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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 Velásquez¹, Maribel Tribaldos Causadias¹, Régulo Valdés², Beatriz Gómez¹,
Jorge Motta^{1,3}, César Cuero⁴, Víctor Herrera¹

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

Corresponding 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.

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3 National estimates of CKD derived from epidemiological studies are lacking.
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5 Recently, a cross-sectional study reported a CKD prevalence of 12.6% in two provinces
6 where 60% of the population resides [13]. Moreover, the study described geographical
7 disparities in age-adjusted standardized mortality rates due to CKD [13]. In 2001, the CSS
8 calculated the yearly costs of care in the peritoneal dialysis (PD) and hemodialysis (HD)
9 programs, resulting in an average per patient of \$ 25,426.64 USD and \$ 18,857.21 USD,
10 respectively. However, neither the costs of RRT nor the years of life lost (YLL), useful
11 measures in prioritizing public health interventions, has been recently evaluated.
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19 The aim of this study is to i) estimate the direct costs associated with CKD dialysis,
20 either HD or PD in public and private Panamanian institutions in 2015, ii) to perform a five
21 year time budget impact analysis, and iii) to calculate the YLL due to CKD in the country.
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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

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3 increased rate from 2010 to 2015 was 10.65% and -4.23% for HD and PD, respectively,
4 with a ratio of 2.5%. No discount rates were included.
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8 **Years of Life Lost (YLL) due to premature CKD mortality**

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11 Data on CKD mortality for the year 2015 was retrieved from the National Mortality
12 Registry at the Institute of Statistics and Census. Linear method was utilized for the
13 analyses using the population aged 20 to 77 years old.
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17 The calculation of the YLLs was performed by subtracting the life expectancy from the age
18 of death of each individual. We then estimated the average life expectancy on the basis of
19 the life table of the Institute of Statistics and Census life tables (77.74 years) and valued for
20 the year 2015 at the country's gross domestic product (GDP) per capita. YLLs of each
21 individual were multiplied by the GDP per capita current prices estimated for 2015,
22 obtaining the YLLs in USD. We applied a 3% discounted present value at a social discount
23 rate (2,3). The estimated total annual YLL by sex was reported according to age-categories:
24 (20-30 years, 31-40 years, 41-50 years, 51-60 years and 71 to 80 years). In addition, YLL
25 were calculated according to provinces.
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34 All analysis was performed in Excel and in Stata version 14.
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37 **Ethical statement:**

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40 Permission to conduct the study was obtained from the medical directors of the respective
41 hospitals. Ethical approval for the study was obtained from the Ethics Review Committee
42 of the Gorgas Memorial Institute for Health Studies.
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46 **Patient and Public Involvement:**

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

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

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3 reasons for the underutilization of PD are presumably multifactorial and may partly be
4 explained by the shortage of trained nephrologists and nurses as well as the lack of health
5 policies [9]. Currently there are 32 nephrologists nationwide, which constitutes a relatively
6 low distribution of density of nephrologists per million population [23]. Furthermore, as
7 opposed to other countries [21], Panama has a small market without local manufacturing
8 facilities of PD bags and largely depends on imported medicines and equipment.
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14 There is compelling evidence that kidney transplantations have led to substantial cost
15 savings for health care systems in high-income countries [24]. Kidney transplantations in
16 Panama began in 1990, and human resources and infrastructure has been enlarged. In 2015,
17 there were 28 kidney transplantations performed in Panama and the number of donors have
18 increased over the years, yet at a slow rate [25].
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24 Taken together and from a macroeconomic standpoint, our results suggest that increasing
25 PD utilization might reduce the overall healthcare expenditure in Panama. Therefore, key
26 strategies such as implementation of policies and incentives favoring PD modality over HD
27 should be advocated [26]. A complementary and vital approach is slowing the progression
28 of CKD to ESRD. Likewise, it is highly recommended that the country improve the kidney
29 transplant programs.
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36 The burden of premature death and health loss from ESRD has been widely described.
37 Between 1990 and 2013, the number of cases of CKD due to diabetes and due to other
38 causes increased by more than 50% worldwide [27]. In addition, the burden of CKD
39 disproportionately impacts low-income and middle-income countries where growth in
40 diabetes, hypertension and obesity is greatest [28]. Moreover, poverty increases the risk of
41 pathologies that predispose CKD to develop, and worsens outcomes in those who already
42 have this disease [29]. Previous studies have reported a relationship between progressive
43 CKD and its impact on household income or poverty, including spending more than 10%
44 on income out of pocket payment [30, 31].
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52 Remarkably, Latin America has the highest CKD death rate in the world [32] where
53 diabetes mellitus, hypertension and recently, CKD of unknown etiology in Central-America
54 are contributors [4, 28]. Interestingly, Coclé, a province with the highest age-adjusted
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3 mortality rate in the country [13], presented considerably elevated YLL in the age-group
4 below 40. Recently, the legal framework for the CKD registration in Panama started
5 through a resolution signed by the MoH, establishing notification of CKD as compulsory
6 for private and health institutions at a national level. In addition, CKD guidelines are
7 currently being revised. On a broader perspective, if the Sustainable Development Goal of
8 poverty reduction is to be accomplished, is essential that health systems protect individuals
9 from the economic burden of CKD and other non-communicable diseases [33].

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

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

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11 **Conflict of interest:** IMV, RV, BG, JM, CC and VH declare no conflict of interest. MTC
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13 submitted work.
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18 Senacyt, Panama.
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24 analyzed the data. CC and RV provided the data. IMV, MTC, RV, BG, JM, CC and VH
25 interpreted the data, critically revised the draft for important intellectual content and
26 approved the final version. All the authors agree to be accountable for all aspects of the
27 work in ensuring that questions related to the accuracy or integrity of any part of the work
28 are appropriately investigated and resolved.
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35 **Data availability:** The datasets used and/or analyzed during the current study are available
36 from the authors on reasonable request.
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References

1. Xie Y, Bowe B, Mokdad AH, Xian H, Yan Y, Li T, Maddukuri G, Tsai CY, Floyd T, Al-Aly Z: **Analysis of the Global Burden of Disease study highlights the global, regional, and national trends of chronic kidney disease epidemiology from 1990 to 2016.** *Kidney Int* 2018.
2. Mills KT, Xu Y, Zhang W, Bundy JD, Chen CS, Kelly TN, Chen J, He J: **A systematic analysis of worldwide population-based data on the global burden of chronic kidney disease in 2010.** *Kidney international* 2015, **88**(5):950-957.
3. Eckardt KU, Coresh J, Devuyst O, Johnson RJ, Kottgen A, Levey AS, Levin A: **Evolving importance of kidney disease: from subspecialty to global health burden.** *Lancet* 2013, **382**(9887):158-169.
4. Obrador GT, Rubilar X, Agazzi E, Estefan J: **The Challenge of Providing Renal Replacement Therapy in Developing Countries: The Latin American Perspective.** *Am J Kidney Dis* 2016, **67**(3):499-506.
5. System USRD: **Medicare Expenditures for Persons with CKD.** [http://www.ajkd.org/article/S0272-6386\(16\)00099-8/pdf](http://www.ajkd.org/article/S0272-6386(16)00099-8/pdf). Accessed April 2016.
6. Abecassis M, Bartlett ST, Collins AJ, Davis CL, Delmonico FL, Friedewald JJ, Hays R, Howard A, Jones E, Leichtman AB *et al*: **Kidney transplantation as primary therapy for end-stage renal disease: a National Kidney Foundation/Kidney Disease Outcomes Quality Initiative (NKF/KDOQIM) conference.** *Clin J Am Soc Nephrol* 2008, **3**(2):471-480.
7. Vanholder R, Van Biesen W, Lameire N: **Renal replacement therapy: how can we contain the costs?** *Lancet* 2014, **383**(9931):1783-1785.
8. Glasscock RJ, Warnock DG, Delanaye P: **The global burden of chronic kidney disease: estimates, variability and pitfalls.** *Nat Rev Nephrol* 2017, **13**(2):104-114.
9. Rosa-Diez G, Gonzalez-Bedat M, Pecoits-Filho R, Marinovich S, Fernandez S, Lugon J, Poblete-Badal H, Elgueta-Miranda S, Gomez R, Cerdas-Calderon M *et al*: **Renal replacement therapy in Latin American end-stage renal disease.** *Clin Kidney J* 2014, **7**(4):431-436.
10. **Instituto Nacional de Estadística y Censo. Available at** https://www.contraloria.gob.pa/inec/Publicaciones/Publicaciones.aspx?ID_SUBCATEGORIA=10&ID_PUBLICACION=491&ID_IDIOMA=1&ID_CATEGORIA=3. Accessed July 31, 2018.

