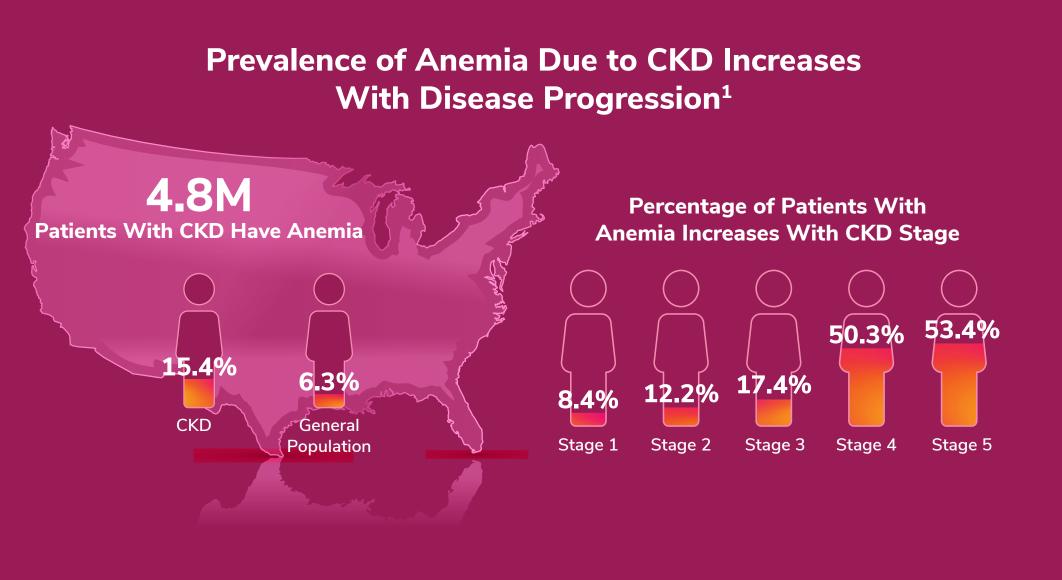
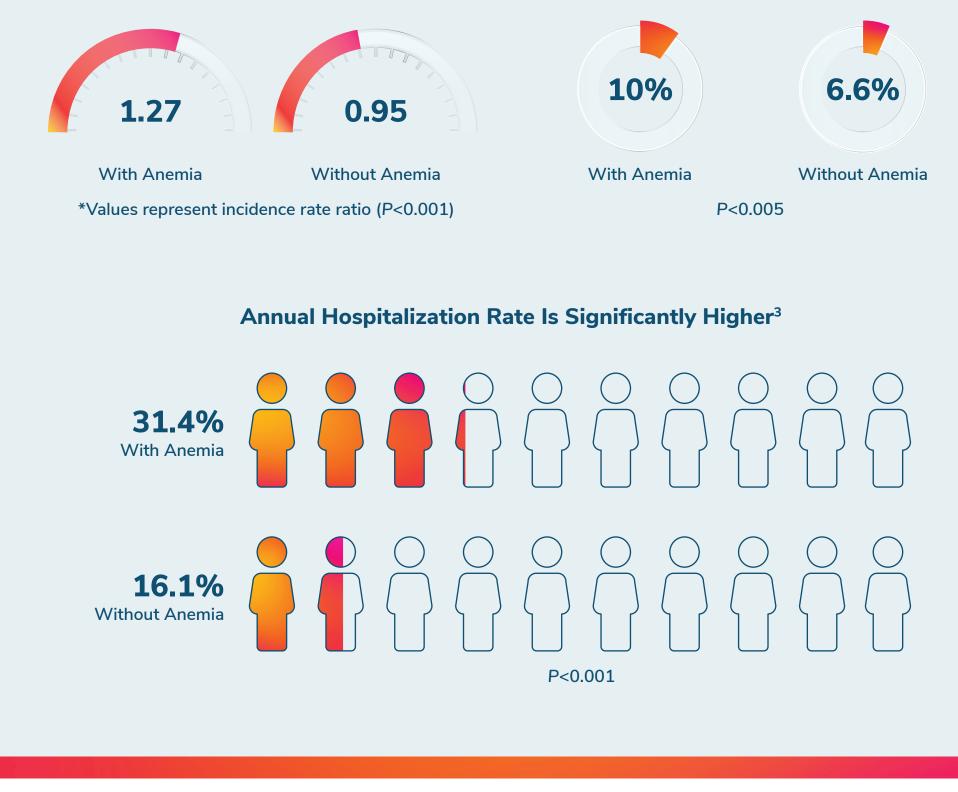
Burden of Anemia Due to Chronic Kidney Disease (CKD)



