

# Global case studies for chronic kidney disease/end-stage kidney disease care



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The prevalence of chronic kidney disease and its risk factors is increasing worldwide, and the rapid rise in global need for end-stage kidney disease care is a major challenge for health systems, particularly in low- and middle-income countries. Countries are responding to the challenge of end-stage kidney disease in different ways, with variable provision of the components of a kidney care strategy, including effective prevention, detection, conservative care, kidney transplantation, and an appropriate mix of dialysis modalities. This collection of case studies is from 15 countries from around the world and offers valuable learning examples from a variety of contexts. The variability in approaches may be explained by country differences in burden of disease, available human or

financial resources, income status, and cost structures. In addition, cultural considerations, political context, and competing interests from other stakeholders must be considered. Although the approaches taken have often varied substantially, a common theme is the potential benefits of multistakeholder engagement aimed at improving the availability and scope of integrated kidney care.

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The prevalence of chronic kidney disease (CKD) and its risk factors is increasing worldwide, and there is a rapid rise in global need for the treatment of end-stage kidney disease (ESKD). The global nephrology community recognizes the need for a plan to address the growing incidence of CKD and a cohesive approach for CKD/ESKD integrated care.<sup>1</sup> This provides a major challenge for health systems, particularly

in lower-middle-income countries (LMICs). Because of the growing demand for expensive kidney replacement therapy (KRT; dialysis or kidney transplantation) and in light of the limited resources, ESKD care must be prioritized against the prevention and treatment of CKD, acute kidney injury (AKI), and other noncommunicable diseases (NCDs).

Countries are responding to the challenge of ESKD in different ways, with variable provision of the components of a kidney care strategy (effective prevention, detection, conservative care, kidney transplantation, and an appropriate mix of dialysis modalities) and World Bank classification of economic status.<sup>2</sup> A key goal stated in the article by Harris *et al.*<sup>1</sup> was to identify a representative selection of country-based case studies showing different levels of development in managing CKD/ESKD care, which offers valuable learning examples. This article illustrates the different approaches that 15 countries have taken toward integrated kidney care (Table 1). Specific areas of approach, in distinct contexts, provide unique experience in CKD, dialysis, and transplantation for ESKD care that are appropriate for each country. Variability in approaches may be explained by country differences in burden of disease, available human or financial resources, and cost structures. In addition, cultural considerations, political context, and competing interests from other stakeholders are confounding factors. This created value to appreciate the similarities and

differences of approaches among the unique pathways obtained from each country's cases.

Finally, the current approach to kidney disease in many countries is neither sufficient nor sustainable. Thus, this series of case studies demands the urgent attention of governments and policymakers in each country to achieve better integrated CKD/ESKD care.

## INTEGRATED CKD/ESKD CARE CASES

### Taiwan (high-income country): evolution of comprehensive integrated CKD/ESKD care

**Background.** High prevalent rates of CKD have continued in Taiwan and are reported to be 6.9% for CKD stage 3 to 5, 9.83% for clinically recognized CKD, and 11.9% for CKD stage 1 to 5. However, overall awareness of CKD is low.<sup>3</sup> The major underlying kidney diseases contributing to ESKD are diabetes mellitus (43.2%), chronic glomerulonephritis (25.1%), hypertension (8.3%), and chronic interstitial nephritis (2.8%).<sup>4</sup> The national kidney care program was initiated in response to high rates and has been successfully implemented across Taiwan, resulting in improvements in outcomes for patients along with sustainable cost reductions for the health care system. The pathway and evolution of the CKD/ESKD program in Taiwan may serve as a template in countries where CKD/ESKD is an emerging health care burden (Table 2 and Appendix 1).

**Action.** To monitor the incidence and burden of ESKD, a national dialysis registry was initiated in 1987 by the Taiwan Society of Nephrology. After this, the Taiwan Society of Nephrology proposed to the Department of Health to make CKD prevention and care a major public health priority. Subsequently, an integrated CKD care program was initiated to promote the screening of high-risk populations (according to the risk factor analysis of epidemiology studies), patient education, and multidisciplinary team care. The CKD care program started in major hospitals in the first phase, then extended to 90 institutes in 2009, and finally rolled out to clinics of general practitioners in 2011. To encourage enrollment in the CKD care program, the Bureau of National Health Insurance reimbursed comprehensive pre-ESKD care for patients with CKD stage 3b to 5 since 2007 and has extended coverage to CKD stage 1 to 3a (early CKD) in 2011.<sup>5-7</sup>

**Table 1 | Summary of the CKD/ESKD care study cases**

Country	Integrated CKD/ESKD care cases
Taiwan	Evolution of comprehensive integrated CKD/ESKD care
Japan	Mature CKD/ESKD care significantly reduced dialysis incidence
China	Promoting CKD/ESKD care with an increased access to KRT in rural patients
Mexico	Moving toward universal access of CKD/ESKD care
Sudan	CKD/ESKD care is a priority fund for lifesaving medicine
Senegal	Fundamental development of CKD/ESKD care
Country	CKD strategy cases
Uruguay	CKD screening and prevention program incorporated into mandatory health programs
Thailand	Mass health care infrastructure implemented for CKD programs
United Arab Emirates	Early CKD detection and management program
Country	Hemodialysis strategy cases
Malaysia	Near-universal coverage for dialysis
Malawi	Unique initiating strategy for ESKD care
Kenya	Upscaling hemodialysis
Country	Peritoneal dialysis strategy cases
South Africa	PD-First policy for children
Country	Transplantation strategy cases
Korea	System development for deceased donor kidney transplantation
Ghana	Framework for the development of living donor kidney donation

CKD, chronic kidney disease; ESKD, end-stage kidney disease; KRT, kidney replacement therapy; PD, peritoneal dialysis.

**Table 2 | Evolutionary pathway and road map of CKD/ESKD integrated care in Taiwan**

- Understanding the burden
  - Registry and data report
- Leadership structure
  - Nephrology society, government, policymaker, patient organization
- Standardization
  - Guidelines for CKD/ESKD care to meet local need and local risk factors
- Implementation
  - Multidisciplinary and multiprofessional approaches
- Sustainability and quality
  - Funding and health care coverage and outcome measures

CKD, chronic kidney disease; ESKD, end-stage kidney disease.

These efforts to combat CKD in Taiwan involve collaboration among government, academia and their respective societies, and nongovernmental organizations (NGOs) to enable a multidisciplinary approach that targets not just CKD but also upstream drivers such as diabetes, hypertension, and hyperlipidemia.

Since November 2003, widely used nephrotoxic Chinese herbs containing aristolochic acid were prohibited through public health legislation. This important step also contributed to CKD/ESKD prevention in Taiwan.

Dedicated nephrologists are key to the success of the program, as this group is crucial for performing roles ranging from CKD screening, education, and treatment to involvement and negotiation of public health policy. The CKD committee within the Taiwan Society of Nephrology was the core for the promotion of CKD prevention activities in collaboration with the government—including the Taiwan Kidney Day campaign, which started in 2005.

**Strategies for CKD/ESKD care.** The strategy and road map for CKD/ESKD care in Taiwan include the following:

- extending the target population from severe CKD to early stages of CKD as well as commencing kidney health promotion in the general population;
- integration of CKD as a target of pay-for-performance health care improvement projects, along with diabetes and cardiovascular disease;
- implementation of early detection and surveillance via national annual physical checkup data for early CKD;
- early referral to proper care clinics/hospitals;
- promoting health literacy to the general public; and
- increased attention to those at highest risk: elderly, multiple diseases, polypharmacy, and so on.

Other factors that have affected the incidence and prevalence of ESKD in Taiwan include universal health coverage (UHC) along with collaboration among government, academia, and NGOs with nephrology societies. Further efforts will be on the prevention and reduction of AKI, outcome monitoring, the promotion of CKD/ESKD shared decision-making, and kidney conservative care. Finally, sustainable quality care of patients with ESKD receiving KRT should be maintained as the ultimate goal.

**Impact.** Outcome measures include the stabilization of the incidence of ESKD in those younger than 75 years, along with lower mortality, better quality of care, less medical costs, better quality of life, and slower rate of progression in patients as demonstrated by findings from the pre-ESKD and early CKD integrated care program<sup>5–7</sup> and diabetes care program.<sup>8</sup> Recent progress of ESKD care has evolved to include more shared decision-making within advance care planning to enable patients and families to choose from various supportive or conservative care options (KRT and withholding/withdrawal of dialysis, where appropriate). The era of CKD care has in parallel progressed to include multidisciplinary care alongside cardiac-kidney-diabetes care with involvement from cardiologists, nephrologists, and endocrinologists. Together these specialists evaluate and educate through

dietary management, medical treatment, and surgical intervention, with the goal of reducing mortality and complications in patients with CKD/ESKD. A new concept of personalized care for patients with multimorbidities on dialysis was initiated to treat patients with evidence-based medicine according to the recommended guidelines while also adjusting and modifying for more personalized therapy. This approach has resulted in the stabilization of diabetes mellitus as a cause of ESKD in Taiwan and has also reduced the use of analgesics in patients with ESKD in the year before the initiation of dialysis.<sup>9</sup> The involvement of vascular surgeons in the care of patients on dialysis has also resulted in a reduction of vascular access reconstruction rates. The overall 5-year survival rate of patients on dialysis is currently ~55.2%, which lies between the rates observed in Japan and Europe. Although the rate of transplantation has been low in Taiwan, the recent promotion of living-related kidney transplantation has increased.

#### **Japan (high-income country): a mature integrated CKD/ESKD care system**

**Background.** Strategies and action plans for kidney disease have been discussed and implemented in collaboration with national and local governments, academic societies, nonprofit organizations, and patient groups in Japan.

**Action.** Strategies for kidney disease in Japan have focused on early diagnosis of kidney disease by health checkups conducted in schools or workplaces, improvement in CKD care, and dialysis therapy. Dialysis therapy has been covered by health insurance since 1967, and patients requiring maintenance dialysis treatment have been exempted from medical expenses since 1972. Kidney transplantation has been covered by health insurance since 1978, and the Organ Transplant Law of Japan was legislated in 1997. The Ministry of Health, Labour and Welfare promotes various areas of research, such as the kidney failure research team (founded in 1989) and the medical care of chronic kidney failure (published guidelines for dialysis initiation in 1991).

Following the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification of Risk, a CKD initiative subcommittee was launched in the Japanese Society of Nephrology (JSN) in 2004.<sup>10</sup> To raise awareness of CKD and its complications to society and promote its measures on a national scale, the Japan Association of Chronic Kidney Disease Initiative was founded by JSN in association with the Japanese Society for Dialysis Therapy and the Japanese Society for Pediatric Nephrology in 2006. Since 2007, Kidney Disease Measures Study Meetings, with participation from physicians, nurses, public health specialists, local government staff, and representatives of kidney disease patient groups, were held by the Ministry of Health, Labour and Welfare. These meetings resulted in the formation of the national action plan of CKD strategies in 2008: Future Kidney Disease Measures to Be Achieved. The aim of the strategies is to slow progression of

kidney dysfunction, prevent the need for KRT, decrease the number of patients with incipient kidney failure, and reduce cardiovascular complications from CKD. Specifically, this action plan called for raising awareness and disseminating knowledge, a medical cooperation system, improvement in medical treatment standards, development of human resources, and promotion of research. The Ministry of Health, Labour and Welfare is currently revising the national action plan for CKD through the second Kidney Disease Measures Study Meeting, discussing a new national action plan to reduce the number of patients on incident dialysis below 35,000 per year by 2028.

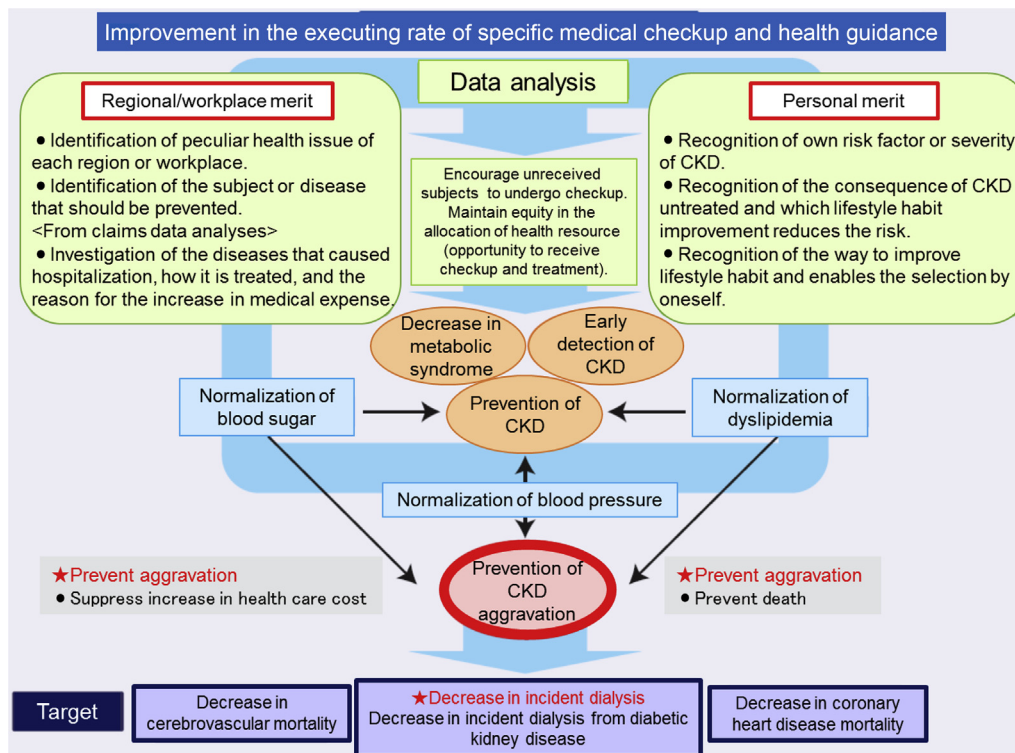
Japanese scientific societies, including JSN, Japanese Society for Dialysis Therapy, and Japan Medical Association, developed various guidelines for referral and care of patients with kidney disease between general practitioners and nephrologists.

