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Strategies to Improve Long-Term Outcomes for Patients with Chronic Kidney Disease in China

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Chronic kidney disease · Management strategies · China

Abstract
Background: Chronic kidney disease (CKD) is an incurable disease requiring lifelong management. China has a high prevalence of CKD, which disproportionately affects older adults and those with chronic risk factors for CKD development. The rising prevalence of CKD in China places a substantial burden on the general population and the healthcare system. ***Summary:*** In China, there are currently many unmet needs for patients with CKD and high-risk individuals, resulting from a lack of education and support to reduce risk factors, delayed diagnoses, limited knowledge of CKD among primary-care physicians, and poor access to treatments among some patient populations. An integrated, nationwide approach is required to improve the current situation of CKD management in China. There are currently several national healthcare frameworks in place that focus on new major health policies to prevent disease and encourage people to adopt healthier lifestyles, and while they do not directly target CKD, they may have a positive indirect impact. We explore the unmet needs for patients with CKD in China and discuss the potential strategies that may be required to overcome them. Such strategies include improving physician and patient education, establishing a targeted screening programme, supporting patients to improve self-management behaviours, accelerating the creation of medical consortia and medical satellite centres, and migrating from hospital- to community-based management. In addition to policy-driven strategies, development of novel therapies will be key to providing new solutions for the long-term management of CKD. ***Key Messages:*** An integrated, nationwide approach is required, incorporating policy-driven changes to the clinical management of CKD, as well as the development of novel CKD treatments.

Introduction

Chronic kidney disease (CKD) is an irreversible and mostly progressive disease, and is defined by the presence of kidney structure or function abnormalities that last >3 months [1]. It is classified according to cause, extent of decreased renal function (indicated by estimated glomerular filtration rate [eGFR]), and extent of kidney damage (indicated by albuminuria or albumin-to-creatinine ratio) [1].

The global burden of CKD is sharply increasing and is projected to become the 5th most common cause of years

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of life lost by 2040 [2]. As global burden disease study reported in 2017, there were 697.5 million (9.1%) adults with CKD, resulting in 35.8 million disability-adjusted life years and 4.6% of total global mortality due to CKD or cardiovascular disease attributable to impaired kidney function [3]. Once CKD progresses into end-stage kidney disease (ESKD), it is associated more than 10 times the risk of death compared with the general population [4]. From 1990 to 2017, global all-age incidence of dialysis and renal transplantation increased by 43.1% and 34.4%, respectively [3]. CKD cases in China (132.3 million cases) and India (115.1 million cases) accounted for almost one-third of cases, and disability-adjusted life years for CKD in China (4.9 million) were 2.6 times of USA (1.9 million) [3].

The spectrum of CKD in China has been evolving toward that of developed countries. Population ageing, diabetes mellitus (DM), hypertension, and metabolic syndromes, all risk factors for CKD, have increased dramatically along with substantial lifestyle and social changes [5–12]. DM has become the top cause of CKD in China, and ESKD due to DM is expected to have a huge impact on the healthcare system in China [13]. The variety of causes, risk factors, mechanisms of progression, and clinical manifestations create many challenges for early CKD diagnosis and intervention, and efforts are urgently needed to improve long-term outcomes for patients with CKD.

The Current State of CKD in China

Prevalence and Disease Awareness

The prevalence of CKD in China is estimated at 9.2–11.6% [14–16], with a recent systematic review and analysis estimating the number of adult cases at 159.8 million [15]. The prevalence of CKD in China differs by region, with the southwest (18.3%) region having the highest prevalence [14]. Consistent with the global trend, the majority of CKD cases in China are early stages (stages 1–3), but there may be a higher proportion of early-stage CKD in China when compared with the global population [14, 16]. Although China has a large population, the total number of patients with CKD may have been underestimated due to large within-country variability and limited data on national studies and CKD registries.

Despite the heavy burden on public health, low patient awareness of CKD has persisted for the last 2 decades. Global awareness of CKD was 19.2% in a 2021 meta-analysis, and this estimation was 26.5% in the setting of patients with eGFR below 60 mL/min per 1.73 m^2 [17]. In China, awareness of CKD was lower than at the global level, with overall awareness of CKD approximately 10% in nationwide samples [18] (8.7% in the setting of middle-aged and elderly [19]). This number remained low even for patients with CKD stage 4 (11.7% and 16.7% for those with normoalbuminuria and albuminuria, respectively) [18]. However, up-to-date data on CKD awareness in China are lacking, and so, further research in this area is needed.

