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Keywords:	cost, haemodialysis, out-of-pocket cost, peritoneal dialysis, productivity loss

Out-of-pocket costs and productivity losses in haemodialysis and peritoneal dialysis from a patient interview survey in Taiwan

Running title: Costs of HD and PD in Taiwan

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ABSTRACT

Objectives: The total medical (economic) costs of haemodialysis (HD) and peritoneal dialysis (PD), including direct medical costs, out-of-pocket (OOP) costs, and productivity losses, have become an important issue. This study aims to compare the direct non-medical costs and indirect medical costs of both modalities in Taiwan.

Design and Setting: This multicentre study included cross-sectional interviews of patients over 20 years old and articulate, who had been continuously receiving long-term HD or PD for more than three months between April 2015 and March 2016. Mann-Whitney U test, Wilcoxon rank sum test, and 1,000 bootstrap procedures with replacement were used for analysis.

Outcome measures: Differences in OOP costs and productivity losses.

Results: There were 308 HD and 246 PD patients available for analysis. HD patients had significantly higher monthly OOP costs than PD patients after bootstrap procedures (NTD 5,912 vs. NTD 5,225, $p<0.001$; NTD, New Taiwan Dollars; 1 US Dollar = 30 NTD). Compared with PD patients, HD patients had higher monthly productivity losses after bootstrap procedures (NTD 14,150 vs. NTD 11,611, $p<0.001$), resulting from more time spent seeking outpatient care (HD, 70.4 hours vs. PD, 4.4 hours, $p<0.001$) and time spent by family caregivers for outpatient care (HD, 66.1 hours vs. PD, 6.1 hours, $p<0.001$). The total costs per patient-month of HD and PD modalities, including OOP costs and productivity losses after adjusted for unemployment rate (3.82%) were NTD 19,522 and NTD 16,392, respectively.

Conclusions: The HD modality has higher OOP costs and productivity losses than the PD modality in Taiwan.

Keywords: cost, haemodialysis; out-of-pocket cost; peritoneal dialysis; productivity loss

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This multicentre study included cross-sectional interviews of long-term HD and PD patients.
- Previous study seldom assessed the information about out-of-pocket payments and productivity losses collected from patient undergoing HD and PD.
- The difference in the proportion of age groups in HD and PD patients are the major drawback of this study.
- The sample size could not represent the general population of HD and PD patients in Taiwan because the sampled patients were also not randomised

INTRODUCTION

Since March 1995, when Taiwan began implementing the National Health Insurance (NHI) system, the per capita healthcare expenditure has increased annually, especially in the care of 'end-stage renal disease' (ESRD) patients. Taiwan has the highest incidence and prevalence rates of ESRD in the world.[1-3] By 2017, the cost of dialysis (New Taiwan Dollar, NTD 36.9 billion; 1 US dollar = 30 NTDs in Dec. 2017) accounted for a staggering 5.73% of the total annual NHI expenditure (NTD 644.1 billion).[3] Haemodialysis (HD) and peritoneal dialysis (PD) are the two major renal replacement modalities in Taiwan with a similar all-cause mortality rate.[4-7] Several studies have provided clear evidence that HD has the higher direct medical costs among the two modalities.[8-14] NHI administrators implemented several strategies besides applying a blanket budget cap on dialysis expenditure to contain the total costs of dialysis and incentivize the use of PD modality. These efforts included increasing the reimbursements for PD and extending the NHI payment scheme covering the automated PD machine costs. As the proportion of PD usage increases, its prevalence in Taiwan has been gradually increasing, from 6.5% in 2003 to 8.5% in 2007, and up to 9.2% in 2014, similar to the average level within the developed countries.[15-18]

ESRD prevalence is increasing with the rise in the number of aging and diabetic nephropathy patients. The total (economic) costs of HD and PD modalities, including direct medical costs, direct non-medical costs, and productivity losses, have become an important issue.[19] Direct medical costs incurred for medical services, such as dialysis costs, physician and nurses' services, diagnostic tests, and hospitalization costs, are the most common type cited in the nephrologic literature. From a payer's perspective (e.g., national insurance organizations), these costs are the most important. However, from a patient's as well as societal perspectives, out-of-pocket (OOP) costs and productivity losses are nominal and meaningful. OOP costs and productivity losses have not been assessed comprehensively in

ESRD patients for two reasons: the methods for collecting these data for the ESRD patients are not well established, and retrospective data collection is difficult. Only two studies have reported that PD had less OOP costs and productivity losses than HD in Brazil and Singapore, but detailed data were not stated.[12 20] These studies highlighted a significant economic burden due to dialysis and a higher direct healthcare costs associated with the use of HD modality; however, little information is available about OOP costs, including expenses on caregivers or transportation, as well as productivity losses, including job loss, worker replacement, and reduced productivity from patients and family. According to the 2016 Annual Report on Kidney Disease in Taiwan, HD patients had higher NHI expenses (NTD 70,000 per patient-month) than PD patients (NTD 51,000 per patient-month), owing to higher cost of outpatient care (HD, NTD 56,000 per patient-month; PD, NTD 43,000 per patient-month) and inpatient care (HD, NTD 13,400 per patient-month; PD, NTD 8,200 per patient-month).[15] However, the extent to which OOP costs and productivity losses contribute to the overall economic burden of HD and PD are yet to be explored in Taiwan. We, therefore, conducted this study from a patient's and societal perspectives, using face-to-face interviews to compare OOP costs and productivity losses between HD and PD patients in Taiwan.

METHODS

Study Design

Ours was a multicentre study using cross-sectional interviews with patients over 20 years old, carried out at the nephrology outpatient clinics of five hospitals and five dialysis clinics located in northern, central, southern, and eastern Taiwan between April 2015 and March 2016. The Joint Institutional Review Board of Taipei Medical University approved this study (No. 201503057). All participants provided informed consent to participate in this study. All aspects of the study were performed in accordance with relevant guidelines and regulations. No patients were asked for input in the creation of this article.

Sampling

Articulate ESRD patients who were receiving long-term HD or PD continuously for more than three months were chosen. Those aged less than 20 years or unable to communicate were excluded. Patients were recruited and enrolled using a 1:1 male-to-female enrolment design. A total of 581 ESRD patients were screened at the contributing sites, of whom 554 were eligible and enrolled. In total, there were 308 HD patients (156 men, 152 women) and 246 PD patients (124 men, 122 women; 117 automated PD, 129 continuous ambulatory PD) available for analysis.

The patient interviews were performed face by face by well-trained nurses from the site or graduate students from the Taipei Medical University. All interviewers had attended prior interviewer training. The patients' baseline characteristics were collected from their medical chart and own response. The patient details collected include sociodemographics, comorbidities, cause of ESRD, and dialysis data (Table 1 and 2). We examine the differences in OOP costs and productivity losses between HD and PD patients. OOP costs included all expenses related to ESRD paid by the patients/family and not reimbursed by the NHI, such as expenses for medicines, medical materials and devices, herbal and alternative medicines, nutritional supplements, transportation costs, and caregiver costs. By using the 'human capital approach',[21] productivity losses were valued and measured by multiplying the loss of time in hours or days with average hourly/daily wage rate reported by the Directorate-General of Budget, Accounting, and Statistics, Taiwan (see supplementary Table S1). There were two sources of time loss being evaluated: patients' and caregivers' time spent in seeking care and time spent in operating the dialysis apparatus at home.

Statistical Analysis

The analyses began with a baseline comparison of patients receiving either HD or PD therapy. Frequencies for categorical variables and means with standard deviations or medians

with interquartile ranges for continuous variables were calculated. Statistical differences between the HD and PD patients were determined with Chi-square ($\chi 2$) tests, Mann-Whitney U test and Wilcoxon rank sum test as appropriate to analyse the patient interview survey data. Finally, as patient characteristics and costs may differ outside clinical settings and in different conditions, a bootstrap analysis was further performed on OOP costs and productivity losses, by applying 1,000 bootstrap procedures of HD and PD patients with replacement, stratified by age groups. The difference between the groups was significant for the two-sided *p*-value <0.05. All the analyses in this study were carried out using the SAS 9.3 software (SAS Institute Inc., Cary, NC, USA).

Sensitivity Analysis

Moreover, the HD and PD patients are a group of patients with a debilitating illness and may receive lower wage rates than the general population resulting in lower productivity losses. To assess the impact of productivity losses on the sum of OOP costs and productivity losses, we adjusted the productivity losses for the mean Taiwan unemployment rate (3.82%) during the interview period (between April 2015 and March 2016) and then set the productivity losses with a 20%, 30%, or 40% decrement of wages as different scenarios to calculate the total amount of these two costs.[22]

RESULTS

A total of 308 HD patients and 246 PD patients were interviewed in the multicentre cross-sectional study. Patient baseline characteristics are shown in Table 1. HD patients were older as more patients were over 70 years old. Diabetes and ischemic heart disease prevalence was higher and hypertension was lower in HD patients. Hypertension and lupus nephritis had a discernibly different causation of ESRD between the HD and PD patients. Marital status, education, and income were not statistically different between the groups. The dialysis-related baseline data are reported in Table 2, where the maximum differences were

found to be the duration of dialysis, haemoglobin, serum albumin, and potassium.

Table 3 shows the results of the per patient-month OOP costs. There were discernible differences between the HD and PD patients in the OOP costs (NTD 5,922 vs. NTD 5,237, p <0.01). The HD patients had significantly lower copayment for outpatient visits, medicine not covered by NHI, and medical equipment, but higher copayment for hospitalizations and transportation than the PD patients. Chinese medication, traditional medicine, and nutritional supplements showed no discernible differences between groups. Another main source of the differences between the HD and PD patients were the transportation costs, owing to more frequent transportation in the former group. However, the results of the mean OOP costs were not consistent in each age group. PD patients had significantly higher OOP costs than the corresponding HD patients in the age groups of 50–59 years old and over 70 years old.

Results of the per patient-month productivity losses are reported in Table 4. Compared with the PD patients, the HD patients had higher monthly productivity losses (NTD 14,147 vs. NTD 11,604, p <0.01), resulting from more time spent seeking outpatient care (HD, 70.4 ± 6.9 hours vs. PD, 4.4 ± 2.5 hours, p <0.001) and time spent by family caregivers for outpatient care (HD, 66.1 ± 51.5 hours vs. PD, 6.1 ± 4.1 hours, p <0.001). However, only 10.4% and 31.3% of HD and PD patients, respectively, had family caregivers who accompanied them for outpatient care. The productivity losses resulting from time spent operating the dialysis apparatus (49.9 ± 27.8 hours) were only seen in PD patients but not HD patients. After the 1,000 bootstrap procedures, the results of the mean productivity losses remained unchanged in each age group. HD patients had significantly lower productivity losses in the age group over 70 years old because no productivity losses were included beyond the age of 70 years.

Table 5 reports the total costs per patient-month, including OOP costs and productivity losses. The productivity losses were further adjusted for mean Taiwan unemployment rate

(3.82%) during the interview survey periods. Models 3–6 show the total costs including OOP costs and productivity losses adjusted for unemployment rate with a 20%, 30%, or 40% decrement of wages as different scenarios. After considering the productivity losses under various scenarios, the differences of total costs between the HD and PD patients slightly decreased in Models 4–6. After stratified by age groups, the total costs per patient-month of HD patients were higher than those of PD patients except in the age group older than 70 years old.

Incorporating the NHI-financed medical costs of HD and PD reported in the 2016 Annual Report on Kidney Disease in Taiwan into the findings in this study [15], Figure 1 shows the per patient-month total costs are NTD 89,522 for HD and NTD 67,392 for PD, to which OOP costs contributed 6.6% and 7.8%, and productivity losses 15.2% and 16.6%, respectively. For the NTD 22,130 per-patient-month difference in the costs of HD and PD, OOP and productivity losses account for 3.1% and 11.0% of the differences, respectively.

DISCUSSION

The main results of this cross-sectional, multicentre interview survey demonstrate that total monthly OOP costs and productivity losses of HD (NTD 19,522) were higher than that of PD (NTD 16,392) after adjusting for unemployment rate. The OOP costs for the HD patients were NTD 687 higher than that for the PD patients, with the greatest difference being found in the costs of copayment to hospitalizations and transportation costs. The main sources of the differences between HD and PD patients for productivity losses were seeking outpatient care and time spent operating the dialysis apparatus.

These findings are rarely assessed in previous studies but important for the care of ESRD patients because the OOP costs and productivity losses constitute an important, but frequently omitted, part of the overall evaluation of economic burden borne by patients and their families. Previous studies reported that a significantly higher total NHI-financed

medical costs were discernible among the HD patients than among the PD patients in several countries, including Taiwan, USA, and UK.[10 15 23] The total costs per patient-month of HD and PD patients, including the OOP costs and productivity losses (Table 5, Model 1), were NTD 19,522 and NTD 16,392, respectively, with a difference of NTD 3,130 per patient-month. From the payer's perspective, the NHI-financed medical costs of PD seems to be a better cost-saving modality; similarly, from a patient's and societal perspective, the total costs per patient-month of HD were higher owing to higher OOP costs except in the age group more than 70 years old (Table 5).

In this study, productivity losses were estimated according to the human capital approach using the reduced future gross income, including lower paid or unpaid production due to seeking medical care and operating the PD apparatus.[21] Productivity losses accounted for 31.7% of the overall costs in the HD patients, which is similar to 31.8% in the PD patients. The mean difference of the productivity losses after bootstrap procedures between HD and PD patients was NTD 2,539 (Table 4). The results reflected that the productivity losses, resulting from the time spent seeking outpatient care and operating the dialysis apparatus were significantly lower in the PD than in the HD patients. The productivity losses in HD patients decreased gradually in the older age groups and was higher than those of PD patients in the same age group (Table 4). Unlike the HD patients, who needed to visit a HD centre three times a week, the PD patients could work freely and spent less time in operating the dialysis apparatus and had lower productivity losses. When compared to HD, PD is a self-care and time-saving modality, which explains the lower productivity losses. To extend the generalisability of our findings to other national health systems, our result demonstrates that PD modality may appear to be more suitable for its markedly lower productivity losses for countries with a younger dialysis patient population (less than 70 years old), or with a higher value hourly wage or daily wage.

The results of this study confirmed HD modality had higher OOP costs and productivity losses than PD modality shown in previous studies.[12 20] This study also found that productivity losses contributed 15.2% and 16.5% to the total economic burden of HD and PD, respectively, which were higher than 12.4% and 9.8% found in the Brazilian study.[20] This discrepancy may reflect the difference in healthcare system in Taiwan, where medical care is mainly financed by National Health Insurance and in Brazil where patients pay out-of-pocket for their medical care.

The results of this study have some limitations. First, the difference in the proportion of age groups in HD and PD patients are the major drawback of this study. From the 2016 Annual Report on Kidney Disease in Taiwan, the mean ages of HD and PD commencement in 2014 were 66.7 and 57.3, respectively, which were older than those of HD and PD patients in this cross-sectional study (61.0 and 56.2, respectively, Table 1).[15] Due to this difference, it was difficult to obtain sampling of these two groups of patients in the similar age range. Therefore, we analysed the results by stratifying into four age groups to compare the differences. Second, the results of this study should be interpreted cautiously. The sample size could not represent the general population of HD and PD patients in Taiwan because the sampled patients were also not randomised, although they were sampled from different parts of Taiwan. Third, the impaired productivity or reduced effectiveness at work associated with HD or PD were not included in this study, so the productivity losses may thus have led to an underestimation.

In this study, we present a patient interview survey in Taiwan to analyse the OOP costs and productivity losses for HD and PD patients. From a patient's and societal perspective, the HD patients have higher OOP costs and productivity losses than the PD patients in the age group less than 70 years old owing to higher productivity losses.

Contributors: CHT and YMS: study concept and design. HHC, MJW, BGH, JCT, CCK, SPL,

and THC: acquisition of data. CCK, CHT and YMS: analysis and interpretation. CHT and YMS: drafted the manuscript. HHC, MJW, BGH, JCT, SPL, and THC: critical revision of the manuscript for important intellectual content. All authors: approved the final paper. CHT and YMS are fully responsible for the paper.

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Competing interests: None declared.

Data sharing statement: All relevant data have been included in the paper.

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Table 1. Patient characteristics of the interview survey patients.

