Supplementary material

Table S1 F statistics for the causal effect of anemia on CVD in MR analysis

Diseases	Data sources	Sample size (cases/controls)	Ancestry	R^2(%) for anemia (Total)	F for anemia (Total)
Heart failure	HERMES	47,309/930,014	European	3.5	279.8
Coronary artery disease	CARDIoGRAMplusC4D	60,801/123,504	Mixed	3.5	280.3
Atrial fibrillation	AFGen	65,446/522,744	European	3.7	273.4
Any stroke	MEGASTROKE	40,585/406,111	European	3.7	254.5
Any ischemic stroke	MEGASTROKE	34,217/406,111	European	3.7	254.5

FinnGen: the FinnGen Consortium; HERMES; Heart Failure Molecular Epidemiology for Therapeutic Targets; CARDIoGRAMplusC4D, Coronary Artery Disease Genome-wide Replication and Meta-analysis plus The Coronary Artery Disease Genetics; AFGen, Atrial Fibrillation Genetics; MEGASTROKE, the MEGASTROKE Consortium.

Note: R^2: Variability explained by genetic instruments. The R^2 was calculated using the formula: $R^2=\beta^2(1\text{-}EAF)*2EAF$. β is the association coefficient between the SNP and phenotype, and EAF is the minor allele frequency.

Furthermore, the F statistics were calculated using the formula: $F= R^2(N\text{-}K\text{-}1)/[K(1\text{-}R^2)]$. R^2 is the proportion of the variability of anemia explained by each instrument, K is the number of SNP-anemia association, N is the sample size of the GWAS for the SNP-anemia association.

Table S2 Pleiotropic associations with used SNPs for anemia in FinnGen study

SNP	Effect_allele	Other_allele	Traits	Direction
rs2476601	A	G	Basophil percentage of granulocytes	+
	A	G	Basophil percentage of white cells	+
	A	G	Granulocyte count	-
	A	G	Lymphocyte count	-
	A	G	Myeloid white cell count	-
	A	G	Neutrophil count	-
	A	G	Sum basophil neutrophil counts	-
	A	G	Sum neutrophil eosinophil counts	-
	A	G	White blood cell count	-
	A	G	Amoxicillin clavulanate drug induced liver injury	NA
	A	G	Crohn disease	NA
	A	G	Drug induced liver injury	NA
	A	G	Drug induced liver injury all cholestatic DILI cases	NA
	A	G	Generalized vitiligo	NA
	A	G	Generalized vitiligo with concomitant other autoimmune disorder	NA
	A	G	Graves disease	NA
	A	G	Graves disease and Hashimotos thyroiditis	NA
	A	G	Hashimotos thyroiditis	NA
	A	G	Hypothyroidism	NA
	A	G	Myasthenia gravis	NA
	A	G	Myasthenia gravis among females	NA
	A	G	Rheumatoid arthritis	NA
	A	G	Rheumatoid arthritis	NA
	A	G	Rheumatoid arthritis	NA
	A	G	Rheumatoid arthritis ACPA positive	NA
	A	G	Rheumatoid arthritis cyclic citrullinated peptide CCP positive	NA
	A	G	Selective immunoglobulin A deficiency IgAD	NA
	A	G	Systemic lupus erythematosus SLE females	NA
	A	G	Type 1 diabetes	NA
	A	G	Crohns disease	-
	A	G	Crohns disease	NA
	A	G	Late onset myasthenia gravis	NA
	A	G	Systemic lupus erythematosus	+
	A	G	Systemic lupus erythematosus or rheumatoid arthritis	NA
	A	G	Type 1 diabetes and autoimmune thyroid diseases	+
	A	G	Diabetes diagnosed by doctor	+
	A	G	Insulin-dependent diabetes mellitus	+
	A	G	Long-standing illness, disability or infirmity	+
	A	G	Medication for cholesterol, blood pressure or diabetes: insulin	+
	A	G	Number of self-reported non-cancer illnesses	+
	A	G	Number of treatments or medications taken	+
	A	G	Other rheumatoid arthritis	+
	A	G	Other serious medical condition or disability diagnosed by doctor	+
	A	G	Self-reported diabetes	+
	A	G	Self-reported hyperthyroidism or thyrotoxicosis	+
	A	G	Self-reported hypothyroidism or myxoedema	+

	A	G	Self-reported pernicious anemia	+
	A	G	Self-reported rheumatoid arthritis	+
	A	G	Self-reported type 1 diabetes	+
	A	G	Started insulin within one year diagnosis of diabetes	+
	A	G	Taking other prescription medications	+
	A	G	Treatment with folic acid product	+
	A	G	Treatment with insulin	+
	A	G	Treatment with insulin product	+
	A	G	Treatment with levothyroxine sodium	+
	A	G	Treatment with methotrexate	+
	A	G	Treatment with thyroxine product	+
	A	G	Treatment with thyroxine sodium	+
	A	G	Rheumatoid arthritis	+
	A	G	Rheumatoid arthritis	+
	A	G	Arthritis rheumatoid	NA
	A	G	Arthritis rheumatoid	NA
	A	G	Arthritis rheumatoid	NA
	A	G	Crohn disease	NA
	A	G	Diabetes mellitus type 1	NA
	A	G	Vitiligo	NA
	A	G	Coronary artery disease	+
rs707926	A	G	Eosinophil count	+
	A	G	Eosinophil percentage of granulocytes	+
	A	G	Eosinophil percentage of white cells	+
	A	G	High light scatter percentage of red cells	+
	A	G	High light scatter reticulocyte count	+
	A	G	Immature fraction of reticulocytes	+
	A	G	Mean platelet volume	-
	A	G	Neutrophil percentage of granulocytes	-
	A	G	Reticulocyte count	+
	A	G	Reticulocyte fraction of red cells	+
	A	G	Sum eosinophil basophil counts	+
	A	G	Age-related macular degeneration	-
	A	G	Age-related macular degeneration	-
	A	G	Advanced age related macular degeneration	NA
	A	G	Primary sclerosing cholangitis	-
	A	G	Asthma	-
	A	G	Hearing difficulty or problems with background noise	+
	A	G	Intestinal malabsorption	-
	A	G	Mouth or teeth dental problems: mouth ulcers	+
	A	G	No blood clot, bronchitis, emphysema, asthma, rhinitis, eczema or allergy diagnosed by doctor	+
	A	G	Past tobacco smoking	-
	A	G	Peak expiratory flow	+
	A	G	Self-reported ankylosing spondylitis	+
	A	G	Self-reported asthma	-
	A	G	Self-reported malabsorption or coeliac disease	-
	A	G	Started insulin within one year diagnosis of diabetes	+
	A	G	Systolic blood pressure	-

	A	G	Time spent using computer	+
	A	G	Treatment with insulin product	+
	A	G	Age at menopause	-
rs3129761	C	G	Body mass index males	-
	C	G	Body mass index	-
	C	G	Hematocrit	-
	C	G	Hemoglobin concentration	-
	C	G	High light scatter percentage of red cells	-
	C	G	High light scatter reticulocyte count	-
	C	G	Lymphocyte count	-
	C	G	Mean corpuscular hemoglobin concentration	-
	C	G	Monocyte count	-
	C	G	Red blood cell count	-
	C	G	Reticulocyte count	-
	C	G	Reticulocyte fraction of red cells	-
	C	G	Crohns disease	-
	C	G	Inflammatory bowel disease	-
	C	G	Ulcerative colitis	-
	C	G	Asthma	+
	C	G	Asthma	+
	C	G	Diabetes diagnosed by doctor	+
	C	G	Doctor diagnosed asthma	+
	C	G	Eye problems or disorders: diabetes related eye disease	+
	C	G	Forced expiratory volume in 1-second	-
	C	G	Forced expiratory volume in 1-second, best measure	-
	C	G	Forced expiratory volume in 1-second, predicted percentage	-
	C	G	Forced vital capacity	-
	C	G	Forced vital capacity, best measure	-
	C	G	Illnesses of father: lung cancer	+
	C	G	Illnesses of siblings: diabetes	+
	C	G	Insulin-dependent diabetes mellitus	+
	C	G	Intestinal malabsorption	+
	C	G	Long-standing illness, disability or infirmity	+
	C	G	Medication for cholesterol, blood pressure or diabetes: insulin	+
	C	G	Nasal polyp	+
	C	G	No blood clot, bronchitis, emphysema, asthma, rhinitis, eczema or allergy diagnosed by doctor	-
	C	G	Number of self-reported non-cancer illnesses	+
	C	G	Number of treatments or medications taken	+
	C	G	Other disorders of pancreatic internal secretion	+
	C	G	Other rheumatoid arthritis	+
	C	G	Other serious medical condition or disability diagnosed by doctor	+
	C	G	Overall health rating	+
	C	G	Self-reported adrenocortical insufficiency or addisons disease	+
	C	G	Self-reported asthma	+
	C	G	Self-reported diabetes	+
	C	G	Self-reported diabetic eye disease	+
	C	G	Self-reported hyperthyroidism or thyrotoxicosis	+
	C	G	Self-reported hypothyroidism or myxoedema	+