**Strategies for CKD/ESKD care.** In 2013, the Ministry of Health, Labour and Welfare developed a formal document targeting CKD within the national health promotion agenda (Basic Direction for Comprehensive Implementation of National Health Promotion). This document included numerical targets to reduce the number of patients on incident dialysis due to diabetic kidney disease by 2022.

Since Japan instituted UHC in 1961, all citizens are covered by some kind of health insurance. The Japan Revitalization Strategy 2013, a growth strategy announced by the

Japanese government extending the nation’s “healthy life expectancy,” was set as one of the themes.<sup>11</sup> Programs to develop a new system of preventive care and health management will be promoted through the requirement of all health insurance societies to analyze data such as health insurance claims. This project program called Data Health Plan will use health data to maintain and improve health conditions of its subscribers, including reduction in the incidence of dialysis. Concrete plans are needed to prevent the onset and worsening of CKD from lifestyle-related disease, such as diabetes or hypertension, identified in specific medical checkups (Figure 1)<sup>12</sup> instituted in 2008. These specific medical checkups are mandated by individual health insurance companies according to the guidelines that outline appropriate laboratory tests to be included, standard inquiries, and the selection and stratification of individuals who require further health guidance. JSN is continuing to emphasize collaboration with other domestic and international societies and regulatory agencies. JSN also achieved its goal of collaborating with the International Society of Nephrology (ISN) and the Japanese Diabetes Society.<sup>13</sup>

**Impact.** The number of kidney transplantation procedures has increased from 749 in 2000 to 1598 in 2011 and remains constant in 2016 with 1648 total transplants (of note, 1471 from living donors, 61 from donors after cardiac death, and 16 from donors after neurological death). As a proportion of the general population, these rates are low compared



**Figure 1 | Relationship between the basic concept of Data Health Plan and chronic kidney disease (CKD), Japan.** Reproduced with permission from [Proposal to achieve a decline in the number of dialysis initiations due to lifestyle related diseases—early detection and prevention of onset and progression of CKD]. *Nihon Jinzo Gakkai Shi*. 2016;58:429–475 [in Japanese].<sup>12</sup> Copyright © 2016 Japanese Society of Nephrology.

to other high-income countries. Standardized incidence ratios of dialysis have significantly decreased since 2008 in Japan (Figure 2).<sup>14</sup> However, the total number of patients on incident dialysis was projected to increase from 36,797 in 2015 to 40,360 in 2025 because of the aging population.

### China (upper-middle-income country): prevention and treatment of ESKD

**Background.** China is the largest LMIC and is home to 20% of the world's population. CKD is common in China and is now the fastest growing cause of death.<sup>15</sup> The government's current NCD policy, along with major national medical research grants, focuses predominantly on 5 diseases—cardiovascular disease, cancer, diabetes, chronic respiratory disease, and mental illness—notably excluding CKD. There is no national program for the prevention and treatment of CKD or chronic dialysis in China, though Chinese nephrologists have made great efforts to reduce the prevalence of ESKD and improve outcomes in this population, particularly during the last decade.

**Strategies for CKD/ESKD care. Understanding CKD and ESKD burden.** CKD is a rapidly growing health burden and is a huge health care challenge in China. Epidemiological studies show that the prevalence of CKD in Chinese adults is 10.8%,<sup>15</sup> representing a population of 120 million patients. As of 2017, there were ~1 million patients with ESKD in China, with only 52% of them having access to KRT.<sup>16</sup> Based on the current average treatment cost, the annual health care expenditure on dialysis in China is ~US\$50 billion.

A recent study, the China Renal Biopsy Series, analyzed 71,151 patients who had a kidney biopsy at 1 of 938 hospitals in 282 cities across China from 2004 to 2014.<sup>17</sup> This analysis found that IgA nephropathy was the most common glomerular disease with a standardized frequency of 28% and the leading cause of progressive CKD in all age groups. Furthermore, the risk of membranous nephropathy has increased by 13% annually during the last decade. The latter could be associated with the increased level of air pollution with

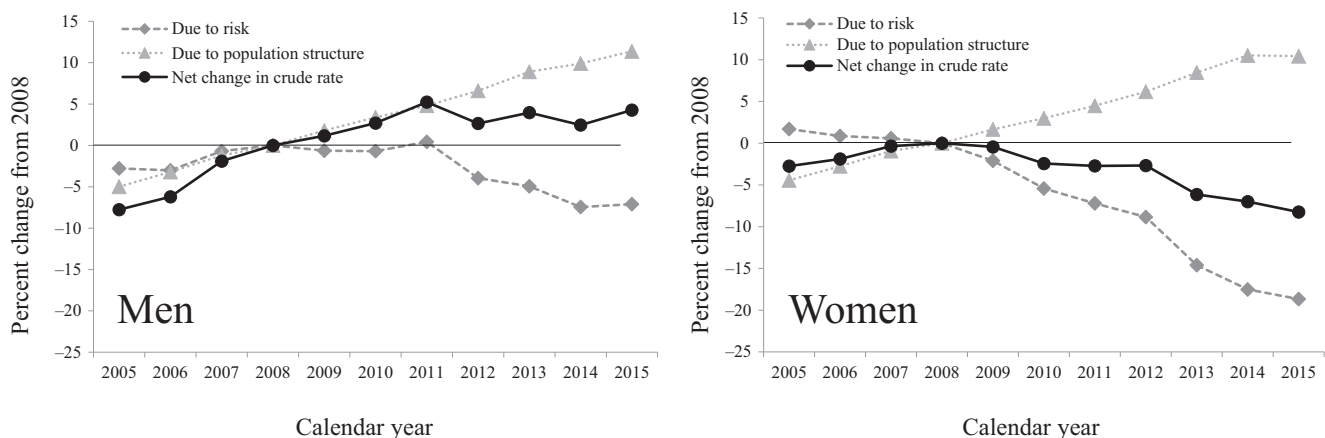
particulate matter <2.5 μm in diameter, a health problem faced by many developing countries.

With the rapid growth of the economy and changes in lifestyle, the prevalence of diabetes mellitus is significantly increasing in China.<sup>18</sup> This increase has changed the pattern of CKD in China. Since 2011, the percentage of CKD due to diabetes has exceeded that of glomerulonephritis-induced CKD in hospitalized patients.<sup>19</sup>

AKI is an important driver of CKD, and in China, the incidence of AKI is 11.6% in hospitalized adults<sup>20</sup> and 19.6% in children,<sup>21</sup> but the detection rate is only 0.99% in hospitalized patients.<sup>22</sup> In addition to other known risk factors, nephrotoxic herbs are a potential risk factor for AKI in Chinese adults.

**Developing population-based prevention approaches for CKD/ESKD according to the risk factor in the Chinese population.** Epidemiological studies have shown that folic acid deficiency is prevalent in Chinese hypertensive populations, particularly in rural areas, and is associated with the risk of development of CKD.<sup>23</sup> A recent large-scale, multicenter, randomized controlled trial conducted in 20 rural communities in China evaluated the efficacy of folic acid supplementation in the prevention of kidney function loss in a hypertensive population without previous cardiovascular disease.<sup>24</sup> Compared to treatment with enalapril alone, the addition of low-dose folic acid significantly reduced the risk of kidney function decline. In patients with CKD at study enrollment, folate supplementation reduced the risk of CKD progression by 56%. Folic acid therapy was also found to reduce the risk of a first stroke<sup>25</sup> and new-onset albuminuria in patients with diabetes.<sup>26</sup> Because folate deficiency has been reported in other developing countries,<sup>27</sup> supplementation of folic acid would be considered a kidney-protective approach for hypertensive populations in these regions.

**Developing intervention approaches for delaying progression of CKD in China.** Once CKD progresses to ESKD, the risk of death and medical costs increase exponentially. Delaying progression of CKD toward ESKD is an important strategy for



**Figure 2 | Incidence rates of dialysis by sex and age group in Japan, 2005–2015.** Reproduced with permission from Wakasugi M, Narita I. Evaluating the impact of CKD initiatives on the incidence of dialysis in Japan. *Jpn J Nephrol.* 2018;60:41–49.<sup>14</sup> Copyright © 2018 Japanese Society of Nephrology and the Japanese Journal of Nephrology.

reducing the burden of ESKD, particularly in LMIC with limited medical resources. The efficacy of renoprotection by angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in patients with CKD has been demonstrated in randomized controlled trials.<sup>28,29</sup> Angiotensin-converting enzyme inhibitors can even be administered in patients with CKD stage 4 and delays the onset of ESKD from 3.5 to 7 years.<sup>30</sup> Uptitration of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker dosages against albuminuria confers further benefit on kidney outcomes in patients with nondiabetic CKD and kidney insufficiency.<sup>31</sup> Given the ~80,000 patients initiating dialysis every year in China, the uptake of these therapies could save US\$120 million annually by delaying dialysis by 1 year for each patient.

**Promoting home-based KRT in China.** The number of patients on peritoneal dialysis (PD) in China rose from 37,942 in 2012 to 55,373 in 2014.<sup>32</sup> China also has the largest variation in PD uptake among regions, ranging from 14% in mainland China to 73% in Hong Kong.<sup>33</sup> The PD-First policy implemented by Hong Kong health authority may contribute to the higher rate of PD uptake. PD has been recommended as a preferred KRT because of its lower cost, reduced requirement for technical support, and less need for trained medical staff. Increasing access to PD could help increase access to KRT for patients with ESKD, particularly in LMIC.

There are still challenges in delivering PD to patients with ESKD living in rural areas with less access to medical care and dialysis. The Flying Angel program is a model developed by a partnership between the Chinese government, medical centers, and the PD industry to overcome the barriers of promoting PD in rural China.<sup>34</sup> This program develops collaboration between central hospitals and community clinics, provides PD training for community medical practitioners, and has a delivery system for PD fluid and materials. This program has increased access to KRT for rural patients with ESKD.<sup>34</sup>

The optimal management of home-based PD is critical for reducing the risk of failure and improving outcomes. By implementing a telephone hotline and mobile phone applications, the collaboration between central hospitals and community clinics is strengthened further, facilitating communication between physicians and patients on PD. Home-based management systems, which include mobile phone applications, also provide lifestyle modification guidance for patients and collect information on treatment response from patients. This model of care increases the compliance of patients on PD and decreases the cost associated with hospital and physician visits.

### **Mexico (upper-middle-income country): moving toward universal access of CKD/ESKD care**

**Background.** Mexico's health system does not offer UHC for patients with kidney disease. Social security benefits, including universal access to dialysis and kidney transplantation, are available to individuals employed by the

private sector or by the government. However, more than half of the population does not have access to social security benefits and cannot afford private health care services. Access to dialysis and kidney transplantation for this population is limited or nonexistent.<sup>35</sup>

**Action.** To reduce health disparities, a constitutional reform was introduced in 1983, recognizing the right of Mexicans to access health insurance.<sup>36</sup> In 1984, legislation on organ and tissue donation and transplantation was passed by the Mexican congress, including the setup of the National Transplantation Registry, to coordinate and facilitate organ procurement and transplantation. In the 1990s, a network of state transplant coordinators and associated organizations were organized throughout the country, as well as a central coordinating center, the National Transplant Center (CENATRA in Spanish).<sup>37</sup>

In 2000, a workshop was convened by the Ministry of Health (MOH) to organize a national dialysis registry, with the participation of representatives of all 32 Mexican state health secretariats; members of the Mexican Society of Nephrology, the Mexican Institute for Nephrology Research, the Mexican Board of Nephrology, and Jalisco Dialysis and Transplant Registry; the directors of the Canadian Organ Replacement Registry and the United States Renal Data System. After this, an *ad hoc* steering committee began a series of meetings at the MOH's National Directorate of Epidemiology to set up the registry<sup>38</sup> and a number of actions for the prevention and control of CKD were included in Mexico's National Health Plan 2001–2006.<sup>39</sup> Among them was the implementation of early screening and treatment of CKD along with a national dialysis registry.

In 2003, a structural reform of the Mexican health system increased financial protection of its citizens by offering publicly subsidized health insurance to more than half of the population not covered by social security. The center of the reform was the creation of Seguro Popular (Popular Health Insurance),<sup>40</sup> which divides personal health services into essential packages of interventions financed by the Fund for Protection against Catastrophic Health Expenditures (FPGC).<sup>41</sup> The law came into effect on January 1, 2004, and dialysis and organ transplantation were among the 7 high-cost interventions included in the FPGC. In 2010, the MOH set up the Strategic Health Services Network Against Chronic Kidney Disease, emphasizing the need for early detection and treatment of CKD.<sup>42</sup>

In 2015, the Mexican Health Foundation (FUNSALUD in Spanish) began organizing a series of meetings with representatives from Mexico's health systems and members of the Mexican nephrology societies to reinstate the setup of the dialysis registry, which had been abandoned by Mexican health authorities. After the ISN Global Kidney Policy Forum held at the ISN World Congress of Nephrology 2017 in Mexico City, the MOH implemented the pilot testing of the National Registry of Chronic Kidney Disease (RENERC in Spanish) as part of the nation's health information system.

**Impact.** Thirty-five years after the constitutional reform of 1983, universal access to kidney care is yet to be realized. Since the implementation of Seguro Popular, the proportion of the population with some type of public health insurance has increased from 41% in 2002 to 81% in 2015<sup>43</sup> and the number of high-cost interventions included in the FPGC has increased from 7 to 68. However, Seguro Popular still does not pay for dialysis. As a result, the marked disparities between the insured and uninsured populations with access to KRT persist. By 2015, the incidence and prevalence of patients receiving treatment for ESKD with social security were 281 and 1357 per million population (pmp), respectively; however, 130 patients pmp on incident dialysis and 200 patients pmp on prevalent dialysis remained uninsured.<sup>35</sup>

The introduction of legislation on organ donation and transplantation in 1984 resulted in a significant increase in kidney transplantation rates, from 1.57 pmp in 1984 to 22.8 pmp in 2015. However, this success is not observed in the population without social security. Because Seguro Popular still does not cover the cost of kidney transplantation and immunosuppressive drugs, transplantation rates remain significantly lower in patients without social security.<sup>35</sup>

Eight years after the setup of the Strategic Health Services Network Against Chronic Kidney Disease, strategies to prevent CKD are yet to become part of the nation's NCD health policies. CKD screening is low or nonexistent across Mexico. Furthermore, uninsured patients with predialysis CKD are often denied access to treatment by Seguro Popular once identified as having kidney disease.<sup>35</sup> Therefore, the opportunity to intervene to delay the progression of CKD is lost.

