Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TMPRSS6 rs855791	Batar et al., 2018													x	Caucasian (Turks)	*Mean ± SD [$10^6 mm^3$]* Wt: 4.0 ± 0.5 Het.: 4.3 ± 0.6 Hom.: 4.2 ± 0.6	Wt: 1 Het.: 1.075 Hom.: 1.050	Het.: *Cohen's d* = 0.055		Het.: P = 0.03 Hom.: NS	8/10	These values refer to IDA subjects, associations in iron normal controls were not significant
	Baeza-Richer et al., 2015		x												Caucasian			*Linear regression for SNP (TT)* Coef (CI 95%): 15.43 (0.07, 30.78)		0.049	3/8	
	Meidtner et al., 2018 †	x													Caucasian	*Mean (95%CI), [pmol/L]* <u>Men</u> GG (Wt): 320.9 (307.0, 335.5) AG: 302.2 (291.4, 313.4) AA: 285.9 (269.8, 303.0)	GG: 1 AG: 0.942 AA: 0.891	<u>Overall</u> β (95% CI): 0.031 (0.009, 0.052) <u>Men</u> β (95% CI): 0.057 (0.023, 0.091)		Overall: 0.0058 Men: 0.0010	8/10	Effect estimates are given for a change in standardized log-transformed ferritin per A allele Associations for women were not significant

Gene and SNP	Source	Iron parameter												Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count	Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TMPRSS6 rs855791	Al-Amer et al., 2020	x												Arabs				*Genotype distribution, [n]* Normal value CC (Wt): 1 CT: 48 TT: 1 Low value CC: 0 CT: 45 TT: 13 X^2= 10.85	0.004	7/10	Low value: ferritin < 15 ng/ml
											x							*Genotype distribution, [n]* Normal value CC (Wt): 1 CT: 36 TT: 1 Low value CC: 0 CT: 57 TT: 13 X^2= 7.18	0.028		Iron deficiency: ferritin < 15 ng/ml & haemoglobin > 12 g/dl
													x					*Odds and risk for IDA for TT compared to CC + CT* OR (95%CI): 22.5 (2.496, 204.836) RR (95%CI): 5.53 (0.897, 34.114)	0.005		

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TMPRSS6 rs855791	An et al., 2012												x		Asian (Chinese)				*Odds for Iron deficiency, OR (95%CI)* 1.55 (1.40, 1.70) *Odds for IDA, OR (95%CI)* 1.78 (1.59, 1.79)	4.96E-8 * 8.43E-9 *	8/8	Iron deficiency: TS < 16% or serum ferritin < 15 ng/ml or FEP/hemoglobin ratio > 3.0 mg/g IDA: hemoglobin < 120 g/L * Bonferroni corrected [a] Associations for hemoglobin were not significant in the Zhuang cohort
											x							*Association of the A allele, β (SE)* HanE: 1.41 (0.24) HanN: -1.45 (0.4) Zhuang: -1.23 (0.36) Meta-analysis: - 1.37 (0.18)		6.90E-9 3.70E-4 7.76E-4 8.28 E-14 *		
						x												*Association of the A allele, β (SE)* [a] HanE: -2.31 (0.59) HanN: -2.65 (1.20) Meta-analysis: -1.99 (0.46)		1.01E-4 0.03 6.51 E-5 *		

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TMPRSS6 rs855791				x														*Association of the A allele, β (SE)* HanE: -0.02 (0.004) HanN: -0.03 (0.01) Zhuang: -0.02 (0.007) Meta-analysis: -0.02 (0.003)		9.92E-10 9.74E-5 8.39E-4 4.47E-15 *		
	Pinto et al., 2017												x		Caucasian				Observed IRIDA twins to be heterozygous carriers		6/10	
	Jallow et al., 2021									x					Black-African	*Mean ± SE [µmol/L]* GG (Wt): 68.29 ± 1.81 GA: 60.79 ± 3.5	Wt: 1 GA: 0.890	β = - 7.5		0.036	7/9	GA has 89% lower average TIBC than Wt per risk allele (A), TIBC reduced by 7.5 units.
								x								*Mean ± SE [ng/mL]* GG (Wt): 9.5 ± 2.3 GA: 4.96 ± 1	Wt: 1 GA: 0.522			0.015		Aboslute values are estimated based on Fig. 4A in Jallow et al. (2021).No values were given for the AA genotype

