

Research Article

The cost-benefit of utilizing post-dialysis haemoglobin for dosing of erythropoiesis-stimulating agent therapy in patients with anaemia on haemodialysis in a low-resource setting

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ABSTRACT

Background: Access to dialysis in South Africa is limited by budgetary constraints. Erythropoiesis-stimulating agents (ESAs) are used to manage anaemia in dialysis patients but are significant cost drivers. We aimed to evaluate haemoglobin and weight variation during dialysis and to assess whether using post-dialysis haemoglobin rather than pre-dialysis haemoglobin was associated with ESA dose reduction and cost benefit.

Methods: In this single-centre cross-sectional study, haemoglobin and weight differences before and after a 4-hour mid-week maintenance haemodialysis session were compared. The ESA doses required to maintain haemoglobin levels within the recommended range of 10 – 11.5g/dL were calculated based on the pre- and post-dialysis haemoglobin results, and the difference was used to determine the cost benefit.

Results: Fifty-five patients on chronic haemodialysis at a tertiary hospital in Johannesburg, South Africa, were enrolled. The mean post-dialysis haemoglobin was higher than pre-dialysis haemoglobin (11.34±1.75 vs 10.92±1.45g/dL, $p=0.003$), representing a 3.95% mean haemoglobin increase. The mean intradialytic weight reduction was 3.32±1.68%, $p<0.0001$. The calculated median ESA dose based on post-dialysis haemoglobin was significantly lower than the ESA dose based on the pre-dialysis haemoglobin (6,000 (IQR 0-12 0000) vs 8,000 (IQR 4,000-12,000) IU/week, $p<0.0001$). The difference in ESA dose translated into a mean cost saving of 21.38%.

Conclusion: In an environment where dialysis access is limited by resource constraints, ESA dosing based on post-dialysis haemoglobin concentrations may translate into significant cost savings. Larger studies are required to validate this approach and assess long-term patient outcomes.

Key words: Anaemia, chronic haemodialysis, post-dialysis haemoglobin, erythropoiesis-stimulating agents

INTRODUCTION

The prevalence of chronic kidney disease (CKD) in South Africa is estimated to be between 6.4% and 10.7%.^(1,2) However, data on the number of patients with end-stage kidney disease (ESKD) are scarce. The South African Renal Registry Report documents that 8,881 patients were receiving kidney replacement therapy (KRT) in South Africa in 2023, 6262 (70.5%) of these patients were on haemodialysis (HD).⁽³⁾ Access to KRT is limited by resource constraints, with an overall dialysis treatment rate of 145 per million population (pmp); 44 pmp in the state sector and 720 pmp in the private sector. This is well below the prevalence of treated ESKD in the United States, which is 2437 pmp.⁽⁴⁾

Anaemia in ESKD primarily results from reduced endogenous erythropoietin production, compounded by factors such as iron deficiency, chronic inflammation, reduced red blood cell lifespan, and blood loss associated with dialysis procedures.⁽⁵⁾ Multiple large international studies have shown that the prevalence of anaemia rises with advancing CKD stage.^(6–8) The reported prevalence of anaemia in CKD in sub-Saharan Africa is from single centres with small sample sizes. It varies widely, from 14% in Nigeria to 89.5% in Ethiopia and 91.8% in South Africa.^(9–11) A systematic review and meta-analysis of anemia among CKD patients in 25 studies from Sub-Saharan Africa ($n=5\ 042$) estimated the pooled prevalence to be 59.15% (95% CI, 50.02–68.27) with a substantial level of heterogeneity between studies.⁽¹²⁾

Anaemia in HD patients is associated with significant risks that impact morbidity and mortality, including cardiovascular complications (left ventricular hypertrophy, heart failure, and ischaemic heart disease), reduced quality of life, increased risk of hospitalisation, worsened cognitive function, a higher prevalence of depression, and complications related to blood transfusions.(13–17)