Finally, the dialysis registry is currently under pilot testing with the participation of several dialysis centers. The sustainability and nationwide expansion of the registry are yet to be seen.

#### **Sudan (lower-middle-income country): evolution of strategies for CKD/ESKD care**

**Background.** During the 1970s, a Sudanese patient was treated in London, UK, for kidney failure by hemodialysis (HD). As he decided to continue his treatment under the care of medical staff of the University Hospital of Khartoum, his HD machine was the basis for the first dialysis unit in Khartoum.

Around the same time, a young surgeon by the name of Omar Beliel was sent by the University Hospital of Khartoum to train in England to be a neurosurgeon. While in the United Kingdom, he had kidney failure and eventually he received a kidney donated by his brother. Dr. Beliel later wrote an autobiography titled *Two Lives: Death Odyssey of a Transplant Surgeon*,<sup>44</sup> in which he describes how kidney transplantation gave him a "second life." He subsequently shifted his training from neurosurgery to transplant surgery and performed the first kidney transplantation procedure in Africa from a living-related donor in 1974. By the mid-1970s, HD, intermittent PD through the use of hard catheters, and living-related kidney transplantation were established services at the

University Hospital of Khartoum. However, these services were limited because of resources and the University Hospital remained mostly an academic and teaching facility.

**Action.** The 1980s saw an expansion in dialysis services to benefit more patients, which was supported by the Ministry of Finance. It was soon evident that these services were costly and further expansion was unlikely to be feasible.

In 1994, the government called for Expert Opinion Conferences on How-Best-to-Do (HBTD) the civil services. The conferences called on scholars and experts in health, education, economy, and other areas to discuss reform of these issues and make recommendations to be executed by the government. A final recommendation in the area of health was to establish the National Centers of Health Care for 5 key areas: kidney disease, heart disease, oncology, gastroenterology and hepatology, and neurosciences. These national centers were required to plan for health care in their respective areas, along with suggestions and the means for successfully operating across the country. Thus, the National Center for Kidney Diseases and Surgery was established in 1995 and has been responsible for CKD/ESKD care across Sudan for the last 2 decades.

The National Medical Supplies Fund was established hand in hand with the National Centers of Health Care. The main objective was to procure and justly distribute medicines nationwide at the lowest cost. An important issue that resulted from the National Medical Supplies Fund policies was the need to have a national regulation for life-saving medicines (LSM), medicines that should be available to all citizens free of charge. After many discussions, it was agreed that the treatment of ESKD was to be considered a lifesaving issue and therefore both dialysis and kidney transplantation would be covered by the LSM bill. Thanks to this huge step forward, the development of both CKD services as preventive measures and ESKD therapy would be managed under the umbrella of the National Center for Kidney Diseases and Surgery.

Another important contribution to the success of managing CKD/ESKD in Sudan is the National Zakat Fund (NZF), which was established in the 1990s. *Zakat* is an Islamic concept where Muslims with the financial means are required to contribute 2.5% of their annual income as charity. The current government decided, for the first time, to create an organized institution to then use these funds in an orderly fashion. As the activities of the fund are regularly published, it became a trustworthy organization and most individuals who pay zakat prefer NZF to find suitable recipients of the aid. Religious scholars agreed that treatment of ESKD through dialysis and transplantation would be eligible to be supported by NZF.

In 2005, the National Medical Supplies Fund accepted continuous ambulatory PD as a viable option for treatment of ESKD, particularly for children and young patients. It has since become an option for ESKD management, albeit on a limited scale.

**Impact.** Using funds obtained from the LSM bill and NZF, the National Center for Kidney Diseases and Surgery is

able to meet the requirements of providing CKD/ESKD care for citizens in Sudan.

**Dialysis facilities and modalities.** Sudan is the second largest country in Africa, with a total population of ~38 million. Nearly all cities and large towns have governmental HD centers to care for patients with ESKD. Currently, the total number of HD centers is 72. There are 7200 patients currently on dialysis; 97% of these are on HD.<sup>45</sup> HD is based on twice weekly sessions for stable patients. The reason for this sub-optimal dialysis schedule is to accommodate as many patients with ESKD as possible under the free-of-charge scheme of the national HD system. A recent survey showed that the 1-year survival of patients on twice weekly HD was 83%.<sup>46</sup> Patients who had functioning arteriovenous fistulas did significantly better than those who were dialyzed via cuffed or noncuffed central venous catheters.<sup>46</sup> Availability of continuous ambulatory PD is still limited to the greater Khartoum state. Although only 3% of patients on dialysis are on continuous ambulatory PD, the outcome and quality of life figures are rewarding. If PD fluid could be manufactured locally, ideally more patients on PD could be accommodated.

**Kidney transplantation.** The kidney transplant activities in Sudan over the last 5 years are increasing. Kidneys are transplanted exclusively from living-related donors. About 80% of the cost of the transplant is covered by either the LSM bill or NZF. All patients (irrespective of where the transplant was done) receive immunosuppressive drugs free of charge.

In summary, the most important milestones in developing a strategy for care for patients with CKD/ESKD in Sudan are as follows:

- The call by the government in 1994 for national conferences to give advice on *how best to do* reforms across the country. This resulted in the birth of the National Center for Kidney Diseases and Surgery, which plans and supervises kidney care nationwide.
- The introduction of the LSM bill was a novel resolution that made it possible to view CKD/ESKD care as a lifesaving issue, using funds to cover almost all citizens free of charge.
- The Islamic system of zakat that requires eligible Muslims to voluntarily pay 2.5% of their annual income to support the poor or programs designed to help the poor. The addition of CKD/ESKD care to be covered by this fund has helped immensely.

### **Senegal (lower-middle-income country): fundamental development of CKD/ESKD care**

**Background.** Senegal is a country on the western tip of Africa, with a population of 15 million, and is one of the poorest countries in the world. Nephrology was unknown in Senegal until the return of the first Senegalese nephrologist after the conclusion of his training in France. Over time, a dedicated nephrology curriculum for undergraduate medical students along with HD and kidney biopsy practices has been introduced. Until 2010, however, there were only 2 HD centers in each of the public and private health sectors, dialysis costs were paid out of pocket by patients without

health coverage, and there were only 3 nephrologists in the country.

**Action. Epidemiology.** The prevalence of CKD in Senegal is estimated at 4.9%.<sup>47</sup> The main cause of CKD is hypertension, followed by chronic glomerulonephritis (especially primary focal segmental glomerulosclerosis), diabetes, and the use of traditional nephrotoxic drugs. The World Health Organization STEPwise survey found the prevalence of hypertension and diabetes in the general Senegalese adult population aged 45 to 49 years to be 25% and 5.4%, respectively. Advocacy and increased awareness among political authorities has made it possible to set up an NCD office at the MOH with a focal point on nephrology for the management of kidney disease. UHC was introduced in 2014, which provides free dialysis for Senegalese patients, but with limited availability. The government provides all dialysis supplies and a bundled payment of 10,000 FRFA (US\$20) for each dialysis session at public dialysis centers. Patients, when dialysis slots are not available, are registered on the first come, first serve waiting list. In the meantime, to survive, patients must pay out of pocket to receive dialysis in the private sector.

**Kidney care.** A national and international nephrology referral service has been developed at the largest university hospital in Senegal. An average of 200 kidney biopsies are done each year, with samples processed and read on site. HD began at the largest public HD center with 25 stations, and HD services grew from 2 HD centers in 2010 to 20 centers all across Senegal. In 2004, the first PD center was established for the management of acute and chronic kidney failure in children and adults using continuous ambulatory PD and automated PD.<sup>48</sup> The costs of dialysis were first fully and then partially borne by the patient until 2012. Since 2012, dialysis costs, with the exception of epoetins and laboratory tests, are fully covered by the government in the public sector and partly covered in the private sector. In the public sector, dialysis supplies are obtained through the National Pharmacy Supply, through 2-year international tenders, permitting regular renegotiations. Kidney transplantation has not yet been done in Senegal. However, a working group with the support of experts drafted texts and laws governing organ transplantation, which passed a National Assembly vote on November 27, 2015. A presidential decree establishing the National Council for Organ Transplantation is on standby.

**Training and education in nephrology.** A nephrology school was opened in 2005 in Dakar to fill the gap of nephrologists in the sub-Saharan Africa region as no single country had more than 5 nephrologists, half the countries had no nephrologists, and Senegal had only 3 nephrologists. Between 2005 and 2017, by combining internal medicine and nephrology, the school trained 104 nephrologists from 21 African countries in a 4-year curriculum (including 2 semesters in France). A 2-year curriculum for nephrology nurses was introduced in 2008 and has trained 90 senior nephrology nurses from 7 African countries. In collaboration with the ISN, 3 training workshops on AKI, CKD, and PD have been organized with

>400 participants per workshop to meet continuing medical education goals.<sup>49</sup>

**Strategies for CKD/ESKD care.** A working group with diverse experts (doctors, biologists, surgeons, pharmacists, and administrative staff) has been set up by the MOH to achieve an integrated CDK/ESKD care strategic plan. This strategy will enhance awareness and prevention, propose ways to reduce the growing number of patients on dialysis waiting lists, and extend PD to rural areas as it costs less than HD and will allow more patients with ESKD to be treated with dialysis. The annual cost per patient is US\$13,650 for PD compared with US\$18,000 for HD.<sup>50</sup> Training standards for health care workers must be developed in conjunction with nephrologists. The National Council for Organ Transplantation will be established, and the support of foreign partners will be needed for the accreditation of the initiation of living-related kidney transplantation.

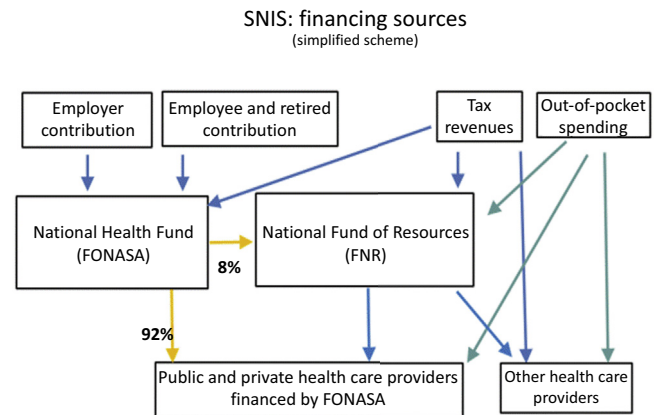
**Impact.** An integrated CDK/ESKD care strategic plan was developed in 2019. The number of patients with CKD on dialysis has grown from 50 in 2010 to >800 currently; this number was doubled in 2019 with the opening of 10 new HD centers across the country. Two new PD centers were opened in 2019. This expanded the treatment of 60 patients with CKD and 20 patients with AKI at the current single center to the treatment of >150 patients with CKD and 50 patients with AKI. From 3 nephrologists in 2008, the country currently has 27 nephrologists and 128 nurses with specialization in nephrology; the goal is to train 5 additional nephrologists and 10 additional specialized nurses per year. The establishment of the National Council for Organ Transplantation will set the rules and criteria for accreditation, enabling the first successful kidney transplantation in Senegal in 2019.

## CKD STRATEGY CASES

### Uruguay (high-income country): prevention and treatment of CKD

**Background.** Uruguay, a developing country in South America with 3.44 million inhabitants, was classified as a non-Organisation for Economic Co-operation and Development high-income country by the World Bank in the last decade. In recent years, there has been a sustained growth in the aging of the population, and life expectancy at birth has increased to 77 years (73 years for men and 81 years for women). A National Integrated Health System (SNIS in Spanish) was launched in 2008 to provide UHC to the entire population. The total expenditure on health per capita in 2016 was ~US\$1800, which represents 8.6% of the nation's gross domestic product.<sup>51</sup>

The SNIS is funded by contributions from employers, employees, retirees, and tax revenues that go to the National Health Fund (FONASA in Spanish) and the National Fund of Resources (FNR in Spanish) (Figure 3).<sup>52</sup> The FNR is a public nongovernmental agency, created by law in 1980 with the purpose of providing funds for highly specialized medical procedures, such as dialysis and transplantation, on the basis of approved protocols. This fund accounts for ~10% of all



**Figure 3 | National Integrated Health System (SNIS in Spanish) financial sources in Uruguay.** Reproduced with permission from Ministerio de Salud Pública. La Construcción del Sistema Nacional Integrado de Salud. 2005–2009. Available at: [http://www.paho.org/hq/dmdocuments/2010/construccion\\_sist\\_nac\\_integrado\\_salud\\_2005-2009-uruguay.pdf](http://www.paho.org/hq/dmdocuments/2010/construccion_sist_nac_integrado_salud_2005-2009-uruguay.pdf). Accessed March 18, 2018.<sup>52</sup>

public expenditures on health; expenses related to dialysis account for ~27% of the entire fund.

**Action and strategies for CKD/ESKD care.** UHC of patients receiving KRT has been available since 1981, with the financial support of the FNR. Data on these patients are collected by the Uruguayan Dialysis Registry.

In April 2004, representatives from the Uruguayan and Latin-American societies of nephrology, the Uruguayan Department of Health, and the FNR signed the Declaration of Montevideo with the aim of enhancing CKD care and recommended an Advisory Committee on Renal Healthcare to develop a National Renal Healthcare Program. Six months later, a pilot program was launched that included (i) education programs on kidney health care, including information on a healthy lifestyle, in the general population, with the aim to reduce cardiovascular and kidney risk factors; (ii) increased accessibility to kidney health care at the primary care level; (iii) promotion of early diagnosis of CKD in the population at risk; (iv) enhanced care given to patients at all stages of CKD; and (v) prevention of cardiovascular morbidity and mortality, as they are high in the target population.<sup>53,54</sup>

The methodology for developing and spreading the National Renal Healthcare Program included several advances: (i) the development of clinical guidelines for identification,<sup>55</sup> evaluation, and management of patients with CKD at the primary care level; (ii) the creation of kidney care teams (including a nephrologist, a dietitian, and a nurse) to work in primary care centers to treat patients referred to them by primary care practitioners; (iii) the management of patients with CKD stage 1 to 3 directly by the laboratory; and (iv) patients with CKD stage 4 and 5 were referred to a CKD advanced clinic, staffed by a formal multidisciplinary team including nephrologists, dietitians, nurses, psychiatrists, vascular surgeons, and social workers.