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TMPRSS6 rs855791	Poggiali et al., 2015					x									Caucasian	*Mean difference [g/dL]* Wt: Ref. Het..: -0.5 g/dL Hom.: -0.8 g/dL				0.08 0.01	5/10	no absolute values were reported by Poggiali et al. (2015)
							x									*Mean difference* MCV *[fL]* Wt: Ref. Het.: -5.0 Hom.: -5.1 MCH *[pg]* Wt: Ref. Het.: -1.7 Hom.:-2.01				0.001 0.002 0.006 0.003		

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TMPRSS6 rs855791	Poggiali et al., 2015											x			Caucasian				*IDA status by genotype* IDA Wt: 22% Het.: 42.5% Hom.: 25.5% Control Wt: 55% Het: 45% Hom.: 0%	*For Homozygotes* X^2 P-value < 0.001	5/10	Odds for heterozygous SNP carriers to have IDA compared to wild types. P-value expresses significant difference in homozygous genotype frequency between IDA patients and iron-normal controls
													x						*Odds for heterozygotes to have IDA* OR (95%CI): 3.70 (1.18, 11.46)	N/R		
	Pei et al., 2014											x			Asian				*IDA status by genotype* IDA TT (Wt): 25.4% TC:62.7 % CC: 11.9% Control TT (Wt): 28% TC: 46.7% CC: 25.2%	Freq. distribution of all genotypes P = 0.06 Freq. Distribution of CC P = 0.03	5/10	"The frequency distribution of the TT, TC, and CC genotypes in both groups showed borderline difference. The proportion of C homozygotes was significantly lower in IDA patients."

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TMPRSS6 rs855791	Pei et al., 2014												x						*Odds for CC to have IDA (compared to TT + TC)* OR (95%CI): 0.4 (0.17, 0.95)	0.04	5/10	
Footnotes Effect directions refer to minor allele A (T on reverse DNA strand); reference genotype: GG (wt) (CC on reverse strand) Allele frequencies: G=0.564810, A=0.435190, T=0.000000 Calculations to obtain Cohen's d are presented in the *Calculations* sheet † Statistical analyses in this study were performed on log-transformed values. Abbreviations: Wt, wild type; Het., heterozygotes; hom., homozygotes; MD, mean difference; NS, not significant; SE, standard error; SD, standard deviation; $^{X}2$ Chi-square test; IRIDA iron refractory iron deficiency anemia; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin																					
TMPRSS6 rs4820268	An et al., 2012										x				Asian (Chinese)			*Association of the G allele, β (SE)* HanE: -1.20 (0.59) HanN: -1.41 (0.4) Zhuang: -1.38 (0.37) Meta-analysis: - 1.28 (0.18)		8.31E-7 5.45E-4 2.23-4 6.42E-12 *		8/8	Iron deficiency: TS < 16% or serum ferritin < 15 ng/ml or FEP/hemoglobin ratio > 3.0 mg/g IDA: hemoglobin < 120 g/L * Bonferroni corrected
				x														*Association of the G allele, β (SE)* HanE: -0.02 (0.004) HanN: -0.02 (0.01) Zhuang: -0.03 (0.01)		1.63E-6 0.001 7.66E-5 5.31E-10 *		

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
																		Meta-analysis: - 0.02 (0.003)				
TMPRSS6 rs4820268	An et al., 2012												x						*Odds for Iron deficiency, OR (95%CI)* 1.53 (1.38, 1.68) *Odds for IDA, OR (95%CI)* 1.72 (1.54, 1.91)	9.00E-8 * 6.49E-8 *	8/8	
	Poggiali et al., 2015											x			Caucasian				*IDA status by genotype* IDA Wt: 25% Het.: 46% Hom.: 29% Control Wt: 55% Het: 45% Hom.: 0%	*For Homozygotes* X^2 P-value < 0.001	5/10	P-value expresses significant difference in homozygous genotype frequency between IDA patients and iron-normal controls
													x						*Odds for heterozygotes to have IDA* OR (95%CI): 3.40 (1.10, 4.71)	N/R		