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 - 60
11. Instituto Nacional de Estadística y Censo población asegurada. Available at: <https://www.contraloria.gob.pa/inec/archivos/P8401421-01.pdf>. Accessed July 31, 2018.
12. Romero LI, Quental C: **The Panamanian health research system: a baseline analysis for the construction of a new phase.** *Health research policy and systems* 2013, **11**:33.
13. Moreno Velasquez I, Castro F, Gomez B, Cuero C, Motta J: **Chronic Kidney Disease in Panama: Results From the PREFREC Study and National Mortality Trends.** *Kidney Int Rep* 2017, **2**(6):1032-1041.
14. Gonzalez-Bedat M, Rosa-Diez G, Pecoits-Filho R, Ferreiro A, Garcia-Garcia G, Cusumano A, Fernandez-Cean J, Noboa O, Douthat W: **Burden of disease: prevalence and incidence of ESRD in Latin America.** *Clin Nephrol* 2015, **83**(7 Suppl 1):3-6.
15. **World Health Organization.** Available at> <http://www.who.int/countries/pan/en/>. Accessed July 27, 2018.
16. Essue BM, Wong G, Chapman J, Li Q, Jan S: **How are patients managing with the costs of care for chronic kidney disease in Australia? A cross-sectional study.** *BMC Nephrol* 2013, **14**:5.
17. Zelmer JL: **The economic burden of end-stage renal disease in Canada.** *Kidney Int* 2007, **72**(9):1122-1129.
18. Couser WG, Remuzzi G, Mendis S, Tonelli M: **The contribution of chronic kidney disease to the global burden of major noncommunicable diseases.** *Kidney Int* 2011, **80**(12):1258-1270.
19. Beaudry A, Ferguson TW, Rigatto C, Tangri N, Dumanski S, Komenda P: **Cost of Dialysis Therapy by Modality in Manitoba.** *Clin J Am Soc Nephrol* 2018.
20. Jain AK, Blake P, Cordy P, Garg AX: **Global trends in rates of peritoneal dialysis.** *J Am Soc Nephrol* 2012, **23**(3):533-544.
21. Karopadi AN, Mason G, Rettore E, Ronco C: **Cost of peritoneal dialysis and haemodialysis across the world.** *Nephrol Dial Transplant* 2013, **28**(10):2553-2569.
22. Neil N, Walker DR, Sesso R, Blackburn JC, Tschosik EA, Sciaraffia V, Garcia-Contreras F, Capsa D, Bhattacharyya SK: **Gaining efficiencies: resources and demand for dialysis around the globe.** *Value Health* 2009, **12**(1):73-79.
23. Osman MA, Alrukhaimi M, Ashuntantang GE, Bellorin-Font E, Benghanem Gharbi M, Braam B, Courtney M, Feehally J, Harris DC, Jha V *et al*: **Global nephrology workforce: gaps and opportunities toward a sustainable kidney care system.** *Kidney International Supplements* 2018, **8**(2):52-63.

- 1
2
3 24. Jarl J, Desatnik P, Peetz Hansson U, Prutz KG, Gerdtham UG: **Do kidney transplantations save money? A study using a before-after design and multiple register-based data from Sweden.** *Clin Kidney J* 2018, **11**(2):283-288.
- 4
5
6
7 25. **Organización Panameña de Transplante.** Available at: <http://190.34.154.93/opt/wp-content/uploads/2017/07/2015anual.pdf>. Accessed July 27, 2018.
- 8
9
10 26. Li PK, Chow KM, Van de Luitgaarden MW, Johnson DW, Jager KJ, Mehrotra R, Naicker S, Pecoits-Filho R, Yu XQ, Lameire N: **Changes in the worldwide epidemiology of peritoneal dialysis.** *Nat Rev Nephrol* 2017, **13**(2):90-103.
- 11
12
13
14 27. Carney EF: **Epidemiology: Global Burden of Disease Study 2013 reports that disability caused by CKD is increasing worldwide.** *Nat Rev Nephrol* 2015, **11**(8):446.
- 15
16
17 28. Neuen BL, Chadban SJ, Demaio AR, Johnson DW, Perkovic V: **Chronic kidney disease and the global NCDs agenda.** *BMJ Glob Health* 2017, **2**(2):e000380.
- 18
19
20 29. Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, Saran R, Wang AY, Yang CW: **Chronic kidney disease: global dimension and perspectives.** *Lancet* 2013, **382**(9888):260-272.
- 21
22
23
24 30. Jaspers L, Colpani V, Chaker L, van der Lee SJ, Muka T, Imo D, Mendis S, Chowdhury R, Bramer WM, Falla A *et al*: **The global impact of non-communicable diseases on households and impoverishment: a systematic review.** *Eur J Epidemiol* 2015, **30**(3):163-188.
- 25
26
27
28 31. Morton RL, Schlackow I, Gray A, Emberson J, Herrington W, Staplin N, Reith C, Howard K, Landray MJ, Cass A *et al*: **Impact of CKD on Household Income.** *Kidney Int Rep* 2018, **3**(3):610-618.
- 29
30
31
32 32. Mortality GBD, Causes of Death C: **Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015.** *Lancet* 2016, **388**(10053):1459-1544.
- 33
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36 33. Jan S, Laba TL, Essue BM, Gheorghe A, Muhunthan J, Engelgau M, Mahal A, Griffiths U, McIntyre D, Meng Q *et al*: **Action to address the household economic burden of non-communicable diseases.** *Lancet* 2018, **391**(10134):2047-2058.
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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).

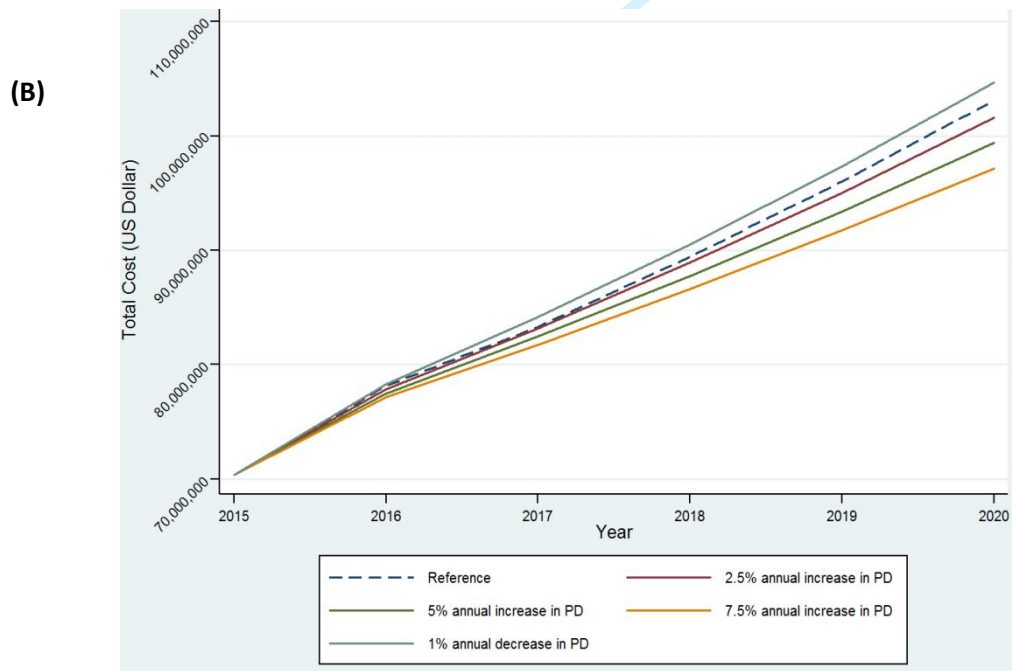
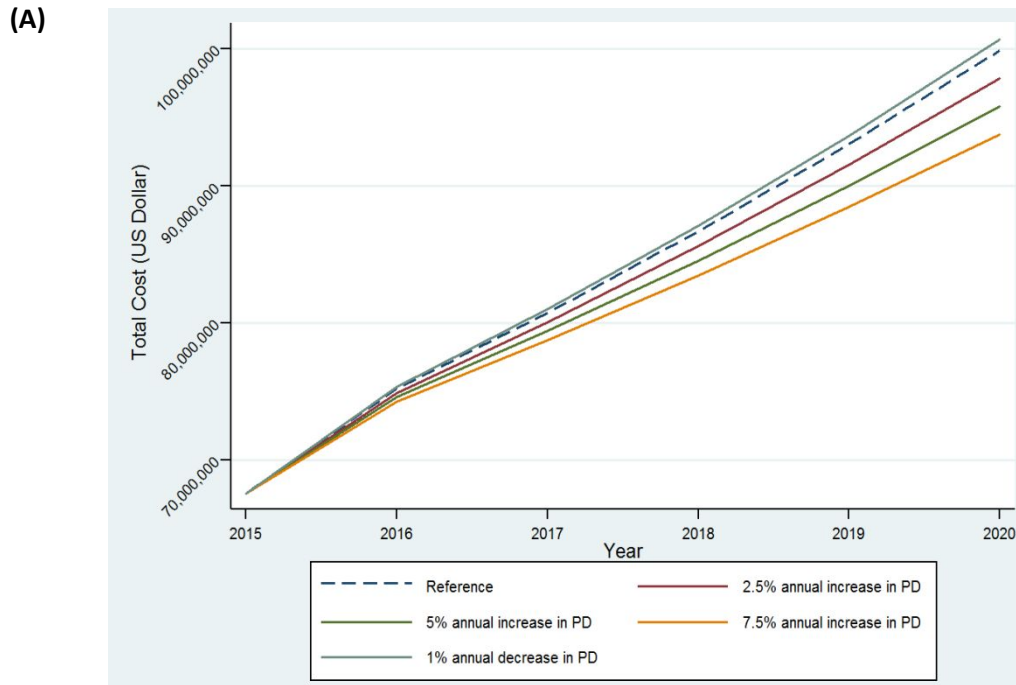
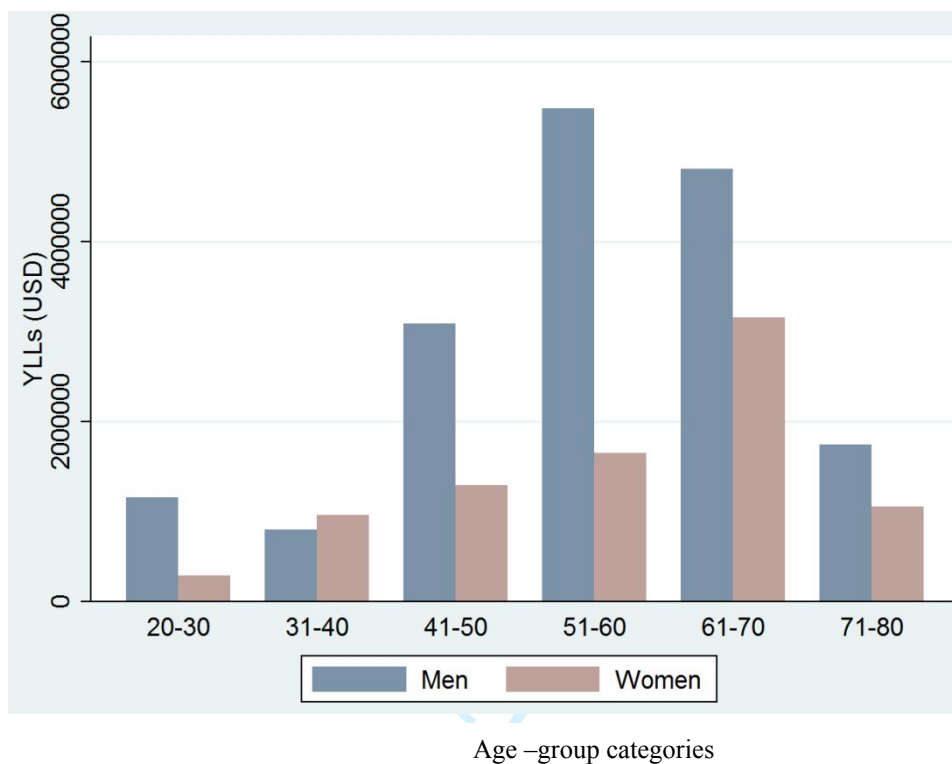


