

2016 Consensus statement on prevention of atherosclerotic cardiovascular disease in the Hong Kong population

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ABSTRACT

Introduction: In Hong Kong, the prevalence of atherosclerotic cardiovascular disease has increased markedly over the past few decades, and further increases are expected. In 2008, the Hong Kong Cardiovascular Task Force released a consensus statement on preventing cardiovascular disease in the Hong Kong population. The present article provides an update on these recommendations.

Participants: A multidisciplinary group of clinicians comprising the Hong Kong Cardiovascular Task Force—10 cardiologists, an endocrinologist, and a family physician—met in September 2014 and June 2015 in Hong Kong.

Evidence: Guidelines from the American College of Cardiology/American Heart Association, the European Society of Hypertension/European Society of Cardiology, and the Eighth Joint National Committee for the Management of High Blood Pressure were reviewed.

Consensus Process: Group members reviewed the 2008 Consensus Statement and relevant international guidelines. At the meetings, each topical recommendation of the 2008 Statement was assessed against the pooled recommendations on that topic from the international guidelines. A final recommendation on each topic was generated by consensus after discussion.

Conclusions: It is recommended that a formal risk scoring system should be used for risk assessment of all adults aged 40 years or older who have at least one cardiovascular risk factor. Individuals can be

classified as having a low, moderate, or high risk of developing atherosclerotic cardiovascular disease, and appropriate interventions selected accordingly. Recommended lifestyle modifications include adopting a healthy eating pattern; maintaining a low body mass index; quitting smoking; and undertaking regular, moderate-intensity physical activity. Pharmacological interventions should be selected as appropriate after lifestyle modification.

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Introduction

Atherosclerotic cardiovascular disease (ASCVD), which includes coronary heart disease (CHD), peripheral vascular disease and stroke, is currently one of the most common causes of morbidity and mortality worldwide.¹ Unfortunately the prevalence of ASCVD is expected to increase further over the next few decades due to a number of factors including an ageing population and increasing industrialisation. The latter is associated with increased exposure to known ASCVD risk factors

such as smoking, low levels of physical activity, and poor dietary habits such as reduced consumption of fruit and vegetables and increased fat and salt intake.²

In Hong Kong, the prevalence of ASCVD risk factors has increased markedly over the past few decades. For example, the 2005–2008 Hong Kong Cardiovascular Risk Factor Prevalence Study-3 (CRISPS-3) reported an 8.6% increase in the prevalence of abdominal obesity (waist circumference ≥ 90 cm in men and ≥ 80 cm in women) and a 21.5%

2016年香港預防動脈粥樣硬化性心血管疾病的共識聲明

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引言：香港動脈粥樣硬化性心血管疾病的患病率在過去數十年顯著增加，預期患者人數還會進一步上升。香港心血管工作小組（Hong Kong Cardiovascular Task Force；HKCTF）於2008年發表了一份關於香港預防動脈粥樣硬化性心血管疾病的共識聲明。本文提供了有關建議的更新。

參與者：HKCTF是由10名心臟病學、1名內分泌學和1名家庭醫學專科醫生組成的多學科小組。他們於2014年9月和2015年6月在香港舉行會議。

證據：建議主要基於以下學會制定的指引：美國心臟病學會／美國心臟協會、歐洲高血壓學會／歐洲心臟病學會和第八屆聯合全國高血壓管理委員會。

共識過程：小組成員基於2008年的共識聲明以及相關國際指引進行審查。會議上根據國際指引中的匯總建議來評估2008年發表的每一項共識聲明。小組成員參與共識的討論制定，以協商方式達成每一項推薦建議。

結論：建議對所有40歲或以上至少有一項心血管危險因素的成年人，利用正式的動脈粥樣硬化性心血管疾病的風險評估系統進行評估，把病人分為低度、中度或高度風險，並選擇相應適當干預。所推薦的生活方式改變包括培養健康飲食習慣、保持體重指數於低水平、戒菸、並定期進行中等強度的體力運動。改變生活方式後才進行藥物治療。

increase in the prevalence of hypertension among a cohort of 1803 subjects recruited from CRISPS-1, the first such survey conducted between 1995 and 1996.³ Of the 551 participants of the Hong Kong Cardiovascular Task Force Risk Management Programme, 65.4% had hypertension, 63.7% dyslipidaemia, and 33.3% diabetes at baseline (BMY Cheung, unpublished data).

