

# Effect of Physician Practice Patterns Regarding Frequency of Hemoglobin Measurement and More Frequent Epoetin Alfa Titrations and Their Association with Time in Range

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### Introduction

- The advent of the new economic bundling rules and changes in FDA label guidelines for ESAs have renewed the focus on current physician practices to achieve greater control of Hb by more frequent measurement and more precise ESA dose titrations.
- One large retrospective analysis found increasing Hb measurements and EPO dose titration frequency decreased patient variability around the facility-level Hb mean.<sup>1</sup>
- However, a second study found that frequent titrations were the most important driver of Hb cycling—potentially resulting in dangerously large fluctuations in Hb levels.<sup>2</sup>
- Recently, a program which limited titration opportunities to once every other month was shown to produce higher proportion of patients in range for Hb.<sup>3</sup> The issue remains controversial.
- We conducted a retrospective database analysis of patient data from Jan 1, 2009 Dec 31, 2010 to quantify the frequency of ESA dose titrations and Hb measurements and their association with keeping patients within the Hb range defined by the CMS Quality Incentive Program requirements in place at the time of the study (10–12 g/dL).

### Methods

- We assessed data from prevalent (≥ 120 days), adult (> 18 years old) hemodialysis patients dialyzing at clinics within a large dialysis organization ≥ 3 times/week between 1/1/2009 and 12/31/2010 (Table 1).
- Physician practice patterns for dose titration were defined as a difference of > 10% between any of:
- the mean dose of 2 consecutive stable periods (≥ 3 doses during which the dose did not change more than 10%);
- the mean dose of a stable period and next/previous dose in a transition (non-stable) period; or
- 2 consecutive doses within a transition period.
- Time in Hb target range was defined as total patient-time in range/total patient-time based on the individual Hb value for each patient.
- Time was calculated as time from current Hb test to the next Hb test. All of that time was assigned to in range or out of range depending on the result of the Hb test.
- Assessments of associations used Pearson product-moment correlation (adjusted for mean BMI, age, and vintage per physician and race, vascular access, and comorbidities based on the % of patients served by the physician).