The latest KDIGO Anaemia in CKD guidelines recommend a haemoglobin (Hb) target of 10–11.5 g/dL in chronic HD patients.(5) Whilst the guideline does not prescribe an exact timing of Hb sampling relative to the dialysis session, it is generally accepted that Hb levels are drawn pre-dialysis.(5) Numerous studies document a variation in serum Hb concentration before, during, and after a HD session.(18–21) The use of pre-HD Hb may underestimate Hb due to volume overload, leading to an over-estimation of ESA dose required to reach target Hb range; however, the use of post-HD Hb for ESA dosing may result in potential underdosing due to haemoconcentration of Hb during a HD session.

Erythropoiesis-stimulating agents (ESAs) play a central role in the management of anaemia in patients undergoing HD. Clinical guidelines emphasise correcting iron deficiency and other reversible causes of anaemia before initiating ESA therapy.(22) Their use has significantly reduced the need for blood transfusions in this population and has been associated with improved patient well-being, physical function, and overall quality of life.(23) Determining the appropriate ESA dose remains challenging due to Hb variability, patient heterogeneity, and the timing of Hb measurement. Hb levels should be monitored regularly to avoid over-correction of Hb or use of high ESA doses, which may increase the risk of hypertension, stroke, vascular access thrombosis, and mortality.(24,25)

ESAs are a significant cost driver in ESKD treatment. In the United States, ESAs account for the single largest drug expenditure for Medicare beneficiaries with ESKD.(26) An Italian cohort study assessed direct healthcare costs in CKD patients treated with ESAs and found that in dialysis patients, the ESA-related cost represented about 6% of total annual costs.(27) In a systematic review of ESKD costs in Africa, medication costs (including ESAs) were explicitly identified among the direct medical cost items. This high per-patient cost of ESAs may represent a major challenge for budgets and sustainability.(28)

In the South African context, where dialysis is already highly resource-intensive, the ESA cost adds further pressure. This study aimed to evaluate variation in Hb and weight during a dialysis session and to assess whether using post-HD Hb rather than pre-HD Hb was associated with changes in ESA dose and potential cost-benefit.

METHODOLOGY

This was a cross-sectional study of patients attending the adult outpatient maintenance HD unit at Charlotte Maxeke

Johannesburg Academic Hospital in Johannesburg, South Africa. Ethical approval for this study was granted by the University of Witwatersrand Human Research Ethics Committee.

All patients were aged 18 or older and on maintenance HD, three times per week for at least 6 months. Each session lasted 4 hours. Exclusion criteria included patients with a co-morbidity associated with altered fluid distribution, such as heart failure or liver failure, current hospitalization, and patients with an incomplete dataset.

Serum Hb monitoring and ESA dose adjustment are undertaken monthly in this unit. The same nephrologist determined all ESA dosing. Each patient had their weight and serum Hb concentrations measured before ('pre') and after ('post') a midweek HD session. All data was collected during one week. The pre-HD Hb sample was taken at the beginning of the HD session, and the post-HD Hb sample was taken immediately after the HD session ended. Hb concentration was measured using Sysmex XN10/20 analysers (Kobe, Japan) by the on site National Health Laboratory Service laboratory. Weight was measured in kilograms with a digital scale in the dialysis unit. Ultrafiltration for each patient was targeted to their individual dry weight.

The Kidney Disease Improving Global Outcomes (KDIGO) Anaemia in CKD guideline recommends a haemoglobin target of 10–11.5 g/dL for patients on chronic HD.(17) The ESA administered in the unit was Epoetin beta, available at our hospital in prefilled syringes of 2000 IU, 4000 IU, and 8000 IU. The patients' prescribed ESA doses were recorded, and the doses required to maintain Hb levels within the recommended range were adjusted for each patient based on their pre-HD Hb results and a theoretical dose based on their post-HD Hb results. The difference in ESA dose was computed and used to calculate the cost-benefit.

