Published in Value in Health Regional Issues Volume 2 2013 (5-12)

Economic evaluation of pravastatin for primary prevention of coronary artery disease based on risk prediction from JALS-ECC in Japan

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Funding sources: This study was supported by the Economic Social Research Institute (ESRI), Cabinet office, Government of Japan; and the Institute for Health Economics and Policy (IHEP).

Keywords: cost-effectiveness, pravastatin, coronary artery disease, primary prevention

Running title: Economic evaluation of pravastatin in Japan

Abstract [First-level Header]

Background: The clinical efficacy of HMG-CoA reductase inhibitor (statin) therapy in cardiovascular disease has been established in clinical trials. Nonetheless, it is unclear to whom and when statin treatment should be initiated for patients without cardiovascular disease with regard to overall absolute risk reduction of cardiovascular disease and the cost-effectiveness of long-term statin therapy.

Objectives: To examine the cost-effectiveness of pravastatin 10 mg/day compared with no drug therapy for primary prevention of coronary artery disease (CAD), using cardiac risk factors from risk predictions for CAD from Japanese cohort studies.

Methods: A Markov transition model was used to evaluate the cost-effectiveness of pravastatin compared with no drug therapy. The incidence of acute myocardial infarction was estimated using risk predictions for CAD in Japan. A hypothetical population from 45 to 75 years old was examined using the cardiac risk factors. Quality-adjusted life-years (QALYs) and incremental cost-effectiveness ratio (ICER) over a lifetime horizon were estimated from a perspective of payers.

Results: ICERs of pravastatin therapy compared with no drug therapy were 9,677,000 yen per QALY in 55-year-old men and 8,648,000 yen per QALY in 65-year-old men with diabetes mellitus, hypertension (grade II), and smoking as cardiac risk factors. Pravastatin therapy was not cost-effective compared with no drug therapy in all subgroups evaluated.

Conclusions: Using risk prediction for CAD based on a Japanese cohort with no history of cardiovascular events, the cost-effectiveness of pravastatin for primary prevention of CAD may not be cost-effective in populations at both low and high cardiac risk.

Background [First-level Header]

National medical expenditure in Japan has been increasing annually due to aging of the population and the introduction of high cost medical care, with an increase from 31 trillion yen in 2004 to 36 trillion yen in 2009 [1]. A westernized lifestyle is one cause of the increase in obese patients with hypertension associated with metabolic disorders, hyperlipidemia, and diabetes mellitus (DM). The number of cases of hyperlipidemia in Japan has also been increasing, with an estimated 1.43 million patients diagnosed with hyperlipidemia in 2006 [2]. Furthermore, an estimated 14.1 million people were predicted to be likely to become hyperlipidemic based on data for high density lipoprotein (HDL) cholesterol levels in the National Health and Nutrition Survey [3]. Nearly 250 billion yen was spent on HMG-CoA reductase inhibitor (statin) therapy in 2008 [4]. The Guidelines of the Japan Atherosclerosis Society (JAS) recommend that drug therapy should be considered after implementation of lifestyle modifications such as diet and exercise [5].

Despite the high prevalence of hyperlipidemia in Japan, the incidence of coronary artery disease (CAD) is less than half that in western countries such as the U.S.A, U.K, and Germany. However, the incidence of stroke is relatively high compared to these countries [6]. Iso reported that different profiles of cardiovascular risk factors in Japanese such as lower serum cholesterol levels and higher prevalence of smoking for men compared with western countries [7]. Therefore, the epidemiological profile of cardiovascular disease (CVD) in Japan may differ from that in western countries.

Statins lower the cholesterol level and reduce the prevalence and mortality of CAD [8]. The clinical efficacy of statins for primary and secondary prevention of CAD among specific populations such as patients with type II DM has been demonstrated in clinical trials in Japan [9]. The Management of Elevated Cholesterol in the Primary Prevention Group of Adult Japanese (MEGA) study was performed as a prospective randomized controlled trial to assess primary prevention of CVD with pravastatin at 10-20 mg/day [10]. The results showed that a low dose of pravastatin significantly reduced CAD events. The Number Needed to Treat (NNT) to prevent one CAD event was 119 for 5.3 years of mean follow-up [10]. The NNT in the MEGA study was more than double the NNT of 50 in the AFCAPS (Air Force/Texas Coronary Atherosclerosis Prevention Study), which was a randomized controlled trial to assess primary prevention of CAD with lovastatin at 20-40 mg/day [11,12].

