

# Standardized Dialysate Temperature of 36 Degrees Celsius: Association with Clinical Outcomes

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### Introduction

- Dialysate cooling below the current standard temperature of 37°C has been proposed as a means to reduce intradialytic hypotension and thereby mitigate the hemodynamic insults associated with dialysis.
- Numerous small trials using dialysate temperatures of 35-35.5°C support this idea, but have also found that patients are more likely to experience discomfort with cooler dialysate.<sup>1</sup>
- Individualized dialysate cooling to 0.5°C below a patient's pre-dialysis body temperature has been shown to preserve brain microarchitecture and cardiac function.<sup>2,3,4</sup>
- Such individualization is unlikely to be practicable at scale.
- We hypothesized that a dialysate temperature of 36°C (dT36), which may be more tolerable to patients than lower dialysate temperatures, might be associated with superior clinical outcomes compared to 37°C (dT37).
- In order to minimize opportunities for confounding on the basis of hemodynamic instability during dialysis, patients' exposure status was based upon the order for their first-ever dialysis treatment.

# Objective

To understand the association between a dialysate temperature of 36°C (vs 37°C) and clinical outcomes

### Methods

- All study data were taken from the electronic health record of a large dialysis organization (LDO).
- To minimize selection bias, we studied a cohort of **incident patients** who received their first-ever dialysis treatment at the LDO, and based exposure status (ie dT36 vs dT37) on the prescribed dialysate temperature for this first-ever treatment.
- We considered adult patients who, between Jan 2011 and Dec 2013 initiated in-center hemodialysis as a first treatment modality for end-stage renal disease, had not previously received dialysis care elsewhere, were not US Veterans' Affairs beneficiaries, and could be assigned to an exposure group.
- Exposure status (dT36 or dT37) was assigned based on the treatment order for the patient's first-ever dialysis treatment.
- dT36 patients were nearest neighbor matched 1:5 without replacement to dT37 controls based on propensity score, which was estimated using a logistic model.
- Patients were followed until death, loss to follow-up, cross-over, 24 months from index date, or end of study (30 June 2015).

- Crossover was defined as a calendar month in which the prescribed dialysate temperature was

consistent with the patient's exposure group for <80% of treatments.</li>
 Death, hospitalization, and missed dialysis treatments were considered as incidence rates. Intradialytic hypotension (defined using the Flythe criterion<sup>5</sup>) was considered as the percent of treatments affected. Formal comparisons were made using mixed linear models with a fixed effects term for exposure group and random effects intercepts for patients. Models were specified as Poisson (death), negative binomial

(hospitalizations and missed treatments) and beta regression (intradialytic hypotension).

## Results

Table 1: Characteristics of Patients by Dialysate Temperature (Prior to Matching)

	Overall N=18,013	37°C N=17,700	36°C N=313	Standardized Difference	P
Age, years, mean ± SD	63.7 ± 14.8	63.7 ± 14.7	65.0 ± 14.9	8.4%	0.14
Sex, female, %	43.3	43.4	40.3	-6.3%	0.27
Race, %					<0.001
White	52.8	52.6	65.5	26.5%	
Black	23.9	24.0	19.8	-10.1%	
Hispanic	13.5	13.6	4.8	-30.9%	
Other	9.8	9.8	9.9	0.2%	
Etiology of ESRD, %					< 0.001
Diabetes	43.4	43.4	44.4	2.1%	
Hypertension	29.5	29.7	15.7	-34.1%	
Other	27.1	26.9	39.9	27.9%	
Vascular access, %					0.22
Arteriovenous fistula	34.8	34.9	30.7	-8.9%	
Arteriovenous graft	6.5	6.5	5.8	-3.0%	
Central venous catheter	58.8	58.7	63.6	10.1%	
Diabetes, %	63.1	63.1	63.3	0.4%	0.94
Heart failure, %	12.3	12.3	15.0	7.9%	0.15
Coronary artery disease, %	11.9	11.8	16.0	12.0%	0.03
Cerebrovascular disease, %	1.6	1.6	2.2	5.0%	0.34
Peripheral vascular disease, %	4.6	4.6	7.3	11.7%	0.02
Albumin, g/dL	$3.6 \pm 0.5$	$3.6 \pm 0.5$	$3.5 \pm 0.5$	-12.9%	0.02
Creatinine, mg/dL	$5.5 \pm 2.2$	$5.5 \pm 2.2$	5.5 ± 2.1	-1.2%	0.84
Hemoglobin, g/dL	10.1 ± 1.2	10.1 ± 1.2	10.3 ± 1.3	15.5%	0.005
Kt/V	$1.4 \pm 0.4$	$1.4 \pm 0.4$	$1.4 \pm 0.3$	-1.4%	0.82
nPCR, g/kg/day	$0.78 \pm 0.27$	$0.78 \pm 0.27$	0.81 ± 0.29	11.0%	0.05