STATISTICAL METHODS

The data were imported into Python 3.8 (Anaconda Inc., Berlin, Germany, 2021) and analysed. Normality was assessed graphically and using the Shapiro–Wilk test. These data were expressed as the mean and standard deviation. Non-parametric data were expressed as median and interquartile range. The principal statistical test employed was a Wilcoxon signed-rank test. Categorical variables were compared using the χ^2 test. $P < 0.05$ was considered statistically significant.

RESULTS

During the study period, sixty adult patients were receiving chronic HD at our facility. Five patients were excluded due to missing data; 55 patients were included in this study (Figure 1).

Baseline characteristics are shown in Table 1. There were thirty females (54.55%) and 25 males (45.45%) in the cohort. The mean age was 42.53 ± 11.98 years. Fifty-three (96.36%)

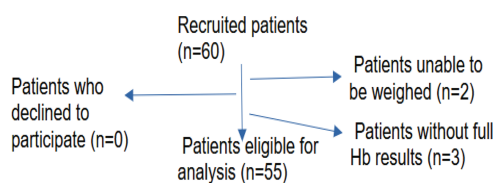


Figure 1: Patient flow diagram of included patients

patients in the sample are of African ethnicity, with the remaining 2 (3.64%) patients being of mixed race. The median dialysis vintage was 7.0 years (IQR 3.50–12.0 years). All patients underwent a 4-hour dialysis session.

The mean pre-HD Hb was significantly lower than the mean post-HD Hb (10.92 ± 1.45 g/dL vs. 11.34 ± 1.75 g/dL, $p = 0.003$), which equates to a 3.95% mean percentage increase in Hb concentration. According to the KDIGO 2012 Anaemia in CKD guideline, using pre-HD Hb measurements, 12 (21.8%) patients had low Hb levels (<10 g/dL) and 21 (38.2%) had on-target Hb levels (10–11.5 g/dL). However, when post-HD Hb values were used, 3 out of 12 (25.0%) patients with a pre-HD Hb <10 g/dL had an Hb within the KDIGO target range, whilst 5 out of 21 (23.8%) patients with a pre-HD Hb of 10–11.5 g/dL had a post-HD Hb above the recommended range of 11.5 g/dL. Table 1.

The mean pre-HD weight and post-HD weights were 62.61 ± 15.41 kg and 60.69 ± 15.12 kg, respectively ($p < 0.0001$). The mean percentage intradialytic weight reduction was $3.23 \pm 1.68\%$ ($p < 0.0001$).

The calculated median ESA dose based on post-HD Hb was 6,000 IU/week (IQR 0–12,000 IU/week), which was significantly lower than the calculated median ESA dose based on the pre-HD Hb, which was 8,000 IU/week (IQR 4,000–12,000 IU/week), $p < 0.0001$.

The patients were grouped according to their intradialytic weight change percentage. Twenty-one (38.18%) patients' weight reduced by $<2.5\%$, 27 (49.09%) by 2.5%–4.9%, and 7 (12.73%) by $\geq 5\%$. The median ESA doses based on pre-HD and post-HD Hb results, grouped by intradialytic

weight change percentage, are shown in Table 2. All groups showed a significant difference in ESA dosing based on pre-HD and post-HD Hb measurements.

The mean reduced cost of the calculated ESA dose based on pre-HD and post-HD Hb values was 21.38%. The mean cost of the ESA dose based on pre-HD Hb was R 1,500.00/patient/week; the price based on post-HD Hb was R 1,000.00/patient/week. Thus, this change in practice could lead to a cost saving of R 26,000.00/patient/ year. The shift in the distribution of ESA doses, rounded to the nearest 2000 IU, was statistically significant ($p < 0.001$).

DISCUSSION

Our study demonstrates that using post-HD Hb values for ESA dosing in chronic HD patients is associated with significant dose reductions and cost savings.