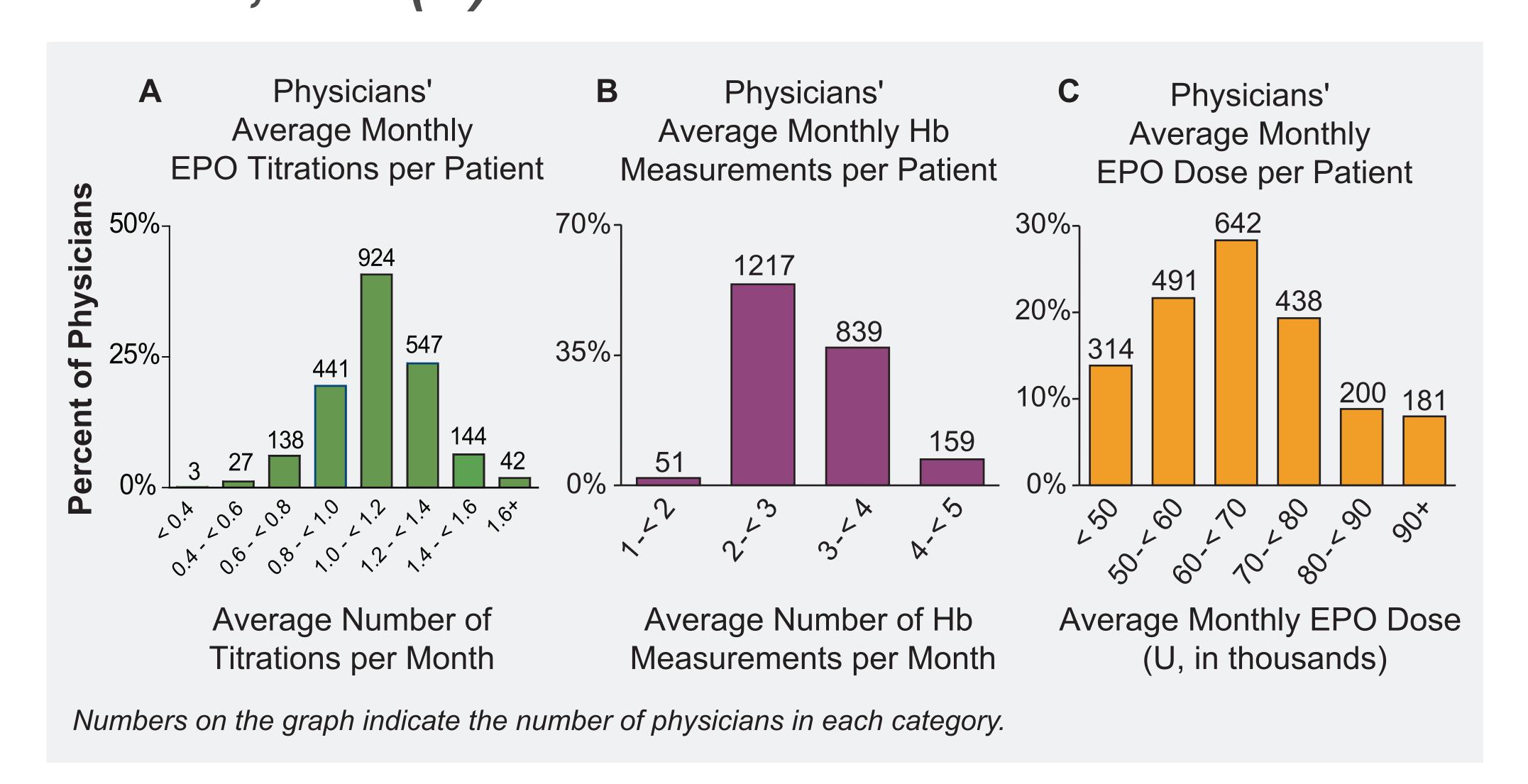
### Results

### Table 1. Demographics

Mean ± SD Patients	
N 81,464	
Mean age ± SD (yr) 63.2 ± 14.7	
% Female 43.0%	
Race and Ethnicity % Caucasian 39.0% % African American 36.7% % Hispanic 16.0% % Asian, Pacific Islander 4.1% % Native American 1.3% % Unknown 0.8%	
% with Diabetes 64.0%	
Mean Vintage ± SD (yr) 2.9 ± 3.6	
BMI $\pm$ SD 28.0 $\pm$ 7.2	

- The majority (> 50%) of physicians titrate patients' EPO dose at least once per month.
- > 95% measure Hb at least twice per month.
- The highest proportion of physicians prescribed between 60,000–70,000 U of EPO per patient per month (Figure 1).

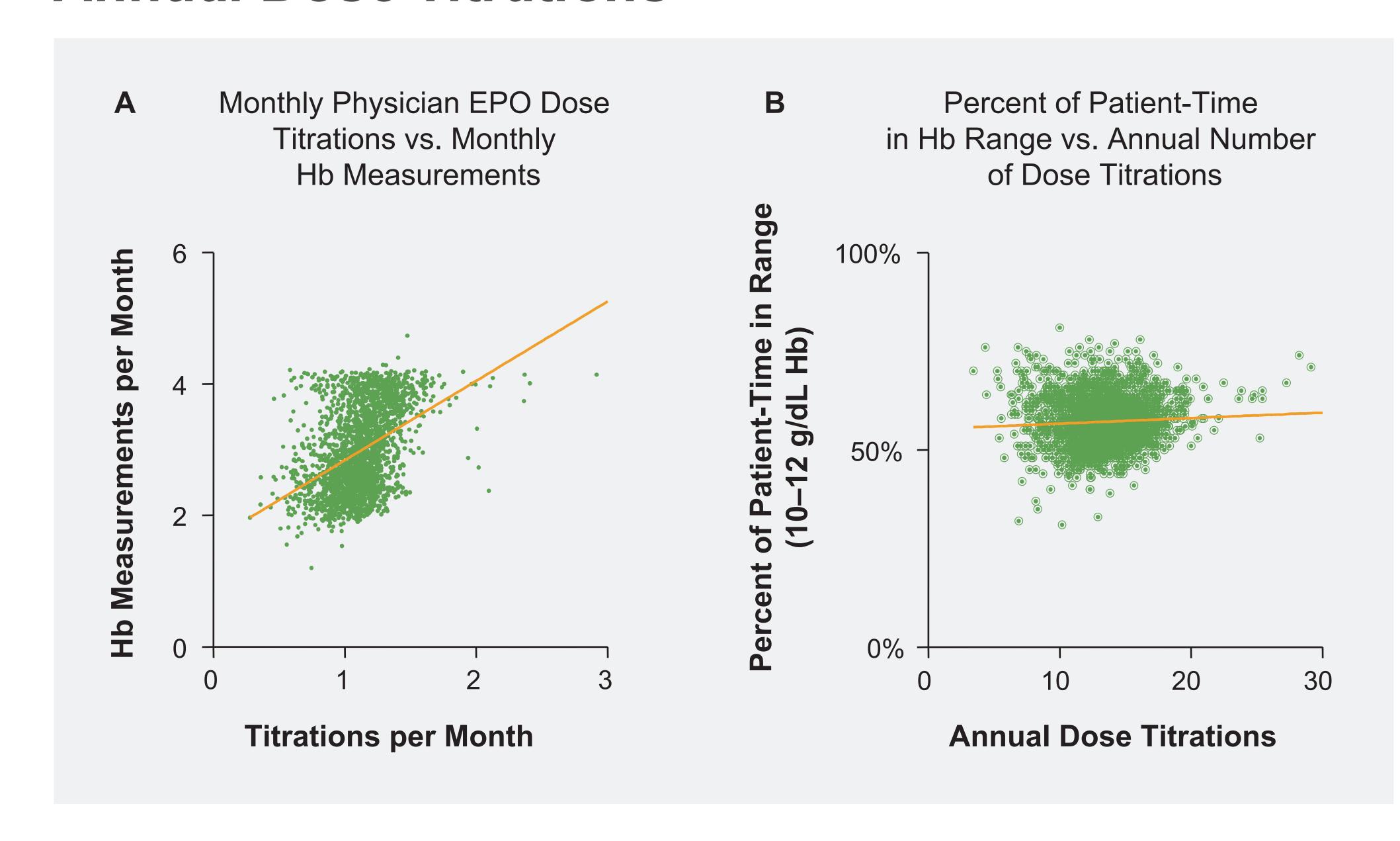
## Figure 1. (A) Physicians' Average Monthly EPO Dose Titrations, (B) Hb Measurements per Patient, and (C) EPO Dose