An online CKD registry housed at the FNR records data on patients with estimated glomerular filtration rate

(eGFR) < 60 ml/min per 1.73 m<sup>2</sup> and persistent albuminuria >300 mg/d (or >30 mg/d in patients with diabetes) and features a centralized alarm system to minimize failure to follow-up.<sup>56</sup> Although the National Renal Healthcare Program is not mandatory for every health care provider, the feasibility of this is being studied.<sup>57</sup>

Since 2009, testing for CKD in high-risk populations (case finding) has been incorporated into the mandatory health checkups of the working population via a decree of the Department of Health. Evaluation includes urine examination and serum creatinine tests in diabetic and hypertensive individuals.<sup>58</sup>

Not all Latin American countries provide the same level of CKD care, which is why the Latin-American Society of Nephrology and Hypertension (SLANH in Spanish) and the Pan American Health Organization declared that all countries should improve CKD care and increase coverage of dialysis treatment. Together, through Pan American Health Organization's virtual space, they launched an online course (in Spanish and Portuguese) on CKD prevention and care in July 2016, aimed at primary care practitioners throughout Latin America.<sup>59</sup>

**Impact. Uruguayan Dialysis Registry.** Data from the Uruguayan Dialysis Registry found that diabetic and hypertensive diseases are the most common causes of ESKD.<sup>60</sup> The prevalence of ESKD was 756 patients pmp, with 90% on HD and 10% on PD in December 2014; the prevalence of ESKD is 1031 pmp when patients with a functioning kidney allograft are included.

**CKD registry.** The target population and the variables included in the registry have already been described elsewhere.<sup>61</sup> Between October 1 and December 31, 2017, 20,879 patients were recorded; the mean age was 66 years, and 47.6% were female. The most frequent causes of CKD were vascular nephropathy (40.8%), diabetic nephropathy (19.1%), obstructive nephropathy (7.9%), and primary glomerulonephritis (4.8%). The most frequent risk factors for kidney disease were hypertension (86.9%), dyslipidemia (54.2%), diabetes (37.3%), and obesity (37.7%). Most patients were referred to a nephrologist at later stages (CKD stage 3 or greater).<sup>62</sup>

Every year, the Advisory Committee on Renal Healthcare carries out an evaluation that assesses the quality of care at the primary level, the achievement of therapeutic goals under nephrology care, the rate of progression of CKD, and the mortality due to ESKD. There has been a sustained increase in blood pressure control care since 2005, with the proportion of patients with systolic blood pressure <140 mm Hg and diastolic blood pressure <90 mm Hg rising from 36.5% to 63.9% and from 58.5% to 86.5%, respectively.<sup>63</sup>

**Table 3** highlights some indicators of kidney care in Uruguay.<sup>64</sup> More than 50% of patients are stabilized with an eGFR loss of <1 ml/min per 1.73 m<sup>2</sup> per year, and 79% of patients with diabetes and albuminuria are taking renin-angiotensin system blockade (despite heterogeneity between groups, ranging from 54% to 96%). The risk of new

**Table 3 | Achievement of quality of care indicators under nephrology care in Uruguay (National Renal Healthcare Program 2004–2016)**

Quality of care indicators	Percentage
Patients with albuminuria over 0.5 g/g creatinine using RAS blocking drugs	79
Patients with LDL cholesterol >100 mg/dl using statins	64
Patients with timely referral (eGFR >30 ml/min per 1.73 m <sup>2</sup> )	80
Patients with blood pressure <140/90 mm Hg	64
Patients with cholesterol <200 mg/dl	60
Patients with LDL cholesterol <100 mg/dl	51
Patients that lose <1 ml/min per 1.73 m <sup>2</sup> per year eGFR	56

eGFR, estimated glomerular filtration rate; LDL, low-density lipoprotein; RAS, renin-angiotensin system.

Data from National Renal Healthcare Program Indicators. Informe del Programa de Salud Renal Año 2016. Available at: [http://www.fnr.gub.uy/sites/default/files/programas/informe\\_renal\\_2016.pdf](http://www.fnr.gub.uy/sites/default/files/programas/informe_renal_2016.pdf). Accessed March 18, 2018.<sup>64</sup>

cardiovascular events was related to previous cardiovascular disease, diabetes, male sex, and increased age and albuminuria and had a U-shaped curve for systolic blood pressure.<sup>65</sup> Other than well-known risk factors such as albuminuria and blood pressure, acidosis was related to greater increase in creatinine.<sup>66</sup> Finally, there is evidence that predialysis CKD care may improve outcomes once patients are established on dialysis in Uruguay.<sup>67</sup>

Since 1981 in Uruguay, there is UHC for dialysis. A CKD screening and prevention program was launched in 2004. Today, these are being incorporated into mandatory health programs, with the aim of making them universal throughout the country. There has been improvement in the quality of care as well as a reduction in CKD progression; the potential benefits of predialysis CKD care seem to extend even to patients who eventually have kidney failure. CKD care requires the commitment of the nephrology community and the national authorities. The former provides guidelines for systematic CKD detection and follow-up, while the latter sets the framework for health care providers and ensures the provision of UHC for treatment from the early stages of CKD to dialysis and kidney transplantation.

### **Thailand (upper-middle-income country): unique CKD prevention program**

**Background.** The prevalence of CKD stage 3 and 4 in Thailand is 9.3% for those older than 18 years, representing 4.8 million people, with a further 4.6 million people with CKD stage 1 and 2.<sup>68</sup> Diabetes mellitus and hypertension are the main causes of CKD.<sup>69</sup> The Ministry of Public Health has divided the country into 12 health care regions (excluding the Bangkok metropolitan area), with each region consisting of 4 to 8 provinces covering a population of ~5 million. Within each province, there are between 6 and 30 districts, each with their own district hospital. Within each district, there are a further 5 to 10 subdistrict health offices. A district hospital usually comprises general practitioners, nurses, pharmacists, a physical therapist, and, in larger hospitals, a nutritionist. At each subdistrict health office, there are 1 to 2 public health officers and 1 to 2 community nurses, caring for anywhere between 3000 and 5000 inhabitants. Community nurses are

responsible for basic drug prescription, on behalf of the district hospital, and for treating common ailments. Moreover, there are village health volunteers, grassroots personnel, who provide a connection between villagers and health personnel and cover public health issues at the village level. Basic health care programs in Thailand are implemented through this infrastructure. Across Thailand, there are ~10,000 subdistrict health offices and >1 million village health volunteers.<sup>70</sup>

Diabetes mellitus and hypertension are the 2 most common NCDs in rural areas. To cope with these problems, general practitioners, diabetes/hypertension case manager nurses, and multidisciplinary care teams work together at the district hospital level. Community nurses and village health volunteers are also responsible for medication refills for stable patients and facilitate patients' self-care and any necessary lifestyle modifications. Key performance indicators from all public hospitals are transferred to the Health Data Center of the Ministry of Public Health. Table 4 illustrates a set of key performance indicators of diabetes and hypertension.<sup>71</sup>

**Action.** It is challenging to use the limited resources available in the country to delay the progression of CKD on a national scale. Community nurses and village health volunteers, who are more present in the community, can be trained to decrease the reliance on multidisciplinary care teams who are present only in hospitals. This is a paradigm shift from hospital-based to a joint hospital-community-based approach.

To test this concept of care, a pilot project was launched a few years ago in Kamphaeng Phet Province, 400 km north of Bangkok. In brief, this study took place at 2 districts within the province.<sup>72</sup> In district hospital A (control), there was no multidisciplinary care team available and patients were cared for as usual by general practitioners and diabetes/hypertension/NCD nurses. There were no home visits by community nurses/village health volunteers. In district hospital B (intervention), multidisciplinary care teams, community nurses, and village health volunteers were trained on CKD with

information on lifestyle modifications and dietary counseling. Educational materials and a protocol checklist were provided in accordance with the Nephrology Society of Thailand and international guidelines on CKD management.<sup>73,74</sup> CKD cases were referred by community nurses/village health volunteers during regular home visits to multidisciplinary care teams at the district hospital. The community nurses/village health volunteers also had a checklist on exercise, smoking cessation, avoidance of analgesic/nonsteroidal anti-inflammatory drugs, and avoidance of high salt and protein intake. Two years later, patients with CKD in the intervention group had lower dietary salt and protein intake and lower rates of eGFR decline than did those in the control group.<sup>75</sup> An economic evaluation demonstrated that this program was cost-effective.<sup>76</sup> The conclusions of this study imply that integrated care provided by multidisciplinary care teams at district hospitals in combination with home visits by community nurses/village health volunteers could help delay the progression of CKD through lifestyle modifications, without the intervention of specialists.

**Strategies for CKD/ESKD care.** In 2015, the Ministry of Public Health announced the prevention of CKD as a national health priority. All referral, provincial, and district hospitals were requested to set up multidisciplinary care teams around CKD. A protocol checklist on the essential parts of CKD management and key performance indicators of CKD were agreed upon. A reference eGFR equation was declared, and the implementation of national serum creatinine standardization is underway.

**Impact.** Our findings illustrate favorable outcomes in a CKD prevention program at a national scale (Table 5).<sup>71</sup> It is yet too early to identify absolute eGFR change over time. We

**Table 4 | Key performance indicators of diabetes mellitus and hypertension reportable to the Ministry of Public Health, Thailand**

Proportion of	2015 (%)	2016 (%)	2017 (%)	No. of people surveyed (millions)
Citizens older than 35 yr screened for diabetes mellitus	66.1	73.7	86.3	16–23
Diabetic patients with HbA <sub>1c</sub> <7%	18.4	20.6	23.0	2.4–2.7
Citizens older than 35 yr screened for hypertension	71.2	77.9	86.2	14.5–19.6
Hypertensive patients with blood pressure <140/90 mm Hg	24.8	30	36.4	5.1–5.6

HbA<sub>1c</sub>, hemoglobin A<sub>1c</sub>.

Data from Health Data Center, Ministry of Public Health, The Royal Thai Government. KPIs for service plan management. Available at: <https://hdcservice.moph.go.th/hdc/main/index.php>. Accessed March 18, 2018.<sup>71</sup>

**Table 5 | Key performance indicators of CKD reportable to the Ministry of Public Health, Thailand**

Proportion of	2015 (%)	2016 (%)	2017 (%)	No. of people surveyed (millions)
Patients with diabetes mellitus/hypertension screened for CKD	49.7	54.3	46.7 <sup>a</sup>	5.5–5.6
Patients with CKD stage 1–4 receiving ACEi/ARB	41.8	44.7	46.9	0.92–1.04
Patients with CKD stage 1–4 having blood pressure <140/90 mm Hg	64.9	65.4	67.2	0.18–1.04
Patients with diabetes mellitus and CKD stage 1–4 with HbA <sub>1c</sub> <7.5%	12.7	14.3	16.47	0.54–0.95
Patients with CKD stage 3 and 4 with the rate of eGFR decline <4 ml/min per 1.73 m <sup>2</sup> per year	63.4	63.7	62.9	0.43–0.58

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blockade; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HbA<sub>1c</sub>, hemoglobin A<sub>1c</sub>.

<sup>a</sup>The screening criteria were changed in 2017 from serum creatinine or albuminuria to serum creatinine and albuminuria.

Data from Health Data Center, Ministry of Public Health, The Royal Thai Government. KPIs for service plan management. Available at: <https://hdcservice.moph.go.th/hdc/main/index.php>. Accessed March 18, 2018.<sup>71</sup>

recognize that the key success factors behind our CKD program are the homogeneity of an existing well-organized primary health care system, the inclusion of an integrated care team at district hospitals, frequent home visits by community nurses and village health volunteers in the program, and, most importantly, a strong sense of belonging to their native homeland of the personnel. Our experience shows that in developing countries such as Thailand, combating CKD progression under limited resources is possible, provided that an integrated care program is developed, including trained multidisciplinary care teams, educational materials, protocol checklists, and dedicated community nurses and village health volunteers. This program could be sustainable and cost-effective.

#### **United Arab Emirates (high-income country): early detection of CKD in Abu Dhabi**

**Background.** In 2012, the prevalence of ESKD and CKD in Abu Dhabi were unknown, but the population on dialysis was doubling approximately every 5 years. Of the new patients starting dialysis, 90% started with <90 days of predialysis care, only 2% of patients had a fistula at their first dialysis session, and patients primarily started on HD. There were no systematic attempts at early detection and management of CKD as the projection of future patients with CKD was unknown.

**Action.** SEHA, the government health system within Abu Dhabi, has a single electronic medical record system that covers the whole country. The data contain patient demographics and information on all patient encounters. Between September 2011 and October 2012, data on 212,314 adults were extracted from the electronic medical record. The eGFR was calculated for every serum creatinine measurement and was used to calculate an estimate of CKD prevalence on the basis of the population breakdown. The prevalence of CKD stage 2 to 5 was estimated to be 22.6% in Emirati men, 12.9% in Emirati women, 26.6% in foreign men, and 16.5% in foreign women.

**Strategies for CKD/ESKD care.** To address the relative high rates of CKD, extensive discussions occurred at both primary and secondary levels of care; a potential solution was introduced in February 2014. This solution included the adoption of several strategies: the automated calculation of eGFR using the CKD Epidemiology Collaboration<sup>77</sup> equation embedded within the electronic medical record; an automated addition of *International Classification of Diseases 9th and 10th Revisions* codes for CKD to the electronic medical record based on *Kidney Disease: Improving Global Outcomes (KDIGO) CKD 2012 criteria*<sup>74</sup>; an algorithm-based management of CKD; online physician decision support for referral and medication management; physician feedback at the individual, practice, and regional level; and kidney nurses working both at the primary level of care and in multidisciplinary advanced CKD clinics.

