Rethinking Ferritin Reference Ranges for Diagnosing Iron Deficiency at Denver Health

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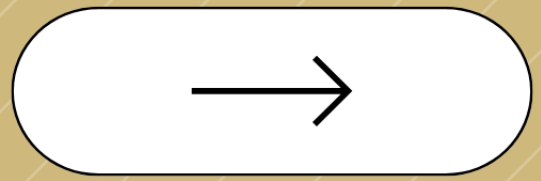
Introduction to Iron Deficiency



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Background

- Iron Deficiency Affects 2 billion people worldwide and is the most common nutritional deficiency

- Leading cause of anemia globally

- Variety of health impacts including:
  - Fatigue/lethargy
  - Exacerbation of underlying medical conditions
  - Poor neurocognitive function

- Per the WHO
  - IDA is among the top 5 causes of years lived with disability

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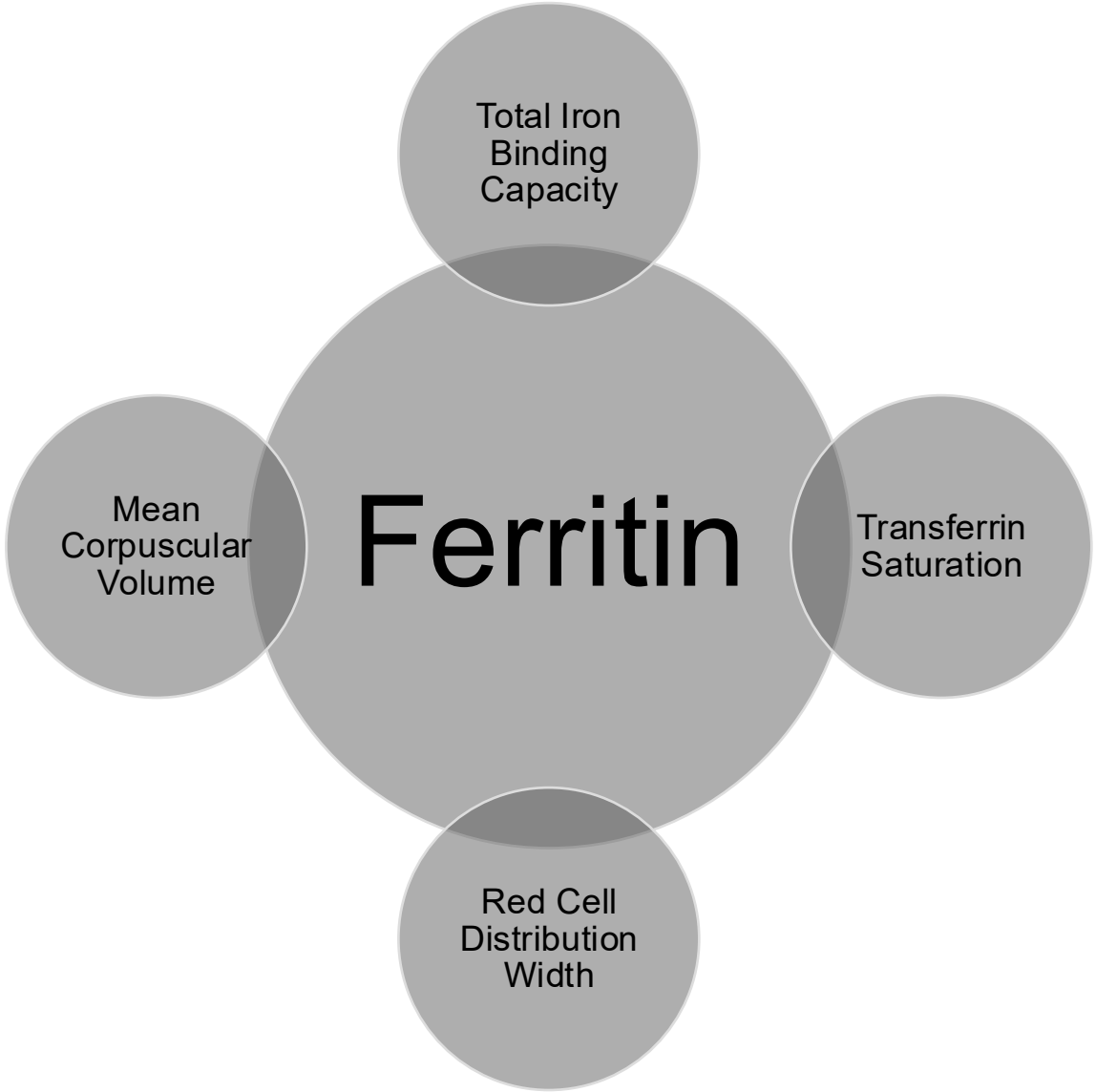
Defining Iron Deficiency



