Aim: The recommended low-density lipoprotein cholesterol (LDL-C) levels of the guideline may be appropriate for Caucasian patients but not for other ethnic groups.

Methods: A cohort study was conducted in Hong Kong, and acute coronary syndrome (ACS) patients who received percutaneous coronary intervention (PCI) between 2005 and 2015 were enrolled. The primary outcomes of interest were the total cost of care and cardiovascular-related cost during one-year follow-up. The cost difference by lipid goal attainments was analyzed by Poisson regression with multivariate treatment effects. The clinical outcomes achieved by lipid goal attainments in terms of major adverse cardiovascular events were analyzed by multivariate Cox regression.

Results: Among the 4638 patients, 79.50%, 48.64%, and 36.14% attained the LDL-C goals of <2.6, <2.0, and <1.8 mmol/L for one year, respectively. Only about 16% patients achieved the ≥50% reduction from baseline. None of these lipid goals was associated with a significant reduction in the total cost of care. We only identified the clinical benefits associated with the lipid goal of <2.6 mmol/L. Other more stringent lipid goals seemed to bring a significant economic burden on cardiovascular-related cost, but their clinical benefits were uncertain.

Conclusions: Lowering LDL-C to achieve the guideline-recommended target levels for post-PCI ACS patients may lead to fewer cardiovascular events, but it may not necessarily lead to economic benefits within one year of follow-up.

Key words: LDL-C, Cost analysis, Chinese, Cardiovascular events, Cost of care

Introduction

Epidemiologic studies and clinical trials constantly suggest that lipid management could reduce the risk of recurrent cardiovascular events1-3). In light of existing evidence, the United States4, 5) and European6, 7) guidelines recommended the lipid goals of 2.6 mmol/L (100 mg/dL) and <1.8 mmol/L (70 mg/dL) for high-risk patients, including those with prior history of coronary heart disease (CHD). The 2013 American College of Cardiology/American Heart Association guidelines recommended a low-density lipoprotein cholesterol (LDL-C) treatment target of ≥50% reduction8). However, most clinical trial data were obtained from Caucasian patients5, 8-12), and the concept of therapeutic LDL-C targets and proper use of lipid-lowering drugs may not be identical between Western and Asian populations13). A rapidly growing body of literature from Asian countries is challenging the “lower is better” hypothesis14-19). The main find-
ing from 13473 acute myocardial infarction (MI) patients in a large-scale, prospective, multicenter Korean MI registry found that patients who achieved the target LDL-C level of <70 mg/dL did not have lower risks for cardiovascular events regardless of statin therapy than patients who did not achieve the target LDL-C. The large-scale Japanese Coronary Revascularization Demonstrating Outcome Study in Kyoto(S) investigated 14866 patients who underwent coronary revascularization and found that the risk for major adverse cardiovascular events (MACEs) was significantly higher in the ≥120 mg/dl group than in patients with lipid goal levels between 80–99 mg/dL; however, the risk for MACEs was not significantly lower in the <80 mg/dL group. Another population-based study using data from 31619 ischemic heart disease patients in Israel concluded that patients with LDL-C levels of 70–100 mg/dL had lower risks of MACEs than those with LDL-C levels at 100–130 mg/dL; however, they failed to observe any additional benefit in the patient group achieving LDL-C <70 mg/dL. According to our previous research findings(21, 22), we failed to identify the clinical benefits associated with the lipid goal of <1.8 mmol/L (70 mg/dL) in Chinese patients. There was an intense debate with regard to the Chinese guidelines on whether the recommended LDL-C reduction target for the high-risk atherosclerotic cardiovascular disease group should be set at LDL-C <1.8 mmol/L (70 mg/dL) or <2.0 mmol/L (80 mg/dL)(23, 24).

In real-world clinical practice, many patients fail to achieve their lipid goals, and the contributing factors vary between individuals, such as use of low doses, limited drug effectiveness, and poor drug adherence(25-27). A retrospective cohort study in 29 countries across Asia, Western Europe, Eastern Europe, the Middle East, and Africa on 35121 patients taking lipid-lowering drugs found that LDL-C goal attainment was suboptimal worldwide, particularly in patients with high and very high cardiovascular risks(27). Treating patients on the basis of guideline-recommended cholesterol levels or even below would lead to higher economic burden(28). The Return on Expenditure Achieved for Lipid Therapy (REALITY) study in Europe(29) was among the first to study the association between attainment of treatment goals and lipid-lowering therapy. In Swedish patients, they found that those attaining the treatment goal of <3.0 mmol/L during the first year had a 28% higher cost of care(28) than nonachievers, but the cost of cardiovascular-related inpatient care in lipid goal achievers was 40% lower than nonachievers after 2–3 years. Compared with the ample pharmacoepidemiologic studies involving Caucasian patients, the economic burden of failure in lipid goal attainments in Asian countries(30) is not well addressed in literature. The REALITY study in Asia(31, 32) focused on the evaluation of the lipid goal attainment rate but left the question of economic burden unanswered.

**Aim**

The aim of the current research was to fill the knowledge gap regarding the following: 1) the lipid goal attainments (namely, the lipid goals of <2.6 mmol/L, <1.8 mmol/L, <2.0 mmol/L, and ≥50% LDL-C reduction) in Hong Kong; 2) the association of lipid goal attainments and MACEs; 3) the short-(one year) and long-term (five years) costs of failure in achieving the lipid goals, including the total cost of care and cardiovascular-related cost per person (among which the one-year cost was evaluated as the primary outcome, complemented with a sensitivity analysis on the five-year cost).

**Methods**

In an attempt to provide such data, we performed a noninterventional secondary cohort analysis of post-percutaneous coronary intervention (PCI) acute coronary syndrome (ACS) patients to assess the costs and consequences of lipid goal attainments under real-life conditions in Hong Kong, China. The current study was based on electronic health records (EHRs) from the Hong Kong Hospital Authority Clinical Data Analysis and Reporting System (CDARS) database.

Our study population consisted of all Chinese ACS patients (identified by the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9 CM) diagnosis codes of 411 and 410) aged above 21 years old who received a first documented PCI in the inclusion period between January 1, 2005, and November 30, 2015 from an acute public hospital, the PCI-capable hospital in the New Territories East Cluster of Hong Kong. The study population was continuously enrolled in CDARS for at least one year after their index PCI procedure and had at least one cholesterol measurement within the first-year follow-up. We defined MACEs in the current study as all-cause death, MI, unstable angina (UA), stroke, and revascularization(33, 34) from 30 days post-PCI to the one-year endpoint and identified MACEs by death records and ICD-9 CM codes of 410.x (MI); 411.x (UA); 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, and 434.91 (stroke); 36.01, 36.02, 36.05, 36.06, and 36.09 (PCI); and 36.1 (coronary artery bypass graft). If the patient died within one month after the PCI, he/she was excluded from...
the analysis regarding the association of MACEs and the latest LDL-C goal before MACE because recurrent events that occurred within the first month might be largely related to the index PCI procedure. The lipid goals under investigation were $\leq 1.8 \text{mmol/L (70 mg/dL)}$, $2.6 \text{mmol/L (100 mg/dL)}$, $< 2.0 \text{mmol/L (80 mg/dL)}$, and $\geq 50\%$ reduction from baseline. The endpoint lipid goal at the one-year follow-up and the latest lipid goal before the first MACE were studied separately. The latest LDL-C measurement before the MACE was taken from the most recent laboratory results prior to the first MACE day, but it might not necessarily be the endpoint lipid measurement at the one-year follow-up. Considering that the measurement of LDL-C levels at the index ACS event was not a routine clinical practice in Hong Kong, the baseline LDL-C measurements were extracted from the laboratory results nearest to the index PCI procedure (within the period between 180 days prior to the index PCI day and 365 days after the index day). For patients who only had one laboratory result during the index day and after 365 days but had no prior LDL-C measurement between -180 and 0 days, their baseline LDL-C levels could be missing. The patients’ prior disease history, including comorbidities of diabetes and hypertension, and prior cardiovascular disease (CVD) history were obtained from the ICD-9 CM codes in the system in the past six months prior to the index PCI procedure day.

The economic evaluation of interest was the total (direct) cost of care and the cardiovascular-related (inpatient and outpatient) cost from the provider perspective. The total cost of care included the costs for inpatient care, outpatient visits, revascularization procedures, lipid-lowering drugs, and laboratory tests (lipid tests) in the public sectors of Hong Kong. The cardiovascular-related cost in this evaluation was defined as the sum of all the costs of the first-year management of the patient for any cardiovascular-related events (identified by ICD-9 CM code 390.xx-459.xx), including inpatient hospitalization, accident and emergency department admission, and outpatient visits for cardiovascular conditions. The cost for inpatient care was estimated using the length of stay in the hospital from the CDARS and standardized daily cost. The estimation of in-hospital care cost by length of stay and cost per hospital bed day was a common practice by the World Health Organization, and the unit cost (cost per hospital bed day) was found in the Hong Kong Government Gazette.

Cost items were also available on all contacts with outpatient hospital services and each attendance at a general clinic would cost HKD 385 (USD 49.4) locally. The unit costs of all direct medical items were based on the 2013 Hong Kong Government Gazette (an official source for medical charges in local public hospitals). All costs were estimated in Hong Kong dollars and were converted to US dollars by using the conversion rate USD 1 = HKD 7.8 as of March 9, 2018, when applicable.