**Impact.** At the outset of the program, 35% of patients with CKD stage 3 to 5 managed within primary care and 20% managed within secondary care were taking nonsteroidal

anti-inflammatory drugs. From 2011 to 2012, these rates fell to 15% and 10%, respectively. To date, 29,000 patients with CKD have been identified, of whom 25% are at high risk of progression as per the KDIGO classification.<sup>74</sup> More than 3500 patients, however, have had a >30% improvement in eGFR over a 2-year follow-up period. The presentation rate for dialysis with <90 days of predialysis care (emergency start) has fallen from 90% to 35%. The proportion of patients commencing dialysis with an arteriovenous fistula has risen each year, with 34% starting dialysis with a fistula in 2018.

This program of early detection and management of CKD has been extremely successful and continues to improve outcomes for Emirati patients. The program has clearly demonstrated the ability to modify physician prescribing behavior and exemplifies value-based health care with improved patient outcomes at a reduced cost to the health system. Data analysis is ongoing, with more work needed on defining the incidence density of progression to KRT and death as well as hazard ratios of progression and the impact of changes in medication regimen.

#### **HD STRATEGY CASES**

##### **Malaysia (upper-middle-income country): near-universal coverage for dialysis**

**Background.** Nephrology services in Malaysia have come a long way, from a humble beginning in the 1960s with steady growth to the mid-1970s, when the country was still categorized as an agricultural-based LMIC. With rapid development in the last 2 decades, a full range of nephrology services is now readily available throughout the country at an affordable cost. For an upper-middle-income country, Malaysia has an impressive treatment rate for patients with ESKD.

**Action and strategies for HD and PD.** *How does Malaysia achieve near-UHC for dialysis?* Over the last 5 decades, the nephrology community in Malaysia has worked toward achieving the World Health Organization indicators of UHC<sup>78</sup> of dialysis via good stewardship and governance (provided by the government), nephrology champions, key opinion leaders, and professional societies via the following strategies.

##### Effective stewardship of health reforms.

- Strong support via the MOH by providing sufficient funding for the development, operation, and subsidy of dialysis centers and services throughout the country.
- Ongoing planning over the last 40 years.
- Cooperation between private corporations and NGOs to develop more HD centers.

##### Effective stewardship of public funds.

- Allocation of more funds from the MOH to expand services, particularly in rural areas.
- Allocation of subsidies to NGOs by the MOH and Treasury.
- Outsourcing of dialysis to private centers by the Public Service Department, Social Security Organization, and zakat. All of the above agreed to consider dialysis as rehabilitation therapy.
- Purchasing HD services from all qualified providers.

These measures were a major departure of standard policies of the public sector in the 1970s and 1980s. The funding of dialysis was one of the very first mixed public, private, and NGO financing operations in Malaysia.

Stewardship in proper training of doctors and allied health staff.

- Emphasizing the importance of a proper training program for nephrologists, kidney nurses, and allied head staff, with a syllabus, logbook, and exit evaluation where trainees are assessed by local and external examiners.

Ensuring quality and integrity.

- Introduced quality initiative efforts, such as the development of practice guidelines on KRT and a document on Hemodialysis Quality Standards.
- Established National Renal Registry (jointly between the MOH and the Malaysian Society of Nephrology) to provide accurate data for health care planners, clinicians, and multinational dialysis industry companies.

Public-private partnership.

- There continues to be collaboration among government, professional societies, private industry, NGOs, and local manufacturers (consumables and solution). There is also widespread implementation of health care laws that have enabled organizations to start an HD facility irrespective of whether they have links to a hospital.

During the last 3 decades of transformation from LMIC to upper-middle-income country, the above measures have resulted in near-universal access to dialysis for all patients with ESKD, at a reasonable cost, with comparable quality to many developed countries.

Malaysia has an interesting dual-tiered system of health care services consisting of a government-led public sector that coexists alongside a private-NGO sector, creating a synergistic public-private/NGO model. The government is the main source of funding for new and existing patients on dialysis (55%–60%); out-of-pocket payments or self-funding for dialysis was ~26% to 30%; and funding from NGOs remained at 11% to 15% over the years.<sup>78</sup> Public financing, mainly through taxation and/or social health insurance (e.g., Social Security Organization), is the dominant form of financing for dialysis. The majority of patients on HD are treated in the private/NGO sector (54%), but almost all patients on PD are treated in government facilities (97%) via financing operations described above.<sup>79</sup> The total health expenditure in Malaysia was 4.21% of the gross domestic product (RM51,742 million) in 2016<sup>80</sup>; the total spending on dialysis was US\$100 million, accounted for 1.72% of the total health expenditure in 2005.<sup>81</sup>

**Strategies for CKD/ESKD care.** In Malaysia, diabetes and hypertension were the most common causes of ESKD,<sup>82</sup> with the prevalence of 17.5% and 30.3%, respectively, in those older than 18 years.<sup>83</sup> The prevalence of CKD stage 5 was 0.36% in those older than 18 years.<sup>84</sup> Recent forecasting estimates that the cost to treat 51,269 patients on dialysis in the year 2020 will be US\$384.5 million.<sup>85</sup> This burden has implications for future health care financing. The prevalence of

ESKD is increasing at an alarming rate. Options proposed to tackle this issue include early medical intervention to slow the progression of CKD in high-risk patients, the promotion of kidney transplantation, and the use of more cost-effective dialysis therapies. In Malaysia, kidney failure prevention initiatives have been carried out nationwide, including patient screening in the primary care setting, the prevention of kidney failure workshops targeting primary care doctors and allied health care staff, the development of clinical practice guidelines on CKD management and nephrology services operational policy, and national public awareness of World Kidney Day. Despite kidney transplantation providing the best KRT option, the transplantation rate remains low at 3 pmp owing to a lack of donors, leaving the choice of KRT between HD and PD.<sup>82</sup>

**Impact.** In Malaysia, citizens can access the subsidized dialysis services provided by the MOH at university hospitals, Ministry of Defense hospitals, and local authorities. Public sector health care services are considered a national health service with its tax-based financing and heavy subsidies. NGOs and political parties also provide support either by providing services (e.g., dialysis services by the National Kidney Foundation), subsidizing part of the payment, or assisting in the appeal for public donations. These measures combined have resulted in expanded coverage of stand-alone dialysis services over the years (Figure 4), with the number of dialysis centers across Malaysia increasing from 205 in 2000 to 758 in 2014.<sup>79,81,86</sup>

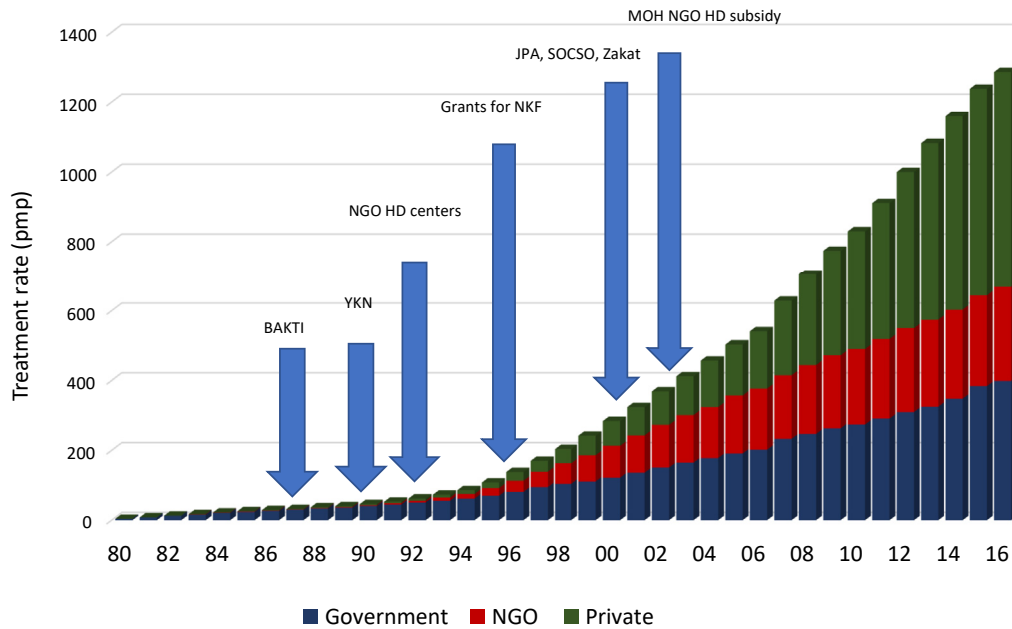
Between 2005 and 2014, private dialysis centers have almost tripled from 6 to 14 pmp, NGO centers increased from 4 to 5 pmp, and the pmp rate of public centers remained unchanged. Private dialysis centers are distributed mainly in economically developed west coast states of Peninsular Malaysia. The government operates most of the dialysis centers in less developed areas.

Reimbursement by government agencies per HD treatment at private and private for-profit HD centers has not changed since 1999 and remains at about RM120 to RM200 and at RM150 to RM200 per dialysis session, respectively.<sup>81</sup> There were 37,183 patients on dialysis in 2015.<sup>79</sup> In 2015, the incidence and prevalence rates of dialysis were 261 and 1295 pmp, respectively.<sup>82</sup> These rates compare favorably to more developed countries in the region, such as Singapore, South Korea, and Hong Kong.<sup>87</sup>

In summary, the number of patients receiving KRT has increased sharply over the last few decades. Malaysia, an upper-middle-income country, has been able to achieve near-UHC for dialysis and consistently reports outcomes; this is usually observed only in industrialized nations. This achievement is due to good stewardship and governance shown by the government, professional societies, NGOs, and clinical champions.

**Malawi (low-income country): unique strategy for ESKD care**

**Background.** Malawi, a country of 16.7 million people, has offered free HD services for both AKI and ESKD since



**Figure 4 | Providing dialysis to meet Malaysian needs.** Dialysis treatment by sector (per million population [pmp]), 1980–2016.<sup>79,81,86</sup>

BAKTI, Badan Amal dan Kebajikan Tenaga Isteri-Isteri Menteri dan Timbalan Menteri (Charitable and welfare bodies of the wives of Ministers and deputy Ministers); HD, hemodialysis; JPA, Jabatan Perkhidmatan Awam (Public Service Department) (civil servants and their dependants would be reimbursed by the government); MOH, Ministry of Health, Malaysia (public health care services are funded through general taxation, with annual health budgets allocated by the Ministry of Finance to the MOH); NGO, nongovernmental organization (NGOs are providing support to access dialysis by either providing some of these services [e.g., dialysis services by the National Kidney Foundation {NKF}], subsidizing part of the payment, or assisting in appealing for public donations [e.g., NKF]); SOCSO, Social Security Organization (a government-run social insurance body that receives mandatory contributions from private-sector employees earning below US\$950 per month); Yayasan Kebajikan Negara; Zakat, state-run Islamic social welfare organizations reimburse eligible patients for certain treatments and dialysis, which was included as a rehabilitation therapy.

1998.<sup>88,89</sup> The first dialysis unit was established in 1998 in Lilongwe with a donation of 4 Gambo AK 95 machines (Baxter International Inc.; Deerfield, IL). As the original HD machines were in poor working order, with spare parts difficult to obtain, patient care was often interrupted and outcomes were generally poor. A second unit was established in Blantyre in 2011 with 4 of the same HD machines to face the increasing demand for services and to reduce the large distances that patients would be required to travel to access dialysis.

**Action.** All HD machines and water plants were replaced at both units between 2013 and 2014. Lilongwe now has 10 stations and Blantyre has 5. A public–private initiative with Fresenius Medical Care (based in South Africa) has provided 5 additional units; the water plant and dialysis machines were offered at no direct capital cost as part of a 5-year contract to purchase consumables from Fresenius. Training of medical and nursing staff has also been a core component of improved service delivery in Blantyre through the Sister Renal Center Program from the ISN. Dialysis is provided on a twice weekly basis, which has increased the number of patients treated, though at a cost of delivering a lower dialysis dose.

**Strategies for CKD/ESKD care.** Although HD services have expanded, providing integrated care for kidney disease remains a challenge. Regular adult and pediatric nephrology clinics help identify patients approaching ESKD, but the overwhelming majority of patients present in extremis,

requiring emergency dialysis for both AKI and ESKD. Screening patients for CKD in high-risk groups such as those with diabetes, hypertension, and HIV remain challenging because of many reasons including the cost of materials such as urine dipstick and laboratory reagents, a low awareness of kidney disease among the public and medical professionals, and the sheer volume of patients.

There is currently no access to transplantation within Malawi; instead, patients are sent overseas for living donor transplants at a cost of ~\$30,000 borne by either the patient or the government. PD has been delivered when suitable supplies of PD fluid and equipment have been available, but these periods are brief and difficult to sustain. Thus, HD remains, and is likely to remain, the predominant dialysis modality in Malawi. Vascular access for HD also remains a challenge, and surgical expertise is urgently required to address this. Some patients do have a native arteriovenous fistula that was created by either a surgeon in Malawi or visiting specialists, but a regular vascular access service has not formally been established. Complications from both temporary and semi-permanent HD catheters are both common and severe.

Significant efforts are being made to provide integrated care for CKD and AKI in Malawi. Both HD units have focused on the development of predialysis nephrology services in terms of clinical activity, teaching, and research. Screening for CKD in high-risk patients such as those with diabetes and HIV has identified an unexpectedly high

prevalence of CKD; this further highlights the importance of robust mechanisms for the early detection and management of CKD.<sup>90,91</sup> Clinical expertise for nephrology in Malawi remains a significant challenge—the country has just received its first qualified nephrologist. The nursing staff in dialysis units represents an excellent source of clinical expertise and have been instrumental in advancing the delivery of dialysis care and education together with physicians and clinical officers.

