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Descriptive analysis of real-world medication use pattern of statins and antiplatelet agents among patients with acute coronary syndrome in Hong Kong and the USA

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ABSTRACT

Objectives The objective was to explore the differences in medication use pattern of lipid-lowering drug (LLD) and antiplatelet agents among post-percutaneous coronary intervention patients with acute coronary syndrome aged <65 in Hong Kong (HK) and the USA.

Design Retrospective study.

Setting This study used deidentified claims data from Clinformatics Data Mart database (OptumInsight, Eden Prairie, Minnesota, USA) and electronic health records from HK Hospital Authority Clinical Data Analysis and Reporting System database.

Participants We used 1 year prescription records of LLDs and antiplatelet agents among 1013 USA patients and 270 HK Chinese patients in 2011–2013.

Primary and secondary outcome measures Continuity was investigated on the assumption that one defined daily dose represented 1 day treatment. Medication possession ratio method was used to evaluate the adherence. Multivariate-adjusted logistic regressions were constructed to compare the good continuity and adherence levels in the merged database with the cutoffs set at 80%, and Cox proportional hazard models were built using the time to discontinuation as the dependent variable, to assess the persistence level.

Results HK Chinese patients were less adherent (67.41% vs 84.60%, adjusted odds ratio (AOR) for Americans over Chinese=2.23 (95% CI=1.60 to 3.12), p<0.001) to antiplatelet agents compared with American patients but better adherent to statins (90.00% vs 78.18%, AOR=0.37 (0.23 to 0.58), p<0.001). The discontinuation with statins was more common in American patients (13.33% vs 34.25%, adjusted hazard ratio (AHR)=2.95 (2.05 to 4.24), p<0.001). Low-to-moderate potency statins and clopidogrel were favoured by our HK local physicians, while American patients received higher doses of statins and prasugrel.

Conclusions We seemed to find HK physicians tended to prescribe cheaper and lower doses of statins and antiplatelet agents when compared with the privately insured patients in the USA, though the adherence and persistence levels of HK patients with statins were relatively good.

Strengths and limitations of this study

- The cost-driven prescription behaviour was a possibility in Hong Kong, but little was known about the prescribing behaviour of statins and antiplatelet agents in the management of young cardiovascular disease patients.
- Our research shed some light on the real-world drug utilisation of lipid-lowering drug (LLD) and antiplatelet agents (clopidogrel, ticagrelor and prasugrel) among acute coronary syndrome patients <65 years in HK public hospitals, compared with a privately and commercially insured US patient cohort.
- We identified the adherence, continuity and discontinuation patterns of HK patients, compared with a typical American privately insured cohort.
- We seemed to find HK physicians tended to prescribe cheaper and lower doses of LLDs and antiplatelet agents compared with the privately insured patients in the USA.

INTRODUCTION

Hong Kong (HK) was thought to be one of the most efficient healthcare systems in the world,[1] with a life expectancy of 84 years in 2016[2] and publicly subsidised public hospitals virtually free to all citizens. It had a population of 7.35 million, accompanying 5.7% of gross domestic product on health expenditure in 2017.[2] In contrast, the USA spent nearly 4.52 times as much per capita on healthcare as HK.[1 3] The government-funded universal healthcare is the cornerstone of HK healthcare system. Universal healthcare provides equal access to medical services to all citizens, and the government controls the price of medication and medical services through negotiation and regulation. In HK, the inpatient hospital stay costed Hong Kong Dollars (HKD) 120 (1 US dollar (USD)=7.8 HKD)

per day for a patient's out-of-pocket spending in 2019.[4] Patients paid 135 HKDs for their first specialist outpatient consultation and 80 HKD per time for the subsequent attendances with an additional 15 HKD per drug item.[4] The drawback with the universal healthcare system is the government focuses on providing basic healthcare.[1 5 6] There is a high possibility that healthcare budget had a ceiling and the government funding decisions are mainly based on cost-saving strategy.[7] In America, it was widely believed that the privately insured patients covered by a commercial health plan were more likely to receive better medical care than the publicly insured.[8 9] In comparison, the government may limit costly services to cut costs for publicly insured patients, which made the underprescribing/treatment a possibility, as reported before[10–12] in HK.

