

*Original Article*

## Incidence, prevalence and mortality trends of dialysis end-stage renal disease in Taiwan from 1990 to 2001: the impact of national health insurance

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### Abstract

**Background.** Incident and prevalent (I&P) rates in dialysis end-stage renal disease (ESRD) patients in Taiwan increased rapidly following the launch of National Health Insurance (NHI) in 1995. Our aim was to explore the impact of NHI on the status and trends of ESRD epidemiology in Taiwan.

**Methods.** This study was conducted using retrospective cohort analysis of data collected from the Taiwan national dialysis registry.

**Results.** From 1990 to 2001, I&P rates of ESRD patients increased 2.6 times from 126 to 331 per million populations (pmp) and 3.46 times from 382 to 1322 pmp, respectively. Increasing ESRD was seen in patients who were middle-aged, elderly and who had diabetic nephropathy as their primary renal disease. The mean age of I&P patients increased by 7.2 years and 7.1 years, respectively. All of these parameters increased markedly in 1995, the year of NHI implementation. First-year mortality decreased to 7.8 per 1000 patient-months in 1994, and then increased to 18.0 in 2001. The cumulative survival rate of the elderly subgroup (age >65) in the incident 1990–1994 cohort was greater than in the 1995–1999 cohort. These data indicated that NHI implementation significantly influenced the inflow and the mortality of ESRD patients.

**Conclusion.** In addition to presenting ESRD epidemiology in Taiwan, this study demonstrated that NHI implementation stimulated the growth of treated ESRD populations. Preventive plans mounted against chronic kidney diseases

will be essential to reduce the growth of ESRD patient numbers and consequent economic burdens.

**Keywords:** dialysis; health insurance; incidence; mortality; prevalence

### Introduction

The impact of end-stage renal disease (ESRD) on public health and health care economics has been a global focus for years [1,2]. In Taiwan, cases of ESRD requiring dialysis have increased progressively over the last decades, becoming an important issue in medical care [3]. In recent years, patients on dialysis represented <0.2% of the general population but consumed over 7.0% of total medical expenditures [4]. Thus, ESRD is an important disease that threatens not only public health but also burdens the financial health of nations [5,6].

When compared to international data using the United States Renal Data System (USRDS), ESRD incidence in Taiwan ranked first and prevalence ranked second in the world from 2002 to 2005 [7,8]. The age groups of 45–65, 65–75 and >75 years had almost the highest incidence and prevalence. Furthermore, the number of patients with diabetic ESRD increased as in other countries [8]. Taiwan implemented National Health Insurance (NHI) in 1995. Patients with ESRD were eligible for any type of renal replacement therapy (RRT) free of charge and without co-payment [4]. This particular change allowed us to study how universal coverage of dialysis therapy affected the size of dialysis populations.

This study aimed to address trends in ESRD incidence, prevalence and mortality from 1990 to 2001. We also attempted to identify factors associated with such changes, and to study the influences of NHI on ESRD epidemiology using analyses from a 12-year ESRD cohort in the national dialysis registry.

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## Materials and methods

### Data sources

Data for this retrospective study were from the Taiwan Society of Nephrology (TSN) Dialysis Registry, 1990–2001, amended and supplemented by the Annual Death Report from the Department of Health (DOH) and by the database of Catastrophic Illness from the Bureau of National Health Insurance (BNHI).

### Data collection by the TSN

The TSN Dialysis Registry is a nationwide, voluntary, non-government system that annually collects information on all dialysis patients. It began in 1987 with a dialysis surveillance project granted by DOH. Since 1994, data have been collected on peritoneal dialysis (PD) patients, and this included demographics, disease-associated conditions, dialysis contents, laboratory data and clinical outcomes on each dialysis patient through an annual dialysis case report form. Since 1997, annual reports of dialysis facilities, treatment quality and patient information have been collected through TSN-designed software. Dialysis centres not reporting their data within the time limit received repeated messages from TSN, resulting in a percentage of reports received each year that approached 100%.

