

## Overview of hemodialysis treatment funded by the Brazilian Unified Health System - An economic perspective

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### ABSTRACT

**Introduction:** End-stage renal disease (ESRD) is a public health problem and, in Brazil, lacks of data on one of the main treatments, hemodialysis, are still identified. **Objective:** To determine, through description of resources used in ESRD treatment and its complications, the cost associated to hemodialysis and supplementary medical therapy in patients attended by Brazilian Public Health (SUS). **Methods:** Methods of cross-sectional and prospective cohort observational analysis were conducted using public data, where information about inpatient and outpatient resource use and patients' characteristics were collected. From described resource use, costs were calculated. In cross-sectional analysis subjects who underwent hemodialysis between January/2008 and November/2012 were considered and in prospective cohort, started in 2009. Descriptive analyses were performed. **Results:** 91,475 and 118,847 hemodialysis procedures were performed in 2008 and 2012, respectively, and 24.8% of increase was estimated until 2017. Analysis by federation unit showed that São Paulo, Minas Gerais and Rio de Janeiro states represented almost half of the procedures observed, with mean cost per patient of US\$ 7,932.52 in 2008 and US\$ 9,112.75 in 2011. In the cohort, composed by 96,600 subjects, the most used drug was alfaepoetin and 8% of the sample used calcitriol 1.0 mcg. The occurrence of complications was observed in 28.2% of patients. **Conclusion:** After data analysis, different aspects of hemodialysis use were demonstrated, with an increase in amount of procedures and, also, in disease related expenses.

**Keywords:** calcitriol; costs and cost analysis; kidney failure, chronic; morbidity; renal dialysis.

### INTRODUCTION

Chronic kidney disease (CKD) is currently considered a global public health issue with prevalence estimated to range between 8% and 16%. Although approximately 80% of the cases of CKD are diagnosed in developed nations, incidence has increased in countries of varied economic profiles.<sup>1</sup> In Brazil, an estimated 1.75 million individuals had CKD in 2006, and 405 per million population were estimated to be on chronic dialysis in 2009.<sup>2,3</sup> In 2012, an estimated 97,586 individuals were on dialysis in Brazil.<sup>4</sup>

The Brazilian Society of Nephrology (SBN) ran the first Brazilian Dialysis Census in 1999. Renal care centers were asked to provide information on areas such as center characteristics, patient prevalence and incidence, and modes of dialysis offered to patients. In 2002, 561 dialysis centers treating a total of 54.523 patients were registered with the SBN. In 2013, the number of registered centers grew to 658. Despite these significant numbers, only 50.8% of the registered renal centers responded the survey of the 2013 Census, thus affecting the accuracy of the published results.<sup>5,6</sup>

The census reports showed the number of patients on dialysis in Brazil increased in the last decade (84.14%). However, the costs associated with treatment were

not covered in the report. According to the DATASUS, approximately R\$ 2 billion were spent in hemodialysis procedures in clinics from all over the country in 2012.<sup>5-7</sup>

Approximately 90% of the individuals with end-stage renal disease (ESRD) are started on dialysis, with significant impact on their survival. The five-year survival of patients with ESRD on dialysis is around 65%.<sup>8,9</sup>

Despite the relevance of treatment for these patients, hemodialysis implies significant economic and social costs. Brazilian studies have shown that the costs associated with renal disease range from R\$ 19,950 to R\$ 26,810.30.<sup>8,10</sup> In addition to hemodialysis, patients with CKD require other medications such as erythropoietin, calcitriol, iron hydroxide, and sevelamer, which add to the costs incurred in by the health care system.<sup>11,12</sup>

Besides, the loss of renal function secondary to the development of CKD may also introduce a series of complications such as anemia, metabolic bone disease, and metabolic acidosis.<sup>13,14</sup>

In order to minimize the occurrence of complications, the *Kidney Disease Outcomes Quality Initiative* (KDOQI) recommends the prescription of phosphorus chelating agents and vitamin D analogues to help support the mineral metabolism of this group of patients.<sup>11</sup> Studies have described an association between higher levels of 25-hydroxyvitamin D and better survival of patients with CKD both on and off dialysis.<sup>15</sup>

In 2009, Martins *et al.*<sup>16</sup> carried out a study to assess how often these medications were prescribed to dialysis patients treated in the State of Bahia, in the only publication to shed light on this aspect of renal disease in Brazil.