Mean Number of CV-Related Mortality Rate Is Higher³ Comorbidities Is Higher^{2,*}

Higher Clinical Burden Is Demonstrated in Patients

With Anemia and CKD (Stages 3-4)



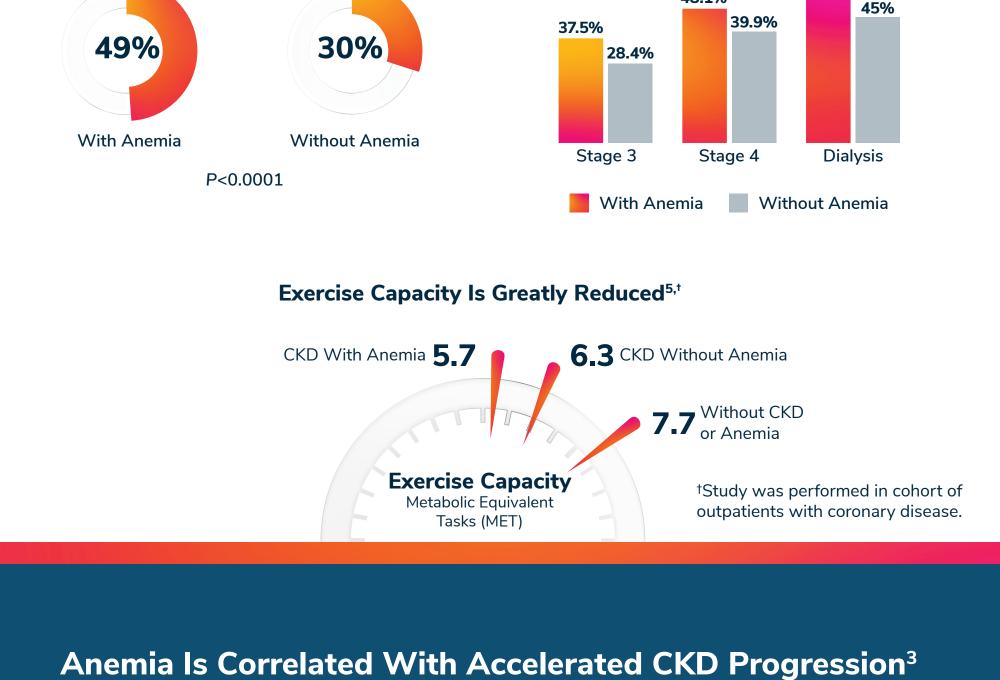
Fatigue Is More Common⁴ **Activity Impairment Increases** With Disease Progression⁴