	C	G	Self-reported malabsorption or coeliac disease	+
	C	G	Self-reported multiple sclerosis	-
	C	G	Self-reported nasal polyps	+
	C	G	Self-reported polymyalgia rheumatica	+
	C	G	Self-reported psoriasis	-
	C	G	Self-reported rheumatoid arthritis	+
	C	G	Self-reported sjogrens syndrome or sicca syndrome	+
	C	G	Self-reported type 1 diabetes	+
	C	G	Self-reported ulcerative colitis	-
	C	G	Started insulin within one year diagnosis of diabetes	+
	C	G	Taking other prescription medications	+
	C	G	Thyrotoxicosis	+
	C	G	Treatment with becotide 50 inhaler	+
	C	G	Treatment with fludrocortisone	+
	C	G	Treatment with folic acid product	+
	C	G	Treatment with hydroxychloroquine	+
	C	G	Treatment with insulin	+
	C	G	Treatment with insulin product	+
	C	G	Treatment with levothyroxine sodium	+
	C	G	Treatment with methotrexate	+
	C	G	Treatment with montelukast product	+
	C	G	Treatment with plaquenil 200mg tablet	+
	C	G	Treatment with prednisolone	+
	C	G	Treatment with salbutamol	+
	C	G	Treatment with seretide 50 evohaler	+
	C	G	Treatment with sulfasalazine	+
	C	G	Treatment with symbicort 100 or 6 turbohaler	+
	C	G	Treatment with thyroxine product	+
	C	G	Treatment with thyroxine sodium	+
	C	G	Treatment with ventolin 100micrograms inhaler	+
	C	G	Ulcerative colitis	-
	C	G	Vitamin and mineral supplements: folic acid or folate	+
	C	G	Wheeze or whistling in the chest in last year	+
	C	G	Rheumatoid arthritis	+
rs7184768	A	G	Arm fat-free mass left	+
	A	G	Arm fat-free mass right	+
	A	G	Arm predicted mass left	+
	A	G	Arm predicted mass right	+
	A	G	Basal metabolic rate	+
	A	G	Height	+
	A	G	Leg fat-free mass left	+
	A	G	Leg fat-free mass right	+
	A	G	Leg predicted mass left	+
	A	G	Leg predicted mass right	+
	A	G	Sitting height	+
	A	G	Trunk fat-free mass	+
	A	G	Trunk predicted mass	+
	A	G	Weight	+
	A	G	Whole body fat-free mass	+

Table S3 Information on instrumental variables for anemia in FinnGen study

SNP	Chr	Position	A1	A2	EAF	Beta	SE	*P*-val
rs149614393	1	112820064	C	A	0.124	0.099	0.020	1.09E-06
rs12615303	2	26917705	C	T	0.336	-0.072	0.014	4.21E-07
rs6728914	2	184421981	T	G	0.007	0.388	0.081	1.86E-06
rs2169706	4	19271294	T	C	0.312	0.070	0.014	1.12E-06
rs35172598	6	103952813	T	C	0.113	-0.116	0.022	8.50E-08
rs847720	7	71116080	T	C	0.727	0.069	0.015	4.32E-06
rs79005670	11	101545718	C	G	0.065	-0.128	0.028	4.16E-06
rs80068492	15	41542957	A	G	0.039	-0.163	0.035	3.61E-06
rs116940507	15	75566965	C	T	0.030	0.181	0.039	4.08E-06
rs7184768	16	81630188	G	A	0.348	-0.067	0.014	2.16E-06
rs117725035	17	59212300	A	G	0.027	0.409	0.040	1.09E-24
rs117372722	17	61401255	G	T	0.025	0.311	0.042	9.22E-14
rs117885142	20	2464755	C	T	0.009	0.337	0.070	1.75E-06
rs145020240	20	23989840	C	T	0.060	-0.152	0.029	2.35E-07

Abbreviation: SNP, single nucleotide polymorphism; Chr, chromosome; A1, Effect_allele; A2, Other_allele; EAF, effect allele frequency; SE, standard error.

Table S4 Mendelian randomization analysis of anemia and heart failure in FinnGen study

SNP	Chr	Position	A1	A2	EAF	Anemia			Heart failure		
						Beta	SE	*P*-val	Beta	SE	*P*-val
rs116940507	15	75566965	T	C	0.03	0.181	0.039	4.08E-06	0.045	0.032	0.167
rs117372722	17	61401255	T	G	0.025	0.311	0.042	9.22E-14	0.055	0.035	0.117
rs117725035	17	59212300	G	A	0.027	0.409	0.04	1.09E-24	0.02	0.03	0.51
rs12615303	2	26917705	T	C	0.336	-0.072	0.014	4.21E-07	-0.023	0.008	0.005
rs145020240	20	23989840	T	C	0.06	-0.152	0.029	2.35E-07	-0.026	0.02	0.194
rs149614393	1	112820064	A	C	0.124	0.099	0.02	1.09E-06	0.01	0.016	0.553
rs2169706	4	19271294	C	T	0.312	0.07	0.014	1.12E-06	0.011	0.008	0.188
rs35172598	6	103952813	C	T	0.113	-0.116	0.022	8.50E-08	0.000	0.01	0.986
rs7184768	16	81630188	A	G	0.348	-0.067	0.014	2.16E-06	-0.013	0.008	0.106
rs79005670	11	101545718	G	C	0.065	-0.128	0.028	4.16E-06	-0.016	0.018	0.377
rs80068492	15	41542957	G	A	0.039	-0.163	0.035	3.61E-06	0.068	0.04	0.085
rs847720	7	71116080	C	T	0.727	0.069	0.015	4.32E-06	-0.002	0.008	0.779

Abbreviation: SNP, single nucleotide polymorphism; Chr, chromosome; A1, Effect_allele; A2, Other_allele; EAF, effect allele frequency; SE, standard error.

Table S5 Mendelian randomization analysis of anemia and coronary artery disease in FinnGen study

SNP	Chr	Position	A1	A2	EAF	Anemia			Coronary artery disease		
						Beta	SE	*P*-val	Beta	SE	*P*-val
rs117372722	17	61401255	T	G	0.025	0.311	0.042	9.22E-14	0.004	0.063	0.951
rs117725035	17	59212300	G	A	0.027	0.409	0.040	1.09E-24	0.025	0.039	0.520
rs12615303	2	26917705	T	C	0.336	-0.072	0.014	4.21E-07	-0.025	0.011	0.017
rs145020240	20	23989840	T	C	0.060	-0.152	0.029	2.35E-07	-0.004	0.035	0.904
rs149614393	1	112820064	A	C	0.124	0.099	0.020	1.09E-06	0.011	0.027	0.689
rs2169706	4	19271294	C	T	0.312	0.070	0.014	1.12E-06	0.014	0.011	0.196
rs35172598	6	103952813	C	T	0.113	-0.116	0.022	8.50E-08	-0.014	0.014	0.306
rs6728914	2	184421981	G	T	0.007	0.388	0.081	1.86E-06	0.008	0.051	0.880
rs7184768	16	81630188	A	G	0.348	-0.067	0.014	2.16E-06	-0.007	0.011	0.501
rs79005670	11	101545718	G	C	0.065	-0.128	0.028	4.16E-06	-0.011	0.029	0.711
rs80068492	15	41542957	G	A	0.039	-0.163	0.035	3.61E-06	0.059	0.058	0.304
rs847720	7	71116080	C	T	0.727	0.069	0.015	4.32E-06	0.010	0.012	0.374

Abbreviation: SNP, single nucleotide polymorphism; Chr, chromosome; A1, Effect_allele; A2, Other_allele; EAF, effect allele frequency; SE, standard error.

