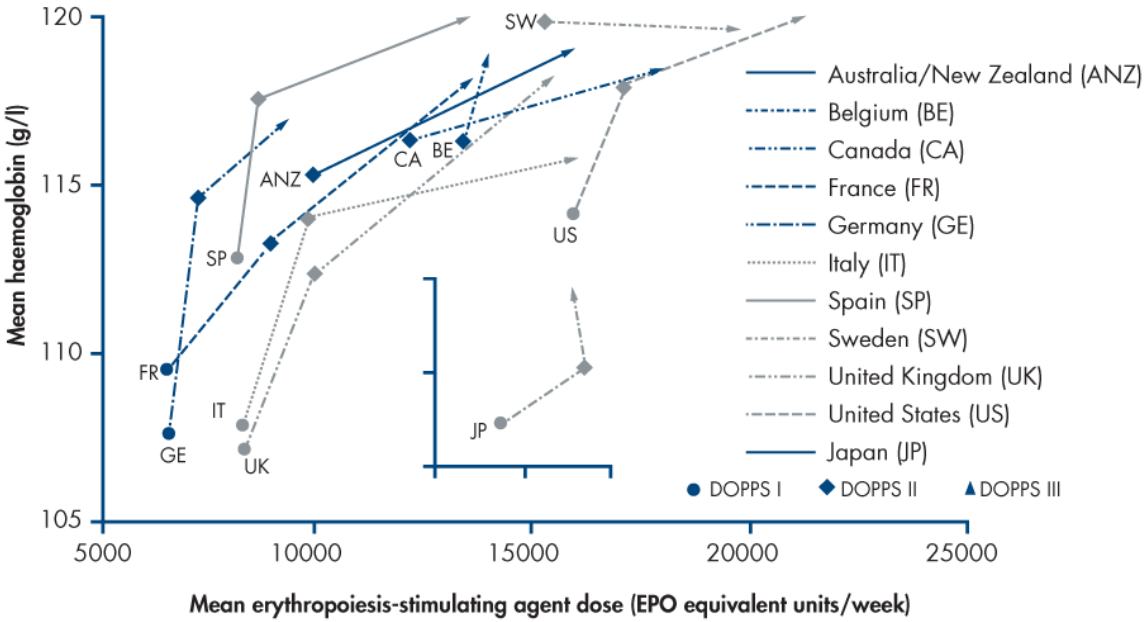
New trends and priorities in anaemia management 2017 update

David Goldsmith, London, UK

ESA doses in patients with CKD have increased

DOPPS I (1996-2001) to DOPPS III (2005-2008)



Nephrol Dial Transplant (2010) 25: 1734–1737
doi: 10.1093/ndt/gfq099
Advance Access publication 2 March 2010

2006-2010 : A testing period for ESAs

Time to Reconsider Evidence for Anaemia Treatment (TREAT) = Essential Safety Arguments (ESA)

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In-Depth Review

2009: A Requiem for rHuEPOs—But Should We Nail Down the Coffin in 2010?

d Goldsmith

Department, Guy's Hospital, King's Health Partners, London, United Kingdom

Clin J Am Soc Nephrol 5: 929–935, 2010. doi: 10.2215/CJN.09131209

NDT Advance Access published September 17, 2010

Nephrol Dial Transplant (2010) 1 of 4
doi: 10.1093/ndt/gfq577

Editorial Review

NDT
Nephrology Dialysis Transplantation

Extraordinary popular delusions and the madness of crowds: puncturing the epoetin bubble—lessons for the future

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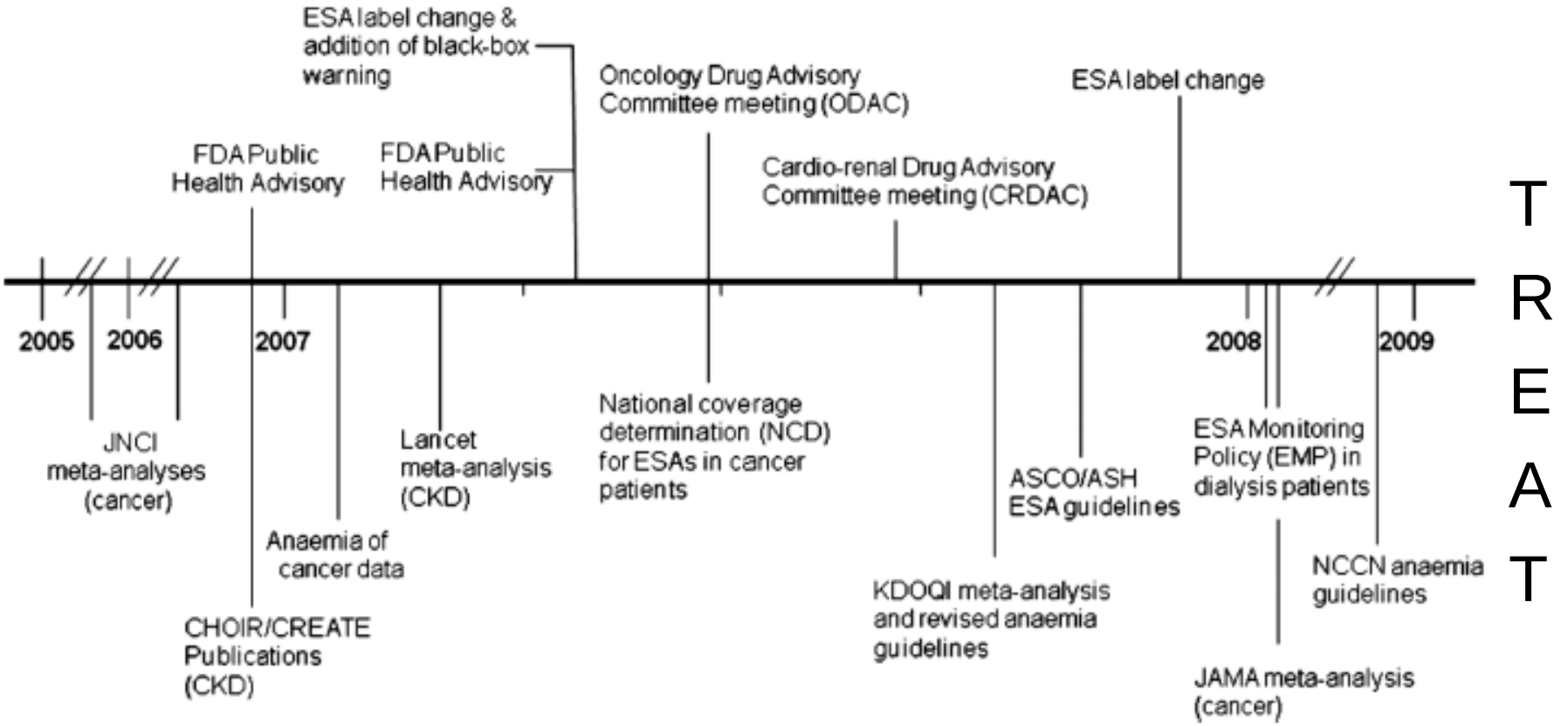
Sign of the Times...

Caution emerges in the renal community….



Renal anaemia management guidelines

CARI
Caring for Australasians with Renal Impairment

CSN
Canadian Society of Nephrology

EBPG
European Best Practice Guidelines

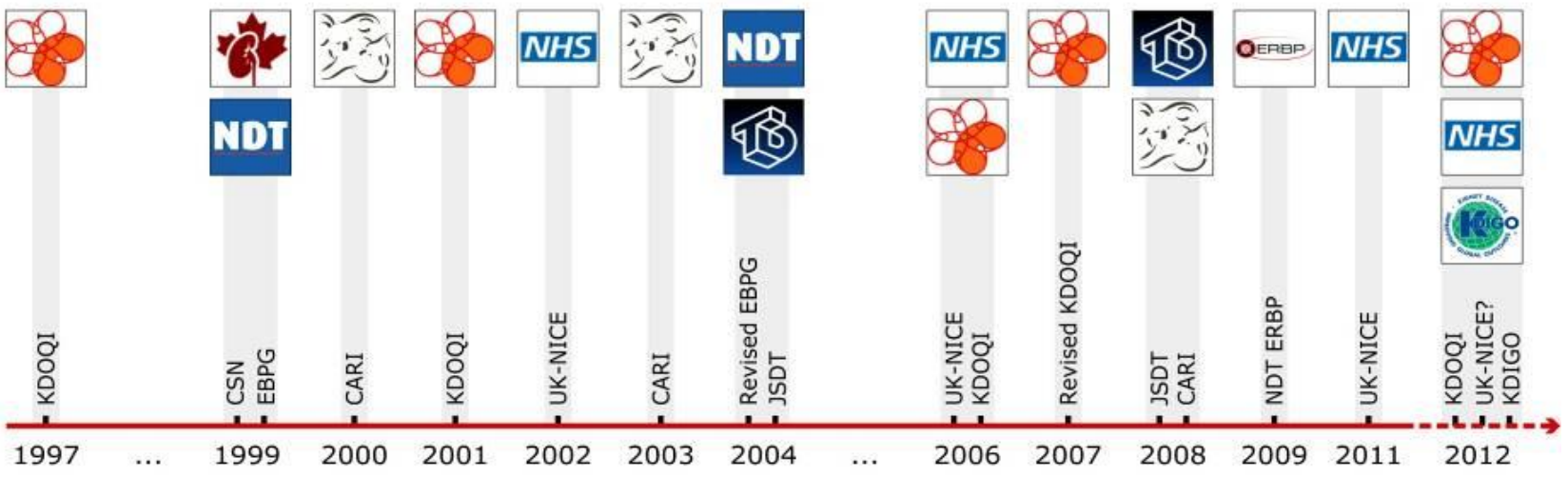
KDOQI
Kidney Disease Outcomes Quality Initiative

UK-NICE
National Institute for Health and Clinical Excellence

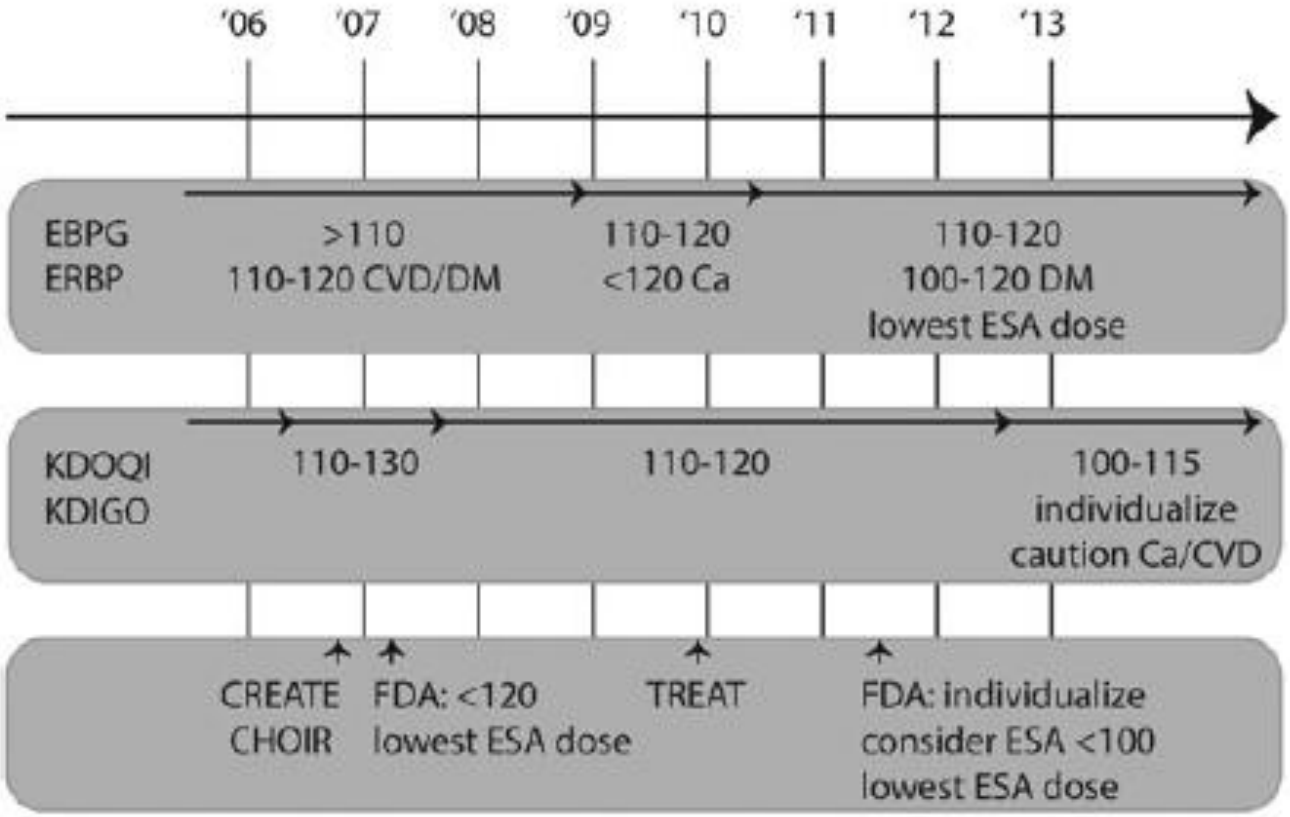
JSDT
The Japanese Society for Dialysis Therapy

