

Variability in Cinacalcet Prescription across US Hemodialysis Facilities

Douglas S. Fuller,¹ Shan Xing,² Vasily Belozeroff,² Alon Yehoshua,² Hal Morgenstern,^{3,4,5} Bruce M. Robinson,¹ Robert J. Rubin,⁶ Nisha Bhatt,² and Ronald L. Pisoni¹

Abstract

Background and objectives Calcimimetic drugs used to treat secondary hyperparathyroidism are being considered for inclusion in the Medicare ESRD Prospective Payment System bundle after an evaluation period. Understanding of utilization patterns of calcimimetics across dialysis facilities may help align financial incentives with clinical objectives. Our study's purpose was to describe the distribution of cinacalcet prescription across United States hemodialysis facilities and to explore factors that may influence cinacalcet utilization.

Design, setting, participants, & measurements We used monthly cross-sectional data from the Dialysis Outcomes and Practice Patterns Study in 2014 to characterize the distribution of cinacalcet prescription across 203 United States hemodialysis facilities (10,521 patients). On the basis of associations with parathyroid hormone levels from patient-level analyses, we used linear mixed-effects regressions to estimate the associations between three facility-level exposures (black race, <65 years old, and having ≥ 3 years on dialysis [vintage]) and the prevalence of cinacalcet prescription, adjusting for facility- and patient-level potential confounders.

Results The mean percentage of patients in each facility with cinacalcet prescription was 23% in June 2014 (median, 22%; interquartile range, 13%–30%). Adjusted for facility-level and nonexposure patient-level variables, the difference in prevalence of cinacalcet prescription between facilities with the highest and lowest quartiles of percentage of black patients was 7.8% (95% confidence interval [95% CI], 0.8% to 14.8%; P for trend =0.03). The adjusted prevalence difference was 7.3% for the percentage of patients aged <65 years (95% CI, –0.1% to 14.7%; P for trend =0.06) and 11.9% for the percentage of patients with ≥ 3 years of dialysis (95% CI, 2.4% to 21.4%; P for trend =0.02). These associations changed appreciably, becoming much weaker or even reversing, after further adjusting for the patient-level exposure variables.

Conclusions Facilities treating more patients who are black, under age 65 years, and having dialysis vintage ≥ 3 years have higher average levels of cinacalcet prescription. However, these differences were strongly attenuated after accounting for the unbalanced distributions of these patient case-mix variables.

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Introduction

Under the Medicare ESRD Prospective Payment System (ESRD PPS; also known as the “bundle”) implemented in 2011, dialysis facilities are reimbursed a flat rate for a bundle of ESKD-related drugs, supplies, and services per dialysis treatment (1). This base rate payment is adjusted to account for several patient-level case-mix and facility-level factors associated with higher costs related to delivery of dialysis care (2–4). Before bundle implementation, multiple dialysis community stakeholders had expressed concern that the resource constraints imposed by the bundled payment system might result in negative and disparate effects for certain subgroups of patients and facilities with higher costs of treatment (5–7).

Among drugs used to manage secondary hyperparathyroidism, marked by persistently elevated serum levels of parathyroid hormone (PTH), only vitamin D analogs (administered both intravenously and orally) have been

incorporated into the bundle as of 2018. The addition of oral-only drugs (e.g., phosphate binders) to the bundle was delayed until 2025 by statutory provision (2,8). Presently, calcimimetic treatments (i.e., oral cinacalcet [9] and intravenous etelcalcetide [10,11]) are separately reimbursed under Medicare Part B through a Transitional Drug Add-on Payment Adjustment classification that began in January 2018 and will remain in effect for at least 2 years. During this time, utilization and cost data are being collected and analyzed by the Centers for Medicare and Medicaid Services to determine appropriate revisions to the bundled payment, including calcimimetics (8).

Current international guidelines suggest maintaining PTH levels at a level between two and nine times the upper normal limit of the assay (approximately 130–585 pg/ml; evidence grade 2C), and adjusting therapy (which may include calcimimetics) to avoid progression to levels outside of this range (evidence

¹Arbor Research Collaborative for Health, Ann Arbor, Michigan; ²Global Health Economics, Amgen, Inc., Thousand Oaks, California; ³Departments of ³Epidemiology and ⁴Environmental Health Sciences, School of Public Health, and ⁵Department of Urology, Medical School, University of Michigan, Ann Arbor, Michigan; and ⁶Division of Nephrology and Hypertension, Georgetown University, Washington, DC

Correspondence: Mr. Douglas S. Fuller, Arbor Research Collaborative for Health, Suite 300, 340 East Huron Street, Ann Arbor, MI 48104. Email: doug.fuller@arborresearch.org

grade 2C) (12). Despite increased use of PTH-controlling medications, including cinacalcet, median PTH levels in the United States hemodialysis population have steadily increased by 24% from 2011 through 2017 (13). However, as of February 2018, approximately 20% of nonblack and 32% of black patients had PTH levels >600 pg/ml (13). Adding calcimimetics to the bundle using a flat rate may reduce utilization of these drugs in favor of secondary hyperparathyroidism treatments outside of the bundle (e.g., phosphate binders and or parathyroidectomy) and potentially increase the occurrence or severity of secondary hyperparathyroidism in patients on dialysis.

Prescription of calcimimetics varies across facilities because of differences in underlying patient health status and severity of secondary hyperparathyroidism, as well as discretionary variation in practice preferences across providers. Factors associated with calcimimetic use across dialysis facilities may differ from the current case-mix and facility-level bundle rate adjusters, which were made on the basis of analyses of dialysis-related costs that excluded calcimimetics (3,14). Etelcalcetide was approved by the US Food and Drug Administration in 2017 (15), and thus real-world utilization data are not yet suitable for analysis. Previous studies have identified patient characteristics that are associated with cinacalcet use; examples include more severe secondary hyperparathyroidism (higher PTH, calcium, and phosphate levels), longer dialysis vintage, younger age, black race, female sex, and comorbidities (16–18). However, there are no studies describing the distribution of calcimimetic use across facilities or assessing the extent to which patient and facility factors contribute to facility variation in calcimimetic use.