### Statistical Methods

Descriptive statistics were used to analyze the demographic data, baseline characteristics, and lipid profile parameters. In Supplementary Table 1, the crude cost items of interest are presented. To identify the influential contributors to the total cost of care, Supplementary Table 1 presents the rundown listing of all the target cost items per person, which include the following: the total cost of care, cardiovascular-related inpatient cost, cardiovascular-related outpatient cost, cardiovascular-related cost (including inpatient and outpatient costs), cost of lipid-lowering therapy (statins and other lipid-lowering drugs), and other management cost (deducting the cardiovascular-related cost from total cost of care). The differences in the abovementioned detailed costs between lipid goal achievers and nonachievers were examined using the treatment effect estimation of multivalued treatment effects by adjusting for available potential confounders such as age, sex, diabetes, hypertension, and prior CVD history (Tables 2 and 3 for “analyzed sample,” Supplementary Table 2 and Supplementary Table 3 for the “full sample,” Supplementary Table 4 for cardiovascular-related inpatient cost and cardiovascular-related outpatient cost). Considering that the costs were all positive and were not necessarily following the normality, we used the Poisson option inside the outcome model specification. Multivariable Cox regression analyses were performed to assess the associations of MACEs with the LDL-C goal attainments before MACE after adjusting for age, sex, diabetes, hypertension, and prior CVD history.

### Sensitivity Analysis

Two sensitivity analyses were conducted to test the robustness of our results. As noticed in the early literature, patients that reached the lipid goals showed a trend of cost reductions over time. To explore if the costs significantly decreased after one year after the index day, we also examined the average five-year total cost of care among the patients who underwent the index PCI between January 1, 2005, and November 30, 2010, and completed the five-year follow-up. The adjusted differences in the total cost of care and cardiovascular-related cost for this patient group could be found in Table 5 and Supplementary Table 5. In absolute terms, the baseline LDL-C levels...
| Description                                                                 | n (Column %) |
|-----------------------------------------------------------------------------|--------------|
| **Total**                                                                  | 4638         |
| Mean age (SD)                                                              | 70.23 (10.99) |
| Sex: Male                                                                  | 3571 (76.99) |
| Previous CVD% (with respective ICD-9 CM code)                              | 2223 (47.93) |
| Hypertensive disease (401-405)                                             | 451 (9.72)   |
| Ischemic heart disease (410-414)                                           | 1278 (27.55) |
| Coronary Artery Disease (414)                                              | 36 (0.78)    |
| CVA, stroke (434.91)                                                       | 13 (0.28)    |
| Atrial fibrillation (427.31)                                               | 46 (0.99)    |
| Heart failure (428)                                                        | 147 (3.17)   |
| Carotid artery stenosis/occlusion (433)                                     | 3 (0.06)     |
| Cerebral atherosclerosis/ischemic cerebrovascular disease (437)            | 6 (0.13)     |
| Others                                                                     | 243 (5.24)   |
| Comorbidity: Hypertension                                                 | 901 (19.43)  |
| Comorbidity: Diabetes                                                      | 795 (17.14)  |
| **Baseline cholesterol**                                                    |              |
| Mean Total (SD)                                                            | 4.65 (1.18)  |
| Mean LDL-C (SD)                                                            | 2.77 (1.05)  |
| Mean HDL-C (SD)                                                            | 1.16 (0.32)  |
| Mean triglycerides (SD)                                                    | 1.6 (0.97)   |
| **Baseline LDL-C category**                                                |              |
| < 1.8 mmol/L                                                               | 675 (16.14)  |
| 1.8-2.6 mmol/L                                                             | 1328 (31.76) |
| > 2.6 mmol/L                                                               | 2179 (52.10) |
| **LDL-C reduction ≥ 50% before MACE**                                      |              |
| 1.8 mmol/L                                                                | 1676 (36.14) |
| 2.0 mmol/L                                                                | 2256 (48.64) |
| 2.6 mmol/L                                                                | 3687 (79.50) |
| Endpoint LDL-C goal attainments                                            |              |
| 1.8 mmol/L                                                                | 1676 (36.14) |
| 2.0 mmol/L                                                                | 2256 (48.64) |
| 2.6 mmol/L                                                                | 3687 (79.50) |
| Endpoint LDL-C                                                             |              |
| < 1.8 mmol/L                                                               | 1676 (36.14) |
| 1.8-2.6 mmol/L                                                             | 2011 (43.36) |
| > 2.6 mmol/L                                                               | 951 (20.5)   |
| **Latest LDL-C category before MACE**                                      |              |
| 1.8 mmol/L                                                                | 1642 (35.50) |
| 2.0 mmol/L                                                                | 2214 (47.87) |
| 2.6 mmol/L                                                                | 3644 (78.79) |
| Latest LDL-C goal attainments before MACE                                   |              |
| 1.8 mmol/L                                                                | 1642 (35.50) |
| 2.0 mmol/L                                                                | 2214 (47.87) |
| 2.6 mmol/L                                                                | 3644 (78.79) |
| Latest LDL-C category before MACE                                          |              |
| < 1.8 mmol/L                                                               | 1642 (35.50) |
| 1.8-2.6 mmol/L                                                             | 2002 (43.29) |
| > 2.6 mmol/L                                                               | 981 (21.21)  |
| **MACE**                                                                   |              |
| Recurrent PCI between 30 and 365 days                                      | 254 (5.56)   |
| Recurrent ACS between 30 and 365 days                                      | 176 (3.75)   |
| Stroke                                                                     | 31 (0.69)    |
| Death between 30 and 365 days                                              | 54 (1.08)    |
| Death within the first 30 days after index PCI                             | 13 (0.30)    |

MACE, major adverse cardiovascular events; CVA, cerebrovascular accident; LDL-C, low-density lipoprotein cholesterol; ACS, acute coronary syndrome; PCI, percutaneous coronary intervention; CDARS, clinical data analysis and reporting system; ICD-9 CM, International Classification of Diseases, Ninth Revision, Clinical Modification; CVD, cardiovascular diseases; HDL-C, high-density lipoprotein cholesterol; SD, standard deviation.
seemed to largely influence the economic and clinical outcomes in terms of their initial effect on physicians’ judgments. Therefore, a sensitivity analysis was conducted among patients with baseline LDL-C beyond 2.6 mmol/L to test the robustness of our results (Tables 2, 3, and 4).

All analyses were performed using Stata 14 (Stata Corporation Lp, College Station, TX). All the patients’ information was de-identified in the database. The study was approved by the Joint Clinical Research Ethics Committee of The Chinese University of Hong Kong and New Territories East Cluster of Hong Kong, and the protocol was compliant with the Declaration of Helsinki.

Results

Our analysis involves 4638 patients (mean age ± standard deviation (SD): 70.23 ± 10.99 years) who have at least one LDL-C measurement via one-year follow-up (Table 1); these patients are referred to as the “full sample” in Supplementary Tables 1, 2, 3, and 4. There were 76.99% males, 19.43% of which were hypertensive, 17.14% were diabetic patients, and 47.93% had previous CVD. At the one-year endpoint, approximately 80% and 50% of patient reached the LDL-C goals of 2.6 and 2.0 mmol/L, respectively, and 36.14% were well controlled under 1.8 mmol/L. Among the 4182 patients who had available baseline LDL-C levels, 52.10% had their initial LDL-C levels above 2.6 mmol/L, and only 15.95% achieved ≥50% reduction. Among all patients, 515 (11.10%) had at least one incidence of MACE between 30 and 365 days after the index procedure. Thirteen patients died within the first month, and these patients were excluded when we analyzed the latest lipid goal attainment before MACE. After the exclusion, 4625 patients comprised the “analyzed sample” (Tables 2, 3, and 4).

Supplementary Table 1 reports the crude costs by lipid goal attainments at the one-year endpoint and before their first MACE between the 30th and 365th day, respectively. From the observed crude numbers of Supplementary Table 1, the lipid goal achievers of <1.8 mmol/L carry the highest total cost of care compared with the nonachievers, and the lipid category of 1.8–2.6 mmol/L seems to be more desirable in terms of costs. The adjusted cost differences in the total cost of care and cardiovascular-related cost are presented in Tables 2 and 3 (Supplementary Tables 2 and 3 for the results of the “full sample”) and were controlled for baseline characteristics. After this adjustment, none of the lipid goal attainments of <2.6 mmol/L, <2.0 mmol/L, <1.8 mmol/L, or ≥50% reduction was associated with any reduction in the total cost of care during the one-year follow-up. After excluding the cardiovascular-related management costs (in Table 3), the lipid goal attainment of 2.6 mmol/L either at the one-year endpoint or before MACE seems to be a cost-saving strategy, particularly the category of 1.8–2.6 mmol/L. This finding could imply that among all the detailed cost items, the cardiovascular-related management cost, particularly the cardiovascular-related inpatient cost (shown in Supplementary Table 4), is the most affected by the lipid goal attainments. Assuming that patients who could attain the lipid goals remarkably differed in baseline characteristics from those who could not, we adjusted for all the available covariates and performed a sensitivity analysis among high-risk patients with LDL-C >2.6 mmol/L at baseline. We constantly find that lowering patients’ LDL-C levels to a more stringent goal leads to an increase in cardiovascular-related cost (Table 2). Upon realizing that the endpoint lipid goal attainment (at the one-year endpoint) was not necessarily the latest lipid goal before the MACE, we evaluated the cost difference by using the latest lipid goal attainments before MACE (Table 2) and the cost difference by lipid goal attainment at the one-year endpoint (Supplementary Table 2). It was still noted that the patients attaining more stringent lipid goals had higher costs in cardiovascular-related management. After excluding the cardiovascular-related (inpatient and outpatient) costs, both LDL-C goal attainment groups of <2.6 and <2.0 mmol/L could substantially increase the cost savings (Table 3). We expected that those having LDL-C levels below each lipid goal would be on more intensive lipid treatments than those above the goal, and this situation would contribute to the increased cost of reaching a lower level of LDL-C. However, from this current observation, the cardiovascular-related inpatient cost (Supplementary Table 4) is a more influential contributor to the total cost of care than the intensive lipid treatment cost (Table 3). In Table 5, among 2686 patients with a complete 5-year follow-up, no significant differences in any cost items between lipid goal achievers and nonachievers were observed starting from the second year.

