

## CKD in China: Evolving Spectrum and Public Health Implications

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Diabetes is the leading cause of kidney failure worldwide, whereas glomerulonephritis has been predominant in developing countries such as China. The prevalence of obesity and diabetes has increased dramatically in developing countries, substantially affecting the patterns of chronic kidney disease (CKD) observed in these regions. Using data from the Hospital Quality Monitoring System to evaluate changes in the spectrum of non-dialysis-dependent CKD in China, we have observed an increase in the percentage of patients with CKD due to diabetes, which has exceeded that of CKD due to glomerulonephritis since 2011, as well as an increase in hypertensive nephropathy and, in some regions, obstructive kidney disease (mostly associated with kidney stones). The growth of non-communicable diseases under profound societal and environmental changes has shifted the spectrum of CKD in China toward patterns similar to those of developed countries, which will have enormous impacts on the Chinese health care system. There is much to be done regarding public health interventions, including the establishment of a national CKD surveillance system, improvement in the management of diabetes and hypertension, and enhancement of the affordability and accessibility of kidney replacement therapy. Reducing the burden of CKD will require joint efforts from government, the medical community (including practitioners other than nephrologists), and the public.

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Kidney failure is a leading cause of morbidity and mortality and is growing as a major public health problem worldwide.<sup>1</sup> In 2010, it was estimated that 2.62 million people were receiving kidney replacement therapy (KRT) for chronic kidney failure, with at least 2.28 million others dying prematurely due to lack of access to KRT.<sup>2</sup> The largest treatment gaps were observed in low-income countries, particularly in Asia and Africa.<sup>2</sup> In many countries, diabetes mellitus (DM) is the leading cause of end-stage kidney disease (ESKD), accounting for one-third of incident cases,<sup>3</sup> while glomerulonephritis (GN) is predominant in most developing countries.<sup>4,5</sup>

However, recent data are limited due in part to the substantial challenge of designing and implementing a survey of chronic kidney disease (CKD) causes in such countries, many of which have undergone substantial lifestyle and societal changes accompanied by economic development and globalization. These changes are often accompanied by dramatic increases in the prevalence of obesity and DM,<sup>6</sup> which may have a substantial impact on CKD in emerging countries such as China.

### The State of CKD in China

#### Survey-Based Prevalence Data

In a nationwide survey conducted between 2009 and 2010 using a multistage stratified sampling method to obtain a representative sample of the adult population, we reported the prevalence of CKD in China to be 10.8%,<sup>7</sup> which was comparable to results from the National Health and Nutrition Examination Survey (NHANES) in the United States.<sup>8</sup> In 2018, we reported that the prevalence of CKD (estimated glomerular filtration rate < 60 mL/min/1.73 m<sup>2</sup>) was higher in the United States than in China (6.5% vs 2.7%).<sup>9</sup> Further analyses revealed that nearly

two-thirds of this difference was accounted for by the prevalence and magnitude of CKD risk factors, including age, sex, DM, hypertension, central obesity, cardiovascular disease, and hyperuricemia.<sup>9</sup>

#### New Opportunities for Monitoring CKD in China

In 2009, China launched a new round of health care system reform that was aimed at improving the medical insurance system. Currently >95% of China's population are covered by the basic health insurance provided by the government. The Chinese government has also made efforts to strengthen the primary care system and build a referral system, although the situation still needs to be improved.

These health care reform activities have opened new opportunities for data capture and analysis. Starting in 2013, our group has had access to a national inpatient database under the support of the National Health Commission (NHC) of the People's Republic of China and the World Health Organization (WHO), with the initial aim to provide evidence for policy making regarding kidney disease.

Details of the database, the Hospital Quality Monitoring System (HQMS), were described elsewhere.<sup>10</sup> In brief, the NHC requires that all tertiary hospitals in China submit inpatient discharge summaries to HQMS in a standardized electronic format on a daily basis. This summary information contains 346 variables, including demographic characteristics and discharge diagnoses (International Classification of Diseases, Tenth Revision [ICD-10]). Although the HQMS was established in 2013, hospitals were requested to retrospectively report data back to January 2010. Currently 74% of tertiary hospitals are reporting data to HQMS, which provides a unique opportunity to investigate the status of CKD in China.