Causes and Risk Factors

In developed countries, causes of CKD generally include old age, DM, hypertension, obesity, and cardiovascular disease. In developing countries, common causes also include glomerular and tubulointerstitial diseases [20]. Based on data from the Hospital Quality Monitoring System in China, glomerulonephritis was the top cause of CKD in China until 2011, when the proportion of CKD due to DM (DM-CKD) first exceeded that of CKD due to glomerulonephritis (GN-CKD) [11]. In 2016, glomerulonephritis had dropped to the fourth most common cause of CKD among hospitalised patients (14.4%), after diabetes (25.7%), hypertensive nephropathy (21.4%), and obstructive nephropathy (16.0%) [21]. This upswing in DM-CKD has also been observed in other Asian regions [11]. For example, in Korea in 2014, diabetic nephropathy and chronic glomerulonephritis were the underlying causes in 48% and 8.2%, respectively, of new ESKD patients [22].

Risk factors associated with CKD can be grouped into the following exposure categories [23, 24]: (1) sociodemographic and socioeconomic, (2) behavioural, (3) cardiovascular, (4) metabolic, (5) genetic, and (6) newly defined factors (shown in Fig. 1). Around two-thirds of the differences between CKD patients in the USA and China could be accounted for by CKD risk factors including DM, hypertension, central obesity, cardiovascular disease, and hyperuricemia [16], but these risk factors continue to evolve. The estimated prevalence of DM in China increased from 10.9% in 2013 to 12.4% in 2018 [6], although prevalence differs by region: a nationwide study of almost 1.4 million participants attending preventative health examinations across 220 cities in 2018 reported that the age- and sex-standardized prevalence of DM was highest in the north (13.1%) and northeast (9.7%), with the prevalence in the north more than double that in the south (6.2%) [25]. A meta-analysis of DM prevalence in China during 2000–2014 revealed a similar trend for higher prevalence in the north (11.5%) and northeast (22.1%) regions [12]. A higher prevalence in urban (11.4%) versus rural (8.2%) areas was also reported [12]. Demonstrating a similar trend to DM, the prevalence of hypertension among adults in mainland China was markedly higher in 2017 compared with 2007 (31.5 vs. 25.7%), as was the prevalence of central obesity (35.4

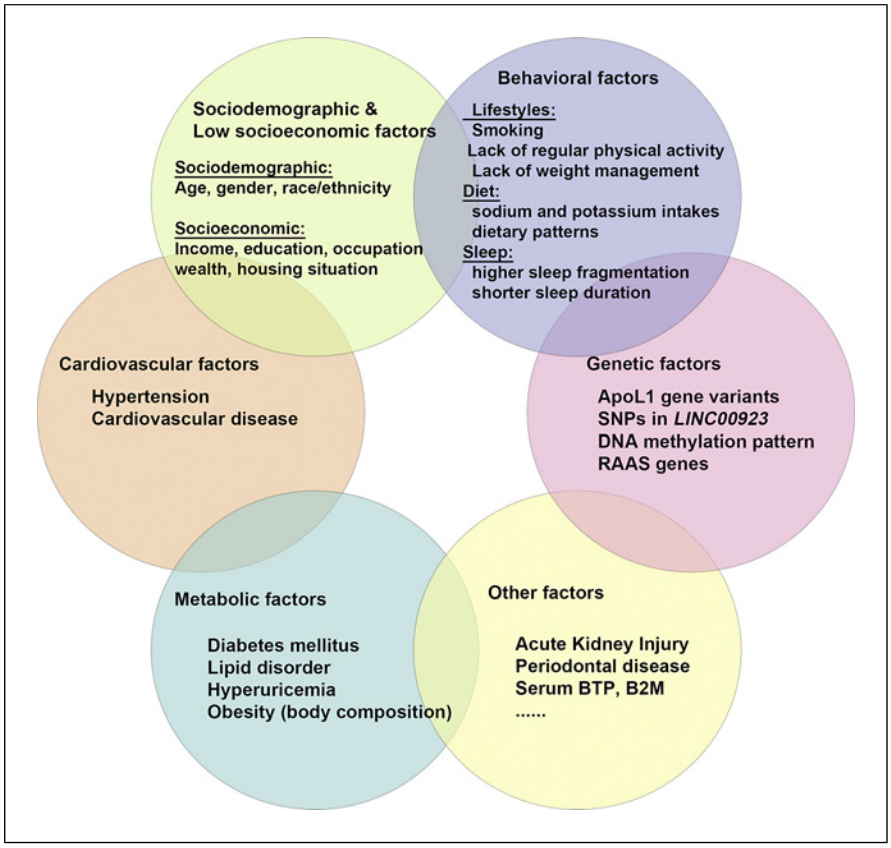

Fig. 1. Risk factors associated with CKD. Risk factors associated with CKD are summarised into following categories: (1) sociodemographic and economic, (2) behavioural, (3) cardiovascular, (4) metabolic, (5) genetic, and (6) newly defined factors. Details of each category were listed in each circle.

vs. 25.9%), although the higher prevalence shifted from urban to rural areas over the decade [26]. The latest China Hypertension Survey also found regional differences in the prevalence of hypertension, with areas of the south, north, and northeast having the highest prevalence [27]. Hyperuricemia, a recently recognised risk factor for both CKD development and CKD progression, has also been increasing in China [28]. The inadequate awareness and management of causes and risk factors aggravate the health and socioeconomic burden of CKD, negatively impacting life expectancy, quality of daily life, and the cost of medical resource [29].

