

Supplemental data to article

Association of ESA hypo-responsiveness and haemoglobin variability with mortality in hemodialysis patients

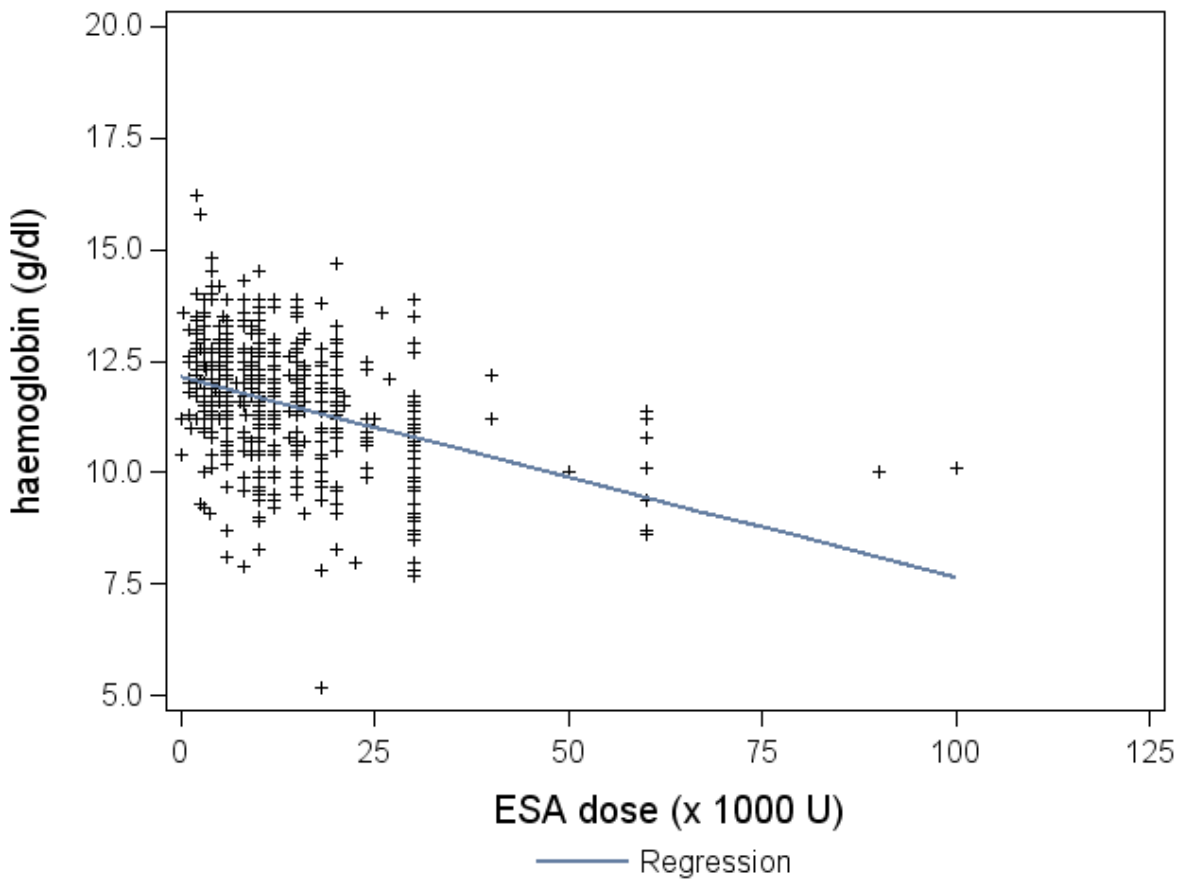
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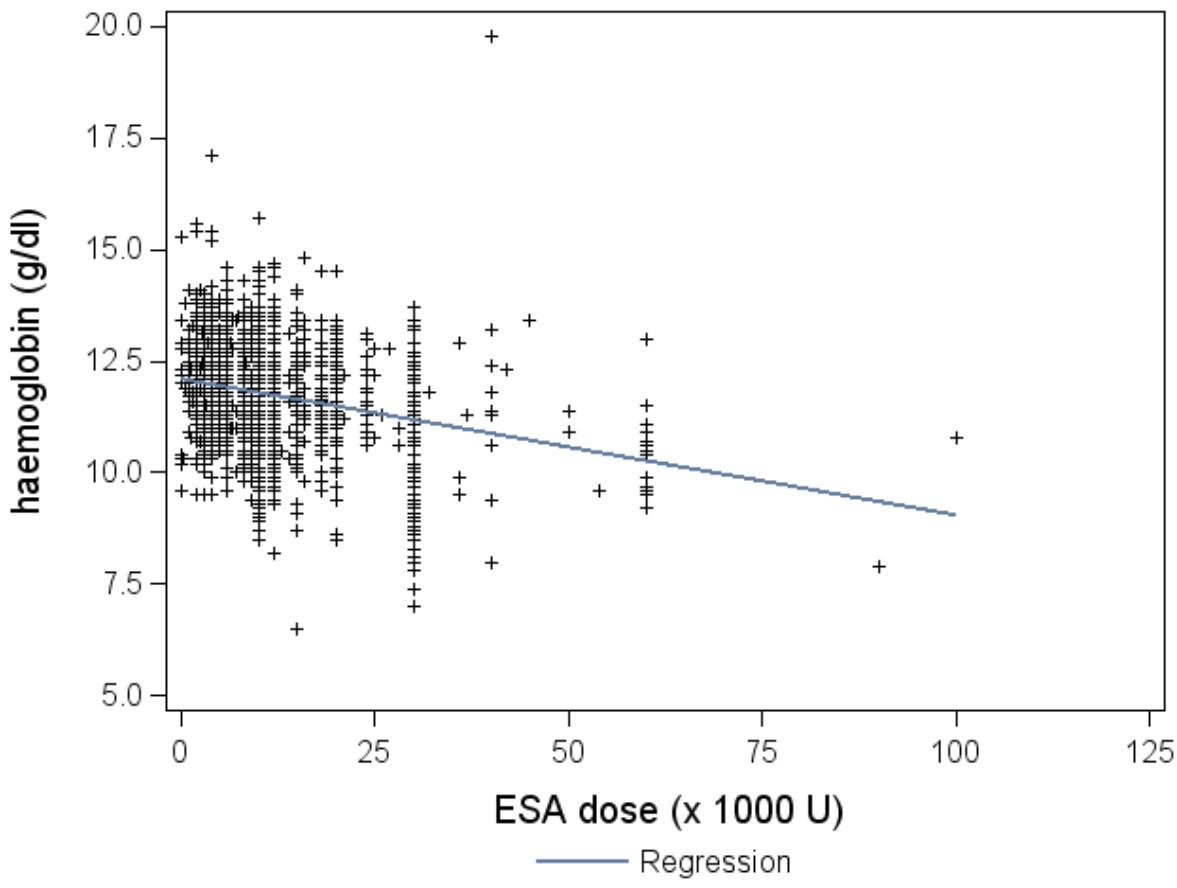
Webfigure 1a