However, there are some limitations, such as the fact that the hospitalized sample is limited to tertiary hospitals. In China, tertiary hospitals are those that have at least 500 beds and are ranked as the top tier of the medical system. As opposed to tertiary hospitals in the Western medical system, their Chinese counterparts provide primary, secondary, and tertiary care and have exposure to a nationwide patient population. The number of patient visits in tertiary hospitals accounts for >50% of total patient visits in the nation.<sup>11</sup> Even so, because the HQMS is confined to data from tertiary hospitals, this may lead to selection bias.

### The Evolving Spectrum of CKD in China

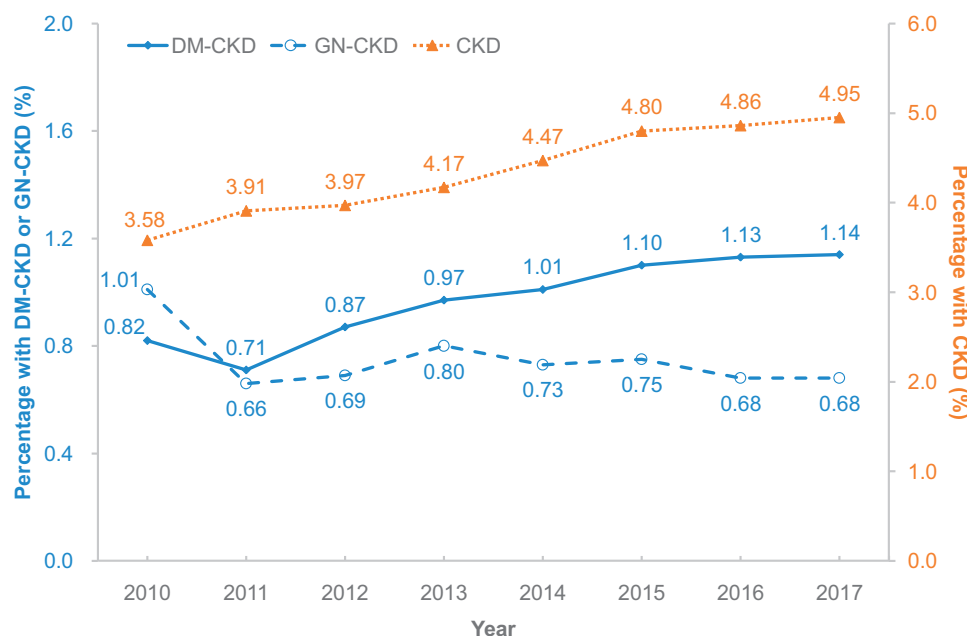
Based on data from the HQMS and using ICD-10 coding of discharge diagnoses to identify patients with CKD, we have evaluated the frequency and spectrum of non-dialysis-dependent CKD among hospitalized patients in China. We observed an increase in the percentage of hospitalized patients with CKD from 2010 (3.58%) to 2017 (4.95%). The percentage with CKD due to DM (DM-CKD) has exceeded that of CKD due to glomerulonephritis (GN-CKD) since 2011.<sup>12</sup> Since 2011, the gap between DM-CKD and GN-CKD has gradually increased, such that in 2017, a total of 1.14% of hospitalized patients had DM-CKD versus 0.68% with GN-CKD (Fig 1). These numbers are substantially lower than the prevalence reported from the national survey in China (10.8%),<sup>7</sup> which could be partly attributable to the low sensitivity of CKD identification by discharge diagnoses.<sup>10</sup> It should be noted that these percentages are based on a combination of actual CKD prevalence, hospitalization rate, and diagnostic rate.

A similar upswing in DM-CKD has been observed in other Asian regions. For example, in South Korea, GN-CKD was the major cause of ESKD until 1993.<sup>13</sup> Since then, DM-CKD has overtaken GN-CKD and accounted for 48% of incident patients with ESKD in 2014.<sup>13</sup> To our knowledge, our analysis is the first to capture the transition among patients with non-dialysis-dependent CKD in China.