Variables	HD (n=308)		PD (n=246)		*p*-value
Male gender	156	(50.7)	124	(50.4)	0.96
Age (y)	61.0	[12.7]	56.2	[13.9]	<0.01
<50	68	(22.1)	71	(28.9)	
50-59	79	(25.7)	67	(27.2)	
60-69	76	(24.7)	70	(28.5)	
≥70	85	(27.6)	38	(15.5)	
Comorbidities					
Diabetes mellitus	130	(42.2)	74	(30.1)	<0.01
Hypertension	204	(66.2)	193	(78.5)	<0.01
Cancer	17	(5.5)	7	(2.9)	0.13
Chronic obstructive pulmonary disease	5	(1.6)	2	(0.81)	0.40
Cirrhosis of liver	5	(1.6)	3	(1.2)	0.91
Dementia	3	(1.0)	4	(1.6)	0.50
Cerebrovascular disease	8	(2.6)	6	(2.4)	0.91
Peripheral vascular disease	15	(4.9)	8	(3.25)	0.34
Cardiac dysrhythmia	36	(11.7)	20	(8.1)	0.17
Ischemic heart disease	22	(7.1)	6	(2.4)	0.01
Myocardial infarction	11	(3.6)	8	(3.3)	0.84
Chronic heart failure	13	(4.2)	9	(3.7)	0.74
Cause of end-stage renal disease					
Chronic glomerulonephritis	111	(36.0)	82	(33.3)	0.44
Diabetes mellitus	118	(38.3)	71	(28.9)	0.11
Hypertension	108	(35.1)	52	(21.1)	0.02
Hereditary polycystic kidney disease	10	(3.3)	6	(2.4)	0.83
Chronic tubulointerstitial nephritis	5	(1.6)	7	(2.9)	0.19
Lupus nephritis	4	(1.3)	11	(4.5)	<0.01
Others	51	(16.6)	43	(17.5)	0.21
Marital status					0.18
Singled	45	(14.6)	52	(21.1)	
Married	210	(68.2)	159	(64.6)	
Divorced	25	(8.1)	15	(6.2)	
Widowed	28	(9.1)	20	(8.1)	
Education years					0.09
Below primary school	26	(8.4)	15	(6.1)	
Primary school	77	(25.0)	51	(20.7)	
Junior high school	50	(16.2)	31	(12.6)	

Senior high school	88	(28.6)	69	(28.1)	
College	59	(19.2)	66	(26.8)	
Above college	8	(2.6)	14	(5.7)	
Family income (NTD)					0.17
<30,000	93	(30.2)	80	(32.5)	
30,000-49,999	99	(32.1)	61	(24.8)	
50,000-69,999	61	(19.8)	46	(18.7)	
70,000-99,999	31	(10.1)	25	(10.1)	
100,000-149,999	9	(2.9)	23	(9.4)	
150,000-199,999	6	(2.0)	8	(3.3)	
≥200,000	9	(2.9)	3	(1.2)	

Data were number (%) or mean [standard deviation]. HD: haemodialysis; NTD: New Taiwan Dollar; PD: peritoneal dialysis.

Table 2. Dialysis related baseline data of interview survey patients.

Variables	HD (n=308)		PD (n=246)		*p*-value
Duration of dialysis (month)	87.8	[78.1]	45.4	[38.6]	<0.001
Systolic blood pressure (mmHg)	141.8	[24.7]	141.0	[23.2]	0.58
Diastolic blood pressure (mmHg)	76.1	[12.6]	82.3	[14.9]	<0.001
Heart rate (beats/min)	77.5	[10.3]	81.8	[15.1]	<0.01
Serum albumin (g/dL)	4.0	[0.4]	3.8	[0.7]	<0.001
Serum potassium (mmol/L)	4.8	[0.8]	4.0	[0.6]	<0.001
Kt/V	1.66	[0.54]	1.97	[0.31]	<0.001
Urea reduction ratio	73.9	[6.2]	—	—	—
Weekly creatinine clearance (ml/min)	—	—	60.1	[12.5]	—
Normalized protein nitrogen appearance	—	—	1.0	[0.2]	—
Hemoglobin (g/dL)	10.5	[1.5]	10.1	[1.5]	<0.01
Body mass index	23.7	[4.5]	23.9	[3.9]	0.22

Data were mean [standard deviation]. HD: haemodialysis; PD: peritoneal dialysis.

Table 3. Per patient-month out-of-pocket costs of the interview survey patients (in NTD).

	HD (n=308)				PD (n=246)				
Variables	Mean	(SD)	Median	(IQR)	Mean	(SD)	Median	(IQR)	*p*-value
Before bootstrap procedures									
Total	5,922	(12,963)	1,794	(488-4,784)	5,237	(7,571)	2,492	(1,018-5,598)	<0.01
Copayment to outpatient care	103	(377)	0	(0-120)	361	(696)	120	(50-400)	<0.001
Copayment to inpatient care	2,209	(11,093)	0	(0-0)	995	(2,163)	0	(0-1,240)	<0.001
Medicine not covered by NHI	591	(1,832)	0	(0-417)	995	(1,911)	125	(0-1,078)	<0.001
Medical equipment	110	(448)	0	(0-0)	439	(726)	208	(0-675)	<0.001
Chinese medication	27	(175)	0	(0-0)	183	(2,153)	0	(0-0)	0.53
Traditional medicine	38	(257)	0	(0-0)	51	(550)	0	(0-0)	0.35
Nutritional supplements	241	(749)	0	(0-0)	542	(2,398)	0	(0-106)	0.26
Transportation costs	1,028	(1,707)	293	(0-1,495)	191	(229)	143	(16-293)	<0.001
Caregiver costs	1,574	(5,453)	0	(0-0)	1,480	(5,309)	0	(0-0)	0.90
Stratified by age groups									
Age <50 (y)	3,766	(5,785)			2,771	(3,150)			0.32
Age 50-59 (y)	4,902	(14,857)			5,824	(7,484)			<0.001
Age 60-69 (y)	7,337	(14,140)			4,091	(6,072)			0.68
Age ≥70 (y)	7,330	(13,980)			10,922	(12,006)			<0.01
After bootstrap procedures									
Total	5,912	(819)			5,225	(485)			<0.001
Stratified by age groups									
Age <50 (y)	3,787	(686)			2,776	(375)			<0.001
Age 50-59 (y)	4,814	(1,678)			5,827	(870)			<0.001
Age 60-69 (y)	7,270	(1,559)			4,111	(701)			<0.001

Age ≥70 (y)	7,348 (1,521)	10,932 (1,855)	<0.001

HD: haemodialysis; IQR: interquartile range; NHI: National health Insurance; NTD, New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars); PD: peritoneal dialysis; SD: standard deviation.

Table 4. Per patient-month productivity losses of the interview survey patients (in NTD).

	HD (n=308)				PD (n=246)				
Variables	Mean	(SD)	Median	(IQR)	Mean	(SD)	Median	(IQR)	*p*-value
Before bootstrap procedures									
Total	14,147	(10,746)	13,936	(6,961-20,921)	11,604	(7,949)	10,576	(5,315-16,764)	<0.01
Time spent operating dialysis apparatus	—	—	—	—	8,655	(6,785)	7,450	(3,138-12,700)	
Seeking outpatient care from patients	11,307	(8,007)	12,874	(0-17,567)	774	(591)	798	(399-1,008)	<0.001
Seeking outpatient care from caregivers	1,608	(5,793)	0	(0-0)	400	(759)	0	(0-833)	<0.001
Seeking inpatient care from patients	799	(1,683)	0	(0-0)	1,037	(1,482)	0	(0-2,918)	0.01
Seeking inpatient care from caregivers	433	(1,251)	0	(0-0)	739	(1,290)	0	(0-733)	<0.001
Stratified by age groups									
Age <50 (y)	19,419	(5,888)			13,177	(7,000)			<0.001
Age 50-59 (y)	19,276	(10,606)			14,424	(7,579)			<0.01
Age 60-69 (y)	17,253	(7,901)			12,826	(6,789)			<0.001
Age ≥70 (y)	2,386	(6,184)			1,207	(1,621)			<0.01
After bootstrap procedures									
Total	14,150	(626)			11,611	(510)			<0.001
Stratified by age groups									
Age <50 (y)	19,381	(715)			13,289	(840)			<0.001
Age 50-59 (y)	19,272	(1,162)			14,415	(878)			<0.001
Age 60-69 (y)	17,212	(857)			12,823	(802)			<0.001
Age ≥70 (y)	2,403	(645)			1,206	(255)			<0.001

HD: haemodialysis; IQR: interquartile range; NTD: New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars); PD: peritoneal dialysis; SD: standard deviation.

Table 5. Total costs of out-of-pocket costs and productivity losses per patient-month of HD and PD patients after bootstrap analysis (in NTD).

Variables	HD	PD	Difference
(1) Out-of-pocket costs	5,912	5,225	687
Stratified by age groups			
Age <50 (y)	3,787	2,776	1,011
Age 50-59 (y)	4,814	5,827	-1,013
Age 60-69 (y)	7,270	4,111	3,159
Age ≥70 (y)	7,348	10,932	-3,584
(2) Productivity losses adjusted for 3.82% unemployment rate[a]	13,610	11,167	2,443
Stratified by age groups			
Age <50 (y)	18,641	12,781	5,860
Age 50-59 (y)	18,536	13,864	4,672
Age 60-69 (y)	16,555	12,333	4,222
Age ≥70 (y)	2,311	1,160	1,151
(3) Total costs, model 1 = (1) + (2)	19,522	16,392	3,130
Stratified by age groups			
Age <50 (y)	22,428	15,557	6,871
Age 50-59 (y)	23,350	19,691	3,659
Age 60-69 (y)	23,825	16,444	7,381
Age ≥70 (y)	9,659	12,092	-2,433
(4) Total costs, model 2 = (1) + (2) x 20% decrement in wages	16,800	14,159	2,641
(5) Total costs, model 3 = (1) + (2) x 30% decrement in wages	15,439	13,042	2,397
(6) Total costs, model 4 = (1) + (2) x 40% decrement in wages	14,078	11,925	2,153

HD: haemodialysis; PD: peritoneal dialysis; NHI: National Health Insurance; NTD: New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars).

[a] Adjusted for mean Taiwan unemployment rate (3.82%) between April 2015 and March 2016.

Figure Legends

Figure 1. Distribution of NHI-financed medical cost [15], out-of-pocket costs, and productivity losses, in HD and PD modalities, and their differences. NHI: National Health Insurance; NTD: New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars); HD: haemodialysis; PD: peritoneal dialysis.

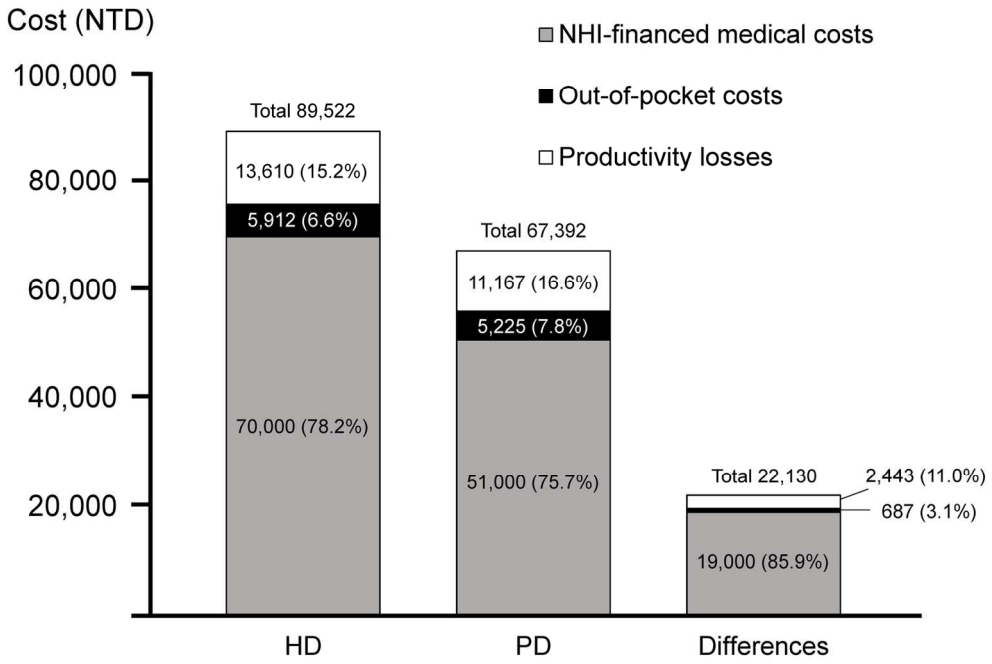

Figure 1. Distribution of NHI-financed medical cost 15, out-of-pocket costs, and productivity losses, in HD and PD modalities, and their differences. NHI: National Health Insurance; NTD: New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars); HD: haemodialysis; PD: peritoneal dialysis.

147x99mm (300 x 300 DPI)

Supplementary Online Content

Out-of-pocket costs and productivity losses in haemodialysis and peritoneal dialysis from a patient interview survey in Taiwan

Chao-Hsiun Tang, Hsi-Hsien Chen, Ming-Ju Wu, Bang-Gee Hsu, Jer-Chia Tsai, Chi-Cheng Kuo, Shih-Pi Lin, Tso-Hsiao Chen, Yuh-Mou Sue

Table S1. Average monthly/hourly wage rate reported by the Directorate-General of Budget, Accounting, and Statistics, Taiwan.

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	Monthly income (NTD)	Hourly income (NTD)[a]
Male[b]		
15 - 19 years	18,300	103
20 - 24 years	25,680	145
25 - 29 years	33,210	187
30 - 34 years	36,090	203
35 - 39 years	40,470	228
40 - 44 years	43,590	245
45 - 49 years	45,930	259
50 - 54 years	44,280	249
55 - 59 years	43,980	248
60 - 64 years	44,760	252
65 - 69 years	34,740	196
70 & over	0	0
Female[b]		
15 - 19 years	16,590	96
20 - 24 years	24,600	143
25 - 29 years	30,420	176
30 - 34 years	32,520	189
35 - 39 years	34,440	200
40 - 44 years	36,000	209
45 - 49 years	36,930	214
50 - 54 years	35,850	208
55 - 59 years	34,830	202
60 - 64 years	34,440	200
65 - 69 years	23,100	134
70 & over	0	0
Caregivers[b]	36,510	208

NTD, New Taiwan Dollar, 1 US Dollar = 30 New Taiwan Dollars.
[a] Average hourly income= average monthly income / average monthly working hours.
[b] Average monthly working hours: male = 177.6 hrs.; female = 172.5 hrs.; caregivers = 175.3 hrs.

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Out-of-pocket costs and productivity losses in haemodialysis and peritoneal dialysis from a patient interview survey in Taiwan

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Out-of-pocket costs and productivity losses in haemodialysis and peritoneal dialysis from a patient interview survey in Taiwan

Running title: Costs of HD and PD in Taiwan

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ABSTRACT

Objectives: The total medical (economic) costs of haemodialysis (HD) and peritoneal dialysis (PD), including direct medical costs, out-of-pocket (OOP) costs, and productivity losses, have become an important issue. This study aims to compare the direct non-medical costs and indirect medical costs of both modalities in Taiwan.

Design and Setting: This multicentre study included cross-sectional interviews of patients over 20 years old and articulate, who had been continuously receiving long-term HD or PD for more than three months between April 2015 and March 2016. Mann-Whitney U test, Wilcoxon rank sum test, and 1,000 bootstrap procedures with replacement were used for analysis.

Outcome measures: Differences in OOP costs and productivity losses.

Results: There were 308 HD and 246 PD patients available for analysis. HD patients had significantly higher monthly OOP costs than PD patients after bootstrap procedures (NTD 5,912 vs. NTD 5,225, $p<0.001$; NTD, New Taiwan Dollars; 1 US Dollar = 30 NTD). Compared with PD patients, HD patients had higher monthly productivity losses after bootstrap procedures (NTD 14,150 vs. NTD 11,611, $p<0.001$), resulting from more time spent seeking outpatient care (HD, 70.4 hours vs. PD, 4.4 hours, $p<0.001$) and time spent by family caregivers for outpatient care (HD, 66.1 hours vs. PD, 6.1 hours, $p<0.001$). The total costs per patient-month of HD and PD modalities, including OOP costs and productivity losses were NTD 20,062 and NTD 16,836, respectively.

Conclusions: The HD modality has higher OOP costs and productivity losses than the PD modality in Taiwan.