Haemoglobin vs ESA dose for first year of treatment



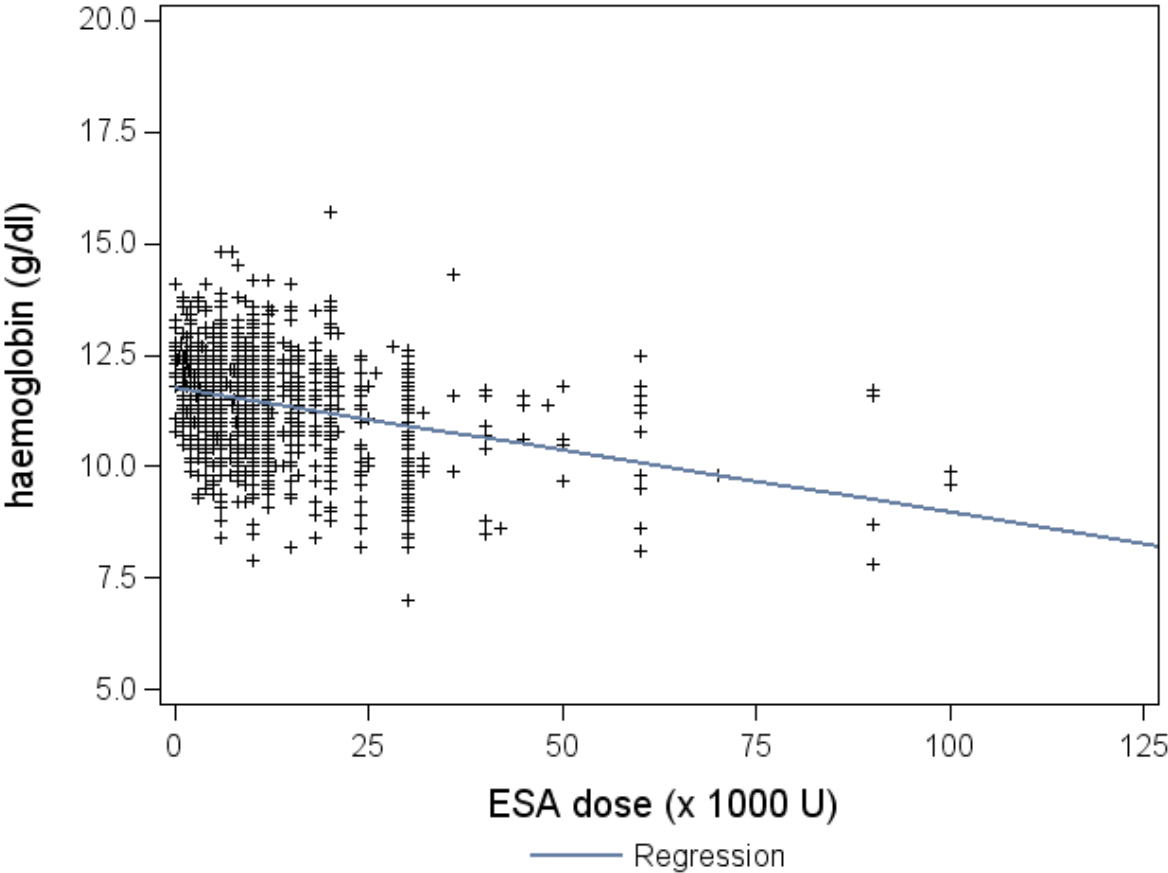
Webfigure 1b

Haemoglobin vs ESA dose for second year of treatment



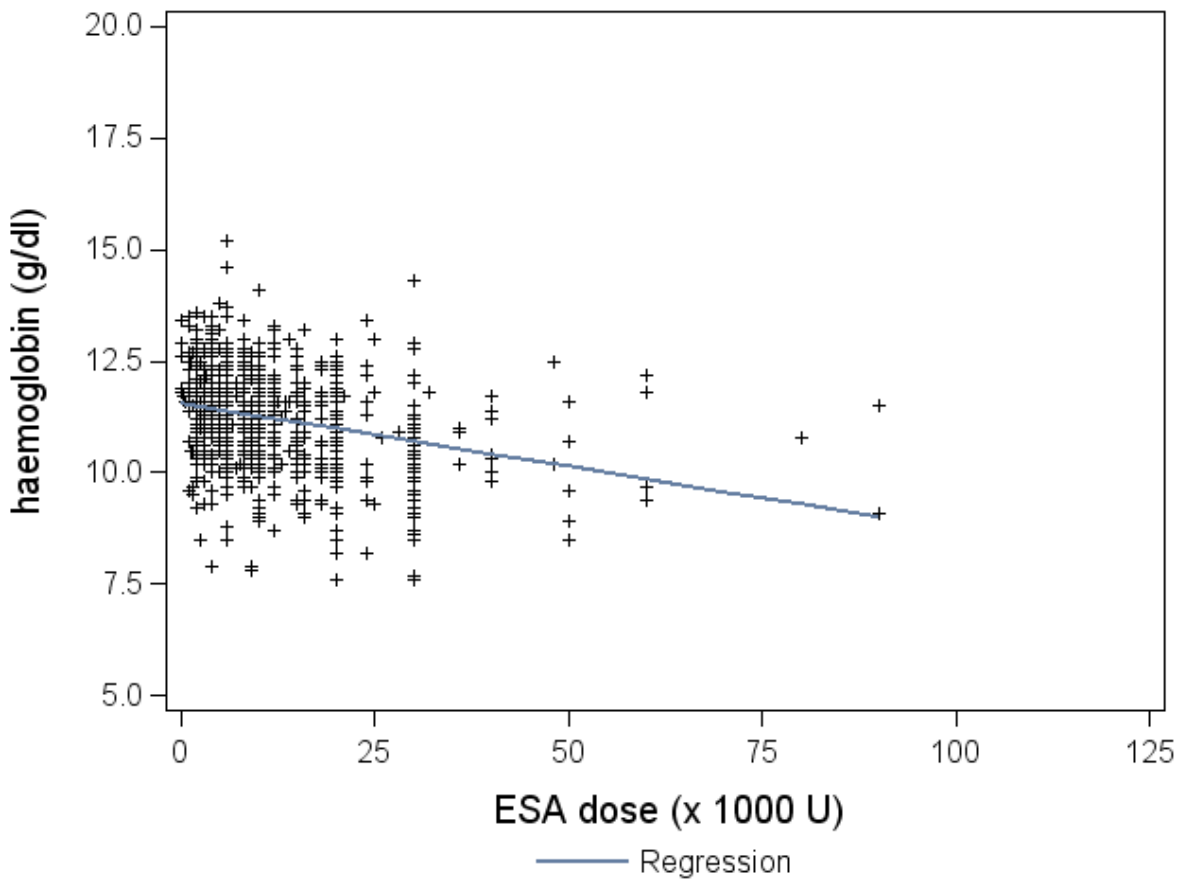
Webfigure 1c

Haemoglobin vs ESA dose for third year of treatment



Webfigure 1d

Haemoglobin vs ESA dose for fourth year of treatment



Webtable 1

Association of haemoglobin variability group with mortality in an unadjusted Cox model (reference group MM).

Parameter	Hazard 95 % confidence			
	Ratio	interval		p-value
HH	1.58	0.98	2.55	0.060
LH	1.71	1.15	2.54	0.008
LL	3.51	1.38	8.93	0.008
LM	1.90	1.24	2.90	0.003
MH	1.18	0.83	1.69	0.361

Webtable 2

Association of haemoglobin variability group with mortality. Cox model is adjusted by the variables listed in the table.

Parameter	Hazard 95 % confidence			
	Ratio	interval		p-value
HH	1.70	1.05	2.75	0.031
LH	1.96	1.31	2.92	0.001
LL	5.97	2.70	13.21	<0.001
LM	2.17	1.42	3.32	<0.001
MH	1.22	0.85	1.76	0.276
Patient age	1.04	1.03	1.05	<0.001
Vintage of dialysis	1.00	1.00	1.00	0.383
Sex (M vs. F)	1.08	0.89	1.31	0.460

Webtable 3

Association of haemoglobin variability group with mortality. Cox model is adjusted by the variables listed in the table.

Parameter	Hazard 95 % confidence			p-value
	Ratio	interval		
HH	1.68	0.46	6.05	0.430
LH	2.38	1.20	4.71	0.013
LL	6.37	2.15	18.82	<0.001
LM	1.85	0.84	4.05	0.127
MH	1.08	0.55	2.10	0.830
Patient age	1.04	1.03	1.06	<0.001
Vintage of dialysis	1.00	0.99	1.00	0.443
Sex (M vs. F)	1.00	0.71	1.41	0.989
Response group (pos. slope vs. neg. slope)	0.72	0.50	1.04	0.079

Webtable 4

Association of haemoglobin variability group with mortality. Missing BMI values were imputed. Cox model is adjusted by the variables listed in the table.