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What is an appropriate Ferritin Cutoff?

Guideline based values

- WHO guidelines <15µg/L
- AGA guidelines <45µg/L
- ASH *suggests* <30µg/L

Physiologic basis: Ferritin >30-50µg/L is the point of reversal of compensatory mechanics

Population factors: Gaussian distribution

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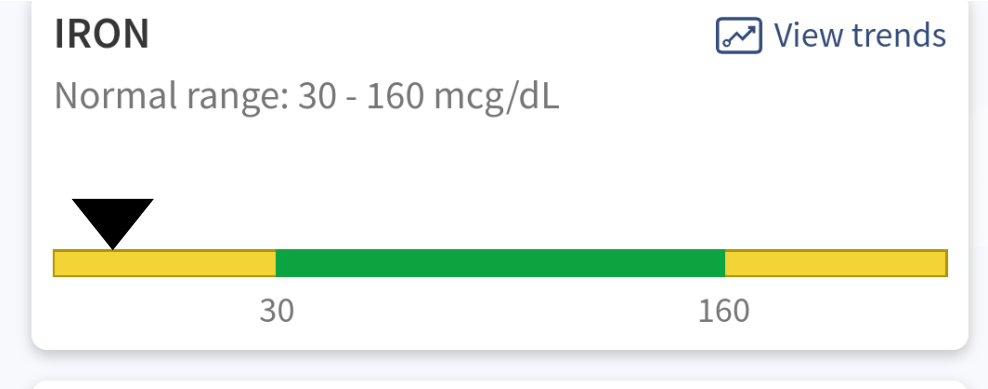
Relevance to Denver Health

- What are the Ferritin Cutoffs at Denver Health?
  - Women: Ferritin Levels **<5ng/mL** are flagged as abnormal
  - Men: Ferritin Levels <28ng/mL are flagged as abnormal
- *Do these abnormal cutoffs lead to undertreatment of Iron Deficiency?*
- In Denver Health primary care clinics, do institutional reference ranges for ferritin levels lead to undertreatment of iron deficiency when compared to a threshold for <30ng/mL



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Methods

- This is an IRB approved, retrospective study looking at adults (>18 years old) who were seen at one of the seven Denver Health primary care clinics and had their ferritin levels measured between January,1st, 2020 and January 1st, 2025
- Data source
  - Extracted from EMR and included demographic data, laboratory values, clinical diagnoses associated with the visit and treatment history (with oral vs IV iron)
- Data analysis
  - Data analyzed in excel, Data analysis performed by Prism by Chi-Squared and Fishers Exact Test

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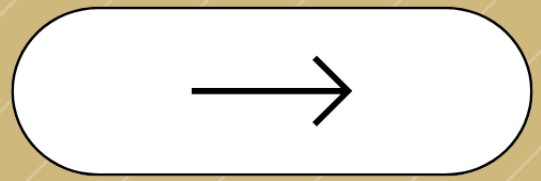
Results