Table 4 shows the results from the multivariate Cox regression analysis of the first occurrence of MACE. Separate regressions were performed for lipid goal attainments before MACEs in the analyzed sample and in the patient group with baseline LDL-C above 2.6 mmol/L. The LDL-C goal of <2.6 mmol/L was associated with a reduction in MACE but not the goals of 1.8 mmol/L, 2.0 mmol/L, and ≥50% reduction. Lowering the LDL-C level attainment from 2.6 mmol/L to 1.8 mmol/L did not improve the clinical
| Analyzed sample                                                                 | N   | Adjusted Coefficient* | (95% Confidence Interval) | p-value | Adjusted Coefficient* | (95% Confidence Interval) | p-value |
|--------------------------------------------------------------------------------|-----|-----------------------|---------------------------|---------|-----------------------|---------------------------|---------|
| Latest LDL-C before MACE achieving the goal of 2.6 mmol/L                      | 4625|                        |                           |         |                       |                           |         |
| Not at goal                                                                    | 947 | Ref                   | -4994.14 (-13597.38, 3609.10) | 0.255   | Ref                   | 4846.70 (1355.73, 8337.66) | 0.007   |
| At goal                                                                        | 3678|                       |                           |         |                       |                           |         |
| Latest LDL-C before MACE achieving the goal of 1.8 mmol/L                      | 4625|                        |                           |         |                       |                           |         |
| Not at goal                                                                    | 2950| Ref                   | -1385.40 (-5911.87, 8682.68) | 0.710   | Ref                   | 3414.99 (-487.42, 7317.40) | 0.086   |
| At goal                                                                        | 1675|                       |                           |         |                       |                           |         |
| Latest LDL-C before MACE achieving the goal of 2.0 mmol/L                      | 4625|                        |                           |         |                       |                           |         |
| Not at goal                                                                    | 2374| Ref                   | -1893.70 (-8656.95, 4869.55) | 0.583   | Ref                   | 3565.83 (-25.09, 7156.76) | 0.052   |
| At goal                                                                        | 2251|                       |                           |         |                       |                           |         |
| Latest LDL-C before MACE achieving the reduction of ≥ 50%                      | 4180|                        |                           |         |                       |                           |         |
| Not at goal                                                                    | 3547| Ref                   | -7485.89 (-5483.54, 20455.32) | 0.258   | Ref                   | 5861.97 (-1088.23, 12812.17) | 0.098   |
| At goal                                                                        | 633 |                       |                           |         |                       |                           |         |
| Latest LDL-C before MACE category of 2.6 mmol/L                                | 4625|                        |                           |         |                       |                           |         |
| >2.6 mmol/L                                                                    | 947 | Ref                   | -2937.15 (-12802.03, 6927.73) | 0.560   | Ref                   | 6005.66 (1690.23, 10321.08) | 0.006   |
| 1.8-2.6 mmol/L                                                                 | 2003| -6770.82 (-15760.27, 2218.63) | 0.140 | 3918.44 (-26.17, 7863.05) | 0.052 |
| <1.8 mmol/L                                                                    | 1675| -2937.15 (-12802.03, 6927.73) | 0.560 | 6005.66 (1690.23, 10321.08) | 0.006 |

| Among those baseline LDL-C > 2.6 mmol/L                                        |      |                       |                           |         |                       |                           |         |
| Latest LDL-C before MACE achieving the goal of 2.6 mmol/L                      | 2177|                        |                           |         |                       |                           |         |
| Not at goal                                                                    | 585 | Ref                   | -9274.95 (-20211.78, 1661.87) | 0.096   | Ref                   | 3009.52 (-1782.19, 7801.23) | 0.218   |
| At goal                                                                        | 1592|                       |                           |         |                       |                           |         |
| Latest LDL-C before MACE achieving the goal of 1.8 mmol/L                      | 2177|                        |                           |         |                       |                           |         |
| Not at goal                                                                    | 1535| Ref                   | -960.01 (-11895.72, 9975.70) | 0.863   | Ref                   | 3486.48 (-2322.27, 9295.23) | 0.239   |
| At goal                                                                        | 642 |                       |                           |         |                       |                           |         |
| Latest LDL-C before MACE achieving the goal of 2.0 mmol/L                      | 2177|                        |                           |         |                       |                           |         |
| Not at goal                                                                    | 1275| Ref                   | -2112.09 (-11778.81, 7554.62) | 0.668   | Ref                   | 5159.30 (-309.52, 10628.12) | 0.064   |
| At goal                                                                        | 903 |                       |                           |         |                       |                           |         |
| Latest LDL-C before MACE achieving the reduction of ≥ 50%                      | 2177|                        |                           |         |                       |                           |         |
| Not at goal                                                                    | 1603| Ref                   | -7611.84 (-4473.77, 19697.46) | 0.217   | Ref                   | 6751.11 (-297.54, 13799.76) | 0.060   |
| At goal                                                                        | 574 |                       |                           |         |                       |                           |         |
| Latest LDL-C before MACE category of >2.6 mmol/L                                | 2177|                        |                           |         |                       |                           |         |
| >2.6 mmol/L                                                                    | 585 | Ref                   | -10335.72 (-21762.04, 1090.59) | 0.076   | Ref                   | 2157.93 (-3304.57, 7620.44) | 0.439   |
| 1.8-2.6 mmol/L                                                                 | 950 | -7167.12 (-20738.06, 6403.83) | 0.301 | 4521.06 (-1791.19, 10833.30) | 0.160 |
| <1.8 mmol/L                                                                    | 642 |                       |                           |         |                       |                           |         |

MACE, major adverse cardiovascular events; LDL-C, low-density lipoprotein cholesterol; HKD, Hong Kong dollars; Ref, reference.
*Adjusted for age, sex, diabetes, hypertension, and prior cardiovascular history
Table 3. Adjusted cost difference in other management cost and the cost of lipid-lowering therapy by lipid goal attainments

| Analyzed sample | Other management cost (defined as total cost of care excluding the cardiovascular-related (inpatient and outpatient) cost) (HKD) | Cost of lipid-lowering therapy (statin and other lipid-lowering drugs) (HKD) |
|-----------------|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
|                 | $N$ | Adjusted Coefficient | Lower limit for 95% CI | Lower limit for 95% CI | $p$-value | Adjusted Coefficient | Lower limit for 95% CI | Lower limit for 95% CI | $p$-value |
| **Analyzed sample** | | | | | | | | | |
| Latest LDL-C before MACE achieving the goal of 2.6 mmol/L | 4625 | | | | | | | | |
| Not at goal | 947 | Ref | | | | | | | |
| At goal | 3678 | -9937.53 | -17166.93 | -2708.14 | 0.007 | 66.43 | -35.63 | 168.50 | 0.202 |
| Latest LDL-C before MACE achieving the goal of 1.8 mmol/L | 4625 | | | | | | | | |
| Not at goal | 2950 | Ref | | | | | | | |
| At goal | 1675 | -2252.01 | -7796.22 | 3292.19 | 0.426 | 272.35 | 183.19 | 361.51 | < 0.001 |
| Latest LDL-C before MACE achieving the goal of 2.0 mmol/L | 4180 | | | | | | | | |
| Not at goal | 2374 | Ref | | | | | | | |
| At goal | 2251 | -5538.07 | -10675.99 | -400.16 | 0.035 | 222.30 | 139.32 | 305.29 | < 0.001 |
| Latest LDL-C before MACE achieving the reduction of ≥ 50% | 4625 | | | | | | | | |
| Not at goal | 3547 | Ref | | | | | | | |
| At goal | 633 | 1578.91 | -8297.82 | 11455.64 | 0.754 | 667.28 | 508.35 | 826.21 | < 0.001 |
| Latest LDL-C before MACE category | 2177 | | | | | | | | |
| >2.6 mmol/L | 947 | Ref | | | | | | | |
| 1.8-2.6 mmol/L | 2003 | -10721.37 | -18081.72 | -3361.01 | 0.004 | -65.52 | -173.06 | 42.03 | 0.232 |
| <1.8 mmol/L | 1675 | -9176.30 | -17309.22 | -1043.37 | 0.027 | 227.61 | 109.81 | 345.41 | < 0.001 |

**Among those baseline LDL-C > 2.6 mmol/L.**

| Latest LDL-C before MACE achieving the goal of 2.6 mmol/L | 2177 | | | | | | | | |
| Not at goal | 585 | Ref | | | | | | | |
| At goal | 1592 | -12256.63 | -21228.51 | -3284.75 | 0.007 | 27.61 | -123.97 | 179.20 | 0.721 |
| Latest LDL-C before MACE achieving the goal of 1.8 mmol/L | 2177 | | | | | | | | |
| Not at goal | 1535 | Ref | | | | | | | |
| At goal | 642 | -4403.03 | -12882.10 | 4076.04 | 0.309 | 325.712 | 167.917 | 483.507 | < 0.001 |
| Latest LDL-C before MACE achieving the goal of 2.0 mmol/L | 2177 | | | | | | | | |
| Not at goal | 1275 | Ref | | | | | | | |
| At goal | 903 | -7310.54 | -14527.17 | -93.91 | 0.047 | 275.38 | 135.93 | 414.82 | < 0.001 |
| Latest LDL-C before MACE achieving the reduction of ≥ 50% | 2177 | | | | | | | | |
| Not at goal | 1603 | Ref | | | | | | | |
| At goal | 574 | 835.75 | -7993.07 | 9664.57 | 0.853 | 757.21 | 582.19 | 932.24 | < 0.001 |

MACE, major adverse cardiovascular events; LDL-C, low-density lipoprotein cholesterol; HKD, Hong Kong dollars; Ref, reference; CI, confidence interval.

