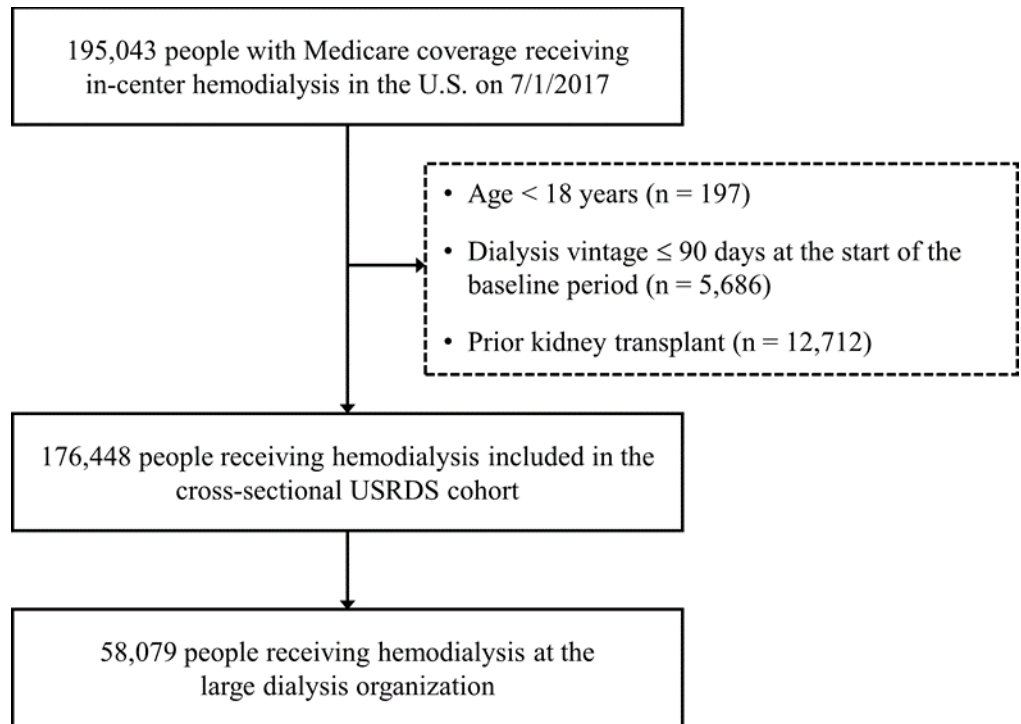
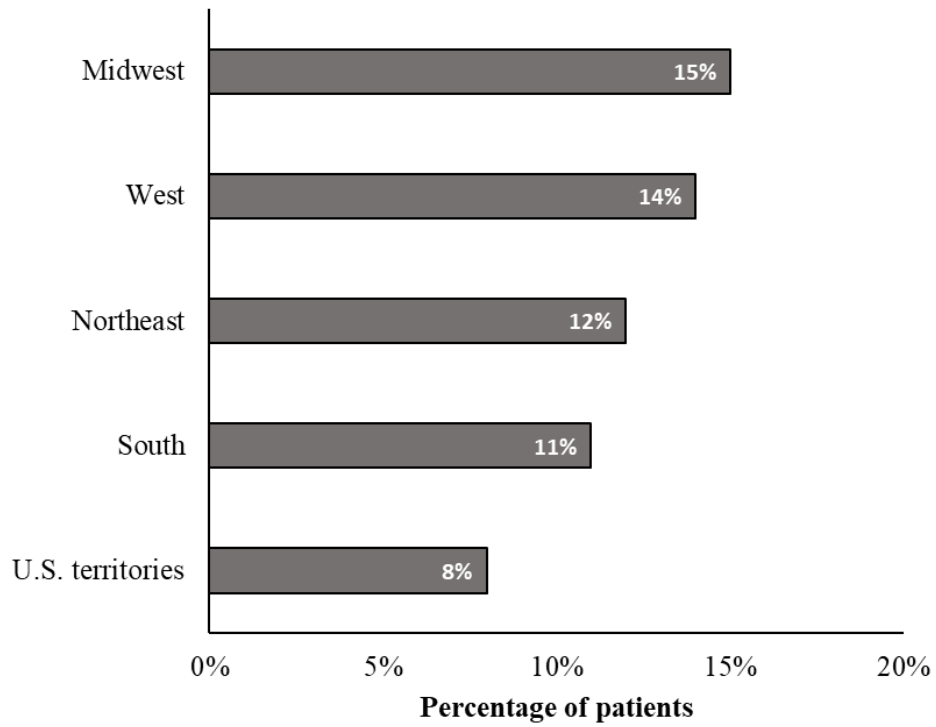