Table S6 Mendelian randomization analysis of anemia and atrial fibrillation in FinnGen study

SNP	Chr	Position	A1	A2	EAF	Anemia			Atrial fibrillation		
						Beta	SE	*P*-val	Beta	SE	*P*-val
rs116940507	15	75566965	T	C	0.030	0.181	0.039	4.08E-06	0.106	0.105	0.313
rs117372722	17	61401255	T	G	0.025	0.311	0.042	9.22E-14	0.168	0.106	0.114
rs117725035	17	59212300	G	A	0.027	0.409	0.040	1.09E-24	0.034	0.059	0.561
rs117885142	20	2464755	T	C	0.009	0.337	0.070	1.75E-06	-0.027	0.186	0.886
rs12615303	2	26917705	T	C	0.336	-0.072	0.014	4.21E-07	0.015	0.013	0.245
rs145020240	20	23989840	T	C	0.060	-0.152	0.029	2.35E-07	-0.010	0.050	0.837
rs149614393	1	112820064	A	C	0.124	0.099	0.020	1.09E-06	0.040	0.034	0.235
rs2169706	4	19271294	C	T	0.312	0.070	0.014	1.12E-06	0.016	0.013	0.235
rs35172598	6	103952813	C	T	0.113	-0.116	0.022	8.50E-08	-0.035	0.017	0.041
rs6728914	2	184421981	G	T	0.007	0.388	0.081	1.86E-06	-0.066	0.061	0.276
rs7184768	16	81630188	A	G	0.348	-0.067	0.014	2.16E-06	-0.009	0.013	0.494
rs80068492	15	41542957	G	A	0.039	-0.163	0.035	3.61E-06	-0.128	0.101	0.205
rs847720	7	71116080	C	T	0.727	0.069	0.015	4.32E-06	0.007	0.014	0.601

Abbreviation: SNP, single nucleotide polymorphism; Chr, chromosome; A1, Effect_allele; A2, Other_allele; EAF, effect allele frequency; SE, standard error.

Table S7 Mendelian randomization analysis of anemia and any stroke in FinnGen study

SNP	Chr	Position	A1	A2	EAF	Anemia			Any stroke		
						Beta	SE	*P*-val	Beta	SE	*P*-val
rs116940507	15	75566965	T	C	0.030	0.181	0.039	4.08E-06	0.009	0.045	0.835
rs117372722	17	61401255	T	G	0.025	0.311	0.042	9.22E-14	-0.036	0.051	0.483
rs117725035	17	59212300	G	A	0.027	0.409	0.040	1.09E-24	-0.054	0.036	0.130
rs117885142	20	2464755	T	C	0.009	0.337	0.070	1.75E-06	0.045	0.069	0.519
rs12615303	2	26917705	T	C	0.336	-0.072	0.014	4.21E-07	-0.011	0.010	0.252
rs145020240	20	23989840	T	C	0.060	-0.152	0.029	2.35E-07	-0.018	0.027	0.513
rs149614393	1	112820064	A	C	0.124	0.099	0.020	1.09E-06	0.038	0.021	0.066
rs2169706	4	19271294	C	T	0.312	0.070	0.014	1.12E-06	-0.005	0.010	0.616
rs35172598	6	103952813	C	T	0.113	-0.116	0.022	8.50E-08	-0.028	0.012	0.019
rs6728914	2	184421981	G	T	0.007	0.388	0.081	1.86E-06	-0.073	0.046	0.112
rs7184768	16	81630188	A	G	0.348	-0.067	0.014	2.16E-06	-0.016	0.010	0.101
rs79005670	11	101545718	G	C	0.065	-0.128	0.028	4.16E-06	0.005	0.023	0.838
rs80068492	15	41542957	G	A	0.039	-0.163	0.035	3.61E-06	0.015	0.053	0.772
rs847720	7	71116080	C	T	0.727	0.069	0.015	4.32E-06	0.010	0.010	0.317

Abbreviation: SNP, single nucleotide polymorphism; Chr, chromosome; A1, Effect_allele; A2, Other_allele; EAF, effect allele frequency; SE, standard error.

Table S8 Mendelian randomization analysis of anemia and any ischemic stroke in FinnGen study

SNP	Chr	Position	A1	A2	EAF	Anemia			Any ischemic stroke		
						Beta	SE	*P*-val	Beta	SE	*P*-val
rs116940507	15	75566965	T	C	0.030	0.181	0.039	4.08E-06	0.011	0.048	0.828
rs117372722	17	61401255	T	G	0.025	0.311	0.042	9.22E-14	-0.054	0.055	0.325
rs117725035	17	59212300	G	A	0.027	0.409	0.040	1.09E-24	-0.054	0.039	0.164
rs117885142	20	2464755	T	C	0.009	0.337	0.070	1.75E-06	0.040	0.075	0.590
rs12615303	2	26917705	T	C	0.336	-0.072	0.014	4.21E-07	-0.013	0.011	0.234
rs145020240	20	23989840	T	C	0.060	-0.152	0.029	2.35E-07	-0.017	0.029	0.550
rs149614393	1	112820064	A	C	0.124	0.099	0.020	1.09E-06	0.042	0.023	0.059
rs2169706	4	19271294	C	T	0.312	0.070	0.014	1.12E-06	-0.005	0.011	0.623
rs35172598	6	103952813	C	T	0.113	-0.116	0.022	8.50E-08	-0.028	0.013	0.032
rs6728914	2	184421981	G	T	0.007	0.388	0.081	1.86E-06	-0.053	0.050	0.295
rs7184768	16	81630188	A	G	0.348	-0.067	0.014	2.16E-06	-0.018	0.010	0.081
rs79005670	11	101545718	G	C	0.065	-0.128	0.028	4.16E-06	0.021	0.025	0.404
rs80068492	15	41542957	G	A	0.039	-0.163	0.035	3.61E-06	0.010	0.057	0.868
rs847720	7	71116080	C	T	0.727	0.069	0.015	4.32E-06	0.008	0.011	0.476

Abbreviation: SNP, single nucleotide polymorphism; Chr, chromosome; A1, Effect_allele; A2, Other_allele; EAF, effect allele frequency; SE, standard error.

Table S9 Associations of genetically predicted anemia with risk of cardiovascular disease in the MR-PRESSO analysis in FinnGen study

Cardiovascular disease	SNP	Outliers	p_glo	p_dis	OR	95% CI	*P*-val
Heart failure	12	0	0.314	NA	1.108	1.03~1.193	0.019
Coronary artery disease	12	0	0.885	NA	1.112	1.041~1.188	0.009
Atrial fibrillation	13	0	0.365	NA	1.109	0.983~1.251	0.119
Any stroke	14	0	0.069	NA	1.038	0.946~1.139	0.441
Any ischemic stroke	14	0	0.133	NA	1.038	0.942~1.143	0.463

Abbreviation: SNPs, singe nucleotide polymorphisms; p_glo, p value for global test; p_dis, p value for distortion test; OR, odds ratio; CI, confidence interval; NA, not available.

