

Articles

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🔔 Tweetorial Alert 🔔

1/

Hey #NephTwitter!

Welcome to a NEW [#tweetorial](#) #xtorial brought to you by [@KIReports](#).

2/

Our author is Melvin [@MChanMD](#) (pediatric nephrologist)

Our topic: Understanding the effects of iron supplementation on Cardiovascular and Kidney Outcomes in CKD Patients

[#MedTwitter](#) [#nephtwitter](#) [@ISNkidneycare](#) [#XTwitter](#)



3/

There are no conflicts of interest. Please also check out [#KIReportsCommunity](#) educational [#blogposts](#) at <https://www.kireportscommunity.org/>. FOLLOW US at [@KIReports](#) for more expert [#MedEd](#) in [#kidneydisease](#). [#FOAMed](#) [@MedTweetorials](#)

4/ Our [#Tweetorial](#) is based on a recent publication by Dr. Bernard Chan and VA [@Husamjz](#): Systematic Review of the Effects of Iron on Cardiovascular, Kidney, and Safety Outcomes in Patients With CKD

Systematic Review of the Effects of Iron on Cardiovascular, Kidney and Safety Outcomes in Patients With Chronic Kidney Disease



Methods



IV or Oral Iron in CKD
Systematic review and meta-analysis of RCT



3 Databases
From inception until February 1, 2024



1ry Composite Endpoint
Heart failure hospitalisation or cardiovascular death

Results



45 Trials
Iron vs placebo

Incidence of SAE
RR 0.90



95% CI 0.82-0.98
moderate certainty
P-heterogeneity=0.09



1ry Composite Endpoint

RR 0.84 95% CI 0.75- 0.94
moderate certainty



Heart Failure Hospitalisation

RR 0.84 95% CI 0.75- 0.94
moderate certainty



Cardiovascular Death

RR 0.81 95% CI 0.65- 1.02
low certainty

CKD: chronic kidney disease; IV: intravenous; SAE: serious adverse events

KIREPORTS
Kidney International Reports

Chan B et al, 2025

Visual abstract by:
Husam Alzayer, MD
X @HusamJZ

Conclusion: Iron therapies may reduce the risk of heart failure or cardiovascular death in patients with CKD. Randomised trials evaluating effects of iron on clinical outcomes are needed, especially in non-dialysis CKD, with or without anaemia.

5/ Intro

Iron is critical for the following:

- 💡 Hemoglobin synthesis
- 💡 Cellular function
- 💡 Oxygen transport

6/ Prevalence and Outcomes

- 💡 1/3 of patients with CKD have low iron stores
- 💡 Low iron is prevalent in patients with heart failure and is associated with more cardiovascular events. However, too much iron can lead to increased atherosclerosis [PMID 32739111].

7/ Recommendations

- 💡 Cardiology societies recommend treating iron deficiency regardless of anemia for patients with heart failure with reduced ejection fractions
- 💡 Kidney societies focus more on anemia for treatment of iron deficiency

8/ Do you normally treat patients for iron deficiency without anemia? We hope this article provides some answers!



9/ Methods

🔍 Meta-Analysis from Database Inception to February 2024, with the following keywords.

📄 "Iron therapies"

📄 "Chronic kidney disease"

📄 "Heart failure"

🔍 Inclusion: RCTs of adults ≥ 18 yo with CKD

🔍 CKD defined as $eGFR < 60 \text{ mL/min/1.73m}^2$ or an albumin/creatinine $> 30 \text{ mg/g}$

10/ Outcomes

📌 Cardiovascular outcomes (heart failure hospitalization, CV deaths)

📌 Heart failure hospitalizations, CV deaths, myocardial infarction, strokes, eGFR, proteinuria, dialysis, all-cause mortality, and serious adverse effects

📌 Compared formulations, route, and dose

11/ Data Analysis

📌 Unpublished trial data were obtained

📌 Hazard ratios for time to event

📌 Treatment ratios for recurrent event analysis

📌 Summarized effects of kidney outcomes due to heterogeneity of outcomes

📌 Stratified patients based on dialysis and non-dialysis groups

12/ Study Characteristics

- 👉 45 eligible studies
- 🔑 18 trials with dialysis patients
- 🔑 26 trials with non-dialysis CKD patients
- 🔑 1 trial with both

