

# Investigation of Blood Lipid Levels and Statin Interventions in Outpatients With Coronary Heart Disease in China

## — The China Cholesterol Education Program (CCEP) —

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**Background** The aim of the China Cholesterol Education Program is to investigate the blood lipid levels, the statin intervention and the rates of achieving the goal of low-density lipoprotein-cholesterol (LDL-C) level in Chinese outpatients with coronary heart disease (CHD).

**Methods and Results** The multicenter study recruited 4,778 outpatients with CHD. The mean level of LDL-C for the total outpatients was  $2.93 \pm 1.00$  mmol/L; 82.2% of the participants received statin therapy. The LDL-C levels were  $3.06 \pm 1.08$  mmol/L and  $2.89 \pm 0.97$  mmol/L in outpatients with high risk and very high risk, respectively ( $p < 0.001$ ). No significant difference was found about the rates of statin intervention in outpatients at high risk and very high risk (81.4% vs 82.5%,  $p > 0.05$ ). Though they had higher rates of statin intervention, only 36.2% of the high-risk outpatients achieved the target LDL-C level ( $< 2.6$  mmol/L); 10.9% of the very high risk outpatients achieved the optimal LDL-C level ( $< 1.82$  mmol/L) suggested by NCEP ATP III. The rate of achieving the target level was only 42.2%, even though LDL-C  $< 2.6$  mmol/L was the goal for patients at very high risk.

**Conclusions** Although the outpatients received a higher rate of statin therapy, the rates of achieving the target cholesterol level were lower. There is a significant gap between the guidelines and clinical practice in China. (Circ J 2008; 72: 2040–2045)

**Key Words:** China Cholesterol Education Program (CCEP); Coronary heart disease; Lipids; Statins

Coronary heart disease (CHD) is still a major worldwide threat to health! Although several risk factors contribute to CHD, low-density lipoprotein-cholesterol (LDL-C) is a major risk factor.<sup>2</sup> Several clinical trials indicate that for every 1% reduction in LDL-C level, the relative risk for a major CHD event is reduced by approximately 1%.<sup>3–11</sup> Recently, more and more clinical trials have proved CHD patients, or equivalent high-risk status patients, could benefit from lowering of the LDL-C level with statins. Recent clinical trials,<sup>12–16</sup> such as HPS and PROVE-IT-TIMI-22,<sup>17</sup> showed further benefit could be achieved by more aggressive LDL-C lowering to well below 100 mg/dl in some patient populations. Based on these recent trials, an LDL-C goal of  $< 70$  mg/dl (1.82 mmol/L) is the recommended therapeutic option for high-risk CHD patients, and  $< 100$  mg/dl (2.6 mmol/L) is a strong recommendation. The purpose of this study was to investigate the treatment of outpatients with CHD, especially with statins, and the rates of achieving the guideline goals in China.

## Methods

### Patients and Data Collection

This study involved 52 centers in 6 cities (Shanghai, Beijing, Guangzhou, Zhejiang, Tianjin and Xinjiang) in China. All participants were known CHD outpatients. They were continuously enrolled from January 2006 to January 2007. Data were collected by questionnaire including demographic data, medical history, and CHD diagnosis, treatment of CHD and laboratory examinations. Body measurements, blood pressure, levels of blood glucose, lipids, aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatine kinase (CK), blood urea nitrogen, serum creatinine (SCr), and uric acid, and smoking status were also recorded.

### Diagnosis of CHD

CHD was diagnosed on clinical grounds judged by physicians, supported by at least 1 objective finding including abnormal stress tests (electrocardiography, scintigraphy, or echocardiography) indicating significant myocardial ischemia, or a coronary angiogram revealing  $> 50\%$  stenosis of the lumen of any major coronary artery, or a history of confirmed myocardial infarction (MI), or evidence of prior MI on electrocardiogram, or a history of a prior coronary revascularization procedure (PCI or CABG). The CHD diagnosis was classified as stable angina pectoris (AP), previous MI, or acute coronary syndromes (ACS), which included unstable AP, ST-segment elevation MI and non-ST-segment elevation MI.