Abbreviations: ESRD, end stage renal disease; nPCR, normalized protein catabolic rate; SD, standard deviation

# Table 2: Characteristics of Patients by Dialysate Temperature (Matched Cohort)

	Overall N=1878	37°C N=1565	36°C N=313	Standardized Difference (%)	P	
Age, years, mean ± SD	64.8 ± 14.6	64.7 ± 14.6	65 ± 14.9	1.4	0.82	
Sex, female, %	37.8	37.3	40.3	6.2	0.32	
Race					0.91	
White	67.0	67.3	65.5	-3.8		
Black	19.0	18.8	19.8	2.4		
Hispanic	4.2	4.1	4.8	1.3		
Other	9.8	9.8	9.9	0.4		
Etiology of ESRD, %					0.73	
Diabetes	44.3	44.3	44.4	0.3		
Hypertension	17.1	17.4	15.7	-4.6		
Other	38.6	38.3	39.9	3.3		
Vascular access, %					0.98	
Arteriovenous fistula	30.2	30.1	30.7	1.3		
Arteriovenous graft	5.7	5.7	5.8	0.3		
Central venous catheter	64.1	64.2	63.6	-1.3		
Diabetes, %	62.6	62.4	63.3	1.7	0.78	
Heart failure, %	15.0	15.0	15.0	0	>0.99	
Coronary artery disease, %	15.6	15.5	16.0	1.2	0.84	
Cerebrovascular disease, %	2.7	2.7	2.2	-3.3	0.61	
Peripheral vascular disease, %	6.9	6.8	7.3	2	0.74	
Albumin, g/dL	$3.5 \pm 0.5$	$3.5 \pm 0.5$	$3.5 \pm 0.5$	-4.7	0.45	
Creatinine, mg/dL	5.4 ± 2.1	5.4 ± 2.1	5.5 ± 2.1	6.0	0.35	
Hemoglobin, g/dL	10.2 ± 1.3	10.2 ± 1.2	10.3 ± 1.3	13.2	0.03	
Kt/V	1.4 ± 0.4	1.4 ± 0.4	1.4 ± 0.3	0.9	0.90	
nPCR, g/kg/day	$0.78 \pm 0.28$	$0.77 \pm 0.27$	0.81 ± 0.29	12.6	0.04	
Abbreviations: ESRD, end stage renal disease; nPCR, normalized protein catabolic rate; SD, standard deviation						

#### Baseline Characteristics

- Within the overall cohort, patients prescribed a dialysate temperature of 36°C were older, less likely to be black or Hispanic, less likely to have hypertension as the etiology of ESRD, more likely to have peripheral vascular disease, and more likely to have coronary artery disease (Table 1).
- In the matched cohort, the two groups were well balanced (Table 2).
- All subsequent analyses were performed in the matched cohort to promote fair comparisons.