The different NNTs in these studies were due to the lower CAD incidence and the lower dose in the MEGA study. This might indicate that statin therapy can be less cost-effective in Japan, with the lower rate of absolute risk reduction for CAD. Studies of the cost-effectiveness for statins have been conducted in Japan. However, the results may have been overestimated since studies have been conducted using western data, such as those from the Framingham study whose incidence of CAD was higher than that in Japan [13,14], or with assumptions based on limited information in Japan [15-18]. Cost-effectiveness using CAD risk prediction based on a Japanese cohort study has not been examined. Therefore, it is unclear to whom and when statin therapy should be initiated for primary prevention of CAD based on the absolute risk reduction of CAD and the cost of long term statin therapy in Japan. The objective of this study was to assess the cost-effectiveness of pravastatin therapy in a population with hyperlipidemia for primary prevention of CAD using cardiac risk factors for CAD prediction based on data from a cohort study in Japan.

Methods [First-level Header]

Effect of pravastatin [Second-level Header]

The effect of pravastatin was obtained from the meta-analysis of primary prevention of CVD by statin treatment [19]. 70,388 people (34%, women) from 10 randomized clinical trials with mean follow-up of 4.1 years were analyzed. The statin included in the meta-analysis have similar clinical efficacy [20]. It is reported that the treatment with statins significantly reduced the risk of major coronary events (Hazard ratio=0.7). According to the study, the treatment effects of statins were similar among clinically defined groups such as age, sex and diabetes status. Therefore, our model applied the efficacy and assumed the similar treatment efficacy of pravastatin among different subgroups [19].

Predicted incidence of CAD [Second-level Header]

The 5-year probability of CAD was estimated using risk prediction formulae for acute myocardial infarction (AMI) based on the Japan Arteriosclerosis Longitudinal Study – Existing Cohorts Combined (JALS-ECC) [21]. The JALS-ECC was a prospective cohort study following 22,430 Japanese men and women aged 40 to 89 years old without a history of CVD events from 10 communities, with an average follow-up of 7.9 years. During this period,

104 subjects experienced AMI and 339 had stroke. A scoring system for the 5-year probability of developing AMI was constructed based on risk factors of age, gender, level of serum TC, serum high density lipoprotein cholesterol (HDL-C), grade of hypertension [19], DM, and smoking status. To estimate the risk of AMI, levels of serum TC of 240 mg/dL and HDL-C of 40 mg/dL were used in this cohort. Twelve subgroups were created based on the risk classifications for primary prevention of the JAS Guidelines for Prevention of Atherosclerotic Cardiovascular Disease, 2007 edition [5]. The cardiac risk factors were combinations of age, gender, TC level, blood pressure (grades I and II) [22], DM, and current smoking status.

Costs and utilities [Second-level Header]

Direct medical costs from the payer's perspective were estimated and adjusted to 2010 values. The cost of pravastatin therapy was calculated based on the 2010 edition of the medical fee index, including laboratory tests, doctor's visits, and pharmacist's fees [23]. Pravastatin 10 mg was listed as 112 yen per day in the 2010 edition of the National Health Index (NHI) drug list [24]. One-way sensitivity analysis was conducted by changing the cost of pravastatin, since this cost varied from 23 to 112 yen per day among brand and generic drugs. The cost of AMI was derived from publicly available data from the All-Japan Hospital Association[25]. The cost of years after AMI was estimated based on a hospital survey [26]. The utility score of healthy state was assumed to be 1. The utility score for the health state after myocardial infarction was obtained from a catalogue of EQ-5D utility weights for chronic diseases in Korea which was used time trade-off techniques to generate the utility score [27]. The number of Quality-adjusted life-years (QALYs) was calculated by life year gained by multiplying a utility score reflecting the Quality of Life (QoL).

Model structure [Second-level Header]

A Markov transition model was used to evaluate the cost effectiveness of pravastatin 10 mg/day compared to no drug therapy. The model was constructed using TreeAge Pro 2011 (TreeAge Software inc., Williamstown, MA, U.S.A.). A similar model was used by Kobayashi et al. to examine primary prevention of CAD in the Japanese population. The model included three health states: healthy, post-myocardial infarction, and death (Figure 1) [17]. The variables and associated distributions used in the model are described in Table 1. The model was examined on a lifetime horizon and simulated in one-year cycles with a half-cycle correction discounting 3% annually until the

