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Complete List of Authors:	Moreno Velásquez, Ilais; Instituto Conmemorativo Gorgas de Estudios de la Salud Tribaldos Causadias, Maribel; Instituto Conmemorativo Gorgas de Estudios de la Salud, Valdés, Régulo; Caja de Seguro Social Gómez, Beatriz; Gorgas Memorial Institute for Health Studies Motta, Jorge; Gorgas Memorial Institute for Health Studies; Secretaria Nacional de Ciencia Tecnologia e Innovacion Cuero, César; Ministerio de Salud Panama, Organización Panameña de Trasplante Herrera, Víctor; Gorgas Memorial Institute for Health Studies
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End-stage renal disease: Financial costs and years of life lost in Panama

Ilais Moreno Velásquez[1], Maribel Tribaldos Causadias[1], Régulo Valdés[2], Beatriz Gómez[1], Jorge Motta[1,3], César Cuero[4], Víctor Herrera[1]

[1]Gorgas Memorial Institute for Health Studies, Panama; [2] Caja de Seguro Social, Panama; [3] National Secretariat for Science and Technology, Panama; [4]Organización Panameña de Trasplante, Ministry of Health, Panama.

Correspondig author:

Ilais Moreno Velasquez
MD, PhD
Gorgas Memorial Institute for Health Studies
0816-02593 Panama City, Panama
Email: imoreno@gorgas.gob.pa

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Abstract

Background: Central-America is a region with an elevated burden of Chronic Kidney Disease (CKD); however, very little is known regarding the costs of treatment for end-stage renal disease. We aim to investigate the direct costs associated with hemodialysis (HD) and peritoneal dialysis (PD) in public and private Panamanian institutions in 2015, to perform a five year time budget impact analysis and, to calculate the years of life lost (YLL) due to CKD.

Methods: Data on direct costs derives from the public and private sectors. A budget impact analysis was calculated from the payer perspective and estimated five scenarios assuming that the mix of dialysis modality use shifts toward greater use of PD over time. The YLL due to CKD was calculated using data from the National Mortality Registry.

Results: In 2015, the total costs for dialysis in the public sector ranged from approximately $7.9 million (PD) to $62 million (HD). Estimated costs were higher in the scenario where a decrease in PD was assumed. The average annual loss due to CKD was 25,501, 808.40 USD-YLL.

Conclusion: End-stage renal disease (ESRD) represents a major challenge for Panama. Our results suggest that an increased use of PD might provide an opportunity to substantially lower overall ESRD treatment costs.

Keywords: Chronic Kidney disease, dialysis, costs, years of life lost, Panama

Strengths and Limitations

- To our knowledge, this is the first comprehensive study on economic costs of HD and PD modalities performed in Panama.
- Costs due to hospitalization, complications and emergency medicines were not evaluated for HD. Therefore, any possible bias is likely to underestimate and not overestimate the cost advantage of PD over HD.
- Indirect costs were not assessed; however, the years of life lost, a contributor of indirect costs, were estimated using the National Mortality Registry data.

1. Background

Chronic Kidney Disease (CKD) is a progressive disease with a substantial public health burden [1]. The majority of individuals with CKD worldwide are living in low-income and middle-income countries [2] where there exist pressure on constrained health-care resources [3]. In many countries, access to renal replacement therapy (RRT) has progressively increased yet, remains largely unaffordable for most patients and imposes a major burden on health systems [4].

The economic evaluation of CKD is important to provide information on which the decision-making process on allocation of resources of the health sector can be based. However, estimating costs of CKD is challenging given that underreporting is most common in the earliest stages of the disease, resulting in bias estimates [5]. Dialysis remains the most commonly employed treatment option for patients with end-stage renal disease (ESRD) due to the fact that not all patients are medically suitable for kidney transplantation and the demand for kidneys far exceeds the supply [6]. The composite cost of dialysis is mostly made up by the treatment itself (including disposables, machines, accommodation, electricity, water and human resources) along with RRT-related medication, transportation, and direct costs from complications, additional hospital admissions, and interventions [7].

Central-America is a region with an elevated burden of CKD [8, 9]; however, very little is known regarding the costs of ESRD. Panama is an upper-middle income country estimated to have a population of 4.1 million inhabitants, as of 2018 [10][10][10]. The country is divided into ten provinces and five “Comarcas,” geographically defined areas populated by several native-American groups. The Panamanian health system encompasses three distinct entities: the Ministry of Health (MoH) and Social Security (Caja de Seguro Social - CSS) which belong to the public health system covering approximately 30% and 70% of the population, respectively [11] and a voluntary paid private health system [12]. Therefore, the direct costs of medical care are at least partly covered by the CSS (the Panamanian public health insurance) or by the state.

National estimates of CKD derived from epidemiological studies are lacking. Recently, a cross-sectional study reported a CKD prevalence of 12.6% in two provinces where 60% of the population resides [13]. Moreover, the study described geographical disparities in age-adjusted standardized mortality rates due to CKD [13]. In 2001, the CSS calculated the yearly costs of care in the peritoneal dialysis (PD) and hemodialysis (HD) programs, resulting in an average per patient of $ 25,426.64 USD and $ 18,857.21 USD, respectively. However, neither the costs of RRT nor the years of life lost (YLL), useful measures in prioritizing public health interventions, has been recently evaluated.

The aim of this study is to i) estimate the direct costs associated with CKD dialysis, either HD or PD in public and private Panamanian institutions in 2015, ii) to perform a five year time budget impact analysis, and iii) to calculate the YLL due to CKD in the country.

2. Materials and Methods

Cost analysis

Data derives from the public (CSS renal program) and private (CETRERSA, the major private hemodialysis out-patient clinic in the country) sectors. Private data only included HD procedures whereas CSS data included PD and HD. We used data collected from January 2015 to December 2015 and the results are presented in US dollars (USD$) and on per patients per year basis.

Costs estimation from the CSS renal program was obtained from the HD National coordinating office and included administration, drugs and consumables and staff wages. Data from CETRERSA were obtained from the administration staff and comprised administration, staff wages, cleaning services, drugs and consumables, electricity, capital expenses (i.e., buildings, machines, instruments), laundry and sterilization. In the present study, PD includes both continuous ambulatory PD, and automated PD. Prevalent HD/PD cost ratio was calculated.

We performed a five year time horizon budget impact analysis on the direct cost related to the renal program in Panama, considering cost from both CSS and the private sector. The budget impact analysis estimates how changes in the mix of dialysis modalities would impact the trajectory of total spending for dialysis services (assuming that the mix of dialysis modality use shifts toward greater use of PD over time). The budget impact model was from the payer perspective and included five scenarios: scenario 1: a 2.5% yearly increase on PD, scenario 2: a 5% yearly increase on the use of PD; scenario 3: a 7.5% yearly increase on the use of PD and scenario 4: a 1% yearly decrease of PD use, from 2015 until 2020.

The estimated annual increase rate was based on prevalences reported previously by the Latin America Dialysis and Transplant Registry in 2010 [14]. The calculated annual

increased rate from 2010 to 2015 was 10.65% and -4.23% for HD and PD, respectively, with a ratio of 2.5%. No discount rates were included.

Years of Life Lost (YLL) due to premature CKD mortality

Data on CKD mortality for the year 2015 was retrieved from the National Mortality Registry at the Institute of Statistics and Census. Linear method was utilized for the analyses using the population aged 20 to 77 years old.

The calculation of the YLLs was performed by subtracting the life expectancy from the age of death of each individual. We then estimated the average life expectancy on the basis of the life table of the Institute of Statistics and Census life tables (77.74 years) and valued for the year 2015 at the country's gross domestic product (GDP) per capita. YLLs of each individual were multiplied by the GDP per capita current prices estimated for 2015, obtaining the YLLs in USD. We applied a 3% discounted present value at a social discount rate (2,3). The estimated total annual YLL by sex was reported according to age-categories: (20-30 years, 31-40 years, 41-50 years, 51-60 years and 71 to 80 years). In addition, YLL were calculated according to provinces.

All analysis was performed in Excel and in Stata version 14.

Ethical statement:

Permission to conduct the study was obtained from the medical directors of the respective hospitals. Ethical approval for the study was obtained from the Ethics Review Committee of the Gorgas Memorial Institute for Health Studies.

Patient and Public Involvement:

The study did not involve patients or public in planning or execution.

3. Results

Costs analysis

The mean direct expenditures for dialysis in summarized in Table 1. As of 2015, 2075 persons were under RRT (PD or HD), and out of those, 87% of the patients were receiving HD. Total costs for dialysis in the public sector ranged from approximately $9.8 million (PD) to $50.5 million (HD). The total cost per year of the programs for the public and private sectors combined was $70.3 million. The HD/PD costs ratio in the public sector was 1.19, whereas in the private and public sector combined was 1.20

Table 1: Estimated costs of Dialysis in the Public and Private sector for the year 2015 in Panama

	Public (CSS)		Private
	PD	HD	HD
Number of patients (n)	265	1746	64
Total annual costs ($USD)	7,915,687.25	62,102,496.24	2,797,380.00
Cost/patient /year ($USD)	29,870.52	35,568.44	43,447.96
	Public (CSS)		Public and Private
	PD+HD		PD+HD
Number of patients (n)	2011		2075
Total cost of programs ($USD)	67,553,921.23		70,351,301.23

CSS: Social Security (in Spanish Caja de Seguro Socia)l

Figure 1 shows the budget impact model according to different scenarios for the public sector –CSS (Panel A) as well as for the public and private sectors combined (Panel B). In the CSS, the estimated costs for the year 2020 ranged from $93.8 million (assuming a 7.5% annual increase in PD) to $100.7 million (assuming a decrease in 1% in PD). Likewise, in the public and private sector, the estimated costs were higher in the scenario where a 1% decrease in peritoneal dialysis was assumed ($104.7 million) (Panel B). Sensitivity analyses were conducted to explore model forecasts under varying assumptions about ESRD growth rates. In general, results of these analyses demonstrate that savings will be greater as the shift toward greater PD use is accomplished sooner.

Years of Life Lost –USD (YLL-USD) due to premature CKD mortality

In the year 2015, CKD was the cause of 440 deaths in Panama, accounting for 2.4 % of the total deaths registered. The number of male deaths was 279 (63.4%), whereas for females it was 161 (36.6%).

The average annual loss was 25,501, 808.40 USD YLL. In men, the higher YLL was observed for the age-group 51-60, whereas in women, the higher YLL was observed for the age-group 61-70, as shown in Figure 2.