Besides documenting an increase in DM-CKD, HQMS data have revealed an increasing trend of hypertensive kidney disease and obstructive nephropathy (mostly associated with kidney stones) during the 2010 to 2015 period.<sup>10</sup> We have also observed substantial geographic variations in the spectrum of CKD. For example, using data from 2015, we reported that more than one-half of urban patients with CKD had DM-CKD or hypertensive nephropathy diagnosed, while among rural residents, the top 3 causes were obstructive nephropathy, GN-CKD, and DM-CKD.<sup>14</sup> In north China, the percentage of hospitalized patients with DM-CKD was relatively higher among urban versus rural residents, while this pattern was reversed for GN-CKD.<sup>10</sup> South China had a higher percentage of patients with obstructive nephropathy.<sup>10</sup> Considering the relatively homogeneous ethnicity in China, lifestyle and environment may be involved in this variation, which deserves further investigation.

### Possible Explanations for the Evolving Spectrum of CKD

In the past 3 decades, along with economic growth and rapid urbanization, China experienced a dramatic shift in



**Figure 1.** Trends in chronic kidney disease (CKD) due to diabetes (DM-CKD) or glomerulonephritis (GN-CKD) among hospitalized patients in China. Percentages are calculated based on overall numbers of hospitalized patients for each year, obtained from the Hospital Quality Monitoring System. *International Classification of Diseases, Tenth Revision* coding of discharge diagnoses was used to identify patients with CKD and extract cases of DM-CKD and GN-CKD.

diet and lifestyle from traditional to Western patterns.<sup>15</sup> It was reported that the overall prevalence of overweight and obesity, based on the WHO standard, increased from 6.6% in 1982 (overweight, 6.0%; obesity, 0.6%) to 21.8% in 2002 (overweight, 18.9%; obesity, 2.9%).<sup>16</sup> This trend in body mass index among the Chinese population has catapulted China upward in the worldwide ranking of the number of severely obese individuals. In 1975, Chinese men and women ranked in 60th and 41st place, respectively, in terms of severe obesity; by 2014, both were ranked second globally.<sup>17</sup>

A recent study estimated that high body mass index was the leading individual-attributable factor for DM in China, responsible for 43.8 million cases, with a population-attributable fraction of 46.8% in 2011.<sup>18</sup> Besides body mass index, physical inactivity, smoking, low whole-grain intake, and high intake of refined grains and sugar-sweetened beverages also contribute substantially to increased risks for the cardiovascular disease and DM burden in China.<sup>18,19</sup> Furthermore, salt has been widely used in many traditional diets as a preservative and as a way to add appeal to monotonous high-carbohydrate diets in China. Sodium intake is substantially higher in northern China than it is in southern regions, which contributes to the variation in the prevalence of hypertension and cardiovascular disease risk.<sup>20</sup>

Diseases such as DM and hypertension have increased rapidly in China. Based on a cross-sectional survey involving 0.3 million participants in 1980, the prevalence of DM was estimated to be 0.67%.<sup>21</sup> Fifteen years later, a nationwide survey revealed that the prevalence of DM and impaired glucose tolerance increased to 2.5% and 3.2%, respectively.<sup>22</sup> In 2007 to 2008, the prevalence almost quadrupled, to 9.7% for DM and 15.5% for prediabetes.<sup>23</sup> A more recent national survey in 2013 reported the prevalence of DM at 10.9%,<sup>24</sup> corresponding to about 122.4 million individuals in China. Similarly, the prevalence of hypertension has increased from 12.5% among men and 10.7% among women in 1991<sup>25</sup> to 31.2% among men and 28.0% among women in 2009 to 2010 (Table 1).<sup>26</sup>

We conclude that the growth of noncommunicable diseases including DM and hypertension under profound societal and environmental changes has shifted the spectrum of CKD in China so that it is now similar to that of developed countries. However, due to substantial variations in the degree of urbanization, lifestyle, and dietary pattern,<sup>27</sup> this transition in the spectrum of CKD varies substantially across China, which needs to be considered when considering management strategies at the population level.

