Individualized Anemia Management in Hemodialysis Patients A Biro¹, S Blumberg¹, R Rachmilewitz², Y Chait^{3,#}, MJ Germain⁴, R Cernes¹, Z Barnea¹, Z Katzir¹

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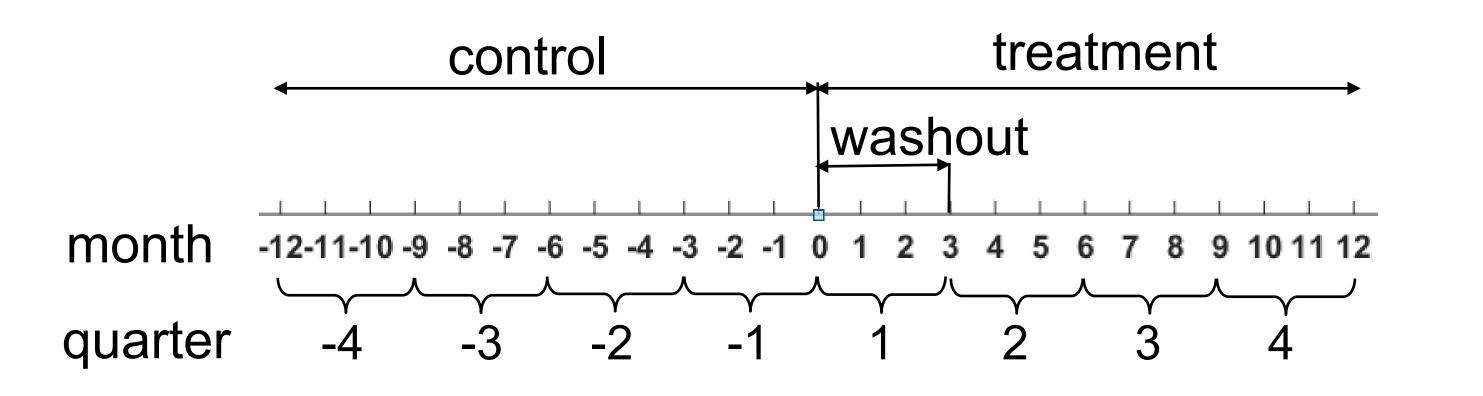
Objective

To test the hypothesis that individualized dosing of erythropoiesis stimulating agents and parenteral iron can increase the percentage of hemoglobin levels within range compared with levels achieved using a standard protocol.

Background

- The optimal use of erythropoiesis stimulating agents (ESAs) to treat anemia in end-stage renal disease (ESRD) remains controversial due to reported associations with adverse events.
- It is generally understood that "one-size fits all" protocols result in suboptimal outcomes. FDA ESA guidelines recommend that "....Therapy should be individualized to the patient..."

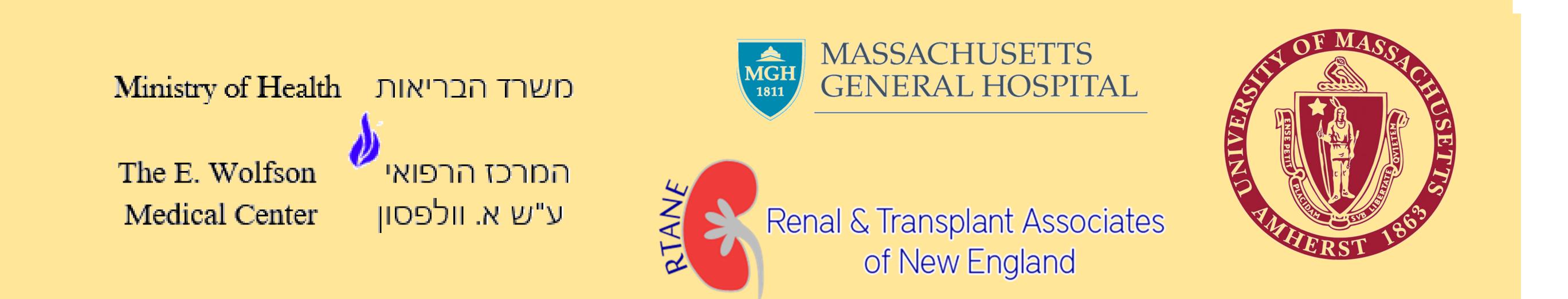
Study: 25 maintenance hemodialysis (HD) patients receiving ESA and parenteral iron; 12 months crossover with patients serving as their own controls:



