Failed Target Weight Achievement Associates with Short-Term Hospital Encounters among Individuals Receiving Maintenance Hemodialysis

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ABSTRACT

Background Hospitalizations and 30-day readmissions are common in the hemodialysis population. Actionable clinical markers for near-term hospital encounters are needed to identify individuals who require swift intervention to avoid hospitalization. Aspects of volume management, such as failed target weight (i.e, estimated dry weight) achievement, are plausible modifiable indicators of impending adverse events. The short-term consequences of failed target weight achievement are not well established.

Methods Statistically deidentified data were taken from a cohort of Medicare-enrolled, prevalent hemodialysis patients treated at a large dialysis organization from 2010 to 2012. We used a retrospective cohort design with repeated intervals, each consisting of 180-day baseline, 30-day exposure assessment, and 30-day follow-up period, to estimate the associations between failed target weight achievement and the risk of 30-day emergency department visits and hospitalizations. We estimated adjusted risk differences using inverse probability of exposure weighted Kaplan–Meier methods.

Results A total of 113,561 patients on hemodialysis contributed 788,722 study intervals to analyses. Patients who had a postdialysis weight >1.0 kg above the prescribed target weight in ≥30% (versus <30%) of exposure period treatments had a higher absolute risk (risk difference) of 30-day: emergency department visits (2.13%; 95% confidence interval, 2.00% to 2.32%); and all-cause (1.47%; 95% confidence interval, 1.34% to 1.62%), cardiovascular (0.31%; 95% confidence interval, 0.24% to 0.40%), and volume-related (0.15%; 95% confidence interval, 0.11% to 0.21%) hospitalizations.

Conclusions In the absence of objective measures of volume status, recurrent failure to achieve target weight is an easily identifiable clinical risk marker for impending hospital encounters among patients on hemodialysis.

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Individuals receiving maintenance hemodialysis in the United States have unacceptably high hospitalization and 30-day readmission rates.[1] Easily discernible and actionable clinical markers for near-term hospital encounters are needed to identify individuals who require swift intervention to avoid hospitalization. Many patient-related hospitalization risk factors, such as heart failure, catheter vascular access, and hypoalbuminemia, are difficult to modify quickly. In contrast, dialysis treatment–related factors, such as aspects of volume management, can often be addressed more promptly. In fact, volume overload is a major contributor to hospitalizations, readmissions, and their associated costs in the hemodialysis population. One report estimated that hospital encounters for volume overload cost Medicare $266 million from 2006 to 2008.[2]

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Both inaccurate prescribed target weight (*i.e.*, estimated dry weight) and failure to achieve prescribed target weight can lead to volume overload. Imprecision in the assessment of volume status and the absence of universally accepted objective volume measurement tools make it challenging to recognize a misestimated target weight. The recurrent occurrence of postdialysis weight exceeding target weight may be an easily identifiable marker of volume overload in some patients. A previous study found that individuals who experienced postdialysis weights >2.0 kg above the prescribed target weight (versus those with postdialysis weights within 2.0 kg of target weight) had a greater long-term mortality risk.[3] However, the short-term consequences of failed target weight achievement are not well established. In addition, some experts have suggested that attention to and adjustment of prescribed target weight after hospital discharge may reduce readmission risk,[4,5] but existing data do not support this seemingly sound hypothesis.

We undertook this study to investigate the association between failed target weight achievement and the short-term risk of emergency department (ED) visits and inpatient hospitalizations in a large, nationally representative cohort of prevalent hemodialysis patients from the United States, using a modern epidemiologic study design and analytic methods. In *post hoc* analyses, we evaluated the association between posthospitalization target weight adjustment and the occurrence of short-term outcomes, including 30-day hospital readmissions.

Significance Statement

Hospitalizations and 30-day readmissions are common and expensive among individuals receiving maintenance hemodialysis. Easily discernible and actionable clinical markers for near-term hospital encounters are needed to identify individuals who require swift intervention to avoid hospitalization. Aspects of volume management, such as failed target weight achievement, may be important, modifiable indicators of impending hospital encounters. Using a failed target weight achievement definition of postdialysis weight ≥1.0 kg above the prescribed target weight, this study reports robust associations between more (versus less) frequent failed target weight achievement and a higher risk of 30-day emergency department visits and hospitalizations. It also shows that adjustment of the target weight prescription after hospital discharge associates with improved 30-day postdischarge outcomes.

METHODS

This study was approved by the University of North Carolina at Chapel Hill Institutional Review Board (17–0011). Data from a large, for-profit dialysis organization with over 1500 outpatient dialysis clinics located across the United States were linked with the US Renal Data System at the patient level.

Study Design and Population

We used a retrospective cohort design with repeated intervals, each consisting of a 180-day baseline, a 30-day exposure assessment, and a 30-day follow-up period, to investigate the associations between postdialysis weight above the prescribed target weight and short-term clinical outcomes among individuals receiving maintenance hemodialysis at the dialysis organization from 2010 to 2012. Study intervals were indexed to equilibrated kt/v (eKt/V) measurement dates to promote consistency with the planned Centers of Medicare and Medicaid ESRD Quality Incentive Program ultrafiltration rate reporting measure.[6] Patients entered the cohort at the time of their first eligible eKt/V measurement during the study period, and subsequent intervals were indexed to later eKt/V measurements. Individual study intervals were constructed, such that (*1*) the exposure period began on the day after the indexing eKt/V measurement, (*2*) the follow-up period began immediately after the end of the exposure period, and (*3*) the baseline period for covariate ascertainment began 180 days before the start of the exposure period (Figure 1A). Within individuals, all exposure/follow-up periods occurring across time were discrete (*i.e.*, did not overlap). However, baseline periods of study intervals occurring later in time could overlap with prior intervals as long as their associated exposure/follow-up periods did not overlap (Supplemental Figure 1).[7]

The study population was composed of Medicare-enrolled, prevalent hemodialysis patients who had at least one eKt/V measurement between January 1, 2010 and December 31, 2012. We studied a prevalent population to minimize confounding from residual kidney function and other dynamic clinical features in the first year of dialysis. Among eligible individuals, baseline/exposure/follow-up intervals were excluded if patients (*1*) had a dialysis vintage <1 year at the time of the index eKt/V measurement, (*2*) were <18 years of age, (*3*) received home hemodialysis or peritoneal dialysis during the baseline or exposure period, (*4*) received fewer than six center-based hemodialysis treatments during the exposure period, (*5*) did not have continuous Medicare Part A/B coverage during the baseline and exposure periods, (*6*) experienced frequent postdialysis weight below the prescribed target weight during the exposure period (postdialysis weight >1.0 kg below target weight in ≥30% of treatments),[3] or (*7*) had a hospital admission that extended from the exposure period into the follow-up period. Additionally, within individual patients, potential study intervals occurring later in time were excluded if their associated exposure/follow-up periods would overlap with the exposure/follow-up period of a previously included interval.