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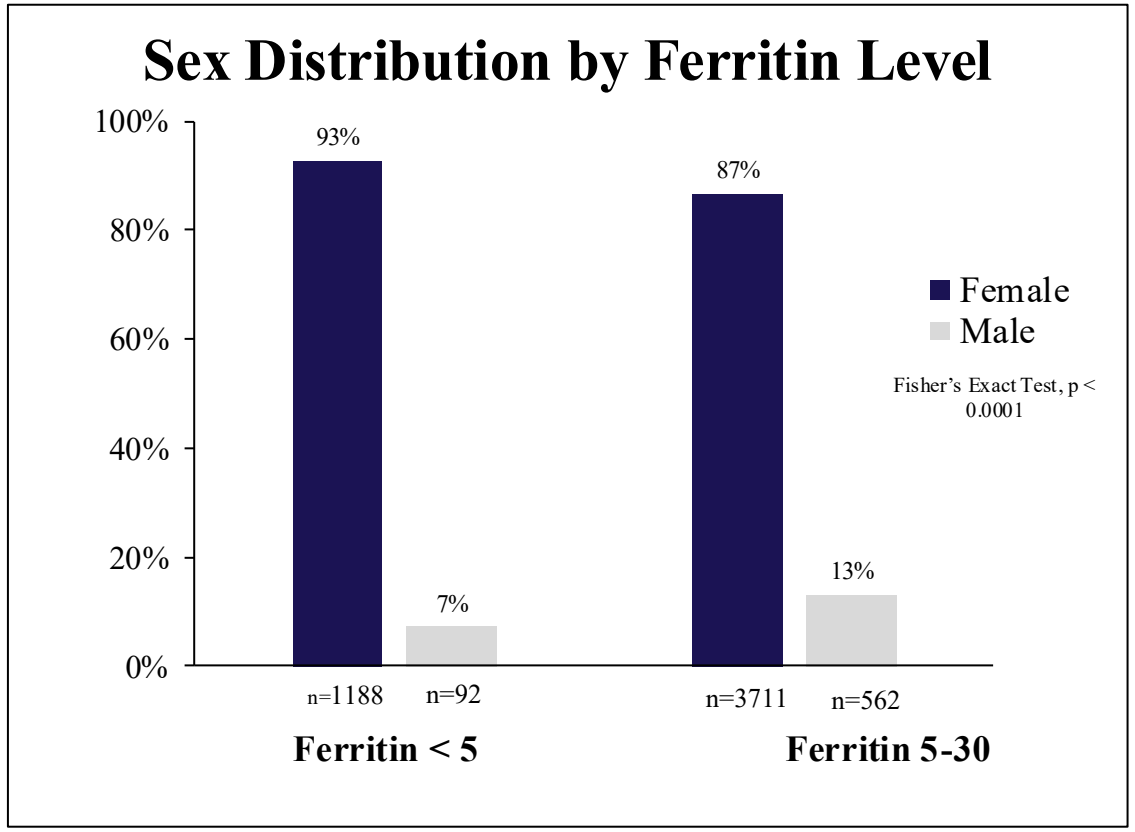
Results

Distribution of Iron Deficiency

- 5553 total patients identified
- Significant sex related difference in distribution
- Women represent a majority of cases of significant iron deficiency at all Ferritin levels <30ng/mL
- *Why are only levels <5ng/mL flagged as abnormal?*