*Adjusted for age, sex, diabetes, hypertension, and prior cardiovascular history.
This was possible because the higher cardiovascular-related cost targeting for more stringent lipid goals offset the savings in other management cost and boosted the total cost of care. In the current analysis, the latest lipid goal attainments before MACEs might not be the same as the lipid goal at the one-year endpoint because lipids changed acutely after MACEs. Therefore, we also tested the cost difference by the latest lipid goal attainments before MACE. The results seemed to be robust to what was found before. Owing to the limitations of the observational study, we could not clarify the causes.

Discussion

To our knowledge, this study was the first to investigate the economic burden of failure in achieving the lipid goals in an Asian/Chinese population. Our findings suggested that any LDL-C goal attainments of <2.6 mmol/L, <2.0 mmol/L, <1.8 mmol/L, and ≥50% reduction did not necessarily bring any reduction in the total cost of care during a one-year follow-up; this finding was in line with the prior cost analysis in Sweden. This was possible because the higher cardiovascular-related cost targeting for more stringent lipid goals offset the savings in other management cost and boosted the total cost of care. In the current analysis, the latest lipid goal attainments before MACEs might not be the same as the lipid goal at the one-year endpoint because lipids changed acutely after MACEs. Therefore, we also tested the cost difference by the latest lipid goal attainments before MACE. The results seemed to be robust to what was found before. Owing to the limitations of the observational study, we could not clarify the causes.

### Table 4. Association of MACEs and lipid goal attainments

|                              | n  | Adjusted Hazard Ratio* | (95% Confidence Interval) | p-value |
|------------------------------|----|------------------------|---------------------------|---------|
| **Analyzed sample**          |    |                        |                           |         |
| Latest LDL-C before MACE achieving the goal of 2.6 mmol/L | 4625 |                         |                           |         |
| Not at goal                  | 981 | 1                      |                           |         |
| At goal                      | 3644| 0.76 (0.62, 0.93)       | 0.007                     |         |
| Latest LDL-C before MACE achieving the goal of 1.8 mmol/L | 4625 |                         |                           |         |
| Not at goal                  | 2983| 1                      |                           |         |
| At goal                      | 1642| 0.97 (0.81, 1.17)       | 0.779                     |         |
| Latest LDL-C before MACE achieving the goal of 2.0 mmol/L | 4625 |                         |                           |         |
| Not at goal                  | 2411| 1                      |                           |         |
| At goal                      | 2214| 0.93 (0.78, 1.10)       | 0.385                     |         |
| Latest LDL-C before MACE achieving the goal of ≥50% reduction | 4180 |                         |                           |         |
| Not at goal                  | 3547| 1                      |                           |         |
| At goal                      | 633 | 0.77 (0.58, 1.03)       | 0.074                     |         |
| Latest LDL-C category before MACE | 4625 |                         |                           |         |
| <1.8 mmol/L                  | 1642| 1                      |                           |         |
| 1.8-2.6 mmol/L               | 2003| 0.92 (0.75, 1.12)       | 0.396                     |         |
| ≥2.6 mmol/L                  | 981 | 1.25 (1.00, 1.57)       | 0.051                     |         |
| **Among those with baseline LDL-C > 2.6 mmol/L** | 2177 |                         |                           |         |
| Latest LDL-C before MACE achieving the goal of 2.6 mmol/L | 2177 |                         |                           |         |
| Not at goal                  | 585 | 1                      |                           |         |
| At goal                      | 1592| 0.56 (0.42, 0.74)       | <0.001                    |         |
| Latest LDL-C before MACE achieving the goal of 1.8 mmol/L | 2177 |                         |                           |         |
| Not at goal                  | 1535| 1                      |                           |         |
| At goal                      | 642 | 0.78 (0.57, 1.06)       | 0.108                     |         |
| Latest LDL-C before MACE achieving the goal of 2.0 mmol/L | 2177 |                         |                           |         |
| Not at goal                  | 1275| 1                      |                           |         |
| At goal                      | 903 | 0.83 (0.63, 1.10)       | 0.186                     |         |
| Latest LDL-C before MACE achieving the goal of ≥50% reduction | 2177 |                         |                           |         |
| Not at goal                  | 1603| 1                      |                           |         |
| At goal                      | 574 | 0.72 (0.52, 1.00)       | 0.051                     |         |
| Latest LDL-C category before MACE | 2177 |                         |                           |         |
| <1.8 mmol/L                  | 642 | 1                      |                           |         |
| 1.8-2.6 mmol/L               | 950 | 1.00 (0.71, 1.41)       | 0.983                     |         |
| ≥2.6 mmol/L                  | 585 | 1.79 (1.26, 2.55)       | 0.001                     |         |

MACE, major adverse cardiovascular events; LDL-C, low-density lipoprotein cholesterol. *Adjusted for age, sex, diabetes, hypertension, and prior cardiovascular history.
atorvastatin and rosuvastatin rather than generic simvastatin. However, as shown in Table 3, the cost of lipid-lowering drugs alone was perceived to have little effect on the total cost of care. Normally the future costs were less than the immediate costs, although the future clinical benefits of a longer follow-up were generally less significant than the immediate benefits\(^5\). As a consequence, we took a closer look at the time series changes among patients with five-year follow-up because one Swedish study found that the cardiovascular-related costs for goal-attaining patients decreased significantly 2–3 years after the treatment started\(^2\). However, our results did not show the same "cost reduction" trend in lipid goal achievers. Starting from the second year, there were no significant cost differences between the lipid goal achievers and nonachievers. The other possible explanation could be that the cost of higher intensive lipid treatment may have been substantially greater because of the use of branded atorvastatin and rosuvastatin rather than generic simvastatin.

Table 5. Adjusted cost difference of the total cost of care and cardiovascular-related cost by lipid goal attainments among 2686 patients with complete five-year follow-up

| Endpoint LDL-C achieving the goal of 2.6 mmol/L | Total cost of care (HKD) | Cardiovascular-related cost (HKD) |
|-----------------------------------------------|--------------------------|-----------------------------------|
|                                               | N                        | Adjusted Coefficient*            | (95% Confidence Interval) | p-value | Adjusted Coefficient* | (95% Confidence Interval) | p-value |
| 1st year: At goal vs Not at goal 2686          | 6548.52 (-3441.94, 16538.97) | 0.20 | 10495.13 (5846.36, 15143.89) | <0.001 |
| 2nd year: At goal vs Not at goal 2686          | 1433.02 (-6835.65, 9701.69) | 0.73 | -1637.26 (-5892.56, 2618.05) | 0.45    |
| 3rd year: At goal vs Not at goal 2686          | 1404.19 (-6251.35, 9059.74) | 0.72 | -7.59 (-3437.71, 3422.53)    | 1.00    |
| 4th year: At goal vs Not at goal 2686          | -4251.30 (-11714.31, 3211.71) | 0.26 | -1776.81 (-5662.26, 2108.64) | 0.37    |
| 5th year: At goal vs Not at goal 2686          | -748.84 (-7558.02, 6060.34) | 0.83 | -1529.18 (-5146.36, 2088.00) | 0.41    |

| Endpoint LDL-C achieving the goal of 1.8 mmol/L | Total cost of care (HKD) | Cardiovascular-related cost (HKD) |
|-----------------------------------------------|--------------------------|-----------------------------------|
|                                               | N                        | Adjusted Coefficient*            | (95% Confidence Interval) | p-value | Adjusted Coefficient* | (95% Confidence Interval) | p-value |
| 1st year: At goal vs Not at goal 2686          | 12764.70 (1199.33, 24330.08) | 0.03 | 8367.48 (1343.69, 15391.27) | 0.02 |
| 2nd year: At goal vs Not at goal 2686          | 1069.42 (1936.13, 19453.32) | 0.02 | 739.51 (-2118.36, 3597.39) | 0.61 |
| 3rd year: At goal vs Not at goal 2686          | 4185.83 (-3570.15, 11941.81) | 0.29 | 2323.03 (-1117.32, 5763.37) | 0.38 |
| 4th year: At goal vs Not at goal 2686          | -2747.02 (-9003.42, 3509.38) | 0.39 | -1263.53 (-4107.77, 1580.71) | 0.38 |
| 5th year: At goal vs Not at goal 2686          | 367.42 (-6025.01, 6759.85) | 0.91 | 21.21 (-2939.33, 2981.74) | 0.99 |

| Endpoint LDL-C achieving the goal of 2.0 mmol/L | Total cost of care (HKD) | Cardiovascular-related cost (HKD) |
|-----------------------------------------------|--------------------------|-----------------------------------|
|                                               | N                        | Adjusted Coefficient*            | (95% Confidence Interval) | p-value | Adjusted Coefficient* | (95% Confidence Interval) | p-value |
| 1st year: At goal vs Not at goal 2686          | 8031.90 (-2052.35, 18116.14) | 0.12 | 7683.58 (1678.83, 13688.32) | 0.01 |
| 2nd year: At goal vs Not at goal 2686          | 6080.24 (-1372.17, 13532.65) | 0.11 | -167.99 (-2973.12, 2637.14) | 0.91 |
| 3rd year: At goal vs Not at goal 2686          | 1853.03 (-5091.22, 8797.29) | 0.60 | 1056.23 (-1890.38, 4002.83) | 0.48 |
| 4th year: At goal vs Not at goal 2686          | -6025.85 (-11884.44, -167.25) | 0.04 | -2474.41 (-5301.74, 352.93) | 0.09 |
| 5th year: At goal vs Not at goal 2686          | -405.39 (-6530.61, 5719.83) | 0.90 | -1076.21 (-3926.35, 1773.94) | 0.46 |

| Endpoint LDL-C achieving the reduction of 50%  | Total cost of care (HKD) | Cardiovascular-related cost (HKD) |
|-----------------------------------------------|--------------------------|-----------------------------------|
|                                               | N                        | Adjusted Coefficient*            | (95% Confidence Interval) | p-value | Adjusted Coefficient* | (95% Confidence Interval) | p-value |
| 1st year: At goal vs Not at goal 2412         | 16472.69 (-2613.22, 35558.59) | 0.09 | 10607.64 (2947.47, 20917.80) | 0.04 |
| 2nd year: At goal vs Not at goal 2412         | 16472.69 (-2613.22, 35558.59) | 0.09 | 10607.64 (2947.47, 20917.80) | 0.04 |
| 3rd year: At goal vs Not at goal 2412         | -1969.65 (-13188.12, 9248.82) | 0.73 | -182.27 (-5121.42, 4756.89) | 0.94 |
| 4th year: At goal vs Not at goal 2412         | -4115.05 (-13228.67, 4998.58) | 0.38 | -2179.64 (-5794.71, 1435.42) | 0.24 |
| 5th year: At goal vs Not at goal 2412         | 2065.28 (-10846.31, 14976.88) | 0.75 | -1675.69 (-5453.84, 2102.45) | 0.38 |

MACE, major adverse cardiovascular events; LDL-C, low-density lipoprotein cholesterol; HKD, Hong Kong dollars; Ref, reference.

