



The burden of chronic kidney disease in Asia region: a review of the evidence, current challenges, and future directions

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The disease burden of chronic kidney disease (CKD) and its impact on healthcare systems has been poorly studied in Asia, a socio-economically diverse region with wide variations in availability, access, and quality of CKD care. The high CKD burden in this region is predominantly driven by an increased prevalence of risk factors including diabetes mellitus, hypertension, obesity, and use of traditional medicines and is further aggravated by challenges associated with effective implementation of population-based screening and surveillance systems in early detection and intervention of CKD. The Asian continent mostly comprised of low- and middle-income countries with resource restraints lacks robust population-based CKD registries resulting in a paucity of data on CKD incidence and prevalence, various treatment modalities, uptake of current guidelines, and the overall impact of implementation of developmental programs. There is an urgent need for a collaborative action plan between the healthcare community and governments in this region to detect CKD in its early stages and prevent its complications including kidney failure, cardiovascular disease, and death. Research-based evidence on the impact of early detection, sustainable treatment options, quality of life, delay or avoidance of dialysis, and related cost analysis is the need of the hour. We highlight successful implementation of strategic and policy-sharing programs adopted in a few countries; also, consolidate available region-specific data, quantify estimates of CKD burden and propose strategies with a multidisciplinary approach involving patients, the healthcare community and governmental bodies to combat CKD and its complications.

Keywords: Asia, Chronic renal insufficiency, Prevalence, Risk factors

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Introduction

Chronic kidney disease (CKD) with a global prevalence of 13.4%, is a major contributor to morbidity and mortality due to noncommunicable diseases [1]. It is the 12th leading cause of death worldwide and is projected to be the 5th leading cause of death by 2040 [2–4]. CKD is an independent predictor of premature mortality, increased hospitalization, economic burden on patients, payers, healthcare infrastructure, and reduced quality of life [5,6]. In 2016, an estimated 1.2 million persons died due to CKD, and it is forecasted that approximately 2.2 to 4.0 million lives will be lost to CKD by 2040 [7]. The change in the burden of CKD from 1990 to 2016 in terms of incidence, prevalence, death, and disability-adjusted life years (DALYs) showed an alarming rise with CKD incidence increasing by 89%, prevalence by 87%, death due to CKD by 98%, and DALYs by 62% [8]. This trend is driven by increased incidences of type 2 diabetes mellitus (T2DM), hypertension (HTN), and obesity in an increasing age population worldwide.

CKD is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health. Glomerular filtration rate (GFR) is a gold standard marker for kidney function. Decreased GFR (60 mL/min/1.73 m²) for >3 months indicates CKD while renal failure is defined as GFR <15 mL/min/1.73 m². CKD is associated with an elevated risk of developing cardiovascular disease (CVD) [6]. Asia has one of the highest CKD prevalence rates worldwide and is currently witnessing an exponential rise in the incidence of diabetes mellitus (DM) and HTN [9]. The Asian continent mostly consists of low- and middle-income countries that have resource restraints with a lack of robust population-based CKD registries resulting in a paucity of data on CKD prevalence, disease burden, and the overall impact of implementation of developmental programs.

This review aims to provide a comprehensive updated overview of the region-specific prevalence and disease burden of CKD in Asia. It also describes the challenges and unmet medical needs unique to this region with diverse socioeconomic and cultural backgrounds. It also aims to provide strategies and guidance for CKD management amidst diversity of the region, providing a platform for regional policy makers to bring healthcare improvement in patients with CKD.

Methodology

A three-step process was implemented for preparing a comprehensive review on the burden of CKD in Asia (Fig. 1). A comprehensive and extensive literature review was conducted to consolidate data as available in the public domain on CKD prevalence and disease burden in Asia (defined as countries in Eastern, Southern, and Southeastern Asia, Asia Pacific excluding Australasian countries). In November 2022, a steering committee meeting consisting of 10 experts from Hong Kong, India, Indonesia, Republic of Korea, Malaysia, the Philippines, Singapore, Taiwan, Thailand, and Vietnam, was convened to review the regional burden, evaluate the role of risk factors on incidence and progression of CKD, and the unmet needs and challenges unique to Asia. The committee aimed to outline region-specific guidance strategies in the early

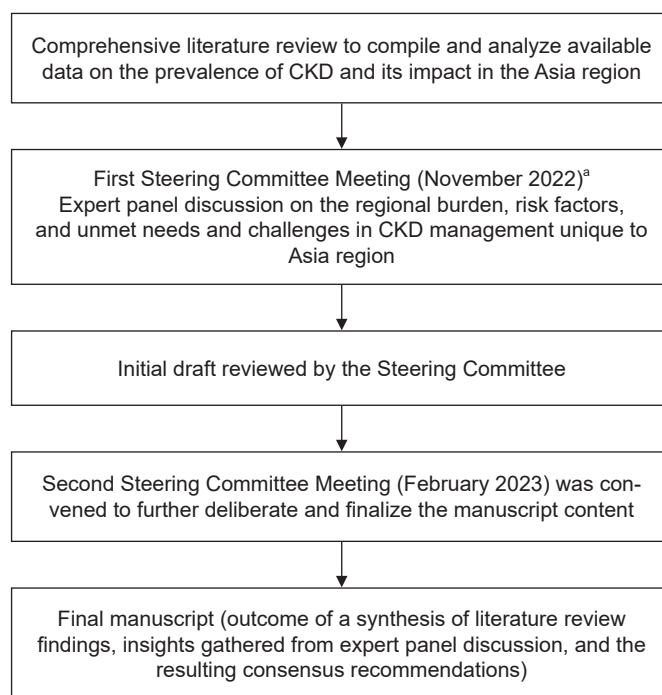


Figure 1. Steering Committee composition and methodology for the development of manuscript.

CKD, chronic kidney disease.

^aSteering Committee comprised of 10 nephrology specialists representing a diverse array of countries including Hong Kong, India, Indonesia, Malaysia, the Philippines, Republic of Korea, Singapore, Taiwan, Thailand, and Vietnam.

detection of CKD and retardation of its progression by implementing effective screening, surveillance programs, and guideline-driven management. The expert panel provided an update on the current CKD screening, surveillance, and management practices and discussed the successful implementation of strategic programs adopted in their respective countries. These strategies incorporated current evidence and adapted to the local healthcare framework.

Comprehensive nonsystematic literature search of the MEDLINE and EMBASE databases using combinations of the key terms: “chronic kidney disease,” “CKD,” “prevalence and disease burden,” “Asia,” “Asia Pacific,” “diabetic kidney disease,” “risk factors” was done. Articles published before the year 2000 were excluded. The panel critically reviewed the published literature and provided a country-specific update on factors impacting the care continuum of CKD in their countries such as commonly used screening methodologies, identification of target population for screening and monitoring, availability of dialysis resources, newer therapeutic agents, healthcare reimbursement policies and patient education strategies and programs. Although mainland China and Japan were included in the evidence review, the disease burden data reported in this manuscript and the strategies and future directions suggested by the panel are specific to the 10 countries represented by the participating experts.

Regional prevalence and disease burden of chronic kidney disease across Asia

There is a substantial variation in the prevalence of CKD between countries in the Asia region that ranges between 7.0% and 34.3% [10]. An estimated 434 million people have CKD across Eastern, Southern, and Southeastern Asia of which 65 million are in advanced stages of CKD (stages 4–5) [10] between 1990 and 2019; all-age incident cases and CKD death counts more than doubled from 3.7 million (range, 3.4 million–4.0 million) to 9.8 million (range, 9.0 million–10.6 million) and 340,636 (316,106–365,632) to 763,024 (696,050–823,829), respectively (Table 1) [9]. The years lived with disability ranged from 60 to <180 per 100,000, with the highest in Thailand, Malaysia, Singapore, and the Philippines. However, the years of life lost (YLLs) were similar in most of the countries in Asia region (400 to <600 per 100,000), with the exception of the Philippines with a YLL rate between 1,000 and 1,200 per 100,000 (Supplementary Fig. 1, available online) [11]. Most countries in Asia reported an increase of 100% or more in the absolute count of CKD incidents, prevalent cases, deaths, and DALYs between 1990 and 2019 [9].