Progression and Prognosis

CKD is an important risk factor for other morbidities and for all-cause and cardiovascular mortality, with patients five-to-ten times more likely to die than progress to ESKD [30]. The absolute number of patients with advanced CKD (eGFR <30 mL/min/1.73 m^2) in China was estimated at the highest globally (26.4 million) [15]. According to the Chinese National Renal Data System (CNRDS), there were a total of 339,748 maintenance haemodialysis patients in China in 2014 [31]. Although ESKD patients constitute a small percentage of the population, they consume a disproportionate share of the medical budget. The China Kidney Disease Network 2015 Annual Data Report showed the number of patients undergoing haemodialysis and peritoneal dialysis constituted only 0.16% and 0.02% of individuals covered by UBMI, while they consumed 2.08% and 0.34% of the overall expenditures of urban basic medical insurance [32].

Current CKD-Related Health Policy in China

Instructed by the Healthy China Initiative, a national medium- to long-term chronic disease prevention plan (2017–2025) targets the burden of chronic disease in the general population and healthcare system in China [33]. Strategic measures include promoting comprehensive healthcare management and controlling risk factors for chronic diseases, but CKD is not directly targeted by this initiative or the more recent Healthy China Action Initiative (2019–2030) [34]. Both frameworks may have indirect benefits on the prevalence and management of CKD in China, with the emphasis of the latter framework