13/ Results

👉 Reduced 📉 outcome by 15% in non-dialysis patients and 16% in dialysis patients

Heart failure hospitalisation or cardiovascular death

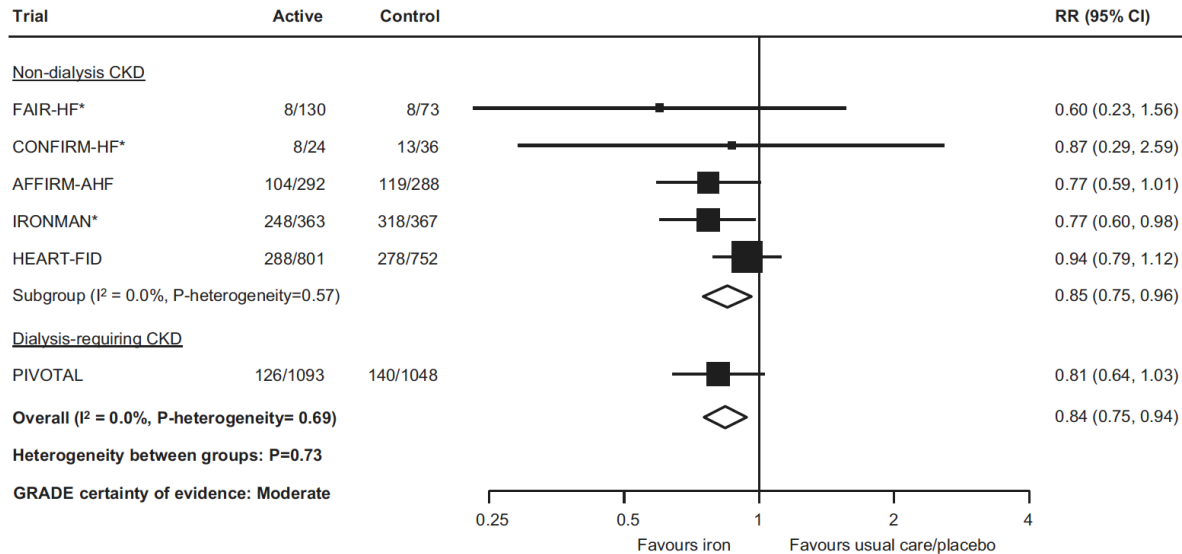
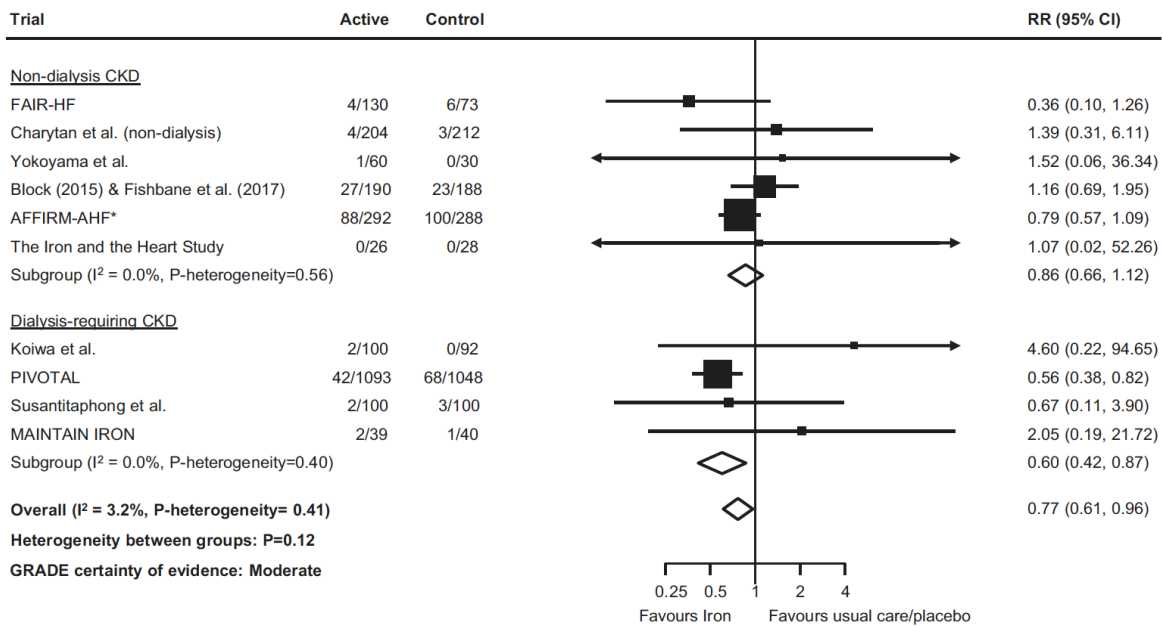


Figure 1. Effect of iron therapies versus usual care or placebo on hospitalization for heart failure or cardiovascular death in people with CKD. *First and recurrent hospitalizations for heart failure or cardiovascular death. CI, confidence interval; CKD, chronic kidney disease; GRADE, Grading of Recommendations, Assessment, Development and Evaluation; RR, relative risk.

