

# Association between serum iron biomarkers and breast cancer incidence

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## Introduction

Iron is both a growth factor that is essential to life and potentially toxic. Extremely high iron stores are associated with increased risk of some cancers. Population-based studies of associations between serum iron levels and breast cancer remain both sparse and inconsistent.

## Aim

Assess breast cancer incidence in relation to three serum iron biomarkers: 1) iron, 2) ferritin, 3) transferrin saturation.

## Study population

5,982 women (including 2,965 incident breast cancer cases) in the Sister Study

- Age 35-74 years at enrollment
- Median follow-up 7.9 years
- Iron biomarkers measured in serum collected at baseline

## Methods

**Model:** Cox models were used in case-cohort analyses to estimate breast cancer hazard ratios.

**Exposure:** Biomarkers were analyzed both as categorical (quartiles) and continuous variables.

- Transferrin Saturation =  $\frac{Iron}{Iron+UIBC} \cdot 100$

## Results

Breast cancer hazard ratios by serum iron covariates

Biomarkers	n events	Models				
		Quartiles covariate				Continuous
		Quartile 1	Quartile 2	Quartile 3	Quartile 4	
<b>Iron</b>						
Median	63	84	103	133		
Unadjusted	2951	ref	1.02 (0.92, 1.13)	1.00 (0.90, 1.11)	1.04 (0.93, 1.15)	1.00 (1.00, 1.00)
Adjusted <sup>a</sup>	2404	ref	1.00 (0.90, 1.12)	1.00 (0.90, 1.13)	1.01 (0.90, 1.14)	1.00 (1.00, 1.00)
<b>Ferritin</b>						
Median	22	52	89	159		
Unadjusted	2940	ref	0.99 (0.89, 1.10)	1.00 (0.90, 1.11)	1.00 (0.90, 1.12)	1.00 (1.00, 1.00)
Adjusted <sup>a</sup>	2405	ref	1.02 (0.91, 1.16)	1.06 (0.94, 1.20)	1.03 (0.91, 1.16)	1.00 (1.00, 1.00)
<b>Transferrin saturation</b>						
Median	18	26	33	42		
Unadjusted	2790	ref	0.97 (0.88, 1.07)	1.01 (0.91, 1.12)	0.97 (0.87, 1.08)	1.00 (1.00, 1.00)
Adjusted <sup>a</sup>	2277	ref	0.94 (0.84, 1.06)	1.01 (0.89, 1.13)	0.95 (0.84, 1.08)	1.00 (1.00, 1.01)

<sup>a</sup> Adjusted for alcohol, education, baseline BMI, age at menarche, age at first birth, early menopause (<=45 years)

Restricting follow-up time to the first four years did not change the hazard ratios.

## Discussion

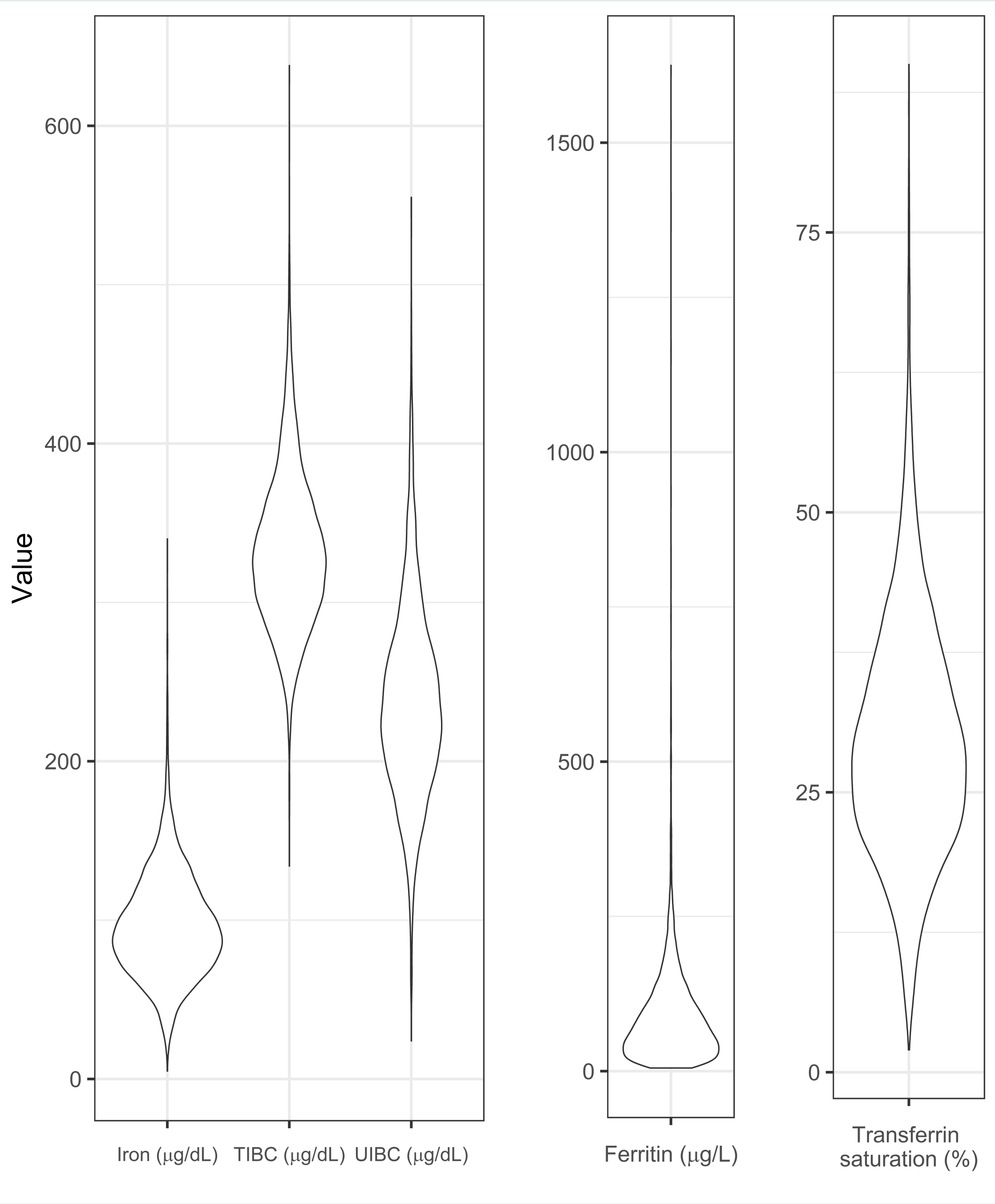
- Given that iron levels can change over time, restricting to the 4 years after baseline should correspond to more accurate exposure assessment.
- Positive associations between red meat intake, rich in heme iron, and breast cancer incidence may be due to factors other than circulating or stored iron.

