

# EARLY DETECTION OF CKD: CASE STUDIES ON SCREENING AND CASE-FINDING

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## Introduction

Chronic kidney disease (CKD) is common, costly, and associated with tremendous morbidity and mortality. The prevalence and burden of CKD are increasing most rapidly in low- and middle-income countries (LMIC), and the corresponding increase in the demand for expensive kidney replacement therapies is a major challenge for health systems worldwide. Unfortunately, kidney replacement is unavailable or unaffordable for most people who live in LMIC, and thus CKD that progresses to kidney failure kills millions of people each year. Since inexpensive treatments can slow the rate of kidney function loss, and because CKD is asymptomatic until its later stages, there is some enthusiasm for population-based screening to enable early intervention in both LMIC and high-income countries (HIC).

Unfortunately, many screening programs are markedly less beneficial than expected. The benefits of population-based screening for CKD are uncertain and screening does not appear to be a wise use of resources even in HIC. There is some potential for harms associated with CKD screening, and screening has substantial opportunity costs that offset its hypothesized benefits, especially in LMIC.

Case-finding approaches that target screening to high-risk populations (e.g., people with diabetes, hypertension, and cardiovascular disease) are more appealing as this may be more cost-effective, and there is already high pre-existing use of kidney testing in such patients.

Work by the International Society of Nephrology (ISN) has generated a list of pre-requisites for successful early detection of CKD, including screening and case-finding (Table 1).

**Table 1 - List of Pre-Requisites for Successful Early Detection of CKD**

1. Document the Burden of Kidney Failure
2. Leadership from Kidney Society
3. Partnership with Government
4. National Health Insurance / Medicare
5. Method of CKD Identification: Screening or Case Finding
6. Focus on High-Risk Groups
7. Availability of Sustained, Effective, Standardized CKD Treatment
8. Multidisciplinary Care
9. Education of the Public, Patients and Carers, Health Care Workers
10. Integration with Management of Other Non-Communicable Diseases, Especially Diabetes
11. Integration with Other Aspects of Health Policy, e.g., Pay-for-Performance (P4P)
12. Continuous Quality Improvement



A series of case studies follows to illustrate how countries have implemented early detection programs, highlighting the use of these pre-requisites. Countries included in the series are:

- Taiwan
- Uruguay
- Canada
- United Kingdom
- Mexico
- Senegal



## Taiwan

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### Background

To monitor the incidence and burden of kidney failure in Taiwan, a national dialysis registry was initiated in 1987 by Taiwan Society of Nephrology (TSN). In response to the high incidence rate of kidney failure, which was published by USRDS (United States Renal Data System) as one of the highest incidence rates among other countries, TSN proposed to the Department of Health to prioritize CKD prevention and care as a major public health issue, arguing against the health economics insurance system. Recognizing the burden of kidney failure, the government included CKD prevention and health care as a significant administrative task since 2003, to reduce the incidence of kidney failure in Taiwan. The task was to encourage CKD screening, prevention, and to improve CKD patient health education and management. Subsequently, an integrated CKD care program was initiated followed by screening of the adult population and case-finding in high-risk populations aiming for CKD patient identification and intervention.

### Goals and Strategies

Since its inception in 1995, Taiwan's National Health Insurance (NHI) has distinguished itself as a high-performing, single-payer national health insurance system that provides universal health coverage to the country's 23.4 million residents based on egalitarian ethical principles. Over the years, the system has encountered numerous obstacles, including significant financial deficits. These crises were managed by the Taiwanese government through a series of policy adjustments and reforms. The Taiwan NHI is a universal coverage health system and reimburses the treatment of kidney failure. However, growing expenditures related to CKD and kidney failure triggered a consideration of strategies to improve care while mitigating the clinical and economic burden. Among the strategies are encouraging different strategies for early detection of CKD (screening; case-finding), improving CKD prevention health education, offering CKD prevention and therapy, and implementing the case management of CKD patients in medical institutes.

### Actions for Identification: Population-based Screening

#### Including CKD screening in general adult health checkups

As a general preventive measure, in 2002 the government provided preventive health checkups for adults, including physical examinations, blood and urine tests, and health consultations. These are provided free to people at age 40-64 every three years, and to those aged 65 or over every year. To provide comprehensive, on-site screening in local communities, the National Health Promotion Administration (NHPA) encouraged county and city governments to consolidate medical resources using these health checkups. In 2019, a total of 1,894,259 people were screened, of whom 444,271 (23.5%) received the health screening service for the first time.



Estimated glomerular filtration rate (eGFR)  $<60$  ml/min/1.73m<sup>2</sup> using the CKD-EPI equation or the presence of proteinuria on dipstick were used to define the presence of CKD. Among those who received health screening in 2019, 15.9% met this criterion and were referred to the national CKD program. The CKD program including CKD stages 3b to 5, was defined as advanced CKD, and CKD stages 1 to 3a were defined as early-CKD to facilitate characterization of the CKD care network. (see “Intervention,” below).

A follow-up analysis using these data found that CKD was associated with increased all-cause mortality in a prospective cohort study in Taiwan. The cohort consisted of 462,293 individuals aged  $>20$  years who participated in a standard medical screening program since 1994; 56,977 (12%) of cohort participants had CKD, but only 3.54% of participants in the cohort were aware of their disorder. The prevalence of CKD was substantially higher in the group with low socioeconomic status than in the high-status group (19.8% vs 7.3%). Participants with CKD had 83% higher mortality for all cause (hazard ratio [HR] 1.83) and 100% higher for cardiovascular diseases (HR 2.00) over median follow-up of 7.5 years. As of Dec 31, 2006, 14 436 deaths were identified. 2,350 (39%) deaths occurred before 65 years of age in those with CKD. 10.3% of deaths in the entire population were attributable to CKD, but 17.5% of deaths in the low socioeconomic status population.<sup>1</sup> The high prevalence of CKD and its related all-cause mortality, especially among people of low socioeconomic status, made CKD a public-health priority for Taiwan.