There is a preponderance of CKD in younger age groups in Asian countries with more than 50% of prevalent cases seen in those below the age of 50 years [12,13]. The Indian Chronic Kidney Disease (ICKD) study, an ongoing compre-

Table 1. The country-wide burden of chronic kidney disease

Country	Prevalence ^a	Incidence	Death	DALYs ^a
China	150.5 (138.6–162.3)	3.1 (2.8–3.4)	0.2 (0.2–0.2) ^a	5.8 (5.0–6.6)
India	115.2 (106.6–124.2)	2.2 (2.0–2.4)	0.2 (0.2–0.3) ^a	7.5 (6.6–8.5)
Indonesia	25.9 (23.8–28.0)	0.4 (0.4–0.4)	0.04 (0.03–0.05) ^a	1.6 (1.4–1.9)
Japan	24.7 (23.1–26.4)	1.0 (0.9–1.1)	0.04 (0.03–0.05) ^a	0.8 (0.7–0.9)
Thailand	11.3 (10.5–12.1)	0.3 (0.3–0.3)	0.03 (0.02–0.03) ^a	0.7 (0.6–0.9)
Philippines	10.2 (9.5–11.1)	0.2 (0.2–0.3)	0.03 (0.03–0.04) ^a	1.1 (0.9–1.3)
Vietnam	10.0 (9.2–10.8)	0.2 (0.2–0.2)	0.02 (0.02–0.02) ^a	0.6 (0.5–0.7)
Republic of Korea	5.5 (5.2–5.8)	0.2 (0.2–0.2)	7,979 (6,931–8,864)	0.2 (0.2–0.2)
Taiwan	3.7 (3.5–3.9)	0.1 (0.1–0.1)	8,248 (6,512–10,329)	0.2 (0.2–0.3)
Malaysia	3.1 (2.9–3.4)	0.1 (0.1–0.1)	6,105 (4,867–7,450)	0.2 (0.2–0.2)
Singapore	0.7 (0.7–0.70)	0.02 (0.02–0.02)	758 (656–830)	0.02 (0.02–0.02)
Hong Kong			NA	

Data are expressed as mean (range). Countries are listed in descending order of prevalence.

DALYs, disability-adjusted life years; NA, not applicable.

^aData presented in millions.

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hensive evaluation of a nationwide cohort of patients with mild-to-moderate CKD found the cohort to be younger as compared to Western cohorts by 5 to 20 years. This trend is seen in other Asian cohorts as well with the exception of Japan [13]. Asia has a high population of patients with advanced CKD as the majority of patients with early stages remain undetected [14–19].

Burden of renal replacement therapy on patients, caregivers, and healthcare system

CKD results in an increased economic burden on the patient, attributable to multiple ambulatory visits, more frequent and longer hospitalizations, and higher treatment costs as a result of associated comorbidities. The health-related quality of life is significantly impacted in CKD patients and is inversely proportional to the stage of CKD, age, and socioeconomic profile of the patients [20,21].

Several estimates forecast the use of kidney replacement therapy (KRT) to more than double by 2030, with the largest increase seen in Asia [22]. The demography of the population requiring hemodialysis (HD) in Asia region differs from the west in two aspects namely the relatively younger age and the higher prevalence of CKD of unknown etiology

[23,24].

The incidence of treated kidney failure in Asian countries ranged from 525 per million population (pmp) (Taiwan) to 116 pmp (mainland China) [25–28] (Fig. 2).

Although most countries in Asia provide all three modalities of KRT—HD, peritoneal dialysis (PD), and kidney transplantation, there remains considerable variability in the availability and costs of treatment (Fig. 3A). A number of the countries have adequate access to KRT and comprehensive KRT registries except a few low- and low-to-middle income countries (Fig. 3B) [17]. The cost implications of KRT are significant, for both patients and healthcare systems. PD is a cost-effective option in this region and can be as low as one-third that of HD and thus has been promoted as the preferred choice in Hong Kong [17,29]. Countries like Japan, Republic of Korea, Hong Kong, and Taiwan have full coverage for KRT via national health insurance while others provide partial coverage with assistance from NGOs.

In China, there were approximately one million kidney failure patients in 2017 with only 52% on KRT [30]. HD is the predominant KRT modality, accounting for approximately 86% of dialysis patients [31]. From 2018 to 2021, overall kidney failure incidence and prevalence rates have increased from 164 to 197 pmp and 1,388 to 1,499 pmp,

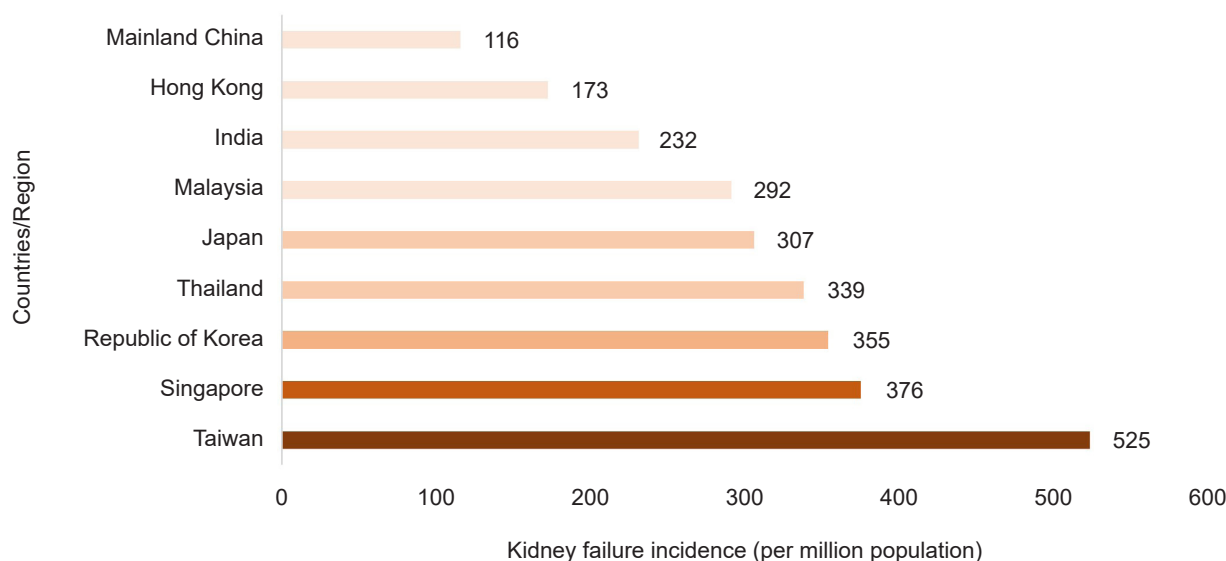


Figure 2. Incidence of kidney failure in the Asian region. The figure offers a comparative overview of the incidence of kidney failure (defined as glomerular filtration rate <15 mL/min/1.73 m²), highlighting the variation across Asian countries.

Data as of 2022; data unavailable from Indonesia, the Philippines, and Vietnam.

Reused from the United States Renal Data System (<https://adr.usrds.org/>) [25].