population reached the age of 100 years old. Hypothetical cohorts of men and women aged 45, 55, 65 or 75 years old were simulated with various cardiac risk factors according to the JAS guidelines [5]. The cohort started from an all healthy state and AMI occurred based on predicted probabilities. The model assumed that post-MI patients were treated for secondary prevention of AMI. In the model, the predicted probabilities of AMI event were adjusted to every 10 years based on the risk score by age (40-49, 50-59, 60-69, 70-79, and 80-89). After 90 years, the predicted probabilities were set at 80-89 due to the lack of the risk score over 90 years from the JALS-ECC study. The predicted incidence of recurrence of AMI was set to 2-fold the predicted primary AMI incidence. The case-fatality rate of AMI was taken from a literature report on the incidence in inpatients and outpatients [28].Annual death rates by age and gender were obtained from the vital statistics of Japan [29]. Willingness to pay was set at 6,000,000 yen/QALY according to Ohkusa's study [30]. Stroke was not included in the model since neither TC nor non-HDL cholesterol was associated with the incidence of stroke in the JALS-ECC study.

Sensitivity analysis [Second-level Header]

Men aged 55 years old with DM, hypertension (Grade II), and smoking was analyzed as a base-case scenario. One-way sensitivity analysis was conducted to evaluate the influence of each parameter in the model for men aged 55 and 65 years old with DM and hypertension (grade II) who were current smokers. Probabilistic sensitivity analysis (PSA) was conducted to examine the uncertainty of the model and 1,000 interactions were performed. The distributions and 95% CIs of the parameters were estimated by R (version 12.3.2) using the Briggs method [31].

Results [First-level Header]

Base-case results [Second-level Header]

The results of the model of lifetime pravastatin therapy initiated from 45, 55, 65, and 75 years old are shown by gender and cardiac risk factors in Tables 2 and 3. Pravastatin therapy in men aged 55 years old with DM, hypertension (grade II), and smoking resulted in a mean QALY gain of 0.097. This therapy was associated with additional mean costs of 935,000 yen per person. Lifetime pravastatin therapy resulted in an ICER of 9,677,000 yen per QALY gain compared to no drug therapy. Pravastatin therapy for men aged 65 years old with DM, hypertension (grade II), and smoking resulted in a mean QALY gain of 0.078 and was associated with additional mean costs of

677,000 yen per person. Lifetime pravastatin therapy resulted in an ICER of 8,648,000 yen per QALY gain compared to no drug therapy. Overall, the ICER was decreased by an increased number of cardiac risk factors. The QALY gain with pravastatin therapy was lower in women, resulting in higher ICERs. The ICER was lower in 65- and 75-year-old men with DM, hypertension (grade II), and smoking.

Sensitivity analysis [Second-level Header]

Table 4 shows the results of one-way sensitivity analysis for 55- and 65-year-old men with DM, hypertension (grade II), and smoking. The results were mostly influenced by the cost and efficacy of pravastatin therapy. If pravastatin 10 mg had a cost of 56 yen/day, the ICER decreased from 9,677,000 yen to 5,084,000 yen in 55-year-old men and from 8,648,000 yen to 4,716,000 yen in 65-year-old men with DM, hypertension (grade II), and smoking, which satisfied the threshold of willingness to pay. At a cost of pravastatin 10 mg of 28 yen/day, the ICER was 4,536,000 and 3,907,000 yen per QALY in men aged 55 and 65 years old, respectively. If the effect of pravastatin on preventing CAD was 7% lower than the base-case scenario, the ICER increased from 9,677,000 to 11,835,000 yen per QALY in 55-year-old men and from 8,648,000 to 10,635,000 yen per QALY in 65-year-old men.

The results of PSA and cost-effectiveness acceptability curves for therapy with pravastatin 10 mg/day are shown in Figure 2 , respectively, for men aged 55 years old with cardiac risk factors of DM, smoking, and hypertension (grade II). The probability of pravastatin being cost-effective was 56% at a threshold of 20,000,000 yen per QALY, 87% at 40,000,000 yen per QALY, and 93% at 60,000,000 yen per QALY.

Discussion [First-level Header]

In this study, the cost-effectiveness of therapy with pravastatin 10 mg/day for primary prevention of CAD was evaluated using a newly developed risk prediction for CAD in Japan. The analysis was performed in 12 subgroup populations that were mostly categorized into middle to high risk groups according to JAS guidelines. In all subgroups, the QALY gain was lower in women and resulted in higher ICERs compared to men. Our results indicate that pravastatin has a superior effect in men aged 65 and 75 years old. The estimated ICERs of pravastatin therapy compared to no drug therapy varied from 8,438,000 to 60,301,000 yen per QALY in men and from 25,282,000 to 157,197,000 yen per QALY in women, depending on the cardiac risk factors, in populations aged 45 to 75 years old.