### Data processing

The TSN used data management procedures to combine annual data from centres into a representative dataset for each year. Then, the dataset for a particular year was combined with the pre-existing database and transformed into a cohort database. Data from the Annual Death Report from DOH were then checked to correct patient death records. After 1995, NHI established a system of Catastrophic Illness to exempt dialysis patients from copayment. These application data were checked with the TSN Dialysis Registry database to confirm information on ESRD patients. Finally, after a comprehensive data cleaning in 2001, the 12-year cohort from 1990 to 2001 containing 114 157 records of 71 734 dialysis patients was established for further analysis.

### Definition of ESRD, incident case, prevalent case and treatment mode

ESRD was defined as patients who suffered from irreversible damage in renal function due to a state of uraemia and received maintenance dialysis therapy for >1 month. Dialysis patients with survival time <1 month were excluded. Incident cases included all new ESRD patients during the reporting year (counted from 1 January to 31 December). A prevalent case was an ESRD patient who survived from the last day of the previous year. The mode of RRT included HD, PD and renal transplantation. Renal transplantation was not included in this analysis, and usually accounted for <5% of total ESRD.

### Statistical analyses

All analyses were performed with SPSS software, version 12.0 (SPSS Inc., Chicago, IL, USA). Statistical analyses included descriptive and inferential analyses. The annual incident rate, calculated by the number of incident cases of the year divided by mid-year populations, was expressed as per million populations. The point prevalence rate, calculated by the number of prevalent cases divided by mid-year populations, was expressed as per million populations. Statistical data on populations were obtained from the Ministry of the Interior, Taiwan. In the observed period, the incidence and prevalence of ESRD were standardized to the 2000 WHO standard population. Populations' categories, such as age and sex, were stratified. One-year mortality among groups and subgroups were calculated. The Kaplan–Meier analysis was applied for probability of survival among the groups.

## Results

### Incident and prevalent cases and trends in incidence and prevalence

As shown in Table 1, numbers of incident and prevalent dialysis cases steadily increased throughout the 1990–2001 study period. In addition, there were marked increases in numbers of total patients as well as in the middle-aged (45–64 years) and elderly groups (65–74 years and >75 years) from 1995 and thereafter. Accordingly, the crude and adjusted incident and prevalent rates of dialysis ESRD, shown in Table 1, show abrupt increases in the incidence and prevalence in 1995, which followed the launch of the NHI system.

### Incidence and prevalence in age-specific groups

Figure 1 shows progressively increasing incident and prevalent rates of dialysis patients over time in the middle-aged (45–64 years), elderly (65–74 years) and senior elderly ( $\geq 75$  years) groups. By adjusting each age-specific population, the aged (65–74 and >75 years) groups showed the greatest increase in the incidence and prevalence with an abrupt increase after the launch of NHI in 1995 and thereafter.

### Changes in average age of incident and prevalent ESRD cases

The average age of incident ESRD patients at initiation of dialysis was 53.8 years in 1990, but it increased to 61.0 years in 2001, which is up 7.2 years during the study period. For prevalent ESRD, the average age increased from 50.8 years in 1990 to 57.9 years in 2001, or up 7.1 years during the study period. Interestingly, there was a prominent increase of 2.1 years in the average age of incident ESRD in 1995, which suggests that certain elderly ESRD patients entered dialysis treatment once they were covered by NHI.