Lower ESA doses are associated with Hb levels less likely to be above the recommended range, thereby reducing the risk of complications associated with higher haemoglobin concentrations. In recent years, several studies have examined the relationship between ESA dosage and mortality in HD patients; a higher ESA exposure has been shown to independently predict adverse cardiovascular outcomes and increased mortality, even after adjusting for Hb levels.(29–31) Incorporating post-HD Hb values into dosing decisions may minimise the risk of overtreatment with ESA

Although KDIGO does not recommend a specific timing for blood sampling, it strongly emphasizes uniformity; advising that Hb be measured at the same point in the dialysis cycle each time. This consistency ensures reliable comparisons and meaningful trend analysis.

Traditional reliance on pre-dialysis Hb may underestimate actual red cell mass due to plasma volume expansion between sessions, leading to overtreatment with ESA.(32) Five of 21 (23.8%) patients within our cohort had a pre-HD Hb measurement within the normal range but a post-HD Hb above target. This potential overestimation of anaemia severity not only increases drug exposure

Table 1: Baseline characteristics of the cohort with haemoglobin and weight change pre- and post-HD

	Total cohort n = 55	Pre-HD value	Post-HD value	p value
Age, years (SD)	42.53 ± 11.98			
Male sex, n (%)	25 (45.45)			
Black ethnicity, n (%)	53 (96.36)			
Time on dialysis session, hours (SD)	4 (0)			
Dialysis vintage, years (IQR)	7 (3.5 – 12)			
Hb, g/dL, (SD)		10.92 (1.45)	11.34 (1.75)	0.003
Weight, kg (SD)		62.61 (15.41)	60.69 (15.12)	< 0.0001

Hb, haemoglobin; HD, haemodialysis; SD, standard deviation

Table 2: Change in ESA doses based on pre-HD and post-HD Hb results in relation to intradialytic weight change

Percentage intradialytic weight loss (%)	Number of patients n (%)	Median ESA dose based on pre – HD Hb value IU/week (IQR)	Median ESA dose based on post – HD Hb value IU/week (IQR)	p-value
<2.5	21(38.18)	8000 (4000–8000)	4000 (0–8000)	<0.01
2.5-4.9	27 (49.09)	8000 (4000–18000)	8000 (0–12000)	<0.01
≥5	7 (12.73)	8000 (8000–16000)	4000 (2000–10000)	0.015

ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; HD, haemodialysis; IQR, interquartile range

but also heightens the risk of adverse events and health care costs associated with higher Hb levels in chronic HD patients.

A key concern with using post-HD Hb levels for ESA dosing is that they may not accurately reflect actual Hb concentrations due to haemoconcentration secondary to excessive ultrafiltration and plasma volume shifts. In our cohort, patients were targeted to achieve their prescribed dry weight through ultrafiltration at each session, which may help mitigate excess haemoconcentration and its confounding impact on post-HD Hb measurements. Multiple studies have demonstrated a rise in serum Hb following an HD session, with this elevation persisting for at least 24 hours.(18–21) Consistent with these findings, our data showed a 3.95% increase in post-HD Hb levels compared to pre-HD values. Castillo et al. reported a post-HD Hb increase of 6.1%. In addition, they examined Hb fluctuations across the dialysis cycle by measuring serum Hb immediately before and after HD, and at 4, 24, and 48 hours post-dialysis.(33) They found no significant difference between the immediate post-HD Hb and values obtained during the interdialytic measurement period, indicating a ‘slow re-equilibration’ and suggesting an extended exposure to the higher post-HD Hb levels that may more closely reflect the patient’s steady-state hematologic status.

Another possible risk of using post-HD Hb for ESA dosing is missing patients with true anaemia. In our cohort, 3 (25%) of 12 patients had a post-HD Hb within the normal range, but pre-HD Hb below target. This potential overestimation of serum Hb levels could lead to an inappropriate reduction in ESA dose, resulting in prolonged anaemia, fatigue, progression of LVH, and increased transfusion risk.

