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The use of Anemia Control Model is Associated with Improved Hemoglobin Target Achievement, Lower Rates of Inappropriate Erythropoietin Stimulating Agents utilization and Severe Anemia Among Dialysis Patients

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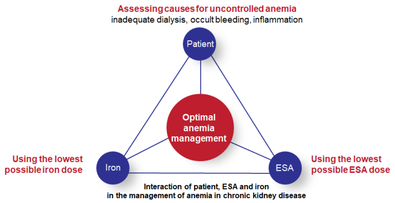
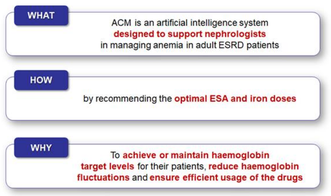
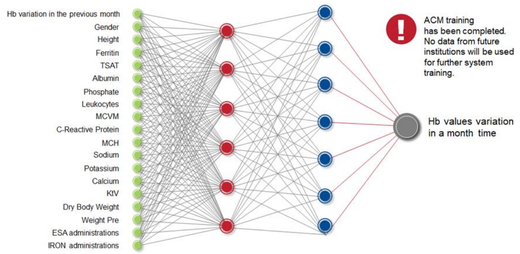
INTRODUCTION AND AIMS

- Responsiveness to treatment depends on iron bioavailability, endogenous EPO concentration, and ESA responsiveness, conditions that fluctuate over time even within the same patient. A large share of patients do not reach therapeutic targets. Additionally, erythropoietin stimulating agents (ESA) are often over-utilized.
- To help nephrologists overcome current challenges in anemia management, we developed the Anemia Control Model (ACM), an AI-based medical device designed to optimize ESA/iron therapy for hemodialysis patients. ACM was previously shown to improve Hb target achievement rates and reduce ESA utilization in two multicenter studies.
- ACM has been used in the Fresenius Medical Care European Dialysis network since 2014. It is currently adopted by 168 Fresenius Medical Care centers in Europe, Asia and Latin America. We sought to evaluate the real-world effectiveness and safety of ACM in the Fresenius Medical Care Nephrocare network and assessed clinical settings where ACM may provide the largest benefit.



THE ANEMIA CONTROL MODEL (ACM)

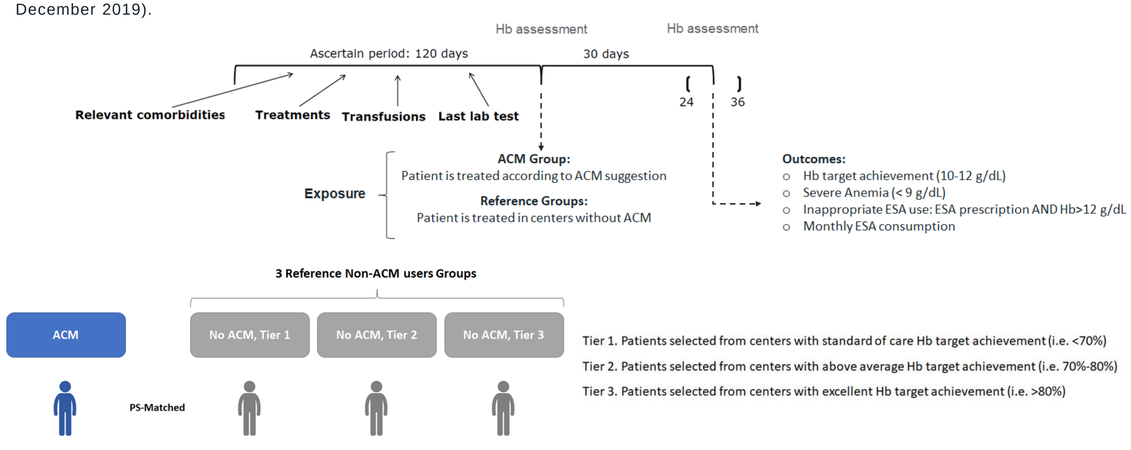




The Anemia Control Model (ACM) is a certified medical device. It has been trained on over 950000 patients' records.

METHODS

- **Design & Setting:** multi-center, matched, retrospective study. Hemodialysis patients treated in the European FMC dialysis Network (June 2013 – December 2019).



- **Statistical Analysis**. *Unit of analysis:* patient-month. *Time-Varying Propensity score (PS):* likelihood of ACM suggestion's acceptance for each patient-month included in the study conditional on previous ESA & Iron prescriptions, comorbidities, socio-demographic characteristics, dialysis treatment parameters, laboratory test results. *Matching:* 1 ACM patient-month matched to 1 Non-ACM patient-month for each reference group. *Inference:* For each endpoint, we estimated event rate per 100 patient-month and compared exposure groups with zero-inflated negative binomial regression. Quantile regression to explore ESA consumption patterns at different percentiles of the ESA dose distribution

RESULTS

Sample Characteristics. 57,382 patients met the inclusion and exclusion criteria for the study, corresponding to 1,525,960 patient-months. In total the ACM and the 3 reference groups consisted of 85512 patient-months each.