More comprehensive data is still needed on the characteristics and costs of hemodialysis in Brazil. Therefore, this study aimed to calculate the cost of hemodialysis and the adjuvant drug therapies paid by the Brazilian public health care system (SUS) based on a description of the items used in the treatment of CKD and its complications.

## METHOD

### STUDY DESIGN

This study used a combination of the cross-sectional observational method and the prospective cohort method as described by Mussolino *et al.*<sup>17</sup>

The cross-sectional observational analysis was carried out with the purpose of providing an overview of the Brazilian public health care system (SUS) and validating the representativeness of the cohort. The prospective cohort portion of the analysis was used to define the hemodialysis patient subgroups followed for 32 months since the first month of treatment started in 2009 and determine the occurrence of cardiac, vascular, bone and parathyroid gland events as described in the International Statistical Classification of Diseases and Related Health Problems - 10th Revision (ICD-10) and recorded in Hospital Admission Authorization (AIH) forms.

### DATA SOURCES

The study included records of the SUS Outpatient Information System (SIA/SUS) and of the SUS Hospital Information System (SIH/SUS) from January 2008 to November 2012.

The SIH/SUS contained information related to the hospital procedures described in the Hospital Admission Authorization (AIH) forms, namely: demographic data (age and gender); municipality of residence; disease code (N18) as per the ICD-10; place of treatment (institution, municipality, and state); procedures performed; length of hospitalization; admission to an intensive care unit (ICU); and death during hospitalization.

The SIA/SUS database had the following information on outpatient procedures: patient profile (age and gender), municipality of residence, disease code as per the ICD-10 (N18), procedures performed, and place of treatment (institution, municipality, state). The information present in the documents used to record Outpatient Procedure Authorizations (APAC) and in the documents used to report medium and high complexity outpatient procedures, including

chronic patient treatment schedules (for patients on dialysis, for example) and oncologic care, were collected.

The occurrence of complications was established based on the codes entered in the SIH/SUS and SIA/SUS databases for the endpoints of interest (cardiac, bone, and vascular events, and parathyroid gland removal). Table 1 describes the procedures performed for each type of complication.

The information collected range from January of 2008, when the Chart of Procedures, Medications, Prosthetics, Orthotics, and Special Materials for the Brazilian Public Health Care System (SUS) was originally published, to November of 2012. Reimbursement fees were estimated from the price list updated on December 17, 2012 by the São Paulo State Secretary of Health considering yearly weighted averages. The resulting values were converted into American Dollars (USD) considering the mean exchange rate from 2008 to 2011.

#### IDENTIFICATION OF INDIVIDUALS IN THE DATABASES

A deterministic approach was used to identify the patients in the SIA/SUS database, with equal records for a unique key being considered a match. However, as there was no such unique key in the SIH/SUS, patients were identified via probabilistic relationships.

The data points related to one same patient in the databases were identified through record linkage. Once the patient identification procedures of the outpatient and hospital settings were different, patients were identified based on probabilistic relationships.

#### STUDY POPULATION

The cross-sectional observational portion of the study included individuals on hemodialysis entered into the SIA/SUS database from January 2008 to November 2012 assigned an N18 ICD-10 code for chronic kidney disease in their AIH forms. A second analysis was then carried out to include the following subgroups: “Hemodialysis I (no more than three sessions a week)”

(SIGTAP: 03.05.01.006-9) and “Hemodialysis II (no more than three sessions a week)” (SIGTAP: 03.05.01.010-7). The subgroups were defined based on the availability of the data in the database; the difference lies basically on the degree of specialization of the center at which the procedures were performed.

The prospective cohort portion of the study included the 96,303 individuals on hemodialysis (I and II, no more than three sessions a week) in 2009. Patients on 1.0 mcg calcitriol (n = 7,728) were analyzed separately due to the described association between prescription of vitamin D analogues and reduced mortality of patients on dialysis.

#### DATA ANALYSIS

The study population was described through measures of central tendency (mean values and standard deviation) for continuous variables and measures of frequency for categorical variables. The data sets were analyzed on Microsoft Excel.

The Forecast function on Microsoft Excel was used to estimate a linear trend line for the data.

