BMJ Open

Effect of Profit Status in Facilities on Mortality Among Patients with Long-term Hemodialysis: A Nationwide Cohort Study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-045832
Article Type:	Original research
Date Submitted by the Author:	14-Oct-2020
Complete List of Authors:	Liu, Sheng-Yu; Taipei Medical University, School of Medicine, College of Medicine, Cheng, Chong-Yi; Taipei Medical University-Wanfang Hospital, Division of Nephrology, Department of Internal Medicine, Wu, Mei-Yi; Taipei Medical University-Shuang Ho Hospital, Taipei, Taiwan , Department of Nephrology Cheng, Cai-Mei ; Taipei Medical University Shuang Ho Hospital Ministry of Health and Welfare Hsu, Chih-Cheng; National Health Research Institutes Institute of Population Health Sciences Wu, Mai Szu; Taipei Medical University Hospital, Lin, Yenchung; Taipei Medical University Hospital, Division of Nephrology; Taipei Medical University, Division of Nephrology, Department of Internal Medicine, School of Medicine, College of Medicine,
Keywords:	Chronic renal failure < NEPHROLOGY, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Dialysis < NEPHROLOGY, End stage renal failure < NEPHROLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Effect of Profit Status in Facilities on Mortality Among Patients with Long-term Hemodialysis: A Nationwide Cohort Study

Sheng-Yu Liu;[1] Chong-Yi Cheng;[2,3,5] Mei-Yi Wu;[2,3,4] Cai-Mei Cheng,[2,3,4] Chih-Cheng Hsu,[6] Mai-Szu Wu,[2,3,4] Yen-Chung Lin [1,2,3]

[1]Division of Nephrology, Department of Internal Medicine, Taipei Medical University Hospital, Taipei, Taiwan;
[2]Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan;
[3]TMU Research Center of Urology and Kidney（TMU-RCUK）, Taipei Medical University, 110 Taipei, Taiwan;
[4]Division of Nephrology, Department of Internal Medicine, Taipei Medical University-Shuang Ho Hospital, 235 New Taipei City, Taiwan;
[5]Division of Nephrology, Department of Internal Medicine, Taipei Medical University-Wanfang Hospital, 116 Taipei City, Taiwan;
[6]Institute of Population Health Sciences, National Health Research Institutes, Maioli country, Taiwan

Short title: Profit status on Patients' Mortality

The author declared no conflict of interests

Corresponding author:
Yen-Chung Lin M.D., PhD and Mai-Szu Wu M.D.
Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan
And Division of Nephrology, Department of Internal Medicine, Shuang Ho Hospital, Taipei Medical University, Taipei, Taiwan
Email: yclin0229@tmu.edu.tw and maiszuwu@gmail.com

Abstract

Objectives: Over the past two decades, there were hot debates in the USA on whether for-profit or not-for-profit dialysis facilities are better regarding patients' prognosis. This issue is equally important in Taiwan since it's prevalence and incidence of dialysis therapy remains top in the world.

Design: A nationwide retrospective conhort study

Setting: A total 31350 patients were divided into two groups by profit status (for-profit, not-for-profit) of dialysis facilities.

Participants: Uremia patients underwent long-term hemodialysis in private medical centers while public facilities are excluded.

Primary and secondary outcome measures:

Survival analyses are performed to compare the prognosis between two groups. Adjustments with patients' basic profile, failities' geographical distribution, level and established time are carried out to minimize possible confounding effect.

Results: The analysis revealed not-for-profit dialysis facilities warrants better outcomes (HR=0.91, 95%CI [0.89 0.93]). Favorable effect remains with the adjustment of facilities' level, geographic distribution (HR=0.89, 95%CI [0.86 – 0.93]), or established time (HR=0.95, 95%CI [0.89 – 0.95]). Survival analysis based on failities' geographical distribution and level showed better prognosis in medical center at six municipality while worse prognosis is found in metropolitan and local hospital.

Conclusion: Our findings suggest in contemporary settings in Taiwan, treatment at not-for-profit dialysis facilities are associated with better outcomes. The result should be interpreted with caution since the possibility of residual confounding and uncertainty of casual relation exist nature to observational study design.

Keywords: Chronic kidney disease; Hemodialysis; Mortality; Profit status; Uremia

Introduction

Taiwan remains on top of the prevalence and incidence of renal replacement therapy in the world [1], where the prevalence and incidence reached up to 3480 per million people and 504 per million people in 2017 [2]. The total amount of national health insurance on uremia patients that underwent dialysis therapy including hemodialysis (HD) or peritoneal dialysis is 62.91 billion points (1 point≈0.8—0.9 NTD), about 8.7—9.2% of the total health expenditure in Taiwan [2]. Therefore, it's vital to determine factors predicting the patient's survival. Not only will these factors influence the patient's outcome, but also impact the cost-effectiveness of hemodialysis. Of all the factors, the profit status of a dialysis facility is an important concern[3].

In the past two decades, there were debates on whether the profit status of dialysis facilities will influence patients' mortality. According to the meta-analysis published in 2002 by Deveraux, *et al*.[4], the pooled estimate demonstrated that private for-profit (FP) dialysis centers were associated with an increased risk of death (RR= 1.08, 95% CI [1.04-1.13], P<0.001). Nevertheless, the retrospective analysis of USRDS (the United States Renal Data System) by Brooks, *et al.* in 2006 [5] indicated that there's no relationship between dialysis center profit status and patient survival after adjusted by the two-stage least squares variant of instrumental variable estimation with the relative proximity of FP and private-not-for-profit (NFP) dialysis centers to the patient's residence as the instrument. Additionally, the retrospective study by Foley, *et al*.[6] featuring more recent patient data from the Medicare database between 1998-2003 compared to that of Deveraux, *et al*. with patients enrolled between 1973-1997. The result also supports that patients dialyzed at FP and NFP facilities had similar mortality risks (adjusted HR=1.02, 95% CI [0.99-1.06], P=0.143). Finally, the retrospective analysis of USRDS by Brunelli, *et al*.[7], concluded that there is no difference in mortality and hospitalization rates between FP and NFP dialysis clinics when appropriate statistical adjustments are made. This study emphasized their "provider level" approach by

adding potential cofounders such as facility's geographic location, length of facility ownership, vascular access at first dialysis session, and pre-dialysis nephrology care into their analysis.

Despite the abundance of HD patients in Taiwan, there are few literatures on this topic. However, this study is largely influenced by the health policy[8], insurance, structure, and distribution of dialysis facilities. Our research aims at evaluating whether the profit status of dialysis facilities affects the patient's mortality.We are assuming that the factor of profit status among HD centers for mortality or survival benefit in Taiwan is minimal. Further analysis will be done to ensure we take the possible confounding factors into account.

A. Method

1. Setting and Participants: A total of 115,535 patients registered on the Taiwan Renal Registry Data System (TWRDS) from 2005—2012 are enrolled. In Taiwan, all the dialysis centers are obligated to upload patients' information quarterly since 1995. The information is inclusive of patients' biochemical profile, past history, dialysis location and timing. After excluding patients with incomplete data, the remaining 76483 patients are included in our study. If the patient underwent dialysis in multiple facilities, we chose the facility where the patient visited most frequently.
2. Grouping: The profit status of dialysis facilities is divided into two groups including "private for-profit (FP)" and "private not-for-profit (NFP)" while public facilities were excluded. Additionally, the facilities are divided into eight categories as a correction factor, according to 4 levels of medical facilities designated by Taiwanese Ministry of Health and Welfare (Medical center, Metropolitan hospital, Local community hospital, Clinic) and 2 types of geographical distribution in Taiwan (Six special municipalities (SMC) or not). The information concerning the level of the dialysis facility and its geographical distribution can be found in the TWRDS lists of dialysis facilities. In addition, the established time of dialysis facilities is also used as a correction factor. The information is

collected through an online search for official websites or telephone interviews. The facilities are divided into four groups inclusive of Group 1 (Established for 0-5 years), Group 2(6-10 years), Group 3(11-20 years), and Group 4(≥20 years).

3. Survival analysis:

   I. Based on profit status differences: We then perform survival analysis based on the patient's all-cause mortality and compare the hazard ratio between FP and NFP group. The patients in both groups are matched before survival analysis, resulting in 31350 patients in each group. With reference to the studies of Brunelli, *et al*.[7], our research is carried out with 4 stages of correction. The crude data only compare the hazard ration between FP and NFP without correction, Model 1 additionally corrects age and sex. Model 2 and Model 3 further correct CAD (coronary artery disease), MI (myocardial infarction), and DM (diabetes mellitus) rate in the population. Furthermore, Model 2 adds the geographical distribution and level of dialysis facilities as a correction factor, and Model 3 adds the established time as a correction factor. Our primary outcome is all-cause mortality in dialysis patients, which is measured by no longer registering on TWRDS anymore.

   II. Based on facilities' level and geographical distribution: Survival analysis is also performed based on the eight categories of facilities' level and geographical distribution without consideration of profit status to evaluate the possible confounding effect of these categories. It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research. The Taipei Medical University-Joint Institutional Review Board permitted this study under the regulation. (ID: N202004151)

4. Patient and Public Involvement: No patient involved

B. Results

1. Survival analysis based on profit status

I. Baseline characteristics between groups (Table 1): After matching, there are 31,350 in each group (FP and NFP). Most of the baseline characteristics are without significant differences between groups, except for the percentage of hypertension (HTN), congestive heart failure (CHF), left ventricular hypertrophy (LVF), and albumin level.

Table 1.

Baseline characteristics between for-profit and not-for profit group after matching

Variable	Type of facilities by profit status		P-value
	for profit	not-for profit	
Number	31350	31350	
Age (years)	62.3±13.5	62.2±13.5	0.66
Male (%)	15831(50%)	15764(50%)	0.59
DM (%)	16136(51%)	16128(51%)	0.95
HTN (%)	13799(44%)	13459(43%)	<.01
CHF (%)	4803(15%)	4585(15%)	<.05
LVH (%)	4556(15%)	4328(14%)	<.01
CVA (%)	2012(6%)	2038(7%)	0.67
CAD (%)	3815(12%)	3762(12%)	0.52
MI (%)	948(3%)	1027(3%)	0.07
HTN drugs (%)	18475(59%)	18274(58%)	0.1
HD duration (years)	3.55±2.61	3.55±2.61	0.99
Albumin (g/dl)	3.75±0.40	3.74±0.41	<.01
Hct(%)	31.09±3.40	31.05±3.15	0.13
Ca(mg/dl)	9.18±0.71	9.18±0.69	0.33
P(mg/dl)	4.84±1.12	4.83±1.11	0.37
ALK-P(u/l)	128.4±97.1	128.5±100.5	0.91
i-PTH(pg/ml)	226.9±184.0	225.5±175.6	0.32

Note: DM= diabetes mellitus, HTN= hypertension, CHF= chronic heart failure, LVH= Left ventricular hypertrophy, CVA= cerebrovascular accident, CAD= cardiovascular disease, MI= myocardial infarction, HD=hemodialysis, ALK-P= Alkaline phosphatase, i-PTH= intact parathyroid hormone

II. Model 1(Table 2): Both crude data and model 1 showed significantly favorable ($p<.0001$) for NFP groups with a hazard ratio (HR) of 0.93 and 0.91 respectively. Figure 1 shows the Kaplan-Meier survival curve of crude data.

Table 2.

Model 1: adjustments of Age and Sex

Group	Crude			Adjusted		
	HR	95% CL	p-value	HR	95% CL	p-value
for profit	Ref.			Ref.		
not-for profit	0.93	[0.9 0.95]	<.0001	0.91	[0.89 0.93]	<.0001
Age(increase per year old)	1.04	[1.04 1.05]	<.0001	1.05	[1.04 1.05]	<.0001
Sex(Male)	1.1	[1.07 1.12]	<.0001	1.21	[1.18 1.24]	<.0001

III. Model 2(Table 3): Data showed significantly favorable (p<.0001) for the NFP group with a hazard ratio (HR) of 0.89.

Table 3.

Model 2: adjustments of Age, Sex, CAD, MI, DM, Geographical distribution and Facility level

Group	Crude			Adjusted		
	HR	95% CL	p-value	HR	95% CL	p-value
for profit	Ref.			Ref.		
non-for profit	0.93	[0.9 0.95]	<.0001	0.89	[0.86 0.93]	<.0001
Age(increase per year old)	1.04	[1.04 1.05]	<.0001	1.04	[1.04 1.05]	<.0001
Sex(Male)	1.1	[1.07 1.12]	<.0001	1.2	[1.18 1.23]	<.0001
CAD(Y)	0.81	[0.78 0.84]	<.0001	0.69	[0.66 0.71]	<.0001
MI(Y)	1.02	[0.96 1.09]	0.56	1	[0.94 1.07]	0.97
DM(Y)	1.51	[1.48 1.55]	<.0001	1.42	[1.39 1.46]	<.0001
Geographic distribution & Facility level						
Medical center SMC	0.75	[0.72 0.78]	<.0001	0.89	[0.84 0.94]	<.0001
Medical center NSMC	0.77	[0.67 0.89]	<.001	0.9	[0.78 1.05]	0.17
Metropolitan hospital SMC	0.98	[0.95 1.02]	0.36	1.03	[0.98 1.08]	0.33
Metropolitan hospital NSMC	1.06	[1.02 1.1]	<.01	1.14	[1.08 1.2]	<.0001
Local hospital SMC	1.02	[0.98 1.06]	0.3	1.06	[1.01 1.1]	0.01
Local hospital NSMC	1.15	[1.1 1.2]	<.0001	1.15	[1.1 1.21]	<.0001
Clinic SMC	Ref.			Ref.		
Clinic NSMC	0.99	[0.94 1.03]	0.58	1	[0.95 1.04]	0.91

Note: SMC= six municipalities, NSMC= not six municipalities, Y=Yes

IV. Model 3(Table 4): Data showed significantly favorable (p<0.0001) for the NFP group with a hazard ratio (HR) of 0.95.

Table 4.

Model 3 with adjustments of Age, Sex, CAD, MI, DM and Establish time of facilities						
Group	Crude			Adjusted		
	HR	95% CL	p-value	HR	95% CL	p-value
for profit	Ref.			Ref.		
non-for profit	0.93	[0.9 0.95]	<.0001	0.95	[0.89 0.95]	<.0001
Age(increase per year old)	1.04	[1.04 1.05]	<.0001	1.05	[1.04 1.05]	<.0001
Sex(Male)	1.1	[1.07 1.12]	<.0001	1.12	[1.16 1.23]	<.0001
CAD(Y)	0.8	[0.78 0.84]	<.0001	0.84	[0.66 0.72]	<.0001
MI(Y)	1.02	[0.96 1.09]	0.56	1.09	[0.86 1.01]	0.08
DM(Y)	1.51	[1.48 1.55]	<.0001	1.55	[1.4 1.49]	<.0001
Establish time of facilities						
Group 1	Ref.			Ref.		
Group 2	1	[0.93 1.06]	0.9	1.04	[0.97 1.11]	0.24
Group 3	1.07	[1.01 1.13]	<.005	1.13	[1.07 1.2]	<.0001
Group 4	0.96	[0.91 1.02]	0.21	1.07	[1.01 1.13]	0.02

Note: Group 1(Established for 0-5 years), Group 2(6-10 y), Group 3(11-20 y), Group 4(≥20 y), Y=Yes

2. Survival analysis based on facilities' level and geographical distribution

I. Baseline characteristics (Table 5): Without matching, most of the parameters in baseline characteristics show significant differences between the eight groups. Of note, there are more patient number-year in the SMC group in every level of the dialysis facility. The difference is most apparent in the medical center (34783 versus 2311) and clinic level (100192 versus 31450), the influence of this difference on the FP and NFP outcome will be discussed later.