Figure 2. Years of Life Lost-(USD) due to premature mortality, according to age-group categories in Panama. Year 2015



Age-group categories

Review only

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 Indigenus	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	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (selection of sectors offering Hemo and peritoneal dialysis) (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Financial costs based on secondary data, and therefore many items are n/a		
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) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed

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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

For peer review only

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	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) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (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
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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

BMJ Open

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

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Primary Subject Heading:	Health economics
Secondary Subject Heading:	Renal medicine
Keywords:	Chronic renal failure < NEPHROLOGY, Dialysis < NEPHROLOGY, costs, years of life lost, Panama

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Manuscripts

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4 **1 End-stage renal disease: Financial costs and years of life lost in Panama**
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9 **3 Ilais Moreno Velásquez¹, Maribel Tribaldos Causadias¹, Régulo Valdés², Beatriz Gómez¹,**
10 **4 Jorge Motta^{1,3}, César Cuero⁴, Víctor Herrera¹**

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13 **5 ¹Gorgas Memorial Institute for Health Studies, Panama; ² Caja de Seguro Social, Panama; ³ National**
14 **6 Secretariat for Science and Technology, Panama; ⁴Organización Panameña de Trasplante, Ministry of**
15 **7 Health, Panama.**
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27 **16 Corresponding author:**

28 **16**
29 **17**
30 **18 Ilais Moreno Velasquez**
31 **19 MD, PhD**
32 **20 Gorgas Memorial Institute for Health Studies**
33 **21 0816-02593 Panama City, Panama**
34 **22 Email: imoreno@gorgas.gob.pa**
35 **23**
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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

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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

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3 155 health coverage to formally employed persons. In addition, there are private insurers with
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5 156 which affiliation is voluntary [14]. Therefore, the direct costs of medical care are at least
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7 157 partly covered by the CSS (the Panamanian public health insurance) or by the state.
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10 159 Electronic health records at public health facilities are in the process of implementation;
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12 160 consequently, a CKD national registry is absent in the country [12]. Further, national
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14 161 estimates of CKD derived from epidemiological studies are lacking. Recently, a cross-
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16 162 sectional study reported a CKD prevalence of 12.6% in two provinces where 60% of the
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18 163 population resides [15]. Moreover, the study described geographical disparities in age-
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20 164 adjusted standardized mortality rates due to CKD [15]. In 2001, the CSS calculated the
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22 165 yearly costs of care in the peritoneal dialysis (PD) and hemodialysis (HD) programs,
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24 166 resulting in an average per patient of \$ 25,426.64 USD and \$ 18,857.21 USD, respectively.
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26 167 However, neither the costs of RRT nor the years of life lost (YLL), useful measures in
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28 168 prioritizing public health interventions, has been recently evaluated.

29 170 The aim of this study is to i) estimate the direct costs associated with ESRD treatment,
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31 171 either HD or PD in public and private Panamanian institutions in 2015, ii) to perform a five
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33 172 year time budget impact analysis, and iii) to calculate the YLL due to CKD in the country.
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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 outpatient clinic in the country (CETRERSA).

Because the information is not systematized homogeneously, 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

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3 215 prevalence reported in 2015 by the CSS and CETRERSA. The calculated annual increased
4 216 rate from 2010 to 2015 was 10.65% and -4.23% for HD and PD, respectively, with a ratio
5 217 of 2.5%. The cost analysis was performed in present value; therefore, no discount rates
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11 220 We performed a five year time horizon budget impact analysis on the direct cost
12 221 related to the renal program in Panama, considering cost from both CSS and the private
13 222 sector. The budget impact analysis estimates how changes in the mix of dialysis modalities
14 223 would impact the trajectory of total spending for dialysis services (assuming that the mix of
15 224 dialysis modality use shifts toward greater use of PD over time). The budget impact model
16 225 was from the payer perspective and included five scenarios: scenario 1: a 2.5% yearly
17 226 increase on PD, scenario 2: a 5% yearly increase on the use of PD; scenario 3: a 7.5%
18 227 yearly increase on the use of PD and scenario 4: a 1% yearly decrease of PD use, from
19 228 2015 until 2020. Scenarios were based on the ratio of sensibility (annual increase rate of
20 229 HD utilization /annual increase rate of PD utilization) =2.5%. In addition, complementary
21 230 analyses were performed under different arbitrary assumptions (10% annual increase in PD,
22 231 2.5% decrease in PD utilization).
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34 234 **Years of Life Lost (YLL) due to premature CKD mortality**

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36 236 Data on CKD mortality for the year 2015 was retrieved from the National Mortality
37 237 Registry at the Institute of Statistics and Census. Deaths recorded as N18 (chronic kidney
38 238 disease, n=221) and N19 (unspecified kidney failures, n=18) were included according to
39 239 the International Classification of Diseases 10th Revision codes. Linear method was utilized
40 240 for the analyses using the population aged 20 to 77 years old.
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49 241 The calculation of the YLLs was performed by subtracting the life expectancy from the age
50 242 of death of each individual. We then estimated the average life expectancy on the basis of
51 243 the life table of the Institute of Statistics and Census life tables (77.74 years) and valued for
52 244 the year 2015 at the country's gross domestic product (GDP) per capita. YLLs of each
53 245 individual were multiplied by the GDP per capita current prices estimated for 2015,
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3 246 obtaining the YLLs in USD. We applied a 3% discounted present value at a social discount
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5 247 rate (2,3). The estimated total annual YLL by sex was reported according to age-categories:
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7 248 (20-30 years, 31-40 years, 41-50 years, 51-60 years and 71 to 80 years). In addition, YLL
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9 249 were calculated according to provinces.

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11 250 All analysis was performed in Excel and in Stata version 14.
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14 251 **Ethical statement:**
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16 252 Permission to conduct the study was obtained from the medical directors of the respective
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18 253 institutions. Ethical approval for the study was obtained from the Ethics Review Committee
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20 254 of the Gorgas Memorial Institute for Health Studies.
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23 255 **Patient and Public Involvement:**
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26 256 The study did not involve patients or public in planning or execution.
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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 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 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

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3 297 toward greater PD use is accomplished sooner (a 10% annual increase in the use of PD in
4 298 CSS resulted in reducing costs by USD 4.5 millions per year).

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10 301 **Years of Life Lost –USD (YLL-USD) due to premature CKD mortality**

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13 303 In the year 2015, CKD was the cause of 440 deaths in Panama, accounting for 2.4 %
14 304 of the total deaths registered. The number of male deaths was 279 (63.4%), whereas for
15 305 females it was 161 (36.6%).

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19 306 The average annual loss was 25,501, 808.40 USD YLL. In men, the higher YLL was
20 307 observed for the age-group 51-60, whereas in women, the higher YLL was observed for the
21 308 age-group 61-70, as shown in Figure 2.

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25 309 The top three provinces with the highest accumulated number of YLL-USD in the age-
26 310 group below 40 years due to CKD were 1) the Province of Panama (1,548,252.11 YLLs) ,
27 311 2) the Province of Coclé, (YLLs of 459,212.85) and the Province of Colón (YLLs
28 312 314,586.97) (Supplementary Table 3).

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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

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3 354 other countries such as Mexico, El Salvador and Guatemala, where the utilization rates
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5 355 were 66%, 76.5% and 56%, respectively [21]. In this context, if the CSS increases the PD
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7 356 utilization by 7.5% per year, the proportion of PD utilization will reach 50% in 5 years. The
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9 357 reasons for the underutilization of PD are presumably multifactorial and may partly be
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11 358 explained by the scarcity of trained nephrologists and nurses as well as the lack of health
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13 359 policies [10]. Currently there are 32 nephrologists nationwide, which constitute a relatively
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15 360 low distribution of density of nephrologists per million population [24]. Furthermore, as
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17 361 opposed to other countries [22], Panama has a small market without local manufacturing
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19 362 facilities of PD bags and largely depends on imported medicines/equipment. Of note,
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21 363 Colombia and Nicaragua have also reported a decrease in the use of PD from the year 2000
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23 364 to 2010, contrasted with the continued expansion of HD [16].

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25 365 There is compelling evidence that kidney transplantations have led to substantial cost
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27 366 savings for health care systems in high-income countries [25]. Kidney transplantations in
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29 367 Panama began in 1990, and human resources and infrastructure has been enlarged.
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31 368 According to the Panamanian Transplant Organization (PTO), in 2015, there were 28
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33 369 kidney transplantations performed in Panama and the number of donors has increased over
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35 370 the years, yet at a slow rate.

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37 371 Taken together and from a macroeconomic standpoint, our results suggest that increasing
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39 372 PD utilization might reduce the overall healthcare expenditure in Panama. Therefore, key
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41 373 strategies such as implementation of policies and incentives favoring PD modality over HD
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43 374 should be advocated [27]. A complementary and vital approach is slowing the progression
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45 375 of CKD to ESRD. Likewise, it is highly recommended to enhance the kidney transplant
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47 376 programs.