Figure S1. Flow diagram of study cohort creation



Abbreviations: U.S., United States; USRDS, United States Renal Data System

Figure S2. Percentage of patients in the USRDS cross-sectional cohort using a diuretic by region of the U.S.



Abbreviations: USRDS, United States Renal Data System; U.S., United States.

Item S1. Detailed methods

Institutional Review Board approval

This study was approved by the University of North Carolina Institutional Review Board (#18-0297), and a waiver of consent was granted because of the study's large size, data anonymity, and retrospective nature.

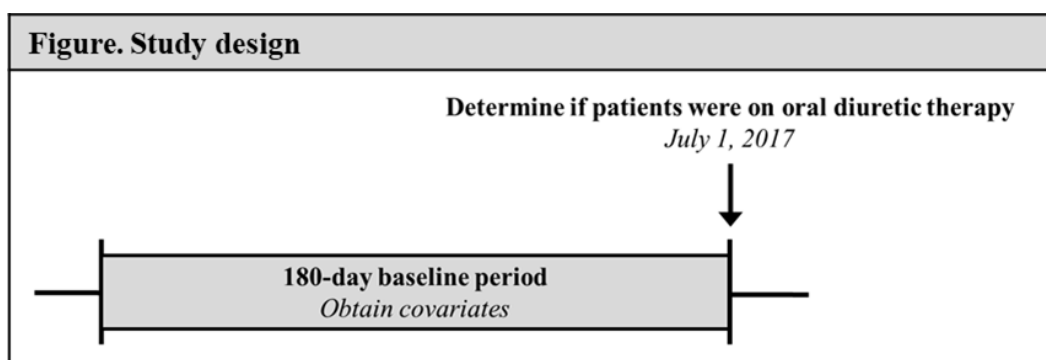
Data sources

We used data from the United States Renal Data System (USRDS) alone, and linked at the patient-level with data from the electronic health record of a large United States dialysis provider. The USRDS database includes: the End Stage Renal Disease (ESRD) Medical Evidence Report, a registration form nephrologists complete for all patients at the outset of maintenance dialysis to establish Medicare eligibility for individuals <65 years of age and to reclassify previously eligible Medicare beneficiaries as having ESRD; the ESRD Death Notification form, a reporting form submitted by dialysis providers to notify the Centers for Medicare & Medicaid Services of patient deaths; and Medicare standard analytic files, including enrollment information and final action hospital (Part A), physician/supplier (Part B), and prescription drug (Part D) insurance claims. The dialysis organization operates more than 2,500 outpatient dialysis clinics throughout the United States, and its electronic health record captures detailed demographic, clinical, laboratory, and dialysis treatment data.

Study overview and design

Using 2017 data from the USRDS, we conducted a cross-sectional study (**Figure**) to describe the oral diuretic utilization and dosing patterns among adults with hemodialysis-dependent kidney failure in the United States. To construct the cross-sectional cohort, we identified people in the USRDS database receiving in-center hemodialysis on 7/1/2017 and during the 180-days prior (i.e., the baseline period). Patients were required to have Medicare coverage during this period and on 7/1/2017. Patients were excluded from the study if they: 1) were < 18 years old on 7/1/2017, 2) had been receiving dialysis \leq 90 days at the start of the baseline period, and 3) had received a prior kidney transplant.

To evaluate the frequency of urine volume monitoring by 24-hour urine collections among patients on diuretic therapy, we identified the subset of patients in the cross-sectional USRDS cohort who were receiving hemodialysis at the large dialysis organization.