Table 5.

Baseline characteristics of 76483 HD patients based on facilities' level and geographical distribution

Variable	Total population	Facilities' level and geographical distribution								P-value
		Medical Center		Metropolitan Hospital		Local Community Hospital		Clinic		
		SMC	NSMC	SMC	NSMC	SMC	NSMC	SMC	NSMC	
Number	78463	7559	510	10286	9824	10229	6040	24327	7708	
Number-year	310404	34783	2311	40047	38421	40236	22964	100192	31450	
Age (years)	62.4±13.6	60.9±13.9	60.1±14.5	63.0±13.5	63.4±13.3	63±13.7	64±13.2	61.8±13.5	62.3±13.4	<.0001
Male (%)	38529(50%)	3785(50%)	248(49%)	5179(50%)	4861(49%)	5149(50%)	3040(50%)	12414(51%)	3853(50%)	0.2757
DM (%)	38847(51%)	3158(42%)	250(49%)	5441(53%)	5277(54%)	5309(52%)	3209(53%)	12384(51%)	3819(50%)	<.0001
HTN (%)	30728(40%)	2878(38%)	296(58%)	3499(34%)	4484(46%)	4339(42%)	2476(41%)	9367(39%)	3389(44%)	<.0001
CHF (%)	9575(13%)	1144(15%)	83(16%)	964(9%)	1681(17%)	1575(15%)	938(16%)	2430(10%)	760(10%)	<.0001
LVH (%)	8990(12%)	1142(15%)	85(17%)	844(8%)	1400(14%)	1342(13%)	710(12%)	2466(10%)	31001(13%)	<.0001
CVA (%)	5306(7%)	421(6%)	29(6%)	485(5%)	733(7%)	916(9%)	460(8%)	1695(7%)	567(7%)	<.0001
CAD (%)	8789(11%)	572(8%)	79(15%)	1001(10%)	1444(15%)	1247(12%)	623(10%)	2813(12%)	1010(13%)	<.0001
MI (%)	2219(3%)	286(4%)	32(6%)	226(2%)	294(3%)	316(3%)	166(3%)	715(3%)	184(2%)	<.0001
HTM drugs (%)	38957(51%)	4049(54%)	256(50%)	5088(49%)	5817(59%)	5093(50%)	2995(50%)	11487(47%)	4172(54%)	<.0001
HD duration (Years)	3.42±2.67	4.01±2.84	3.93±2.66	3.24±2.61	3.25±2.59	3.28±2.65	3.14±2.59	3.48±2.66	3.46±2.67	<.0001
Albumin(g/dl)	3.77±0.41	3.85±0.39	3.6±0.37	3.71±0.43	3.68±0.44	3.76±0.43	3.69±0.46	3.84±0.36	3.8±0.36	<.0001
Hct(%)	31±3.3	3.85±0.39	3.6±0.37	3.71±0.43	3.68±0.44	3.76±0.43	3.69±0.46	3.84±0.36	3.8±0.36	<.0001
Ca(mg/dl)	9.2±0.7	31.1±3.5	30.9±2.7	30.8±3.2	31±3.1	30.9±3.4	30.6±3.4	31±3.2	31.5±3.2	<.0001
P(mg/dl)	4.79±1.13	9.2±0.68	9.15±0.63	9.16±0.7	9.15±0.7	9.24±0.73	9.14±0.73	9.23±0.68	9.23±0.69	<.0001
ALK-P(u/l)	124.8±97.3	4.94±1.09	4.75±1.11	4.82±1.12	4.81±1.17	4.71±1.15	4.63±1.18	4.81±1.11	4.73±1.09	<.0001
i-PTH(pg/ml)	215.5±173.7	107±76.1	215.2±147.1	135±113.2	130.7±103.8	138.8±113	153.4±116.7	110.9±80.5	118.0±74.3	<.0001

II. Survival analysis (Table 6): Survival analysis with adjustments on age, sex, CAD MI, DM are also performed to compare the impact of facility level and geographic distribution on patients' outcomes. The clinic SMC group is designated as a reference group. There are trends for better outcomes in the medical center level while worse outcomes are observed in the metropolitan hospital and local hospital groups. Non-significant p-values is observed in the medical center NSMC and Clinic NSMC groups, which indicate the outcome is similar to that of clinic SMC.

Table 6.

Survival analysis based on facilities' level and geographical distribution with adjustments

Group	Crude			Adjusted		
	HR	95% CL	p-value	HR	95% CL	p-value
Medical center SMC	0.84	[0.81 0.88]	<.0001	0.83	[0.8 0.87]	<.0001
Medical center NSMC	0.9	[0.79 1.04]	0.144	0.92	[0.8 1.06]	0.23
Metropolitan hospital SMC	1.15	[1.11 1.19]	<.0001	1.08	[1.04 1.11]	<.0001
Metropolitan hospital NSMC	1.18	[1.14 1.22]	<.0001	1.1	[1.06 1.14]	<.0001
Local hospital SMC	1.2	[1.16 1.25]	<.0001	1.16	[1.12 1.2]	<.0001
Local hospital NSMC	1.28	[1.23 1.34]	<.0001	1.18	[1.13 1.23]	<.0001
Clinic SMC	Ref.			Ref.		
Clinic NSMC	1.02	[0.98 1.06]	0.3361	1.02	[0.98 1.06]	0.44
Age(increase per year old)	1.04	[1.04 1.04]	<.0001	1.04	[1.04 1.04]	<.0001
Sex(Male)	1.09	[1.07 1.12]	<.0001	1.18	[1.16 1.2]	<.0001
CAD(Y)	1.45	[1.42 1.48]	<.0001	1.37	[1.34 1.4]	<.0001
MI(Y)	1	[0.94 1.06]	<.0001	1.02	[0.96 1.08]	0.57
DM(Y)	0.78	[0.76 0.81]	<.0001	0.67	[0.65 0.7]	<.0001

Note: SMC= six municipalities, NSMC= not six municipalities, Y=Yes

C. Discussion

In summary, the result of our analysis revealed that private not-for-profit (NFP) dialysis facilities warrant better outcomes in comparison to private for-profit (FP) facilities. The

favorable effect remains with the adjustment of facilities' level, geographic distribution, or established time.

The possible reasons why NFP and FP facilities have different outcomes have been discussed extensively in previous studies[4, 9-11]. By definition, the FP facilities are owned by investors or shareholders. They usually distribute part of their profit directly to owners and aim at increasing the wealth of shareholders. In contrast, NFP facilities are owned by members (communities, religious organizations, non-governmental organizations or universities, etc.) to fulfill certain missions (provide health service, teaching, or research). The revenue should be used for their stated mission and cannot distribute to the members of the organization[11]. Theoretically, the FP facilities result in greater efficiency if there were no barriers to entering the market and there is an observable and measurable outcome[11-13]. Nevertheless, the barrier is often abundant (e.g. high capital investment, technology, faculty training, regulation, and certification) while the outcomes are hardly measurable for customers (patients). The barrier to market, asymmetrical information, risk, and uncertainty nature of the healthcare industry making it prone to become a market failure[14]. The PFP hospitals are associated with higher payments for care in a meta-analysis by Devereaux et al.[15], which indicates the shortcoming of FP facilities when it comes to efficiency. To make matters worse, the FP facilities are often confronted with difficult economic challenges. Shareholders expect 10-15% returns of their investments[9] and taxes may account for 5-6% of total expenses[16]. FP facilities must generate these profits and pay taxes while making an effort to provide the same quality of care as NFP facilities that are free of these excessive expenses[4]. In a health care system in which the funding and resource are relatively fixed, as with the national health insurance in Taiwan, the FP facility may try to cut off other forms of spending to generate more profit. The possible approach to reducing expenses is to employ fewer personnel per run and less-highly skilled personnel[17, 18], shorter duration of dialysis treatment[18, 19], or use less expensive medical

supplies. These approaches may also be associated with higher mortality in FP facilities[19].

Despite concordant with previous results[1, 4], there are some confounding specials to the setting of Taiwan that might influence the outcome disparity between FP and NFP. Table 7 demonstrates the distribution of FP and NFP facilities at each level. All of the medical centers and the majority of metropolitan hospitals are considered as NFP facilities, while most of the clinics are FP facilities. Table 5 shows the person-year data in medical centers and clinics are disproportionate towards six-municipalities (SMC). With table 6 illustrating the favorable outcome in the medical center of SMC, the NFP population could be strongly cofounded by those who went to medical centers in SMC for dialysis therapy. On the other hand, the FP population is less cofounded by the patients of clinics in SMC since no statistical difference is found between the clinic in SMC and NSMC (Table 6). To conclude, the NFP population is affected by the good prognosis of the patient from the medical center in SMC; the FP population is less affected by the neutral outcome of the patient from the clinic in SMC.

There are several limitations to our study. Firstly, as mentioned in previous studies[4, 6, 7], it's impractical and highly unlikely that any randomized control trial will be done on this topic. Namely, the current studies unquestionably suffer from all limitations inherent to observational designs. There may be residual confounding yet to be corrected and the causal relationships between profit status and the patient outcome cannot be directly derived from an observational study design. Secondly, due to the personal information protection law in Taiwan, we are unable to directly gain access to the established time data of the facilities and had to do online search and telephone interviews for the information needed. There are about 30% of the facilities that refused to report any information on established time, resulting in missing data and insufficient correction in Model 3. Correction with geographic distribution and established time (Model 2 + Model 3) is also not performed due to the problem in Model 3. Lastly, most of the high-level medical facilities in Taiwan (Table 7, medical center, and metropolitan hospital)

are established as foundations and are deemed as private not-for-profit facilities. Nonetheless, some of the facilities were established as foundations for the sake of tax exemption and are de facto a for-profit facility. This cofounding cannot be properly addressed through statistics.

Our findings suggest that in contemporary hemodialysis settings in Taiwan, treatment at not-for-profit dialysis facilities is associated with better outcomes. The result should be interpreted with caution since the possibility of residual confounding and uncertainty of casual relation exist in the setting of an observational study. However, the favorable effects of private not-for-profit facilities are demonstrated even in the latest unpublished meta-analysis from the United States[20]. Studies also show shorter hospitalized days or hospitalization rate due to complications in NFP facilities[21, 22]. The effect of the profit status of hemodialysis facility on patient prognosis is a widespread and longstanding problem yet to be corrected. Government regulations should be made for the welfare of dialysis patients and more research with robust study design is needed to investigate the problem more thoroughly.

Table 7.

Level of dialysis facilities and profit status

Level	Private for-profit (FP)	Private not-for-profit (NFP)
Medical center	0	15
Metropolitan hospital	8	45
Local hospital	78	49
Clinic	353	5

D. Conflict of interest:

There is no conflict of interest with both of the authors and the study is not funded.

E. Acknowledgement:

This study is supported by the grant from the Ministry of Science and Technology, R.O.C (MOST 106-2813-C-038-019-B) and Taipei Medical University Hospital (107TMU-TMUH-04)

F. Reference

1. Saran R, R.B., Abbott KC, et al. , *US Renal Data System 2018 Annual Data Report: epidemiology of kidney disease in the United States. .* Am J Kidney Dis., 2019. **73**((3)): p. Svii-Sxxii, S1-S772.
2. Wu, M.S.e.a., *2019 Annual Report on Kidney Disease in Taiwan*, in *Taiwan ESRD Registry*, C.C. Hsu, Editor. 2019: Taiwan Society of Nephrology. p. 4, 28, 50.
3. Chevreul, K., et al., *France: Health System Review.* Health Syst Transit, 2015. **17**(3): p. 1-218, xvii.
4. Devereaux, P.J., et al., *Comparison of mortality between private for-profit and private not-for-profit hemodialysis centers: a systematic review and meta-analysis.* Jama, 2002. **288**(19): p. 2449-57.
5. Brooks, J.M., et al., *Effect of dialysis center profit-status on patient survival: a comparison of risk-adjustment and instrumental variable approaches.* Health Serv Res, 2006. **41**(6): p. 2267-89.
6. Foley, R.N., et al., *Comparative mortality of hemodialysis patients at for-profit and not-for-profit dialysis facilities in the United States, 1998 to 2003: a retrospective analysis.* BMC Nephrol, 2008. **9**: p. 6.
7. Brunelli, S.M., et al., *Confounders of mortality and hospitalization rate calculations for profit and nonprofit dialysis facilities: analytic augmentation.* BMC Nephrol, 2014. **15**: p. 121.
8. Lin, y.-c., et al., *Health policies on dialysis modality selection: A nationwide population cohort study.* BMJ Open, 2017. **7**: p. e013007.
9. Nudelman, P.M. and L.M. Andrews, *The "value added" of not-for-profit health plans.* N Engl J Med, 1996. **334**(16): p. 1057-9.
10. Woolhandler, S. and D.U. Himmelstein, *When money is the mission--the high costs of investor-owned care.* N Engl J Med, 1999. **341**(6): p. 444-6.
11. Herrera, C.A., et al., *Does ownership matter? An overview of systematic reviews of the performance of private for-profit, private not-for-profit and public healthcare providers.* PLoS One, 2014. **9**(12): p. e93456.
12. Rosenthal, G. and W. Newbrander, *Public policy and private sector provision of health services.* Int J Health Plann Manage, 1996. **11**(3): p. 203-16.
13. BH, G., *For-Profit Enterprise in Health Care*. 1986, Institute of Medicine. National Academy Press, Washington DC.
14. I, I., H. A.H, and M. Juni, *MARKET FAILURE IN HEALTH CARE: A REVIEW.* International Journal of Public Health and Clinical Sciences, 2018. **5**: p. 16-25.
15. Devereaux, P.J., et al., *Payments for care at private for-profit and private not-for-profit hospitals: a systematic review and meta-analysis.* CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne, 2004. **170**(12): p. 1817-1824.
16. Friedman, B., P. Hattis, and R. Bogue, *Tax exemption and community benefits of not-for-*

profit hospitals. Advances in health economics and health services research, 1990. **11**: p. 131-58.