Global efforts are underway to promote ASCVD prevention and reduce the risk of major ASCVD events. These efforts have yielded benefits—between 1990 and 2013, a substantial reduction in cardiovascular mortality was seen in central Europe (5.2%) and western Europe (12.8%), attributed primarily to birth cohorts' decreased exposure to tobacco smoking, improvements in diet, improved treatment of cardiometabolic risk factors, and improved treatment of CVD.⁴

Methods

A multidisciplinary group of clinicians comprising the Hong Kong Cardiovascular Task Force—10 cardiologists, an endocrinologist, and a family physician—met in September 2014 and June 2015 in Hong Kong with the aim of updating the first

Consensus Statement on Preventing Cardiovascular Disease in the Hong Kong Population published in 2008.⁵ Prior to the consensus meetings, group members reviewed the 2008 Consensus Statement and relevant guidelines from the American College of Cardiology/American Heart Association, the European Society of Hypertension/European Society of Cardiology, and the Eighth Joint National Committee for the Management of High Blood Pressure, among others.⁵⁻⁹ At the meetings, each topical recommendation of the 2008 Statement was assessed against the pooled recommendations on that topic from the international guidelines reviewed. A final recommendation on each topic was generated by consensus after discussion.

The recommendations included in this consensus statement constitute the consensus opinion of the members of the Hong Kong Cardiovascular Task Force regarding the most appropriate interventions for the Hong Kong population.

Recommendations

Risk assessment

Total cardiovascular risk

Total ASCVD risk is based on the complex interactions of a number of different risk factors that together have a multiplicative effect. That is, the risk of ASCVD is amplified to a greater extent by the interaction of multiple risk factors than would be expected due to the cumulative effect of each risk factor alone.^{7,9} The present standard of practice for the primary prevention of ASCVD is to determine a patient's total ASCVD risk using a formal risk scoring algorithm.^{1,7,9}

Who to assess?

In Hong Kong, it is recommended that ASCVD prevention efforts should be focused on adults aged 40 years or older who have at least one ASCVD risk factor.^{1,9} The total ASCVD risk should be formally calculated for such individuals, and they should receive ASCVD prevention advice and/or treatment according to their determined level of risk (high, moderate, or low).^{1,9} High-risk patients will benefit most from treatment and include:

- patients with overt ASCVD (CHD, previous myocardial infarction, previous stroke, or peripheral vascular disease) or those who are symptomatic (eg have experience with angina)
- patients with diabetes mellitus
- patients with one major ASCVD risk factor (eg moderate-to-severe hypertension, severely elevated lipid levels)⁹

These patients automatically meet the threshold for intensive risk factor treatment and need not undergo formal risk scoring.^{1,9}

How to assess?

It is important to note that the current recommendations do not espouse a preference for any particular method of risk projection, but recommend that formal ASCVD risk scoring should be performed for all potentially at-risk patients.

