ADJUSTMENT FOR EXPOSURE HISTORY AND IMPORTANT CONFOUNDERS MARKEDLY ATTENUATES ELEVATED MORTALITY RISK ASSOCIATED WITH EPOETIN ALFA (EPO) DOSE

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Previous studies by other researchers have associated high EPO doses measured as a mean over a 3-month baseline period with elevated 1-year mortality using USRDS data. These analyses did not account for exposure more proximal to death or confounding by possibly important unmeasured mortality predictors unavailable in the USRDS, and thus may have been biased. Here, we examine the influence of these potential biases using more detailed data from a large dialysis provider.

Eligible (N=23,802) patients were 18+ years of age receiving dialysis at a large dialysis organization (LDO) facility from 07/2000-06/2001, had ≥6 consecutive months of EPO or hemoglobin (Hb) data (6-month entry period), and survived into the follow-up period. EPO dose was defined as the mean per admin dose in month 6 (last month in entry period); patient characteristics were assessed in, or as close as possible to, month 6. Exposure history (EH) was assessed using the mean Hb and EPO dose during months 1-5, markers of bone marrow response and health status. We used Cox models to estimate the mortality risk during the 90-day follow-up period with and without adjustment for EH and other potential confounders (variables commonly available in USRDS and additional variables available in LDO data).

Table: 90-day mortality HR and 95% CI by quartile of EPO dose

EPO (IU)	Crude		USRDS adjustment		Additional adjustment	
	HR	95% CI	HR	95% CI	HR	95% CI
<2708	1.0	--	1.0	--	1.0	--
2708-5000	1.3	1.1–1.6	1.2	1.0–1.5	1.2	0.9–1.4
5001-8800	1.7	1.4–2.1	1.5	1.2–1.8	1.3	1.1–1.6
>8800	2.7	2.3–3.3	2.1	1.7–2.6	1.7	1.4–2.1
	EH adjustment		EH + USRDS adjustment		EH + additional adjustment	
<2708	1.0	--	1.0	--	1.0	--
2708-5000	1.1	0.9–1.4	1.0	0.8–1.3	1.0	0.8–1.2
5001-8800	1.3	1.0–1.7	1.1	0.8–1.4	1.0	0.8–1.3
>8800	1.8	1.3–2.4	1.3	0.9–1.7	1.1	0.8–1.5

Our results indicate that analyses that ignore exposure history and fail to account for important confounding factors resulted in a strong relationship between EPO dose and mortality.