Table S10 F statistics for the causal effect of cardiovascular disease on anemia in MR analysis in FinnGen study

Diseases	Data sources	Sample size (cases/controls)	Ancestry	R^2(%) for CVDs (Total)	F for CVDs (Total)
Heart failure	HERMES	47,309/930,014	European	1.3	1221.8
Coronary artery disease	CARDIoGRAMplusC4D	60,801/123,504	Mixed	8.1	647.1
Atrial fibrillation	AFGen	65,446/522,744	European	NA	NA
Any stroke	MEGASTROKE	40,585/406,111	European	1.2	767.7
Any ischemic stroke	MEGASTROKE	34,217/406,111	European	1.3	966.2

FinnGen: the FinnGen Consortium; HERMES; Heart Failure Molecular Epidemiology for Therapeutic Targets; CARDIoGRAMplusC4D, Coronary Artery Disease Genome-wide Replication and Meta-analysis plus The Coronary Artery Disease Genetics; AFGen, Atrial Fibrillation Genetics; MEGASTROKE, the MEGASTROKE Consortium.
Note: R^2: Variability explained by genetic instruments. The R^2 was calculated using the formula[1]: $R^2=\beta^2(1-EAF)*2EAF$. β is the association coefficient between the SNP and phenotype, and EAF is the minor allele frequency. Furthermore, the F statistics were calculated using the formula[2]: $F= R^2(N-K-1)/[K(1-R^2)]$. R^2 is the proportion of the variability of CVD explained by each instrument, K is the number of SNP-CVD association, N is the sample size of the GWAS for the SNP-CVD association.

Table S11 Mendelian randomization analysis of heart failure and anemia in FinnGen study

SNP	Chr	Position	A1	A2	EAF	Heart failure			Anemia		
						Beta	SE	*P*-val	Beta	SE	*P*-val
rs11745324	5	137676482	A	G	0.228	-0.053	0.010	2.35E-08	-0.017	0.016	0.285
rs1510226	6	160395377	T	C	0.981	-0.162	0.029	1.27E-08	-0.119	0.063	0.057
rs17042102	4	110747470	A	G	0.115	0.110	0.012	5.71E-20	0.049	0.019	0.012
rs17617337	10	119667372	T	C	0.221	-0.056	0.010	3.65E-09	-0.022	0.016	0.174
rs4135240	6	36679903	T	C	0.659	0.049	0.008	6.84E-09	0.008	0.014	0.567
rs4746140	10	73657491	C	G	0.154	-0.067	0.011	1.10E-09	-0.026	0.018	0.135
rs55730499	6	160584578	T	C	0.069	0.106	0.016	1.83E-11	0.091	0.032	0.004
rs56094641	16	53772541	A	G	0.584	-0.045	0.008	1.21E-08	-0.013	0.014	0.351
rs600038	9	133276354	T	C	0.791	-0.057	0.010	3.68E-09	-0.066	0.016	3.84E-05
rs660240	1	109275216	T	C	0.213	-0.061	0.010	3.25E-10	-0.023	0.016	0.152

Abbreviation: SNP, single nucleotide polymorphism; Chr, chromosome; A1, Effect_allele; A2, Other_allele; EAF, effect allele frequency; SE, standard error.

Table S12 Mendelian randomization analysis of coronary artery disease and anemia in FinnGen study

SNP	Chr	Position	A1	A2	EAF	Coronary artery disease			Anemia		
						Beta	SE	*P*-val	Beta	SE	*P*-val
rs10455872	6	160589086	G	A	0.054	0.285	0.027	9.23E-27	0.092	0.032	0.004
rs10947786	6	39188634	A	G	0.208	-0.072	0.013	1.77E-08	-0.022	0.015	0.138
rs113113862	19	11072901	A	G	0.218	-0.075	0.013	2.78E-09	-0.046	0.016	0.005
rs11556924	7	130023656	T	C	0.298	-0.069	0.013	4.00E-08	0.002	0.014	0.895
rs1332329	10	89243662	C	A	0.362	0.079	0.011	2.68E-13	0.001	0.014	0.939
rs1510226	6	160395377	C	T	0.027	0.226	0.035	6.16E-11	0.119	0.063	0.057
rs1870634	10	43985363	G	T	0.618	0.070	0.011	8.35E-11	-0.021	0.015	0.150
rs2019090	11	103798234	T	A	0.642	-0.065	0.011	3.65E-09	-0.001	0.016	0.952
rs2327426	6	133881552	C	T	0.298	-0.063	0.011	1.22E-08	-0.015	0.016	0.337
rs2505083	10	30046193	C	T	0.395	0.061	0.011	6.93E-09	0.003	0.014	0.824
rs2681472	12	89615182	G	A	0.194	0.073	0.013	6.11E-09	-0.028	0.025	0.278
rs28451064	21	34221526	A	G	0.119	0.122	0.018	6.10E-12	-0.003	0.019	0.880
rs35700460	1	222638065	G	A	0.647	0.082	0.012	1.91E-11	-0.003	0.015	0.834
rs41290120	19	44879418	A	G	0.032	-0.186	0.031	2.62E-09	-0.035	0.040	0.376
rs4773141	13	110302006	G	C	0.345	0.080	0.013	4.69E-10	0.000	0.015	0.982
rs4977574	9	22098575	G	A	0.482	0.189	0.010	4.58E-75	0.021	0.014	0.124
rs653178	12	111569952	T	C	0.558	-0.077	0.012	2.84E-11	-0.044	0.014	0.001
rs7173743	15	78849442	C	T	0.432	-0.064	0.010	7.75E-10	-0.011	0.014	0.436
rs72689147	4	155718736	T	G	0.180	-0.074	0.013	1.65E-08	-0.020	0.016	0.212
rs72934535	2	203104250	C	T	0.093	0.141	0.019	3.36E-14	-0.024	0.023	0.306
rs7528419	1	109274570	G	A	0.202	-0.101	0.013	9.92E-16	-0.024	0.016	0.136
rs9349379	6	12903725	G	A	0.411	0.131	0.011	9.37E-35	0.026	0.013	0.053
rs9970807	1	56499992	T	C	0.084	-0.111	0.018	1.81E-09	-0.017	0.022	0.433

Abbreviation: SNP, single nucleotide polymorphism; Chr, chromosome; A1, Effect_allele; A2, Other_allele; EAF, effect allele frequency; SE, standard error.

Table S13 Mendelian randomization analysis of atrial fibrillation and anemia in FinnGen study

SNP	Chr	Position	A1	A2	EAF	Atrial fibrillation			Anemia		
						Beta	SE	*P*-val	Beta	SE	*P*-val
rs11264280	1	154890476	T	C	NA	0.115	0.014	6.41E-17	0.014	0.014	0.314
rs1152591	14	64214130	A	G	NA	0.082	0.013	1.04E-10	-0.017	0.014	0.217
rs11598047	10	103582915	A	G	NA	-0.162	0.017	1.67E-22	-0.020	0.023	0.389
rs11718898	3	12807323	T	C	NA	-0.073	0.013	4.68E-08	0.017	0.014	0.208
rs12664873	6	122142045	T	G	NA	0.078	0.014	1.19E-08	-0.006	0.016	0.704
rs2106261	16	73017721	T	C	NA	0.185	0.016	8.18E-32	0.010	0.016	0.533
rs2288327	2	178546938	A	G	NA	-0.089	0.016	2.05E-08	0.034	0.018	0.057
rs28681402	4	110850907	T	G	NA	0.138	0.013	7.90E-26	-0.011	0.014	0.444
rs2967791	5	137677417	T	C	NA	0.072	0.013	2.73E-08	0.013	0.013	0.346
rs337711	5	114412874	T	C	NA	0.070	0.013	2.93E-08	-0.004	0.014	0.775
rs3771537	2	69811660	A	C	NA	0.085	0.012	7.92E-12	0.022	0.013	0.101
rs4946333	6	118244502	A	G	NA	-0.074	0.012	1.89E-09	-0.001	0.013	0.967
rs520525	1	170669192	A	G	NA	0.113	0.014	6.39E-16	0.012	0.016	0.428
rs6843082	4	110796911	A	G	NA	-0.371	0.014	3.41E-155	-0.038	0.015	0.009
rs7026071	9	94730238	T	C	NA	0.091	0.013	1.31E-12	0.019	0.014	0.180
rs74022964	15	73384923	T	C	NA	0.111	0.017	2.37E-11	-0.019	0.017	0.264
rs7508	8	18056461	A	G	NA	0.088	0.014	5.16E-10	0.014	0.015	0.353
rs75190942	11	128894676	A	C	NA	0.159	0.028	1.59E-08	0.020	0.023	0.381
rs7915134	10	73660422	T	C	NA	-0.113	0.018	1.68E-10	-0.027	0.019	0.152
rs80056983	10	103750144	T	C	NA	0.115	0.018	8.41E-11	0.016	0.021	0.436
rs883079	12	114355435	T	C	NA	0.108	0.014	1.80E-15	-0.007	0.014	0.643

Abbreviation: SNP, single nucleotide polymorphism; Chr, chromosome; A1, Effect_allele; A2, Other_allele; EAF, effect allele frequency; SE, standard error.