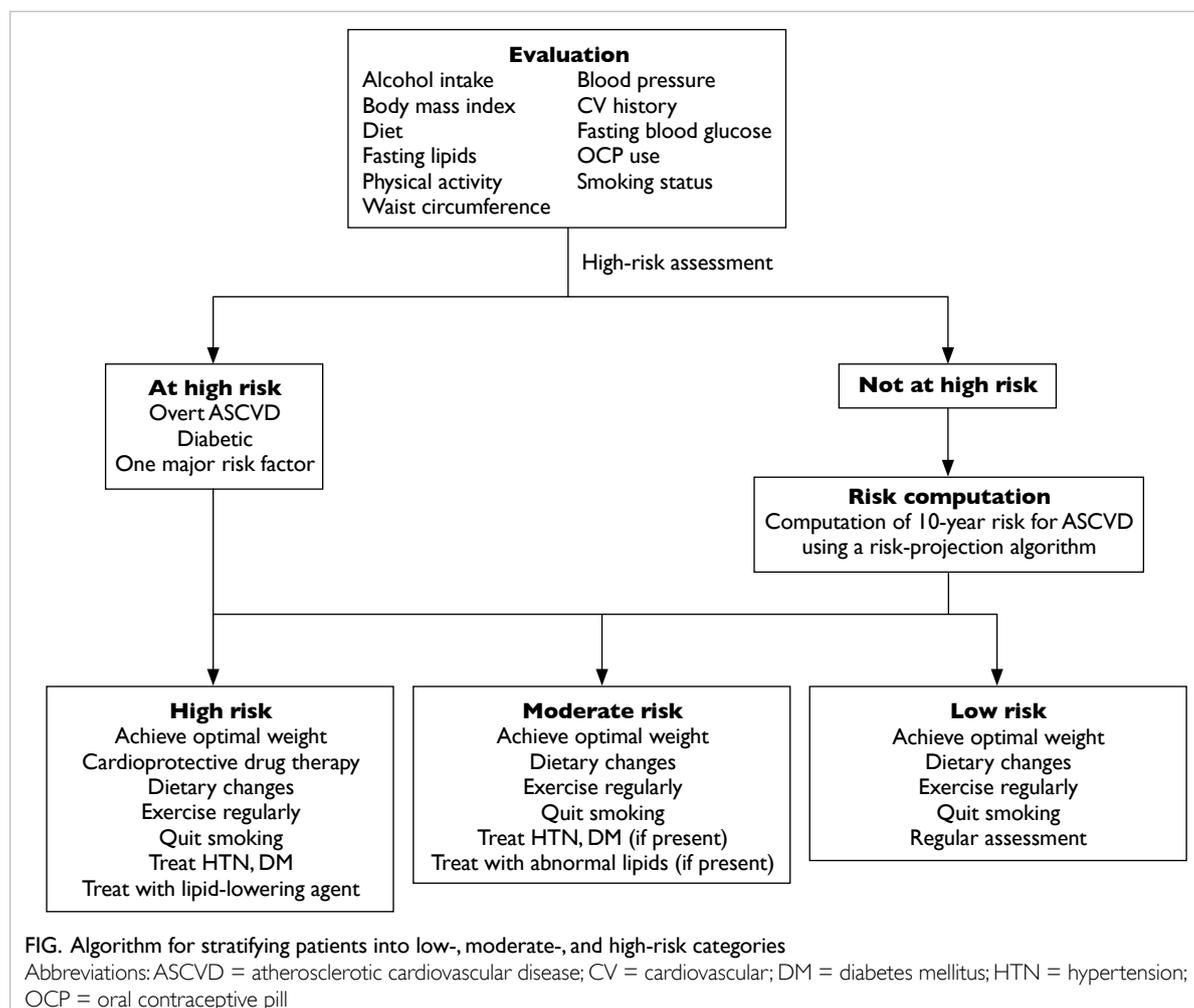
A patient's 10-year (total) risk for ASCVD may be calculated using a variety of methods. The most recently published algorithm uses the American Pooled Cohort Risk Assessment Equations that are sex- and race-specific estimates for African-American and White men and women aged 40 to 79 years. They utilise age, total and high-density lipoprotein (HDL) cholesterol, systolic blood pressure (BP), diabetes, and current smoking status to calculate the total ASCVD risk.¹ The European Systematic Coronary Risk Evaluation (SCORE) system is another well-validated system that uses sex, age, systolic BP, total cholesterol, and current smoking status to predict the risk of fatal cardiovascular events.⁷ Another risk assessment system, QRISK2, includes the risk factor of 'self-assigned ethnicity' (including Chinese) in the computation^{10,11}; however, the model was validated

for Chinese immigrants to the United Kingdom and, thus, its applicability to the local Chinese population is unknown.

The calculated risk score is used to stratify patients into low-, moderate-, and high-risk categories (Fig). When interpreting these scores, the clinician should bear in mind that they were developed and validated for western populations. In addition, it must be remembered that any calculated ASCVD score is simply an indicator of total cardiovascular risk.⁹ Although it can guide patient treatment, it cannot be a substitute for individualised patient evaluation and management. The clinician is advised to take all factors into account and to treat the patient individually rather than treat the risk score.

Risk interventions

There is robust scientific evidence that the development of ASCVD in at-risk patients may be slowed and/or prevented by lifestyle modification, reduction of metabolic risk factors, and pharmacological treatment.^{7,9-19} Listed below are



the major modifiable risk factors for ASCVD. The treatment goal is stated for each risk factor, along with general recommendations on how this goal may be achieved. Existing hypertension,^{7,8} dyslipidaemia,^{1,6} and diabetes²⁰⁻²² treatment guidelines incorporate the latest evidence on how to treat these conditions and to what appropriate targets. The clinician is referred to these guidelines for further guidance.

Diet

Treatment goal: an overall healthy eating pattern

All patients at increased risk of ASCVD should be given advice and specific recommendations for eating a healthy diet. Advice should include⁹:

- matching energy intake with energy needs;
- eating a variety of fruits, vegetables, grains, low- or non-fat dairy products, legumes, fish, poultry, and lean meats;
- reducing saturated and trans fats to <10% of total daily caloric intake, through replacement with polyunsaturated fats (vegetables, nuts, seeds, and seafood);
- reducing cholesterol intake;
- reducing salt intake; and
- limiting alcohol intake to no more than two drinks per day for men and one drink per day for women.