**Table 1.** Number of crude as well as adjusted incident and prevalent rates of ESRD in Taiwan from 1990 to 2001

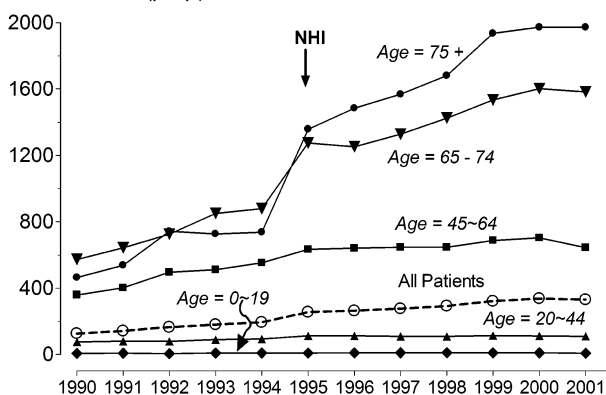
Year	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
No. of incident cases	2562	2916	3424	3793	4107	5446	5680	5999	6396	7116	7505	7423
Crude incidence (pmp)	126	142	165	181	194	255	264	276	292	322	337	331
Adjusted incidence <sup>a</sup> (pmp)	146	162	190	203	215	271	274	281	294	314	327	313
Adjusted incidence <sup>b</sup> (pmp)	150	167	195	210	221	280	282	290	303	324	337	323
Incidence by gender (pmp)												
Male	63.3	72.7	84.3	87.1	92.6	121.4	122.2	128.3	137.5	151.8	160.1	160.9
Female	62.1	68.6	80.0	92.6	99.4	127.4	133.2	140.3	150.1	164.1	176.6	170.1
No. of prevalent cases	8051	9806	11804	14087	16650	19978	22888	25627	28082	30497	32052	31876
Crude prevalence (pmp)	395	476	567	671	786	935	1063	1179	1281	1380	1439	1423
Adjusted prevalence <sup>a</sup> (pmp)	444	532	633	741	857	1002	1116	1214	1289	1360	1388	1341
Adjusted prevalence <sup>b</sup> (ppm)	461	552	655	767	886	1037	1155	1255	1334	1407	1435	1387
Prevalence by gender (pmp)												
Male	210.4	250.6	295.9	341.9	393.2	462.1	518.7	567.2	609.8	654.9	673.8	661.7
Female	183.4	224.2	270.2	326.8	388.8	467.8	538.9	605.1	664.6	720.7	761.1	758.2

pmp, per million populations.

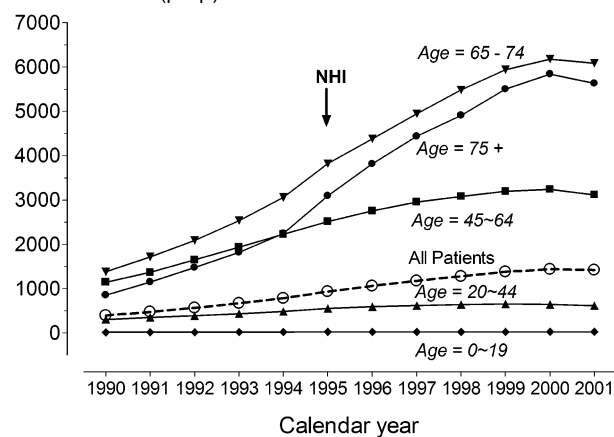
<sup>a</sup>Adjustment based on the WHO standard population, 2000.

<sup>b</sup>Adjustment based on the Taiwan population, 2000.

#### Incidence rate (pmp)



#### Prevalence rate (pmp)



**Fig. 1.** Incident (upper panel) and prevalent (lower panel) rates of all dialysis patients, stratified by age groups, from 1990 to 2001. After the launch of the National Health Insurance in 1995, both prevalence and incidence progressively increased in the all patient group, and in the middle age (45–64 years), elderly (65–74 years) and senior elderly ( $\geq 75$  years) groups. Population data for each year were obtained from the Ministry of Interior, Taiwan.

#### Trends in incidence and prevalence by gender

From 1990 to 2001, the percent of female dialysis patients increased progressively. The male to female prevalent rate ratio of 1:0.87 in 1990 reversed in 1995, and reached 1:1.15 by 2001. Similarly, the incident rate male to female ratio of 1:0.98 in 1990 reversed in 1993, and was 1:1.06 by 2001 (Table 1).

#### Changes in percentages of primary diseases

Chronic glomerulonephritis (CGN) was the main cause of ESRD, comprising 38.6% of incident patients and 47.1% of prevalent patients in 1990. In contrast, diabetes mellitus (DM) caused 24.7% of incident patients and 14.6% of prevalent patients. However, percentages for CGN declined yearly, but increased for DM. The crossover point for incident patients occurred in 2001 when DM became the leading cause of ESRD (35.3%). The percentage of DM in prevalent ESRD cases also increased, and reached almost one-fourth of all prevalent cases in 2001.