In the largest, most comprehensive, U.S. study to date, we found little evidence to support an association between serum iron biomarkers and breast cancer incidence.

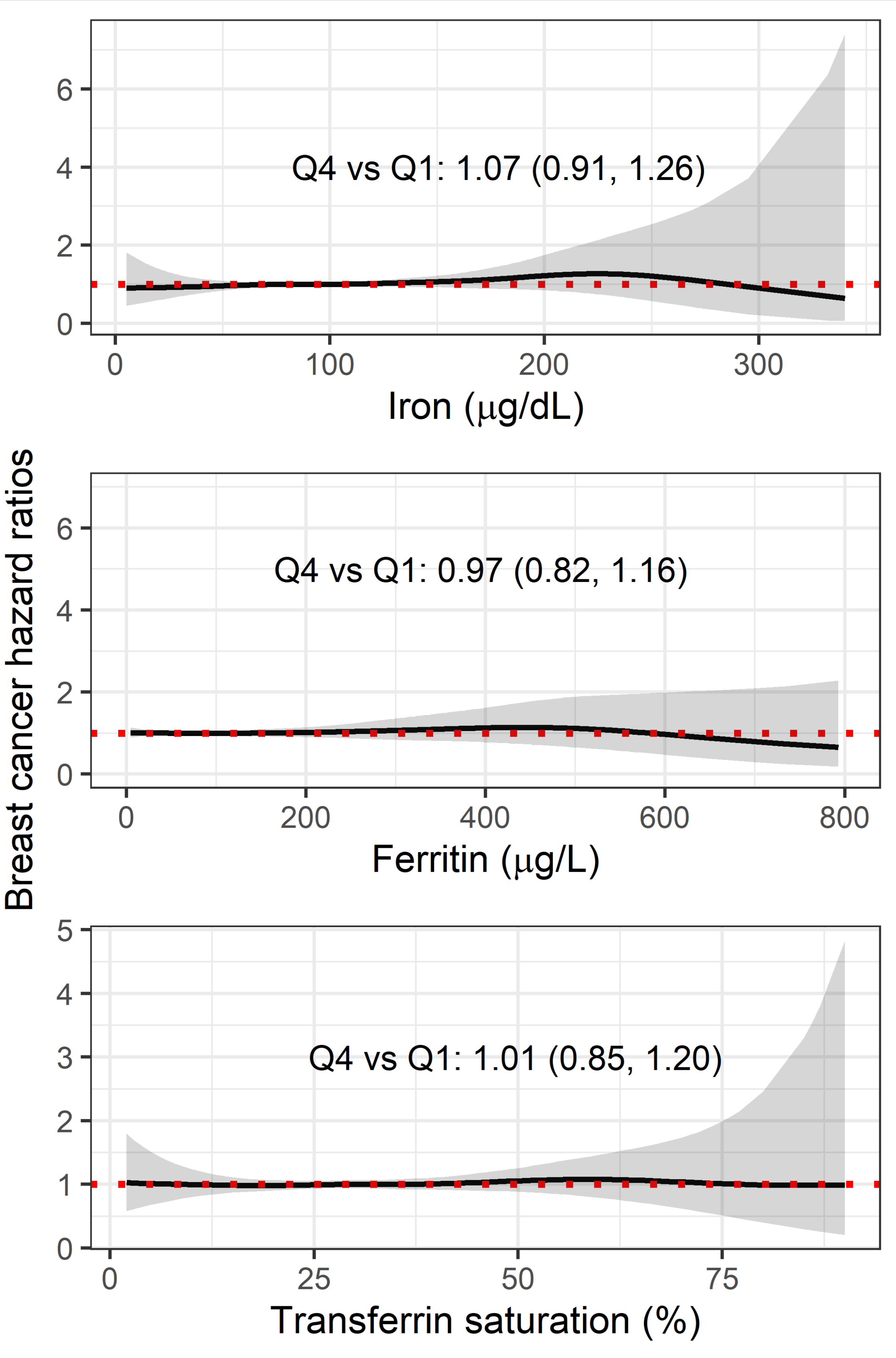


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## Serum iron distributions



Breast cancer hazard ratios for extreme quartiles and splines fit to iron covariates, restricted to first four years of follow-up



Note: Black lines represent the fitted splines; red dotted lines represent a horizontal line at hazard ratio=1; shaded area represents 95% confidence intervals.