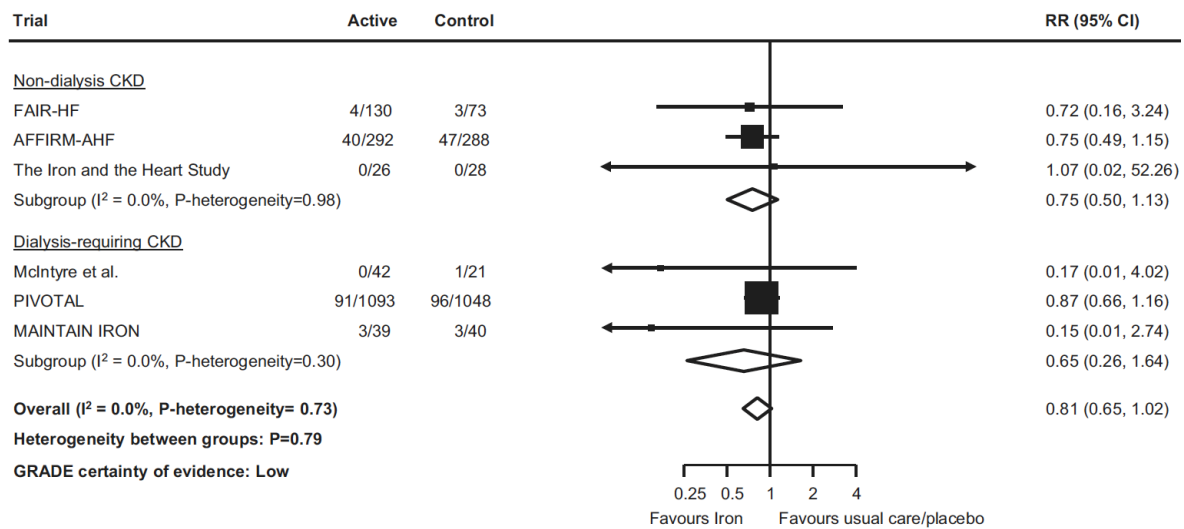
14/ Results

- 👉 Reduced heart failure hospitalization by 40% in dialysis patients. No significant difference in non-dialysis patients.
- 👉 No significant impact on cardiovascular death in dialysis or non-dialysis patients.

