### Incorporating the cardiovascular-kidneymetabolic health framework into the local healthcare system: a position statement from the Hong Kong College of Physicians

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### Introduction

# What is cardiovascular-kidney-metabolic syndrome?

Cardiovascular-kidney-metabolic (CKM) syndrome is a new entity that emphasises interconnections among atherosclerotic cardiovascular disease (ASCVD), atrial fibrillation (AF), heart failure (HF), chronic kidney disease (CKD), excess adiposity, metabolic syndrome, and diabetes.<sup>1</sup> It is categorised into five stages (Table 1), reflecting the progressive nature of the pathophysiology behind this multifaceted syndrome and the increasing risk of adverse cardiovascular outcomes associated with higher CKM stages.<sup>2-6</sup> The CKM health framework incorporates screening, staging, and management for early identification of potential CKM-related events.<sup>7,8</sup>

Adaptation of the CKM model is influenced by access, financing, and care delivery. A multispecialty working group of the Hong Kong College of Physicians (HKCP) developed this Position Statement concerning incorporation of the CKM health framework into the local healthcare system, taking into consideration local healthcare needs, existing resources and limitations, as well as future healthcare directions and initiatives in Hong Kong.

at risk for suboptimal CKM health to enable timely intervention and slow disease progression. Optimal care delivery remains challenging despite improvements in local health literacy. A recent local population health survey revealed that many individuals were unaware of overweight or obesity status, as well as hypertension, diabetes, and elevated cholesterol.<sup>9</sup>

The ageing local population (~21% of individuals are aged  $\geq 65$  years<sup>10</sup>) further strains healthcare resources due to increasing numbers of patients with CKM risks, as well as end-organ damage. A lack of public awareness about CKM health and limitations in primary healthcare constitute barriers to implementing the CKM health framework.

The Hospital Authority has largely focused on specialist care, while our primary healthcare system is comparatively underdeveloped.<sup>11</sup> Public health expenditures reflect this focus.<sup>12</sup> The Health Bureau's Primary Healthcare Blueprint (2022) and the 3-year Chronic Disease Co-Care (CDCC) Pilot Scheme are promising initiatives, but their integration with specialist care remains unclear.

### Screening

Screening asymptomatic individuals for metabolic risk factors (eg, overweight/obesity, central adiposity, dysglycaemia, hypertension, and dyslipidaemia) is a key component of the CKM health framework.

### Patient care challenges in real-world settings

The CKM concept aims to identify individuals

TABLE 1. Stages of cardiovascular-kidney-metabolic sy	indrome proposed by the American Heart Association