Study Exposure, Outcomes, and Covariates

The exposure of interest was postdialysis weight above the prescribed target weight. In primary analyses, patients were classified as failing to achieve target weight if their postdialysis weight was >1.0 kg above their prescribed target weight in ≥30% of exposure period hemodialysis treatments. Patients with a postdialysis weight >1.0 kg above their target weight in <30% of exposure period treatments served as the referent group. In secondary analyses, we considered (*1*) alternative

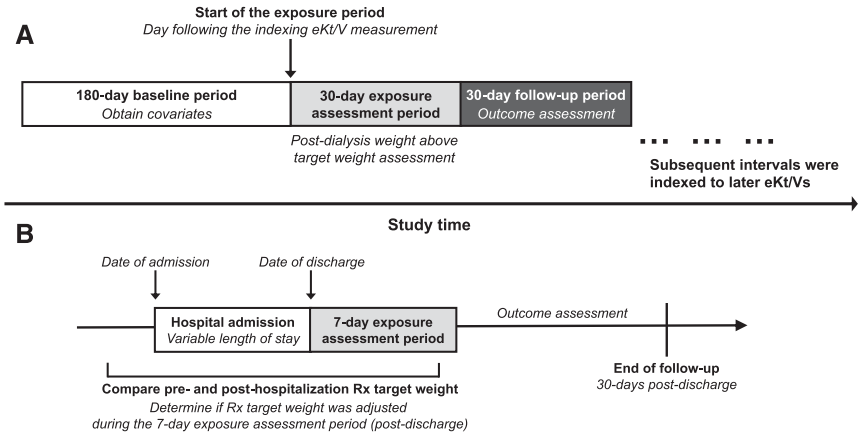

Figure 1. Study designs. (A) In primary and secondary analyses, a retrospective cohort design with repeated intervals, each consisting of a 180-day baseline, a 30-day exposure assessment and a 30-day follow-up period was used. Exposure periods were anchored on eKt/V measurements occurring during the study period. This figure illustrates a single study interval; individuals could contribute multiple study intervals to analyses. Individual study intervals were constructed such that the: 1) exposure period began on the day after the indexing eKt/V measurement; 2) follow-up period began immediately after the end of the exposure period; and 3) baseline period for covariate ascertainment began 180 days prior to the start of the exposure period. (B) The study design for *post hoc* analyses involved identifying hospitalization events that occurred during 30-day follow-up intervals in the primary study. Exposure periods were anchored on hospital discharge dates. This figure illustrates a single study interval; individuals could contribute multiple study intervals to analyses. For each eligible hospitalization event the: 1) 7-day exposure period began on the day following hospital discharge; and 2) the follow-up period began immediately after the end of the exposure period and continued up to day 30 post-hospitalization. eKt/V, equilibrated kt/v; Rx, prescribed.

binary exposures using different weight thresholds, including postdialysis weights >1.5, >2.0, and >2.5 kg above the prescribed target weight in ≥30% versus <30% of exposure period treatments; (*2*) a multilevel categorical exposure parameterized as <5% (referent), 5%–29%, 30%–49%, and ≥50% of exposure period treatments with a postdialysis weight >1.0 kg above the prescribed target weight; and (*3*) a mean-based exposure comparing individuals with an average postdialysis weight minus prescribed target weight of >1.0 versus ≤1.0 kg during the exposure period.

Our primary study outcomes included short-term (7-, 14-, and 30-day) (*1*) ED visits[8] and (*2*) inpatient hospitalizations (all-cause, cardiovascular, and volume related).[9,10] Secondary outcomes included short-term all-cause and cardiovascular mortality.[9] All study outcomes were assessed separately, and their definitions are provided in Supplemental Table 1.

Covariates were identified in each eligible 180-day baseline period and included demographic characteristics, comorbid conditions, laboratory data, dialysis treatment parameters, and metrics of health care utilization (Supplemental Table 2). Missing baseline laboratory variables were imputed using the Markov Chain Monte Carlo method with ten imputations.[11] All baseline covariates were included in the imputation.

Statistical Analyses

All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). Baseline characteristics were described across individuals who did and did not experience frequent postdialysis weight >1.0 kg above prescribed target weight as count (percentage) for categorical variables and mean±SD for continuous variables. Baseline covariate distributions were compared using standardized differences. A standardized difference >10.0% represents an imbalance between exposure groups.[12]