## RESULTS

#### PRESCRIPTION OF HEMODIALYSIS IN BRAZIL, 2008-2017

A total of 91,475 and 118,847 individuals were on hemodialysis in 2008 and 2012, respectively. The estimated linear trend indicated that the number of patients on hemodialysis would grow by 24.8% from 2012 to 2017, reaching a total of 148,315 patients in the latter year.

When the patients on three hemodialysis sessions per week were analyzed separately from the individuals who underwent one additional weekly hemodialysis session, the total number of patients in 2008 added up to 91,431 and 38,911 respectively, while in 2012 the numbers came to 118,793 and 46,858 respectively. The number of patients on one additional hemodialysis session associated to three weekly sessions was estimated to grow by 20.4% by 2017, while the ranks of individuals on three hemodialysis sessions per week was estimated to grow by 24.8% by the same time.

**TABLE 1** PROCEDURES CONSIDERED FOR THE REPORTING OF COMPLICATIONS AND THEIR RESPECTIVE CODES IN THE SUS CHART OF PROCEDURES, DRUGS, ORTHOTICS, AND PROSTHETICS (SIGTAP)

Complications	SIGTAP Code
<b>Cardiac complications</b>	
Diagnosis and/or emergency consultation with general practitioner	03.01.06.008-8
Coronary angioplasty	04.06.03.001-4
Coronary angioplasty, two stents implanted	04.06.03.002-2
Coronary angioplasty with stenting	04.06.03.003-0
Primary coronary angioplasty (includes catheterization)	04.06.03.004-9
Therapeutic electrophysiological study I (atrial flutter ablation)	04.06.05.002-3
Therapeutic electrophysiological study II (atrial fibrillation ablation)	04.06.05.007-4
Transvenous placement of multi-site pacing devices	04.06.01.063-3
Implantation of prosthetic heart valves	04.06.01.069-2
Valvuloplasty	04.06.01.080-3
Valvuloplasty with myocardial revascularization	04.06.01.081-1
Valvuloplasty and/or multiple valve change	04.06.01.082-0
Treatment with multiple surgical procedures	04.15.01.001-2
Treatment of arrhythmia	03.03.06.002-6
Treatment of acute pulmonary edema	03.03.06.013-1
Treatment of acute myocardial infarction	03.03.06.019-0
Treatment of heart failure	03.03.06.021-2
Treatment of acute coronary syndrome	03.03.06.028-0
Valve change with myocardial revascularization	04.06.01.120-6
Percutaneous aortic valve replacement	04.06.03.011-1
Percutaneous mitral valve repair	04.06.03.012-0
Percutaneous pulmonary valve replacement	04.06.03.013-8
Parathyroid complications	
Parathyroid gland removal	04.02.01.002-7
Vascular complications	
Amputation/disarticulation of finger	04.08.06.004-2
Amputation/disarticulation of lower limbs	04.08.05.001-2
Amputation/disarticulation of feet and tarsum	04.08.05.002-0
Intraluminal angioplasty of vessels in the extremities (uncoated stent)	04.06.04.006-0
Intraluminal angioplasty of vessels in the extremities (without stenting)	04.06.04.005-2
Intraluminal angioplasty of visceral vessels with coated stent	04.06.04.011-7
Intraluminal angioplasty of supra-aortic vessels in the neck/trunk (coated stent)	04.06.04.013-3
Diagnosis and/or emergency consultation with surgeon	03.01.06.007-0
Arterial embolectomy	04.06.02.012-4
Detachable balloon embolization of carotid-cavernous fistula	04.03.07.009-0
Embolization of arteriovenous vascular malformation (includes angiogram)	04.06.04.020-6
Other procedures with sequential surgical procedures	04.15.02.003-4
Myocardial revascularization with extracorporeal circulation	04.06.01.092-7
Myocardial revascularization with extracorporeal circulation (two or more grafts)	04.06.01.093-5
Myocardial revascularization without extracorporeal circulation (two or more grafts)	04.06.01.095-1
CABG/thromboendarterectomy of other distal arteries	04.06.02.043-4
CABG/proximal femoropopliteal thromboendarterectomy	04.06.02.045-0
Treatment with multiple surgical procedures	04.15.01.001-2