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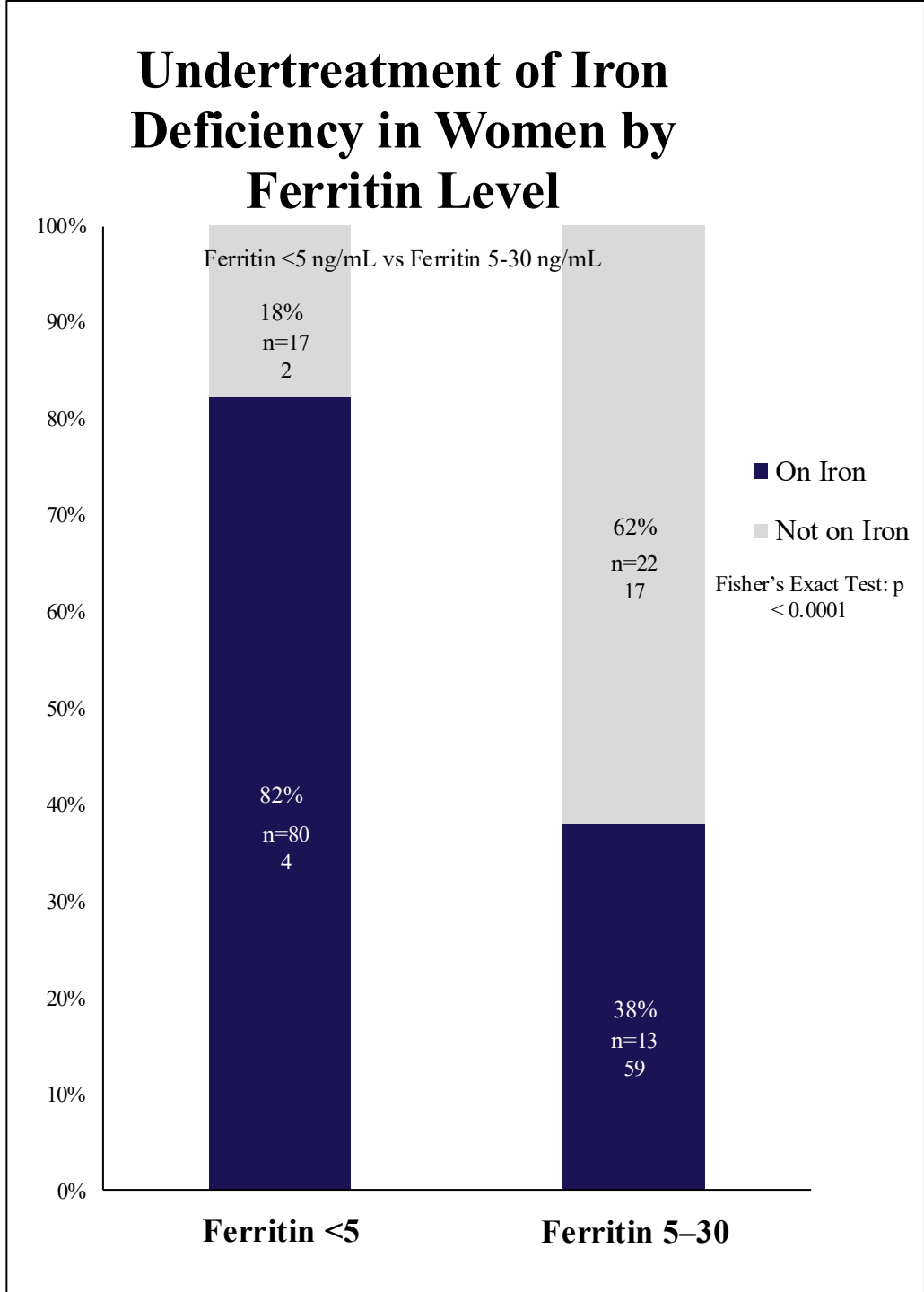
Results