Physical activity

Treatment goal: a minimum of 30 minutes of moderate-intensity physical activity at least 5 times a week, or a minimum of 15 minutes of vigorous-intensity physical activity at least 5 times a week⁹

- ‘Moderate intensity’ is defined as exercising at 64% to 76% of maximum heart rate (ie 220 minus age); activities include brisk walking, slow cycling, vacuuming, gardening, golf, tennis (doubles), ballroom dancing, and water aerobics.⁹ ‘Vigorous intensity’ is defined as exercising at 77% to 93% of maximum heart rate; activities include race walking, jogging or running, bicycling, heavy gardening, swimming laps, and tennis (singles).⁹
- The practice of the popular Chinese soft martial art *tai chi* may also be beneficial for individuals at risk of ASCVD. A systematic review has shown that *tai chi* has physiological and psychosocial benefits, and it also appears to be safe and effective in promoting flexibility, balance control, and cardiovascular fitness in older patients with chronic conditions.²³
- All patients should consult their doctor prior to initiating graded exercise programmes.

Overweight/obesity

Treatment goal: maintenance of normal body mass index and waist circumference

- Normal body mass index is 18.5-22.9 kg/m² for

Asians,²⁴ and normal waist circumference is <90 cm (35.4 inches) for men and <80 cm (31.5 inches) for women.²⁵

- Patients who are overweight or obese should strive to achieve normal body weight by restricting caloric intake and increasing physical activity.
- Drug therapy or surgical interventions may be a helpful adjunct for the treatment of severe obesity in some patients.

Smoking

Treatment goal: complete smoking cessation

- Assess the patient’s tobacco use and strongly urge the patient to stop smoking.
- Determine the patient’s degree of nicotine addiction and his/her readiness to quit smoking. For patients identified as willing to quit, a plan should be developed that may involve pharmacotherapy, counselling, cessation support mechanisms (eg follow-up calls and visits), and referral to specialised programmes, if available.^{20,26}

Hypertension

Risk factor reduction goal: blood pressure of <140/90 mm Hg for the general population aged <60 years, including patients with previous stroke or transient ischaemic attack; patients with coronary heart disease; and patients with chronic kidney disease. For patients with diabetes, a target blood pressure of <140/85 mm Hg is recommended. For the general population aged ≥60 years, a target blood pressure of <150/90 mm Hg is recommended⁷⁻⁹

- Patients with a systolic BP of ≥130 mm Hg or diastolic BP of ≥80 mm Hg should be given advice and specific recommendations on reducing lifestyle risk factors.
- Patients who do not meet their primary goals as defined above should be given drug therapy tailored to their circumstances.
- The choice of first-line therapy is the prerogative of the attending physician. Suitable antihypertensive drugs include calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, and angiotensin receptor blockers (ARBs), either alone or in combination (Tables 1 and 2).^{7,9} Diuretics (chlorthalidone and indapamide) and β-blockers may also be used, but their long-term use is associated with increased risk of new-onset diabetes^{30,31}; of note, there is no evidence that hydrochlorothiazide—one of the most commonly prescribed antihypertensives—in its usual dose of 12.5 to 25 mg daily reduces myocardial infarction, stroke, or death.³²
- When target BP cannot be achieved with monotherapy or with a two-drug combination,

TABLE I. Summary of blood pressure management guidelines^{7,8,27-29}

Study group	Recommended target BP (mm Hg)			
	2011 NICE Clinical Guideline for the Management of Hypertension, 2009 Clinical Guideline for the Management of Type 2 Diabetes, and 2014 Clinical Guideline for the Management of Chronic Kidney Disease	2013 ESH-ESC Task Force Guideline for the Management of Arterial Hypertension	2014 JNC 8 Guideline for the Management of High Blood Pressure in Adults	2016 Hong Kong Cardiovascular Task Force Recommendations
General population (age in years)	Age <80: <140/90 Age ≥80: <150/90	Age <80: <140/90 Age ≥80: <140-150/90	Age <60: <140/90 Age ≥60: <150/90	Age <60: <140/90 Age ≥60: <150/90
Patients with diabetes	<140/80 (<130/80 For people with kidney, eye, or cardiovascular damage)	<140/85	<140/90	<140/85
Patients with chronic kidney disease	<140/90 (<130/80 In patients with CKD and diabetes)	<140/90 (systolic BP reading <140 should be considered. When overt proteinuria is present, values <130 may be considered, provided that changes in eGFR are monitored)	<140/90	<140/90
Patients with CHD, ACS, HF	Patients with CHD: <140/90	<140/90	Not specified	<140/90
Other special populations (age in years)	Patients identified as having a 'white coat' effect: consider ambulatory or home BP monitoring. Aim for usual target BP during waking hours of: Age <80: <135/85 Age ≥80: <145/85	Patients with organ damage: <140/90	Not specified	Not specified