HK healthcare system by large followed UK National Health Service (NHS), for it was a British colony for 155 years. Where it lacked from the UK system was mostly clinical audit and quality assurance. UK claimed its commitment in the 2014 Pharmaceutical Price Regulation Scheme,[13] that 'the UK should compare itself with other countries if it is to deliver a world-class NHS' and 'develop and evolve an approach to the analysis and publication of comparative information on international medicines use on a periodic basis'. When this was compared with HK, where public health services were facing the same challenges, a small effort was made to make an international comparison to identify the underlying issues regarding the medication use pattern.

In recent years, risk factors associated with lifestyles has gradually led to the prevalence of cardiovascular diseases in young adults aged <65 worldwide.[14] However, young patients were rarely studied,[15] and little was known about how the young patients were managed after they were identified as atherosclerotic cardiovascular disease (ASCVD) patients. There was no study comparing the prescribing patterns of cardiovascular drugs in HK government-subsidised system with those in the private health insurance system presumably due to the difficulty in obtaining useful data and that HK does not have a private healthcare system which is transparent and well developed compared with other countries on this agenda. In terms of the delivery of care, 90% of healthcare services in HK were provided by 44 public hospitals.[16] In HK, public and private healthcare operate in separate systems, and the main legislation on data protection limited the sharing system between the public and private sectors, which made it less feasible to extract patients' information from any private insurance providers for the comparison purpose.

Lipid-lowering drugs (LLDs) and antiplatelet agents were found to be the least adherent medications in post-percutaneous coronary intervention (PCI) acute coronary syndrome (ACS) patients from our pilot study.[17] Therefore, in this study, we chose these two worst-adhered classes of cardiovascular drugs as the focus. There is a rich literature to describe the local prescribing patterns of statin[18] and antiplatelet[19] agents in HK. However, the international comparison between HK and other countries is lacking. Clinician in HK mainly followed the US and European guidelines as many other countries did,[20] but they were meanwhile aware of the emerging clinical evidence and recommendations by mainland China. That may sometimes put them in a dilemma[21] at the absence of nuanced guidance on specific scenarios. For example, the mainland Chinese guideline held a conservative attitude against high-potency statin,[22] while the most recent American guideline highly recommended the use of high-potency statins.[23]

In the current research, with a limited health budget available for pharmacy in HK, we attempted to identify the medication use patterns of HK patients, compared with privately insured Americans, a typical cohort which should be prescribed sufficient drugs[24] accompanying the rapid updating of guidelines by American College of Cardiology/American Heart Association. A broad spectrum of factors is likely to lead to observed differences between HK Chinese and American patients. This type of comparison mainly enabled the health policy makers and health practitioners in HK to compare itself with other countries, and to understand the potentially mixed effects from both healthcare systems and the contextual difference[25] in implementing the clinical practice guidelines for Chinese patients.

METHODS

This was a retrospective and comparative analysis using two cohorts: one from HK Hospital Authority (HA) Clinical Data Analysis and Reporting System (CDARS) database, representing all the local Chinese citizens in the New Territories East Cluster admitted to a PCI-capable acute public hospital; and the other from the 1% random cohort of the deidentified Clinformatics Data Mart database (OptumInsight, Eden Prairie, Minnesota, USA), which was referred as 'Optum' below, comprising administrative claims data for commercially insured multiethnic population in the parallel inclusion period between January 2011 and December 2012. New Territories East Cluster is one of the seven hospital clusters managed by Hospital Authority in HK, which accounted for roughly 7% of Hong Kong's population and took up 10% of the health budget of the government per year.[26]