52%

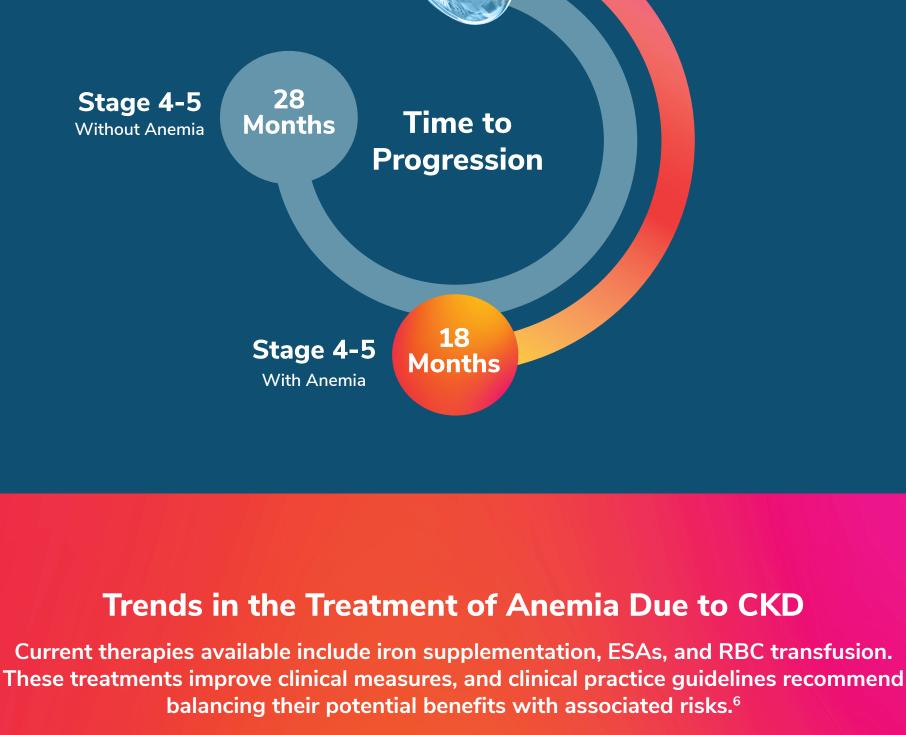
48.1%

Reduced Quality of Life Is Associated With Anemia

in Patients With CKD (Stages 3-5D)



Stage 3



Regulations

FDA approval for first ESA

treatment for anemia due to CKD, epoetin alfa (Epogen®)¹⁰ Guidelines

Clinical Evidence

1989

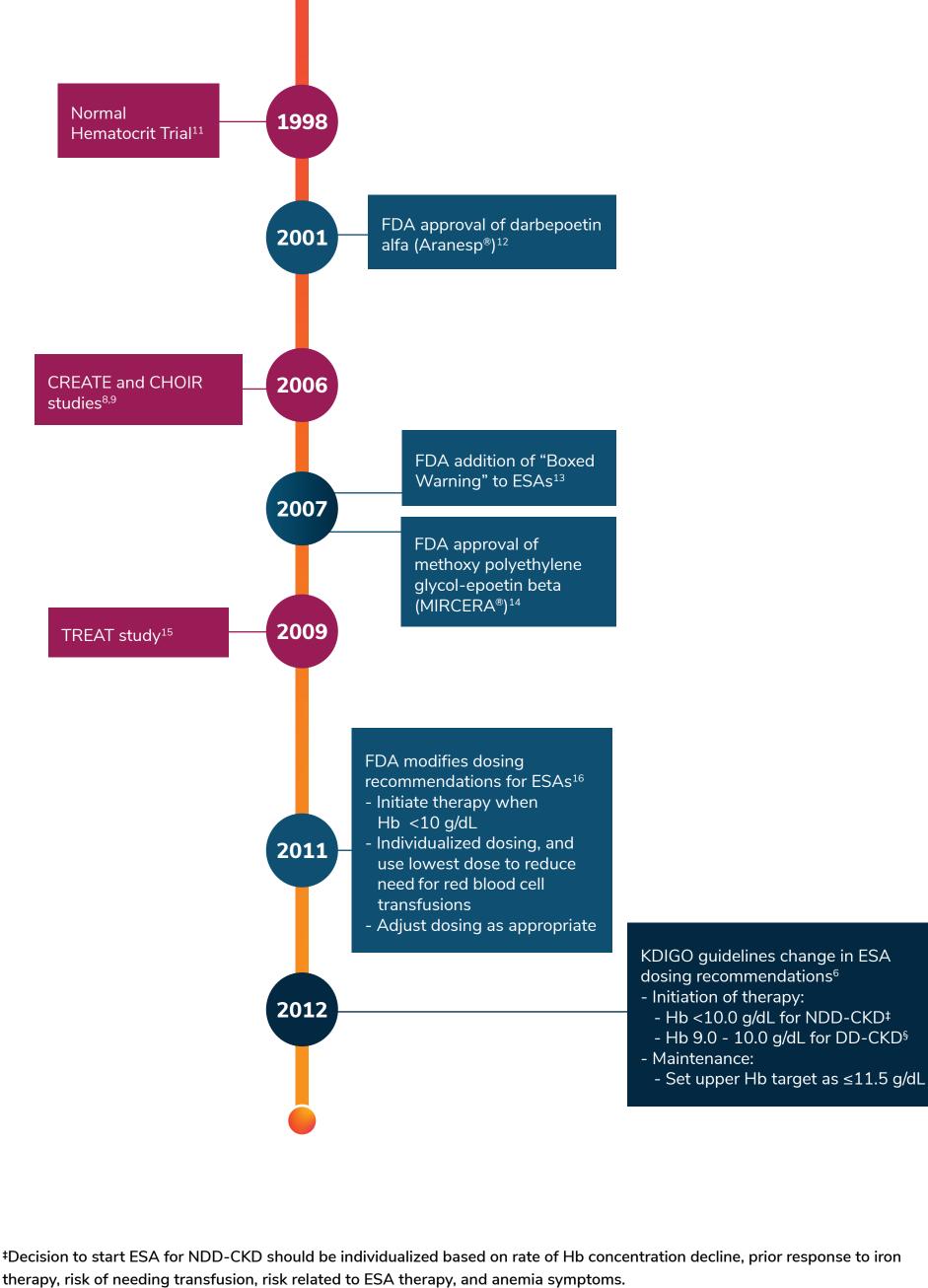
The introduction of ESAs represented a breakthrough in therapy.^{6,7} They have remained a mainstay for the treatment of anemia due to CKD for the past 30 years by increasing