*Adjusted for age, sex, diabetes, hypertension, and prior cardiovascular history.

of the additional cardiovascular-related cost in the “treat-to-target” approaches for the LDL-C goals of < 2.0 mmol/L, < 1.8 mmol/L, and ≥ 50% reduction compared with the less intensive LDL-C goal of < 2.6 mmol/L. One possible reason could be that physicians aggressively treated patients who were at higher risk at baseline to reach a more stringent lipid goal, thus causing additional economic burden. Bearing this potential explanation in mind, we looked at the cost differences in high-risk patients with baseline LDL-C beyond 2.6 mmol/L and still found that lipid categories of 1.8 mmol/L, 2.0 mmol/L, 2.6 mmol/L, and ≥ 50% reduction denoted higher cardiovascular-related costs. The other possible explanation could be that the cost of higher intensive lipid treatment may have been substantially greater because of the use of branded atorvastatin and rosuvastatin rather than generic simvastatin. However, as shown in Table 3, the cost of lipid-lowering drugs alone was perceived to have little effect on the total cost of care. Normally the future costs were less than the immediate costs, although the future clinical benefits of a longer follow-up were generally less significant than the immediate benefits\(^5\). As a consequence, we took a closer look at the time series changes among patients with five-year follow-up because one Swedish study found that the cardiovascular-related costs for goal-attaining patients decreased significantly 2–3 years after the treatment started\(^2\). However, our results did not show the same “cost reduction” trend in lipid goal achievers. Starting from the second year, there were no significant cost differences between the lipid goal achievers and nonachieve-
ers.

Taken together, if attainment of a more stringent lipid goal accompanied a higher cardiovascular-related cost, it would be important to determine if the attainment of the lower lipid goal could also lead to improved clinical outcomes. Therefore, we examined if the lipid goal attainment of 1.8 mmol/L, 2.0 mmol/L, 2.6 mmol/L, and ≥ 50% reduction could lead to significant reduction in MACEs after controlling for known baseline variables. Our results suggested that only the lipid goal of 2.6 mmol/L was associated with a reduction in MACEs during the one-year follow-up. Patients attaining the lipid goals of 1.8 mmol/L, 2.0 mmol/L, or ≥ 50% reduction were not having fewer MACEs, and lowering the patient's LDL-C from 1.8–2.6 mmol/L further to <1.8 mmol/L did not seem to be associated with any significant clinical benefits. On the basis of our exploration on the clinical benefits and costs of lipid goal attainments in Hong Kong Chinese patients, our study questioned if the lipid goal of 2.6 mmol/L could be a better fit for Chinese patients, with significant clinical benefits and lower cardiovascular-related management costs, and raised the question of the most cost-effective lipid goal, which would need to be addressed by a prospective clinical trial. Despite the sensitivity analysis, our study has a limitation associated with real-world data (RWD). It may provide a large sample size and can be more representative of the general population, but we were unable to adjust for the confounders that were not captured in real-world clinical practice. The following could be a more cautious interpretation of our results: the reason for aiming for a more stringent lipid goal (for example, <1.8 mmol/L) was due to the fact that patients had multiple risk factors such as obesity, smoking, and comorbidities. This possibility was beyond our scope, and our findings were limited to the nature of the type of RWD generated from EHRs.

Given its retrospective nature, the study was limited to the following aspects. First, the main problem with the basic data was that it was retrospective and observational and had very limited power to challenge the evidence of a randomized controlled trial. The groups of patients above and below the various lipid goals during follow-up were not matched at the start when they were first identified as a CVD patient and probably differed in terms of true and original baseline lipids. Therefore, it is important to be very cautious when comparing these groups. Second, several risk factors, such as body mass index and smoking status, which might be relevant to lipid goal attainments and MACEs, were not available for the current analysis. Therefore, patients who attained the respective lipid goal could differ from those who did not attain the goal. Although we adopted the estimation of multivalued treatment effects, adjusted for the confounders at baseline, and performed sensitivity analysis, it should be still viewed as a potential violation to our results because we lacked an evaluation of the patients’ full risk profile at baseline. Third, we observed the higher cardiovascular-related costs associated with lower lipid goals but failed to identify the reason leading to the difference.

Conclusion

In this first examination of the clinical outcomes and economic burden of lipid goal attainments in post-PCI Chinese patients with ACS, we found that none of the LDL-C goals of <2.6 mmol/L, <2.0 mmol/L, <1.8 mmol/L, and ≥ 50% reduction could lead to the reduction of the total costs of care within one-year follow-up. Furthermore, we found that any further lipid decrease could bring a remarkable economic burden on cardiovascular-related management. However, we failed to identify the clinical benefits associated with lipid goals of <1.8 mmol/L, 2.0 mmol/L, and ≥ 50% reduction despite of the higher cardiovascular-related costs related to these groups of patients.

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## Supplementary Table 1. Crude cost items by lipid goal attainments

| Lipid goal attainments | N   | All management cost | All management cost excluding all the cardiovascular-related cost | Cardiovascular-related inpatient cost |
|------------------------|-----|---------------------|---------------------------------------------------------------|--------------------------------------|
|                        |     | HKD (USD)           | HKD (USD)                                                     | HKD (USD)                            |
| **Full sample (n = 4638)** |     |                     |                                                               |                                      |
| Endpoint LDL-C achieving the goal of 2.6 mmol/L | 4638 | 84021.88 (10772.04) | 37598.98 (4820.38) | 34294.78 (4396.77) |
| Not at goal            | 950  | 85979.66 (11023.03) | 44935.63 (5760.98) | 29061.01 (3725.77) |
| At goal                | 3688 | 83516.90 (10707.30) | 35706.62 (4577.77) | 35644.75 (4569.84) |
| Endpoint LDL-C achieving the goal of 1.8 mmol/L | 4638 | 82682.57 (10600.33) | 38365.84 (4918.70) | 32431.62 (4157.90) |
| Not at goal            | 2962 | 8143.60 (10659.44)  | 35210.52 (4514.17) | 37307.04 (4791.03) |
| At goal                | 1676 | 86388.86 (11075.49) | 36243.71 (4646.63) | 37587.55 (4818.92) |
| Endpoint LDL-C achieving the goal of 2.0 mmol/L | 4638 | 83143.60 (10659.44) | 38541.63 (4941.24) | 34225.65 (4387.90) |
| Not at goal            | 2382 | 85297.01 (10935.51) | 38541.63 (4941.24) | 34225.65 (4387.90) |
| At goal                | 2256 | 82223.61 (10541.49) | 33773.27 (4329.91) | 37244.65 (4774.95) |
| Endpoint LDL-C achieving the reduction of ≥ 50% | 4182 | 82682.57 (10600.33) | 38365.84 (4918.70) | 32431.62 (4157.90) |
| Not at goal            | 3549 | 85297.01 (10935.51) | 38541.63 (4941.24) | 34225.65 (4387.90) |
| At goal                | 633  | 82223.61 (10541.49) | 33773.27 (4329.91) | 37244.65 (4774.95) |
| Endpoint LDL-C category | 4638 | 85979.66 (11023.03) | 44935.63 (5760.98) | 29061.01 (3725.77) |
| > 2.6 mmol/L           | 950  | 82682.57 (10600.33) | 38365.84 (4918.70) | 32431.62 (4157.90) |
| 1.8-2.6 mmol/L         | 2012 | 81123.37 (10400.43) | 35258.99 (4520.38) | 34025.58 (4362.25) |
| ≤ 1.8 mmol/L           | 1676 | 86388.86 (11075.49) | 36243.71 (4646.63) | 37587.55 (4818.92) |

| Analyzed sample (n = 4625) |     |                     |                                                               |                                      |
| Latest LDL-C before MACE achieving the goal of 2.6 mmol/L | 4625 | 83927.13 (10759.89) | 37691.60 (4832.26) | 34133.48 (4376.09) |
| Not at goal              | 981  | 89092.49 (11422.11) | 46677.64 (5984.31) | 30467.26 (3906.06) |
| At goal                  | 3644 | 82536.57 (10581.61) | 35272.47 (4522.11) | 35120.47 (4502.62) |
| Latest LDL-C before MACE achieving the goal of 1.8 mmol/L | 4625 | 83178.75 (10663.94) | 38433.26 (4927.34) | 32886.29 (4216.19) |
| Not at goal              | 2983 | 83178.75 (10663.94) | 38433.26 (4927.34) | 32886.29 (4216.19) |
| At goal                  | 1642 | 85286.70 (10934.19) | 36344.23 (4659.52) | 36399.25 (4666.57) |
| Latest LDL-C before MACE achieving the goal of 2.0 mmol/L | 4625 | 84468.93 (10829.35) | 40280.41 (5164.16) | 32329.59 (4144.82) |
| Not at goal              | 2411 | 84468.93 (10829.35) | 40280.41 (5164.16) | 32329.59 (4144.82) |
| At goal                  | 2214 | 83337.12 (10684.25) | 34872.44 (4470.83) | 36097.89 (4627.93) |
| Latest LDL-C before MACE achieving the reduction of ≥ 50% | 4180 | 85314.22 (10937.72) | 38541.63 (4941.24) | 34225.65 (4387.90) |
| Not at goal              | 3547 | 85314.22 (10937.72) | 38541.63 (4941.24) | 34225.65 (4387.90) |
| At goal                  | 633  | 82223.61 (10541.49) | 33773.27 (4329.91) | 37244.65 (4774.95) |
| Latest LDL-C before MACE category | 4625 | 89092.49 (11422.11) | 46677.64 (5984.31) | 30467.26 (3906.06) |
| > 2.6 mmol/L             | 981  | 89092.49 (11422.11) | 46677.64 (5984.31) | 30467.26 (3906.06) |
| 1.8-2.6 mmol/L           | 2002 | 80280.96 (10292.43) | 34393.44 (4409.41) | 34071.63 (4368.16) |
| ≤ 1.8 mmol/L             | 1642 | 85286.70 (10934.19) | 36344.23 (4659.52) | 36399.25 (4666.57) |