17. Hirth, R., M. Chernew, and S. Orzol, *Ownership, Competition, and the Adoption of New Technologies and Cost-Saving Practices in a Fixed-Price Environment.* Inquiry : a journal of medical care organization, provision and financing, 2000. **37**: p. 282-94.
18. Held, P.J., et al., *Price of Dialysis, Unit Staffing, and Length of Dialysis Treatments.* American Journal of Kidney Diseases, 1990. **15**(5): p. 441-450.
19. Held, P.J., et al., *Mortality and Duration of Hemodialysis Treatment.* JAMA, 1991. **265**(7): p. 871-875.
20. al., D.S.e., *Mortality at Private for-Profit and Private not-for-Profit Hemodialysis Centers: A Systematic Review and Meta-analysis* J Gen Intern Med, 2019. **34**(Suppl 2): p. 289.
21. Lee, D.K.K., G.M. Chertow, and S.A. Zenios, *Reexploring differences among for-profit and nonprofit dialysis providers.* Health services research, 2010. **45**(3): p. 633-646.
22. Dalrymple, L.S., et al., *Comparison of hospitalization rates among for-profit and nonprofit dialysis facilities.* Clin J Am Soc Nephrol, 2014. **9**(1): p. 73-81.

Figure legend Liu SY et al.

Figure 1: The Kaplan-Meier survival curve in HD patients: The survival rate for-profit group about 8.75% decreased comparing to non-profit control group ($P < 0.0001$)

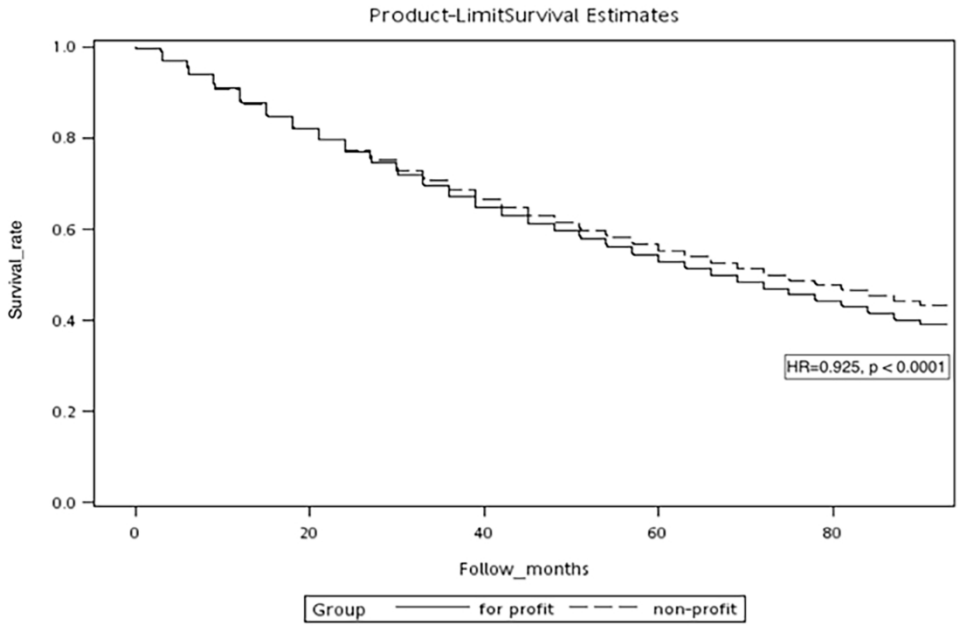

Figure 1: The Kaplan-Meier survival curve in HD patients: The survival rate for-profit group about 8.75% decreased comparing to non-profit control group (P < 0.0001)

181x118mm (300 x 300 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
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	4
		(*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	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
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	5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	
		(*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	
		(*e*) Describe any sensitivity analyses	6
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	6
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	-
		Cross-sectional study—Report numbers of outcome events or summary measures	-
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	7-9, Table 2-4
		(*b*) Report category boundaries when continuous variables were categorized	4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-11, Table 5-6
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
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	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
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	14

*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

Effect of Profit Status in Facilities on Mortality Among Patients with Long-term Hemodialysis: A Nationwide Cohort Study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-045832.R1
Article Type:	Original research
Date Submitted by the Author:	20-Apr-2021
Complete List of Authors:	Liu, Sheng-Yu; Taipei Medical University, School of Medicine, College of Medicine, Cheng, Chung-Yi; Taipei Medical University-Wanfang Hospital, Division of Nephrology, Department of Internal Medicine, Wu, Mei-Yi; Taipei Medical University-Shuang Ho Hospital, Taipei, Taiwan , Department of Nephrology Zheng, Cai-Mei ; Taipei Medical University Shuang Ho Hospital Ministry of Health and Welfare Hsu, Chih-Cheng; National Health Research Institutes Institute of Population Health Sciences Wu, Mai Szu; Taipei Medical University Hospital, Lin, Yen-Chung; Taipei Medical University Hospital, Division of Nephrology; Taipei Medical University, Division of Nephrology, Department of Internal Medicine, School of Medicine, College of Medicine,
Primary Subject Heading:	Renal medicine
Secondary Subject Heading:	Epidemiology, Health policy, Health economics, Health services research
Keywords:	Chronic renal failure < NEPHROLOGY, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Dialysis < NEPHROLOGY, End stage renal failure < NEPHROLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Effect of Profit Status in Facilities on Mortality Among Patients with Long-term Hemodialysis: A Nationwide Cohort Study

Sheng-Yu Liu;[1] Chong-Yi Cheng;[2,3,5] Mei-Yi Wu;[2,3,4] Cai-Mei Zheng,[2,3,4] Chih-Cheng Hsu,[6] Mai-Szu Wu,[2,3,4] Yen-Chung Lin [1,2,3]

[1]Division of Nephrology, Department of Internal Medicine, Taipei Medical University Hospital, Taipei, Taiwan; [2]Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan; [3]TMU Research Center of Urology and Kidney（TMU-RCUK）, Taipei Medical University, 110 Taipei, Taiwan; [4]Division of Nephrology, Department of Internal Medicine, Taipei Medical University-Shuang Ho Hospital, 235 New Taipei City, Taiwan; [5]Division of Nephrology, Department of Internal Medicine, Taipei Medical University-Wanfang Hospital, 116 Taipei City, Taiwan; [6]National Health Research Institutes Institute of Population Health Sciences. Zhunan, Maoli county, Taiwan

Short title: Profit status on Patients' Mortality

The author declared no conflict of interests

Corresponding author:
Yen-Chung Lin M.D., PhD and Mai-Szu Wu M.D.
Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan
And Division of Nephrology, Department of Internal Medicine, Shuang Ho Hospital, Taipei Medical University, Taipei, Taiwan
Email: yclin0229@tmu.edu.tw and maiszuwu@gmail.com

Abstract

Objectives: Over the past two decades, there were hot debates in the USA on whether the profit status of dialysis facilities would influence patients' prognosis. Taiwan remains the highest prevalence and incidence of kidney replacement therapy in the world, but no similar research has been conducted. We aim to be the first study to address this issue.

Design: A nationwide retrospective cohort study based on Taiwan Renal Registry Data System (TWRDS).

Setting: Patients were divided into two groups by profit status (for-profit, not-for-profit) of dialysis facilities, with 31350 patients in each group. The patients are followed up from 2005-2012.

Participants: Uremia patients underwent long-term hemodialysis in private dialysis facilities while public facilities are excluded.

Primary and secondary outcome measures:

Survival analyses are performed to compare the prognosis between two groups. Adjustments with patients' basic profile, facilities' geographical distribution, level and length of ownership are carried out to minimize possible confounding effect.

Results: The analysis revealed not-for-profit dialysis facilities are with better outcome (HR=0.91, 95%CI [0.89 0.93]). Favorable effect remains with the adjustment of facilities' level, geographic distribution (HR=0.89, 95%CI [0.86 – 0.93]), or length of ownership (HR=0.95, 95%CI [0.89 – 0.95]). Survival analysis based on facilities' geographical distribution and level is also conducted, which shows better prognosis in medical center at the six municipality while worse prognosis is found in local hospital not located in the six municipality.

Conclusion: Our findings suggest in contemporary settings in Taiwan, treatment at not-for-profit dialysis facilities are associated with better prognosis. The result should be interpreted with caution since the possibility of residual confounding and uncertainty of casual relation exist nature to

observational study design.

Keywords: Chronic kidney disease; Hemodialysis; Mortality; Profit status; Uremia

Strengths and limitations

- Our study is based on relatively large sample size from a nationwide database (TWRDS).
- Potential confounding effect of the study are minimized by matching study groups, adjusting with facilities' geographic distribution, level and length of ownership.
- Uncontrolled/residual confounding may interfere the association between profit status of facilities and patients' prognosis due to observational study design.
- Missing data from facilities' length of ownership limited further adjustment of this study.
- The study result has limited generalizability to other country on account of different healthcare landscape and insurance system.

Introduction

Taiwan remains on top of the prevalence and incidence of kidney replacement therapy in the world [1], where the prevalence and incidence reached up to 3480 per million people and 504 per million people in 2017 [2]. The total amount of national health insurance on uremia patients that underwent dialysis therapy including hemodialysis (HD) or peritoneal dialysis is about 62 billion NTD (New Taiwanese dollar, converted $2179 million in USD), 8.7 – 9.2% of the total health expenditure in Taiwan in 2019 [2]. Therefore, it's vital to determine factors predicting patients' survival. Not only will these factors influence patient outcome, but also impact the cost-effectiveness of hemodialysis. Of all the factors, the profit status of a dialysis facility is an important concern [3].

In the past two decades, there were debates on whether the profit status of dialysis facilities will influence patients' mortality. According to the meta-analysis published in 2002 by Deveraux, *et al*. [4], the pooled estimation demonstrated that private for-profit (FP) dialysis

facilities were associated with an increased risk of death (RR= 1.08, 95% CI [1.04-1.13], P<0.001). Nevertheless, the retrospective analysis of USRDS (the United States Renal Data System) by Brooks, *et al.* in 2006 [5] indicated that there's no relationship between dialysis facilities' profit status and patient survival after adjusted by two-stage least squares variant of instrumental variable estimation with relative proximity of facilities to the patient's residence as the instrument. Additionally, the retrospective study by Foley, *et al*. [6] featuring more recent patient data from the Medicare database between 1998-2003 compared to that of Deveraux, *et al*. with patients enrolled between 1973-1997. The result also showed no significant difference in patients' mortality between FP and NFP facilities (adjusted HR=1.02, 95% CI [0.99-1.06], P=0.143). Finally, the retrospective analysis of USRDS by Brunelli, *et al*. [7], concluded there is no difference in mortality and hospitalization rates between FP and NFP dialysis facilities when appropriate statistical adjustments are made. This study emphasized their "provider level" approach by adding potential cofounders such as facility's geographic location, length of facility ownership, vascular access at first dialysis session, and pre-dialysis nephrology care into their analysis.

Despite the abundance of HD patients in Taiwan, there are few literatures on this topic. However, this study is largely influenced by the health policy [8], insurance, structure, and distribution of dialysis facilities. The National health insurance (NHI) system of Taiwan covers nearly the total population of Taiwan and a broad range of medical service, inclusive of HD. Patients only need to pay for about $ 3 USD of registration fee for each dialysis course. The fee in similar across different levels of facilities and no specific referral system restrict patients from directly seek dialysis treatment in high level facilities. Under a unified payment system in Taiwan, it's a good opportunity to uncover the pure effect of ownership that might be confounded by the complex setting in the health care market in the United States [9]. Our research aims at evaluating whether the profit status of dialysis facilities affects the patient's

mortality. We are assuming that the factor of profit status among HD centers for mortality or survival benefit in Taiwan is minimal. Further analysis will be done to ensure we take the possible confounding factors into account.

Method:

1. Setting and Participants: Patients registered in the Taiwan Renal Registry Data System (TWRDS) from 2005 – 2012 are enrolled (N=115535). In Taiwan, all the dialysis facilities are obligated to upload patient information quarterly since 1987 [10]. The information is inclusive of patients' biochemical profile, past history, dialysis location and timing. After excluding patients treated with peritoneal dialysis(N=9232), shift between different dialysis modality(N=4661), underwent HD at public facilities(N=20609), with missing biochemical/comorbidity profile(N=2570), remaining 76483 patients are included in our study (Figure 1). If the patient underwent dialysis in multiple facilities, we chose the facility where the patient visited most frequently. Figure 1
2. Patient and Public Involvement: No patient involved.
3. Grouping:
   I. By facilities' ownership and profit status: The profit status of dialysis facilities is divided into two groups including "private for-profit (FP)" and "private not-for-profit (NFP)" while public facilities were excluded. A facility is regarded as private when it's not established by government authority, government-owned enterprises, or public schools [11]. Furthermore, a facility is considered private not-for-profit (NFP) if it's established or operated by a medical foundation [11]. NFP facilities are required to contribute no less than 20% of revenue on research, training, health education, community service or charity. As compensation, NFP facilities are exempt from corporate tax, land and property tax, personal income tax. Reduction on corporate tax tax is also offered [9].

II. By facilities' level and geographical distribution: Facilities are divided into eight categories as a correction factor, according to 4 levels of medical facilities designated by Taiwanese Ministry of Health and Welfare (Medical center, Metropolitan hospital, Local community hospital, Clinic) and 2 types of geographical distribution in Taiwan (Six special municipalities (SMC) or not). The Ministry of Health and Welfare of Taiwan hold hospital accreditation yearly and categorize medical facilities into four levels. A medical center should be a teaching and research hospital with over 500 beds and 23 medical specialties. Metropolitan hospital should be a teaching hospital with more than 300 beds and most of the medical specialties (inclusive of pathology, anesthesiology, radiology, rehabilitation). Local community hospital should be no more than 100 beds and provide general/emergency healthcare service. Clinics are not subject to hospital accreditation with relatively smaller in size [12]. The special municipalities are defined as regions with population of not less than 1,250,000 and have special requirements in their political, economic, cultural, and metropolitan developments [13]. Currently, there are six special municipalities in Taiwan. The information concerning the level of the dialysis facility and its geographical distribution can be found in the TWRDS lists of dialysis facilities. In addition, the dialysis facilities' length of ownership is also used as a correction factor. The information is collected through an online search for official websites or telephone interviews. The facilities are divided into four groups inclusive of Group 1 (Established for 0-5 years), Group 2(6-10 years), Group 3(11-20 years), and Group 4(≥20 years).