In Keelung, Taiwan, from 1999 to 2009, a prospective cohort study was conducted with an integrated community-based multiple screening program of 106,094 adults aged  $>20$  years. The mean age of the participants was  $47.7 \pm 15.4$  years. The estimated prevalence was 15.5% for total CKD and 9.06% for CKD stages 3–5. The incidence was 27.21/1,000 person-years (PY) for total CKD and 16.89/1,000- PY for CKD stages 3–5. Patients who were older, male, or had comorbidities such as diabetes, hypertension, or metabolic syndrome had greater CKD prevalence and incidence rates than their counterparts.<sup>2</sup>

### Case-finding in the Three-Highs Survey

Among the subset of the general population who were found to have one of the “Three-Highs” (high blood pressure, high blood sugar, high blood lipids), the proportion of people with CKD was found to be higher than in the overall population. Despite self-reported healthy condition, after health checkups review, 392,000 people (21.3%) had high blood pressure, 162,000 people (8.8%) had high blood sugar, and 475,000 people (25.8%) had high blood lipids at age over 40 years. Compared with those without Three-Highs, the people who had one, two, or three types of Three-Highs, were 1.5, 1.8, and 2.1 times, respectively, more likely to have early CKD. In data collected between 2002 and 2009, 13.4% to 17.7% of people with one or more of the Three-Highs conditions had CKD; this proportion was 18.9% among people with two of these conditions and 22.9% among those with all three conditions. This phenomenon is also evident in the advanced CKD condition, the more types of Three-Highs people had, the higher rate of advanced CKD they would develop.

In addition, advanced CKD was found in 18.3% in the Three-Highs age group (over 65 years old), which is 3.5 times higher than the middle-age group (40 to 64 years old) that also had Three-Highs (5.2% of those with advanced CKD). These data indicate that the more types of Three-Highs people had, the higher the likelihood that they would develop advanced CKD. These patients when identified by health checkups, were followed up at medical institutions for CKD management.

### Diabetes Shared Care Program and CKD Identification

Due to the high prevalence of diabetic nephropathy, a shared care program was established to help improve outcomes among patients with diabetes. The program partners primary care practitioners with more than 4,000 certified diabetes educators (CDEs), including health professionals such as physicians, nurses, dieticians, and pharmacists.<sup>3</sup> In 22 counties and towns, the program was supported by



“Standards for Accreditation of Diabetes Shared Care Networks Medical Staff” and an accreditation scheme, as well as a CKD case management and information system. During 2003–2008, a program called Diabetic Management Integrated Delivery System (DMIDS) was implemented to assess the effect of educational action on diabetic control.

Pay for performance (P4P) has been used as a strategy to improve quality for patients with chronic illness. Outcomes included life-years, quality-adjusted life-years (QALYs), program intervention costs, cost-savings, and incremental cost-effectiveness ratios (ICERs). A study using population-based longitudinal databases compared costs and effectiveness between P4P and non-P4P diabetes patient groups in two cohorts. QALYs for P4P patients and non-P4P patients were 2.80 and 2.71 for the diabetes mellitus (DM) alone cohort and 2.74 and 2.66 for the DM Hypertension Hyperlipidemia (DMHH) patient cohort. The average incremental intervention costs per QALYs was US\$5,222 in the DM alone cohort and US\$4,542 in the DMHH cohort. The average incremental all-cause medical costs saved by the P4P program per QALYs were US\$13,578 in DM alone cohort and US\$15,807 in the DMHH cohort. The findings indicated that the P4P program for both cohorts were cost-effective. Thus, the diabetes P4P program in both cohorts enabled the long-term cost-effective use of resources and cost-savings, especially for patients with diabetes.<sup>4</sup>

The prevalence of diabetic kidney disease (DKD) was found to be between 10.5% and 17.9% out of this screening program.<sup>5</sup> In contrast to the control group, diabetic patients treated by health professionals after educational management showed that the diabetic shared care program was cost-effective in preventing nephropathy, especially in patients with HbA1c levels of >10% and those who received continuous educational intervention and case management for >4 years.<sup>6</sup>

These identified CKD patients were then referred to CKD Care Programs (early CKD, advanced CKD) for multidisciplinary care to delay the progression of the disease and prepare for dialysis. The program has recruited 785,484 people to date, with 142,525 new cases in 2019. In 2018, 3.9% had advanced stages of CKD, and 0.6% died.

### Actions for Intervention: Early-CKD and Advanced-CKD Programs

In 2002, TSN and NHPA launched a national CKD Care Program to help patients with CKD who were diagnosed by different screening programs. In the first step, the CKD treatment program was implemented in major hospitals, then expanded to 90 institutes in 2009, and eventually to general practitioner clinics in 2011. Since 2007, the National Health Insurance Administration has reimbursed extensive services for patients with non-dialysis dependent CKD, and in 2011, coverage was expanded to early-CKD to facilitate participation in the CKD care network.

Between 2002 and 2019, a total of 407,484 patients were enrolled in the early-CKD program, with 100,294 new cases in 2019. Most (42.2%) had CKD stage 1, with 32.6% and 25% having stage 2 and stage 3 CKD respectively. Patients in the Kidney Care Program received multidisciplinary team care including education and funding for medications.

Over median follow-up of 6 years, 5.8% of patients developed kidney failure, and 0.4% died, as compared to 1.3% and 0% of historical controls. Between 2002 and 2019, there were 90,347 patients enrolled in the Pre-ESRD (i.e., kidney failure) program, with 24,232 new cases in 2019. Of these, 37.9% had CKD stage 3b, with 33.6% had stage 4, and 19.5% had stage 5. Over median follow-up of 8 years, 14.5% of patients developed kidney failure, and 8.8% died, as compared to 11.2% and 8.8% of historical controls.