MACE indicates major adverse cardiovascular events; LDL-C, low-density lipoprotein cholesterol; HKD, Hong Kong Dollars; USD, United States Dollars.
### (Cont. Supplementary Table 1)

| Lipid goal attainments | Cardiovascular-related outpatient cost | Cardiovascular-related inpatient and outpatient cost | Lipid-lowering therapy (statins and other lipid-lowering drugs) |
|------------------------|----------------------------------------|------------------------------------------------------|---------------------------------------------------------------|
|                        | HKD (USD)                              | HKD (USD)                                           | HKD (USD)                                                    |
| **Full sample** (n = 4638) |                                        |                                                      |                                                              |
| Endpoint LDL-C achieving the goal of 2.6 mmol/L |                                        |                                                      |                                                              |
|  Not at goal            | 11835.23 (1517.34)                     | 40731.76 (5222.02)                                  | 675.92 (86.66)                                               |
|  At goal                | 12055.40 (1545.56)                     | 47301.87 (6064.34)                                  | 787.70 (100.99)                                              |
| Endpoint LDL-C achieving the goal of 1.8 mmol/L |                                        |                                                      |                                                              |
|  Not at goal            | 11701.03 (1500.13)                     | 43767.36 (5611.20)                                  | 640.65 (82.14)                                               |
|  At goal                | 12556.75 (1609.84)                     | 49820.39 (6387.23)                                  | 984.14 (126.17)                                              |
| Endpoint LDL-C achieving the goal of 2.0 mmol/L |                                        |                                                      |                                                              |
|  Not at goal            | 11679.77 (1497.41)                     | 42828.18 (5490.79)                                  | 635.40 (81.46)                                               |
|  At goal                | 12359.20 (1584.51)                     | 49255.83 (6314.85)                                  | 901.39 (115.56)                                              |
| Endpoint LDL-C achieving the reduction of ≥ 50% |                                        |                                                      |                                                              |
|  Not at goal            | 12504.82 (1603.18)                     | 46712.21 (5988.74)                                  | 638.31 (81.83)                                               |
|  At goal                | 11205.70 (1436.63)                     | 48450.35 (6211.58)                                  | 1484.50 (190.32)                                             |
| **Analyzed sample** (n = 4625) |                                        |                                                      |                                                              |
| Latest LDL-C before MACE achieving the goal of 2.6 mmol/L |                                        |                                                      |                                                              |
|  Not at goal            | 11909.24 (1526.83)                     | 42298.15 (5422.84)                                  | 714.08 (91.55)                                               |
|  At goal                | 12076.03 (1548.21)                     | 47009.73 (6026.89)                                  | 781.03 (100.13)                                              |
| Latest LDL-C before MACE achieving the goal of 1.8 mmol/L |                                        |                                                      |                                                              |
|  Not at goal            | 11764.48 (1508.27)                     | 44578.84 (5715.24)                                  | 667.50 (85.58)                                               |
|  At goal                | 12542.37 (1608.00)                     | 48611.00 (6232.18)                                  | 947.28 (121.45)                                              |
| Latest LDL-C before MACE achieving the goal of 2.0 mmol/L |                                        |                                                      |                                                              |
|  Not at goal            | 11749.64 (1506.36)                     | 43994.11 (5640.27)                                  | 658.84 (84.47)                                               |
|  At goal                | 12357.57 (1584.30)                     | 48206.02 (6180.26)                                  | 884.43 (113.39)                                              |
| Latest LDL-C before MACE achieving the reduction of ≥ 50% |                                        |                                                      |                                                              |
|  Not at goal            | 12511.87 (1604.09)                     | 46738.55 (5992.12)                                  | 652.17 (83.61)                                               |
|  At goal                | 11205.70 (1436.63)                     | 48450.35 (6211.58)                                  | 1454.30 (186.45)                                             |
| Latest LDL-C before MACE category |                                        |                                                      |                                                              |
|  > 2.6 mmol/L           | 11909.24 (1526.83)                     | 42298.15 (5422.84)                                  | 714.08 (91.55)                                               |
|  1.8-2.6 mmol/L         | 11693.55 (1499.17)                     | 45696.40 (5858.51)                                  | 644.68 (82.65)                                               |
|  < 1.8 mmol/L           | 12542.37 (1608.00)                     | 48611.00 (6232.18)                                  | 947.28 (121.45)                                              |
## Supplementary Table 2. Adjusted cost difference in total cost of care and cardiovascular-related cost by lipid goal attainments

|                  | Full sample                                                                 | Among those with baseline LDL-C > 2.6 mmol/L (n = 2179) |
|------------------|------------------------------------------------------------------------------|--------------------------------------------------------|
|                  | Total cost of care (HKD) | Cardiovascular-related inpatient and outpatient cost (HKD) |
|                  | $N$ | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | $p$-value | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | $p$-value |
| Endpoint LDL-C achieving the goal of 2.6 mmol/L | 4638 | 950 | Ref | Ref | 3688 | -759.60 | -9253.72 | 7734.53 | 0.861 | 6739.87 | 3337.06 | 10142.69 | <0.001 |
| Not at goal      |                                          | 2962 | Ref | Ref | 1676 | 2891.58 | -4362.46 | 10145.62 | 0.435 | 5358.43 | 1418.34 | 9298.53 | 0.008 |
| At goal          |                                          | 2382 | Ref | Ref | 2256 | 1162.69 | -5568.53 | 7893.90 | 0.735 | 5765.66 | 2185.53 | 9342.79 | 0.002 |
| Endpoint LDL-C achieving the goal of 1.8 mmol/L | 4638 | 950 | Ref | Ref | 2179 | -2594.92 | -11501.67 | 6311.83 | 0.568 | 5078.77 | 1283.27 | 8874.28 | 0.009 |
| Not at goal      |                                          | 2179 | Ref | Ref | 1630 | -916.76 | -11958.09 | 10124.56 | 0.871 | 6964.52 | 2373.71 | 11555.33 | 0.003 |
| At goal          |                                          | 1512 | Ref | Ref | 1512 | -9921.49 | -13649.60 | 13191.20 | 0.973 | 8709.78 | 2657.14 | 14762.41 | 0.005 |
| Endpoint LDL-C achieving the goal of 2.0 mmol/L | 2179 | 549 | Ref | Ref | 2179 | -11958.09 | 10124.56 | 11555.33 | 0.003 |
| Not at goal      |                                          | 1577 | Ref | Ref | 1577 | -11958.09 | 10124.56 | 11555.33 | 0.003 |
| At goal          |                                          | 1512 | Ref | Ref | 1512 | -9921.49 | -13649.60 | 13191.20 | 0.973 | 8709.78 | 2657.14 | 14762.41 | 0.005 |
| Endpoint LDL-C achieving the reduction of ≥50% | 4638 | 950 | Ref | Ref | 2179 | -2594.92 | -11501.67 | 6311.83 | 0.568 | 5078.77 | 1283.27 | 8874.28 | 0.009 |
| Not at goal      |                                          | 2179 | Ref | Ref | 1630 | -916.76 | -11958.09 | 10124.56 | 0.871 | 6964.52 | 2373.71 | 11555.33 | 0.003 |
| At goal          |                                          | 1512 | Ref | Ref | 1512 | -9921.49 | -13649.60 | 13191.20 | 0.973 | 8709.78 | 2657.14 | 14762.41 | 0.005 |
| Endpoint LDL-C category | 2179 | 549 | Ref | Ref | 2179 | -11958.09 | 10124.56 | 11555.33 | 0.003 |
| >2.6 mmol/L      |                                          | 1577 | Ref | Ref | 1577 | -11958.09 | 10124.56 | 11555.33 | 0.003 |
| 1.8-2.6 mmol/L   |                                          | 1512 | Ref | Ref | 1512 | -9921.49 | -13649.60 | 13191.20 | 0.973 | 8709.78 | 2657.14 | 14762.41 | 0.005 |
| <1.8 mmol/L      |                                          | 1512 | Ref | Ref | 1512 | -9921.49 | -13649.60 | 13191.20 | 0.973 | 8709.78 | 2657.14 | 14762.41 | 0.005 |

MACE indicates major adverse cardiovascular events; LDL-C, low-density lipoprotein cholesterol; HKD, Hong Kong Dollars; Ref, reference; CI, confidence interval.