Across all analyses, we used Kaplan–Meier methods to estimate (*1*) risk differences (RDs), an absolute effect measure (null value =0.00%); and (*2*) risk ratios, a relative effect measure (null value =1.00).[7,13] To assess the relationship between failure to achieve target weight and the risk of short-term ED visits and hospitalizations, we estimated the 30-day cumulative incidence function of each outcome within each exposure group using the complement of the Kaplan–Meier estimator. We then estimated 7-, 14-, and 30-day RDs and risk ratios from these cumulative incidence functions. To account for the within-person correlation of the repeated measures (*i.e.*, multiple intervals per patient), we obtained 95% confidence intervals (95% CIs) using a cluster-based bootstrap procedure[14] on the basis of 250 resamples. Inverse probability of exposure (IPE) weighting was used for confounding control. We used multivariable logistic regression to calculate the predicted probability (*i.e.*, propensity score) of exposure as a function of baseline covariates. Propensity scores were then used to generate IPE weights.[15] Statistical adjustment was performed by applying IPE weights to the Kaplan–Meier estimator. Across each study interval, patients surviving the exposure period were followed forward in historical time to the first occurrence of a study outcome or censoring event. Censoring

events included (*1*) kidney transplantation, (*2*) dialysis modality change, (*3*) recovery of kidney function, (*4*) loss of Medicare Part A/B coverage, (*4*) lost to follow-up, and (*5*) end of the specified follow-up period (7, 14, or 30 days). In hospitalization analyses, death was treated as an additional censoring event. We also calculated incidence rate differences per 100 person-years, an absolute effect measure (null value =0.00), by subtracting outcome rates in the (−) failure to achieve target weight group from outcome rates in the (+) failure to achieve target weight group.[16] Finally, to assess the robustness of our primary study findings, we evaluated the failed target weight achievement-hospital encounter associations among individuals with and without exposure period target weight adjustments.

Post Hoc Analyses

We conducted *post hoc* analyses to explore the potential benefit of adjusting prescribed target weight immediately after inpatient hospitalizations. Among individuals who experienced an all-cause hospitalization during follow-up in our primary study, we evaluated the association between prescribed target weight adjustment within 7 days of hospital discharge (versus not) and the occurrence of 30-day ED visits, hospital readmissions, and a composite outcome of an ED visit, hospitalization, or death (Figure 1B, Supplemental Figure 2). For each eligible hospitalization, the day after hospital discharge was designated as the start of the 7-day exposure assessment period. Study follow-up began immediately after the end of the exposure period and continued up to day 30 posthospitalization. In addition to the covariates used in primary analyses, we adjusted *post hoc* analyses for length of hospital stay and primary hospitalization cause (cardiovascular, infectious, or other).

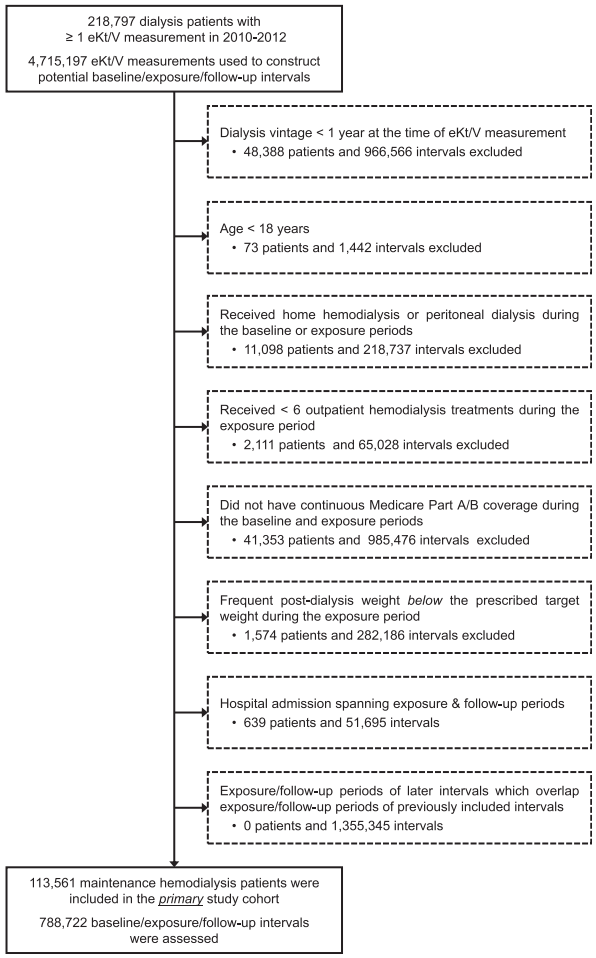

Figure 2. Flow diagram depicting the assembly of the primary cohort. eKt/V, equilibrated kt/v.

RESULTS

Study Cohort Characteristics

Figure 2 displays a flow diagram of study cohort selection. A total of 113,561 patients on hemodialysis contributed 788,722 intervals (7.0±4.5 intervals per patient) to analyses. Individuals underwent an average of 12.4±1.5 treatments during exposure assessment periods. Overall, study patients had an average age of 61.1±14.8 years, 45.1% were female, 42.4% were black, and the most common ESRD cause was diabetes (44.5%).

Baseline characteristics of the primary cohort stratified by target weight achievement status (postdialysis weight >1.0 kg above the prescribed target weight in ≥30% and <30% of exposure period treatments) are presented in Table 1. Individuals who experienced postdialysis weights above the prescribed target weight more (versus less) frequently during exposure periods were younger and had larger body sizes, a greater cardiovascular disease burden, shorter delivered dialysis treatment times, larger interdialytic weight gains, and more missed outpatient hemodialysis treatments. After IPE weighting, all baseline covariates were well balanced between exposure groups (standardized differences <10.0%).

Primary Analyses

In primary analyses, we evaluated the associations between failed target weight achievement and 30-day hospital encounters using a binary exposure variable. During the exposure period, the median [quartile 1, quartile 3] postdialysis weight minus target weight was 1.3 [0.5, 2.4] kg among patients who had a postdialysis weight >1.0 kg above target weight in ≥30% compared with 0.0 [−0.4, 0.4] kg among patients who had a postdialysis weight >1.0 kg above target weight in <30% exposure period treatments. Experiencing a postdialysis weight >1.0 kg above target weight in ≥30% (versus <30%) of exposure period treatments was associated with higher 7-, 14-, and 30-day risks of ED visits and hospitalizations. The 30-day adjusted RDs (95% CIs) were 2.13% (95% CI, 2.00% to 2.32%) for ED visits and 1.47% (95% CI, 1.34% to 1.62%) for all-cause hospitalizations. Thus, failing to achieve target weight (versus not) was associated with 21 excess ED visits and

Table 1. Baseline characteristics of individuals experiencing postdialysis weight >1.0 kg above prescribed target weight in ≥30% versus <30% of exposure period treatments