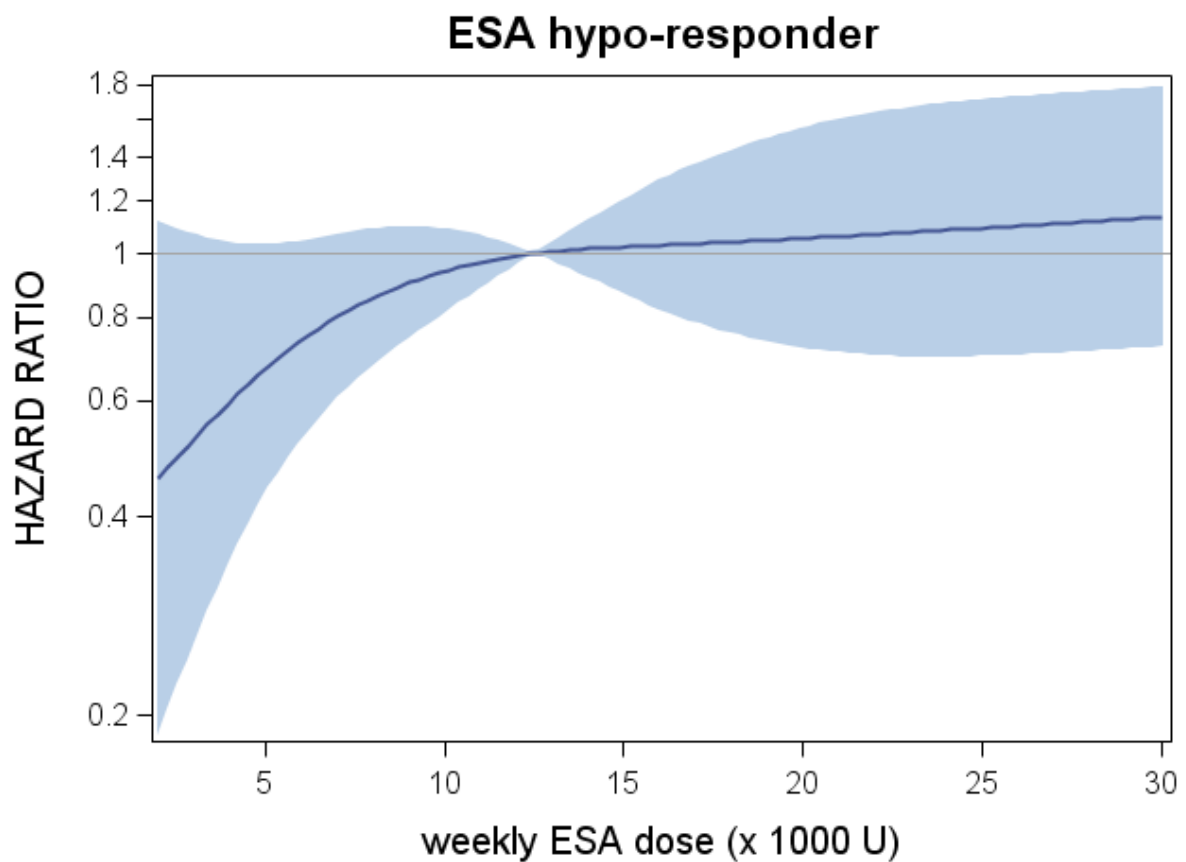
Parameter	Hazard 95 % confidence			p-value
	Ratio	interval		
HH	1,69	0,46	6,18	0.425
LH	2,32	1,17	4,62	0.017
LL	5,59	1,97	15,85	0.001
LM	1,83	0,83	4,03	0.133
MH	1,06	0,54	2,07	0.861
Patient age	1,04	1,03	1,06	<0.001
Vintage of dialysis	1,00	0,99	1,00	0.592
Sex (M vs. F)	1,01	0,71	1,42	0.961
Response group (pos. slope vs. neg. slope)	0,71	0,49	1,03	0.073
Diabetes (yes vs. no)	0,73	0,50	1,07	0.110
BMI	1.00	0,95	1,05	0.931

Hazard ratios for ESA dose

In Webfigure 2a and 2b a reference value of 12500 U/week was used (hazard ratio=1), which corresponds to the median of the analysed population.

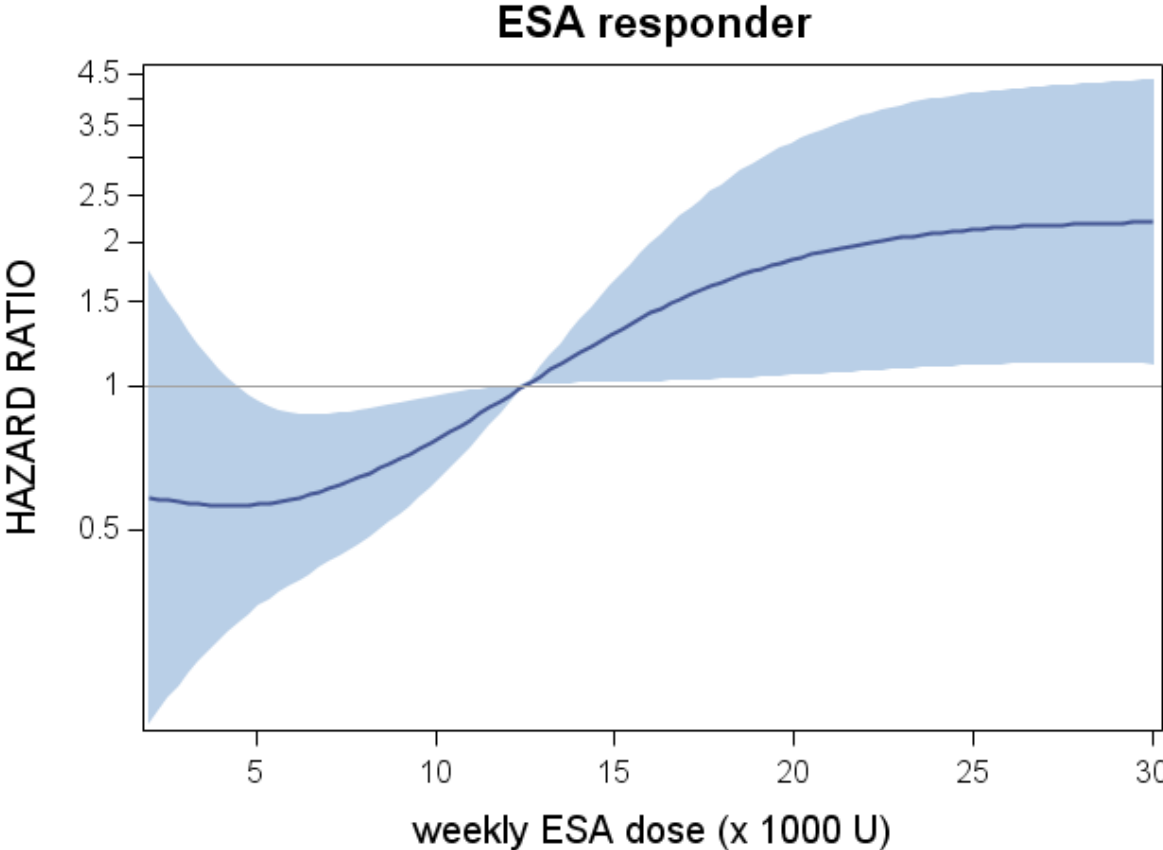
Webfigure 2a

Hazard ratio for ESA dose in ESA hypo-responders (restricted cubic spline with 4 knots). Colored bands depict the 95 % confidence intervals. The following variables were included in the model: haemoglobin, ESA dose, age, sex and vintage of dialysis.



Webfigure 2b

Hazard ratio for ESA dose in ESA responders (restricted cubic spline with 4 knots). Colored bands depict the 95 % confidence intervals. The following variables were included in the model: haemoglobin, ESA dose, age, sex and vintage of dialysis.



Differentiation of patients by haemoglobin level

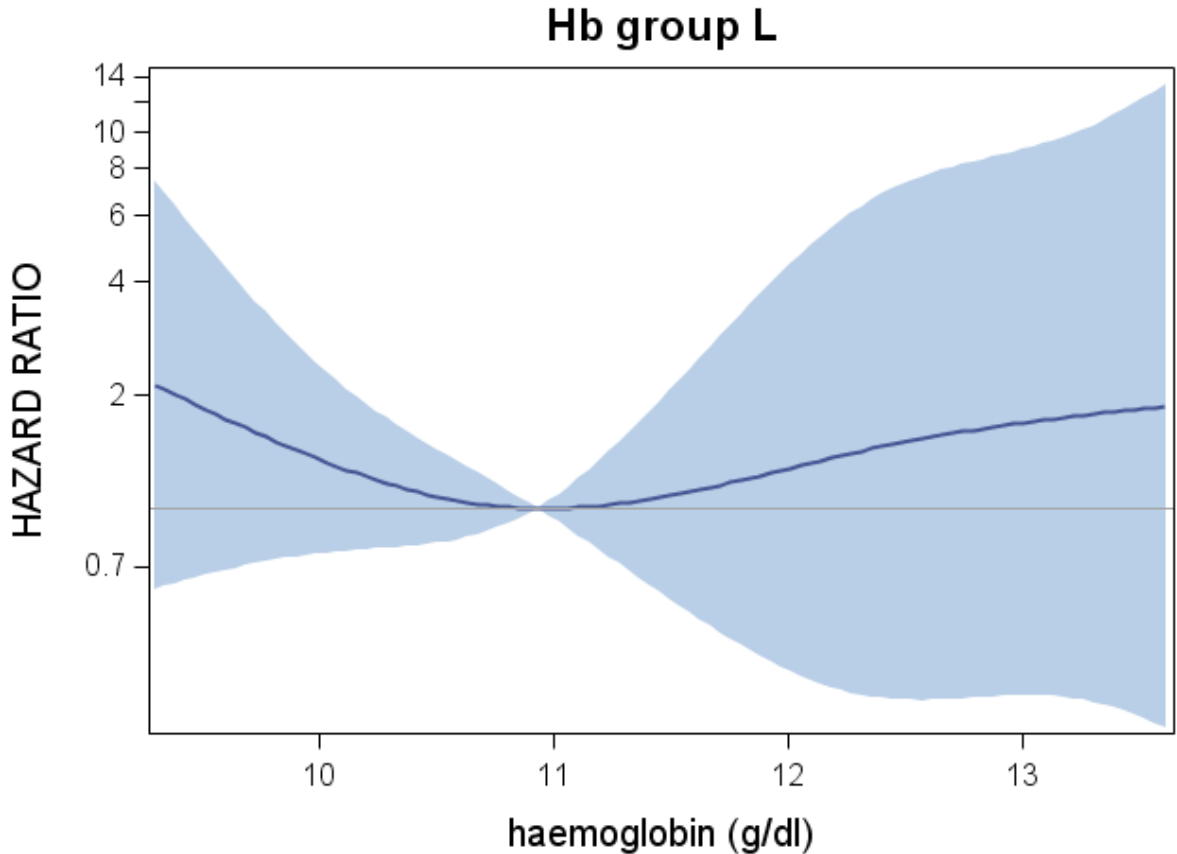
Patients were assigned to groups L, M, and H as describe in the Methods section of the article. Cox models were computed with restricted splines for baseline haemoglobin and ESA dose with 4 knots.