Kidney services in Malawi have been supported by bidirectional teaching and training programs with Barts Health NHS Trust in the United Kingdom. This partnership has helped develop clinical, research, and teaching expertise. The volume of patients with kidney disease in Malawi, both acute and chronic, has required the development of a specialist kidney ward to care for patients with both AKI and ESKD at Queen Elizabeth Central Hospital in Blantyre. To address the needs of patients who do not proceed with dialysis, a partnership with palliative care services has been established. This service provides holistic and symptomatic care for patients with ESKD in the absence of dialysis.<sup>92,93</sup>

Preliminary discussions around providing transplantation in Malawi have identified attendant laboratory, pharmacy, clinical, legal, and ethical challenges; although difficult, they are not impossible to overcome. Although transplantation in Malawi will ultimately lead to a better quality of life for patients and lower direct cost to the government, it remains some years away.

**Impact.** The total number of patients on dialysis in Malawi has dramatically increased with the provision of new equipment, allowing better access to dialysis for both patients with ESKD and those with AKI.<sup>88</sup> Increasing dialysis has saved lives but at a high cost to the health economy, and the HD capacity is not yet sufficient to treat every case of ESKD. Patient dialysis groups in Malawi have become strong and vocal advocates for services for patients with kidney disease and are instrumental in sustaining and improving HD services in conjunction with clinicians. The educational activities undertaken over the last 7 years have strengthened the clinical and research expertise in Malawi. There are significant challenges ahead for kidney care in Malawi, but working with the ISN on the Kidney Care Network project has the potential to make a major impact on the care of AKI, ultimately saving lives. Strengthening the breadth and depth of clinical nephrology expertise sustainably will require continued financial and operational support from the Malawi government and is essential to a national kidney strategy in Malawi.

### Kenya (lower-middle-income country): upscaling HD

**Background.** Kenya, with a population of >50 million, has a huge number of patients with kidney failure and who would potentially benefit from KRT.

HD was first offered in Kenya in 1964 when an HD machine had to be flown in from England along with a team of doctors for a British soldier. In 1970, regular HD was offered in an intensive care unit at the referral hospital, Kenyatta

National Hospital (KNH) in the capital Nairobi. PD was introduced in 1971, but this expertise was available only in Nairobi. A kidney unit was established at KNH in 1979, and it remained the only unit in the country until 1982, when private hospitals started offering both HD and PD. As these units were located only in Nairobi, other regions still had no access to HD and anybody who needed dialysis traveled to the capital city. By 1990, most provincial hospitals had the personnel to provide acute PD and a few patients started on continuous ambulatory PD. With the introduction of the double bag system in 2002, PD slowly became costlier than HD and few patients opted for this modality. Starting in 2002, satellite HD units appeared outside Nairobi; by 2006, however, there were still only 4 government hospitals offering HD across the country.

In 1978, the first ever kidney transplantation was carried out in a patient whose horseshoe kidneys had been mistaken for an abdominal mass and inadvertently removed; she lived for 1 year after surgery. A few private hospitals started kidney transplantation in 1984, though the numbers were low and irregular. By 1988, KNH was also doing kidney transplantation; however, over the next 20 years, only 130 had been done.

In 2010, it became clear that the government could no longer cope with the growing burden of ESKD and the Kenya Renal Association drafted a plan to increase kidney services (Table 6<sup>94–99</sup>).

**Actions and strategies for CKD/ESKD care.** A partnership between KNH and Novartis Pharmaceuticals was established in 2010 to retrain the transplantation team at KNH. Over the next few years, with travel between Spain and Kenya, the team was fully equipped to run a successful transplantation program. The number of transplantations increased, and expertise was shared with some of the private hospitals.

Because of lobbying from powerful dialysis patient groups to improve the situation in the country, the government implemented the Kenya Renal Association recommendations to increase kidney services in 2015. Recommendations that were implemented included the establishment of at least 1 HD unit in each of the 47 counties with 5 machines each over a 2-year period. This task involved the government creating new structures in regions that did not have the necessary infrastructure. Currently, 90% of the county units, representing 40% of dialysis units in the country, are in place and delivering services to patients.

The National Hospital Insurance Fund, established in 1966, provides UHC to all Kenyans 18 years or older and who have a monthly income of >US\$10; monthly contributions

**Table 6 | Progress of kidney services in Kenya since 1995**

Category	1995 <sup>94</sup>	2000 <sup>95</sup>	2005 <sup>96</sup>	2010 <sup>97</sup>	2015 <sup>98</sup>	2017 <sup>99</sup>
Doctors/nephrologists	12	13	15	16	21	26
Kidney nurses	20	25	50	75	100	260
Hemodialysis units	4	5	6	17	40	100
Patients on hemodialysis	120	120	200	500	1500	2300

Data from compilation of annual audit reports of the Kenya Renal Association from 1995.<sup>94–99</sup> Values are numbers.

range from US\$5 to US\$17. The National Hospital Insurance Fund has the aim of ensuring access to affordable, sustainable, equitable, and quality care and was entrusted by the government to provide funds to reimburse dialysis centers.

Kenya has been entrusted with the East African Kidney Institute of Urology, Nephrology, and Transplantation as part of a new initiative set up by the African Development Bank. The overall objective of this institute is to develop a world class institution that facilitates the realization of the vision to strengthen health training, research capacity, and provision of services to the local and international communities, more so in the East and Central African regions. Although a full nephrology fellowship program is 2 years in length, to address the urgent need for trained doctors, the institute created a 3-month preceptorship.

Despite the advancements in infrastructure, many challenges remain (Table 7). A good supportive structure is needed to ensure the success of the program. Involving partners such as the World Health Organization, United Nations, and ISN to support the program and endorse safety is important. Adapting good guidelines that suit the patient needs is critical.

The MOH is charged with implementing this program and to ensure standards are met by empowering the medical board. Funding comes from the National Hospital Insurance Fund, and the supply of medicines comes from the Kenya Medical Supplies Authority, a state corporation whose mandate is to procure, warehouse, and distribute drugs and medical supplies for prescribed public health programs.

**Impact.** In 2017, a health bill was passed into law, which enables public hospitals in Kenya to start deceased donor (DD) kidney transplantation. Once implemented, this law will ease the number of patients waiting for a kidney transplantation. The Kenya Renal Association, which oversees the program, has started creating a registry for dialysis and transplantation. Nephrologists work closely with the MOH to ensure standards for safe HD are met by each unit. A national

epidemiological survey to determine the number of patients with kidney disease in Kenya is being planned. Despite all these systems being put into place, further team efforts are required to ensure success.

## PD STRATEGY CASES

### South Africa (upper-middle-income country): pediatric PD for ESKD

**Background.** ESKD in pediatric patients is a significant problem in South Africa as it is in many parts of the world. Adults often get preference in terms of dialysis and transplantation.

**Action.** Facilities are present in 3 of the larger academic centers—Johannesburg, Durban, and Cape Town—to provide KRT and transplantation to children who have access to these centers. There is lobbying at the local hospital level for the purchase of pediatric and, in some centers, infant dialysis equipment. Provision for pediatric facilities has also been facilitated in some private facilities. There has been some lobbying at the government level for specific pediatric support but with limited success.

Like adult centers in South Africa, pediatric centers do not provide chronic dialysis for children unless they are suitable for transplantation. This has proved difficult as many children have started on acute dialysis, only to be changed to conservative care as their family and home facilities are not suitable for long-term dialysis. This transition plan has been difficult for some centers, and thus long-term dialysis has been started in some children without a satisfactory plan for future dialysis.

**Strategies for CKD/ESKD care.** The first strategy in developing a pediatric dialysis program in South Africa is to create pediatric programs where adult programs exist. Adult programs can then provide the initial knowledge and technical support associated with caring for adolescents and bigger children.

The next strategy is to use a PD-First approach for children who have been accepted for transplantation and thus dialysis. This uses automated home cycle machines for overnight dialysis while children are sleeping, enabling them to continue school during the day. Families are trained during an inpatient visit over a period of 2 weeks and then examined on their technique before discharge. In most centers, a single home visit is done to see if this is a suitable option as well as to advise them in practical matters of having a dialysis machine at home. There are currently 2 marketed machines for home automated PD in children: Homechoice Claria by Baxter International Inc. and Sleepsafe by Fresenius Medical Care (Waltham, MA).

Advanced technology (Claria Baxter) now allows the remote daily follow-up of overnight dialysis patterns.

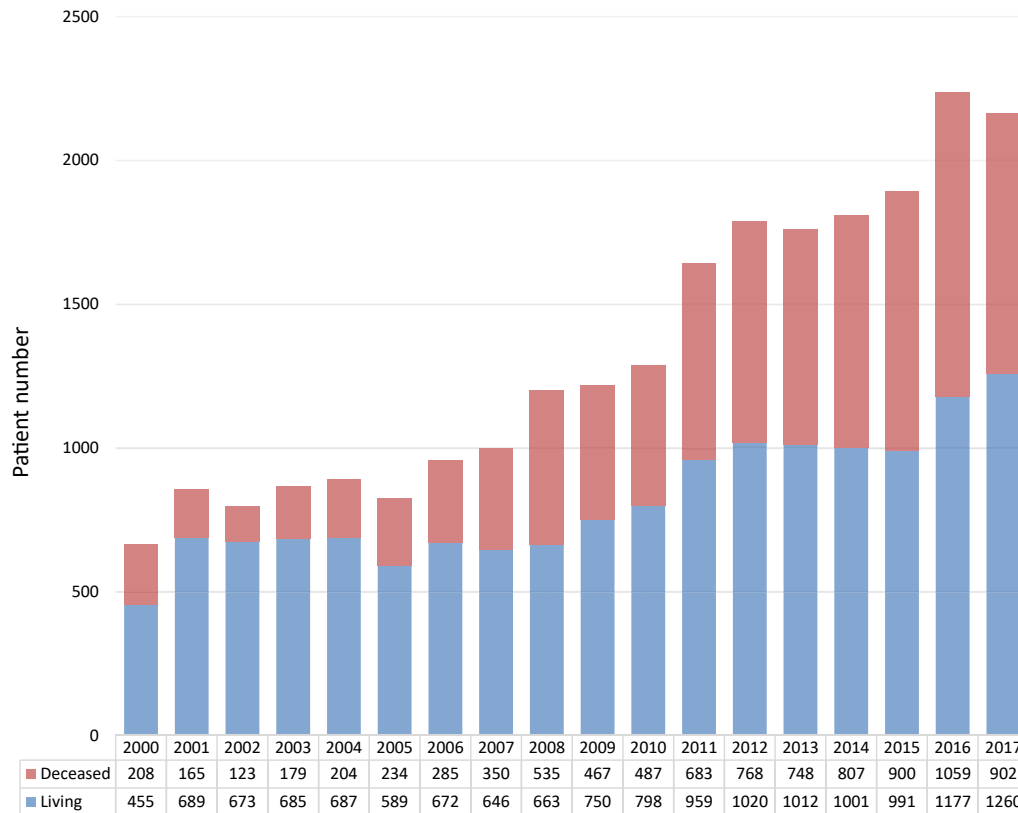
Other strategies include the training and employment of specialized advanced nurse practitioners who can operate in- and outpatient PD programs.

Children who have failed PD and would go onto HD provide the challenge to appropriate pediatric and infant HD lines and filters. While pediatric centers are being established,

**Table 7 | Challenges for the growing kidney replacement therapy program in Kenya**

- Patients come into the hospital with crush syndrome and require urgent dialysis through temporary catheters
- Long distance to the dialysis facility
- Despite the many units, they are quickly filling up and many patients must be turned away
- Lack of sufficiently trained personnel—biomed engineers, nephrologists, kidney nurses, and vascular surgeons
- Vascular access—creation, failure, infection, and thrombosis
- Poor control of blood pressure and volume with patients on twice weekly hemodialysis
- Costs of medications, especially erythropoietin and iron
- Costs of screening for HIV and hepatitis B and C
- Cost of vaccination for hepatitis B and screening for antibody
- Costs of laboratory tests for follow-up of BMD and anemia
- Cost of water analysis
- Low number of kidney transplantations
- Lack of support for PD
- Output from this institute will not be sufficient

BMD, bone mineral density; PD, peritoneal dialysis.



**Figure 5 | Number of kidney transplantation cases in South Korea.** Data from Ahn HJ, Kim HW, Han M, et al. Changing patterns of foreigner transplants in Korea and overseas organ transplants among Koreans. *Transplantation*. 2018;102:310–317.<sup>100</sup> Copyright © 2018 Wolters Kluwer Health, Inc.

bigger children will often initially dialyze in adult facilities. This emphasizes the need for training of medical and nursing staff in both adult and pediatric centers.

The ultimate goal in pediatrics is to arrange kidney transplantation as soon as possible; this avoids stunting due to long-term dialysis. To ensure the success of a pediatric transplantation program, it is critical to have a few dedicated centralized areas across the country. This will centralize the skills base and improve results.

**Impact.** Over the last 10 years, pediatric nephrology has grown in South Africa from 10 to 27 active pediatric nephrologists. Over the last 15 years, at the Red Cross Children's Hospital alone, we have trained a further 24 pediatric nephrologists from elsewhere in Africa.

The challenge remains to increase the training of nurses, technicians, and advanced nurse practitioners to provide dialysis and transplantation for children.