Study exposure and covariates

We used Medicare Part D prescription drug claims to determine if patients were using an oral diuretic on 7/1/2017. Diuretic classes of interest included: 1) loop diuretics (furosemide, bumetanide, torsemide, and ethacrynic acid), 2) thiazide and thiazide-like diuretics (hydrochlorothiazide, chlorothiazide, bendroflumethiazide, methyclothiazide, trichlormethiazide, chlorthalidone, indapamide, and metolazone), 3) potassium sparing diuretics (amiloride, triamterene, spironolactone, and eplerenone), and 4) carbonic anhydrase

inhibitors (acetazolamide). Among patients taking a loop diuretic, we determined their daily furosemide-equivalent dose based on the dispensed pill strength, quantity, and days supply.

Covariates (patient demographics and comorbid conditions) were ascertained during the 180-day baseline period. Comorbid conditions were considered present if an applicable discharge diagnosis code, located in any billing position, was associated with ≥ 1 institutional or physician supplier claim during the baseline period.

Statistical analysis

All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC). Baseline characteristics of the study cohort overall and stratified by diuretic use status are displayed as count (%) for categorical variables and as mean \pm standard deviation or median [interquartile range] for continuous variables. We compared baseline covariate distributions between patients taking and not taking diuretics using absolute standardized differences and considered a standardized difference > 0.10 to indicate an imbalance between groups.

In primary analyses, we calculated the proportion of patients in the full USRDS cross-sectional cohort taking a diuretic, overall and by diuretic type, on 7/1/2017. Then among patients on a loop diuretic, we determined the proportion of patients taking varying furosemide-equivalent doses. In a secondary analysis, we evaluated the frequency of urine volume monitoring during the 180-day period prior to 7/1/2017 among the subset of diuretic users and non-users who were in both the USRDS and large dialysis organization databases.

Table S1. Combinations of diuretics used by patients in the USRDS cross-sectional cohort^a

Diuretics used	n (%)
<i>Use of one diuretic</i>	
Loop diuretic	19,027 (85%)
Thiazide/thiazide-like diuretic	1,106 (5%)
Aldosterone antagonist	923 (4%)
Other potassium sparing diuretic	37 (0%)
Carbonic anhydrase inhibitor	113 (1%)
<i>Use of two diuretics</i>	
Loop diuretic + thiazide/thiazide-like diuretic	665 (3%)
Loop diuretic + aldosterone antagonist	342 (2%)
Loop diuretic + other potassium sparing diuretic	< 11 (0%) ^b
Loop diuretic + carbonic anhydrase inhibitor	32 (0%)
Thiazide/thiazide-like diuretic + aldosterone antagonist	17 (0%)
Thiazide/thiazide-like diuretic + other potassium sparing diuretic	< 11 (0%) ^b
Thiazide/thiazide-like diuretic + carbonic anhydrase inhibitor	< 11 (0%) ^b
<i>Use of three diuretics</i>	
Loop diuretic + aldosterone antagonist + thiazide/thiazide-like diuretic	26 (0%)

^a Among the 22,296 diuretic users in the USRDS cross-sectional cohort.

^b Per USRDS contractual requirements, researchers are required to report counts of 10 or fewer individuals as < 11.

Abbreviations: USRDS, United States Renal Data System.

Table S2. Characteristics of the USRDS cross-sectional cohort and the subset of patients treated at the large dialysis organization^a