Our inclusion criterion was, the study cohorts in both databases should be ACS patients identified by International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes of 411.xx (unstable angina) and 410.xx (myocardial infarction),[27 28] ≥21 years who received a first documented PCI (ICD-9-CM procedure codes 36.0x[29]) during the inclusion period between January 2011 and December 2012, and were continuously enrolled in the respective database for 1 year after their index PCI. The patients who had any prior ACS diagnosis or underwent PCI in the preceding 6 months were excluded. The available LLDs in HK localised HA Drug Formulary were atorvastatin,

Table 1 DDD defined by WHO

ATC code	Name	DDD	Unit	Administrative route
B01AC06	Acetylsalicylic acid	1	tablet	Oral
B01AC04	Clopidogrel	75	mg	Oral
B01AC22	Prasugrel	10	mg	Oral
B01AC24	Ticagrelor	0.18	g	Oral
C10AA05	Atorvastatin	20	mg	Oral
C10AA04	Fluvastatin	60	mg	Oral
C10AA02	Lovastatin	45	mg	Oral
C10AA03	Pravastatin	30	mg	Oral
C10AA07	Rosuvastatin	10	mg	Oral
C10AA01	Simvastatin	30	mg	Oral
C10A×09	Ezetimibe	10	mg	Oral
C10AC01	Colestyramine	14	g	Oral
C10AD02	Nicotinic acid	2	g	Oral
C10AB05	Fenofibrate	0.2	g	Oral
C10AB04	Gemfibrozil	1.2	g	Oral

ATC, anatomical therapeutic chemical; DDD, daily defined dose.

cholestyramine, ezetimibe, fenofibrate, fluvastatin, gemfibrozil, rosuvastatin, simvastatin and evolocumab. The LLDs in Optum were identified through the American Hospital Formulary Service Therapeutic Class codes. The antiplatelet agents under investigation were clopidogrel, ticagrelor and prasugrel in both databases. Since aspirin was an over-the-counter medication in the USA and the non-prescription drugs taken by the patients were not captured in claims data, we chose not to include aspirin in this analysis.

The patients' age, sex, procedures, prescriptions, and visits to outpatient and inpatient clinics were extracted from both systems during the study period between −6 months and +12 months of the index procedure. The analysis of all prescriptions was made within 12 months that followed from the index PCI, and both entities had the advantage of making a follow-up of patients' prescriptions.

The utilisation of all drugs was expressed as the number of defined daily doses (DDDs)/inhabitant/year, a standard unit (table 1) calculated according to the Anatomical Therapeutic Chemical (ATC)/DDD methodology,[30] which allowed the international comparison between countries and regions and quantified the annual prevalence of use. We evaluated the continuity under the assumption that 1 DDD represented 1 day treatment, and the patients should get 365 DDDs[31] within 1 year in the respective databases. The limit between good and poor continuity was defined as 80%.[31] The measurement of adherence was reported as medication possession ratio (MPR),[32] the sum of the days' supply for all fills of a given drug in a particular time period divided by the number of days in the study window, and was evaluated to report the percentage of the time when a patient had medication available. Patients were deemed non-adherent if the MPR value was <80%.[32] We also assessed the persistence level[33] by the time to discontinuation as other did before,[34] namely the time from first having the prescription dispensed to the discontinuation day (defined as with a >14 days' gap from the recent refill record).

Statistical analysis

Because the underlying factors (such as age, sex, comorbidities of diabetes (ICD code of 250.xx, 362.0x, 366.41) and hypertension (ICD code of 401.x-405.x, 362.11, 437.2) and prior cardiovascular disease history (ICD code of 390.x-459.x)) between Chinese and American patient cohorts could lead to variation in prescriptions, the multivariable logistic regressions adjusted for these covariates were used to test if the good continuity and adherence with statins and antiplatelet agents varied between these two cohorts in the merged database. Good continuity and adherence were the dichotomous outcomes in the logistic regressions, and the patient cohorts (USA vs HK) was analysed as a categorical variable.