KDIGO
Kidney Disease Improving Global Outcomes

ERBP
European Renal Best Practice

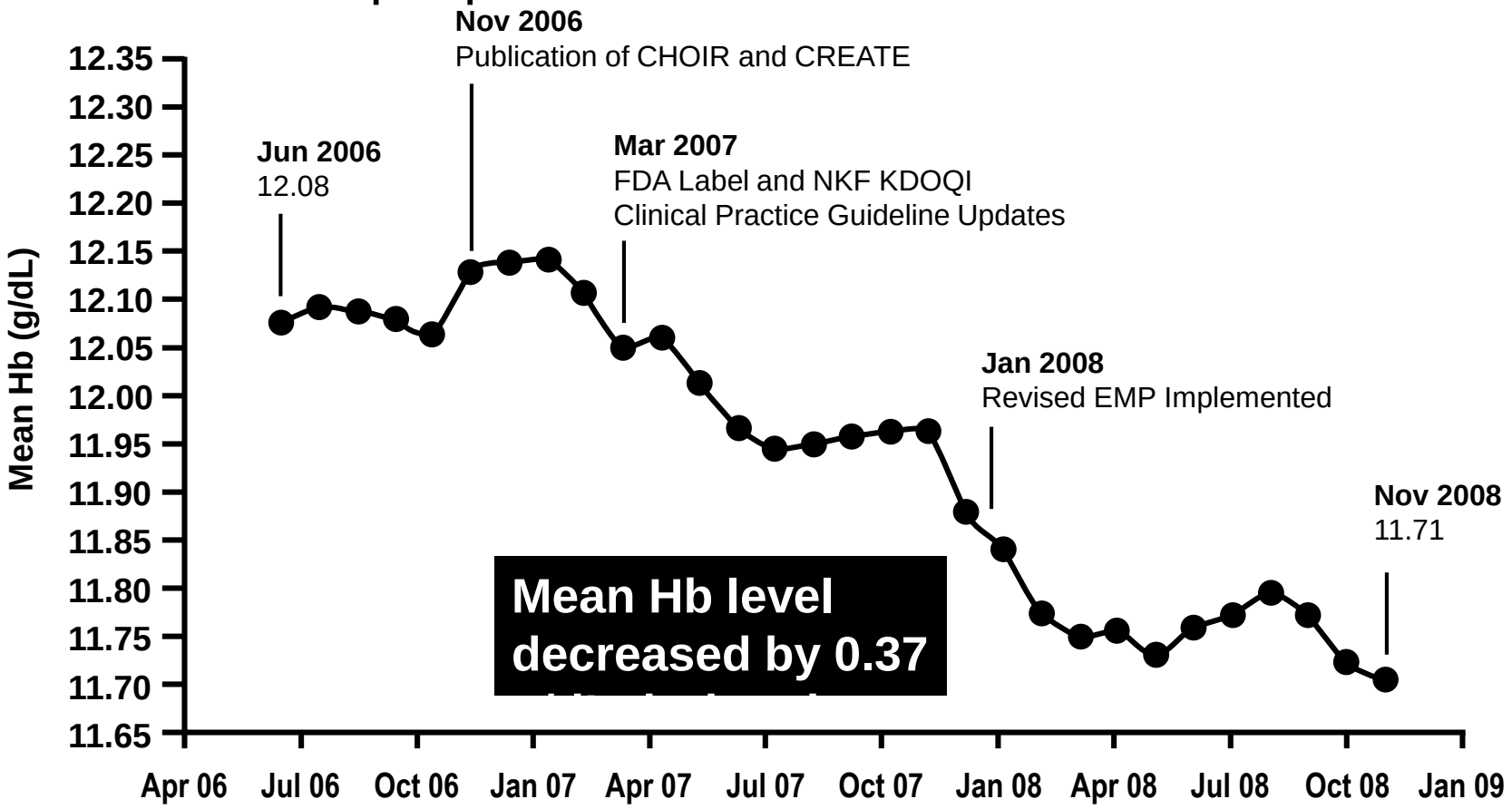


Trials, and Guidelines, for Hb 2006-2014



Decrease in Hb levels since 2006

- Retrospective observational study using patient-level data from ~87% of dialysis centres in the US (2006-2008): ~ 743 000 unique patients



NDT Advance Access published August 4, 2015

Nephrol Dial Transplant (2015) 0: 1–8
doi: 10.1093/ndt/gfv298

Original Article

Trends in haemoglobin, erythropoietin-stimulating agents and iron use in Swedish chronic kidney disease patients between 2008 and 2013

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Table 2. Trends in the use of ESA in a referred CKD-ND population during the period 2008–13

	2008–09 Adj. RR	95% CI	*P*-value
ESA use[a]	Ref.	0.81; 0.96 0.87; 1.04	0.003
ESA dose[a]	Ref.	95% CI −0.03; 0.12 −0.11; 0.05	*P*-value 0.16

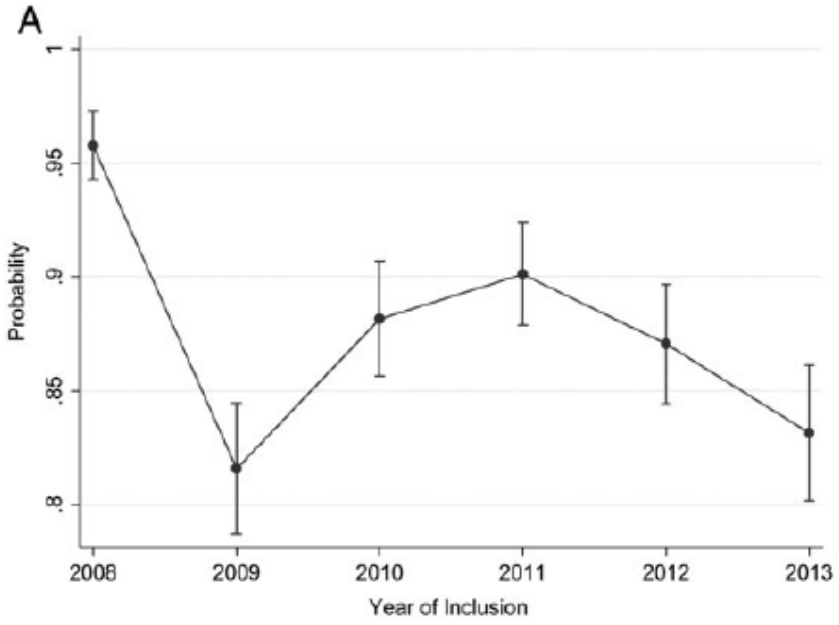


Table 6. Trends in the use of ESA

	2008–09 Adj. RR	95% CI	*P*-value
ESA use[a]	Ref.	0.92; 0.97 0.92; 0.98	<0.01
ESA dose[a]	Ref.	95% CI −0.15; −0.04 −0.08; 0.03	*P*-value <0.01

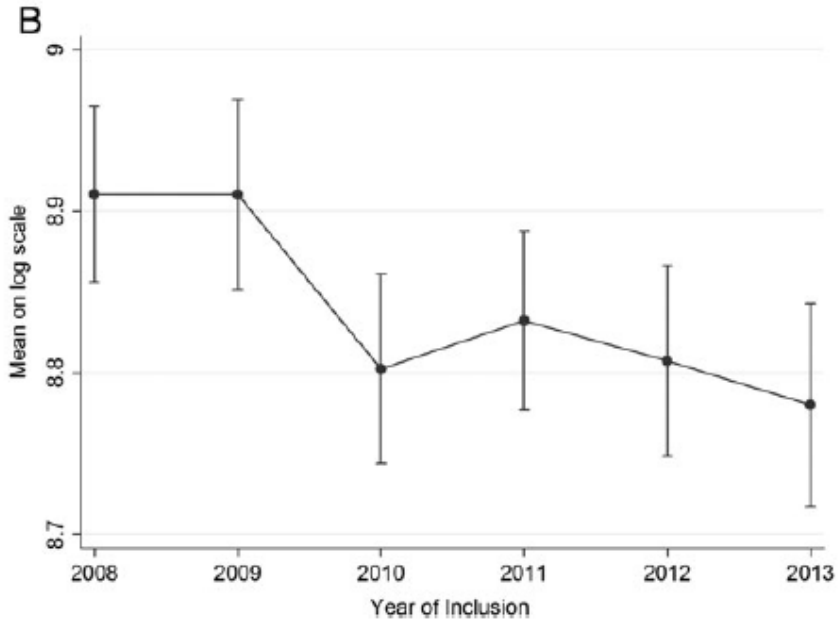


Table 7. Trends in haemoglobin levels in stable incident HD patients during the period 2008–13

	2008–09	2010–11	95% CI	2012–13	95% CI	*P*-value
	Adj. coeff.	Adj. coeff.		Adj. coeff.		
Haemoglobin[a]						
ESA users	Ref.	−1.29	−2.33; −0.25	−1.72	−2.81; −0.64	<0.01
		Ref.		−0.44	−1.51; 0.64	
ESA non-users	Ref.	−0.47	−3.91; 2.96	0.09	−3.18; 3.36	0.94
		Ref.		0.57	−2.69; 3.82	
		Adj. RR	95% CI	Adj. RR	95% CI	*P*-value
Hb >120 g/L[a]						
ESA users	Ref.	0.88	0.80; 0.97	0.89	0.81; 0.99	<0.02
		Ref.		1.01	0.91; 1.12	

Adj., adjusted; coeff., coefficient; haemoglobin: to convert g/L to mg/dL multiply by 0.1.
[a]Model adjusted for age, sex, primary renal disease, BMI, use of iron, type of access, use of haemodiafiltration, CRP, *p*-albumin and standard Kt/*V*.

Table 8. Trends in the use of iron medication and ferritin levels in stable incident HD patients 2008–13

	2008–09	2010–11	95% CI	2012–13	95% CI	*P*-value
	Adj. RR	Adj. RR		Adj. RR		
Iron medication						
ESA users[a]	Ref.	1.04	0.99; 1.09	1.05	1.00; 1.10	0.05
		Ref.		1.01	0.96; 1.06	
ESA non-users[a,b]	Ref.	1.40	1.11; 1.77	1.42	1.14; 1.77	<0.01
		Ref.		1.02	0.85; 1.22	
		Adj. coeff.[c]	95% CI	Adj. coeff.[c]	95% CI	*P*-value
Ferritin (µg/L)						
ESA users and non-users[a]	Ref.	0.05	−0.03; 0.13	−0.06	−0.14; 0.02	0.18
		Ref.		−0.11	−0.19; −0.03	

CJASN ePress. Published on August 18, 2015 as doi: 10.2215/CJN.02600315

Article

Understanding the Recent Increase in Ferritin Levels in United States Dialysis Patients: Potential Impact of Changes in Intravenous Iron and Erythropoiesis-Stimulating Agent Dosing

Angelo Karaboyas, Jarcy Zee,* Hal Morgenstern,*†‡ Jacqueline G. Nolen,§ Raymond Hakim,‖ Kamyar Kalantar-Zadeh,¶ Philip Zager,** Ronald L. Pisoni,* Friedrich K. Port,* and Bruce M. Robinson*††*

*Arbor Research Collaborative for Health, Ann Arbor,

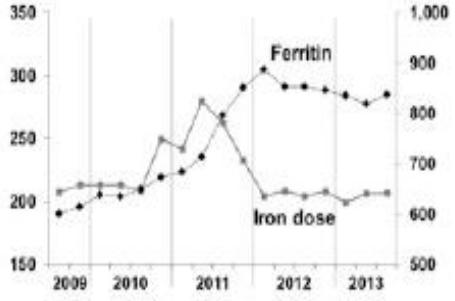
All patients

Group A: Facility mean IV iron dose increased >50 mg/mo from 2010 to 2011

Group B: Facility mean IV iron dose increased <50 mg/mo from 2010 to 2011

Group C: Facility mean IV iron dose decreased from 2010 to 2011

T1



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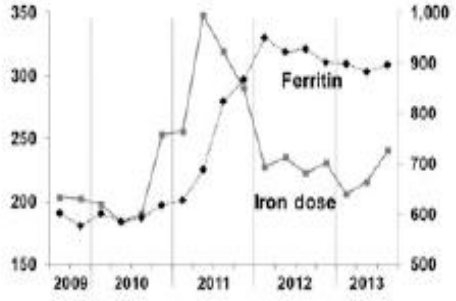

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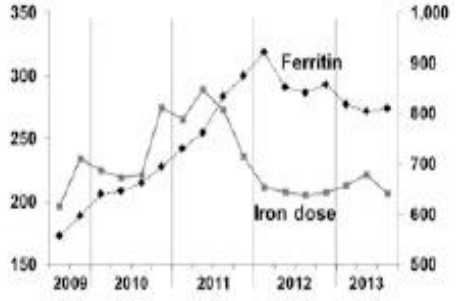

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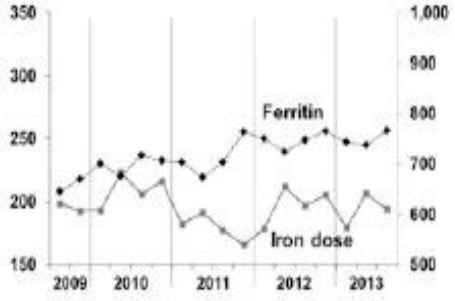

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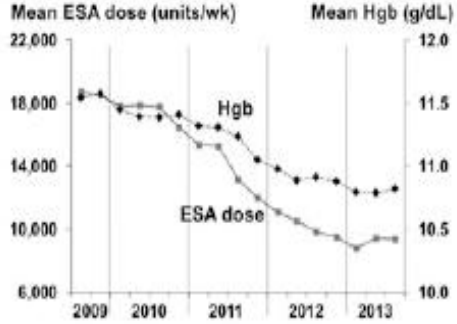

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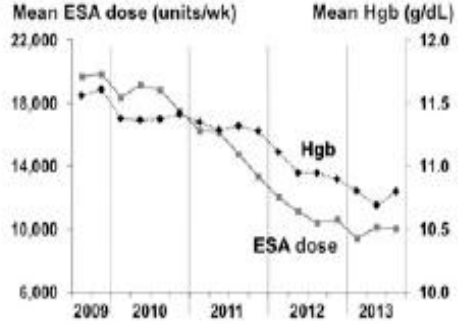