4. Statistical analysis: Descriptive statistics are expressed as means ± SD (standard deviations) for continuous variables and proportions for categorical variables. One-way ANOVA test or Kruskal Wallis test is used for the analysis of differences between

continuous variables, and the nominal variables are compared by the χ^2 test. Kaplan-Meier analysis is performed by Log-rank test. Level of significance is set at 0.05, two-tailed for all tests. Cox regression model for survival analysis is performed to estimate the hazard ratios (HR) of all-cause mortality in HD patients. Primary endpoint of our study is all-cause mortality. An individual is considered to be dead if he or she is lost to follow-up in the TWRDS based on the complete national coverage provided by the NHI policy for all kidney replacement therapy expenditures in Taiwan. All descriptive and multivariate analyses are performed using the Statistical Package for the Social Sciences software version 17.0 for Windows XP (SPSS Inc., Chicago, IL, USA) and SAS version 9.1 (SAS Institute, Cary, NC).

I. Survival analysis based on facilities' profit status: We perform survival analysis to compare the HR between FP and NFP group. Propensity score matching by patients' age, sex, biochemical/comorbidity profile (Table 1) are conducted before survival analysis, resulting in 31350 patients in each group. With reference to the studies of Brunelli, *et al*. [7], our research is carried out with 4 models each correcting for different parameters. The crude data compares the hazard ratio between FP and NFP without correction, Model 1 additionally corrects age and sex. Model 2 and Model 3 further correct CAD (coronary artery disease), MI (myocardial infarction), and DM (diabetes mellitus) rate in the population. Furthermore, Model 2 adds the geographical distribution and level of dialysis facilities as a correction factor, and Model 3 adds the length of ownership as a correction factor.

II. Survival analysis based on facilities' level and geographical distribution: Survival analysis is also performed based on the eight categories of facilities' level and geographical distribution without consideration of profit status to evaluate the possible confounding effect of these categories.

Results

1. Survival analysis based on profit status

I. Baseline characteristics between groups (Table 1): After matching, there are 31,350 in each group (FP and NFP). Most of the baseline characteristics are without significant differences between groups, except for the prevalence of hypertension (HTN), congestive heart failure (CHF), left ventricular hypertrophy (LVF), and albumin level.

Table 1.

Baseline characteristics between for-profit and not-for profit group after matching

Variable	Type of facilities by profit status		P-value
	for profit	not-for profit	
Number	31350	31350	
Age (years)	62.3±13.5	62.2±13.5	0.66
Male (%)	15831(50%)	15764(50%)	0.59
DM (%)	16136(51%)	16128(51%)	0.95
HTN (%)	13799(44%)	13459(43%)	<.01
CHF (%)	4803(15%)	4585(15%)	<.05
LVH (%)	4556(15%)	4328(14%)	<.01
CVA (%)	2012(6%)	2038(7%)	0.67
CAD (%)	3815(12%)	3762(12%)	0.52
MI (%)	948(3%)	1027(3%)	0.07
HTN drugs (%)	18475(59%)	18274(58%)	0.1
HD duration (years)	3.55±2.61	3.55±2.61	0.99
Albumin (g/dl)	3.75±0.40	3.74±0.41	<.01
Hct (%)	31.09±3.40	31.05±3.15	0.13
Ca(mg/dl)	9.18±0.71	9.18±0.69	0.33
P(mg/dl)	4.84±1.12	4.83±1.11	0.37
ALK-P(u/l)	128.4±97.1	128.5±100.5	0.91
i-PTH(pg/ml)	226.9±184.0	225.5±175.6	0.32

Note: DM= diabetes mellitus, HTN= hypertension, CHF= chronic heart failure, LVH= Left ventricular hypertrophy, CVA= cerebrovascular accident, CAD= cardiovascular disease, MI= myocardial infarction, HD=hemodialysis, ALK-P= Alkaline phosphatase, i-PTH= intact parathyroid hormone

II. Model 1(Table 2, Figure 2): The follow up time is 96 months (from 2005-2012). Both crude data and model 1 showed significantly favorable outcome(p<.0001) for NFP group with a hazard ratio (HR) of 0.93 and 0.91 respectively. Figure 2 shows the Kaplan-Meier survival curve of crude data.

Table 2.

Model 1: adjustments of Age and Sex

Group	Crude				Adjusted			
	HR	95% CI		p-value	HR	95% CI		p-value
for profit	Ref.				Ref.			
not-for profit	0.93	[0.9	0.95]	<.0001	0.91	[0.89	0.93]	<.0001
Age(increase per year old)	1.04	[1.04	1.05]	<.0001	1.05	[1.04	1.05]	<.0001
Sex(Male)	1.1	[1.07	1.12]	<.0001	1.21	[1.18	1.24]	<.0001

Note: 95% CI= 95% Confidence interval

Figure 2

III. Model 2(Table 3): Data showed significantly favorable outcome(p<.0001) for the NFP group with a hazard ratio (HR) of 0.89.

Table 3.

Model 2: adjustments of Age, Sex, CAD, MI, DM, Geographical distribution and Facility level

Group	Crude			Adjusted			
	HR	95% CI	p-value	HR	95% CI		p-value
for profit	Ref.			Ref.			
non-for profit	0.93	[0.9 0.95]	<.0001	0.89	[0.86	0.93]	<.0001
Age(increase per year old)	1.04	[1.04	1.05] <.0001	1.04	[1.04	1.05]	<.0001
Sex(Male)	1.1	[1.07	1.12] <.0001	1.2	[1.18	1.23]	<.0001
CAD(Y)	0.81	[0.78	0.84] <.0001	0.69	[0.66	0.71]	<.0001
MI(Y)	1.02	[0.96	1.09] 0.56	1	[0.94	1.07]	0.97
DM(Y)	1.51	[1.48	1.55] <.0001	1.42	[1.39	1.46]	<.0001
Geographic distribution & Facility level							
Medical center SMC	0.75	[0.72	0.78] <.0001	0.89	[0.84	0.94]	<.0001
Medical center NSMC	0.77	[0.67	0.89] <.001	0.9	[0.78	1.05]	0.17
Metropolitan hospital SMC	0.98	[0.95	1.02] 0.36	1.03	[0.98	1.08]	0.33
Metropolitan hospital NSMC	1.06	[1.02 1.1]	<.01	1.14	[1.08 1.2]		<.0001
Local hospital SMC	1.02	[0.98	1.06] 0.3	1.06	[1.01 1.1]		0.01
Local hospital NSMC	1.15	[1.1 1.2]	<.0001	1.15	[1.1 1.21]		<.0001
Clinic SMC	Ref.			Ref.			
Clinic NSMC	0.99	[0.94	1.03] 0.58	1	[0.95	1.04]	0.91

Note: SMC= six municipalities, NSMC= not six municipalities, Y=Yes

IV. Model 3(Table 4): Data showed significantly favorable outcome($p<0.0001$) for the NFP group with a hazard ratio (HR) of 0.95.

Table 4.

Model 3 with adjustments of Age, Sex, CAD, MI, DM and Establish time of facilities

Group	Crude				Adjusted			
	HR	95% CI		p-value	HR	95% CI		p-value
for profit	Ref.				Ref.			
non-for profit	0.93	[0.9 0.95]		<.0001	0.95	[0.89	0.95]	<.0001
Age(increase per year old)	1.04	[1.04	1.05]	<.0001	1.05	[1.04	1.05]	<.0001
Sex(Male)	1.1	[1.07	1.12]	<.0001	1.12	[1.16	1.23]	<.0001
CAD(Y)	0.8	[0.78	0.84]	<.0001	0.84	[0.66	0.72]	<.0001
MI(Y)	1.02	[0.96	1.09]	0.56	1.09	[0.86	1.01]	0.08
DM(Y)	1.51	[1.48	1.55]	<.0001	1.55	[1.4	1.49]	<.0001
Facilities' length of ownership								
Group 1	Ref.				Ref.			
Group 2	1	[0.93	1.06]	0.9	1.04	[0.97	1.11]	0.24
Group 3	1.07	[1.01	1.13]	<.005	1.13	[1.07	1.2]	<.0001
Group 4	0.96	[0.91	1.02]	0.21	1.07	[1.01	1.13]	0.02

Note: Group 1(Established for 0-5 years), Group 2(6-10 y), Group 3(11-20 y), Group 4(≥20 y), Y=Yes

2. Survival analysis based on facilities' level and geographical distribution

I. Baseline characteristics (Table 5): Without matching, most of the parameters in baseline characteristics show significant differences between the eight groups. Of note, there are more patient number-year in the SMC group in every level of the dialysis facility. The difference is most apparent in the medical center (34783 versus 2311) and clinic (100192 versus 31450), the influence of this difference on the FP and NFP outcome will be discussed later in the article.

Table 5.

Baseline characteristics of 76483 HD patients based on facilities' level and geographical distribution

Variable	Total population	Facilities' level and geographical distribution								P-value
		Medical Center		Metropolitan Hospital		Local Community Hospital		Clinic		
		SMC	NSMC	SMC	NSMC	SMC	NSMC	SMC	NSMC	
Number	76483	7559	510	10286	9824	10229	6040	24327	7708	
Person-year	310404	34783	2311	40047	38421	40236	22964	100192	31450	
Age (years)	62.4±13.6	60.9±13.9	60.1±14.5	63.0±13.5	63.4±13.3	63±13.7	64±13.2	61.8±13.5	62.3±13.4	<.0001
Male (%)	38529(50%)	3785(50%)	248(49%)	5179(50%)	4861(49%)	5149(50%)	3040(50%)	12414(51%)	3853(50%)	0.2757
DM (%)	38847(51%)	3158(42%)	250(49%)	5441(53%)	5277(54%)	5309(52%)	3209(53%)	12384(51%)	3819(50%)	<.0001
HTN (%)	30728(40%)	2878(38%)	296(58%)	3499(34%)	4484(46%)	4339(42%)	2476(41%)	9367(39%)	3389(44%)	<.0001
CHF (%)	9575(13%)	1144(15%)	83(16%)	964(9%)	1681(17%)	1575(15%)	938(16%)	2430(10%)	760(10%)	<.0001
LVH (%)	8990(12%)	1142(15%)	85(17%)	844(8%)	1400(14%)	1342(13%)	710(12%)	2466(10%)	31001(13%)	<.0001
CVA (%)	5306(7%)	421(6%)	29(6%)	485(5%)	733(7%)	916(9%)	460(8%)	1695(7%)	567(7%)	<.0001
CAD (%)	8789(11%)	572(8%)	79(15%)	1001(10%)	1444(15%)	1247(12%)	623(10%)	2813(12%)	1010(13%)	<.0001
MI (%)	2219(3%)	286(4%)	32(6%)	226(2%)	294(3%)	316(3%)	166(3%)	715(3%)	184(2%)	<.0001
HTM drugs (%)	38957(51%)	4049(54%)	256(50%)	5088(49%)	5817(59%)	5093(50%)	2995(50%)	11487(47%)	4172(54%)	<.0001
HD duration (Years)	3.42±2.67	4.01±2.84	3.93±2.66	3.24±2.61	3.25±2.59	3.28±2.65	3.14±2.59	3.48±2.66	3.46±2.67	<.0001
Albumin(g/dl)	3.77±0.41	3.85±0.39	3.6±0.37	3.71±0.43	3.68±0.44	3.76±0.43	3.69±0.46	3.84±0.36	3.8±0.36	<.0001
Hct(%)	31±3.3	3.85±0.39	3.6±0.37	3.71±0.43	3.68±0.44	3.76±0.43	3.69±0.46	3.84±0.36	3.8±0.36	<.0001
Ca(mg/dl)	9.2±0.7	31.1±3.5	30.9±2.7	30.8±3.2	31±3.1	30.9±3.4	30.6±3.4	31±3.2	31.5±3.2	<.0001
P(mg/dl)	4.79±1.13	9.2±0.68	9.15±0.63	9.16±0.7	9.15±0.7	9.24±0.73	9.14±0.73	9.23±0.68	9.23±0.69	<.0001
ALK-P(u/l)	124.8±97.3	4.94±1.09	4.75±1.11	4.82±1.12	4.81±1.17	4.71±1.15	4.63±1.18	4.81±1.11	4.73±1.09	<.0001
i-PTH(pg/ml)	215.5±173.7	107±76.1	215.2±147.1	135±113.2	130.7±103.8	138.8±113	153.4±116.7	110.9±80.5	118.0±74.3	<.0001

1
2

II. Survival analysis (Table 6): Survival analysis with adjustments on age, sex, CAD MI, DM are also performed to compare the impact of facility level and geographic distribution on patients' prognosis. The clinic SMC is designated as a reference group. There are trends for better outcome in the medical center level while worse outcome are observed in the metropolitan hospital and local hospital. Non-significant p-values is observed in the medical center NSMC and clinic NSMC, which indicate the outcome is similar to that of clinic SMC.

Table 6.

Survival analysis based on facilities' level and geographical distribution with adjustments

Group	Crude			Adjusted		
	HR	95% CI	p-value	HR	95% CI	p-value
Medical center SMC	0.84	[0.81 0.88]	<.0001	0.83	[0.8 0.87]	<.0001
Medical center NSMC	0.9	[0.79 1.04]	0.144	0.92	[0.8 1.06]	0.23
Metropolitan hospital SMC	1.15	[1.11 1.19]	<.0001	1.08	[1.04 1.11]	<.0001
Metropolitan hospital NSMC	1.18	[1.14 1.22]	<.0001	1.1	[1.06 1.14]	<.0001
Local hospital SMC	1.2	[1.16 1.25]	<.0001	1.16	[1.12 1.2]	<.0001
Local hospital NSMC	1.28	[1.23 1.34]	<.0001	1.18	[1.13 1.23]	<.0001
Clinic SMC	Ref.			Ref.		
Clinic NSMC	1.02	[0.98 1.06]	0.3361	1.02	[0.98 1.06]	0.44
Age(increase per year old)	1.04	[1.04 1.04]	<.0001	1.04	[1.04 1.04]	<.0001
Sex(Male)	1.09	[1.07 1.12]	<.0001	1.18	[1.16 1.2]	<.0001
CAD(Y)	0.78	[0.76 0.81]	<.0001	0.67	[0.65 0.7]	<.0001
MI(Y)	1	[0.94 1.06]	<.0001	1.02	[0.96 1.08]	0.57
DM(Y)	1.45	[1.42 1.48]	<.0001	1.37	[1.34 1.4]	<.0001

Note: SMC= six municipalities, NSMC= not six municipalities, Y=Yes

Table 7.

Level of dialysis facilities and profit status		
Level	Private for-profit (FP)	Private not-for-profit (NFP)
Medical center	0	14
Metropolitan hospital	7	41
Local hospital	71	45
Clinic	207	2

Discussion

In summary, the result of our analysis revealed that private not-for-profit (NFP) dialysis facilities are with better patient outcome in comparison to private for-profit (FP) facilities. The favorable effect remains with the adjustment of facilities' level, geographic distribution, or length of ownership.

