

Is there a benefit to lowering the creatinine reference interval?

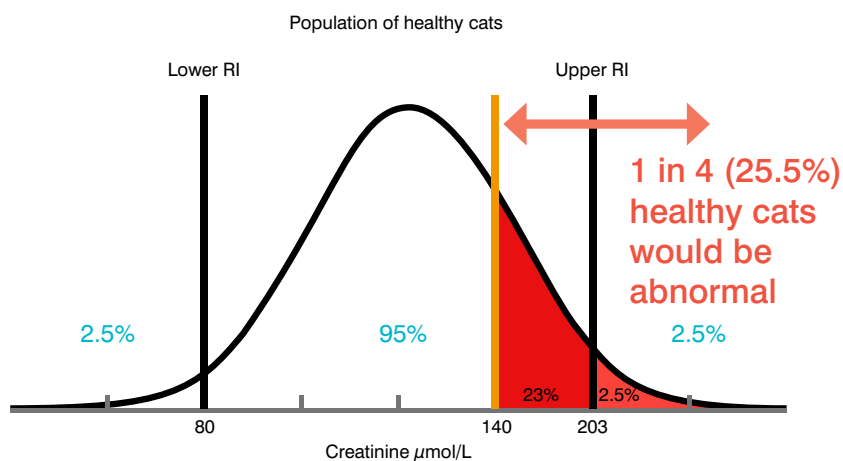
We are often asked, “Why does the upper limit of the feline reference interval (203 $\mu\text{mol/L}$ or 2.3 mg/dL)[†] for creatinine (CREA) not match the threshold for International Renal Interest Society (IRIS) chronic kidney disease (CKD) stage 1 (140 $\mu\text{mol/L}$ or 1.6 mg/dL)?”

The first step to understanding why changing a reference interval does not improve the diagnostic quality of a biomarker is knowing the facts:

- IDEXX follows strict guidelines from the Clinical and Laboratory Standards Institute (CLSI) to establish reference intervals across our reference laboratories and in-house diagnostics.¹
- Reference intervals are based on populations determined to be clinically normal by veterinarians.
- Reference intervals are not universal - they may differ based on laboratory, methodology, and population.
- The IRIS recommended cutoffs used to stage CKD are decision points determined by the IRIS committee for use after the diagnosis of CKD.²

What happens if the upper limit of the feline reference interval is changed to 140 $\mu\text{mol/L}$ (1.6 mg/dL)?

Lowering the upper limit of the reference interval for creatinine is not beneficial for most feline patients when diagnosing CKD - it risks inappropriate diagnosis and treatment of apparently healthy cats with CKD, an irreversible and progressive condition which may lead to unnecessary treatment.



Changing the upper limit of the reference interval to 140 $\mu\text{mol/L}$ (1.6 mg/dL) would describe **one in four known clinically healthy cats** as abnormal with reduced GFR and possible disease.³

[†]The refers to the reference interval used at IDEXX Reference Laboratories. The equivalent Catalyst® Creatinine method-specific reference interval is 71 to 212 $\mu\text{mol/L}$ (or 0.8 to 2.4 mg/dL). The same logic would apply.

References:

1. Clinical and Laboratory Standards Institute. Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline, 3rd ed. https://clsi.org/media/1421/ep28a3c_sample.pdf. Clinical and Laboratory Standards Institute, 2010;28(30). EP28-A3c.
2. International Renal Interest Society. IRIS Guidelines. IRIS website. <http://www.iris-kidney.com/guidelines/index.html>. Accessed November 1, 2019.
3. Data on file at IDEXX Laboratories, Inc. Westbrook, Maine USA.