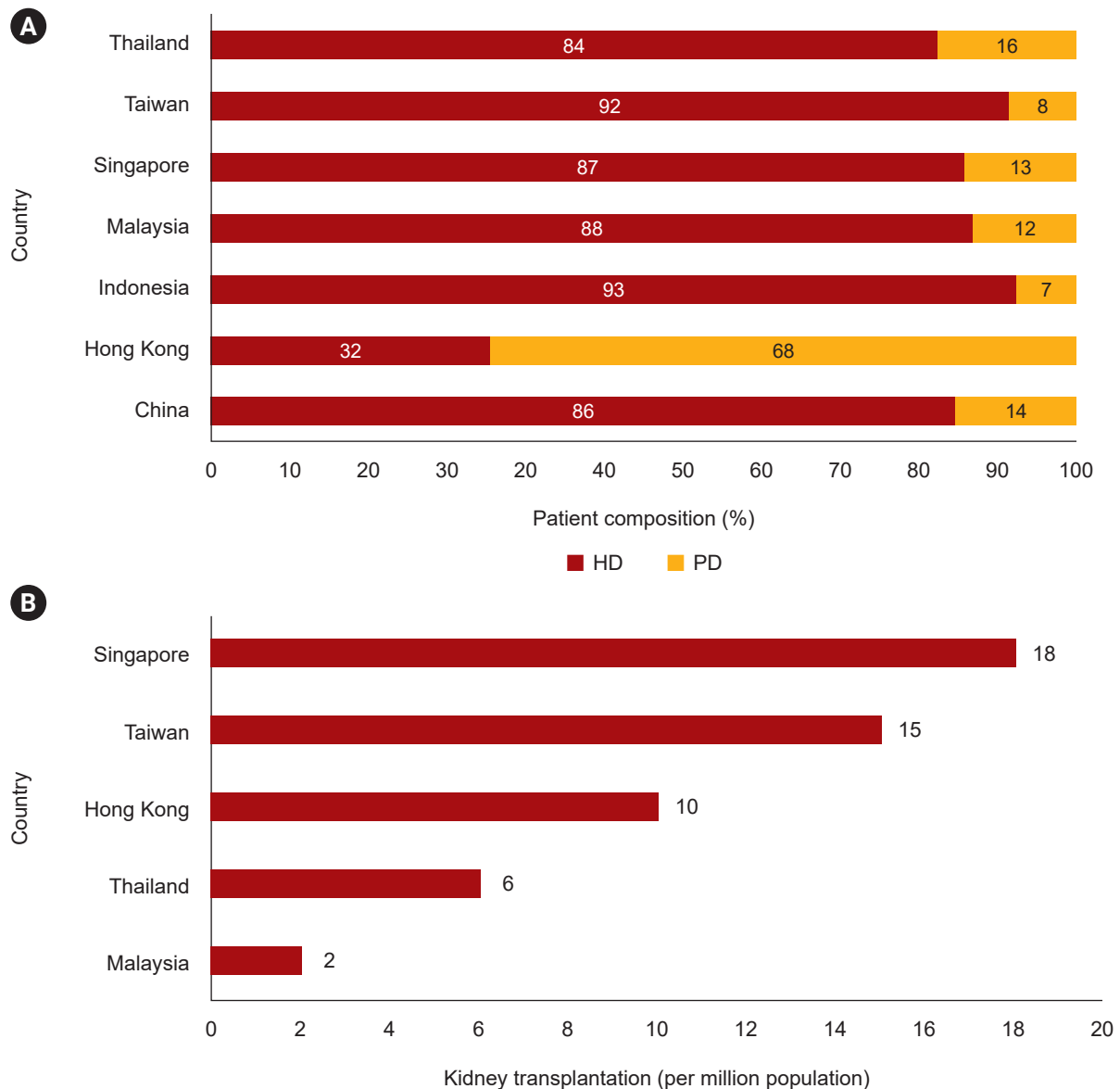


Figure 3. Trend in the utilization of kidney replacement modalities by country among patients with kidney failure. (A) Hemodialysis (HD) and peritoneal dialysis (PD). (B) Kidney transplantation. Most Asian countries showed a higher utilization of HD spanning from 84% to 93%. Notably, Hong Kong exhibited a greater preference for PD (68%).

Data as of 2022; data unavailable from Republic of Korea, the Philippines, India, and Vietnam.

Reused from the United States Renal Data System (<https://adr.usrds.org/>) [25].

respectively. In the Philippines, although a PD-first policy was implemented, it was less successful and HD continues to be the most common modality of KRT [32]. In Vietnam, though there is a paucity of data on the number of patients with kidney failure in need of dialysis, it is estimated to be over 100,000 persons with approximately 30% on HD [33]. In Indonesia, HD continues to be the KRT of choice,

however, initiatives are underway to increase the uptake of PD to reduce costs [34]. In Malaysia, there is a PD-first policy within the Ministry of Health centers but overall in the country, 85.2% of kidney failure patients are on HD and only 11.2% on PD [19]. A population-based study in India reported the crude- and age-adjusted kidney failure incidence rates as 151 and 232 pmp, respectively [35,36]. How-

ever, only 175,000 and 8,500 people were receiving HD and PD, respectively, as per a survey conducted in 2018 [37,38]. Since most of the HD facilities are located in urban regions, home-based PD that can be self-administered by patients or caregivers is being advocated to be included as the first option KRT in policies in several Asian countries such as India, Indonesia, and Vietnam. Cost-utility and budget impact analyses from Thailand, China, Indonesia, Singapore, and Malaysia using real-practice dialysis data show PD as a cost-effective and sustainable form of initial treatment relative to HD from both governmental and patient perspectives [39–42].

In Thailand, over 0.1 million patients require dialysis [18,43,44] and >20,000 people with kidney failure need treatment with HD or PD every year. Its PD-first policy has saved the lives of nearly 50,000 kidney failure patients under the universal coverage scheme [45]. The economic burden of CKD is available for Singapore where the annual expenditure for dialysis accounts for USD 230 million [46,47] and Malaysia where the total annual expenditure on kidney failure by the public sector has grown 94% within a span of 7 years, from USD 405 million (purchasing power

parity [PPP]) in 2010 to USD 785 million (PPP) in 2016 [48].

Risk factors for chronic kidney disease and its progression in Asia

The risk factors associated with CKD can be classified as susceptibility factors that increase an individual's susceptibility to renal damage, initiating factors that directly initiate renal damage, and progression factors that worsen renal damage resulting in rapid decline of renal function (Fig. 4) [49].

DM and HTN are the more common risk factors of CKD in developed countries, whereas glomerulonephritis and unknown causes account for higher incidence of CKD in developing countries [23,50]. The prevalence of kidney failure is higher among men, despite a higher prevalence of CKD in women [51–53]. With considerable variation in CKD etiology, chronic glomerulonephritis (e.g., immunoglobulin A [IgA] nephropathy) continues to be the leading cause of CKD in several countries like Japan, China, and Thailand while infectious disease-related CKD or CKD of unknown origin (CKDu) are highly prevalent in certain

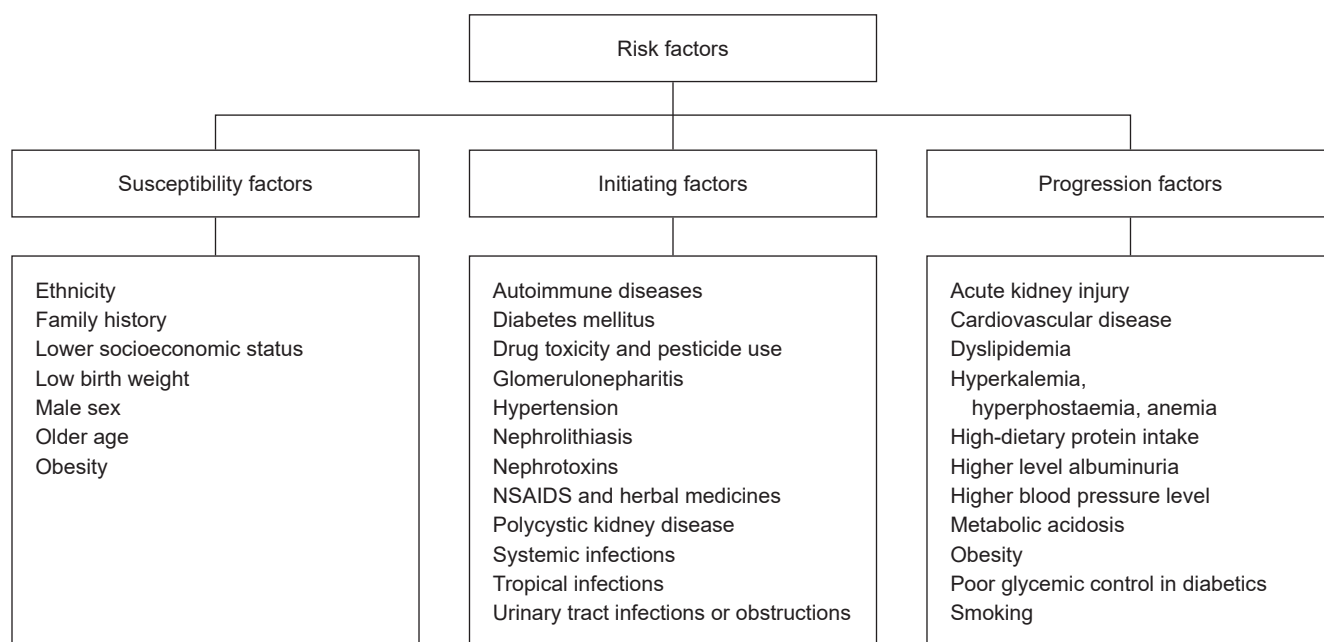


Figure 4. Risk factors for chronic kidney disease initiation and progression. Figure depicts the risk factors associated with the initiation and progression of chronic kidney disease that lead to exacerbation of kidney damage leading to a rapid decline in kidney function. NSAIDs, nonsteroidal anti-inflammatory drugs.

other parts of the region such as India [54–56].

Diabetes mellitus

The Global Burden of Disease Study of 2019 showed DM to be the cause of the majority of CKD incidence worldwide with Asia accounting for the highest prevalence of DM-CKD, especially in South and Eastern regions [57]. The prevalence of CKD in patients with DM ranged from 25% to 53% [19,58–65]. Though the prevalence of CKD in patients with DM is not reported, a high proportion of CKD has been reported in Philippines (35.9%) [66]. In Singapore, DM remains the leading cause of kidney failure in new patients starting dialysis, accounting for 68.2% of cases in 2019 [67]. Based on the recent 2021 registry data, diabetic nephropathy accounts for 66.9% of incident dialysis and 56.3% of prevalent dialysis in the Singaporean population [28].