Pravastatin therapy was found not to be cost-effective compared to no drug therapy in this study population based on a cost-effectiveness threshold of 6,000,000 yen per QALY.

A previous study evaluated in Japan found that pravastatin was not cost-effective at low and high cardiac risk among most subgroup [17]. In our study, pravastatin was also found not to be cost-effective for patients at high cardiac risk among all subgroup. One of the causes in the previous study may be the relative risks of CAD were obtained from a number of observational studies where the patients selection might be biased. Our study is the first cost-effectiveness study using risk prediction of CAD based on community cohorts without a history of CVD in Japan. Thus, the results might be applicable to the general population in Japan. The results also clarified the relationships between cardiac risk factors and the efficacy of pravastatin by showing the absolute risk of a CAD event in five years, along with cardiac risks. Sensitivity analysis showed significant improvement of cost-effectiveness in pravastatin therapy when the cost of the drug was reduced. With this reduction, pravastatin could be cost-effective for high risk populations such as 65- to 75-year-old men with DM, hypertension (grade II), and smoking. In our study, the ICER per QALY differed by age, gender and cardiac risk factors. The population with hyperlipidemia is increasing in Japan [2], but the characteristics of hyperlipidemia vary and give different cardiac risks. Therefore, it is important to identify subgroups that will benefit from statin treatment and to establish the best timing for initiation of this treatment as well as the acceleration of generics use for statin.

The following limitations and uncertainties should be considered. Firstly, the effect of pravastatin may have been overestimated by using results from clinical trials, in which the adherence to the drug is generally better than that in actual clinical practice [32]. Secondly, stroke was not included in the model due to the non-significant results in MEGA study and no association with the incidence of stroke in the JALS-ECC study [21]. However, the effect of pravastatin may have been underestimated by not considering risk reductions such as that for stroke . Thirdly, adverse drug reactions associated with statin therapy such as rhabdomyolysis, liver disorders, thrombocytopenia, interstitial pneumonia, and myopathy were not considered in the model since the incidences were unclear [33], and thus the clinical benefit of pravastatin may have been overestimated. Fourthly, the population in the JALS-ECC study was healthier than the general population since cohort selection was based on a community health check-up. Therefore, the results might have underestimated the incidence of CAD. Furthermore, the predicted event rate of CAD from JALS-ECC study might be underestimated by not considering patients who were already on statin

treatment. Lastly, it should be remembered that the predicted event rate had limitations on the validity of data compared to the actual observed rate. In our model, the utility score of the first year after AMI event was weighted same as the subsequent years after AMI event. Therefore, the results might have underestimated the effectiveness of pravastatin by not considering the lower utility score at the onset of the CAD events. The utility score for post-AMI was obtained from a Korean chronic disease index [27] since this score was not available for Japanese patients. However, this utility score was similar to a previously reported value [34] and the results from one-way sensitivity analysis of the utility score indicated little influence on the model. Therefore, the results of the model are likely to be reliable. Disutility of taking a pill daily was not considered in the model since the utility score for taking a pill daily was not found to be high [35]. Cost-effectiveness was evaluated from the payer's perspective, and thus any economic burden related to indirect cost was excluded in the analysis. This may also have biased the results for the cost-effectiveness of pravastatin and further evaluations are needed from a societal perspective in different risk populations.

Conclusion [First-level Header]

In this study, the cost-effectiveness of pravastatin for primary prevention of CAD was evaluated. The estimated ICERs depended on age, gender, and number of cardiac risk factors. Using thresholds based on Japanese criteria, pravastatin therapy for primary prevention of CAD may not be cost-effective compared to no drug therapy.

Acknowledgements [First-level Header]

This study was supported by the Economic Social Research Institute (ESRI), Cabinet office, Government of Japan; and the Institute for Health Economics and Policy (IHEP)

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Figure 1. Structure of the Markov transition model for cost-effectiveness of pravastatin 10 mg/day