Keywords: cost, haemodialysis; out-of-pocket cost; peritoneal dialysis; productivity loss

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This multicentre study included cross-sectional interviews of long-term HD and PD patients.
- Previous study seldom assessed the information about out-of-pocket payments and productivity losses collected from patient undergoing HD and PD.
- The difference in the proportion of age groups in HD and PD patients are the major drawback of this study.
- The sample size could not represent the general population of HD and PD patients in Taiwan because the sampled patients were also not randomised

INTRODUCTION

Since March 1995, when Taiwan began implementing the National Health Insurance (NHI) system, the per capita healthcare expenditure has increased annually, especially in the care of 'end-stage renal disease' (ESRD) patients. Taiwan has the highest incidence and prevalence rates of ESRD in the world.[1-3] By 2017, the cost of dialysis (New Taiwan Dollar, NTD 36.9 billion; 1 US dollar = 30 NTDs in Dec. 2017) accounted for a staggering 5.73% of the total annual NHI expenditure (NTD 644.1 billion).[3] Haemodialysis (HD) and peritoneal dialysis (PD) are the two major renal replacement modalities in Taiwan with a similar all-cause mortality rate.[4-7] Several studies have provided clear evidence that HD has the higher direct medical costs among the two modalities.[8-14] NHI administrators implemented several strategies besides applying a blanket budget cap on dialysis expenditure to contain the total costs of dialysis and incentivize the use of PD modality. These efforts included increasing the reimbursements for PD and extending the NHI payment scheme covering the automated PD machine costs. As the proportion of PD usage increases, its prevalence in Taiwan has been gradually increasing, from 6.5% in 2003 to 8.5% in 2007, and up to 9.2% in 2014, similar to the average level within the developed countries.[15-18]

ESRD prevalence is increasing with the rise in the number of aging and diabetic nephropathy patients. The total (economic) costs of HD and PD modalities, including direct medical costs, direct non-medical costs, and productivity losses, have become an important issue.[19] Direct medical costs incurred for medical services, such as dialysis costs, physician and nurses' services, diagnostic tests, and hospitalization costs, are the most common type cited in the nephrologic literature. From a payer's perspective (e.g., national insurance organizations), these costs are the most important. However, from a patient's as well as societal perspectives, out-of-pocket (OOP) costs and productivity losses are nominal and meaningful. OOP costs and productivity losses have not been assessed comprehensively in

ESRD patients for two reasons: the methods for collecting these data for the ESRD patients are not well established, and retrospective data collection is difficult. Only two studies have reported that PD had less OOP costs and productivity losses than HD in Brazil and Singapore, but detailed data were not stated.[12 20] These studies highlighted a significant economic burden due to dialysis and a higher direct healthcare costs associated with the use of HD modality; however, little information is available about OOP costs, including expenses on caregivers or transportation, as well as productivity losses, including job loss, worker replacement, and reduced productivity from patients and family. According to the 2016 Annual Report on Kidney Disease in Taiwan, HD patients had higher NHI expenses (NTD 70,000 per patient-month) than PD patients (NTD 51,000 per patient-month), owing to higher cost of outpatient care (HD, NTD 56,000 per patient-month; PD, NTD 43,000 per patient-month) and inpatient care (HD, NTD 13,400 per patient-month; PD, NTD 8,200 per patient-month).[15] However, the extent to which OOP costs and productivity losses contribute to the overall economic burden of HD and PD are yet to be explored in Taiwan. We, therefore, conducted this study from a patient's and societal perspectives, using face-to-face interviews to compare OOP costs and productivity losses between HD and PD patients in Taiwan.

METHODS

Study Design

Ours was a multicentre study using cross-sectional interviews with patients over 20 years old, carried out at the nephrology outpatient clinics of five hospitals and five dialysis clinics located in northern, central, southern, and eastern Taiwan between April 2015 and March 2016. The Joint Institutional Review Board of Taipei Medical University approved this study (No. 201503057). All participants provided informed consent to participate in this study. All aspects of the study were performed in accordance with relevant guidelines and regulations.

Patient and Public Involvement

No patients were asked for input in the creation of this article.

Sampling

Articulate ESRD patients who were receiving long-term HD or PD continuously for more than three months were chosen. Those aged less than 20 years or unable to communicate were excluded. Patients were recruited and enrolled using a 1:1 male-to-female enrolment design. A total of 581 ESRD patients were screened at the contributing sites, of whom 554 were eligible and enrolled. In total, there were 308 HD patients (156 men, 152 women) and 246 PD patients (124 men, 122 women; 117 automated PD, 129 continuous ambulatory PD) available for analysis.

The patient interviews were performed face by face by well-trained nurses from the site or graduate students from the Taipei Medical University during HD therapy or monthly PD clinic visit. All interviewers had attended prior interviewer training. The patients' baseline characteristics were collected from their medical chart and own response. The patient details collected include sociodemographics, comorbidities, cause of ESRD, and dialysis data (Table 1 and 2). We examine the differences in OOP costs and productivity losses between HD and PD patients. OOP costs included all expenses related to ESRD paid by the patients/family and not reimbursed by the NHI, such as expenses for medicines, medical materials and devices, herbal and alternative medicines, nutritional supplements, transportation costs, and caregiver costs. By using the 'human capital approach',[21] productivity losses were valued and measured by multiplying the loss of time in hours or days with average hourly/daily wage rate reported by the Directorate-General of Budget, Accounting, and Statistics, Taiwan (see supplementary Table S1). There were two sources of time loss being evaluated: patients' and caregivers' time spent in seeking care and time spent in operating the dialysis apparatus at home.

Statistical Analysis

The analyses began with a baseline comparison of patients receiving either HD or PD therapy. Frequencies for categorical variables and means with standard deviations or medians with interquartile ranges for continuous variables were calculated. Statistical differences between the HD and PD patients were determined with Chi-square ($\chi 2$) tests, Mann-Whitney U test and Wilcoxon rank sum test as appropriate to analyse the patient interview survey data. Finally, as patient characteristics and costs may differ outside clinical settings and in different conditions, a bootstrap analysis was further performed on OOP costs and productivity losses, by applying 1,000 bootstrap procedures of HD and PD patients with replacement, stratified by age groups. The difference between the groups was significant for the two-sided *p*-value <0.05. All the analyses in this study were carried out using the SAS 9.3 software (SAS Institute Inc., Cary, NC, USA).

Sensitivity Analysis

Moreover, the HD and PD patients are a group of patients with a debilitating illness and may receive lower wage rates than the general population resulting in lower productivity losses. To assess the impact of productivity losses on the sum of OOP costs and productivity losses, we adjusted the productivity losses for the mean Taiwan unemployment rate (3.82%) during the interview period (between April 2015 and March 2016) and then set the productivity losses with a 20%, 30%, or 40% decrement of wages as different scenarios to calculate the total amount of these two costs.[22]

RESULTS

A total of 308 HD patients and 246 PD patients were interviewed in the multicentre cross-sectional study. Patient baseline characteristics are shown in Table 1. HD patients were older as more patients were over 70 years old. Diabetes and ischemic heart disease prevalence was higher and hypertension was lower in HD patients. Hypertension and lupus nephritis had a discernibly different causation of ESRD between the HD and PD patients.

Marital status, education, and income were not statistically different between the groups. The dialysis-related baseline data are reported in Table 2, where the maximum differences were found to be the duration of dialysis, haemoglobin, serum albumin, and potassium.

Table 3 shows the results of the per patient-month OOP costs. There were discernible differences between the HD and PD patients in the OOP costs (NTD 5,922 vs. NTD 5,237, p <0.01). The HD patients had significantly lower copayment for outpatient visits, medicine not covered by NHI, and medical equipment, but higher copayment for hospitalizations and transportation than the PD patients. Chinese medication, traditional medicine, and nutritional supplements showed no discernible differences between groups. Another main source of the differences between the HD and PD patients were the transportation costs, owing to more frequent transportation in the former group. However, the results of the mean OOP costs were not consistent in each age group. PD patients had significantly higher OOP costs than the corresponding HD patients in the age groups of 50–59 years old and over 70 years old.

Results of the per patient-month productivity losses are reported in Table 4. Compared with the PD patients, the HD patients had higher monthly productivity losses (NTD 14,147 vs. NTD 11,604, p <0.01), resulting from more time spent seeking outpatient care (HD, 70.4 ± 6.9 hours vs. PD, 4.4 ± 2.5 hours, p <0.001) and time spent by family caregivers for outpatient care (HD, 66.1 ± 51.5 hours vs. PD, 6.1 ± 4.1 hours, p <0.001). However, only 10.4% and 31.3% of HD and PD patients, respectively, had family caregivers who accompanied them for outpatient care. The productivity losses resulting from time spent operating the dialysis apparatus (49.9 ± 27.8 hours) were only seen in PD patients but not HD patients. After the 1,000 bootstrap procedures, the results of the mean productivity losses remained unchanged in each age group. HD patients had significantly lower productivity losses in the age group over 70 years old because no productivity losses were included beyond the age of 70 years.

Table 5 reports the total costs per patient-month, including OOP costs and productivity losses. The productivity losses were further adjusted for mean Taiwan unemployment rate (3.82%) during the interview survey periods. Models 2–4 show the total costs including OOP costs and productivity losses adjusted for unemployment rate with a 20%, 30%, or 40% decrement of wages as different scenarios. After considering the productivity losses under various scenarios, the differences of total costs between the HD and PD patients slightly decreased in Models 2–4. After stratified by age groups, the total costs per patient-month of HD patients were higher than those of PD patients except in the age group older than 70 years old.

Incorporating the NHI-financed medical costs of HD and PD reported in the 2016 Annual Report on Kidney Disease in Taiwan into the findings in this study [15], Figure 1 shows the per patient-month total costs are NTD 90,062 for HD and NTD 67,836 for PD, to which OOP costs contributed 6.6% and 7.7%, and productivity losses 15.7% and 17.1%, respectively. For the NTD 22,227 per-patient-month difference in the costs of HD and PD, OOP and productivity losses account for 3.1% and 11.4% of the differences, respectively.

DISCUSSION

The main results of this cross-sectional, multicentre interview survey demonstrate that total monthly OOP costs and productivity losses of HD (NTD 19,522) were higher than that of PD (NTD 16,392) after adjusting for unemployment rate. The OOP costs for the HD patients were NTD 687 higher than that for the PD patients, with the greatest difference being found in the costs of copayment to hospitalizations and transportation costs. The main sources of the differences between HD and PD patients for productivity losses were seeking outpatient care and time spent operating the dialysis apparatus. The total economic costs of HD (NT 90,062), including NHI expenses, OPP costs and productivity losses, were higher than those of PD (NT 67,836), which were most contributed by NHI expenses (NT 19,000,

85.5%) (Figure 1).

These findings are rarely assessed in previous studies but important for the care of ESRD patients because the OOP costs and productivity losses constitute an important, but frequently omitted, part of the overall evaluation of economic burden borne by patients and their families. Previous studies reported that a significantly higher total NHI-financed medical costs were discernible among the HD patients than among the PD patients in several countries, including Taiwan, USA, and UK.[10 15 23] The total costs per patient-month of HD and PD patients, including the OOP costs and productivity losses (Table 5, Model 1), were NTD 20,063 and NTD 16,836, respectively, with a difference of NTD 3,227 per patient-month. From the payer's perspective, the NHI-financed medical costs of PD seems to be a better cost-saving modality; similarly, from a patient's and societal perspective, the total costs per patient-month of HD were higher owing to higher OOP costs except in the age group more than 70 years old (Table 5). Aged ESRD patients often have comorbidities, such as diabetes mellitus with retinopathy and poor vision acuity. Considering the necessity of caregiver's support to complete the every day's procedures, most patients would not choose PD as a favour choice to prevent the OOP cost of caregiver. Compared with HD patients, PD patients with diabetes mellitus or age more than 65 years old also had increased death rate. All these factors would discourage patients to choosing PD as their renal replacement modality.[5]

In this study, productivity losses were estimated according to the human capital approach using the reduced future gross income, including lower paid or unpaid production due to seeking medical care and operating the PD apparatus.[21] Productivity losses accounted for 31.7% of the overall costs in the HD patients, which is similar to 31.8% in the PD patients. The mean difference of the productivity losses after bootstrap procedures between HD and PD patients was NTD 2,539 (Table 4). The results reflected that the productivity losses,

resulting from the time spent seeking outpatient care and operating the dialysis apparatus were significantly lower in the PD than in the HD patients. The productivity losses in HD patients decreased gradually in the older age groups and was higher than those of PD patients in the same age group (Table 4). Unlike the HD patients, who needed to visit a HD centre three times a week, the PD patients could work freely and spent less time in operating the dialysis apparatus and had lower productivity losses. When compared to HD, PD is a self-care and time-saving modality, which explains the lower productivity losses. In patients with chronic kidney disease stage 5 near ESRD, facing with numerous decisions across the trajectory of their illness are needed. Using shared decision making approach offers a patient-centered method to nudge patients facing health-related decisions, including the choice of HD, PD, kidney transplantation or hospice care. The OPP costs and productivity losses have significant impact on quality of lives and cost of healthcare delivery. Exploring the detailed information will provide evidence based, high-quality decision aids and be able to meet patients' informational needs. To extend the generalisability of our findings to other national health systems, our result demonstrates that PD modality may appear to be more suitable for its markedly lower productivity losses for countries with a younger dialysis patient population (less than 70 years old), or with a higher value hourly wage or daily wage.

The results of this study confirmed HD modality had higher OOP costs and productivity losses than PD modality shown in previous studies.[12 20] This study also found that productivity losses contributed 15.2% and 16.5% to the total economic burden of HD and PD, respectively, which were higher than 12.4% and 9.8% found in the Brazilian study.[20] This discrepancy may reflect the difference in healthcare system in Taiwan, where medical care is mainly financed by National Health Insurance and in Brazil where patients pay out-of-pocket for their medical care.

The results of this study have some limitations. First, the difference in the proportion of

age groups in HD and PD patients are the major drawback of this study. From the 2016 Annual Report on Kidney Disease in Taiwan, the mean ages of HD and PD commencement in 2014 were 66.7 and 57.3, respectively, which were older than those of HD and PD patients in this cross-sectional study (61.0 and 56.2, respectively, Table 1).[15] Due to this difference, it was difficult to obtain sampling of these two groups of patients in the similar age range. Therefore, we analysed the results by stratifying into four age groups to compare the differences. Second, the results of this study should be interpreted cautiously. The sample size could not represent the general population of HD and PD patients in Taiwan because the sampled patients were also not randomised, although they were sampled from different parts of Taiwan. Third, the impaired productivity or reduced effectiveness at work associated with HD or PD were not included in this study, so the productivity losses may thus have led to an underestimation.

In this study, we present a patient interview survey in Taiwan to analyse the OOP costs and productivity losses for HD and PD patients. From a patient's and societal perspective, the HD patients have higher OOP costs and productivity losses than the PD patients in the age group less than 70 years old owing to higher productivity losses.

Contributors: CHT and YMS: study concept and design. HHC, MJW, BGH, JCT, CCK, SPL, and THC: acquisition of data. CCK, CHT and YMS: analysis and interpretation. CHT and YMS: drafted the manuscript. HHC, MJW, BGH, JCT, SPL, and THC: critical revision of the manuscript for important intellectual content. All authors: approved the final paper. CHT and YMS are fully responsible for the paper.

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Competing interests: None declared.

Data sharing statement: All relevant data have been included in the paper.

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Table 1. Patient characteristics of the interview survey patients.

Variables	HD (n=308)		PD (n=246)		*p*-value
Male gender	156	(50.7)	124	(50.4)	0.96
Age (y)	61.0	[12.7]	56.2	[13.9]	<0.01
<50	68	(22.1)	71	(28.9)	
50-59	79	(25.7)	67	(27.2)	
60-69	76	(24.7)	70	(28.5)	
≥70	85	(27.6)	38	(15.5)	
Comorbidities					
Diabetes mellitus	130	(42.2)	74	(30.1)	<0.01
Hypertension	204	(66.2)	193	(78.5)	<0.01
Cancer	17	(5.5)	7	(2.9)	0.13
Chronic obstructive pulmonary disease	5	(1.6)	2	(0.81)	0.40
Cirrhosis of liver	5	(1.6)	3	(1.2)	0.91
Dementia	3	(1.0)	4	(1.6)	0.50
Cerebrovascular disease	8	(2.6)	6	(2.4)	0.91
Peripheral vascular disease	15	(4.9)	8	(3.25)	0.34
Cardiac dysrhythmia	36	(11.7)	20	(8.1)	0.17
Ischemic heart disease	22	(7.1)	6	(2.4)	0.01
Myocardial infarction	11	(3.6)	8	(3.3)	0.84
Chronic heart failure	13	(4.2)	9	(3.7)	0.74
Cause of end-stage renal disease					
Chronic glomerulonephritis	111	(36.0)	82	(33.3)	0.44
Diabetes mellitus	118	(38.3)	71	(28.9)	0.11
Hypertension	108	(35.1)	52	(21.1)	0.02
Hereditary polycystic kidney disease	10	(3.3)	6	(2.4)	0.83
Chronic tubulointerstitial nephritis	5	(1.6)	7	(2.9)	0.19
Lupus nephritis	4	(1.3)	11	(4.5)	<0.01
Others	51	(16.6)	43	(17.5)	0.21
Marital status					0.18
Singled	45	(14.6)	52	(21.1)	
Married	210	(68.2)	159	(64.6)	
Divorced	25	(8.1)	15	(6.2)	
Widowed	28	(9.1)	20	(8.1)	
Education years					0.09
Below primary school	26	(8.4)	15	(6.1)	
Primary school	77	(25.0)	51	(20.7)	
Junior high school	50	(16.2)	31	(12.6)	

Senior high school	88	(28.6)	69	(28.1)	
College	59	(19.2)	66	(26.8)	
Above college	8	(2.6)	14	(5.7)	
Family income (NTD)					0.17
<30,000	93	(30.2)	80	(32.5)	
30,000-49,999	99	(32.1)	61	(24.8)	
50,000-69,999	61	(19.8)	46	(18.7)	
70,000-99,999	31	(10.1)	25	(10.1)	
100,000-149,999	9	(2.9)	23	(9.4)	
150,000-199,999	6	(2.0)	8	(3.3)	
≥200,000	9	(2.9)	3	(1.2)	

Data were number (%) or mean [standard deviation]. HD: haemodialysis; NTD: New Taiwan Dollar; PD: peritoneal dialysis.