We assume that the cost of prescribing calcimimetics within a hemodialysis facility is proportional to the number of patients who are prescribed them, and that the need for a bundling reimbursement adjustment should depend on the proportion of patients in the facility who are prescribed calcimimetics. Therefore, if that proportion depends on certain patient factors that usually require more of these drugs, a bundling adjustment should be considered, and that adjustment should be on the basis of the distribution of those patient factors in the facility. An investigation of facility variation in calcimimetic use, and how patient-level and facility-level factors may induce such variation, can also help inform whether inclusion of calcimimetic drugs into the bundle may introduce unexpected disincentives or financial burdens to facilities using calcimimetics to treat patients with more severe secondary hyperparathyroidism. Thus, this study describes the distribution of cinacalcet prescription prevalence across a national sample of United States hemodialysis facilities and explores key factors that influence systematic differences in the prevalence of cinacalcet prescription.

Materials and Methods

Data Source and Variables

We analyzed cross-sectional US Dialysis Outcomes and Practice Patterns Study (DOPPS) data from 2014. Preliminary data from 2016 were used in a sensitivity analysis. DOPPS uses a two-stage stratified random sample of United States hemodialysis facilities and patients to provide nationally representative estimates of dialysis practices and care metrics

over time. Demographic variables and a detailed medical history for each patient are obtained at study enrollment from electronic records or internet-based data entry, and laboratory values and kidney-related medication prescriptions are updated monthly during follow-up. DOPPS sampling and analysis methods have been published elsewhere (19–21).

The outcome variable in this study was cinacalcet prescription status for each patient, which was measured monthly in 2014. Three binary variables known to be associated with cinacalcet prescription were selected to define the facility-level exposures of interest: percentages of patients who were black, under age 65 years, and had dialysis vintage ≥ 3 years (16–18). These percentages were categorized into quartiles in the full sample and treated as the main exposures in the primary analyses. We also investigated several other facility variables available in DOPPS that may be associated with cinacalcet prescription: geographic region (four regions; Supplemental Figure 1), facility size (≥ 25 patients versus < 25 patients), rural location (versus urban), dialysis chain size (large and medium organizations [ten or more units] versus smaller organizations [fewer than ten units], independent, and hospital-based facilities), facility profit status (for-profit versus nonprofit), and setting (free-standing versus hospital-based). Rural location was defined using Rural-Urban Commuting Area codes (22) 7.0–10.6, which denote areas with a population $< 10,000$. For each month during 2014, we reported the overall distribution of the percentage of patients in each facility who were prescribed cinacalcet using percentiles and box-whisker plots. For this trend, facilities could contribute once per month as long as the facility remained in the DOPPS sample. We also described the distribution of the percentage of patients in each facility with a cinacalcet prescription using percentiles and box-whisker plots, both overall and grouped by each exposure variable (e.g., percentage of black patients in the facility). For these cross-sectional descriptions, each facility contributed only once using the observation that was closest to July 1. We report the distribution of key facility factors and patient case-mix factors according to weighted quartiles of facility cinacalcet prescription. Within quartiles of the three main facility-level exposures, we also report facility-aggregated distributions of median PTH and the percentages of patients with PTH ≥ 600 pg/ml, albumin-corrected serum calcium < 8.4 or ≥ 9.5 mg/dl, and serum phosphorus ≥ 5.5 mg/dl.

We estimated mean differences between exposure groups in prevalence of patient cinacalcet prescription (the binary outcome) using linear mixed-effect models for each exposure variable separately with progressive adjustments for patient and facility covariates. Model 1 included each main exposure with no covariates. Model 2 adjusted the estimated effect of each exposure for facility chain affiliation, facility size, and rural location. Model 3 added adjustment for the patient's age, race (black versus other), vintage, sex, and postdialysis weight, excluding the patient-level covariate corresponding to the facility-level exposure of interest; for example, excluding black race when estimating the association between percentage black and the outcome. Model 4 added the patient-level covariate corresponding to the facility-level exposure of interest; for example, including black race when estimating the association between percentage black and the outcome. Additional covariates added to

model 3 (as supplemental analyses) included facility setting, facility profit status, geographic location, patient PTH, albumin-corrected calcium, and prescription of active or analog vitamin D.

Patients with a parathyroidectomy before study entry ($n=33$) or missing data regarding cinacalcet prescription ($n=145$) were excluded from analyses. Additionally, one facility with 13 sampled patients was excluded for lack of race information, and one facility with 35 sampled patients was excluded for lack of profit status information.

Missing values for patient factors were singly imputed by the chained-equations method using IVEware for SAS. Analyses were weighted to account for nonproportional sampling of facilities in the DOPPS and to account for unequal patient sampling fractions across facilities (12,21). Data management was performed and weighted distributions were created using SAS v9.4. Weighted mixed-effects model analyses were performed using STATA/MP 15.0.

Results

During 2014, the median percentage of patients in facilities with cinacalcet prescription increased steadily, from 22% to 24%—a difference of only 2%–3% (slope per 30 days =0.09%; 95% confidence interval [95% CI], 0.02% to 0.2%; P for trend =0.01; Figure 1). By contrast, we observed large variability in cinacalcet prescription across facilities within each month, with absolute differences between the 25th and 75th percentiles (interquartile range [IQR]) varying from 16% to 20% across months in 2014. The estimated

monthly percentages were slightly higher in a sensitivity analysis using preliminary data from 2016, but no other notable differences were observed compared with the main analysis of 2014 data.

Estimated quartile cut-off points for the percentage of patients within a facility having a cinacalcet prescription in the June 2014 cross-sectional sample (203 facilities; 10,521 patients) were 13% (quartile 1), 22% (quartile 2), and 32% (quartile 3) (Table 1). Patients in facilities in the highest quartile compared with the lowest quartile of cinacalcet prescription had lower mean age (61 [SD 15] versus 64 years [SD 16]), longer median dialysis vintage (3.4 [IQR, 1.4–6.5] versus 2.5 [IQR, 1.2–4.4] years), and were more likely to be black (50% versus 32%). Results from linear mixed-effects regression models showed strong positive relationships between cinacalcet prescription and the patient characteristics of younger age, black race, longer dialysis vintage, and higher postdialysis weight (see also Supplemental Table 1). Associations with other patient variables were much weaker. The percentage of facility patients with cinacalcet prescriptions was higher in the South and West, in facilities affiliated with large and medium dialysis organizations, and in for-profit facilities.