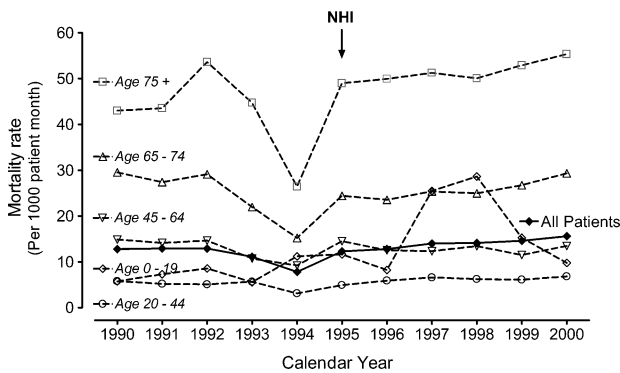
#### Changes in first-year mortality

From 1990 to 1994, first-year mortality decreased in all age groups with the lowest point in 1994 (Figure 2). However, it increased sharply in 1995 and continued to increase in the 64–75 and over 75 year age groups. This result may reflect the increase in elderly ESRD patients on dialysis and the high risk of mortality in these patients.

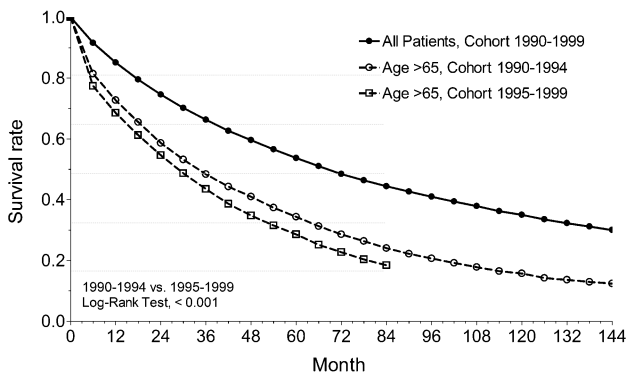
The top five leading causes of death during the study period were cardiovascular diseases (32–42%), infections (10–24%), central nervous system diseases (7–14%), liver diseases (5–9%), malignancies (6–8%) and other causes (13–27%).

#### Changes in cumulative survival rates

Cumulative survival rates for all patients who survived  $>30$  days after initiation of dialysis at 12, 24 and 60 months were 85.1%, 74.6% and 53.7%, respectively, and were 35.0% at



**Fig. 2.** First-year mortality in all dialysis patients and in different age groups from 1990 to 2001. Mortality rates gradually declined before 1995, but increased abruptly in the elderly patient groups thereafter. Data are expressed as person mortality per 1000 patient-months.



**Fig. 3.** Cumulative survival rates of all patients in the 1990–1999 incident cohort, in the elderly group (age over 65 years) 1990–1994 incident cohort and in the 1995–1999 elderly group cohort. A greater cumulative survival rate was noted in the 1990–1994 elderly group incident cohort ( $P < 0.001$ , log-rank test) than in the 1995–1999 cohort.

120 months and 30.0% at 144 months (Figure 3). The cumulative survival rate was slightly higher in females and significantly different from males ( $P < 0.001$ ) at 12 (86.3% versus 85.0%), 60 (56.1% versus 52.1%) and 120 months (37.6% versus 33.0%), respectively. Survival rates were lower in the diabetes versus non-diabetes groups at 12 (81.5% versus 89.4%), 60 (37.1% versus 63.5%) and 120 months (17.5% versus 44.0%), respectively ( $P < 0.001$ ).

Cumulative survival rates were worse in groups aged over 65 years compared to the all-patient group. However, survival rates were better in the 1990–1994 incident cohort than in the 1995–1999 cohort ( $P < 0.001$ ), which suggested an influence of NHI on patient survival (Figure 3).

## Discussion

The high incidence and prevalence of ESRD in Taiwan have been described in preliminary reports [9]. Although several possible causes have been proposed, none are supported by definitive evidence. The present study clearly demonstrated increasing trends of ESRD incidence and prevalence from 1990 to 2001 in Taiwan, and is the first to show that these increments are closely related to implementation of NHI in 1995.