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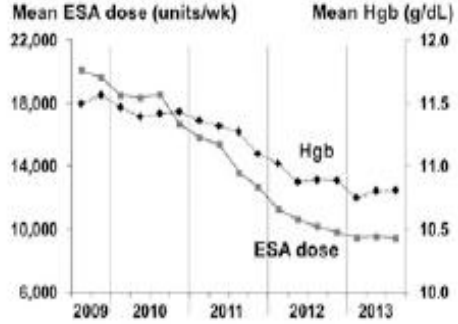

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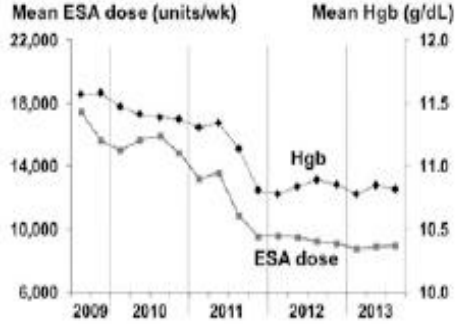

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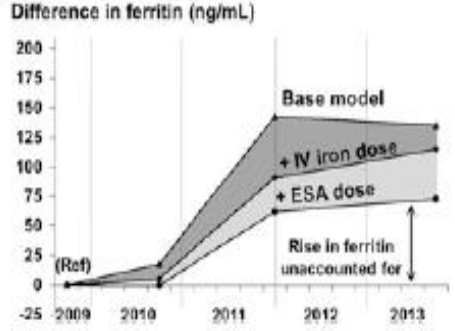

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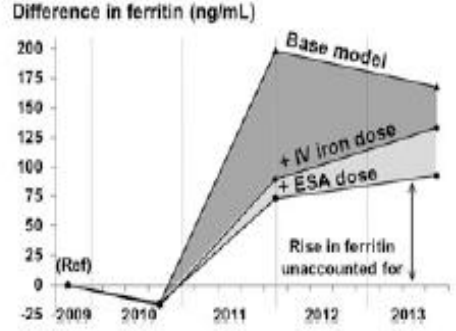

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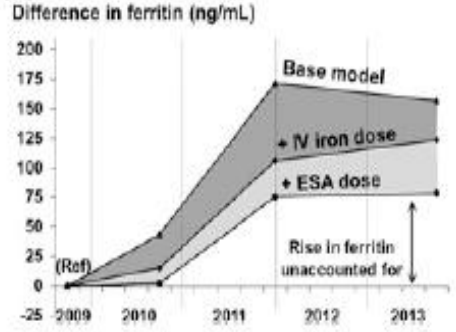

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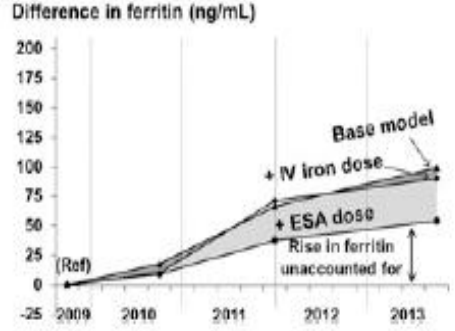

Patient characteristics trends

Table 2. Trends in patient characteristics in United States dialysis patients

Patient Characteristic	August 2010	August 2011	August 2012	August 2013
Age (yr)	63 (52, 73)	63 (52, 73)	63 (52, 73)	63 (53, 73)
Vintage (yr)	2.7 (1.1, 5.1)	2.8 (1.2, 5.5)	2.9 (1.3, 5.7)	2.9 (1.3, 5.7)
Vintage <90 d (%)	5.2	4.1	4.8	4.9
Men (%)	56	55	56	56
Black race (%)	32	33	37	34
Body mass index (kg/m^2)	27.0 (22.9, 32.2)	27.3 (23.3, 32.1)	27.5 (23.4, 32.3)	27.2 (23.5, 32.4)
Diabetes (%)	64	63	61	62
Systolic BP (mmHg)	148 (131, 163)	147 (131, 163)	148 (132, 165)	146 (130, 163)
Treatment time (min)	212 (195, 240)	212 (195, 240)	215 (196, 240)	215 (199, 241)
Single pool Kt/V	1.56 (1.41, 1.72)	1.58 (1.43, 1.75)	1.62 (1.47, 1.78)	1.60 (1.44, 1.77)
Serum phosphorus (mg/dl)	4.9 (4.1, 6.0)	4.9 (4.1, 5.9)	4.8 (3.9, 5.8)	4.8 (4.0, 5.8)
Serum parathyroid hormone (pg/ml)	247 (163, 379)	307 (192, 488)	311 (196, 501)	322 (198, 496)
Serum albumin (g/dl)	3.84 (3.57, 4.06)	3.85 (3.59, 4.07)	3.89 (3.61, 4.10)	3.90 (3.69, 4.17)
Transfusions (%)[a]	2.5	3.1	3.3	–
Catheter use (%)	18	19	16	16

Original Report: Patient-Oriented, Translational Research

American Journal of Nephrology

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DOI: 10.1159/000370334

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Major Declines in Epoetin Dosing after Prospective Payment System Based on Dialysis Facility Organizational Status

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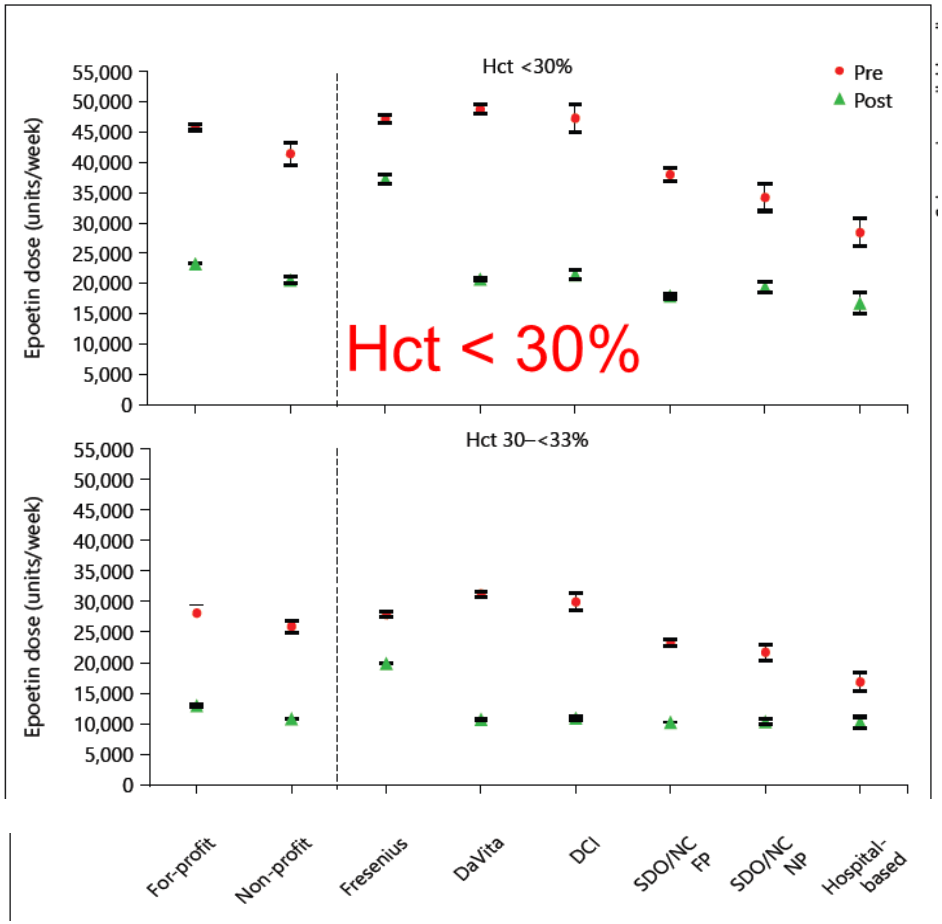
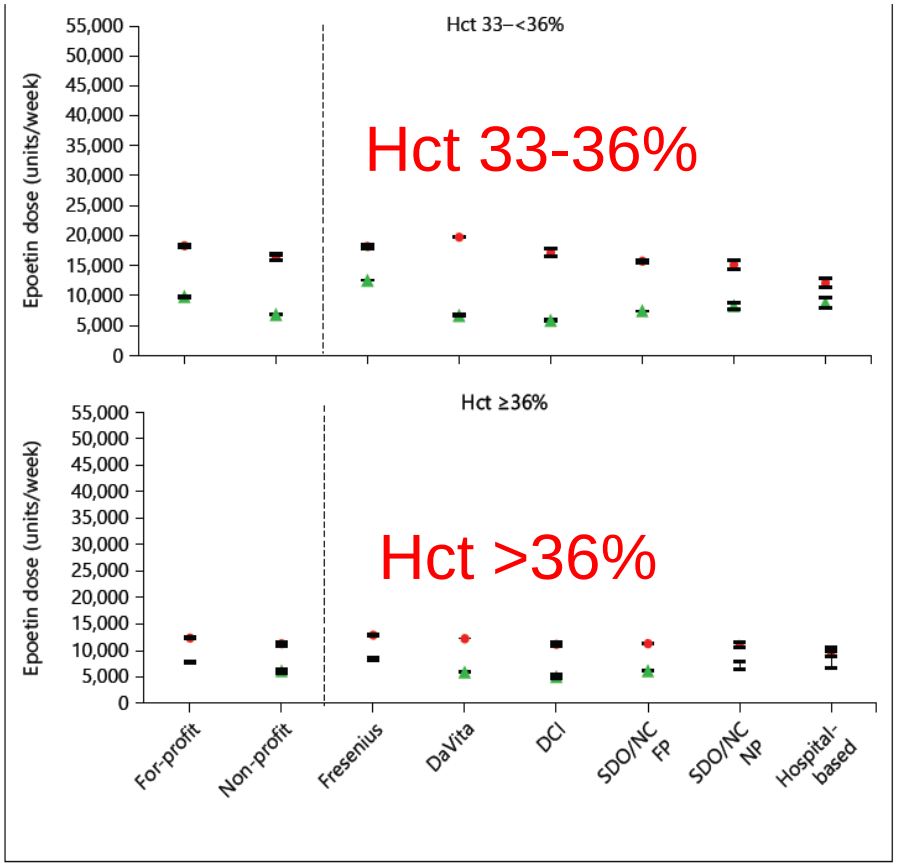
Miguel A. Hernán[c]

[a]Medical Technology and Practice Patterns Institute, Bethesda, Md., [b]Department of Medicine and Research Service, VA NY Harbor Healthcare System and New York University School of Medicine, New York, N.Y., and [c]Departments of Epidemiology and Biostatistics, Harvard School of Public Health, Harvard-MIT Division of Health Sciences and Technology, Boston, Mass., USA


Hct <30%
Pre
Post
Epoetin dose (units/week)
55,000
50,000
45,000
40,000
35,000
30,000
25,000
20,000
15,000
10,000
5,000
0
Hct < 30%
Hct 30–<33%
For-profit
Non-profit
Fresenius
DaVita
DCI
SDO/NC FP
SDO/NC NP
Hospital-based

Hct 30-33%


Hct 33–<36%
Epoetin dose (units/week)
55,000
50,000
45,000
40,000
35,000
30,000
25,000
20,000
15,000
10,000
5,000
0
Hct 33-36%
Hct ≥36%
Hct >36%
For-profit
Non-profit
Fresenius
DaVita
DCI
SDO/NC FP
SDO/NC NP
Hospital-based

The times and tides of Hb levels (g/dL)

13

7…8

9….11

1997

2004

2011

2017

Eriksson *et al. BMC Nephrology* (2016) 17:97
DOI 10.1186/s12882-016-0312-9

BMC Nephrology

RESEARCH ARTICLE Open Access

Cross-sectional survey in CKD patients across Europe describing the association between quality of life and anaemia

Daniel Eriksson[1†], David Goldsmith[2†], Siguroli Teitsson[1], James Jackson[3] and Floortje van Nooten[4*]