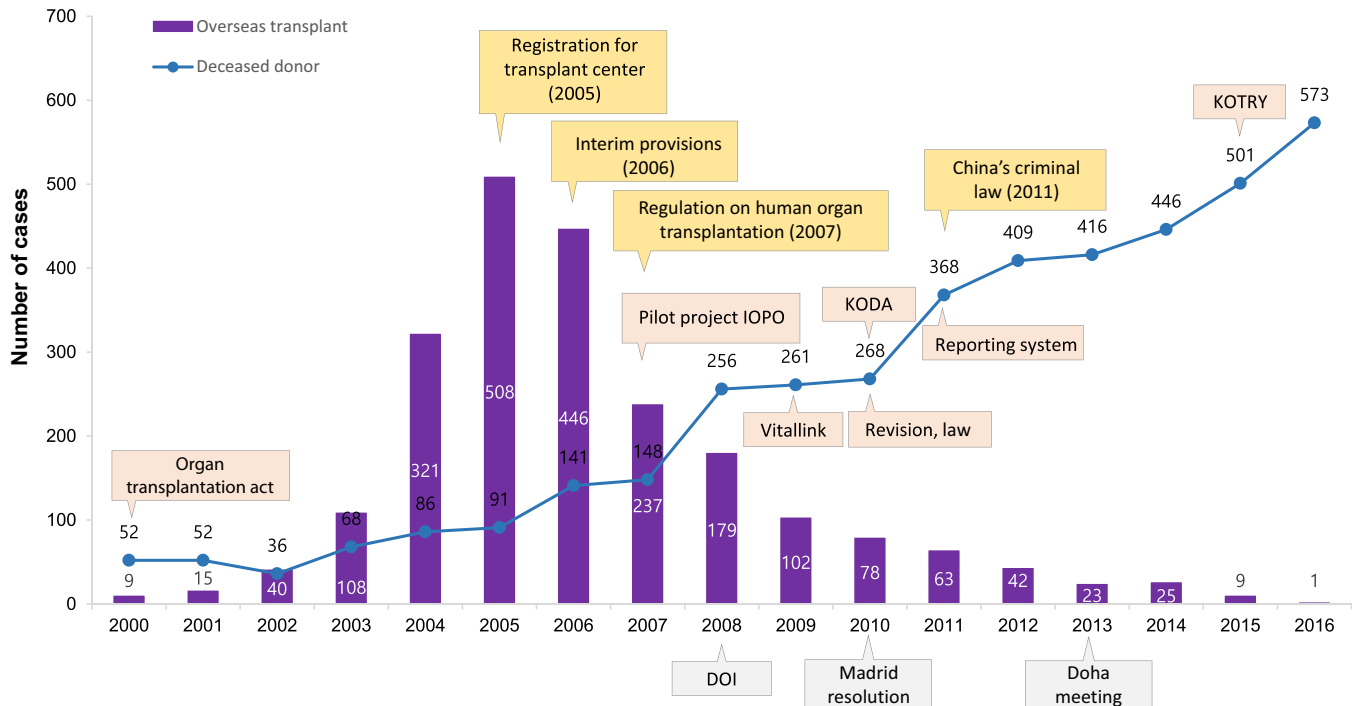
Overall, the situation is slowly improving: in December 2016, the South African Renal Registry found that there were 54, 53, and 86 patients younger than 19 years on PD and HD, and with a functioning transplanted kidney, respectively (with permission from Razeen Davids, Webmaster of South African Renal Registry). The result of staff training as well as collaboration with adult nephrology teams gives hope for the future of pediatric patients with nephrology disorders in South Africa as well as in other parts of Africa.

## TRANSPLANTATION STRATEGY CASES

### South Korea (high-income country): system development for DD kidney transplantation

**Background.** Kidney transplantation improves the quality of life of patients with ESKD and is cost-effective. The first living-donor kidney transplantation in Korea was conducted in 1969, and the first DD kidney transplantation was conducted in 1976. The number of hospitals performing kidney transplantation has since rapidly increased. However, as most kidneys are donated within families and there is an increasing trend of smaller families, living donor kidney donation has stagnated. Furthermore, the revered traditional Confucian view teaches that *your entire body was given to you by your parents* and people are taught to value their bodies. The meaning of this teaching has been overinterpreted to mean *value all parts of human body even after death*, resulting in the rejection of organ procurement from DDs.

**Actions and strategies for CKD/ESKD care.** To address the shortage, in 1988, the Korean Society for Transplantation proposed DD organ transplantation legislation to the congress. Although DD kidney transplantation was being conducted by several hospitals at the time, it took 10 years to secure legal support for it. This situation resulted in kidneys from the poor being traded on the black market. Thus, a renewed legal review of brain death was initiated, and the Organ Transplantation Law was passed in 1999 and the



**Figure 6 | Relationship between the number of overseas organ transplantation cases and the number of deceased organ donors in South Korea.** Doha: Doha, Qatar; DOI, Declaration of Istanbul; IOPO, independent organ procurement organization; KODA, Korea Organ Donation Agency; KOTRY, Korean Organ Transplantation Registry. Reproduced with permission from Ahn HJ, Kim HW, Han M, et al. Changing patterns of foreigner transplants in Korea and overseas organ transplants among Koreans. *Transplantation*. 2018;102:310–317.<sup>100</sup> Copyright © 2018 Wolters Kluwer Health, Inc.

Korean Network for Organ Sharing was established in 2000. The major role of the Korean Network for Organ Sharing was to review the legal and ethical relationship between living donors and their recipients. It also became responsible for the management of the transplantation wait-list and the allocation of DDs. Over time, the Korean Network for Organ Sharing became a national authority, regulating organ transplantation–related activities.

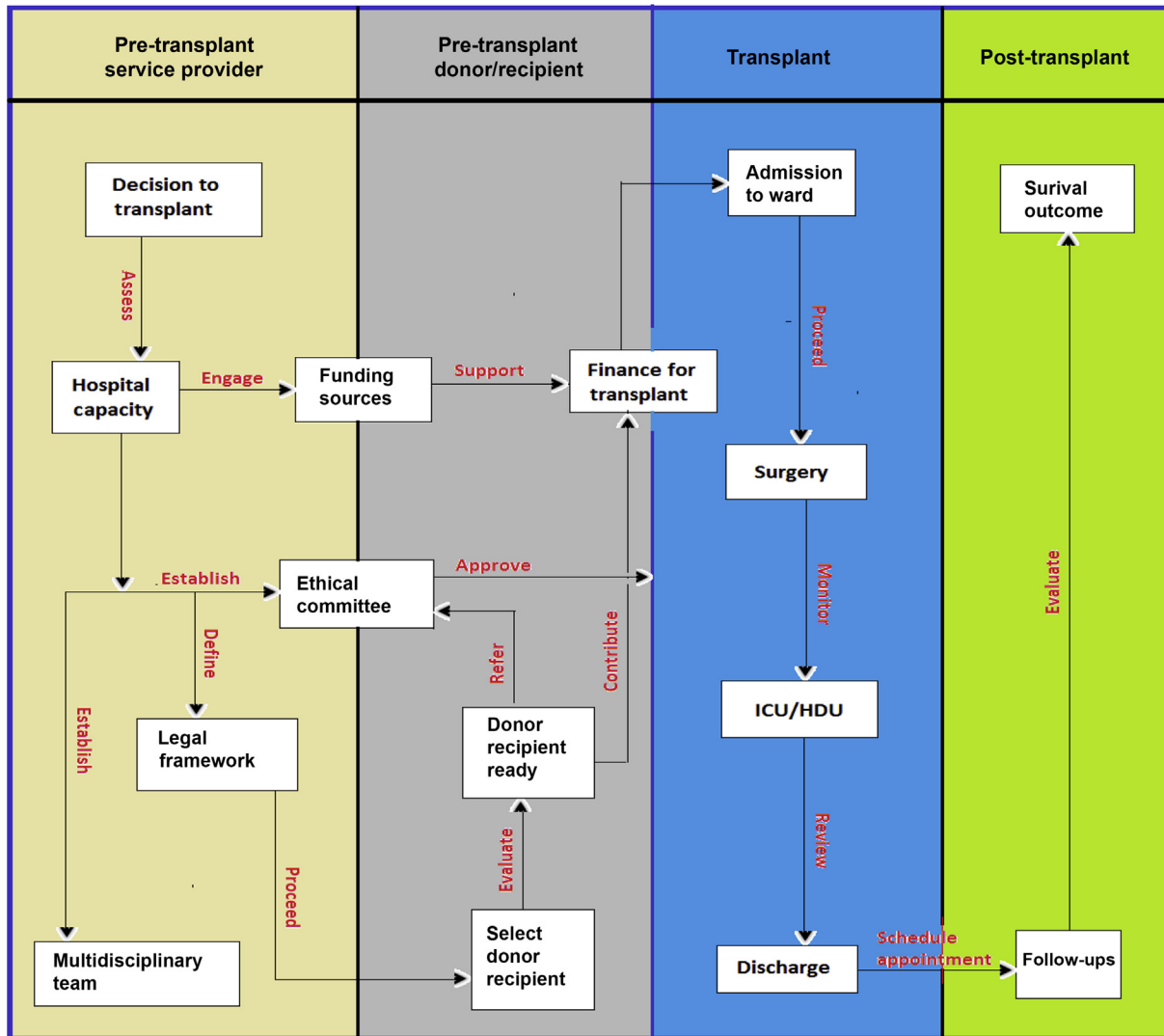
The overly tight regulation of each process soon resulted in a decline in kidney transplantation, and the annual number of patients who died while waiting for organ transplantation increased. Patients became increasingly desperate, and overseas transplantation rapidly increased starting in 2002. The Organ Allocation Study Group, under the Korean Society for Transplantation, elected to change its name to the Deceased Organ Donation Improvement Program Committee in 2009 and started devoting its efforts to formulating strategic plans for reactivating DD organ transplantation. The Organ Allocation Study Group cooperated with the congress in revising the existing law in 2010, adding a law on mandatory reporting, the establishment of an independent organ procurement organization, and the implementation of a transplantation registry.

Vitallink is an NGO that was established by the Korean Society for Transplantation in August 2009 to promote public awareness of DD organ donation. Vitallink educates medical and high school students about organ donation. Vitallink also established the Korean Organ Donation Network in 2010 to

conduct consistent education for NGO leaders. They jointly collaborate with Catholic and Buddhist NGOs to host various campaigns. Finally, Vitallink has been supporting the development of the Asian organ transplantation program through annual workshops and the provision of training courses for medical professionals from Korea and abroad.

The Korea Organ Donation Agency was established in 2009. Currently, this agency has jurisdiction over 3 regional divisions. The main responsibility of procurement coordinators is to discover potential DDs by visiting hospitals. When the Korea Organ Donation Agency receives notification of a potential brain death donor, they first visit the hospital to conduct a primary medical evaluation for donor eligibility and then obtain consent from the family, process the evaluation of brain death, and contact and coordinate the organ procurement teams and operations. After donation, they collect the body to transfer to the family and provide emotional support. The Korea Organ Donation Agency is also in charge of education for medical professionals and donor families.

In 2014, the Korean Society for Transplantation established a web-based registry, the Korean Organ Transplantation Registry. The Korean Organ Transplantation Registry collects data on ~85% of all organ transplantation and issues an annual report. They have hosted various seminars and provide research grants and awards. The Korean Organ Transplantation Registry has now started the Asian Organ Transplantation Registry (ASTREG).



**Figure 7 | Model for kidney transplantation in Ghana.** HDU, high-dependency unit; ICU, intensive care unit.

**Impact.** The rate of DD organ transplantation in Korea has greatly increased because of the adoption of new strategies (Figure 5).<sup>100</sup> This increase has led to a decrease in the number of overseas transplantation (Figure 6).<sup>100</sup> As of 2017, the number of DD organ donations in Korea was 10.7 pmp, the highest in Asia; however, Korea is still ranked only 37th worldwide. To provide a better life for patients with ESKD in Korea, partnerships will be required with other Asian countries in organ transplantation.

**Ghana (lower-middle-income country): framework for the development of living donor kidney donation**

**Background.** In 2008, a living donor kidney transplantation program was established in Ghana in collaboration with the Transplant Links Community and the Queen Elizabeth Hospital Birmingham, part of University Hospitals Birmingham NHS Foundation Trust–ISN Sister Renal Center. Our model for developing a kidney transplant program involved 3 stages (Figure 7): the *pre-transplant* stage, crucial in ensuring effective planning and long-term sustainability; and the *transplant* and *post-transplant* stages, important for

clinical capacity building, patient care, monitoring, and evaluation, which then feed back into the pre-transplant stage to optimize the transplantation process.

**Pre-transplant planning.** The decision to undertake living donor kidney donation was based on the youthfulness of patients on dialysis, the cost of HD (beyond the means of most patients), and the opportunity for an improved quality of life. First, a knowledgeable and committed *champion* was identified to lead, drive, and coordinate the program through effective and ongoing engagement with all stakeholders.<sup>101</sup>

The second step involved an assessment of the capacity of the hospital to ensure that it could support kidney transplantation. A checklist was developed to assess *infrastructure*: personnel, policies, protocols, laboratory support, and medicine availability. This was implemented by a team including heads of departments of medicine, surgery, pharmacy, pathology, and anesthesia. The assessment of clinical capacity included identification of comprehensive protocols for both donor and recipient work-up and immunosuppressant management, including a choice of affordable generic

**Table 8 | Featured strategies of CKD/ESKD care stratified by World Bank economic classification**

Country	Featured strategy
Integrated CKD/ESKD care (high-income countries)	
Japan	UHC for dialysis; reduced incidence ratios of dialysis with CKD program. Increased transplantation since 2011
Taiwan	UHC for dialysis; multidisciplinary team care for high-risk populations of patients with pre-ESKD and CKD
Uruguay	UHC for dialysis; creation of kidney care teams to work in health care centers and treat patients with CKD at the primary care level
United Arab Emirates	Modification of physician prescribing behavior to reduce NSAID usage. Early detection and management of CKD by using the electronic medical record system
South Korea	Promotion of deceased donor organ transplantation through registries, seminars, research grants, and awards
Increasing access of CKD care and KRT (upper-middle-income countries)	
China	Developing population-based prevention approaches for CKD/ESKD; increasing home-based KRT, including rural areas, along with optimal management
Mexico	Creation of measures to move toward UHC for patients with kidney disease
Thailand	Use of community nurses and village health volunteers to provide information on lifestyle modifications and referral of CKD cases during home visits
Malaysia	Funding dialysis through a mix of public, private, and NGO financing
South Africa	Increasing access to KRT for pediatric patients through increased dialysis and training of pediatric nephrologists
Building capacity for kidney care (lower-middle-income countries)	
Senegal	Establishment of a nephrology school to train nephrologists and nurses in the sub-Saharan Africa region
Kenya	Upscaling hemodialysis and partnership with a private entity to enable retraining of transplantation surgeons
Sudan	Use of charitable funds to increase access to dialysis across the country
Ghana	Institution of a living donor kidney donation program through collaboration with international nephrology centers
Building capacity for KRT (low-income country)	
Malawi	Expansion and better access of dialysis services over the last 20 yr

CKD, chronic kidney disease; ESKD, end-stage kidney disease; KRT, kidney replacement therapy; NGO, nongovernmental organization; NSAID, nonsteroidal anti-inflammatory drug; UHC, universal health coverage.

immunosuppressants. Identified key gaps included no legal framework for organ transplantation, a lack of transplantation surgeons, and the nonavailability of protocols and some immunosuppressive drugs.