Characteristic	USRDS cross-sectional cohort				Subset of patients treated at the large dialysis organization			
	Overall N = 176,448	Diuretic user n = 22,296	Diuretic non-user n = 154,152	Std diff ^b	Overall N = 58,079	Diuretic user n = 6,659	Diuretic non-user n = 51,420	Std diff ^b
Age (years)	64 ± 14	66 ± 13	63 ± 14	0.17	64 ± 14	67 ± 13	63 ± 14	0.25
Female	80,412 (46%)	10,527 (47%)	69,885 (45%)	0.04	26,624 (46%)	3,143 (47%)	23,481 (46%)	0.03
Race								
White	94,129 (53%)	14,464 (65%)	79,665 (52%)	0.27	30,855 (53%)	4,325 (65%)	26,530 (52%)	0.27
Black	70,535 (40%)	6,316 (28%)	64,219 (42%)	0.28	23,354 (40%)	1,874 (28%)	21,480 (42%)	0.29
Other	11,784 (7%)	1,516 (7%)	10,268 (7%)	0.01	3,870 (7%)	460 (7%)	3,410 (7%)	0.01
Hispanic	29,132 (17%)	3,611 (16%)	25,521 (17%)	0.01	10,659 (18%)	1,129 (17%)	9,530 (19%)	0.04
Cause of ESKD								
Diabetes	85,305 (48%)	12,879 (58%)	72,426 (47%)	0.22	28,116 (48%)	3,813 (57%)	24,303 (47%)	0.20
Hypertension	54,492 (31%)	6,011 (27%)	48,481 (31%)	0.10	18,293 (31%)	1,826 (27%)	16,467 (32%)	0.10
Glomerular disease	14,819 (8%)	1,318 (6%)	13,501 (9%)	0.11	4,685 (8%)	385 (6%)	4,300 (8%)	0.10
Cystic	3,884 (2%)	378 (2%)	3,506 (2%)	0.04	1,232 (2%)	106 (2%)	1,126 (2%)	0.04
Other	17,948 (10%)	1,710 (8%)	16,238 (11%)	0.10	5,753 (10%)	529 (8%)	5,224 (10%)	0.08
Dialysis vintage								
< 1.0 year	6,683 (4%)	1,530 (7%)	5,153 (3%)	0.16	2,103 (4%)	487 (7%)	1,616 (3%)	0.19
1.0-2.9 years	52,797 (30%)	9,880 (44%)	42,917 (28%)	0.35	17,088 (29%)	2,921 (44%)	14,167 (28%)	0.35
≥3.0 years	116,968 (66%)	10,886 (49%)	106,082 (69%)	0.42	38,888 (67%)	3,251 (49%)	35,637 (69%)	0.43
Arrhythmia	47,894 (27%)	6,438 (29%)	41,456 (27%)	0.04	15,547 (27%)	2,011 (30%)	13,536 (26%)	0.09
Conduction disorder	19,477 (11%)	2,629 (12%)	16,848 (11%)	0.03	6,406 (11%)	830 (12%)	5,576 (11%)	0.05
Dyslipidemia	110,427 (63%)	15,739 (71%)	94,688 (61%)	0.19	33,560 (58%)	4,473 (67%)	29,087 (57%)	0.22
Heart failure	70,904 (40%)	10,917 (49%)	59,987 (39%)	0.20	23,222 (40%)	3,382 (51%)	19,840 (39%)	0.25
Hypertension	154,865 (88%)	20,392 (91%)	134,473 (87%)	0.14	50,723 (87%)	6,096 (92%)	44,627 (87%)	0.15
Ischemic heart disease	75,581 (43%)	10,864 (49%)	64,717 (42%)	0.14	24,884 (43%)	3,411 (51%)	21,473 (42%)	0.19
Peripheral arterial disease	57,666 (33%)	7,634 (34%)	50,032 (32%)	0.04	18,658 (32%)	2,342 (35%)	16,316 (32%)	0.07
Stroke	34,309 (19%)	4,467 (20%)	29,842 (19%)	0.02	11,194 (19%)	1,405 (21%)	9,789 (19%)	0.05
Valvular disease	34,703 (20%)	4,675 (21%)	30,028 (19%)	0.04	11,414 (20%)	1,487 (22%)	9,927 (19%)	0.08
Asthma/COPD	46,932 (27%)	6,982 (31%)	39,950 (26%)	0.12	15,300 (26%)	2,151 (32%)	13,149 (26%)	0.15
Liver disease	21,637 (12%)	2,638 (12%)	18,999 (12%)	0.02	4,281 (7%)	505 (8%)	3,776 (7%)	0.01

^a Values displayed as count (%) for categorical variables and as mean ± standard deviation for continuous variables.

^b Absolute standardized differences comparing diuretics users to diuretic non-users. A standardized difference > 0.10 represents an imbalance between groups

Flythe et al, Kidney Med, "Diuretic Use Among Hemodialysis Patients in the United States"

Abbreviations: COPD, chronic obstructive pulmonary disease; ESKD, end-stage kidney disease; std diff, standardized difference