### Long-term Public Health Implications for the Health Care System

ESKD due to DM can be expected to have a huge impact on the health care system in China. The Hong Kong Diabetes Registry reported an incidence of ESKD among Chinese patients with DM of 8.69 (95% confidence interval,

7.78-9.60) per 1,000 person years.<sup>28</sup> Given the lack of corresponding national data, we extrapolated from data from the Hong Kong Diabetes Registry and estimated the potential number of Chinese mainland patients with ESKD due to DM to be approximately 1.06 million, which is much larger than the number of prevalent dialysis patients in 2015 (0.40 million).<sup>29</sup> Because dialysis is covered by the Basic Health Insurance policy in China,<sup>30</sup> 1.06 million incident dialysis patients each year would correspond to an additional 106 billion Renminbi (RMB; about US \$15.3 billion) annually. This translates to dialysis expenses of 1.59 trillion RMB in next 5 years, which would equal 1.3 times the annual government health expenditure in 2015.<sup>31</sup> Considering the increasing trend of ESKD due to other metabolic diseases besides DM, as well as increased health care resource utilization for patients with non-dialysis-dependent CKD, the long-term impact of CKD on the health care system in China would be enormous and needs to be addressed urgently.

## What Needs to Be Done

### Establishment of a CKD Surveillance System

Population-based surveillance of disease has become an important component of addressing common chronic diseases such as hypertension and DM. Such systems have the potential to guide screening, prevention, and treatment resources, but are only beginning to be implemented for CKD in a few countries.<sup>32</sup> In Asia, Japan has made efforts to investigate risk factors for progression of CKD and ESKD development. The CKD-Japan Cohort (CKD-JAC) study has been active since 2007, with a sample size limited to 3,000 patients with CKD.<sup>33</sup> For emerging countries such as China that are experiencing an increased burden and evolving disease spectrum, a CKD surveillance system would be even more important given the absence of updated nationwide data on CKD.

Currently there are some regional attempts to monitor CKD<sup>34</sup> but no government-funded national surveillance system for kidney disease in China. The China Kidney Disease Network (CK-NET), which is funded by Peking University, is working on building a surveillance system and releasing annual data reports of kidney disease in China by integrating administrative and claims data.<sup>14,35</sup> However, those data are not collected for research purposes, and the estimation of prevalence based on those data involve several assumptions, such as using ICD-10 codes or items of medical service claim instead of laboratory results to ascertain patients.

Integrating feasible screening methods for kidney disease into existing government-funded chronic disease surveillance systems is also needed. Because of the efforts of the Chinese Society of Nephrology, since 2018, the Chinese Center for Disease Control and Prevention has included both estimated glomerular filtration rate and urinary albumin-creatinine ratio in the China Chronic Disease and Nutrition Surveillance, which will provide

**Table 1.** Summary of Several Nationwide Surveys of the Prevalence of Overweight and Obesity, Diabetes, and Hypertension in China

Year of Survey	Sample Size	Age, y	Prevalence, %	Sampling Method	Strength	Limitation
Overweight and Obesity						
1982	238,134	—	6.6% (overweight: 6.0%; obesity: 0.6%)	Multistage stratified cluster sampling	Nationally representative sample	Focused on investigating the nutritional status; without creatinine and urine tests
2002	252,912	—	21.8% (overweight: 18.9%; obesity: 2.9%)			
Diabetes						
1980	304,537	—	0.67%	Convenience sampling & stratified sampling	First national survey of the prevalence of diabetes	Original screening methods; without creatinine and urine tests
1994	213,515	25~64	2.5% (impaired glucose tolerance: 3.2%)	Convenience sampling & stratified sampling	First national survey of the prevalence of impaired glucose tolerance	
2007-2008	46,239	≥20	9.7% (prediabetes: 15.5%)	Multistage stratified sampling	Nationally representative sample; based on WHO criteria	Without creatinine and urine tests
2013	170,287	≥18	10.9% (prediabetes: 35.7%)			
Hypertension						
1991	950,356	≥15	11.6% (men: 12.5%; women: 10.7%)	Multistage stratified cluster sampling	Nationally representative sample; first using BP level & antihypertensive drug use to define hypertension	Without creatinine and urine tests
2009-2010	50,171	≥18	29.6% (men: 31.2%; women: 28.0%)	Multistage stratified cluster sampling	Nationally representative sample; with creatinine and urine tests	Originally designed to investigate the prevalence of CKD

Abbreviations: BP, blood pressure; CKD, chronic kidney disease; WHO, World Health Organization.  
Based on data in references<sup>16,21-26</sup>.