### Classification of Risk

Patients at high risk were those with CHD, or with CHD

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risk equivalents such as non-coronary forms of atherosclerotic disease [peripheral arterial disease (PAD), abdominal aortic aneurysm, and carotid artery disease (transient ischemic attacks or stroke of carotid origin or >50% obstruction of a carotid artery)], and diabetes mellitus (DM).

Patients at very high risk were those with established cardiovascular disease plus (1) multiple major risk factors (especially DM), (2) severe and poorly controlled risk factors (eg, continued cigarette smoking), (3) multiple risk factors of the metabolic syndrome (triglycerides (TG)  $\geq 200$  mg/dl plus non-high-density lipoprotein-cholesterol (HDL-C)  $\geq 130$  mg/dl with low HDL-C  $< 40$  mg/dl), and (4) ACS.

#### Other Criteria

Hypertension was defined as systolic blood pressure  $\geq 140$  mmHg, and/or diastolic blood pressure  $\geq 90$  mmHg, and/or current antihypertensive medication.<sup>18</sup> DM was defined as: (1) fasting plasma glucose concentration  $> 7.0$  mmol/L in the absence of treatment; (2) fasting plasma glucose concentration  $\geq 11.0$  mmol/L, 2 h after a 75-g oral glucose load; or (3) current treatment with hypoglycemic drugs.<sup>19</sup> Ischemic stroke was defined as a history of physician-diagnosed cerebral attack or self-reporting of a prior cerebral revascularization procedure. PAD was defined as partial or complete atherosclerotic obstruction of the peripheral arteries on angiography, or intermittent claudication.<sup>20</sup> Dyslipidemia was defined as total cholesterol (TC)  $\geq 5.2$  mmol/L, and/or HDL-C  $\leq 0.9$  mmol/L, and/or LDL-C  $\geq 3.12$  mmol/L, and/or TG  $\geq 1.69$  mmol/L, or undergoing current lipid-lowering treatment. Smoking was considered positive in those who smoked at least 1 cigarette/day for at least 1 year.

The data collection protocol was approved by the Beijing University Research Ethics Committee. All participants signed informed consent statements allowing access to their medical records.

#### Statistical Analysis

All case record form data were entered into dual Epidata 3.02 databases by different people. The 2 databases were compared and any necessary corrections were made. All analyses were performed with the Statistics Package for Social Science, version 13.0 (Chicago, IL, USA). Continuous variables are expressed as mean  $\pm$  SD, and discrete variables

**Table 1 Baseline Characteristics of the Outpatients in CCEP**

	n	%
Total	4,778	100
Age (years)	62 $\pm$ 10	
35–45	183	3.8
46–55	803	16.8
56–65	1,285	26.9
66–75	1,689	35.4
76–85	735	15.4
86–95	83	1.7
Sex		
Male	3,059	64.0
Female	1,719	36.0
Hypertension	3,279	68.9
SBP (mmHg)	132 $\pm$ 18	
DBP (mmHg)	79 $\pm$ 10	
DM	1,079	22.7
PAD	588	12.5
Non-coronary forms of atherosclerotic disease	986	21.0
Dyslipidemia	3,707	78.5
Smoking		
Never	2,881	61.2
Former	1,032	21.9
Current	795	16.9
Family history		
Hypertension	1,818	38.0
DM	668	14.0
Stroke	675	14.1
CHD	1,156	24.2
Risk category		
High-risk	1,171	24.5
Very-high-risk	3,607	75.5
Lipid levels		
TC (mmol/L)	4.95 $\pm$ 1.52	
TG (mmol/L)	1.88 $\pm$ 1.07	
HDL-C (mmol/L)	1.24 $\pm$ 0.46	
LDL-C (mmol/L)	2.93 $\pm$ 1.00	
Statin therapy	3,929	82.2
Simvastatin	921	17.8
Atorvastatin	2,067	43.3
Pravastatin	554	11.6
Lovastatin	63	1.3
Fluvastatin	224	4.7
Other	100	2.1

CCEP, China Cholesterol Education Program; SBP, systolic blood pressure; DBP, diastolic blood pressure; DM, diabetes mellitus; PAD, peripheral artery disease; CHD, coronary heart disease; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol.