Furthermore, an analysis was done with a threshold of 12 g/dL used for assignment of patients to haemoglobin group 0 or 1, which means below and equal or greater 12 g/dL.

Again a Cox model with restricted splines for baseline haemoglobin and ESA dose (4 knots) was computed.

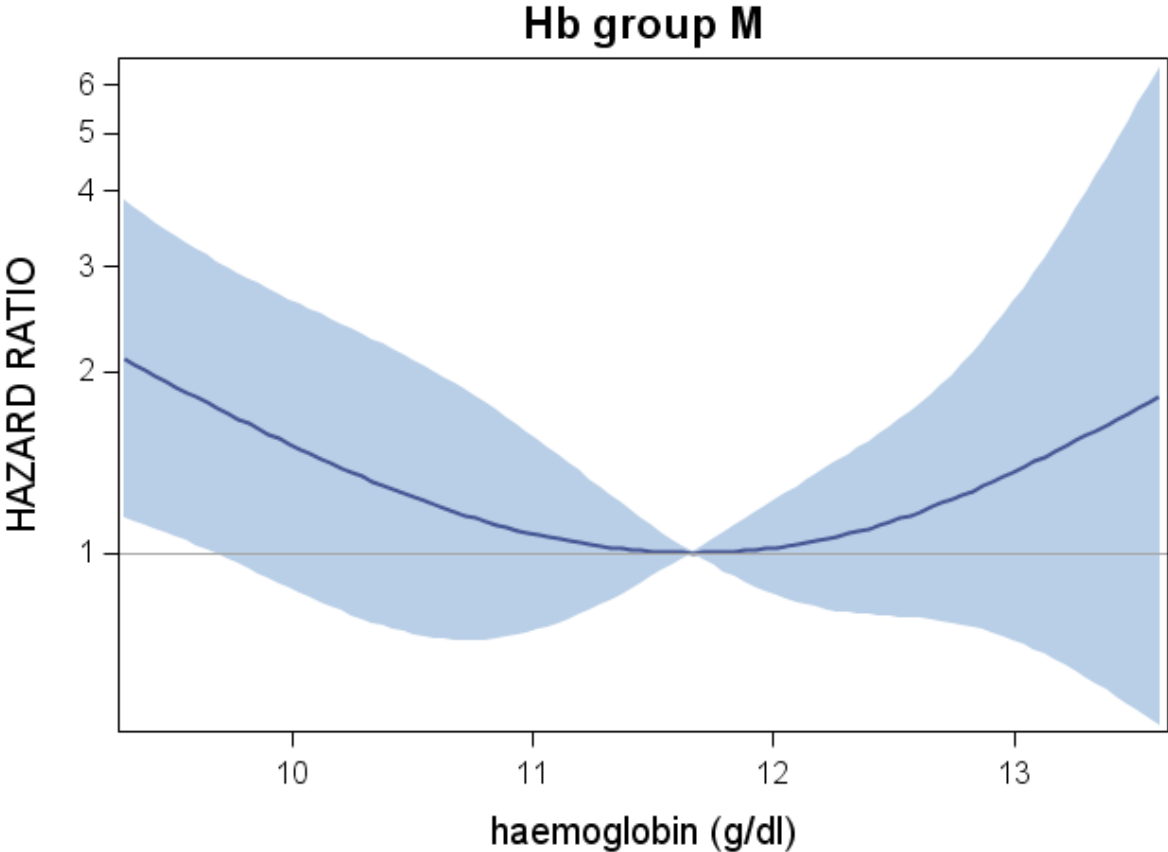
Webfigure 3a

Dependency of hazard ratio of achieved haemoglobin levels for patients with baseline haemoglobin corresponding to group L (minimum HR is at 10.9 g/dl).



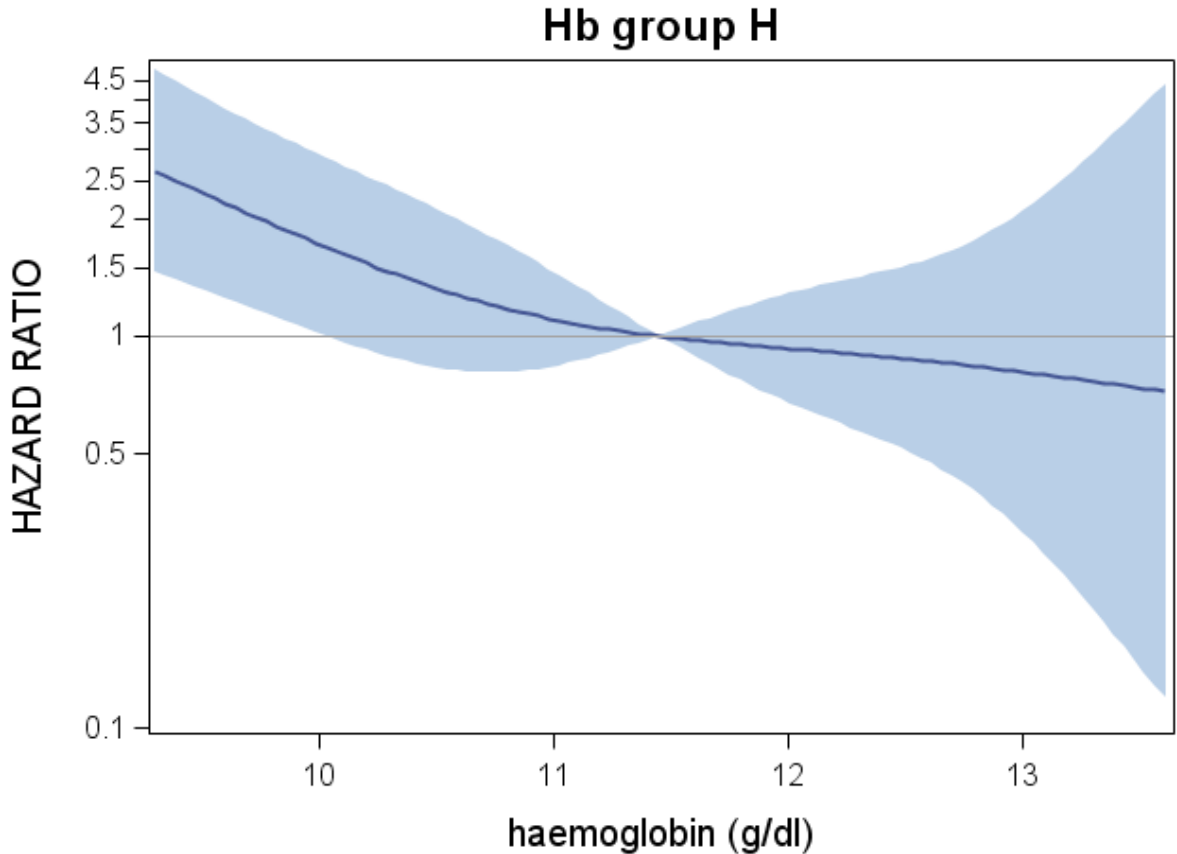
Webfigure 3b

Dependency of hazard ratio of achieved haemoglobin levels for patients with baseline haemoglobin corresponding to group M (minimum HR is at 11.7 g/dl).