## International status of ESRD

International comparisons by the USRDS [8] and other national reports on ESRD epidemiology [10–12] show great variations in ESRD incidence and prevalence. In the USA, already high ESRD incidence and prevalence rates also showed increasing trends in the 1990s [13]. A projection study assessing the number and growth of ESRD cases predicted that the number of ESRD patients would double by the end of 2010 [14]. Annual reports from the EDTA/ERA [10,15] showed great variations among the reported countries in Europe, with increasing trends in the ESRD prevalence and incidence comparable to those in Taiwan. However, incidence and prevalence rates in Europe were much lower than in Taiwan [10,15], and these rates were also lower in Australia and New Zealand, as reported by the ANZDATA [16]. In contrast, data from Japan showed a higher prevalence of ESRD than in Taiwan but a lower incidence [17]. Overall, ESRD in Japan showed a high prevalence and incidence, a high percent of aged patients, an increase in diabetic ESRD, a low dialysis mortality and a low PD penetration rate [11,18,19]. This is very similar to Taiwan, but is occurring in a larger population in Japan [11]. These differences in ESRD parameters between countries are multi-factorial and may be attributed in part to variations in method of data collection, definitions of studied groups, use of different analytic tools, socioeconomic status, cultural background and most importantly, the system of health insurance [12,20,21].

## Impact of advanced age and diabetic nephropathy on ESRD

We found that annually increasing percentages of aged and diabetic patients were the main causes of increases in the ESRD prevalence and incidence in Taiwan. The increasing numbers of middle-aged and elderly ESRD patients, as indicated by the increase in mean age of both the incidence and prevalence cohorts, can be attributed to an ageing society. Improvements in public health and medical care have prolonged life expectancy, and this has increased the elderly population in Taiwan, making it an aged society in 1993 with the elderly (>65 years) comprising 7.1% of the total population [22]. The increasing prevalence of diabetes in Taiwan has increased the number of patients at risk for diabetic nephropathy and those that progress to ESRD. The prevalence of diabetes in Taiwan has been estimated at ~6.2–8.0% of the population aged over 40 years [23], and of these the percentage of diabetic nephropathy may reach as high as 39.0% with ~1% of diabetic patients developing ESRD [24]. This large proportion of middle-aged and elderly patients, with or without diabetes, prompts us to suggest that preventive measures should be taken to slow the increases in middle-aged and aged chronic kidney disease (CKD) patients as well as in diabetic patients, and that these conditions should be tightly monitored.

## Factors other than age and diabetes

Besides these, there are still other unsolved findings from the present data set. For example, despite similar racial and

socio-cultural factors, Japan has the highest prevalence of ESRD in the world, but an incidence rate that is nearly 100 pmp is lower than that in Taiwan [7]. The average age at initiation of dialysis is older in Japan than in Taiwan [17], and thus ageing is probably not the only factor that explains the high incidence of ESRD in Taiwan. In addition, the number of diabetic ESRD patients cannot explain the results because the percentage of diabetic ESRD patients in Taiwan is lower than in the USA, Australia and other European countries [25].

Chinese herbal drugs are very popular in Taiwan, and there have been reports of chronic tubulointerstitial nephritis caused by these herbs [26] or by herbs containing an aristolochic acid [27]. In addition to the use of Chinese herbal drugs, abuse of various analgesics including non-steroid anti-inflammatory drugs (NSAIDs) may also explain the high incidence and prevalence of ESRD in Taiwan. Drug-induced chronic interstitial nephritis may be underestimated as the primary cause of ESRD because few CKD patients are willing to allow kidney biopsy for pathological diagnosis. Medication abuse is further aggravated by differences in socio-economic status. Such abuse is worse in rural areas where younger people have left in order to find work in cities, leaving aged family members with insufficient care. All these factors may contribute to the growing rate of ESRD in Taiwan.