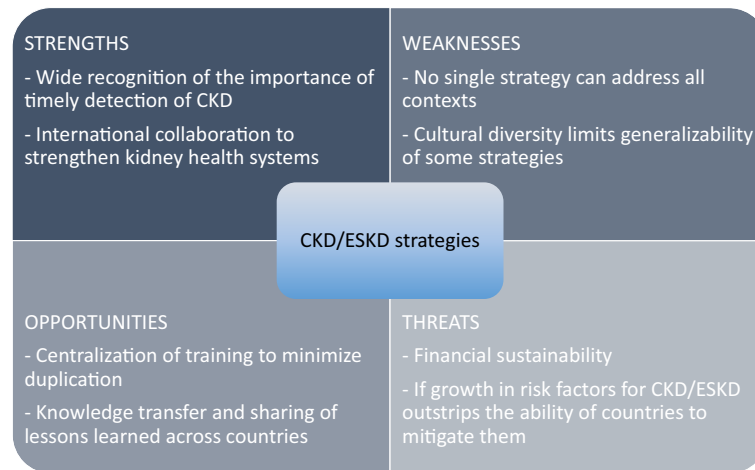
The third step was the development of a *legal and ethical framework for living donor kidney donation*. In the absence of a national legal framework for transplantation, hospital management and the MOH decided to adopt the Declaration of Istanbul on organ trafficking and transplant tourism as a means of ensuring best practices.<sup>102,103</sup> To work within the principles of the Declaration of Istanbul, only living-related donors were considered. In addition, a *transplant ethics committee* was established, guided by the UK Human Tissue Act (2004), the World Health Organization Guiding Principles on Human Cell, Tissue and Organ Transplantation, and the Declaration of Istanbul, to independently assess the transplantation process and to avoid coercion and organ trafficking.<sup>104–106</sup> The committee comprised a retired professor of surgery, a priest, a lawyer, a clinical psychologist, and a professor in public health.

The final step was *financing*. Given the projected costs of a transplantation program, the hospital engaged funders including the National Health Insurance Scheme and the Social Security and National Insurance Trust. The hospital also provided letters to patients to solicit funds for transplantation. The Transplant Links Community raised enough funds to cover the costs of the visiting transplantation team, volunteers who visited during their holidays. The National Kidney Foundation–Ghana raised funds to support medicines and laboratory investigations. The cost of a kidney transplantation was estimated at US\$10,000 per transplantation,

including pre- and post-transplantation laboratory investigations, hospital admission, both operations (donor and recipient), postoperative management, and a 3-month supply of immunosuppressive drugs. Corporate organizations sponsored transplantation patients to ensure that all patients, even those who could not afford it, were provided for, including ongoing immunosuppressants, which average US\$3600 to US\$4000 per year.

#### **Impact.**

- (i) *Development of local clinical capacity for transplantation:* A multidisciplinary clinical team made up of local nephrologists, urologists, anesthesiologists, clinical pharmacists, and critical care nurses was created. Clinical expertise in kidney transplantation was achieved with periods of training of surgeons and physicians in South Africa and the United Kingdom through ISN fellowship awards.
- (ii) *Donor and recipient selection:* Recipients along with suitable living donors were selected from dialysis centers. Two local nephrologists applied standard guidelines to evaluate donor and recipient pairs. Donors and recipients were provided with counseling and educational materials on the risks and alternatives available. Materials were provided in English; however, a team of local nurses were able to counsel in the local language. After the medical evaluation, donors and recipients were further evaluated by the transplantation surgeon and the anesthesiologist. The ethics committee provided an independent assessment and interviewed each pair separately and together. Once the committee was satisfied that the pair were genuinely related, that the donor was not acting under any coercion, and that the Declaration of Istanbul was adhered to,



**Figure 8 | Strengths, weaknesses, opportunities, and threats (SWOT) analysis of chronic kidney disease (CKD)/end-stage kidney disease (ESKD) strategies.**

- written approval was given to proceed to the transplant stage. Two other nephrologists from the international team reevaluated the donor-recipient pair before surgery.
- (iii) *Transplantation procedure and follow-up:* The University Hospitals Birmingham NHS Foundation Trust and Transplant Links Community teams made 2 initial visits before the first transplantation and then performed the kidney transplantations on subsequent visits. These visits enabled hands-on training of local surgeons, anesthetists, nurses, and theater technicians. The Ghanaian team adopted the University Hospitals Birmingham NHS Foundation Trust protocols, with minor modifications, for patient management and follow-up pre-, intra-, and postoperation.
- (iv) *Monitoring and evaluation of the program involved entering all patients into a database for ongoing follow-up:* After the first set of kidney transplantations done in 2008, the donor work-up process was reevaluated and a new donor work-up sheet was designed to reduce the cost of the donor work-up ([Appendix 2](#)). Outcome of the transplantation program has been good: in the first 17 transplantations done, there was 100% 1-year patient survival and 91.7% graft survival.<sup>106</sup>

### SUMMARY

ESKD is a global problem and cuts across all sociodemographic differences and cultural context. Despite the diversity in countries discussed here, common themes emerged in the approach to reducing the burden of CKD/ESKD:

- the importance of screening high-risk populations and multidisciplinary care in slowing the rate of progression of CKD;
- improving access to KRT options (HD, PD, DD, and living donor transplantation) to all patients (including rural) affected by ESKD;
- moving toward financially sustainable KRT options; and
- the recognition of the harm of nephrotoxic drugs.

Countries have made great strides to date in recognizing the importance of and developing strategies to address CKD/ESKD across different income status ([Table 8](#)). Future work

needs to continue to rely on strong data collection and analysis to identify key risk factors across populations, enact strategies that delay the onset and progression of CKD, increase universal access to appropriate KRT, and use the leverage of international collaboration to strengthen systems around the world ([Figure 8](#)). Capitalizing on partnerships that can limit the financial burden on LMIC should continue to be explored. A cohesive collaborative approach among experts around the globe will continue to strengthen the international nephrology community and improve outcomes for patients with CKD/ESKD.

### Appendix 1 | Evolutionary pathway of CKD/ESKD integrated care in Taiwan

- I. Understanding burden and risks for ESKD/CKD in Taiwan
  1. Understanding the ESKD/CKD burden
    - National Dialysis Registry since 1987 by TSN, a mandatory reporting system
    - CKD prevalence estimation by an epidemiology study (national and local)
    - Impacts on medical economics and financial burdens of NHI; NHI launched in 1995
  2. Identifying risk factors and target populations through national and local studies
    - Patients with diabetes and hypertension
    - Patients with a family history of CKD
    - Individuals receiving potentially nephrotoxic drugs, herbs, or substances or taking indigenous medicine
    - Individuals older than 65 years
- II. Plans and actions taken in strategy consideration and time sequence, facts exposure, and collaboration with the government
  - Report ESKD data to the academic organization for international comparisons (USRDS) – 2001
  - Exposure to media and legislators and promote government concern as an important public health issue – 2001
  - Collaboration with DOH – TSN president and Committee of Chronic Diseases Prevention, DOH – 2001
  - Active participation in policymaking within government institutes: NBHP and BNHI – 2002
1. Organize CKD prevention committee within TSN – 2003
- Design overall CKD prevention project with national perspectives:
  - Play the pivotal role of opinion, education, and action leaders
  - Arrange CKD educational programs extensively at regional and annual meetings

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### Appendix 1 | (Continued) Evolutionary pathway of CKD/ESKD integrated care in Taiwan

- Design and initiate a training course of multidisciplinary CKD care for nephrologists, CKD nurse educators, and kidney dietitians
  - Set up project for organizing the CKD prevention institutions as the key unit of CKD patient care, early prevention measure, and public education at the hospital level
2. Action taken for patient education and multidisciplinary team care in CKD prevention institutions through the Taiwan CKD Prevention Project – 2002
- Pilot Project of Integrated Care of CKD from major hospitals – 2002 (NBHP)
  - Project expansion to include more CKD prevention organizations (rolled out to clinics) – 2003–present (NBHP + TSN)
  - CKD Information System for register and case management – 2005 (NBHP)
  - Project of integrated care for patients with pre-ESKD (CKD stage 3b, 4, and 5) and screening for high-risk patients with reimbursement from NHI – 2007–present (BNHI)
  - Project of care for patients with early CKD (CKD stage 1, 2, and 3a) and extension to general medicine discipline – 2011–present (BNHI)
- III. Collaboration among government, academic societies, and other NGOs
1. Public promotion
- Use extensive public media for educating CKD concept and promoting prevention actions
  - Initiate the public health promotion activity of Taiwan Kidney Day – 2005 (1 year ahead of the World Kidney Day)
  - Continue public promotion of the *wherever, whenever, and whoever* strategy
2. Reduction in risk factors through the national health promotion program by DOH
- Diabetes control
  - Hypertension control
  - Hyperlipidemia control
  - Prohibition of aristolochic acid-containing herbs since 2003
3. CKD early detection through the adult and elderly physical checkup project
- Report eGFR from serum creatinine measurements and urine protein from the dipstick test
  - Make CKD staging accordingly
  - Refer individual detected with CKD to the health care system
- IV. Outcome monitoring and future goals
1. Outcome measures
- Long-term goals: reduction in ESKD incidence as the final goal
  - Short-term goals: improving quality of CKD care
  - Reduction in the incidence of emergent dialysis
    - a. Increased rate of prepared vascular access before dialysis
    - b. Increased penetration of PD, a less expensive treatment in Taiwan
    - c. Promote kidney transplantation, a difficult concept in Taiwan
    - d. Slowing the kidney progression rate by medical and multidisciplinary care
    - e. Improved quality of CKD care on the basis of various clinical parameters
    - f. Reduction of medical expenses before and after the initiation of dialysis
  - The rising incidence rate of ESKD began to stabilize in the age group younger than 75 years from 2006
2. Future goals: set by DOH in 2011, to work with TSN
- Decrease the dialysis incidence rate — by 2%/yr to move out of the ranking of the fifth world highest incidence in 10 years
  - Keep good dialysis survival rate – 5-year survival rate of dialysis must be kept higher than that observed in the ERA-EDTA registry
  - Increase the number of new kidney transplants – 15% increment in 5 years
  - Increase the penetration rate of PD – 20% of incident dialysis cases, 13% of prevalent dialysis cases as PD

BNHI, Bureau of National Health Insurance; CKD, chronic kidney disease; DOH, Department of Health; eGFR, estimated glomerular filtration rate; ERA-EDTA, European Renal Association – European Dialysis and Transplant Association; ESKD, end-stage kidney disease; NBHP, National Bureau of Health Promotion; NGO, nongovernmental organization; NHI, National Health Insurance; PD, peritoneal dialysis; TSN, Taiwan Society of Nephrology; USRDS, United States Renal Data System.

### Appendix 2 | Work-up checklist for living donor kidney donation in Ghana

Recipient work-up		Donor work-up	
Name	X	Name	X
Date of birth/age	X	Date of birth/age	X
<b>Phase 1A</b>	X	<b>Phase 1A</b>	X
Blood group	X	Blood group	X
Relationship	X	Relationship	X
Hemodialysis			
Dialysis access	X		
Diagnosis	X		
General clinical assessment	X	General clinical assessment	X
Past medical history	X	Past medical history	X
Family history	X	Family history	X
Blood pressure	X	Blood pressure	X
Examination of the heart	X	Examination of the heart	X
Examination of the chest	X	Examination of the chest	X
Examination of the abdomen	X	Examination of the abdomen	X
Other features	X	Other features	X
<b>Phase 1B</b>	X	<b>Phase 1B</b>	X
ECG	X	ECG	X
ECHO	X	ECHO	X
CXR	X	CXR	X
Hemoglobin	X	Hemoglobin	X
WBC	X	WBC	X
Neutrophils %	X	Neutrophils %	X
Platelets	X	Platelets	X
Hb electrophoresis	X	Hb electrophoresis	X
Fasting glucose	X	Fasting glucose	X
G6PD	X	G6PD	X
Sodium	X	Sodium	X
Potassium	X	Potassium	X
Urea	X	Urea	X
Creatinine	X	Creatinine	X
Total bilirubin	X	Total bilirubin	X
Conjugated bilirubin	X	Conjugated bilirubin	X
ALP	X	ALP	X
AST	X	AST	X
ALT	X	ALT	X
GGT	X	GGT	X
Total protein	X	Total protein	X
Albumin	X	Albumin	X
INR	X	INR	X
PTT	X	PTT	X
		Urine dipstick protein	X
		Urine dipstick blood	X
		Urine culture	X
Hepatitis B	X	Hepatitis B	X
Hepatitis C	X	Hepatitis C	X
HIV	X	HIV	X
CMV	X	CMV	X
TPHA	X	TPHA	X
<b>Phase 2A</b>		<b>Phase 2A</b>	
		Urine dipstick	X
		24-h urine protein ×2	X
		Creatinine clearance ×2	X
		MDRD GFR	X
		Ultrasound of kidneys	X
		PSA	X
Total cholesterol	X	Total cholesterol	X
LDL	X	LDL	X
HDL	X	HDL	X
Triglycerides	X	Triglycerides	X
Chol/HDL ratio	X	Chol/HDL ratio	X
Uric acid	X	Uric acid	X
<b>Phase 2B</b>		<b>Phase 2B</b>	
		Pap smear	X
		Mammogram	X
		ECG	X

(Continued on next page)

## Appendix 2 | (Continued) Work-up checklist for living donor kidney donation in Ghana

Recipient work-up		Donor work-up	
		CXR	X
		Echo	X
<b>Phase 3</b>		<b>Phase 3</b>	
Tissue typing	X	Tissue typing	X
Crossmatch	X	Crossmatch	X
<b>Phase 4</b>		<b>Phase 4</b>	
		MR/CT kidney angiogram)	X
		Isotopic GFR	X
<b>Phase 5</b>		<b>Phase 5</b>	
Independent Assessment	X	Independent Assessment Committee clearance	X
Committee clearance			

### DISCLOSURE

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