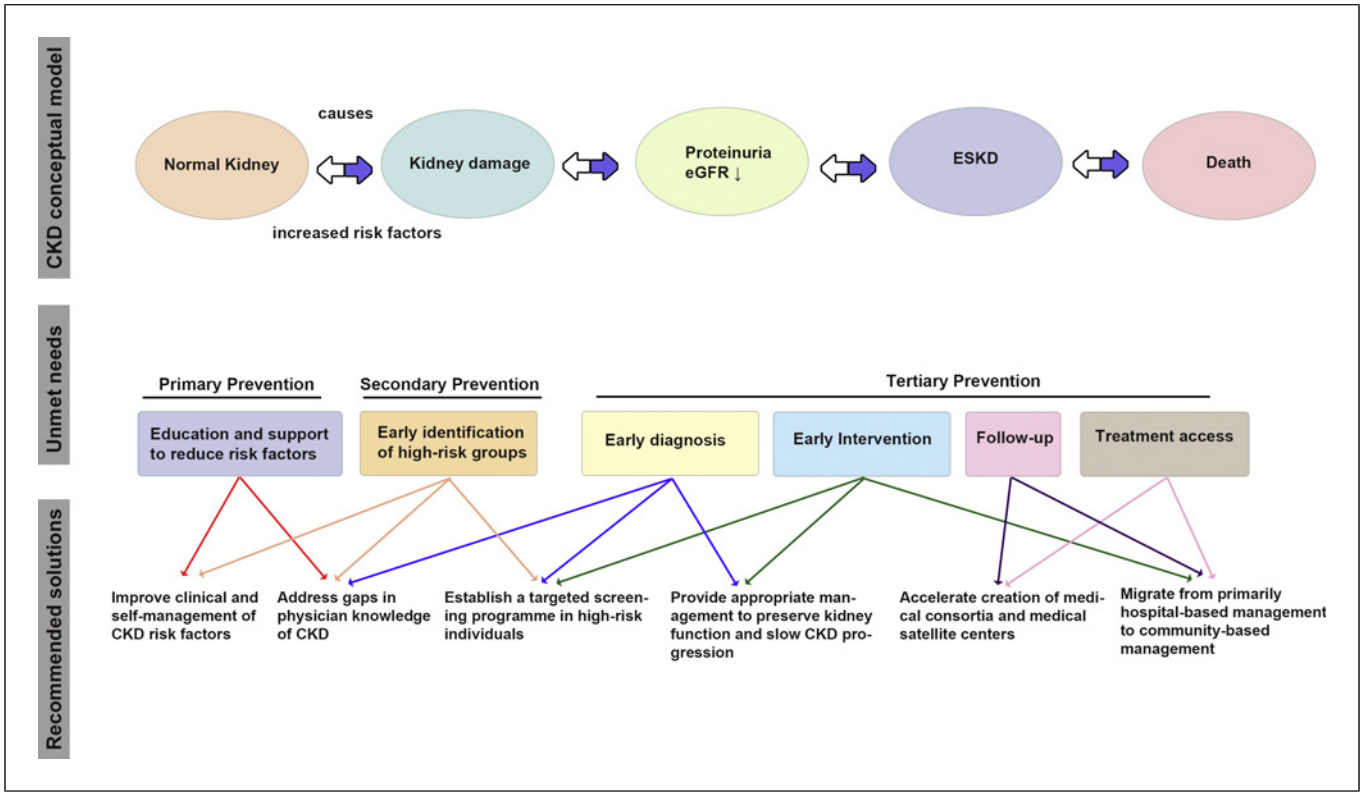

Fig. 2. Unmet needs for CKD patients in China and recommended solutions – a holistic approach based on conceptual CKD model. Unmet needs and corresponding recommended solutions of CKD management were summarised from the perspective of three-class prevention along with conceptual model of CKD development and progression. CKD, chronic kidney disease.

incorporating new major health policies, preventing disease and encouraging people to adopt healthier lifestyles [34]. Core indicators include the number of people taking part in physical exercise, level of health literacy among residents, the number of registered doctors and nurses per 1,000 residents, and the proportion of personal health spending [34]. The National Health Commission of the People's Republic of China reports that several measures are currently under way to improve the prevention, diagnosis, and management of CKD in China [35]. We discuss hereon the unmet needs for patients with CKD in China and discuss the holistic approach required to overcome them (shown in Fig. 2).

Unmet Needs in the Prevention, Diagnosis, and Management of CKD in China

Education and Support to Reduce Risk Factors

About 25% CKD patients experience low health literacy, which has been shown to be associated with poor health outcomes [36]. There is currently insufficient support for patients nationwide to effectively identify and reduce risk factors for CKD, which is related to lack of awareness among healthcare professionals (including nephrologists) of targets and strategies to prevent disease deterioration [37].

Early Identification of High-Risk Groups

Primary prevention of CKD focuses on identifying individuals with risk factors for CKD, and despite the existence of guidelines on screening, early diagnosis, and prevention of CKD [38], in China there is a currently substantial gap in the identification of high-risk individuals. Low awareness of common risk factors for CKD mainly accounts this gap. A cross-sectional study in rural China found that among a population of whom 25% had hypertension, only 20% previously had a blood pressure measurement [39]. Among adults with DM in 2018, only 36.7% reported being aware of their condition and 32.9% reported being treated [6]. To the best of our knowledge, there are no ongoing nationwide initiatives that aim to

identify high-risk patients for CKD in the general population or to screen asymptomatic CKD cases among high-risk groups.

Early Diagnosis

Despite large investments in the primary healthcare system, the quality of healthcare provided by primary services remains insufficient for timely diagnosis or appropriate referral. For example, simple tests (e.g., for albuminuria) are available to identify those at risk or with early-stage CKD, although these are not widely utilised [40]. A major challenge in China to improve primary healthcare is attracting physicians to community and regional healthcare practices. Consequently, the level of education among healthcare professionals at the community level is poor. There also appears to be limited knowledge of current CKD guidelines [1, 38, 41–46] among non-specialist physicians and shortfalls in the awareness of important risk factors for CKD in primary healthcare settings.

Early and Effective Management

Unmet needs concerning the management of patients with CKD in China are summarised in Table 1.

Treatment Access

Health reforms have achieved almost universal health insurance coverage among Chinese residents, but health expenses remain high, mainly for those from lower socioeconomic backgrounds. For ESKD patients, the financial burden is particularly high. Over 10 years, the cost of peritoneal dialysis and haemodialysis is approximately USD 118,000 and USD 131,000, respectively. These costs are accompanied by 6.55 (peritoneal dialysis) and 6.42 (haemodialysis) quality-of-life years [47]. Despite peritoneal dialysis being more cost-effective than haemodialysis in China, the latter is the major renal replacement therapy used (>90%) [21]. This is largely due to limited access geographically, which may be influenced by socioeconomic factors [47].