The national kidney care program was developed in response to high rates of CKD and has been successfully implemented across Taiwan. In 2006, the National Health Insurance Administration initiated a nationwide P4P program to improve quality of care for patients with advanced CKD.



In a longitudinal observational matched cohort study using two nationwide population-based datasets, the major outcomes of interests were incidence of dialysis, all-cause mortality, direct medical costs, life years (LYs) and incremental cost-effectiveness ratio comparing matched P4P and non-P4P advanced CKD patients. Sub distribution hazard ratio (95% confidence intervals) for advanced CKD patients enrolled in the P4P program, compared with those who did not enroll, were 0.845 (0.779–0.916) for incidence of dialysis and 0.792 (0.673–0.932) for all-cause mortality. LYs for P4P and non-P4P patients who initiated dialysis were 2.83 and 2.74, respectively. The adjusted incremental CKD-related costs and other-cause-related costs were US\$3,823 and US\$1,080 for P4P and non-P4P patients who initiated dialysis, respectively, and US\$114 and US\$1,572 for P4P and non-P4P patients who did not initiate dialysis, respectively, during the 3-year follow-up period.<sup>7</sup>

Another study showed that among the 26 588 patients, 25.5% participated in the P4P program. The P4P group received significantly better quality of care, including a higher frequency of glomerular filtration rate measurement and CKD complications survey, a higher rate of vascular access preparation, and more frequent use of arteriovenous fistulas than the non-P4P group did. The P4P group had a 68.4% reduction of the 4-year total healthcare expenditure (excluding dialysis fee), which is equivalent to US\$345.7 million, and a significant 22% reduction in three-year mortality after dialysis (HR 0.78, 95% confidence interval: 0.75–0.82,  $P < 0.001$ ) compared with the non-P4P group.

In summary, the P4P program improved the quality of care for people with advanced CKD and was associated with better survival and long-term cost savings among dialysis patients.<sup>8</sup>

Multidisciplinary pre-dialysis education (MPE) was implemented in the national CKD program and improved patient outcomes. In a study enrolling 573 patients, 287 received MPE. Dialysis was initiated in 13.9% and 43% of the patients in the MPE and non-MPE groups, respectively ( $P < 0.001$ ). In the mean follow-up period of  $11.7 \pm 0.9$  months, the overall mortality was 1.7% and 10.1% in the MPE and non-MPE groups, respectively ( $P < 0.001$ ).<sup>9</sup>

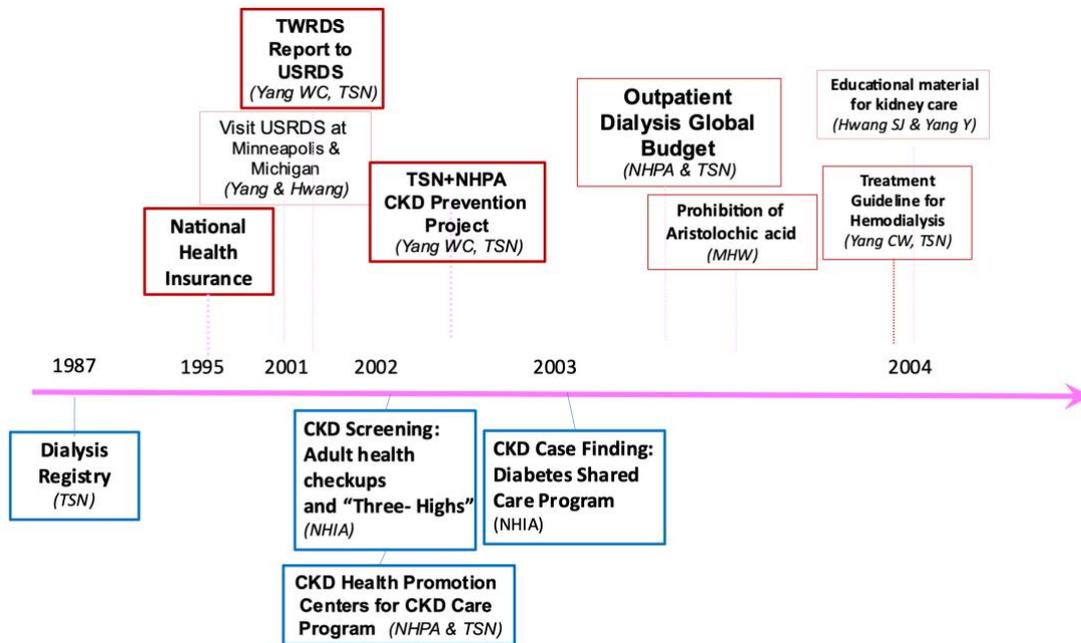
## Outcome and Impact

Using screening and case-finding for early detection of CKD was achieved by coordinating activity across multiple stakeholders, including Health Promotion Administration, National Health Insurance Administration, National Health Research Institutes, the Taiwan Society of Nephrology, participating hospitals and clinics and integrated settings. These early detection programs were linked to multidisciplinary care intervention programs for identified patients, which seemed to increase the quality of kidney care and improve clinical outcomes while also reducing costs. This multi-pronged, integrated approach within a universal health care system was enabled by continuous advocacy from the kidney community, strengthened by links to stakeholders representing other key non-communicable diseases (NCDs), and implemented with strong support from government. Key successes of the program have been the stabilization of diabetes mellitus as a cause of kidney failure in Taiwan and lower use of analgesics in CKD patients during the year before dialysis initiation.