Hypertension

Patients with CKD and HTN are at a higher risk of kidney failure than patients with blood pressure (BP) within normal limits [68]. A recent systematic review reports the overall prevalence estimate of HTN in the Southeast Asian urban population as 33.82% [69]. In a narrative review by Teo et al. [70], it was found that HTN-associated CKD, particularly in the Asia region, accounts for the largest proportion of CKD burden. The prevalence of HTN in the general population and in CKD patients are tabulated for Asian countries as available (Supplementary Table 1, available online) [14,19,43,70–75]. The overall prevalence of HTN among the adult population in 2013 was 25.2% in males from 29% in 2008, and 19.3% in females from 22%, while the prevalence of DM increased to 5.6% from 4% in males, and 5.3% from 5.5% in females. With the current population of the Philippines at 100 million, this represents a substantial population at risk for CKD. Notably, HTN is decreasing while DM is significantly increasing from 3% in 2003 to 5.4% in 2014.

Glomerulonephritis and immunoglobulin A nephropathy

IgA nephropathy, the most common form of primary glomerulonephritis (30%–40%) worldwide, is highly prevalent in the Asian population and is the leading cause of

CKD and subsequent kidney failure with a poor prognosis [54,55]. Patients of Asian descent diagnosed with IgA nephropathy tend to have a poorer prognosis and an increased risk of progression to kidney failure [76]. In a registry-based study on patients of Pacific Asian origin in North America with biopsy-proven idiopathic IgA nephropathy, the risk of renal failure (end-stage renal disease) was approximately 1.5 times higher along with a faster decline in estimated GFR (eGFR). The most common form of glomerulonephritis in Singapore is membranous glomerulonephritis; however, there is a rising prevalence of focal segmental glomerulosclerosis as well, similar to Malaysia, Thailand, and China [56]. In Indonesia, primary glomerulopathy (comprised of 8% of CKD patients) and autoimmune diseases (around 1% of CKD patients have systemic lupus erythematosus) are some of the significant risk factors for CKD [14]. According to the CKD registry of the Indian Society of Nephrology, glomerulonephritis is the second most common cause of CKD in India [13].

Lifestyle and environmental factors

Lifestyle factors, i.e., diet, physical inactivity, alcohol consumption, tobacco smoking, a higher salt intake, and obesity are major drivers for CKD. Numerous population-based studies have shown an association between obesity and development of proteinuria, decreased eGFR, and rapid progression of CKD [77,78]. Asia has seen an alarming rise in obesity [79,80]. High sodium diet is linked with an increased risk of acid reflux, high BP, and resistance to the effects of renin-angiotensin system (RAS) blockers which may contribute to kidney failure [81].

Epidemiological studies suggest a plausible link between exposure to ambient fine particulate matter PM_{2.5} and kidney disease [82].

Tropical diseases

Certain tropical diseases and conditions endemic to Asia can cause severe renal injury and complicate preexisting renal disease. Tropical infections such as malaria, leishmaniasis, leptospirosis, and dengue can involve the kidneys, varying from transient urinary abnormalities to severe acute kidney injury (AKI) [83,84]. It has been reported that a significant proportion of patients with no preexisting

kidney disease who recover from AKI develop CKD and patients with preexisting kidney disease suffer progression [85].

In Indonesia, Weil's disease and infections such as leptospirosis are known to contribute to CKD progression [86].

Indigenous medicines and chronic kidney disease of unknown origin

In South Asian countries such as Sri Lanka, Thailand, and India, CKDu is suspected to be due to the presence of environmental toxins (heavy metals, pesticides) in combination with factors such as heat stress, and underground water with high fluoride levels [87,88]. CKDu is distinct in the clinicopathologic characteristics with lower age group being commonly affected with minimal to no proteinuria. The disease progresses rapidly leading to stage 5 CKD needing KRT over a span of several months [87]. Regular use of certain herbal medicines has also been a documented cause of CKD in certain Asian populations. The use of aristolochic acid-containing herbs is responsible for the high prevalence of CKD in Taiwan [89]. Heavy metals (mercury) contained in traditional medicines can cause chronic poisoning, which can cause membranous nephropathy [90].

Anemia and electrolyte disturbances in chronic kidney disease

Anemia is a common complication that contributes to the disease burden of CKD [91]. It significantly increases the risk of morbidity and mortality in CKD patients particularly those with comorbidities of DM and/or HTN. The development of anemia in CKD patients is due to an absolute or relative deficiency of erythropoietin. Prevalence of anemia is higher in uncontrolled HTN than in well-controlled, suggesting that HTN is independently associated with increased anemia risk [92]. Hyperkalemia is a common finding in CKD which is associated with decreased renal ion excretion, as well as the use of some medications for CKD or DM and heart failure [93]. Hyperphosphatemia is common in CKD [94]. It has a significant effect on vascular calcifications, and the onset of the complex mineral and bone disorders associated with CKD, together with hypocalcemia and decreased 1-25(OH)₂ vitamin D levels

[92]. Similarly, metabolic acidosis occurs in about 20% of patients with CKD and contributes to CKD progression. Early intervention and correction of metabolic acidosis can impede the progression of CKD [95].

Acute kidney injury

AKI is a critical risk factor for CKD [96]. In a meta-analysis on the global burden of AKI, the incidence of AKI in the hospitalized population ranged from 11.6% to 31.0% [97–99]. The high prevalence of AKI in Asia is mostly due to the use of nephrotoxic medicines, exposure to environmental nephrotoxins, drug-induced AKI, and infections.

Existing framework for diagnosis and management of chronic kidney disease in Asia

Early detection of CKD is crucial for initiating timely therapeutic interventions, thereby delaying further progression and subsequently limiting the risk of long-term morbidity and mortality associated with the disease [51]. Despite the enormous health burden of CKD in Asian countries, only a few accepted guidelines are available for implementing effective screening and surveillance programs facilitating early identification of CKD in high-risk populations in this region.

Persistently elevated serum creatinine and albuminuria are important diagnostic and prognostic biomarkers of CKD. For initial assessment, measurement of eGFR using serum creatinine is considered the gold standard because of its affordability, easy accessibility, and long history of clinical use. Estimating equations for eGFR measurement such as Chronic Kidney Disease Epidemiology Collaboration (CKD EPI) and Modification of Diet in Renal Disease (MDRD) are widely accepted across the Asian region in routine clinical practice [100]. However, these equations have been mainly derived and validated in the Western population and are associated with inherent inaccuracies in GFR estimation due to racial variation, which limits their general use across diverse Asian ethnicities. In an attempt to improve eGFR, some investigators proposed modifications in the original CKD-EPI equation allowing adjustment for racial differences, which resulted in more accurate eGFR estimations in Asian, Taiwanese, and Chinese CKD patients [61,101–103]. It can be challenging to establish the

best GFR estimating equation for a population, due to a lack of evidence supporting its application to a particular setting or racial ethnicity [104]. Kidney Disease: Improving Global Outcomes (KDIGO) 2012 guidelines recommend using the 2009 CKD-EPI creatinine equation in adults for initial and subsequent eGFR estimation unless an alternative modified equation has been validated in the local population [105]. Recently, the Task Force from the National Kidney Foundation and American Society of Nephrology recommended the implementation of a new 2021 CKD-EPI equation for calculating eGFR without racial co-efficient to improve generalizability across different populations; however, studies validating its performance in Asian population are warranted [106].

Cystatin C is recommended by KDIGO 2012 guidelines as a reliable biomarker of kidney function which is less influenced by racial differences, compared to creatinine. Increased cystatin C levels have been found to be associated with a higher risk of developing CKD, CVD, kidney failure, and mortality [107–109]. Staging of CKD mainly based on serum creatinine might lead to misclassification of patients due to false positives and therefore, the use of equations involving both serum cystatin C and creatinine have been suggested to improve diagnostic accuracy, risk stratification assessment for CKD and reduced requirement of follow-up testing [105,110]. However, the use of serum cys-

tin C is limited by less availability and high cost, compared to serum creatinine [111].

Persistent albuminuria is a definite marker of impaired renal function, irrespective of eGFR [105]. Measurement of albuminuria by a spot urine sample using either albumin-specific dipsticks or urine albumin-to-creatinine ratio (UACR) is most accepted by physicians and nephrologists. KDIGO preferentially recommends using UACR, followed by urine protein-to-creatinine ratio over total protein urinalysis strips (either automated or manual) in assessing albuminuria in CKD diagnosis and follow-up. Although quantitative assessment of albuminuria using UACR is favored and recommended by the guidelines, it is unaffordable in certain developing Asian countries and dipstick screening is considered acceptable to be followed by appropriate confirmatory testing [112]. Commonly used diagnostic tests used in countries across Asia are listed in Table 2.