Current and Recommended Strategies to Improve Prevention, Diagnosis, and Management of CKD in China

Improve Clinical and Self-Management of CKD Risk Factors

Self-management is fundamental in controlling risk factors for CKD. A meta-analysis and systematic review of self-management interventions for CKD found that self-management (e.g., lifestyle modifications such as for nutrition and physical exercise, and/or medical behaviour modifications such as treatment adherence and complication control) can lead to lower blood pressure, C-reactive protein, and glycated haemoglobin (HbA1c) levels in CKD patients [48]. Despite the reported benefits, self-management is poorly understood by patients and physicians [49] and each has frequently cited lack of CKD knowledge and difficulties in making necessary lifestyle changes as barriers to effective self-management [49]. The Chinese practices Tai Chi and Qigong have been independently found to improve modifiable CKD risk factors (e.g., hypertension) [50, 51], suggesting their incorporation into a self-management programme may benefit some patients. Emerging e-health technologies may also help optimise long-term management and follow-up of patients engaged in self-management practices [52].

Establish a Targeted Screening Programme in High-Risk Individuals

Secondary prevention of CKD may be best achieved by identifying those at high risk of CKD before a substantial decline in kidney function. The CKD Prognosis Consortium has developed two equations for predicting the 5-year risk of reduced eGFR by using data from more than 5 million individuals from 34 multinational cohorts [53]. These two models demonstrated high discrimination and variable calibration in DM and non-DM subgroups [53]. Other risk scores to identify patients at risk for developing CKD generally include easy-to-collect patient factors such as age, sex, diabetes, and blood pressure [54, 55]. A recently published prediction tool based on a comprehensive general population health survey between 2000 and 2015 was included (n = 22,200) indicating that self-reported lifestyle and health behaviour information may assist in predicting incident CKD [56].

The consensus from the Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference recommended that screening coupled with risk stratification and treatment should be implemented immediately for high-risk individuals [57]. Adding individuals with low socioeconomic status, rather than elderly individuals, to traditional CKD high-risk groups may help detect those with a higher risk for future cardiovascular events and renal function decline [58]. A KDIGO US commentary on the KDIGO 2012 guidelines highlighted the economic implications of an ineffective screening programme, i.e., using tests with unproven or limited value [59]. However, in general, the cost of diagnostic tests for CKD is low, while cost of treatment during advanced stages of the disease is high [60]. A systematic review of nine studies on primary screening for CKD

Table 1. Unmet needs in the early and effective management of CKD in China

Unmet need	Description
A cure for CKD	• Current kidney-preserving care is a life-sustaining conservative management therapy with the primary goal of slowing CKD progression and preserving kidney function [51] • Current approaches aim to prolong survival, improve cardiovascular health, and improve health-related quality of life through effective treatment of renal and nonrenal comorbidities and their associated symptoms [6]
Limited treatment to reduce risk for progression or adverse cardiovascular events	• Current recommended treatments for slowing CKD progression, such as RAASis (ACEis and ARBs) [6], have been shown to reduce the risk of kidney failure by 30–39% and cardiovascular events by 18–24% [61]. However, 15–68% of patients with stage 3–5 CKD do not initiate RAASi therapy [62] • Among those who receive RAASi therapy, dose reduction and discontinuation are common, mostly due to hyperkalaemia [63]. Suboptimal dosing of RAASis increases the risk of mortality and major adverse cardiovascular events in patients with CKD [63]
Optimal management for patients who experience disease progression	• There is limited awareness of CKD management among physicians in China: only 46.9% of doctors in secondary and tertiary hospitals in China reported that they had adopted the KDOQI and/or KDIGO guidelines in their clinical practice [27] • In the event of CKD progression, referral to a nephrologist is recommended by KDIGO guidelines [6], but there is a lack of coordination and cooperation between healthcare tiers in China [64, 65], impacting referral and continuous management. In the USA, seeing a non-nephrologist versus a nephrologist [66] and late versus early referral [67] is associated with poorer management in patients with advanced CKD
Consistency of care	• The quality of healthcare and patient satisfaction with healthcare provided is not consistent between hospital tiers [65, 68], regions [31, 69], and patients from different socioeconomic backgrounds [69] • The lack of consistency in patient care may hamper nationwide efforts to intervene early in (or before) the development of CKD across the general population in China and to provide appropriate management for all CKD patients in China throughout their disease course

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; KDIGO, Kidney Disease: Improving Global Outcomes; KDOQI, Kidney Disease Outcomes Quality Initiative; RAASi, renin-angiotensin-aldosterone system inhibitor.

concluded that CKD screening using eGFR or proteinuria-based testing may be cost-effective (<$50,000/QALY [2011 US dollars]) in patients with DM or hypertension (i.e., high-risk populations), and cited the incidence of CKD, rate of progression, and effectiveness of drug therapy as major drivers of cost-effectiveness. Accordingly, a cost-utility analysis of the National Health Screening Program for CKD in Korea found that screening was more cost-effective in patients with DM or hypertension than in the general population [61]. Use of CKD risk scores may be a cost-effective way for clinicians to identify broader populations for CKD screening with proteinuria-based testing than screening only patients with DM or hypertension [62]. Given that a high proportion of patients with CKD in China fall into one or more conventional high-risk categories, and patients overwhelmingly prefer earlier CKD screening and diagnosis, we believe a targeted screening programme in China is likely to be successful.

