PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Out-of-pocket costs and productivity losses in haemodialysis and peritoneal dialysis from a patient interview survey in Taiwan
AUTHORS	SUE, YUH-MOU; Tang, Chao-Hsiun; Chen, Hsi-Hsien; Wu, Ming-Ju; Hsu, Bang-Gee; Tsai, Jer-Chia; Kuo, Chi-Cheng; Lin, Shih-Pi; Chen, Tso-Hsiao

VERSION 1 - REVIEW

REVIEWER	James Heaf Dept. Medicine Zealand University Hospital Sygehusvej 10 4000 Roskilde Denmark
REVIEW RETURNED	14-Apr-2018

GENERAL COMMENTS	The paper studies patient-related costs for HD compared to PD. HD costs are found to be higher, primarily related to loss of income related to the HD procedure. This finding is not surprising, and confirms previous studies. Generally, I feel that the paper is more suited for a national than an international audience. There are some methodological problems. 1) Many of the factors studied are specific to Taiwan and/or the Taiwanese health system, and may not be applicable to other populations. 2) The estimation of lost income is problematic. Apparently, these are calculated for average wages corrected for unemployment rate and age (page 7, margin no. 42). Thus, no account is made for the patient's individual income, or rates and sizes of invalidity and old-age pensions (which will be age-dependent). Is it true that patients over 70 have no work income at all (Suppl table 1), or is data just not available? Patients receiving pensions, or in part-time work may not have any income loss associated with the dialysis procedure. 3) Many of the procedures performed by PD patients are made immediately before, or after, sleep, and presumably are not associated with productivity losses. 4) Previous studies have demonstrated better chances of rehabilitation for PD patients than HD, i.e. lower risk of job loss and requirement for invalidity pension. This is not included in the model. Including them would lead to a paradoxical situation, where the patient (and society in general) benefits form the improved rehabilitation, but individual patient-related costs increase. Minor Comments 1) Non-parametrically distributed variables, e.g. duration of dialysis, should (also) be reported as median values (IQR). 2) Table 2. It is not clear how Kt/V is calculated. PD Kt/V is presumably per week, and HD Kt/V per dialysis. These figures are not comparable. HD Kt/V should be converted to standard Kt/V in units/week.

REVIEWER	Carlos Bechara Loyola School of Medicine, Maywood, IL, USA.
REVIEW RETURNED	06-Aug-2018

GENERAL COMMENTS	The authors present an interesting paper on "Out of pocket costs and productivity losses in haemodialysis and peritoneal dialysis from a patient interview survey in Taiwan". Here are my comments: 1- It seems the patient were interviewed at dialysis centers, but PD was done at home. Can the authors clarify that. 2- The HD group were older with higher incidence of diabetes and ischemic heart disease. Maybe thats why they didn't get PD! Please comment. 3- The authors added cost of over the counter medication and herbal medication, do they believe PD patients being younger might be more concerned about their health and buy these herbal medicines. 4- How did they actually calculate the costs? Did they look at receipts or get an estimate for medication cost, transportation cost... I really couldn't understand the reasoning and how they factored the inflation rate and unemployment into their costs! 5- How do the authors envision this research will impact dialysis patients in Taiwan? 6- I am sure it's no surprise to the authors that the cost of transportation for HD patients was the main driver for higher oop costs. Do they believe home HD will offset the costs and match PD costs?

VERSION 1 – AUTHOR RESPONSE

#Reviewer(s)' Comments to Author:

#Reviewer: 1

Reviewer Name: James Heaf

Institution and Country: Dept. Medicine, Zealand University Hospital, Sygehusvej 10, 4000 Roskilde, Denmark.

Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below:

The paper studies patient-related costs for HD compared to PD. HD costs are found to be higher, primarily related to loss of income related to the HD procedure. This finding is not surprising, and confirms previous studies. Generally, I feel that the paper is more suited for a national than an international audience. There are some methodological problems.

1. Many of the factors studied are specific to Taiwan and/or the Taiwanese health system, and may not be applicable to other populations.