Characteristic	Unweighted			Weighted		
	Postdialysis Weight >1.0 kg above Target Weight during the Exposure Period		Standardized Difference, %[a]	Postdialysis Weight >1.0 kg above Target Weight during the Exposure Period		Standardized Difference, %[a]
	≥30% of Treatments, *n*=234,102	<30% of Treatments, *n*=554,620		≥30% of Treatments, *n*=232,716	<30% of Treatments, *n*=555,520	
Age, yr	59.0±14.6	62.0±14.8	20.7	61.2±14.8	61.2±14.8	0.1
Women	107,579 (46.0)	248,399 (44.8)	2.3	105,163 (45.2)	251,151 (45.2)	0.0
Race			6.2			0.6
White	117,371 (50.1)	292,493 (52.7)		120,559 (51.8)	288,521 (51.9)	
Black	104,189 (44.5)	229,884 (41.4)		99,217 (42.6)	235,559 (42.4)	
Other	12,542 (5.4)	32,243 (5.8)		12,939 (5.6)	31,439 (5.7)	
Hispanic	40,066 (17.1)	95,570 (17.2)	0.3	39,839 (17.1)	95,377 (17.2)	0.1
Cause of ESRD			13.7			0.3
Diabetes	115,433 (49.3)	235,842 (42.5)		104,082 (44.7)	247,710 (44.6)	
Hypertension	63,533 (27.1)	170,722 (30.8)		68,885 (29.6)	164,849 (29.7)	
Glomerular disease	24,977 (10.7)	66,229 (11.9)		26,766 (11.5)	64,116 (11.5)	
Other	30,159 (12.9)	81,827 (14.8)		32,982 (14.2)	78,845 (14.2)	
Dialysis vintage, yr			4.8			0.6
1.0–1.9	46,772 (20.0)	100,705 (18.2)		43,163 (18.5)	103,799 (18.7)	
2.0–3.9	67,688 (28.9)	160,790 (29.0)		66,970 (28.8)	160,774 (28.9)	
≥4.0	119,642 (51.1)	293,125 (52.9)		122,583 (52.7)	290,947 (52.4)	
History of a prior kidney transplant	16,581 (7.1)	41,924 (7.6)	1.8	17,278 (7.4)	41,166 (7.4)	0.1
Body mass index, kg/m^2			25.3			0.4
<18.5	6815 (2.9)	20,905 (3.8)		8337 (3.6)	19,646 (3.5)	
18.5–24.9	67,713 (28.9)	205,804 (37.1)		81,127 (34.9)	192,824 (34.7)	
25.0–29.9	63,469 (27.1)	164,421 (29.6)		66,961 (28.8)	160,337 (28.9)	
≥30.0	96,105 (41.1)	163,490 (29.5)		76,292 (32.8)	182,713 (32.9)	
Ischemic heart disease	75,683 (32.3)	150,146 (27.1)	11.5	67,390 (29.0)	159,724 (28.8)	0.5
Heart failure	77,476 (33.1)	129,440 (23.3)	21.8	62,159 (26.7)	146,591 (26.4)	0.7
Hypertension	170,828 (73.0)	349,941 (63.1)	21.3	154,740 (66.5)	367,449 (66.1)	0.7
Diabetes	155,491 (66.4)	322,189 (58.1)	17.2	141,610 (60.9)	336,892 (60.6)	0.4
Malignancy	18,084 (7.7)	47,263 (8.5)	2.9	19,515 (8.4)	46,095 (8.3)	0.3
History of noncompliance[b]	13,099 (5.6)	13,855 (2.5)	15.8	8107 (3.5)	19,166 (3.5)	0.2
Albumin,[c] g/dl			16.5			0.8
≤3.0	8594 (3.7)	11,675 (2.1)		6251 (2.7)	14,637 (2.6)	
3.1–3.5	32,504 (13.9)	59,112 (10.7)		27,731 (11.9)	65,147 (11.7)	
3.6–4.0	110,949 (47.4)	255,785 (46.1)		108,276 (46.5)	258,059 (46.5)	
≥4.1	82,055 (35.1)	228,048 (41.1)		90,458 (38.9)	217,676 (39.2)	
Calcium,[c] mg/dl			10.4			0.4
≤8.4	43,847 (18.7)	82,481 (14.9)		37,160 (16.0)	88,968 (16.0)	
8.5–10.2	181,612 (77.6)	449,080 (81.0)		186,020 (79.9)	444,156 (80.0)	
≥10.3	8643 (3.7)	23,059 (4.2)		9535 (4.1)	22,396 (4.0)	
Phosphorus,[c] mg/dl			22.2			0.6
≤3.4	21,073 (9.0)	62,677 (11.3)		24,637 (10.6)	59,030 (10.6)	
3.5–5.5	114,487 (48.9)	317,257 (57.2)		126,630 (54.4)	303,638 (54.7)	
≥5.6	98,542 (42.1)	174,686 (31.5)		81,449 (35.0)	192,851 (34.7)	
Potassium,[c] mEq/L			14.6			0.2
≤3.9	16,506 (7.1)	51,316 (9.3)		20,011 (8.6)	47,772 (8.6)	
4.0–6.0	203,915 (87.1)	485,456 (87.5)		203,241 (87.3)	485,333 (87.4)	
≥6.1	13,681 (5.8)	17,848 (3.2)		9464 (4.1)	22,414 (4.0)	
Hemoglobin,[c] g/dl			8.2			0.4
≤9.4	18,333 (7.8)	32,057 (5.8)		15,142 (6.5)	35,757 (6.4)	
9.5–11.9	158,480 (67.7)	381,544 (68.8)		158,743 (68.2)	380,010 (68.4)	