**Table 2 Baseline Laboratory Results of the Outpatients in CCEP**

Baseline	High-risk patients (n=1,171)	Very-high-risk patients (n=3,607)	p value
TC (mmol/L)	5.06 $\pm$ 1.52	4.91 $\pm$ 1.52	0.003
TG (mmol/L)	1.87 $\pm$ 1.07	1.88 $\pm$ 1.06	0.748
HDL-C (mmol/L)	1.31 $\pm$ 0.46	1.22 $\pm$ 0.46	<0.001
LDL-C (mmol/L)	3.06 $\pm$ 1.08	2.89 $\pm$ 0.97	<0.001
Glucose (mmol/L)	5.62 $\pm$ 2.51	6.07 $\pm$ 2.44	<0.001
ALT (U/L)	24.58 $\pm$ 14.15	26.73 $\pm$ 15.95	<0.001
AST (U/L)	26.21 $\pm$ 23.38	37.81 $\pm$ 58.75	<0.001
CK (U/L)	94.37 $\pm$ 195.92	140.34 $\pm$ 324.61	<0.001
hsCRP (mg/L)	7.59 $\pm$ 18.52	10.14 $\pm$ 24.08	0.182
Hemoglobin A1c (%)	5.49 $\pm$ 1.72	6.44 $\pm$ 2.27	0.003
BUN (mmol/L)	6.02 $\pm$ 2.06	6.15 $\pm$ 2.18	0.160
SCr ( $\mu$ mol/L)	80.53 $\pm$ 29.62	84.73 $\pm$ 31.72	0.003
UA (mmol/L)	335.23 $\pm$ 96.59	332.24 $\pm$ 104.98	0.543

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; hsCRP, high-sensitivity C-reactive protein; BUN, blood urea nitrogen; SCr, serum creatinine; UA, uric acid. See Table 1 for other abbreviations.

**Table 3 Therapeutic Interventions in the Outpatients in CCEP**

Therapy	High-risk patients (n=1,171)	Very-high-risk patients (n=3,607)	Total	p value
Lifestyle change (%)	84.5	82.2	82.8	0.062
Nitrates (%)	60.5	72.2	69.4	<0.001
Diuretics (%)	12.8	15.1	14.5	0.053
Antiplatelet drugs (%)	86.2	92.8	91.2	<0.001
Anticoagulation drugs (%)	9.5	18.2	16.1	<0.001
$\beta$ -blocker (%)	61.8	64.5	63.8	0.104
CCB (%)	40.0	38.6	38.9	0.393
ACEI (%)	36.6	46.8	44.3	<0.001
ARB (%)	24.8	23.4	23.7	0.34
Statins (%)	81.4	82.5	82.2	0.382
Simvastatin	19.5	19.2	19.3	
Atorvastatin	42.5	43.5	43.3	
Pravastatin	9.4	12.3	11.6	
Lovastatin	1.4	1.3	1.3	
Fluvastatin	5.0	4.6	4.7	
Others	3.6	1.6	2.1	
Fibrates (%)	6.1	4.4	4.9	0.018

CCB, calcium-channel blocker; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-II receptor blocker. See Table 1 for other abbreviation.