Hb levels and decreasing the need for RBC transfusions.⁶

Several randomized clinical trials have demonstrated that higher hemoglobin targets

(≥13.0 to 14.0 g/dL) with ESA use are associated with increased cardiovascular risk,

leading to changes in regulatory and clinical practice guidance outlined below.^{6,8,9}



§For DD-CKD, ESA should be initiated to prevent a decline in Hb to <9.0 g/dL. Epogen® (epoetin alfa) and Aranesp® (darbepotein alfa) are products of Amgen Inc. MIRCERA® (methoxy polyethylene glycol-epoetin beta) is a product of Vifor (International) Inc.

Mean Hemoglobin Levels in ESA-Treated Hemodialysis Patients¹⁷

2007: FDA Boxed Warning¹³

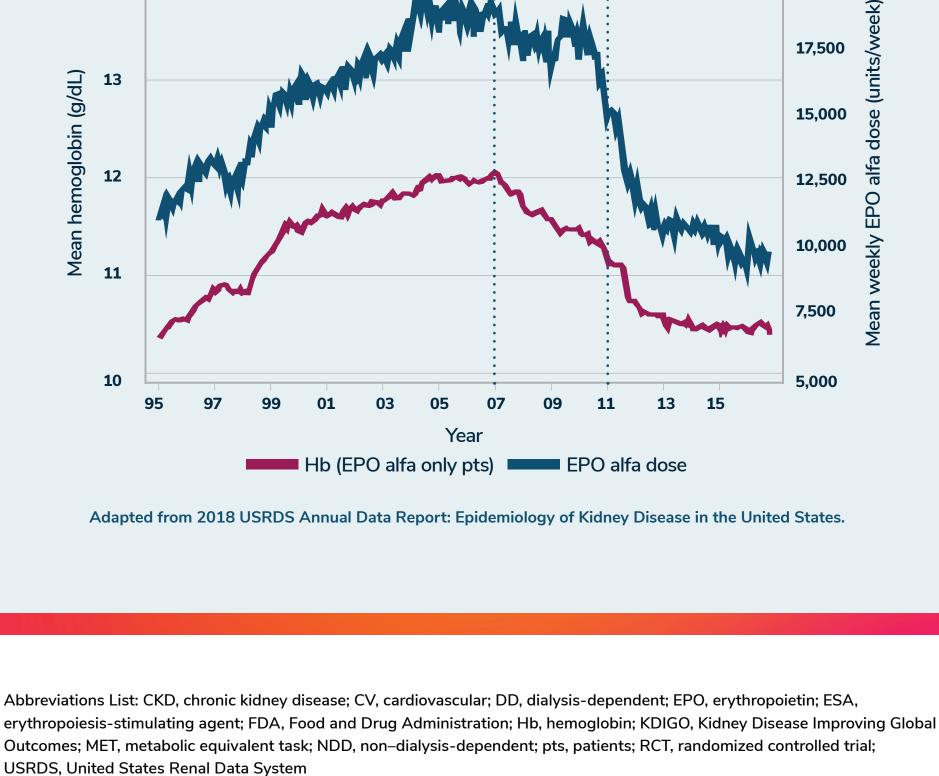
2011: FDA Dose Modification

Recommendation¹⁶

20,000

17,500

15,000



References: 1. Stauffer ME, Fan T. PLoS One. 2014;9:e84943. 2. Covic A, et al. Adv Ther. 2017;34:1662-1672. 3. Portolés J, et al. BMC Nephrol. 2013;14:2. 4. Eriksson D, et al. BMC Nephrol. 2016;17:97. 5. Odden MC, et al. J Am Soc Nephrol. 2004;15(11):2908-

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