

Erythropoietin Stimulating Agents Resistance and Survival on Dialysis



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1. Background:

Definition: 'failure to reach the target Hb level despite SC epoetin dose >300 IU/kg/week (450 IU/kg/week IV epoetin) or darbepoetin dose >1.5mcg/kg/week'.

European best practice Guidelines 14-16: inadequate response to epoetin. Nephrol Dial Transplant 2000; 15 Suppl 4: 43-50.

Erythropoietin resistance index (ERI)- IU/kg/week/g per 100 ml

Factors that condition the response to erythropoietin in patients on haemodialysis and their relation to mortality. Lopez-Gomez et al Kidney International, Vol 74, 575-81

2. Aim:

To describe the prevalence of ESA resistance, to identify predictors for ESA resistance and to investigate 1 year survival in the UK dialysis population.

3. Methods:

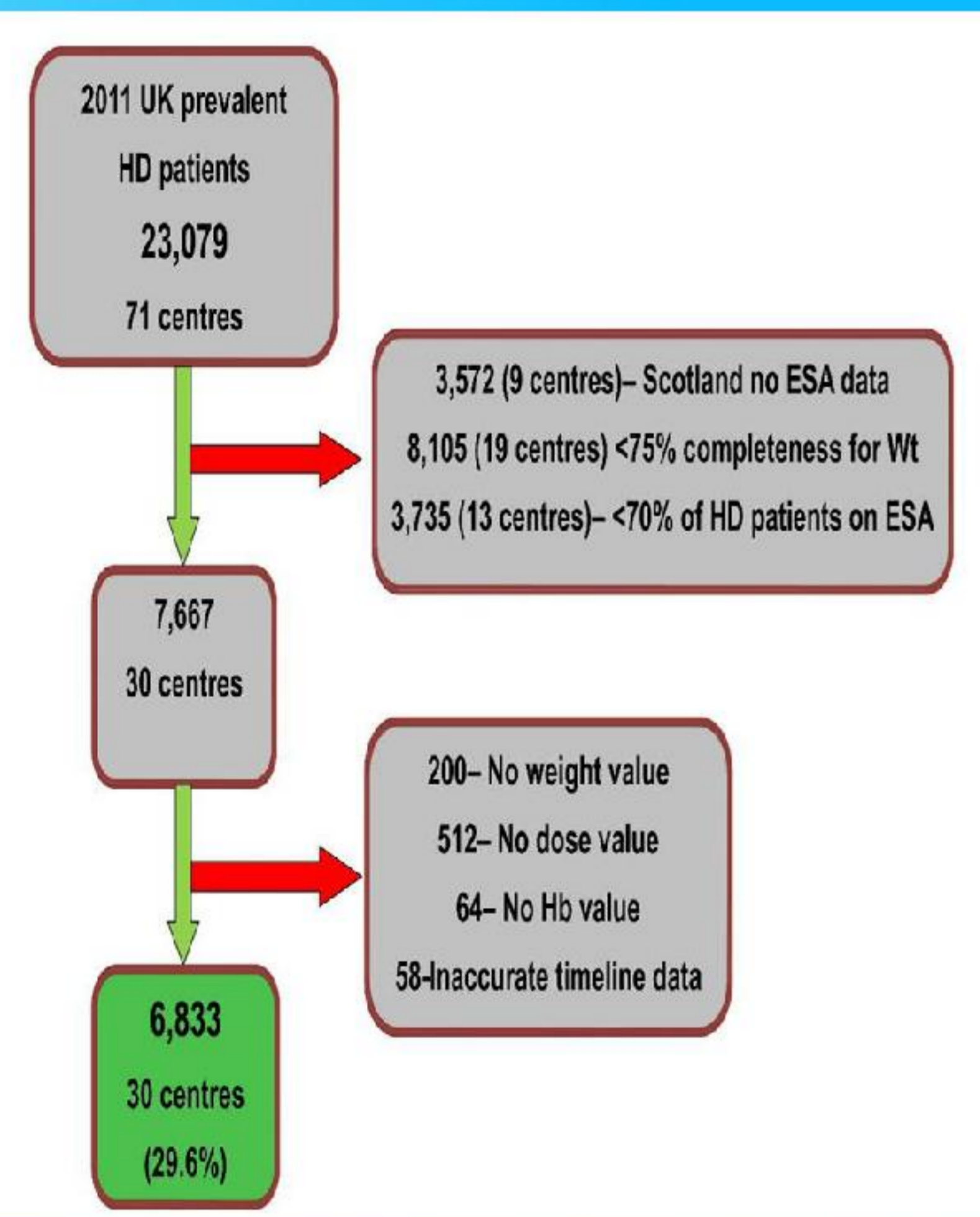
Retrospective observational cohort study
Prevalent cohort 2011