**Table 4 Statin Therapy and Percentage of Patients Achieving the Target LDL-C Level**

	Dose (mg)	Average duration (months)	Achieving target* (%)	LDL-C (mmol/L)
<b>High-risk group (n=1,171)</b>				
Simvastatin	21±10	18.1	42.6	2.04±0.40
Atorvastatin	16±5	6.9	38.6	2.01±0.42
Pravastatin	19±5	13.3	41.7	2.08±0.39
Lovastatin	20±9	26.5	33.3	1.99±0.46
Fluvastatin	39±4	13.3	37.5	2.08±0.39
Others	44±64	14.4	33.3	2.11±0.37
<b>Very-high-risk group (n=3,607)</b>				
Simvastatin	21±8	13.5	10.5	1.49±0.26
Atorvastatin	16±7	6.4	11.3	1.48±0.29
Pravastatin	20±5	11.2	9.3	1.48±0.28
Lovastatin	28±10	14.6	11.1	1.46±0.30
Fluvastatin	38±6	10.4	9.8	1.54±0.21
Others	18±9	9.8	6.1	1.48±0.32

LDL-C <2.6 mmol/L is the target level for high-risk patients; LDL-C <1.82 mmol/L is the goal for very-high-risk patients. See Table 1 for abbreviation.

bles as percentages. The differences in continuous variables between groups were examined by t-test. The differences in discrete variables between groups were calculated by the Pearson  $\chi^2$  test.

## Results

### Recruitment

Case record forms were collected for 4,861 patients; 83 patients were excluded because of protocol violations and abnormal laboratory examination results (eg, AST or ALT levels  $\geq$ 3-fold the upper limit of normal). The eligible 4,778 patients were divided into 2 groups according to risk category.

### Baseline Characteristics

The baseline demographics of the CHD outpatients are shown in Table 1. More of the participants were male (64%). The average age was 62 years. Most CHD occurred in the patients between the ages of 65 and 75 years (35.4%); 24.2% of the outpatients had a family history of premature CHD. Table 1 also shows the disease history of the partici-

pants. The most frequent disease was dyslipidemia (78.5%), although hypertension was also common (68.9%). The mean LDL-C level was 2.93±1.00 mmol/L. Statins were prescribed in 82.2% of the outpatients.

Table 2 shows the baseline laboratory results. The outpatients at high risk had a higher TC level than those at very high risk (5.06±1.52 mmol/L vs 4.91±1.52 mmol/L, p=0.003). The baseline levels of HDL-C and LDL-C in outpatients at high risk were significantly higher than the levels in those at very high risk (p<0.001), although the reverse was true for glucose, ALT, CK, hemoglobin A<sub>1c</sub>, and SCr.

Table 3 illustrates the baseline medical interventions. There was no significant difference between the 2 risk groups for the proportion of patients taking statins (81.4% vs 82.5%, p=0.382).

Statin therapy and the percentage of patients achieving the target LDL-C level are shown in Table 4 (all statins listed are generic). Of the 1,171 patients at high risk, 81.4% were taking statins as lipid-lowering therapy; statins were also used in 82.5% of the 3,607 patients at very high risk (Fig 1). Table 4 and Fig 1 illustrate that only 36.2% of the

high-risk outpatients achieved the target LDL-C level (<2.6 mmol/L); 10.9% of the very-high-risk outpatients achieved the optimal LDL-C level (<1.82 mmol/L) as suggested by NCEP ATPIII<sup>21</sup>

Achievement rates with different statins were also investigated. There was no significance in the rate of achievement among the statins in either the high-risk or very-high-risk patients. The rate of achieving the target level was only 42.2%, even though the LDL-C <2.6 mmol/L was the goal for patients at very high risk.

## Discussion

Many clinical trials of statin therapy have been published<sup>3-9,11,14</sup> NCEP reviewed the results of the major trials and assesses their implications for cholesterol management. They recommend the LDL-C goal of <100 mg/dl in high-risk persons, but when the risk is very high, an LDL-C goal of <70 mg/dl is a therapeutic option<sup>21</sup> China has also updated its guideline for the treatment of dyslipidemia in CHD patients<sup>22</sup>

This is the first, large multicenter study with systematic availability of medical records surveying lipid level and statin interventions in CHD outpatients in China. It may well represent the situation in many areas of China. LDL-C is an independent risk factor for CHD<sup>23-25</sup> and the CCEP survey revealed the average LDL-C level in the participants was 2.93 mmol/L, which is higher than the 2.6 mmol/L suggested by NCEP ATPIII. Therefore, statins should be prescribed for Chinese CHD patients, besides their benefit of lipid lowering<sup>26-30</sup> In this study, 82.2% of the participants received statin therapy, which was higher than a result from Japan (36.3%)<sup>31</sup> and from Hong Kong where a report showed that only 37% of participants received lipid-lowering drugs.<sup>32</sup> It is also higher than the results of small trials in China and other reports.<sup>33</sup> In other words, Chinese medical practitioners have realized that lowering LDL-C is the basic treatment for patients with CHD.