Moreover, we conducted sensitivity analyses through estimating the average treatment effect (ATE) and the average treatment effect for the treated (ATT) on the basis of the abovementioned covariates age, sex, comorbidities of diabetes and hypertension, and prior cardiovascular disease history and assessing the continuity and adherence in the logistic regressions by propensity score (PS) weighting for ATT or ATE,[35 36] because HK and American cohorts could differ substantially across the baseline characteristics. We did PS weighting, instead of PS matching, because normally PS matching would result in a significant reduction in the cohorts size.[37] Multivariate-adjusted and PS-weighted Cox proportional hazards models were constructed for the outcome time to discontinuation, after adjustment for the covariates in the merged database. Patients were censored if they died or reached the end of the 1-year follow-up.

All statistical analyses were carried out using STATA V.14.0 (Stata Corp LP, College Station, Texas, USA).

Patient and public involvement

This research did not involve a prospective intervention to any human subjects. Both datasets were deidentified. The major findings through this international comparison could add knowledge to the existing literature and will be disseminated to the public in HK.

RESULTS

We identified 270 Chinese ACS patients from HK CDARS database and 1013 American patients from US Optum. Table 2 shows the baseline characteristics of the two cohorts. Apparently, American patients tend to carry a higher prevalence of hypertension than Chinese (44.13% vs 12.22% in table 2). The rate of prior cardiovascular

Table 2 Baseline characteristics of Hong Kong Chinese patients and American patients in Optum

	Hong Kong CDARS—Chinese	US Optum—American	P value
Total	270	1013	
Gender, no. (%)			0.001
Male	237 (87.78)	797 (78.68)	
Female	33 (12.22)	216 (21.32)	
Age, years, mean±SD	57.69 (5.61)	57.12 (6.11)	0.168
Comorbidities, no. (%)			
Diabetes	36 (13.33)	114 (11.25)	0.345
Hypertension	33 (12.22)	447 (44.13)	<0.001
Prior cardiovascular disease	33 (12.22)	32 (3.16)	<0.001

CDARS, Clinical Data Analysis and Reporting System; SD, Standard Deviation.

disease history in Chinese was much higher (12.22%) than that of American patients (3.16%). ACS patients in both cohorts were more likely to be men (78.68% American and 87.78% Chinese) and have diabetes at the index day (13.33% American and 11.25% Chinese).

Table 3 classifies the use of LLDs and antiplatelet agents in these two cohorts: the majority (97.41% of Chinese and 95.26% of American) receive at least one prescription of statins. The average DDDs/inhabitant/year of LLDs in American patients is almost twice of HK patients. Non-statin LLDs account for about 10% of the annual use of LLDs in the USA, but the use of non-statin drugs is rare (0.47%) in HK (table 3). In HK, simvastatin is widely used (65.78% of the annual DDDs of statins) as the initial dosing strategy (85.93%), followed by relatively little use of rosuvastatin (7.04%) and atorvastatin (4.44%). In contrast, in Optum, atorvastatin was more prevalent (59.38% of the annual DDDs of statins). Almost equivalent numbers of American patients were first put on atorvastatin (39.68%) and simvastatin (35.64%). Ever use of antiplatelet agents was found in 100% of HK patients and 96.94% of American patients, respectively. The annual use of antiplatelet agents was almost the same as HK Chinese patients (331.74 vs 326.62 DDDs/inhabitant/year). Clopidogrel was highly preferred in Chinese patients, taking up 88.37% of the annual DDDs of antiplatelet agents. In the USA, only about the half of the annual DDDs belonged to clopidogrel and the other 32.65% were prasugrel, implying that American physicians preferred prasugrel over ticagrelor.

