

# Iron deficiency in middle age is linked with higher risk of developing heart disease

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Approximately 10% of new coronary heart disease cases occurring within a decade of middle age could be avoided by preventing iron deficiency, suggests a study published today in *ESC Heart Failure*, a

journal of the European Society of Cardiology (ESC).

"This was an observational study and we cannot conclude that iron deficiency causes heart disease," said study author Dr. Benedikt Schrage of the University Heart and Vasculature Centre Hamburg, Germany. "However, evidence is growing that there is a link and these findings provide the basis for further research to confirm the results."

Previous studies have shown that in patients with cardiovascular diseases such as [heart failure](#), iron deficiency was linked to worse outcomes including hospitalisations and death. Treatment with intravenous iron improved symptoms, [functional capacity](#), and quality of life in patients with heart failure and iron deficiency enrolled in the FAIR-HF trial. Based on these results, the FAIR-HF 2 trial is investigating the impact of intravenous iron supplementation on the risk of death in patients with heart failure.

The current study aimed to examine whether the association between iron deficiency and outcomes was also observed in the [general population](#).

The study included 12,164 individuals from three European population-based cohorts. The median age was 59 years and 55% were women. During the baseline study visit, cardiovascular risk factors and comorbidities such as smoking, obesity, diabetes and cholesterol were assessed via a thorough clinical assessment including [blood samples](#).

Participants were classified as iron deficient or not according to two definitions: 1) absolute iron deficiency, which only includes stored iron (ferritin); and 2) functional iron deficiency, which includes iron in storage (ferritin) and iron in circulation for use by the body (transferrin).

Dr. Schrage explained: "Absolute iron deficiency is the traditional way

of assessing iron status but it misses circulating iron. The functional definition is more accurate as it includes both measures and picks up those with sufficient stores but not enough in circulation for the body to work properly."

Participants were followed up for incident coronary heart disease and stroke, death due to [cardiovascular disease](#), and all-cause [death](#). The researchers analysed the association between iron deficiency and incident coronary heart disease, stroke, cardiovascular mortality, and all-cause mortality after adjustments for age, sex, smoking, cholesterol, blood pressure, diabetes, body mass index, and inflammation. Participants with a history of coronary heart disease or stroke at baseline were excluded from the incident disease analyses.

At baseline, 60% of participants had absolute iron deficiency and 64% had functional iron deficiency. During a median follow-up of 13.3 years there were 2,212 (18.2%) deaths. Of these, a total of 573 individuals (4.7%) died from a cardiovascular cause. Incidence coronary heart disease and stroke were diagnosed in 1,033 (8.5%) and 766 (6.3%) participants, respectively.

Functional iron deficiency was associated with a 24% higher risk of coronary heart disease, 26% raised risk of cardiovascular mortality, and 12% increased risk of all-cause mortality compared with no functional iron deficiency. Absolute iron deficiency was associated with a 20% raised risk of coronary heart disease compared with no absolute iron deficiency, but was not linked with mortality. There were no associations between iron status and incident stroke.

The researchers calculated the population attributable fraction, which estimates the proportion of events in 10 years that would have been avoided if all individuals had the risk of those without iron deficiency at baseline. The models were adjusted for age, sex, smoking, cholesterol,

blood pressure, diabetes, body mass index, and inflammation. Within a 10-year period, 5.4% of all deaths, 11.7% of cardiovascular deaths, and 10.7% of new coronary heart disease diagnoses were attributable to functional iron deficiency.

"This analysis suggests that if iron deficiency had been absent at baseline, about 5% of deaths, 12% of cardiovascular deaths, and 11% of new [coronary heart disease](#) diagnoses would not have occurred in the following decade," said Dr. Schrage.

"The study showed that iron deficiency was highly prevalent in this middle-aged population, with nearly two-thirds having functional [iron deficiency](#)," said Dr. Schrage. "These individuals were more likely to develop [heart disease](#) and were also more likely to die during the next 13 years."

Dr. Schrage noted that future studies should examine these associations in younger and non-European cohorts. He said: "If the relationships are confirmed, the next step would be a randomized trial investigating the effect of treating [iron deficiency](#) in the general population."

**More information:** Schrage B, Rübsamen N, Ojeda FM, et al. Association of iron deficiency with incident cardiovascular diseases and mortality in the general population. ESC Heart Fail. 2021. [DOI: 10.1002/ehf2.13589](#)

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