Definition and classification of chronic kidney disease

The definition and indications of CKD have been described in current KDIGO guidelines. Classification of CKD is based on the cause, GFR category, and albuminuria category (Supplementary Tables 2 and 3, available online).

Table 2. Commonly used diagnostic tests across Asia

Country	Test				
	Blood pressure	eGFR	UACR	Dipstick	Serum creatinine
China	No	Yes (CKD-EPI)	Yes	Yes	No
Hong Kong	No	Yes	Yes	Yes	No
India	No	Yes	Yes (or UPCR)	Yes	No
Indonesia	No	Yes (CKD-EPI)	Yes (or UPCR)	Yes	No
Japan	No	No	No	Yes	Yes
Singapore	No	Yes (calculated)	Yes	No	Yes
Malaysia	No	Yes (CKD-EPI)	Yes (for DM patients if dipstick is negative)	Yes	No
Philippines	No	Yes	Yes	No	No
Republic of Korea	Yes	Yes (calculated)	Yes (or UPCR)	Yes	No
Taiwan	No	Yes (MDRD)	Yes		No
Thailand	No	Yes (CKD-EPI)	Yes (only in CKD patients)	Yes (for screening)	No
Vietnam	No	Yes	Yes	Yes	No

Countries are listed in alphabetical order.

CKD, chronic kidney disease; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; MDRD, modification of diet in renal disease; UACR, urinary albumin-to-creatinine ratio; UPCR, urine protein-to-creatinine ratio.

Existing chronic kidney disease management strategies

Both KDIGO and Asian Pacific Society of Nephrology clinical practice guidelines advocate annual screening of patients with T2DM for CKD, starting from the time of diagnosis and beginning 5 years after the diagnosis of type 1 DM [113,114]. A comprehensive multidisciplinary management approach is recommended to target these risk factors with lifestyle modifications such as proper nutrition, regular physical activity, weight control, and abstinence from smoking, with regular risk factor assessment every 3 to 6 months. As per the latest KDIGO 2022 guidelines, sodium-glucose cotransport 2 inhibitors can be initiated as first-line therapy in patients with T2DM and CKD with eGFR ≥ 20 mL/min/1.73 m² (updated from ≥ 30 mL/min/1.73 m² in the 2020 guidelines) and continued till the initiation of dialysis or KRT. This recommendation is strongly based on findings from recent clinical trials, which have clearly demonstrated the efficacy and safety of dapagliflozin in patients with eGFR ≥ 5 mL/min/1.73 m² and albumin-to-creatinine ratio ≥ 200 to 5,000 mg/g (DAPA CKD trial) and empagliflozin among patients with eGFR ≥ 20 mL/min/1.73 m² and heart failure (EMPEROR and EMPA Kidney trial) [115–117]. Additionally, hyperparathyroidism (HPT) has been linked to adverse renal and cardiovascular outcomes in patients with CKD. In 2021, KDIGO recommended the use of standardized BP measurement, treated with a target systolic BP < 120 mmHg [118]. Treatment with antihypertensive medications such as RAS inhibitors (angiotensin-converting enzyme inhibitor [ACEi] or angiotensin receptor blocker [ARB]) is the recommended first-line therapy for patients with HPT, CKD, and moderate to severe albuminuria (G1–G4, A2–A3), with or without DM. These recommendations discourage using any combination of ACEi, ARB, and direct renin inhibitors in patients with severe kidney impairment (Supplementary Fig. 2, available online).

Successful chronic kidney disease care strategies or policy-sharing programs across Asia

Worldwide the nephrology community recognizes the compelling need for a strategic plan to effectively address the growing incidence of CKD and an integrated approach for its management. The mindset has transitioned from

treating kidney failure to preventing its development in the first place. Effective prevention, early detection, conservative management, an appropriate combination of dialysis modalities, and optimizing the availability of kidney transplantation form the cornerstone of CKD care strategies. Asia region is faced with unique challenges such as wide disparities in the socioeconomic profiles, burden of CKD, culture, ethnicity, and political landscape. A collaborative effort among the government and policymakers of each country to achieve better integrated CKD/kidney failure care will improve kidney care of patients in the region. Developmental programs aimed at improving clinical outcomes and optimizing healthcare costs associated with CKD management are undertaken by several countries (Table 3 [119–124]). Several screening strategies aimed at the general and high-risk population are currently undertaken at national levels (Table 4).

Unmet needs and challenges unique to Asia

Limited screening and surveillance systems impacting chronic kidney disease prevention

Four of the 10 International Society of Nephrology world regions are located in the Asia sector, ie, North and East, Oceania and South-East Asia South Asia, and the Middle East [125]. The region is socioeconomically, culturally, and ethnically diverse. As per the World Bank, China, India, Thailand, Vietnam, Indonesia, Malaysia, and the Philippines are middle-income economies, whereas Hong Kong, Singapore, Republic of Korea, Taiwan, and Japan are high-income economies. CKD screening and targeted early identification while asymptomatic or at an early stage can enable effective interventions that can delay disease progression and reduce the incidence of associated complications such as cardiovascular risk, dyslipidemia, anemia, and bone and mineral disease (Fig. 5) [4,126].

Multiple barriers prove to be hindrances in the implementation of screening programs in Asia attributable to patient-related factors or the health system in general. Social risk factors, such as limited financial resources and low health literacy are significant patient-level barriers. Educational materials may be unavailable in the local vernacular which may be an obstacle in the rural areas of Asian countries. Lack of regional data leads to the application of West-

Table 3. Developmental programs and initiatives for CKD screening

Country	Developmental programs
Taiwan	The national kidney care program has resulted in improved clinical outcomes along with a reduction in health care system costs. The Department of Health made CKD prevention and care a major public health priority and an integrated CKD care program was initiated to promote the screening of high-risk populations, patient education, and multidisciplinary team care. Nephrotoxic Chinese herbs containing aristolochic acid were prohibited through public health legislation in 2003. National pay-for-performance programs for CKD were implemented as part of health care improvement projects, along with diabetes mellitus and cardiovascular disease care in 2006 (pre-ESKD program) and 2011 (early CKD program) [119]. The Taiwan model has been proposed for adoption by the Indonesian Ministry of Health as well.
Republic of Korea	The Korean National Health Screening Program for CKD was implemented in 2002 with biannual screening starting at the age of 40 years for CKD by proteinuria (dipstick) and eGFR testing. Korean organ transplantation policies have ensured an increase in the availability of donor transplants, the Korean Society for Transplantation established a web-based registry, the Korean Organ Transplantation Registry to educate patients, donor families, and healthcare professionals.
Philippines	The Philippines' national insurance covers kidney transplantation as a single largest payment for any surgical procedure.
Thailand	The Chronic Kidney Disease Prevention in the Northeast Thailand (CKDNET) is an initiative to reduce the CKD burden in the region. Pamphlets, posters, brochures, and other media are distributed for CKD education and awareness at the community level. Locally suitable practice guidelines have been formulated [120].
Hong Kong	The Screening for Hong Kong Asymptomatic Renal Population and Evaluation (SHARE) program is an effective screening program at the primary care level that identified potential subjects for further evaluation and aided in educating the public about the significance of following up even asymptomatic renal diseases [121].
Singapore	The HALT-CKD program was started in 2017, the 'Holistic Approach in Lowering and Tracking Chronic Kidney Disease (HALT-CKD)' program concentrates on a concerted effort for timely detection and delaying the progression of CKD in primary care settings through an integrated and multi-faceted approach. The program focuses on a series of lifestyle modifications (low-salt diet, physical activity, smoking cessation) and medical interventions such as optimization of RAASi, MRA, and SGLT2i government has also authorized subsidies and reimbursements to reduce the financial burden in CKD patients [122].
Malaysia	Under the "Strategic Action Plan for Healthy Kidneys (ACT-KID) 2018-2025" there are various initiatives utilizing multi-sectoral collaborations to promote public and healthcare practitioner awareness of CKD which emphasize the need for screening and early detection, as well as guideline-directed CKD management [123].
Indonesia	The government NHIS launched a noncommunicable and chronic disease management program named Indonesian Chronic Disease Management Program (PROLANIS) in 2014 with T2DM and hypertension as the main focus. It is specifically designed to be implemented at the primary care level (government-owned community healthcare centers, primary care clinics, or private doctors). As an integrated health service program, it controls the clinical and laboratory outcomes, prevents disease complications and improves patients' quality of life [124]. This program gives additional benefits to its participants through monthly regular meetings for medical consultation, peer group education by healthcare professionals, healthcare visit reminders, peer club activities, and home visits.