CKM stage	Cardiovascular condition	Kidney condition	Metabolic condition
Stage 0	No subclinical or clinical ASCVD, HF, or AF	No evidence of CKD	<ul> <li>All of the following:</li> <li>Normal BMI and WC based on ethnicity-specific thresholds (ie, BMI &lt;23 kg/m<sup>2</sup> and WC &lt;90 cm [for men] or &lt;80 cm [for women] of Asian ethnicity)</li> <li>FG &lt;5.6 mmol/L</li> <li>HbA1c &lt;5.7%</li> <li>SBP &lt;130 and DBP &lt;80 mmHg</li> <li>TG &lt;1.52 mmol/L</li> </ul>
Stage 1	No subclinical or clinical ASCVD, HF, or AF	No evidence of CKD	<ul> <li>Any of the following:</li> <li>Presence of overweight or obesity (ie, BMI ≥23 kg/m² or WC ≥90 cm [for men] or ≥80 cm [for women] of Asian ethnicity</li> <li>FG ≥5.6 and ≤6.9 mmol/L</li> <li>HbA1c ≥5.7% and ≤6.4%</li> </ul>
Stage 2	No subclinical or clinical ASCVD, HF, or AF	<ul> <li>CKD with any of the following stages:</li> <li>CKD stage 3 with normoalbuminuria (UACR &lt;3 mg/mmol)</li> <li>CKD stages 1-3a with moderately increased albuminuria (UACR 3-30 mg/mmol)</li> <li>CKD stages 1-2 with severely increased albuminuria (UACR &gt;30 mg/mmol)</li> </ul>	<ul> <li>Any of the following:</li> <li>Diabetes</li> <li>Hypertension (SBP ≥130 mmHg and/or DBP ≥80 mmHg or use of antihypertensive medications)</li> <li>TG ≥1.52 mmol/L</li> <li>Presence of metabolic syndrome, defined as three of five abnormalities (elevated WC, TG, BP, FG, and low HDL-C [&lt;1.0 mmol/L for men and &lt;1.3 mmol/L for women])</li> </ul>
Stage 3	<ul> <li>Any of the following:</li> <li>Subclinical ASCVD</li> <li>Presence of coronary artery calcification on CT angiography or coronary catheterisation</li> <li>Subclinical HF</li> <li>NT-proBNP ≥125 pg/mL</li> <li>hsTrop ≥22 ng/L (men) or 14 ng/L (women)</li> <li>Findings on echocardiography</li> <li>High predicted 10-year CVD risk*</li> </ul>	<ul> <li>CKD with any of the following stages:</li> <li>CKD stage ≥4</li> <li>CKD stage 3b with moderately increased albuminuria (UACR 3-30 mg/mmol)</li> <li>CKD stage 3a with severely increased albuminuria (UACR &gt;30 mg/mmol)</li> </ul>	Presence of excess or dysfunctional adiposity, or metabolic risk factors
Stage 4	Clinical ASCVD (CHD, stroke, PVD), HF, or AF	<ul><li>Presence of any CKD</li><li>4a: without kidney failure</li><li>4b: with kidney failure</li></ul>	Presence of excess or dysfunctional adiposity, or metabolic risk factors

Abbreviations: AF = atrial fibrillation; ASCVD = atherosclerotic cardiovascular disease; BMI = body mass index; BP = blood pressure; CHD = chronic heart disease; CKD = chronic kidney disease; CKM = cardiovascular-kidney-metabolic; CT = computed tomography; CVD = cardiovascular disease; DBP = diastolic blood pressure; FG = fasting glucose; HbAIc = glycated haemoglobin; HDL-C = high-density lipoprotein cholesterol; HF = heart failure; hsTrop = high-sensitivity troponin T; NT-proBNP = N-terminal pro B-type natriuretic peptide; PVD = peripheral vascular disease; SBP = systolic blood pressure; TG = triglyceride; UACR = urine albumin-to-creatinine ratio; WC = waist circumference

\* Risk determined using the PREVENT (American Heart Association Predicting Risk of Cardiovascular Events) equation<sup>6</sup>

For adults aged  $\geq 21$  years, this includes annual measurements of body mass index (BMI) and waist circumference, along with periodic assessments of blood pressure (BP), lipid levels, and glycaemic status. Screening intervals depend on CKM stage: every 3-5 years for CKM stage 0 (healthy and lean), every 2-3 years for CKM stage 1 (overweight/obese or prediabetes), and annually for CKM stage 2 (diabetes, hypertension, or hypertriglyceridaemia).<sup>1</sup> These recommendations align with the American Diabetes Association's guidance that asymptomatic adults aged  $\geq 35$  years, or overweight/obese adults with risk factors—such as physical inactivity, family history of diabetes, hypertension, high triglyceride

levels, or polycystic ovarian syndrome—undergo screening for prediabetes or diabetes every 3 years if no abnormalities are detected.<sup>13</sup> The need for triglyceride screening remains unclear, and discussions continue regarding BMI thresholds for overweight/obesity in Asian populations.<sup>14</sup>

The CDCC Pilot Scheme, launched by the Hong Kong SAR Government in November 2023, offers subsidised screening in the private sector for residents aged  $\geq$ 45 years without known diabetes or hypertension.<sup>15</sup> Initial assessments include BP and glycated haemoglobin), with follow-up tests (lipid profile, estimated glomerular filtration rate [eGFR], urinalysis) if hypertension or diabetes is detected.