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	*Transferrin*	*TS %*	*Hematocrit*	*Hemoglobin*	*MCV, MCH*	*Hepcidin*	*UIBC*	*TIBC*	*Serum Iron*	*Genotype frequency*	*Iron deficiency/ IDA risk*	*RBC count*	*Ancestry*	*Absolute Values and Mean Difference*	*Factor*	*Effect size*	*Other*	*P-value*	*JBI assessment*	
TMPRSS6 rs4820268	Pinto et al., 2017												x		Caucasian				Observed IRIDA twins to be heterozygous carriers		6/10	
	Batar et al., 2018									x					Caucasian (Turks)	*Mean ± SE [µg/dL]* Wt: 342.6 ± 120.8 Het.: 375.3 ± 68.6 Hom.: 392.9 ± 59.3 *Mean difference, MD ± SD* Wt.: Ref. Het.: 32.7 ± 822.96 Hom.: 50.3 ± 421.22	Wt: 1 Het.: 1.095 Hom.: 1.147	Het.: *Cohen's d* = 0.0397 Hom.: *Cohen's d* = 0.119		0.04 0.03	8/10	
	Jallow et al., 2021							x							Black-African	*Mean ± SE [ng/mL]* AA (Wt): 9.5 ± 2.5 GA: 3.6 ± 0.8 GG: 3.3 ± 0.7	Wt: 1 GA: 0.379 GG: 0.374			<u>GG vs. Wt</u> P = 0.002	7/9	Absolute values are estimated based on Fig. 4A in Jallow et al., 2021

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TMPRSS6 rs4820268	Jallow et al., 2021								x						Black-African	*Mean ± SE [µmol/L]* AA (Wt): 53.76 ± 2.27 AG: 50.47 ± 3.64 GG: 43.51 ± 3.61	Wt: 1 GA: 0.939 GG: 0.809	AA: Ref. AG: β = -3.29 GG: β = -10.25		P = 0.368 (NS) P = 0.005	7/9	
										x						*Mean ± SE [µmol/L]* AA (Wt): 68.29 ± 1.81 AG: 63.33 ± 2.98 GG: 58.76 ± 2.86	Wt: 1 GA: 0.927 GG: 0.860	AA: Ref. AG: β= -4.96 GG: β= -9.54		P = 0.089 (NS) P = 0.001		

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TMPRSS6 rs4820268	Ji et al., 2018	x													Caucasian			*Odds for low ferritin, OR(95%CI)* [a] AG: 3.443 (1.312, 9.021)	*Genotypes by Ferritin status Values for women only* AA (Wt) Low ferritin: n= 6 Medium ferritin: n= 93 High ferritin: n= 10 AG Low ferritin: n= 27 Medium ferritin: n= 125 High ferritin: n= 20 GG Low ferritin: n= 7 Medium ferritin: n= 60 High ferritin: n= 10	Genotype freq.: P = 0.025 [b] OR: P = 0.012	5/8	Ferritin low ≤ 8ng/mL medium 8-60ng/mL high >60ng/mL [a] Value after adjusting for significant donor parameters; Pre-adjustment OR (95%CI): 3.348 (1.328-8.438), P = 0.010 [b] P-value after adjusting for significant donor parameters; Pre-adjustment P = 0.043
Footnotes Effect directions refer to minor allele G; reference genotype: AA (wt) Allele frequencies: G=0.459037, A=0.540963, C=0.000000 Cohen's d represents the nr. of SD that hepcidin levels in heterozygous carrieres deviate drom the mean levels in Wt. (after controling for the variability (SE)). Calculations to obtain Cohen's d are presented in the *Calculations* sheet																						
TMPRSS6 rs2235321	Lee et al., 2012			x											Caucasian	*Mean ± SD [%]* Wt: 13 ± 16 SNP: 6 ± 4 MD: - 7 ± 10	Wt: 1 SNP: 0.462	*Cohen's d* = - 0.424		0.0021	6/8	
												x							SNP more frequent in subjects with TS < 10%	0.0135		

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TMPRSS6 rs2235321	Poggiali et al., 2015											x			Caucasian				*IDA status by genotype* IDA Wt: 47.8% Het.: 40.7% Hom.: 11.5% Control Wt: 75.5% Het: 24.5% Hom.: 0%	*For Homozygotes* X^2 P-value = 0.004	5/10	P-value expresses significant difference in homozygous genotype frequency between IDA patients and iron-normal controls
													x						*Odds for Heterozygotes to be IDA* OR (95%CI): 1.90 (0.72, 5.09)			
	Pinto et al., 2017												x		Caucasian				Observed IRIDA twins to be heterozygous carriers		6/10	
	Jallow et al., 2021						x									*Mean ± SE* MCV *[fL]* GG (Wt): 77.8 ± 1.54 AA: 83.7 ± 1.79 MCH *[pg]* GG (Wt): 26.4 ± 0.60 AA: 29.0 ± 0.70	MCV GG: 1 AA: 1.076 MCH GG: 1 AA: 1.098	GG: Ref. MCV AA: β = 5.81 MCH AA: β = 2.55		P = 0.002 P = 0.000	7/9	Differences between Wt and heterozygotes (GA) were not significant.