Timelines from 1987-present are shown in Figures 1 and 2. The pathway and roadmap of CKD identification and intervention in Taiwan is shown in Table 2 and the evolution of CKD identification and CKD/kidney failure integrated care in Taiwan in Appendix 1.<sup>10</sup> Note that **some of the material in this case study was taken from ISN's 2020 *Global case studies for chronic kidney disease/end-stage kidney disease care* paper.**<sup>10</sup>

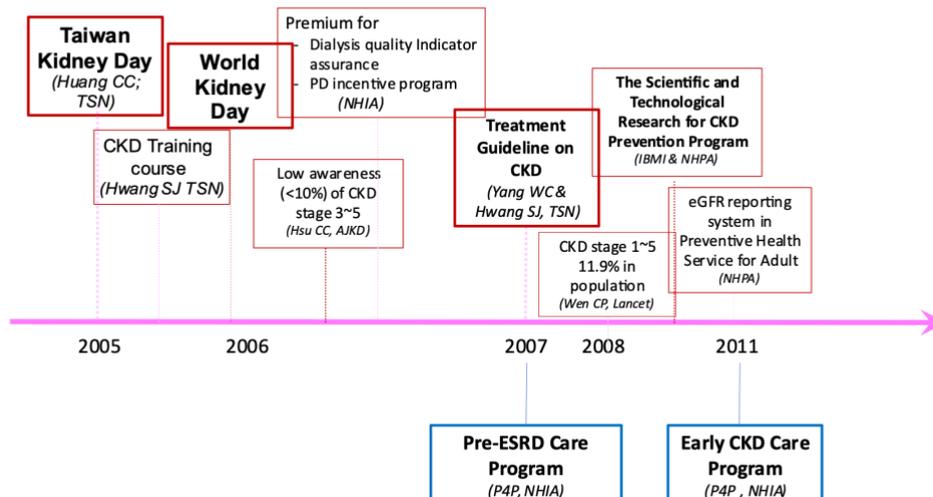


Figure 1: Timeline 1987-2004



TWRDS: Taiwan Renal Data System; USRDS: United States Renal Data System; TSN: Taiwan Society of Nephrology; NHPA: National Health Promotion Administration; CKD: chronic kidney disease; MHW: Ministry of Health and Welfare

Figure 2: Timeline 2005-present



NHPA: National Health Promotion Administration; NHIA: National Health Insurance Administration; TSN: Taiwan Society of Nephrology; P4P: Pay for Performance; MHW: Ministry of Health and Welfare; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate; ESRD: end-stage renal disease; PD: peritoneal dialysis



**Table 2: Evolutionary Pathway and Roadmap of CKD Identification and Intervention in Taiwan**

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**1. Understanding the burden**

Registry and data report

**2. Leadership structure**

Nephrology society, government, policymaker, patient organization

**3. CKD case Identification**

By screening: Annual health checkups and Three-Highs

By case-finding: Diabetes Shared Care Program

**4. Standardization**

Guidelines for CKD/kidney failure care to meet local need and risk factors

**5. Intervention and Implementation**

Multidisciplinary and multi-professional approaches for CKD care

**6. Sustainability and Quality Improvement**

Funding, universal health care coverage, and outcome measures

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CKD: chronic kidney disease

Modified with permission from The International Society of Nephrology.<sup>10</sup>



## Uruguay

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### Background

Uruguay is a developing country with 3.461,734 inhabitants by 2019. It was classified as a non- OECD HIC by the World Bank<sup>11</sup> with a Gross National Income per capita of US\$16,230, and a Human Capital Index of 0.6. In recent years, there has been a sustained growth in the ageing of the population, and life expectancy at birth has increased to 77.9 years old (73 for men and 81 for women).

### National Health Insurance

The Uruguayan healthcare system is a mixed public and private system that gives universal coverage for health. A National Integrated Health System (SNIS in Spanish) was launched in 2008 to provide universal health coverage to the entire population. The total expenditure on health per capita in 2016 was approximately US\$1,800, which represents 8.6% of the nation's Gross Domestic Product.

The SNIS a combination of public healthcare system (for those without social security operated by the Administration of State Health Services) and private system 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).<sup>12</sup> The FNR is a public non-governmental agency, that provides funds for highly specialized medical procedures, such as dialysis and transplantation, and accounts for approximately 10% of all public expenditures on health; expenses related to dialysis account for about 27% of the entire fund.

### Document the Burden of Kidney Failure

The FNR provides financial support for universal coverage of kidney replacement therapy (KRT) since 1981. Data on these patients is collected by the Uruguayan Dialysis Registry (UDR).<sup>13</sup> Prevalence of patients with kidney failure on dialysis was 756 patients per million populations (pmp) by December 2014, reaching almost 1000 pmp when transplant patients with a functioning kidney graft are included.

### Leadership from Kidney Society CKD Identification and Intervention Program

In April 2004, by initiative of the Uruguayan Society of Nephrology, with the Department of Health and the FNR, the "Declaration of Montevideo" was signed with the aim of improving and enhancing CKD care and recommended an Advisory Committee on Renal Healthcare (ACRH) to develop a National Renal Healthcare Program (NRHP).

This ACRH was created initially with members of the Uruguayan Society of Nephrology, National Fund of Resources, and Medical School of University of the Republic. This program was launched six months later, as a pilot that included: i) education on kidney healthcare, including information on a healthy lifestyle, with the aim to reduce cardiovascular and kidney disease risk factors; ii) increased accessibility to kidney healthcare at the primary care level; iii) promotion of early diagnosis of CKD among 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>14</sup>

For spreading the NRHP there were several advancements. First, the development of clinical guidelines for identification,<sup>15</sup> evaluation and management of patients with CKD at the primary care level. Second, the creation of "Kidney Care Teams" (including a nephrologist, a dietitian, and a nurse) to work in



primary care centers to treat patients referred by primary care practitioners. Third, the management of patients with CKD stage 1 to 3 directly by first level of attention. Finally, patients with CKD stage 4-5 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 eGFR lower than 60 ml/min/1.73 m<sup>2</sup>, persistent proteinuria higher than 300 mg/day (or microalbuminuria higher than 30 mg/day in diabetic patients) and features a centralized “alarm system” to minimize failure to follow-up.<sup>16</sup> Although the NRHP is not mandatory for every healthcare provider,<sup>17</sup> the feasibility of this is being studied.