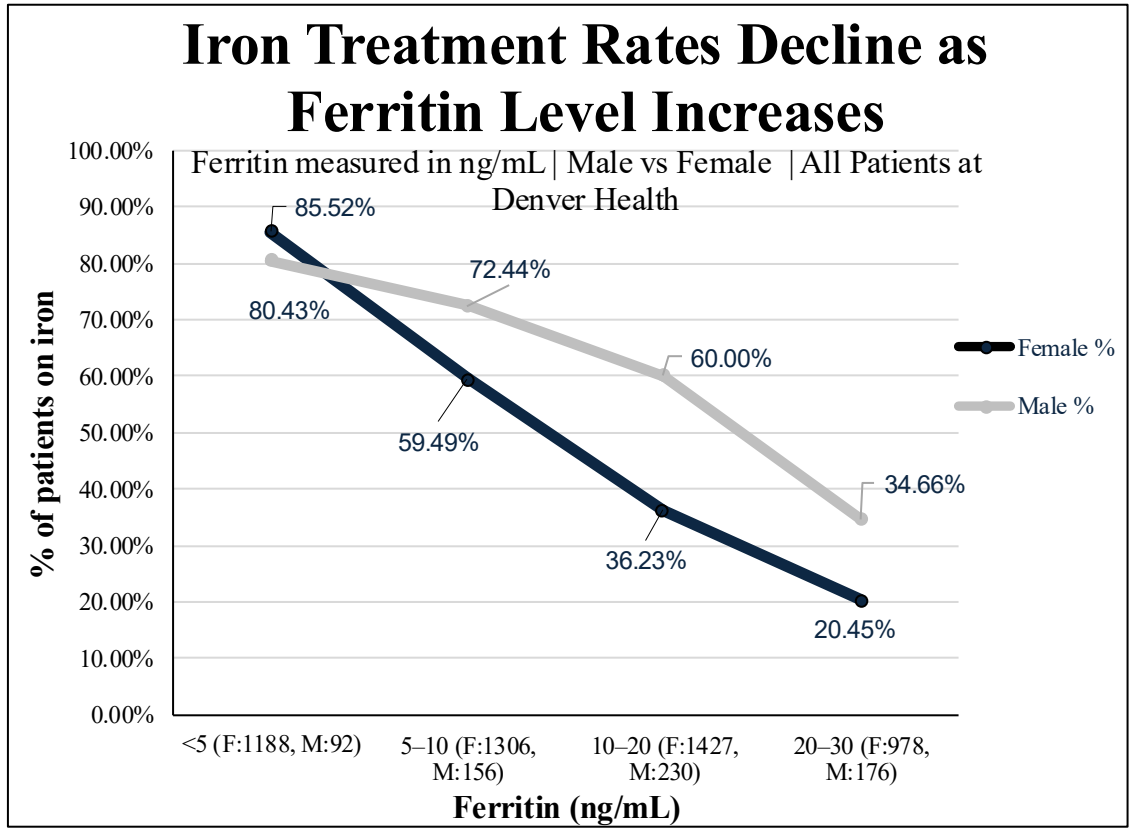
Treatment rates of Iron Deficiency in Women

- Women are more likely to receive treatment for iron deficiency when Ferritin levels are >5ng/mL compared to Ferritin levels 5-30ng/mL



Results

- Both women and men have significantly undertreated iron deficiency based upon guideline (<30ng/mL)
- Even for men where the ferritin levels <28ng/mL is flagged as abnormal, undertreatment persists