a Heart failure hospitalisation



b Cardiovascular death

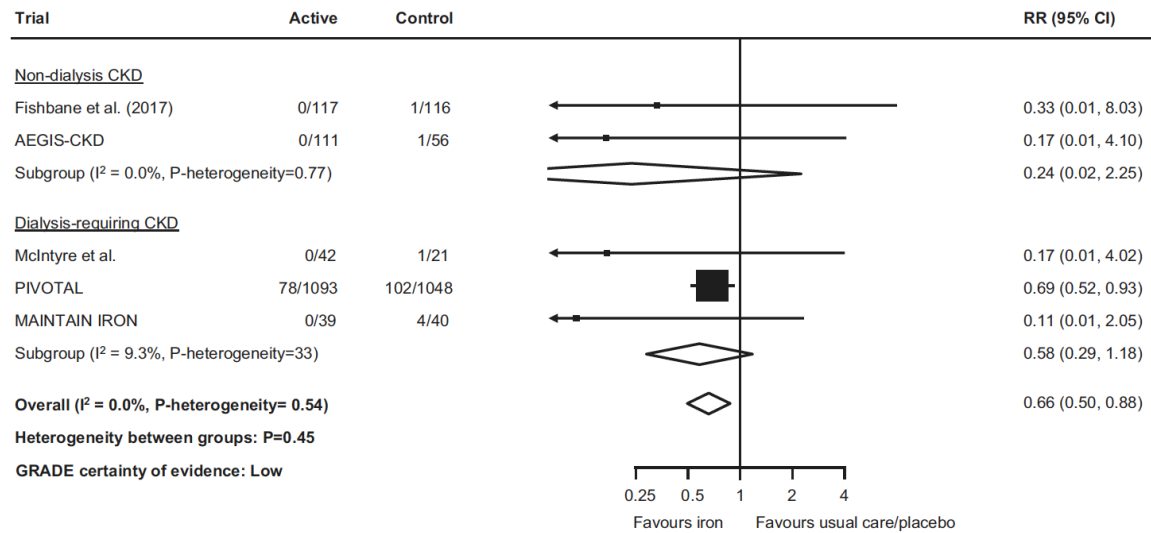


15/ Results

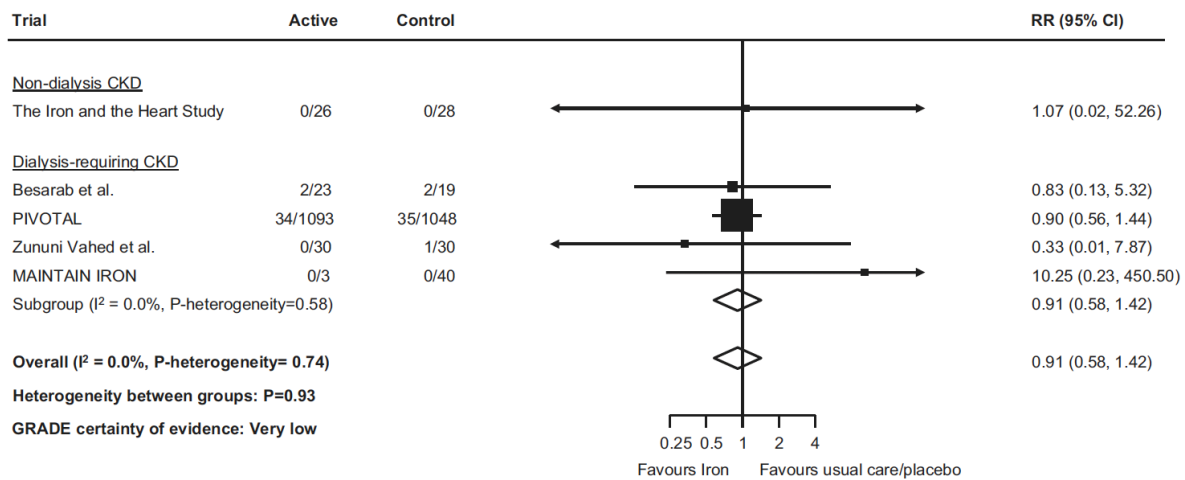
👉 No significant impact on myocardial infarction rates when looking at dialysis or non-dialysis patients separately, but is significant as a total cohort.

👉 No significant impact on strokes in either groups or total cohort.