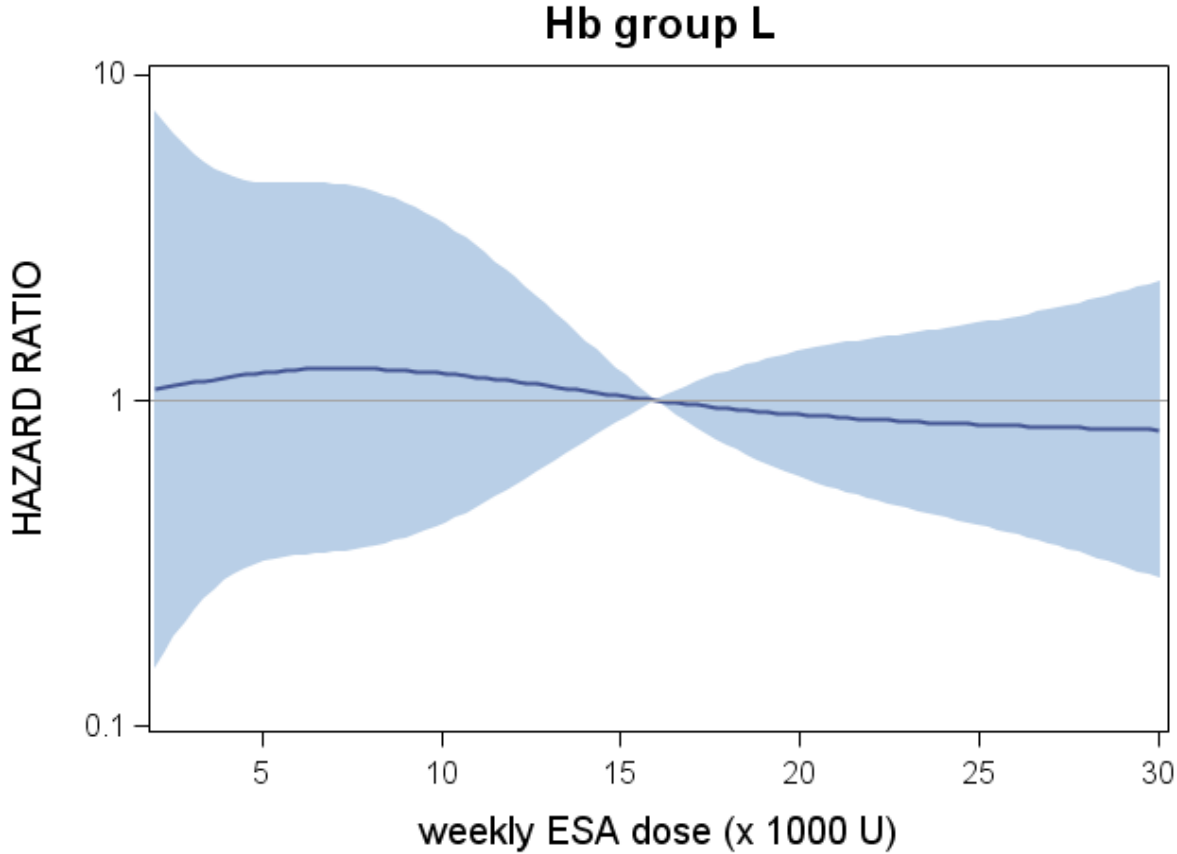
Webfigure 3c

Dependency of hazard ratio of achieved haemoglobin levels for patients with baseline haemoglobin corresponding to group H.



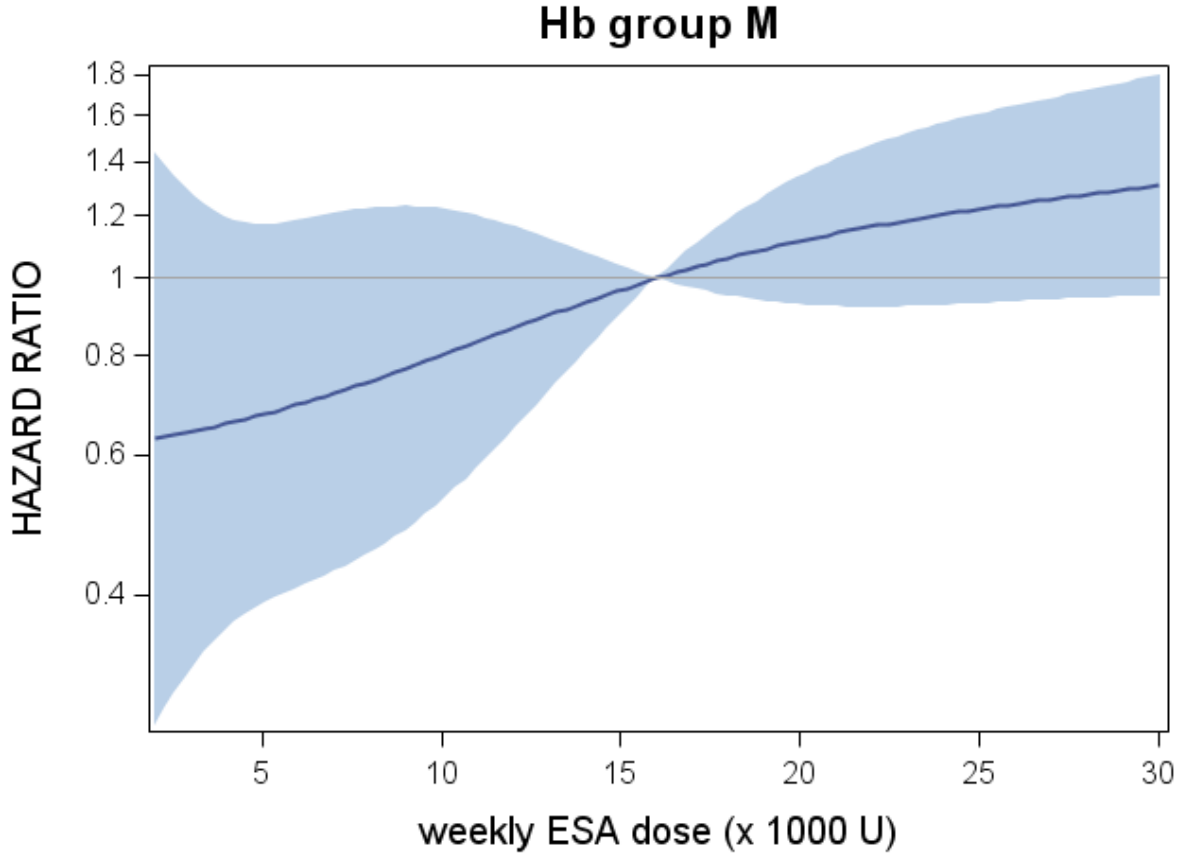
Webfigure 4a

Dependency of hazard ratio of ESA dose levels for patients with baseline haemoglobin corresponding to group L.



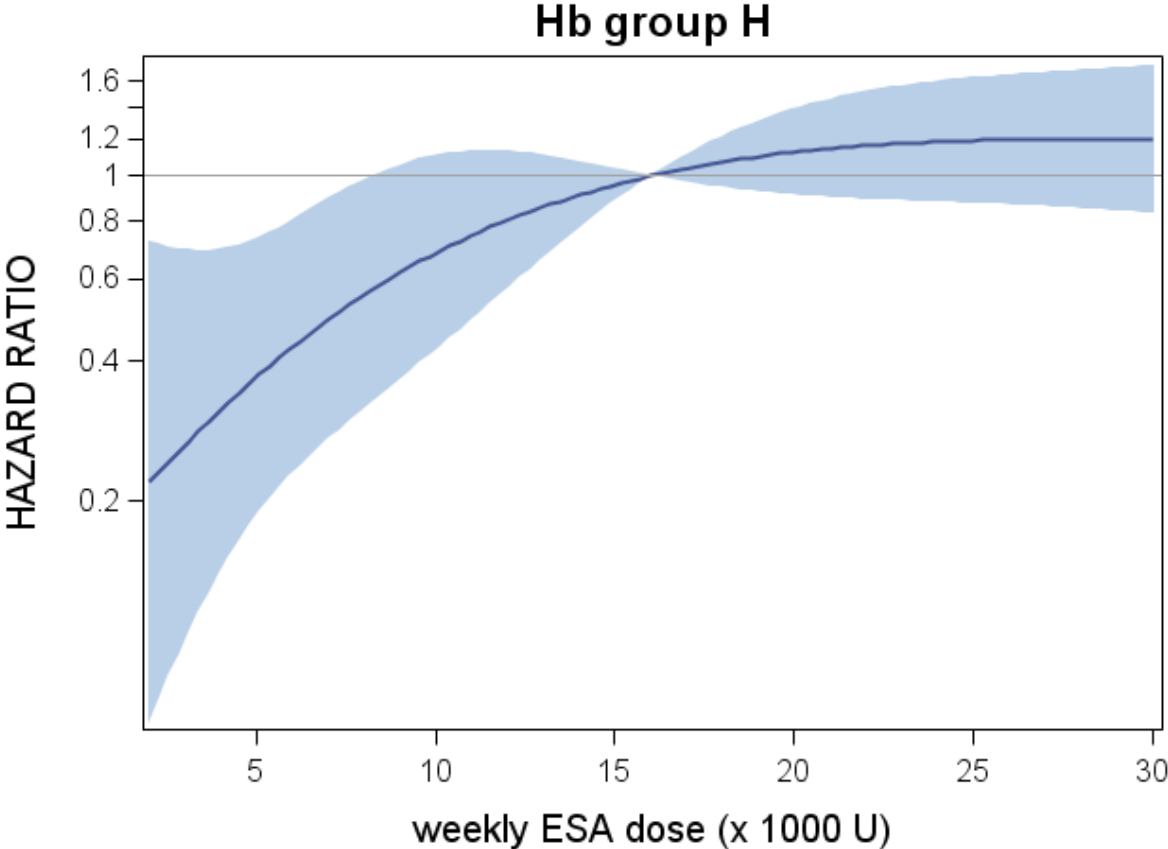
Webfigure 4b

Dependency of hazard ratio of ESA dose levels for patients with baseline haemoglobin corresponding to group M.