From an economic perspective, the implications are substantial. Previous analyses have demonstrated that even modest reductions in ESA dose translate into considerable savings when extrapolated across dialysis populations.(26,34) Our study showed a mean ESA cost reduction on 21.38% when using post-HD rather than pre-HD Hb levels. This change in practice could lead to a cost saving of R 26,000.00/patient/year. For the 55 patients included in the study, this results in a cost reduction of

R 1,430,000.00/year for our unit. According to the 2023 South African Renal Registry, there are 6262 patients on haemodialysis in South Africa. This change in routine practice could lead to a saving of R 162,812,000.00/year. Cost reduction could be further extrapolated to include benefits from lower hospitalisation rates, cardiovascular mortality, and vascular access thrombosis, resulting from fewer patients with Hb above the target and excessive ESA exposure. Studies by Castillo et al. and Sagheb et al. have mirrored this significant reduction in cost with the application of post-HD Hb to calculate ESA dose.(21,33)

LIMITATIONS

This study has several limitations. First, its cross-sectional design and relatively small sample size from a single dialysis centre limit the generalizability of the findings to broader HD populations. The lack of longitudinal follow-up precluded the assessment of sustained ESA dose reduction, long-term anaemia control, and patient-centred outcomes, such as fatigue, quality of life, and hospitalization rates, limiting the ability to assess the broader clinical impact of this dosing strategy. The absence of body composition monitoring and lung ultrasound assessments represents an additional limitation, as these tools could have provided valuable insights into patients’ fluid status and help verify that the observed post-HD Hb concentrations were not influenced by excessive ultrafiltration or residual volume overload.

CONCLUSIONS

In an environment where dialysis access is limited by resource constraints, the findings of this study provide preliminary evidence supporting the use of post-HD Hb concentration as a practical, cost-effective guide for optimizing ESA therapy. Thus ESA dosing based on post-HD Hb concentrations may yield significant cost savings and reduce the risk of inappropriately high ESA doses in patients on chronic HD. These results provide a strong rationale for future multicentre, longitudinal studies to validate this approach, assess long-term patient outcomes, and evaluate its integration into standardized anaemia management protocols.

CONFLICT OF INTEREST: None.

AUTHORS' CONTRIBUTIONS

NM, KM, GP and ND participated in the initial conceptualization and drafting of the research topic and protocol. AG and EG collected the data. NM performed the data analysis. NM and ND prepared the initial manuscript. All authors reviewed and approved the final manuscript.