Ideally, screening of high-risk groups would occur in a primary-care setting [57]. This could be realised by incorporating findings from other countries. For example, an Australian study found that point-of-care testing for pathology measurements can be incorporated into a CKD screening programme, removing the need to transport samples for centralised testing [63].

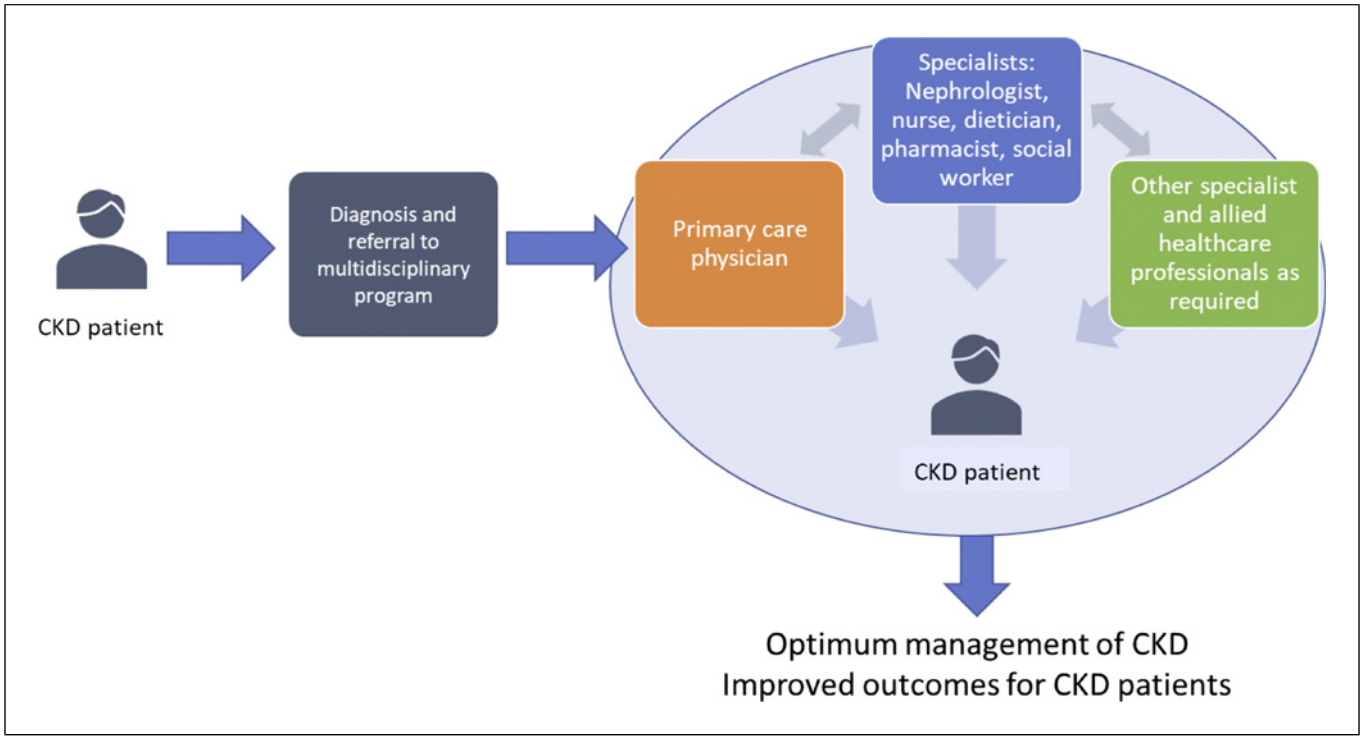

Fig. 3. Multidisciplinary model for CKD management. Multidisciplinary management of CKD allows simultaneous and complementary management by primary-care physicians, specialists, and allied healthcare professionals, and may lead to improved outcomes for CKD patients. There is currently no consensus on the optimum composition of a specialist multidisciplinary team, although commonly they comprise a nephrologist, nurse, dietician, and either a pharmacist or social worker. CKD, chronic kidney disease.