Reply:

The current study demonstrates how the roles of out-of-pocket payment and productivity losses play in determining the economic costs of chronic dialysis in a country with a universal health care program such as Taiwan. Our findings provide policy implications for countries who have or are contemplating to have public financing in health care such as dialysis treatment. First, out-of-pocket payment as a percentage of the total costs (6.6% for HD and 7.7% for PD, Figure 1) reflects the financial hardship patients are enduring and should be monitored by the government to ensure the government are providing adequate financial protection when patients fall ill. Second, HD appears to have higher productivity loss than PD (NT 14,150 vs. NT 11,611). For countries with higher wage rate, or with higher proportion of patients younger than 70, may benefit from cost-savings in choosing PD. (1st paragraph, page 11)

2. The estimation of lost income is problematic. Apparently, these are calculated for average wages corrected for unemployment rate and age (page 7, margin no. 42). Thus, no account is made for the patient's individual income, or rates and sizes of invalidity and old-age pensions (which will be age-dependent). Is it true that patients over 70 have no work income at all (Suppl table 1), or is data just not available? Patients receiving pensions, or in part-time work may not have any income loss associated with the dialysis procedure.

Reply:

We took the Human Capital approach (last paragraph, page 10) to estimate the opportunity costs of time lost for receiving dialysis treatment. Hence it is the wage income that is relevant when we are evaluating the value of time loss. We applied national average hourly wage rate released on an annual basis by Directorate General of Budget, Accounting and Statistics (DGBAS), to assess the value of time lost for dialysis treatment. Patients over 70 were mostly retired and wage date was reported only for working population under 70 years old.

3. Many of the procedures performed by PD patients are made immediately before, or after, sleep, and presumably are not associated with productivity losses.

Reply:

The value of time lost when receiving dialysis treatment is defined as the potential benefits forgone if the patients would have spent the time undertaking activities other than dialysis treatment. So there surely are opportunity costs associated with the time spent in dialysis, no matter at what time the dialysis treatment is performed. Indeed, economists even go further to argue that the value of leisure time (such as the time before or after sleep) is even higher than that of the daily working hours.

4. Previous studies have demonstrated better chances of rehabilitation for PD patients than HD, i.e. lower risk of job loss and requirement for invalidity pension. This is not included in the model. Including them would lead to a paradoxical situation, where the patient (and society in general) benefits form the improved rehabilitation, but individual patient-related costs increase.

Reply:

The costs of illness we estimated in this study is the costs associated with ESRD. The opportunity costs of time is to reflect the potential benefits forgone of the alternative use of time, regardless whether the patient is in the labor force and not in the labor force. The issues regarding risk of job loss and requirement for invalidity pension are not in the scope of this present study.

Minor Comments

1. Non-parametrically distributed variables, e.g. duration of dialysis, should (also) be reported as median values (IQR).

Reply:

The duration of dialysis variables has been reported as median values (IQR).

2. Table 2. It is not clear how Kt/V is calculated. PD Kt/V is presumably per week, and HD Kt/V per dialysis. These figures are not comparable. HD Kt/V should be converted to standard Kt/V in units/week.

Reply:

The Kt/V of HD has be converted to standard Kt/V to compare with the Kt/V of PD.

#Reviewer: 2

Reviewer Name: Carlos Bechara

Institution and Country: Loyola School of Medicine, Maywood, IL, USA.

Please state any competing interests or state ‘None declared’: none

Please leave your comments for the authors below:

The authors present an interesting paper on "Out of pocket costs and productivity losses in haemodialysis and peritoneal dialysis from a patient interview survey in Taiwan". Here are my comments:

1. It seems the patient were interviewed at dialysis centers, but PD was done at home. Can the authors clarify that.

Reply:

The patient interviews were performed face by face during HD therapy or monthly PD clinic visit. The manuscript has been revised (3rd paragraph, page 6).

2. The HD group were older with higher incidence of diabetes and ischemic heart disease. Maybe that’s why they didn't get PD! Please comment.

Reply:

Aged ESRD patients often have comorbidities, such as diabetes mellitus with retinopathy and poor vision acuity. Considering the necessity of caregiver’s support to complete the every day’s procedures, most patients would not choose PD as a favour choice to prevent the OOP cost of caregiver. Compared with HD patients, PD patients with diabetes mellitus or age more than 65 years old also had increased death rate. All these factors would discourage patients to choosing PD as their renal replacement modality. The manuscript has been revised. (2nd paragraph, page 10)

3. The authors added cost of over the counter medication and herbal medication, do they believe PD patients being younger might be more concerned about their health and buy these herbal medicines.

Reply:

This study showed PD patients tend to have higher costs of Chinese (herbs) medicine and tradition medicine than those of HD, however, the differences does not reach statistical significance. This may be due to a mixture of the following two forces. First, PD patients are younger and have higher health awareness, which resulted to their more frequent use of Chinese and traditional medicine; and Second, PD patients tend to be younger and are more likely to actively participate in labor force, and thus are financially more capable of paying out-of-pocket for Chinese and traditional medicine.