About 45% Chinese patients and 70% American patients received ≥80% of 365 DDDs' statin (table 3). American patients are treated with higher daily doses of statins and the continuity tends to be higher (multivariate-adjusted OR (AOR) (95% confidence interval (95% CI)), 3.01 (2.23 to 4.06), P<0.001, table 4), but their adherence (MPR ≥80%) appears to be poorer (AOR (95% CI) for American over Chinese, 0.37 (0.23 to 0.58), p<0.001, in table 4) .

The sensitivity analyses, adjusted for PS weight for ATT and ATE, demonstrate the similar patterns (table 4). For antiplatelet agents, there are significant between-group differences (p<0.001) regarding the continuity and adherence levels between Chinese and American patients—American patients are more adherent to antiplatelet agents (table 4) and receive higher doses (table 3). In table 5, Chinese patients demonstrate a lower discontinuation rate for statins but a higher rate for antiplatelet agents.

DISCUSSION

Our study assessed the between-group difference in the medication use patterns of LLDs and antiplatelet agents between US Optum and HK CDARS databases. We found Chinese patients demonstrated a higher adherence level with statins than American patients, while discontinuation from stains was more frequent in Optum patients. Our study was not the first to identify this. According to a previous study among high cardiovascular risk patients in the USA, 53.0% of patients withdrew from statin therapy throughout 15 months' follow-up.[38] The likelihood existed that the American patients in our cohort discontinued the statins due to the high incidence of safety events, however, the likelihood should be minor in this case given that Asian patients were more liable for the intolerance to statin.[39]

The continuity level, measured by ≥80% of 1 year DDDs, of HK patients was lower because the dosing scheme of statins in Chinese patients was mainly dominated by low-to-moderate potency statin. DDD could be taken as a proxy for average annual consumption per person and had the advantage of being internationally recognised as assigned and published by the WHO[40 41]; however, it had the major limitations that across different ethnic or risk groups, the recommended dosing scheme could vary, and purely relying on an international standardised measure of dose equivalence for all patients can, therefore, be misleading.[42] For example, the DDD by the WHO ATC/DDD standard for simvastatin was 30 mg per day, which belonged to moderate-potency statin. However, according to the most recent ACC/AHA guidelines,[43] ACS patients

Table 3 Drug use pattern of statin and antiplatelet in Hong Kong Chinese patients and American patients in Optum

	Hong Kong CDARS—Chinese		US Optum—All	
	No. (%) patients	Mean±SD	No. (%) patients	Mean±SD
Total	270		1013	
DDD of all lipid-lowering drugs	270 (100.00)	352.53 (240.43)	1013 (100.00)	636.14 (472.03)
DDD of statin	270 (100.00)	350.86 (240.39)	1013 (100.00)	576.76 (416.70)
DDD of simvastatin	270 (100.00)	230.81 (180.59)	1013 (100.00)	117.31 (202.39)
DDD of atorvastatin	270 (100.00)	62.60 (222.05)	1013 (100.00)	342.48 (466.29)
DDD of rosuvastatin	270 (100.00)	57.18 (168.43)	1013 (100.00)	87.38 (259.56)
DDD of fluvastatin	270 (100.00)	0 (0)	1013 (100.00)	0 (0)
DDD of pitavastatin	270 (100.00)	0 (0)	1013 (100.00)	2.48 (47.38)
DDD of pravastatin	270 (100.00)	0 (0)	1013 (100.00)	28.22 (115.24)
DDD of lovustatin	270 (100.00)	0 (0)	1013 (100.00)	1.74 (19.24)
Average days per year on statins	270 (100.00)	338.06 (81.86)	1013 (100.00)	304.94 (109.60)
Good continuity (DDD/year ≥ 80%×365 days) with statins	121 (44.81)		711 (70.19)	
Good adherence (MPR≥80%) with statins	243 (90.00)		792 (78.18)	
Discontinuation rate of statin	36 (13.33)		347 (34.25)	
Statin use pattern				
Constantly high-potency statin user	12 (4.44)		364 (35.93)	
Constantly moderate-potency statin user	132 (48.89)		392 (38.70)	
Constantly low-potency statin user	42 (15.56)		18 (1.78)	
Switched statin potency	77 (28.52)		191 (18.85)	
Never used statin	7 (2.59)		48 (4.74)	
The intensity of first dose statin				
High	15 (5.56)		422 (41.66)	
Moderate	171 (63.33)		508 (50.15)	
Low	77 (28.52)		35 (3.46)	
Not any	7 (2.59)		48 (4.74)	
First statin chosen				
Atorvastatin	12 (4.44)		402 (39.68)	
Fluvastatin	0 (0)		0 (0)	
Rosuvsatin	19 (7.04)		116 (11.45)	
Simvastatin	232 (85.93)		361 (35.64)	
Lovastatin	0 (0)		12 (1.18)	
Pravastatin	0 (0)		74 (7.31)	
Pitavastatin	0 (0)		0 (0)	
None	7 (2.59)		48 (4.74)	