Table S14 Mendelian randomization analysis of any stroke and anemia in FinnGen study

SNP	Chr	Position	A1	A2	EAF	Any stroke			Anemia		
						Beta	SE	*P*-val	Beta	SE	*P*-val
rs10774624*	12	111395984	A	G	0.529	-0.065	0.009	4.04E-12	-0.046	0.014	0.001
rs11242678	6	1336945	T	C	0.255	0.064	0.011	8.71E-10	-0.016	0.015	0.273
rs11587860	1	156187160	C	G	0.355	-0.069	0.010	2.54E-12	0.002	0.014	0.896
rs1537375	9	22116072	T	C	0.498	-0.052	0.009	1.24E-08	-0.025	0.014	0.062
rs2107595	7	19009765	A	G	0.167	0.080	0.012	3.59E-11	0.028	0.017	0.099
rs2634074	4	110755885	A	T	0.789	-0.084	0.011	6.56E-14	-0.036	0.016	0.025
rs475937	11	102816969	A	C	0.132	0.076	0.014	2.92E-08	-0.017	0.016	0.285
rs4942561	13	46635212	T	G	0.758	0.064	0.011	2.05E-09	0.008	0.016	0.608

Abbreviation: SNP, single nucleotide polymorphism; Chr, chromosome; A1, Effect_allele; A2, Other_allele; EAF, effect allele frequency; SE, standard error; "rs10774624*" was removed as outliers in the MR-PRESSO analysis.

Table S15 Mendelian randomization analysis of any ischemic stroke and anemia in FinnGen study

SNP	Chr	Position	A1	A2	EAF	Any ischemic stroke			Anemia		
						Beta	SE	*P*-val	Beta	SE	*P*-val
rs11242678	6	1336945	T	C	0.255	0.072	0.011	2.70E-10	-0.016	0.015	0.273
rs2066864	4	154604543	A	G	0.245	0.063	0.012	3.51E-08	0.019	0.015	0.196
rs2107595	7	19009765	A	G	0.167	0.088	0.013	2.33E-11	0.028	0.017	0.099
rs2634074	4	110755885	A	T	0.788	-0.094	0.012	5.91E-15	-0.036	0.016	0.025
rs3184504	12	111446804	T	C	0.472	0.078	0.010	1.23E-14	0.040	0.014	0.003
rs473238*	11	102829629	T	C	0.133	0.083	0.015	1.65E-08	-0.018	0.016	0.263
rs4942561	13	46635212	T	G	0.759	0.066	0.012	1.77E-08	0.008	0.016	0.608
rs635634*	9	133279427	T	C	0.192	0.077	0.013	9.18E-09	0.071	0.017	2.55E-05

Abbreviation: SNP, single nucleotide polymorphism; Chr, chromosome; A1, Effect_allele; A2, Other_allele; EAF, effect allele frequency; SE, standard error; "rs2634074*" and "rs4942561*" was removed as outliers in the MR-PRESSO analysis.

Table S16 Associations of genetically predicted anemia with risk of cardiovascular disease in the MR-PRESSO analysis in FinnGen study

Cardiovascular disease	SNP	Outliers	*P*_glo	*P*_dis	OR	95%CI	*P*-val
Heart failure	10	0	0.441	NA	1.639	1.372~1.958	4.10E-04
Coronary artery disease	23	0	0.098	NA	1.155	1.066~1.252	0.002
Atrial fibrillation	21	0	0.343	NA	1.064	1.009~1.121	0.032
Any stroke	8	1	0.02	0.175	1.223	0.961~1.558	0.146
Any stroke*	7	0	0.093	NA	1.133	0.905~1.419	0.317
Any ischemic stroke	8	2	0.001	0.988	1.307	1.014~1.685	0.078
Any ischemic stroke*	6	0	0.153	NA	1.302	1.057~1.603	0.056

Abbreviation: SNPs, singe nucleotide polymorphisms; p_glo, p value for global test; p_dis, p value for distortion test; OR, odds ratio; CI, confidence interval; NA, not available; Any stroke*, "rs10774624" was removed as outliers in the MR-PRESSO analysis; Any ischemic stroke*, "rs2634074" and "rs4942561" was removed as outliers in the MR-PRESSO analysis.

Table S17 MR-Steiger test in two-sample bidirectional Mendelian randomization analysis in FinnGen study

Exposure	Outcome	SNP_r^2.exposure	SNP_r^2.outcome	Correct_causal_direction	Steiger_pval
Anemia	Heart failure	0.020	1.51E-06	TRUE	2.01E-27
Anemia	Coronary artery disease	0.020	2.10E-05	TRUE	1.41E-25
Heart failure	Anemia	0.000	1.59E-05	TRUE	6.31E-10
Coronary artery disease	Anemia	0.003	5.67E-05	TRUE	2.18E-63
Atrial fibrillation	Anemia	0.002	2.95E-05	TRUE	1.31E-84
Any ischemic stroke	Anemia	0.001	1.33E-05	TRUE	1.07E-17

Table S18 Information on instrumental variables for anemia in UK Biobank study

SNP	Chr	A1	A2	EAF	Beta	SE	*P*-val
rs11863726	16	G	A	0.501	0.094	0.456	1.22E-06
rs1894251	22	T	C	0.078	0.183	0.915	5.99E-07
rs35239007	6	A	C	0.118	0.143	0.666	3.24E-06
rs7189975	16	A	G	0.472	0.093	0.450	1.18E-06
rs8099569	18	A	G	0.077	0.184	0.929	4.62E-07

Abbreviation: SNP, single nucleotide polymorphism; Chr, chromosome; A1, Effect_allele; A2, Other_allele; EAF, effect allele frequency; SE, standard error.

Table S19 Mendelian randomization analysis of anemia and cardiovascular disease in UK Biobank study