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51 378 The burden of premature death and health loss from CKD has been widely described.
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53 379 Between 1990 and 2013, the number of cases of CKD due to diabetes and due to other
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55 380 causes increased by more than 50% worldwide [28]. In addition, the burden of CKD
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57 381 disproportionately impacts low-income and middle-income countries where growth in
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59 382 diabetes, hypertension and obesity is greatest [29]. Moreover, poverty increases the risk of
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383 pathologies that predispose CKD to develop, and worsens outcomes in those who already

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3 384 have this disease [30]. Previous studies have reported a relationship between progressive
4 385 CKD and its impact on household income or poverty, including spending more than 10%
5 386 on income out of pocket payment [31, 32].

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9 387 Remarkably, Latin America has the highest CKD death rate in the world [33] where
10 388 diabetes mellitus, hypertension and recently, CKD of unknown etiology in Central-America
11 389 are contributors [5, 29]. In Panama, the trends in mortality rates due to CKD have been
12 390 declining from 2006, however geographical disparities exist [15]. Interestingly, Coclé, a
13 391 province with the highest age-adjusted mortality rate in the country [15], presented
14 392 considerably elevated YLL in the age-group below 40. Taken together, the sum of the
15 393 estimated YLL and the dialysis costs is unsustainable for the health system, highlighting
16 394 the importance on prevention. Recently, the legal framework for the CKD registration in
17 395 Panama started through a resolution signed by the MoH, establishing notification of all
18 396 stages of CKD as compulsory for private and health institutions at a national level. In
19 397 addition, CKD guidelines are currently being revised. On a broader perspective, if the
20 398 Sustainable Development Goal of poverty reduction is to be accomplished, is essential that
21 399 health systems protect individuals from the economic burden of CKD and other non-
22 400 communicable diseases [34].

23 401 This study has strengths and limitations. Costs due to hospitalization, complications,
24 402 emergency medicines, transportation were not included in the HD calculation, and hence,
25 403 any possible bias is likely to underestimate and not overestimate the cost advantage of PD
26 404 over HD. Of note, patients frequently have to travel long distances, often with families, to
27 405 receive specialized care adding a dimension of social and economic consequences that was
28 406 beyond the scope of this study. Despite the exclusion of these costs, we estimated YLL, a
29 407 contributor of indirect costs. However, it is it likely that the reliance on diagnostic code
30 408 data alone to define CKD as a cause of death and the underreporting resulted in
31 409 underestimation of people with early stages of CKD. Finally, because the public systems
32 410 operate independently of each other and the information (health and costs) is not
33 411 systematized homogenously, costs data derived from the MoH could not be obtained.
34 412 Therefore, the total costs from the public sector are underestimated and the estimated yearly
35 413 increase rate should be interpreted with caution. Likewise, we could not perform a cost-

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3 414 effectiveness analysis. Despite the lack of registries, the Panamanian Society of
4 415 Nephrology and Hypertension, along with the PTO have been actively recording the
5 416 number of cases undergoing RRT. Currently, there are three institutions from the MoH
6 417 offering dialysis within the country. According to the PTO, in 2015 there were n=26 and
7 418 n=204 patients receiving PD and HD treatment, respectively in these institutions.

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13 419 In conclusion, CKD represents a major challenge for Panama. Our results suggest
14 420 that an increased utilization of PD provides an opportunity to lower overall ESRD
15 421 treatment costs. In the long term, an important factor to reduce the overall annual cost is to
16 422 reduce the number of patients with ESRD. Therefore, CKD in early stages (which affects
17 423 far more patients and who are frequent users of the health system) should not be ignored by
18 424 policy makers. Altogether, the huge cost associated with CKD provides a compelling
19 425 economic incentive for improving the prevention, detection and management of CKD and
20 426 its health policies in Panama.

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38 434 **Conflict of interest:** IMV, RV, BG, JM, CC and VH declare no conflict of interest. MTC
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51 442 analyzed the data. CC and RV provided the data. IMV, MTC, RV, BG, JM, CC and VH
52 443 interpreted the data, critically revised the draft for important intellectual content and
53 444 approved the final version. All the authors agree to be accountable for all aspects of the

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3 445 work in ensuring that questions related to the accuracy or integrity of any part of the work
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5 446 are appropriately investigated and resolved.
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7 447 **Data availability:** The datasets used and/or analyzed during the current study are available
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9 448 from the authors on reasonable request.
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451 **References**

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- 453 1. Xie Y, Bowe B, Mokdad AH, Xian H, Yan Y, Li T, Maddukuri G, Tsai CY, Floyd T, Al-Aly Z:
454 **Analysis of the Global Burden of Disease study highlights the global, regional, and**
455 **national trends of chronic kidney disease epidemiology from 1990 to 2016.** *Kidney Int*
456 2018.
- 457 2. Dienemann T, Fujii N, Orlandi P, Nessel L, Furth SL, Hoy WE, Matsuo S, Mayer G, Methven
458 S, Schaefer F *et al*: **International Network of Chronic Kidney Disease cohort studies (iNET-**
459 **CKD): a global network of chronic kidney disease cohorts.** *BMC Nephrol* 2016, **17**(1):121.
- 460 3. Mills KT, Xu Y, Zhang W, Bundy JD, Chen CS, Kelly TN, Chen J, He J: **A systematic analysis of**
461 **worldwide population-based data on the global burden of chronic kidney disease in**
462 **2010.** *Kidney international* 2015, **88**(5):950-957.
- 463 4. Eckardt KU, Coresh J, Devuyst O, Johnson RJ, Kottgen A, Levey AS, Levin A: **Evolving**
464 **importance of kidney disease: from subspecialty to global health burden.** *Lancet* 2013,
465 **382**(9887):158-169.
- 466 5. Obrador GT, Rubilar X, Agazzi E, Estefan J: **The Challenge of Providing Renal Replacement**
467 **Therapy in Developing Countries: The Latin American Perspective.** *Am J Kidney Dis* 2016,
468 **67**(3):499-506.
- 469 6. System USRD: **Medicare Expenditures for Persons with CKD.**
470 [http://www.ajkd.org/article/S0272-6386\(16\)00099-8/pdf](http://www.ajkd.org/article/S0272-6386(16)00099-8/pdf). Accessed April 2016.
- 471 7. Abecassis M, Bartlett ST, Collins AJ, Davis CL, Delmonico FL, Friedewald JJ, Hays R, Howard
472 A, Jones E, Leichtman AB *et al*: **Kidney transplantation as primary therapy for end-stage**
473 **renal disease: a National Kidney Foundation/Kidney Disease Outcomes Quality Initiative**
474 **(NKF/KDOQITM) conference.** *Clin J Am Soc Nephrol* 2008, **3**(2):471-480.
- 475 8. Vanholder R, Van Biesen W, Lameire N: **Renal replacement therapy: how can we contain**
476 **the costs?** *Lancet* 2014, **383**(9931):1783-1785.
- 477 9. Glasscock RJ, Warnock DG, Delanaye P: **The global burden of chronic kidney disease:**
478 **estimates, variability and pitfalls.** *Nat Rev Nephrol* 2017, **13**(2):104-114.
- 479 10. Rosa-Diez G, Gonzalez-Bedat M, Pecoits-Filho R, Marinovich S, Fernandez S, Lugon J,
480 Poblete-Badal H, Elgueta-Miranda S, Gomez R, Cerdas-Calderon M *et al*: **Renal**
481 **replacement therapy in Latin American end-stage renal disease.** *Clin Kidney J* 2014,
482 **7**(4):431-436.
- 483 11. **Instituto Nacional de Estadística y Censo. Available at>**
484 **https://www.contraloria.gob.pa/inec/Publicaciones/Publicaciones.aspx?ID_SUBCATEG**

- 1
2
3 485 **ORIA=10&ID_PUBLICACION=491&ID_IDIOMA=1&ID_CATEGORIA=3.** Accessed July 31,
4 486 **2018.**
- 6 487 12. **Ministry of Health. Available at:**
7 488 **http://www.minsa.gob.pa/sites/default/files/publicaciones/asis_final_2018c.pdf.**
8 489 **Accessed on December 2018.**
- 10 490 13. **Instituto Nacional de Estadística y Censo población asegurada. Available at:**
11 491 **<https://www.contraloria.gob.pa/inec/archivos/P8401421-01.pdf>.** Accessed July 31,
12 492 **2018.**
- 15 493 14. Romero LI, Quental C: **The Panamanian health research system: a baseline analysis for**
16 494 **the construction of a new phase.** *Health research policy and systems* 2013, **11**:33.
- 18 495 15. Moreno Velasquez I, Castro F, Gomez B, Cuero C, Motta J: **Chronic Kidney Disease in**
19 496 **Panama: Results From the PREFREC Study and National Mortality Trends.** *Kidney Int Rep*
20 497 **2017, 2(6):1032-1041.**
- 22 498 16. Gonzalez-Bedat M, Rosa-Diez G, Pecoits-Filho R, Ferreiro A, Garcia-Garcia G, Cusumano A,
23 499 Fernandez-Cean J, Noboa O, Douthat W: **Burden of disease: prevalence and incidence of**
24 500 **ESRD in Latin America.** *Clin Nephrol* 2015, **83(7 Suppl 1):3-6.**
- 27 501 17. Couser WG, Remuzzi G, Mendis S, Tonelli M: **The contribution of chronic kidney disease**
28 502 **to the global burden of major noncommunicable diseases.** *Kidney Int* 2011, **80(12):1258-**
29 503 **1270.**
- 31 504 18. Essue BM, Wong G, Chapman J, Li Q, Jan S: **How are patients managing with the costs of**
32 505 **care for chronic kidney disease in Australia? A cross-sectional study.** *BMC Nephrol* 2013,
33 506 **14:5.**
- 35 507 19. Zelmer JL: **The economic burden of end-stage renal disease in Canada.** *Kidney Int* 2007,
36 508 **72(9):1122-1129.**
- 39 509 20. Beaudry A, Ferguson TW, Rigatto C, Tangri N, Dumanski S, Komenda P: **Cost of Dialysis**
40 510 **Therapy by Modality in Manitoba.** *Clin J Am Soc Nephrol* 2018.
- 42 511 21. Jain AK, Blake P, Cordy P, Garg AX: **Global trends in rates of peritoneal dialysis.** *J Am Soc*
43 512 *Nephrol* 2012, **23(3):533-544.**
- 45 513 22. Karopadi AN, Mason G, Rettore E, Ronco C: **Cost of peritoneal dialysis and haemodialysis**
46 514 **across the world.** *Nephrol Dial Transplant* 2013, **28(10):2553-2569.**
- 48 515 23. Neil N, Walker DR, Sesso R, Blackburn JC, Tschosik EA, Sciaraffia V, Garcia-Contreras F,
49 516 Capsa D, Bhattacharyya SK: **Gaining efficiencies: resources and demand for dialysis**
50 517 **around the globe.** *Value Health* 2009, **12(1):73-79.**
- 53 518 24. Osman MA, Alrukhaimi M, Ashuntantang GE, Bellorin-Font E, Benghanem Gharbi M,
54 519 Braam B, Courtney M, Feehally J, Harris DC, Jha V *et al*: **Global nephrology workforce:**