Classification:

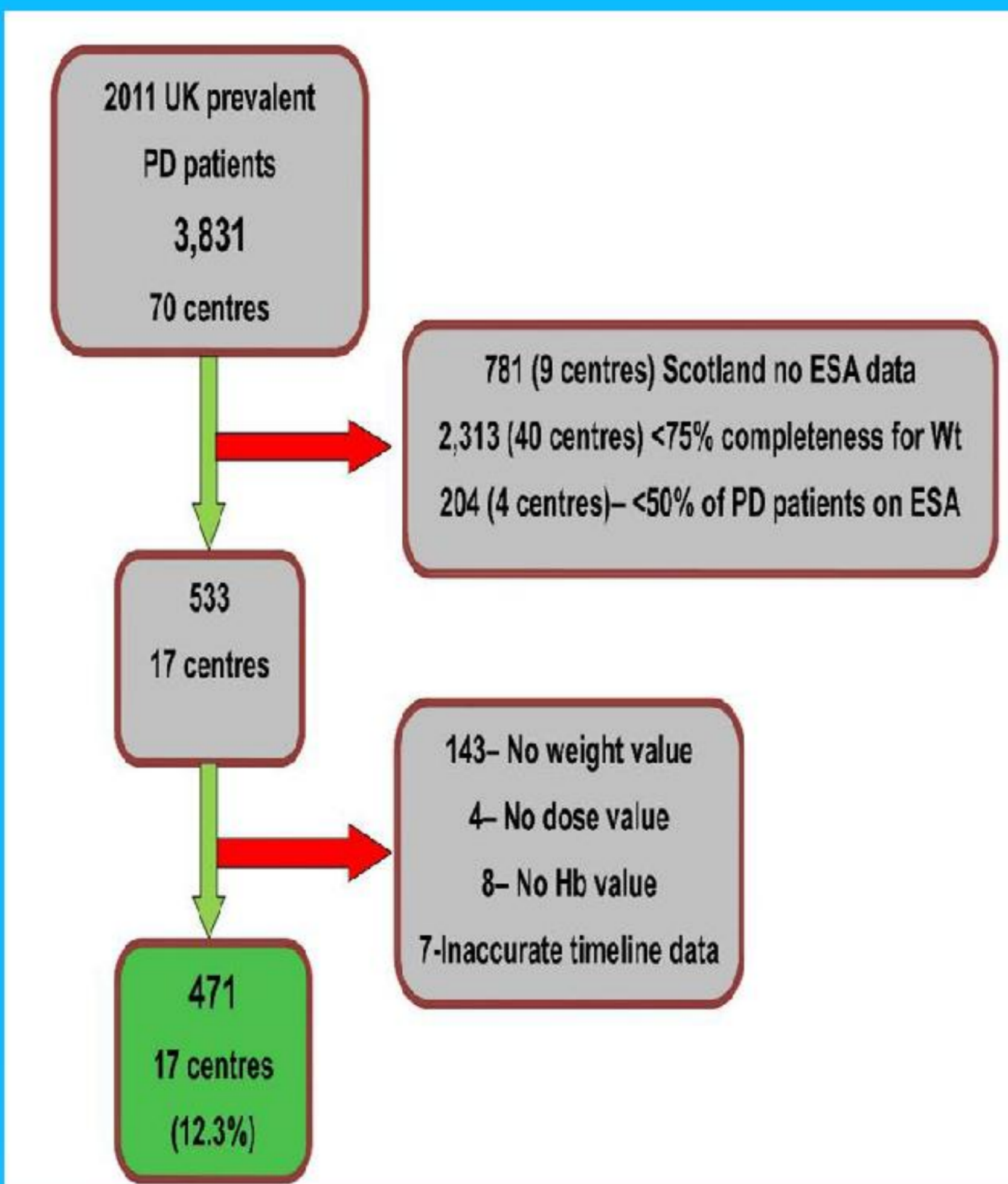
ESA Resistance	
HD	> 450 IU/kg/week & Hb <10 g/dl
PD	> 300 IU/kg/week & Hb <10 g/dl