### Table 2. Physician-Level Results

	Mean ± SD	Median
Physicians (n = 2,266)		
ESA Dose Titrations per Patient-Month	$1.12 \pm 0.23$	1.12
Hb Measurements per Patient-Month	$2.98 \pm 0.64$	2.87
Annual % of Patient-Time in 10–12 g/dL Range	57.2 ± 6.1%	56.7%
ESA Dose per Patient-Month (U)	66,279 ± 16,540	64,989

Figure 2. Scatter Plot of (A) Monthly Hb Measurements vs. Monthly EPO Dose Titrations and (B) Percent of Patient-Time in Hb Range vs. Annual Dose Titrations



- At the physician level, after adjustment for case mix factors, the frequency of Hb measurements was associated with ESA dose titrations (r = 0.47; p < 0.0001). Unadjusted data shown in Figure 2A.
- The adjusted association between EPO dose titrations and achievement of time in 10–12 g/dL Hb range annually was negligible (r = 0.07; p = 0.0005). Unadjusted data is shown in Figure 2B.
- An analysis of EPO utilization showed that an increase of 1 titration per patient-month at the physician level was associated with an extra 17,000 U of EPO (p<0.001) used per month.</li>

### Conclusions

- The average physician measures Hb ~ 3 times per month per patient, titrates ESAs ≥ 1 time per month per patient, and prescribes 60,000–70,000 U of EPO per patient.
- More frequent Hb testing is associated with more frequent ESA dose titration.
- More frequent ESA dose titration was not associated to any meaningful degree with longer time in the 10-12 g/dL Hb range targeted at the time of the study, yet was associated with an increase in EPO dose (17,000 U of EPO per month for every additional titration per patient-month).

#### References

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- 2. Fishbane S and Berns JS: Hemoglobin cycling in hemodialysis patients treated with recombinant human erythropoietin. *Kidney Int.* 68:1337–1343, 2005.
- 3. Lines S, Lindley E, Tattersall J and Wright M. A predictive algorithm for the management of anaemia in haemodialysis patients based on ESA pharmacodynamics: better results for less work et al. *NDT*, ePub, Dec 29, 2011.

### Acknowledgements

Our sincere appreciation to the teammates in more than 1600 DaVita clinics who work every day to take care of patients but also to ensure the extensive data collection on which our work is based. We thank DaVita Clinical Research® (DCR®), and specifically acknowledge Karen M. Spach, PhD of DCR for editorial contributions in preparing this poster. DCR is committed to advancing the knowledge and practice of kidney care.

This analysis was funded by Affymax Inc. and Takeda Pharmaceutical Company Limited.

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American Nephrology Nurses' Association 43rd National Symposium, April 29–May 2, 2012, Orlando, FL.