Cardiovascular disease	Method	SNP	Beta	SE	OR	95%CI	*P*-val
Heart failure	IVW (fixed effects)	5	0.046	0.056	1.047	0.939~1.168	0.409
	IVW (multiplicative random effects)	5	0.046	0.025	1.047	0.997~1.099	0.064
	Maximum likelihood	5	0.100	0.293	1.105	0.623~1.961	0.733
	MR Egger	5	0.021	0.225	1.021	0.656~1.589	0.932
	Weighted median	5	0.012	2.709	1.012	0.005~204.651	0.996
	RAPS	5	0.100	0.310	1.105	0.602~2.028	0.748
	MR-PRESSO	5	0.046	0.025	1.047	0.997~1.099	0.137
Coronary artery disease	IVW (fixed effects)	5	-0.004	0.068	0.996	0.872~1.138	0.955
	IVW (multiplicative random effects)	5	-0.004	0.067	0.996	0.874~1.135	0.955
	Maximum likelihood	5	-7.753	89.250	0.000	0~4.02E+72	0.931
	MR Egger	5	-0.078	0.296	0.925	0.518~1.653	0.810
	Weighted median	5	0.014	0.240	1.014	0.633~1.625	0.952
	RAPS	5	0.563	3.973	1.756	0.001~4230.364	0.887
	MR-PRESSO	5	-0.004	0.067	0.996	0.874~1.135	0.957
Atrial fibrillation	IVW (fixed effects)	5	-0.024	0.089	0.976	0.819~1.163	0.786
	IVW (multiplicative random effects)	5	-0.024	0.109	0.976	0.788~1.209	0.824
	Maximum likelihood	5	-1.598	11.678	0.202	0~1763400900	0.891
	MR Egger	5	0.001	0.509	1.001	0.369~2.715	0.998
	Weighted median	5	-0.142	0.141	0.868	0.658~1.145	0.315
	RAPS	5	-2.339	49.644	0.096	0~1.75E+41	0.962
	MR-PRESSO	5	-0.024	0.109	0.976	0.788~1.209	0.835
Any stroke	IVW (fixed effects)	5	-0.054	0.071	0.947	0.824~1.088	0.442
	IVW (multiplicative random effects)	5	-0.054	0.080	0.947	0.809~1.108	0.498
	Maximum likelihood	5	-1.433	11.683	0.239	0~2100028637	0.902
	MR Egger	5	0.171	0.341	1.186	0.608~2.312	0.651
	Weighted median	5	-0.028	0.604	0.972	0.298~3.174	0.963
	RAPS	5	-2.116	49.380	0.120	0~1.3E+41	0.966
	MR-PRESSO	5	-0.054	0.080	0.947	0.809~1.108	0.535
Any ischemic stroke	IVW (fixed effects)	5	-0.052	0.075	0.949	0.819~1.1	0.486
	IVW (multiplicative random effects)	5	-0.052	0.086	0.949	0.802~1.123	0.541
	Maximum likelihood	5	-1.356	7.803	0.258	0~1130136.753	0.862
	MR Egger	5	0.203	0.366	1.226	0.598~2.51	0.617
	Weighted median	5	-0.048	0.786	0.954	0.204~4.452	0.952
	RAPS	5	-2.450	59.290	0.086	0~2.5E+49	0.967
	MR-PRESSO	5	-0.052	0.086	0.949	0.802~1.123	0.574

Abbreviation: SNPs, Single nucleotide polymorphisms; SE, standard error; OR, Odds ratio; CI, Confidence interval; IVW, inverse-variance weighted; IVW (fixed), fixed-effects inverse-variance weighted; MR-RAPS, MR-robust adjusted profile score; MR-PRESSO, MR-pleiotropy residual sum and outlier.

Table S20 Associations of genetically predicted anemia with risk of cardiovascular disease in sensitivity analysis in UK Biobank study

Cardiovascular disease	Heterogeneity test MR-Egger			Heterogeneity test IVW			Pleiotropy test		
	Q	Q_df	Q_pval	Q	Q_df	Q_pval	egger_ intercept	SE	*P*-val
Heart failure	0.779	3	0.854	0.792	4	0.939	0.003	0.029	0.916
Coronary artery disease	3.778	3	0.287	3.862	4	0.425	0.011	0.041	0.813
Atrial fibrillation	5.990	3	0.112	5.995	4	0.199	-0.003	0.066	0.962
Any stroke	4.456	3	0.216	5.149	4	0.272	-0.029	0.043	0.544
Any ischemic stroke	4.429	3	0.219	5.200	4	0.267	-0.034	0.046	0.522

Abbreviation: MR, Mendelian randomization; Q, heterogeneity statistic Q; Q_df, degree of freedom.

Table S21 Mendelian randomization analysis of cardiovascular disease and anemia in UK Biobank study

Cardiovascular disease	Method	SNP	Beta	SE	OR	95%CI	*P*-val
Heart failure*	IVW (fixed effects)	5	0.003	0.000	1.003	1.002~1.004	1.58E-10
	IVW (multiplicative random effects)	5	0.003	0.000	1.003	1.002~1.004	1.94E-10
	Maximum likelihood	5	0.003	0.001	1.003	1.002~1.004	1.66E-08
	MR Egger	5	0.002	0.001	1.002	1~1.004	0.201
	Weighted median	5	0.003	0.001	1.003	1.002~1.004	3.01E-06
	RAPS	5	0.003	0.001	1.003	1.002~1.004	9.95E-08
	MR-PRESSO	5	0.003	0.000	1.003	1.002~1.004	0.003
Coronary artery disease*	IVW (fixed effects)	10	-0.001	0.001	0.999	0.998~1	0.231
	IVW (multiplicative random effects)	10	-0.001	0.001	0.999	0.998~1.001	0.381
	Maximum likelihood	10	-0.001	0.001	0.999	0.998~1	0.206
	MR Egger	10	0.001	0.003	1.001	0.995~1.008	0.726
	Weighted median	10	-0.002	0.001	0.998	0.996~1	0.031
	RAPS	10	0.000	0.001	1.000	0.998~1.002	0.903
	MR-PRESSO	10	-0.001	0.001	0.999	0.998~1.001	0.404
Atrial fibrillation*	IVW (fixed effects)	10	0.001	0.000	1.001	1~1.001	0.094
	IVW (multiplicative random effects)	10	0.001	0.000	1.001	1~1.002	0.248
	Maximum likelihood	10	0.001	0.000	1.001	1~1.001	0.092
	MR Egger	10	-0.001	0.001	0.999	0.997~1	0.089
	Weighted median	10	0.001	0.001	1.001	1~1.002	0.196
	RAPS	10	0.000	0.001	1.000	0.999~1.001	0.888
	MR-PRESSO	10	0.001	0.000	1.001	1~1.002	0.278
Any stroke	IVW (fixed effects)	4	0.003	0.000	1.003	1.003~1.003	7.50E-120
	IVW (multiplicative random effects)	4	0.003	0.001	1.003	1.001~1.005	0.002
	Maximum likelihood	4	0.003	0.001	1.003	1.002~1.004	1.49E-07
	MR Egger	4	-0.026	0.069	0.974	0.851~1.114	0.739
	Weighted median	4	0.003	0.001	1.003	1.001~1.005	0.006
	RAPS	4	0.001	0.002	1.001	0.998~1.005	0.498
	MR-PRESSO	4	0.003	0.001	1.003	1.001~1.005	0.052
Any ischemic stroke	IVW (fixed effects)	5	0.002	0.000	1.002	1.002~1.003	1.17E-110
	IVW (multiplicative random effects)	5	0.002	0.001	1.002	1.001~1.004	0.003
	Maximum likelihood	5	0.003	0.001	1.003	1.001~1.004	0.000
	MR Egger	5	-0.048	0.019	0.953	0.919~0.989	0.084
	Weighted median	5	0.002	0.001	1.002	1~1.005	0.055
	RAPS	5	0.001	0.001	1.001	0.999~1.004	0.296
	MR-PRESSO	5	0.002	0.001	1.002	1.001~1.004	0.039

Abbreviation: SNPs, Single nucleotide polymorphisms; SE, standard error; OR, Odds ratio; CI, Confidence interval; IVW, inverse-variance weighted; IVW (fixed), fixed-effects inverse-variance weighted; MR-RAPS, MR-robust adjusted profile score; MR-PRESSO, MR-pleiotropy residual sum and outlier; Heart failure*, “rs11745324” was removed as outliers in the MR-PRESSO analysis; Coronary artery disease*, “rs1870634” and “rs653178” were removed as outliers in the MR-PRESSO analysis; Atrial fibrillation*, “rs12664873” and “rs6843082” were removed as outliers in the MR-PRESSO analysis.