The possible reasons why NFP and FP facilities have different outcome have been discussed extensively in previous studies [4, 14-16]. By definition, the FP facilities are owned by investors or shareholders. They usually distribute part of their profit directly to owners and focus on increasing the wealth of shareholders. In contrast, NFP facilities are owned by members (communities, religious organizations, non-governmental organizations or universities, etc.) to fulfill certain missions (provide health service, teaching, or research). The revenue should be used for their stated mission and cannot distribute to the members of the organization [16]. Theoretically, the FP facilities result in greater efficiency if there were no barriers to entering the market and there is an observable and measurable outcome [16-18] Nevertheless, the barrier are numerous (e.g. high capital investment, technology, faculty training, regulation, and certification) while the outcomes are hardly visible for customers (patients). The barriers to market, asymmetrical information, risk, and uncertainty nature of the healthcare industry making it prone to become a market failure [19]. The PFP hospitals are

associated with higher payments for care in a meta-analysis by Devereaux et al. [20], which indicates the shortcoming of FP facilities when it comes to efficiency. To make matters worse, the FP facilities are often confronted with economic challenges. Shareholders expect 10-15% returns of their investments [14] and taxes may account for 5-6% of total expenses [21]. FP facilities must generate these profits and pay taxes while making an effort to provide the same quality of care as NFP facilities that are free of these excessive expenses [4]. In a health care system in which the funding and resource are relatively fixed, as with the national health insurance in Taiwan, the FP facility may try to cut off other forms of spending to generate more profit. The possible approach to reducing expenses is to employ fewer personnel per run and less-highly skilled personnel [22, 23], unwilling to extension personal dialysis time and use less high performance dialyzers [23, 24]. These approaches may also be associated with higher mortality in FP facilities [24].

Despite our study result is in concordance with previous studies [1, 4], there are some possible confounding specific to the setting of Taiwan. Table 7 demonstrates the distribution of FP and NFP facilities at each level. All of the medical centers and the majority of metropolitan hospitals are NFP facilities, while most of the clinics are FP facilities. Table 5 shows the majority of person-year data in medical centers and clinics are contributed by the six-municipalities (SMC). Table 6 illustrated the “medical center SMC” are with the best outcome (HR=0.84, p<.0001), while the “clinic SMC and “clinic NSMC” show no significant survival benefits (HR=ref. and 1.02 respectively, p=0.3361). To conclude, the NFP population may be affected by the good prognosis of the “medical center SMC”; the FP population is less affected by the neutral outcome of the “clinic SMC” .

There are several limitations to our study. Firstly, as mentioned in previous studies [4, 6, 7], it’s impractical and highly unlikely that any randomized control trial will be done on this topic. Namely, the current studies unquestionably suffer from all limitations inherent to observational

designs. There may be residual confounding yet to be corrected and the causal relationships between profit status and the patient outcome cannot be directly derived from an observational study design. Secondly, due to the personal information protection law in Taiwan, we are unable to directly access the facilities' length of ownership data and had to do online search and telephone interviews for the information needed. There are about 30% of the facilities that refused to report information on their length of ownership, resulting in missing data and insufficient correction in Model 3. Correction with geographic distribution and length of ownership (Model 2 + Model 3) is also not performed due to the problem in Model 3. Thirdly, most of the high-level medical facilities in Taiwan (Table 7, medical center, and metropolitan hospital) are established as foundations and are deemed as private not-for-profit facilities. Nonetheless, some of the facilities were established as foundations for the sake of tax exemption and are de facto a for-profit facility. This cofounding cannot be properly addressed through statistics. Lastly, immortal time bias is an important issue in analysis of prevalent patient and survival, especially in our study design with a retrospective, long-term nationwide population-based cohort. Only could we decrease the impact of this bias by time dependent cox regression model for hazard ratio of mortality, and fortunately, a follow-up time up to 7 years (Figure 2) of our cohort may alleviate the bias.

Our findings suggest that in contemporary hemodialysis settings in Taiwan, treatment at not-for-profit dialysis facilities is associated with better outcome. The result should be interpreted with caution since the possibility of residual confounding and uncertainty of casual relation exist in the setting of an observational study. However, the favorable effects of private not-for-profit facilities are demonstrated in the latest unpublished meta-analysis from the United States [25]. Studies also show shorter hospitalized days or hospitalization rate due to complications in NFP facilities [26, 27]. The effect of the profit status of hemodialysis facility on patient prognosis is a widespread and longstanding problem yet to be corrected. Government

regulations should be made for the welfare of dialysis patients and more research with robust study design is needed to investigate the problem more thoroughly.

Conflict of interest

There is no conflict of interest with both of the authors and the study is not funded.

Funding

This study is supported by the grant from the
Ministry of Science and Technology, R.O.C (MOST 106-2813-C-038-019-B) and Taipei Medical University Hospital (107TMU-TMUH-04)

Data Availability Statement

No additional data are available

Ethical Approval Statement

The Taipei Medical University-Joint Institutional Review Board permitted this study under the regulation. (ID: N202004151)

Contributorship statement

Liu SY: manuscript draft
Cheng CY, Wu MY, Zheng CM: study design
Lin YC: data analysis, review of draft
Hsu CC: statistical consultant
Wu MS: grant application, review of draft

Reference

1. Saran R, R.B., Abbott KC, et al. , *US Renal Data System 2018 Annual Data Report: epidemiology of kidney disease in the United States.* . Am J Kidney Dis., 2019. **73**((3)): p. Svii-Sxxii, S1-S772.
2. Wu, M.S.e.a., *2019 Annual Report on Kidney Disease in Taiwan*, in *Taiwan ESRD Registry*, C.C. Hsu, Editor. 2019: Taiwan Society of Nephrology. p. 4, 28, 50.
3. Chevreul, K., et al., *France: Health System Review.* Health Syst Transit, 2015. **17**(3): p. 1-218, xvii.
4. Devereaux, P.J., et al., *Comparison of mortality between private for-profit and private not-for-profit hemodialysis centers: a systematic review and meta-analysis.* Jama, 2002. **288**(19): p. 2449-57.
5. Brooks, J.M., et al., *Effect of dialysis center profit-status on patient survival: a comparison of risk-adjustment and instrumental variable approaches.* Health Serv Res, 2006. **41**(6): p. 2267-89.
6. Foley, R.N., et al., *Comparative mortality of hemodialysis patients at for-profit and not-for-*

profit dialysis facilities in the United States, 1998 to 2003: a retrospective analysis. BMC Nephrol, 2008. **9**: p. 6.

7. Brunelli, S.M., et al., *Confounders of mortality and hospitalization rate calculations for profit and nonprofit dialysis facilities: analytic augmentation.* BMC Nephrol, 2014. **15**: p. 121.
8. Lin, y.-c., et al., *Health policies on dialysis modality selection: A nationwide population cohort study.* BMJ Open, 2017. **7**: p. e013007.
9. Lien, H.-M., S.-Y. Chou, and J.-T. Liu, *Hospital ownership and performance: Evidence from stroke and cardiac treatment in Taiwan.* Journal of Health Economics, 2008. **27**(5): p. 1208-1223.
10. Lin, Y.C., *Incidence and Prevalence of ESRD in Taiwan Renal Registry Data System (TWRDS): 2005-2012.* Acta nephrologica, 2014. **28**: p. 65-68.
11. Taiwan(R.O.C), M.o.H.a.W.o., *Medical Care Act, Article 3*. 2020-01-15.
12. Welfare, M.o.H.a., *Code of Practice on Hospital Accreditation and Teaching Hospital Accreditation*. 2019.
13. Taiwan(R.O.C.), M.o.t.I., *Local Government Act, Article 4*, M.o.t.I. Taiwan(R.O.C.), Editor. 2016-06-22: Laws & Regulations Database of The Republic of China.
14. Nudelman, P.M. and L.M. Andrews, *The "value added" of not-for-profit health plans.* N Engl J Med, 1996. **334**(16): p. 1057-9.
15. Woolhandler, S. and D.U. Himmelstein, *When money is the mission--the high costs of investor-owned care.* N Engl J Med, 1999. **341**(6): p. 444-6.
16. Herrera, C.A., et al., *Does ownership matter? An overview of systematic reviews of the performance of private for-profit, private not-for-profit and public healthcare providers.* PLoS One, 2014. **9**(12): p. e93456.
17. Rosenthal, G. and W. Newbrander, *Public policy and private sector provision of health services.* Int J Health Plann Manage, 1996. **11**(3): p. 203-16.
18. BH, G., *For-Profit Enterprise in Health Care*. 1986, Institute of Medicine. National Academy Press, Washington DC.
19. I, I., H. A.H, and M. Juni, *MARKET FAILURE IN HEALTH CARE: A REVIEW.* International Journal of Public Health and Clinical Sciences, 2018. **5**: p. 16-25.
20. Devereaux, P.J., et al., *Payments for care at private for-profit and private not-for-profit hospitals: a systematic review and meta-analysis.* CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne, 2004. **170**(12): p. 1817-1824.

21. Friedman, B., P. Hattis, and R. Bogue, *Tax exemption and community benefits of not-for-profit hospitals.* Advances in health economics and health services research, 1990. **11**: p. 131-58.

22. Hirth, R., M. Chernew, and S. Orzol, *Ownership, Competition, and the Adoption of New Technologies and Cost-Saving Practices in a Fixed-Price Environment.* Inquiry : a journal of medical care organization, provision and financing, 2000. **37**: p. 282-94.

23. Held, P.J., et al., *Price of Dialysis, Unit Staffing, and Length of Dialysis Treatments.* American Journal of Kidney Diseases, 1990. **15**(5): p. 441-450.

24. Held, P.J., et al., *Mortality and Duration of Hemodialysis Treatment.* JAMA, 1991. **265**(7): p. 871-875.

25. al., D.S.e., *Mortality at Private for-Profit and Private not-for-Profit Hemodialysis Centers: A Systematic Review and Meta-analysis* J Gen Intern Med, 2019. **34**(Suppl 2): p. 289.

26. Dalrymple, L.S., et al., *Comparison of hospitalization rates among for-profit and nonprofit dialysis facilities.* Clin J Am Soc Nephrol, 2014. **9**(1): p. 73-81.

27. Lee, D.K.K., G.M. Chertow, and S.A. Zenios, *Reexploring differences among for-profit and nonprofit dialysis providers.* Health services research, 2010. **45**(3): p. 633-646.

Figure legend
Liu SY et al.

Figure 1: Flowchart of patient selection process

Figure 2: The Kaplan-Meier survival curve in HD patients: The survival rate for-profit group about 8.75% decreased comparing to non-profit control group ($P < 0.0001$)

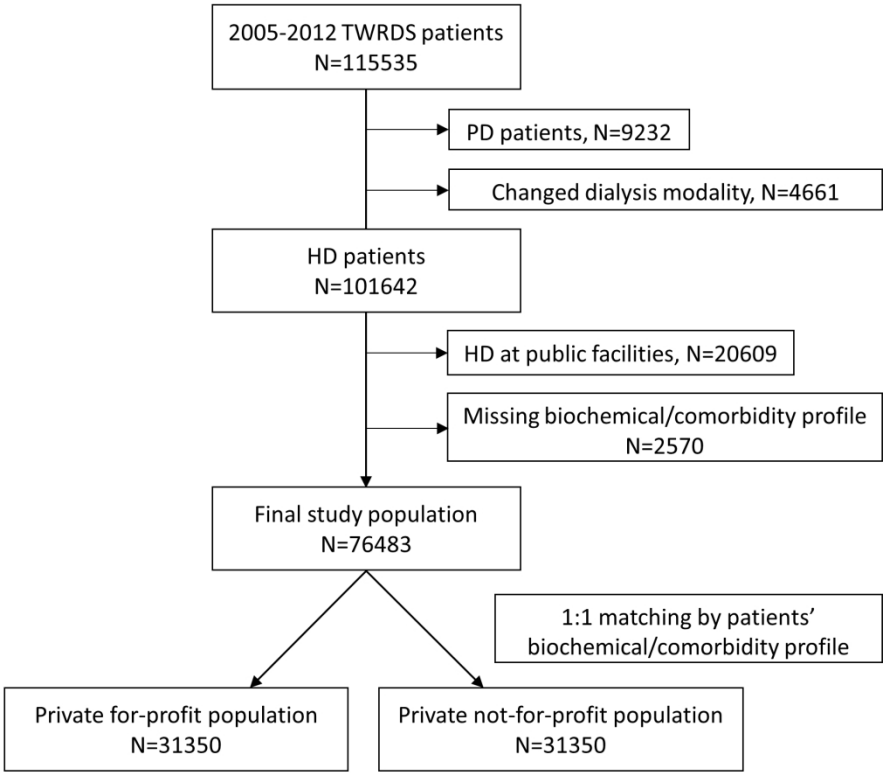

Figure 1: Flowchart of patient selection process

180x160mm (300 x 300 DPI)

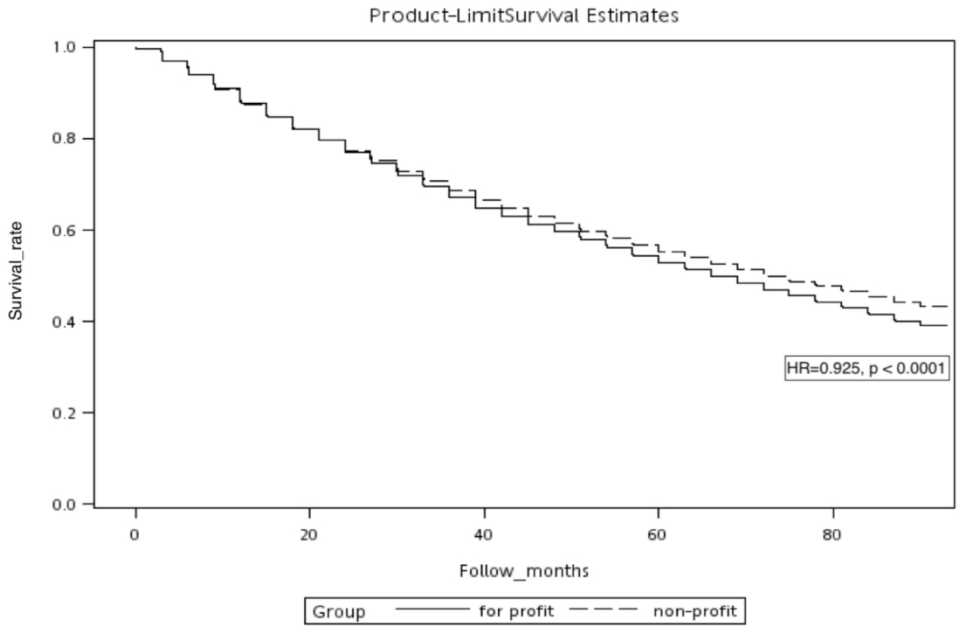

Figure 2: The Kaplan-Meier survival curve in HD patients: The survival rate for-profit group about 8.75% decreased comparing to non-profit control group (P < 0.0001)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any pre-specified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
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	5
		(*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	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
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	5-6
Bias	9	Describe any efforts to address potential sources of bias	5-6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(c) Explain how missing data were addressed	5
		(*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	6