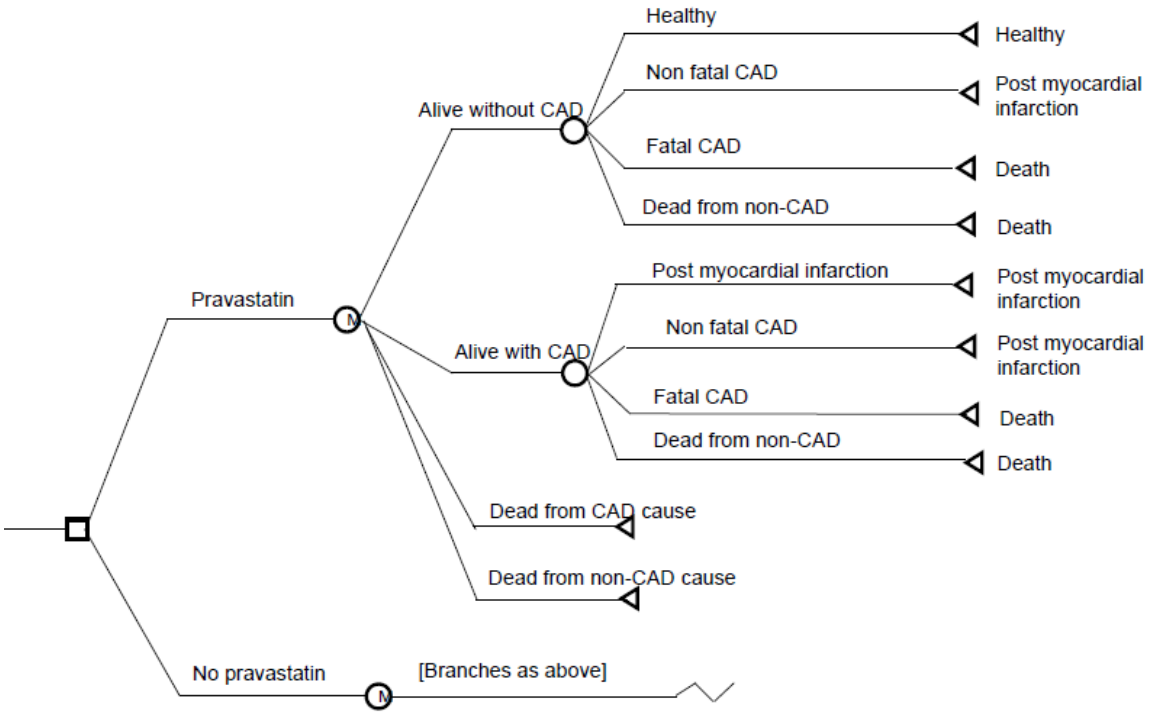

Figure 2. Cost-effectiveness acceptability curve for therapy with pravastatin 10 mg/day