	ACM arm matched	Tier 1	Tier 2	Tier 3	ES
n	85512	85512	85512	85512	
	Mean (std), Median (IQR) or n (%) where appropriate				
Men	53323 (62.4)	49422 (57.8)	50758 (59.4)	49974 (58.4)	0.036
Age (years)	67.3 (14.7)	65.5 (14.7)	64.4 (14.5)	65.4 (14.2)	0.006
Hb (g/dL)	11.5 (1.4)	11.2 (1.4)	11.4 (1.3)	11.4 (1.3)	0.010
Ferritin (ng/mL)	479.6 [337.6]	521.5 [617.9]	509.1 [578.6]	503.0 [552.2]	0.017
T.Sat. (%)	30.5 (13.8)	31.2 (16.3)	30.8 (15.2)	30.7 (16.3)	0.001
MCV (fL)	94.9 (6.6)	98.9 (173.3)	95.0 (10.0)	95.1 (9.4)	0.000
MCH (pg/cell)	32.7 (2.4)	32.6 (2.3)	32.6 (2.4)	32.5 (2.3)	0.002
CHF	19265 (22.5)	23153 (27.1)	23524 (27.5)	22072 (25.8)	0.044
CAD	17544 (20.5)	19954 (23.3)	21920 (25.6)	24342 (28.5)	0.071
Diabetes	28891 (33.8)	26089 (30.5)	25491 (29.8)	28882 (33.7)	0.030

Table 1. Sample Characteristics. Matched samples. .

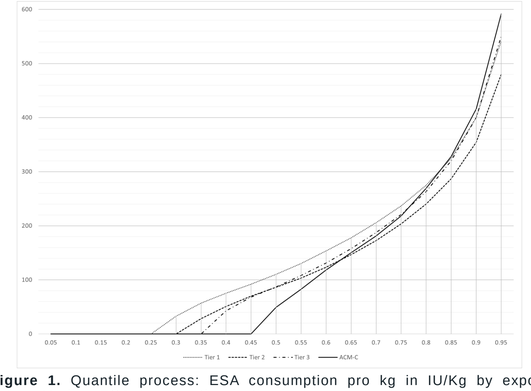


Figure 1. Quantile process: ESA consumption pro kg in IU/Kg by exposure group. Median ESA consumption in the four comparison groups was 49.4 (IQR: 218.2), 110.3 (IQR: 236.8), 86.5 (IQR: 203.5), and 87.1 (IQR: 220.9) for ACM, tier 1, tier 2 and tier 3 respectively (p<0.001 for all comparisons based on Mann-Whitney test).

Hb target achievement:

- ✓ **ACM: 87.49 (95% CI: 87.27 - 87.71)**
- ✓ Tier 1: 73.89 (95% CI: 73.59 - 74.18) *
- ✓ Tier 2: 80.76 (95% CI: 80.50 - 81.03) *
- ✓ Tier 3: 86.30 (95% CI: 86.07 - 86.53) *

Severe Anemia:

- ✓ **ACM: 2.03 (95% CI: 1.94 - 2.13)**
- ✓ Tier 1: 4.90 (95% CI: 4.76 - 5.05) *
- ✓ Tier 2: 3.16 (95% CI: 3.05 - 3.28) *
- ✓ Tier 3: 2.17 (95% CI: 2.07 - 2.27)

Inappropriate ESA use:

- ✓ **ACM: 3.97 (95% CI: 3.85 - 4.11)**
- ✓ Tier 1: 10.79 (95% CI: 10.59 – 11.00) *
- ✓ Tier 2: 8.18 (95% CI: 8.00 - 8.37) *
- ✓ Tier 3: 6.04 (95% CI: 5.88 - 6.20) *

Table 2. Hb Target achievement, Severe Anemia and Inappropriate ESA use by comparison group. * Denotes statistically significant differences compared to ACM group .

CONCLUSIONS

- Increased target achievement among ACM patients, was partially explained by smaller rates of severe anemia (i.e., Hb < 9 g/dl), a common complication of CKD-related anemia, compared to both tier 1, 2 and 3 controls, a finding possibly associated with reduced blood transfusions risk.
- Additionally, the risk of inappropriate administrations was almost 3-fold higher, 2-fold higher and 50% higher among control tier 1, tier 2 and tier 3 patients respectively compared to patients treated according to ACM recommendations.
- We observed smaller ESA dosage in the ACM arm, a reduction that was mostly explained by a greater rate of no-ESA prescriptions. Given that excessive ESA dose are associated with the risk of thrombosis, cardiovascular hospitalizations and mortality, minimizing the use of ESA and avoiding inappropriate overdosage when the level of Hb is already above the upper recommended limit (i.e., > 12 g/dl) is an important goal of therapy.
- Our large-scale analyses suggest that ACM may improve the quality of anemia management over current standard of care especially in centers where less than 80% of patients achieve hemoglobin therapeutic targets. Importantly we showed that both severe anemia and inappropriate ESA use were less frequent among patients treated in accordance with ACM suggestions.