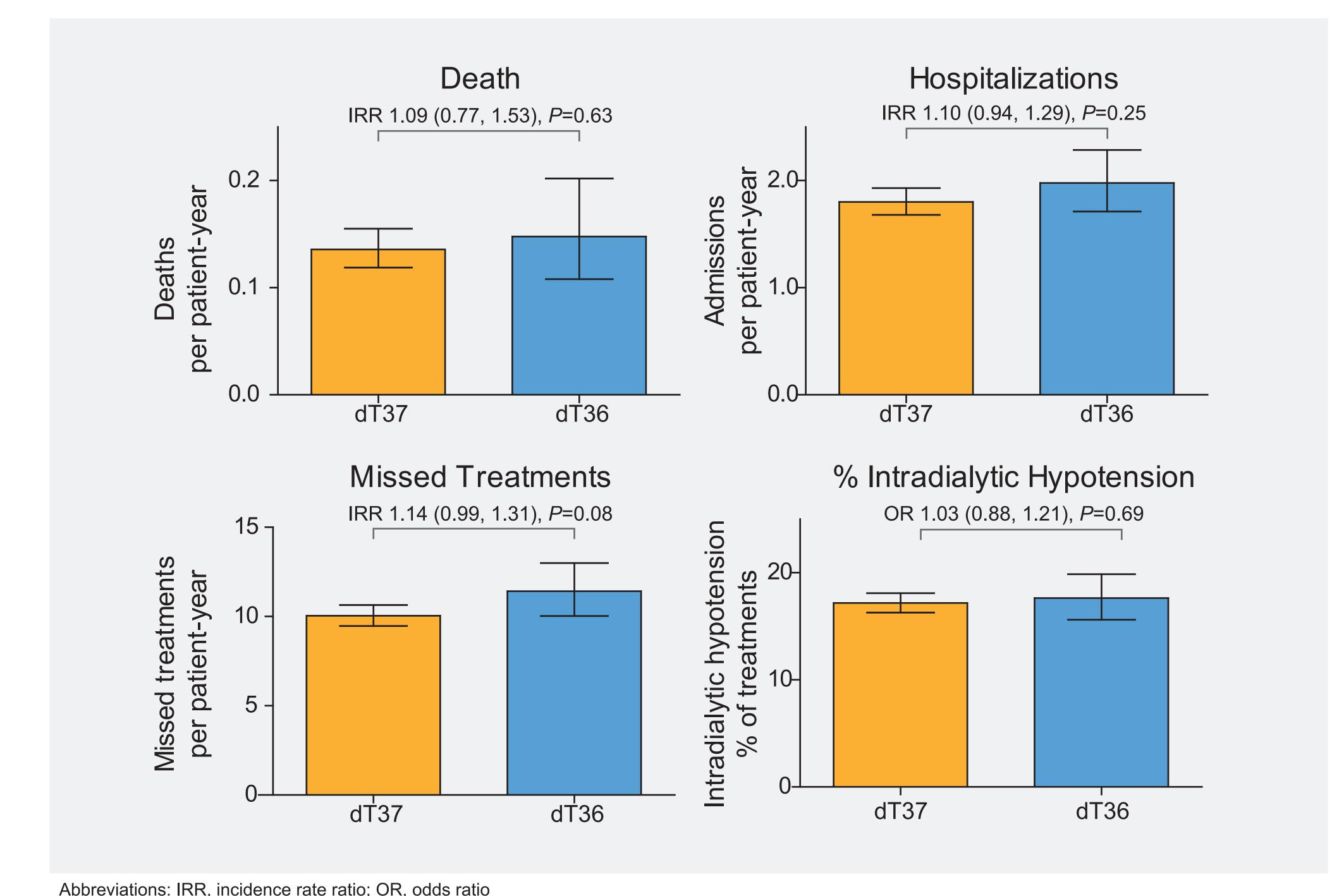
#### **Primary Outcomes**

- Rates of death, hospitalization, and missed treatments, and the percent of treatments affected by intradialytic hypotension were not statistically significantly different between dT36 and dT37 patients (Figure 1).
- Nominal risk was greater for dT36 patients (IRR or OR >1 for each outcome).

#### Secondary Outcomes

• Post-dialysis blood pressure was slightly higher, and ultrafiltration rate slightly lower, among dT36 vs dT37 patients. No other statistically significant differences were observed (Table 3).

# Figure 1: Comparison of Primary Outcomes by Dialysate Temperature



# Temperature 27°C 26°C OR (05% C

Table 3: Comparison of Secondary Outcomes by Dialysate

	37°C	36°C	OR (95% CI)	P				
Premature cessation of treatment, %	10.0 (9.4, 10.6)	10.7 (9.3, 12.4)	1.08 (0.91, 1.29)	0.36				
	37°C	36°C	Mean diff (95% CI)	P				
<b>IDWG</b> , kg	2.1 (2.0, 2.1)	2.1 (2.0, 2.2)	-0.01 (-0.14, 0.11)	0.82				
IDWG, % body weight	2.6 (2.6, 2.7)	2.6 (2.5, 2.7)	0 (0, 0)	0.62				
Ultrafiltration Volume, L	2.1 (2.1, 2.2)	2.1 (2.0, 2.2)	0 (-0.13, 0.12)	0.96				
Ultrafiltration Rate, mL/hour/kg	7.9 (7.7, 8.1)	7.4 (7.0, 7.8)	-0.51 (-0.97, -0.05)	0.03				
Pre-dialysis Blood Pressure, mmHg	145.1 (144.0, 146.2)	144.5 (142.1, 147.0)	-0.5 (-3.2, 2.2)	0.71				
Post-dialysis Blood Pressure, mmHg	136.6 (135.7, 137.5)	139.1 (136.8, 141.4)	2.5 (0.1, 5.0)	0.04				
Nadir Blood Pressure, mmHg	109.8 (109.0, 110.6)	111.2 (109.2, 113.3)	1.4 (-0.8, 3.7)	0.20				
Abbreviations: CI, confidence interval; diff, difference; IDWG, interdialytic weight gain; OR, odds ratio								

### Conclusions

- No clinical benefit of a dialysate temperature of 36°C could be detected within the subpopulation of patients whose characteristics might lead clinicians to prescribe a lower dialysate temperature.
- This conclusion applies only to the matched population and cannot necessarily be generalized to the entire patient population.
- Conclusions cannot be extrapolated to other dialysis temperatures, to individualized dialysate cooling, or other outcomes.

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