Table 1. Continued

Characteristic	Unweighted			Weighted		
	Postdialysis Weight >1.0 kg above Target Weight during the Exposure Period		Standardized Difference, %[a]	Postdialysis Weight >1.0 kg above Target Weight during the Exposure Period		Standardized Difference, %[a]
	≥30% of Treatments, *n*=234,102	<30% of Treatments, *n*=554,620		≥30% of Treatments, *n*=232,716	<30% of Treatments, *n*=555,520	
≥12	57,289 (24.5)	141,019 (25.4)		58,831 (25.3)	139,753 (25.2)	
Transferrin saturation,[c] %			4.2			0.3
≤19	39,215 (16.8)	85,039 (15.3)		36,908 (15.9)	87,728 (15.8)	
20–29	88,517 (37.8)	209,354 (37.7)		87,964 (37.8)	209,720 (37.8)	
≥30	106,370 (45.4)	260,227 (46.9)		107,843 (46.3)	258,071 (46.5)	
Creatinine,[c] mg/dl			4.8			0.3
≤6.7	56,706 (24.2)	140,693 (25.4)		58,079 (25.0)	139,287 (25.1)	
6.8–8.5	57,280 (24.5)	140,693 (25.4)		58,454 (25.1)	139,510 (25.1)	
8.6–10.6	58,604 (25.0)	138,145 (24.9)		58,111 (25.0)	138,508 (24.9)	
≥10.7	61,512 (26.3)	135,089 (24.4)		58,071 (25.0)	138,215 (24.9)	
eKt/V<1.2	3743 (1.6)	4113 (0.7)	8.0	2361 (1.0)	5638 (1.0)	0.0
Vascular access			11.9			0.6
Fistula	145,596 (62.2)	363,740 (65.6)		149,365 (64.2)	357,969 (64.4)	
Graft	56,877 (24.3)	136,849 (24.7)		57,400 (24.7)	136,497 (24.6)	
Catheter	31,629 (13.5)	54,031 (9.7)		25,950 (11.2)	61,053 (11.0)	
Treatment time ≥240 min	50,415 (21.5)	97,027 (17.5)	10.2	43,344 (18.6)	103,870 (18.7)	0.6
Interdialytic weight gain, kg			57.3			0.0
≤1.9	32,338 (13.8)	164,915 (29.7)		57,493 (24.7)	138,637 (25.0)	
2.0–2.5	45,576 (19.5)	151,701 (27.4)		58,241 (25.0)	138,805 (25.0)	
2.6–3.3	62,187 (26.6)	134,825 (24.3)		58,436 (25.1)	138,780 (25.0)	
≥3.4	94,001 (40.2)	103,179 (18.6)		58,545 (25.2)	139,298 (25.1)	
Postdialysis weight, kg			27.4			0.0
≤64.3	47,813 (20.4)	149,380 (26.9)		58,587 (25.2)	139,242 (25.1)	
64.4–76.4	51,282 (21.9)	145,886 (26.3)		58,021 (24.9)	138,886 (25.0)	
76.5–92.0	57,712 (24.7)	139,472 (25.1)		58,254 (25.0)	138,858 (25.0)	
≥92.1	77,295 (33.0)	119,882 (21.6)		57,854 (24.9)	138,534 (24.9)	
Predialysis systolic BP, mm Hg			7.7			0.0
≤129	42,599 (18.2)	96,055 (17.3)		41,789 (18.0)	98,162 (17.7)	
130–149	76,266 (32.6)	192,410 (34.7)		78,824 (33.9)	188,988 (34.0)	
150–169	74,252 (31.7)	182,660 (32.9)		75,250 (32.3)	180,618 (32.5)	
≥170	40,985 (17.5)	83,495 (15.1)		36,853 (15.8)	87,752 (15.8)	
No. of hospital admissions[d]			30.8			0.0
0	121,583 (51.9)	362,690 (65.4)		141,050 (60.6)	339,835 (61.2)	
1–2	79,213 (33.8)	153,143 (27.6)		69,734 (30.0)	164,024 (29.5)	
≥3	33,306 (14.2)	38,787 (7.0)		21,932 (9.4)	51,661 (9.3)	
No. of missed dialysis treatments (unexcused)[e]			10.4			0.4
0	204,900 (87.5)	503,016 (90.7)		208,431 (89.6)	498,294 (89.7)	
1–2	18,551 (7.9)	31,374 (5.7)		14,984 (6.4)	35,347 (6.4)	
≥3	10,651 (4.5)	20,230 (3.6)		9301 (4.0)	21,879 (3.9)	

A total of 113,561 unique patients on hemodialysis contributed 788,722 intervals to the analysis. In each study interval, covariates were measured during the 180-day baseline period before the 30-day exposure period. Values are given as count (%) for categorical variables and mean±SD for continuous variables. eKt/V, equilibrated kt/v; No., number.

[a]A standardized difference >10.0% represents meaningful imbalance between groups.

[b]The claims-based definition of noncompliance included International Classification of Diseases, Ninth Revision discharge diagnosis code V15.81 (personal history of noncompliance with medical treatment, presenting hazards to health).

[c]Values were imputed using the Markov Chain Monte Carlo method using ten imputations when missing (albumin, *n*=216; calcium, *n*=216; creatinine, *n*=26,787; hemoglobin, *n*=13; phosphorus, *n*=140; potassium, *n*=214; and transferrin saturation, *n*=1059).[11]

[d]Number of inpatient hospitalizations during the entire 180-day baseline period.

[e]Number of missed hemodialysis treatments (unexcused) in the last 30 days of the 180-day baseline period.

15 excess all-cause hospitalizations per 1000 persons during the 30-day follow-up period. Analyses considering cause-specific hospitalizations (cardiovascular and volume related) yielded similar results (Supplemental Table 3, Table 2).

Prescribed target weight was adjusted in 277,294 (35.2%) exposure periods. A total of 136,776 exposure periods had at least one downward target weight adjustment, and a total of 164,488 exposure periods had at least one upward adjustment. Across all study intervals, the median [quartile 1, quartile 3] number of prescribed target weight adjustments during exposure periods was 0 [0, 1]. Sensitivity analyses considering individuals with and without changes in prescribed target weight (separately) during the exposure period generated results similar to those of our primary analyses (Supplemental Table 4).