Abbreviations: ACS = acute coronary syndrome; BP = blood pressure; CHD = coronary heart disease; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; ESH-ESC = European Society of Hypertension/European Society of Cardiology; HF = heart failure; JNC 8 = Eighth Joint National Committee; NICE = National Institute for Health and Care Excellence

doses can be increased; if target BP cannot be achieved by a two-drug combination at full doses, switching to another two-drug combination, or adding a third drug, may be considered.⁷⁻⁹ In patients with uncontrolled BP despite treatment with maximally tolerated doses of three antihypertensive medications, addition of the aldosterone antagonist spironolactone has achieved larger reductions in systolic BP than addition of the β-blocker bisoprolol, the alpha-adrenergic blocker doxazosin, or placebo.³³

Dyslipidaemia

Risk factor reduction goal: low-density lipoprotein cholesterol level of <3 mmol/L. For patients with overt atherosclerotic cardiovascular disease, the target level should be <1.8 mmol/L⁹

- Low-density lipoprotein cholesterol (LDL-C) reduction decreases cardiovascular events.⁹
- Recommended target LDL-C level for patients stratified by ASCVD risk is as follows:
 - o Very high ASCVD risk: LDL-C <1.8 mmol/L, or a ≥50% reduction if the baseline is between 1.8 and 3.5 mmol/L (Table 3)
 - o High ASCVD risk: LDL-C <2.6 mmol/L, or a

- o ≥50% reduction if the baseline is between 2.6 and 5.1 mmol/L
- o Low-to-moderate ASCVD risk: LDL-C <3.0 mmol/L⁹
- Patients at low and moderate risk should be given advice and specific recommendations on lowering LDL-C through dietary adjustments, increased physical activity, and weight reduction. If the target is not met after 6 months, they should be given a lipid-lowering agent (Tables 4 and 5).³⁵
- Patients at high risk should immediately be started on lipid-lowering therapy with a high-intensity statin (Tables 4 and 5).³⁵ Importantly, however, pharmacokinetic studies have shown that Chinese patients achieve a higher plasma concentration of statin compared with Caucasians, and this may be associated with an increased risk of adverse effects.³⁶ Consequently, the maximum approved doses of the statins available in Asia are around half the maximum approved doses in the United States.³⁷ The clinician should, therefore, exercise caution when prescribing high-intensity statin therapy.
- Inhibitors of proprotein convertase subtilisin/kexin type 9 have recently been approved for use

TABLE 2. Classes of antihypertensive drugs

Drug class	Agents available in Hong Kong	Mechanism of action	Conditions favouring use of drug class	Compelling contra-indications	Possible contra-indications
ACE inhibitors	Captopril Enalapril Imidapril Lisinopril Perindopril Quinapril Ramipril	Blocks conversion of angiotensin I to angiotensin II by inhibiting ACE	Congestive heart failure, post-MI patients with reduced LV ejection fraction, diabetes mellitus, renal dysfunction	Pregnancy, hyperkalaemia, bilateral renal artery stenosis	-
Alpha-blockers	Doxazosin Prazosin	Blocks α 1-adrenoceptors in the vasculature, causing a clinically significant reduction in blood pressure as a result of a reduction in systemic vascular resistance	Benign prostatic hypertrophy	-	Orthostatic hypotension
Angiotensin II antagonists	Azilsartan Candesartan Eprosartan Irbesartan Losartan Olmesartan Telmisartan Valsartan	Blocks angiotensin II type I receptors	Diabetes mellitus, post-MI patients, patients with contra-indications to ACE inhibitors, renal dysfunction	Pregnancy, hyperkalaemia, bilateral renal artery stenosis	-
Beta-blockers	Atenolol Bisoprolol Carvedilol Esmolol Metoprolol Nebivolol Pindolol Propranolol	Competitively antagonises effect of catecholamines at β -adrenergic receptor sites	Angina, post-MI patients, congestive heart failure, glaucoma	Asthma, AV block	Peripheral artery disease, metabolic syndrome, glucose intolerance, physically active patients, COPD
Calcium antagonists (dihydropyridines)	Amlodipine Felodipine Lercanidipine Nifedipine	Dilates coronary and peripheral arteries as a result of inhibition of cellular Ca^{2+} influx	Angina, LV hypertrophy	-	Tachyarrhythmias, heart failure
Calcium antagonists	Diltiazem Verapamil	(ditto)	(ditto)	AV block, heart failure	-
Thiazide diuretics	Hydrochlorothiazide Indapamide Metolazone	Inhibits the Na^+/Cl^- cotransporter in the distal tubule	Elderly patients with no co-morbid conditions	Gout	Metabolic syndrome, glucose intolerance, pregnancy