Table 2. Dialysis related baseline data of interview survey patients.

Variables	HD (n=308)		PD (n=246)		*p*-value
Duration of dialysis (month)	63	(26-135)	37	(16-63)	<0.001
Systolic blood pressure (mmHg)	141.8	[24.7]	141.0	[23.2]	0.58
Diastolic blood pressure (mmHg)	76.1	[12.6]	82.3	[14.9]	<0.001
Heart rate (beats/min)	77.5	[10.3]	81.8	[15.1]	<0.01
Serum albumin (g/dL)	4.0	[0.4]	3.8	[0.7]	<0.001
Serum potassium (mmol/L)	4.8	[0.8]	4.0	[0.6]	<0.001
Standard Kt/V (HD) or Kt/V (PD)	2.39	[0.32]	1.97	[0.31]	<0.001
Urea reduction ratio	73.9	[6.2]	—	—	—
Weekly creatinine clearance (ml/min)	—	—	60.1	[12.5]	—
Normalized protein nitrogen appearance	—	—	1.0	[0.2]	—
Hemoglobin (g/dL)	10.5	[1.5]	10.1	[1.5]	<0.01
Body mass index	23.7	[4.5]	23.9	[3.9]	0.22

Data were median (interquartile range) or mean [standard deviation]. HD: haemodialysis; PD: peritoneal dialysis.

Table 3. Per patient-month out-of-pocket costs of the interview survey patients (in NTD).

	HD (n=308)				PD (n=246)				
Variables	Mean	(SD)	Median	(IQR)	Mean	(SD)	Median	(IQR)	*p*-value
Before bootstrap procedures									
Total	5,922	(12,963)	1,794	(488-4,784)	5,237	(7,571)	2,492	(1,018-5,598)	<0.01
Copayment to outpatient care	103	(377)	0	(0-120)	361	(696)	120	(50-400)	<0.001
Copayment to inpatient care	2,209	(11,093)	0	(0-0)	995	(2,163)	0	(0-1,240)	<0.001
Medicine not covered by NHI	591	(1,832)	0	(0-417)	995	(1,911)	125	(0-1,078)	<0.001
Medical equipment	110	(448)	0	(0-0)	439	(726)	208	(0-675)	<0.001
Chinese medication	27	(175)	0	(0-0)	183	(2,153)	0	(0-0)	0.53
Traditional medicine	38	(257)	0	(0-0)	51	(550)	0	(0-0)	0.35
Nutritional supplements	241	(749)	0	(0-0)	542	(2,398)	0	(0-106)	0.26
Transportation costs	1,028	(1,707)	293	(0-1,495)	191	(229)	143	(16-293)	<0.001
Caregiver costs	1,574	(5,453)	0	(0-0)	1,480	(5,309)	0	(0-0)	0.90
Stratified by age groups									
Age <50 (y)	3,766	(5,785)			2,771	(3,150)			0.32
Age 50-59 (y)	4,902	(14,857)			5,824	(7,484)			<0.001
Age 60-69 (y)	7,337	(14,140)			4,091	(6,072)			0.68
Age ≥70 (y)	7,330	(13,980)			10,922	(12,006)			<0.01
After bootstrap procedures									
Total	5,912	(819)			5,225	(485)			<0.001
Stratified by age groups									
Age <50 (y)	3,787	(686)			2,776	(375)			<0.001
Age 50-59 (y)	4,814	(1,678)			5,827	(870)			<0.001
Age 60-69 (y)	7,270	(1,559)			4,111	(701)			<0.001

Age ≥70 (y)	7,348 (1,521)	10,932 (1,855)	<0.001

HD: haemodialysis; IQR: interquartile range; NHI: National health Insurance; NTD, New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars); PD: peritoneal dialysis; SD: standard deviation.

Table 4. Per patient-month productivity losses of the interview survey patients (in NTD).

	HD (n=308)				PD (n=246)				
Variables	Mean	(SD)	Median	(IQR)	Mean	(SD)	Median	(IQR)	*p*-value
Before bootstrap procedures									
Total	14,147	(10,746)	13,936	(6,961-20,921)	11,604	(7,949)	10,576	(5,315-16,764)	<0.01
Time spent operating dialysis apparatus	—	—	—	—	8,655	(6,785)	7,450	(3,138-12,700)	
Seeking outpatient care from patients	11,307	(8,007)	12,874	(0-17,567)	774	(591)	798	(399-1,008)	<0.001
Seeking outpatient care from caregivers	1,608	(5,793)	0	(0-0)	400	(759)	0	(0-833)	<0.001
Seeking inpatient care from patients	799	(1,683)	0	(0-0)	1,037	(1,482)	0	(0-2,918)	0.01
Seeking inpatient care from caregivers	433	(1,251)	0	(0-0)	739	(1,290)	0	(0-733)	<0.001
Stratified by age groups									
Age <50 (y)	19,419	(5,888)			13,177	(7,000)			<0.001
Age 50-59 (y)	19,276	(10,606)			14,424	(7,579)			<0.01
Age 60-69 (y)	17,253	(7,901)			12,826	(6,789)			<0.001
Age ≥70 (y)	2,386	(6,184)			1,207	(1,621)			<0.01
After bootstrap procedures									
Total	14,150	(626)			11,611	(510)			<0.001
Stratified by age groups									
Age <50 (y)	19,381	(715)			13,289	(840)			<0.001
Age 50-59 (y)	19,272	(1,162)			14,415	(878)			<0.001
Age 60-69 (y)	17,212	(857)			12,823	(802)			<0.001
Age ≥70 (y)	2,403	(645)			1,206	(255)			<0.001

HD: haemodialysis; IQR: interquartile range; NTD: New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars); PD: peritoneal dialysis; SD: standard deviation.

Table 5. Total costs of out-of-pocket costs and productivity losses per patient-month of HD and PD patients after bootstrap analysis (in NTD).

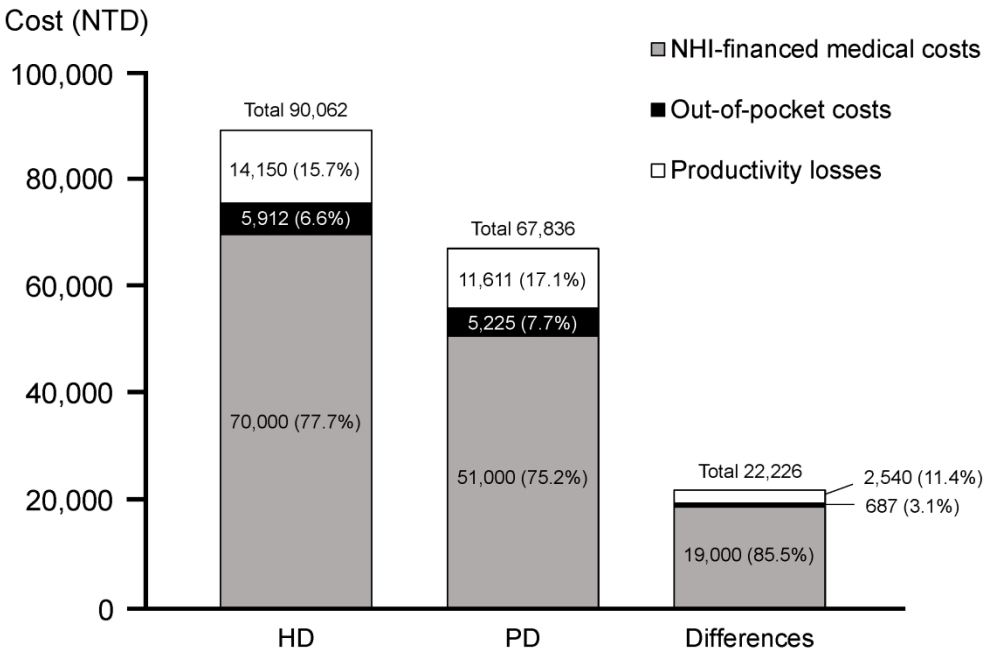
Variables	HD	PD	Difference
(1) Out-of-pocket costs	5,912	5,225	687
Stratified by age groups			
Age <50 (y)	3,787	2,776	1,011
Age 50-59 (y)	4,814	5,827	-1,013
Age 60-69 (y)	7,270	4,111	3,159
Age ≥70 (y)	7,348	10,932	-3,584
(2) Productivity losses	14,150	11,611	2,540
Stratified by age groups			
Age <50 (y)	19,381	13,289	6,093
Age 50-59 (y)	19,272	14,415	4,858
Age 60-69 (y)	17,213	12,823	4,390
Age ≥70 (y)	2,403	1,206	1,197
(3) Total costs			
Model 1 = (1) + (2)	20,062	16,836	3,227
Stratified by age groups			
Age <50 (y)	23,168	16,065	7,103
Age 50-59 (y)	24,086	20,242	3,844
Age 60-69 (y)	24,483	16,934	7,549
Age ≥70 (y)	9,751	12,138	-2,387
Model 2 = (1) + (2) x 20% decrement in wages x (1-0.0382)[a]	16,800	14,159	2,641
Model 3 = (1) + (2) x 30% decrement in wages x (1-0.0382)[a]	15,439	13,042	2,397
Model 4 = (1) + (2) x 40% decrement in wages x (1-0.0382)[a]	14,078	11,925	2,153

HD: haemodialysis; PD: peritoneal dialysis; NHI: National Health Insurance; NTD: New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars).

[a] Adjusted for mean Taiwan unemployment rate (3.82%) between April 2015 and March 2016.

Figure Legends

Figure 1. Distribution of NHI-financed medical cost [15], out-of-pocket costs, and productivity losses, in HD and PD modalities, and their differences. NHI: National Health Insurance; NTD: New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars); HD: haemodialysis; PD: peritoneal dialysis.



221x150mm (300 x 300 DPI)

Supplementary Online Content

Out-of-pocket costs and productivity losses in haemodialysis and peritoneal dialysis from a patient interview survey in Taiwan

Chao-Hsiun Tang, Hsi-Hsien Chen, Ming-Ju Wu, Bang-Gee Hsu, Jer-Chia Tsai, Chi-Cheng Kuo, Shih-Pi Lin, Tso-Hsiao Chen, Yuh-Mou Sue

Table S1. Average monthly/hourly wage rate reported by the Directorate-General of Budget, Accounting, and Statistics, Taiwan.

Table S1. Average monthly/hourly wage rate reported by the Directorate-General of Budget, Accounting, and Statistics, Taiwan.

	Monthly income (NTD)	Hourly income (NTD)[a]
Male[b]		
15 - 19 years	18,300	103
20 - 24 years	25,680	145
25 - 29 years	33,210	187
30 - 34 years	36,090	203
35 - 39 years	40,470	228
40 - 44 years	43,590	245
45 - 49 years	45,930	259
50 - 54 years	44,280	249
55 - 59 years	43,980	248
60 - 64 years	44,760	252
65 - 69 years	34,740	196
70 & over	0	0
Female[b]		
15 - 19 years	16,590	96
20 - 24 years	24,600	143
25 - 29 years	30,420	176
30 - 34 years	32,520	189
35 - 39 years	34,440	200
40 - 44 years	36,000	209
45 - 49 years	36,930	214
50 - 54 years	35,850	208
55 - 59 years	34,830	202
60 - 64 years	34,440	200
65 - 69 years	23,100	134
70 & over	0	0
Caregivers[b]	36,510	208

NTD, New Taiwan Dollar, 1 US Dollar = 30 New Taiwan Dollars.

[a] Average hourly income= average monthly income / average monthly working hours.

[b] Average monthly working hours: male = 177.6 hrs.; female = 172.5 hrs.; caregivers = 175.3 hrs.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	Out-of-pocket costs and…
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	Results: There were…
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5	However, from a patient's as
Objectives	3	State specific objectives, including any prespecified hypotheses	5	We, therefore, conducted
Methods				
Study design	4	Present key elements of study design early in the paper	5	Study design
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5	Ours was a multicentre study …
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6	*Cross-sectional study* Sampling Articulate ESRD patients who were…
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6	We examine the differences in OOP costs...
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6	OOP costs included all expenses related…
Bias	9	Describe any efforts to address potential sources of bias	7	Sensitivity analysis
Study size	10	Explain how the study size was arrived at	6	Sampling

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7	The patient interviews…
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7	Frequencies for categorical...
		(*b*) Describe any methods used to examine subgroups and interactions	NA	
		(*c*) Explain how missing data were addressed	NA	*Cross-sectional study*, face by face interviews, no missing data.
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	7	Finally, as patient characteristics…
		(*e*) Describe any sensitivity analyses	7	Sensitivity analysis
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7	A total of 308 HD patients and 246 PD patients…
		(b) Give reasons for non-participation at each stage	NA	
		(c) Consider use of a flow diagram	NA	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7, 15-17	Table 1 and table 2
		(b) Indicate number of participants with missing data for each variable of interest	NA	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA	*Cross-sectional study*
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA	
		Cross-sectional study—Report numbers of outcome events or summary measures	8, 18-20	Table 3 and table 4
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8, 18-20	Table 3 and table 4
		(*b*) Report category boundaries when continuous variables were categorized	8, 18-20	Table 3 and table 4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful	NA	

		time period		
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9, 21	Table 5
Discussion				
Key results	18	Summarise key results with reference to study objectives	9	The main results of…
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11	The results of this study have some limitations…
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-11	These findings are…
Generalisability	21	Discuss the generalisability (external validity) of the study results	11	To extend the generalisability of…
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12	Funding: This study

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Out-of-pocket costs and productivity losses in haemodialysis and peritoneal dialysis from a patient interview survey in Taiwan

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Secondary Subject Heading:	Medical management
Keywords:	cost, haemodialysis, out-of-pocket cost, peritoneal dialysis, productivity loss

Out-of-pocket costs and productivity losses in haemodialysis and peritoneal dialysis from a patient interview survey in Taiwan

Running title: Costs of HD and PD in Taiwan

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ABSTRACT

Objectives: The total medical (economic) costs of haemodialysis (HD) and peritoneal dialysis (PD), including direct medical costs, out-of-pocket (OOP) costs, and productivity losses, have become an important issue. This study aims to compare the direct non-medical costs and indirect medical costs of both modalities in Taiwan.

Design and Setting: This multicentre study included cross-sectional interviews of patients over 20 years old and articulate, who had been continuously receiving long-term HD or PD for more than three months between April 2015 and March 2016. Mann-Whitney U test, Wilcoxon rank sum test, and 1,000 bootstrap procedures with replacement were used for analysis.

Outcome measures: Differences in OOP costs and productivity losses.

Results: There were 308 HD and 246 PD patients available for analysis. HD patients had significantly higher monthly OOP costs than PD patients after bootstrap procedures (NTD 5,912 vs. NTD 5,225, $p<0.001$; NTD, New Taiwan Dollars; 1 US Dollar = 30 NTD). Compared with PD patients, HD patients had higher monthly productivity losses after bootstrap procedures (NTD 14,150 vs. NTD 11,611, $p<0.001$), resulting from more time spent seeking outpatient care (HD, 70.4 hours vs. PD, 4.4 hours, $p<0.001$) and time spent by family caregivers for outpatient care (HD, 66.1 hours vs. PD, 6.1 hours, $p<0.001$). The total costs per patient-month of HD and PD modalities, including OOP costs and productivity losses were NTD 20,062 and NTD 16,836, respectively.

Conclusions: The HD modality has higher OOP costs and productivity losses than the PD modality in Taiwan.