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; MRA, mineralocorticoid receptor antagonists; NHIS, National Health Insurance System; RAASi, renin-angiotensin-aldosterone system inhibitors; SGLT2i, sodium glucose cotransporter-2 inhibitor; T2DM, type 2 diabetes mellitus.

ern guidelines in a population that is markedly different in racial, ethnic, and sociocultural profile. Patient adherence to follow-up is a major challenge as patients are apprehensive of fear of repercussions at the workplace and do not avail of medical reimbursements and insurance schemes. In Indonesia for example, the National Health Insurance reported low screening uptake among patients with DM and HTN for CKD screening despite the screening program being covered by national insurance. Rampant practice of self medications and use of alternative medicines that are potentially nephrotoxic also hinder preventive efforts [89]. There are no national-level screening programs in some

countries like India. There is a dearth of key strategies for screening and early detection of CKD at a community level and sensitizing primary care clinicians on its importance. Sparse educational initiatives for patients, inadequate patient follow-up routines, and lack of multidisciplinary care are barriers that are attributable to the healthcare system.

Lack of adequate healthcare resources and policies on chronic kidney disease impacting effective chronic kidney disease management

There are considerable gaps in health care capacity, work-

Table 4. Strategies for regular screening in diabetic/hypertensive populations

Country	Campaigns/strategies for regular screening		
	General population	High-risk population	CKD population
Hong Kong	None	Diabetic patients – annual complications screening	Covered in regular clinic visits
India	None	Physician-directed	
Indonesia	PROLANIS under NHS		
Republic of Korea	<ul style="list-style-type: none"> • World kidney day campaign annually by KSN • Big walk for kidney campaign by KSN • School Urine Screening Program for all elementary, middle, and high school students annually (urinalysis) • Conscription examination for 19-year-old men (including urinalysis) • NHI checkup • Local household, workplace subscriber, family members of 40 years old or older, and dependents • Conducted once every 2 years, and every year for non-office workers • 40- and 66-years-old people are subject to a life-changing period of health checkups • Employment and recruitment physical examination (including urinalysis) 	Campaign for shared decision-making for choosing renal replacement therapy (SDM-ART) in CKD patients	
Malaysia	<ul style="list-style-type: none"> • Under <i>Skim Peduli Kesihatan untuk Kumpulan B40 (PeKa B40)</i>, Malaysian citizens aged >40 years and with household incomes in the bottom 40% are eligible for free health screening in private primary care clinics which includes renal function tests and urine full and microscopic examination • Government health clinics (<i>Klinik Kesihatan</i>) in Malaysia provide free health screening for NCDs for Malaysians aged 40 years and above through walk-in or online appointments at selected locations • The Social Security Organization (SOCSO) offers free health screening to active SOCSO contributors for more than 12 months who are aged 40 years and above, or between ages 30 to 39 years with NCD health risks • Screening for high-risk populations is recommended by local clinical practice guidelines for management of CKD, and the Malaysian Society of Nephrology has organized a structured webinar training program for primary care doctors on CKD prevention, early detection, and management 		
Philippines	<ul style="list-style-type: none"> • Tests included in the primary health benefit of the NHI program • Annual tests included for all government employees, private corporations <p>Local government units use different strategies for their constituents—they can have the laboratory tests during annual vaccination programs—coincide the tests with other annual programs like community meetings or religious occasions</p>		
Singapore	<ul style="list-style-type: none"> • National Diabetes Workgroup set up to screen and improve care and care delivery for diabetic patients working with primary care teams and setting up of registry • HALT-CKD workgroup targets on screening of high-risk groups maximizing treatment for kidney retardation and lifestyle change with collaboration between community and healthcare institution physicians • Upcoming Healthier SG program will incorporate approaches for healthier lifestyles for the nation starting with prevention with an emphasis on a community approach • ACE Workgroup (ACE clinical guidelines) at the national level to provide objective and credible healthcare guidance, enabling stakeholders to make better-informed choices through evidence-based practice 		
Taiwan	Several national programs cover students, military personnel, pregnant women, employees, and any adult >45 years for regular CKD screening using eGFR and urine dipstick test	<ol style="list-style-type: none"> 1. NHI reimburses all high-risk groups for CKD screening using eGFR and ACR 2. Extra incentives for regular CKD screenings in the DM population (pay by performance in DM program) 	<ol style="list-style-type: none"> 1. NHI reimburses all the CKD population for regular renal function follow-up 2. Extra incentives for CKD regular follow-ups (pay by performance in early CKD and pre-ESKD program)
Thailand	None	DM, hypertension, autoimmune disease, renal stone, aging, cardiovascular disease, genetic disease, strong family history of CKD	
Vietnam	Not regularly	Screening for CKD done in high-risk population	

ACE, Agency for Care Effectiveness; ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HALT, Holistic Approach in Lowering and Tracking; KSN, Korean Society of Nephrology; NCD, noncommunicable diseases; NHI, National Health Insurance; NHS, National Health Service; PROLANIS, Indonesian Chronic Disease Management Program.

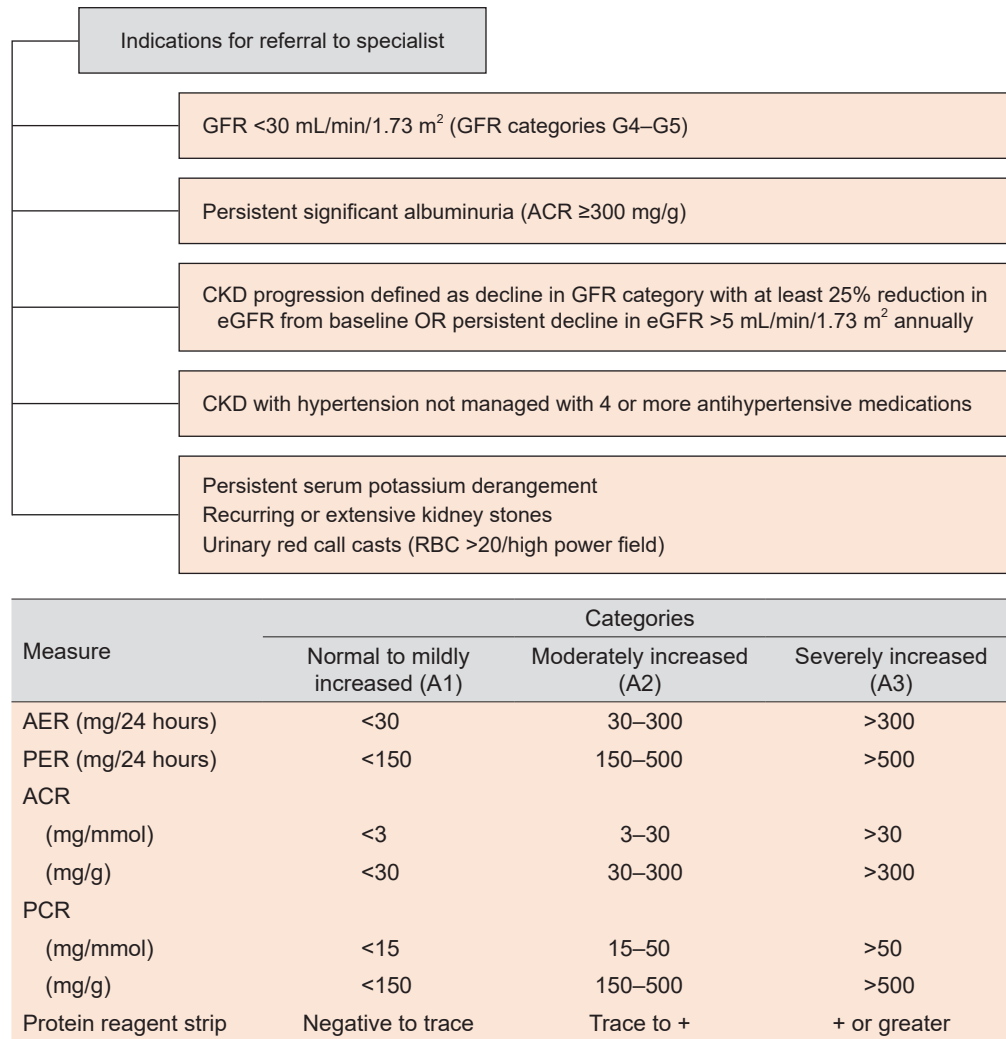


Figure 5. Indications requiring referral to kidney specialists. Referral indications based on CKD staging and specific conditions warranting comprehensive evaluation and management are elaborated. These indications emphasize the importance of specialized assessment and intervention by kidney specialists to optimize patient care and outcomes in CKD management. Albuminuria and proteinuria can be measured using excretion rates in timed urine collections, the ratio of concentrations to creatinine concentration in spot urine samples, and using reagent strips in spot urine samples. Relationships among measurement methods within a category are not exact. For example, the relationships between AER and ACR and between PER and PCR are based on the assumption that average creatinine excretion rate is approximately 1.0 g/day or 10 mmol/day. The conversions are rounded for pragmatic reasons (for an exact conversion from mg/g of creatinine to mg/mmol of creatinine, multiply by 0.113). Creatinine excretion varies with age, sex, race, and diet; therefore, the relationship among these categories is approximate only. ACR <10 mg/g (<1 mg/mmol) is considered normal; ACR 10–30 mg/g (1–3 mg/mmol) is considered “high normal.” ACR >2,200 mg/g (>220 mg/mmol) is considered “nephrotic range.” The relationship between urine reagent strip results and other measures depends on urine concentration.