Abbreviations: ACE = angiotensin-converting enzyme; AV = atrioventricular; COPD = chronic obstructive pulmonary disease; LV = left ventricular; MI = myocardial infarction

in the United Kingdom and the United States as an adjunct to diet and maximally tolerated statin therapy for the treatment of individuals with primary hypercholesterolaemia or mixed dyslipidaemia, or those with clinical ASCVD who require additional lowering of LDL-C.^{38,39} Clinical trials have demonstrated decreases in LDL-C by up to 60% in subjects receiving these agents³⁸; definitive evidence of reduced cardiovascular event rates associated with their use may be provided by ongoing trials.

Diabetes

Risk factor treatment goal: glycated haemoglobin < 7%²⁰⁻²²

- All diabetic patients are considered high risk

for the development of ASCVD^{9,21} and should receive appropriate management upon diagnosis. This includes guidance on diet modification and increased physical activity in conjunction with pharmacotherapy.²⁰⁻²² Early initiation of medication is recommended to avoid any delay in treatment. Insulin is administered if treatment goals are not achieved with oral therapy.²⁰⁻²² Treatment goal for glycaemia should be tailored according to the patient profile in order to avoid hypoglycaemia in those with co-morbidities or in elderly patients.^{22,40}

- In diabetic patients, treat other ASCVD risk factors more aggressively,²² including hypertension. Nevertheless, present evidence suggests that a BP target of <140/85 mm Hg is appropriate in patients with diabetes, with a lower

TABLE 3. Summary of lipid management goals^{6,9,34}

	Recommended lipid levels (mmol/L or % reduction)			
	2016 European Guidelines on Cardiovascular Disease Prevention in Clinical Practice	2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults	2014 NICE Clinical Guideline on Lipid Modification	2016 Hong Kong Cardiovascular Task Force Recommendations
Primary prevention	LDL-C <1.8 to <3.0 mmol/L according to SCORE risk	↓ LDL-C ≥30% if 10-year risk ≥7.50%	↓ Non HDL-C ≥40%	LDL-C <1.8 mmol/L to <3.0 mmol/L according to individual CV risk level
Secondary prevention	LDL-C <1.8 mmol/L or ↓ LDL-C ≥50%	↓ LDL-C ≥50%	↓ Non HDL-C ≥40%	LDL-C <1.8 mmol/L
Familial hypercholesterolaemia	No recommendation	↓ LDL-C ≥50%	↓ Non HDL-C ≥40%	LDL-C <2.5 mmol/L
Diabetes	LDL-C <1.8 mmol/L or ↓ LDL-C ≥50%	↓ LDL-C ≥50% if 10-year ASCVD risk ≥7.50% or ↓ LDL-C ≥30-50%	↓ Non HDL-C ≥40%	LDL-C <1.8 mmol/L to 2.5 mmol/L According to individual CV risk level
CKD	Severe: LDL-C <1.8 mmol/L or ↓ LDL-C ≥50% Moderate: LDL-C <2.6 mmol/L or ↓ LDL-C ≥50%	No target specified	↓ Non HDL-C ≥40%	LDL-C <1.8 mmol/L to 2.5 mmol/L According to individual CV risk level

Abbreviations: ACC/AHA = American College of Cardiology/American Heart Association; ASCVD = atherosclerotic cardiovascular disease; CKD = chronic kidney disease; CV = cardiovascular; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; NICE = National Institute for Health and Care Excellence; SCORE = Systematic Coronary Risk Evaluation