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TMPRSS6 rs2235321								x							Black-African	*Mean ± SE [ng/mL]* GG (Wt): 9.5 ± 2.4 GA: 4.2 ± 0.8 AA: 6.6 ± 1.5	Wt: 1 GA: 0.442 AA: 0.695			P = 0.035		Absolute values are estimated based on Figure 4A in Jallow et al., 2021
									x							*Mean ± SE [µmol/L]* GG (Wt): 53.76 ± 2.27 GA: 45.59 ± 3.83 AA: 44.40 ± 3.30	Wt: 1 GA: 0.848 AA: 0.826	GG: Ref. GA: β = -8.17 AA: β = -9.36		P = 0.036 P = 0.006	7/9	
										x						*Mean ± SE [µmol/L]* GG (Wt): 68.29 ± 1.81 GA: 61.63 ± 3.06 AA: 58.78 ± 2.63	Wt: 1 GA: 0.902 AA: 0.861	GG: Ref. GA: β = -6.66 AA: β = -9.51		P = 0.032 P = 0.000		

Footnotes

Effect directions refer to minor allele A; reference genotype GG (wt)

Allele frequencies: G=0.636033, A=0.363967, C=0.000000

Calculations to obtain Cohen's d are presented in the *Calculations* sheet

Abbreviations: Wt, wild type; het., heterozygotes; MD, mean difference; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TMPRSS6 rs2235324	Lee et al., 2012			x											Caucasian				SNP more frequent in subjects with TS ≥ 10%	0.0001	6/8	
	Poggiali et al., 2015											x			Caucasian				*IDA status by genotype* IDA Wt: 52% Het.: 38% Hom.: 10% Control Wt: 94% Het: 6% Hom.: 0%	*For Homozygotes* X^2 P-value = 0.005	5/10	P-value expresses significant difference in homozygous genotype frequency between IDA patients and iron-normal controls
													x						*Odds for heterozygotes to have IDA* OR (95%CI): 8.70 (2.01, 37.91)	N/R		
Footnotes Effect directions refer to minor allele C; reference genotype TT (Wt). Allele frequencies: T=0.619381, C=0.380619, G=0.000000 Abbreviations: Wt, wild type; het., heterozygotes; OR, odds ratio																						
TMPRSS6 rs2413450	Batar et al., 2018									x					Caucasian	*Mean ± SE for IDA subjects, [µg/dL]* Wt: 330.6 ± 132.2 Het.: 416.6 ± 53.1 MD ± SD: 86 ± 771.26	Wt: 1 Het.: 1.260	*Cohen's d* = 0.112		0.04	8/10	

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
	Melis et al., 2008											x			Caucasian				SNP observed in IRIDA patients		5/10	
Footnotes Effect directions refer to minor allele T; reference genotype CC (Wt) Allele frequencies: C=0.546368, T=0.453632 Calculations to obtain Cohen's d are presented in the *Calculations* sheet Abbreviations: Wt, wild type; het., heterozygotes; MD, mean difference																						
HFE rs1800562	Terada et al., 2009	x													274 Caucasians + 234 non-Caucasians	*Median (IQR) [µg/L]* GG (Wt): 94.9 (57.8, 158.2) GA: 162.1 (69.6, 232.2)	Wt: 1 GA: 1.708			0.06	8/8	
	Meidtner et al., 2018 †	x													Caucasian	*Mean (SD) [pmol/L]* Men GG (Wt): 301.0 (293.2, 309.1) GA: 336.1 (309.5, 365.0) AA: 1'183.7 (654.8, 2,139.7) Women GG (Wt): 118.8 (116.3,	Men WT: 1 GA: 1.117 AA: 3.933 Women WT: 1 GA: 1.125 AA: 1.882	All β (95%CI): 0.165(0.116, 0.213) Men β (95%CI): 0.188 (0.11, 0.266) Women β (95%CI): 0.149 (0.087, 0.212)			3.81E-11 2.08E-6 3.08E-6	8/10	EPIC cohort (n= 9347)