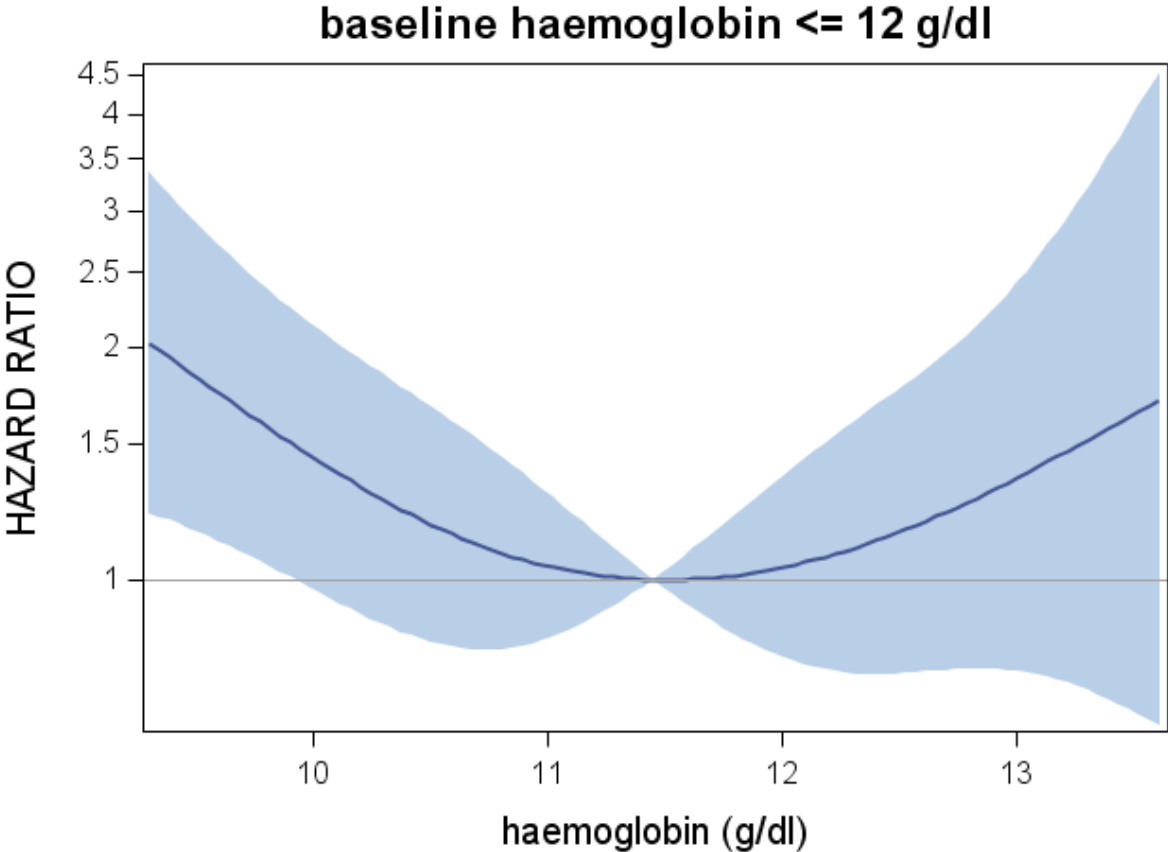
Webfigure 4c

Dependency of hazard ratio of ESA dose levels for patients with baseline haemoglobin corresponding to group H.



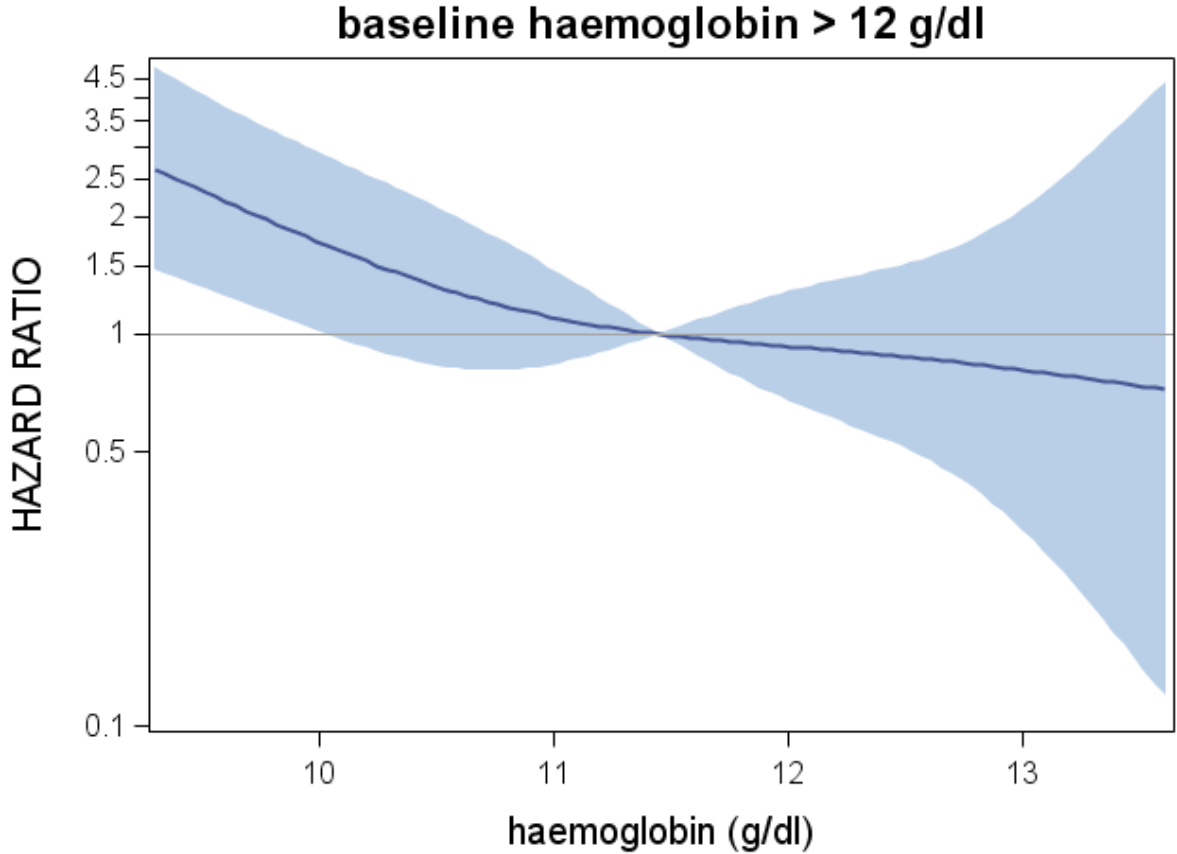
Webfigure 5a

Dependency of hazard ratio of achieved haemoglobin levels for patients with baseline haemoglobin ≤ 12 g/dL.