The mean percentage of patients in each facility with a cinacalcet prescription increased monotonically from 18% to 31% as the percentage of black patients in the facility increased from the lowest to the highest quartile (Figure 2, left panel). Similar monotonic associations with cinacalcet prescription in a facility were also observed for the percentages of patients younger than age 65 years (Figure 2,

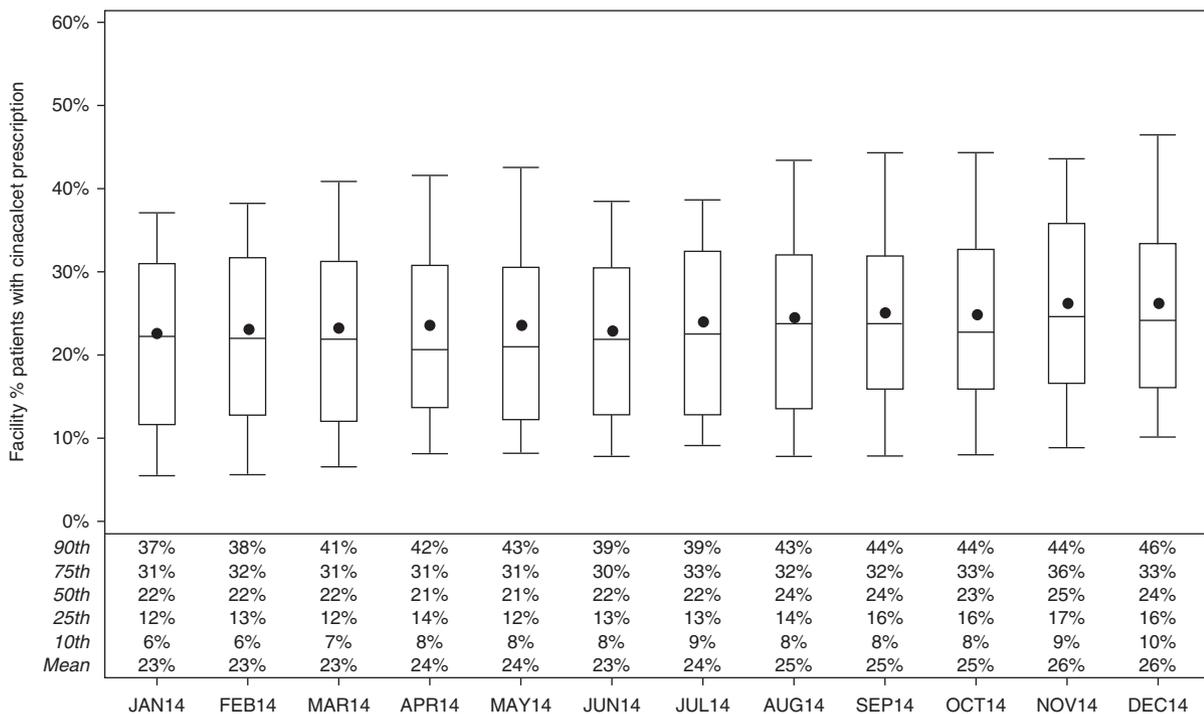


Figure 1. | The median percentage of patients who were prescribed cinacalcet across facilities increased during 2014. Box-whisker plot distributions of the percentage of patients in a facility who were prescribed cinacalcet each month, 2014. Circle markers denote mean values. Boxes extend to 25th and 75th percentiles. Error bars extend to 10th and 90th percentiles. Frequency weights were applied to account for nonproportional sampling of facilities in the DOPPS.

Table 1. Characteristics of patients and facilities in the study sample

Facility % with Cinacalcet Prescription	Weighted Quartile of Facility % Cinacalcet Prescription				Missing (%)
	<12.7	12.7–22.4	22.5–31.9	≥32.0	
Facilities, <i>N</i>	55	63	41	44	
Patient characteristics (n=10,521)					
Age, yr, mean (SD)	64 (16)	65 (15)	63 (15)	61 (15)	<1
ESKD vintage, yr, median [IQR]	2.5 [1.2–4.4]	2.9 [1.3–5.5]	2.8 [1.1–5.4]	3.4 [1.4–6.5]	8
Black, %	32	38	22	50	4
Men, %	56	57	55	56	<1
Body mass index, kg/m ² , mean (SD)	28.7 (7.4)	28.3 (7.0)	28.5 (6.8)	29.0 (7.0)	9
Body surface area, m ² , mean (SD)	1.9 (0.3)	1.9 (0.3)	1.9 (0.3)	1.9 (0.3)	8
Parathyroid hormone, pg/ml, median [IQR]	355 [214–623]	356 [218–575]	428 [248–701]	340 [203–554]	16
Albumin-corrected serum calcium, mg/dl, mean (SD)	9.2 (0.7)	9.2 (0.7)	9.1 (0.7)	9.1 (0.7)	7
Serum phosphorus, mg/dl, mean (SD)	5.3 (1.6)	5.1 (1.5)	5.2 (1.6)	5.2 (1.5)	6
IV active vitamin D use, %	70	78	62	86	<1
IV active vitamin D weekly dose, mcg, paricalcitol-equivalent, median [IQR]	6.0 [3.5–9.9]	7.0 [3.5–12.0]	6.0 [4.5–10.5]	8.8 [4.5–11.8]	7
Facility characteristics (n=203)					
DOPPS Practice Monitor region ^a					
<i>Central</i>	34	28	18	17	
<i>East</i>	20	24	25	12	
<i>South</i>	22	25	16	49	
<i>West</i>	24	22	42	22	
Dialysis chain size					
≥10 units	74	88	93	89	
<10 units, independent, or hospital-based	26	12	7	11	
Facility setting					
<i>Free-standing</i>	97	96	98	98	
<i>Hospital-based</i>	3	4	2	2	
Facility profit status					
<i>For-profit</i>	77	93	82	89	
<i>Not for-profit</i>	23	7	18	11	
Facility location					
<i>Nonrural</i>	78	91	95	83	
<i>Rural</i>	22	9	5	17	
Facility census size					
≥25	4	3	0.3	3	
<25	96	97	99.7	97	
Facility % black patients					
<7	36	23	36	4	
7–31	25	30	30	16	
31–57	21	21	23	34	
≥57	18	36	11	46	
Facility % patients aged <65 yr					
<38	40	34	16	11	
38–49	23	25	36	14	
49–64	22	24	24	27	
≥64	15	16	25	48	
Facility % patients on dialysis ≥3 yr					
<41	54	24	7	15	
41–48	12	30	48	8	
48–56	11	27	38	27	
≥56	23	19	7	50	

Facility characteristics category percentages add to 100% within columns of facility % cinacalcet use. IQR, interquartile range; IV, intravenous; DOPPS, Dialysis Outcomes and Practice Patterns Study.