*Adjusted for age, sex, diabetes, hypertension, and prior cardiovascular history.
Supplementary Table 3. Adjusted cost difference in other management cost and cardiovascular-related cost al by lipid goal attainments

| Endpoint LDL-C achieving the goal of 2.6 mmol/L | N  | Other management cost (defined as total cost of care excluding the cardiovascular-related (inpatient and outpatient) cost) (HKD) | Cost of lipid-lowering therapy (statins and other lipid-lowering drugs) (HKD) |
|-----------------------------------------------|----|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Not at goal                                   | 4638 | | |
| At goal                                       | 3688 | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value |
|                                               | 950  | -7649.69 | -14780.03 | -519.35 | 0.035 | 111.84 | 11.39 | 212.30 | 0.029 |

| Endpoint LDL-C achieving the goal of 1.8 mmol/L | N  | Other management cost (defined as total cost of care excluding the cardiovascular-related (inpatient and outpatient) cost) (HKD) | Cost of lipid-lowering therapy (statins and other lipid-lowering drugs) (HKD) |
|-----------------------------------------------|----|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Not at goal                                   | 4638 | | |
| At goal                                       | 1676 | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value |
|                                               | 2962 | -2295.23 | -7762.20 | 3171.74 | 0.411 | 336.07 | 247.01 | 425.12 | <0.001 |

| Endpoint LDL-C achieving the goal of 2.0 mmol/L | N  | Other management cost (defined as total cost of care excluding the cardiovascular-related (inpatient and outpatient) cost) (HKD) | Cost of lipid-lowering therapy (statins and other lipid-lowering drugs) (HKD) |
|-----------------------------------------------|----|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Not at goal                                   | 4638 | | |
| At goal                                       | 2256 | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value |
|                                               | 2382 | -4634.13 | -9738.11 | 469.84 | 0.075 | 265.48 | 183.11 | 347.84 | <0.001 |

| Endpoint LDL-C achieving the reduction of ≥ 50% | N  | Other management cost (defined as total cost of care excluding the cardiovascular-related (inpatient and outpatient) cost) (HKD) | Cost of lipid-lowering therapy (statins and other lipid-lowering drugs) (HKD) |
|-----------------------------------------------|----|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Not at goal                                   | 4182 | | |
| At goal                                       | 633  | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value |
|                                               | 3549 | 2870.41 | -6875.75 | 12616.56 | 0.564 | 721.86 | 565.70 | 878.02 | <0.001 |

| Endpoint LDL-C category | N  | Other management cost (defined as total cost of care excluding the cardiovascular-related (inpatient and outpatient) cost) (HKD) | Cost of lipid-lowering therapy (statins and other lipid-lowering drugs) (HKD) |
|-------------------------|----|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| > 2.6 mmol/L            | 2179 | | |
| Not at goal             | 2179 | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value |
| At goal                 | 1630 | -7662.03 | -16812.44 | 1488.38 | 0.101 | 93.92 | -56.79 | 244.63 | 0.222 |

| Endpoint LDL-C achieving the goal of 1.8 mmol/L | N  | Other management cost (defined as total cost of care excluding the cardiovascular-related (inpatient and outpatient) cost) (HKD) | Cost of lipid-lowering therapy (statins and other lipid-lowering drugs) (HKD) |
|-----------------------------------------------|----|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Not at goal                                   | 1630 | | |
| At goal                                       | 1512 | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value |
|                                               | 549  | -4392.23 | -12755.67 | 3971.20 | 0.303 | 402.64 | 246.53 | 558.76 | <0.001 |

| Endpoint LDL-C achieving the goal of 2.0 mmol/L | N  | Other management cost (defined as total cost of care excluding the cardiovascular-related (inpatient and outpatient) cost) (HKD) | Cost of lipid-lowering therapy (statins and other lipid-lowering drugs) (HKD) |
|-----------------------------------------------|----|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Not at goal                                   | 2179 | | |
| At goal                                       | 1577 | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value |
|                                               | 602  | 2805.23 | -5949.90 | 11560.35 | 0.530 | 813.85 | 642.16 | 985.54 | <0.001 |

| Endpoint LDL-C achieving the reduction of ≥ 50% | N  | Other management cost (defined as total cost of care excluding the cardiovascular-related (inpatient and outpatient) cost) (HKD) | Cost of lipid-lowering therapy (statins and other lipid-lowering drugs) (HKD) |
|-----------------------------------------------|----|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Not at goal                                   | 2179 | | |
| At goal                                       | 1250 | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value |
|                                               | 929  | -6035.74 | -13535.69 | 1464.20 | 0.115 | 329.98 | 191.73 | 468.22 | <0.001 |

Among those baseline LDL-C > 2.6 mmol/L.

| Endpoint LDL-C achieving the goal of 2.6 mmol/L | N  | Other management cost (defined as total cost of care excluding the cardiovascular-related (inpatient and outpatient) cost) (HKD) | Cost of lipid-lowering therapy (statins and other lipid-lowering drugs) (HKD) |
|-----------------------------------------------|----|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Not at goal                                   | 2179 | | |
| At goal                                       | 1630 | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value |
|                                               | 549  | -7662.03 | -16812.44 | 1488.38 | 0.101 | 93.92 | -56.79 | 244.63 | 0.222 |

| Endpoint LDL-C achieving the goal of 1.8 mmol/L | N  | Other management cost (defined as total cost of care excluding the cardiovascular-related (inpatient and outpatient) cost) (HKD) | Cost of lipid-lowering therapy (statins and other lipid-lowering drugs) (HKD) |
|-----------------------------------------------|----|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Not at goal                                   | 2179 | | |
| At goal                                       | 1512 | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value |
|                                               | 549  | -4392.23 | -12755.67 | 3971.20 | 0.303 | 402.64 | 246.53 | 558.76 | <0.001 |

| Endpoint LDL-C achieving the goal of 2.0 mmol/L | N  | Other management cost (defined as total cost of care excluding the cardiovascular-related (inpatient and outpatient) cost) (HKD) | Cost of lipid-lowering therapy (statins and other lipid-lowering drugs) (HKD) |
|-----------------------------------------------|----|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Not at goal                                   | 2179 | | |
| At goal                                       | 1577 | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value |
|                                               | 602  | 2805.23 | -5949.90 | 11560.35 | 0.530 | 813.85 | 642.16 | 985.54 | <0.001 |

| Endpoint LDL-C achieving the reduction of ≥ 50% | N  | Other management cost (defined as total cost of care excluding the cardiovascular-related (inpatient and outpatient) cost) (HKD) | Cost of lipid-lowering therapy (statins and other lipid-lowering drugs) (HKD) |
|-----------------------------------------------|----|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Not at goal                                   | 2179 | | |
| At goal                                       | 1577 | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value |
|                                               | 602  | 2805.23 | -5949.90 | 11560.35 | 0.530 | 813.85 | 642.16 | 985.54 | <0.001 |

MACE indicates major adverse cardiovascular events; LDL-C, low-density lipoprotein cholesterol; HKD, Hong Kong Dollars; Ref, reference; CI, confidence interval.

* Adjusted for age, sex, diabetes, hypertension, and prior cardiovascular history
Supplementary Table 4. Adjusted cost difference in cardiovascular-related inpatient and outpatient costs al by lipid goal attainments

|                       | Cardiovascular-related inpatient cost (HKD) | Cardiovascular-related outpatient cost (HKD) |
|------------------------|-------------------------------------------|---------------------------------------------|
|                        | N             | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | p-value |
| **Full sample**        |               |                      |                         |                         |         |                      |                         |                         |         |
| Endpoint LDL-C achieving the goal of 2.6 mmol/L |               |                      |                         |                         |         |                      |                         |                         |         |
| Not at goal            | 4638          | 950                  | Ref                     | Ref                     |         |                      |                         |                         |         |
| At goal                |               | 3688                 | 6563.44                 | 3567.08                 | 9559.81 | <0.001               | 404.88                   | -764.31                 | 1574.07 | 0.497   |
| Endpoint LDL-C achieving the goal of 1.8 mmol/L |               |                      |                         |                         |         |                      |                         |                         |         |
| Not at goal            | 4638          | 2962                 | Ref                     | Ref                     |         |                      |                         |                         |         |
| At goal                |               | 1676                 | 4583.37                 | 921.54                  | 8245.20 | 0.01                 | 784.66                   | -106.42                 | 1675.74 | 0.084   |
| Endpoint LDL-C achieving the goal of 2.0 mmol/L |               |                      |                         |                         |         |                      |                         |                         |         |
| Not at goal            | 4638          | 2382                 | Ref                     | Ref                     |         |                      |                         |                         |         |
| At goal                |               | 2256                 | 5343.24                 | 2032.67                 | 8653.81 | 0.002                | 674.53                   | -174.16                 | 1523.21 | 0.119   |
| Endpoint LDL-C achieving the reduction of 50% |               |                      |                         |                         |         |                      |                         |                         |         |
| Not at goal            | 4182          | 3549                 | Ref                     | Ref                     |         |                      |                         |                         |         |
| At goal                |               | 633                  | 7821.31                 | 1379.81                 | 14262.81| 0.02                 | -48.28                   | -1176.01               | 1079.44 | 0.933   |
| Endpoint LDL-C category |               |                      |                         |                         |         |                      |                         |                         |         |
| > 2.6 mmol/L           | 4638          | 950                  | Ref                     | Ref                     |         |                      |                         |                         |         |
| 1.8-2.6 mmol/L         |               | 2012                 | -2815.61                | -6868.01                | 1236.78 | 0.173                | -780.33                  | -1694.82               | 134.16  | 0.094   |
| < 1.8 mmol/L           |               | 1676                 | -8168.68                | -12054.67               | -4282.69| 0.00                 | -797.55                  | -2091.59               | 496.49  | 0.227   |
| **Analyzed sample**   |               |                      |                         |                         |         |                      |                         |                         |         |
| Latest LDL-C before MACE achieving the goal of 2.6 mmol/L |               |                      |                         |                         |         |                      |                         |                         |         |
| Not at goal            | 4625          | 947                  | Ref                     | Ref                     |         |                      |                         |                         |         |
| At goal                |               | 3678                 | 4640.73                 | 1550.45                 | 7731.00 | 0.003                | 310.31                   | -854.52                 | 1475.14 | 0.602   |
| Latest LDL-C before MACE achieving the goal of 1.8 mmol/L |               |                      |                         |                         |         |                      |                         |                         |         |
| Not at goal            | 4625          | 2950                 | Ref                     | Ref                     |         |                      |                         |                         |         |
| At goal                |               | 1675                 | 3026.64                 | -574.43                 | 6627.71 | 0.10                 | 698.51                   | -205.20                 | 1602.23 | 0.130   |
| Latest LDL-C before MACE achieving the goal of 2.0 mmol/L |               |                      |                         |                         |         |                      |                         |                         |         |
| Not at goal            | 4625          | 2374                 | Ref                     | Ref                     |         |                      |                         |                         |         |
| At goal                |               | 2251                 | 3177.62                 | -121.41                 | 6476.64 | 0.059                | 569.77                   | -286.25                 | 1425.79 | 0.192   |
| Latest LDL-C before MACE achieving the reduction of 50% |               |                      |                         |                         |         |                      |                         |                         |         |
| Not at goal            | 4180          | 3547                 | Ref                     | Ref                     |         |                      |                         |                         |         |
| At goal                |               | 633                  | 6407.96                 | -189.79                 | 13005.72| 0.06                 | -556.08                  | -1639.01               | 526.85  | 0.314   |
| Latest LDL-C before MACE category |               |                      |                         |                         |         |                      |                         |                         |         |
| > 2.6 mmol/L           | 4625          | 947                  | Ref                     | Ref                     |         |                      |                         |                         |         |
| 1.8-2.6 mmol/L         |               | 2003                 | 3939.56                 | 402.93                  | 7476.19 | 0.029                | -34.05                   | -1246.45               | 1178.34 | 0.956   |
| < 1.8 mmol/L           |               | 1675                 | 5625.88                 | 1740.87                 | 9510.88 | <0.001               | 679.57                   | -617.86                 | 1977.01 | 0.305   |
(Cont. Supplementary Table 4)