Table S22 Associations of genetically predicted cardiovascular disease with risk of anemia in sensitivity analysis in UK Biobank study

Cardiovascular disease	Heterogeneity test MR-Egger			Heterogeneity test IVW			Pleiotropy test		
	Q	Q_ df	Q_pval	Q	Q_ df	Q_pval	egger_ intercept	SE	*P*-val
Heart failure	23.473	4	1.02E-04	23.484	5	2.73E-04	-8.38E-06	1.87E-04	0.966
Heart failure*	2.900	3	0.407	4.040	4	0.401	8.53E-05	7.99E-05	0.364
Coronary artery disease	29.873	10	8.99E-04	29.933	11	0.002	-4.44E-05	3.11E-04	0.889
Coronary artery disease*	16.129	8	0.041	16.816	9	0.052	-0.00016	2.74E-04	0.576
Atrial fibrillation	22.148	9	0.008	26.538	10	0.003	1.50E-04	1.12E-04	0.214
Atrial fibrillation*	7.982	8	0.435	18.876	9	0.026	2.53E-04	7.67E-05	0.011
Any stroke	152.197	2	8.93E-34	165.843	3	1.00E-35	0.002	0.004	0.713
Any ischemic stroke	65.275	3	4.38E-14	220.099	4	1.79E-46	0.004	0.001	0.076

Abbreviation: MR, Mendelian randomization; Q, heterogeneity statistic Q; Q_df, degree of freedom. Heart failure*, “rs11745324” was removed as outliers in the MR-PRESSO analysis; Coronary artery disease*, “rs1870634” and “rs653178” were removed as outliers in the MR-PRESSO analysis; Atrial fibrillation*, “rs12664873” and “rs6843082” were removed as outliers in the MR-PRESSO analysis.

Table S23 Associations of genetic liability to anemia with risk of cardiovascular disease in UK Biobank and FinnGen studies

Cardiovascular disease	Studies	SNP	OR	LCI	UCI	*P*-val
Heart failure	UK Biobank	5	1.047	0.939	1.168	0.409
	FinnGen	12	1.108	1.037	1.184	0.002
	Combined		1.092	1.032	1.155	0.002
Coronary artery disease	UK Biobank	5	0.996	0.872	1.138	0.955
	FinnGen	12	1.112	1.017	1.216	0.020
	Combined		1.075	0.998	1.158	0.056
Atrial fibrillation	UK Biobank	5	0.947	0.824	1.088	0.442
	FinnGen	13	1.038	0.963	1.120	0.330
	Combined		1.017	0.951	1.087	0.627
Any stroke	UK Biobank	5	0.947	0.824	1.088	0.442
	FinnGen	14	1.038	0.963	1.120	0.330
	Combined		1.017	0.951	1.087	0.627
Any ischemic stroke	UK Biobank	5	0.949	0.819	1.100	0.486
	FinnGen	14	1.038	0.956	1.127	0.374
	Combined		1.016	0.946	1.092	0.662

Abbreviation: SNPs, Single nucleotide polymorphisms; OR, Odds ratio; LCI, Lower confidence interval; UCI, Upper confidence interval.

Table S24 Associations of genetic liability to cardiovascular disease with risk of anemia in UK Biobank and FinnGen studies

Cardiovascular disease	Studies	SNP	OR	LCI	UCI	*P*-val
Heart failure	UK Biobank	6	1.002	1.002	1.003	1.01E-07
	FinnGen	10	1.639	1.386	1.938	7.60E-09
	Combined		1.272	0.786	2.060	0.328
Coronary artery disease	UK Biobank	10	0.999	0.998	1.000	0.231
	FinnGen	23	1.155	1.080	1.235	2.32E-05
	Combined		1.070	0.928	1.233	0.351
Atrial fibrillation	UK Biobank	10	1.001	1.000	1.002	0.248
	FinnGen	21	1.064	1.012	1.118	0.015
	Combined		1.001	1.000	1.002	0.045
Any stroke	UK Biobank	4	1.003	1.001	1.005	0.002
	FinnGen	7	1.133	0.964	1.332	0.13
	Combined		1.003	1.001	1.005	0.003
Any ischemic stroke	UK Biobank	5	1.002	1.001	1.004	0.003
	FinnGen	6	1.302	1.112	1.524	0.001
	Combined		1.128	0.874	1.457	0.355

Abbreviation: SNPs, Single nucleotide polymorphisms; OR, Odds ratio; LCI, Lower confidence interval; UCI, Upper confidence interval.

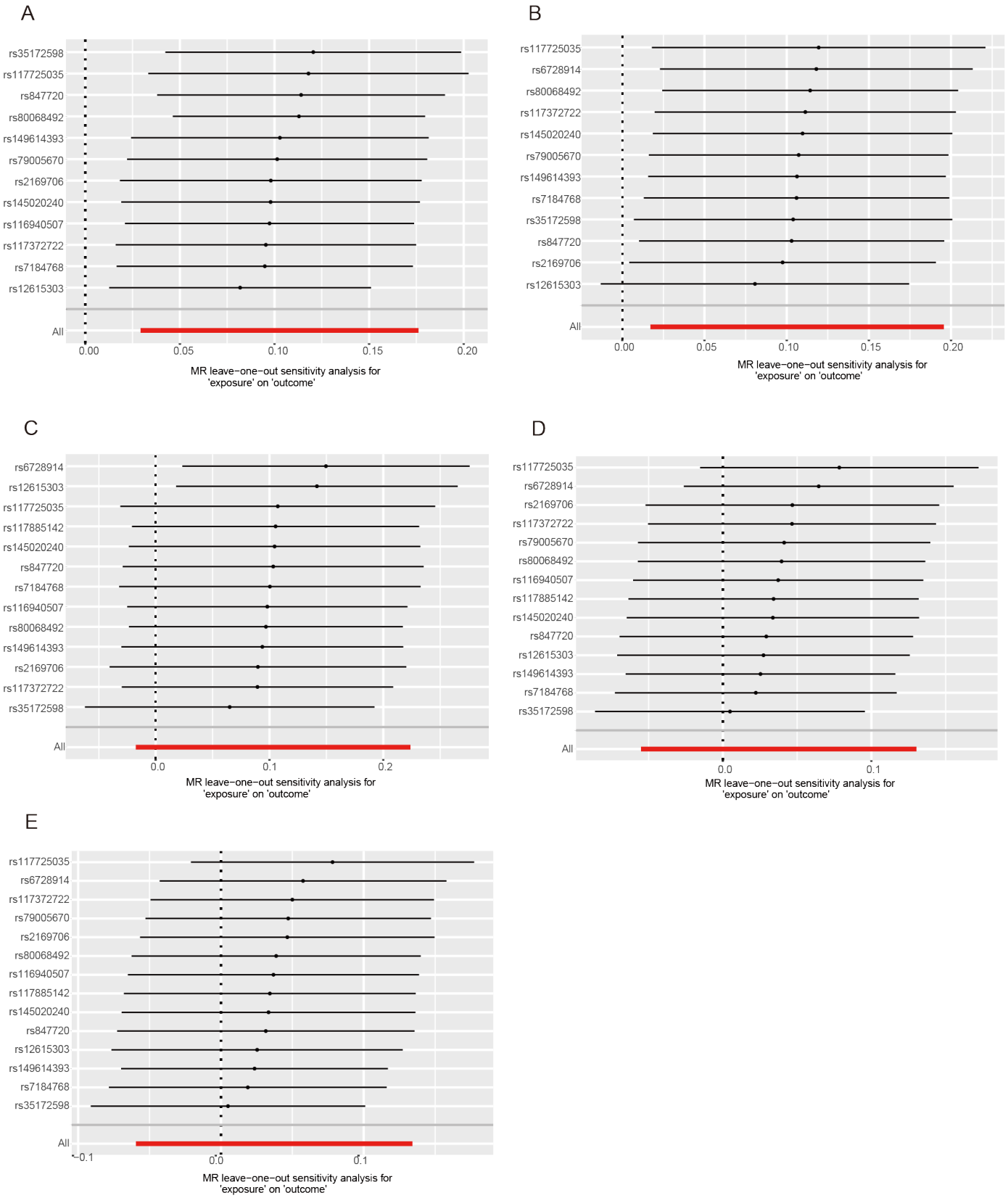

Figure S1 Leave-one-out sensitivity analysis in the Mendelian randomization analysis of anemia and cardiovascular disease in FinnGen study. (A) Anemia and Heart failure; (B) Anemia and Coronary artery disease; (C) Anemia and Atrial fibrillation; (D) Anemia and Any stroke; (E) Anemia and Any ischemic stroke.