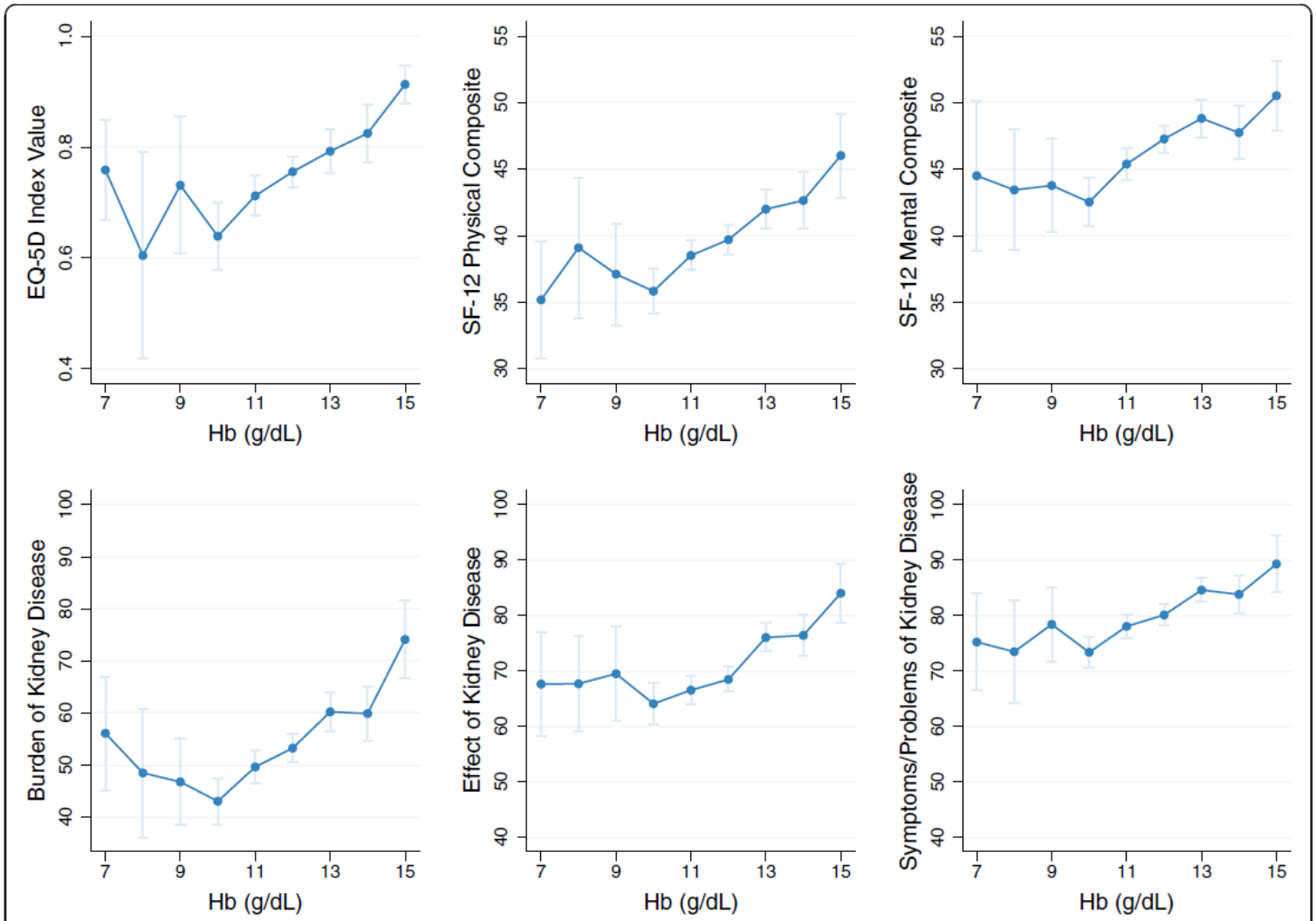


Fig. 1 HRQoL measures by serum haemoglobin level. Significant but modest Spearman's correlation coefficients between HRQoL measures and Hb (range 0.19–0.23; all *P*-values < 0.0001). Hb levels recorded on the x-axis represent the midpoint of the Hb range (e.g. 7 g/dL refers to levels 6.5 ≤ Hb < 7.5 g/dL). Vertical lines represent the 95 % confidence interval around the mean. EQ-5D, $n = 1147$; SF-12, $n = 1086$; burden of kidney disease, $n = 1169$; effect of kidney disease, $n = 1149$; symptoms of/problems with kidney disease, $n = 1140$. Hb, haemoglobin; SF-12, 12-Item Short Form Health Survey; HRQoL, health-related quality of life

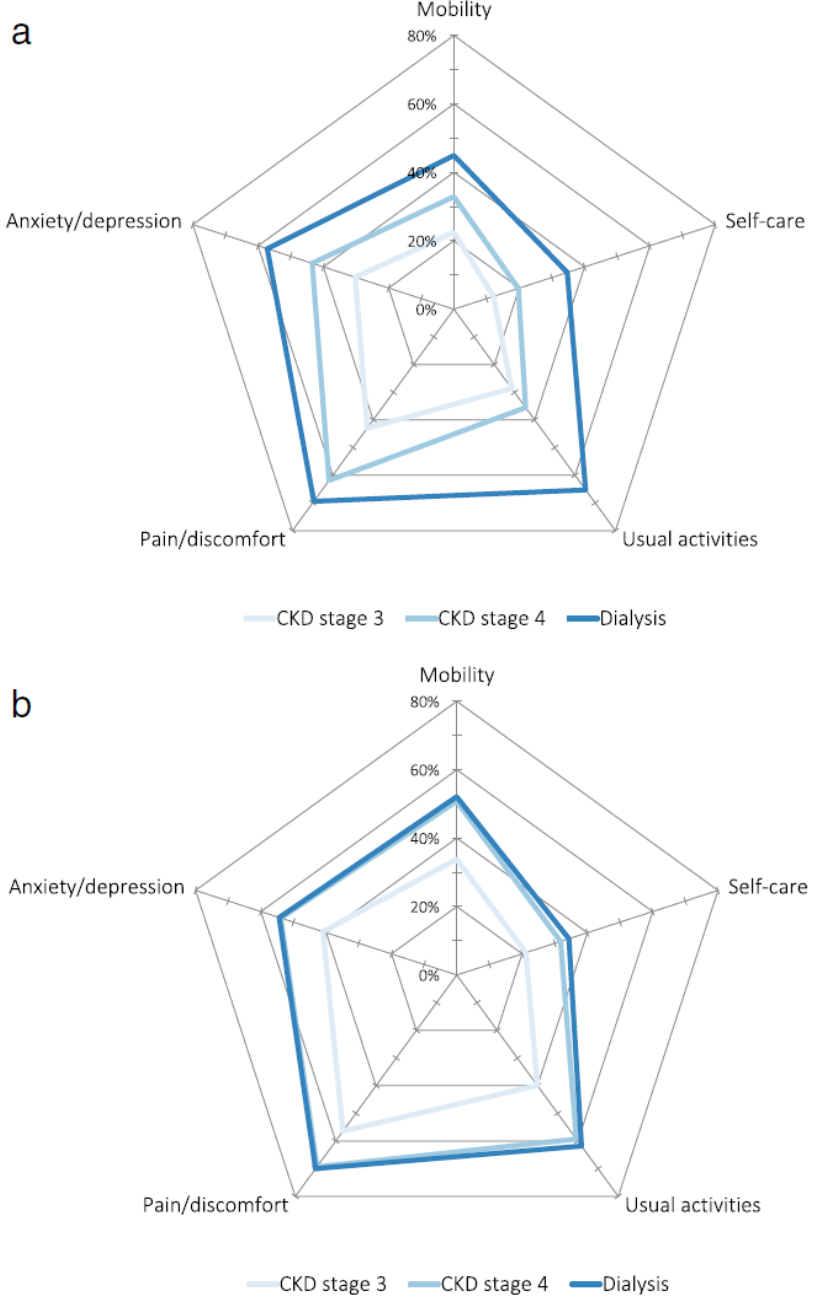


Fig. 2 Proportion of patients reporting problems for the five EQ-5D dimensions by stages of chronic kidney disease. **a** Non-anaemic patients and **b** anaemic patients. CKD, chronic kidney disease

Table 5 Health-related quality of life scores by erythropoiesis stimulating agent/supplemental iron use in patients with CKD stages 3 and 4 and those on dialysis

Subscales of the KDQOL-36	No ESA/supplemental iron use Mean (SD)	ESA and/or supplemental iron use Mean (SD)	*P*-value
Symptoms/problems list	83.5 (17.1)	77.1 (17.6)	<0.0001
Effect of Kidney Disease	76.9 (19.0)	64.5 (21.0)	<0.0001
Burden of Kidney Disease	61.5 (25.8)	46.9 (25.8)	<0.0001
SF-12 physical composite summary	42.4 (10.1)	37.6 (9.5)	<0.0001
CKD stage 3	44.6 (9.3)	40.8 (9.9)	0.0019
CKD stage 4	40.5 (10.3)	36.9 (8.9)	0.0007
Dialysis	39.0 (10.4)	37.1 (9.7)	0.1441
SF-12 mental composite summary	47.9 (9.3)	45.4 (10.1)	<0.0001
CKD stage 3	49.7 (8.6)	46.9 (10.0)	0.0206
CKD stage 4	46.9 (9.4)	44.9 (9.8)	0.0653
Dialysis	44.3 (10.0)	45.3 (10.3)	0.4347

Abbreviations: *CKD* chronic kidney disease, *ESA* erythropoiesis stimulating agent, *KDQOL-36* Kidney Disease Quality of Life Instrument, *SD* standard deviation, *SF-12* 12-Item Short Form Health Survey

Saudi J Kidney Dis Transpl 2016;27(6 Suppl 1):S51-S61
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Saudi Journal of Kidney Diseases and Transplantation

Original Article

Gulf Cooperation Council-Dialysis Outcomes and Practice Patterns Study: An Overview of Anemia Management Trends at the Regional and Country Specific Levels in the Gulf Cooperation Council Countries

Characteristic	Country						
	Bahrain	Kuwait	Oman	Qatar	Saudi Arabia	UAE	Overall
Facility characteristics							
Facilities (*n*)	1	4	4	2	21	9	41
Facility size, median (IQR)	287 (287,287)	164 (130,198)	103 (70,203)	167 (65,268)	57 (37,85)	144 (48,193)	142 (71,296)
Sample patients (*n*)	25	116	89	58	419	220	927
Demographics							
Age, years	51.0 (54.7)	55.5 (38.5)	51.4 (40.3)	61.6 (33.1)	50.9 (32.3)	54.5 (33.0)	53.2 (35.4)
Male (%)	56	54	52	61	55	61	56
Arab National (%)	100	84	97	49	83	57	77
Years on dialysis	2.92 (1.08, 3.85)	1.82 (1.03, 3.66)	3.52 (1.09, 5.87)	2.48 (1.18, 4.51)	2.71 (0.77, 7.24)	2.55 (1.21, 4.82)	2.55 (0.93, 5.01)
Body mass index, (kg/m^2)	27.2 (24.6)	28.9 (17.9)	23.9(19.2)	26.7 (16.0)	25.7(13.6)	26.4(13.2)	26.3 (15.2)
Labs							
Hb (g/dL)	10.4 (5.5)	11.1 (3.3)	10.7 (4.4)	11.1 (3.3)	10.9 (3.1)	10.7 (3.5)	10.9 (3.4)
Ferritin (ng/ml)	383 (70,735)	438 (218,752)	304 (148,580)	397 (295,602)	388 (180,547)	449 (208,702)	390 (179,621)
Transferrin saturation (%)	16.2 (25.9)	26.4 (27.7)	28.2 (42.2)	30.7 (32.1)	30.0 (28.9)	27.2 (27.0)	28.4 (29.9)
Medications prescribed (%)							
ESAs	100	87	94	97	80	91	88
Intravenous iron	68	68	61	73	38	55	53
Oral iron	4	10	6	0	37	14	20
Medications details							
ESAs type (%)							
Epoetin	76	0	100	64	52	43	50
Darbepoetin	16	98	0	24	45	56	47
Pegylated epoetin beta	8	2	0	12	3	1	3
Subcutaneous ESA use (%)	0	4	0	0	15	2	6
Epoetin dose equivalent (units/weak)	12000 (3500, 15,000)	8000 (4800, 12,000)	8667 (7333, 12,000)	10000 (4000, 16,000)	8000 (5333, 12,000)	9333 (5333, 14,000)	8667 (5333, 13,333)
Intravenous iron type (%)							
Sucrose only	6	60	100	100	47	64	0.617
Gluconate only	0	0	0	0	3	0	1
Dextran only	35	0	0	0	11	19	11
Other	59	40	0	0	39	17	27

HD: Hemodialysis, Hb: Hemoglobin, ESAs: Erythropoiesis-stimulating agents

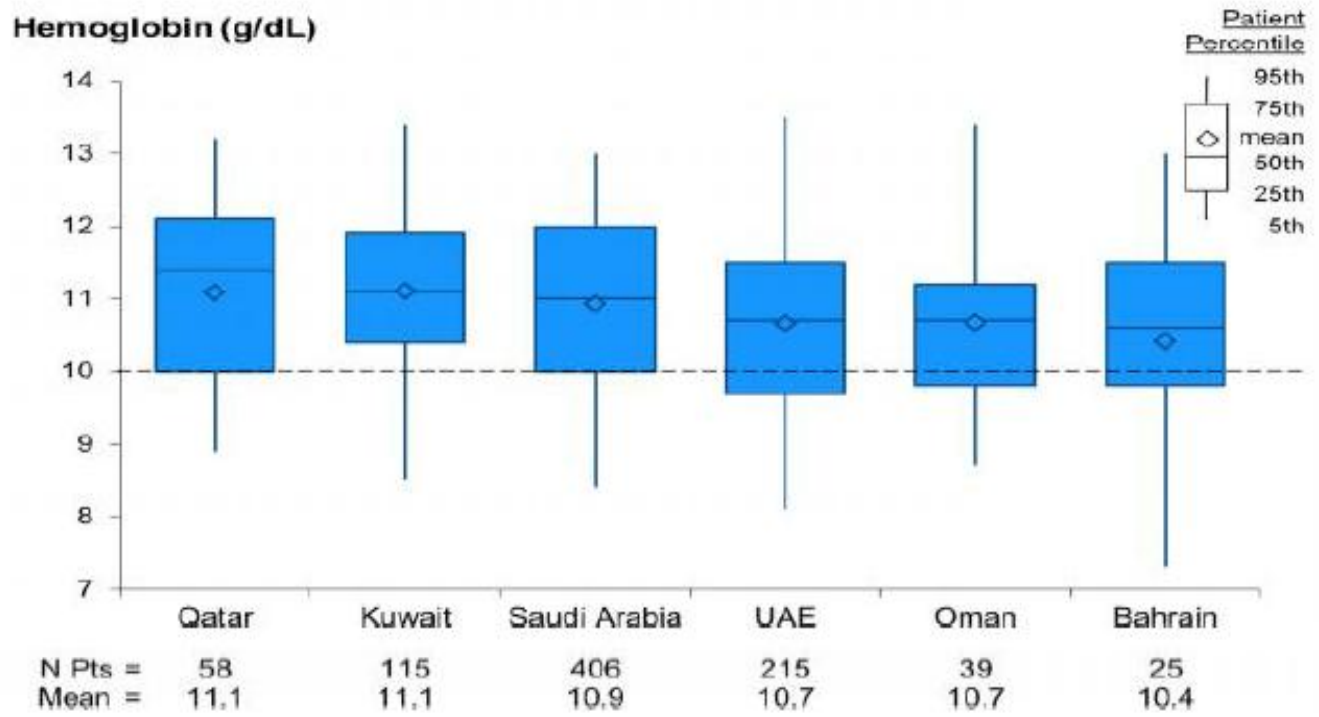


Figure 3. Achieved hemoglobin level distribution by country for the Gulf Cooperation Council-Dialysis Outcomes and Practice Patterns Study hemodialysis population (2012, 2013). Some variability in Hb levels was evident between GCC countries, with the highest mean Hb level of 11.1 g/dL observed in Kuwait and Qatar.