|                          | Cardiovascular-related inpatient cost (HKD) |                       | Cardiovascular-related outpatient cost (HKD) |                       |
|--------------------------|---------------------------------------------|-----------------------|---------------------------------------------|-----------------------|
|                          | \( N \) | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | \( p \)-value | \( N \) | Adjusted Coefficient* | Lower limit for 95% CI | Lower limit for 95% CI | \( p \)-value |
| Among those baseline LDL-C > 2.6 mmol/L |                          |                       |                                  |                          |          |                          |                       |                                  |          |
| Endpoint LDL-C achieving the goal of 2.6 mmol/L | 2179 | 549 | Ref | 7425.07 | 3397.85 | 11452.29 | <0.001 | Ref | -522.06 | -2070.39 | 1026.28 | 0.509 |
| Not at goal              | 1630   | 1512 | Ref | 5010.12 | -258.74 | 10278.98 | 0.062 | Ref | 317.90 | -860.70 | 1496.49 | 0.597 |
| At goal                  | 2179   | 1250 | Ref | 6119.90 | 1068.21 | 11171.58 | 0.02 | Ref | 251.80 | -853.84 | 1357.44 | 0.655 |
| Endpoint LDL-C achieving the goal of 1.8 mmol/L | 2179 | 929 | 10619.90 | 1068.21 | 11171.58 | 0.02 | Ref | 251.80 | -853.84 | 1357.44 | 0.655 |
| Not at goal              | 1577   | 1512 | Ref | 5010.12 | -258.74 | 10278.98 | 0.062 | Ref | 317.90 | -860.70 | 1496.49 | 0.597 |
| At goal                  | 2179   | 1250 | Ref | 6119.90 | 1068.21 | 11171.58 | 0.02 | Ref | 251.80 | -853.84 | 1357.44 | 0.655 |
| Endpoint LDL-C achieving the goal of 2.0 mmol/L | 2179 | 929 | 10619.90 | 1068.21 | 11171.58 | 0.02 | Ref | 251.80 | -853.84 | 1357.44 | 0.655 |
| Not at goal              | 1577   | 1512 | Ref | 5010.12 | -258.74 | 10278.98 | 0.062 | Ref | 317.90 | -860.70 | 1496.49 | 0.597 |
| At goal                  | 2179   | 1250 | Ref | 6119.90 | 1068.21 | 11171.58 | 0.02 | Ref | 251.80 | -853.84 | 1357.44 | 0.655 |
| Latest LDL-C before MACE achieving the goal of 2.6 mmol/L | 2177 | 585 | Ref | 3885.39 | -384.12 | 8154.91 | 0.074 | Ref | -878.64 | -2371.55 | 614.28 | 0.249 |
| Not at goal              | 1592   | 1535 | Ref | 3319.74 | -2132.71 | 8772.18 | 0.23 | Ref | 161.66 | -1008.74 | 1332.06 | 0.787 |
| At goal                  | 2177   | 1275 | Ref | 4957.06 | -163.92 | 10078.04 | 0.058 | Ref | 193.57 | -915.19 | 1302.34 | 0.732 |
| Latest LDL-C before MACE achieving the goal of 1.8 mmol/L | 2177 | 642 | 3319.74 | -2132.71 | 8772.18 | 0.23 | Ref | 161.66 | -1008.74 | 1332.06 | 0.787 |
| Not at goal              | 1535   | 1275 | Ref | 4957.06 | -163.92 | 10078.04 | 0.058 | Ref | 193.57 | -915.19 | 1302.34 | 0.732 |
| At goal                  | 2177   | 1275 | Ref | 4957.06 | -163.92 | 10078.04 | 0.058 | Ref | 193.57 | -915.19 | 1302.34 | 0.732 |
| Latest LDL-C before MACE achieving the reduction of 50% | 2177 | 1603 | Ref | 6942.93 | 231.22 | 13654.65 | 0.04 | Ref | -202.58 | -1382.28 | 977.12 | 0.736 |
| Not at goal              | 1603   | 574 | Ref | 6942.93 | 231.22 | 13654.65 | 0.04 | Ref | -202.58 | -1382.28 | 977.12 | 0.736 |
| At goal                  | 2177   | 585 | Ref | 6942.93 | 231.22 | 13654.65 | 0.04 | Ref | -202.58 | -1382.28 | 977.12 | 0.736 |

MACE indicates major adverse cardiovascular events; LDL-C, low-density lipoprotein cholesterol; HKD, Hong Kong Dollars; Ref, reference; CI, confidence interval.

*Adjusted for age, sex, diabetes, hypertension, and prior cardiovascular history.
### Supplementary Table 5. Adjusted cost difference by lipid goal attainments among 2686 patients with complete five-year follow-up

| Endpoint LDL-C category | Total cost of care (HKD) | Cardiovascular-related cost (HKD) |
|-------------------------|--------------------------|----------------------------------|
|                         | Adjusted Coefficient*    | Lower limit for 95% CI | Lower limit for 95% CI | p-value | Adjusted Coefficient*    | Lower limit for 95% CI | Lower limit for 95% CI | p-value |
| 1st year:               |                          |                          |                          |         |                          |                          |                          |         |
| > 2.6 mmol/L           | Ref                      |                          |                          |         | Ref                      |                          |                          |         |
| 1.8-2.6 mmol/L         | 1510.38                  | -9054.15                 | 12074.92                 | 0.78    | 8280.74                  | 3097.21                   | 13464.26                  | <0.001  |
| < 1.8 mmol/L           | 13910.13                 | 710.44                   | 27109.82                 | 0.04    | 13887.91                 | 6831.99                   | 20943.83                  | <0.001  |
| 2nd year:              |                          |                          |                          |         |                          |                          |                          |         |
| > 2.6 mmol/L           | Ref                      |                          |                          |         | Ref                      |                          |                          |         |
| 1.8-2.6 mmol/L         | -3520.93                 | -11949.96                | 4908.09                  | 0.41    | -2387.03                 | -6707.04                  | 1932.98                   | 0.28    |
| < 1.8 mmol/L           | 8408.82                  | -2255.99                 | 19073.64                 | 0.12    | -753.36                  | -5383.72                  | 3876.99                   | 0.75    |
| 3rd year:              |                          |                          |                          |         |                          |                          |                          |         |
| > 2.6 mmol/L           | Ref                      |                          |                          |         | Ref                      |                          |                          |         |
| 1.8-2.6 mmol/L         | -211.90                  | -8450.38                 | 8026.58                  | 0.96    | -1234.08                 | -4663.44                  | 2195.28                   | 0.48    |
| < 1.8 mmol/L           | 4022.09                  | -5283.34                 | 13327.51                 | 0.40    | 1649.37                  | -2653.99                  | 5952.72                   | 0.45    |
| 4th year:              |                          |                          |                          |         |                          |                          |                          |         |
| > 2.6 mmol/L           | Ref                      |                          |                          |         | Ref                      |                          |                          |         |
| 1.8-2.6 mmol/L         | -3680.62                 | -11771.91                | 4410.68                  | 0.37    | -1411.23                 | -5648.60                  | 2826.13                   | 0.51    |
| < 1.8 mmol/L           | -5277.79                 | -13619.73                | 3064.16                  | 0.21    | -2267.74                 | -6382.58                  | 1847.10                   | 0.28    |
| 5th year:              |                          |                          |                          |         |                          |                          |                          |         |
| > 2.6 mmol/L           | Ref                      |                          |                          |         | Ref                      |                          |                          |         |
| 1.8-2.6 mmol/L         | -1029.39                 | -8780.01                 | 6721.23                  | 0.79    | -1541.59                 | -5687.27                  | 2604.09                   | 0.47    |
| < 1.8 mmol/L           | -342.22                  | -8003.73                 | 7319.29                  | 0.93    | -1061.03                 | -4991.50                  | 2869.43                   | 0.60    |

MACE indicates major adverse cardiovascular events; LDL-C, low-density lipoprotein cholesterol; HKD, Hong Kong Dollars; Ref, reference; CI, confidence interval.

*Adjusted for age, sex, diabetes, hypertension, and prior cardiovascular history