The top three provinces with the highest accumulated number of YLL-USD in the age-group below 40 years due to CKD were 1) the Province of Panama (1,548,252.11 YLLs) , 2) the Province of Coclé, (YLLs of 459,212.85) and the Province of Colón (YLLs 314,586.97) (Supplementary Table 1).

4. Discussion

In the present study, we found that treatment with dialysis constitutes a substantial burden in terms of the provision of health services and in YLL.

In Panama, the total health care expenditure represented approximately 8% of the GDP in 2014 [15]. In the context of our findings, during the year 2015, approximately 1.6 % of the health care budget was invested in dialysis considering only the costs derived from the CSS. In addition, the average annual loss in terms of YLL due to CKD represented 0.59% of the GDP allocated to health. Similar levels of expenditure are reported for high-income countries [16, 17]. Of note, it has been shown that the economic burden associated with milder forms of CKD are even higher: more than twice the total cost of ESRD [18].

Assuming our reference scenario, it is estimated that the accumulated costs in five years will be approximately $505 million for the CSS and $525 million for both, private and public sectors combined. Noteworthy, this estimate excludes the ongoing costs derived from the MoH, which also adds a financial pressure to the health system. In this perspective, the cost of therapy per se and medicines were the major costs drivers in HD. Therefore, strategies aimed at reducing these costs would help to reduce annual cost in the short term.

All forms of dialysis outside hospital are more cost effective than in hospital-based dialysis [19]. In fact, the number of patients treated with PD rose worldwide from 1997 to 2008, with a 2.5-fold increase in the prevalence of PD patients in developing countries [20]. In agreement with previous studies, we observed a considerable cost saving related to PD modalities over HD [21]. Our HD/PD cost ratio was lower than the one reported in Mexico, but higher than those stated previously in other countries of the region [22]. Despite several advantages including the possibility of being offered in the remotest locations, our results indicate that PD is still an underused therapy in Panama as compared with reports from other countries such as Mexico, El Salvador and Guatemala, where the utilization rates were 66%, 76.5% and 56%, respectively [20]. In this context, if the CSS increases the PD utilization by 7.5% per year, the proportion of PD utilization will reach 50% in 5 years. The

reasons for the underutilization of PD are presumably multifactorial and may partly be explained by the shortage of trained nephrologists and nurses as well as the lack of health policies [9]. Currently there are 32 nephrologists nationwide, which constitutes a relatively low distribution of density of nephrologists per million population [23]. Furthermore, as opposed to other countries [21], Panama has a small market without local manufacturing facilities of PD bags and largely depends on imported medicines and equipment.

There is compelling evidence that kidney transplantations have led to substantial cost savings for health care systems in high-income countries [24]. Kidney transplantations in Panama began in 1990, and human resources and infrastructure has been enlarged. In 2015, there were 28 kidney transplantations performed in Panama and the number of donors have increased over the years, yet at a slow rate [25].

Taken together and from a macroeconomic standpoint, our results suggest that increasing PD utilization might reduce the overall healthcare expenditure in Panama. Therefore, key strategies such as implementation of policies and incentives favoring PD modality over HD should be advocated [26]. A complementary and vital approach is slowing the progression of CKD to ESRD. Likewise, it is highly recommended that the country improve the kidney transplant programs.

The burden of premature death and health loss from ESRD has been widely described. Between 1990 and 2013, the number of cases of CKD due to diabetes and due to other causes increased by more than 50% worldwide [27]. In addition, the burden of CKD disproportionately impacts low-income and middle-income countries where growth in diabetes, hypertension and obesity is greatest [28]. Moreover, poverty increases the risk of pathologies that predispose CKD to develop, and worsens outcomes in those who already have this disease [29]. Previous studies have reported a relationship between progressive CKD and its impact on household income or poverty, including spending more than 10% on income out of pocket payment [30, 31].

Remarkably, Latin America has the highest CKD death rate in the world [32] where diabetes mellitus, hypertension and recently, CKD of unknown etiology in Central-America are contributors [4, 28]. Interestingly, Coclé, a province with the highest age-adjusted

mortality rate in the country [13], presented considerably elevated YLL in the age-group below 40. Recently, the legal framework for the CKD registration in Panama started through a resolution signed by the MoH, establishing notification of CKD as compulsory for private and health institutions at a national level. In addition, CKD guidelines are currently being revised. On a broader perspective, if the Sustainable Development Goal of poverty reduction is to be accomplished, is essential that health systems protect individuals from the economic burden of CKD and other non-communicable diseases [33].

This study has strengths and limitations. Costs due to hospitalization, complications, emergency medicines, transportation were not included in the HD calculation, and hence, any possible bias is likely to underestimate and not overestimate the cost advantage of PD over HD. Of note, patients frequently have to travel long distances, often with families, to receive specialized care adding a dimension of social and economic consequences that was beyond the scope of this study. Despite the exclusion of these costs, we estimated YLL, a contributor of indirect costs. However, it is it likely that the reliance on diagnostic code data alone to define CKD as a cause of death and the underreporting resulted in underestimation of people with early stages of CKD. Finally, costs data derived from the MoH could not be obtained, underestimating the total costs from the public sector. Currently, there are three institutions from the MoH offering dialysis within the country. According to the Panamanian Transplant Organization, in 2015 there were n=26 and n=204 patients receiving PD and HD treatment, respectively in these institutions.

In conclusion, ESRD represents a major challenge for Panama. Our results suggest that an increased utilization of PD provides an opportunity to lower overall ESRD treatment costs. In the long term, an important factor to reduce the overall annual cost is to reduce the number of patients with ESRD. Therefore, CKD in early stages (which affects far more patients) should not be ignored by policy makers. Altogether, the huge cost associated with RRT provides a compelling economic incentive for improving the prevention, detection and management of CKD and its health policies in Panama.

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Conflict of interest: IMV, RV, BG, JM, CC and VH declare no conflict of interest. MTC currently works at Sanofi Pasteur, nonetheless, her responsibilities do not relate with the submitted work.

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Contributorship statement: IMV wrote the draft of the work. IMV MTC and VH analyzed the data. CC and RV provided the data. IMV, MTC, RV, BG, JM, CC and VH interpreted the data, critically revised the draft for important intellectual content and approved the final version. All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data availability: The datasets used and/or analyzed during the current study are available from the authors on reasonable request.

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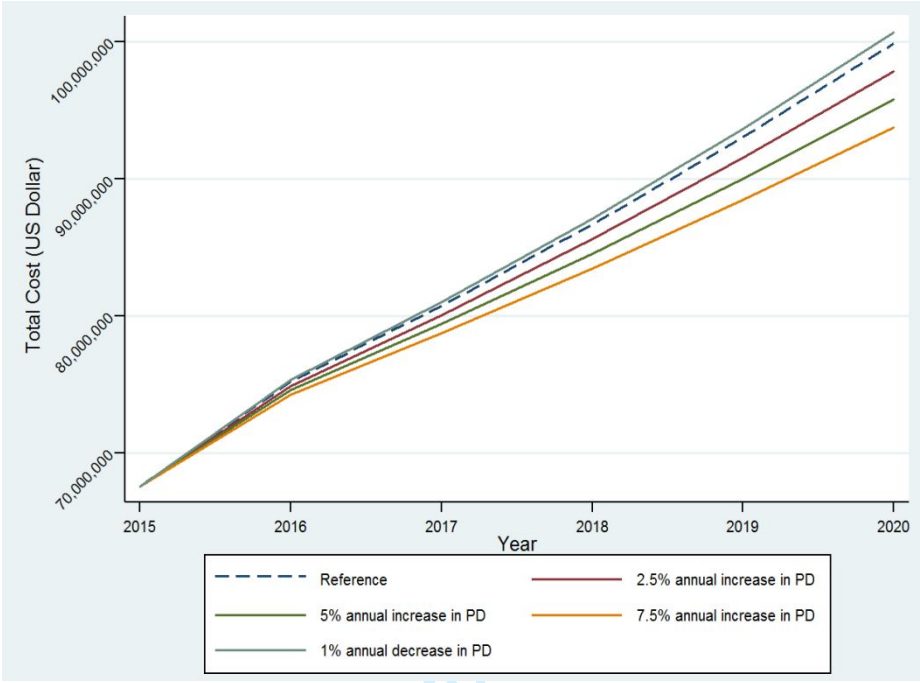
Figure 1. Estimated cost (US Dollars) of the dialysis program according to different scenarios in the public sector (A) and in the combined public and private sector (B).

(A)



(B)