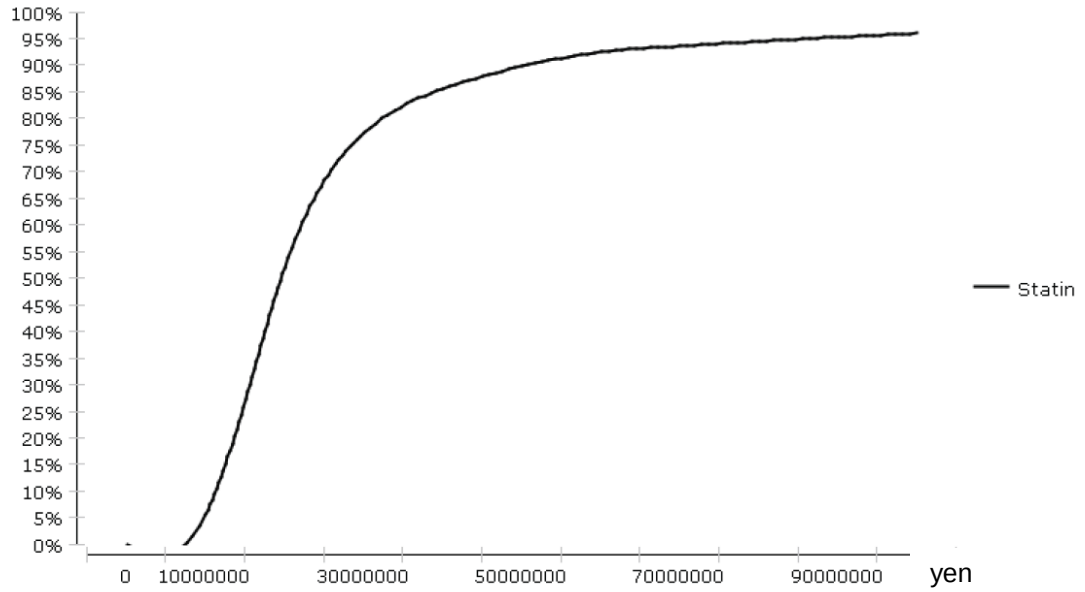

Table 1. Model variables and associated distributions and ranges

Variables	Men	Women	Distribution	References
Predicted incidence of AMI (per 10,000/year) (with DM, hypertension (grade II), and smoking)				
45-54 years of age	7.6 (3.2-13.9)	2.6 (0.5-6.6)	Beta	Cohort study [21]
55-64 years of age	20.1 (12.3-29.8)	6.6 (2.5-12.5)		
65-74 years of age	39.8 (28.4-53.1)	13.2 (7.1–21.2)		
75-84 years of age	64.3 (50.0-81.4)	21.4 (13.3–31.4)		
≥85 years of age	110.7 (91.14-132.1)	37.2 (26.2–50.0)		
Overall one-year mortality rate due to myocardial infarction	0.21 (0.14-0.30)	0.21 (0.14-0.30)	Beta	Literature[28]
Treatment efficacy of pravastatin	0.7 (0.50-0.97)	0.7 (0.50-0.97)	Log-normal	Meta-analysis[19]
Cost of pravastatin 10 mg (yen/year)	65,400 (64,900-65,902)	65,400 (64,900-65,902)	Gamma	Medical treatment and drug fee index[23] [24]
Cost of post myocardial infarction - first year (yen)	2,149,000 (2,146,128-2151874)	2,149,000 (2,146,128-2151874)	Gamma	All Japan Hospital Association[25]
Cost of post myocardial infarction - subsequent years (yen)	245,070 (244,100-246,041)	245,070 (244,100-246,041)	Gamma	Cohort study[26]
Utilities post-myocardial infarction	0.88 (0.81-0.94)	0.88 (0.81-0.94)	Beta	Cohort study[27]

Table 2. Five-year probabilities of CAD risk, incremental QALYs and cost, and ICERs in men and women aged 45 and 55 years old

		5-year CAD risk	Incre-mental QALYs	Incre-mental cost (×1,000 yen)	ICER (×1,000 yen per QALY)	5-year CAD risk	Incre-mental QALYs	Incre-mental cost (×1,000 yen)	ICER (×1,000 yen per QALY)
Age	Cardiac risk factors	Men				Women			
45	No risk factor	0.08%	0.022	1,311	60,301	0.03%	0.009	1,477	157,197
	Smoking	0.12%	0.031	1,295	42,118	0.04%	0.013	1,470	109,660
	Hypertension grade I	0.12%	0.031	1,295	42,118	0.04%	0.013	1,470	109,660
	Hypertension grade II	0.18%	0.046	1,269	27,402	0.06%	0.020	1,458	71,397
	Diabetes Mellitus (DM)	0.13%	0.033	1,292	39,370	0.04%	0.013	1,470	109,660
	Smoking, Hypertension grade I	0.17%	0.043	1,274	29,342	0.05%	0.019	1,461	78,595
	Smoking, Hypertension grade II	0.25%	0.065	1,238	19,139	0.08%	0.029	1,444	49,954
	Smoking, DM	0.18%	0.046	1,269	27,402	0.06%	0.020	1,458	71,397
	DM, Hypertension grade I	0.18%	0.046	1,269	27,402	0.06%	0.020	1,458	71,397
	DM, Hypertension grade II	0.27%	0.069	1,231	17,852	0.09%	0.031	1,441	46,772
	DM, Hypertension grade I, Smoking	0.25%	0.065	1,238	19,139	0.08%	0.029	1,444	49,954
	DM, Hypertension grade II, Smoking	0.38%	0.098	1,184	12,123	0.13%	0.043	1,422	33,251
55	No risk factor	0.22%	0.022	1,067	49,447	0.07%	0.010	1,259	129,770
	Smoking	0.31%	0.031	1,050	34,413	0.10%	0.014	1,252	90,228
	Hypertension Grade I	0.31%	0.031	1,050	34,413	0.10%	0.014	1,252	90,228
	Hypertension Grade II	0.47%	0.046	1,023	22,286	0.15%	0.021	1,239	58,421
	Diabetes Mellitus (DM)	0.33%	0.033	1,047	32,128	0.11%	0.014	1,252	90,228
	Smoking, Hypertension grade I	0.44%	0.043	1,028	23,885	0.14%	0.019	1,243	64,734