Secondary Analyses

In secondary analyses, we evaluated the associations between failed target weight achievement and 30-day hospital encounters using alternative exposure specifications. First, we varied the weight threshold used to define postdialysis weight above the prescribed target weight ($>$1.5, $>$2.0, and $>$2.5 kg). As the weight threshold for exposure classification increased, the magnitude of the observed associations between postdialysis weight above the prescribed target weight and short-term hospital encounters also increased (Figure 3, Supplemental Table 5). Second, we considered failed target weight achievement as a multilevel categorical variable ($<$5% [referent], 5%–29%, 30%–49%, and $\geq$50% of exposure period dialysis treatments with a postdialysis weight $>$1.0 kg above the prescribed target weight). Failing to achieve prescribed target weight on a more frequent basis was associated with an incrementally greater risk of 30-day ED visits and hospitalizations (Table 3, Supplemental Table 6). Third, we assessed the association between having an average postdialysis weight minus target weight of $>$1.0 kg (versus $\leq$1.0 kg) during the exposure period and 30-day hospital encounters. Results were analogous to primary study findings (Supplemental Table 7).

Finally, we assessed the association between failed target weight achievement and mortality. Experiencing a postdialysis weight $>$1.0 kg above target weight in $\geq$30% (versus $<$30%) of exposure period treatments was associated with higher short-term all-cause and cardiovascular mortality (Supplemental Table 3).

Post Hoc Analyses

We conducted *post hoc* analyses to investigate the potential role of prescribed target weight adjustment in modifying posthospitalization outcomes. We examined the association between having (versus not having) a prescribed target weight adjustment within 7 days of hospital discharge and 30-day posthospitalization outcomes among individuals who experienced inpatient hospitalizations in our primary study cohort (44,460 patients on hemodialysis contributed 71,120 posthospitalization intervals). Individuals whose target weight was (versus was not) adjusted within 7 days of hospital discharge had lower risks of 30-day ED visits, all-cause hospitalizations, and the composite outcome of an ED visit, hospitalization, or death (Figure 4, Supplemental Table 8). On the basis of the estimated RDs, we computed the number needed to treat (95% CI) for each outcome. Target weight adjustment within

Table 2. Associations between postdialysis weight $>$1.0 kg above target weight in $\geq$30% versus $<$30% of exposure period treatments and 7-, 14-, and 30-day hospital encounters

Outcome	Postdialysis Weight >1.0 kg above Target Weight during the Exposure Period in ≥30% versus <30% of Treatments (ref.)		
	Adjusted Risk Difference, % (95% CI)	Adjusted Incidence Rate Difference per 100 person-yr (95% CI)	Adjusted Risk Ratio (95% CI)
All-cause ED visits			
7-d Follow-up	0.71 (0.61 to 0.82)	38.82 (33.68 to 44.86)	1.14 (1.12 to 1.17)
14-d Follow-up	1.24 (1.12 to 1.37)	35.62 (32.25 to 39.47)	1.14 (1.12 to 1.15)
30-d Follow-up	2.13 (2.00 to 2.32)	31.74 (29.76 to 34.53)	1.13 (1.12 to 1.14)
All-cause hospitalizations			
7-d Follow-up	0.43 (0.35 to 0.52)	23.19 (18.85 to 27.60)	1.14 (1.11 to 1.17)
14-d Follow-up	0.85 (0.73 to 0.95)	23.43 (20.27 to 26.38)	1.14 (1.13 to 1.16)
30-d Follow-up	1.47 (1.34 to 1.62)	20.46 (18.64 to 22.45)	1.13 (1.12 to 1.14)
Cardiovascular hospitalizations			
7-d Follow-up	0.11 (0.07 to 0.15)	5.70 (3.60 to 7.91)	1.12 (1.07 to 1.17)
14-d Follow-up	0.17 (0.12 to 0.24)	4.61 (3.24 to 6.45)	1.10 (1.07 to 1.14)
30-d Follow-up	0.31 (0.24 to 0.40)	3.95 (3.07 to 5.05)	1.09 (1.07 to 1.11)
Volume-related hospitalizations			
7-d Follow-up	0.06 (0.04 to 0.09)	3.11 (1.91 to 4.48)	1.17 (1.10 to 1.25)
14-d Follow-up	0.07 (0.04 to 0.11)	1.90 (1.00 to 2.92)	1.11 (1.05 to 1.17)
30-d Follow-up	0.15 (0.11 to 0.21)	1.90 (1.36 to 2.61)	1.11 (1.08 to 1.15)

Adjusted risk differences are percentages (%). The null value for a risk difference is 0.00%, the null value for an incidence rate difference is 0.00, and the null value for a risk ratio is 1.00. 95% CI, 95% confidence interval; ED, emergency department; ref., referent.