**CONTINUED TABLE 1**

Treatment of stroke (ischemic or acute hemorrhagic)	03.03.04.014-9
Treatment of arterial insufficiency with critical ischemia	03.03.06.020-4
Endovascular treatment of arteriovenous fistula	04.06.04.032-0
Bone complications	
Diagnosis and/or emergency consultation with surgeon	03.01.06.007-0
Two-level anterior neck fusion	04.08.03.007-0
Three-level anterior neck fusion	04.08.03.006-2
One-level anterior neck fusion	04.08.03.011-9
Posterior two-level thoracolumbar and sacral fusions, including instrumentation	04.08.03.029-1
Posterior six-level thoracolumbar and sacral fusions, including instrumentation	04.08.03.031-3
Partial hip replacement	04.08.04.005-0
Primary cemented total hip replacement	04.08.04.008-4
Primary non-cemented/hybrid total hip replacement	04.08.04.009-2
Diagnosis and/or emergency consultation with general practitioner	03.01.06.008-8
Closed reduction of shaft fracture/physeal injury in the proximal femur	04.08.05.023-3
Closed reduction of knee fracture or physeal injury	04.08.05.025-0
Closed reduction of dislocated/fractured-dislocated knee	04.08.05.026-8
Closed reduction of disjointed/dislocated/fractured/fractured-dislocated pelvic ring	04.08.04.020-3
Removal of foreign body from the cervical spine via anterior approach	04.08.03.057-7
Removal of plate and/or pins	04.08.06.037-9
Treatment with multiple surgical procedures	04.15.01.001-2
Surgery for avulsion of tuberosities/spines and iliac crest without injury to the pelvic ring	04.08.04.024-6
Surgery for combined fractured/dislocated/fractured-dislocated/disjointed pelvic ring	04.08.04.025-4
Surgery for proximal (neck) femur (synthesis) physeal fracture/injury	04.08.05.048-9
Surgery for fractured/dislocated/fractured-dislocated/disjointed anteroposterior pelvic ring	04.08.04.026-2
Surgery for coxofemoral fracture/dislocation with fractured femoral shaft	04.08.04.028-9
Surgery for femur shaft fractures	04.08.05.051-9
Surgery for acetabular fractures	04.08.04.029-7
Surgery for intercondylar distal femur fractures	04.08.05.058-6
Surgery for physeal injury/fracture at the level of the knee	04.08.05.059-4
Surgery for subtrochanteric fractures	04.08.05.061-6
Surgery for femur supracondylar fractures (distal metaphysis)	04.08.05.062-4
Surgery for transtrochanteric fractures	04.08.05.063-2
Surgery for dislocation/fracture-dislocation at the level of the knee	04.08.05.068-3
Multiple trauma patient surgery	04.15.03.001-3
Conservative treatment for fracture/ligament injury/bone avulsion at the level of the pelvis	03.03.09.013-8
Conservative treatment of fractured pelvic rings	03.03.09.019-7
Conservative treatment of fractured lower limbs with immobilization	03.03.09.020-0
Conservative treatment of thoracolumbar and sacral spine with orthotics	03.03.09.023-5
Conservative treatment of spinal cord injury	03.03.04.011-4
Treatment of fractured spine with spinal cord injury	03.03.04.023-8

**PRESCRIPTION AND COST OF HEMODIALYSIS PER STATE IN BRAZIL, 2008-2011**

Table 2 shows the analysis of hemodialysis prescriptions per Brazilian State based only on the

records referring to Hemodialysis I and II procedures - three sessions a week. In 2008 and 2011, a total of 9,868,978 and 11,382,988 hemodialysis sessions were carried out in Brazil, respectively.