	Smoking, Hypertension grade II	0.66%	0.064	991	15,486	0.22%	0.030	1,224	41,085
	Smoking, DM	0.47%	0.046	1,023	22,286	0.15%	0.021	1,239	58,421
	DM, Hypertension grade I	0.47%	0.046	1,023	22,286	0.15%	0.021	1,239	58,421
	DM, Hypertension grade II	0.71%	0.068	984	14,472	0.23%	0.032	1,221	38,306
	DM, Smoking, Hypertension grade I	0.66%	0.064	991	15,486	0.22%	0.030	1,224	41,085
	DM, Smoking, Hypertension grade II	1.00%	0.097	935	9,677	0.33%	0.044	1,200	27,413

Note: Hypertension Grade I: Systolic Blood Pressure (140-159 mmHg), Diastolic Blood Pressure (90-99 mmHg)

Hypertension Grade II: Systolic Blood Pressure (160-179 mmHg), Diastolic Blood Pressure (100-109 mmHg)

Table 3. Five-year probabilities of CAD risk, incremental QALYs and cost, and ICERs in men and women aged 65 and 75 years old

		5-year CAD risk	Incre-mental QALYs	Incre-mental cost (×1,000 yen)	ICER (×1,000 yen per QALY)	5-year CAD risk	Incre-mental QALYs	Incre-mental cost (×1,000 yen)	ICER (×1,000 yen per QALY)
Age	Cardiac risk factors	Men				Women			
65	No risk factor	0.44%	0.018	795	45,155	0.14%	0.008	991	118,425
	Smoking	0.62%	0.025	780	31,197	0.20%	0.012	984	82,092
	Hypertension (I)	0.62%	0.025	780	31,197	0.20%	0.012	984	82,092
	Hypertension (II)	0.93%	0.038	756	20,059	0.31%	0.018	972	53,304
	Diabetes Mellitus (DM)	0.66%	0.027	777	29,050	0.22%	0.012	984	82,092
	Smoking, Hypertension (I)	0.87%	0.035	760	21,478	0.29%	0.016	976	60,425
	Smoking, Hypertension (II)	1.32%	0.064	991	15,486	0.44%	0.025	959	37,722
	Smoking, DM	0.93%	0.038	756	20,059	0.31%	0.018	972	53,304
	DM, Hypertension (I)	0.93%	0.038	756	20,059	0.31%	0.018	972	53,304
	DM, Hypertension (II)	1.41%	0.055	722	13,107	0.47%	0.027	955	35,083
	DM, Smoking, Hypertension (I)	1.32%	0.052	728	14,024	0.44%	0.025	959	37,722
	DM, Smoking, Hypertension (II)	1.99%	0.078	677	8,648	0.66%	0.037	937	25,279
75	No risk factor	0.71%	0.012	518	44,736	0.23%	0.006	681	120,601
	Smoking	1.00%	0.017	506	30,472	0.33%	0.008	676	83,378
	Hypertension (I)	1.00%	0.017	506	30,472	0.33%	0.008	676	83,378
	Hypertension (II)	1.51%	0.025	487	19,491	0.50%	0.012	667	53,985
	Diabetes Mellitus (DM)	1.07%	0.018	504	28,348	0.35%	0.008	676	83,378
	Smoking, Hypertension (I)	1.41%	0.024	490	20,752	0.47%	0.010	671	64,737

	Smoking, Hypertension (II)	2.13%	0.034	468	13,936	0.71%	0.017	657	38,789
	Smoking, DM	1.51%	0.025	487	19,491	0.50%	0.012	667	53,985
	DM, Hypertension (I)	1.51%	0.025	487	19,491	0.50%	0.012	667	53,985
	DM, Hypertension (II)	2.28%	0.036	462	12,693	0.76%	0.018	655	36,014
	DM, Smoking, Hypertension (I)	2.13%	0.034	468	13,936	0.71%	0.017	657	38,789
	DM, Smoking, Hypertension (II)	3.21%	0.051	429	8,438	1.07%	0.025	640	25,282

Note: Hypertension Grade I: Systolic Blood Pressure (140-159 mmHg), Diastolic Blood Pressure (90-99 mmHg)

Hypertension Grade II: Systolic Blood Pressure (160-179 mmHg), Diastolic Blood Pressure (100-109 mmHg)

Table 4. One-way sensitivity analysis of ICERs for men aged 55 and 65 years old with DM, hypertension (grade II), and current smoking

