

Call to action: bridging gaps in lipid management in Hong Kong

Bryan PY Yan^{1*}, MD, FRCP, Kui Kai Lau², DPhil, FRCP, Andrea OY Luk³, MD, FRCP, Martin CS Wong^{4,5}, MD, MPH

¹ Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong SAR, China

² Division of Neurology, Department of Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China

³ Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong SAR, China

⁴ The Jockey Club School of Public Health and Primary Care, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China

⁵ Editor-in-Chief, Hong Kong Medical Journal

* Corresponding author: bryan.yan@cuhk.edu.hk

This article was published on 10 Apr 2024 at www.hkmj.org.

Hong Kong Med J 2024;30:90-3

<https://doi.org/10.12809/hkmj245158>

Atherosclerotic cardiovascular disease in Hong Kong

Cardiovascular disease is the third leading cause of death in Hong Kong, contributing to 13% of all deaths in 2020.¹ According to the Hong Kong Population Health Survey conducted between 2020 and 2022, the prevalence of high blood cholesterol among individuals aged 15 to 84 years in the Hong Kong general population increased from 8.4% in 2003/2004² to 51.9% in 2022.³ Low-density lipoprotein cholesterol (LDL-C) has been recognised as one of the most important modifiable risk factors for atherosclerotic cardiovascular disease (ASCVD).⁴ Accordingly, optimal LDL-C management is essential for reducing the incidence of and mortality from ASCVD. Despite the availability of effective and safe lipid-lowering therapies (LLTs) and guidelines for managing elevated LDL-C and other lipids, implementation remains a key challenge in clinical practice.

Advancements in lipid-lowering therapies

A lower LDL-C level is highly beneficial because of the direct correlation between the absolute reduction in LDL-C level and reduced cardiovascular risk, such that an incremental reduction in LDL-C level leads to a proportional reduction in the number of cardiovascular events.⁵ Statins are well-established as effective LLTs; this recognition has been extended to other non-statin therapies, including proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9is), ezetimibe, bempedoic acid, evinacumab, and inclisiran.^{6,7} Clinical trials have demonstrated that PCSK9is effectively lower LDL-C levels, thereby surpassing previous recommendations (high risk: <2.6 mmol/dL; very high risk: <1.8 mmol/dL) to offer additional cardiovascular benefits to patients (particularly those with high or very high ASCVD risk) who failed to meet their target LDL-C goal

despite maximally tolerated high-intensity statin therapy.^{6,8}

Adapting the latest evidence into current guidelines

The European Society of Cardiology and European Atherosclerosis Society (ESC/EAS) revised their guidelines in 2019 to integrate recent evidence concerning ASCVD prevention.⁵ These updates include a more aggressive approach with new LDL-C targets across all cardiovascular risk categories, as well as recommendations for lipid-lowering strategies. Since these updates, other cardiology societies (Table)^{5,9-11} and medical associations^{12,13} have also begun to recommend achieving the lowest possible LDL-C levels, especially for patients with very high ASCVD risk.

The 2019 ESC/EAS guidelines recommend the following LDL-C targets for the prevention of ASCVD in very high- and high-risk patients: <1.4 mmol/L and <1.8 mmol/L (and 50% reduction from baseline), respectively.⁵ Consistent with these recommendations, the 2024 American Diabetes Association guidelines recommend that patients with diabetes aged 40 to 70 years receive moderate-intensity statins, and such patients with one or more ASCVD risk factors receive high-intensity statins, to achieve LDL-C level <1.8 mmol/L and ≥50% reduction from baseline.¹² Statin therapy should also be considered for young adults aged 20 to 39 years, depending on their existing risk factors.¹² The American Heart Association/American Stroke Association guidelines recommend a target LDL-C level of <1.8 mmol/L for patients who have experienced transient ischaemic attack/ischaemic stroke with atherosclerotic disease.¹³