## Partnership with Government Focus on High-risk Groups

Since 2009, screening for CKD in high-risk populations (“case-finding”) has been incorporated into the mandatory health check-ups of the working population via a decree of the Department of Health. Evaluation includes a urine exam and serum creatinine tests in diabetic and hypertensive individuals.<sup>18</sup>

Health check-ups are required every two years for sports persons, students, and employed individuals (between the ages of 15-89). The check-up includes glycemia, VDRL and urine exams. However, for individuals who are diabetic or hypertensive of any age, it also includes a serum creatinine test.<sup>19</sup>

For healthy individuals, the frequency of these check-ups is every two years. If abnormalities are found, a General Practitioner (GP) appointment is required as follow up to see if referral to a nephrologist is needed. Within six months of the check-up the individual needs to have a letter from their GP or nephrologist which confirms the abnormality. If the abnormality is confirmed, they will then receive follow up.

## Continuous Quality Improvement

The evaluation of the program can be done based on the CKD Registry. The target population and the variables included in the registry have already been described elsewhere.<sup>20</sup> Currently the CKD Registry includes over 25,000 patients from all the administrative regions of the country including private and public system assisted patients.

Every year, the ACRH 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 rate and kidney failure rate. It has been seen that 57.9% of patients are stabilized with an eGFR loss of less than 1 ml/min/year.<sup>21</sup>

Risk of new cardiovascular events was related to previous cardiovascular disease, diabetes, male gender and increased age and proteinuria, and had a U-shaped curve for systolic blood pressure.<sup>22</sup> Other than well-known risk factors such as proteinuria and blood pressure, acidosis was related to greater increase in creatinine,<sup>23</sup> with no influence on progression according to the type of Renin-Angiotensin-System Blocker used.<sup>24</sup>

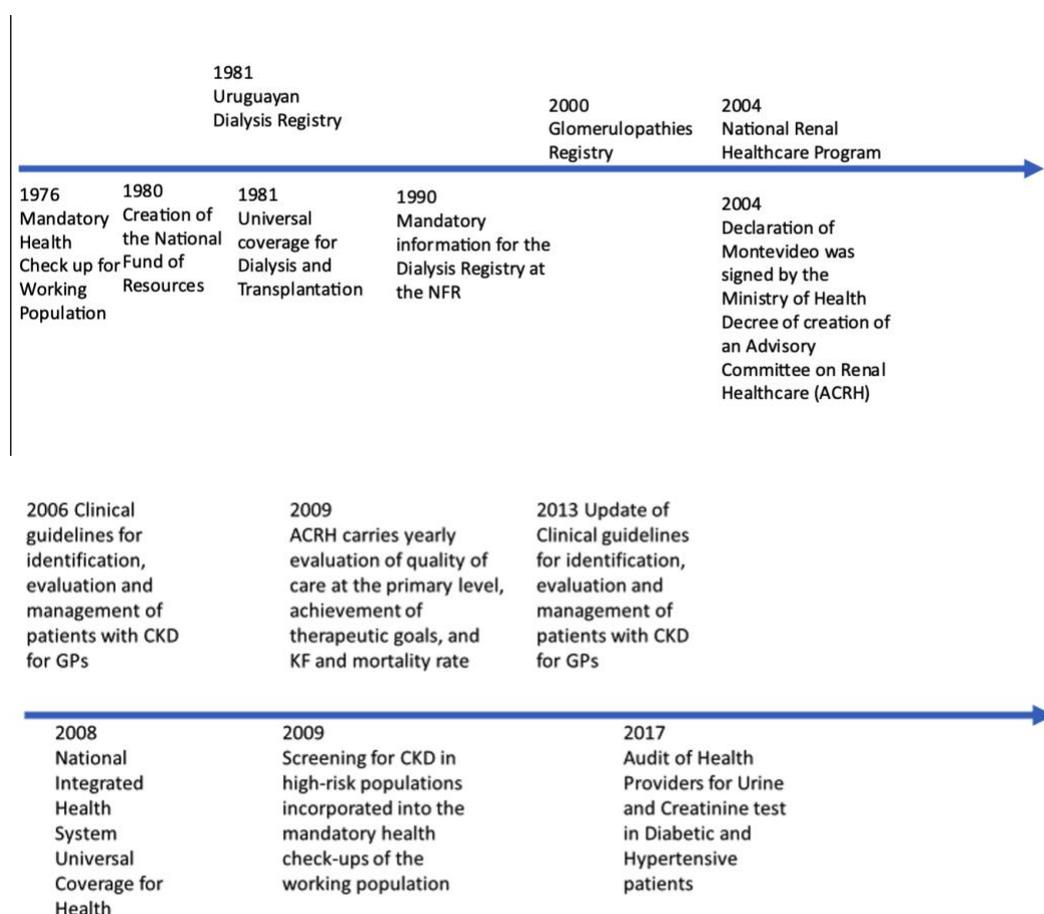
There is evidence that pre-dialysis CKD care may improve outcomes once patients are established on dialysis in Uruguay. Among patients who began dialysis, those with pre-dialysis nephrological care for over a year had more frequent vascular access placement prior to dialysis (45.1 vs 37.1%), and better anemia management with hemoglobin levels higher than 10 g/dL (55.4 vs 43.5%).<sup>25</sup> Finally, NRHP multidisciplinary care has shown to be associated with timely initiation of KRT and 30% lower mortality rate.<sup>26</sup>



There has been improvement in the quality of care, as well as a reduction in CKD progression; the potential benefits of pre-dialysis CKD care seem to extend even to patients that eventually develop 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 universal healthcare coverage for treatment from the early stages of CKD to dialysis and kidney transplantation.