- 1
2
3 520 **gaps and opportunities toward a sustainable kidney care system. *Kidney International*
4 521 *Supplements* 2018, **8**(2):52-63.**
- 6 522 25. Jarl J, Desatnik P, Peetz Hansson U, Prutz KG, Gerdtham UG: **Do kidney transplantations**
7 523 **save money? A study using a before-after design and multiple register-based data from**
8 524 **Sweden.** *Clin Kidney J* 2018, **11**(2):283-288.
- 10 525 26. **Organización Panameña de Transplante.** Available at: [http://190.34.154.93/opt/wp-](http://190.34.154.93/opt/wp-content/uploads/2017/07/2015annual.pdf)
12 526 [content/uploads/2017/07/2015annual.pdf](http://190.34.154.93/opt/wp-content/uploads/2017/07/2015annual.pdf). Accessed July 27, 2018.
- 14 527 27. Li PK, Chow KM, Van de Luitgaarden MW, Johnson DW, Jager KJ, Mehrotra R, Naicker S,
15 528 Pecoits-Filho R, Yu XQ, Lameire N: **Changes in the worldwide epidemiology of peritoneal**
16 529 **dialysis.** *Nat Rev Nephrol* 2017, **13**(2):90-103.
- 18 530 28. Carney EF: **Epidemiology: Global Burden of Disease Study 2013 reports that disability**
19 531 **caused by CKD is increasing worldwide.** *Nat Rev Nephrol* 2015, **11**(8):446.
- 21 532 29. Neuen BL, Chadban SJ, Demaio AR, Johnson DW, Perkovic V: **Chronic kidney disease and**
22 533 **the global NCDs agenda.** *BMJ Glob Health* 2017, **2**(2):e000380.
- 24 534 30. Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, Saran R, Wang AY, Yang CW:
25 535 **Chronic kidney disease: global dimension and perspectives.** *Lancet* 2013, **382**(9888):260-
26 536 272.
- 28 537 31. Jaspers L, Colpani V, Chaker L, van der Lee SJ, Muka T, Imo D, Mendis S, Chowdhury R,
29 538 Bramer WM, Falla A *et al*: **The global impact of non-communicable diseases on**
30 539 **households and impoverishment: a systematic review.** *Eur J Epidemiol* 2015, **30**(3):163-
31 540 188.
- 33 541 32. Morton RL, Schlackow I, Gray A, Emberson J, Herrington W, Staplin N, Reith C, Howard K,
34 542 Landray MJ, Cass A *et al*: **Impact of CKD on Household Income.** *Kidney Int Rep* 2018,
35 543 **3**(3):610-618.
- 37 544 33. Mortality GBD, Causes of Death C: **Global, regional, and national life expectancy, all-**
38 545 **cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a**
39 546 **systematic analysis for the Global Burden of Disease Study 2015.** *Lancet* 2016,
40 547 **388**(10053):1459-1544.
- 42 548 34. Jan S, Laba TL, Essue BM, Gheorghe A, Muhunthan J, Engelgau M, Mahal A, Griffiths U,
43 549 McIntyre D, Meng Q *et al*: **Action to address the household economic burden of non-**
44 550 **communicable diseases.** *Lancet* 2018, **391**(10134):2047-2058.

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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).

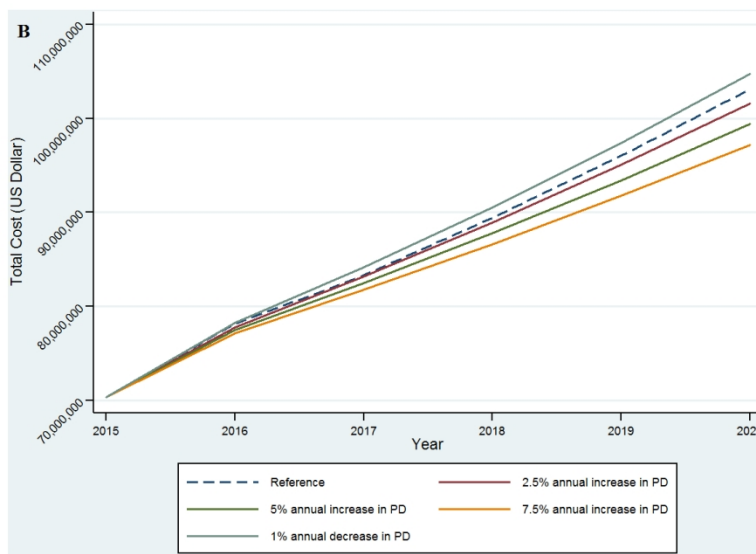
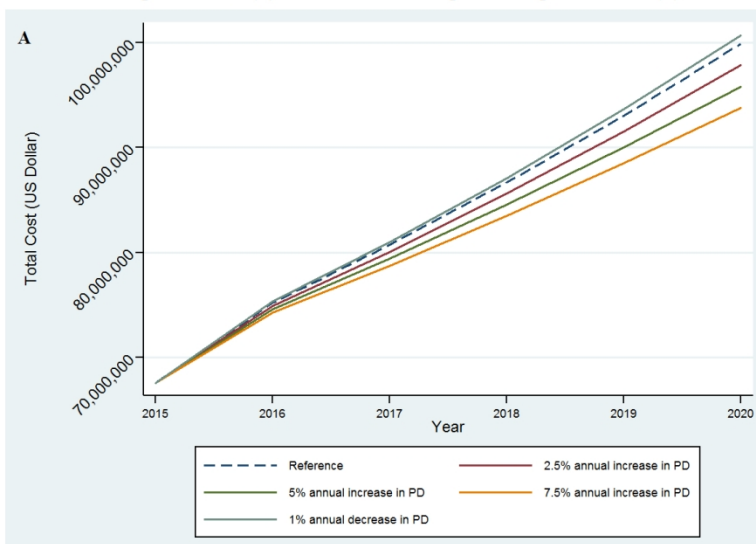
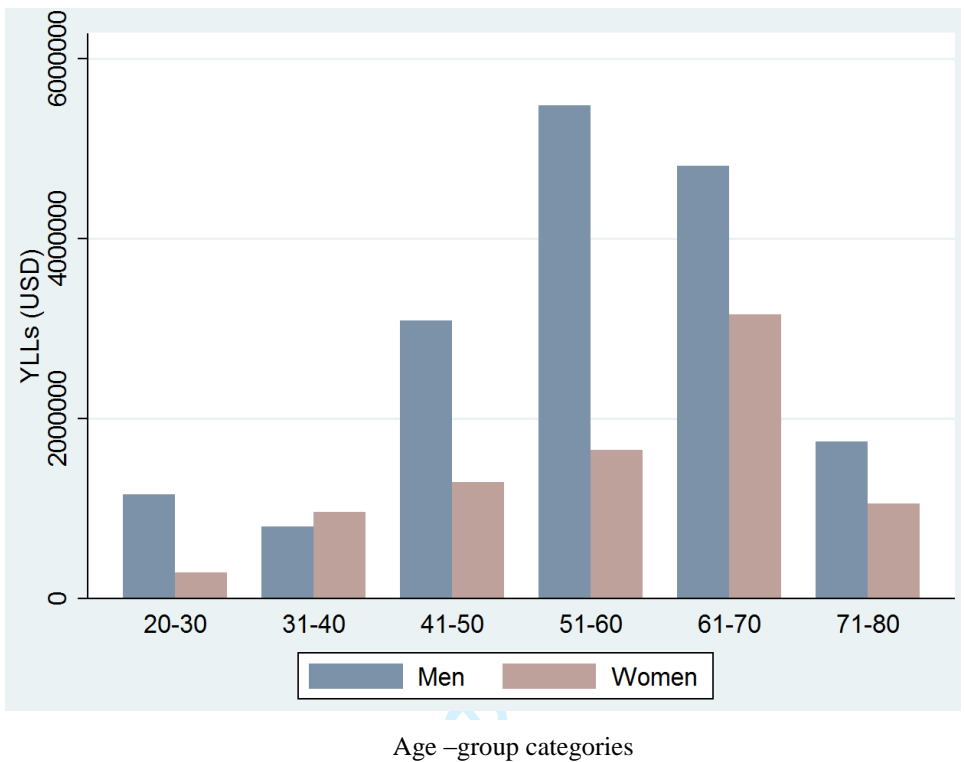


Figure 2. Years of Life Lost-(USD) due to premature mortality, according to age-group categories in Panama. Year 2015



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
Paricalcitol	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	6,7	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (selection of sectors offering Hemo and peritoneal dialysis) (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Financial costs based on secondary data, and therefore many items are not applicable		
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) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —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

BMJ Open

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

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Keywords:	Chronic renal failure < NEPHROLOGY, Dialysis < NEPHROLOGY, costs, years of life lost, Panama

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4 **1 End-stage renal disease: Financial costs and years of life lost in Panama.**
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11 4 Ilais Moreno Velásquez¹, Maribel Tribaldos Causadias¹, Régulo Valdés², Beatriz Gómez¹,
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13 5 Jorge Motta^{1,3}, César Cuero⁴, Víctor Herrera-Ballesteros¹
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15
16 6 ¹Gorgas Memorial Institute for Health Studies, Panama; ²Caja de Seguro Social, Panama; ³ National
17 7 Secretariat for Science and Technology, Panama; ⁴Organización Panameña de Trasplante, Ministry of
18 8 Health, Panama.
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26 14
27 15
28 16 **Corresponding author:**
29

30 17
31 18 Ilais Moreno Velásquez
32 19 MD, PhD
33 20 Gorgas Memorial Institute for Health Studies
34 21 0816-02593 Panama City, Panama
35 22 Email: imoreno@gorgas.gob.pa
36 23
37 24
38 25

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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

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4 78 **Strengths and Limitations**
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- 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,

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3 154 whereas the CSS provides health coverage to formally employed persons. In addition, there
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5 155 are private insurers with which affiliation is voluntary [14]. Therefore, the direct costs of
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7 156 medical care are at least partly covered by the CSS (the Panamanian public health
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9 157 insurance) or by the state.