Continued

Table 3 Continued

	Hong Kong CDARS—Chinese		US Optum—All	
	No. (%) patients	Mean±SD	No. (%) patients	Mean±SD
DDD of any antiplatelet agent (clopidogrel/ticagrelor/prasugrel)	270 (100.00)	326.62 (813.73)	1013 (100.00)	331.74 (105.04)
DDD of clopidogrel	270 (100.00)	288.65 (817.85)	1013 (100.00)	184.66 (163.07)
DDD of ticagrelor	270 (100.00)	13.30 (75.79)	1013 (100.00)	7.67 (48.29)
DDD of prasugrel	270 (100.00)	24.67 (89.39)	1013 (100.00)	108.00 (152.58)
Averages days per year on antiplatelet agents	270 (100.00)	262.69 (148.40)	1013 (100.00)	330.81 (73.89)
Good continuity (DDD/year≥80%×365 days) with antiplatelet agents	172 (63.70)		802 (79.17)	
Good adherence (MPR≥80%) withantiplatelet agents	182 (67.41)		857 (84.60)	
Discontinuation rate of antiplatelet agents	125 (46.30)		316 (31.19)	
First antiplatelet agent chosen				
Clopidogrel	246 (91.11)		600 (59.23)	
Ticagrelor	19 (7.04)		27 (2.67)	
Prasugrel	5 (1.85)		335 (35.04)	
Not any	0 (0)		31 (3.06)	

CDARS, Clinical Data Analysis and Reporting System; DDD, daily defined dose; MPR, medical possession ratio; SD, Standard Deviation.

should be treated with the high-potency statins as long as they were <75 years old and could tolerate. As observed, 41.66% of US patients were put on high-potency statins after their index PCI, which would result in more DDDs than an annual use of 365 DDDs for each patient, therefore denoting a higher continuity while a lower adherence level was present.

Moreover, in Optum, atorvastatin was commonly used in treating American patients. For a long while, no statins could denote any advantage over atorvastatin (Lipitor).[44] The other higher-potency statin rosuvastatin (Crestor) failed to bring in any incremental benefits and so was less likely to take the market share[44] at this stage. It was obvious that by average American patients consumed more statin drugs than HK Chinese patients. Our observation that HK patients were treated with less intensive and lower quantity of statins was not surprising: the safety issue of high-potency statins among Chinese patients was widely discussed[39 45] and meanwhile Chinese patients were labelled as 'hyper-responders' to low-to-moderate potency statin. Compared with Caucasians, Chinese achieved a higher blood concentration of statins for a given dose of statin.[46 47] The most remarkable study challenging the use of the high-potency statins in Chinese was HPS2-THRIVE trial,[48] which found the rate of myopathy on simvastatin alone was higher among Chinese individuals, but they also concluded this 'small absolute excess' of myopathy with simvastatin 40 mg daily was less likely to outweigh the cardiovascular benefits in the high-risk group. The solid evidence, in terms of results from clinical trials, to support the higher risk of severe statin toxicity in Chinese was lacking. However, the fact we could assure was, both in mainland China[49] and HK,[50] the majority of the patients seldom received high-potency statins, and meanwhile substantial numbers of high-risk patients did not reach the lipid goals. Although the cardiologists in HK hospital setting mainly referred to the western guidelines, very interestingly, we found physicians were less willing to prescribe high-potency statins to local patients. Moreover, the use of non-statin LLDs was rare in HK patients. At the time of our study period, the routine use of non-statin lipid-lowering agents was not fully encouraged. However, the 2017 Focused Update[51] of ACC guideline made it clear that addition of non-statin lipid-lowering agents to maximally tolerated statin therapy was recommended among patients with clinical ASCVD when the additional LDL lowering should be achieved. Therefore, we suggested the future studies look at the influence of new guidelines on the medication use pattern of non-statin LLDs.