ACR, albumin-to-creatinine ratio; AER, albumin excretion rate; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; PCR, protein-to-creatinine ratio; PER, protein excretion rate; RBC, red blood cell.

force limitations, and quality of care in Asia.

Work force limitations

Primary care physicians who are the first clinical con-

tact in almost all cases of CKD and play a vital role in the detection and management of early-stage CKD, lack the competencies and understanding of current guidelines in the diagnosis and management of CKD. There is a per-

sistence of traditional, less accurate diagnostic procedures and limited availability and affordability of tests for more reliable biomarkers of CKD such as eGFR and UACR [127]. There is uncertainty regarding the right time to refer to a nephrologist causing a delay in timely intervention. Referrals are further adversely impacted by patient-level barriers such as nonavailability of appointments and referral centers being too far. The role of community health workers is paramount especially in rural communities and there is a general lack of understanding and low risk perception regarding CKD within this group resulting in delayed diagnosis at a primary care level. Continuous in-service training is crucial in the management of CKD patients and has not been successfully implemented across Asia.

Inadequate reimbursement systems

The availability of specialist nephrologists (ratio of nephrologists per patient and ratio of nephrologists per patient on KRT) shows a significant disparity in Asian countries, as this is driven by policies specific to the country. Availability of KRT shows significant disparity with some Asian countries such as Singapore, Thailand, Taiwan, Hong Kong, and Malaysia having adequate KRT facilities and the treatment being mostly publicly funded; whereas, in other countries, KRT facilities are limited with inadequate or nonexistent reimbursement policies such as India where patients bear the expenses of KRT. KRT reimbursement policies of countries in Asia are listed below (Table 5).

Lack of adequate data, policies, and programs

There is a lack of exact estimates of CKD burden in Asia with limited screening and surveillance systems. Current data collection efforts are focused on KRT through dialysis and transplantation registries; however, systematic assessment of CKD in its early stages is critical as well [128]. Kidney failure registries are currently maintained in Taiwan (Taiwan Renal Data System), Hong Kong (Renal Registry of Hong Kong), Malaysia (Malaysian Dialysis and Transplant Registry), Indonesia (Indonesian Renal Registry), Japan (Japan Kidney Disease Registry), Thailand (Thailand Renal Replacement Therapy Registry), Singapore (Singapore Renal Registry), and Republic of Korea (Korean Renal Data System). However, there is a definite gap in the quality of data collected in the registries; especially at the patient

level that includes demographics, current treatment, and clinical outcomes [129]. There are wide variations between the registries as well with a few being very specific capturing granular details such as ethnic differences, while others lack basic data. Most countries also do not maintain a systematic repository of data consisting of disease, occurrence, prevalence, clinical outcomes, demographic data, and cost of treatments (Fig. 6). Although a few registries were developed, the data collection was manual with limitations in data quality and quantity. The use of technology may aid in more granular data collection.

Emerging research and future actionable directions in chronic kidney disease detection and management in Asia: consensus recommendations

Early stages of CKD and the subsequent transition to advanced stages and finally to kidney failure, both pose high clinical risks and carry substantial healthcare-related costs. Research-based evidence about the impact of early detection, sustainable treatment options, quality of life, delay or complete avoidance of dialysis, and related cost analysis is the need of the hour. Initiatives directed at effective detection and management of CKD can be categorized into three levels: patient, physician and medical societies, and policy makers and government.

Patient advocacy groups for increasing CKD awareness and eliminating negative perceptions about the disease among CKD patients have been particularly beneficial in India as primary care physicians are often busy in hospitals and have limited time for such activities. In Republic of Korea, short educational videos engage the younger population with access to the internet and smartphones and create CKD awareness. This is similar to the situation in Malaysia, where social media platforms such as internet websites are managed by nephrologists to provide public and patient information, and patient chat groups have been established to provide support and counteract health misinformation. At the physician and medical society level, appropriate management of co-morbid metabolic diseases and risk factors especially cardiovascular events can be prioritized. Appropriate and timely transition of care for younger patients with DM and CKD to pediatricians who often follow their patients into early adulthood is crucial. At

Table 5. KRT reimbursement policies in Asia

Country	Type of reimbursement for HD and PD		Key expenses excluded in coverage ^a	HD to PD reimbursement ratio	Specific eligibility criteria	PD-first policy (year of implementation)
	HD	PD				
Hong Kong	Complete	Complete	Transportation	32%:68%	None	Yes (1985)
India	Complete	Complete			Income criteria specified for government reimbursement	No
Indonesia	Yes	Yes	Yes	80%:100% based on hospital policies	No PD policy preferred	No
Republic of Korea	90%	90%	All drugs have their own strict criteria for coverage	Similar	PD homecare management pilot project launched for PD penetration	No
Malaysia	Complete/near-complete for MOH, Public Service Department, and Social Security Services-funded patients. The government provides subsidies to NGOs (e.g., NKF) and various religious organizations also provide charity KRT services		Transportation	Overall 88.3%:11.7% HD:PD utilization but within MOH the ratio 59.4%:40.6% for now, respectively	None	Yes for MOH services
Philippines	Partial	Complete for 3 exchanges daily		4:3	All diagnosed kidney failure patients eligible	For some hospitals and the national health insurance program
Singapore	Public and private health-care schemes. Additionally, subsidies available from the government and VWOs e.g., NKF, KDF EPO is reimbursed up to 80% with a maximum cap Blood tests are covered as part of dialysis package	Subsidy framework similar to HD	Transportation	Similar	Eligibility for VWO is based on means testing that is reviewed on regular basis	No PD preferred
Taiwan	Complete	Complete	Full coverage	1.07:1	No	No
Thailand	Yes	Yes	Transportation	80:20	No	Yes (2008)
Vietnam	80%	80%	EPO, drugs, blood tests	Equal	Based on health insurance	No

In Taiwan, the policy encourages PD, in Indonesia the MOH target for PD:HD is 10:90, in the Philippines, the national health insurance program is considering increasing coverage to of HD to 156 sessions/yr. PD (increase to 4 exchanges/day) when indicated, cover icodextrin and cyclor therapy to make the benefit higher than HD. In Singapore, PD is encouraged. There is the provision of a national home visit program, to empower and handhold in the initial phase of therapy, followed by regular review in the latter phases.

EPO, erythropoietin; KDF, Kidney Dialysis Foundation; KRT, kidney replacement therapy; HD, hemodialysis; MOH, Ministry of Health; NGO, nongovernment organization; NKF, National Kidney Foundation; PD, peritoneal dialysis; VWO, voluntary welfare organization.

^ae.g., EPO, drugs, blood tests, transportation.

the government level, policies to ensure the screening of at-risk populations and universal coverage of CKD diagnostic tests would aid in the early detection and management of CKD.