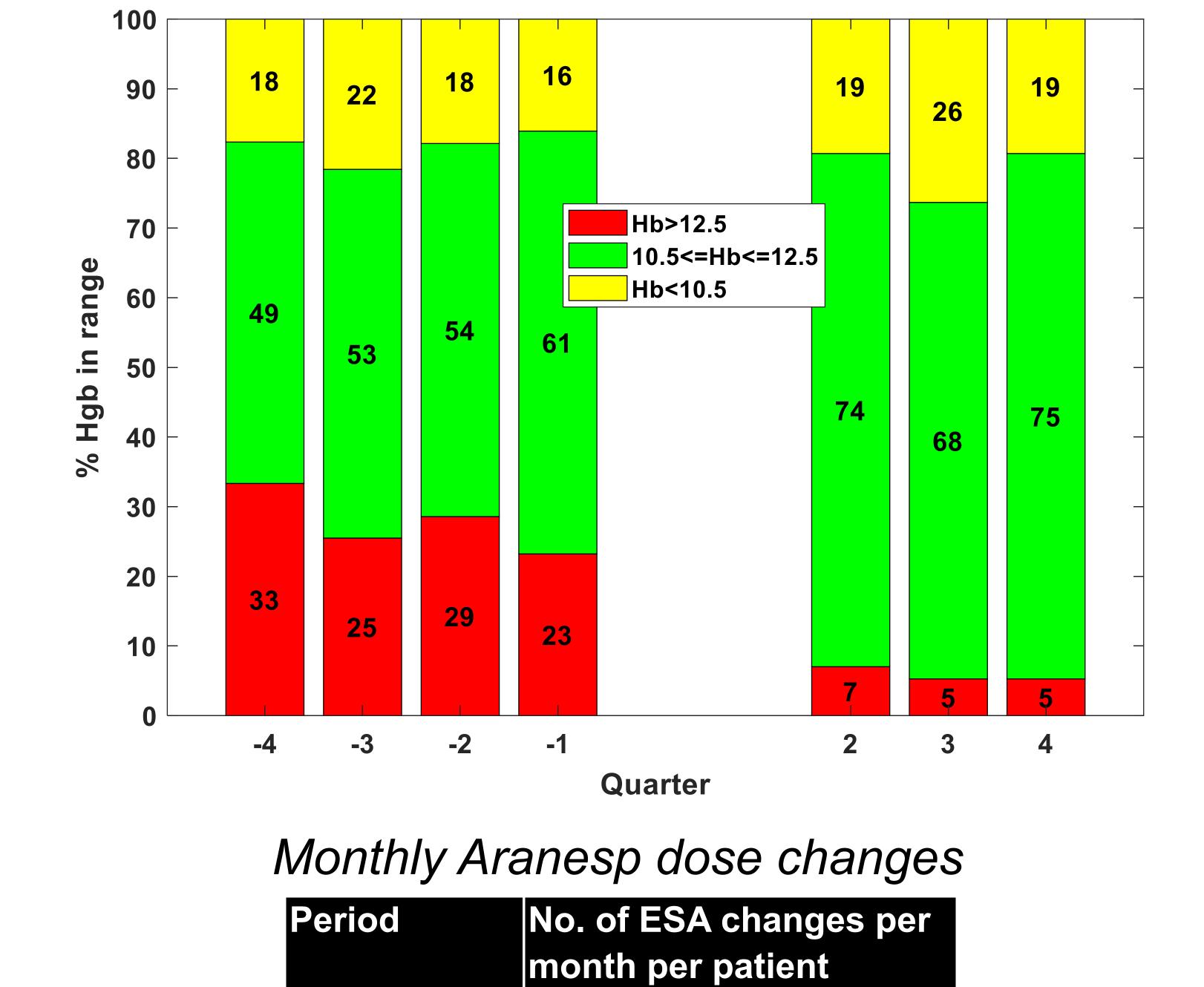


Baseline characteristics for the study population

Ν	25 [§]
Age, yr , mean (SD)	70.8(12)
Female, n (%)	10 (40)
Vintage, yr, mean (SD)	3.7 (3.2)
Diabetes mellitus, n (%)	8 (32%)
CHF/IHD	9 (36%)



Quarterly Hgb distributions: above, within, and below target (n=18)



 Individual patient's response to ESAs cannot be accurately modelled using population statistics. The heterogeneity is Hgb response is due to many factors including, chronic inflammation, red-blood cell lifespan, acute blood loss, nutrition, and other comorbidities.

Methods

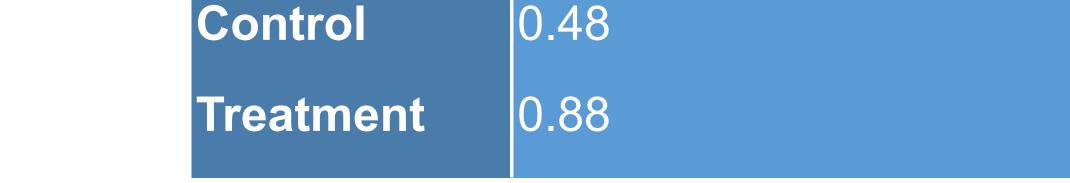
Standard Protocol: Biweekly hemoglobin lab draws, biweekly ESA (Aranesp) dose titration with biweekly dose administration, monthly iron parameters with biweekly dose administration.

Individualization:

- Biweekly hemoglobin lab draws, biweekly ESA (Aranesp) dose titration with weekly dose administration, monthly iron parameters with weekly dose administration.
- ESA dose-response profile for each patient derived from 3 months Hgb and ESA data using validated mathematical model. ESA dose adjustment guided by a robust feedback control algorithm.