We are curious why the LDL-C level was higher in outpatients with high risk than in those with very high risk (Table 2). The probable reason is that outpatients at very high risk knew the dangers of their disease, paid more attention to their health and their compliance was good, including with the advice given by doctors. It is also possible that the patients were on higher doses of statins or taking a more potent statin. The total effect of these differences might have contributed to the lower LDL-C level in these patients.

The outpatients also implemented lifestyle changes and received antiplatelet drugs, ACEIs, statins, etc. Both high-risk and very-high-risk patients had higher rates of statin interventions. Most Chinese medical practitioners knew the benefit of statin therapy, so the rate of statin interventions was much higher.

Although most of the outpatients in both the high-risk and very-high-risk groups received lipid-lowering therapy, only 36.2% of the high-risk outpatients reached the target LDL-C level (2.6 mmol/L), and only 10.9% of the very-high-risk outpatients achieved their goal (1.82 mmol/L). The rate of achieving the target was only 42.2%, even though LDL-C <2.6 mmol/L was the target level for patients at very high risk. A report from Japan shows the rate of achieving the target level in patients with CHD was 29.9%;<sup>31</sup> and the rate was only 15% in patients with coronary artery disease in Hong Kong.<sup>32</sup> Our result was also higher accord-

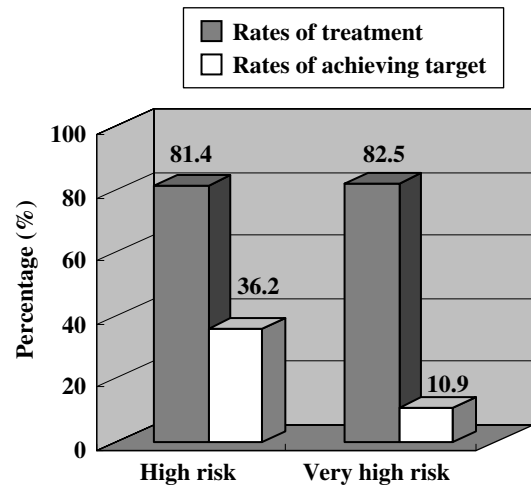


Fig 1. Rates of treatment and achieving the target low-density lipoprotein-cholesterol level using statins in patients at high risk and very high risk of coronary heart disease.

ing to NCEP ATPIII compared with other low reported rates of success in achieving NCEP goal.<sup>34</sup> However, all the success rates were much lower. The NCEP report has been accepted by most Chinese medical practitioners in recent years; however, there is still a significant gap between the guidelines and clinical practice. The possible reasons are that physicians paid more attentions to the outpatients, but there was not good follow-up for the LDL-C level. The duration of the statin intervention may be shorter than 6 weeks for outpatients who first consulted a doctor. Different statins have different effects in lowering LDL-C and some may have not been appropriate for some of the outpatients. All the doses of statins were moderate, so maybe more intensive LDL-C therapy should have been used in those outpatients who did not achieve the goals. Though the LDL-C level was higher than the goals, maybe the reduction in the LDL-C level was larger than 30% in some outpatients; and the adherence of outpatients to therapy should also be investigated. Another question is whether Chinese medical practitioners are hesitant to prescribe statins or give intensive statins intervention because of the safety issue regarding these drugs.