**TABLE 2** NUMBER OF HEMODIALYSIS SESSIONS AND REIMBURSEMENTS PAID PER STATE, 2008-2011

	2008	2009	2010	2011
São Paulo				
Number of sessions	2,395,134	2,468,270	2,534,919	2,645,313
Reimbursement paid (USD)	175,896,850.06	195,851,803.38	204,989,954.80	225,667,374.36
Minas Gerais				
Number of sessions	1,300,663	1,365,671	1,430,601	1,490,897
Reimbursement paid (USD)	95,351,782.33	108,359,564.38	115,718,184.58	127,186,012.18
Rio de Janeiro				
Number of sessions	1,126,630	1,157,190	1,187,748	1,204,781
Reimbursement paid (USD)	82,558,528.29	91,757,527.29	96,026,758.76	102,777,861.65
Rio Grande do Sul				
Number of sessions	733,779	757,295	762,411	761,428
Reimbursement paid (USD)	58,890,091.43	60,085,587.97	61,652,630.87	64,948,375.49
Bahia				
Number of sessions	576,071	621,916	670,203	712,044
Reimbursement paid (USD)	42,304,307.11	49,347,668.81	54,228,055.18	60,743,322.21
Paraná				
Number of sessions	538,469	554,140	576,015	594,772
Reimbursement paid (USD)	39,492,461.35	43,917,034.02	46,558,350.52	50,690,799.77
Pernambuco				
Number of sessions	482,471	523,236	557,491	577,016
Reimbursement paid (USD)	35,435,135.22	41,517,627.33	45,099,815.49	49,224,301.88
Ceará				
Number of sessions	387,915	409,182	434,503	460,860
Reimbursement paid (USD)	28,492,383.47	32,467,693.03	35,148,228.82	39,315,221.35
Goiás				
Number of sessions	322,193	360,897	391,898	412,992
Reimbursement paid (USD)	23,674,492.93	28,636,384.03	31,693,829.31	35,231,679.68
Santa Catarina				
Number of sessions	269,821	280,305	285,728	296,499
Reimbursement paid (USD)	19,820,552.44	22,240,999.48	23,106,165.18	25,293,593.75
Espírito Santo				
Number of sessions	204,634	217,342	225,946	250,282
Reimbursement paid (USD)	15,031,338.72	17,245,610.26	18,268,828.73	21,351,152.70
Maranhão				
Number of sessions	174,322	190,446	210,458	226,070
Reimbursement paid (USD)	12,800,659.35	15,111,471.91	17,021,769.87	19,285,666.13
Rio Grande do Norte				
Number of sessions	162,025	178,636	197,010	203,276
Reimbursement paid (USD)	11,898,214.99	14,174,238.79	54,462,553.61	17,341,146.85
Pará				
Number of sessions	112,703	135,356	181,573	201,117
Reimbursement paid (USD)	8,278,760.83	10,740,201.58	14,698,050.43	17,156,966.05
Piauí				
Number of sessions	145,387	160,560	173,566	192,356
Reimbursement paid (USD)	10,684,191.39	12,740,083.24	14,043,984.45	16,409,579.31

**CONTINUED TABLE 2**

Alagoas				
Number of sessions	142,656	159,322	169,909	180,315
Reimbursement paid (USD)	10,486,201.09	12,641,850.92	13,747,443.71	15,382,381.07
Mato Grosso				
Number of sessions	104,734	127,171	150,421	156,940
Reimbursement paid (USD)	8,427,480.31	10,090,739.50	12,169,874.31	13,388,297.67
Distrito Federal				
Number of sessions	134,201	139,419	145,523	156,583
Reimbursement paid (USD)	9,856,494.79	11,062,591.31	11,772,430.81	13,340,780.85
Mato Grosso do Sul				
Number of sessions	121,190	132,213	142,476	147,563
Reimbursement paid (USD)	8,906,533.66	10,490,811.05	11,523,464.07	12,588,360.91
Paraíba				
Number of sessions	125,227	134,406	139,962	143,037
Reimbursement paid (USD)	9,196,100.03	10,664,820.89	11,316,223.04	12,202,255.17
Sergipe				
Number of sessions	65,167	74,659	76,753	89,198
Reimbursement paid (USD)	4,791,770.22	5,924,027.66	6,205,203.54	7,609,337.14
Amazonas				
Number of sessions	75,450	78,413	80,121	81,325
Reimbursement paid (USD)	5,537,394.10	6,221,899.21	6,476,672.97	6,937,704.24
Rondônia				
Number of sessions	63,923	63,939	63,807	74,770
Reimbursement paid (USD)	4,692,376.04	5,073,419.42	5,158,916.58	6,378,507.79
Tocantins				
Number of sessions	45,705	51,296	54,056	56,754
Reimbursement paid (USD)	3,357,331.22	4,070,224.76	4,371,965.46	4,841,591.96
Acre				
Number of sessions	19,043	23,524	25,396	29,326
Reimbursement paid (USD)	1,081,306.32	1,787,372.98	2,053,371.68	2,501,753.64
Amapá				
Number of sessions	16,044	19,525	21,736	22,903
Reimbursement paid (USD)	911,015.93	1,108,675.45	1,234,221.32	1,300,486.67
Roraima				
Number of sessions	13,421	14,515	15,084	14,771
Reimbursement paid (USD)	987,934.92	1,159,668.40	1,217,976.95	1,260,090.12
Total				
Number of sessions	9,868,978	10,398,944	10,905,314	11,382,988
Reimbursement paid (USD)	723,841,688.56	824,489,642.60	881,438,722.58	970,354,599.98