REFERENCES

1. Hariparshad S, Bhimma R, Nandlal L, et al. The prevalence of chronic kidney disease in South Africa: limitations of studies comparing prevalence with sub-Saharan Africa, Africa, and globally. *BMC Nephrol.* 2023; 24:62. doi:10.1186/s12882-023-03109-1
2. Bello AK, Levin A, Lunney M, et al. Status of care for end stage kidney disease in countries and regions worldwide: international cross-sectional survey. *BMJ.* 2019; 367:15873. doi:10.1136/bmj.15873
3. Jardine T, Marais N, Sebastian S, et al. South African Renal Registry annual report 2023. *Afr J Nephrol.* 2025; 28(1):62–74. doi:10.21804/28-1-7789
4. United States Renal Data System. 2024 USRDS annual data report: epidemiology of kidney disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2024. Available from: <https://usrds-adr.niddk.nih.gov/2024>
5. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO clinical practice guideline for anemia in chronic kidney disease. *Kidney Int Suppl.* 2012; 2(4):279–335. doi:10.1038/kisup.2012.37
6. Dmitrieva O, de Lusignan S, Macdougall IC, et al. Association of anaemia in primary care patients with chronic kidney disease: cross-sectional study of quality improvement in chronic kidney disease (QICKD) trial data. *BMC Nephrol.* 2013; 14:24. doi:10.1186/1471-2369-14-24
7. Chai YF, Lin HB, Ding GH, et al. Prevalence and treatment of anemia in chronic kidney disease patients based on regional medical big data. *Zhonghua Liu Xing Bing Xue Za Zhi.* 2023; 44(7):1046–1053. doi:10.3760/cma.j.cn112338-20221201-01028
8. Kovesdy CP, Davis JR, Duling I, Little DJ. Prevalence of anaemia in adults with chronic kidney disease in a representative sample of the United States population: analysis of the 1999–2018 National Health and Nutrition Examination Survey. *Clin Kidney J.* 2023; 16(2):303–311. doi:10.1093/ckj/sfac240
9. Haupt L, Weyers R. Determination of functional iron deficiency status in haemodialysis patients in central South Africa. *Int J Lab Hematol.* 2016; 38(4):352–359. doi:10.1111/ijlh.12492
10. Iyawe IO, Adejumo OA, Iyawe LI, Oviasu EO. Assessment of iron status in predialysis chronic kidney disease patients in a Nigerian Tertiary Hospital. *Saudi J Kidney Dis Transpl.* 2018; 29(6):1431–1440. doi:10.4103/1319-2442.248296
11. Abate A, Birhan W, Alemu A. Association of anemia and renal function test among diabetes mellitus patients attending Fenote Selam Hospital, West Gojam, Northwest Ethiopia: a cross-sectional study. *BMC Hematol.* 2013; 13(1):6. doi:10.1186/2052-1839-13-6
12. Taderegew MM, Wondie A, Terefe TF, et al. Anemia and its predictors among chronic kidney disease patients in Sub-Saharan African countries: a systematic review and meta-analysis. *PLoS One.* 2023; 18(2):e0280817. doi:10.1371/journal.pone.0280817
13. Singh AK, Szczech L, Tang KL, et al. Correction of anaemia with epoetin alfa in chronic kidney disease. *N Engl J Med.* 2006; 355(20):2085–2098. doi:10.1056/nejmoa065485
14. Foley RN, Parfrey PS, Harnett JD, et al. Clinical epidemiology of cardiovascular disease in chronic kidney disease. *Am J Kidney Dis.* 1998; 32(5 Suppl 3): S112–S119. doi:10.1053/ajkd.1998.v32.pm9820470
15. Stauffer ME, Fan T. Prevalence of anaemia in chronic kidney disease in the United States. *PLoS One.* 2014; 9(1):e84943. doi:10.1371/journal.pone.0084943
16. Kurella M, Yaffe K, Shlipak MG, Wenger NK, Chertow GM. Cognitive impairment in chronic kidney disease. *J Am Geriatr Soc.* 2004; 52(11):1863–1869. doi:10.1111/j.1532-5415.2004.52508.x
17. Taddio A, Stevens B, Craig KD. Blood transfusions and allo-immunization in dialysis patients. *Nephrol Dial Transplant.* 2007; 22(1):12–15.
18. Vlassopoulos D, Sonikian M, Dardioti V, Hadjiconstantinou V. Target haematocrit during erythropoietin treatment in dialysis patients: which value is “true-functional haematocrit”? *Nephrol Dial Transplant.* 1999; 14(5):1340–1341. doi:10.1093/ndt/14.5.1340
19. Bellizzi V, Minutolo R, Terracciano V, et al. Influence of the cyclic variation of hydration status on hemoglobin levels in hemodialysis patients. *Am J Kidney Dis.* 2002; 40(3):549–555. doi:10.1053/ajkd.2002.34913
20. Movilli E, Pertica N, Camerini C, et al. Predialysis versus postdialysis hematocrit evaluation during erythropoietin therapy. *Am J Kidney Dis.* 2002; 39(4):850–853. doi:10.1053/ajkd.2002.32007
21. Sagheb MM, Fallahzadeh MA, Moaref A, Fallahzadeh MH, Dormanesh B. Comparison of hemoglobin levels before and after hemodialysis and their effects on erythropoietin dosing and cost. *Nephrourol Mon.* 2016; 8(4):e38495. doi:10.5812/numonthly.38495
22. Macdougall IC, Bircher AJ, Eckardt KU, et al. Iron management in chronic kidney disease: conclusions from a “Kidney Disease: Improving Global Outcomes” (KDIGO) Controversies Conference. *Kidney Int.* 2016; 89(1):28–39. doi:10.1016/j.kint.2015.10.002
23. Tonelli M, Klarenbach S, Wiebe N, et al. Erythropoiesis-stimulating agents for anemia of chronic kidney disease: systematic review and economic evaluation. In: Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews [Internet]. York (UK): Centre for Reviews and Dissemination; 2008. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK75874/>
24. Driecke, T.B. Lessons from clinical trials with erythropoiesis-stimulating agents (ESAs). *Ren Replace Ther.* 2018; 4:46. doi:10.1186/s41100-018-0187-2
25. Koulouridis I, Alfayez M, Trikalinos TA, Balk EM, Jaber BL. Dose of erythropoiesis-stimulating agents and adverse outcomes in CKD: a metaregression analysis. *Am J Kidney Dis.* 2013; 61(1):44–56. doi:10.1053/j.ajkd.2012.07.014