The drug-specific adherence pattern was identified in HK local management. Compared with American patients, HK patients were less adherent to antiplatelet agents but better adherent to statins. Uncertainty remained among cardiologists regarding the uptake of 1 year antiplatelet agents after ACS. In HK hospitals, the recommended treatment duration of clopidogrel after PCI has gradually increased over these years from 1 to 6–12 months, which may explain why the adherence with antiplatelet

Table 4 OR for good adherence and continuity with statins and antiplatelet agents

	OR*	95% CI	P value
Good adherence (MPR≥80%) with statins			
US Optum versus HK CDARS (adjusted†)	0.37	(0.23 to 0.58)	<0.001
US Optum versus HK CDARS (PS weights for ATE‡)	0.42	(0.22 to 0.81)	0.009
US Optum versus HK CDARS (PS weights for ATT§)	0.44	(0.21 to 0.92)	0.030
Good continuity (DDD/year≥80%×365 days) with statins			
US Optum versus HK CDARS (adjusted†)	3.01	(2.23 to 4.06)	<0.001
US Optum versus HK CDARS (PS weights for ATE‡)	4.28	(2.94 to 6.22)	<0.001
US Optum versus HK CDARS (PS weights for ATT§)	4.90	(3.25 to 7.38)	<0.001
Good adherence (MPR≥80%) with antiplatelet agents			
US Optum versus HK CDARS (adjusted†)	2.23	(1.60 to 3.12)	<0.001
US Optum versus HK CDARS (PS weights for ATE‡)	2.09	(1.40 to 3.13)	<0.001
US Optum versus HK CDARS (PS weights for ATT§)	2.07	(1.31 to 3.26)	0.002
Good continuity (DDD/year≥80%×365 days) with antiplatelet agents			
US Optum versus HK CDARS (adjusted†)	1.87	(1.36 to 2.56)	<0.001
US Optum versus HK CDARS (PS weights for ATE‡)	1.70	(1.16 to 2.49)	0.007
US Optum versus HK CDARS (PS weights for ATT§)	1.64	(1.06 to 2.54)	0.026

*Relative to Chinese patients in HK CDARS.
†Adjusted for sex, age, comorbidities of diabetes and hypertension and prior cardiovascular disease.
‡PS weights for ATE.
§PS weights for the ATT.
ATE, average treatment effect; ATT, average treatment effect for the treated; CDARS, Clinical Data Analysis and Reporting System; CI, confidence interval; DDD, defined daily doses; MPR, medical possession ratio; OR, odds ratio; PS, propensity score.

agents appeared less in HK. It was less likely that difference in drug price was the significant contributor to this, as clopidogrel (HKD 0.91 (USD 0.12)/75 mg) in local pharmacy was available as inexpensive generics, whose price was comparable to that of moderate-potency simvastatin (HKD 0.245 (USD 0.031) /40 mg). Previous qualitative research proposed several possibilities for patients' discontinuation behaviour[52 53]: The patients' compliance with statins appeared to link to the patients' belief about cholesterol level and LLDs, and inefficient physician–patient communication.[52 53] Another study[54] found that the major reasons for LLD discontinuation were adverse side events, and the less common reasons were the drug price, and the mistrust, confusion and preference for other therapies of the patient. Patients who discontinued LLDs were more likely to challenge the necessity of LLDs than patients who discontinued clopidogrel.[54] Reasons for discontinuing the clopidogrel included the confusion