Keywords: cost, haemodialysis; out-of-pocket cost; peritoneal dialysis; productivity loss

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This multicentre study included cross-sectional interviews of long-term HD and PD patients.
- Previous study seldom assessed the information about out-of-pocket payments and productivity losses collected from patient undergoing HD and PD.
- The difference in the proportion of age groups in HD and PD patients are the major drawback of this study.
- The sample size could not represent the general population of HD and PD patients in Taiwan because the sampled patients were also not randomised

INTRODUCTION

Since March 1995, when Taiwan began implementing the National Health Insurance (NHI) system, the per capita healthcare expenditure has increased annually, especially in the care of 'end-stage renal disease' (ESRD) patients. Taiwan has the highest incidence and prevalence rates of ESRD in the world.[1-3] By 2017, the cost of dialysis (New Taiwan Dollar, NTD 36.9 billion; 1 US dollar = 30 NTDs in Dec. 2017) accounted for a staggering 5.73% of the total annual NHI expenditure (NTD 644.1 billion).[3] Haemodialysis (HD) and peritoneal dialysis (PD) are the two major renal replacement modalities in Taiwan with a similar all-cause mortality rate.[4-7] Several studies have provided clear evidence that HD has the higher direct medical costs among the two modalities.[8-14] NHI administrators implemented several strategies besides applying a blanket budget cap on dialysis expenditure to contain the total costs of dialysis and incentivize the use of PD modality. These efforts included increasing the reimbursements for PD and extending the NHI payment scheme covering the automated PD machine costs. As the proportion of PD usage increases, its prevalence in Taiwan has been gradually increasing, from 6.5% in 2003 to 8.5% in 2007, and up to 9.2% in 2014, similar to the average level within the developed countries.[15-18]

ESRD prevalence is increasing with the rise in the number of aging and diabetic nephropathy patients. The total (economic) costs of HD and PD modalities, including direct medical costs, direct non-medical costs, and productivity losses, have become an important issue.[19] Direct medical costs incurred for medical services, such as dialysis costs, physician and nurses' services, diagnostic tests, and hospitalization costs, are the most common type cited in the nephrologic literature. From a payer's perspective (e.g., national insurance organizations), these costs are the most important. However, from a patient's as well as societal perspectives, out-of-pocket (OOP) costs and productivity losses are nominal and meaningful. OOP costs and productivity losses have not been assessed comprehensively in

ESRD patients for two reasons: the methods for collecting these data for the ESRD patients are not well established, and retrospective data collection is difficult. Only two studies have reported that PD had less OOP costs and productivity losses than HD in Brazil and Singapore, but detailed data were not stated.[12 20] These studies highlighted a significant economic burden due to dialysis and a higher direct healthcare costs associated with the use of HD modality; however, little information is available about OOP costs, including expenses on caregivers or transportation, as well as productivity losses, including job loss, worker replacement, and reduced productivity from patients and family. According to the 2016 Annual Report on Kidney Disease in Taiwan, HD patients had higher NHI expenses (NTD 70,000 per patient-month) than PD patients (NTD 51,000 per patient-month), owing to higher cost of outpatient care (HD, NTD 56,000 per patient-month; PD, NTD 43,000 per patient-month) and inpatient care (HD, NTD 13,400 per patient-month; PD, NTD 8,200 per patient-month).[15] However, the extent to which OOP costs and productivity losses contribute to the overall economic burden of HD and PD are yet to be explored in Taiwan. We, therefore, conducted this study from a patient's and societal perspectives, using face-to-face interviews to compare OOP costs and productivity losses between HD and PD patients in Taiwan.

METHODS

Study Design

Ours was a multicentre study using cross-sectional interviews with patients over 20 years old, carried out at the nephrology outpatient clinics of five hospitals and five dialysis clinics located in northern, central, southern, and eastern Taiwan between April 2015 and March 2016. The Joint Institutional Review Board of Taipei Medical University approved this study (No. 201503057). All participants provided informed consent to participate in this study. All aspects of the study were performed in accordance with relevant guidelines and regulations.

Patient and Public Involvement

No patients were asked for input in the creation of this article.

Sampling

Articulate ESRD patients who were receiving long-term HD or PD continuously for more than three months were chosen. Those aged less than 20 years or unable to communicate were excluded. Patients were recruited and enrolled using a 1:1 male-to-female enrolment design. A total of 581 ESRD patients were screened at the contributing sites, of whom 554 were eligible and enrolled. In total, there were 308 HD patients (156 men, 152 women) and 246 PD patients (124 men, 122 women; 117 automated PD, 129 continuous ambulatory PD) available for analysis.

The patient interviews were performed face by face by well-trained nurses from the site or graduate students from the Taipei Medical University during HD therapy or monthly PD clinic visit. All interviewers had attended prior interviewer training. The patients' baseline characteristics were collected from their medical chart and own response. The patient details collected include sociodemographics, comorbidities, cause of ESRD, and dialysis data (Table 1 and 2). We examine the differences in OOP costs and productivity losses between HD and PD patients. OOP costs included all expenses related to ESRD paid by the patients/family and not reimbursed by the NHI, such as expenses for medicines, medical materials and devices, herbal and alternative medicines, nutritional supplements, transportation costs, and caregiver costs. By using the 'human capital approach',[21] productivity losses were valued and measured by multiplying the loss of time in hours or days with average hourly/daily wage rate reported by the Directorate-General of Budget, Accounting, and Statistics, Taiwan (see supplementary Table S1). There were two sources of time loss being evaluated: patients' and caregivers' time spent in seeking care and time spent in operating the dialysis apparatus at home.

Statistical Analysis

The analyses began with a baseline comparison of patients receiving either HD or PD therapy. Frequencies for categorical variables and means with standard deviations or medians with interquartile ranges for continuous variables were calculated. Statistical differences between the HD and PD patients were determined with Chi-square ($\chi 2$) tests, Mann-Whitney U test and Wilcoxon rank sum test as appropriate to analyse the patient interview survey data. Finally, as patient characteristics and costs may differ outside clinical settings and in different conditions, a bootstrap analysis was further performed on OOP costs and productivity losses, by applying 1,000 bootstrap procedures of HD and PD patients with replacement, stratified by age groups. The difference between the groups was significant for the two-sided *p*-value <0.05. All the analyses in this study were carried out using the SAS 9.3 software (SAS Institute Inc., Cary, NC, USA).

Sensitivity Analysis

Moreover, the HD and PD patients are a group of patients with a debilitating illness and may receive lower wage rates than the general population resulting in lower productivity losses. To assess the impact of productivity losses on the sum of OOP costs and productivity losses, we first defined the total costs of out-of-pocket costs and productivity losses after bootstrap analysis as Model 1. Then we adjusted the productivity losses for the mean Taiwan unemployment rate (3.82%) during the interview period (between April 2015 and March 2016) and then set the productivity losses with a 20%, 30%, or 40% decrement of wages as different scenarios (Model 2–4) to calculate the total amount of these two costs.[22]

RESULTS

A total of 308 HD patients and 246 PD patients were interviewed in the multicentre cross-sectional study. Patient baseline characteristics are shown in Table 1. HD patients were older as more patients were over 70 years old. Diabetes and ischemic heart disease

prevalence was higher and hypertension was lower in HD patients. Hypertension and lupus nephritis had a discernibly different causation of ESRD between the HD and PD patients. Marital status, education, and income were not statistically different between the groups. The dialysis-related baseline data are reported in Table 2, where the maximum differences were found to be the duration of dialysis, haemoglobin, serum albumin, and potassium.

Table 3 shows the results of the per patient-month OOP costs. There were discernible differences between the HD and PD patients in the OOP costs (NTD 5,922 vs. NTD 5,237, p <0.01). The HD patients had significantly lower copayment for outpatient visits, medicine not covered by NHI, and medical equipment, but higher copayment for hospitalizations and transportation than the PD patients. Chinese medication, traditional medicine, and nutritional supplements showed no discernible differences between groups. Another main source of the differences between the HD and PD patients were the transportation costs, owing to more frequent transportation in the former group. However, the results of the mean OOP costs were not consistent in each age group. PD patients had significantly higher OOP costs than the corresponding HD patients in the age groups of 50–59 years old and over 70 years old.

Results of the per patient-month productivity losses are reported in Table 4. Compared with the PD patients, the HD patients had higher monthly productivity losses (NTD 14,147 vs. NTD 11,604, p <0.01), resulting from more time spent seeking outpatient care (HD, 70.4 ± 6.9 hours vs. PD, 4.4 ± 2.5 hours, p <0.001) and time spent by family caregivers for outpatient care (HD, 66.1 ± 51.5 hours vs. PD, 6.1 ± 4.1 hours, p <0.001). However, only 10.4% and 31.3% of HD and PD patients, respectively, had family caregivers who accompanied them for outpatient care. The productivity losses resulting from time spent operating the dialysis apparatus (49.9 ± 27.8 hours) were only seen in PD patients but not HD patients. After the 1,000 bootstrap procedures, the results of the mean productivity losses remained unchanged in each age group. HD patients had significantly lower productivity

losses in the age group over 70 years old because no productivity losses were included beyond the age of 70 years.

Table 5 reports the total costs per patient-month, including OOP costs and productivity losses. The productivity losses were further adjusted for mean Taiwan unemployment rate (3.82%) during the interview survey periods. Models 2–4 show the total costs including OOP costs and productivity losses adjusted for unemployment rate with a 20%, 30%, or 40% decrement of wages as different scenarios. After considering the productivity losses under various scenarios, the differences of total costs between the HD and PD patients slightly decreased in Models 2–4. After stratified by age groups, the total costs per patient-month of HD patients were higher than those of PD patients except in the age group older than 70 years old.

Incorporating the NHI-financed medical costs of HD and PD reported in the 2016 Annual Report on Kidney Disease in Taiwan into the findings in this study [15], Figure 1 shows the per patient-month total costs are NTD 90,062 for HD and NTD 67,836 for PD, to which OOP costs contributed 6.6% and 7.7%, and productivity losses 15.7% and 17.1%, respectively. For the NTD 22,227 per-patient-month difference in the costs of HD and PD, OOP and productivity losses account for 3.1% and 11.4% of the differences, respectively.

DISCUSSION

The main results of this cross-sectional, multicentre interview survey demonstrate that total monthly OOP costs and productivity losses of HD (NTD 19,522) were higher than that of PD (NTD 16,392) after adjusting for unemployment rate. The OOP costs for the HD patients were NTD 687 higher than that for the PD patients, with the greatest difference being found in the costs of copayment to hospitalizations and transportation costs. The main sources of the differences between HD and PD patients for productivity losses were seeking outpatient care and time spent operating the dialysis apparatus. The total economic costs of

HD (NT 90,062), including NHI expenses, OPP costs and productivity losses, were higher than those of PD (NT 67,836), which were most contributed by NHI expenses (NT 19,000, 85.5%) (Figure 1).

These findings are rarely assessed in previous studies but important for the care of ESRD patients because the OOP costs and productivity losses constitute an important, but frequently omitted, part of the overall evaluation of economic burden borne by patients and their families. Previous studies reported that a significantly higher total NHI-financed medical costs were discernible among the HD patients than among the PD patients in several countries, including Taiwan, USA, and UK.[10 15 23] The total costs per patient-month of HD and PD patients, including the OOP costs and productivity losses (Table 5, Model 1), were NTD 20,063 and NTD 16,836, respectively, with a difference of NTD 3,227 per patient-month. From the payer's perspective, the NHI-financed medical costs of PD seems to be a better cost-saving modality; similarly, from a patient's and societal perspective, the total costs per patient-month of HD were higher owing to higher OOP costs except in the age group more than 70 years old (Table 5). Aged ESRD patients often have comorbidities, such as diabetes mellitus with retinopathy and poor vision acuity. Considering the necessity of caregiver's support to complete the every day's procedures, most patients would not choose PD as a favour choice to prevent the OOP cost of caregiver. Compared with HD patients, PD patients with diabetes mellitus or age more than 65 years old also had increased death rate. All these factors would discourage patients to choosing PD as their renal replacement modality.[5]

In this study, productivity losses were estimated according to the human capital approach using the reduced future gross income, including lower paid or unpaid production due to seeking medical care and operating the PD apparatus.[21] Productivity losses accounted for 31.7% of the overall costs in the HD patients, which is similar to 31.8% in the PD

patients. The mean difference of the productivity losses after bootstrap procedures between HD and PD patients was NTD 2,539 (Table 4). The results reflected that the productivity losses, resulting from the time spent seeking outpatient care and operating the dialysis apparatus were significantly lower in the PD than in the HD patients. The productivity losses in HD patients decreased gradually in the older age groups and was higher than those of PD patients in the same age group (Table 4). Unlike the HD patients, who needed to visit a HD centre three times a week, the PD patients could work freely and spent less time in operating the dialysis apparatus and had lower productivity losses. When compared to HD, PD is a self-care and time-saving modality, which explains the lower productivity losses. In patients with chronic kidney disease stage 5 near ESRD, facing with numerous decisions across the trajectory of their illness are needed. Using shared decision making approach offers a patient-centered method to nudge patients facing health-related decisions, including the choice of HD, PD, kidney transplantation or hospice care. The OPP costs and productivity losses have significant impact on quality of lives and cost of healthcare delivery. Exploring the detailed information will provide evidence based, high-quality decision aids and be able to meet patients' informational needs. To extend the generalisability of our findings to other national health systems, our result demonstrates that PD modality may appear to be more suitable for its markedly lower productivity losses for countries with a younger dialysis patient population (less than 70 years old), or with a higher value hourly wage or daily wage. The population characteristics, summarized in Table 1, serves as a basis for considering extending the results to other populations/medical systems. If the baseline characteristics (demographics, clinical need) are similar across populations, the generalizability seems more convincing.

The results of this study confirmed HD modality had higher OOP costs and productivity losses than PD modality shown in previous studies.[12 20] This study also found that

productivity losses contributed 15.2% and 16.5% to the total economic burden of HD and PD, respectively, which were higher than 12.4% and 9.8% found in the Brazilian study.[20] This discrepancy may reflect the difference in healthcare system in Taiwan, where medical care is mainly financed by National Health Insurance and in Brazil where patients pay out-of-pocket for their medical care.

The results of this study have some limitations. First, the difference in the proportion of age groups in HD and PD patients are the major drawback of this study. From the 2016 Annual Report on Kidney Disease in Taiwan, the mean ages of HD and PD commencement in 2014 were 66.7 and 57.3, respectively, which were older than those of HD and PD patients in this cross-sectional study (61.0 and 56.2, respectively, Table 1).[15] Due to this difference, it was difficult to obtain sampling of these two groups of patients in the similar age range. Therefore, we analysed the results by stratifying into four age groups to compare the differences. Second, the results of this study should be interpreted cautiously. The sample size could not represent the general population of HD and PD patients in Taiwan because the sampled patients were also not randomised, although they were sampled from different parts of Taiwan. Third, the impaired productivity or reduced effectiveness at work associated with HD or PD were not included in this study, so the productivity losses may thus have led to an underestimation.

In this study, we present a patient interview survey in Taiwan to analyse the OOP costs and productivity losses for HD and PD patients. From a patient's and societal perspective, the HD patients have higher OOP costs and productivity losses than the PD patients in the age group less than 70 years old owing to higher productivity losses.

Contributors: CHT and YMS: study concept and design. HHC, MJW, BGH, JCT, CCK, SPL, and THC: acquisition of data. CCK, CHT and YMS: analysis and interpretation. CHT and YMS: drafted the manuscript. HHC, MJW, BGH, JCT, SPL, and THC: critical revision

of the manuscript for important intellectual content. All authors: approved the final paper. CHT and YMS are fully responsible for the paper.

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Data sharing statement: All relevant data have been included in the paper.

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Table 1. Patient characteristics of the interview survey patients.