Blood pressure thresholds for hypertension vary across guidelines.<sup>16,17</sup> The HKCP previously endorsed defining hypertension as BP  $\geq 140/90$  mmHg<sup>18</sup>; the CKM framework utilises a lower threshold of 130/80 mmHg based on recent evidence. Home BP monitoring and standardised office BP measurements are both acceptable. Early detection of CKM risk factors aligns with the Primary Healthcare Blueprint,<sup>19</sup> which promotes chronic disease prevention through a family-centric, communitybased primary care system. A key concept, "family doctor for all," aims to enhance public access to care, including screening and diagnosis of prediabetes, early diabetes, and hypertension via coordination with family doctors in the Primary Care Register. Timely screening and intervention can reduce complications such as CKD, cardiovascular disease (CVD), and hospitalisations.

### Roles of physician specialists and primary care doctors in the cardiovascular-kidneymetabolic health framework

The increasing incidence of kidney failure and growing healthcare burden of CKD, which now affects 10% of the global population, have made CKD an international health priority. Nephrologists play a central role in managing individuals across CKM stages. Chronic kidney disease substantially increases risks of cardiovascular morbidity and mortality; many patients, especially those aged  $\geq 75$ years, die of CVD before exhibiting kidney failure or requiring dialysis.<sup>20</sup> Among dialysis patients in Hong Kong, CVD and stroke caused 30.3% of deaths in 2022.<sup>21</sup> Diabetes or hypertension was the primary diagnosis for 63% of patients initiating kidney replacement therapy. Early CKD detection, particularly in at-risk individuals, allows preventive measures during asymptomatic stages. Primary care doctors are needed to identify and manage these individuals.

Cardiovascular risk factors, including CKD, often remain unrecognised until disease becomes clinically apparent. The CKM staging system prioritises early detection of cardiovascular risk factors, recommending eGFR and urine albumin-tocreatinine ratio assessments for at-risk individuals. such as those with hypertriglyceridaemia, metabolic syndrome, diabetes, hypertension (stage  $\geq 2$ ), or clinical CVD. Indeed, evaluation of albuminuria should also be considered in CKM stage 1, characterised by obesity or dysfunctional adiposity, which manifests as prediabetes-both risk factors for CKD.<sup>22,23</sup> These recommendations aim to improve kidney health awareness and promote CKD screening among primary care doctors, family physicians, and specialists, who are often the first to encounter patients in early stages of CKM.

The Predicting Risk of CVD Events

(PREVENT) equation from the American Heart Association is recommended to assess 10-year CVD risk in asymptomatic individuals without ASCVD or HF. This tool estimates overall CVD risk and guides preventive therapy initiation.<sup>6</sup> Caution is needed because the equation may overestimate risk in individuals of Asian descent.24,25 The PREVENT equation is preferred over the Pooled Cohort Equations<sup>26</sup> in the CKM framework<sup>27</sup> because it includes CKM-specific factors that constitute novel CVD risk factors. Although the social deprivation index is specific to the United States, the inclusion of socioeconomic background during CVD risk estimation is relevant in Hong Kong. The risk score can be calculated using the online tool provided by the American Heart Association.<sup>28</sup> The PREVENT equation, designed for primary prevention in individuals aged 30-79 years without coronary heart disease, stroke, or HF, helps tailor patient-centred preventive therapies according to guidelines.<sup>26,29</sup>

Coronary artery calcium (CAC) testing is recommended for further CVD risk stratification and statin use guidance during primary prevention.<sup>26,27</sup> However, routine CAC testing is not advised in Hong Kong for CKM screening or staging due to concerns about increased downstream testing and the lack of a structured follow-up programme. When CAC results are available, even for asymptomatic individuals, they should inform CKM staging and guide therapies following established guidelines.<sup>26,27,29</sup>