Address Gaps in Physician Knowledge of CKD

Current educational investments, such as in-service training, may help attract more qualified workers into primary healthcare settings [35, 64]. Additional investment to improve knowledge of international [1, 42, 43, 65] and regional [38, 41, 44–46] CKD guidelines among specialist physicians may help improve timely management of CKD, its common comorbidities, and associated complications such as mineral and bone disorder. CKD has a heterogenous array of underlying causes and risk factors and is itself a risk factor for renal failure and other diseases due its impact on cardiovascular risk. Several different interventions [41], including nutritional support [45], may therefore be required to adequately manage CKD. CKD has been shown to respond favourably to an integrated, multidisciplinary management approach [66], which can provide patients with complementary knowledge, skills, and experience that may not be available from their nephrologist. A multidisciplinary approach allows different specialists to collaboratively treat the same disease and, with regard to CKD, allows simultaneous management of, e.g., blood pressure, proteinuria, mineral bone disorder, cardiovascular risk reduction, diabetes, lifestyle interventions, medication adherence, and self-management [67]. Globally, there is no consensus on the optimum composition of a multidisciplinary team for CKD management, which is likely due to the differences between countries in terms of patients, clinicians, other stakeholders, and healthcare systems [67]. However, multidisciplinary CKD teams commonly comprise a nephrologist, nurse, dietician, and either a social worker or a pharmacist, but may also include other specialists and allied health professionals such as a surgeon, counsellor or personal support volunteer, manager or coordinator, diabetes educator, or psychologist [67] (Fig. 3). Primary-care physicians also play an essential role in the long-term care of patients with CKD [68, 69], reinforcing the importance of improving knowledge of CKD through all levels of the healthcare system.

Accelerate Creation of Supporting Bodies and Expand the National CKD Surveillance Programme

Medical Consortia

Medical consortia, led by a major city or country hospital, facilitate cooperation between medical teams

and hospital tiers and improve resource allocation, operational efficiency, and healthcare service continuity. Moreover, a two-way referral system between upper/lower hospitals and general/specialised services can reduce medical and travel costs for patients [70]. Migration from primarily hospital- to community-based management has proven successful in reducing blood pressure and improving secondary prevention of stroke among patients in rural China [71], while use of medical consortia has also shown improved outcomes among cancer patients in China [72].

Satellite Centres

Creation of community-based dialysis satellite centres in recent years has helped improve the care of ESKD patients in rural China, reduce travel costs, and relieve the burden on hospital-based dialysis centres in larger cities. Further improvements can be made by creating additional satellite centres in areas not already serviced and by utilising data from the CNRDS [73]. The prospective data collected by the CNRDS can be retrospectively analysed to reveal information and trends on prevalence, incidence, mortality, technical failures, and peritonitis among dialysis patients [74], which may help inform future resource allocation.

National Medical Research Centres

To date, several national medical research centres for CKD have been established, including the Nanjing General Hospital of the People's Liberation Army, the Chinese People's Liberation Army General Hospital, and the Nanfang Hospital of Southern Medical University. These centres integrate ongoing research in prevention and treatment of CKD on a national level, cultivate leaders in the field of nephrology research, carry out training for primary healthcare workers, optimise primary health service models, and guide primary health diagnosis and treatment capabilities [35].

National CKD Surveillance Programme

Using electronic health data, a national CKD surveillance programme should be established to monitor disease trends, study risk factors, and mobilise public health resources for CKD prevention and management. The China Kidney Disease Network (CK-NET), which provides reports on the burden of CKD in China, is now rapidly expanding, with more than 60 large renal centres and access to data from several large databases [21]. The CK-NET-Yinzhou study is an expansion of CK-NET, incorporating longitudinal electronic health data from >1 million people in Yinzhou district [75], with the aim of monitoring the incidence, prevalence, prognosis, complications, and management of CKD, as well as optimising the management of CKD via development of an intelligent clinical decision support system [75].

Provide Appropriate Management to Slow Disease Progression

Conventional Management

Similar to the management of risk factors, progression of CKD can be attenuated via a combination of lifestyle and dietary interventions (e.g., increasing physical activity, restricting sodium intake, eating a higher proportion of plant-based protein, stopping smoking) and pharmacological interventions that reduce the risk of cardiovascular disease via the management of hypertension or diabetes [1, 76]. Management can be individualised, but adherence to all interventions is important in reducing the burden of CKD.

The KDIGO guidelines recommend a target systolic blood pressure <130 mm Hg for all patients with urine albumin excretion ≥30 mg/24 h. Additionally, in CKD patients with DM, KDIGO guidelines recommend an individualised HbA1c target ranging from <6.5% to <8.0% in non-dialysis patients [1, 43]. Renin-angiotensin-aldosterone system inhibitor therapy is currently recommended in adults with diabetes and 30–300 mg/day albumin excretion, and in diabetic and non-diabetic adults with albumin excretion >300 mg/day [1]. Maximum approved tolerated RAASi dosing is recommended, with angiotensin-converting enzyme inhibitors or angiotensin receptor blocker-associated hyperkalaemia managed by measures that reduce potassium rather than decreasing or stopping ACEi or ARB treatment [43].