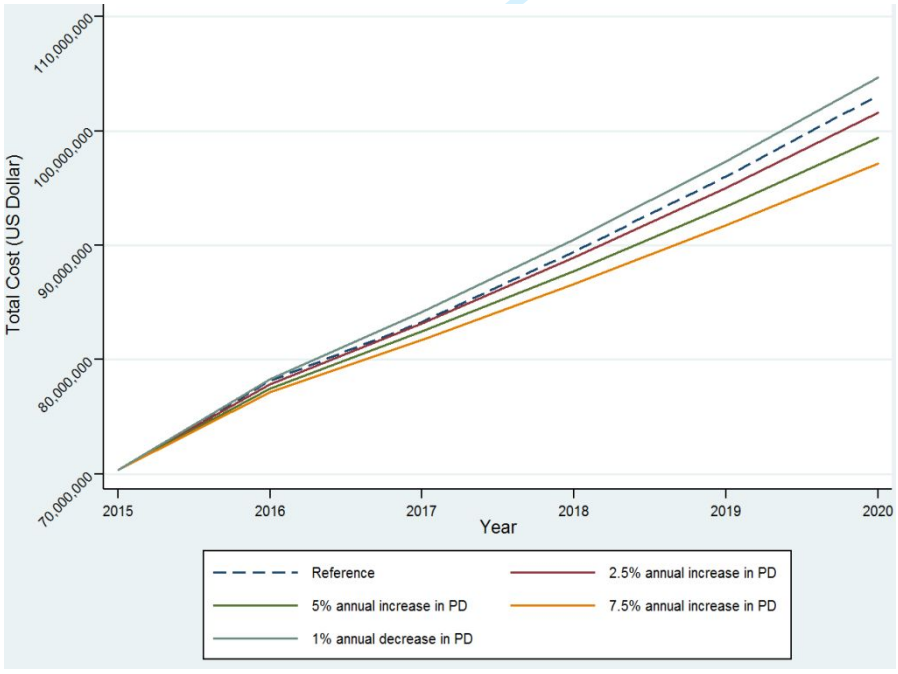
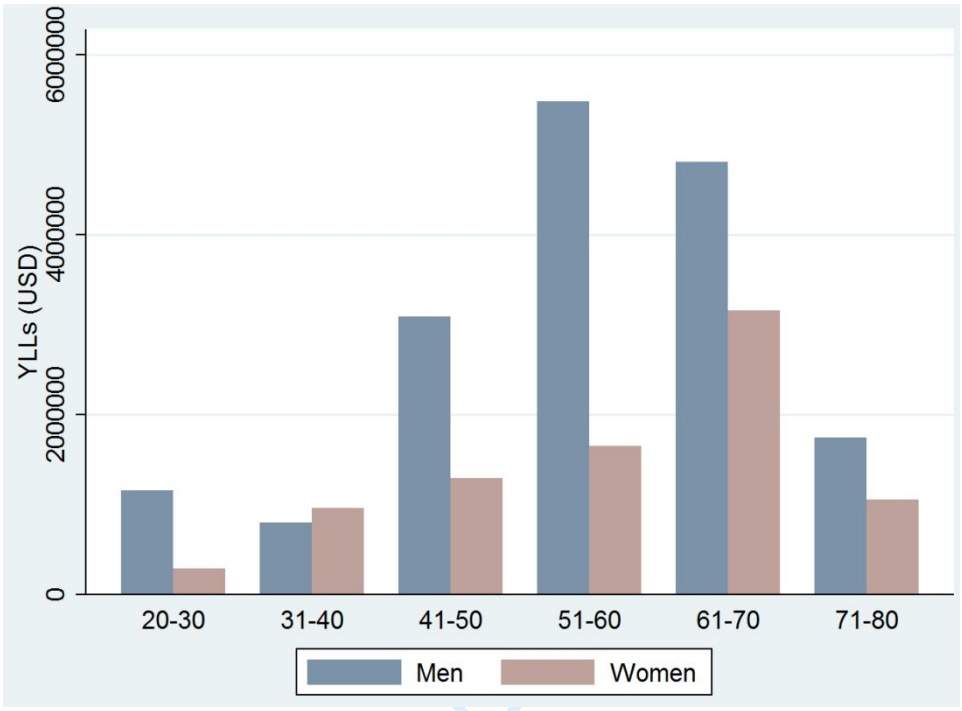


Figure 2. Years of Life Lost-(USD) due to premature mortality, according to age-group categories in Panama. Year 2015



Supplementary Table 1

Years of Life Lost (USD) due to CKD mortality below the age of 40 years, according to provinces in Panama. Year 2015

Province*	YLLs-USD
Panamá	1,548,252.11
Coclé	459,212.85
Colón	314,586.97
Chiriquí	301,269.05
Panamá Oeste	298,389.39
Emberá Indigenous	160,991.2
Bocas del Toro	152,671.82
Los Santos	143,929.82

** Provinces with recorded deaths due to CKD in the age below 40 years.*

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

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants Financial costs based on secondary data, and therefore many items are n/a	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 (selection of sectors offering Hemo and peritoneal dyalisis)
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
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
Bias	9	Describe any efforts to address potential sources of bias
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
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*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

Continued on next page

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
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data N/A	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(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 N/A	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
		(*b*) Report category boundaries when continuous variables were categorized
		(*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
Discussion		
Key results	18	Summarise key results with reference to study objectives
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
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
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

*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.

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End-stage renal disease: Financial costs and years of life lost in Panama

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End-stage renal disease: Financial costs and years of life lost in Panama

Ilais Moreno Velásquez[1], Maribel Tribaldos Causadias[1], Régulo Valdés[2], Beatriz Gómez[1], Jorge Motta[1,3], César Cuero[4], Víctor Herrera[1]

[1]Gorgas Memorial Institute for Health Studies, Panama; [2] Caja de Seguro Social, Panama; [3] National Secretariat for Science and Technology, Panama; [4]Organización Panameña de Trasplante, Ministry of Health, Panama.

Correspondig author:

Ilais Moreno Velasquez
MD, PhD
Gorgas Memorial Institute for Health Studies
0816-02593 Panama City, Panama
Email: imoreno@gorgas.gob.pa

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Abstract

Objectives: Central-America is a region with an elevated burden of Chronic Kidney Disease (CKD); however, the cost of treatment for end-stage renal disease remains an understudied area. This study aims to investigate the direct costs associated with hemodialysis (HD) and peritoneal dialysis (PD) in public and private institutions from Panama in 2015, to perform a five year time budget impact analysis and, to calculate the years of life lost (YLL) due to CKD.

Design: A retrospective cost-analysis study, using hospital costs and registry-based data.

Setting: Data on direct costs derives from the public and private sectors at two institutions from Panama. Data on CKD mortality were obtained from the National Mortality Registry.

Methods: A budget impact analysis was calculated from the payer perspective and estimated five scenarios assuming that the mix of dialysis modality use shifts toward greater use of PD over time. The YLL due to CKD was calculated using data recorded between 1 January 2015 and 31 December 2015. Linear method was utilized for the analyses using the population aged 20 to 77 years old.

Results: In 2015, the total costs for dialysis in the public sector ranged from approximately $7.9 million (PD) to $62 million (HD). Estimated costs were higher in the scenario where a decrease in PD was assumed. The average annual loss due to CKD was 25,501, 808.40 USD-YLL.

Conclusion: End-stage renal disease represents a major challenge for Panama. Our results suggest that an increased use of PD might provide an opportunity to substantially lower overall ESRD treatment costs.

Keywords: Chronic Kidney disease, dialysis, costs, years of life lost, Panama

Strengths and Limitations

- To our knowledge, this is the first comprehensive study on economic costs of HD and PD modalities performed in Panama.
- Costs due to hospitalization, complications and emergency medicines were not evaluated for HD. Therefore, any possible bias is likely to underestimate and not overestimate the cost advantage of PD over HD.
- Indirect costs were not assessed; however, the years of life lost, a contributor of indirect costs, were estimated using the National Mortality Registry data.

1. Background

Chronic Kidney Disease (CKD) is a progressive disease with a substantial public health burden [1]. Early detection can prevent or delay progression to end-stage renal disease (ESRD) [2] . The majority of individuals with CKD worldwide are living in low-income and middle-income countries [3] where there exist pressure on constrained health-care resources [4]. In many countries, access to renal replacement therapy (RRT) has progressively increased yet, remains largely unaffordable for most patients and imposes a major burden on health systems [5].

The economic evaluation of CKD is important to provide information on which the decision-making process on allocation of resources of the health sector can be based. However, estimating costs of CKD is challenging given that underreporting is most common in the earliest stages of the disease, resulting in bias estimates [6]. Dialysis remains the most commonly employed treatment option for patients with ESRD due to the fact that not all patients are medically suitable for kidney transplantation and the demand for kidneys far exceeds the supply [7]. The composite cost of dialysis is mostly made up by the treatment itself (including disposables, machines, accommodation, electricity, water and human resources) along with RRT-related medication, transportation, and direct costs from complications, additional hospital admissions, and interventions [8].

Central-America is a region with an elevated burden of CKD [9, 10]; however, very little is known regarding the costs of milder forms of CKD and ESRD. Panama is an upper-middle income country estimated to have a population of 4.1 million inhabitants, as of 2018 [11]. The country is divided into ten provinces and five “Comarcas,” geographically defined areas populated by several native-American groups. Panama has a fragmented health system with public and private health coverage schemes that encompasses three distinct entities [12]. The Ministry of Health (MoH) and Social Security (Caja de Seguro Social - CSS), which belong to the public health system, operate independently from each other and cover approximately 30% and 70% of the population, respectively [13]. The MoH provides health coverage to the unemployed population, whereas the CSS provides

health coverage to formally employed persons. In addition, there are private insurers with which affiliation is voluntary [14]. Therefore, the direct costs of medical care are at least partly covered by the CSS (the Panamanian public health insurance) or by the state.

Electronic health records at public health facilities are in the process of implementation; consequently, a CKD national registry is absent in the country [12]. Further, national estimates of CKD derived from epidemiological studies are lacking. Recently, a cross-sectional study reported a CKD prevalence of 12.6% in two provinces where 60% of the population resides [15]. Moreover, the study described geographical disparities in age-adjusted standardized mortality rates due to CKD [15]. In 2001, the CSS calculated the yearly costs of care in the peritoneal dialysis (PD) and hemodialysis (HD) programs, resulting in an average per patient of $ 25,426.64 USD and $ 18,857.21 USD, respectively. However, neither the costs of RRT nor the years of life lost (YLL), useful measures in prioritizing public health interventions, has been recently evaluated.

The aim of this study is to i) estimate the direct costs associated with ESRD treatment, either HD or PD in public and private Panamanian institutions in 2015, ii) to perform a five year time budget impact analysis, and iii) to calculate the YLL due to CKD in the country.

2. Materials and Methods

Cost analysis-ESRD

Three sectors were selected based on their dialysis coverage and formally invited to participate in the study via an Institutional letter: CSS (comprising all HD and PD at the national level), Hospital Santo Tomás (MoH), and the major private hemodialysis out-patient clinic in the country (CETRERSA).

Because the information is not systematized homogenously, data on costs was not possible to obtain from the MoH. Therefore, in the present study, data derives from the public (CSS renal program) and private (CETRERSA) sectors. Private data only included HD procedures whereas CSS data included PD and HD. We used data collected from January 2015 to December 2015 and the results are presented in US dollars (USD$) and on per patients per year basis.

Costs estimation from the CSS renal program was obtained from the HD National coordinating office and included administration, drugs and consumables and staff wages (Supplementary Table 1). Data from CETRERSA were obtained from the administration staff and comprised administration, staff wages, cleaning services, drugs and consumables, electricity, capital expenses (i.e., buildings, machines, instruments), laundry and sterilization (Supplementary Table 2). Data was provided to researchers in different formats. For the private sector, data on HD costs was grouped according to categories using the format shown in Supplementary Table 2. For the CSS, data on HD and PD costs was provided in several electronic PDF files and costs were distributed according to the categories stipulated previously.

In the present study, PD includes both continuous ambulatory PD, and automated PD. Prevalent HD/PD cost ratio was calculated for the public sector. The estimated annual increase rate of HD and PD utilization was calculated according to the prevalence reported previously by the Latin America Dialysis and Transplant Registry in 2010 [16] and the

prevalence reported in 2015 by the CSS and CETRERSA. The calculated annual increased rate from 2010 to 2015 was 10.65% and -4.23% for HD and PD, respectively, with a ratio of 2.5%. The cost analysis was performed in present value; therefore, no discount rates were included.