If there is inadequate LDL-C reduction with maximally tolerated statins, the addition of non-statin options (eg, PCSK9is or ezetimibe) can be considered according to the extent of reduction required to reach the LDL-C goal.^{5,7,9-13}

TABLE. Target low-density lipoprotein cholesterol goals established by various regional guidelines

	AHA/ACC 2018 ¹¹	ESC/EAS 2019 ⁵	APSC 2021 ⁹	China 2023 ¹⁰
Risk assessment	PCE to predict the 10-year ASCVD risk	SCORE chart to predict the 10-year risk of fatal CVD	APSC Coronary-Vascular-Disease system for identifying high-risk and very-high-risk patients	Risk factor enumeration
Secondary prevention				
Very high risk	<1.8 mmol/L and ≥50% reduction from baseline	<1.4 mmol/L and ≥50% reduction from baseline	<1.4 mmol/L and ≥50% reduction from baseline	<1.4 mmol/L and ≥50% reduction from baseline
Not very high risk	≥50% reduction from baseline	<1.0 mmol/L if a second event is experienced within 2 years from starting maximum statin-based therapy	N/A	<1.8 mmol/L and ≥50% reduction from baseline
Primary prevention				
High risk	≥50% reduction from baseline*	<1.8 mmol/L and ≥50% reduction from baseline	<1.8 mmol/L and ≥50% reduction from baseline	<2.6 mmol/L and ≥50% reduction from baseline
Moderate risk	30%-49% reduction from baseline*	<2.6 mmol/L	N/A	<2.6 mmol/L
Low risk	N/A	<3.0 mmol/L	N/A	<3.4 mmol/L

Abbreviations: AHA/ACC = American Heart Association/American College of Cardiology; APSC = Asian Pacific Society of Cardiology; ASCVD = atherosclerotic cardiovascular disease; CVD = cardiovascular disease; ESC/EAS = European Society of Cardiology/European Atherosclerosis Society; N/A = not available; PCE = Pooled Cohort Equation; SCORE = Systematic Coronary Risk Estimation

* Adults aged 40 to 75 years with low-density lipoprotein cholesterol levels of 1.7-4.8 mmol/L without diabetes

Low-density lipoprotein cholesterol target achievement remains challenging in Hong Kong

Low-density lipoprotein cholesterol management in Hong Kong has gradually improved, but considerable gaps in care persist. A territory-wide study conducted between 2016 and 2021 revealed poor achievement of LDL-C target goals among patients hospitalised for acute coronary syndrome.¹⁴ The study showed low rates of prescription for high-intensity statins (53%) and combination LLTs (1.3%-3.8%) at discharge; LLT and statin treatments were rarely intensified after discharge.¹⁴ Notably, approximately 22% of patients did not undergo follow-up lipid profile assessment after discharge.¹⁴ This lack of follow-up has been identified as an independent risk factor for all-cause death and cardiovascular-related death.¹⁴

A separate study involving over 700 000 patients revealed gross underutilisation of statins among patients with diabetes in Hong Kong, such that most of this population failed to meet LDL-C targets.¹⁵ Importantly, women and younger individuals were particularly undertreated, highlighting the need to address these age and sex disparities in lipid management.¹⁵ Consistent with current evidence,⁵ a large cohort of local patients with ischaemic stroke (with or without significant large artery atherosclerosis) demonstrated that the achievement of a target LDL level <1.8 mmol/L was associated with a reduced risk of subsequent major adverse cardiovascular events.¹⁶

Outdated recommendations in local settings can hinder optimal lipid management. As a result, physicians may fail to initiate appropriate LLT, prioritise regular monitoring, or provide appropriate follow-up care to assess treatment efficacy. Patients may not recognise the dangers of elevated LDL-C levels or understand the importance of lifestyle modification and medication adherence, leading to suboptimal outcomes.