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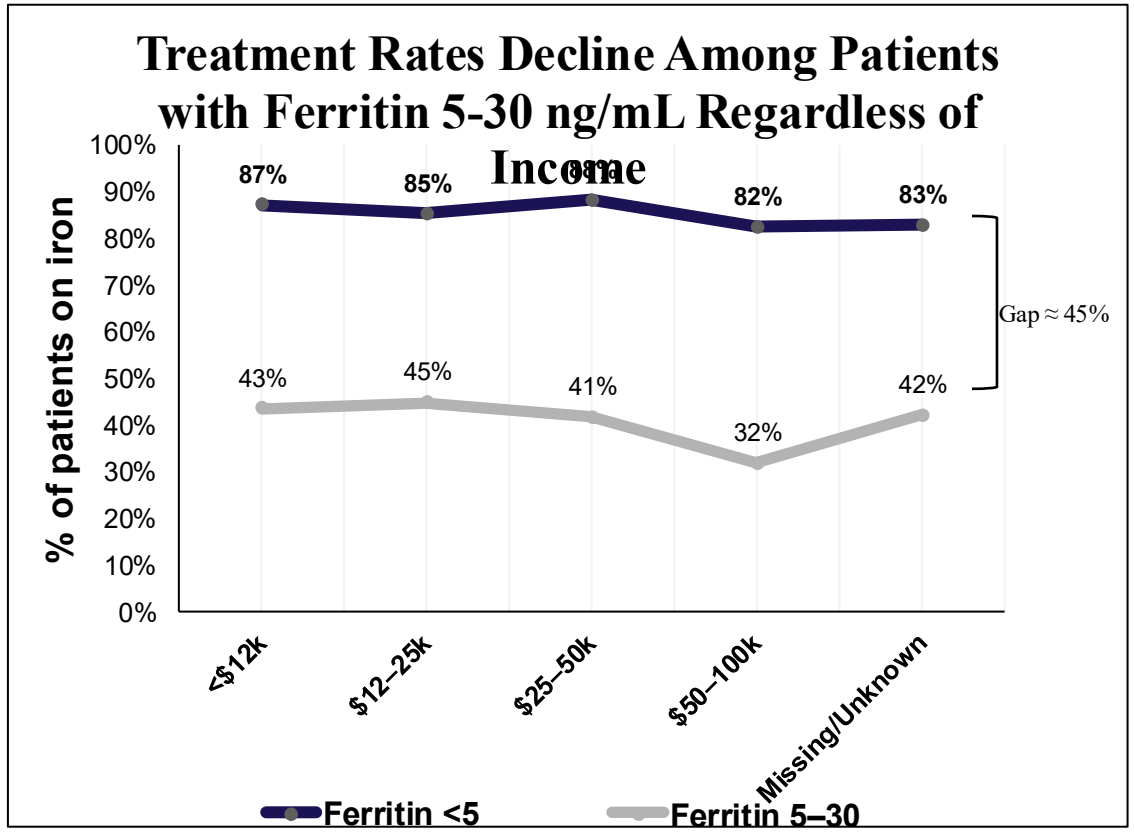
Results

Income Levels and Treatment Rates

- Overall similar trend of Ferritin levels between 5-30ng/mL being more undertreated compared to levels <5ng/mL
- No significant difference in treatment rates by income level based upon the two ferritin subgroups
- Not visualized: Borderline significance in racial differences in ferritin levels (p=0.0567) with black patients being overrepresented