### Study limitations

Firstly, this was a cross-sectional study and only represents larger cities in China. Secondly, the rates of achieving the targets were low and the exact reasons for this were not found, although there are several possible explanations.<sup>35</sup>

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### References

1. Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular disease. Part I: General considerations, the epidemiologic transition, risk factors, and impact of urbanization. *Circulation* 2001; **104**: 2746-2753.
2. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation* 1998; **97**: 1837-1847.
3. Heart Protection Study Collaborative Group. MRC/BHF Heart Pro-

- tection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: A randomised placebo-controlled trial. *Lancet* 2002; **360**: 7–22.
4. Shepherd J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM, et al; PROSPER study group. PROspective Study of Pravastatin in the Elderly at Risk. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): A randomised controlled trial. *Lancet* 2002; **360**: 1623–1630.
  5. Sever PS, Dahlof B, Poulter NR, Wedel H, Beevers G, Caulfield M, et al; ASCOT investigators. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial–Lipid Lowering Arm (ASCOT-LLA): A multicentre randomised controlled trial. *Lancet* 2003; **361**: 1149–1158.
  6. ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group; The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Major outcomes in moderately hypercholesterolemic, hypertensive patients randomized to pravastatin vs usual care: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT-LLT). *JAMA* 2002; **288**: 2998–3007.
  7. Scandinavian Simvastatin Survival Study. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: The Scandinavian Simvastatin Survival Study (4S). *Lancet* 1994; **344**: 1383–1389.
  8. Sacks FM, Pfeffer MA, Moye LA, Rouleau JL, Rutherford JD, Cole TG, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels: Cholesterol and Recurrent Events Trial investigators. *N Engl J Med* 1996; **335**: 1001–1009.
  9. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. *N Engl J Med* 1998; **339**: 1349–1357.
  10. Shepherd J, Cobbe SM, Ford I, Isles CG, Lorimer AR, MacFarlane PW, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia: West of Scotland Coronary Prevention Study Group. *N Engl J Med* 1995; **333**: 1301–1307.
  11. Downs JR, Clearfield M, Weis S, Whitney E, Shapiro DR, Beere PA, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: Results of AFCAPS/TexCAPS. Air Force/Texas Coronary Atherosclerosis Prevention Study. *JAMA* 1998; **279**: 1615–1622.
  12. Smilde TJ, van Wissen S, Wollersheim H, Trip MD, Kastelein JJ, Stalenhoef AF. Effect of aggressive versus conventional lipid lowering on atherosclerosis progression in familial hypercholesterolaemia (ASAP): A prospective, randomised, double-blind trial. *Lancet* 2001; **357**: 577–581.
  13. Taylor AJ, Kent SM, Flaherty PJ, Coyle LC, Markwood TT, Vernalis MN. ARBITER: Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol: A randomized trial comparing the effects of atorvastatin and pravastatin on carotid intima medial thickness. *Circulation* 2002; **106**: 2055–2060.
  14. Nissen SE, Tuzcu EM, Schoenhagen P, Brown BG, Ganz P, Vogel RA, et al; REVERSAL Investigators. Effect of intensive compared with moderate lipid-lowering therapy on progression of coronary atherosclerosis: A randomized controlled trial. *JAMA* 2004; **291**: 1071–1080.
  15. LaRosa JC, Grundy SM, Waters DD, Shear C, Barter P, Fruchart JC, et al; Treating to New Targets (TNT) Investigators. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. *N Engl J Med* 2005; **352**: 1425–1435.
  16. O'Keefe JH, Cordain L, Harris WH, Moe RM, Vogel R. Optimal low-density lipoprotein is 50 to 70 mg/dl: Lower is better and physiologically normal. *J Am Coll Cardiol* 2004; **43**: 2142–2146.
  17. Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, et al; Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 Investigators. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med* 2004; **350**: 1495–1504.
  18. 1999 World Health Organization–International Society of Hypertension Guidelines Subcommittee. Guidelines for the Management of Hypertension. *J Hypertens* 1999; **17**: 151–183.