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
																121.4) GA: 133.7 (125.0, 142.9) AA: 223.6 (146.9, 340.3)						
HFE rs1800562	Baeza-Richer et al., 2015 †	x													Caucasian			*Linear regression for SNP (GA) and logFerritin* Coef (95%CI): 0.17 (0.00, 0.34)		0.048	3/8	Parameter: LogFerritin - transformed due to skewedness
			x															*Linear regression for SNP (GA)* Coef (95%CI): -39.35 (64.67, -14.02)		0.0025		

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
HFE rs1800562													x						*Odds for GA to have abnormal iron* [a] OR (95%CI): 0.169 (0.058, 0.490)	0.0011	3/8	[a] Back-step logistic regression OR informs of the probability of disease: being anaemic vs. deficient/normal and anaemic/deficient vs. Normal Iron deficiency: Hb ≥ 12 g/dL and Ferritin < 20 µg/L or Hb ≤ 12 g/dL and Ferritin > 20 µg/L IDA: Hb < 12 g/dL and Ferritin < 20µg/L
	McLaren et al., 2011								x						Caucasian			GWAS Coef: -44.27 Follow-up Coef: -42.7	Meta-analysis Variance explained: 4.1%	GWAS: 3.15E-7 Follow-up: 0.0004 Meta-analysis: 5.72E-10*	9/10	* genome-wide corrected P = 0.00019
										x								GWAS Coef: -35.36 Follow-up Coef: -21.58	Meta-analysis Variance explained: 3.4%	GWAS: 1.31E-7* Follow-up: 0.035 Meta-analysis: 2.68E-8**		* genome-wide corrected P = 0.043 ** genome-wide corrected P = 0.0089

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
HFE rs1800562											x							GWAS Coef: 9.07 Follow-up Coef: -21.16	Meta-analysis Variance explained: 1.9%	GWAS: 0.0091 Follow-up: 0.0005 Meta-analysis: 1.93E-5	9/10	
	Blanco-Rojo et al., 2011		x												Caucasian			Effect per A allele: -44.87	100% probability of association Variance explained: 3.07 %		7/8	
	Beiranvand et al., 2015											x			Iranian				In contrast to Caucasian populations, the frequency of rs1800562 was even smaller (0.008 - 0%) in Asian and Middle Eastern people. SNP might have negible effect in these populations.		5/8	
	Aranda et al., 2010			x											Caucasian	*Mean ±SD [%]* GG (Wt): 26.7 ± 11.2 GA: 32.7 ± 11.9 MD ± SD: 6 ± 16.34	Wt: 1 GA: 1.225	Multilinear regression All: β (SE) = 5.75 (2.75) Women: β (SE) = 6.43 (3.03)		Mean values P < 0.05 MLR All: 0.037 Women: 0.035	6/8	

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
Footnotes Effect directions refer to minor allele A; reference genotype: GG (wt) Allele frequencies: G=0.947281, A=0.052719 † Statistical analyses in this study were performed on log-transformed ferritin values. Abbreviations: IQR, interquartile range (25th, 75th percentile); Wt, wild type; MD, mean difference; SD, standard deviation																						
HFE rs1800562 x rs1799945	Aranda et al., 2010			x											Caucasian	*Mean ± SD [%]* Men Wt: 37.7 ± 20.8 Het.: 53.4 ± 19 MD ±SD: 15.7 ± 28.17 Women Wt: 26.7 ± 11.2 Het.: 40.5 ± 5.4 MD ± SD: 13.8 ± 12.43	Men Wt: 1 Het.: 1.416 Women Wt: 1 Het.: 1.517	Men *Cohen's d* = 0.56 Women *Cohen's d* = 1.11 Multilinear regression *Whole cohort:* β (SE)= 16.4 (4.2) *Women:* β (SE)= 13.11 (5.59) *Men:* β (SE)= 13.21 (6.59)		Mean values Men P < 0.05 Women P< 0.01 MLR All: P < 0.001 Women: P = 0.02 Men: P = 0.045	6/8	
		x																Multilinear regression *Whole cohort:* β(SE) = 0.32 (0.18)		0.049		