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12 159 Electronic health records are in the process of being implemented at public health facilities;
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14 160 consequently, there is currently no CKD national registry in Panama [12]. Furthermore,
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16 161 national estimates of CKD derived from epidemiological studies are lacking. Recently, a
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18 162 cross-sectional study reported a CKD prevalence of 12.6% in the two provinces in which
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20 163 60% of the population resides [15]. Moreover, the study described geographical disparities
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22 164 in age-adjusted standardized mortality rates due to CKD [15]. In 2001, the CSS calculated
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24 165 the annual costs of care for the peritoneal dialysis (PD) and haemodialysis (HD)
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26 166 programmes, resulting in average per patient costs of \$25,426.64 USD and \$18,857.21
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28 167 USD, respectively. However, neither the costs of RRT nor the years of life lost (YLL),
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30 168 which are useful measures to consider when prioritizing public health interventions, has
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32 169 been recently evaluated.

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34 171 The aim of this study was to i) estimate the direct costs associated with ESRD treatment,
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36 172 whether HD or PD, in public and private Panamanian institutions in 2015, ii) to perform a
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38 173 five-year budget impact analysis, and iii) to calculate the YLL due to CKD in the country.

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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

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3 216 prevalence reported in 2015 by the CSS and CETRERSA. The calculated annual changes in
4 217 rates from 2010 to 2015 were 10.65% and -4.23% for HD and PD, respectively, with a ratio
5 218 of 2.5%. The cost analysis was performed using present values; therefore, no discounted
6 219 rates were included.
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11 221 We performed a five-year time horizon budget impact analysis on the direct costs
12 222 related to the renal programme in Panama, considering costs from both the CSS and the
13 223 private sector. The budget impact analysis estimated how changes in the mix of dialysis
14 224 modalities would impact the trajectory of the total spending for dialysis services (assuming
15 225 that the mix of dialysis modalities used shifts towards a greater use of PD over time). The
16 226 budget impact model was from the payer perspective and included the following five
17 227 scenarios from 2015 until 2020: scenario 1 was a 2.5% yearly increase in the use of PD,
18 228 scenario 2 was a 5% yearly increase in the use of PD, scenario 3 was a 7.5% yearly increase
19 229 in the use of PD, and scenario 4 was a 1% yearly decrease in the use of PD. The scenarios
20 230 were based on the ratio of sensibility (annual increase in the rate of HD utilization/annual
21 231 increase in the rate of PD utilization) =2.5%. In addition, complementary analyses were
22 232 performed with different arbitrary assumptions (10% annual increase in PD, 2.5% decrease
23 233 in PD utilization).
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36 236 **Years of life lost due to premature CKD mortality**

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38 238 Data on CKD mortality for the year 2015 were retrieved from the National
39 239 Mortality Registry at the Institute of Statistics and Census. Deaths recorded as N18
40 240 (chronic kidney disease, n=221) and N19 (unspecified kidney failures, n=18) were included
41 241 according to the International Classification of Diseases 10th Revision codes. The linear
42 242 method was utilized for the analyses in the population aged 20 to 77 years old.
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50 243 The YLLs were calculated by subtracting the life expectancy from the age of death of each
51 244 individual. We estimated the average life expectancy on the basis of the Institute of
52 245 Statistics and Census life table (77.74 years) and the value of the country's gross domestic
53 246 product (GDP) per capita in 2015. The YLLs for each individual were multiplied by the
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3 247 GDP per capita estimated for 2015, obtaining the YLLs in USD. We applied a 3%
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5 248 discounted present value at a social discount rate. The estimated total annual YLLs were
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7 249 reported stratified by sex and the following age categories: 20-30 years, 31-40 years, 41-50
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9 250 years, 51-60 years and 71-80 years. In addition, YLLs were stratified by province.

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11 251 All analyses were performed in Excel and Stata version 14.

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14 252 **Ethical statement:**

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16 253 Permission to conduct the study was obtained from the medical directors of the respective
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18 254 institutions. Ethical approval for the study was obtained from the Ethics Review Committee
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20 255 of the Gorgas Memorial Institute for Health Studies.

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23 256 **Patient and public involvement:**

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25 257 The study did not involve patients or the public in its planning or execution.

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274 3. Results

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276 Cost analysis

277 The mean direct expenditures for dialysis are summarized in Table 1. As of 2015,
 278 2075 persons were receiving RRT (PD or HD), and of those, 87% were receiving HD. The
 279 total costs for dialysis in the public sector ranged from approximately \$9.8 million (PD) to
 280 \$50.5 million (HD). The total cost per year of the programmes in the public and private
 281 sectors combined was \$70.3 million. The HD/PD cost ratio in the public sector was 1.19.

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

284 **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

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

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287 The total estimated costs (USD) during the five years for the reference scenarios were 503
 288 million (CSS) and 520 million (combined sectors). Figure 1 shows the budget impact
 289 model according to the different scenarios for the public sector (CSS) (Panel A) and for the
 290 public and private sectors combined (Panel B). In the CSS, the estimated costs for the year
 291 2020 ranged from \$93.8 million (assuming a 7.5% annual increase in the use of PD) to
 292 \$100.7 million (assuming a 1% decrease in the use of PD).

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

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3 297 greater if the shift towards greater PD use is accomplished sooner (a 10% annual increase
4 298 in the use of PD in CSS resulted in reducing costs by USD 4.5 million per year).

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10 301 **Years of life lost –USD (YLL-USD) due to premature CKD mortality**

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13 303 In 2015, CKD was the cause of 440 deaths in Panama, accounting for 2.4% of the
14 304 total deaths registered. There were 279 male deaths (63.4%) and 161 female deaths
15 305 (36.6%).

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19 306 The average annual loss was 25,501,808.40 YLL-USD. In men, a higher YLL-USD was
20 307 observed in the 51-60 years age group than in the other age groups, whereas in women, a
21 308 higher YLL-USD was observed in the 61-70 years age group than in the other age groups,
22 309 as shown in Figure 2.

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27 310 The three provinces with the highest accumulated numbers of YLL-USD due to CKD in the
28 311 age group younger than 40 years were 1) the Province of Panama (1,548,252.11 YLLs), 2)
29 312 the Province of Coclé, (459,212.85 YLLs) and the Province of Colón (314,586.97 YLLs)
30 313 (Supplementary Table 3).

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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

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3 355 are 66%, 76.5% and 56%, respectively [21]. In this context, if the CSS increases the
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5 356 utilization of PD by 7.5% per year, the proportion of dialysis accounted for by PD will
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7 357 reach 50% in 5 years. The reasons for the underutilization of PD are presumably
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9 358 multifactorial and may partly be explained by the scarcity of trained nephrologists and
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11 359 nurses as well as the lack of relevant health policies [10]. Currently, there are 32
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13 360 nephrologists nationwide, which results in a relatively low number of nephrologists per
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15 361 million population [24]. Furthermore, as opposed to other countries [22], Panama has a
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17 362 small market, lacks local manufacturing facilities for PD bags and largely depends on
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19 363 imported medicines/equipment. Notably, Colombia and Nicaragua have also reported a
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21 364 decrease in the use of PD and an expansion of the use of HD from 2000 to 2010 [16].

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23 365 There is compelling evidence that kidney transplantations have led to substantial cost
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25 366 savings for health care systems in high-income countries [25]. Kidney transplantations in
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27 367 Panama began in 1990, and the necessary human resources and infrastructure have been
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29 368 expanded. According to the Panamanian Transplant Organization (PTO), in 2015, there
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31 369 were 28 kidney transplantations performed in Panama, and the number of donors has
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33 370 increased over the years [26], albeit at a slow rate.

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35 371 Taken together and considered from a macroeconomic standpoint, our results suggest that
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37 372 increasing PD utilization might reduce the overall healthcare expenditure in Panama.
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39 373 Therefore, key strategies such as the implementation of policies and incentives favouring
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41 374 PD over HD should be advocated [27]. A critical complementary approach is slowing the
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43 375 progression of CKD to ESRD. Likewise, enhancing kidney transplant programmes is
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45 376 strongly recommended

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49 378 The burdens imposed by premature death and the loss of health due to CKD have been
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51 379 widely described. Between 1990 and 2013, the number of cases of CKD due to diabetes
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53 380 and other causes increased by more than 50% worldwide [28]. In addition, the burden of
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55 381 CKD disproportionately impacts low-income and middle-income countries where the
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57 382 prevalences of diabetes, hypertension and obesity are growing the most [29]. Moreover,
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59 383 poverty increases the risk of pathologies that predispose individuals to CKD and worsen
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384 outcomes in those who already have the disease [30]. Previous studies have reported a