We performed a five year time horizon budget impact analysis on the direct cost related to the renal program in Panama, considering cost from both CSS and the private sector. The budget impact analysis estimates how changes in the mix of dialysis modalities would impact the trajectory of total spending for dialysis services (assuming that the mix of dialysis modality use shifts toward greater use of PD over time). The budget impact model was from the payer perspective and included five scenarios: scenario 1: a 2.5% yearly increase on PD, scenario 2: a 5% yearly increase on the use of PD; scenario 3: a 7.5% yearly increase on the use of PD and scenario 4: a 1% yearly decrease of PD use, from 2015 until 2020. Scenarios were based on the ratio of sensibility (annual increase rate of HD utilization /annual increase rate of PD utilization) =2.5%. In addition, complementary analyses were performed under different arbitrary assumptions (10% annual increase in PD, 2.5% decrease in PD utilization).

Years of Life Lost (YLL) due to premature CKD mortality

Data on CKD mortality for the year 2015 was retrieved from the National Mortality Registry at the Institute of Statistics and Census. Deaths recorded as N18 (chronic kidney disease, n=221) and N19 (unspecified kidney failures, n=18) were included according to the International Classification of Diseases 10th Revision codes. Linear method was utilized for the analyses using the population aged 20 to 77 years old.

The calculation of the YLLs was performed by subtracting the life expectancy from the age of death of each individual. We then estimated the average life expectancy on the basis of the life table of the Institute of Statistics and Census life tables (77.74 years) and valued for the year 2015 at the country's gross domestic product (GDP) per capita. YLLs of each individual were multiplied by the GDP per capita current prices estimated for 2015,

obtaining the YLLs in USD. We applied a 3% discounted present value at a social discount rate (2,3). The estimated total annual YLL by sex was reported according to age-categories: (20-30 years, 31-40 years, 41-50 years, 51-60 years and 71 to 80 years). In addition, YLL were calculated according to provinces.

All analysis was performed in Excel and in Stata version 14.

Ethical statement:

Permission to conduct the study was obtained from the medical directors of the respective institutions. Ethical approval for the study was obtained from the Ethics Review Committee of the Gorgas Memorial Institute for Health Studies.

Patient and Public Involvement:

The study did not involve patients or public in planning or execution.

3. Results

Costs analysis

The mean direct expenditures for dialysis in summarized in Table 1. As of 2015, 2075 persons were under RRT (PD or HD), and out of those, 87% of the patients were receiving HD. Total costs for dialysis in the public sector ranged from approximately $9.8 million (PD) to $50.5 million (HD). The total cost per year of the programs for the public and private sectors combined was $70.3 million. The HD/PD costs ratio in the public sector was 1.19.

Table 1: Estimated costs of Dialysis in the Public and Private sector for the year 2015 in Panama

	Public (CSS)		Private
	PD	HD	HD
Number of patients (n)	265	1746	64
Total annual costs ($USD)	7,915,687.25	62,102,496.24	2,797,380.00
Cost/patient /year ($USD)	29,870.52	35,568.44	43,447.96
	Public (CSS)		Public and Private
	PD+HD		PD+HD
Number of patients (n)	2011		2075
Total cost of programs ($USD)	67,553,921.23		70,351,301.23

CSS: Social Security (in Spanish Caja de Seguro Socia)l

The total estimated costs (USD) during the five years for the reference scenarios were 503 million (CSS) and 520 million (combined sectors). Figure 1 shows the budget impact model according to different scenarios for the public sector-CSS (Panel A) as well as for the public and private sectors combined (Panel B). In the CSS, the estimated costs for the year 2020 ranged from $93.8 million (assuming a 7.5% annual increase in PD) to $100.7 million (assuming a decrease in 1% in PD).

Likewise, in the public and private sector, the estimated costs were higher in the scenario where a 1% decrease in peritoneal dialysis was assumed ($104.7 million) (Panel B). Sensitivity analyses were conducted to explore model forecasts under varying assumptions. In general, results of these analyses demonstrate that savings will be greater as the shift

toward greater PD use is accomplished sooner (a 10% annual increase in the use of PD in CSS resulted in reducing costs by USD 4.5 millions per year).

Years of Life Lost –USD (YLL-USD) due to premature CKD mortality

In the year 2015, CKD was the cause of 440 deaths in Panama, accounting for 2.4 % of the total deaths registered. The number of male deaths was 279 (63.4%), whereas for females it was 161 (36.6%).

The average annual loss was 25,501, 808.40 USD YLL. In men, the higher YLL was observed for the age-group 51-60, whereas in women, the higher YLL was observed for the age-group 61-70, as shown in Figure 2.

The top three provinces with the highest accumulated number of YLL-USD in the age-group below 40 years due to CKD were 1) the Province of Panama (1,548,252.11 YLLs) , 2) the Province of Coclé, (YLLs of 459,212.85) and the Province of Colón (YLLs 314,586.97) (Supplementary Table 3).

4. Discussion

In the present study, we found that treatment with dialysis constitutes a substantial burden in terms of the provision of health services and in YLL.

In Panama, the total health care expenditure represented approximately 8% of the GDP in 2014. In the context of our findings, during the year 2015, approximately 1.6 % of the health care budget was invested in dialysis considering only the costs derived from the CSS. Of note, the costs associated with milder forms of CKD (early stages of the disease without RRT) were not evaluated and it has been reported that the economic burden associated with milder forms of CKD is more than twice the total cost of ESRD [17]. In addition, the average annual loss in terms of YLL due to CKD represented 0.59% of the GDP allocated to health. Similar levels of expenditure have been reported in high-income countries [18, 19].

Assuming our reference scenario, it is estimated that the accumulated costs in five years will be approximately $505 million for the CSS and $525 million for both, private and public sectors combined. Noteworthy, this estimate excludes the ongoing costs derived from the MoH, which also adds a financial pressure to the health system. In this perspective, the cost of therapy per se and medicines were the major costs drivers in HD in at the CSS, whereas the staff wages represented the highest cost for the private sector. Therefore, strategies aimed at reducing these costs would help to reduce annual cost in the short term.

All forms of dialysis outside hospital are more cost effective than in hospital-based dialysis [20]. In fact, the number of patients treated with PD rose worldwide from 1997 to 2008, with a 2.5-fold increase in the prevalence of PD patients in developing countries [21]. In agreement with previous studies, we observed a considerable cost saving related to PD modalities over HD [22]. Our HD/PD cost ratio was lower than the one reported in Mexico, but higher than those stated previously in other countries of the region [23]. Despite several advantages including the possibility of being offered in the remotest locations, our results indicate that PD is still an underused therapy in Panama as compared with reports from

other countries such as Mexico, El Salvador and Guatemala, where the utilization rates were 66%, 76.5% and 56%, respectively [21]. In this context, if the CSS increases the PD utilization by 7.5% per year, the proportion of PD utilization will reach 50% in 5 years. The reasons for the underutilization of PD are presumably multifactorial and may partly be explained by the scarcity of trained nephrologists and nurses as well as the lack of health policies [10]. Currently there are 32 nephrologists nationwide, which constitute a relatively low distribution of density of nephrologists per million population [24]. Furthermore, as opposed to other countries [22], Panama has a small market without local manufacturing facilities of PD bags and largely depends on imported medicines/equipment. Of note, Colombia and Nicaragua have also reported a decrease in the use of PD from the year 2000 to 2010, contrasted with the continued expansion of HD [16].

There is compelling evidence that kidney transplantations have led to substantial cost savings for health care systems in high-income countries [25]. Kidney transplantations in Panama began in 1990, and human resources and infrastructure has been enlarged. According to the Panamanian Transplant Organization (PTO), in 2015, there were 28 kidney transplantations performed in Panama and the number of donors has increased over the years, yet at a slow rate.

Taken together and from a macroeconomic standpoint, our results suggest that increasing PD utilization might reduce the overall healthcare expenditure in Panama. Therefore, key strategies such as implementation of policies and incentives favoring PD modality over HD should be advocated [27]. A complementary and vital approach is slowing the progression of CKD to ESRD. Likewise, it is highly recommended to enhance the kidney transplant programs.

The burden of premature death and health loss from CKD has been widely described. Between 1990 and 2013, the number of cases of CKD due to diabetes and due to other causes increased by more than 50% worldwide [28]. In addition, the burden of CKD disproportionately impacts low-income and middle-income countries where growth in diabetes, hypertension and obesity is greatest [29]. Moreover, poverty increases the risk of pathologies that predispose CKD to develop, and worsens outcomes in those who already

have this disease [30]. Previous studies have reported a relationship between progressive CKD and its impact on household income or poverty, including spending more than 10% on income out of pocket payment [31, 32].

Remarkably, Latin America has the highest CKD death rate in the world [33] where diabetes mellitus, hypertension and recently, CKD of unknown etiology in Central-America are contributors [5, 29]. In Panama, the trends in mortality rates due to CKD have been declining from 2006, however geographical disparities exist [15]. Interestingly, Coclé, a province with the highest age-adjusted mortality rate in the country [15], presented considerably elevated YLL in the age-group below 40. Taken together, the sum of the estimated YLL and the dialysis costs is unsustainable for the health system, highlighting the importance on prevention. Recently, the legal framework for the CKD registration in Panama started through a resolution signed by the MoH, establishing notification of all stages of CKD as compulsory for private and health institutions at a national level. In addition, CKD guidelines are currently being revised. On a broader perspective, if the Sustainable Development Goal of poverty reduction is to be accomplished, is essential that health systems protect individuals from the economic burden of CKD and other non-communicable diseases [34].

This study has strengths and limitations. Costs due to hospitalization, complications, emergency medicines, transportation were not included in the HD calculation, and hence, any possible bias is likely to underestimate and not overestimate the cost advantage of PD over HD. Of note, patients frequently have to travel long distances, often with families, to receive specialized care adding a dimension of social and economic consequences that was beyond the scope of this study. Despite the exclusion of these costs, we estimated YLL, a contributor of indirect costs. However, it is it likely that the reliance on diagnostic code data alone to define CKD as a cause of death and the underreporting resulted in underestimation of people with early stages of CKD. Finally, because the public systems operate independently of each other and the information (health and costs) is not systematized homogenously, costs data derived from the MoH could not be obtained. Therefore, the total costs from the public sector are underestimated and the estimated yearly increase rate should be interpreted with caution. Likewise, we could not perform a cost-

effectiveness analysis. Despite the lack of registries, the Panamanian Society of Nephrology and Hypertension, along with the PTO have been actively recording the number of cases undergoing RRT. Currently, there are three institutions from the MoH offering dialysis within the country. According to the PTO, in 2015 there were n=26 and n=204 patients receiving PD and HD treatment, respectively in these institutions.