The number of sessions grew by 15.3% within the studied time period. Similar increases were observed in each Brazilian State. Although the states of São Paulo, Minas Gerais, and Rio de Janeiro accounted for almost half of the procedures prescribed

at a national level, their numbers decreased slightly in the studied time period, from 48.8% to 46.9%, showing the growing importance of other states.

The fees paid to dialysis centers for hemodialysis sessions were raised by 34.1%

from 2008 to 2011, an increase equivalent to roughly twice the growth of the number of procedures. In 2011, the mean cost of a patient on dialysis was USD 9,112.75 ( $\pm$  650.05) *versus* USD 7,932.52 ( $\pm$  514.55) in 2008.

#### PROSPECTIVE COHORT ANALYSIS: COSTS, COMPLICATIONS, AND PRESCRIBED MEDICATIONS

##### STUDY POPULATION PROFILE

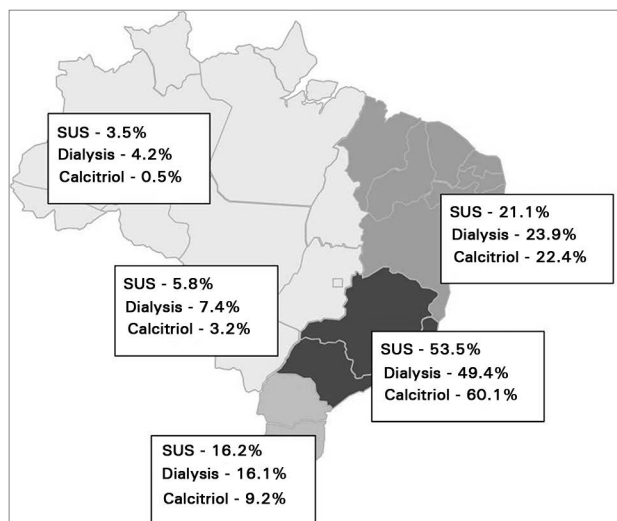
The prospective cohort analysis included 96,600 patients, most of which (57.6%) were males. The majority of the patients on dialysis were aged between 40 and 69 years (62.9%). A significant portion of them (24.2%) resided in the state of São Paulo.

The patients in the cohort were followed up for 32 months since they were first observed in 2009. Twelve months into follow-up, 71.3% of the patients were still on dialysis. After 24 and 32 months, 55.1% and 42.7% remained on dialysis, respectively.

##### PRESCRIPTION OF CALCITRIOL

Eight percent of the patients were on 1.0 mcg calcitriol. Figure 1 shows the calcitriol prescription distribution between different regions in Brazil; more prescriptions were observed among patients seen in the Southeast and Northeast regions of the country.

**Figure 1.** Calcitriol prescriptions per region in Brazil.



The occurrence of prescriptions of 1.0 mcg calcitriol decreased from 8.0% to 6.1% after 32 months of follow-up. Calcitriol was introduced a mean of 8.1 ( $\pm$  9.7) months after the start of dialysis.

##### PRESCRIPTION OF OTHER MEDICATIONS

Table 3 shows the prescription of medications other than calcitriol. Epoetin alfa was the most commonly prescribed medication (65.1%), but sevelamer, although less frequently used (26.0%), had a higher cost impact when compared to other drugs. Ferric saccharate was frequently prescribed (50.6%) and had the lowest cost impact per patient per year - USD 56.14. The total cost incurred in with medications other than calcitriol was USD 35,964,856.25 - a mean of USD 598.81 per patient per year.

##### INCIDENCE OF COMPLICATIONS

Over a quarter (28.2%) of the patients suffered with complications. Cardiac events were recorded in 17.1% of the patients, vascular events in 4.3%, bone-related events in 6.8%, and parathyroid gland complications in 0.2%. Patients on 1.0 mcg calcitriol had fewer complications in general, with the exception of parathyroid-related events (Table 4).