Timeline for CKD care in Uruguay is shown in Figure 3. Note that **some of the material in this case study was taken from ISN's 2020 *Global case studies for chronic kidney disease/end-stage kidney disease care* paper.**<sup>10</sup>

**Figure 3. Timeline for Chronic Kidney Disease Care in Uruguay**



NFR: National Fund of Resources; CKD: chronic kidney disease; GPs: General Practitioners; KF: kidney failure



## United Kingdom

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In 2009, the United Kingdom introduced a national prevention program for the early detection and management of certain NCDs and their major risk factors (heart disease, stroke, diabetes, CKD). The program is named Health Check, and invites people aged 40-74 years and without a history of the target conditions to attend every five years. A clinical history is taken, blood pressure and body mass index are measured, and laboratory tests are arranged. Blood is drawn for serum creatinine if blood pressure is  $>140/90$ ; urinalysis and albuminuria are not assessed. If eGFR is  $<60$  ml/min/ $1.73\text{m}^2$  at the prevention visit, a confirmatory test is arranged within two weeks. Depending on the findings of the assessment, lifestyle advice is provided, referrals for counselling or specialist assessment are arranged, and statin prescription is considered for people with estimated 10y cardiovascular risk  $>10\%$ .<sup>27</sup>

Lower-than-expected attendance is a key limitation of this population-based program: attendance has increased over time but ranged between 41.3 and 49.2% by region in 2017/18, as compared to the target of 75%.<sup>28</sup> There have been concerns that the program may reduce health equity, as attendance is lower among those residing in lower income or racialized communities.

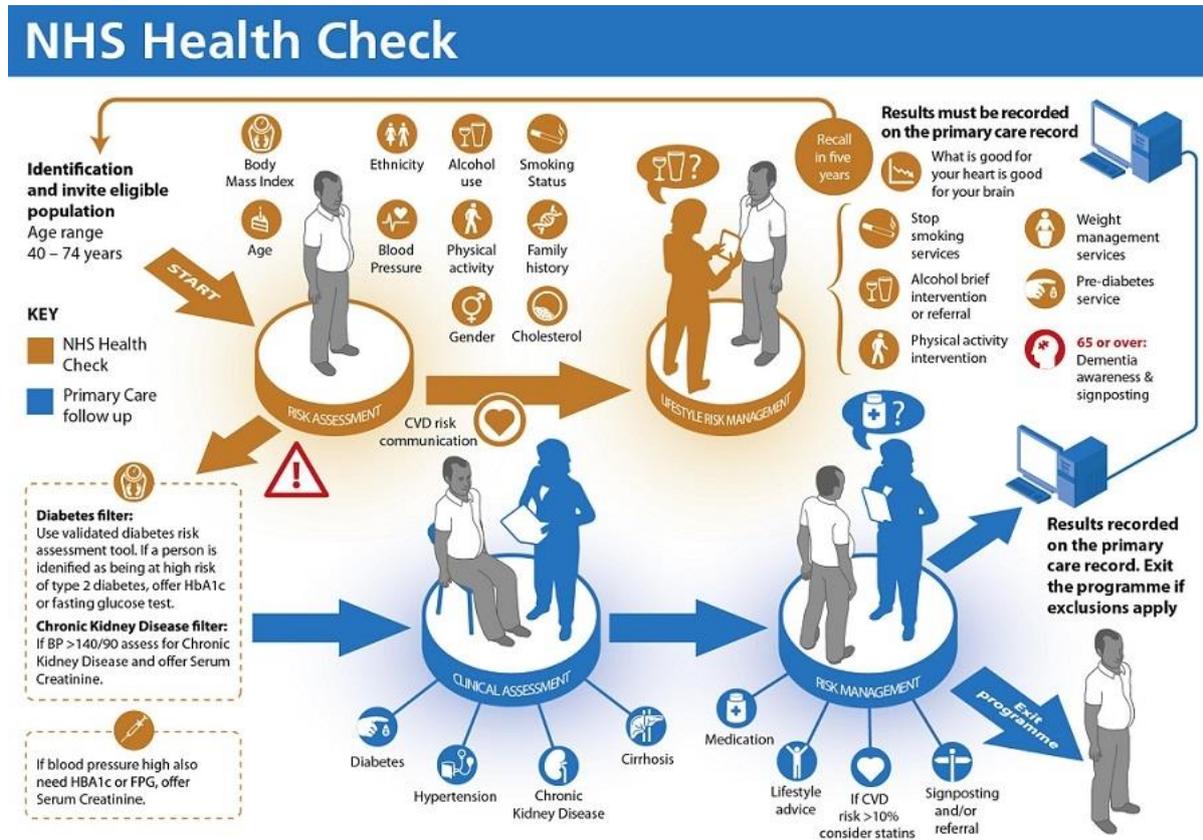
As compared to those who were invited but did not attend, attendance at National Health Service (NHS) Health Checks is associated with small reductions in body mass index (BMI) ( $0.3$  kg/ $\text{m}^2$ ), the prevalence of smoking (absolute reduction 2%), systolic blood pressure ( $1.43$  mmHg) and total cholesterol ( $0.05$  mmol/l) over 6 years.<sup>29</sup> The odds of detecting new CKD was higher among people attending (vs those invited but not attending): 1.83, 95% CI 1.52, 2.21.<sup>30</sup> When expressed in terms of the number of people attending an appointment, the estimated number needed to screen (NNS) to detect one new case of CKD is 568 at 6 months<sup>31</sup> or 265 at 12 months.<sup>32</sup> However, if expressed in terms of the number of people invited to an appointment, the NNS is 1,616 at 12 months.<sup>33</sup> No published data examine the effects of the NHS Health Check on process-based outcomes or the rate of CKD progression among people with newly identified CKD.