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
Footnotes Effect directions refer to heterozygosity for rs1800562 and rs1799945; reference: wild types for both SNPs. Calculations to obtain Cohen's d are presented in the *Calculations* sheet Abbreviations: Wt, wild type; het., heterozygotes; MD, mean difference																						
rs1800562 x rs1375515	Baeza-Richer et al., 2015 †	x													Caucasian	*Mean ± SD [ng/mL]* rs1375515: AA (Wt) or AG Rs1800562: GG (Wt): 1.182 ± 0.384 GA: 1.377 ± 0.336	AX / GG: 1 AX / GA: 1.165			0.027	3/8	Iron parameter: LogFerritin
Footnotes Effect directions refer to heterozygosity(GA) for rs1800562 simultaneously as genotypes AA/GA in rs1375515; reference: GG (Wt) for rs1800562 Effect directions refer to minor allele A; reference genotype: GG (wt) † Statistical analyses in this study were performed on log-transformed ferritin values. Abbreviations: Wt, wild type; SD, standard deviation																						
HFE rs1799945	Meidtner et al., 2018 †	x													Caucasian	*Mean (95%CI), [pmol/L]* Men CC (Wt): 296.7 (288.0, 305.7) CG: 323.3 (307.4, 340.0) GG: 372.4 (317.3, 437.0)	Wt: 1 CG: 1.090 GG: 1.255	Overall β = 0.056 95% CI (0.026, 0.085) Men β = 0.097 95% CI (0.050, 0.145)		Sex-diff.: < 0.05 0.003 0.0001	8/10	EPIC cohort (n= 9347)

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
HFE rs1799945	Beiranvand et al., 2015	x													Iranian	*Mean(SD), [ng/mL]* Wt (Healthy): 119.53 ± 46.75 SNP (HH patients): 278.6 ± 63	Wt: 1 SNP: 2.331		Mean level of serum ferritin in HH men was 3x higher than healthy men * CI: 152.62 ± 196.14	* P ≤ 0.001	5/8	
				x												*Mean ± SD [%]* (only men) Wt (Healthy): 37.83 ± 9.5 SNP (HH patients): 89.56 ± 17.32	Wt: 1 SNP: 2.367		TS level was higher in HH patients without being affected by gender and it was also higher than the normal range (up to 45%) * CI: 44.55 ± 64.31	* P ≤ 0.001		
	Aranda et al., 2010			x											Caucasian	*Mean ± SD [%] values only of women* Wt: 26.7 ± 11.2 Het.: 30.6 ± 14.5 Hom.: 34.9 ± 13.1	Wt: 1 Het.: 1.146 Hom.: 1.307	Het. Cohen's *d* = 0.213 Hom. Cohen's *d* = 0.476 <u>MLR</u> Het.: β (SE) = 3.00 (1.24) Hom.: β (SE) = 7.26 (2.66)		< 0.01 < 0.01 0.015 0.006	6/8	

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
HFE rs1799945	Blanco-Rojo et al., 2011		x												Caucasian			Effect per G allele: -15.73	85.6% probability of association Variance explained: 2.40 %		7/8	
	Baeza-Richer et al., 2015		x												Caucasian			*Linear regression for CG + GG* Coef (95%CI): -16.79 (-29.64, -3.95)		0.011	3/8	
Footnotes Effect directions refer to minor allele G; reference genotype: CC (wt) Allele frequencies: C=0.863913, G=0.136087 † Statistical analyses in this study were performed on log-transformed values. Calculations to obtain Cohen's d are presented in the *Calculations* sheet Abbreviations: HH hereditary hemochromatosis, CI, confidence interval																						
TF rs3811647	Blanco-Rojo et al., 2011			x											Caucasian	*Mean ± SD [%]* GG (Wt): 21.8 ± 10.9 AA + AG: 18.2 ± 8.7 MD ± SD: - 3.6 ± 13.96	Wt: 1 AA + AG: 0.835	*Cohen's d* = - 0.258		0.007	7/8	

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TF rs3811647			x												Caucasian	*Mean ± SD [mg/dL]* GG (Wt): 292.2 ± 48.7 GA: 314.6 ± 51.6 AA: 342.2 ± 67.3	Wt: 1 GA: 1.077 AA: 1.171	GA Cohen's *d* = 0.316 AA Cohen's *d* = 0.602 Effect per A allele: 20.32	100% probability of association Variance explained: 8.08 %	<u>Mean values</u> P < 0.001		
	Kutalik et al., 2011 †		x												Caucasian			CH: β = 0.362 AUSI: β = 0.358 AUSII: β = 0.353 Meta-analysis: β (SE) = 0.358 (0.029)		1.27E-10 5.25E-19 8.80E-9 1.45E-35	5/8	
	Baeza-Richer et al., 2015		x												Caucasian	*Mean ± SD [mg/dL]* GG (Wt): 302.039 ± 54.097 GA: 324.634 ± 55.870 AA: 354.571 ± 62.296	Wt: 1 GA: 1.075 AA: 1.174	GA Cohen's *d* = 0.2905 AA Cohen's *d* = 0.636	*Linear regression* GA: Coef (95%CI): 21.29 (8.74, 33.84) AA: Coef (95%CI): 51.48 (30.88, 72.02)	< 0.0001	'3/8	