In conclusion, CKD represents a major challenge for Panama. Our results suggest that an increased utilization of PD provides an opportunity to lower overall ESRD treatment costs. In the long term, an important factor to reduce the overall annual cost is to reduce the number of patients with ESRD. Therefore, CKD in early stages (which affects far more patients and who are frequent users of the health system) should not be ignored by policy makers. Altogether, the huge cost associated with CKD provides a compelling economic incentive for improving the prevention, detection and management of CKD and its health policies in Panama.

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Conflict of interest: IMV, RV, BG, JM, CC and VH declare no conflict of interest. MTC currently works at Sanofi Pasteur, nonetheless, her responsibilities do not relate with the submitted work.

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Contributorship statement: IMV wrote the draft of the work. IMV MTC and VH analyzed the data. CC and RV provided the data. IMV, MTC, RV, BG, JM, CC and VH interpreted the data, critically revised the draft for important intellectual content and approved the final version. All the authors agree to be accountable for all aspects of the

work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data availability: The datasets used and/or analyzed during the current study are available from the authors on reasonable request.

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Figure 1. Estimated cost (US Dollars) of the dialysis program according to different scenarios in the public sector (A) and in the combined public and private sector (B).

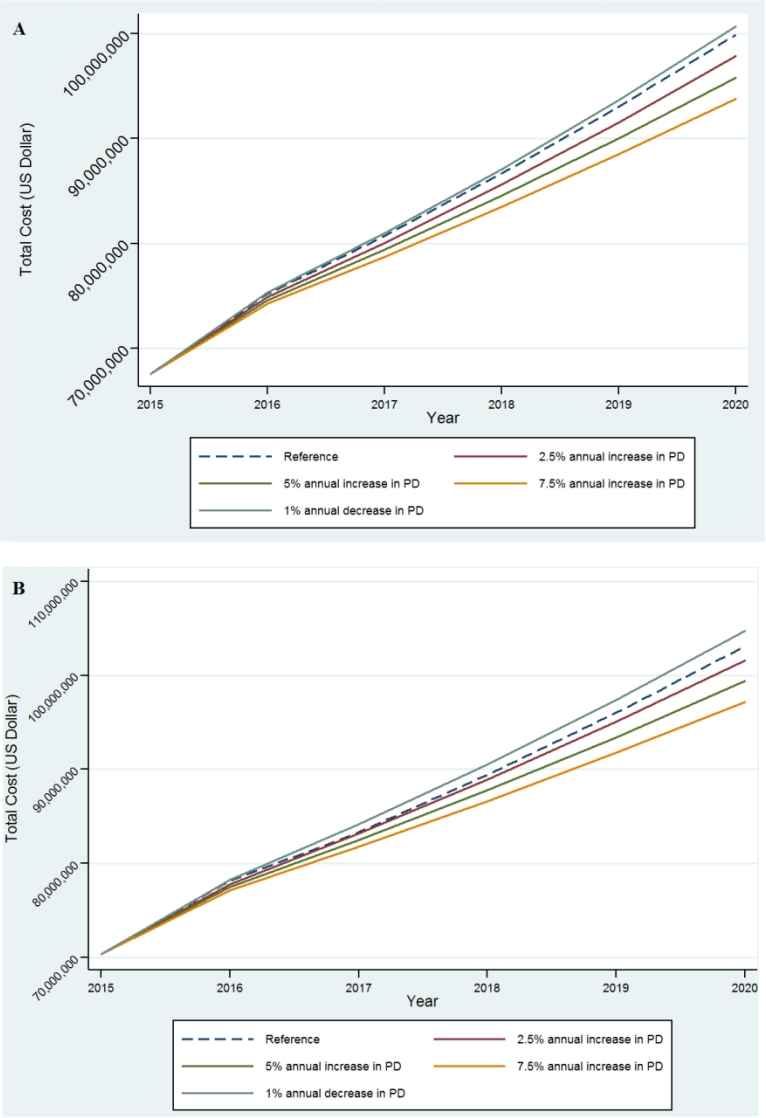
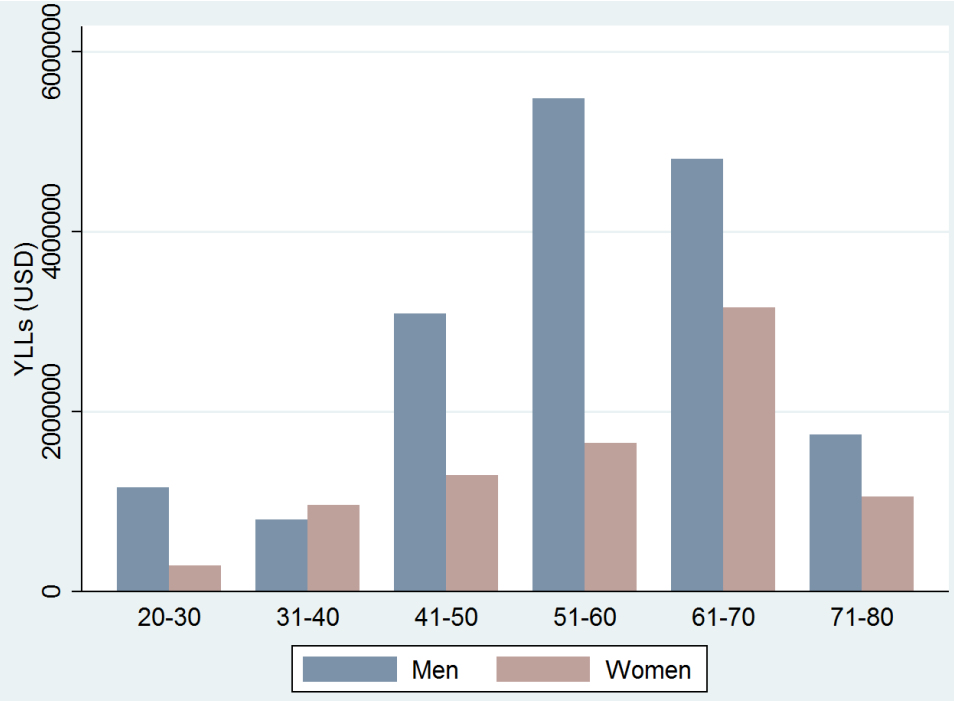


Figure 2. Years of Life Lost-(USD) due to premature mortality, according to age-group categories in Panama. Year 2015



Supplementary Table 1. Estimated cost of HD and PD (USD) in CSS, year 2015

HD + PD (PUBLIC)				
	Monthly cost	**Yearly cost/patient**	**Patients (factor)**	**Total Cost (USD)**
PD		18,766.00	265	4,972,990.00
HD	1,739.66	20,875.92	1746	36,449,356.32
Eritropoyetin	507.00	6,084.00	2011	12,234,924.00
Paricalcitiol	299.00	3,588.00	1423	5,105,724.00
Sevelamer	207.00	2,484.00	1751	4,349,484.00
Peritoneal Dialysis		18,766.00	265	4,972,990.00
Total				**63,112,478.32**
National Coordination		26,500.00	1	26,500.00
National Coordination (teaching)		11,000.00	1	11,000.00
National coordination (personnel)	5,982.84	71,794.08	1	71,794.08
National Coordination (physicians)	10,248.42	122,981.04	1	122,981.04
Sub total				**232,275.12**
Nephrologists (salary)	62,682.52	752,190.24	0.87*	654,405.51
Nephrologists (shifts)	41,600.00	499,200.00	0.87*	434,304.00
Nephrologists (productivity)	2,142.00	25,704.00	1	25,704.00
Sub total				**1,114,413.51**
General practitioners (salary)	71,029.00	852,348.00	1	852,348.00
General practitioners (shifts)	19,960.00	239,520.00	1	239,520.00
Sub total				**1,091,868.00**
Nurses (salary)	129,680.19	1,556,162.28	1	1,556,162.28
Nurses (shifts)	37,227.00	446,724.00	1	446,724.00
Sub total				**2,002,886.28**
TOTAL (HD+PD)				**67,553,921.23**
Yearly cost / patient (HD+PD)				**38,580.19 USD**

**Shifts are calculated only for HD (Prevalence of HD =0.87).*

Supplementary Table 2. Estimates Costs of HD (USD) in CETRERSA, year 2015

HD (PRIVATE)			
	Monthly cost 2015	**Yearly Cost**	**Cost/HD**
Human resources	**Private**		
Personal (Nephrologists, General Practitioners, Nurses, etc.)	**123757.00**	**1485084.00**	**147.86**
Subtotal Human Resources	**123757.00**	**1,485,084.00**	**147.86**
Basic Services		**Private**	
Water	400.00	4,800.00	0.48
Electricity	3,886.00	46,632.00	4.64
Subtotal Basic Services	**4,286.00**	**51,432.00**	**5.12**
Travel expenses	**Private**		
Food/Travel expenses companions	57.00	684.00	0.07
Travel expenses patients	1605.00	19260.00	1.92
Subtotal Travel expenses	**1,662.00**	**19,944.00**	**1.99**
Infrastructure	**Private**		
Maintenance and buildings	1,235.00	14,820.00	1.48
Maintenance of equipment	7,018.00	84,216.00	8.38
Estimation of the use of buildings	29,151.00	349,812.00	34.83
Equipment utilization	4,184.00	50,208.00	5.00
Subtotal Infrastructure	**41,588.00**	**499,056.00**	**49.69**
Materials and supplies	**Private**		
Food-patients and human resources	2572.00	30864.00	3.07
Cost of clothing: sheets, patient gowns, disposable bed cover,	3048.00	36576.00	3.64
Diesel	1026.00	12312.00	1.23
Medicines	10091.00	121092.00	12.06
Pharmaceuticals supplies	38224.00	458688.00	45.67
Cleaning articles	639.00	7668.00	0.76
Laboratories	1125.00	13500.00	1.34
Office materials	773.00	9276.00	0.92
Surgical Medical Instruments	4324.00	51888.00	5.17
Subtotal Materials and Supplies	**61,822.00**	**741,864.00**	73.86
Machinery and equipment	**Private**		
Number of HD			**10044**
Number of patients			**64**
	Monthly cost 2015	**Yearly Cost**	**Cost/HD**
Total	**233,115.00**	**2,797,380.00**	**278.51**

Cost/patient
43,447.96 USD

Supplementary Table 3. Years of Life Lost-USD due to CKD mortality below 40 years of age, according to provinces in Panama. Year 2015

Province*	YLLs-USD
Panamá	1,548,252.11
Coclé	459,212.85
Colón	314,586.97
Chiriquí	301,269.05
Panamá Oeste	298,389.39
Emberá Indigenous	160,991.2
Bocas del Toro	152,671.82
Los Santos	143,929.82

** Provinces with recorded deaths due to CKD in the age below 40 years.*

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

	Page	Recommendation
Title and abstract	2	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	4	Explain the scientific background and rationale for the investigation being reported
Objectives	5	State specific objectives, including any prespecified hypotheses
Methods		
Study design	6	Present key elements of study design early in the paper
Setting	6	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants Financial costs based on secondary data, and therefore many items are not applicable	6,7	(*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 (selection of sectors offering Hemo and peritoneal dyalisis)
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	6+Supplementary Table	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	6,7	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
Bias	7	Describe any efforts to address potential sources of bias
Study size	n/a	Explain how the study size was arrived at
Quantitative variables	n/a	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	7,8	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*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
Results		
Participants	9,10	(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
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	n/a	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(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	9,10	*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	n/a	(*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
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	10	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	11-13	Summarise key results with reference to study objectives
Limitations	13-14	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	11-14	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	13-14	Discuss the generalisability (external validity) of the study results
Other information		
Funding	14	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

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End-stage renal disease: Financial costs and years of life lost in Panama. A cost-analysis study

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End-stage renal disease: Financial costs and years of life lost in Panama. A cost-analysis study.