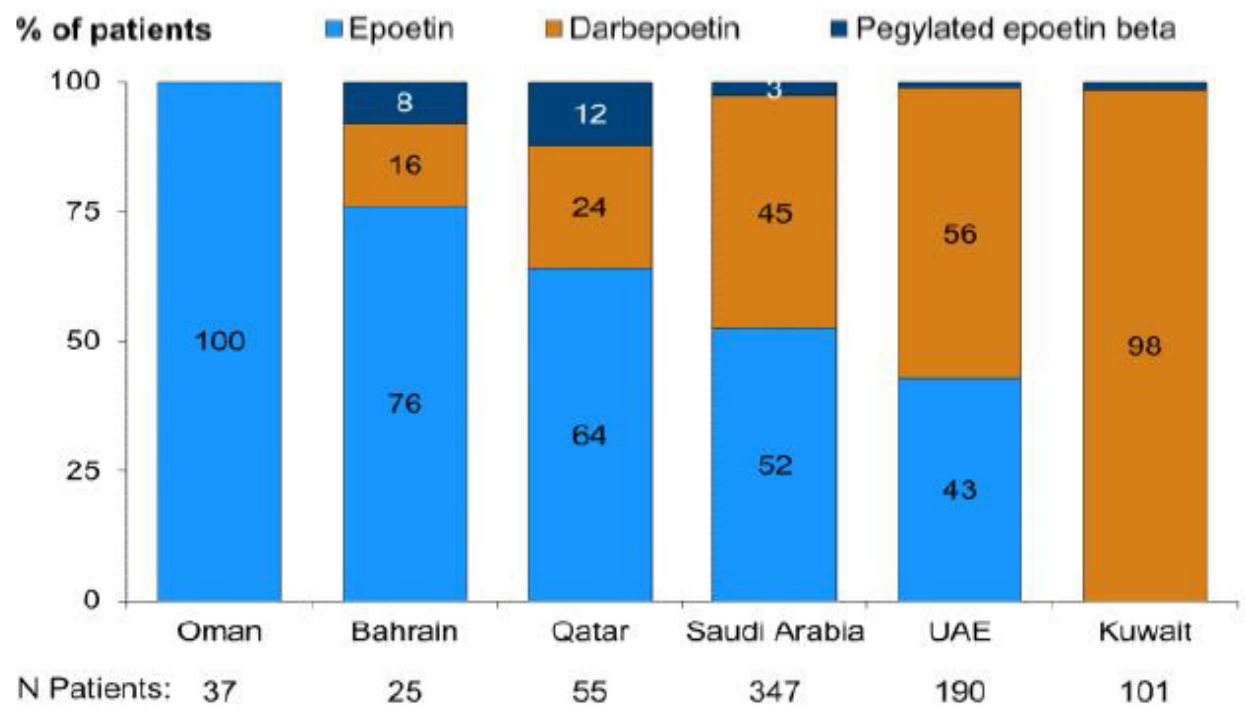


Figure 4. Type of erythropoiesis stimulating agents prescribed by country for the Gulf Cooperation Council-Dialysis Outcomes and Practice Patterns Study hemodialysis population (2012, 2013), among patients with an active ESA prescription at any time during the month of enrollment into DOPPS. Significant variability was observed in ESA type being used across GCC countries. Epoetin was predominantly used in Oman, Bahrain, and Qatar whereas darbepoetin was predominant in Kuwait. An almost even split in the use of epoetin and darbepoetin was seen in the UAE and Saudi Arabia.

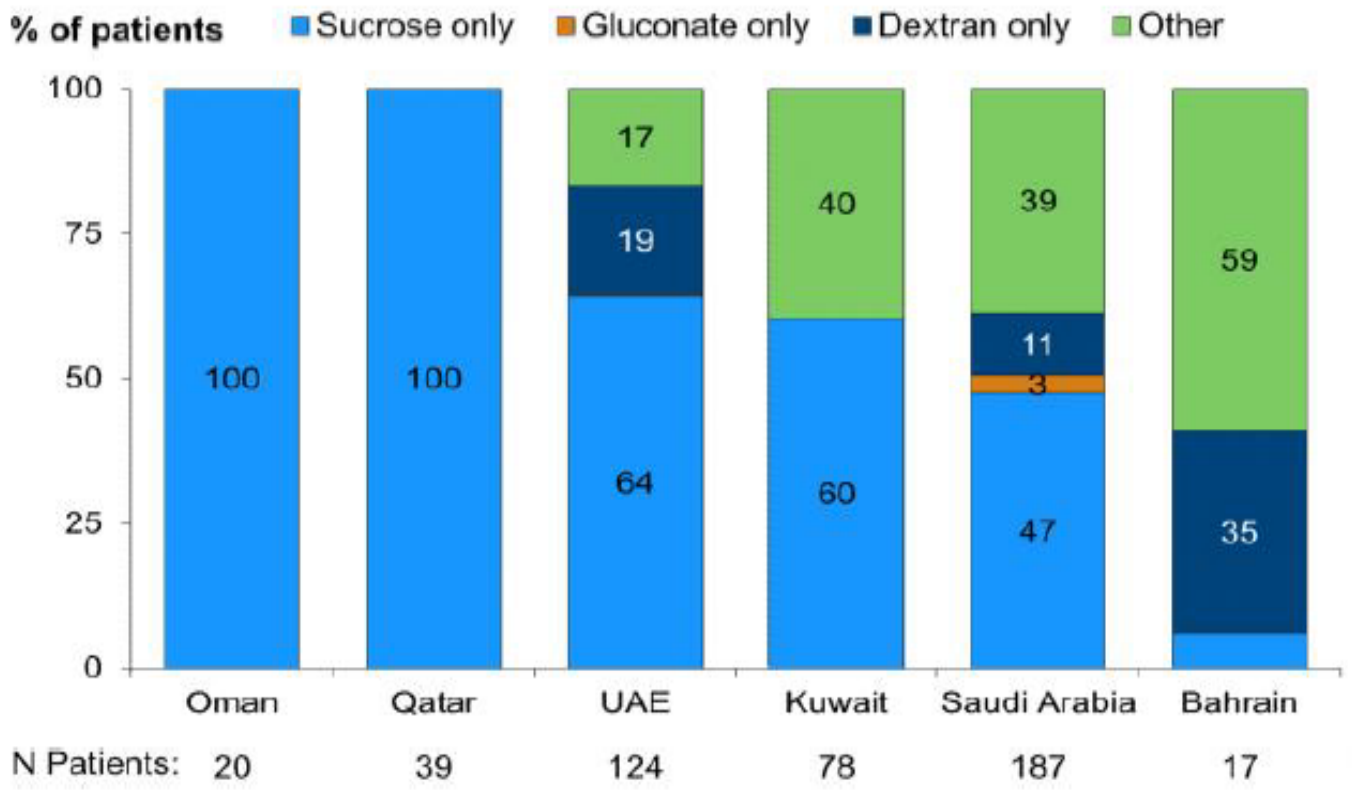


Figure 5. Intravenous iron formulation prescribed by country for the Gulf Cooperation Council- Dialysis Outcomes and Practice Patterns Study hemodialysis population (2012, 2013), among patients with an active i.v. iron prescription any time during the month of enrollment into DOPPS. A wide variation was observed in the use of i.v. iron agents among GCC countries. Iron sucrose was the only formulation used in Oman and Qatar and also the predominant one in UAE, Kuwait, and Saudi Arabia. In Bahrain, its use constituted only 6%, with 35% using dextran, and the remaining being on the other non-sucrose, non-gluconate forms of i.v. iron.

Ferritin

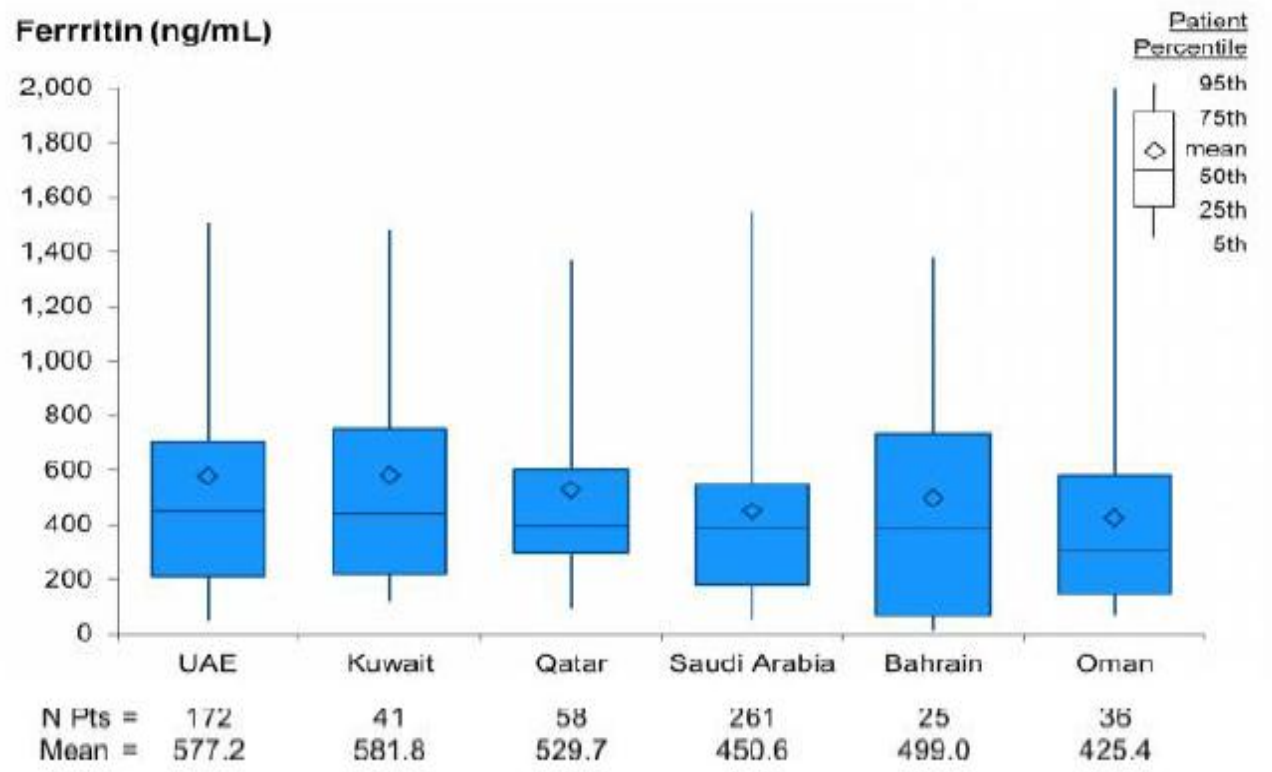


Figure 6. Ferritin level distribution by country for the Gulf Cooperation Council-Dialysis Outcomes and Practice Patterns Study hemodialysis population (2012, 2013). Median serum ferritin levels were consistently >200 ng/mL across all GCC countries with highest levels seen in the UAE and Kuwait. The lowest median ferritin level was observed in Oman at 304 ng/mL.

TSAT

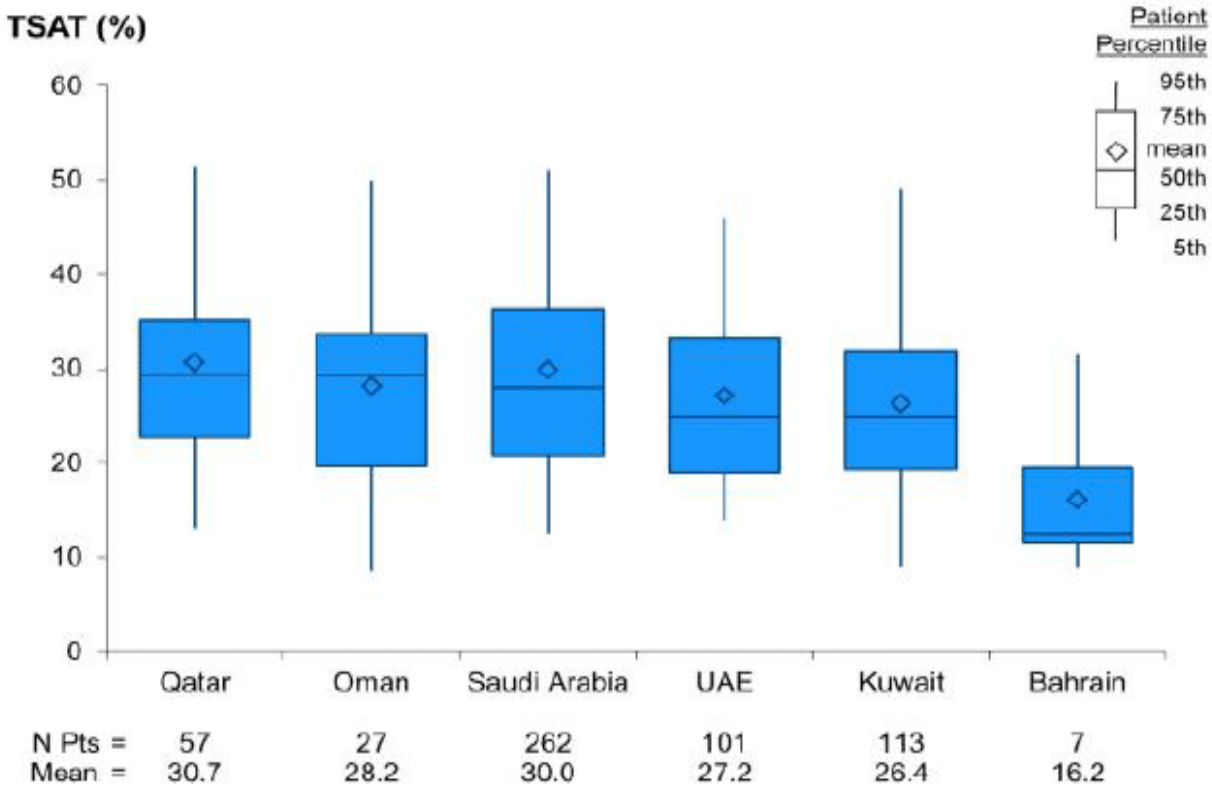


Figure 7. Transferrin saturation (TSAT) level distribution by country for the Gulf Cooperation Council-Dialysis Outcomes and Practice Patterns Study hemodialysis population (2012, 2013). Some variability was observed in the mean TSAT percentage across GCC countries with highest levels seen in Qatar and Saudi Arabia (30.7% and 30% ,respectively) and lowest in Bahrain at 16.2%.