#### *Impact of NHI on the growth of ESRD*

A low incidence and prevalence of ESRD may have been reported in developing countries because they were not able to afford the financial burden of dialysis therapy [28]. However, many developed countries (e.g., Australia and certain countries in Europe) have only a modest incidence and prevalence of ESRD compared to Japan, the USA and Taiwan [7]. These findings raise the question of whether the health insurance systems in each country affect the status of RRT. Japan, the USA and Taiwan all have complete insurance coverage of dialysis therapy and free access to dialysis treatment [29,30], which may not be the case in other developed countries [5].

In 1995, the NHI system of Taiwan for the first time was able to cover a significant portion of the population who had previously been without any health insurance benefits [31]. Furthermore, patients with ESRD received free RRT and even exemption from copayment [4]. Evidence that this coverage and these benefits facilitated the growth of the ESRD population includes the following: (1) sharp increases in the incident and prevalence of ESRD case numbers and rates were noted in 1995; (2) the increase in ESRD case numbers was most pronounced in the elderly subgroups aged 65 and above, indicating an immediate effect of NHI coverage on these groups that had not previously received medical insurance; (3) there was an abrupt increase in average age of incident and prevalent ESRD cases in 1995; (4) the marked increase in first-year mortality in patients as a whole was most obvious after the launch of NHI in elderly groups aged over 65 years, which reflects a new influx of older ESRD patients having worse prognosis and high first-year mortality; (5) the superior cumulative survival rate of elderly patients in the 1990–1994 incident cohort compared

to the 1995–1999 incident cohort further supports the above conclusion and (6) with NHI coverage, more diabetic patients were able to have better care, which increased the chances of developing end-stage diabetic nephropathy instead of dying from other acute or chronic complications. Furthermore, the financial report of the BNHI showed that medical expenses for dialysis therapy in the outpatient sector increased from 18.2 billion NTD (New Taiwan Dollar) in 1999 to 25.5 billion NTD in 2003. This steady growth in medical expenses from dialysis therapy has forced the BNHI to change the payment system to a dialysis global budget in the years following 2001 [32]. The effect of this change on dialysis should be assessed in future studies.

#### *Mortality and survival rates*

First-year mortality rates of ESRD patients decreased to their lowest level in 1994, but then rebounded in 1995 and continued to increase in subsequent years. This biphasic change in mortality could be explained by the fewer incoming patients not covered by medical insurance before NHI, especially elderly ESRD or diabetic patients with multiple complications who frequently refused dialysis therapy or eventually gave up because of the financial burden and family care problems. More recently, increasing numbers of dialysis clinics and facilities have been accommodating more patients that are relatively younger and less sick. In addition, the national dialysis surveillance programme, initiated in 1987, has improved the quality of dialysis therapy. All these factors may have played a role in contributing to improvements in dialysis quality and to the decrease in the first-year mortality from 1990 to 1994. At the same time, the launch of the NHI provided free access and total coverage of medical expenses for dialysis therapy, which caused an abrupt increase in first-year mortality because of recruitment of more elderly and diabetic ESRD patients into the pool of patients needing dialysis therapy.

Despite the increase in first-year mortality after 1995, overall cumulative survival rates were low compared to the USA and were comparable to those of Japan [19] and Europe [33]. Diabetic and older patients had a poor survival rate compared to non-diabetic and younger patients, and cumulative survival rates were slightly lower in males. These findings are similar to those in Japan over a similar time span [34], and the longer life expectancy in females was given as an explanation.

#### *Limitations of the study*

This study retrospectively analysed secondary data from the Dialysis Registry of TSN. Despite vigorous efforts to correct errors, unavoidable errors remained in the analysis. Since all dialysis centres report data from the prior year to TSN at the beginning of the next year, patients who died or were transferred in the middle of the year may have been underreported.

#### **Conclusion**

The Taiwan National Health Insurance programme has facilitated the growth of ESRD incidence and prevalence,

especially in elderly and diabetic groups, and is probably the most important factor affecting ESRD epidemiology in the past decade. To prevent the further growth and burden of this disease, a nationwide project for prevention of chronic kidney diseases has been initiated in Taiwan.

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**Conflict of interest statement.** None declared.

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