ERI Groups	
A	Hb>=10, no ESA
B	ERI<5
C	ERI=5-15
D	ERI>15
E	Hb<10, no ESA

Inclusion & Exclusion criteria: Hemodialysis (HD)



Peritoneal Dialysis (PD)



Statistical analyses:

- Done using SAS 9.3
1. Prevalence rates
 2. Univariate analysis
 3. Multivariate analysis
- Logistic regression
Cox proportional hazards models

4. Results:

Prevalence by ESA resistance

Modality	Hb <10g/dl		Total N (%)
	and on high dose ESA	and not currently on ESA	
	N	N	
Haemodialysis (HD)			
N=6833	24	58	82 (1.2)
30 centres			
Peritoneal dialysis (PD)			
N=471	7	6	13 (2.8)
17 centres			

Prevalence by ERI

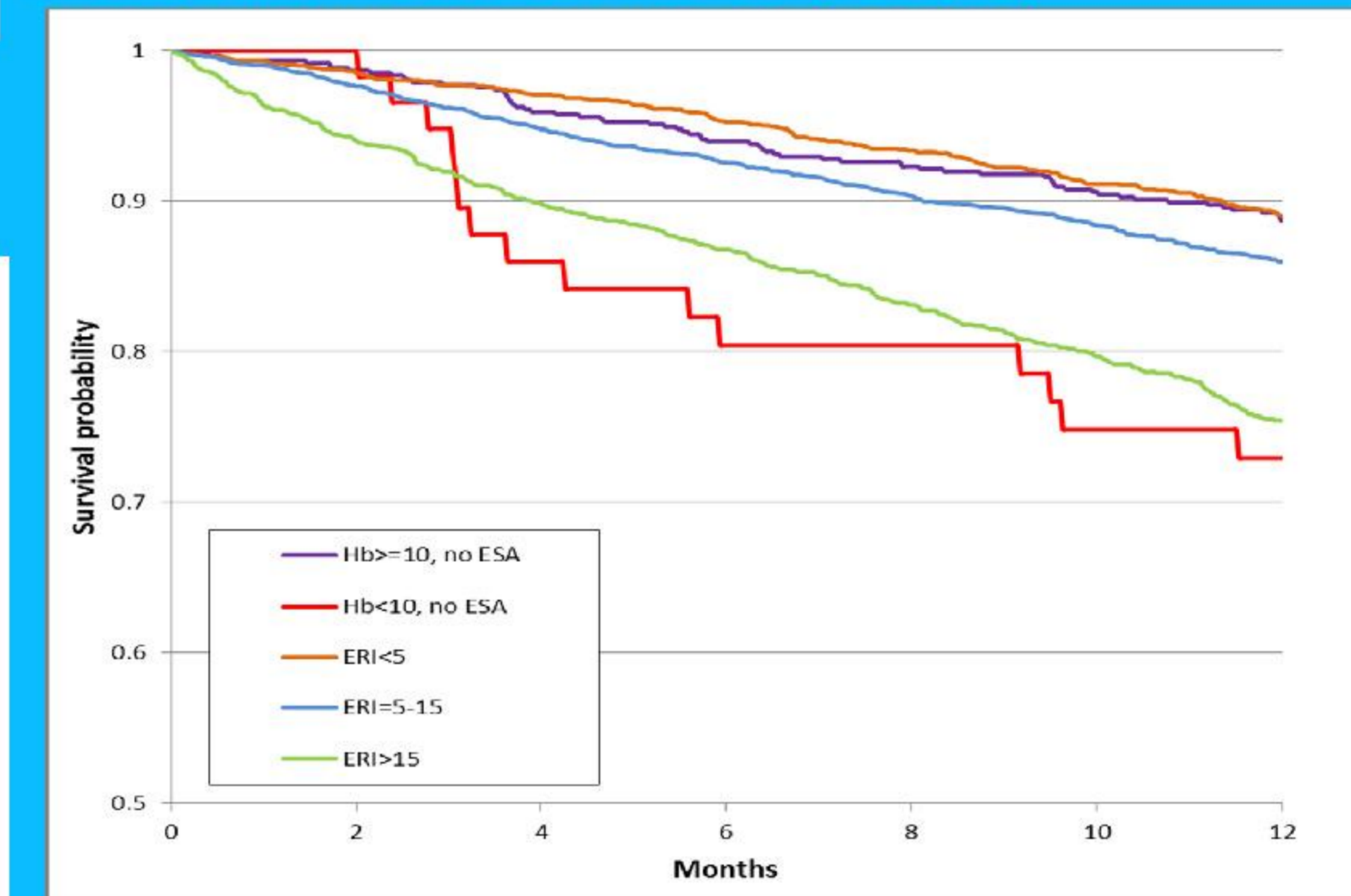
Group		HD N (%)
A	Hb>=10, no ESA	631 (9.2)
B	ERI<5	1750 (25.6)
C	ERI=5-15	2967 (43.4)
D	ERI>15	1427 (20.9)
E	Hb<10, no ESA	58 (0.9)