Ilais Moreno Velásquez[1], Maribel Tribaldos Causadias[1], Régulo Valdés[2], Beatriz Gómez[1], Jorge Motta[1,3], César Cuero[4], Víctor Herrera-Ballesteros[1]

[1]Gorgas Memorial Institute for Health Studies, Panama; [2] Caja de Seguro Social, Panama; [3] National Secretariat for Science and Technology, Panama; [4]Organización Panameña de Trasplante, Ministry of Health, Panama.

Corresponding author:

Ilais Moreno Velásquez
MD, PhD
Gorgas Memorial Institute for Health Studies
0816-02593 Panama City, Panama
Email: imoreno@gorgas.gob.pa

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Abstract

Objectives: Central America is a region with an elevated burden of chronic kidney disease (CKD); however, the cost of treatment for end-stage renal disease remains an understudied area. This study aimed to investigate the direct costs associated with haemodialysis (HD) and peritoneal dialysis (PD) in public and private institutions in Panama in 2015, to perform a five-year budget impact analysis and to calculate the years of life lost (YLL) due to CKD.

Design: A retrospective cost-analysis study using hospital costs and registry-based data.

Setting: Data on direct costs were derived from the public and private sectors from two institutions from Panama. Data on CKD-related mortality were obtained from the National Mortality Registry.

Methods: A budget impact analysis was performed from the payer perspective, and five scenarios were estimated, with the assumption that the mix of dialysis modality use shifts towards a greater use of PD over time. The YLL due to CKD was calculated using data recorded between 1 January 2015, and 31 December 2015. The linear method was utilized for the analyses with the population aged 20 to 77 years old.

Results: In 2015, the total costs for dialysis in the public sector ranged from approximately $7.9 million (PD) to $62 million (HD). The estimated costs were higher in the scenario in which a decrease in PD was assumed. The average annual loss due to CKD was 25,501,808.40 USD-YLL.

Conclusion: End-stage renal disease represents a major challenge for Panama. Our results suggest that an increased use of PD might provide an opportunity to substantially lower overall ESRD treatment costs.

Keywords: Chronic kidney disease, dialysis, costs, years of life lost, Panama

Strengths and Limitations

- To the best of our knowledge, this is the first comprehensive study on the economic costs of HD and PD modalities performed in Panama.
- Costs due to hospitalization, complications and emergency medicines were not evaluated for HD. Therefore, any possible bias is likely to result in underestimation and not overestimation of the cost advantage of PD over HD.
- Indirect costs were not assessed; however, the years of life lost, a contributor to indirect costs, were estimated using National Mortality Registry data.

1. Background

Chronic kidney disease (CKD) is a progressive disease that imposes a substantial public health burden [1]. Early detection can prevent or delay progression to end-stage renal disease (ESRD) [2]. The majority of individuals with CKD worldwide are living in low-income and middle-income countries [3], where there exists pressure on limited health-care resources [4]. In many countries, access to renal replacement therapy (RRT) has progressively increased, yet it remains largely unaffordable for most patients and imposes a major burden on health systems [5].

The evaluation of the economic impact of CKD is important to provide information on which decisions regarding the allocation of healthcare resources can be based. However, estimating the costs associated with CKD is challenging given that underreporting is most common in the earliest stages of the disease, resulting in biased estimates [6]. Dialysis remains the most commonly employed treatment option for patients with ESRD because not all patients are medically suitable for kidney transplantation, and the demand for kidneys far exceeds the supply [7]. The total cost of dialysis is mostly composed of the costs of the treatment itself (including disposables, machines, accommodation, electricity, water and human resources) and the costs of medications, transportation, complications, additional hospital admissions, and interventions [8].

Central America is a region with an elevated burden of CKD [9, 10]; however, very little is known regarding the costs associated with milder forms of CKD and ESRD. Panama is an upper-middle income country estimated to have a population of 4.1 million inhabitants as of 2018 [11]. The country is divided into ten provinces and five “Comarcas,” which are geographically defined areas populated by several indigenous American groups. Panama has a fragmented health system with public and private health coverage schemes that encompass three distinct entities [12]. The Ministry of Health (MoH) and Social Security (Caja de Seguro Social - CSS), which belong to the public health system, operate independently from each other and cover approximately 30% and 70% of the population, respectively [13]. The MoH provides health coverage to the unemployed population,

whereas the CSS provides health coverage to formally employed persons. In addition, there are private insurers with which affiliation is voluntary [14]. Therefore, the direct costs of medical care are at least partly covered by the CSS (the Panamanian public health insurance) or by the state.

Electronic health records are in the process of being implemented at public health facilities; consequently, there is currently no CKD national registry in Panama [12]. Furthermore, national estimates of CKD derived from epidemiological studies are lacking. Recently, a cross-sectional study reported a CKD prevalence of 12.6% in the two provinces in which 60% of the population resides [15]. Moreover, the study described geographical disparities in age-adjusted standardized mortality rates due to CKD [15]. In 2001, the CSS calculated the annual costs of care for the peritoneal dialysis (PD) and haemodialysis (HD) programmes, resulting in average per patient costs of $25,426.64 USD and $18,857.21 USD, respectively. However, neither the costs of RRT nor the years of life lost (YLL), which are useful measures to consider when prioritizing public health interventions, has been recently evaluated.

The aim of this study was to i) estimate the direct costs associated with ESRD treatment, whether HD or PD, in public and private Panamanian institutions in 2015, ii) to perform a five-year budget impact analysis, and iii) to calculate the YLL due to CKD in the country.

2. Materials and Methods

Cost analysis-ESRD

The following three sectors were selected based on their dialysis coverage and formally invited to participate in the study via an institutional letter: CSS (comprising all HD and PD at the national level), Hospital Santo Tomás (MoH), and the major private haemodialysis outpatient clinic in the country (CETRERSA).

Because the information was not homogenously systematized, data on costs were not available from the MoH. Therefore, in the present study, the data were derived from the public (CSS renal programme) and private (CETRERSA) sectors. Private data only included HD procedures, whereas CSS data included PD and HD. We used data collected from January 2015 to December 2015, and the results are presented in US dollars (USD) and on a per-year basis.

The estimation of the costs of the CSS renal programme was based on data from the HD national coordinating office and included costs associated with administration, drugs and consumables and staff wages (Supplementary Table 1). Data from CETRERSA were obtained from the administrative staff and included costs associated with administration, staff wages, cleaning services, drugs and consumables, electricity, capital expenses (i.e., buildings, machines, instruments), and laundry and sterilization (Supplementary Table 2). Data were provided to researchers in different formats. For the private sector, data on HD costs were grouped according to categories using the format shown in Supplementary Table 2. For the CSS, data on HD and PD costs were provided in several electronic PDF files, and costs were distributed according to the categories stipulated previously.

In the present study, PD includes both continuous ambulatory PD and automated PD. The prevalent HD/PD cost ratio was calculated for the public sector. The estimated annual increase in the rate of HD and PD utilization was calculated according to the prevalence reported by the Latin America Dialysis and Transplant Registry in 2010 [16] and the

prevalence reported in 2015 by the CSS and CETRERSA. The calculated annual changes in rates from 2010 to 2015 were 10.65% and -4.23% for HD and PD, respectively, with a ratio of 2.5%. The cost analysis was performed using present values; therefore, no discounted rates were included.

We performed a five-year time horizon budget impact analysis on the direct costs related to the renal programme in Panama, considering costs from both the CSS and the private sector. The budget impact analysis estimated how changes in the mix of dialysis modalities would impact the trajectory of the total spending for dialysis services (assuming that the mix of dialysis modalities used shifts towards a greater use of PD over time). The budget impact model was from the payer perspective and included the following five scenarios from 2015 until 2020: scenario 1 was a 2.5% yearly increase in the use of PD, scenario 2 was a 5% yearly increase in the use of PD, scenario 3 was a 7.5% yearly increase in the use of PD, and scenario 4 was a 1% yearly decrease in the use of PD. The scenarios were based on the ratio of sensibility (annual increase in the rate of HD utilization/annual increase in the rate of PD utilization) =2.5%. In addition, complementary analyses were performed with different arbitrary assumptions (10% annual increase in PD, 2.5% decrease in PD utilization).

Years of life lost due to premature CKD mortality

Data on CKD mortality for the year 2015 were retrieved from the National Mortality Registry at the Institute of Statistics and Census. Deaths recorded as N18 (chronic kidney disease, n=221) and N19 (unspecified kidney failures, n=18) were included according to the International Classification of Diseases 10th Revision codes. The linear method was utilized for the analyses in the population aged 20 to 77 years old.

The YLLs were calculated by subtracting the life expectancy from the age of death of each individual. We estimated the average life expectancy on the basis of the Institute of Statistics and Census life table (77.74 years) and the value of the country's gross domestic product (GDP) per capita in 2015. The YLLs for each individual were multiplied by the

GDP per capita estimated for 2015, obtaining the YLLs in USD. We applied a 3% discounted present value at a social discount rate. The estimated total annual YLLs were reported stratified by sex and the following age categories: 20-30 years, 31-40 years, 41-50 years, 51-60 years and 71-80 years. In addition, YLLs were stratified by province.