The CKM framework proposes testing for B-type natriuretic peptide (BNP),<sup>27</sup> N-terminal pro-BNP, or high-sensitivity troponin in at-risk individuals to detect subclinical HF.27 Although two randomised studies demonstrated the utility of this approach for guiding renin-angiotensin-aldosterone system-modifying agent therapy,<sup>30,31</sup> routine cardiac biomarker testing in asymptomatic individuals is not recommended within Hong Kong. Angiotensinconverting enzyme inhibitors (ACEi) are already recommended as first-line therapy, particularly for patients with diabetes,32 and local cost-effectiveness data are unavailable. Furthermore, it can be challenging to interpret BNP, N-terminal pro-BNP, and troponin levels in moderate to advanced CKD (a component of CKM syndrome) due to renal excretion of these biomarkers. When available, cardiac biomarker data should be considered for management of HF medications with proven benefits, even in asymptomatic individuals.<sup>33</sup>

### **Prevention of complications**

The CKM health framework prioritises identifying and treating CKM risk factors during the preclinical phase to prevent clinical ASCVD, AF, HF, and kidney failure. Locally, patients with hypertension and diabetes in General Out-patient Clinics undergo regular screening for complications through the RAMP (Risk Assessment and Management Programs) for Hypertension and Diabetes, respectively.<sup>34,35</sup> Patients with diabetes in public hospital clinics also undergo regular complications screening, including cardiovascular risk assessments, urine albumin-to-creatinine ratio testing, and, in some centres, vascular Doppler studies.<sup>34,35</sup> In the private sector, the Health Bureau of Hong Kong has established Reference Frameworks<sup>36,37</sup> for diabetes and hypertension care, highlighting the importance of regular diabetic complications screening.

The incidences of CKD, metabolic diseases, and obesity are rising, even in younger individuals; greater emphasis on CKD prevention is needed, particularly regarding screening methods and timing. The CKM framework recommends CKD screening before age 21 among individuals with risk factors such as obesity, hypertriglyceridaemia, diabetes, or hypertension. Although not widely adopted locally, the HKCP supports earlier CKD detection to improve kidney survival and quality of life.<sup>38</sup> Screening gaps exist for albuminuria in high-risk groups, including overweight or obese individuals and those with clinical CVD.

Because most patients in early stages of CKM are asymptomatic, primary care and family doctors play a central role in ensuring regular follow-up. This role includes monitoring glycaemic status, lipid profiles, and BP, along with surveillance for CKM complications, such as CKD progression or clinical CVD.

## Clinical management: an interdisciplinary care model in Hong Kong

The НКСР supports the guideline-directed management approach in the CKM health framework, although anthropometric thresholds for interventions slightly differ due to population variations. The BMI threshold for metabolic and bariatric surgery was recently updated to  $\geq 27.5 \text{ kg/m}^2$ for Asian populations.<sup>39</sup> This threshold also applies the use of glucagon-like peptide-1 receptor agonists (GLP1RAs) for obesity treatment in patients with type 2 diabetes, aligning with the World Health Organization's recommended BMI action point for high-risk individuals in Asian populations.<sup>40</sup> If pharmacotherapy cost constraints are addressed, the threshold could be lowered to  $\geq 25$  kg/m<sup>2</sup>, as indicated in some Asian guidelines.41 In Hong Kong, access to newer CKM pharmacotherapies is limited. Among GLP1RAs approved for managing obesity in individuals without diabetes, only daily liraglutide is currently available, whereas weekly semaglutide is not. Icosapent ethyl, an omega-3 fatty acid treatment for hypertriglyceridaemia, is unavailable in the public sector. The CKM framework recommends initiating cardioprotective

antidiabetic agents regardless of glycaemic control, even before metformin in individuals with glycated haemoglobin level <7.5%. However, affordability and patient preferences may impact implementation. Glycaemic control optimisation remains essential because early and effective control improves cardiorenal outcomes and reduces mortality.<sup>42</sup> Notably, statin pharmacokinetics differ between Chinese and Western populations<sup>43,44</sup>; rosuvastatin dosages should not exceed 20 mg daily in Chinese individuals due to rhabdomyolysis risk.