Call to action: bridging gaps in lipid management

The International Atherosclerosis Society issued a call to action for improvements in lipid management, based on a multinational survey that involved 1758 physicians comprising cardiologists, endocrinologists, neurologists/stroke specialists, nephrologists, and general medicine practitioners from Japan, Germany, Colombia and the Philippines; the survey was designed to identify knowledge gaps in clinical practice.¹⁷ The results highlighted three major gaps in beliefs and behaviour across the four countries: (1) physicians lacked clear guidance concerning the management of higher-risk patients who may benefit from aggressive LLT; (2) although most physicians believed that they followed guideline recommendations, only half knew the LDL-C target for high-risk patients, and more than one-third had no opinion concerning the safety of low LDL-C levels; and (3) physicians were unsure of the potential effects of statins on cognitive, renal, and hepatic functions,

as well as the increased risk of haemorrhagic stroke associated with low LDL-C levels.¹⁷ Taken together, these findings highlighted key areas for enhanced education and research efforts to bridge gaps in lipid management.¹⁷ Physicians' limited familiarity with the rapidly changing guidelines hinders optimal LDL-C management.

The Hong Kong Cardiovascular Task Force published a consensus statement regarding ASCVD prevention in 2016, based on the 2011 ESC/EAS guidelines and the 2013 American Heart Association/American College of Cardiology guidelines.¹⁸ Although the consensus is valuable, it primarily constitutes expert opinion and lacks endorsement from any medical societies. Additionally, although various international societies have established guidelines for optimal lipid management, differences among these recommendations (eg, pharmacological treatment, lifestyle modification, and therapeutic targets) may lead to confusion and uncertainty among primary care physicians regarding the best approach.¹⁹

Efforts to bridge current gaps in lipid management in Hong Kong will require identifying local therapeutic limitations and barriers to optimising lipid management among physicians and patients. Based on knowledge of these issues, a consensus among local experts (ie, cardiologists, endocrinologists, neurologists, nephrologists, internists, general practitioners, nutritionists, and other healthcare specialists) can be achieved to provide practical recommendations that are consistent with international guidelines and adapted to local clinical practice.¹¹ Considering the complexities and time involved in developing local guidelines, a practical course of action would involve local medical societies across various specialties collaborating to issue a joint statement that recommends the adoption of appropriate guidelines, thereby ensuring a more cohesive and unified approach to lipid management in Hong Kong.

Local recommendations should also address pertinent issues, such as greater adherence to established guidelines—specifically, by encouraging the prompt initiation and intensification of statin therapy in eligible patients. Because the overall ASCVD risk assessment is the basis for treatment decisions in patients with dyslipidaemia,^{5,7,9} appropriate tools—adapted to the local population—should be used in routine clinical practice to ensure that patients are adequately assessed and managed. Additionally, the benefits of long-term adherence to LLT should be consistently and effectively communicated to patients.

Author contributions

All authors contributed to the development of the manuscript, approved the final version for publication, and take full

responsibility for its accuracy and integrity.

Conflicts of interest

KK Lau has received grants from the Croucher Foundation, Research Fund Secretariat of the Health Bureau, Innovation, Technology and Industry Bureau, Research Grants Council, Amgen, Boehringer Ingelheim, Eisai, and Pfizer, as well as consultation fees from Amgen, Boehringer Ingelheim, Daiichi Sankyo, and Sanofi, all unrelated to the submitted work. AOY Luk has served as a member of advisory panels for Amgen, AstraZeneca, Boehringer Ingelheim, and Sanofi and has received research support from Amgen, Asia Diabetes Foundation, Bayer, Biogen, Boehringer Ingelheim, Lee's Pharmaceutical, MSD, Novo Nordisk, Roche, Sanofi, Sugardown Ltd, and Takeda, unrelated to the submitted work. As editors of the journal, BPY Yan, KK Lau and MCS Wong were not involved in the peer review process.

Acknowledgement

Medical writing support was provided by Dr Veronica Yap and Dr Anlyn Lizaso of Weber Shandwick Health HK.