a Myocardial infarction



b Stroke

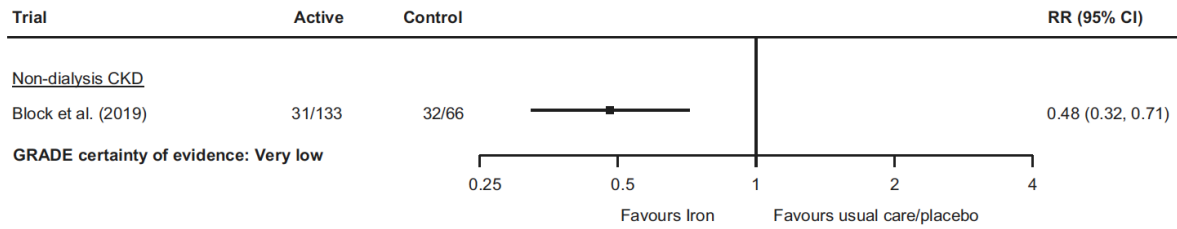


16/ Results

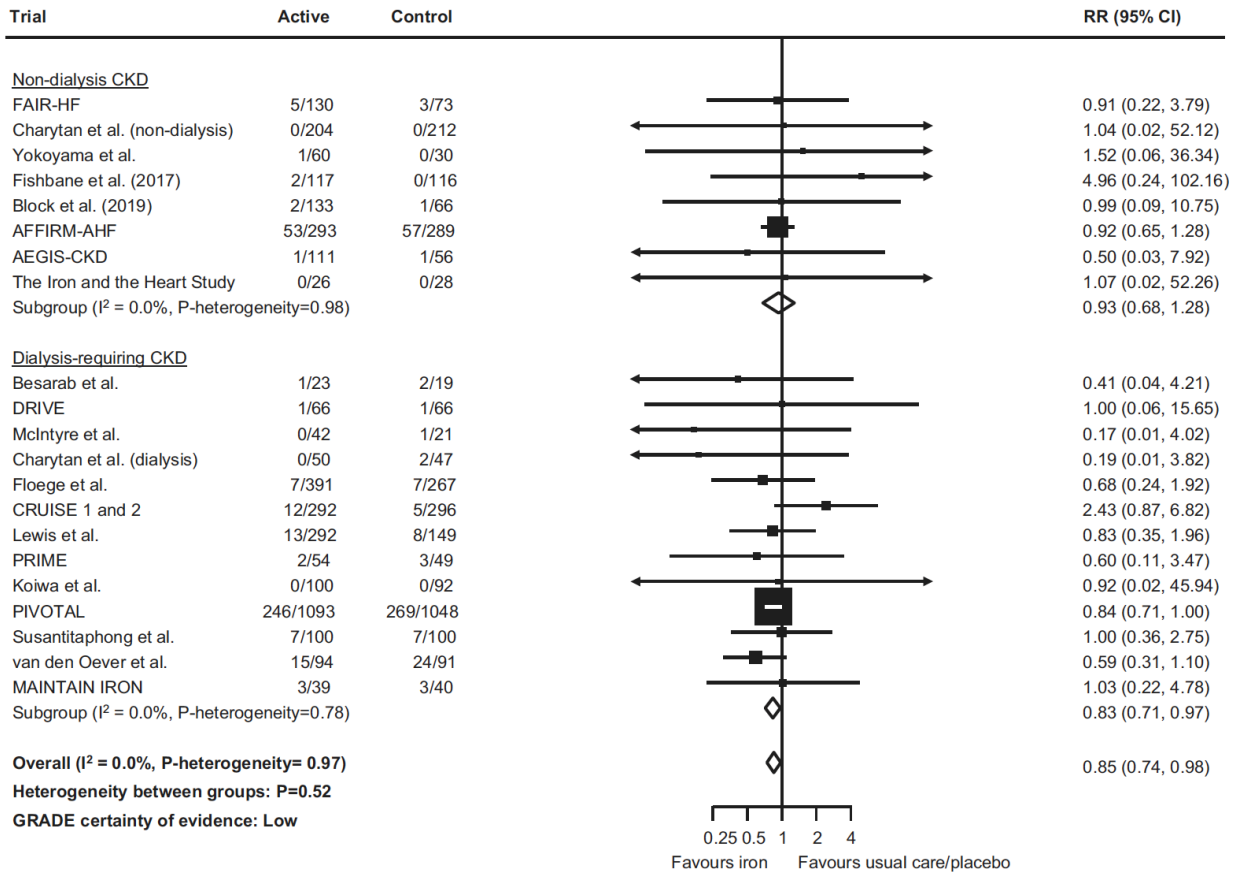
👉 Suggests that it may impact longitudinal dialysis needs although no effects on eGFR slope or proteinuria.

👉 Reduced the risk of all-cause mortality in dialysis patients by 17%, without impact on non-dialysis patients. Reduced total cohort's risk by 15%.