Transfusion rates, mid 2000s

- A retrospective study was conducted of patients with CKD and chronic anemia from 2002 through 2007 in the Veterans Administration Healthcare System. Included patients had stage 3 CKD or higher and anemia (one or more hemoglobin [Hb] levels <11 g/dl or received anemia therapy [erythropoiesis-stimulating agents [ESAs], iron, or both]).

Lawler EV, Bradbury BD, Fonda JR, Gaziano JM, Gagnon DR. Transfusion burden among patients with chronic kidney disease and anemia. Clin J Am Soc Nephrol. 2010 Apr;5(4):667-72.

Transfusion rates, mid 2000s

- Among 97,636 patients with CKD and anemia, there were 68,556 transfusion events (61 events per 100 person-years), 86.6% of which occurred in inpatient settings.
- At all Hb levels, transfusion events were highest during periods of no ESA treatment and increased with declining Hb levels.
  - Between an Hb of 10.0 and 10.9 g/dl, the transfusion rate was 2.0% for those who received an ESA, iron, or both and 22% for those who received no treatment;
  - at an Hb level of 7.0 to 7.9 g/dl, the transfusion rate was 10 to 12% for treated and 58% for untreated patients.

Lawler EV, Bradbury BD, Fonda JR, Gaziano JM, Gagnon DR. Transfusion burden among patients with chronic kidney disease and anemia. Clin J Am Soc Nephrol. 2010 Apr;5(4):667-72.

Dialysis Practice snapshots

USA free-standing and chain dialysis units

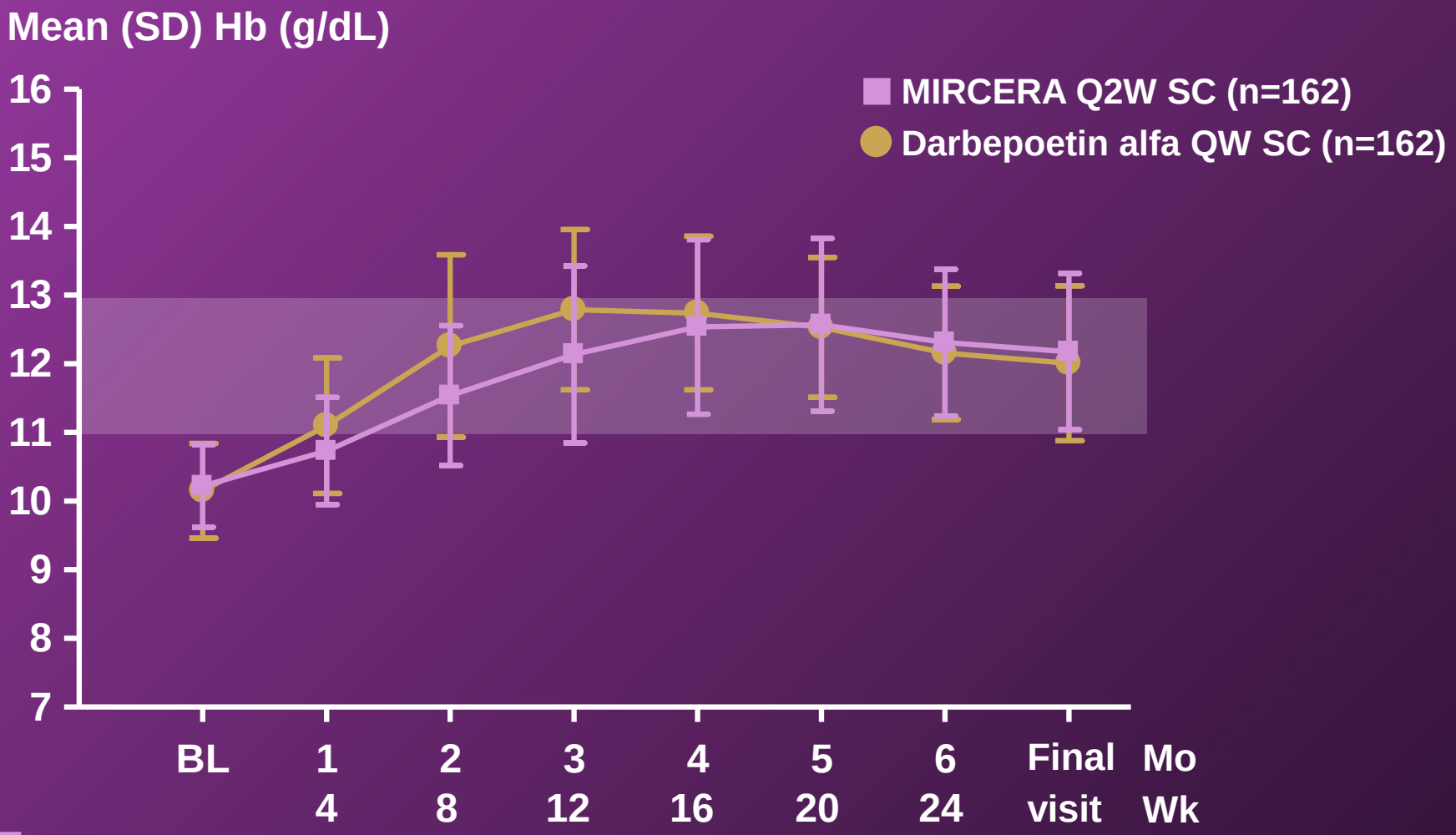
- Percentages of patients with haemoglobin levels <10 g/dL increased every year from 2007 (6%) to 2011 (~11%). Epoetin alfa doses, iron doses, and transfusion rates changed in 2011.
- Median monthly epoetin alfa and iron doses decreased 25% and 43.8%, respectively, and monthly transfusion rates increased from 2.8% to 3.2% in 2011, a 14.3% increase, starting in 2010-11.
- Patients in facilities with the highest prevalence of haemoglobin levels <10 g/dL over 3 months were at ~30% elevated risk of receiving RBC transfusions within the next 3 months (relative risk, 1.28; 95% CI, 1.22-1.34).

Am J Kidney Dis. 2014 Jun;63(6):997-1006. doi: 10.1053/j.ajkd.2013.10.052.

What we want….

- Stable regulatory, product, and safety environment
  - No new shocks, or changes
- Predictable efficacy
- Tolerability, safety, proven ability
- Minimisation of both symptoms and rbc transfusions
- Aiming for Hb 10 – 12 g/dL using iron (sensibly) first, then adding a long-acting ESA preferentially
  - Pegylated Epoetin-Beta, or Darbepoetin

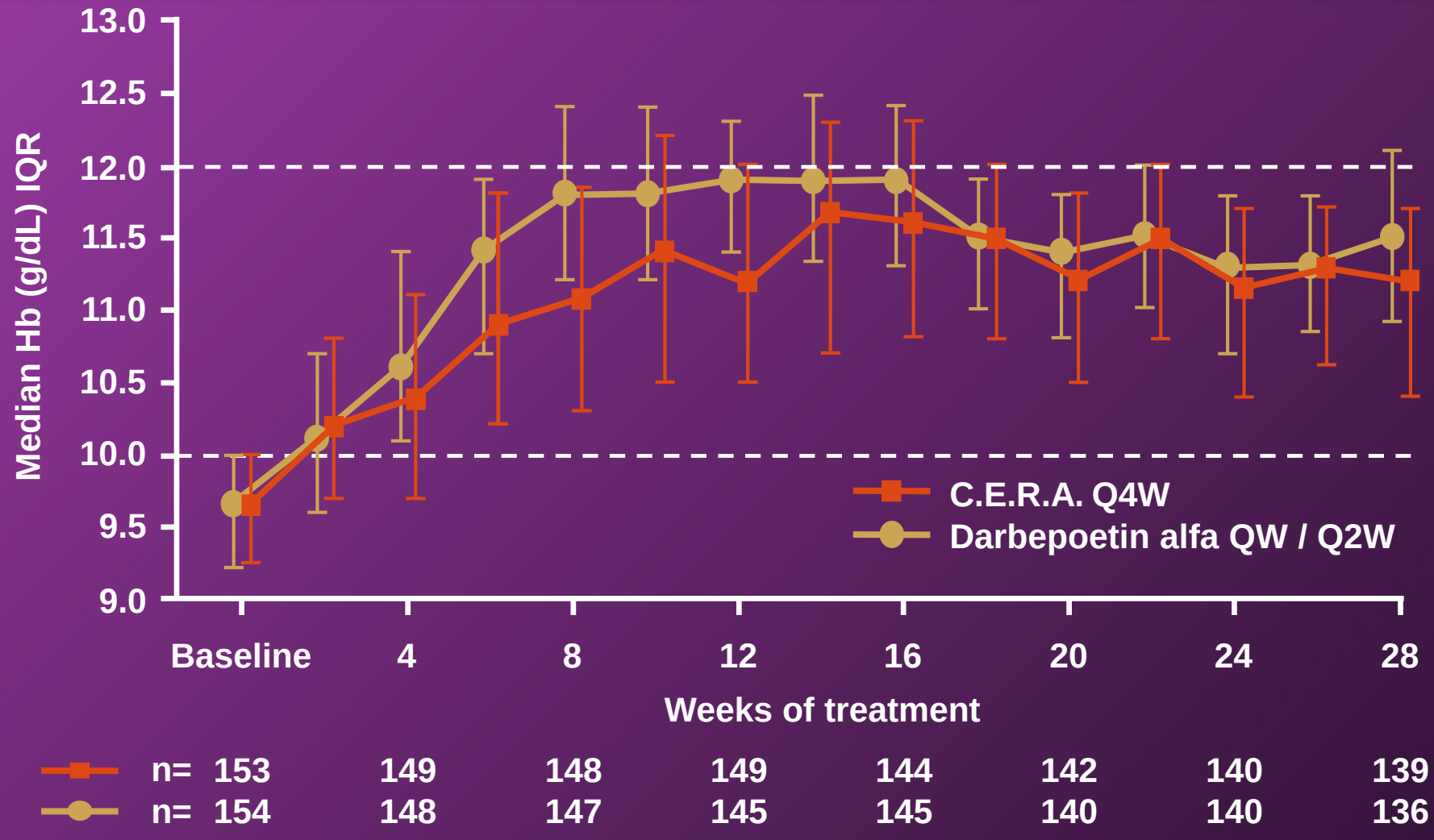
SC MIRCERA Provides a Smooth and Steady Rise in Hb Level



ITT populations

Macdougall et al. *Clin J Am Soc Nephrol*. 2008;3:337-347

C.E.R.A. Q4W offers a smooth and steady rise in Hb levels compared with darbepoetin alfa QW / Q2W



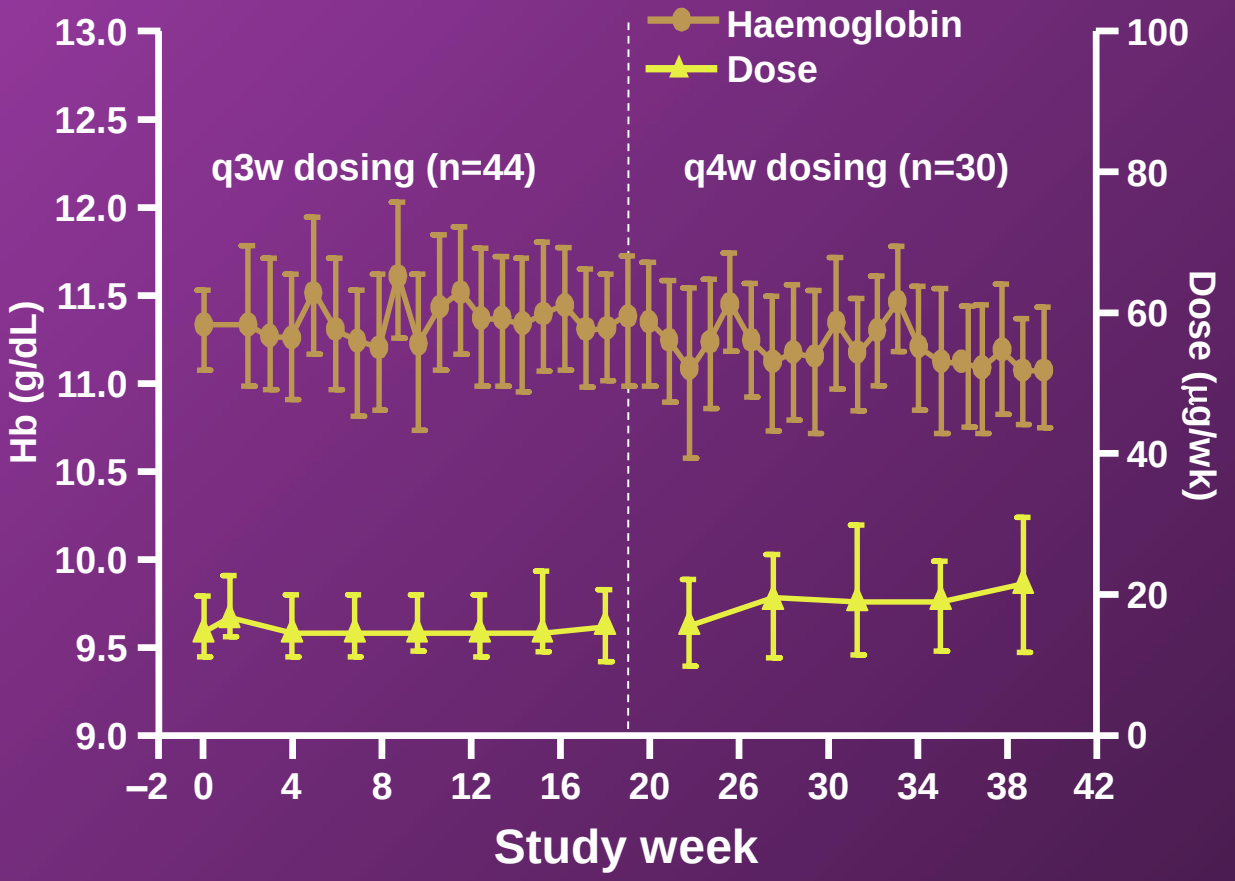
Roger SD, et al. Nephrol Dial Transplant 2011;26:3980–3986