4. How did they actually calculate the costs? Did they look at receipts or get an estimate for medication cost, transportation cost... I really couldn't understand the reasoning and how they factored the inflation rate and unemployment into their costs!

Reply:

1) During the patient interview, patients were asked to recall how much out-of-pocket expenses they spent on their health problems associated with ESRD. To avoid recall biases, out-of-pocket costs associated with physician visits and hospitalization were related to the most recent one within 3 months or 12 months prior to the interview. For other out-of-pocket expenses, such as folk medicine, vitamin supplements, or domestic caregivers, patients were asked to recall the itemized expenses occurred in the past 12 months in total.

2) Thank you for your question regarding why the unemployment rate needs to be factored in when estimating the opportunity costs of time lost. This is to reflect the situation when another worker from the pool of unemployed replaces the individual who is absent due to an illness. In such as case, there should be no productivity loss due to an illness. Therefore, a more conservative estimate of the value of the productivity loss is approximated by deducting the unemployment rate from the calculation. To clarify this process of calculation, we have showed both the numbers before and after unemployment rate is taken into account.

Koopmanschap, M.A. 1995. The friction cost method for measuring indirect costs of disease. Journal of Health Economics, 14(2), 171-189.

5. How do the authors envision this research will impact dialysis patients in Taiwan?

Reply:

In patients with chronic kidney disease stage 5 near ESRD, facing with numerous decisions across the trajectory of their illness are needed. Using shared decision making approach offers a patient-centered method to nudge patients facing health-related decisions, including the choice of HD, PD, kidney transplantation or hospice care. The OPP costs and productivity losses have significant impact on quality of lives and cost of healthcare delivery. Exploring the detailed information will provide evidence based, high-quality decision aids and be able to meet patients' informational needs. The manuscript has been revised. (1st paragraph, page 11)

6. I am sure it's no surprise to the authors that the cost of transportation for HD patients was the main driver for higher OOP costs. Do they believe home HD will offset the costs and match PD costs?

Reply:

After reducing the transportation cost of HD by the current data, the OOP cost will be offset and even lower than that of PD. However, these data were not obtained based on the face to face interview survey of home HD patients. We need to speculate these data carefully. Furthermore, home

HD is not available in Taiwan owing to the limitation of medical law, nor is the detailed information of NHI-financed medical cost.

VERSION 2 – REVIEW

REVIEWER	Carlos Bechara Loyola School of Medicine, IL USA.
REVIEW RETURNED	19-Sep-2018

GENERAL COMMENTS	The authors did an excellent job responding to the reviewers. However, despite accepting the manuscript, I have a problem with how they calculated out of pocket expenses based on response number 4 to reviewer #2. The authors wrote "patients were asked to recall the itemized expenses occurred in the past 12 months in total." I have a problem on asking patients to recall expenses for the past 12 months. I can't even remember how much money I spent last week on medication! This requires a review by a statistician.

REVIEWER	Frank Li Department of Biostatistics and Bioinformatics, Duke University School of Medicine
REVIEW RETURNED	25-Nov-2018

GENERAL COMMENTS	This article describes a comparative study on direct non-medical costs/indirect medical costs among patients receiving hemodialysis (HD) and peritoneal dialysis (PD). The cost information was collected through medical charts and interviews, and a series of statistical tests were carried out for comparisons, possibly stratified by age groups. Given that comparisons on indirect medical costs were relatively limited in the literature in this context, the current analysis is considered necessary. I have the following comments that the authors could consider in improving the current manuscript. 1. One of my biggest concern, regarding this study, is selection bias/confounding. There are notable differences among the groups of people receiving HD and PD (demographics and clinical need). The receipt of HD or PD is non-randomized, and patients select themselves into one of the two groups based on their clinical need/health status, and so a valid descriptive comparison shares some similarity with an observational study. Therefore, I wonder how one should interpret the current results (raw comparison) as they ignore the covariate (demographics and clinical need variables) information. In health services research, estimating differences in medical costs (such as among racial groups) is common and have always taken into account the clinical need information (either through regression-based approach or propensity score approach). Should we consider such approaches to address the study question in this context? If not, I would like to see a more convincing argument/discussion on why this should not be done.