Table 4 shows the incidence and costs related to the complications observed in the study group. Patients on 1.0 mcg calcitriol had fewer complications but higher overall treatment costs when compared to individuals on dialysis in all complication categories. The largest share of the costs incurred in the treatment of patients not given calcitriol was associated with parathyroid gland removal procedures (mean cost per patient per year: USD 2,016.03); for patients on calcitriol, the largest share of the expenditure was devoted to heart complications (mean cost per patient per year: US\$ 2,100.24). Bone complications accounted for the smallest share of the costs observed in both groups (mean cost per patient per year: USD 695.68 and USD 791.44).



**TABLE 3** FREQUENCY OF USE AND COST OF OTHER DRUGS PRESCRIBED TO THE STUDIED POPULATION

	N (%)	Total cost (USD)	Mean/Patient/Year (USD)
Epoetin alfa	59,475 (61.8)	15,148,812.77	254.82
Ferric saccharate	48,711 (50.6)	2,725,644.11	56.14
Sevelamer	25,008 (26.0)	17,841,220.19	713.29
Alfacalcidol	1,621 (1.7)	125,113.82	77.05
Desferroxamine	396 (0.4)	124,035.09	313.16
Total	60,082 (62.4)	35,964,856.25	598.81

**TABLE 4** FREQUENCY OF OCCURRENCE AND COST OF COMPLICATIONS OBSERVED IN INCLUDED PATIENTS (N = 96,303) AND PATIENTS ON CALCITRIOL (N = 7,056)

	Patients with complications N (%)	Mean Cost/Patient/ Year (US\$)	Patients on calcitriol presenting complications N (%)	Mean Cost/Patient on calcitriol (USD)
Cardiac	16,490 (17.1)	1,894.40	347 (5.9)	2,100.24
Vascular	4,189 (4.3)	1,061.68	78 (1.1)	985.17
Bone	6,570 (6.8)	695.68	10 (0.1)	791.44
Parathyroid gland removal	174 (0.2)	2,016.03	165 (2.3)	1,983.01
Total	27,118 (28.2)	1,812.94	593 (8.4)	1,923.57

## DISCUSSION

This study aimed to provide a comprehensive understanding of the costs and characteristics of the hemodialysis procedures and the drug therapies offered to patients with chronic kidney disease treated through the Brazilian Public Health Care system (SUS). The used hemodialysis procedures were described, along with the characteristics of the patients prescribed hemodialysis in terms of their geographic distribution, genders, ages, prescribed drugs, and incidence of complications. Secondary data analysis allowed the assessment of large patient cohorts from every Brazilian state, which helped achieve the goals set for the study. However, a limitation of the study was the impossibility of defining treatment start dates. Additionally, patients prescribed hemodialysis for acute kidney injury may have been included in the study population. The method used in the study also posed other constraints as a consequence of the secondary nature of the analyzed databases, which limited the scope of the conclusions presented herein. The limitations included the way patients and costs were identified, resource

utilization was assessed, and hospitalizations due to complications were defined; moreover, although infection is a common adverse event among hemodialysis patients, cases of infection were not considered in the study.

The number of hemodialysis procedures offered through the SUS grew by 29.9% between 2008 and 2012. Estimates indicate this number will grow by 24.8% between 2012 and 2017. The 2012 Dialysis Census, however, reported an increase of 12.1% in the number of patients on hemodialysis from 2008 to 2012.<sup>4</sup> The census survey, organized by the Brazilian Society of Nephrology (SBN), included dialysis centers from the entire country reimbursed by the SUS and other parties. The disagreement between the census and this study may stem from the low response rate seen in the census. In 2008, only 47.8% of the 684 dialysis centers registered with the SBN responded the survey. In 2012, 651 (39.1%) centers registered with the SBN responded the survey.<sup>4,18</sup> Nonetheless, the trend of an increase in the prevalence and incidence of hemodialysis in the SUS was previously reported to have reached 3.6% and 1.8% a year, respectively, from 2000 to 2012.<sup>19</sup>

In addition to presenting the totals concerning patients on dialysis in Brazil, the Dialysis Census also offered the breakdown for each Brazilian State. Most of the individuals included in this study were on hemodialysis in southeastern states, as also described in the census for the same time period (2008-2011) and by other authors.<sup>18,20-23</sup> However, the dialysis census surveys suggest that this finding may have been biased by the availability of dialysis centers in the southeast region, which accounted for 49.2% to 52.1% of the responding centers in the 2009-2011 time period.<sup>20-22</sup> The higher prevalence of kidney disease reported in this region of the country - 453 patients per million population in the state of São Paulo *versus* a national prevalence of 354 patients per million population - may have been biased by easier access to treatment in the country's southeast region.<sup>23</sup> Underreporting and incomplete patient records may have also led to underestimated incidence and prevalence rates in other regions of the country.