Time to Hb response was more controlled with C.E.R.A. than with darbepoetin alfa

	C.E.R.A. Q4W (n=153)	Darbepoetin alfa QW / Q2W (n=154)
Responders, n (%)	144 (94.1)	144 (93.5)
Median time to response, days	43	29
95% CI	37; 43	29; 41
IQR	28; 57	22; 43

Castelao et al. Oral presentation Su057 at ERA-EDTA 2010

Limited evidence of efficacy in HD patients for once-monthly darbepoetin alfa



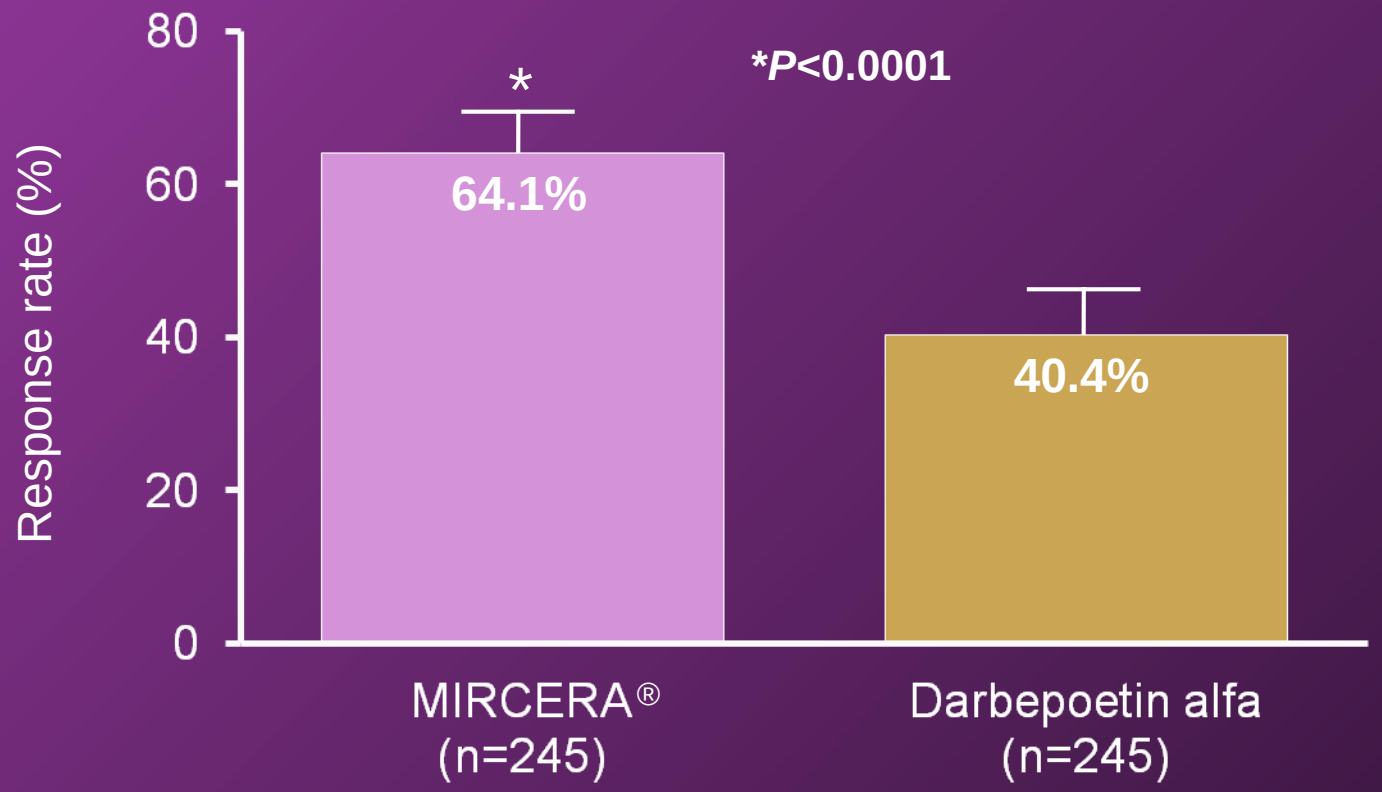
- Patients on darbepoetin alfa q2w converted to q3w dosing and, if Hb stable (10–13 g/dL), to q4w dosing
- **Limited conversion to q4w dosing:**
  Of 54 patients entering the study, 36 patients were converted to q4w dosing
- **Limited maintenance on q4w dosing:**
  Of 36 patients converting to q4w dosing, 30 patients maintained Hb >10 g/dL over 20 weeks

Hb, haemoglobin; HD, haemodialysis

Jadoul M et al. *Nephrol Dial Transplant.* 2004;19:898-903

Once-monthly MIRCERA® exhibited a superior response rate compared with once-monthly darbepoetin alfa

Primary end point

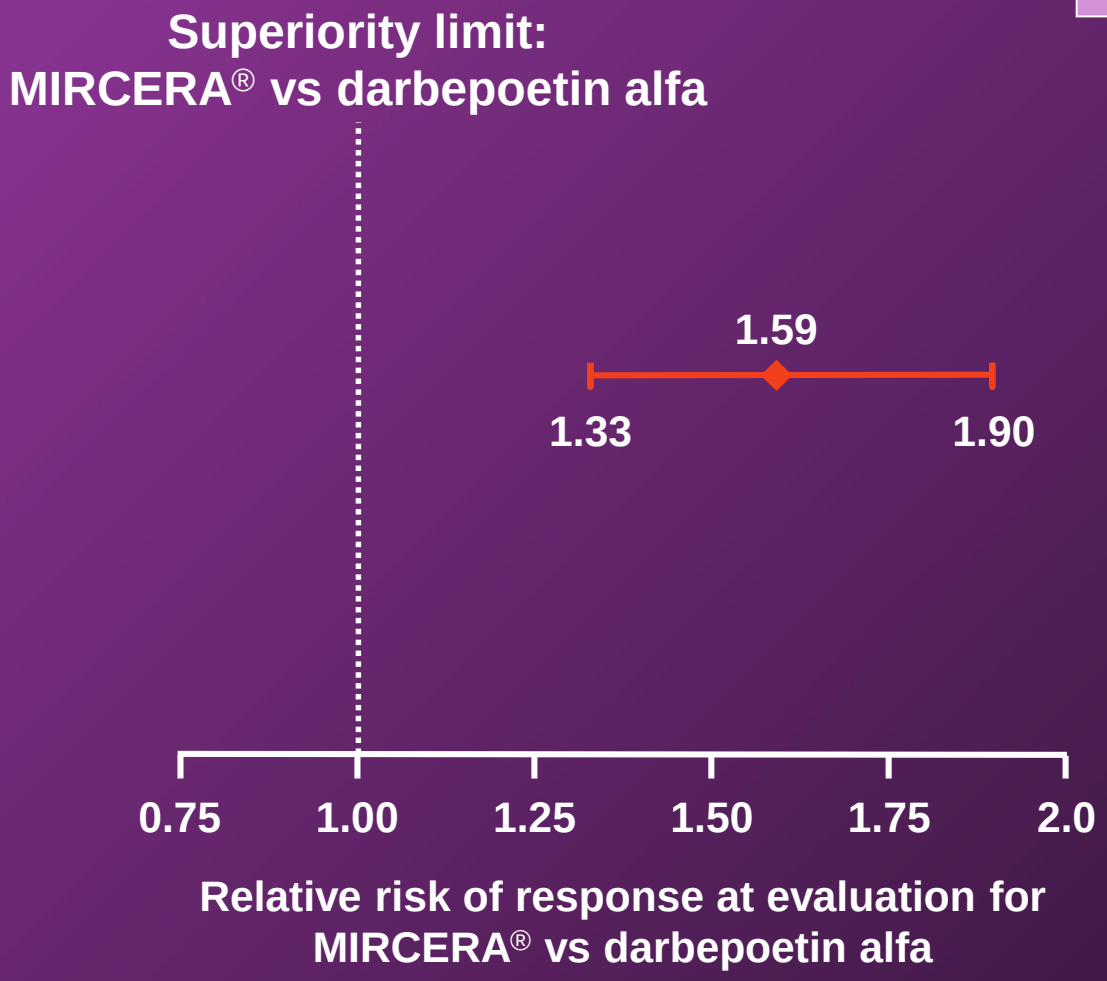


CI, confidence interval

Dosing once a month is not indicated for darbepoetin alfa in dialysis, except in Switzerland

Once-monthly MIRCERA® shows a 59% higher likelihood of response compared with once-monthly darbepoetin alfa

Primary end point



Dosing once a month is not indicated for darbepoetin alfa in dialysis, except in Switzerland

Adv Ther (2016) 33:610–625
DOI 10.1007/s12325-016-0309-6

ORIGINAL RESEARCH

Once-Monthly Continuous Erythropoietin Receptor Activator (C.E.R.A.) in Patients with Hemodialysis-Dependent Chronic Kidney Disease: Pooled Data from Phase III Trials

Francesco Locatelli · Gabriel Choukroun · Matt Truman · Alfons Wiggenhauser · Danilo Fliser

ClinicalTrials.gov identifiers: NCT00413894/NCT00545571/NCT00517413/NCT00560404/NCT00882713/NCT00550680/NCT00576303/NCT00660023/NCT00717821/NCT00642850/NCT00605293/NCT00661505/NCT00699348.
Funding: F. Hoffmann-La Roche Ltd, Basel, Switzerland.

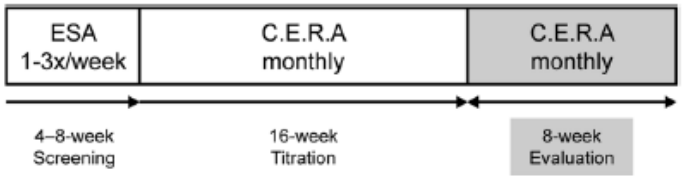
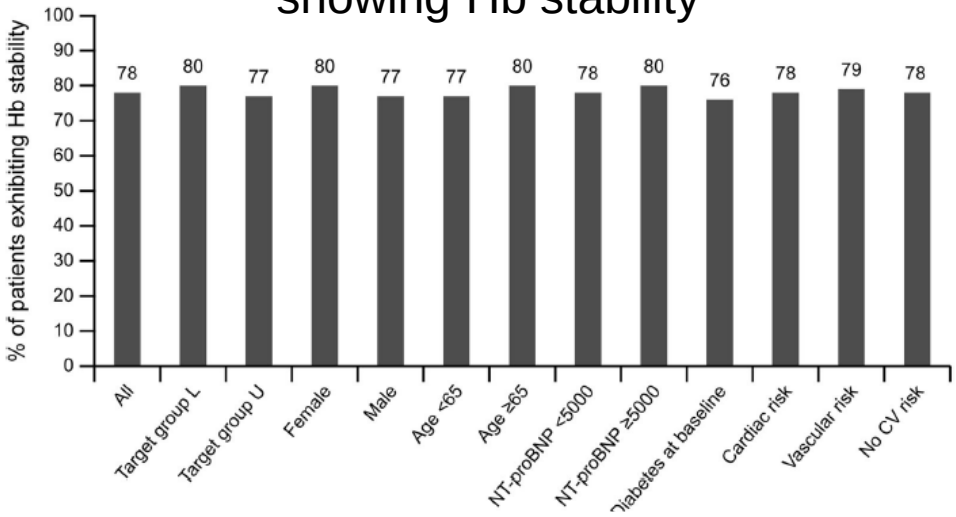
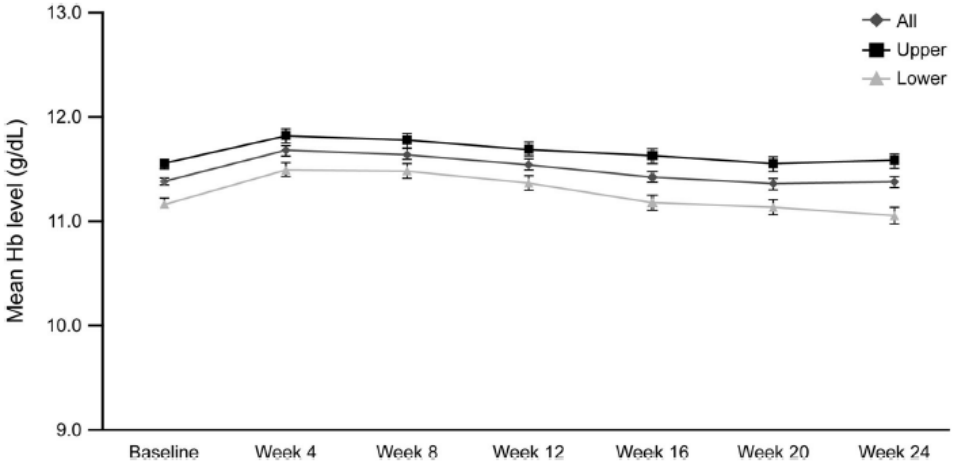