^aAs defined in Supplemental Figure 1.

middle panel) and with a dialysis vintage ≥3 years (Figure 2, right panel).

Patients in the quartile of facilities having the highest percentage of black patients had the highest median PTH level (396 pg/ml [IQR, 313–490]), the largest percentages of patients with PTH ≥600 pg/ml (28%) and albumin-corrected serum calcium <8.4 mg/dl (31%), but a lower

percentage of patients with phosphorus levels ≥5.5 mg/dl (34%) relative to patients in the first two quartiles (Table 2, top). Patients in the top two quartiles of facilities with the largest percentage under age 65 years had the highest median PTH levels (394 [IQR, 342–436] and 386 [IQR, 273–423] pg/ml), almost twice the percentage of patients with PTH ≥600 pg/ml (24% and 21%) than in the lowest

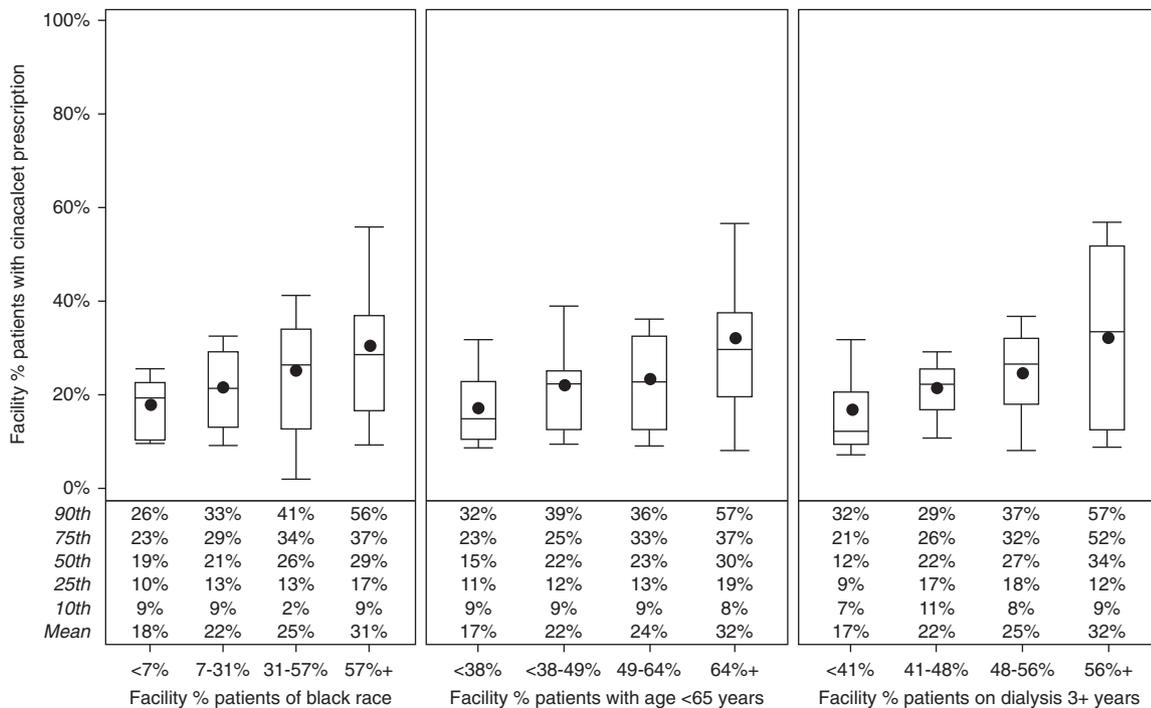


Figure 2. | Cinacalcet use within a facility is associated with the proportion of patients in that facility who are black, age <65 years, or have vintage 3+ years. Box-whisker plots, unadjusted distributions of the percentage of patients in a facility who were prescribed cinacalcet, by quartiles of facility percentage black, facility percentage age <65 years, and facility percentage on dialysis ≥3 years. *n*=203 facilities participating in DOPPS during 2014. Each facility contributed the monthly observation nearest to July 1. Circle markers denote mean values. Boxes extend to 25th and 75th percentiles. Error bars extend to 10th and 90th percentiles. Frequency weights were applied to account for non-proportional sampling of facilities in the DOPPS.

quartile, and the highest percentage of patients with calcium levels ≥9.5 mg/dl (12% and 15%) (Table 2, middle). Patients in the quartile of facilities with the smallest percentage of patients with vintage ≥3 years had the lowest median PTH levels (314 [IQR, 271–391] pg/ml) and the lowest percentage of patients with PTH ≥600 pg/ml (14%) (Table 2, bottom).

In unadjusted models, we observed positive monotonic (“dose-response”) associations between each of the three facility exposures and the prevalence of cinacalcet prescription (Table 3, model 1). Adjustment for facility chain affiliation, facility size, and rural location in model 2 did not appreciably affect the associations, but adjustment for several patient case-mix variables in model 3 mildly weakened the associations. The adjusted difference in cinacalcet prescription prevalence between the highest and lowest quartiles of percentage of black patients in model 3 was 7.8% (95% CI, 0.8% to 14.8%; *P* for trend =0.03). The same estimated association was 7.3% for the percentage of patients aged <65 years (95% CI, -0.1% to 14.7%; *P* for trend =0.06) and 11.9% for the percentage of patients with ≥3 years of dialysis (95% CI, 2.4% to 21.4%; *P* for trend =0.02). These associations changed appreciably, becoming much weaker or even reversing for percentage black, when also adjusting for the patient-level exposure variables in model 4.