  19. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med* 1998; **15**: 539–553.
  20. Hirsch AT, Haskal ZJ, Hertzner NR, Bakal CW, Creager MA, Halperin JL, et al; American Association for Vascular Surgery; Society for Vascular Surgery; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine and Biology; Society of Interventional Radiology; ACC/AHA Task Force on Practice Guidelines Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease; American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; Vascular Disease Foundation. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): A collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease); Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *Circulation* 2006; **113**: e463–e654.
  21. Grundy SM, Cleeman JI, Merz CN, Brewer HB Jr, Clark LT, Hunninghake DB, et al; National Heart, Lung, and Blood Institute; American College of Cardiology Foundation; American Heart Association. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation* 2004; **110**: 227–239.
  22. The Writing Committee for the Treatment of Dyslipidemia in Chinese Adult. The guideline for the treatment of dyslipidemia in Chinese adult. *Chin J Cardiol* 2007; **35**: 390–420 (in Chinese).
  23. Liu J, Hong Y, D'Agostino RB Sr, Wu Z, Wang W, Sun J, et al. Predictive value for the Chinese population of the Framingham CHD risk assessment tool compared with the Chinese Multi-Provincial Cohort Study. *JAMA* 2004; **291**: 2591–2599.
  24. Critchley J, Liu J, Zhao D, Wei W, Capewell S. Explaining the increase in coronary heart disease mortality in Beijing between 1984 and 1999. *Circulation* 2004; **110**: 1236–1244.
  25. Wu Z, Yao C, Zhao D, Wu G, Wang W, Liu J, et al. Cardiovascular disease risk factor levels and their relations to CVD rates in China: Results of Sino-MONICA project. *Eur J Cardiovasc Prev Rehabil* 2004; **11**: 275–283.
  26. Mizuguchi Y, Oishi Y, Miyoshi H, Iuchi A, Nagase N, Oki T. Impact of statin therapy on left ventricular function and carotid arterial stiffness in patients with hypercholesterolemia. *Circ J* 2008; **72**: 538–544.
  27. Sato H, Kinjo K, Ito H, Hirayama A, Nanto S, Fukunami M, et al; Osaka Acute Coronary Insufficiency Study (OACIS)-LIPID Study Investigators. Effect of early use of low-dose pravastatin on major adverse cardiac events in patients with acute myocardial infarction: The OACIS-LIPID Study. *Circ J* 2008; **72**: 17–22.
  28. Yamada T, Azuma A, Sasaki S, Sawada T, Matsubara H; REACH Study Group. Randomized evaluation of atorvastatin in patients with coronary heart disease: A serial intravascular ultrasound study. *Circ J* 2007; **71**: 1845–1850.
  29. Kawano H, Yano K. Pravastatin decreases blood pressure in hypertensive and hypercholesterolemic patients receiving antihypertensive treatment. *Circ J* 2006; **70**: 1116–1121.
  30. Tasaki H, Miyamoto M, Kubara T, Kamezaki F, Tanaka S, Yamashita K, et al. Cross-over trial of intensive monotherapy with atorvastatin and combined therapy with atorvastatin and colestimide for Japanese familial hypercholesterolemia. *Circ J* 2006; **70**: 14–20.
  31. Nagashima H, Kasanuki H. The status of lipid management in 1,836 patients with coronary artery disease: A multicenter survey to evaluate the percentage of Japanese coronary artery disease patients achieving the target low-density lipoprotein cholesterol level specified by the Japan Atherosclerosis Society. *J Atheroscler Thromb* 2005; **12**: 338–342.
  32. Majumdar SR, Gurwitz JH, Soumerai SB. Undertreatment of hyperlipidemia in the secondary prevention of coronary artery disease. *J Gen Intern Med* 1999; **14**: 711–717.
  33. McBride P, Schrott HG, Plane MB, Underbakke G, Brown RL. Primary care practice adherence to National Cholesterol Education Program guidelines for patients with coronary heart disease. *Arch Intern Med* 1998; **158**: 1238–1244.
  34. Schrott HG, Bittner V, Vittinghoff E, Herrington DM, Hulley S. Adherence to National Cholesterol Education Program Treatment goals in postmenopausal women with heart disease: The Heart and Estrogen/Progestin Replacement Study (HERS). The HERS Research Group. *JAMA* 1997; **277**: 1281–1286.