CKD Novel Therapies

Antihyperglycaemic agents used to manage type 2 DM, namely, sodium-glucose transport protein-2 (SGLT2) inhibitors, have shown promising renoprotective effects, independent of their ability to decrease blood glucose levels. SGLT2 inhibitors are recommended in combination with metformin as first-line therapy for glycaemic control in patients with CKD and DM [43].

SGLT2 Inhibitors

Several large cardiovascular outcome trials have demonstrated the efficacy of SGLT2 inhibitors such as dapagliflozin [77], canagliflozin [78, 79], and empagliflozin [80] in reducing cardiovascular risk in CKD patients with DM. The agents also improved renal outcomes among the same patient populations [79, 81]. These benefits appear to translate into real-world clinical practice [82].

The Food and Drug Administration and European Medicines Agency approved dapagliflozin in April and August 2021, respectively, for patients with CKD regardless of DM status. This came 2 decades after the last approval of a new therapy to slow the progression of CKD. Approval was based on results of the DAPA-CKD trial (32.4% non-diabetic patients in dapagliflozin arm), which revealed a significantly lower risk of a composite sustained decline in the eGFR of at least 50%, ESKD, or death from renal or cardiovascular causes with dapagliflozin versus placebo (HR 0.56, 95% CI: 0.45–0.68; $p < 0.001$) [83]. In a prespecified analysis, outcomes were similar between patients with and without DM: for the primary composite outcome, relative risk reduction for patients with and without DM was 36% (HR 0.64, 95% CI: 0.52–0.79) and 50% (HR 0.50, 95% CI: 0.35–0.72), respectively ($p_{interaction} = 0.24$). Results were also similar for the kidney-specific composite outcome (HR 0.57 [95% CI: 0.45–0.73] vs. 0.51 [95% CI: 0.34–0.75]; $p_{interaction} = 0.57$), hospital admission for heart failure (HR 0.70 [95% CI: 0.53–0.92] vs. 0.79 [95% CI: 0.40–1.55]; $p_{interaction} = 0.78$), and all-cause mortality (HR 0.74 [95% CI: 0.56–0.98] vs. 0.52 [95% CI: 0.29–0.93]; $p_{interaction} = 0.25$) [84].

In the DAPA-HF and EMPEROR-Reduced trials, SGLT2 inhibitor treatment led to a reduced risk of cardiovascular death or hospitalisation for heart failure and a reduced risk of renal outcome versus placebo in patients with heart failure and reduced ejection fraction. A trial investigating empagliflozin in patients with CKD with/without DM is ongoing (EMPA-KIDNEY; NCT03594110).

Other Therapies under Investigation

Both the SONAR and FIDELIO-DKD trials enrolled CKD patients with DM and investigated renal outcomes. SONAR found that atrasentan, an endothelin receptor agonist, reduced the relative risk of the primary composite renal endpoint by 35%. Hospitalisations for heart failure increased versus placebo, although this was not statistically significant [85]. The FIDELIO-DKD trial showed that finerenone, a mineralocorticoid receptor agonist, reduced the relative risk of the primary composite outcome by 18% [86].

Monitoring and Management of Complications

Effective CKD management also involves counselling on avoidance of nephrotoxic drugs and the monitoring and treatment of kidney failure, electrolyte imbalances, bone and mineral abnormalities, and anaemia [1, 41, 42, 46, 87]. Regular monitoring is recommended (with intervals determined by disease stage and the magnitude of abnormality) as it allows timely adaptation and individualisation of management strategies.

Conclusions

CKD is an incurable disease requiring lifelong management. There are currently many unmet needs for patients with CKD and high-risk individuals with modifiable risk factors. Without an integrated, nationwide strategy, the current burden of CKD in China is unlikely to improve. We believe a holistic approach is necessary to address the unmet needs experienced by CKD patients in China. Key to the success of this approach will be the implementation of evidence-based policy to promote primary intervention and early identification, improve doctor and patient understanding of the disease, increase cooperation between healthcare tiers, and improve access to therapies and medical services. Novel therapies will also provide new solutions for the management of CKD, but the focus of future clinical trials should be on all CKD patients rather than only those with specific conditions.

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Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Ping Fu, Jing Liu, and Yunying Shi proposed the initial concept and contributed to the first draft; Yongshu Diao and Xiaoxi Zeng collected relevant literature and data for the manuscript; Ping Fu and Xiaoxi Zeng reviewed and provided critical feedback on manuscript drafts. Jing Liu, Yunying Shi, Yongshu Diao, Xiaoxi Zeng, and Ping Fu approved the final version for publication.

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