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	6-7
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	5
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	5, Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	5, Figure 1
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	8, Figure 2
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	8, Figure 2
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Not Applicable
		Cross-sectional study—Report numbers of outcome events or summary measures	Not Applicable
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	9-11, Table 2-4
		(*b*) Report category boundaries when continuous variables were categorized	6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not Applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12-14, Table 5-7
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
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	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
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	17

*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

Effect of Profit Status in Facilities on the Mortality of Patients on Long-term Hemodialysis: A Nationwide Cohort Study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-045832.R2
Article Type:	Original research
Date Submitted by the Author:	18-Aug-2021
Complete List of Authors:	Liu, Sheng-Yu; Taipei Medical University, School of Medicine, College of Medicine, Cheng, Chung-Yi; Taipei Medical University-Wanfang Hospital, Division of Nephrology, Department of Internal Medicine, Wu, Mei-Yi; Taipei Medical University-Shuang Ho Hospital, Taipei, Taiwan , Department of Nephrology Zheng, Cai-Mei ; Taipei Medical University Shuang Ho Hospital Ministry of Health and Welfare Hsu, Chih-Cheng; National Health Research Institutes Institute of Population Health Sciences Wu, Mai Szu; Taipei Medical University Hospital, Lin, Yen-Chung; Taipei Medical University Hospital, Division of Nephrology; Taipei Medical University, Division of Nephrology, Department of Internal Medicine, School of Medicine, College of Medicine,
Primary Subject Heading:	Renal medicine
Secondary Subject Heading:	Epidemiology, Health policy, Health economics, Health services research
Keywords:	Chronic renal failure < NEPHROLOGY, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Dialysis < NEPHROLOGY, End stage renal failure < NEPHROLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Effect of Profit Status in Facilities on the Mortality of Patients on Long-term Hemodialysis: A Nationwide Cohort Study

Sheng-Yu Liu,[1] Chung-Yi Cheng,[2,3,5] Mei-Yi Wu,[2,3,4] Cai-Mei Zheng,[2,3,4] Chih-Cheng Hsu,[6] Mai-Szu Wu,[2,3,4] Yen-Chung Lin[1,2,3]

[1]Division of Nephrology, Department of Internal Medicine, Taipei Medical University Hospital, Taipei, Taiwan
[2]Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan
[3]TMU Research Center of Urology and Kidney (TMU-RCUK), Taipei Medical University, 110 Taipei, Taiwan
[4]Division of Nephrology, Department of Internal Medicine, Taipei Medical University-Shuang Ho Hospital, 235 New Taipei City, Taiwan
[5]Division of Nephrology, Department of Internal Medicine, Taipei Medical University-Wanfang Hospital, 116 Taipei City, Taiwan
[6]National Health Research Institutes Institute of Population Health Sciences, 350 Zhunan, Taiwan

Corresponding author:
Yen-Chung Lin, MD, PhD
Department of Internal Medicine, School of Medicine
College of Medicine, Taipei Medical University, Taipei, Taiwan
Email: yclin0229@tmu.edu.tw

Mai-Szu Wu, MD
Division of Nephrology, Department of Internal Medicine
Shuang Ho Hospital, Taipei Medical University, Taipei, Taiwan
Email: maiszuwu@gmail.com

Short title: Profit status on patients' mortality

ABSTRACT

Objectives: Over the past two decades, debates on whether the profit status of dialysis facilities influences patient prognosis have been popular in the United States. Taiwan is one of the regions with the highest rate per capita of kidney replacement therapy worldwide, but no similar research has been conducted to date. This is the first study to address this issue.

Design: This was a nationwide retrospective cohort study based on the Taiwan Renal Registry Data System (TWRDS).

Setting: Patients were categorized into two groups based on the profit status (for-profit, not-for-profit [NFP]) of dialysis facilities, with 31,350 patients in each group. The patients were followed up from 2005 to 2012.

Participants: Patients with uremia who underwent long-term hemodialysis in private dialysis facilities and public facilities were excluded.

Primary and Secondary Outcome Measures: Survival analyses were performed to compare prognosis between the two groups. Adjustments to patients' basic profile, and facilities' geographical distribution, level, and length of ownership were carried out to minimize possible confounding effects.

Results: Analysis revealed that NFP dialysis facilities had better outcomes (hazard ratio [HR]=0.91, 95% confidence interval [CI] [0.89, 0.93]). A favorable effect remains with the adjustment of the facilities' level, geographic distribution (HR=0.89, 95% CI [0.86–0.93]), or length of ownership (HR=0.95, 95% CI [0.89–0.95]). Survival analysis based on the geographical distribution and level of facilities was also conducted, which showed better prognosis in medical centers in the six municipalities, whereas worse prognosis was found in local hospitals not located in these municipalities.

Conclusion: Our findings suggest that in contemporary settings in Taiwan, treatment at NFP dialysis facilities was associated with a better prognosis. The results should be interpreted with caution since

the possibility of residual confounding effects and uncertainty of casual relations exist due to the nature of observational studies.

Keywords: Kidney replacement therapy; Hemodialysis; Survival analysis; Profit status; Uremia

Strengths and limitations of the study

- This study was based on a relatively large sample size from a nationwide database (TWRDS).
- Potential confounding effects of the study were minimized by matching study groups, adjusting for facilities' geographic distribution, level, and length of ownership.
- Uncontrolled/residual confounding factors may interfere with the association between the profit status of facilities and patient prognosis due to the observational study design.
- Missing data from facilities' length of ownership limited further adjustment of this study.
- The study results have limited generalizability to other countries on account of different healthcare landscapes and insurance systems.

INTRODUCTION

Taiwan remains one of the countries with the highest prevalence and incidence of kidney replacement therapy worldwide,[1] as they reached 3,480 per million individuals and 504 per million individuals, respectively, in 2017.[2] The total amount of National Health Insurance for patients with uremia who underwent dialysis therapy, including hemodialysis (HD) or peritoneal dialysis, is approximately 62 billion NTD (New Taiwanese dollar, or US$2,179 million), with 8.7%–9.2% of the total health expenditure in Taiwan in 2019.[2] Therefore, it is vital to determine the factors predicting patients' survival. These factors not only influence patient outcomes, but also impact the cost-effectiveness of HD. Of all the factors, the profit status of a dialysis facility is an important concern.[3]

In the past two decades, there has been debate on whether the profit status of dialysis facilities has an influence on patient mortality. According to a meta-analysis published in 2002 by Deveraux et al.,[4] the pooled estimation demonstrated that private for-profit (FP) dialysis facilities were associated with an increased risk of death (risk ratio [RR] = 1.08, 95% confidence interval [CI] [1.04–1.13], P<0.001). Nevertheless, a retrospective analysis of the United States Renal Data System (USRDS) by Brooks et al. in 2006 [5] indicated that no relationship exists between dialysis facilities' profit status and patient survival after adjusting for the two-stage least squares variant of instrumental variable estimation with the relative proximity of facilities to the patient's residence as the instrument. Additionally, a retrospective study comparing Foley et al.'s study [6], featuring more recent patient data from the Medicare database between 1998 and 2003, with that of Deveraux et al.'s study, with patients enrolled between 1973 and 1997, showed no significant difference in patient mortality between FP and not-for-profit (NFP) facilities (adjusted hazard ratio [HR] = 1.02, 95% CI [0.99–1.06], P = 0.143). Finally, a retrospective analysis of the USRDS by Brunelli et al. [7] concluded that no difference was observed in mortality and hospitalization rates between FP and NFP dialysis facilities when appropriate statistical adjustments were made, which emphasized the

"provider-level" approach by adding potential cofounders such as facility's geographic location, length of facility ownership, vascular access at first dialysis session, and pre-dialysis nephrology care into their analysis.

Despite the abundance of HD patients in Taiwan, few studies are available on this topic. However, this study is largely influenced by the health policy,[8] insurance, structure, and distribution of dialysis facilities. The National Health Insurance (NHI) system of Taiwan covers nearly the entire population of Taiwan and a broad range of medical services, including HD. Patients only need to pay a registration fee of approximately US$3 for each dialysis course. The fee is similar across different levels of facilities, and no specific referral system restricts patients from directly seeking dialysis treatment in high-level facilities. Under a unified payment system in Taiwan, it is a good opportunity to uncover the actual effect of ownership that might be confounded by the complex setting of the healthcare market in the United States.[9] Our research aimed to evaluate whether the profit status of dialysis facilities affects patient mortality. We assume that the effect of profit status among HD centers on mortality or survival benefit in Taiwan is minimal. Further analysis should be performed to ensure that the possible confounding factors are taken into account.

METHODS

Setting and participants

Patients registered in the Taiwan Renal Registry Data System (TWRDS) from 2005 to 2012 were enrolled (N=115,535). In Taiwan, all dialysis facilities have been obligated to upload patient information quarterly since 1987.[10] Information included patients' biochemical profiles, past history, dialysis location, and timing. After excluding patients treated with peritoneal dialysis (N = 9,232), that shift between different dialysis modalities (N = 4,661), who underwent HD at public facilities (N = 20,609), and with missing biochemical/comorbidity profile (N = 2,570), the remaining 76,483 patients were included in our study (Figure 1). If the patient underwent dialysis in

multiple facilities, we chose the facility where the patient visited most frequently. The independent Ethics Committee of Taipei Medical University approved this study (no.: N202004151; Principle investigator: Cai-Mei Zheng) and supervised it in accordance with the tenets of the Declaration of Helsinki (1975) and its later amendment (2013). The study fits all the applicable regulations for waiver of the informed consent.

Patient and Public Involvement:

No patient involved

Figure 1

Grouping

By facilities' ownership and profit status:

The profit status of dialysis facilities was divided into two groups, including "private FP" and "private NFP," whereas public facilities were excluded. A facility was regarded as private when it is not established by government authorities, government-owned enterprises, or public schools.[11] Furthermore, a facility was considered private NFP if it is established or operated by a medical foundation.[11] NFP facilities are required to contribute no less than 20% of revenue on research, training, health education, community service, or charity. As compensation, NFP facilities are exempt from corporate tax, land and property taxes, and personal income tax. A reduction in the corporate tax is also offered.[9]

By facilities' level and geographical distribution:

Facilities were divided into eight categories as a correction factor, according to four levels of medical facilities designated by the Taiwanese Ministry of Health and Welfare (medical center, metropolitan hospital, local community hospital, and clinic) and two types of geographical distribution in Taiwan (six special municipalities [SMC] or not). The Ministry of Health and Welfare of Taiwan holds hospital accreditation yearly and categorizes medical facilities into four levels. A

medical center should be a teaching and research hospital with over 500 beds and 23 medical specialties. Metropolitan hospitals should be teaching hospitals with more than 300 beds and most medical specialties (including pathology, anesthesiology, radiology, and rehabilitation). Local community hospitals should have no more than 100 beds and provide general/emergency healthcare services. Clinics are not subject to hospital accreditation, which are relatively small in size.[12] Special municipalities are defined as regions with populations of not less than 1,250,000 and have special requirements in their political, economic, cultural, and metropolitan development.[13] Currently, there are six municipalities in Taiwan. Information concerning the level of the dialysis facility and its geographical distribution can be found in the TWRDS lists of dialysis facilities. The dialysis facility's length of ownership was also used as a correction factor. Information was collected through an online search of official websites or telephone interviews. The facilities were divided into four groups: Group 1 (established for 0–5 years), Group 2 (6–10 years), Group 3 (11–20 years), and Group 4 (≥20 years).

Statistical analysis

Descriptive statistics were expressed as mean ± standard deviation for continuous variables and proportions for categorical variables. One-way analysis of variance or the Kruskal-Wallis test was used for the analysis of differences between continuous variables, and the nominal variables were compared using the χ^2 test. Kaplan-Meier analysis was performed using the log-rank test. The level of significance was set at 0.05, two-tailed for all tests. A Cox regression model for survival analysis was used to estimate the HRs of all-cause mortality in HD patients. The primary endpoint of our study was all-cause mortality. If a patient switched to other dialysis modalities or received kidney transplant during follow-up period, the patient would be censored. An individual was considered deceased if he or she was lost to follow-up in the TWRDS based on the complete national coverage provided by the NHI policy for all kidney replacement therapy expenditures in Taiwan. All

descriptive and multivariate analyses were performed using the Statistical Package for the Social Sciences software (version 17.0) for Windows XP (SPSS Inc., Chicago, IL, USA) and SAS version 9.1 (SAS Institute, Cary, NC).

Survival analysis based on the profit status of the facilities:

Survival analysis was performed to compare the HRs between the FP and NFP groups. Propensity score matching by patient age, sex, and biochemical/comorbidity profile (Table 1) was conducted before survival analysis, resulting in 31,350 patients in each group. With reference to the studies by Brunelli et al.,[7] our research was carried out with four models, each correcting different parameters. Crude data compared the HR between FP and NFP without correction. Model 1 additionally corrects for age and sex. Models 2 and 3 further correct coronary artery disease (CAD), myocardial infarction (MI), and diabetes mellitus (DM) rates in the population. Furthermore, Model 2 adds the geographical distribution and level of dialysis facilities as a correction factor, and Model 3 adds the length of ownership as a correction factor.

Survival analysis based on facilities' level and geographical distribution:

Survival analysis was also performed based on the eight categories of facilities' level and geographical distribution without consideration of the profit status to evaluate the possible confounding effect of these categories.

RESULTS

Survival analysis based on profit status

Baseline characteristics between groups (Table 1):

After matching, there were 31,350 patients in each group (FP and NFP). Most baseline characteristics were not significantly different between the groups, except for the prevalence of hypertension, congestive heart failure, left ventricular hypertrophy, and albumin level.

Table 1. Baseline characteristics between the for-profit and not-for-profit groups after matching

Variable	Type of facilities by profit status		P-value
	For-profit	Not-for-profit	
Number	31,350	31,350	
Age (years)	62.3±13.5	62.2±13.5	0.66
Male (%)	15,831 (50%)	15,764 (50%)	0.59
DM (%)	16,136 (51%)	16,128 (51%)	0.95
HTN (%)	13,799 (44%)	13,459 (43%)	<0.01
CHF (%)	4,803 (15%)	4,585 (15%)	<0.05
LVH (%)	4,556 (15%)	4,328 (14%)	<0.01
CVA (%)	2,012 (6%)	2,038 (7%)	0.67
CAD (%)	3,815 (12%)	3,762 (12%)	0.52
MI (%)	948 (3%)	1,027 (3%)	0.07
HTN drugs (%)	18,475 (59%)	18,274 (58%)	0.1
HD duration (years)	3.55±2.61	3.55±2.61	0.99
Albumin (g/dL)	3.75±0.40	3.74±0.41	<0.01
Hct (%)	31.09±3.40	31.05±3.15	0.13
Ca (mg/dL)	9.18±0.71	9.18±0.69	0.33
P (mg/dL)	4.84±1.12	4.83±1.11	0.37
ALK-P (μ/L)	128.4±97.1	128.5±100.5	0.91
i-PTH (pg/mL)	226.9±184.0	225.5±175.6	0.32

Note: DM = diabetes mellitus, HTN = hypertension, CHF = chronic heart failure, LVH = left ventricular hypertrophy, CVA = cerebrovascular accident, CAD = coronary artery disease, MI = myocardial infarction, HD = hemodialysis, ALK-P = alkaline phosphatase, i-PTH = intact parathyroid hormone, Ca =calcium , Hct = hematocrit , P = phosphate

Model 1 (Table 2, Figure 2):

The follow-up period was 96 months (2005–2012). Both crude data and Model 1 showed significantly favorable outcomes ($P < 0.0001$) for the NFP group, with HRs of 0.93 and 0.91, respectively. Figure 2 shows the Kaplan-Meier survival curve of the crude data.