35. Cheng CW, Woo KS, Chan JC, Tomlinson B, You JH. Association between adherence to statin therapy and lipid control in Hong Kong Chinese patients at high risk of coronary heart disease. *Br J Clin Pharmacol* 2004; **58**: 528–535.

### Appendix 1

*Beijing*: Beijing People's Hospital: Dayi Hu; Tongren Hospital: Dayi Hu; Xiehe Hospital: Xiaowei Yan; Shijitan Hospital: Shuixiang Yang; Beijing Hospital: Qing He; Dianli Hospital: Buxing Chen; Shijingshan Hospital: Mingsheng Wang; Beida Hospital: Yong Huo, Meilin Liu; Xuanwu Hospital: Ming Feng; Fuwai Hospital: Zhe Qi; Tiantan Hospital: Fenghe Du; Puren Hospital: Lizhi Ke, Feng He; The General Hospital of the Air Force PLA: Zhaozhong Liu; 304 Hospital of PLA: Dong Shen; 306 Hospital of PLA: Xiaofei Wang; 721 Hospital of PLA: Bin Wang; The Sixth Hospital: Xiaoping Xiang; Meitan Hospital: Jinghua Liu; China–Japan Friendship Hospital: Yuannan Ke, Zhigang Zheng; General Hospital of Beijing Military Area Command of PLA: Xian Wang; The Third Hospital of Beijing University: Wei Gao; Dongfang Hospital: Yang Wu; Zhongyi Hospital: Hongxu Liu; Youyi Hospital: Hongwei Li; Jishuitan Hospital: Huayi Sun; Wujing Hospital: Huiliang Liu.

*Shanghai*: The Tenth People's Hospital: Yawei Xu; Eastern Hospital: Daifu Zhang; Tongji Hospital: Mingzhong Zhao; Yueyang Hospital: Haiming Luo; Changhai Hospital: Yongwen Qin; Zhongshan Hospital:

Junbo Ge; Ruijing Hospital: Guoping Lu; Changzheng Hospital: Zonggui Wu; Renji Hospital: Jianping Liu; The First People's Hospital: Baogui Sun; Central Hospital of Jing'an District: Minghe Wang; Xinhua Hospital: Yigang Li; Central Hospital of Minhang District: Dadong Zhang; Central Hospital of Yangpu District: Shufu Zhang; Central Hospital of Luwan District: Jianrong Zhao; Central Hospital of Putuo District: Huigen Jin; Huashan Hospital: Haiming Shi; People's Hospital of Putuo District: Qiliang Liu; Shuguang Hospital: Meixian Jiang; Longhua Hospital: Ning Zhu.

*Guangzhou*: Guangzhou Southern Hospital: Pingsheng Wu; The First Hospital: Guanglian Li; People's Hospital of Guangdong Province: Yingling Zhou; The First Hospital Affiliated to Zhongshan University: Xugang Dong. *Xinjiang*: Xinjiang People's Hospital: Jianxin Lei; Zhongyi Hospital: Gang Wu; General Hospital of Xinjiang Military Area Command of PLA: Maoru Ma.

*Zhejiang*: The First Hospital of Ningbo: Shenghuang Wang; Lihuili Hospital of Ningbo: Shijun Ge; Central Hospital of Jinhua: Hang Chen; The First Hospital Affiliated to Wenzhou Medical College: Huaiqin Zhang; The Second Hospital Affiliated to Wenzhou Medical College: Jun Wang; The second Hospital of Zhengjiang Province: Geng Xu; The First Hospital of Hangzhou: Ningfu Wang; Shaoyifu Hospital: Guosheng Fu; Zhongyi Hospital: Zhaoquan Huang; Zhejiang Hospital: Farong Shen.

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