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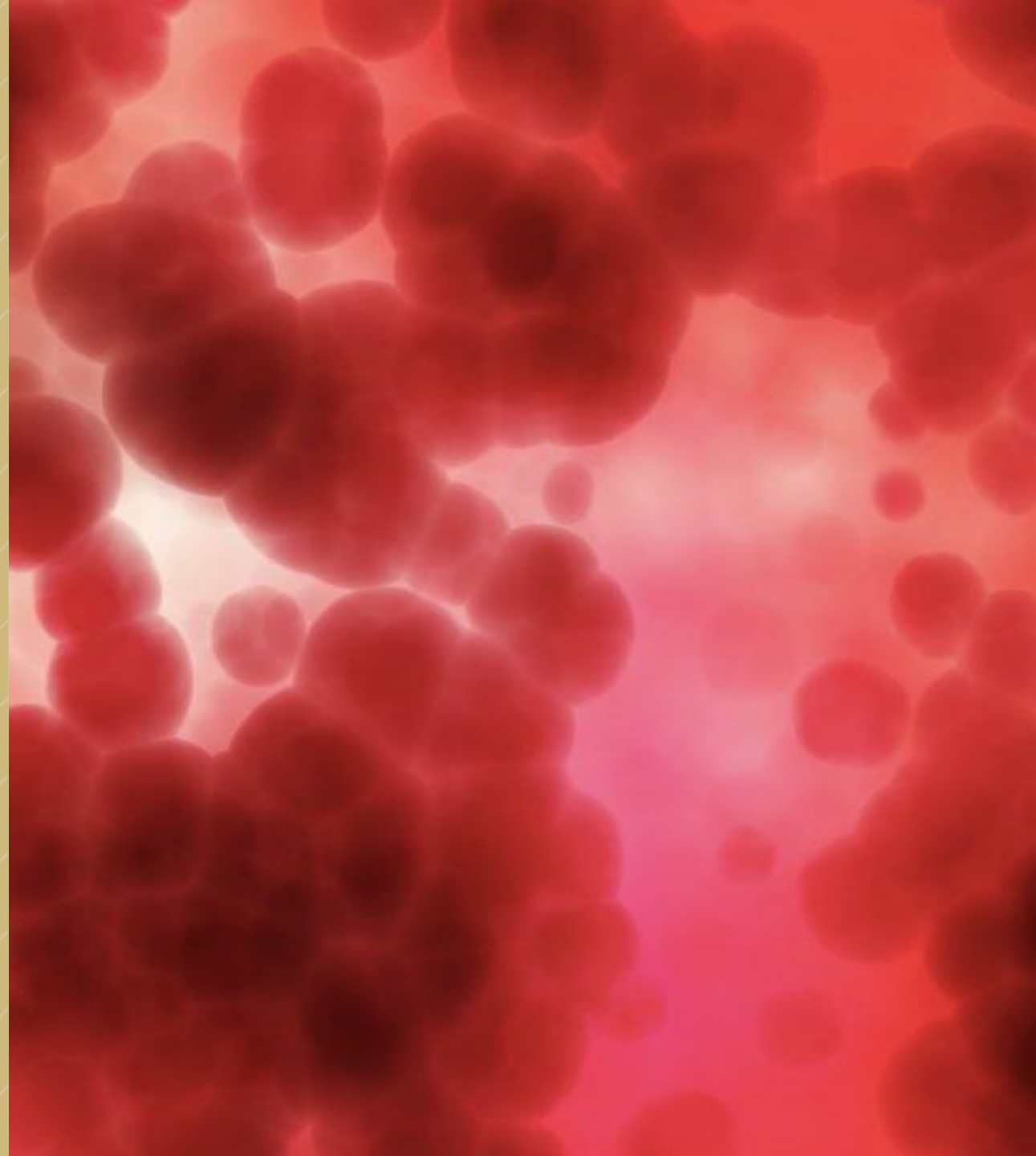
Conclusions

Conclusions

Reference ranges at Denver Health are set below evidence-based threshold for iron deficiency treatment. Many patients have clinically significant low ferritin levels that is untreated

Ferritin thresholds appear to drive clinical decision rather than current clinical guidelines

Disproportionately, women have higher rates of iron deficiency and poor treatment rates

