Item S1. Detailed methods and associations between prescribed ultrafiltration rate and all-cause mortality

Table *a*. Associations between prescribed ultrafiltration rate and all-cause mortality using a time-updated exposure window approach.[a]

	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Mean UF rate dichotomized at 10 mL/h/kg		
≤10 mL/h/kg	1.00 (reference)	1.00 (reference)
>10 mL/h/kg	1.00 (0.97-1.02)	1.17 (1.14-1.20)
Mean UF rate dichotomized at 13 mL/h/kg		
≤13 mL/h/kg	1.00 (reference)	1.00 (reference)
>13 mL/h/kg	1.10 (1.07-1.14)	1.26 (1.22-1.30)
Mean UF rate categorized		
<10 mL/h/kg	1.00 (reference)	1.00 (reference)
10-13 mL/h/kg	0.93 (0.90-0.95)	1.07 (1.04-1.10)
>13 mL/h/kg	1.08 (1.05-1.12)	1.29 (1.24-1.33)

[a] *Marginal structural model represented by weighted cox proportional hazards models with the robust sandwich estimator of the variance specified. Adjusted for fixed baseline covariates age (continuous), gender (female vs. male), race (black vs. non-black), ethnicity (Hispanic vs. non-Hispanic), time on dialysis (1-2, 3-4, ≥5 vs. <1 year), history of heart failure (yes vs. no), history of cardiovascular disease (yes vs. no), history of diabetes (yes vs. no), and time dependent vascular access (graft, fistula vs. catheter), pre-HD systolic blood pressure (131-150, 151-170, >170 vs. ≤130 mmHg), missed sessions (≥3 vs. <3), albumin (3.1-3.5, 3.6-4.0, >4.0 vs. ≤3.0 g/dL), creatinine (continuous), phosphorous (4.1-5.0, 5.1-6.0, >6.0 vs. ≤4.0 mg/dL), hemoglobin (10.0-11.9, ≥12.0 vs. <10.0 g/dL), and urea reduction ratio (continuous).*

We conducted sensitivity analyses in which we assessed the association between time-updated prescribed UF rate and all-cause mortality using marginal structural proportional hazards models. Marginal structural models estimate the effect of a time-varying exposure on an outcome by appropriately controlling for the effects of time-dependent confounders. (Robins *et al*. Epidemiology. 2000;11(5): 5500-60 and Hernan *et al*. Epidemiology. 2000;11(5): 561-70). The exposure of interest, prescribed UF rate, was defined in discrete 30-day intervals and time-dependent confounders were defined in 30 day periods before each 30-day exposure interval. A 30 day lag period was used to avoid undue influence from changes in the UF rate—mortality association in the immediate peri-death period. Longitudinal analyses were then conducted on the basis of parameters defined in successive 30-day increments from the start to end of follow-up time (the latter defined by occurrence of either the outcome of interest or censoring event).

Figure *a*. Timing of time-updated covariates, exposure (UF rates), and outcome windows.[a]
UF rate was assessed in a 30-day window. Time-dependent confounders were defined during a 30-day period before the exposure window, and the outcome was defined during 30 days after the exposure window (with a 30-day lag period to avoid undue influence from changes in the UF rate—mortality association in the immediate peri-death period). Longitudinal analyses were performed on the basis of parameters defined in successive 30-day increments of the below series of windows from the study entry to end of follow-up for each individual. The end of follow-up time was defined by the occurrence of either the outcome of interest or a censoring event.
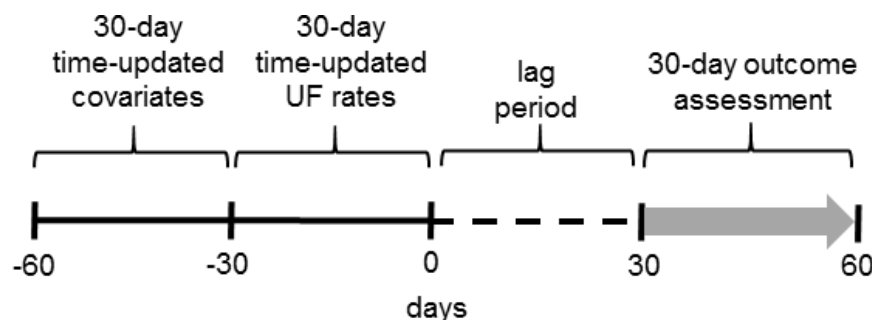
[a] Adapted from Miskulin DC, *et al*. Intravenous iron exposure and mortality in patients on hemodialysis. *Clin J Am Soc Nephrol* 2014 Nov 7;9(11):1930-39.