Table 2. Adjustments for age and sex (Model 1)

Group	Crude			Adjusted		
	HR	95% CI	P-value	HR	95% CI	P-value
For-profit	Ref.			Ref.		
Not-for-profit	0.93	[0.9, 0.95]	<0.0001	0.91	[0.89, 0.93]	<0.0001
Age (increase per year old)	1.04	[1.04, 1.05]	<0.0001	1.05	[1.04, 1.05]	<0.0001
Sex (male)	1.1	[1.07, 1.12]	<0.0001	1.21	[1.18, 1.24]	<0.0001

Note: 95% CI = 95% confidence interval, HR = hazard ratio

Figure 2

Model 2 (Table 3):

Table 3. Adjustments for age, sex, CAD, MI, DM, geographical distribution, and facility level (Model 2)

Group	Crude			Adjusted		
	HR	95% CI	P-value	HR	95% CI	P-value
For-profit	Ref.			Ref.		
Not-for-profit	0.93	[0.9, 0.95]	<0.0001	0.89	[0.86, 0.93]	<0.0001
Age (increase per year old)	1.04	[1.04, 1.05]	<0.0001	1.04	[1.04, 1.05]	<0.0001
Sex (male)	1.1	[1.07, 1.12]	<0.0001	1.2	[1.18, 1.23]	<0.0001
CAD (Y)	0.81	[0.78, 0.84]	<0.0001	0.69	[0.66, 0.71]	<0.0001
MI (Y)	1.02	[0.96, 1.09]	0.56	1	[0.94, 1.07]	0.97
DM (Y)	1.51	[1.48, 1.55]	<0.0001	1.42	[1.39, 1.46]	<0.0001
Geographic distribution and facility level						
Medical center SMC	0.75	[0.72, 0.78]	<0.0001	0.89	[0.84, 0.94]	<0.0001
Medical center NSMC	0.77	[0.67, 0.89]	<0.001	0.9	[0.78, 1.05]	0.17
Metropolitan hospital SMC	0.98	[0.95, 1.02]	0.36	1.03	[0.98, 1.08]	0.33
Metropolitan hospital NSMC	1.06	[1.02, 1.1]	<0.01	1.14	[1.08, 1.2]	<0.0001
Local hospital SMC	1.02	[0.98, 1.06]	0.3	1.06	[1.01, 1.1]	0.01
Local hospital NSMC	1.15	[1.1, 1.2]	<0.0001	1.15	[1.1, 1.21]	<0.0001
Clinic SMC	Ref.			Ref.		
Clinic NSMC	0.99	[0.94, 1.03]	0.58	1	[0.95, 1.04]	0.91

Note: SMC = six municipalities, NSMC = not six municipalities, Y = yes, 95% CI = 95% confidence interval, HR = hazard ratio, MI = myocardial infarction, DM = diabetes mellitus, CAD = coronary artery disease

Data show significantly favorable outcomes (P < 0.0001) for the NFP group with an HR of 0.89.

Model 3 (Table 4)

Data show a significantly favorable outcome (P < 0.0001) for the NFP group with an HR of 0.95.

Table 4. Model 3 with adjustments for age, sex, CAD, MI, DM, and establishment of facilities

Group	Crude			Adjusted		
	HR	95% CI	P-value	HR	95% CI	P-value
For-profit	Ref.			Ref.		
Not-for-profit	0.93	[0.9, 0.95]	<0.0001	0.92	[0.89, 0.95]	<0.0001
Age (increase per year old)	1.04	[1.04, 1.05]	<0.0001	1.05	[1.04, 1.05]	<0.0001
Sex (male)	1.1	[1.07, 1.12]	<0.0001	1.12	[1.16, 1.23]	<0.0001
CAD (Y)	0.8	[0.78, 0.84]	<0.0001	0.69	[0.66, 0.72]	<0.0001
MI (Y)	1.02	[0.96, 1.09]	0.56	0.93	[0.86, 1.01]	0.08
DM (Y)	1.51	[1.48, 1.55]	<0.0001	1.45	[1.4, 1.49]	<0.0001
Facilities' length of ownership						
Group 1	Ref.			Ref.		
Group 2	1	[0.93, 1.06]	0.9	1.04	[0.97, 1.11]	0.24
Group 3	1.07	[1.01, 1.13]	<0.005	1.13	[1.07, 1.2]	<0.0001
Group 4	0.96	[0.91, 1.02]	0.21	1.07	[1.01, 1.13]	0.02

Note: Group 1 (established for 0–5 years), Group 2 (6–10 y), Group 3 (11–20 y), Group 4 (≥20 y); Y = yes, 95% CI = 95% confidence interval, HR = hazard ratio, MI = myocardial infarction, DM = diabetes mellitus, CAD = coronary artery disease

Survival analysis based on facilities' level and geographical distribution

Baseline characteristics (Table 5)

Without matching, most parameters in the baseline characteristics showed significant differences between the eight groups. Of note, there were several patients in the SMC group at every level of the dialysis facility. The difference is most apparent in the medical centers (34,783 versus 2,311) and clinics (10,0192 versus 31,450), and the influence of this difference on the FP and NFP outcomes will be discussed later in this article.

1

Table 5. Baseline characteristics of 76,483 HD patients based on facilities' level and geographical distribution

Variable	Total population	Facilities' level and geographical distribution								P-value
		Medical center		Metropolitan hospital		Local community hospital		Clinic		
		SMC	NSMC	SMC	NSMC	SMC	NSMC	SMC	NSMC	
Number	76,483	7,559	510	10,286	9,824	10,229	6,040	24,327	7,708	
Person-year	310,404	34,783	2,311	40,047	38,421	40,236	22,964	10,0192	31,450	
Age (years)	62.4±13.6	60.9±13.9	60.1±14.5	63.0±13.5	63.4±13.3	63±13.7	64±13.2	61.8±13.5	62.3±13.4	<0.0001
Male (%)	38,529 (50%)	3,785 (50%)	248 (49%)	5,179 (50%)	4,861 (49%)	5,149 (50%)	3,040 (50%)	12,414 (51%)	3,853 (50%)	0.2757
DM (%)	38,847 (51%)	3,158 (42%)	250 (49%)	5,441 (53%)	5,277 (54%)	5,309 (52%)	3,209 (53%)	12,384 (51%)	3,819 (50%)	<0.0001
HTN (%)	30,728 (40%)	2,878 (38%)	296 (58%)	3,499 (34%)	4,484 (46%)	4,339 (42%)	2,476 (41%)	9,367 (39%)	3,389 (44%)	<0.0001
CHF (%)	9,575 (13%)	1,144 (15%)	83 (16%)	964 (9%)	1,681 (17%)	1,575 (15%)	938 (16%)	2,430 (10%)	760 (10%)	<0.0001
LVH (%)	8,990 (12%)	1,142 (15%)	85 (17%)	844 (8%)	1,400 (14%)	1,342 (13%)	710 (12%)	2,466 (10%)	31,001 (13%)	<0.0001
CVA (%)	5,306 (7%)	421 (6%)	29 (6%)	485 (5%)	733 (7%)	916 (9%)	460 (8%)	1,695 (7%)	567 (7%)	<0.0001
CAD (%)	8,789 (11%)	572 (8%)	79 (15%)	1,001 (10%)	1,444 (15%)	1,247 (12%)	623 (10%)	2,813 (12%)	1,010 (13%)	<0.0001
MI (%)	2,219 (3%)	286 (4%)	32 (6%)	226 (2%)	294 (3%)	316 (3%)	166 (3%)	715 (3%)	184 (2%)	<0.0001
HTN drugs (%)	38,957 (51%)	4,049 (54%)	256 (50%)	5,088 (49%)	5,817 (59%)	5,093 (50%)	2,995 (50%)	11,487 (47%)	4,172 (54%)	<0.0001
HD duration (years)	3.42±2.67	4.01±2.84	3.93±2.66	3.24±2.61	3.25±2.59	3.28±2.65	3.14±2.59	3.48±2.66	3.46±2.67	<0.0001
Albumin (g/dL)	3.77±0.41	3.85±0.39	3.6±0.37	3.71±0.43	3.68±0.44	3.76±0.43	3.69±0.46	3.84±0.36	3.8±0.36	<0.0001
Hct (%)	31±3.3	31.1±3.5	30.9±2.7	30.8±3.2	31.0±3.1	30.9±3.4	30.6±3.4	31.0±3.2	31.5±3.2	<0.0001
Ca (mg/dL)	9.2±0.7	9.2±0.68	9.15±0.63	9.16±0.7	9.15±0.7	9.24±0.73	9.14±0.73	9.23±0.68	9.23±0.69	<0.0001
P (mg/dL)	4.79±1.13	4.94±1.09	4.75±1.11	4.82±1.12	4.81±1.17	4.71±1.15	4.63±1.18	4.81±1.11	4.73±1.09	<0.0001
ALK-P (μ/L)	124.8±97.3	107±76.1	215.2±147.1	135±113.2	130.7±103.8	138.8±113	153.4±116.7	110.9±80.5	118.0±74.3	<0.0001
i-PTH (pg/mL)	215.5±173.7	240±181	240.4±176.6	231.8±176.8	215.9±171.1	212.4±176.8	193.3±166.4	210.6±170.2	204.9±173.4	<0.0001

Note: DM = diabetes mellitus, HTN = hypertension, CHF = chronic heart failure, LVH = left ventricular hypertrophy, CVA = cerebrovascular accident, MI = myocardial infarction, HD = hemodialysis, ALK-P = alkaline phosphatase, i-PTH = intact parathyroid hormone, SMC = six municipalities, NSMC = not six municipalities, Ca = calcium, CAD =coronary artery disease , P =phosphate

Table 6. Survival analysis based on facilities' level and geographical distribution with adjustments

Group	Crude			Adjusted		
	HR	95% CI	P-value	HR	95% CI	P-value
Medical center SMC	0.84	[0.81, 0.88]	<0.0001	0.83	[0.8, 0.87]	<0.0001
Medical center NSMC	0.9	[0.79, 1.04]	0.144	0.92	[0.8, 1.06]	0.23
Metropolitan hospital SMC	1.15	[1.11, 1.19]	<0.0001	1.08	[1.04, 1.11]	<0.0001
Metropolitan hospital NSMC	1.18	[1.14, 1.22]	<0.0001	1.1	[1.06, 1.14]	<0.0001

Local hospital SMC	1.2	[1.16, 1.25]	<0.0001	1.16	[1.12, 1.2]	<0.0001
Local hospital NSMC	1.28	[1.23, 1.34]	<0.0001	1.18	[1.13, 1.23]	<0.0001
Clinic SMC	Ref.			Ref.		
Clinic NSMC	1.02	[0.98, 1.06]	0.3361	1.02	[0.98, 1.06]	0.44
Age (increase per year old)	1.04	[1.04, 1.04]	<0.0001	1.04	[1.04, 1.04]	<0.0001
Sex (male)	1.09	[1.07, 1.12]	<0.0001	1.18	[1.16, 1.2]	<0.0001
CAD (Y)	0.78	[0.76, 0.81]	<0.0001	0.67	[0.65, 0.7]	<0.0001
MI (Y)	1	[0.94, 1.06]	1	1.02	[0.96, 1.08]	0.57
DM (Y)	1.45	[1.42, 1.48]	<0.0001	1.37	[1.34, 1.4]	<0.0001

Note: SMC = six municipalities, NSMC = not six municipalities, Y = yes, 95% CI = 95% confidence interval, HR = hazard ratio, MI = myocardial infarction, DM = diabetes mellitus, CAD =coronary artery disease

Survival analysis (Table 6)

Survival analyses with adjustments for age, sex, CAD, MI, and DM were also performed to compare the impact of the facility level and geographic distribution on patient prognosis. The clinic SMC was designated as the reference group. Trends for better outcomes were observed at the medical center level, whereas worse outcomes were observed in metropolitan hospitals and local hospitals. Nonsignificant p-values were observed in the medical center NSMC and clinic NSMC, indicating that the outcome is similar to that of clinic SMC.

Table 7. Level of dialysis facilities and profit status

Level	Private for-profit	Private not-for-profit
Medical center	0	14
Metropolitan hospital	7	41
Local hospital	71	45
Clinic	207	2

DISCUSSION

In summary, our results revealed that private NFP dialysis facilities have better patient outcomes than private FP facilities. The favorable effect remains with the adjustment of the facilities' level, geographic distribution, or length of ownership.

The possible reasons why NFP and FP facilities have different outcomes have been discussed extensively in previous studies.[4, 14-16] By definition, FP facilities are owned by investors or shareholders. They usually distribute part of their profits directly to owners and focus on increasing shareholder wealth. In contrast, NFP facilities are owned by members (communities, religious organizations, nongovernmental organizations, universities, etc.) to fulfill certain missions (providing health services, teaching, or research). Revenue should be used for their stated mission and cannot be distributed to the members of the organization.[16] Theoretically, FP facilities result in greater efficiency if there are no barriers to entering the market and there is an observable and measurable outcome.[16-18] Nevertheless, numerous barriers exist (e.g., high capital investment, technology, faculty training, regulation, and certification), whereas the outcomes are hardly visible to customers (patients). The barriers to market, asymmetrical information, risk, and the uncertain nature of the healthcare industry make it prone to market failure.[19] In a meta-analysis by Devereaux et al.,[20] NFP hospitals are associated with higher payments for care, which indicates the shortcoming of FP facilities in terms of efficiency. To make matters worse, FP facilities are often faced with economic challenges. Shareholders expect 10%–15% returns on their investments,[14] and taxes may account for 5%–6% of the total expenses.[21] FP facilities must generate these profits and pay taxes while making an effort to provide the same quality of care as NFP facilities that are free of these excessive expenses.[4] In a healthcare system in which funding and resources are relatively fixed, as with the NHI in Taiwan, the FP facility may try to cut off other forms of spending to generate more profit. Although both business models ought to be confronted with costings on doing audit, ongoing training and purchasing medical supplies, there are several reasons that could result in

the better efficiency of NFP facilities. Firstly, due to the relatively larger scale of NFP facilities(Table 7), economies of scale could be achieved. Facilities of larger scale could reduce the proportion on these expenditure by setting up standard operation procedures(SOP). Discounts may be provided by outsourcing training company or medical supply company. Secondly, according to the regulations in Taiwan [11], NFP facilities are exempt from about 20% of costings on tax while no less than 20% of revenue on research, training, health education, community medical service or charity are required. The expenditure is roughly equal to the surplus from tax exemption. Additionally, NFP hospitals are entitled to receive charitable contributions. Several financial studies comparing NFP and FP hospitals also indicated that financial performance of NFP hospitals were better than FP hospitals[9, 22]. Possible approaches for FP facilities to reducing expenses are employing fewer personnel per run and less highly skilled personnel,[23, 24] unwillingness to extend personal dialysis time, and using low-performance dialyzers.[24, 25] These approaches may also be associated with higher mortality rates in the FP facilities.[25]

Although our study results are in concordance with those of previous studies,[1, 4] some confounding factors specific to the setting in Taiwan may exist. Table 7 shows the distribution of the FP and NFP facilities at each level. All medical centers and most metropolitan hospitals are NFP facilities, whereas most clinics are FP facilities. Table 5 shows that the majority of person-year data in medical centers and clinics are contributed by the SMC. Table 6 illustrates that “medical center SMC” have the best outcome (HR = 0.84, P < 0.0001), whereas “clinic SMC and “clinic NSMC” show no significant survival benefits (HR = ref. and 1.02, respectively; P = 0.3361). In conclusion, the NFP population may be affected by the good prognosis of the “medical center SMC”; the FP population is less affected by the neutral outcome of the “clinic SMC.”