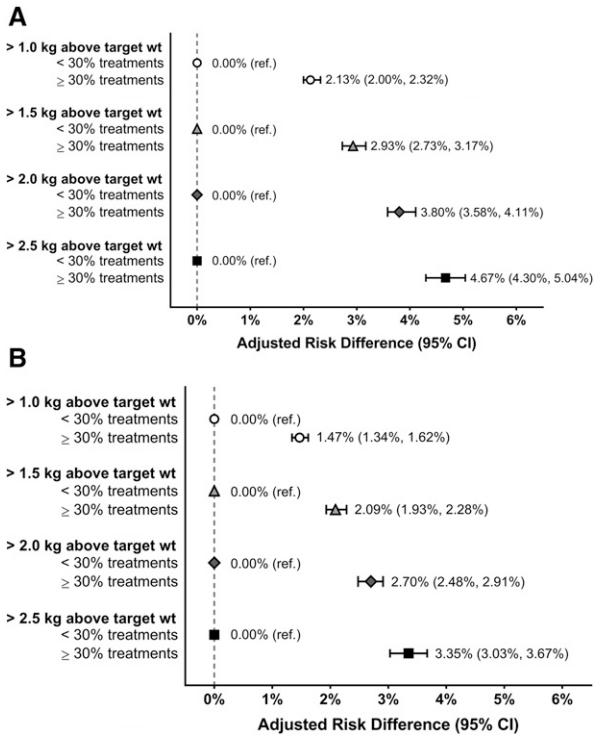

Figure 3. Associations between postdialysis weight above target weight in ≥30% versus <30% of exposure period treatments and 30-day all-cause hospital encounters across varying kilogram thresholds of failed target weight achievement. (A) Depicts the association between post-dialysis weight above the prescribed target weight in ≥30% versus <30% of exposure period treatments and 30-day all-cause ED visits across varying kilogram thresholds of failed target weight achievement. (B) Depicts the association between post-dialysis weight above the prescribed target weight in ≥30% versus <30% of exposure period treatments and 30-day all-cause hospitalizations across varying kilogram thresholds of failed target weight achievement. The null value for a risk difference is 0.00%. As the weight threshold for failure to attain target weight increased, the magnitude of the observed associations between postdialysis weight above the prescribed target weight and short-term hospital encounters also increased. ED, emergency department; ref., referent; wt, weight.

7 days of hospital discharge in 114 (95% CI, 60 to 512) individuals may prevent one 30-day ED visit postdischarge, 61 (95% CI, 44 to 110) individuals may prevent one 30-day readmission, and 49 (95% CI, 35 to 74) individuals may prevent one 30-day composite outcome event (an ED visit, hospitalization, or death).

DISCUSSION

To our knowledge, this is the first study evaluating the association between failed target weight achievement and short-term clinical outcomes among individuals receiving maintenance hemodialysis. We found that experiencing a postdialysis weight >1.0 kg above the prescribed target weight in ≥30% (versus <30%) of exposure period treatments was associated with higher risks of 7-, 14-, and 30-day ED visits and hospitalizations (all-cause, cardiovascular, and volume related). The observed associations were (*1*) more potent when we defined failure to achieve target weight using larger postdialysis weight above prescribed target weight thresholds, (*2*) incremental when different frequencies of failed target weight achievement were considered, and (*3*) consistent when we considered failed target weight achievement as a mean-based exposure. Finally, our *post hoc* analyses showed that adjustment of the target weight prescription after hospital discharge was associated with improved 30-day postdischarge outcomes.

Existing observational evidence suggests that failed target weight achievement is associated with increased long-term mortality. In a prospective study of 182 prevalent Italian hemodialysis patients, Movilli *et al.*[17] reported that an average postdialysis weight of ≥0.3 kg (versus <0.3 kg) above prescribed target was associated with greater 3-year all-cause and cardiovascular mortality. In a retrospective cohort study of 10,785 patients on hemodialysis from the United States, Flythe *et al.*[3] found that individuals who experienced postdialysis weights >2.0 kg above prescribed target weight in ≥30% (versus <30%) of dialysis treatments had higher rates of all-cause and cardiovascular mortality over a median follow-up time of 2.1 years. Both of these studies considered long-term mortality outcomes, and neither examined the relationship of failed target weight achievement and subsequent hospital encounters.

To expand on this evidence base, we used a modern epidemiologic study design where individual patients could contribute multiple baseline/exposure/follow-up intervals to analyses and evaluated the association between postdialysis weight above target weight and short-term clinical outcomes. Recently, a National Institutes of Health working group called out the historical underemphasis of short-term clinical risk prediction,[18] and others have noted that dynamic clinical factors (*e.g.*, biochemical indices, interdialytic weight gain, and ultrafiltration volume) tend to be stronger predictors of near- versus long-term clinical events.[19] In addition, short-term outcome risk prediction is becoming increasingly important in today's health care environment, where cost containment and population health management are increasingly valued. Health care models, such as ESRD Seamless Care Organizations and other integrated health care groups, strive to reduce costs by identifying and intervening in individuals who have the highest risk for cost-intensive health care services. Reductions in hospitalizations and 30-day readmissions have been a major focus in this effort.[20,21] Our findings suggest that dialysis clinic personnel could use frequent failed target weight achievement as a clinical marker to identify individuals at risk for imminent hospital encounters. Our *post hoc* analyses offer potential support for this premise. Individuals who had their target weights adjusted after hospitalizations were at lower risk for a 30-day hospital readmission compared with individuals

Table 3. Associations between postdialysis weight >1.0 kg above target weight during the exposure period and 30-day hospital encounters using varied frequency thresholds for failed target weight achievement

Outcome	Postdialysis Weight >1.0 kg above Target Weight during the Exposure Period			
	<5% of Treatments	5%–29% of Treatments	30%–49% of Treatments	≥50% of Treatments
All-cause ED visits				
Adjusted risk difference, % (95% CI)	0.00 (ref.)	1.19 (1.00 to 1.37)	1.98 (1.73 to 2.24)	3.07 (2.82 to 3.34)
Adjusted incidence rate difference (95% CI)	0.00 (ref.)	17.52 (14.86 to 20.25)	29.04 (25.71 to 33.12)	45.96 (42.66 to 49.99)
Adjusted risk ratio (95% CI)	1.00 (ref.)	1.07 (1.06 to 1.09)	1.12 (1.11 to 1.14)	1.19 (1.17 to 1.21)
All-cause hospitalizations				
Adjusted risk difference, % (95% CI)	0.00 (ref.)	0.69 (0.52 to 0.83)	1.20 (0.98 to 1.41)	2.08 (1.90 to 2.29)
Adjusted incidence rate difference (95% CI)	0.00 (ref.)	9.41 (7.13 to 11.60)	16.45 (13.80 to 19.20)	28.89 (25.83 to 31.91)
Adjusted risk ratio (95% CI)	1.00 (ref.)	1.06 (1.05 to 1.08)	1.11 (1.09 to 1.13)	1.19 (1.17 to 1.21)
Cardiovascular hospitalizations				
Adjusted risk difference, % (95% CI)	0.00 (ref.)	0.16 (0.04 to 0.23)	0.21 (0.09 to 0.35)	0. 45 (0.33 to 0.58)
Adjusted incidence rate difference (95% CI)	0.00 (ref.)	1.97 (0.81 to 3.16)	2.64 (0.93 to 4.34)	5.70 (4.38 to 7.18)
Adjusted risk ratio (95% CI)	1.00 (ref.)	1.04 (1.01 to 1.07)	1.06 (1.03 to 1.10)	1.13 (1.09 to 1.16)
Volume-related hospitalizations				
Adjusted risk difference, % (95% CI)	0.00 (ref.)	0.00 (−0.07 to 0.06)	0.03 (−0.05 to 0.11)	0.21 (0.13 to 0.28)
Adjusted incidence rate difference (95% CI)	0.00 (ref.)	0.04 (−0.62 to 0.78)	0.35 (−0.57 to 1.39)	2.61 (1.68 to 3.64)
Adjusted risk ratio (95% CI)	1.00 (ref.)	1.00 (0.95 to 1.04)	1.02 (0.96 to 1.08)	1.15 (1.09 to 1.21)