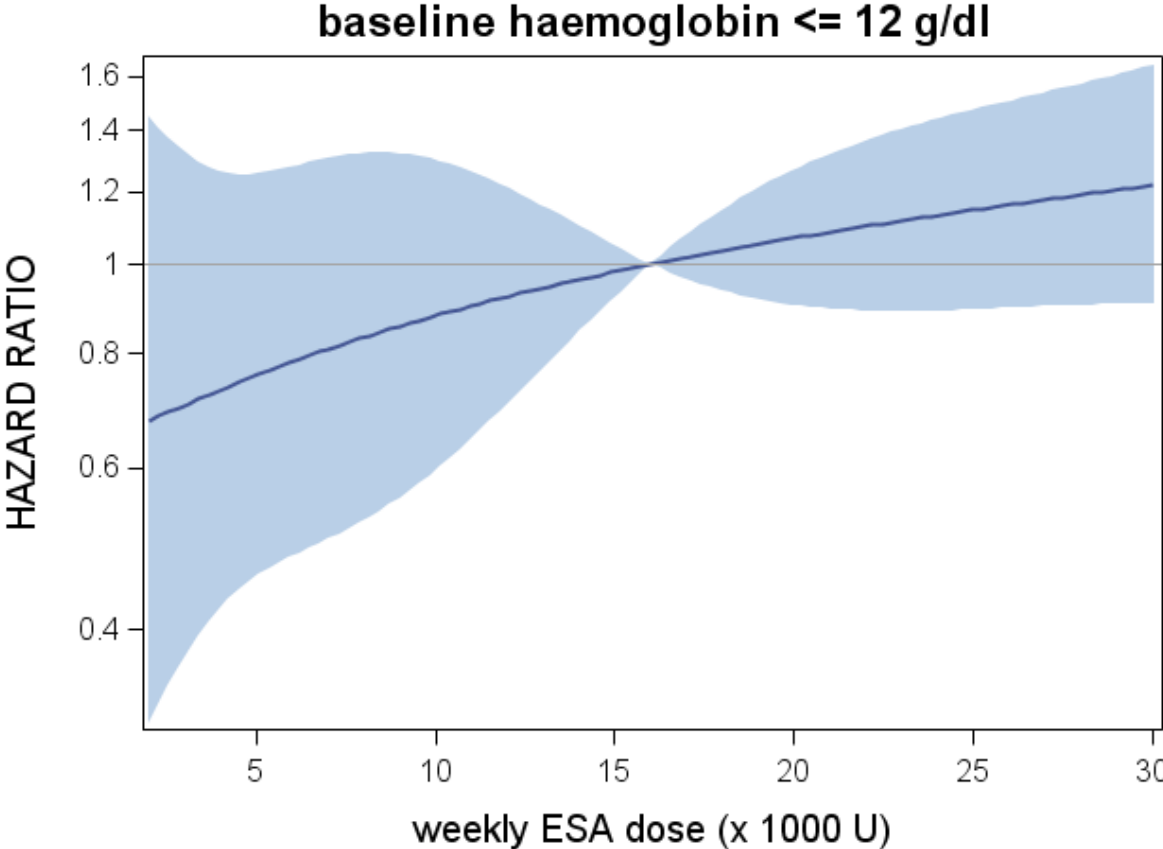
Webfigure 5b

Dependency of hazard ratio of achieved haemoglobin levels for patients with baseline haemoglobin ≥ 12 g/dL.



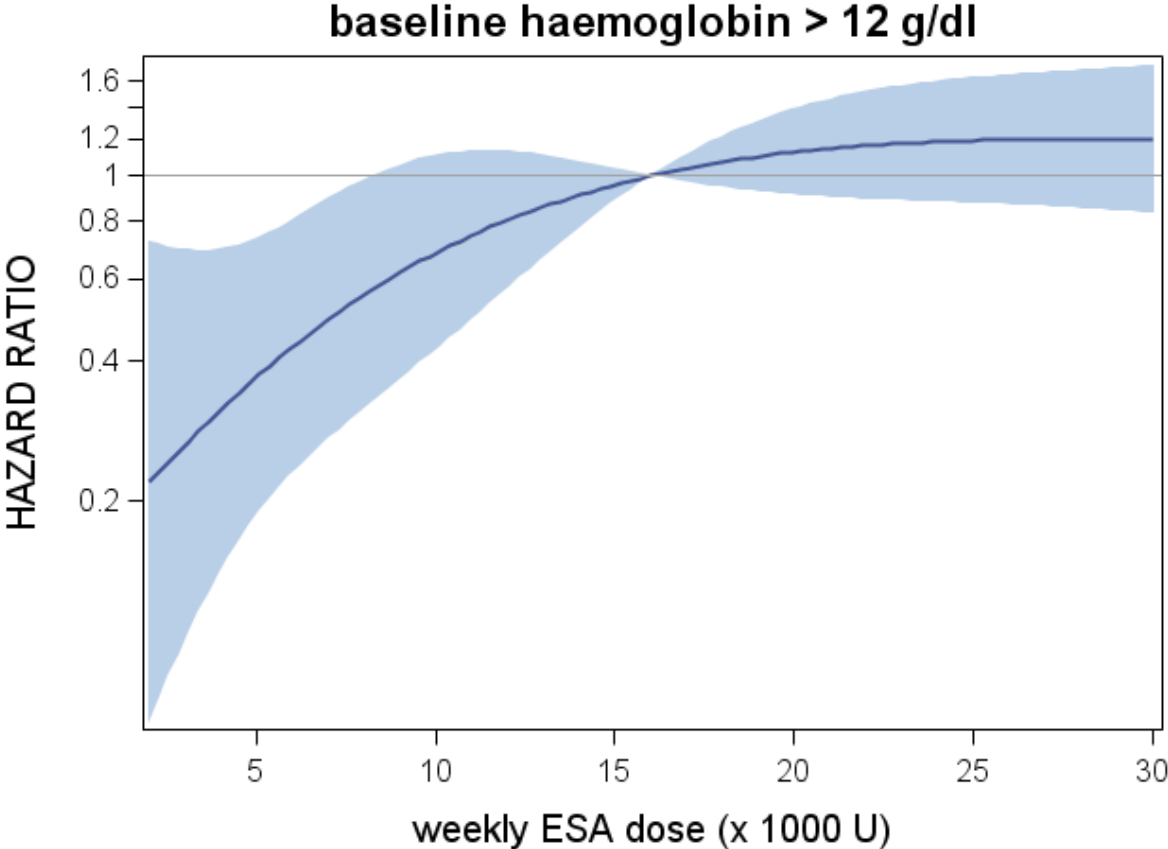
Webfigure 6a

Dependency of hazard ratio of ESA dose levels for patients with baseline haemoglobin ≤ 12 g/dL. Values of ESA are per 1000 U/week.



Webfigure 6b

Dependency of hazard ratio of ESA dose levels for patients with baseline haemoglobin > 12 g/dL. Values of ESA are per 1000 U/week.

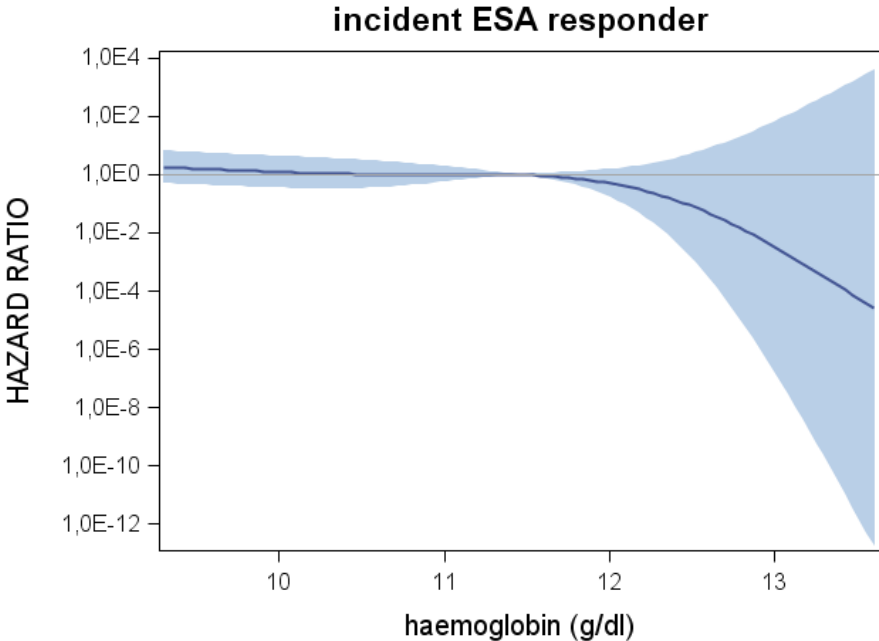
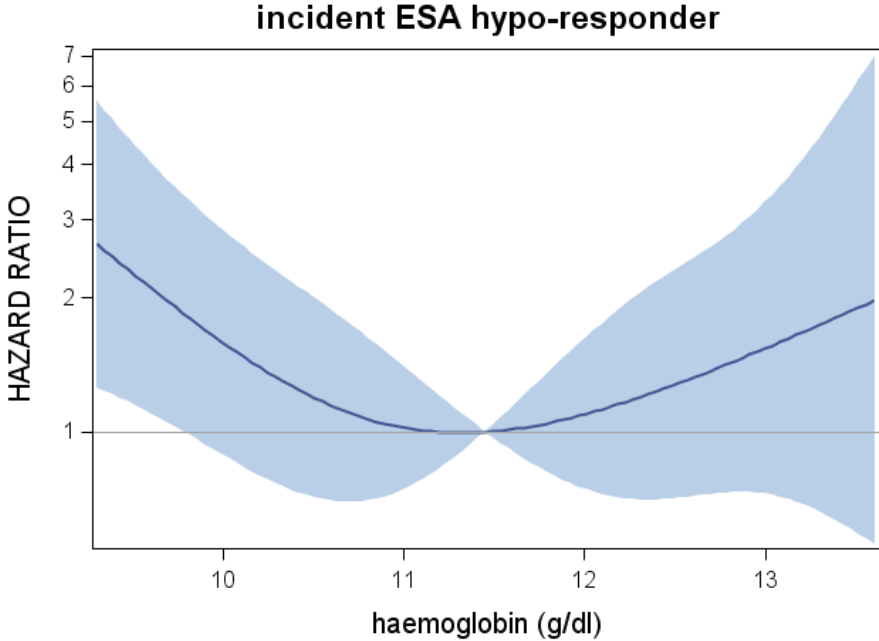