Overall, the Health Check's integrated approach to NCD detection and management is appealing and offers potential advantages as compared to an early detection program for CKD alone (Figure 4 shows the current format of the NHS Health Check<sup>34</sup>). However, data are lacking on whether it improves kidney-related outcomes specifically. The yield of new CKD cases is relatively low, likely due in part to the fact that serum creatinine is measured only in people with elevated blood pressure during the screening visit. Future studies would ideally investigate whether more liberal use of serum creatinine testing (with or without testing for albuminuria) would increase diagnostic yield and/or improve clinical outcomes.

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Figure 4: Current Format of the NHS Health Check



NHS Health Check. NHS Health Check: Commissioners and providers. Delivery. 2020. Available from: <https://www.healthcheck.nhs.uk/commissioners-and-providers/delivery/>.34 Reproduced under the Open Government Licence v3.0.

NHS: National Health Service; HbA1C: hemoglobin A1C; BP: blood pressure; FPG: fasting plasma glucose; CVD: cardiovascular disease



## Canada

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Similar to the situation in Australia and the United States, Indigenous people in Canada have a high burden of CKD and kidney failure.<sup>35,36</sup> Indigenous people in Canada are also more likely to live in rural or remote communities and to have reduced access to specialist care as compared to otherwise similar non-Indigenous people. For these reasons there has been considerable interest in early detection of CKD among Canada's Indigenous communities. In 2013, a carefully designed program was established to screen residents of rural and remote Indigenous communities in Manitoba, Canada. Testing was done using point-of-care equipment to measure estimated GFR and albumin:creatinine ratio (ACR) as well as A1C. Risk of progressive CKD was assessed with the Kidney Failure Risk Equation<sup>37</sup>; participants whose estimated risk of kidney failure was >3% within 5 years or with urine-albumin: creatinine ratio (UACR) >100 mg/mmol were referred for nephrology assessment. All participants received recommendations for follow-up and management, including blood pressure (BP) control, glycemic control (if appropriate) and use of angiotensin-converting-enzyme inhibitors (ACEI)/ angiotensin II receptor blockers (ARB) and statins. There was no formal integration between the program and other specialist services such as endocrinology or cardiology, although screening personnel could make such referrals at their own discretion.<sup>35</sup>

The program confirmed a high prevalence of CKD in these communities (~ two-fold higher than in the general Canadian population). Using a pre- post- design over an interval of three years, the effects of the program were assessed among participants who were judged to face "at least some risk of kidney failure", defined by one or more of ACR>3 mg/mmol, BP>160/90, A1C>7.0% or risk of progression to kidney failure >0% at 5 years. Participation in the program was associated with substantial improvements in the likelihood of comprehensive laboratory testing and nephrology referral but did not lead to large increases in the use of potentially beneficial medications. For example, the proportion of participants receiving an ACEI or ARB increased by 0.8% (95% CI -7.7 to 9.4%) among rural-dwellers and by 3.3% (95%CI -4.1 to 10.6%) among remote-dwellers (see Table 3). Findings were similar when participants were compared to a matched group of people living in remote or rural Indigenous communities that did not participate in the program.<sup>38</sup>

These benefits are encouraging but whether they will lead to improvements in clinical outcomes on the population scale is uncertain. Similar to other Canadian studies aiming to promote more timely treatment of people with CKD,<sup>39</sup> detection of new cases did not necessarily translate into increased use of beneficial medications. Further work should explore barriers to uptake of guideline-concordant care in screen-detected populations.

*The authors thank Professor Paul Komenda for reviewing an earlier draft of this summary.*



Table 3: Effects of Screening on Processes of Care Among Participants in the Program

	Rural dwellers n = 280			Remote dwellers n = 326		
	% before screening	% after screening	% difference (95% CI)*	% before screening	% after screening	% difference (95% CI)*
Comprehensive testing (eGFR + UACR or UPCR testing)	26.8	55.7	28.9 (21.1 to 36.7)	68.7	75.5	6.8 (-0.1 to 13.6)
Nephrology visits	suppressed**	4.6	–	3.4	11.7	8.3 (4.3 to 12.3)
Use of statin	50.4	51.8	1.4 (-6.9 to 9.7)	52.3	57.7	5.5 (-2.1 to 13.2)
Use of ACE inhibitor or ARB <sup>38</sup>	63.4	64.2	0.8 (-7.7 to 9.4)	66.8	70.0	3.3 (-4.1 to 10.6)

eGFR: estimated glomerular filtration rate; UACR: urine albumin to creatinine ratio; UPCR: urine protein to creatinine ratio; ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; CI = confidence interval

\* The % difference was calculated as follows: (the % frequency in the postintervention period – the % frequency in the preintervention period)

\*\* value was suppressed owing to small cell size



## Mexico

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The Kidney Early Evaluation (KEEP) Program was developed by the US National Kidney Foundation. KEEP focused on case-finding of CKD among adults with diabetes, hypertension, or family history of diabetes, hypertension, and/or CKD. In 2008, KEEP was adapted for use in Mexico by the Mexican Kidney Foundation. In 2010, a pilot study's results showed a prevalence of CKD of 22% and 33% in Mexico City (N=1519) and Jalisco (N=2020), respectively, which was similar to the 26% prevalence reported by KEEP US.<sup>40</sup> CKD stages 1 and 2 were more prevalent in KEEP Mexico City than in KEEP US, where stage 3 predominated. Only 1% of KEEP Mexico City participants were aware of the CKD diagnosis, despite that 71% had been seen by a doctor at least once in the previous year. These data indicated that CKD is underdiagnosed and underrecognized among high-risk individuals in Mexico.