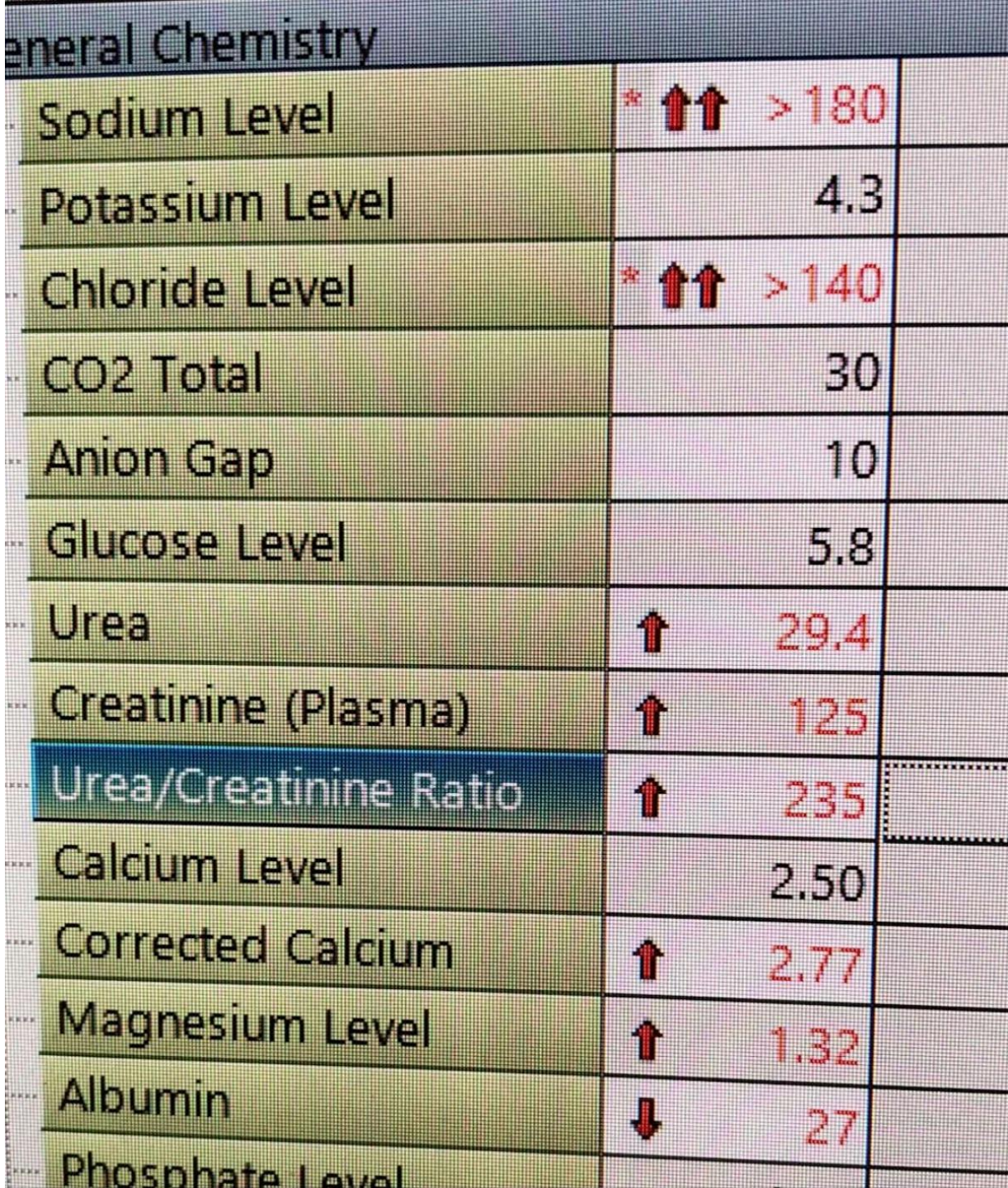


Clinical Implications

Re-aligning ferritin reference ranges with clinical practice represents a low cost and high impact evidence-based intervention to treat iron deficiency and address disparities

An assumed normal distribution of iron deficiency can conflict with clinical guidelines and lead to undertreatment of the condition

Future research could examine physicians' understanding of clinical guidelines and how markers of normal/abnormal lab values impact treatment rates



Limitations and considerations

- Anemia as a potential confounder to treatment of iron deficiency/ low ferritin
- Assessment of iron deficiency with elevated ferritin levels
- Potential downstream effects of increasing the Ferritin Cutoffs
  - More extensive diagnostic studies

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Next Steps

- Analysis of reference ranges at surrounding institutions
- Data analysis of iron deficiency in the setting of normal to elevated ferritin levels
- Meetings with institutional leadership to discuss changing reference ranges

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Questions?

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