26. Gauthier-Loiselle M, Michalopoulos SN, Cloutier M, et al. Costs associated with the administration of erythropoiesis-stimulating agents for the treatment of anemia in patients with non-dialysis-dependent chronic kidney disease: a US societal perspective. *J Manag Care Spec Pharm.* 2021; 27(12):1703–1713. doi:10.18553/jmcp.2021.27.12.1703
27. Ingrasciotta Y, Sultana J, Formica D, et al. Direct healthcare costs of chronic kidney disease management in Italy: what cost-savings can be achieved with higher biosimilar uptake and more appropriate use of erythropoiesis-stimulating agents? *Pharmacoepidemiol Drug Saf.* 2021; 30(1):65–77. doi:10.1002/pds.5152
28. Yakubu AO, Olusesi OT, Lawal FI, et al. Economic cost of end-stage renal disease in Africa: a systematic review. *BMC Nephrol.* 2025; 26:551. doi:10.1186/s12882-025-04478-5
29. Regidor DL, Kopple JD, Kovesdy CP, et al. Associations between changes in hemoglobin and administered erythropoiesis-stimulating agent and survival in hemodialysis patients. *J Am Soc Nephrol.* 2006; 17(4):1181–1191. doi:10.1681/ASN.2005090997
30. Streja E, Park J, Chan TY, et al. Erythropoietin dose and mortality in hemodialysis patients: marginal structural model to examine causality. *Int J Nephrol.* 2016; 2016:6087134. doi:10.1155/2016/6087134
31. Pan S, Zhao DL, Li P, et al. Relationships among the dosage of erythropoiesis-stimulating agents, erythropoietin resistance index, and mortality in maintenance hemodialysis patients. *Blood Purif.* 2022; 51(2):171–181. doi:10.1159/000506536
32. Lundby C, Ponte B, Lundby AK, Robach P, de Seigneux S. Red blood cell volume is not decreased in ESA-naive anemic patients with chronic kidney disease. *Physiol Rep.* 2018; 6(21):e13900. doi:10.14814/phy2.13900
33. Castillo N, García-García P, Rivero A, et al. Should we adjust erythropoiesis-stimulating agent dosage to postdialysis hemoglobin levels? A pilot study. *BMC Nephrol.* 2012; 13:60. doi:10.1186/1471-2369-13-60
34. Schiller B, Doss S, De Cock E, Del Aguila MA, Nissenson AR. Costs of managing anemia with erythropoiesis-stimulating agents during hemodialysis: a time and motion study. *Hemodial Int.* 2008; 12(4):441–449. doi:10.1111/j.1542-4758.2008.00308.x