In CKM stage 4 (established CVD), recurrent cardiovascular event risk is high, but many patients fail to achieve the recommended low-density lipoprotein cholesterol target of <1.8 mmol/L.45 Identification of high-risk individuals and intensification of lipid-lowering therapy with high-intensity statins, ezetimibe, and proprotein convertase subtilisin/ kexin type 9 inhibitors are needed to achieve therapeutic goals.<sup>26</sup> In patients with HF, particularly those exhibiting reduced left ventricular ejection guideline-directed medical therapy fraction, (GDMT) classes-beta-blockers, angiotensin receptor blockers (ARBs)/neprilysin inhibitors, sodium-glucose co-transporter 2 inhibitors, and mineralocorticoid receptor antagonists-should be initiated and titrated appropriately.33 Among patients with AF exhibiting CKM syndrome and stroke risk factors, anticoagulation is advised.46 Comorbidities such as severe obesity and CKD should be carefully considered because they may influence direct oral anticoagulant efficacy.

Patients across all CKD and CVD stages<sup>47</sup> should be evaluated for kidney-protective therapies, many of which also provide cardiovascular benefits. These include ACEi or ARBs, sodium-glucose co-transporter 2 inhibitors, GLP1RAs, and the nonsteroidal mineralocorticoid receptor antagonist finerenone, as appropriate. Most patients should receive an ACEi or ARB at the maximum tolerated dose, with additional agents introduced based on individual needs and tolerability. Goals include optimising BP, reducing albuminuria, stabilising eGFR, and lowering cardiovascular risk. Some therapies may cause short-term haemodynamic effects on kidney function or adverse effects, leading to premature discontinuation. The CKM framework emphasises initiation and maintenance of these therapies. The HKCP supports their timely uptake and continued use by specialists and primary care physicians.

Implementation of the CKM health framework in Hong Kong faces challenges, including discrepancies in drug formularies between primary care and specialty clinics and inadequate coordination between these services. Patients are sometimes referred to specialty clinics solely for medications unavailable in primary care. Such referral increases waiting times at overburdened specialty clinics and delays GDMT initiation. Follow-up intervals may be extended due to heavy patient loads, impacting treatment adherence and monitoring. The CDCC Pilot Scheme provides targeted subsidies to support the diagnosis and management of chronic diseases, particularly hypertension and diabetes, in the private sector. This co-care model aims to benefit patients across various CKM stages and mitigate complications.

### Conclusions and the way forward

Cardiovascular-kidney-metabolic syndrome has substantial implications for patients and society. The HKCP emphasises the need for collaborative interdisciplinary care within the CKM healthcare framework, integrating primary care, specialist care, and medical subspecialties to prevent complications and protect organs. Although GDMT ensures evidence-based care, clinicians must tailor management to the unique characteristics of each patient, addressing gaps in trial data and local applicability. Conditions such as hyperglycaemia, dyslipidaemia, obesity, kidney insufficiency, and hypertension should not be viewed as "risk factors" but as chronic conditions requiring early intervention to prevent CVD and CKD. Kidney health is central to CKM syndrome, given the high prevalence of kidney failure among patients with diabetes or CVD.

Considering the strengths and limitations of the local healthcare system (Table 2), multiple actions are needed to mitigate the increasing impact of CKM syndrome. The public and healthcare professionals must be educated regarding its adverse effects and access to effective interventions. Integrated care across primary and specialist services is essential, supported by healthcare policy focusing on organ protection to ensure coordination, minimise duplication, and optimise resource use. A collaborative care model involving all stakeholders and providers is essential. The HKCP hopes this position statement will raise awareness and prompt timely strategies to address the growing challenges of CKM syndrome, ultimately improving cardiovascular, metabolic, and kidney health in the community.