Variables	HD (n=308)		PD (n=246)		*p*-value
Male gender	156	(50.7)	124	(50.4)	0.96
Age (y)	61.0	[12.7]	56.2	[13.9]	<0.01
<50	68	(22.1)	71	(28.9)	
50-59	79	(25.7)	67	(27.2)	
60-69	76	(24.7)	70	(28.5)	
≥70	85	(27.6)	38	(15.5)	
Comorbidities					
Diabetes mellitus	130	(42.2)	74	(30.1)	<0.01
Hypertension	204	(66.2)	193	(78.5)	<0.01
Cancer	17	(5.5)	7	(2.9)	0.13
Chronic obstructive pulmonary disease	5	(1.6)	2	(0.81)	0.40
Cirrhosis of liver	5	(1.6)	3	(1.2)	0.91
Dementia	3	(1.0)	4	(1.6)	0.50
Cerebrovascular disease	8	(2.6)	6	(2.4)	0.91
Peripheral vascular disease	15	(4.9)	8	(3.25)	0.34
Cardiac dysrhythmia	36	(11.7)	20	(8.1)	0.17
Ischemic heart disease	22	(7.1)	6	(2.4)	0.01
Myocardial infarction	11	(3.6)	8	(3.3)	0.84
Chronic heart failure	13	(4.2)	9	(3.7)	0.74
Cause of end-stage renal disease					
Chronic glomerulonephritis	111	(36.0)	82	(33.3)	0.44
Diabetes mellitus	118	(38.3)	71	(28.9)	0.11
Hypertension	108	(35.1)	52	(21.1)	0.02
Hereditary polycystic kidney disease	10	(3.3)	6	(2.4)	0.83
Chronic tubulointerstitial nephritis	5	(1.6)	7	(2.9)	0.19
Lupus nephritis	4	(1.3)	11	(4.5)	<0.01
Others	51	(16.6)	43	(17.5)	0.21
Marital status					0.18
Singled	45	(14.6)	52	(21.1)	
Married	210	(68.2)	159	(64.6)	
Divorced	25	(8.1)	15	(6.2)	
Widowed	28	(9.1)	20	(8.1)	
Education years					0.09
Below primary school	26	(8.4)	15	(6.1)	
Primary school	77	(25.0)	51	(20.7)	
Junior high school	50	(16.2)	31	(12.6)	

Senior high school	88	(28.6)	69	(28.1)	
College	59	(19.2)	66	(26.8)	
Above college	8	(2.6)	14	(5.7)	
Family income (NTD)					0.17
<30,000	93	(30.2)	80	(32.5)	
30,000-49,999	99	(32.1)	61	(24.8)	
50,000-69,999	61	(19.8)	46	(18.7)	
70,000-99,999	31	(10.1)	25	(10.1)	
100,000-149,999	9	(2.9)	23	(9.4)	
150,000-199,999	6	(2.0)	8	(3.3)	
≥200,000	9	(2.9)	3	(1.2)	

Data were number (%) or mean [standard deviation]. HD: haemodialysis; NTD: New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars); PD: peritoneal dialysis.

Table 2. Dialysis related baseline data of interview survey patients.

Variables	HD (n=308)		PD (n=246)		*p*-value
Duration of dialysis (month)	63	(26-135)	37	(16-63)	<0.001
Systolic blood pressure (mmHg)	141.8	[24.7]	141.0	[23.2]	0.58
Diastolic blood pressure (mmHg)	76.1	[12.6]	82.3	[14.9]	<0.001
Heart rate (beats/min)	77.5	[10.3]	81.8	[15.1]	<0.01
Serum albumin (g/dL)	4.0	[0.4]	3.8	[0.7]	<0.001
Serum potassium (mmol/L)	4.8	[0.8]	4.0	[0.6]	<0.001
Standard Kt/V (HD) or Kt/V (PD)	2.39	[0.32]	1.97	[0.31]	<0.001
Urea reduction ratio	73.9	[6.2]	—	—	—
Weekly creatinine clearance (ml/min)	—	—	60.1	[12.5]	—
Normalized protein nitrogen appearance	—	—	1.0	[0.2]	—
Hemoglobin (g/dL)	10.5	[1.5]	10.1	[1.5]	<0.01
Body mass index	23.7	[4.5]	23.9	[3.9]	0.22

Data were median (interquartile range) or mean [standard deviation]. HD: haemodialysis; PD: peritoneal dialysis.

Table 3. Per patient-month out-of-pocket costs of the interview survey patients (in NTD).

Variables	HD (n=308) Mean	(SD)	Median	(IQR)	PD (n=246) Mean	(SD)	Median	(IQR)	*p*-value
Before bootstrap procedures									
Total	5,922	(12,963)	1,794	(488-4,784)	5,237	(7,571)	2,492	(1,018-5,598)	<0.01
Copayment to outpatient care	103	(377)	0	(0-120)	361	(696)	120	(50-400)	<0.001
Copayment to inpatient care	2,209	(11,093)	0	(0-0)	995	(2,163)	0	(0-1,240)	<0.001
Medicine not covered by NHI	591	(1,832)	0	(0-417)	995	(1,911)	125	(0-1,078)	<0.001
Medical equipment	110	(448)	0	(0-0)	439	(726)	208	(0-675)	<0.001
Chinese medication	27	(175)	0	(0-0)	183	(2,153)	0	(0-0)	0.53
Traditional medicine	38	(257)	0	(0-0)	51	(550)	0	(0-0)	0.35
Nutritional supplements	241	(749)	0	(0-0)	542	(2,398)	0	(0-106)	0.26
Transportation costs	1,028	(1,707)	293	(0-1,495)	191	(229)	143	(16-293)	<0.001
Caregiver costs	1,574	(5,453)	0	(0-0)	1,480	(5,309)	0	(0-0)	0.90
Stratified by age groups									
Age <50 (y)	3,766	(5,785)			2,771	(3,150)			0.32
Age 50-59 (y)	4,902	(14,857)			5,824	(7,484)			<0.001
Age 60-69 (y)	7,337	(14,140)			4,091	(6,072)			0.68
Age ≥70 (y)	7,330	(13,980)			10,922	(12,006)			<0.01
After bootstrap procedures									
Total	5,912	(819)			5,225	(485)			<0.001
Stratified by age groups									
Age <50 (y)	3,787	(686)			2,776	(375)			<0.001
Age 50-59 (y)	4,814	(1,678)			5,827	(870)			<0.001
Age 60-69 (y)	7,270	(1,559)			4,111	(701)			<0.001

Age ≥70 (y)	7,348 (1,521)	10,932 (1,855)	<0.001

HD: haemodialysis; IQR: interquartile range; NHI: National health Insurance; NTD, New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars); PD: peritoneal dialysis; SD: standard deviation.

Table 4. Per patient-month productivity losses of the interview survey patients (in NTD).

	HD (n=308)				PD (n=246)				
Variables	Mean	(SD)	Median	(IQR)	Mean	(SD)	Median	(IQR)	*p*-value
Before bootstrap procedures									
Total	14,147	(10,746)	13,936	(6,961-20,921)	11,604	(7,949)	10,576	(5,315-16,764)	<0.01
Time spent operating dialysis apparatus	—	—	—	—	8,655	(6,785)	7,450	(3,138-12,700)	
Seeking outpatient care from patients	11,307	(8,007)	12,874	(0-17,567)	774	(591)	798	(399-1,008)	<0.001
Seeking outpatient care from caregivers	1,608	(5,793)	0	(0-0)	400	(759)	0	(0-833)	<0.001
Seeking inpatient care from patients	799	(1,683)	0	(0-0)	1,037	(1,482)	0	(0-2,918)	0.01
Seeking inpatient care from caregivers	433	(1,251)	0	(0-0)	739	(1,290)	0	(0-733)	<0.001
Stratified by age groups									
Age <50 (y)	19,419	(5,888)			13,177	(7,000)			<0.001
Age 50-59 (y)	19,276	(10,606)			14,424	(7,579)			<0.01
Age 60-69 (y)	17,253	(7,901)			12,826	(6,789)			<0.001
Age ≥70 (y)	2,386	(6,184)			1,207	(1,621)			<0.01
After bootstrap procedures									
Total	14,150	(626)			11,611	(510)			<0.001
Stratified by age groups									
Age <50 (y)	19,381	(715)			13,289	(840)			<0.001
Age 50-59 (y)	19,272	(1,162)			14,415	(878)			<0.001
Age 60-69 (y)	17,212	(857)			12,823	(802)			<0.001
Age ≥70 (y)	2,403	(645)			1,206	(255)			<0.001

HD: haemodialysis; IQR: interquartile range; NTD: New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars); PD: peritoneal dialysis; SD: standard deviation.

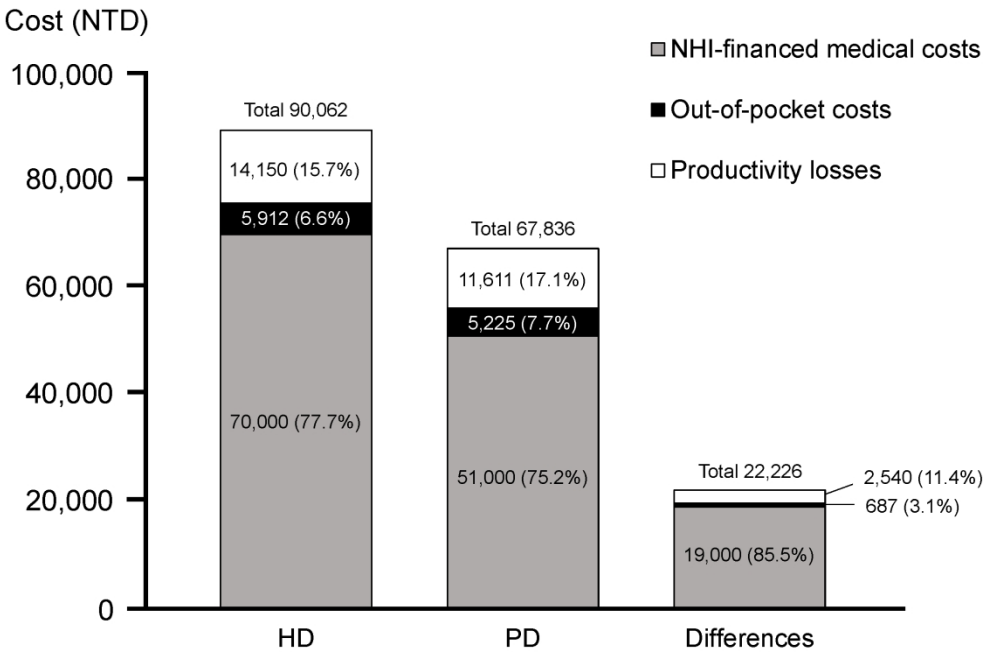
Table 5. Total costs of out-of-pocket costs and productivity losses per patient-month of HD and PD patients after bootstrap analysis (in NTD).

Variables	HD	PD	Difference
(1) Out-of-pocket costs	5,912	5,225	687
Stratified by age groups			
Age <50 (y)	3,787	2,776	1,011
Age 50-59 (y)	4,814	5,827	-1,013
Age 60-69 (y)	7,270	4,111	3,159
Age ≥70 (y)	7,348	10,932	-3,584
(2) Productivity losses	14,150	11,611	2,540
Stratified by age groups			
Age <50 (y)	19,381	13,289	6,093
Age 50-59 (y)	19,272	14,415	4,858
Age 60-69 (y)	17,213	12,823	4,390
Age ≥70 (y)	2,403	1,206	1,197
(3) Total costs			
Model 1 = (1) + (2)	20,062	16,836	3,227
Stratified by age groups			
Age <50 (y)	23,168	16,065	7,103
Age 50-59 (y)	24,086	20,242	3,844
Age 60-69 (y)	24,483	16,934	7,549
Age ≥70 (y)	9,751	12,138	-2,387
Model 2 = (1) + (2) x 20% decrement in wages x (1-0.0382)[a]	16,800	14,159	2,641
Model 3 = (1) + (2) x 30% decrement in wages x (1-0.0382)[a]	15,439	13,042	2,397
Model 4 = (1) + (2) x 40% decrement in wages x (1-0.0382)[a]	14,078	11,925	2,153

HD: haemodialysis; PD: peritoneal dialysis; NHI: National Health Insurance; NTD: New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars).
[a] Adjusted for mean Taiwan unemployment rate (3.82%) between April 2015 and March 2016.

Figure Legends

Figure 1. Distribution of NHI-financed medical cost [15], out-of-pocket costs, and productivity losses, in HD and PD modalities, and their differences. NHI: National Health Insurance; NTD: New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars); HD: haemodialysis; PD: peritoneal dialysis.



221x150mm (300 x 300 DPI)

Supplementary Online Content

Out-of-pocket costs and productivity losses in haemodialysis and peritoneal dialysis from a patient interview survey in Taiwan

Chao-Hsiun Tang, Hsi-Hsien Chen, Ming-Ju Wu, Bang-Gee Hsu, Jer-Chia Tsai, Chi-Cheng Kuo, Shih-Pi Lin, Tso-Hsiao Chen, Yuh-Mou Sue

Table S1. Average monthly/hourly wage rate reported by the Directorate-General of Budget, Accounting, and Statistics, Taiwan.

Table S1. Average monthly/hourly wage rate reported by the Directorate-General of Budget, Accounting, and Statistics, Taiwan.

	Monthly income (NTD)	Hourly income (NTD)[a]
Male[b]		
15 - 19 years	18,300	103
20 - 24 years	25,680	145
25 - 29 years	33,210	187
30 - 34 years	36,090	203
35 - 39 years	40,470	228
40 - 44 years	43,590	245
45 - 49 years	45,930	259
50 - 54 years	44,280	249
55 - 59 years	43,980	248
60 - 64 years	44,760	252
65 - 69 years	34,740	196
70 & over	0	0
Female[b]		
15 - 19 years	16,590	96
20 - 24 years	24,600	143
25 - 29 years	30,420	176
30 - 34 years	32,520	189
35 - 39 years	34,440	200
40 - 44 years	36,000	209
45 - 49 years	36,930	214
50 - 54 years	35,850	208
55 - 59 years	34,830	202
60 - 64 years	34,440	200
65 - 69 years	23,100	134
70 & over	0	0
Caregivers[b]	36,510	208

NTD, New Taiwan Dollar, 1 US Dollar = 30 New Taiwan Dollars.

[a] Average hourly income= average monthly income / average monthly working hours.

[b] Average monthly working hours: male = 177.6 hrs.; female = 172.5 hrs.; caregivers = 175.3 hrs.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	Out-of-pocket costs and…
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	Results: There were…
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5	However, from a patient's as
Objectives	3	State specific objectives, including any prespecified hypotheses	5	We, therefore, conducted
Methods				
Study design	4	Present key elements of study design early in the paper	5	Study design
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5	Ours was a multicentre study …
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6	*Cross-sectional study* Sampling Articulate ESRD patients who were…
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6	We examine the differences in OOP costs...
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6	OOP costs included all expenses related…
Bias	9	Describe any efforts to address potential sources of bias	7	Sensitivity analysis
Study size	10	Explain how the study size was arrived at	6	Sampling

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7	The patient interviews…
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7	Frequencies for categorical...
		(*b*) Describe any methods used to examine subgroups and interactions	NA	
		(*c*) Explain how missing data were addressed	NA	*Cross-sectional study*, face by face interviews, no missing data.
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	7	Finally, as patient characteristics…
		(*e*) Describe any sensitivity analyses	7	Sensitivity analysis
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7	A total of 308 HD patients and 246 PD patients…
		(b) Give reasons for non-participation at each stage	NA	
		(c) Consider use of a flow diagram	NA	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7, 15-17	Table 1 and table 2
		(b) Indicate number of participants with missing data for each variable of interest	NA	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA	*Cross-sectional study*
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA	
		Cross-sectional study—Report numbers of outcome events or summary measures	8, 18-20	Table 3 and table 4
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8, 18-20	Table 3 and table 4
		(*b*) Report category boundaries when continuous variables were categorized	8, 18-20	Table 3 and table 4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful	NA	

		time period		
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9, 21	Table 5
Discussion				
Key results	18	Summarise key results with reference to study objectives	9	The main results of…
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11	The results of this study have some limitations…
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-11	These findings are…
Generalisability	21	Discuss the generalisability (external validity) of the study results	11	To extend the generalisability of…
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12	Funding: This study

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Out-of-pocket costs and productivity losses in haemodialysis and peritoneal dialysis from a patient interview survey in Taiwan

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Secondary Subject Heading:	Medical management, Health economics
Keywords:	cost, haemodialysis, out-of-pocket cost, peritoneal dialysis, productivity loss

Out-of-pocket costs and productivity losses in haemodialysis and peritoneal dialysis from a patient interview survey in Taiwan

Running title: Costs of HD and PD in Taiwan

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ABSTRACT

Objectives: The total medical (economic) costs of haemodialysis (HD) and peritoneal dialysis (PD), including direct medical costs, out-of-pocket (OOP) costs, and productivity losses, have become an important issue. This study aims to compare the direct non-medical costs and indirect medical costs of both modalities in Taiwan.

Design and Setting: This multicentre study included cross-sectional interviews of patients over 20 years old and articulate, who had been continuously receiving long-term HD or PD for more than three months between April 2015 and March 2016. Mann-Whitney U test, Wilcoxon rank sum test, and 1,000 bootstrap procedures with replacement were used for analysis.

Outcome measures: Differences in OOP costs and productivity losses.