(c) Kidney failure requiring dialysis



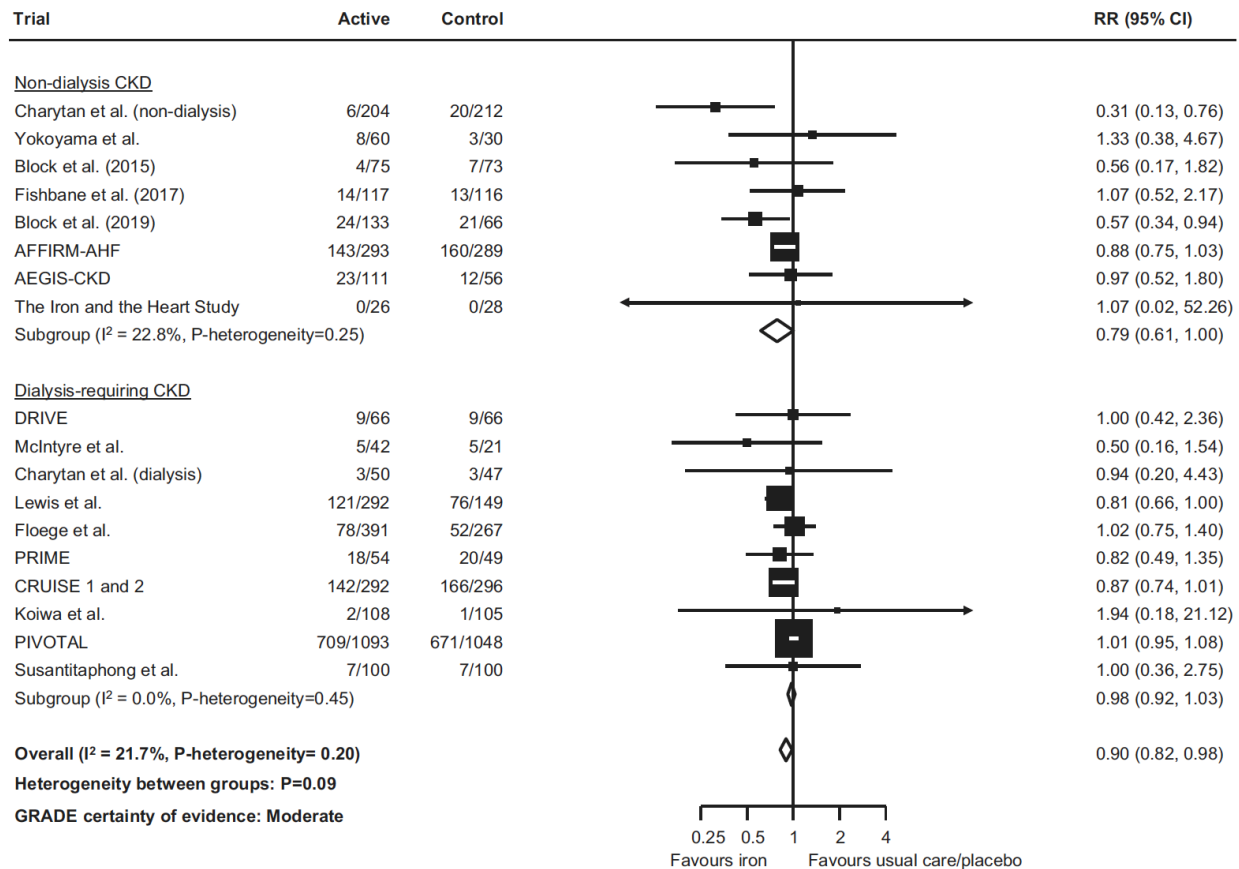
All-cause mortality



17/ Results

👉 No significant serious adverse events with iron supplementation in dialysis or non-dialysis groups, although there may be favorable side effects with iron as a total cohort.

Serious adverse events



18/ Key Learning Points

- 🔑 Suggests that dialysis and non-dialysis patients may benefit by reducing the risk of
 - Heart failure
 - Cardiovascular death
 - Myocardial infarction
 - All cause mortality
- 🔑 Side effect profile is reassuring for 1st year

19a/ Strengths

- 🧠 Most comprehensive looking at renal outcomes

Limitations

- 😞 Most cardiovascular outcomes were based on patients with heart failure and reduced ejection fraction, whereas most CKD patients have heart failure and preserved ejection fraction

19b/

- 😞 Only one trial with CKD cohort looking at iron deficiency rather than anemia
- 😞 Lack of subgroup analysis related to transferrin saturation, ferritin, and hemoglobin

😬 Increased confounding given that cardiovascular and kidney outcomes are closely linked to cardio-kidney-metabolic syndrome.

20/ Future Directions

🩺 More randomized control study involving CKD patient outcomes and looking at strictly iron stores rather than anemia

🩺 More studies involving patients with HFpEF

21/ Now let's see if you have learned something!

What does iron supplementation not seem to reduce the risk for?

1. Heart failure
2. Myocardial infarction
3. Mortality
4. Proteinuria

22/ The answer is Proteinuria. We hope this #tweetorial has improved your knowledge on iron supplementation and CKD outcomes. Please share this [#tweetorial](#) with your followers and friends! Thanks to [@MChanMD](#) for authoring & *** for great feedback! [#FOAMed](#) [#nephtwitter](#) [@ISNkidneycare](#) [@KIReports](#)