Predictors of ESA resistance:

Parameter	Multivariate models HD		Multivariate models PD		
	OR (95% CI)	p value	OR (95% CI)	p value	
Age (yrs)	50-65	1.0	1.0	-	
	<50	1.56 (1.27-1.92)	0.70 (0.27-1.82)	0.47	
	>65	0.93 (0.79-1.10)	0.50 (0.22-1.16)	0.10	
Sex (Male, Female)	1.63 (1.42-1.86)	<.0001	1.27 (0.60-2.70)	0.53	
Time on dialysis (yrs)	1.01 (0.97-1.03)	0.07	1.27 (1.12-1.43)	0.0001	
Ferritin µg/L	200-500	1.0	1.0	-	
	<200	1.12(0.91-1.40)	0.28	1.45 (0.49-4.28)	0.50
	500-800	0.91 (0.77-1.07)	0.26	1.68 (0.64-4.40)	0.29
	>800	1.26 (1.03-1.53)	0.03	4.50 (1.43-14.48)	0.01
Albumin (g/l)	0.91 (0.90-0.92)	<.0001	0.90 (0.84-0.96)	0.002	
URR (<65, ≥65%)	1.42 (1.16-1.74)	<.0001	-	-	

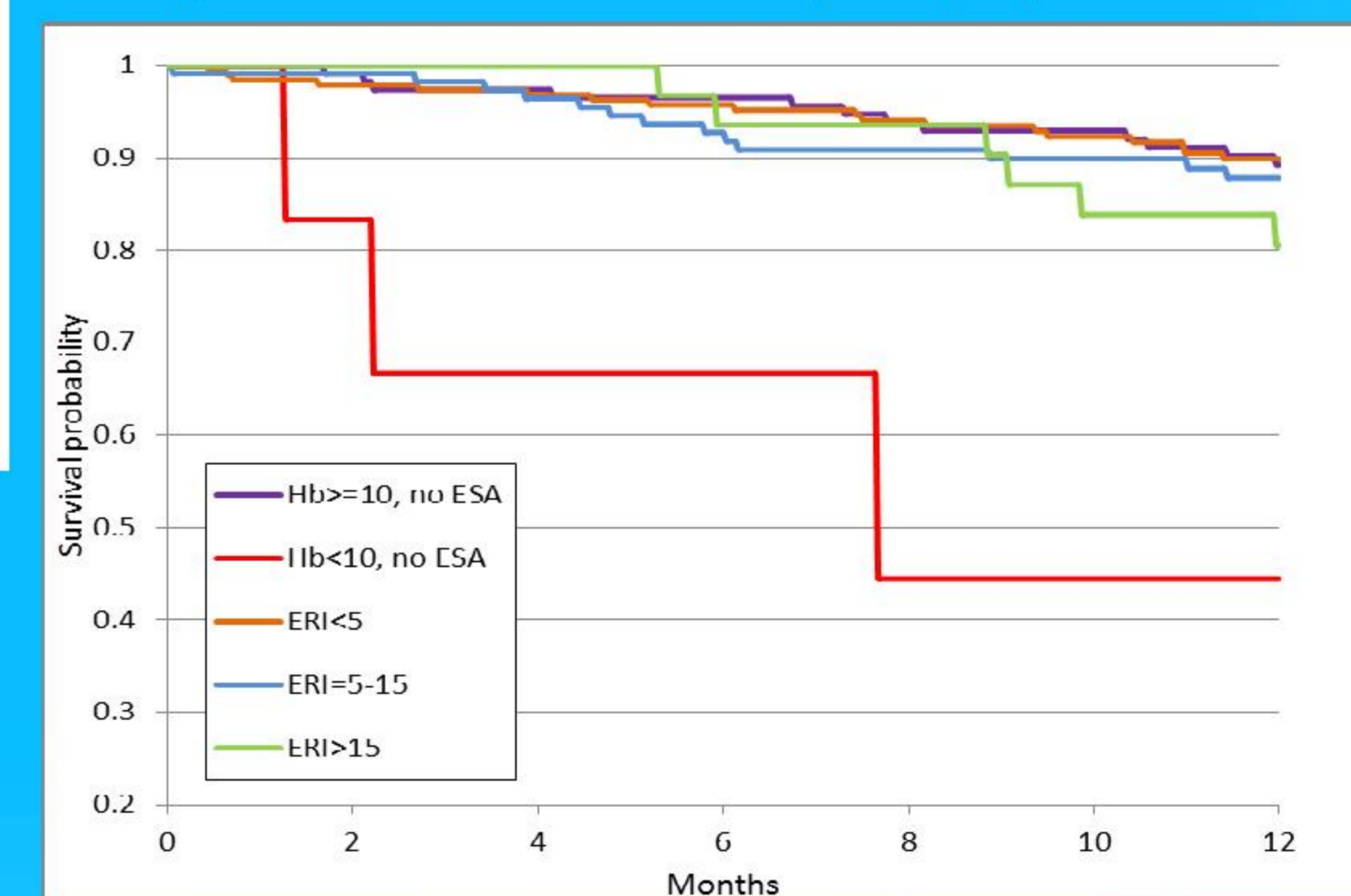
ESA resistance and survival

KM Kaplan-Meier Survival Plot by ERI (HD)



HD (N=5743)	
Group	Unadjusted
A	-
B	1.0 (0.88)
C	1.2 (0.13)
D	2.5 (<.0001)
E	2.9 (0.0009)

KM Kaplan-Meier Survival Plot by ERI (PD)



PD (N=459)	
Group	Unadjusted
A	-
B	0.9 (0.82)
C	1.1 (0.77)
D	1.6 (0.41)
E	8.4 (0.001)

Adjusted 1 year survival, HR and (p-value), for HD & PD patients

Group	HD (N=5743)		PD (N=459)	
	Adj for age & sex	Adj for age, sex, URR, time on dialysis & albumin	Adj for age & sex	Adj for age, sex, time on dialysis & albumin
A	-	-	-	-
B	0.9 (0.43)	0.9 (0.40)	0.8 (0.57)	0.8 (0.60)
C	1.1 (0.35)	1.1 (0.66)	1.4 (0.44)	1.2 (0.68)
D	2.5 (<.0001)	2.0 (<.0001)	1.6 (0.37)	0.7 (0.55)
E	3.7 (<.0001)	2.2 (0.02)	9.9 (0.0004)	5.2 (0.01)

5. Conclusion:

1. ESA resistance has implications beyond the management of anaemia.
2. High ERI portends mortal outcomes.
3. ERI may not be a reliable surrogate for inflammation.

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