Results: There were 308 HD and 246 PD patients available for analysis. HD patients had significantly higher monthly OOP costs than PD patients after bootstrap procedures (NTD 5,912 vs. NTD 5,225, $p<0.001$; NTD, New Taiwan Dollars; 1 US Dollar = 30 NTD). Compared with PD patients, HD patients had higher monthly productivity losses after bootstrap procedures (NTD 14,150 vs. NTD 11,611, $p<0.001$), resulting from more time spent seeking outpatient care (HD, 70.4 hours vs. PD, 4.4 hours, $p<0.001$) and time spent by family caregivers for outpatient care (HD, 66.1 hours vs. PD, 6.1 hours, $p<0.001$). The total costs per patient-month of HD and PD modalities, including OOP costs and productivity losses were NTD 20,062 and NTD 16,836, respectively.

Conclusions: The HD modality has higher OOP costs and productivity losses than the PD modality in Taiwan.

Keywords: cost, haemodialysis; out-of-pocket cost; peritoneal dialysis; productivity loss

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This multicentre study included cross-sectional interviews of long-term HD and PD patients.
- Previous study seldom assessed the information about out-of-pocket payments and productivity losses collected from patient undergoing HD and PD.
- The difference in the proportion of age groups in HD and PD patients are the major drawback of this study.
- The sample size could not represent the general population of HD and PD patients in Taiwan because the sampled patients were also not randomised.
- The 12-month recall period of healthcare utilization in this study could make sure all out-of-pocket information in the previous year captured in the answer but possibly caused a recall bias.

INTRODUCTION

Since March 1995, when Taiwan began implementing the National Health Insurance (NHI) system, the per capita healthcare expenditure has increased annually, especially in the care of 'end-stage renal disease' (ESRD) patients. Taiwan has the highest incidence and prevalence rates of ESRD in the world.[1-3] By 2017, the cost of dialysis (New Taiwan Dollar, NTD 36.9 billion; 1 US dollar = 30 NTDs in Dec. 2017) accounted for a staggering 5.73% of the total annual NHI expenditure (NTD 644.1 billion).[3] Haemodialysis (HD) and peritoneal dialysis (PD) are the two major renal replacement modalities in Taiwan with a similar all-cause mortality rate.[4-7] Several studies have provided clear evidence that HD has the higher direct medical costs among the two modalities.[8-14] NHI administrators implemented several strategies besides applying a blanket budget cap on dialysis expenditure to contain the total costs of dialysis and incentivize the use of PD modality. These efforts included increasing the reimbursements for PD and extending the NHI payment scheme covering the automated PD machine costs. As the proportion of PD usage increases, its prevalence in Taiwan has been gradually increasing, from 6.5% in 2003 to 8.5% in 2007, and up to 9.2% in 2014, similar to the average level within the developed countries.[15-18]

ESRD prevalence is increasing with the rise in the number of aging and diabetic nephropathy patients. The total (economic) costs of HD and PD modalities, including direct medical costs, direct non-medical costs, and productivity losses, have become an important issue.[19] Direct medical costs incurred for medical services, such as dialysis costs, physician and nurses' services, diagnostic tests, and hospitalization costs, are the most common type cited in the nephrologic literature. From a payer's perspective (e.g., national insurance organizations), these costs are the most important. However, from a patient's as well as societal perspectives, out-of-pocket (OOP) costs and productivity losses are nominal and meaningful. OOP costs and productivity losses have not been assessed comprehensively in

ESRD patients for two reasons: the methods for collecting these data for the ESRD patients are not well established, and retrospective data collection is difficult. Only two studies have reported that PD had less OOP costs and productivity losses than HD in Brazil and Singapore, but detailed data were not stated.[12 20] These studies highlighted a significant economic burden due to dialysis and a higher direct healthcare costs associated with the use of HD modality; however, little information is available about OOP costs, including expenses on caregivers or transportation, as well as productivity losses, including job loss, worker replacement, and reduced productivity from patients and family. According to the 2016 Annual Report on Kidney Disease in Taiwan, HD patients had higher NHI expenses (NTD 70,000 per patient-month) than PD patients (NTD 51,000 per patient-month), owing to higher cost of outpatient care (HD, NTD 56,000 per patient-month; PD, NTD 43,000 per patient-month) and inpatient care (HD, NTD 13,400 per patient-month; PD, NTD 8,200 per patient-month).[15] However, the extent to which OOP costs and productivity losses contribute to the overall economic burden of HD and PD are yet to be explored in Taiwan. We, therefore, conducted this study from a patient's and societal perspectives, using face-to-face interviews to compare OOP costs and productivity losses between HD and PD patients in Taiwan.

METHODS

Study Design

Ours was a multicentre study using cross-sectional interviews with patients over 20 years old, carried out at the nephrology outpatient clinics of five hospitals and five dialysis clinics located in northern, central, southern, and eastern Taiwan between April 2015 and March 2016. The Joint Institutional Review Board of Taipei Medical University approved this study (No. 201503057). All participants provided informed consent to participate in this study. All aspects of the study were performed in accordance with relevant guidelines and regulations.

Patient and Public Involvement

No patients were asked for input in the creation of this article.

Sampling

Articulate ESRD patients who were receiving long-term HD or PD continuously for more than three months were chosen. Those aged less than 20 years or unable to communicate were excluded. Patients were recruited and enrolled using a 1:1 male-to-female enrolment design. A total of 581 ESRD patients were screened at the contributing sites, of whom 554 were eligible and enrolled. In total, there were 308 HD patients (156 men, 152 women) and 246 PD patients (124 men, 122 women; 117 automated PD, 129 continuous ambulatory PD) available for analysis.

The patient interviews were performed face by face by well-trained nurses from the site or graduate students from the Taipei Medical University during HD therapy or monthly PD clinic visit. All interviewers had attended prior interviewer training. The patients' baseline characteristics were collected from their medical chart and own response. The patient details collected include sociodemographics, comorbidities, cause of ESRD, and dialysis data (Table 1 and 2). We examine the differences in OOP costs and productivity losses between HD and PD patients. OOP costs included all expenses related to ESRD paid by the patients/family and not reimbursed by the NHI, such as expenses for medicines, medical materials and devices, herbal and alternative medicines, nutritional supplements, transportation costs, and caregiver costs. By using the 'human capital approach',[21] productivity losses were valued and measured by multiplying the loss of time in hours or days with average hourly/daily wage rate reported by the Directorate-General of Budget, Accounting, and Statistics, Taiwan (see supplementary Table S1). There were two sources of time loss being evaluated: patients' and caregivers' time spent in seeking care and time spent in operating the dialysis apparatus at home.

Statistical Analysis

The analyses began with a baseline comparison of patients receiving either HD or PD therapy. Frequencies for categorical variables and means with standard deviations or medians with interquartile ranges for continuous variables were calculated. Statistical differences between the HD and PD patients were determined with Chi-square ($\chi 2$) tests, Mann-Whitney U test and Wilcoxon rank sum test as appropriate to analyse the patient interview survey data. Finally, as patient characteristics and costs may differ outside clinical settings and in different conditions, a bootstrap analysis was further performed on OOP costs and productivity losses, by applying 1,000 bootstrap procedures of HD and PD patients with replacement, stratified by age groups. The difference between the groups was significant for the two-sided *p*-value <0.05. All the analyses in this study were carried out using the SAS 9.3 software (SAS Institute Inc., Cary, NC, USA).

Sensitivity Analysis

Moreover, the HD and PD patients are a group of patients with a debilitating illness and may receive lower wage rates than the general population resulting in lower productivity losses. To assess the impact of productivity losses on the sum of OOP costs and productivity losses, we first defined the total costs of out-of-pocket costs and productivity losses after bootstrap analysis as Model 1. Then we adjusted the productivity losses for the mean Taiwan unemployment rate (3.82%) during the interview period (between April 2015 and March 2016) and then set the productivity losses with a 20%, 30%, or 40% decrement of wages as different scenarios (Model 2–4) to calculate the total amount of these two costs.[22]

RESULTS

A total of 308 HD patients and 246 PD patients were interviewed in the multicentre cross-sectional study. Patient baseline characteristics are shown in Table 1. HD patients were older as more patients were over 70 years old. Diabetes and ischemic heart disease

prevalence was higher and hypertension was lower in HD patients. Hypertension and lupus nephritis had a discernibly different causation of ESRD between the HD and PD patients. Marital status, education, and income were not statistically different between the groups. The dialysis-related baseline data are reported in Table 2, where the maximum differences were found to be the duration of dialysis, haemoglobin, serum albumin, and potassium.

Table 3 shows the results of the per patient-month OOP costs. There were discernible differences between the HD and PD patients in the OOP costs (NTD 5,922 vs. NTD 5,237, p <0.01). The HD patients had significantly lower copayment for outpatient visits, medicine not covered by NHI, and medical equipment, but higher copayment for hospitalizations and transportation than the PD patients. Chinese medication, traditional medicine, and nutritional supplements showed no discernible differences between groups. Another main source of the differences between the HD and PD patients were the transportation costs, owing to more frequent transportation in the former group. However, the results of the mean OOP costs were not consistent in each age group. PD patients had significantly higher OOP costs than the corresponding HD patients in the age groups of 50–59 years old and over 70 years old.

Results of the per patient-month productivity losses are reported in Table 4. Compared with the PD patients, the HD patients had higher monthly productivity losses (NTD 14,147 vs. NTD 11,604, p <0.01), resulting from more time spent seeking outpatient care (HD, 70.4 ± 6.9 hours vs. PD, 4.4 ± 2.5 hours, p <0.001) and time spent by family caregivers for outpatient care (HD, 66.1 ± 51.5 hours vs. PD, 6.1 ± 4.1 hours, p <0.001). However, only 10.4% and 31.3% of HD and PD patients, respectively, had family caregivers who accompanied them for outpatient care. The productivity losses resulting from time spent operating the dialysis apparatus (49.9 ± 27.8 hours) were only seen in PD patients but not HD patients. After the 1,000 bootstrap procedures, the results of the mean productivity losses remained unchanged in each age group. HD patients had significantly lower productivity

losses in the age group over 70 years old because no productivity losses were included beyond the age of 70 years.

Table 5 reports the total costs per patient-month, including OOP costs and productivity losses. The productivity losses were further adjusted for mean Taiwan unemployment rate (3.82%) during the interview survey periods. Models 2–4 show the total costs including OOP costs and productivity losses adjusted for unemployment rate with a 20%, 30%, or 40% decrement of wages as different scenarios. After considering the productivity losses under various scenarios, the differences of total costs between the HD and PD patients slightly decreased in Models 2–4. After stratified by age groups, the total costs per patient-month of HD patients were higher than those of PD patients except in the age group older than 70 years old.

Incorporating the NHI-financed medical costs of HD and PD reported in the 2016 Annual Report on Kidney Disease in Taiwan into the findings in this study [15], Figure 1 shows the per patient-month total costs are NTD 90,062 for HD and NTD 67,836 for PD, to which OOP costs contributed 6.6% and 7.7%, and productivity losses 15.7% and 17.1%, respectively. For the NTD 22,227 per-patient-month difference in the costs of HD and PD, OOP and productivity losses account for 3.1% and 11.4% of the differences, respectively.

DISCUSSION

The main results of this cross-sectional, multicentre interview survey demonstrate that total monthly OOP costs and productivity losses of HD (NTD 19,522) were higher than that of PD (NTD 16,392) after adjusting for unemployment rate. The OOP costs for the HD patients were NTD 687 higher than that for the PD patients, with the greatest difference being found in the costs of copayment to hospitalizations and transportation costs. The main sources of the differences between HD and PD patients for productivity losses were seeking outpatient care and time spent operating the dialysis apparatus. The total economic costs of

HD (NT 90,062), including NHI expenses, OPP costs and productivity losses, were higher than those of PD (NT 67,836), which were most contributed by NHI expenses (NT 19,000, 85.5%) (Figure 1).

These findings are rarely assessed in previous studies but important for the care of ESRD patients because the OOP costs and productivity losses constitute an important, but frequently omitted, part of the overall evaluation of economic burden borne by patients and their families. Previous studies reported that a significantly higher total NHI-financed medical costs were discernible among the HD patients than among the PD patients in several countries, including Taiwan, USA, and UK.[10 15 23] The total costs per patient-month of HD and PD patients, including the OOP costs and productivity losses (Table 5, Model 1), were NTD 20,063 and NTD 16,836, respectively, with a difference of NTD 3,227 per patient-month. From the payer's perspective, the NHI-financed medical costs of PD seems to be a better cost-saving modality; similarly, from a patient's and societal perspective, the total costs per patient-month of HD were higher owing to higher OOP costs except in the age group more than 70 years old (Table 5). Aged ESRD patients often have comorbidities, such as diabetes mellitus with retinopathy and poor vision acuity. Considering the necessity of caregiver's support to complete the every day's procedures, most patients would not choose PD as a favour choice to prevent the OOP cost of caregiver. Compared with HD patients, PD patients with diabetes mellitus or age more than 65 years old also had increased death rate. All these factors would discourage patients to choosing PD as their renal replacement modality.[5]

In this study, productivity losses were estimated according to the human capital approach using the reduced future gross income, including lower paid or unpaid production due to seeking medical care and operating the PD apparatus.[21] Productivity losses accounted for 31.7% of the overall costs in the HD patients, which is similar to 31.8% in the PD

patients. The mean difference of the productivity losses after bootstrap procedures between HD and PD patients was NTD 2,539 (Table 4). The results reflected that the productivity losses, resulting from the time spent seeking outpatient care and operating the dialysis apparatus were significantly lower in the PD than in the HD patients. The productivity losses in HD patients decreased gradually in the older age groups and were higher than those of PD patients were in the same age group (Table 4). Unlike the HD patients, who needed to visit a HD centre three times a week, the PD patients could work freely, spent less time in operating the dialysis apparatus, and had lower productivity losses. When compared to HD, PD is a self-care and timesaving modality, which explains the lower productivity losses. In patients with chronic kidney disease stage 5 near ESRD, facing with numerous decisions across the trajectory of their illness are needed. Using shared decision-making approach offers a patient-centered method to nudge patients facing health-related decisions, including the choice of HD, PD, kidney transplantation or hospice care. The OPP costs and productivity losses have significant impact on quality of lives and cost of healthcare delivery. Exploring the detailed information will provide evidence based, high-quality decision aids and be able to meet patients' informational needs. To extend the generalisability of our findings to other national health systems, our result demonstrates that PD modality may appear to be more suitable for its markedly lower productivity losses for countries with a younger dialysis patient population (less than 70 years old), or with a higher value hourly wage or daily wage. The population characteristics, summarized in Table 1, serves as a basis for considering extending the results to other populations/medical systems. If the baseline characteristics (demographics, clinical need) are similar across populations, the generalizability seems more convincing.

The results of this study confirmed HD modality had higher OOP costs and productivity losses than PD modality shown in previous studies.[12 20] This study also found that

productivity losses contributed 15.2% and 16.5% to the total economic burden of HD and PD, respectively, which were higher than 12.4% and 9.8% found in the Brazilian study.[20] This discrepancy may reflect the difference in healthcare system in Taiwan, where medical care is mainly financed by National Health Insurance and in Brazil where patients pay out-of-pocket for their medical care.

The results of this study have some limitations. First, the difference in the proportion of age groups in HD and PD patients are the major drawback of this study. From the 2016 Annual Report on Kidney Disease in Taiwan, the mean ages of HD and PD commencement in 2014 were 66.7 and 57.3, respectively, which were older than those of HD and PD patients in this cross-sectional study (61.0 and 56.2, respectively, Table 1).[15] Due to this difference, it was difficult to obtain sampling of these two groups of patients in the similar age range. Therefore, we analysed the results by stratifying into four age groups to compare the differences. Second, the results of this study should be interpreted cautiously. The sample size could not represent the general population of HD and PD patients in Taiwan because the sampled patients were also not randomised, although they were sampled from different parts of Taiwan. Third, the impaired productivity or reduced effectiveness at work associated with HD or PD were not included in this study, so the productivity losses may thus have led to an underestimation. Fourth, when designing a question asking patients about their healthcare utilization, the optimum recall period is always an issue to tackle. While a shorter recall period of healthcare utilization may decrease the likelihood of a recall error, at the same time, it also increases the likelihood of missing information. In this study, we chose 12 months as the recall period to make sure all out-of-pocket information in the previous year captured in the answer and this possibly caused a recall bias.

In this study, we present a patient interview survey in Taiwan to analyse the OOP costs and productivity losses for HD and PD patients. From a patient's and societal perspective, the

HD patients have higher OOP costs and productivity losses than the PD patients do in the age group less than 70 years old owing to higher productivity losses.

Contributors: CHT and YMS: study concept and design. HHC, MJW, BGH, JCT, CCK, SPL, and THC: acquisition of data. CCK, CHT and YMS: analysis and interpretation. CHT and YMS: drafted the manuscript. HHC, MJW, BGH, JCT, SPL, and THC: critical revision of the manuscript for important intellectual content. All authors: approved the final paper. CHT and YMS are fully responsible for the paper.