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TF rs3811647	An et al., 2012		x												Asian (Chinese			*Association for A allele, β (SE)* HanE: 18.46 (1.68) HanN: 16.42 (3.36) Zhuang: 17.61 (1.91) Meta-analysis: 17.88 (1.18)		8.18 E-27 1.53E-6 4.86E-19 3.77E-51*	8/8	* Bonferroni corrected HanE, HanN & Zhuang represent the different cohorts studied. The Meta-analysis contains the pooled sample. [a] Associations for HuanN & Meta-analysis were not significant.
											x							*Association for A allele, β (SE)* [a] HanE: 0.52 (0.25) - 0.042 Zhuang: -0.76 (0.34)		0.042 0.03		

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TF rs3811647										x								*Association for A allele, β (SE)* HanE: 3.71 (0.41) HanN: 3.56 (0.79) Zhuang: 3.70 (0.52) Meta-analysis: 3.68 (0.30)		7.49E-19 8.57E-6 4.21E-12 3.40E-34*		
	McLaren et al., 2011									x					Caucasian			GWAS Coef: 21.49 Follow-up Coef: 16.69	Meta-analysis variance explained: 4.2%	GWAS: 0.0023 Follow-up: 0.012 Meta-analysis: 0.00015	9/10	
	Al-Amer et al., 2018										x				Arabic				*Genotype distribution, [n]* Iron normal GG (Wt): 24 GA: 14 Low Iron GG (Wt): 26 GA: 44 X^2: 6.7	0.035	4/8	IDA: Ferritin < 15ng/mL and Hb < 12g/dL Iron deficiency: Ferritin < 15ng/mL and Hb > 12g/dL

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TF rs3811647		x																	*Genotype distribution, [n]* Iron normal GG (Wt): 34 GA: 18 Low Iron GG (Wt): 23 GA: 33 X^2: 6.4	0.04		

Footnotes
Effect directions refer to minor allele A; reference genotype: GG (wt)
Allele frequencies: G=0.666694, A=0.333306
Calculations to obtain Cohen's d are presented in the *Calculations* sheet
[†] The phenotypes were log-transformed prior to association analyses, normalized to have zero mean & unit variance and adjusted for the effects of sex, age, self-reported smoking status, alcohol intake and principal components
Abbreviations: MD, mean difference; X^2 Chi-square test

TF rs3811647 x rs1799852	Blanco-Rojo et al., 2011		x												Caucasian	*Mean ± SD [mg/dL]* GG (Wt) + CC (Wt): 301.4 ± 46.5 GG + CT: 276.4 ± 48.7 MD ± SD: - 25 ± 67.3	GG + CC: 1 GG + CT: 0.917	*Cohen's d* = - 0.37		0.007	7/8	

Footnotes
Calculations to obtain Cohen's d are presented in the *Calculations* sheet
Abbreviations: MD, mean difference; SD, standard deviation

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
TF rs1799852	Blanco-Rojo et al., 2011		x												Caucasian			Effect per A allele: -20.25	78% probability of association variance explained: 5.5 %		7/8	
	Baeza-Richer et al., 2015		x												Caucasian			*Linear regression for SNP (CT)* Coef (95%CI): -25.45 (-39.29, -11.61)		0.0004	3/8	
TF rs1799852	Baeza-Richer et al., 2015				x										Caucasian	*Mean ± SD [%]* CC (Wt): 38.371 ± 3.601 CT: 37.169 ± 3.804 MD(SD): -1.20 ± 5.24	Wt: 1 CT: 0.969	*Cohen's d* = - 0.23 *Linear regression for SNP (CT)* Coef (CI 95%): -1.09 (-1.96, -0.23)		Mean values P = 0.018 Linear regression P = 0.014	3/8	
						x										*Mean ± SD [g/dL]* CC (Wt): 12.826 ± 1.330 CT: 12.385 ± 1.496 MD ± SD: -0.441 ± 2	Wt: 1 CT: 0.966	*Cohen's d* = - 0.22 *Linear regression for SNP (CT)* Coef (CI 95%): -0.39 (-0.71, -0.07)		Mean values 0.022 Linear regression 0.019		