TABLE 4. Agents recommended for achieving lipid-lowering goals^{6,9,34}

	Recommended lipid-lowering agents		
	2016 European Guidelines on Cardiovascular Disease Prevention in Clinical Practice ⁹	2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults ⁶	2014 NICE Clinical Guideline on Lipid Modification
Primary prevention	Statin	10-Year risk ≥7.5%: moderate* to high†-intensity statin	10-Year risk ≥10%: atorvastatin 20 mg Age ≥85 years: consider atorvastatin 20 mg
Secondary prevention	Statin	≤75 Years: high-intensity statin† >75 Years: moderate statin*	Atorvastatin 80 mg
Familial hypercholesterolaemia	Statin	High-intensity statin†	Atorvastatin 20 mg Consider ezetimibe for FH
Diabetes	Statin	10-Year risk ≥7.5%: high-intensity statin† 10-Year risk <7.5%: moderate-intensity statin*	Type 1: consider atorvastatin 20 mg Type 2 and 10-year risk ≥10%: atorvastatin 20 mg
CKD	Statin	No specific recommendation	Atorvastatin 20 mg If non-HDL-C ↓ <40%: consider higher dose
Combination with non-statin	If target not reached with highest tolerated statin	If target not reached with highest tolerated statin	Do not offer fibrates, niacin, BAS, or omega-3 fatty acid

Abbreviations: ACC/AHA = American College of Cardiology/American Heart Association; BAS = bile acid sequestrant; CKD = chronic kidney disease; FH = familial hypercholesterolaemia; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; NICE = National Institute for Health and Care Excellence

* Moderate-to-high-intensity statin: Expected to reduce LDL-C by 30%-50%, eg atorvastatin 10-20 mg, rosuvastatin 5-10 mg, simvastatin 20-40 mg, pravastatin 40-80 mg, lovastatin 40 mg

† High-intensity statin: Expected to reduce LDL-C by ≥50%, eg atorvastatin 40-80 mg, rosuvastatin 20-40 mg

BP (systolic BP of <130 mm Hg) as an option in patients with hypertension and nephropathy. It should be noted that lower BP may be associated with increased risk of adverse events, especially

in older patients or those with a long duration of diabetes, and the risk and benefit of intensive BP lowering needs to be considered individually according to the patient profile.²²

TABLE 5. Classes of lipid-lowering agents

Drug class	Agents available in Hong Kong	Mechanism of action	Conditions favouring use of drug class	Compelling contra-indications	Possible contra-indications
Statins	Atorvastatin Fluvastatin Lovastatin Pravastatin Rosuvastatin Simvastatin	Inhibit the enzyme HMG-CoA reductase, which plays a central role in cholesterol synthesis	Existing cardiovascular disease, very high LDL-C levels, diabetes, patients with a high 10-year risk of MI	Should not be used in patients with active or chronic liver disease, or by pregnant or lactating women	Liver function should be tested before, after 6-12 weeks of therapy, and with any dose increase. Advise patient to consult immediately if signs of muscle pain suggesting myopathy occur
Fibrates	Bezafibrate Fenofibrate Gemfibrozil	Varies depending on the agent. Bezafibrate, fenofibrate reduce the concentration of VLDL by increasing the activity of lipoprotein lipase. Gemfibrozil inhibits lipolysis, reduces hepatic fatty acid uptake, and reduces secretion of VLDL from the liver	Very high levels of plasma triglycerides	Not recommended in patients with severe renal or hepatic impairment, hypoalbuminaemia, primary biliary cirrhosis, gallbladder disease, or nephrotic syndrome. Should not be used by pregnant or lactating women	Use with caution in mild-to-moderate renal impairment; monitor serum transaminase levels regularly. May cause myalgia, myopathy. Rarely used with statins, may interact with anticoagulant therapy
Bile-acid sequestrants (resins)	Cholestyramine	Binds with bile acids to form an insoluble complex that is excreted in the faeces. The increasing loss of bile acid increases the oxidation of cholesterol to bile acids	Patients for whom statin therapy is contra-indicated or those who cannot tolerate statin therapy	Contra-indicated in complete biliary obstruction, high fasting triglycerides	May decrease folate levels
Selective cholesterol absorption inhibitor	Ezetimibe	Localises in the brush border of the small intestine where it inhibits absorption of cholesterol, decreasing its delivery to the liver. This decrease in cholesterol stored in the liver increases cholesterol clearance from the blood	Patients for whom statin therapy is contra-indicated or those who cannot tolerate statin therapy	Active liver disease. Should not be used by pregnant or lactating women	Use with caution in patients with renal or hepatic impairment
Combination cholesterol absorption inhibitor and statin	Ezetimibe-simvastatin	Simvastatin inhibits the HMG-CoA reductase enzyme and thus cholesterol synthesis, while ezetimibe inhibits cholesterol absorption in the small intestine, reducing liver cholesterol stores and increasing cholesterol clearance from the blood	Patients who cannot achieve target LDL-C levels despite receiving the maximum tolerated statin dose	Contra-indications include hypersensitivity, active liver disease or unexplained persistent elevations of serum transaminases, pregnancy and lactation, and concomitant administration of potent CYP3A4 inhibitors, gemfibrozil, cyclosporine or danazol	-
Nicotinic acid	Nicotinic acid	The exact mechanisms are currently unknown, but are not related to its role as a vitamin	Patients who cannot tolerate statin therapy, and for those with very low levels of HDL-C and/or high triglyceride levels	Contra-indications include - hypersensitivity reactions to nicotinic acid, liver disease, impaired glucose tolerance, diabetes mellitus, and gouty arthritis	-