Additional results extending model 3 from Table 3 to other facility- and patient-level adjustments are available in Supplemental Tables 2 and 3. Adjustments for facility setting, profit status, and geographic region had minimal

effect on the model 3 estimates from Table 3 and are available in Supplemental Table 2. Supplemental Table 3 shows the results after further adjusting model 3 for patient PTH, calcium, and active or analog vitamin D prescription. Because these variables may be affected by race, age, and/or vintage, they may lie in the causal pathway leading to cinacalcet use. Thus, adjustment for those clinical variables probably reflects overadjustment, *i.e.*, partial blocking of the effects by covariate adjustment.

Discussion

In this study, we estimated the facility variation in the distribution of cinacalcet prescriptions across United States hemodialysis facilities in 2014. We found that the median percentage of patients with cinacalcet prescription in each facility was 22% (IQR, 13%–32%). We also identified three aggregated facility variables (the percentages of facility patients who were black, under age 65 years, and having dialysis vintage ≥3 years) that were positively and monotonically associated with the prevalence of cinacalcet prescription, adjusting for several potential confounders. Adjusting for patient-level analogs of these aggregated variables in model 4 strongly reduced, or even reversed, the associations observed in models 1–3, suggesting that these facility-level associations were primarily due to compositional effects of age, race, and vintage (*i.e.*, unbalanced distributions of these variables among facilities) rather than contextual effects of the facility exposures themselves,

Table 2. Distributions (median and interquartile range) of facility-aggregated laboratory values, by facility percentage of black patients, facility percentage of patients aged <65 years, and facility percentage of patients on dialysis ≥3 years

Facility-aggregated laboratory values				
	<7	Facility % Black Patients		
		7–31	31–57	≥57
Facility median PTH, pg/ml	311 [274, 343]	369 [298, 412]	382 [292, 408]	396 [313, 490]
Facility % patients with PTH ≥600 pg/ml	16 (4, 27)	20 (10, 29)	18 (13, 24)	28 (22, 38)
Facility % patients with corrected calcium <8.4 mg/dl	22 (19, 30)	27 (22, 37)	24 (21, 31)	31 (25, 40)
Facility % patients with corrected calcium ≥9.5 mg/dl	13 (7, 16)	9 (6, 15)	12 (7, 16)	12 (8, 15)
Facility % patients with phosphorus ≥5.5 mg/dl	39 (21, 57)	36 (32, 43)	32 (25, 37)	34 (23, 41)
		Facility % Patients Aged <65 yr		
		38–49	49–64	≥64
Facility median PTH, pg/ml	310 [271, 381]	317 [284, 468]	394 [342, 436]	386 [273, 423]
Facility % patients with PTH ≥600 pg/ml	11 (4, 22)	25 (17, 38)	24 (19, 34)	21 (11, 29)
Facility % patients with corrected calcium <8.4 mg/dl	29 (22, 35)	26 (21, 44)	22 (15, 30)	26 (19, 38)
Facility % patients with corrected calcium ≥9.5 mg/dl	8 (4, 13)	9 (4, 16)	12 (9, 16)	15 (10, 17)
Facility % patients with phosphorus ≥5.5 mg/dl	34 (21, 40)	41 [36, 57]	32 (26, 42)	33 (28, 42)
		Facility % Patients on Dialysis ≥3 yr		
		41–48	48–56	≥56
Facility median PTH, pg/ml	314 [271, 391]	374 [286, 421]	390 [308, 404]	368 [295, 492]
Facility % patients with PTH ≥600 pg/ml	14 (7, 22)	25 (13, 33)	19 (13, 27)	25 (20, 37)
Facility % patients with corrected calcium <8.4 mg/dl	25 (21, 33)	26 (18, 37)	23 (14, 30)	33 (25, 40)
Facility % patients with corrected calcium ≥9.5 mg/dl	10 (6, 18)	14 (4, 16)	13 (7, 18)	9 (7, 12)
Facility % patients with phosphorus ≥5.5 mg/dl	38 (22, 41)	39 (25, 47)	32 (23, 36)	39 (29, 49)

PTH, parathyroid hormone.

i.e., being treated in a facility with a larger percentage of patients who were under 65 years, black, or with longer vintages.

The ESRD PPS recognizes the heterogeneity of the patient population by allowing several patient-level case-mix adjustments for adults: patient age (five categories), body surface area, low body mass index, two chronic and two acute comorbidities, and new onset of dialysis (120 days) (23). These case-mix adjustments were developed to provide higher facility payments and reduced disincentives for treating higher-cost patients (1,3). Our study found that younger patient age, longer dialysis vintage, and black race were associated with higher cinacalcet prescription, consistent with findings from other studies evaluating associations of PTH and cinacalcet use (16–18,24,25). The current patient-level bundle adjustments provide higher reimbursement for patients younger than 70 or older than 79 years and for patients within the first 120 days on dialysis (14). Additional economic analyses should therefore be conducted to assess whether the current adjustment multipliers for age and vintage are sufficient to account for increased use of calcimimetics among younger patients and patients with longer dialysis vintage.

The proportion of patients in a dialysis facility who are black is known to be associated with higher dialysis facility costs; thus, black race has been proposed as another case-mix adjuster by the nephrology community (1,3,4,26,27). However, inclusion of race as a case-mix adjuster is limited by difficulties in accurate classification and social acceptability (1,3,4). Although a causal biologic basis for more severe secondary hyperparathyroidism in black patients has not yet been clearly identified, black patients have higher mean and median PTH levels than nonblack patients (13,28,29). During the implementation of the ESRD PPS (August 2010 to April 2011), the prevalence of PTH levels >600 mg/dl increased more rapidly among black patients (from 17% to 28%) than among other races

(from 9% to 14%) (13,30). Although an early evaluation of the bundle's effect on anemia and mineral metabolism outcomes found no exacerbation of existing racial inequalities for hemoglobin levels or PTH, black patients had lower hemoglobin levels and higher PTH levels than nonblack patients at baseline (31). Additionally, small chain dialysis facilities, which may have less capability to absorb the financial effect of reimbursement changes, were observed to experience greater racial inequalities for anemia after bundle implementation compared with the overall ESKD facility population (32). Current international guidelines suggest maintaining PTH levels at a level between two and nine times the upper normal limit of the assay (approximately 130–585 pg/ml; evidence grade 2C), and adjusting therapy (which includes calcimimetics) to avoid progression to levels outside of this range (evidence grade 2C) (12). Modification of the bundle to include calcimimetics should strive to avoid exacerbation of PTH levels outside the guideline range, particularly among black patients, and should also consider the effect on patients dialyzing in small chain facilities.