	55-year-old men			65-year-old men		
	Incremental QALYs	Incremental cost (×1,000 yen)	ICER (×1,000 yen per QALY)	Incremental QALYs	Incremental cost (×1,000 yen)	ICER (×1,000 yen per QALY)
Base-case scenario	0.097	935	9,677	0.078	678	8,648
Pravastatin 10 mg pill cost (base-case 112 yen/day)						
56 yen/day	0.118	604	5,084	0.092	430	4,716
28 yen/day	0.097	438	4,536	0.078	3,061	3,907
Pravastatin 10 mg effectiveness (base-case 0.7)						
0.75	0.081	952	11,835	0.065	694	10,635
0.80	0.064	970	15,072	0.052	711	13,616
Discount rate (base-case cost 3%, health outcome 3%)						
Cost 2%, health outcome 2%	0.119	1,041	8,768	0.091	734	8,056
Cost 3%, health outcome 2%	0.119	935	7,871	0.092	678	7,433
Cost 3%, health outcome 1%	0.147	935	6,340	0.107	678	6,348
Utility score for AMI (base-case 0.88)						
Utility score 0.84	0.105	935	8,878	0.085	678	7,924
Utility cost 0.92	0.088	935	10,633	0.072	678	9,506

Supplement:

Table 1. Lipid management goals based on risk assessment

Principle of therapeutic strategy	Category		Lipid management goals (mg/dL)		
		Major risk factors other than LDL-C*	LDL-C	HDL-C	TG
Primary prevention Lifestyle should be changed before consideration of drug therapy	I (Low-risk group)	0	<160	>=40	<150
	II (Incremental-risk group)	1~2	<140		
	III (High-risk group)	3 or more	<120		
Secondary prevention Both drug therapy and lifestyle modification are considered.	History of coronary artery disease		< 100		

Management of serum lipids as well as intervention of other risk factors (smoking, hypertension or diabetes) is necessary.

*Major risk factors other than LDL-C, Aging (male >=45 years, female >=55 years), hypertension, diabetes (including impaired glucose tolerance), smoking, family history of coronary artery disease, low HDL cholesterol (<40 mg/dL)

・Category III, if complicated by diabetes mellitus, cerebral infarction or arteriosclerosis obliterans.

(Reference) Teramoto T, Sasaki J, Ueshima H, et al. Exective summary of Japan Atherosclerosis Society (JAS) guideline for diagnosis and prevention of atherosclerotic cardiovascular disease for Japanese. J Atheroscier Thromb, 2007;14:45-50.

Figure 1. Scoring system for estimating the 5-year probability of developing AMI

Table 6. Scoring System for Estimating 5-Year Probability of Developing AMI

Non-HDL-C model				TC model			
Items	Score	Items	Score	Items	Score	Items	Score
Serum non-HDL-C (mg/dl)†		Age (years)		Serum TC (mg/dl)‡		Age (years)	
		40–49	0			40–49	0
90	–9.5	50–59	14	150	–8.0	50–59	14
100	–7.6	60–69	24	160	–6.4	60–69	24
110	–5.7	70–79	31	170	–4.8	70–79	31
120	–3.8	80–89	39	180	–3.2	80–89	39
130	–1.9	Serum HDL-C		190	–1.6	Serum HDL-C	
140	0.0	40 mg/dl+	0	200	0.0	40 mg/dl+	0
150	1.9	<40 mg/dl	7	210	1.6	<40 mg/dl	11
160	3.8	Grade of hypertension§		220	3.2	Grade of hypertension§	
170	5.7	Normal or less	0	230	4.8	High-normal or less	0
180	7.6			240	6.4		
190	9.5	Grade 1	5	250	8.0	Grade 1	5
200	11.4	Grade 2+	11	260	9.6	Grade 2+	11
210	13.3	Diabetes mellitus		270	11.2	Diabetes mellitus	
220	15.2	No	0	280	12.8	No	0
230	17.1	Yes	5	290	14.4	Yes	6
240	19.0	Smoking		300	16.0	Smoking	
Sex				Sex			
Men	16	Never or former	0	Men	16	Never or former	0
Women	0	Current	5	Women	0	Current	5

The score increases †0.19 or ‡0.16 along with every+1 mg/dl.
Every 10 increase in the score represents 2-fold increase in the incidence rate of AMI.
§Based on the 1999 criteria of World Health Organization and International Society of Hypertension.
Tables 6,7 and the Japanese versions will be available on the website of the JALS (http://jals.gr.jp/). The Japanese version has also been published in *Doumyakukouka Yobou* 2009; **8**(1): 20–25.
Abbreviations see in Table 1.

Tanabe N, Iso H, Okada K, et al.. Serum Total and Non-High-Density Lipoprotein Cholesterol and the Risk Prediction of Cardiovascular Events – The JALS-ECC. Circ J 2010; 74: 1352 (Table 6)