	2. As reviewer 1 has pointed out, this is indeed a study specific to Taiwan and the findings may not be easily generalized to other populations. In my perspective, the generalizability critically depends on the population/sample characteristics. The authors could perhaps point out in the discussion that, the population characteristics, summarized in Table 1, serves as a basis for considering extending the results to other populations/medical systems. If the baseline characteristics (demographics, clinical need) are similar across populations, the generalizability seems more convincing. Such discussions may help reader critically assess the utility of the current analysis. 3. Page 9 Line 3- the authors have not defined Model 2-4 in the prior texts. While there are some explanations in Table 5, it is more appropriate to define what these models are before discussing them.

VERSION 2 – AUTHOR RESPONSE

Response to Reviewers

Reviewer(s)' Comments to Author:

Reviewer: 2

Reviewer Name: Carlos Bechara

Institution and Country: Loyola School of Medicine, IL USA.

Please state any competing interests or state ‘None declared’: none

Please leave your comments for the authors below

The authors did an excellent job responding to the reviewers. However, despite accepting the manuscript, I have a problem with how they calculated out of pocket expenses based on response number 4 to reviewer #2. The authors wrote "patients were asked to recall the itemized expenses occurred in the past 12 months in total."

I have a problem on asking patients to recall expenses for the past 12 months. I can't even remember how much money I spent last week on medication! This requires a review by a statistician.

Reply

When designing a question asking patients about their healthcare utilization, there is always an issue about what the optimum recall period should be. There is no easy way to tackle this issue. While a shorter recall period may decrease the likelihood of recall error, at the same time, it also increases the likelihood of missing information. We chose 12-month to be the recall period because we wanted to make sure all out-of-pocket information in the previous year can be captured in the answer.

Reviewer: 3

Reviewer Name: Frank Li

Institution and Country: Department of Biostatistics and Bioinformatics, Duke University School of Medicine

Please state any competing interests or state ‘None declared’: None

Please leave your comments for the authors below

This article describes a comparative study on direct non-medical costs/indirect medical costs among patients receiving hemodialysis (HD) and peritoneal dialysis (PD). The cost information was collected through medical charts and interviews, and a series of statistical tests were carried out for comparisons, possibly stratified by age groups. Given that comparisons on indirect medical costs were relatively limited in the literature in this context, the current analysis is considered necessary. I have the following comments that the authors could consider in improving the current manuscript.

1. One of my biggest concern, regarding this study, is selection bias/confounding. There are notable differences among the groups of people receiving HD and PD (demographics and clinical need). The receipt of HD or PD is non-randomized, and patients select themselves into one of the two groups based on their clinical need/health status, and so a valid descriptive comparison shares some similarity with an observational study. Therefore, I wonder how one should interpret the current results (raw comparison) as they ignore the covariate (demographics and clinical need variables) information. In health services research, estimating differences in medical costs (such as among racial groups) is common and have always taken into account the clinical need information (either through regression-based approach or propensity score approach). Should we consider such approaches to address the study question in this context? If not, I would like to see a more convincing argument/discussion on why this should not be done.

Reply:

To solve the problem of selection bias of the patient interview data and that they may not be a reasonable representative population of HD and PD patients, we employed the bootstrapped method by resampling the HD and PD sample data (Please see the bootstrapped process we have described on Page 7). This would allow us to draw inferences about the HD and PD population, and compare their differences in the means of the productivity costs and out-of-pocket costs between HD and PD patients.

2. As reviewer 1 has pointed out, this is indeed a study specific to Taiwan and the findings may not be easily generalized to other populations. In my perspective, the generalizability critically depends on the population/sample characteristics. The authors could perhaps point out in the discussion that, the population characteristics, summarized in Table 1, serves as a basis for considering extending the results to other populations/medical systems. If the baseline characteristics (demographics, clinical need) are similar across populations, the generalizability seems more convincing. Such discussions may help reader critically assess the utility of the current analysis.

Reply:

We have made the appropriate changes to the “Discussion” (1st paragraph, page 11).

3. Page 9 Line 3- the authors have not defined Model 2-4 in the prior texts. While there are some explanations in Table 5, it is more appropriate to define what these models are before discussing them.

Reply:

We have made the appropriate changes to the “Sensitivity Analysis” section of METHODS (2nd paragraph, page 7).

VERSION 3 – REVIEW

REVIEWER	Frank Li Department of Biostatistics and Bioinformatics, Duke University School of Medicine USA
REVIEW RETURNED	22-Jan-2019

GENERAL COMMENTS	Thank you for addressing my comments. I have no further comments at this time.