In a demonstration project sponsored by the Secretariat of Health, the Mexican Kidney Foundation, and the National Institute of Public Health, serum creatinine was measured in 7,689 patients after validation and calibration with a correction factor.<sup>41,42</sup> The overall prevalence of CKD was 44% (40% for those with diabetes and 47% for those with both diabetes and hypertension).<sup>43</sup>

In a longitudinal analysis of 434 KEEP Mexico participants, testing was repeated at least one year after a baseline KEEP. CKD incidence at one year was 14%. The percentage of patients who remained positive regardless of stage in the follow-up KEEP was 40% for those with stage 1 at baseline, 52% for those with stage 2, 65% for those with stage 3, and 100% for those with stages 4 or 5.<sup>44</sup>

A recent analysis of 6,885 participants in KEEP Mexico showed that the age-adjusted CKD prevalence had increased to 30.2% by 2017, with CKD 1-2 being the most frequent CKD stages. The prevalence of CKD stage 1 decreased, and stages 3, 4, and 5 remained virtually unchanged over time.<sup>45</sup>

The KEEP methodology has also been used to assess areas of Mexico where the apparent prevalence of CKD is higher than expected ("CKD hotspots"), specifically in Tierra Blanca, Veracruz,<sup>46</sup> and Tepeji, Hidalgo.



## Senegal<sup>47</sup>

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In 2012, investigators in Senegal conducted a community-based cross-sectional survey of a sample drawn from individuals aged  $\geq 18$  years and living in Saint-Louis for at least 3 months. A two-stage cluster sampling method was used to select a representative sample of adults living in urban and rural areas of Saint-Louis. Data were collected during home visits or at the nearest health centre. Questionnaires were used to obtain information on age, sex, education, income, smoking status, physical activity, history of diabetes and hypertension, family history of kidney disease and medication use.

Serum creatinine was measured and GFR was estimated with the Modification of Diet in Renal Disease (MDRD) equation. Urine samples were first tested using dipsticks and those with  $>2+$  albuminuria had urine albumin quantified in a 24h urine sample. Fasting blood glucose was measured using a glucose oxidase method. All participants were personally informed of their screening results and those with abnormal values were referred to a specialist for further management.

The survey found that approximately 6.1% of participants had CKD, many of whom had additional NCDs such as hypertension and diabetes. Approximately 76% of those with CKD were unaware of their condition. All participants with CKD were referred for specialist follow-up, but according to the research team, few such participants could afford ongoing follow-up, and thus most derived little benefit from their diagnosis.

As a research project, this work had several key strengths including its community-based design, relatively large sample size, and efficient use of resources. The research team should be congratulated for establishing the burden of CKD in Senegal (the first pre-requisite in Table 1 - the table of pre-requisites for successful CKD detection) and for executing this project under challenging conditions.

This initiative also had important strengths. First, the survey had the benefit of raising awareness about CKD and its major risk factors in the Saint-Louis community. In addition, the program measured blood pressure and glycemia, so there was evidence of potentially beneficial integration with the management of other major NCDs (pre-requisite #10 in Table 1).

On the other hand, nearly one quarter of participants with CKD were aware of their diagnosis, and thus derived little if any benefit from screening. The remaining three-quarters were not provided with access to ongoing management for their CKD. Some may have been able to afford appropriate long-term CKD care during the years following the screening visit; thus, deriving benefit from early detection. However, for those who were informed that they had CKD but were not able to afford ongoing kidney care, the screening program actually caused harm.

In the context of setting up an effective screening program, planning further management after detection of disease requires consideration of potential barriers such as travel time to specialist clinics, failure to grasp the importance of timely CKD treatment, unpaid time off work, costs of travel or the costs of care, including medications. Patients with mild or moderate CKD do not necessarily need to be seen by specialists and follow-up may be more likely to succeed with primary care physicians who are more readily accessible (and may charge less), provided that these primary care physicians have the expertise to properly manage CKD. All these point to the importance of public, patient, and provider education (pre-requisite #9).

This case study illustrates some of the challenges associated with establishing and maintaining early detection programs in lower resource settings.

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## Appendix 1

### The Evolution of CKD Identification and CKD/Kidney Failure Integrated Care in Taiwan

#### I. Understanding burden and risks for kidney failure/CKD in Taiwan

##### 1. Understanding the CKD/kidney failure burden:

- National Dialysis Registry since 1987 by Taiwan Society of Nephrology (TSN), a mandatory reporting system
- CKD prevalence estimation by an epidemiology study (national and local)
- Impacts on medical economics and financial burdens of NHIA; NHI launched in 1995 with universal health coverage

##### 2. Identifying risk factors and target populations through national and local studies:

- Population screening by health checkups
- Patients with diabetes and hypertension and hyperlipidemia (Three-Highs)
- Case-Finding in diabetic patients by Diabetes Shared Care Program
- 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 kidney failure 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 MHW – TSN president and Committee of Chronic Diseases Prevention, MHW – 2001
- Active participation in policymaking within government institutes: NHPA and NHIA – 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
- 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 (NHPA)
- Project expansion to include more CKD prevention organizations (rolled out to clinics) – 2003–present (NHPA+TSN)
- CKD Information System for register and case management – 2005 (NHPA)
- Project of integrated care for patients with pre-kidney failure (CKD stage 3b, 4, and 5) and screening for high-risk patients with reimbursement from NHIA– 2007–present (NHIA)



- Project of care for patients with early CKD (CKD stage 1, 2, and 3a) and extension to general medicine discipline – 2011–present (NHIA)

### 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 MHW*

- 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
- Stage CKD 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 kidney failure 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 based on various clinical parameters
  - f) Reduction of medical expenses before and after the initiation of dialysis
- The rising incidence rate of kidney failure began to stabilize in the age group younger than 75 years from 2006

#### 2. *Future goals: set by MHW 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 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

NHPA: National Health Promotion Administration; NHIA: National Health Insurance Administration; TSN: Taiwan Society of Nephrology; MHW: Ministry of Health and Welfare; CKD: chronic kidney disease; USRDS: United States Renal Data System; NGO: non-government organization; eGFR: estimated glomerular filtration rate; PD: peritoneal dialysis; ERA-EDTA: European Renal Association – European Dialysis and Transplant Association  
Modified with permission from the International Society of Nephrology.<sup>10</sup>



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