## Perspective

updated information regarding the prevalence, awareness, treatment, and control of CKD in China. This study has investigated a nationally representative sample of adults based on the multistage cluster random sampling method, and data collection from 302 monitoring sites in China has been completed.

### Improving the Management of DM and Hypertension at the Population Level

Management of DM and hypertension at the population level in China is far from satisfactory. According to a Chinese national survey based on the general population, among patients with DM, only 32.2% received treatment for DM, and only 49.2% of treated patients had a hemoglobin A<sub>1c</sub> level < 7.0%.<sup>24</sup> In a nationally representative sample of Chinese adults, only 27.4% of treated hypertensive patients had blood pressure < 140/90 mm Hg.<sup>26</sup> Furthermore, although renin-angiotensin system inhibitors are effective in reducing the risk for adverse kidney outcomes, including ESKD,<sup>36,37</sup> in our hospitalized population data set, less than one-third of patients with DM-CKD were using these medications (unpublished data). By comparison, 70% to 80% of patients with DM-CKD in the United States are treated with renin-angiotensin system inhibitors.<sup>38</sup>

Suboptimal disease management is not unique to China. According to the Joint Asia Diabetes Evaluation study, based on 41,209 patients with DM from 9 Asian countries or regions, <20% of patients had their blood glucose, blood pressure, and low-density lipoprotein cholesterol levels under control.<sup>39</sup> Hence, the joint efforts by general practitioners, multidisciplinary physicians, and the public to improve the management of metabolic diseases as a means of primary prevention of CKD are urgently needed in developing countries such as China.

### Improving the Affordability and Accessibility of KRT

Historically, affordability has been a major constraint on the use of KRT in China. Since 2003, the government has initiated universal health insurance coverage to narrow the gap between demand and supply for KRT.<sup>40</sup> Current insurance policies cover the costs of KRT, with the proportion of payment that is out of pocket varying from 10% to 40% according to geographic region.<sup>40</sup> In 2016, the Chinese government announced that the Urban Resident Basic Medical Insurance and the New Rural Co-operative Medical Care Scheme would be merged into 1 system in the next few years. This will have the effect of further increasing the affordability of KRT for rural residents. Another driver of increased affordability of KRT could be commercial insurance. Although currently commercial insurance constitutes <10% of overall health care expenditures in China, there is substantial enthusiasm in both the government and the companies to increase this proportion.

Accessibility is another important constraint to delivering KRT in China. With support from the government, the number of hemodialysis centers in China has increased

from 3,511 in 2011 to 4,089 in 2015.<sup>29</sup> Originally the government required all hemodialysis centers to be affiliated with public hospitals, but in December 2016, the NHC announced a new policy of allowing independent hemodialysis centers in China.<sup>41</sup> Since then, more than 150 independent hemodialysis facilities have been set up, most at the county and township level, substantially improving the accessibility of KRT in these less well-developed areas.

Despite these efforts, considering the potential massive increase in the number of patients reaching ESKD, affordability and accessibility will still be a huge challenge in the future. An additional complicating factor is that the ratio of nephrologists to patients with CKD in China is 1:15,000.<sup>42</sup> Furthermore, because the referral system has not been well established in China, many nephrologists are also exposed to patients without kidney diseases or who could be treated by general practitioners, which imposes further challenges to CKD care. To improve the situation, establishment of a well-functioned referral system, as well as training general practitioners, would be necessary.

### Conclusions

During a period of major economic expansion and urbanization, the spectrum of CKD in China has been evolving toward that of developed countries. This shift will have enormous impact on the health care system in China. Reducing the burden of CKD needs joint efforts from government, the medical community (including but not limited to nephrologists), and the public.

### Article Information

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## Perspective

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