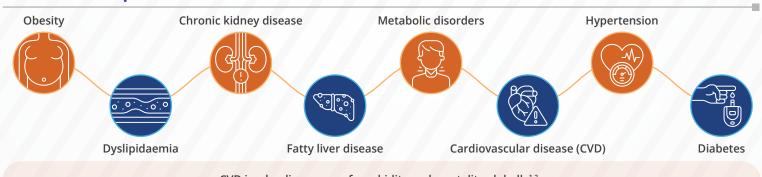


Hypertension, Dyslipidaemia, and Cardiometabolic Disease – Insights on Pathophysiology, Interplay, and Therapeutic Management

Understanding the association between hypertension, dyslipidaemia, and cardiometabolic disease in the Asia Pacific region

Lifestyle-related diseases are tightly interlinked through complex and synergistic mechanisms, ultimately leading to cardiovascular complications<sup>1</sup>



CVD is a leading cause of morbidity and mortality globally<sup>1,2</sup>

Hypertension and dyslipidaemia are independent and well-established risk factors of CVD2

Treatments targeting hypertension and dyslipidaemia have demonstrated a reduction in the subsequent risk of CVD and associated mortality<sup>2</sup>



However, the mortality rate continues to remain high, underscoring the need for comprehensive risk assessment and treatments that address multiple risk factors

Understanding the interplay between hypertension, dyslipidaemia, and metabolic dysfunction in the development of CVD can aid improved therapeutic management

#### Uncontrolled hypertension is characterised by excessively high blood pressure (BP) levels<sup>2,3</sup>

Systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg





Family history of hypertension

## Non-modifiable risk factors<sup>3</sup>

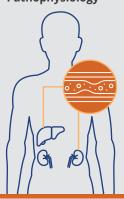


Presence of other comorbidities including diabetes and chronic kidney diseases



Age >65 years

### Pathophysiology<sup>4</sup>



#### **Altered renal function**

- Higher sodium retention
- Increased release of renin (an enzyme that activates the renin-angiotensin system)
- Altered pressure diuresis and natriuresis
- Modulation of systemic sympathetic tone and enhanced renal afferent nerve traffic
- Immune activation

## Vascular perturbations

- Systemic vascular resistance
- Increase in angiotensin II, catecholamines, and vasopressin → enhanced vasoconstriction and diminished vasodilation
- Endothelial dysfunction and impaired vasodilation
- Reduced nitric oxide (vasodilator) bioavailability
- Vascular stiffening
- Immune activation and thrombosis

# Central nervous system alterations

- Sympathetic neural activation
- Enhanced renal sodium resorption and inflammation
- Altered vagal activity and defective immune reflex

Inappropriate activation of the renin-angiotensin-aldosterone system and sympathetic nervous system

Oxidative stress

Diabetic nephropathy

Arterial stiffness

Inflammation

Mitochondrial dysfunction

Enhanced renal and endothelial sodium channel activation

Abnormal release of extracellular vesicles and related microRNAs

## Obesity-induced hypertension4,5



Afferent nerve stimulation in the adipose tissue triggered by a high-fat diet increases BP and insulin resistance

#### Dyslipidaemia and hypertension<sup>2,4,5</sup>

Dyslipidaemia is characterised by alterations in the plasma lipid profile

- Total cholesterol



Triglycerides



Low-density lipoprotein cholesterol (LDL-C)



High-density lipoprotein cholesterol (HDL-C)

- Endothelial dysfunction
- Increase in atherosclerosis
- Arterial stiffening
- Enhanced vasoconstriction
- · Increased lipid oxidation and generation of reactive oxygen species
- Heightened risk of ischaemic heart disease and stroke

#### Cardiometabolic syndrome represents a group of metabolic abnormalities associated with an elevated CVD risk5.6.7



Abdominal obesity (high body mass index and/or large waist circumference)



Insulin-resistant glucose metabolism (hyperinsulinaemia, impaired fasting glucose, impaired glucose tolerance, type 2 diabetes)



Dyslipidaemia (high serum triglyceride and low serum HDL-C concentrations)



Increased BP

## Guidelines for hypertension and dyslipidaemia management<sup>8</sup> Non-pharmacological interventions Reduction in **Dietary modifications** Reduction in alcohol Weight loss and caloric restriction consumption salt intake KG Reduction or cessation Reduction in caffeine Improvements in of smoking consumption physical activity **Pharmacological interventions for hypertension** Angiotensin-converting enzyme inhibitors - captopril, enalapril, lisinopril, perindopril, ramipril Angiotensin receptor blockers - candesartan, losartan, olmesartan, telmisartan, valsartan Beta blockers - atenolol, bisoprolol, carvedilol, metoprolol, nebivolol, propranolol Alpha blockers - doxazosin, prazosin Calcium channel blockers - amlodipine, cilnidipine, lercanidipine, nifedipine Diuretics - bendroflumethiazide, chlorthalidone, chlorothiazide, hydrochlorothiazide, indapamide Mineralocorticoid receptor antagonists - eplerenone, spironolactone A combination of two or more drugs may be used in individuals with high initial BP or a high CVD risk **Lipid-lowering agents Statins** Cholesteryl ester transfer protein inhibitors Ezetimibe Fish oils **Fibrates** Nicotinic acid Proprotein convertase subtilisin/kexin type 9 inhibitors Drug costs Medication adherence

Barriers to effective hypertension and dyslipidaemia

management<sup>8,9,10</sup>

Asymptomatic disease

Perceived side-effects

Healthcare access in low-resource settings

Health insurance and reimbursements/coverage

Therapeutic inertia or lack of treatment

Suboptimal awareness and undertreatment

intensification

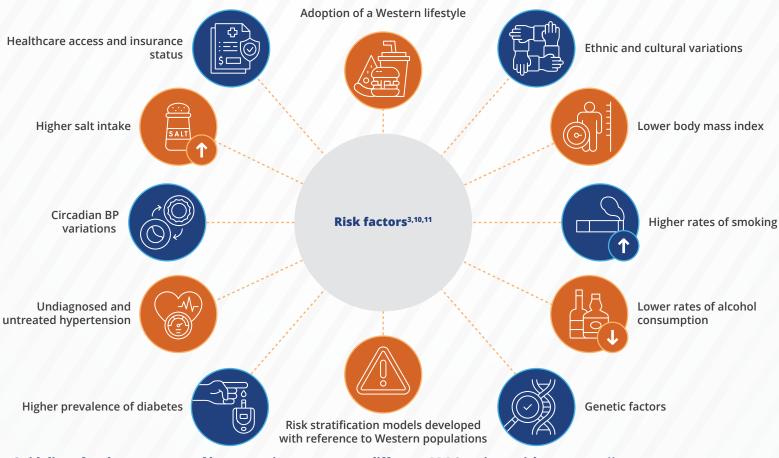


APAC countries account for a major proportion of the global population<sup>10</sup>



However, treatment guidelines for the management of hypertension and dyslipidaemia are largely based on data derived from non-Asian populations<sup>10,11</sup>

## CVD risk varies considerably for individuals from APAC countries compared to their Western counterparts



Guidelines for the treatment of hypertension vary across different APAC regions with respect to<sup>11</sup>:



Threshold for diagnosis

Threshold for treatment

Target BP

A unified pan-Asian guideline can help streamline patient care and optimise the management of hypertension

#### **Key message**

Regular monitoring of BP and blood glucose, risk assessment, lifestyle modifications, and comprehensive therapeutic management can help reduce cardiovascular complications and associated mortality

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