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3 385 relationship between progressive CKD and its impact on household income or poverty,
4 386 including spending more than 10% of the household income on out of pocket payments [31,
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9 388 Remarkably, Latin America has the highest CKD-related death rate in the world [33], and
10 389 diabetes mellitus, hypertension and, recently, CKD of unknown aetiology are contributors
11 390 to CKD-related death in Central America [5, 29]. In Panama, the CKD-related mortality
12 391 rate has been decreasing since 2006; however, geographical disparities exist [15].
13 392 Interestingly, Coclé, a province with the highest age-adjusted mortality rate in the country
14 393 [15], was found to have markedly elevated YLLs in the under-40 years age group. Taken
15 394 together, the sum of the estimated YLLs and the costs of the dialysis is unsustainable for
16 395 the health system, highlighting the importance of prevention. Recently, the legal framework
17 396 for CKD registration in Panama started with a resolution signed by the MoH, establishing
18 397 the notification of all stages of CKD as compulsory for private and health institutions at a
19 398 national level. In addition, the CKD guidelines are currently being revised. From a broader
20 399 perspective, if the Sustainable Development Goal of poverty reduction is to be
21 400 accomplished, it is essential that health systems protect individuals from the economic
22 401 burdens imposed by CKD and other non-communicable diseases [34].
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34 402 This study has strengths and limitations. Costs due to hospitalization, complications,
35 403 emergency medicines, and transportation were not included in the HD calculation; hence,
36 404 any possible bias is likely to result in the underestimation and not the overestimation of the
37 405 cost advantage of PD over HD. It is noteworthy that patients frequently have to travel long
38 406 distances, often with their families, to receive specialized care, adding a dimension of social
39 407 and economic consequences that was beyond the scope of this study. Although we excluded
40 408 these costs, we estimated the YLLs, which is a measure of indirect costs. However, it is
41 409 likely that the reliance on diagnostic code data alone to define CKD as a cause of death and
42 410 the effects of underreporting resulted in the underestimation of people with early stages of
43 411 CKD. Finally, because the public systems operate independently of each other and the
44 412 information (health and costs) is not homogeneously systematized, cost data could not be
45 413 obtained from the MoH. Therefore, the total costs from the public sector were
46 414 underestimated, and the estimated yearly increase in the rates of utilization should be
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3 415 interpreted with caution. Likewise, we could not perform a cost-effectiveness analysis.
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5 416 Despite the lack of registries, the Panamanian Society of Nephrology and Hypertension and
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7 417 the PTO have been actively recording the number of cases undergoing RRT. Currently,
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9 418 there are three institutions in the MoH offering dialysis within the country. According to
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11 419 the PTO, in 2015, there were 26 and 204 patients receiving PD and HD treatment,
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13 420 respectively, in these institutions.

14 421 **Conclusion**

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16 422 In conclusion, CKD represents a major challenge for Panama. Our results suggest
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18 423 that increasing the utilization of PD will lower the overall ESRD treatment costs. In the
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20 424 long term, an important method of reducing the overall annual cost is to reduce the number
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22 425 of patients with ESRD. Consequently, patients with CKD in the early stages (who are more
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24 426 abundant and more frequent users of the health system) should not be ignored by policy
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26 427 makers. Altogether, the enormous cost associated with CKD provides a compelling
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28 428 economic incentive for improving the prevention, detection and management of CKD and
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30 429 the relevant health policies in Panama.

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32
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36
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39 435 in the decision to submit the article for publication.

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42 437 **Competing interests:** IMV, RV, BG, JM, CC and VH declare no conflict of interest. MTC
43
44 438 currently works at Sanofi Pasteur, nonetheless, her responsibilities do not relate with the
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46 439 submitted work.

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51 442 Senacyt, Panama.

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56 445 analyzed the data. CC and RV provided the data. IMV, MTC, RV, BG, JM, CC and VH

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3 446 interpreted the data, critically revised the draft for important intellectual content and
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5 447 approved the final version. All the authors agree to be accountable for all aspects of the
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7 448 work in ensuring that questions related to the accuracy or integrity of any part of the work
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9 449 are appropriately investigated and resolved.

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11 450 **Data availability:** The datasets used and/or analyzed during the current study are available
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13 451 from the authors on reasonable request.

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For peer review only

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3 453 **References**
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- 9 455 1. Xie Y, Bowe B, Mokdad AH, Xian H, Yan Y, Li T, Maddukuri G, Tsai CY, Floyd T, Al-Aly Z:
10 456 **Analysis of the Global Burden of Disease study highlights the global, regional, and**
11 457 **national trends of chronic kidney disease epidemiology from 1990 to 2016.** *Kidney Int*
12 458 2018.
- 13
14 459 2. Dienemann T, Fujii N, Orlandi P, Nessel L, Furth SL, Hoy WE, Matsuo S, Mayer G, Methven
15 460 S, Schaefer F *et al*: **International Network of Chronic Kidney Disease cohort studies (iNET-**
16 461 **CKD): a global network of chronic kidney disease cohorts.** *BMC Nephrol* 2016, **17**(1):121.
- 17
18 462 3. Mills KT, Xu Y, Zhang W, Bundy JD, Chen CS, Kelly TN, Chen J, He J: **A systematic analysis of**
19 463 **worldwide population-based data on the global burden of chronic kidney disease in**
20 464 **2010.** *Kidney international* 2015, **88**(5):950-957.
- 21
22
23 465 4. Eckardt KU, Coresh J, Devuyst O, Johnson RJ, Kottgen A, Levey AS, Levin A: **Evolving**
24 466 **importance of kidney disease: from subspecialty to global health burden.** *Lancet* 2013,
25 467 **382**(9887):158-169.
- 26
27 468 5. Obrador GT, Rubilar X, Agazzi E, Estefan J: **The Challenge of Providing Renal Replacement**
28 469 **Therapy in Developing Countries: The Latin American Perspective.** *Am J Kidney Dis* 2016,
29 470 **67**(3):499-506.
- 30
31 471 6. System USRD: **Medicare Expenditures for Persons with CKD.**
32 472 **[http://www.ajkd.org/article/S0272-6386\(16\)00099-8/pdf](http://www.ajkd.org/article/S0272-6386(16)00099-8/pdf).** Accessed April 2016.
- 33
34
35 473 7. Abecassis M, Bartlett ST, Collins AJ, Davis CL, Delmonico FL, Friedewald JJ, Hays R, Howard
36 474 A, Jones E, Leichtman AB *et al*: **Kidney transplantation as primary therapy for end-stage**
37 475 **renal disease: a National Kidney Foundation/Kidney Disease Outcomes Quality Initiative**
38 476 **(NKF/KDOQITM) conference.** *Clin J Am Soc Nephrol* 2008, **3**(2):471-480.
- 39
40 477 8. Vanholder R, Van Biesen W, Lameire N: **Renal replacement therapy: how can we contain**
41 478 **the costs?** *Lancet* 2014, **383**(9931):1783-1785.
- 42
43
44 479 9. Glassock RJ, Warnock DG, Delanaye P: **The global burden of chronic kidney disease:**
45 480 **estimates, variability and pitfalls.** *Nat Rev Nephrol* 2017, **13**(2):104-114.
- 46
47 481 10. Rosa-Diez G, Gonzalez-Bedat M, Pecoits-Filho R, Marinovich S, Fernandez S, Lugon J,
48 482 Poblete-Badal H, Elgueta-Miranda S, Gomez R, Cerdas-Calderon M *et al*: **Renal**
49 483 **replacement therapy in Latin American end-stage renal disease.** *Clin Kidney J* 2014,
50 484 **7**(4):431-436.
- 51
52 485 11. Instituto Nacional de Estadística y Censo. Available at
53 486 **[https://www.contraloria.gob.pa/inec/Publicaciones/Publicaciones.aspx?ID_SUBCATEG](https://www.contraloria.gob.pa/inec/Publicaciones/Publicaciones.aspx?ID_SUBCATEGORIA=10&ID_PUBLICACION=491&ID_IDIOMA=1&ID_CATEGORIA=3)**
54 487 **[ORIA=10&ID_PUBLICACION=491&ID_IDIOMA=1&ID_CATEGORIA=3](https://www.contraloria.gob.pa/inec/Publicaciones/Publicaciones.aspx?ID_SUBCATEGORIA=10&ID_PUBLICACION=491&ID_IDIOMA=1&ID_CATEGORIA=3).** Accessed July 31,
55 488 **2018.**

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2
3 489 12. **Ministry of Health. Available at:**
4 490 **http://www.minsa.gob.pa/sites/default/files/publicaciones/asis_final_2018c.pdf.**
5 491 **Accessed on December 2018.**
6
7 492 13. **Instituto Nacional de Estadística y Censo población asegurada. Available at:**
8 493 **<https://www.contraloria.gob.pa/inec/archivos/P8401421-01.pdf>. Accessed July 31,**
9 494 **2018.**
10
11 495 14. **Romero LI, Quental C: The Panamanian health research system: a baseline analysis for**
12 496 **the construction of a new phase. *Health research policy and systems* 2013, **11**:33.**
13
14 497 15. **Moreno Velasquez I, Castro F, Gomez B, Cuero C, Motta J: Chronic Kidney Disease in**
15 498 **Panama: Results From the PREFREC Study and National Mortality Trends. *Kidney Int Rep***
16 499 **2017, **2**(6):1032-1041.**
17
18 500 16. **Gonzalez-Bedat M, Rosa-Diez G, Pecoits-Filho R, Ferreiro A, Garcia-Garcia G, Cusumano A,**
19 501 **Fernandez-Cean J, Noboa O, Douthat W: Burden of disease: prevalence and incidence of**
20 502 **ESRD in Latin America. *Clin Nephrol* 2015, **83**(7 Suppl 1):3-6.**
21
22 503 17. **Couser WG, Remuzzi G, Mendis S, Tonelli M: The contribution of chronic kidney disease**
23 504 **to the global burden of major noncommunicable diseases. *Kidney Int* 2011, **80**(12):1258-**
24 505 **1270.**
25
26 506 18. **Essue BM, Wong G, Chapman J, Li Q, Jan S: How are patients managing with the costs of**
27 507 **care for chronic kidney disease in Australia? A cross-sectional study. *BMC Nephrol* 2013,**
28 508 **14**:5.
29
30 509 19. **Zelmer JL: The economic burden of end-stage renal disease in Canada. *Kidney Int* 2007,**
31 510 **72**(9):1122-1129.
32
33 511 20. **Beaudry A, Ferguson TW, Rigatto C, Tangri N, Dumanski S, Komenda P: Cost of Dialysis**
34 512 **Therapy by Modality in Manitoba. *Clin J Am Soc Nephrol* 2018.**
35
36 513 21. **Jain AK, Blake P, Cordy P, Garg AX: Global trends in rates of peritoneal dialysis. *J Am Soc***
37 514 ***Nephrol* 2012, **23**(3):533-544.**
38
39 515 22. **Karopadi AN, Mason G, Rettore E, Ronco C: Cost of peritoneal dialysis and haemodialysis**
40 516 **across the world. *Nephrol Dial Transplant* 2013, **28**(10):2553-2569.**
41
42 517 23. **Neil N, Walker DR, Sesso R, Blackburn JC, Tschosik EA, Sciaraffia V, Garcia-Contreras F,**
43 518 **Capsa D, Bhattacharyya SK: Gaining efficiencies: resources and demand for dialysis**
44 519 **around the globe. *Value Health* 2009, **12**(1):73-79.**
45
46 520 24. **Osman MA, Alrukhaimi M, Ashuntantang GE, Bellorin-Font E, Benghanem Gharbi M,**
47 521 **Braam B, Courtney M, Feehally J, Harris DC, Jha V *et al*: Global nephrology workforce:**
48 522 **gaps and opportunities toward a sustainable kidney care system. *Kidney International***
49 523 ***Supplements* 2018, **8**(2):52-63.**
50
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52
53
54
55
56
57
58
59
60