Analysis of incident vs. prevalent patients

Incident patients

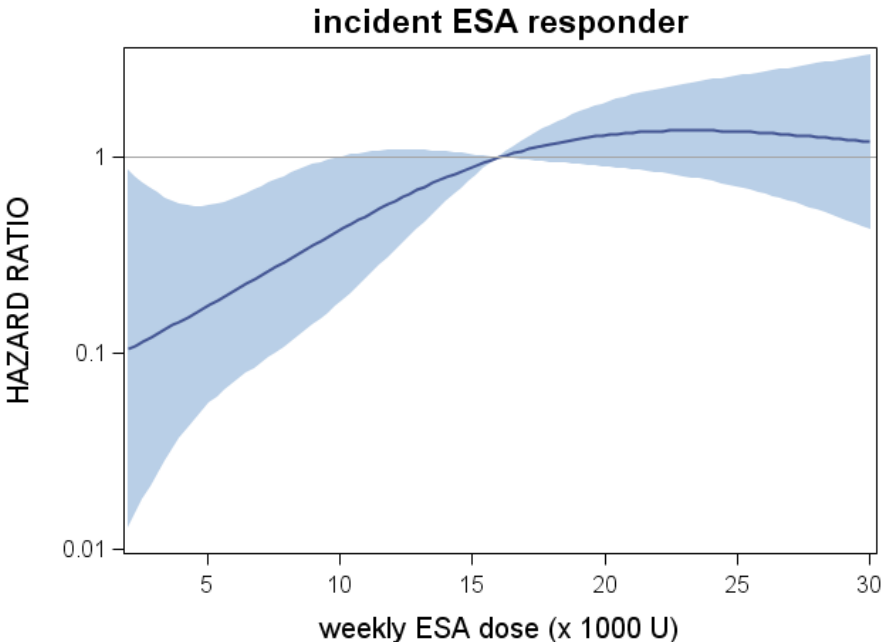
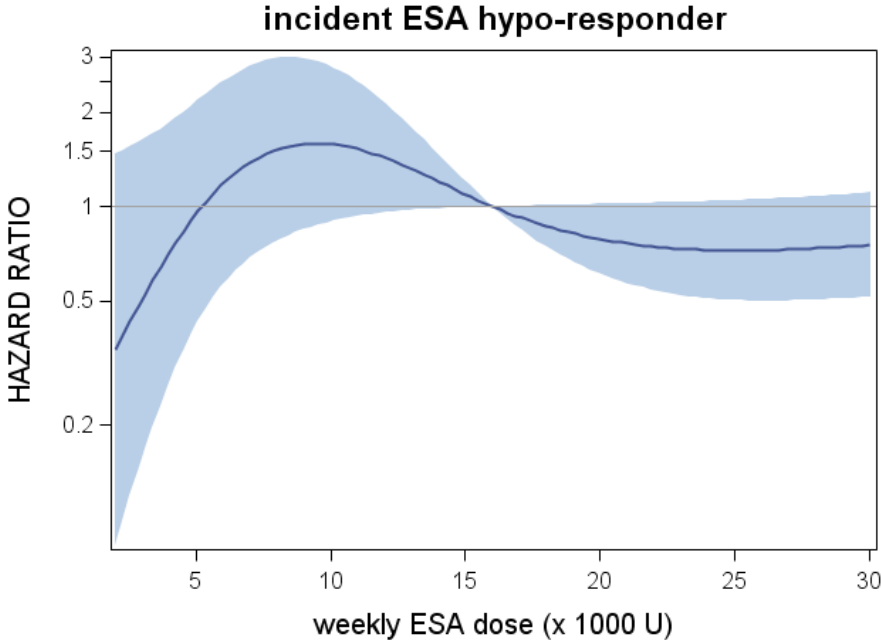
Webfigure 7

Hazard ratio for haemoglobin levels of incident patients stratified in groups of ESA responsiveness.



Webfigure 8

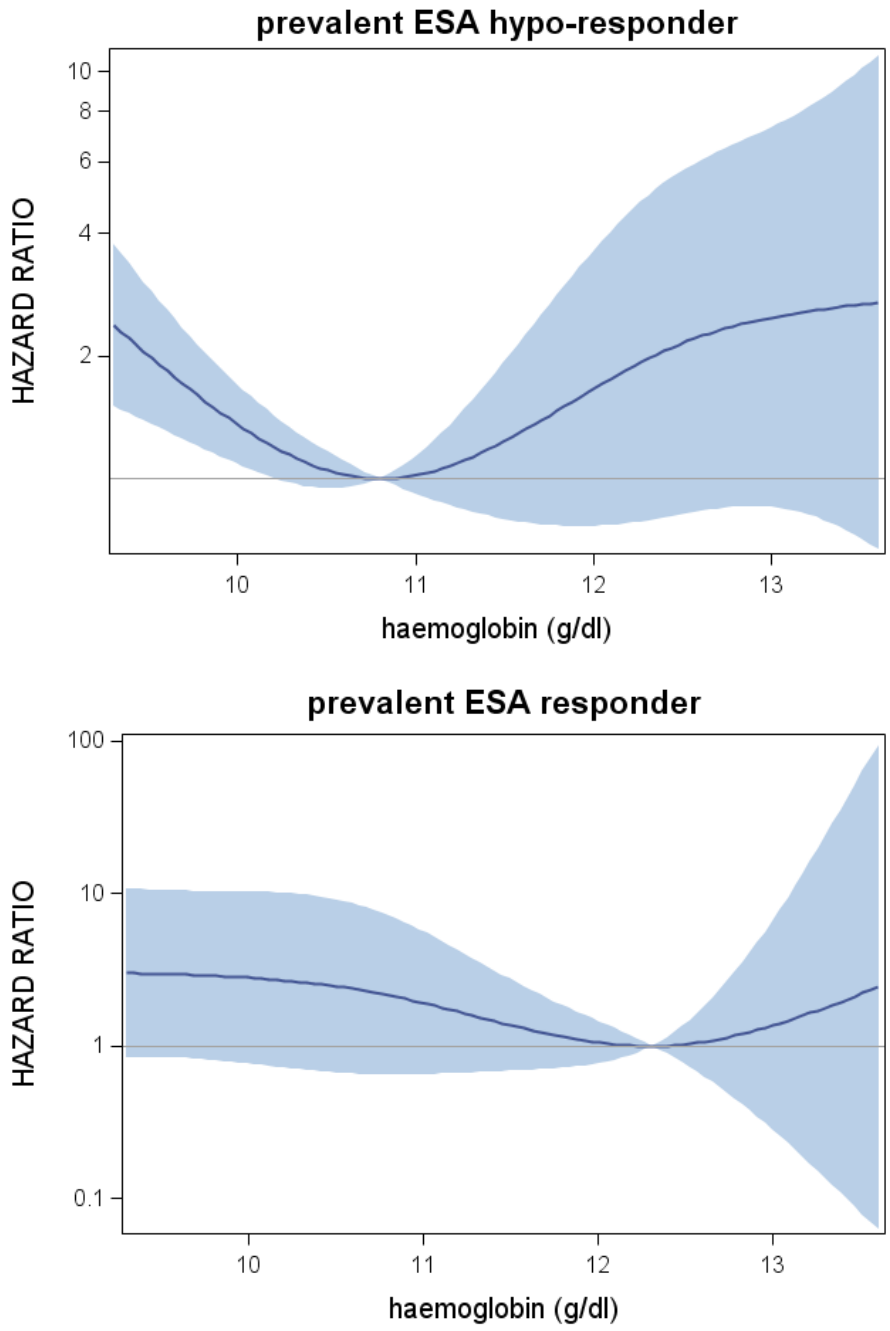
Hazard ratio for ESA dose of incident patients stratified in groups of ESA responsiveness.



Prevalent patients

Webfigure 9

Hazard ratio for haemoglobin levels of prevalent patients stratified in groups of ESA responsiveness.



Webfigure 10

Hazard ratio for ESA dose of prevalent patients stratified in groups of ESA responsiveness.