[§]6 (24%) died (country rate 20%), mean age 77 yr, mean vintage 5.5 yr; 1 discontinued.

Patient Hgb trajectory over time (n=25) target range -12-11-10 -9 -8 -7 -6 -5 -4 -3 -2 -1 4 5 6 7 8 9 10 11 12 Month $\underline{\qquad}$



Monthly means in each quarter (n=18)

Parameter		Control			Treatment			
	quarter	-4	-3	-2	-1	2	3	4
Hgb (gr/dl)	mean	11.6	11.6	11.6	11.6	11.3	11.2	11.1
	(SD)	(1.8)	(1.7)	(1.5)	(1.5)	(0.9)	(0.9)	(1.1)
TSAT (%)	mean	25.7	27.8	30.5	26.4	22.7	22.7	22.7
	(SD)	(11)	(8.5)	(11.5)	(8.9)	(7.4)	(9)	(9)
Ferritin (ng/ml	mean	626	660	529	524	495	466	473
	(SD)	(349)	(352)	(315)	(220)	(193)	(190)	(237)
Aranesp	mean	258	251	226	243	169	209	194
	(SD)	(361)	(289)	(164)	(177)	(148)	(170)	(153)
Venofer	mean	283	239	200	221	137	156	171
	(SD)	(248)	(180)	(179)	(270)	(101)	(135)	(114)

Conclusions

 Individualized Aranesp and Venofer dosing, derived using model-based feedback concepts, improved Hgb outcomes compared with standard protocol outcomes.

 Decreased TSAT levels suggest the need for a more aggressive parenteral iron protocol at higher Hgb target levels.