Fig. 1 Common study design. In all 13 studies, enrolled patients entered a 4- to 8-week screening period followed by a 16-week C.E.R.A. dose-titration period, and an 8-week evaluation period. *C.E.R.A.* continuous erythropoietin receptor activator, *ESA* erythropoiesis-stimulating agents

Proportion of patients showing Hb stability





Adv Ther (2016) 33:610–625
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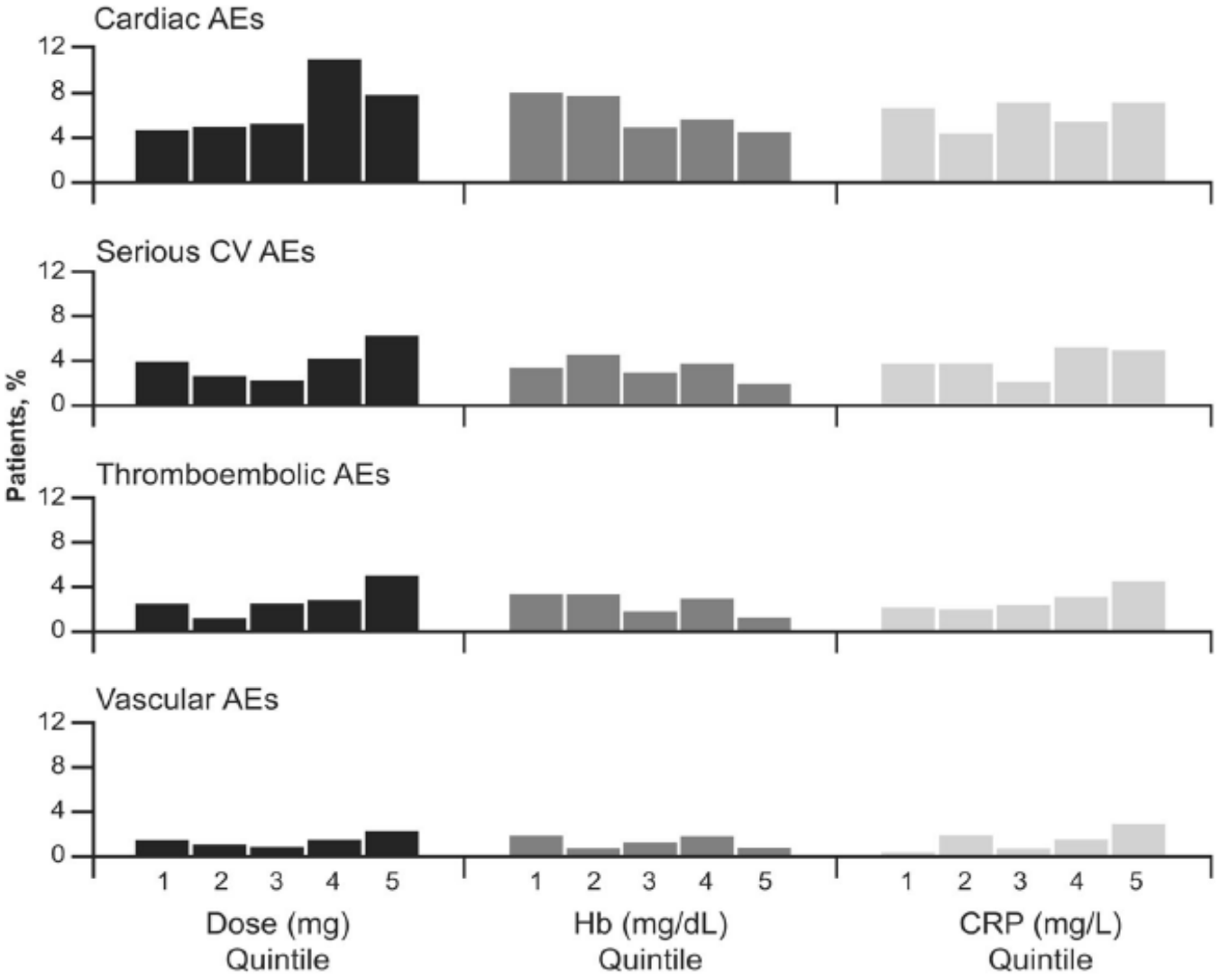


Quintiles	1	2	3	4	5
C.E.R.A dose (mg)	<70	70–110	110–125	125–185	>185
Hb (g/dL)	<10.65	10.65–11.2	11.2–11.7	11.7–12.25	>12.25
CRP (mg/L)	<2.26	2.26–4.14	4.14–7.21	7.21–14	>14

New things….

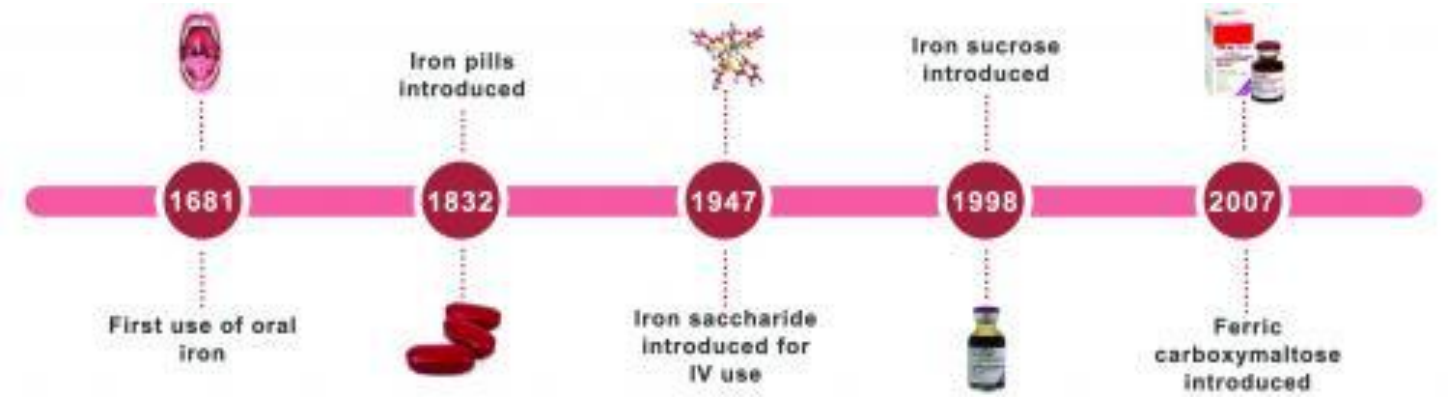
Prominent cause of ESA resistance

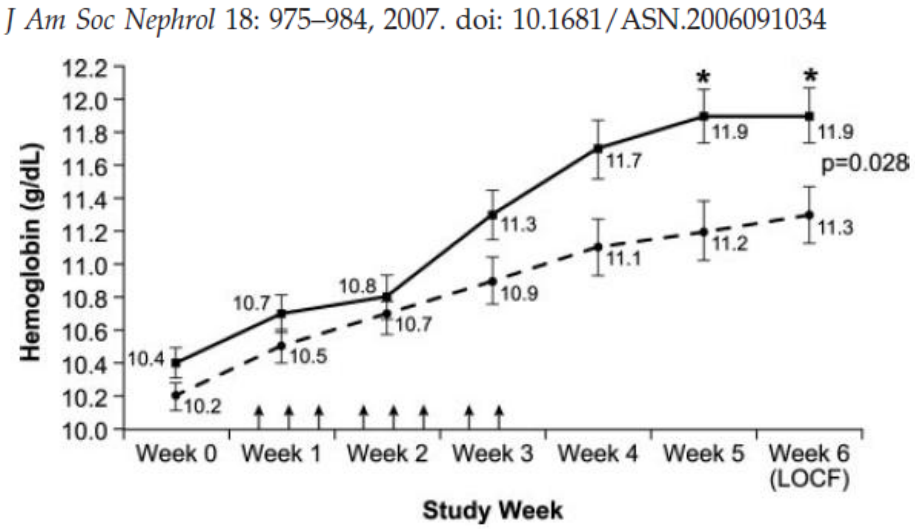
- Old “defunct” allografts – smouldering rejection and inflammation
  - (ongoing) HLA sensitisation
  - Anaemia
  - Extirpation versus continued IS

Iron – the time and tides

- According to DOPPS serum ferritin levels have progressively increased in recent years in the USA, with nearly 40% of the HD population having ferritin levels >800 ng/mL [20]. The increase in mean IV iron dose (from 210 mg/month in 2009–10 to a peak of 280 mg/month in 2011, then back to 200 mg/month in 2013) combined with lower ESA doses accounted for 46% of the increase in ferritin over time.
- Something similar has happen in the EU too
- High ferritin levels have been related to poor survival in both non-dialysis and dialysis patients, but the ferritin levels at which mortality risk increases is still matter of debate. As for iron therapy, observational studies have the confounding bias that serum ferritin is also a marker of inflammation, and thus of comorbidity.

The iron saga





DRIVE study forcing more IV iron (and ESA) into TSAT < 25 and ferritin 500-1200 patients

Iron bound to transferrin in the plasma, to ferritin in storage sites, or to metalloproteins and enzymes in tissues, is kept in a safe and catalytically inactive state.
Improperly liganded ferrous iron reacts with H2O2, generated by mitochondria and inflammatory cells. This leads to formation of hydroxyl radical (•OH), which is the most reactive and cytotoxic free radical known (H2O2+Fe2+ =•OH+OH–+ Fe3+), and conversion of Fe2 to ferric iron (Fe3+).
Fe3+ is then transformed back to Fe2+ by superoxide (Fe3+ + O2•- = Fe2+ + O2), which is produced by mitochondria leading to sustained production of •OH which causes cytotoxicity and tissue damage

Iron usage in CKD

- PIVOTAL – a ground-breaking trial of worldwide importance in CKD
- Two different IV iron regimes (“high”) and (“low”) targeting different ferritin concentrations
- Safety and efficacy end-points
- 2 years, 2100 patients (now all recruited)
  - Probably reporting 2018-2019

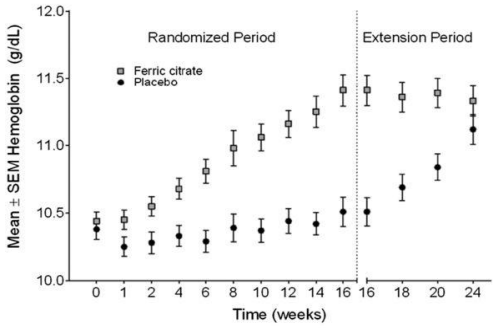
Ferric Citrate

January 12, 2017,
doi: 10.1681/ASN.2016101053
JASN January 12, 2017
ASN.2016101053

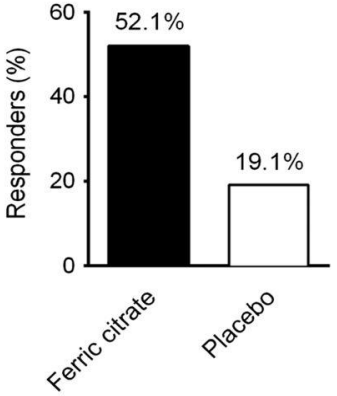
Fishbane et al.

Iron deficient CKD (non dialysis)

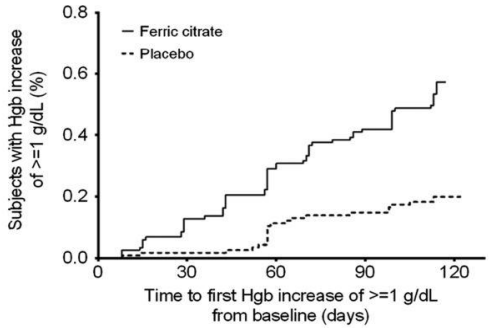
A Hemoglobin



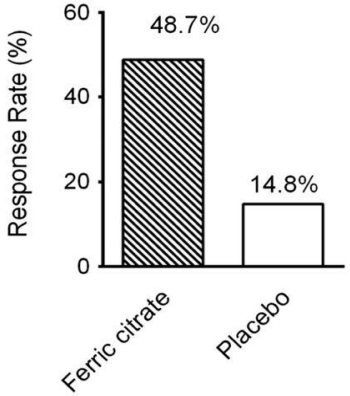
B Percent responders achieving ≥ 1g/dL Rise in Hemoglobin



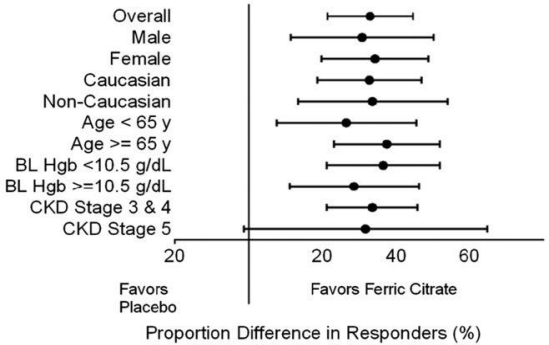
C Time to first response of ≥ 1g/dL Hemoglobin rise



D Sustained effect of >0.75 g/dL over any 4 week period



E Proportion Difference in Responders



Conclusions

In conclusion, the confluence of new financial incentives bundling epoetin payments and mounting scientific evidence linking higher epoetin doses to adverse outcomes culminated in fewer hemodialysis patients receiving epoetin therapy, lower epoetin doses administered and lower target hematocrit levels across nearly all dialysis providers in the first year after PPS. The effects of these changes in anemia management on mortality and quality of life among the dialysis population are uncertain and will require careful future assessment.

But we can't just wait for symptoms to become bad, and we can't just let Hb drift down to where LVH a risk, and transfusions become necessary

"out of the frying pan and into the fire"


FIRE SALE
10
FRYING PAN SALE
CARTOONSTOCK .com
Search ID: wda1927


GRAND KITCHEN of EUROPE
A STEW
A PICKLE