TABLE 2. Strengths and limitations of the current Hong	g Kong health system for implementin	g the cardiovascular-kidney-metabolic health framework

Domains of CKM health	Strengths	Limitations
Cardiovascular	<ul> <li>Regular screening for complications, including cardiovascular risk factors, is available for patients with hypertension and diabetes under RAMP-HT and RAMP-DM in the public sector</li> <li>The Reference Framework formulated by the Health Bureau of Hong Kong promotes regular screening for complications in patients with diabetes and hypertension</li> <li>ACEis are already recommended as first-line medications, particularly for patients with diabetes</li> </ul>	<ul> <li>Routine coronary artery calcium testing is not recommended for asymptomatic individuals</li> <li>Routine screening of cardiac biomarkers, such as BNP, NT- proBNP, or hsTrop, is not recommended for asymptomatic individuals</li> <li>Discrepancies in drug formularies exist between primary care and specialty clinics in the public sector</li> <li>Follow-up intervals for monitoring treatment adherence are often prolonged in the public sector</li> </ul>
Kidney	<ul> <li>Regular screening for complications, including eGFR and UACR measurements, is available for patients with hypertension and diabetes under RAMP-HT and RAMP-DM in the public sector</li> <li>The Reference Framework formulated by the Health Bureau of Hong Kong promotes regular screening for complications in patients with diabetes and hypertension</li> </ul>	<ul> <li>There is a notable service gap in screening for albuminuria among high-risk patients, including overweight/obese individuals and those with clinical CVD</li> <li>Discrepancies in drug formularies exist between primary care and specialty clinics in the public sector</li> <li>Follow-up intervals for monitoring treatment adherence are often prolonged in the public sector</li> </ul>
Metabolic	<ul> <li>The vision of "family doctor for all" in the Primary Healthcare Blueprint aims to improve screening and diagnosis of metabolic dysfunction through community coordination and networking with matched family doctors in primary care</li> <li>The launch of the Chronic Disease Co-Care Pilot Scheme provides subsidised diabetes and hypertension screening services for local residents aged ≥45 years</li> </ul>	<ul> <li>Screening for elevated triglyceride levels is less established but often included in lipid profile testing</li> <li>Some newer pharmacotherapies for CKM health (eg, semaglutide 2.4 mg weekly to treat obesity in individuals without diabetes, icosapent ethyl) are either not registered locally or not widely available in the public sector</li> <li>Access to some antidiabetic agents (eg, SGLT2is, GLP1-RAs) is limited by patient affordability and preference</li> <li>Differences in pharmacokinetics between Chinese and Western populations (eg, statins) must be considered</li> <li>Discrepancies in drug formularies exist between primary care and specialty clinics in the public sector</li> <li>Follow-up intervals for monitoring treatment adherence are often prolonged in the public sector</li> </ul>

Abbreviations: ACEis = angiotensin-converting enzyme inhibitors; BNP = B-type natriuretic peptide; CKM = cardiovascular-kidney-metabolic; CVD = cardiovascular disease; eGFR = estimated glomerular filtration rate; GLPI-RAs = glucagon-like peptide-I receptor agonists; hsTrop = high-sensitivity troponin T; NT-proBNP = N-terminal pro B-type natriuretic peptide; RAMP-DM = Risk Assessment and Management Program for Diabetes; RAMP-HT = Risk Assessment and Management Program for Hypertension; SGLT2is = sodium-glucose co-transporter 2 inhibitors; UACR = urine albumin-to-creatinine ratio

### Author contributions

Concept or design: SCW Tang and TM Chan. Acquisition of data: CHL, G Tan and SCW Tang. Analysis or interpretation of data: CHL, G Tan, SCW Tang and TM Chan. Drafting of the manuscript: CHL, G Tan and SCW Tang.

Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

### **Conflicts of interest**

CH Lee has received advisory board and lecture honoraria from AstraZeneca, Bayer, Boehringer Ingelheim, Eli Lilly, Gilead, GSK, Novo Nordisk, and Sanofi Aventis. SCW Tang has reported consulting fees from Boehringer Ingelheim, Novartis, and Travere Therapeutics, as well as speaker fees from AstraZeneca, Baxter, Bayer, Boehringer Ingelheim/ Eli Lilly, GSK, and Novartis. The other co-authors have no competing interests relevant to this manuscript.

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