Point of care testing (POCT) that allows rapid measure-

ment of serum creatinine and eGFR levels can enable healthcare professionals to diagnose and institute appropriate care earlier. Patient access to POCT to monitor their serum creatinine and eGFR values, similar to diabetics who routinely record their blood glucose results would promote

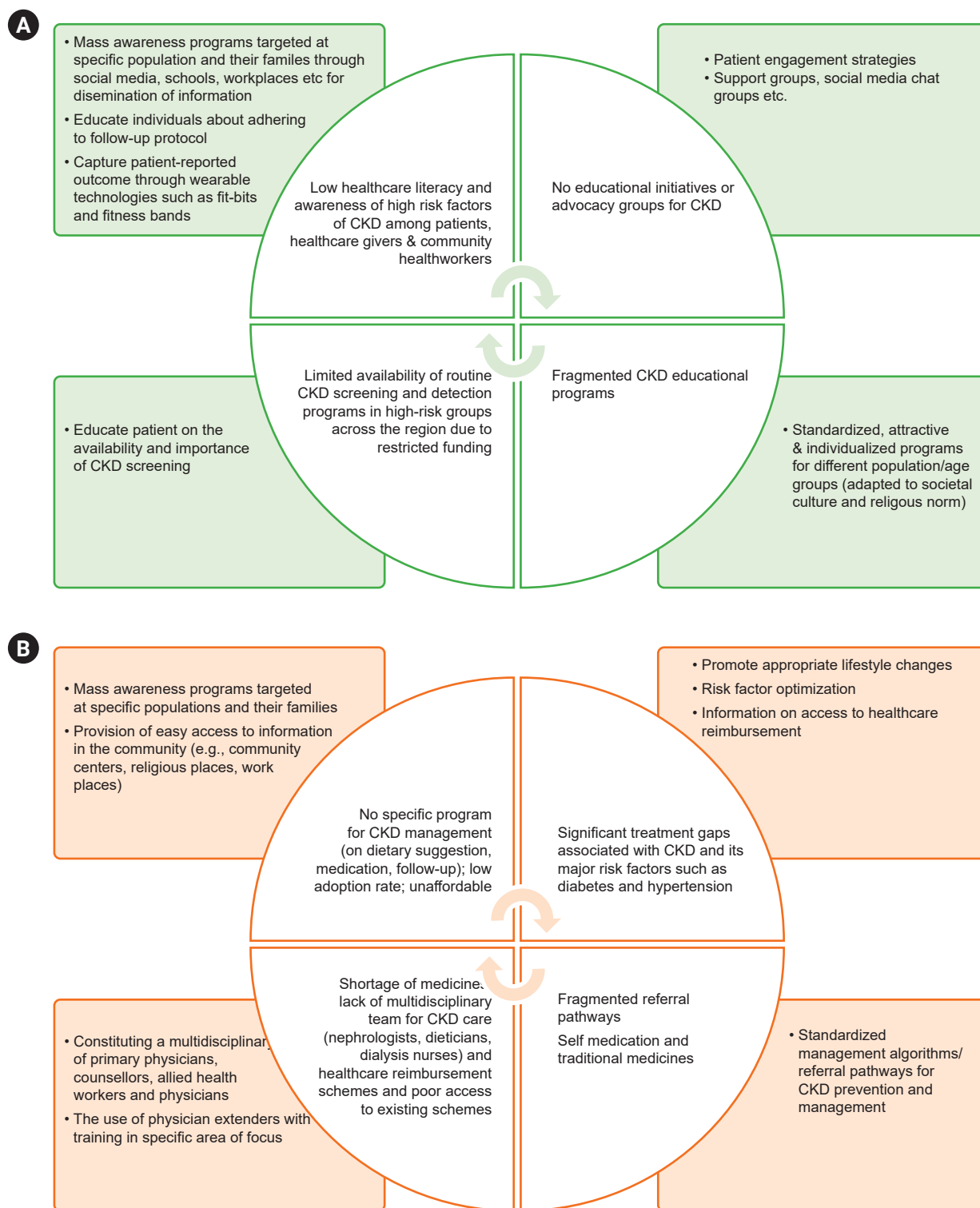


Figure 6. Unmet challenges and proposed mitigation strategies targeted at (A) individual, (B) community, and (C) national levels. AI, artificial intelligence; CKD, chronic kidney disease; KRT, kidney replacement therapy. (Continued to the next page)

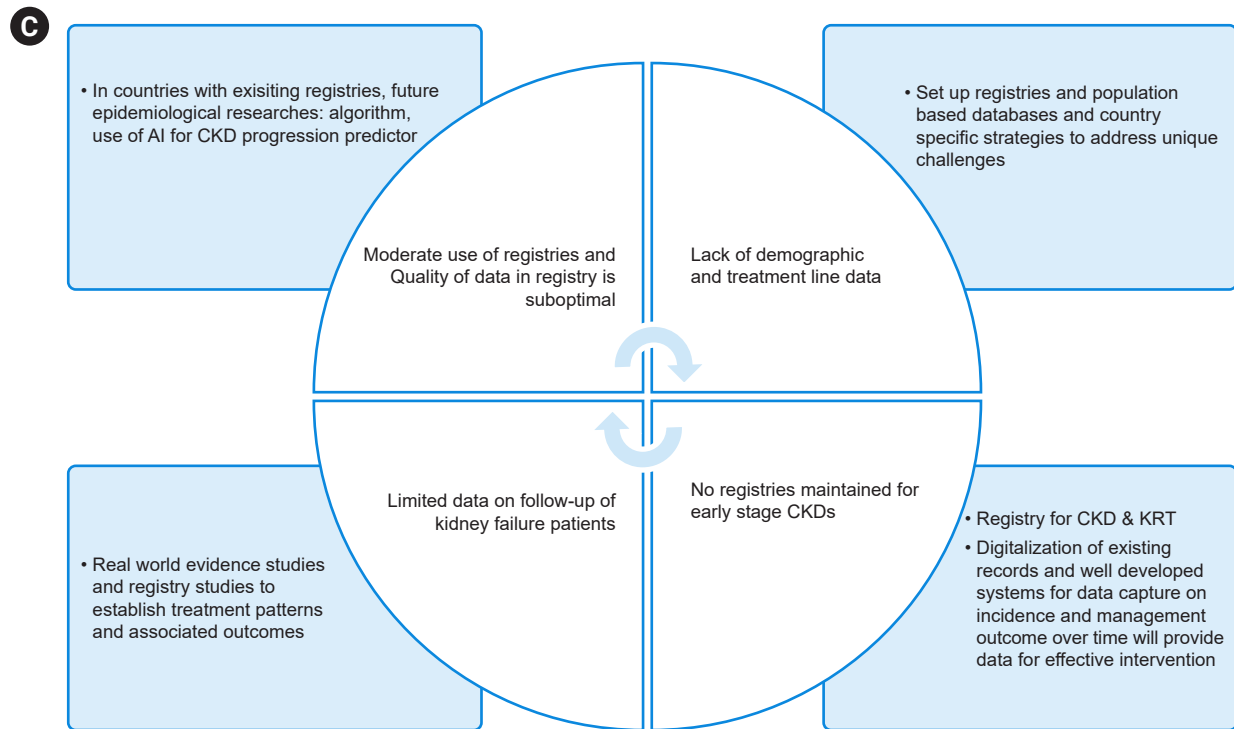


Figure 6. Continued

patient empowerment, encouraging patients to take stock of their own health and wellbeing.

Conclusion

Asia is a vast and diverse region comprising highly populated countries with unique features and challenges. Each country's socioeconomic situation, geographic location, and governmental funding structure for CKD detection and management have an impact on the availability, access, and quality of CKD care. There is an urgent need for a collaborative action plan between the healthcare community and governments in this region to detect CKD in its early stages and prevent its complications including kidney failure, CVD, and death. Individual countries should be encouraged to develop strategies for effective prevention, early identification, and timely intervention. Initiatives for preventive interventions to decrease the incidence of CKD and kidney failure should be undertaken. Patient and physician awareness of kidney disease as a complication of other chronic diseases should be reinforced. Government spending on CKD-focused healthcare needs should

be increased. Finally, CKD research capacity needs to be enhanced by the nephrology community through a multi-disciplinary approach.

Conflicts of interest

ST reports receiving honoraria from Boehringer Ingelheim, GlaxoSmithKline, AstraZeneca, Novartis, Baxter, and Bayer, is the President (2022–2024) of the Asian Pacific Society of Nephrology and an executive member (2020–2023) of KDIGO. RD reports receiving honoraria from AstraZeneca, Novartis, Bayer, Boehringer Ingelheim, Astellas Pharma, Corbridge, and Philippine Council for Health Research and Development and travel support from AstraZeneca, Boehringer Ingelheim, Corbridge, and Macro Pharma, and is part of Maria Corazon Torres Y Javier (MCTJ) Foundation and Transplantation Society of the Philippines. SK reports receiving research grant support from the National Evidence-based Healthcare Collaborating Agency and Korea Evaluation Institute of Industrial Technology and serves on the advisory board of the Korean Society of Nephrology. YWC reports receiving honoraria from AstraZeneca, Bax-

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Data sharing statement

The data presented in this study are available from the corresponding author upon reasonable request.

Authors' contributions

Conceptualization, Methodology: All authors

Writing-original draft: All authors

Writing-review & editing: All authors

All authors read and approved the final manuscript.

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