Funding/support

This editorial received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

1. Centre for Health Protection, Department of Health, Hong Kong SAR Government. Heart diseases. Available from: <https://www.chp.gov.hk/en/healthtopics/content/25/57.html>. Accessed 23 Jan 2024.
2. Centre for Health Protection, Department of Health, Hong Kong SAR Government and Department of Community Medicine, The University of Hong Kong. Population Health Survey 2003/2004. Available from: https://www.chp.gov.hk/files/pdf/report_on_population_health_survey_2003_2004_en.pdf. Accessed 23 Jan 2024.
3. Non-Communicable Disease Branch, Centre for Health Protection, Department of Health, Hong Kong SAR Government. Population Health Survey 2020-22 (Part II). Published April 2023. Available from: https://www.chp.gov.hk/files/pdf/dh_phs_2020-22_part_2_report_eng_rectified.pdf. Accessed 23 Jan 2024.
4. Borén J, Chapman MJ, Krauss RM, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease: pathophysiological, genetic, and therapeutic insights: a consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur Heart J* 2020;41:2313-30.
5. Mach F, Baigent C, Catapano AL, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J* 2020;41:111-88.
6. Furtado RH, Giugliano RP. What lessons have we learned and what remains to be clarified for PCSK9 inhibitors? A review of FOURIER and ODYSSEY outcomes trials. *Cardiol Ther* 2020;9:59-73.
7. Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 2022 ACC Expert consensus decision pathway on the role of nonstatin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: a report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol* 2022;80:1366-

- 418.
8. Catapano AL, Graham I, De Backer G, et al. 2016 ESC/EAS Guidelines for the management of dyslipidaemias. *Eur Heart J* 2016;37:2999-3058.
 9. Koh N, Ference BA, Nicholls SJ, et al. Asian Pacific Society of Cardiology consensus recommendations on dyslipidaemia. *Eur Cardiol* 2021;16:e54.
 10. Li JJ, Zhao SP, Zhao D, et al. 2023 Chinese guideline for lipid management. *Front Pharmacol* 2023;14:1190934.
 11. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2019;73:e285-350.
 12. American Diabetes Association Professional Practice Committee. 10. Cardiovascular disease and risk management: standards of care in diabetes—2024. *Diabetes Care* 2024;47(Suppl 1):S179-218.
 13. Kleindorfer DO, Towfighi A, Chaturvedi S, et al. 2021 Guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/American Stroke Association. *Stroke* 2021;52:e364-467.
 14. Sun H, Lai A, Tan GM, Yan B. Therapeutic gaps in low-density lipoprotein cholesterol management have narrowed over time but remain wide: a Hong Kong-wide study of 40,141 acute coronary syndrome patients from 2016 to 2021. Presented at the European Society of Cardiology Congress 2023; 2023 Aug 25-28; Amsterdam: Netherlands.
 15. Wu H, Lau ES, Yang A, et al. Trends in diabetes-related complications in Hong Kong, 2001-2016: a retrospective cohort study. *Cardiovasc Diabetol* 2020;19:60.
 16. Lau KK, Chua BJ, Ng A, et al. Low-density lipoprotein cholesterol and risk of recurrent vascular events in Chinese patients with ischemic stroke with and without significant atherosclerosis. *J Am Heart Assoc* 2021;10:e021855.
 17. Barter PJ, Yamashita S, Laufs U, et al. Gaps in beliefs and practice in dyslipidaemia management in Japan, Germany, Colombia and the Philippines: insights from a web-based physician survey. *Lipids Health Dis* 2020;19:131.
 18. Cheung BM, Cheng CH, Lau CP, et al. 2016 consensus statement on prevention of atherosclerotic cardiovascular disease in the Hong Kong population. *Hong Kong Med J* 2017;23:191-201.
 19. Singh M, McEvoy JW, Khan SU, et al. Comparison of transatlantic approaches to lipid management: the AHA/ACC/Multisociety Guidelines vs the ESC/EAS Guidelines. *Mayo Clin Proc* 2020;95:998-1014.