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Competing interests: None declared.

Data sharing statement: All relevant data have been included in the paper.

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Table 1. Patient characteristics of the interview survey patients.

Variables	HD (n=308)		PD (n=246)		*p*-value
Male gender	156	(50.7)	124	(50.4)	0.96
Age (y)	61.0	[12.7]	56.2	[13.9]	<0.01
<50	68	(22.1)	71	(28.9)	
50-59	79	(25.7)	67	(27.2)	
60-69	76	(24.7)	70	(28.5)	
≥70	85	(27.6)	38	(15.5)	
Comorbidities					
Diabetes mellitus	130	(42.2)	74	(30.1)	<0.01
Hypertension	204	(66.2)	193	(78.5)	<0.01
Cancer	17	(5.5)	7	(2.9)	0.13
Chronic obstructive pulmonary disease	5	(1.6)	2	(0.81)	0.40
Cirrhosis of liver	5	(1.6)	3	(1.2)	0.91
Dementia	3	(1.0)	4	(1.6)	0.50
Cerebrovascular disease	8	(2.6)	6	(2.4)	0.91
Peripheral vascular disease	15	(4.9)	8	(3.25)	0.34
Cardiac dysrhythmia	36	(11.7)	20	(8.1)	0.17
Ischemic heart disease	22	(7.1)	6	(2.4)	0.01
Myocardial infarction	11	(3.6)	8	(3.3)	0.84
Chronic heart failure	13	(4.2)	9	(3.7)	0.74
Cause of end-stage renal disease					
Chronic glomerulonephritis	111	(36.0)	82	(33.3)	0.44
Diabetes mellitus	118	(38.3)	71	(28.9)	0.11
Hypertension	108	(35.1)	52	(21.1)	0.02
Hereditary polycystic kidney disease	10	(3.3)	6	(2.4)	0.83
Chronic tubulointerstitial nephritis	5	(1.6)	7	(2.9)	0.19
Lupus nephritis	4	(1.3)	11	(4.5)	<0.01
Others	51	(16.6)	43	(17.5)	0.21
Marital status					0.18
Singled	45	(14.6)	52	(21.1)	
Married	210	(68.2)	159	(64.6)	
Divorced	25	(8.1)	15	(6.2)	
Widowed	28	(9.1)	20	(8.1)	
Education years					0.09
Below primary school	26	(8.4)	15	(6.1)	
Primary school	77	(25.0)	51	(20.7)	
Junior high school	50	(16.2)	31	(12.6)	

Senior high school	88	(28.6)	69	(28.1)	
College	59	(19.2)	66	(26.8)	
Above college	8	(2.6)	14	(5.7)	
Family income (NTD)					0.17
<30,000	93	(30.2)	80	(32.5)	
30,000-49,999	99	(32.1)	61	(24.8)	
50,000-69,999	61	(19.8)	46	(18.7)	
70,000-99,999	31	(10.1)	25	(10.1)	
100,000-149,999	9	(2.9)	23	(9.4)	
150,000-199,999	6	(2.0)	8	(3.3)	
≥200,000	9	(2.9)	3	(1.2)	

Data were number (%) or mean [standard deviation]. HD: haemodialysis; NTD: New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars); PD: peritoneal dialysis.

Table 2. Dialysis related baseline data of interview survey patients.

Variables	HD (n=308)		PD (n=246)		*p*-value
Duration of dialysis (month)	63	(26-135)	37	(16-63)	<0.001
Systolic blood pressure (mmHg)	141.8	[24.7]	141.0	[23.2]	0.58
Diastolic blood pressure (mmHg)	76.1	[12.6]	82.3	[14.9]	<0.001
Heart rate (beats/min)	77.5	[10.3]	81.8	[15.1]	<0.01
Serum albumin (g/dL)	4.0	[0.4]	3.8	[0.7]	<0.001
Serum potassium (mmol/L)	4.8	[0.8]	4.0	[0.6]	<0.001
Standard Kt/V (HD) or Kt/V (PD)	2.39	[0.32]	1.97	[0.31]	<0.001
Urea reduction ratio	73.9	[6.2]	—	—	—
Weekly creatinine clearance (ml/min)	—	—	60.1	[12.5]	—
Normalized protein nitrogen appearance	—	—	1.0	[0.2]	—
Hemoglobin (g/dL)	10.5	[1.5]	10.1	[1.5]	<0.01
Body mass index	23.7	[4.5]	23.9	[3.9]	0.22

Data were median (interquartile range) or mean [standard deviation]. HD: haemodialysis; PD: peritoneal dialysis.

Table 3. Per patient-month out-of-pocket costs of the interview survey patients (in NTD).

Variables	HD (n=308) Mean	(SD)	Median	(IQR)	PD (n=246) Mean	(SD)	Median	(IQR)	*p*-value
Before bootstrap procedures									
Total	5,922	(12,963)	1,794	(488-4,784)	5,237	(7,571)	2,492	(1,018-5,598)	<0.01
Copayment to outpatient care	103	(377)	0	(0-120)	361	(696)	120	(50-400)	<0.001
Copayment to inpatient care	2,209	(11,093)	0	(0-0)	995	(2,163)	0	(0-1,240)	<0.001
Medicine not covered by NHI	591	(1,832)	0	(0-417)	995	(1,911)	125	(0-1,078)	<0.001
Medical equipment	110	(448)	0	(0-0)	439	(726)	208	(0-675)	<0.001
Chinese medication	27	(175)	0	(0-0)	183	(2,153)	0	(0-0)	0.53
Traditional medicine	38	(257)	0	(0-0)	51	(550)	0	(0-0)	0.35
Nutritional supplements	241	(749)	0	(0-0)	542	(2,398)	0	(0-106)	0.26
Transportation costs	1,028	(1,707)	293	(0-1,495)	191	(229)	143	(16-293)	<0.001
Caregiver costs	1,574	(5,453)	0	(0-0)	1,480	(5,309)	0	(0-0)	0.90
Stratified by age groups									
Age <50 (y)	3,766	(5,785)			2,771	(3,150)			0.32
Age 50-59 (y)	4,902	(14,857)			5,824	(7,484)			<0.001
Age 60-69 (y)	7,337	(14,140)			4,091	(6,072)			0.68
Age ≥70 (y)	7,330	(13,980)			10,922	(12,006)			<0.01
After bootstrap procedures									
Total	5,912	(819)			5,225	(485)			<0.001
Stratified by age groups									
Age <50 (y)	3,787	(686)			2,776	(375)			<0.001
Age 50-59 (y)	4,814	(1,678)			5,827	(870)			<0.001
Age 60-69 (y)	7,270	(1,559)			4,111	(701)			<0.001

Age ≥70 (y)	7,348 (1,521)	10,932 (1,855)	<0.001

HD: haemodialysis; IQR: interquartile range; NHI: National health Insurance; NTD, New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars); PD: peritoneal dialysis; SD: standard deviation.

Table 4. Per patient-month productivity losses of the interview survey patients (in NTD).

	HD (n=308)				PD (n=246)				
Variables	Mean	(SD)	Median	(IQR)	Mean	(SD)	Median	(IQR)	*p*-value
Before bootstrap procedures									
Total	14,147	(10,746)	13,936	(6,961-20,921)	11,604	(7,949)	10,576	(5,315-16,764)	<0.01
Time spent operating dialysis apparatus	—	—	—	—	8,655	(6,785)	7,450	(3,138-12,700)	
Seeking outpatient care from patients	11,307	(8,007)	12,874	(0-17,567)	774	(591)	798	(399-1,008)	<0.001
Seeking outpatient care from caregivers	1,608	(5,793)	0	(0-0)	400	(759)	0	(0-833)	<0.001
Seeking inpatient care from patients	799	(1,683)	0	(0-0)	1,037	(1,482)	0	(0-2,918)	0.01
Seeking inpatient care from caregivers	433	(1,251)	0	(0-0)	739	(1,290)	0	(0-733)	<0.001
Stratified by age groups									
Age <50 (y)	19,419	(5,888)			13,177	(7,000)			<0.001
Age 50-59 (y)	19,276	(10,606)			14,424	(7,579)			<0.01
Age 60-69 (y)	17,253	(7,901)			12,826	(6,789)			<0.001
Age ≥70 (y)	2,386	(6,184)			1,207	(1,621)			<0.01
After bootstrap procedures									
Total	14,150	(626)			11,611	(510)			<0.001
Stratified by age groups									
Age <50 (y)	19,381	(715)			13,289	(840)			<0.001
Age 50-59 (y)	19,272	(1,162)			14,415	(878)			<0.001
Age 60-69 (y)	17,212	(857)			12,823	(802)			<0.001
Age ≥70 (y)	2,403	(645)			1,206	(255)			<0.001

HD: haemodialysis; IQR: interquartile range; NTD: New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars); PD: peritoneal dialysis; SD: standard deviation.

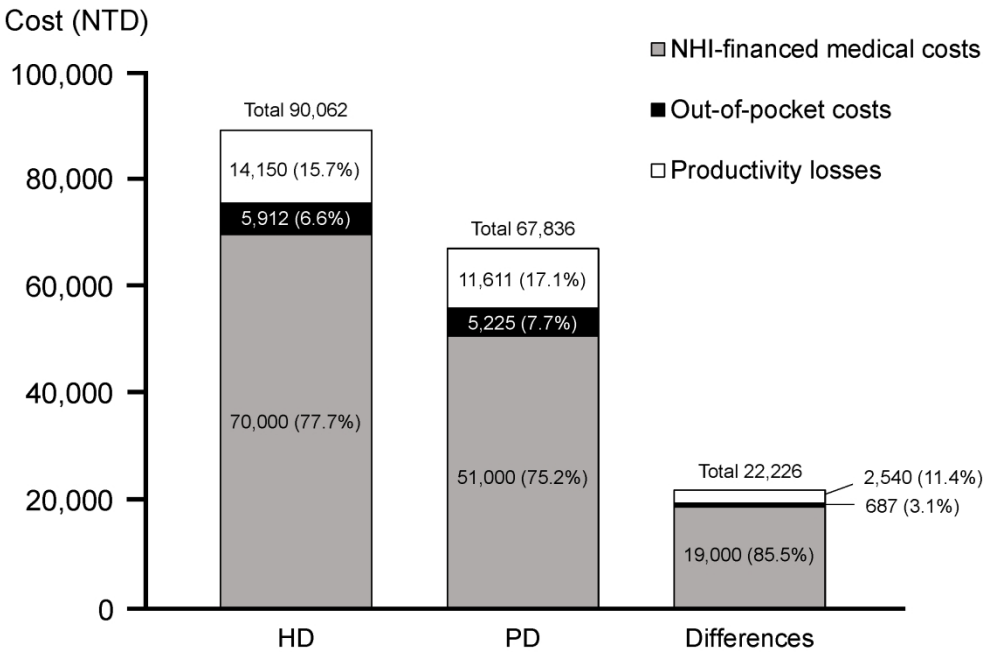
Table 5. Total costs of out-of-pocket costs and productivity losses per patient-month of HD and PD patients after bootstrap analysis (in NTD).

Variables	HD	PD	Difference
(1) Out-of-pocket costs	5,912	5,225	687
Stratified by age groups			
Age <50 (y)	3,787	2,776	1,011
Age 50-59 (y)	4,814	5,827	-1,013
Age 60-69 (y)	7,270	4,111	3,159
Age ≥70 (y)	7,348	10,932	-3,584
(2) Productivity losses	14,150	11,611	2,540
Stratified by age groups			
Age <50 (y)	19,381	13,289	6,093
Age 50-59 (y)	19,272	14,415	4,858
Age 60-69 (y)	17,213	12,823	4,390
Age ≥70 (y)	2,403	1,206	1,197
(3) Total costs			
Model 1 = (1) + (2)	20,062	16,836	3,227
Stratified by age groups			
Age <50 (y)	23,168	16,065	7,103
Age 50-59 (y)	24,086	20,242	3,844
Age 60-69 (y)	24,483	16,934	7,549
Age ≥70 (y)	9,751	12,138	-2,387
Model 2 = (1) + (2) x 20% decrement in wages x (1-0.0382)[a]	16,800	14,159	2,641
Model 3 = (1) + (2) x 30% decrement in wages x (1-0.0382)[a]	15,439	13,042	2,397
Model 4 = (1) + (2) x 40% decrement in wages x (1-0.0382)[a]	14,078	11,925	2,153

HD: haemodialysis; PD: peritoneal dialysis; NHI: National Health Insurance; NTD: New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars).
[a] Adjusted for mean Taiwan unemployment rate (3.82%) between April 2015 and March 2016.

Figure Legends

Figure 1. Distribution of NHI-financed medical cost [15], out-of-pocket costs, and productivity losses, in HD and PD modalities, and their differences. NHI: National Health Insurance; NTD: New Taiwan Dollar (1 US Dollar = 30 New Taiwan Dollars); HD: haemodialysis; PD: peritoneal dialysis.



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Supplementary Online Content

Out-of-pocket costs and productivity losses in haemodialysis and peritoneal dialysis from a patient interview survey in Taiwan

Chao-Hsiun Tang, Hsi-Hsien Chen, Ming-Ju Wu, Bang-Gee Hsu, Jer-Chia Tsai, Chi-Cheng Kuo, Shih-Pi Lin, Tso-Hsiao Chen, Yuh-Mou Sue

Table S1. Average monthly/hourly wage rate reported by the Directorate-General of Budget, Accounting, and Statistics, Taiwan.

Table S1. Average monthly/hourly wage rate reported by the Directorate-General of Budget, Accounting, and Statistics, Taiwan.

	Monthly income (NTD)	Hourly income (NTD)[a]
Male[b]		
15 - 19 years	18,300	103
20 - 24 years	25,680	145
25 - 29 years	33,210	187
30 - 34 years	36,090	203
35 - 39 years	40,470	228
40 - 44 years	43,590	245
45 - 49 years	45,930	259
50 - 54 years	44,280	249
55 - 59 years	43,980	248
60 - 64 years	44,760	252
65 - 69 years	34,740	196
70 & over	0	0
Female[b]		
15 - 19 years	16,590	96
20 - 24 years	24,600	143
25 - 29 years	30,420	176
30 - 34 years	32,520	189
35 - 39 years	34,440	200
40 - 44 years	36,000	209
45 - 49 years	36,930	214
50 - 54 years	35,850	208
55 - 59 years	34,830	202
60 - 64 years	34,440	200
65 - 69 years	23,100	134
70 & over	0	0
Caregivers[b]	36,510	208

NTD, New Taiwan Dollar, 1 US Dollar = 30 New Taiwan Dollars.

[a] Average hourly income= average monthly income / average monthly working hours.

[b] Average monthly working hours: male = 177.6 hrs.; female = 172.5 hrs.; caregivers = 175.3 hrs.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	Out-of-pocket costs and…
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	Results: There were…
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5	However, from a patient's as
Objectives	3	State specific objectives, including any prespecified hypotheses	5	We, therefore, conducted
Methods				
Study design	4	Present key elements of study design early in the paper	5	Study design
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5	Ours was a multicentre study …
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6	*Cross-sectional study* Sampling Articulate ESRD patients who were…
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6	We examine the differences in OOP costs...
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6	OOP costs included all expenses related…
Bias	9	Describe any efforts to address potential sources of bias	7	Sensitivity analysis
Study size	10	Explain how the study size was arrived at	6	Sampling

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7	The patient interviews…
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7	Frequencies for categorical...
		(*b*) Describe any methods used to examine subgroups and interactions	NA	
		(*c*) Explain how missing data were addressed	NA	*Cross-sectional study*, face by face interviews, no missing data.
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	7	Finally, as patient characteristics…
		(*e*) Describe any sensitivity analyses	7	Sensitivity analysis
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7	A total of 308 HD patients and 246 PD patients…
		(b) Give reasons for non-participation at each stage	NA	
		(c) Consider use of a flow diagram	NA	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7, 15-17	Table 1 and table 2
		(b) Indicate number of participants with missing data for each variable of interest	NA	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA	*Cross-sectional study*
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA	
		Cross-sectional study—Report numbers of outcome events or summary measures	8, 18-20	Table 3 and table 4
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8, 18-20	Table 3 and table 4
		(*b*) Report category boundaries when continuous variables were categorized	8, 18-20	Table 3 and table 4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful	NA	

		time period		
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9, 21	Table 5
Discussion				
Key results	18	Summarise key results with reference to study objectives	9	The main results of…
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11	The results of this study have some limitations…
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-11	These findings are…
Generalisability	21	Discuss the generalisability (external validity) of the study results	11	To extend the generalisability of…
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12	Funding: This study

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.