The addition of calcimimetics into the ESRD PPS will likely change the landscape of secondary hyperparathyroidism treatment as dialysis facilities adapt to new financial incentives. According to a Medicare Payment Advisory Commission analysis in 2017, the overall use of dialysis drugs included in the bundle declined from 2011 (*i.e.*, the first year that the ESRD PPS was implemented) to 2013, whereas spending for calcimimetics (cinacalcet) and phosphate binders, which remained separately reimbursable, increased by 22% (2). Spoendlin *et al.* (33) recently reported a 10% reduction in the rate of intravenous vitamin D initiation and a 7% reduction in starting intravenous vitamin D dose after ESRD PPS implementation. Since the ESRD PPS, the DOPPS Practice Monitor (13) has also noted

Table 3. Associations of three facility-level aggregate exposures with patient cinacalcet prescription

Facility-Level Exposure	Model 1		Model 2		Model 3		Model 4	
	APD	95% CI	APD	95% CI	APD	95% CI	APD	95% CI
Facility % black patients								
<7 (ref)	0%	(ref)	0%	(ref)	0%	(ref)	0%	(ref)
7–31	3.9%	(−0.6% to 8.3%)	3.6%	(−1.0% to 8.2%)	4.2%	(0.5% to 7.9%)	2.4%	(−1.2% to 5.9%)
31–57	7.4%	(−0.05% to 14.9%)	7.4%	(−0.02% to 14.8%)	5.4%	(−1.2% to 12.0%)	0.9%	(−5.4% to 7.3%)
57+	12.4%	(3.9% to 20.8%)	12.6%	(4.2% to 20.8%)	7.8%	(0.8% to 14.8%)	−0.04%	(−7.1% to 7.0%)
<i>P</i> value for linear trend		0.003		0.002		0.03		0.9
Facility % patients aged 65 yr								
<38 (ref)	0%	(ref)	0%	(ref)	0%	(ref)	0%	(ref)
38–49	5.0%	(−0.02% to 10.0%)	4.9%	(−0.1% to 9.8%)	2.7%	(−1.8% to 7.2%)	2.2%	(−2.3% to 6.8%)
49–64	6.4%	(0.3% to 12.4%)	6.1%	(−0.05% to 12.3%)	3.0%	(−2.5% to 8.7%)	2.0%	(−3.7% to 7.5%)
64+	14.7%	(5.9% to 23.6%)	14.4%	(5.4% to 23.3%)	7.3%	(−0.1% to 14.7%)	5.6%	(−1.8% to 13.1%)
<i>P</i> value for linear trend		0.001		0.002		0.06		0.2
Facility % patient on dialysis 3+ yr								
<41 (ref)	0%	(ref)	0%	(ref)	0%	(ref)	0%	(ref)
41–48	4.2%	(−0.9% to 9.4%)	3.3%	(−2.0% to 8.5%)	5.7%	(0.3% to 11.0%)	3.0%	(−2.0% to 8.0%)
48–56	7.7%	(0.9% to 14.4%)	6.9%	(0.1% to 13.7%)	6.0%	(−1.3% to 13.3%)	2.4%	(−4.3% to 9.1%)
56+	15.4%	(6.4% to 24.3%)	16.2%	(6.9% to 25.5%)	11.9%	(2.4% to 21.4%)	5.1%	(−3.9% to 14.1%)
<i>P</i> value for linear trend		0.001		0.001		0.02		0.3

Shown are the associations between the prevalence of patient cinacalcet prescription and each main facility-level exposure (using separate models) as an adjusted prevalence difference (APD) with 95% confidence interval (95% CI). The first quartile of each main facility-level exposure is treated as the reference group, and the estimated associations are cumulatively adjusted for potential confounders using linear mixed-effect models. Model 1 included each main exposure with no covariates. Model 2 adjusted the estimated effect of each exposure for facility chain affiliation, small facility volume (± 25 patients), and rural versus urban location. Model 3 added adjustment for the patient's age, race (black versus other), vintage, sex, body mass index, and body surface area, excluding the patient-level covariate corresponding to the facility-level exposure of interest; *e.g.*, excluding black race when estimating the association between facility percentage black patients and the outcome. Model 4 added the patient-level covariate corresponding to the facility-level exposure of interest, *e.g.*, including black race when estimating the association between facility percentage black patients and the outcome.

large-scale shifts in the use of vitamin D preparation (from paricalcitol to doxercalciferol) and route (from intravenous to oral). After the Transitional Drug Add-on Payment Adjustment period ends and calcimimetics are added to the bundle, it is possible that transition to other treatments for secondary hyperparathyroidism may occur, such as oral vitamin D, phosphate binders, and parathyroidectomy (34). The net effect on patient outcomes should be carefully monitored. In addition, Medicare beneficiaries are usually responsible for cost-sharing payments toward covered ESKD services, which is typically 20% after a deductible amount has been paid each year (8). Thus, higher bundle payments to dialysis facilities to cover calcimimetic treatments may also raise cost-sharing amounts attributable to the patient. Consideration should be given to creating an equitable allocation of financial burden across facilities and patients.

This cross-sectional analysis was intended to describe variation in cinacalcet use across United States hemodialysis facilities and readily identifiable variables associated with higher PTH levels, which may be related to systematic differences in cinacalcet prescription. We note as a key limitation of this study that there may be other variables, such as private insurance or Medicare/Medicaid dual coverage, that induce similar systematic differences across facilities or that explain the differences we observed. Thus, causal interpretation is limited. We did not have information regarding the acute and chronic comorbid adjustments to the ESRD PPS available for this analysis; however, these conditions are relatively rare and not typically associated with CKD-mineral bone disorder, and thus are not likely to influence our findings. We note as an additional limitation that etelcalcetide was approved in 2017 but not commercially available in United States facilities during our study period. However, the systematic factors we have described here that are pertinent to cinacalcet use likely may also be relevant to etelcalcetide use.

In summary, we found considerable variability in the percentage of patients prescribed cinacalcet across United States hemodialysis facilities. Facilities treating more patients who are black, under age 65 years, and having dialysis vintage ≥ 3 years have systematically higher levels of cinacalcet prescription. These differences were only slightly influenced by facility situational factors, but were strongly attenuated after accounting for the unbalanced distributions of these patient-level case-mix variables. Existing ESRD PPS adjustments may not fully account for these imbalances, and thus additional studies evaluating the clinical and financial effects on facilities of adding calcimimetics to the bundle with respect to these three factors are warranted.