All analyses were performed in Excel and Stata version 14.

Ethical statement:

Permission to conduct the study was obtained from the medical directors of the respective institutions. Ethical approval for the study was obtained from the Ethics Review Committee of the Gorgas Memorial Institute for Health Studies.

Patient and public involvement:

The study did not involve patients or the public in its planning or execution.

3. Results

Cost analysis

The mean direct expenditures for dialysis are summarized in Table 1. As of 2015, 2075 persons were receiving RRT (PD or HD), and of those, 87% were receiving HD. The total costs for dialysis in the public sector ranged from approximately $9.8 million (PD) to $50.5 million (HD). The total cost per year of the programmes in the public and private sectors combined was $70.3 million. The HD/PD cost ratio in the public sector was 1.19.

Table 1: Estimated costs of dialysis in the public and private sectors for the year 2015 in Panama

	Public (CSS)		Private
	PD	HD	HD
Number of patients (n)	265	1746	64
Total annual costs (USD)	7,915,687.25	62,102,496.24	2,797,380.00
Cost/patient/year (USD)	29,870.52	35,568.44	43,447.96
	Public (CSS)		Public and Private
	PD+HD		PD+HD
Number of patients (n)	2011		2075
Total cost of programmes (USD)	67,553,921.23		70,351,301.23

CSS: Social Security (in Spanish Caja de Seguro Social)

The total estimated costs (USD) during the five years for the reference scenarios were 503 million (CSS) and 520 million (combined sectors). Figure 1 shows the budget impact model according to the different scenarios for the public sector (CSS) (Panel A) and for the public and private sectors combined (Panel B). In the CSS, the estimated costs for the year 2020 ranged from $93.8 million (assuming a 7.5% annual increase in the use of PD) to $100.7 million (assuming a 1% decrease in the use of PD).

Likewise, in the public and private sectors, the estimated costs were higher in the scenario in which a 1% decrease in the use of PD was assumed ($104.7 million) (Panel B). Sensitivity analyses were conducted to explore the model forecasts under varying assumptions. In general, the results of these analyses demonstrate that the savings will be

greater if the shift towards greater PD use is accomplished sooner (a 10% annual increase in the use of PD in CSS resulted in reducing costs by USD 4.5 million per year).

Years of life lost –USD (YLL-USD) due to premature CKD mortality

In 2015, CKD was the cause of 440 deaths in Panama, accounting for 2.4% of the total deaths registered. There were 279 male deaths (63.4%) and 161 female deaths (36.6%).

The average annual loss was 25,501,808.40 YLL-USD. In men, a higher YLL-USD was observed in the 51-60 years age group than in the other age groups, whereas in women, a higher YLL-USD was observed in the 61-70 years age group than in the other age groups, as shown in Figure 2.

The three provinces with the highest accumulated numbers of YLL-USD due to CKD in the age group younger than 40 years were 1) the Province of Panama (1,548,252.11 YLLs), 2) the Province of Coclé, (459,212.85 YLLs) and the Province of Colón (314,586.97 YLLs) (Supplementary Table 3).

4. Discussion

In the present study, we found that treatment with dialysis imposes substantial burdens in terms of the provision of health services and YLLs.

In Panama, the total health care expenditure represented approximately 8% of the GDP in 2014. In the context of our findings, in 2015, approximately 1.6% of the health care budget was invested in dialysis, considering only the costs derived from the CSS. Notably, the costs associated with milder forms of CKD (early stages of the disease without RRT) were not evaluated, and it has been reported that the economic burden associated with milder forms of CKD is more than twice the total cost of ESRD [17]. In addition, the average annual loss in terms of YLLs due to CKD represented 0.59% of the GDP allocated to health. Similar levels of expenditure have been reported in high-income countries [18, 19].

Assuming our reference scenario, it is estimated that the accumulated costs in five years will be approximately $505 million for the CSS and $525 million for both the private and public sectors combined. Noteworthy, this estimate excludes the ongoing costs derived from the MoH, which also adds financial pressure to the health system. In this study, the cost of therapy per se and medicines were the major drivers of the total cost of HD for the CSS, whereas staff wages represented the highest cost in the private sector. Therefore, strategies aimed at reducing these costs would help reduce the annual cost in the short term.

All forms of dialysis that occur outside of the hospital setting are more cost effective than in-hospital-based dialysis forms [20]. In fact, the number of patients treated with PD rose worldwide from 1997 to 2008, with a 2.5-fold increase in the prevalence of patients receiving PD in developing countries [21]. In agreement with the results of previous studies, we observed a considerable cost savings related to the use of PD instead of HD [22]. Our HD/PD cost ratio was lower than the one reported in Mexico but higher than those reported previously in other countries in the region [23]. Despite several advantages, including the possibility of being offered in the remotest locations, our results indicate that PD is still an underused therapy in Panama; this contrasts with the results of reports from other countries, such as Mexico, El Salvador and Guatemala, where the PD utilization rates

are 66%, 76.5% and 56%, respectively [21]. In this context, if the CSS increases the utilization of PD by 7.5% per year, the proportion of dialysis accounted for by PD will reach 50% in 5 years. The reasons for the underutilization of PD are presumably multifactorial and may partly be explained by the scarcity of trained nephrologists and nurses as well as the lack of relevant health policies [10]. Currently, there are 32 nephrologists nationwide, which results in a relatively low number of nephrologists per million population [24]. Furthermore, as opposed to other countries [22], Panama has a small market, lacks local manufacturing facilities for PD bags and largely depends on imported medicines/equipment. Notably, Colombia and Nicaragua have also reported a decrease in the use of PD and an expansion of the use of HD from 2000 to 2010 [16].

There is compelling evidence that kidney transplantations have led to substantial cost savings for health care systems in high-income countries [25]. Kidney transplantations in Panama began in 1990, and the necessary human resources and infrastructure have been expanded. According to the Panamanian Transplant Organization (PTO), in 2015, there were 28 kidney transplantations performed in Panama, and the number of donors has increased over the years [26], albeit at a slow rate.

Taken together and considered from a macroeconomic standpoint, our results suggest that increasing PD utilization might reduce the overall healthcare expenditure in Panama. Therefore, key strategies such as the implementation of policies and incentives favouring PD over HD should be advocated [27]. A critical complementary approach is slowing the progression of CKD to ESRD. Likewise, enhancing kidney transplant programmes is strongly recommended

The burdens imposed by premature death and the loss of health due to CKD have been widely described. Between 1990 and 2013, the number of cases of CKD due to diabetes and other causes increased by more than 50% worldwide [28]. In addition, the burden of CKD disproportionately impacts low-income and middle-income countries where the prevalences of diabetes, hypertension and obesity are growing the most [29]. Moreover, poverty increases the risk of pathologies that predispose individuals to CKD and worsen outcomes in those who already have the disease [30]. Previous studies have reported a

relationship between progressive CKD and its impact on household income or poverty, including spending more than 10% of the household income on out of pocket payments [31, 32].

Remarkably, Latin America has the highest CKD-related death rate in the world [33], and diabetes mellitus, hypertension and, recently, CKD of unknown aetiology are contributors to CKD-related death in Central America [5, 29]. In Panama, the CKD-related mortality rate has been decreasing since 2006; however, geographical disparities exist [15]. Interestingly, Coclé, a province with the highest age-adjusted mortality rate in the country [15], was found to have markedly elevated YLLs in the under-40 years age group. Taken together, the sum of the estimated YLLs and the costs of the dialysis is unsustainable for the health system, highlighting the importance of prevention. Recently, the legal framework for CKD registration in Panama started with a resolution signed by the MoH, establishing the notification of all stages of CKD as compulsory for private and health institutions at a national level. In addition, the CKD guidelines are currently being revised. From a broader perspective, if the Sustainable Development Goal of poverty reduction is to be accomplished, it is essential that health systems protect individuals from the economic burdens imposed by CKD and other non-communicable diseases [34].

This study has strengths and limitations. Costs due to hospitalization, complications, emergency medicines, and transportation were not included in the HD calculation; hence, any possible bias is likely to result in the underestimation and not the overestimation of the cost advantage of PD over HD. It is noteworthy that patients frequently have to travel long distances, often with their families, to receive specialized care, adding a dimension of social and economic consequences that was beyond the scope of this study. Although we excluded these costs, we estimated the YLLs, which is a measure of indirect costs. However, it is likely that the reliance on diagnostic code data alone to define CKD as a cause of death and the effects of underreporting resulted in the underestimation of people with early stages of CKD. Finally, because the public systems operate independently of each other and the information (health and costs) is not homogenously systematized, cost data could not be obtained from the MoH. Therefore, the total costs from the public sector were underestimated, and the estimated yearly increase in the rates of utilization should be

interpreted with caution. Likewise, we could not perform a cost-effectiveness analysis. Despite the lack of registries, the Panamanian Society of Nephrology and Hypertension and the PTO have been actively recording the number of cases undergoing RRT. Currently, there are three institutions in the MoH offering dialysis within the country. According to the PTO, in 2015, there were 26 and 204 patients receiving PD and HD treatment, respectively, in these institutions.

Conclusion

In conclusion, CKD represents a major challenge for Panama. Our results suggest that increasing the utilization of PD will lower the overall ESRD treatment costs. In the long term, an important method of reducing the overall annual cost is to reduce the number of patients with ESRD. Consequently, patients with CKD in the early stages (who are more abundant and more frequent users of the health system) should not be ignored by policy makers. Altogether, the enormous cost associated with CKD provides a compelling economic incentive for improving the prevention, detection and management of CKD and the relevant health policies in Panama.

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Competing interests: IMV, RV, BG, JM, CC and VH declare no conflict of interest. MTC currently works at Sanofi Pasteur, nonetheless, her responsibilities do not relate with the submitted work.

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Contributorship statement: IMV wrote the draft of the work. IMV MTC and VH analyzed the data. CC and RV provided the data. IMV, MTC, RV, BG, JM, CC and VH

interpreted the data, critically revised the draft for important intellectual content and approved the final version. All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data availability: The datasets used and/or analyzed during the current study are available from the authors on reasonable request.

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Figure Legends

Figure 1. *Estimations based on data from the public (CSS renal programme) and private (CETRERSA) sectors.*

Figure 2. *Deaths recorded as N18 (chronic kidney disease, n=221) and N19 (unspecified kidney failures, n=18).*

Figure 1. Estimated cost (US Dollars) of the dialysis program according to different scenarios in the public sector (A) and in the combined public and private sector (B).