Table 5 HR for discontinuation with statins and antiplatelet agents

	HR*	95% CI	P value
Discontinuation with statins			
US Optum versus HK CDARS (adjusted†)	2.95	(2.05 to 4.24)	<0.001
US Optum versus HK CDARS (PS weights for ATE‡)	3.51	(2.12 to 5.81)	<0.001
US Optum versus HK CDARS (PS weights for ATT§)	3.76	(2.06 to 6.88)	<0.001
Discontinuation with antiplatelet agents			
US Optum versus HK CDARS (adjusted†)	0.55	(0.43 to 0.69)	<0.001
US Optum versus HK CDARS (PS weights for ATE‡)	0.62	(0.48 to 0.82)	0.001
US Optum versus HK CDARS (PS weights for ATT§)	0.65	(0.48 to 0.88)	0.006

*Relative to Chinese patients in HK CDARS.
†Adjusted for sex, age, comorbidities of diabetes and hypertension and prior cardiovascular disease.
‡PS weights for ATE.
§PS weights for the ATT.
ATE, average treatment effect; ATT, average treatment effect for the treated; CDARS, Clinical Data Analysis and Reporting System; HR, hazard ratio; PS, propensity score.

on the duration of the therapy, possible side effects, and drug price.[54] In the study, the possibility existed that statins were better prescribed than antiplatelet agents in HK due to the availability of lab results to monitor patients' lipid levels and slow uptake of antiplatelet agents in the local clinical practice.

Additionally, the choice of antiplatelet agents differed substantially between two cohorts. In HK, clopidogrel was the most dominant. In contrast, more American patients were prescribed prasugrel as the first antiplatelet agent but very few took ticagrelor. Ticagrelor was not available in the USA until July 2011, which could greatly affect its prescribing from the other two antiplatelet agents. The early guidelines in 2011,[55] during our study period, did not endorse any of antiplatelet agents over another, because at that time, the clinical benefits of prasugrel over ticagrelor was not that confirmative. From our prior research in HK,[56] we found the ticagrelor was more cost-effective than clopidogrel, however, the uptake of ticagrelor was still slow, probably because the price of ticagrelor (11 HKD (USD 1.41) /90 mg per tablet) was much higher than clopidogrel (0.91 HKD (USD 0.12) /75 mg).

There is no golden standard in justifying which country is doing better. Our research studied the patients in 2011–2012. There were several guideline updates to the management of ACS patients since this research was conducted, all of which could affect the prescribing practices of these medications. From the current research, we could hardly answer the question if HK physicians were 'policy-driven' and if they were following the cost-saving strategies when they prescribed. It was very likely the medication adherence and continuity in HK was determined by the system and the doctors rather than the patient when it was measured this way. The cost-saving prescription behaviour was widely reported[10–12] to our local environment.

Some of the limitations bore mentioning. Due to the availability of data in Optum, we lacked a complete record of lab results and the exact reason for patients' discontinuation. Evaluation of adherence and continuity based on a patient's refill history could hardly account for the actual drug use and taking the medication in the correct way, instead, it was just an objective and relatively easy measurement.[57] The reason for patients' actual medication use was beyond our reach. Some known predictors for the medication use, for example, socioeconomic status and ethnic minority status, were beyond our reach.

CONCLUSION

Our research shed some light on the real-world medication use pattern of HK—we found relatively good adherence with statins but bad adherence with antiplatelet agents in HK Chinese patients, compared with the privately insured patients in the USA. We identified the needs for the future qualitative and quantitative research to explore the factors leading to the medication use pattern.

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