Our study had several limitations. First, as mentioned in previous studies,[4, 6, 7] it is impractical and highly unlikely that any randomized control trial will be conducted on this topic. Specifically, current studies unquestionably suffer from limitations inherent to observational designs.

There may be residual confounding effects yet to be corrected, and the causal relationships between profit status and patient outcome cannot be directly derived from an observational study design. Second, due to the personal information protection law in Taiwan, we are unable to directly access the facilities' length of ownership data and have to conduct online searches and telephone interviews for the information needed. Approximately 30% of the facilities refused to report information on their length of ownership, resulting in missing data and insufficient correction in Model 3. Correction with geographic distribution and length of ownership (Model 2 + Model 3) was also not performed because of the problem in Model 3. Similarly, due to limited access to more granular socioeconomic data of participants, more detailed geographic fixed effects of facilities, and type of vascular access of each patient, adjustments regarding these factors counldn't be carried out. Third, most high-level medical facilities in Taiwan (Table 7, medical center and metropolitan hospital) are established as foundations and are deemed private NFP facilities. Nonetheless, some facilities were established as foundations for the sake of tax exemption and are de facto FP facilities. This finding cannot be properly addressed through statistical analysis. Lastly, immortal time bias is an important issue in the analysis of prevalence and patient survival, especially in our retrospective, long-term, nationwide population-based cohort study design. We could only decrease the impact of this bias using a time-dependent Cox regression model for the HR of mortality, and fortunately, a follow-up period of up to 7 years (Figure 2) may alleviate the bias.

Our findings suggest that in contemporary HD settings in Taiwan, treatment at NFP dialysis facilities is associated with better outcomes. The result should be interpreted with caution, since the possibility of residual confounding effects and uncertainty of casual relations exist in the setting of an observational study. However, the favorable effects of private not-for-profit facilities have been demonstrated in a recent unpublished meta-analysis from the United States [26]. Studies also show shorter hospitalization days or hospitalization rates due to complications in NFP facilities [27, 28]. The effect of the profit status of hemodialysis facilities on patient prognosis is a widespread and

longstanding problem that needs to be corrected. Government regulations should be made for the welfare of dialysis patients, and more research with a robust study design is needed to investigate the problem more thoroughly.

Funding statement

This study was supported by a grant from the Ministry of Science and Technology, R.O.C. (MOST 106-2813-C-038-019-B) and Taipei Medical University Hospital (107TMU-TMUH-04).

Competing interest statement

The authors have no conflicts of interest to declare.

Data availability statement

No additional data available

Acknowledgement

We would like to thank Mr. Kuang-wen Wang for analytical assistance.

Author contributions

Conceived and designed the experiments: YL (Yen-Chung Lin); MW (Mai-Szu Wu); SL(Sheng-Yu Liu). Performed the experiments: YL; SL. Analyzed the data: YL; SL; CH (Chih-Cheng Hsu). Contributed reagents/materials/analysis tools: YL; MW; SL; CC(Chong-Yi Cheng); MW(Mei-Yi Wu,); CZ(Cai-Mei Zheng). Wrote the manuscript: SL; YL . All authors read and approved the final manuscript.

Ethics Statement:

The independent Ethics Committee of Taipei Medical University approved this study (no.: N202004151; Principle investigator: Cai-Mei Zheng) and supervised it in accordance with the tenets of the Declaration of Helsinki (1975) and its later amendment (2013). The study fits all the applicable regulations for waiver of the informed consent.

References

1. Saran R, R.B., Abbott KC, et al. , *US Renal Data System 2018 Annual Data Report: epidemiology of kidney disease in the United States. .* Am J Kidney Dis., 2019. **73**((3):Svii–Sxxii, S1–S772.
2. Hsu CC, et al. Summary Report of the 2019 Annual Report on Kidney Disease in Taiwan. Acta Nephrologica 35(1): 3-14, 2021DOI:10.6221/AN.202103_35(1).0002.
3. Chevreul K, et al. France: health system review. *Health Syst Transit* 2015;17(3):1–218, xvii.
4. Devereaux PJ, et al. Comparison of mortality between private for-profit and private not-for-profit hemodialysis centers: a systematic review and meta-analysis. *JAMA* 2002;288(19):2449–57.
5. Brooks JM, et al. Effect of dialysis center profit-status on patient survival: a comparison of risk-adjustment and instrumental variable approaches. *Health Serv Res* 2006;41(6):2267–89.
6. Foley RN, et al. Comparative mortality of hemodialysis patients at for-profit and not-for-profit dialysis facilities in the United States, 1998 to 2003: a retrospective analysis. *BMC Nephrol* 2008;9:6.
7. Brunelli SM, et al. Confounders of mortality and hospitalization rate calculations for profit and nonprofit dialysis facilities: analytic augmentation. *BMC Nephrol* 2014;15:121.
8. Lin YC, et al. Health policies on dialysis modality selection: a nationwide population cohort study. *BMJ Open* 2017;7:e013007.
9. Lien HM, Chou SY, Liu JT. Hospital ownership and performance: evidence from stroke and cardiac treatment in Taiwan. *J Health Econ* 2008;27(5):1208–23.
10. Lin YC. Incidence and prevalence of ESRD in Taiwan Renal Registry Data System (TWRDS): 2005-2012. *Acta Nephrologica* 2014;28:65–8.
11. Medical Care Act, Article 3. MOHW, Taiwan (R.O.C). Amended date: 2020-01-15.
12. Code of Practice on Hospital Accreditation and Teaching Hospital Accreditation. MOHW, Taiwan (R.O.C). 2019.
13. Ministry of Interior, Taiwan (R.O.C.). Local Government Act, Article 4. Amended date: 2016-06-22: Laws & Regulations Database of The Republic of China.
14. Nudelman PM, Andrews LM. The “value added” of not-for-profit health plans. *N Engl J Med* 1996;334(16):1057–9.
15. Woolhandler S, Himmelstein DU. When money is the mission--the high costs of investor-owned care. *N Engl J Med* 1999;341(6):444–6.
16. Herrera CA, et al. Does ownership matter? An overview of systematic reviews of the

performance of private for-profit, private not-for-profit and public healthcare providers. *PLoS One* 2014;9(12):e93456.

17. Rosenthal G, Newbrander W. Public policy and private sector provision of health services. *Int J Health Plan Manag* 1996;11(3):203–16.
18. Gray BH, For-Profit Enterprise in Health Care. Institute of Medicine. Washington, DC: National Academy Press 1986.
19. Iszaid I, Hafizan A.H,Muhamad J. Market failure in health care: a review. *IJPHCS* 2018;5:16–25.
20. Devereaux PJ, et al. Payments for care at private for-profit and private not-for-profit hospitals: a systematic review and meta-analysis. *CMAJ* 2004;170(12):1817–24.
21. Friedman B, Hattis P, Bogue R. Tax exemption and community benefits of not-for-profit hospitals. *Adv Health Econ Health Serv Res* 1990;11:131–58.
22. Lin, W.-H., et al., Financial performance of non-profit hospitals in Taiwan. Journal of Information and Optimization Sciences, 2011; 32(2); 419–431.
23. Hirth R, Chernew M, Orzol S. Ownership, competition, and the adoption of new technologies and cost-saving practices in a fixed-price environment. *Inquiry* 2000;37:282–94.
24. Held PJ, et al. Price of dialysis, unit staffing, and length of dialysis treatments. *Am J Kidney Dis* 1990;15(5):441–50.
25. Held PJ, et al. Mortality and duration of hemodialysis treatment. JAMA 1991;265(7):871–5.
26. Samuel L , et al. Mortality at private for-profit and private not-for-profit hemodialysis centers: a systematic review and meta-analysis. J Gen Intern Med 2019;34(Suppl 2):289.
27. Dalrymple LS, et al. Comparison of hospitalization rates among for-profit and nonprofit dialysis facilities. *Clin J Am Soc Nephrol* 2014;9(1):73–81.
28. Lee DKK, Chertow GM, Zenios SA. Reexploring differences among for-profit and nonprofit dialysis providers. *Health Serv Res* 2010;45(3):633–46.

Figure legends

Figure 1. Flowchart of the patient selection process

Figure 2. The Kaplan-Meier survival curve in HD patients. The survival rate in the FP group (approximately 8.75%) was decreased compared to that in the NFP control group ($P < 0.0001$)

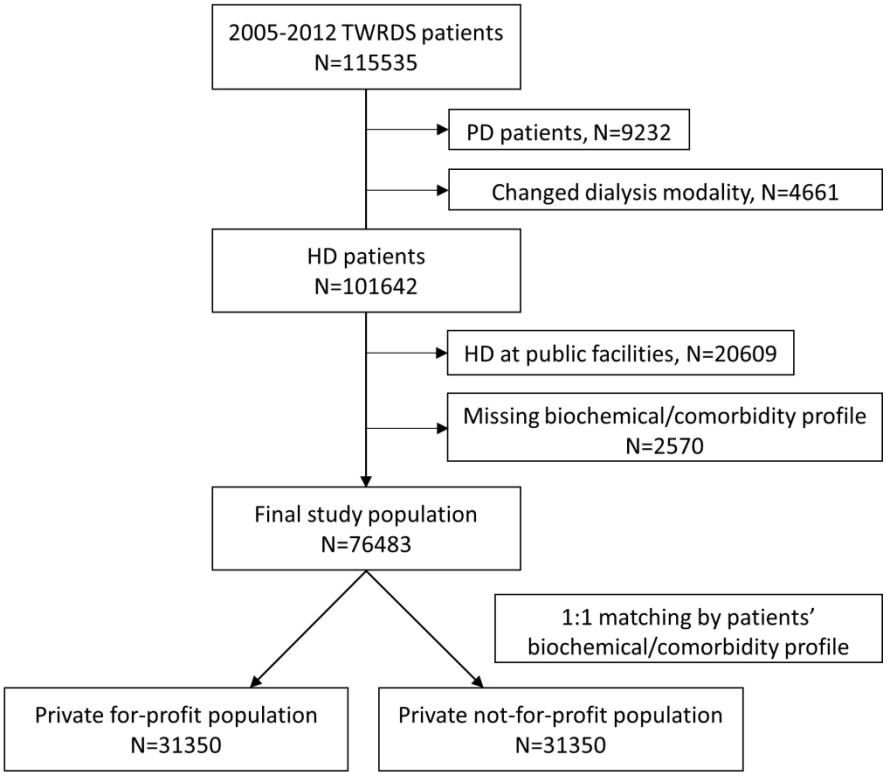

Figure 1: Flowchart of patient selection process

180x160mm (300 x 300 DPI)

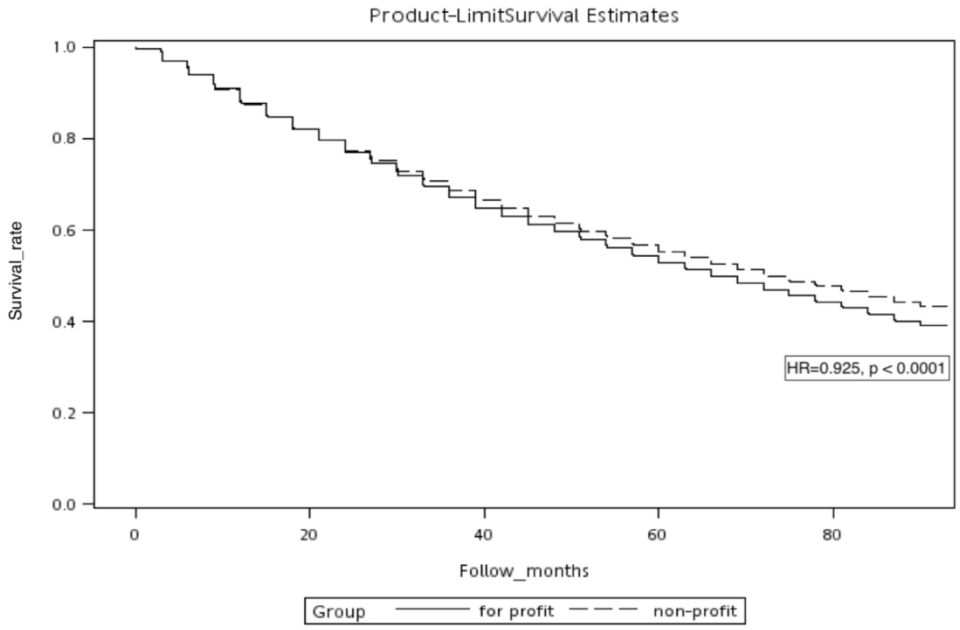

Figure 2: The Kaplan-Meier survival curve in HD patients: The survival rate for-profit group about 8.75% decreased comparing to non-profit control group (P < 0.0001)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any pre-specified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
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	5
		(*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	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
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	5-6
Bias	9	Describe any efforts to address potential sources of bias	5-6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(c) Explain how missing data were addressed	5
		(*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	6

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	6-7
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	5
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	5, Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	5, Figure 1
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	8, Figure 2
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	8, Figure 2
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Not Applicable
		Cross-sectional study—Report numbers of outcome events or summary measures	Not Applicable
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	9-11, Table 2-4
		(*b*) Report category boundaries when continuous variables were categorized	6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not Applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12-14, Table 5-7
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
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	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
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	17

*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.