Abbreviations: HDL-C = high-density lipoprotein cholesterol; HMG-CoA = 3-hydroxy-3-methyl coenzyme A; LDL-C = low-density lipoprotein cholesterol; MI = myocardial infarction; VLDL = very-low-density lipoproteins

Discussion

The gap between evidence and practice

Although clear, evidence-based guidelines and recommendations for ASCVD prevention have

been available for a number of years and are regularly updated, there is evidence that they are not routinely implemented in clinical practice.^{9,41,42} For example, Yusuf et al⁴³ reported worldwide poor use of medications for the secondary prevention of

ASCVD. Their study included 153 996 adults aged 35 to 70 years from rural and urban communities in high-, upper-middle-, lower-middle-, and low-income countries, 5650 of whom had had a self-reported CHD event and 2292 a stroke. Few individuals with ASCVD took antiplatelet drugs (25.3%), β -blockers (17.4%), ACE inhibitors or ARBs (19.5%), or statins (14.6%). As expected, drug use was higher in high-income countries, with 11.2% of patients in these countries not receiving any drugs compared with 45.1% of patients in upper-middle-income countries, 69.3% in lower-middle-income countries, and 80.2% in low-income countries. Notably, despite the relative accessibility of drugs for secondary prevention of ASCVD in high- and upper-middle-income countries, many patients remained untreated.

Of the patients who do receive treatment for ASCVD risk factors, only a few attain their treatment goals. Findings from the Hong Kong Cardiovascular Task Force Risk Management Programme indicate that 84% of enrolled hypertensive patients were treated with one or two antihypertensive drugs, most commonly ARBs (63.5%) and calcium channel blockers (47.2%; BMY Cheung, unpublished data). Similarly 64% of the diabetic patients were treated with metformin (68.8%) and/or gliptins (36%), while 78.1% of patients with dyslipidaemia were treated with a statin. Notably, however, treatment goals for hypertension (<130/80 mm Hg for diabetic patients, <140/90 mm Hg for non-diabetics) and diabetes (glycated haemoglobin <7%) were met by just over 50% of hypertensive patients and approximately 60% of diabetics.

Ensuring physician compliance with evidence-based guidelines and improving clinician understanding of factors affecting patient compliance with treatment may be the key to decreasing ASCVD risk in the Hong Kong population.

Differences between the 2008 and 2016 consensus statements

The present update of the 2008 Consensus Statement introduces the use of the new American Pooled Cohort Risk Assessment Equations that have superseded the Framingham Risk Evaluation; ASCVD risk can be assessed using either these equations or the European SCORE system to stratify patients into low-, moderate-, or high-risk categories to aid targeting of therapies as well as the establishment of suitable treatment goals. The risk factor reduction goals for hypertension and dyslipidaemia have been updated to reflect the most current recommendations from the Eighth Joint National Committee, the European guidelines on the management of arterial hypertension, and the European guidelines on cardiovascular disease prevention in clinical practice. The HDL-C target

included in the 2008 Consensus Statement has been omitted from the current update as increased HDL-C has not been proven to reduce ASCVD risk.

Conclusions

The development of ASCVD in at-risk patients may be slowed and/or prevented by lifestyle modification, reduction of metabolic risk factors, and pharmacological treatment. The clinician plays a central role in ASCVD prevention—identifying at-risk patients, calculating the total ASCVD risk score, encouraging lifestyle changes, and providing targeted interventions to achieve specific treatment goals. Nonetheless, it is vital that the clinician is not overly focused on the treatment of isolated ASCVD risk factors but should instead adopt a ‘whole-person’ approach to diagnosis and therapy. Many patients present with multiple risk factors and, therefore, individualised, nuanced patient evaluation and management is essential to achieve optimum outcomes. Finally, none of these interventions will result in ASCVD prevention without the cooperation of the patient. Clinicians are encouraged to build strong partnerships with their patients, with the aim of establishing individual ownership of their treatment plans and, thus, improved treatment compliance.

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