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
Footnotes Effect directions refer to the minor allele T (A on reverse DNA strand); reference genotype: CC (wt) Allele frequencies: C=0.891421, T=0.108579 Calculations to obtain Cohen's d are presented in the *Calculations* sheet																						
BMP2 rs235756	Al-Amer et al., 2021	x													Arab				*Genotype distribution, [n]* Normal value TT (Wt): 4 TC: 45 CC: 1 Low value TT: 2 TC: 48 CC: 8 $X^2 = 5.65$	0.05	5/10	IDA: Ferritin < 15ng/mL and Hb < 12g/dL Iron deficiency: Ferritin < 15ng/mL and Hb > 12g/dL
													x						*Odds and Risk for iron deficiency for CC* OR (95% CI): 29.3 (1.494, 575.401) RR (95%CI): 7.65 (0.549, 106.47)	0.026		

Gene and SNP	Source	Iron parameter													Ancestry	Outcome					Risk of bias	Notes
		Ferritin	Transferrin	TS %	Hematocrit	Hemoglobin	MCV, MCH	Hepcidin	UIBC	TIBC	Serum Iron	Genotype frequency	Iron deficiency/ IDA risk	RBC count		Absolute Values and Mean Difference	Factor	Effect size	Other	P-value	JBI assessment	
BMP2 rs235756	Al-Amer et al., 2021											x			Arab				*Genotype distribution, [n]* Control TT (Wt): 4 (8%) TC: 45 (90%) CC: 1 (2%) IDA TT: 2 (3.45%) TC: 48 (82.76%) CC: 8 (13.79%) $X^2 = 5.65$	0.05	5/10	
	Ji et al., 2018	x													Caucasian				"rs235756 was significantly associated with ferritin levels in male donors before and after adjusting for donor parameters"	adjusted P = 0.038 unadjusted P = 0.029	5/8	

Footnotes
Effect directions refer to minor allele C (G on reverse DNA strand); reference group: TT (wt) (AA on reverse DNA strand)
Allele frequencies: A=0.644149, C=0.000000, G=0.355851
Abbreviations: X2 Chi-square test

Gene and SNP	*Source*	***Iron parameter***													*Ancestry*	***Outcome***					***Risk of bias***	***Notes***
		Ferritin	*Transferrin*	*TS %*	*Hematocrit*	*Hemoglobin*	*MCV, MCH*	*Hepcidin*	*UIBC*	*TIBC*	*Serum Iron*	*Genotype frequency*	*Iron deficiency/ IDA risk*	*RBC count*		*Absolute Values and Mean Difference*	*Factor*	*Effect size*	*Other*	*P-value*	*JBI assessment*	
Chromosome 2 rs2698530	McLaren et al., 2011									x					Caucasian			GWAS Coef: 20.72 Follow-up Coef: 16.27	Meta-analysis Variance explained: 3.0 %	GWAS: 5.01E-7 * Follow-up: 0.032 Meta-analysis: 1.67E-7 **	9/10	* genome-wide corrected P = 0.17 ** genome-wide corrected P = 0.055
				x														GWAS Coef: -0.20 Follow-up Coef: -0.02	Meta-analysis Variance explained: 2.3 %	GWAS: 3.70E-7 * Follow-up: 0.71 Meta-analysis: 3.51E-6		* genome-wide corrected P = 0.12
									x									GWAS Coef: 28.75 Follow-up Coef: 14.25	Meta-analysis Variance explained: 3.0 %	GWAS: 5.96E-8 * Follow-up: 0.11 Meta-analysis: 1.40E-7 *		* genome-wide corrected P = 0.02 ** genome-wide corrected P = 0.046

Footnotes
Effect estimates refer to minor allele C; reference genotype: AA (wt)
Allele frequencies: A=0.757795, C=0.242205
Corr.: genome-wide corrected P-value
Genome-wide statistical significance was defined as P < 1.51E-7 (corrected P=0.05)

Source allele frequencies: *dbSNP, https://www.ncbi.nlm.nih.gov/snp/*