- 1
2
3 524 25. Jarl J, Desatnik P, Peetz Hansson U, Prutz KG, Gerdtham UG: **Do kidney transplantations**
4 525 **save money? A study using a before-after design and multiple register-based data from**
5 526 **Sweden.** *Clin Kidney J* 2018, **11**(2):283-288.
- 7 527 26. **Organización Panameña de Transplante.** Available at: [http://190.34.154.93/opt/wp-](http://190.34.154.93/opt/wp-content/uploads/2017/07/2015anual.pdf)
8 528 [content/uploads/2017/07/2015anual.pdf](http://190.34.154.93/opt/wp-content/uploads/2017/07/2015anual.pdf). Accessed July 27, 2018.
- 10 529 27. Li PK, Chow KM, Van de Luitgaarden MW, Johnson DW, Jager KJ, Mehrotra R, Naicker S,
11 530 Pecoits-Filho R, Yu XQ, Lameire N: **Changes in the worldwide epidemiology of peritoneal**
12 531 **dialysis.** *Nat Rev Nephrol* 2017, **13**(2):90-103.
- 14 532 28. Carney EF: **Epidemiology: Global Burden of Disease Study 2013 reports that disability**
15 533 **caused by CKD is increasing worldwide.** *Nat Rev Nephrol* 2015, **11**(8):446.
- 17 534 29. Neuen BL, Chadban SJ, Demaio AR, Johnson DW, Perkovic V: **Chronic kidney disease and**
18 535 **the global NCDs agenda.** *BMJ Glob Health* 2017, **2**(2):e000380.
- 20 536 30. Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, Saran R, Wang AY, Yang CW:
21 537 **Chronic kidney disease: global dimension and perspectives.** *Lancet* 2013, **382**(9888):260-
22 538 272.
- 24 539 31. Jaspers L, Colpani V, Chaker L, van der Lee SJ, Muka T, Imo D, Mendis S, Chowdhury R,
25 540 Bramer WM, Falla A *et al*: **The global impact of non-communicable diseases on**
26 541 **households and impoverishment: a systematic review.** *Eur J Epidemiol* 2015, **30**(3):163-
27 542 188.
- 29 543 32. Morton RL, Schlackow I, Gray A, Emberson J, Herrington W, Staplin N, Reith C, Howard K,
30 544 Landray MJ, Cass A *et al*: **Impact of CKD on Household Income.** *Kidney Int Rep* 2018,
31 545 **3**(3):610-618.
- 33 546 33. Mortality GBD, Causes of Death C: **Global, regional, and national life expectancy, all-**
34 547 **cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a**
35 548 **systematic analysis for the Global Burden of Disease Study 2015.** *Lancet* 2016,
36 549 **388**(10053):1459-1544.
- 38 550 34. Jan S, Laba TL, Essue BM, Gheorghe A, Muhunthan J, Engelgau M, Mahal A, Griffiths U,
39 551 McIntyre D, Meng Q *et al*: **Action to address the household economic burden of non-**
40 552 **communicable diseases.** *Lancet* 2018, **391**(10134):2047-2058.

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3 557 **Figure Legends**
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6 558 **Figure 1.** *Estimations based on data from the public (CSS renal programme) and private*
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8 559 *(CETRERSA) sectors.*

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10 560 **Figure 2.** *Deaths recorded as N18 (chronic kidney disease, n=221) and N19 (unspecified*
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12 561 *kidney failures, n=18).*

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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).

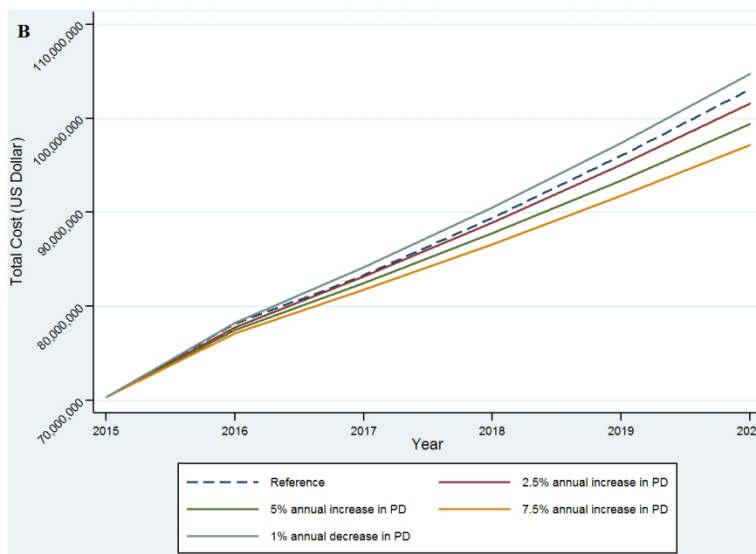
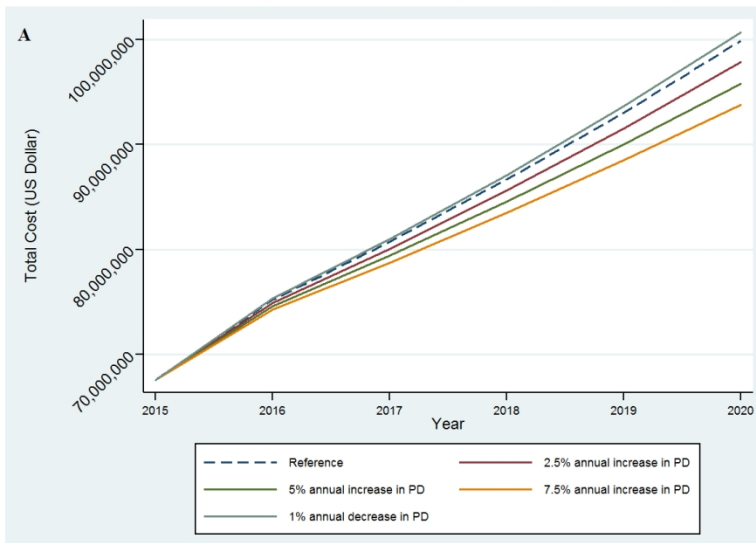
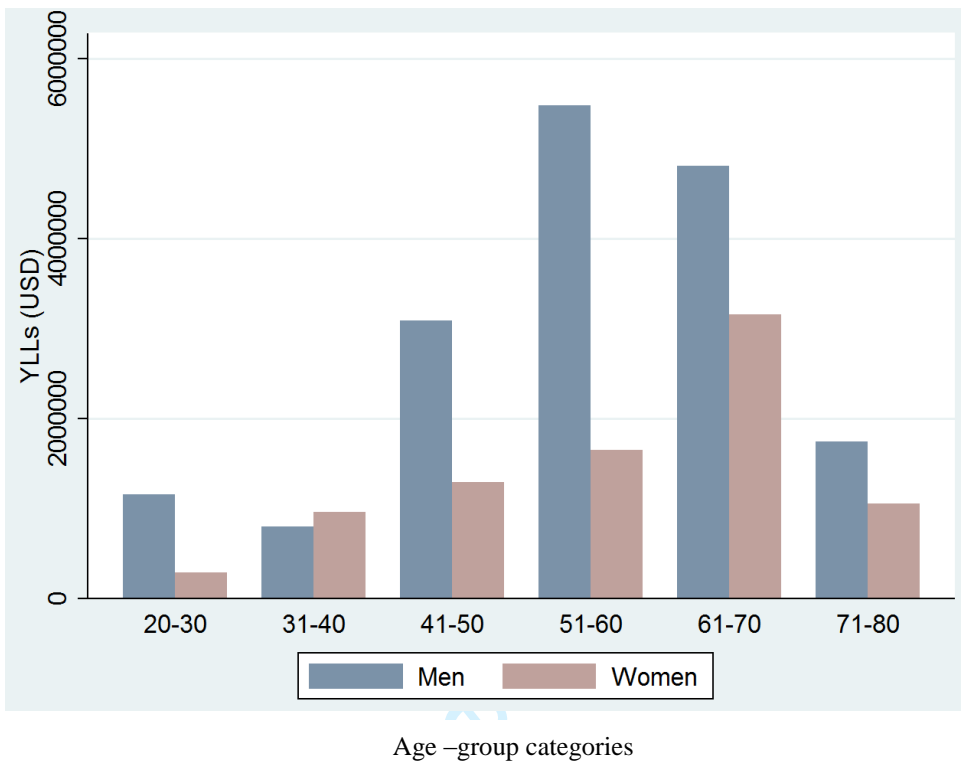


Figure 2. Years of Life Lost-(USD) due to premature mortality, according to age-group categories in Panama. Year 2015



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
Paricalcitol	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	6,7	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (selection of sectors offering Hemo and peritoneal dialysis) (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Financial costs based on secondary data, and therefore many items are not applicable		
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) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —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