Moura *et al.*<sup>19</sup> looked into the number of patients on hemodialysis in each Brazilian state and also found greater numbers of patients in the southeastern states and percent rates similar to the ones reported in this study.

The reimbursements paid by the SUS in 2008 and 2011 for hemodialysis procedures added to USD 723,841,688.56 and USD 970,354,599.98, respectively, or an estimated mean annual cost per patient of USD 7,932.52 in 2008 and USD 9,112.75 in 2011. Three studies have been carried out in Brazil on the costs of CKD, with reported mean annual costs per patient ranging widely between USD 7,980 and USD 28,570.<sup>8,10,24</sup> The values reported in this study were closer to the figures described by Sesso *et al.*,<sup>8</sup> in a study using primary data and cost descriptions from the standpoint of the Ministry of Health, which corroborated our findings. The greatest discrepancy was observed in relation to the study published by Abreu *et al.*,<sup>24</sup> in which the mean cost of hemodialysis per patient per year of USD 28,570 included indirect costs not considered in this study.

In addition to the pattern of hemodialysis prescription in Brazil, this study also described the use of costly medication to treat patients with CKD in general terms and of calcitriol in particular.

Vitamin D analogues are recommended by the KDOQI, and 8.0% of the studied patients were on calcitriol on any dosage.<sup>11</sup> Martins *et al.*<sup>16</sup> assessed the cost of these drugs for 747 patients on hemodialysis in Salvador, Brazil, and found that 31.9% of them were on calcitriol on any dosage. Despite the disagreement, these are the only studies in which the use of calcitriol by individuals on hemodialysis in Brazil has been described.

The study also revealed that 62.4% of the patients were on other medications, such as epoetin alfa, ferric saccharate, sevelamer, alfacalcidol, or desferroxamine. Epoetin alfa was the most commonly prescribed drug with 61.8% of the patients, as described in the 2008-2011 dialysis census surveys.<sup>5,18,20-22</sup>

Complications were observed in 28.2% of the patients and 8.4% of the individuals on calcitriol on any dosage. The incidence of complications among patients on regular hemodialysis has not been clearly defined, as only aspects concerning each type of complication have been described.<sup>8,25-30</sup> Cardiac adverse events were the most common complication described in this study. Other authors have ranked it as the number one cause of death of individuals with CKD and a factor associated with higher hospitalization costs when compared to individuals not manifesting this type of complication.<sup>8,25</sup>

## CONCLUSION

The analysis of the data collected from the DATASUS database allowed the description of different aspects of the treatment of chronic kidney disease and hemodialysis, and the presentation of a comprehensive overview of renal disease in Brazil.

The number of individuals in need of dialysis grew from 91,475 in 2008 to 118,847 in 2012. By 2017, the number of patients on dialysis has been estimated to grow to 148,315.

Similarly, the costs associated with treating chronic kidney disease have increased. The reimbursements paid by the SUS for hemodialysis procedures grew by 34.1% from 2008 to 2011, elevating the mean cost per patient per year from USD 7,932.52 in 2008 to USD 9,112.75 in 2011.

Cohort analysis of the patients on dialysis included in the DATASUS database shed light on the use of vitamin D analogues and the incidence of various types of complications. Complications were reported for 28.2% of the patients, with cardiac adverse events topping the list. Eight percent of the patients were started on 1 mcg calcitriol a mean of 8.1 months after the start of dialysis. More than 50% of the patients were on other medications such as epoetin alfa and ferric saccharate. The mean cost per patient per year with complications was USD 1,923.57 and USD 1,812.94 for patients on and off 1 mcg calcitriol, respectively.

Despite the insights brought by this study into the reality of chronic kidney disease in Brazil, the limitations posed by the chosen method call for the organization of further studies on the subject.

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