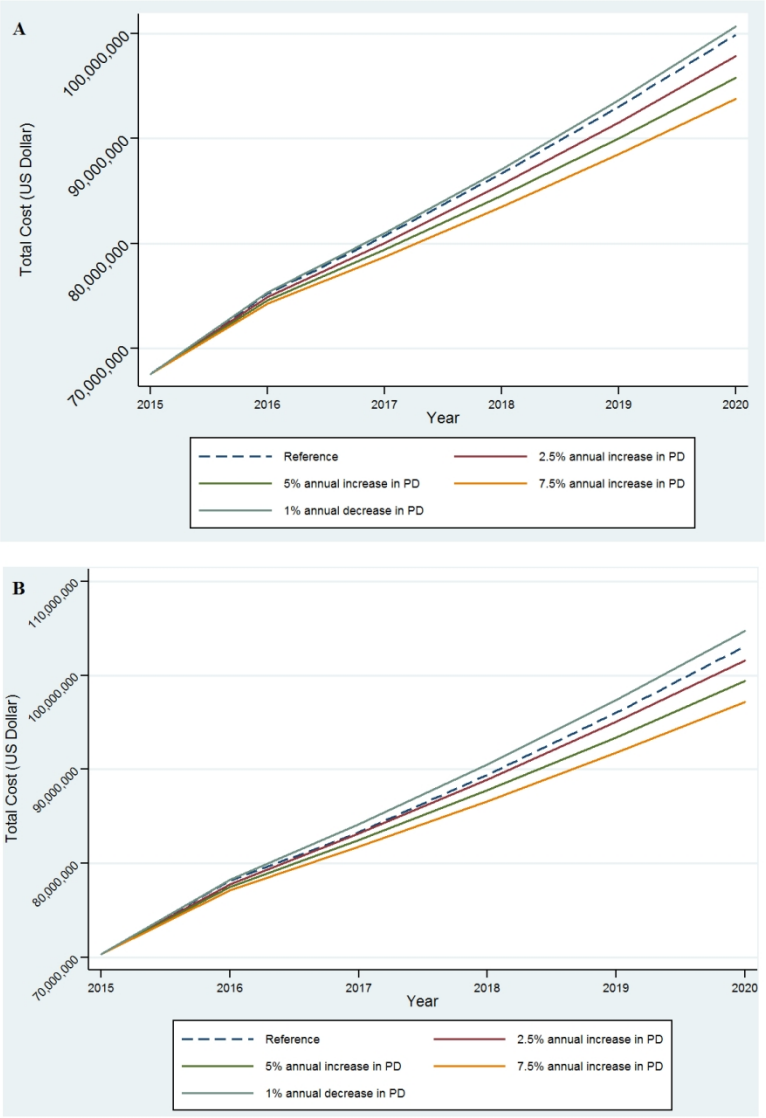
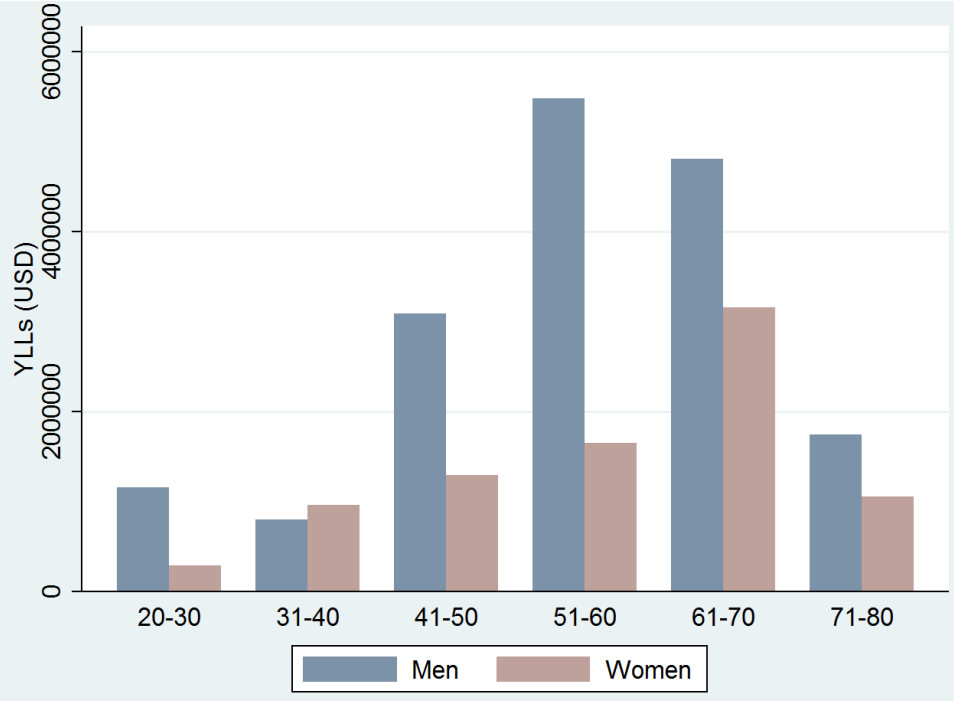


Figure 2. Years of Life Lost-(USD) due to premature mortality, according to age-group categories in Panama. Year 2015



Supplementary Table 1. Estimated cost of HD and PD (USD) in CSS, year 2015

HD + PD (PUBLIC)				
	Monthly cost	**Yearly cost/patient**	**Patients (factor)**	**Total Cost (USD)**
PD		18,766.00	265	4,972,990.00
HD	1,739.66	20,875.92	1746	36,449,356.32
Eritropoyetin	507.00	6,084.00	2011	12,234,924.00
Paricalcitiol	299.00	3,588.00	1423	5,105,724.00
Sevelamer	207.00	2,484.00	1751	4,349,484.00
Peritoneal Dialysis		18,766.00	265	4,972,990.00
Total				**63,112,478.32**
National Coordination		26,500.00	1	26,500.00
National Coordination (teaching)		11,000.00	1	11,000.00
National coordination (personnel)	5,982.84	71,794.08	1	71,794.08
National Coordination (physicians)	10,248.42	122,981.04	1	122,981.04
Sub total				**232,275.12**
Nephrologists (salary)	62,682.52	752,190.24	0.87*	654,405.51
Nephrologists (shifts)	41,600.00	499,200.00	0.87*	434,304.00
Nephrologists (productivity)	2,142.00	25,704.00	1	25,704.00
Sub total				**1,114,413.51**
General practitioners (salary)	71,029.00	852,348.00	1	852,348.00
General practitioners (shifts)	19,960.00	239,520.00	1	239,520.00
Sub total				**1,091,868.00**
Nurses (salary)	129,680.19	1,556,162.28	1	1,556,162.28
Nurses (shifts)	37,227.00	446,724.00	1	446,724.00
Sub total				**2,002,886.28**
TOTAL (HD+PD)				**67,553,921.23**
Yearly cost / patient (HD+PD)				**38,580.19 USD**

**Shifts are calculated only for HD (Prevalence of HD =0.87).*

Supplementary Table 2. Estimates Costs of HD (USD) in CETRERSA, year 2015

HD (PRIVATE)			
	Monthly cost 2015	**Yearly Cost**	**Cost/HD**
Human resources	**Private**		
Personal (Nephrologists, General Practitioners, Nurses, etc.)	**123757.00**	**1485084.00**	**147.86**
Subtotal Human Resources	**123757.00**	**1,485,084.00**	**147.86**
Basic Services		**Private**	
Water	400.00	4,800.00	0.48
Electricity	3,886.00	46,632.00	4.64
Subtotal Basic Services	**4,286.00**	**51,432.00**	**5.12**
Travel expenses	**Private**		
Food/Travel expenses companions	57.00	684.00	0.07
Travel expenses patients	1605.00	19260.00	1.92
Subtotal Travel expenses	**1,662.00**	**19,944.00**	**1.99**
Infrastructure	**Private**		
Maintenance and buildings	1,235.00	14,820.00	1.48
Maintenance of equipment	7,018.00	84,216.00	8.38
Estimation of the use of buildings	29,151.00	349,812.00	34.83
Equipment utilization	4,184.00	50,208.00	5.00
Subtotal Infrastructure	**41,588.00**	**499,056.00**	**49.69**
Materials and supplies	**Private**		
Food-patients and human resources	2572.00	30864.00	3.07
Cost of clothing: sheets, patient gowns, disposable bed cover,	3048.00	36576.00	3.64
Diesel	1026.00	12312.00	1.23
Medicines	10091.00	121092.00	12.06
Pharmaceuticals supplies	38224.00	458688.00	45.67
Cleaning articles	639.00	7668.00	0.76
Laboratories	1125.00	13500.00	1.34
Office materials	773.00	9276.00	0.92
Surgical Medical Instruments	4324.00	51888.00	5.17
Subtotal Materials and Supplies	**61,822.00**	**741,864.00**	73.86
Machinery and equipment	**Private**		
Number of HD			**10044**
Number of patients			**64**
	Monthly cost 2015	**Yearly Cost**	**Cost/HD**
Total	**233,115.00**	**2,797,380.00**	**278.51**

Cost/patient
43,447.96 USD

Supplementary Table 3. Years of Life Lost-USD due to CKD mortality below 40 years of age, according to provinces in Panama. Year 2015

Province*	YLLs-USD
Panamá	1,548,252.11
Coclé	459,212.85
Colón	314,586.97
Chiriquí	301,269.05
Panamá Oeste	298,389.39
Emberá Indigenous	160,991.2
Bocas del Toro	152,671.82
Los Santos	143,929.82

** Provinces with recorded deaths due to CKD in the age below 40 years.*

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

	Page	Recommendation
Title and abstract	2	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	4	Explain the scientific background and rationale for the investigation being reported
Objectives	5	State specific objectives, including any prespecified hypotheses
Methods		
Study design	6	Present key elements of study design early in the paper
Setting	6	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants Financial costs based on secondary data, and therefore many items are not applicable	6,7	(*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 (selection of sectors offering Hemo and peritoneal dyalisis)
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	6+Supplementary Table	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	6,7	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
Bias	7	Describe any efforts to address potential sources of bias
Study size	n/a	Explain how the study size was arrived at
Quantitative variables	n/a	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	7,8	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*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
Results		
Participants	9,10	(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
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	n/a	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(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	9,10	*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	n/a	(*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
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	10	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	11-13	Summarise key results with reference to study objectives
Limitations	13-14	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	11-14	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	13-14	Discuss the generalisability (external validity) of the study results
Other information		
Funding	14	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