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Data and analytic support are available to qualified researchers for approved scientific uses. To make the best possible use of this important resource, the DOPPS Steering Committee encourages investigators, whether previously affiliated with the DOPPS, to submit proposals for collaboration and ancillary studies to DOPPS at <https://www.dopps.org/PartnerwithUs.aspx>.

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Disclosures

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Supplemental Material

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Supplemental Table 1. Associations of patient cinacalcet prescription with patient case-mix variables.

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Supplemental Figure 1. Geographic regions, as defined in the DOPPS Practice Monitor (DPM).

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Variability in Cinacalcet Prescription Across US Hemodialysis Facilities

Douglas S. Fuller, MS, Shan Xing, PhD, Vasily Belozeroff, PhD, Alon Yehoshua, MS, Hal Morgenstern, PhD,

Bruce M. Robinson, MD, Robert J. Rubin, MD, Nisha Bhatt, MD, Ronald L. Pisoni, PhD

Supplemental Material Table of Contents

Supplemental Table 1: Associations of patient cinacalcet prescription with patient case-mix variables

Supplemental Table 2. Associations of three facility-level aggregate exposures with patient cinacalcet prescription, adjusted for additional facility variables

Supplemental Table 3. Associations of three facility-level aggregate exposures with patient cinacalcet prescription, adjusted for additional patient variables

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Supplemental Table 1: Associations of patient cinacalcet prescription with patient case-mix variables

Patient characteristic	APD	95% CI
Age, per 10 years older	-2.0%	(-2.9%, -1.2%)
Time on dialysis, per 1 year longer	3.3%	(2.9%, 3.7%)
Black race, vs. other	11.2%	(7.5%, 14.9%)
Male gender, vs. female	-1.2%	(-5.5%, 3.1%)
Post-dialysis weight, per 1 kg higher	1.2%	(0.5%, 1.9%)

Shown are the associations between the prevalence of patient cinacalcet prescription and each patient-level covariate as an adjusted prevalence difference (APD) with 95% confidence interval (CI). The estimated associations are estimated using linear mixed-effects models and adjusted for facility chain affiliation and the other patient-level variables listed in the table.

Supplemental Table 2. Associations of three facility-level aggregate exposures with patient cinacalcet prescription, adjusted for additional facility variables

Facility-level exposure	Model 3		Model 3 + facility setting		Model 3 + facility profit status		Model 3 + DPM region	
	APD	95% CI	APD	95% CI	APD	95% CI	APD	95% CI
Facility % black patients								
<7 (ref)	0%	(ref)	0%	(ref)	0%	(ref)	0%	(ref)
7-31	4.2%	(0.5%, 7.9%)	4.2%	(0.5%, 7.9%)	4.2%	(-0.4%, 8.8%)	2.9%	(-1.1%, 6.9%)
31-57	5.4%	(-1.2%, 12.0%)	5.5%	(-1.1%, 12.1%)	5.4%	(-1.8%, 12.6%)	3.1%	(-4.3%, 10.5%)
57+	7.8%	(0.8%, 14.8%)	7.9%	(0.9%, 14.9%)	7.8%	(0.6%, 15.0%)	6.6%	(0.1%, 13.2%)
P-value for linear trend	0.03		0.03		0.04		0.06	
Facility % patients <65 years old								
<38 (ref)	0%	(ref)	0%	(ref)	0%	(ref)	0%	(ref)
38-49	2.7%	(-1.8%, 7.2%)	2.7%	(-1.8%, 7.2%)	3.0%	(-1.9%, 7.9%)	2.2%	(-2.9%, 7.3%)
49-64	3.0%	(-2.5%, 8.7%)	3.0%	(-2.6%, 8.7%)	3.1%	(-2.6%, 8.7%)	3.5%	(-2.0%, 9.0%)
64+	7.3%	(-0.1%, 14.7%)	7.3%	(-0.1%, 14.7%)	7.3%	(-0.1%, 14.7%)	6.8%	(-1.0%, 14.7%)
P-value for linear trend	0.06		0.06		0.06		0.08	
Facility % patients on dialysis ≥3 years								
<41 (ref)	0%	(ref)	0%	(ref)	0%	(ref)	0%	(ref)
41-48	5.7%	(0.3%, 11.0%)	5.6%	(0.3%, 11.0%)	5.7%	(0.04%, 11.4%)	6.4%	(0.9%, 11.8%)
48-56	6.0%	(-1.3%, 13.3%)	5.9%	(-1.4%, 13.3%)	6.0%	(-1.2%, 13.3%)	6.8%	(0.4%, 13.2%)
56+	11.9%	(2.4%, 21.4%)	11.9%	(2.4%, 21.4%)	11.9%	(2.4%, 21.4%)	12.5%	(2.7%, 22.3%)
P-value for linear trend	0.02		0.02		0.02		0.01	

Shown are the associations between the prevalence of patient cinacalcet prescription and each exposure (using separate models) as an adjusted prevalence difference (APD) with 95% confidence interval (CI). The first quartile of each facility-level exposure is treated as the reference group, and the estimated associations are adjusted using linear mixed-effects models. Model 3 (from Table 3 in the main analysis) includes adjustments for facility chain affiliation, facility rural location, facility size, and the patient's age, race (black vs. other), vintage, sex, body mass index, and body surface area, excluding the patient-level covariate corresponding to the facility-level exposure of interest; e.g., excluding black race when estimating the association between facility percentage black patients and the outcome.

