



# Exploring the association between Ferritin levels and mortality in the UK haemodialysis population



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## 1. Background:

- Intravenous (IV) iron facilitates maintenance of target haemoglobin levels and improves anaemia management with lowering of ESA requirements in haemodialysis (HD) patients.
- Most UK centres use serum ferritin to evaluate iron status and to guide dosing.
- The 2014 UK Renal Registry report shows that twenty centres had greater than 20% (20–60%) of their HD patients with ferritin  $\geq 800$  mg/L.

## 2. Aim:

To explore in the UK haemodialysis population, risks linked to achieving higher ferritin levels as a consequence of iron dosing having adjusted for other acute phase proteins.

## 3. Methods:

- Retrospective observational cohort study
- Prevalent cohort 31<sup>st</sup> December 2011
- Groups stratified by ferritin levels  $\leq 200$ , 201 to  $\leq 500$ , 501 to  $< 800$ ,  $\geq 800$  micro g/L in accordance with the Renal Association recommendations.

**Statistical analyses:** Done using SAS 9.3

- Cox proportional hazards models.
- Adjusted for clinical covariates (That could confound the association between ferritin and all-cause mortality)

**Model 1:** Unadjusted (KM plot)

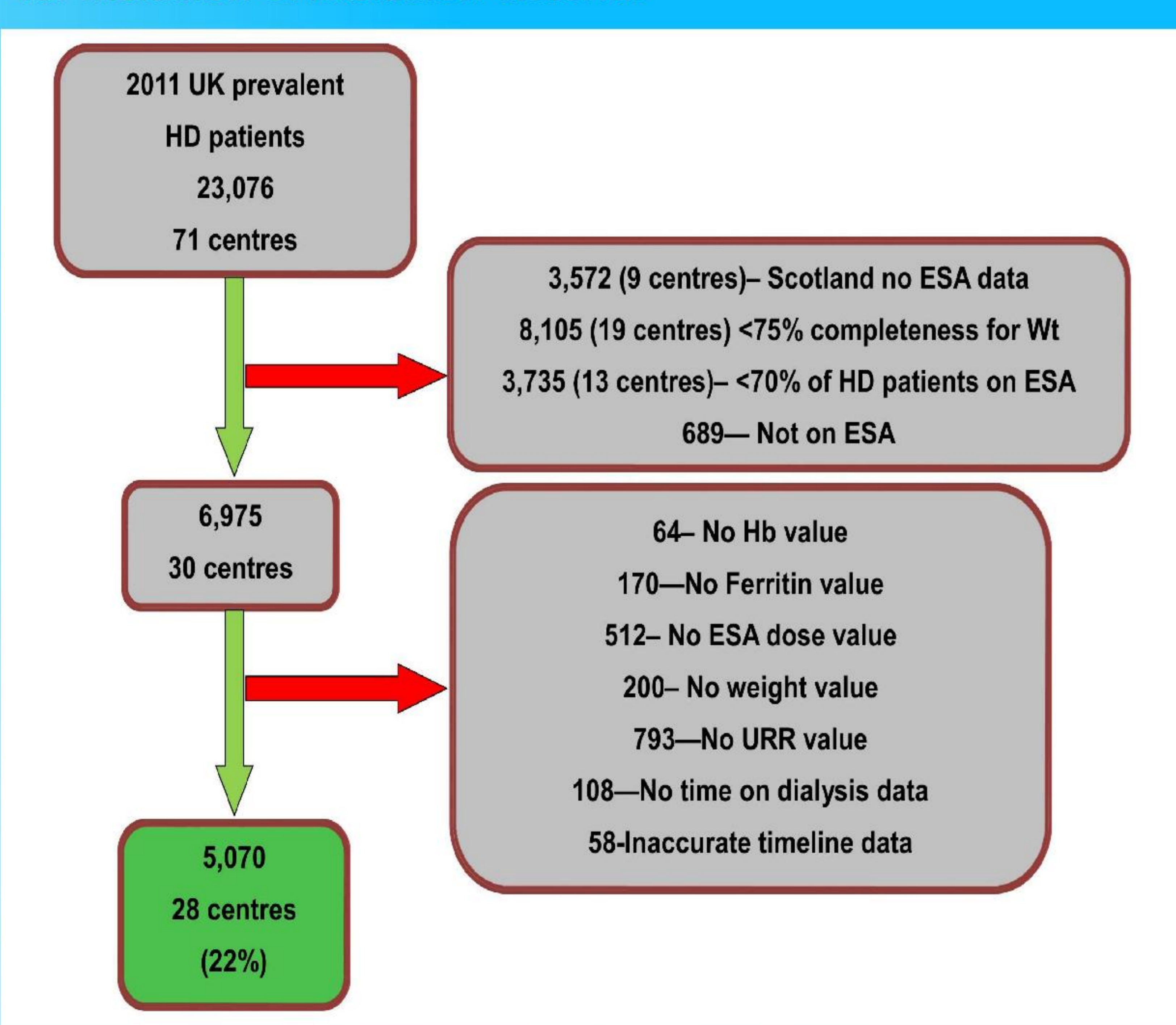
**Model 2:** Age & Sex

**Model 3:** Haemoglobin ( $<10$ , 10-12,  $>12$ g/dl), ESA dose ( $<150$  &  $\geq 150$  IU/Kg/week)

**Model 4:** Time on dialysis, URR ( $<65$  &  $\geq 65$ ) & albumin)

## 4. Results:

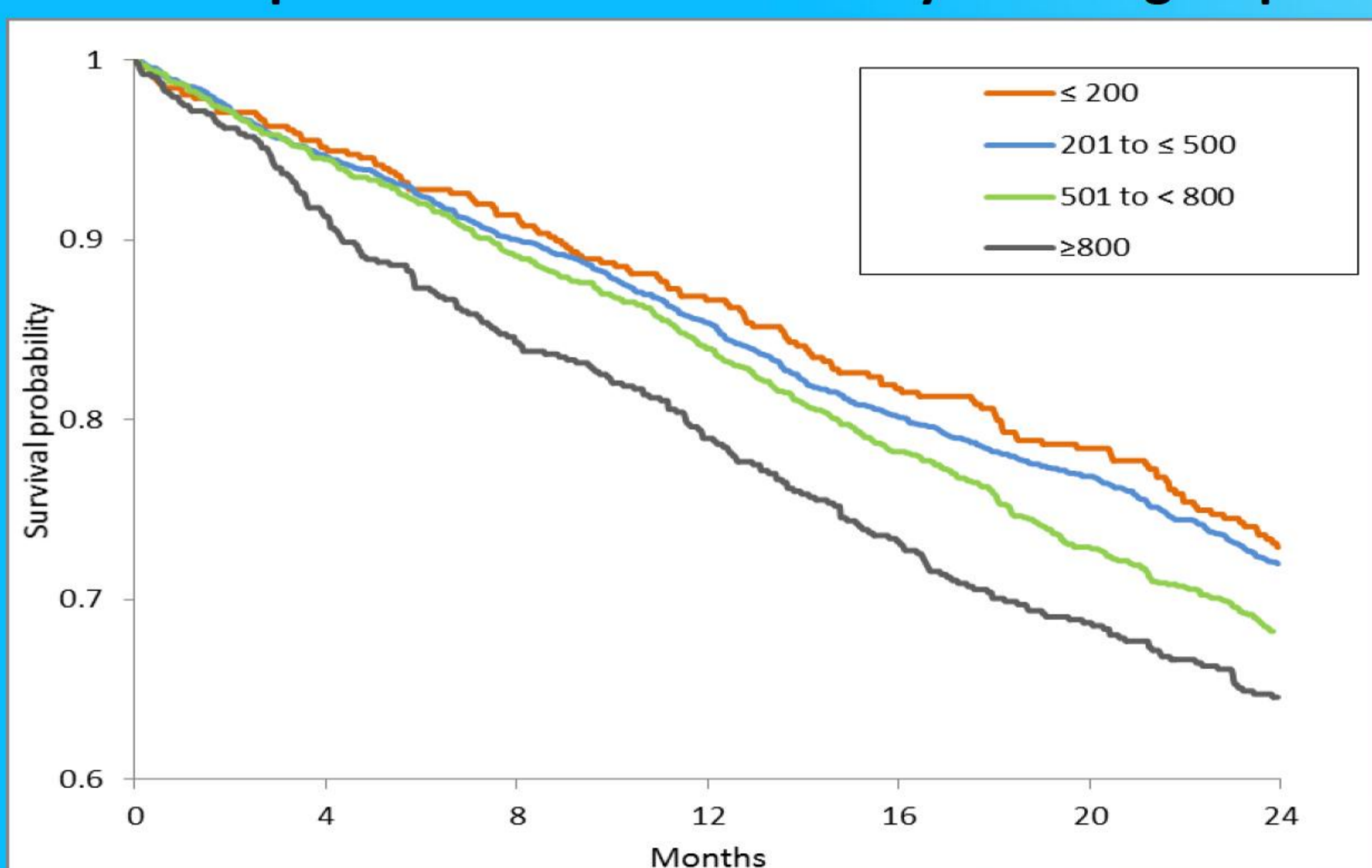
### 4a. Inclusion & Exclusion criteria:



## 4b. Table of baseline characteristics:

Ferritin Level	$\leq 200$	201 to $\leq 500$	501 to $< 800$	$\geq 800$	p value	
N	519	2584	1331	636		
Age (95% CI)	61.9 (60.5-63.4)	66.6 (66.0-67.2)	66.7 (65.9-67.5)	67.2 (66.0-68.4)	$<.0001$	
Sex-Male N (%)	330 (63.6)	1598 (61.8)	746 (56.1)	351 (55.2)	$<.0001$	
Haemoglobin g/dl	$<10$ N (%)	94 (18.1)	411 (15.9)	245 (18.4)	170 (26.7)	$<.0001$
	10-12 N (%)	271 (52.2)	1598 (61.8)	784 (59.0)	323 (50.8)	$<.0001$
	$>12$ N (%)	154 (29.7)	575 (22.3)	302 (22.7)	143 (22.5)	$<.0001$
ESA dose IU/kg/week	$<150$ N (%)	151 (29.1)	623 (24.1)	316 (23.7)	176 (27.7)	0.03
	$>150$ N (%)	368 (70.9)	1961 (75.9)	1015 (76.3)	460 (72.3)	
Albumin g/l (95% CI)	37.0 (36.6-37.5)	36.8 (36.6-37.0)	36.7 (36.1-36.6)	35.6 (35.1-36.0)	$<0.001$	
URR	$<65\%$ N (%)	97 (18.7)	276 (10.7)	135 (10.1)	57 (9.0)	$<0.001$
	$\geq 65\%$ N (%)	422 (81.3)	2308 (89.3)	1196 (89.9)	579 (91.0)	$<0.001$
Median time on dialysis (yrs) (IQR)	2.6 (1.0-4.0)	3.2 (1.6-5.8)	3.7 (1.8-6.1)	3.7 (1.7-6.4)	$<0.001$	

## 4c. KM Kaplan-Meier Survival Plot by ferritin groups



## 4d. Table: Unadjusted and adjusted 2-year survival, HR and (p-value), for HD patients

Ferritin groups micro g/L	HD (N=5,070)			
	Model 1	Model 2	Model 3	Model 4
$\leq 200$	0.95 (0.60)	1.1(0.28)	1.06 (0.51)	1.08 (0.43)
201 to $\leq 500$	-	-	-	-
501 to $<800$	1.15 (0.02)	1.18 (0.008)	1.20(0.003)	1.15 (0.02)
$\geq 800$	1.36 ( $<.0001$ )	1.40 ( $<.0001$ )	1.35 (0.0001)	1.26 (0.003)

## 5a. Strengths:

- Registry analysis with large population and good statistical power.
- Good generalizability.

## 5b. Limitations:

- Missing data.
- Residual confounding.
- Does not establish causality.

## 6. Conclusion:

- High ferritin was associated with increased mortality risk despite controlling for acute phase proteins such as albumin.
- In observational data this association needs explored further using causal models.
- Alternatively PIVOTAL, a large UK randomised control trial, will hopefully also be able to better inform the renal community on long-term safety of IV iron in this patient population.

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