Adjusted risk differences are percentages (%). Adjusted incidence rate differences are per 100 person-yr. The null value for a risk difference is 0.00%, the null value for an incidence rate difference is 0.00, and the null value for a risk ratio is 1.00. ED, emergency department; 95% CI, 95% confidence interval; ref., referent.

who did not. Such easily recognized risk markers for volume-related hospital encounters are especially important given the limited availability of objective volume status measurement tools in United States outpatient dialysis clinics and the substantial costs associated with volume-related hospitalizations.[2]

Although our findings suggest that frequent failed target weight achievement may be a clinical marker for an impending hospital encounter, we cannot assess whether the observed risk stems from extracellular volume overload, inadequate volume management, or both. Incorporation of objective volume measurement tools into routine clinical practice to help make this distinction is a critical unmet need in hemodialysis patient care. However, in the absence of objective measures, surrogate risk markers may have clinical utility. Occasional postdialysis-target weight mismatch is expected (*e.g.*, in patients with fluctuating health status, and during intentional target weight challenge). Conversely, frequent postdialysis weight-target weight mismatch likely suggests that a clinical or care process problem exists. Typically, risk stratification approaches rely on computationally complex algorithms performed at the centralized, corporate dialysis provider level.[20] In contrast, failed target weight achievement is a simple clinical marker that can be easily identified by a range of clinical care team members, including patent care technicians, nurses, dietitians, medical providers, and patients, rendering it a potentially attractive risk stratification tool that can be used to quickly focus attention to patients at imminent risk for hospital encounters.

Our study has many strengths. First, we selected a study design with repeated intervals, each consisting of separate baseline, exposure, and follow-up periods. Repeatedly ascertaining each patient's baseline characteristics and exposure status across time ensured that the most current clinical information was considered when assessing failed target weight achievement—short-term outcome associations. Utilization of this design also minimizes biases common to longitudinal observational studies, such as time-varying confounding, immortal person time bias, and selection bias. Second, we used a detailed data source that enabled us to account for numerous demographic, clinical, and dialysis treatment–related variables in our analyses. Covariate imbalances between exposure groups were diminished after IPE weighting. Third, we defined our study exposure,

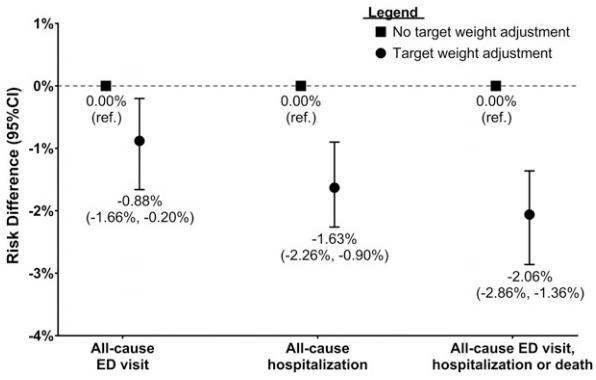

Figure 4. Associations between having versus not having a prescribed target weight adjustment within 7 days of hospital discharge and 30-day posthospitalization outcomes. The null value for a risk difference is 0.00%. Individuals whose target weight was (versus was not) adjusted within 7 days of hospital discharge had lower risks of 30-day ED visits, all-cause hospitalizations, and the composite outcome. 95% CI, 95% confidence interval; ED, emergency department; ref., referent.

postdialysis weight above the prescribed target weight, using several approaches. Regardless of exposure specification, failure to achieve target weight was consistently associated with a higher risk of short-term adverse outcomes.

Our results must be considered in the context of study limitations. First, our study was observational, and it is possible that residual confounding may exist. To minimize confounding from difficult to measure factors, such as ambient health status, we controlled for variables, including albumin, phosphorus, creatinine, and a history of noncompliance, in our analyses. Second, target weights were prescribed by treating nephrologists in the setting of routine clinical practice. The approach to target weight estimation and adjustment may have varied across clinical providers. Related, target weight changes are made in response to a variety of clinical scenarios and likely have varying consequences. Although we did not assess the association between target weight adjustment and outcomes in our primary analyses, the findings from our *post hoc* analyses suggest that target weight adjustment soon after hospital discharge associates with improved posthospitalization outcomes. Third, comorbid condition designations were based upon the International Classification of Diseases, Ninth Revision diagnosis codes. Comorbidities not requiring a health care encounter during the 180-day baseline period may have been missed. Fourth, our study included adult, center-based hemodialysis patients with a dialytic vintage of 1 year or longer. Our results may not extrapolate to excluded populations, such as incident hemodialysis, home hemodialysis or peritoneal dialysis patients.

In summary, we found that frequent postdialysis weight $\geq$1.0 kg above the prescribed target weight was associated with short-term ED visits and hospitalizations. We also observed that target weight adjustment in the period immediately after hospital discharge was associated with a reduced risk of 30-day readmissions. Recurrent failed target weight achievement may represent an easily identifiable risk maker for impending hospital encounters among individuals receiving maintenance hemodialysis. Prospective studies testing clinical monitoring programs that use failed target weight achievement as a clinic-based risk stratification tool for the identification of individuals at high risk for impending hospital encounters are warranted.

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Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

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DISCLOSURES

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