Supplemental Table 3. Associations of three facility-level aggregate exposures with patient cinacalcet prescription, adjusted for additional patient variables

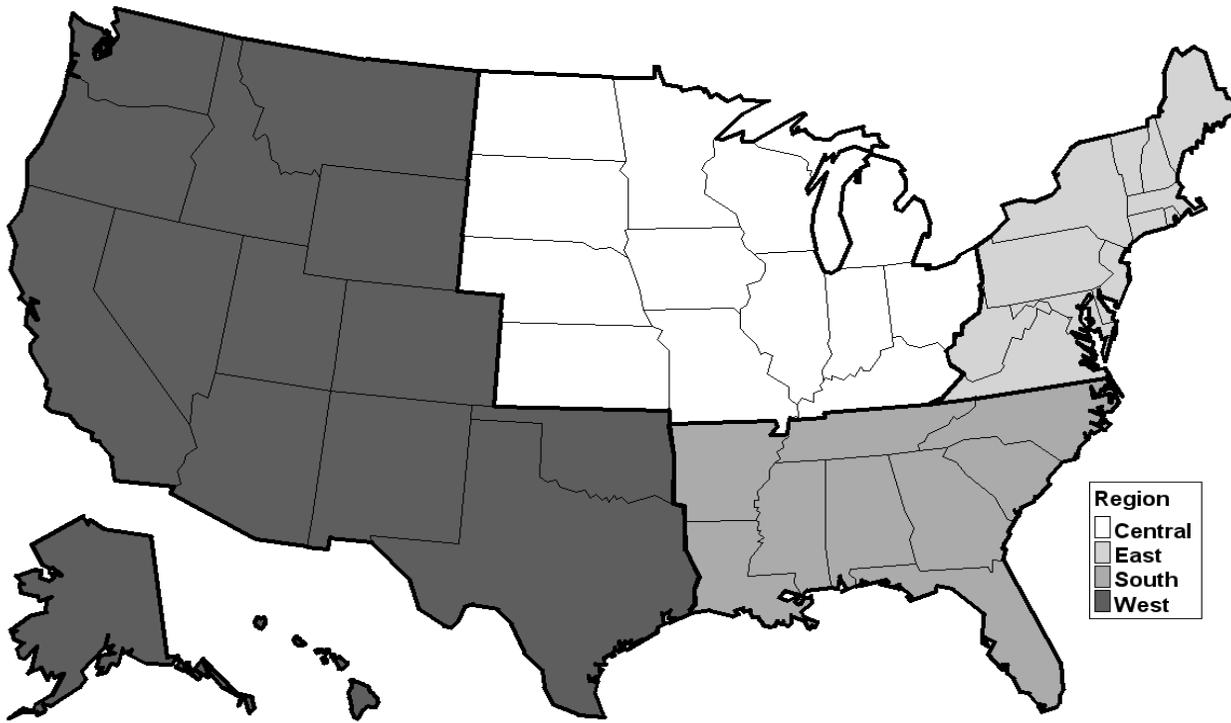
Facility-level exposure	Model 3		Model 3A (PTH)		Model 3A (Calcium)		Model 3A (IV vitamin D use)		Model 3A (All)	
	APD	95% CI	APD	95% CI	APD	95% CI	APD	95% CI	APD	95% CI
Facility % black patients										
<7 (ref)	0%	(ref)	0%	(ref)	0%	(ref)	0%	(ref)	0%	(ref)
7-31	4.2%	(0.5%, 7.9%)	4.9%	(0.9%, 9.0%)	4.2%	(0.5%, 8.0%)	1.9%	(-2.2%, 6.0%)	2.9%	(-1.3%, 7.0%)
31-57	5.4%	(-1.2%, 12.0%)	5.6%	(-1.3%, 12.6%)	5.5%	(-1.1%, 12.1%)	1.6%	(-4.3%, 7.4%)	2.4%	(-3.7%, 8.5%)
57+	7.8%	(0.8%, 14.8%)	8.7%	(0.8%, 16.6%)	7.9%	(0.9%, 15.0%)	3.4%	(-3.8%, 10.6%)	4.9%	(-2.9%, 12.6%)
P-value for linear trend	0.03		0.04		0.03		0.4		0.3	
Facility % patients <65 years old										
<38 (ref)	0%	(ref)	0%	(ref)	0%	(ref)	0%	(ref)	0%	(ref)
38-49	2.7%	(-1.8%, 7.2%)	0.7%	(-4.3%, 5.7%)	2.6%	(-1.9%, 7.2%)	4.8%	(0.1%, 9.6%)	2.7%	(-2.4%, 7.8%)
49-64	3.0%	(-2.5%, 8.7%)	0.8%	(-5.5%, 7.0%)	2.9%	(-2.8%, 8.6%)	2.4%	(-3.2%, 7.9%)	0.5%	(-5.6%, 6.6%)
64+	7.3%	(-0.1%, 14.7%)	7.7%	(-0.01%, 15.5%)	7.2%	(-0.2%, 14.6%)	5.9%	(-1.4%, 13.2%)	6.4%	(-1.2%, 14.0%)
P-value for linear trend	0.06		0.06		0.07		0.2		0.2	
Facility % patients on dialysis ≥3 years										
<41 (ref)	0%	(ref)	0%	(ref)	0%	(ref)	0%	(ref)	0%	(ref)
41-48	5.7%	(0.3%, 11.0%)	3.8%	(-1.8%, 9.4%)	5.6%	(0.2%, 11.0%)	7.4%	(2.1%, 12.7%)	5.4%	(0.02%, 10.9%)
48-56	6.0%	(-1.3%, 13.3%)	4.9%	(-3.2%, 12.9%)	6.1%	(-1.3%, 13.4%)	5.2%	(-1.9%, 12.2%)	4.3%	(-3.4%, 12.1%)
56+	11.9%	(2.4%, 21.4%)	12.0%	(1.6%, 22.3%)	12.1%	(2.6%, 21.6%)	11.0%	(1.9%, 20.0%)	11.2%	(1.5%, 20.9%)
P-value for linear trend	0.02		0.03		0.02		0.03		0.04	

Shown are the associations between the prevalence of patient cinacalcet prescription and each exposure (using separate models) as an adjusted prevalence difference (APD) with 95% confidence interval (CI). The first quartile of each facility-level exposure is treated as the reference group, and the estimated associations are adjusted using linear mixed-effects models. Model 3 (from Table 3 in the main analysis) includes adjustments for facility chain affiliation, facility rural location, facility size, and the patient's age, race (black vs. other), vintage, sex, body mass index, and body surface area, excluding the patient-level covariate corresponding to the facility-level exposure of interest; e.g., excluding black race when estimating the association between facility percentage black patients and the outcome.

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Supplemental Figure 1. Geographic regions, as defined in the DOPPS Practice Monitor (DPM).

DPM Geographic Regions



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