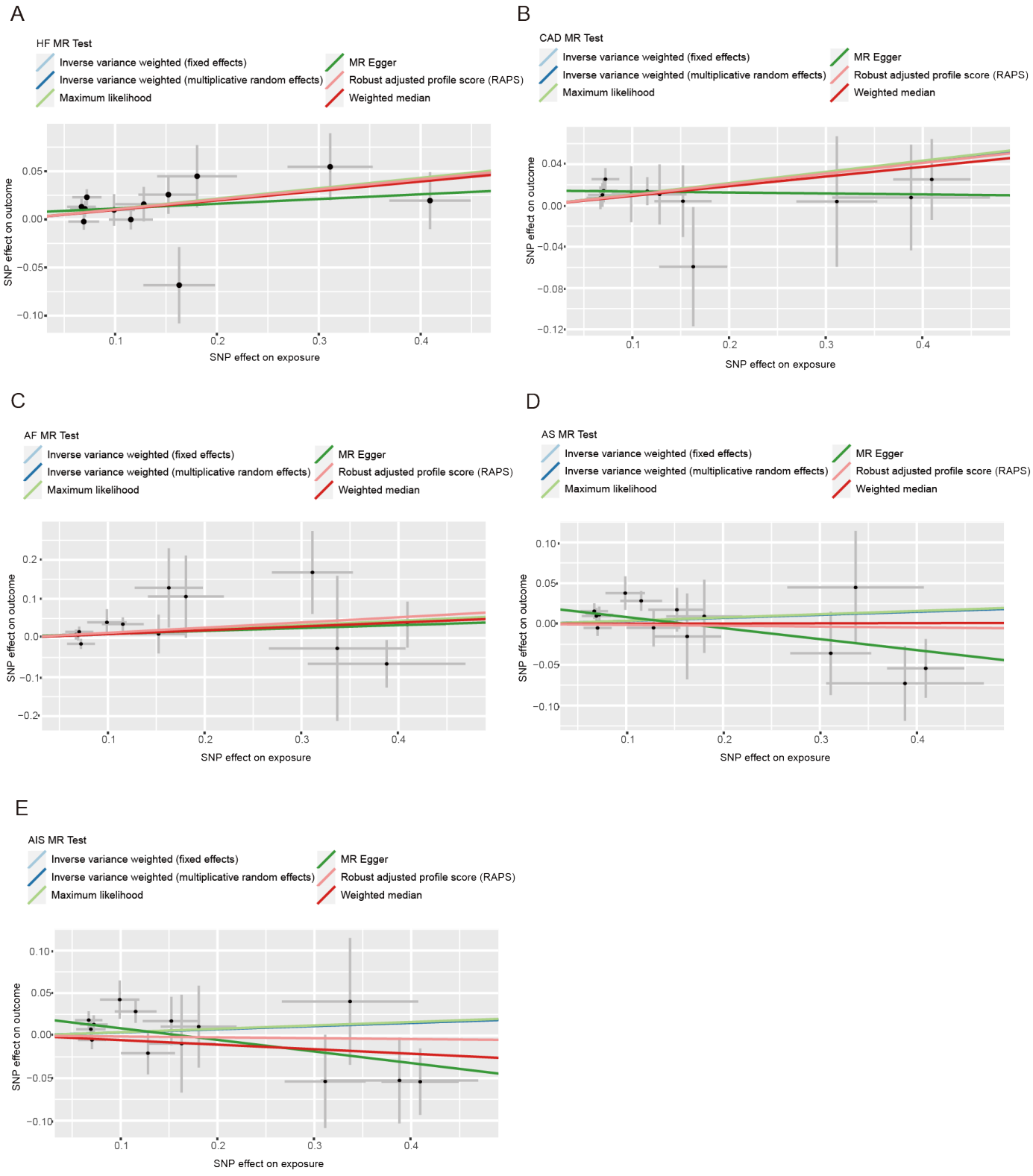

Figure S2 Scatter_plot in the Mendelian randomization analysis of anemia and cardiovascular disease in FinnGen study. (A) Anemia and Heart failure; (B) Anemia and Coronary artery disease; (C) Anemia and Atrial fibrillation; (D) Anemia and Any stroke; (E) Anemia and Any ischemic stroke.

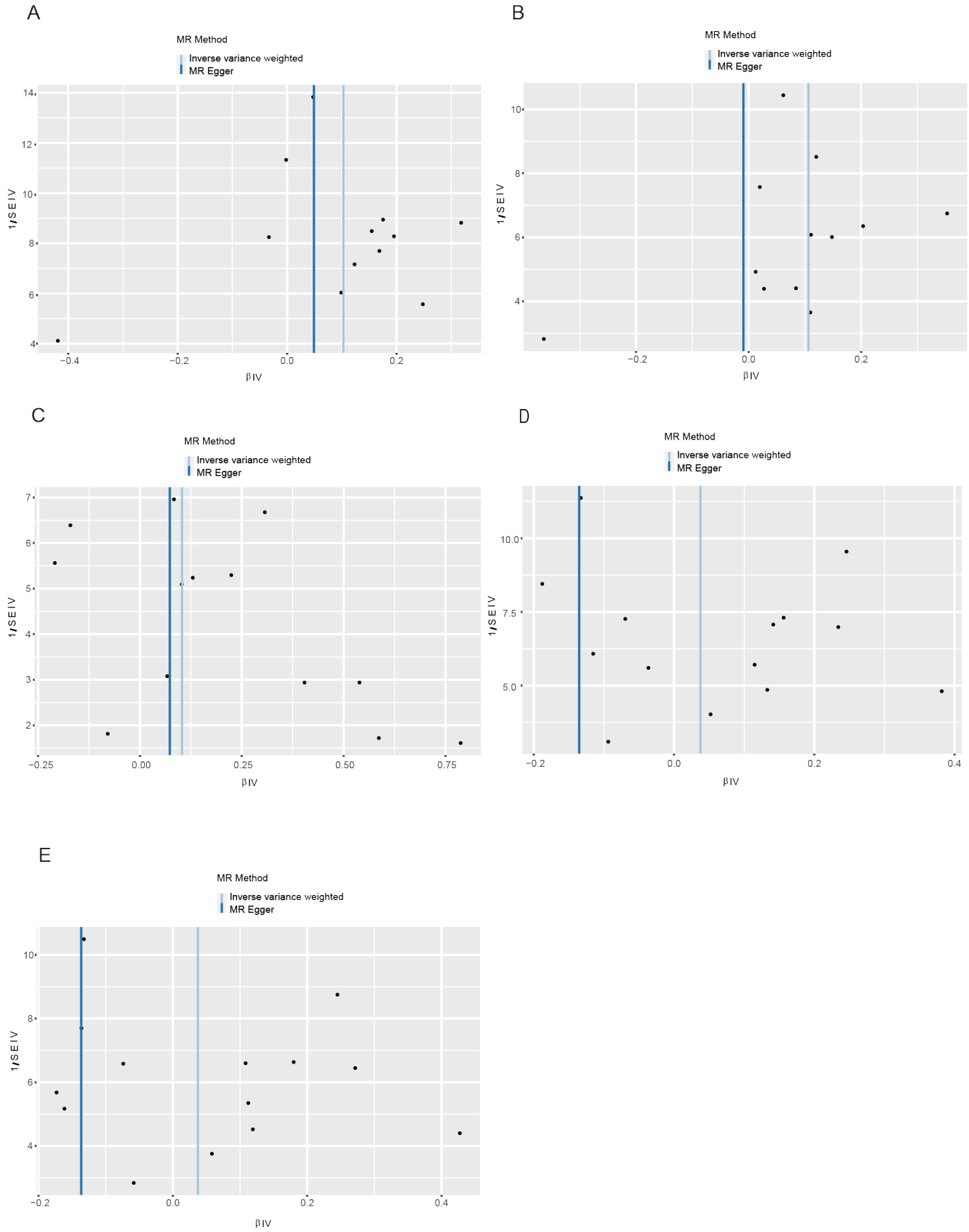

Figure S3 Funnel_plot in the Mendelian randomization analysis of anemia and cardiovascular disease in FinnGen study. (A) Anemia and Heart failure; (B) Anemia and Coronary artery disease; (C) Anemia and Atrial fibrillation; (D) Anemia and Any stroke; (E) Anemia and Any ischemic stroke.

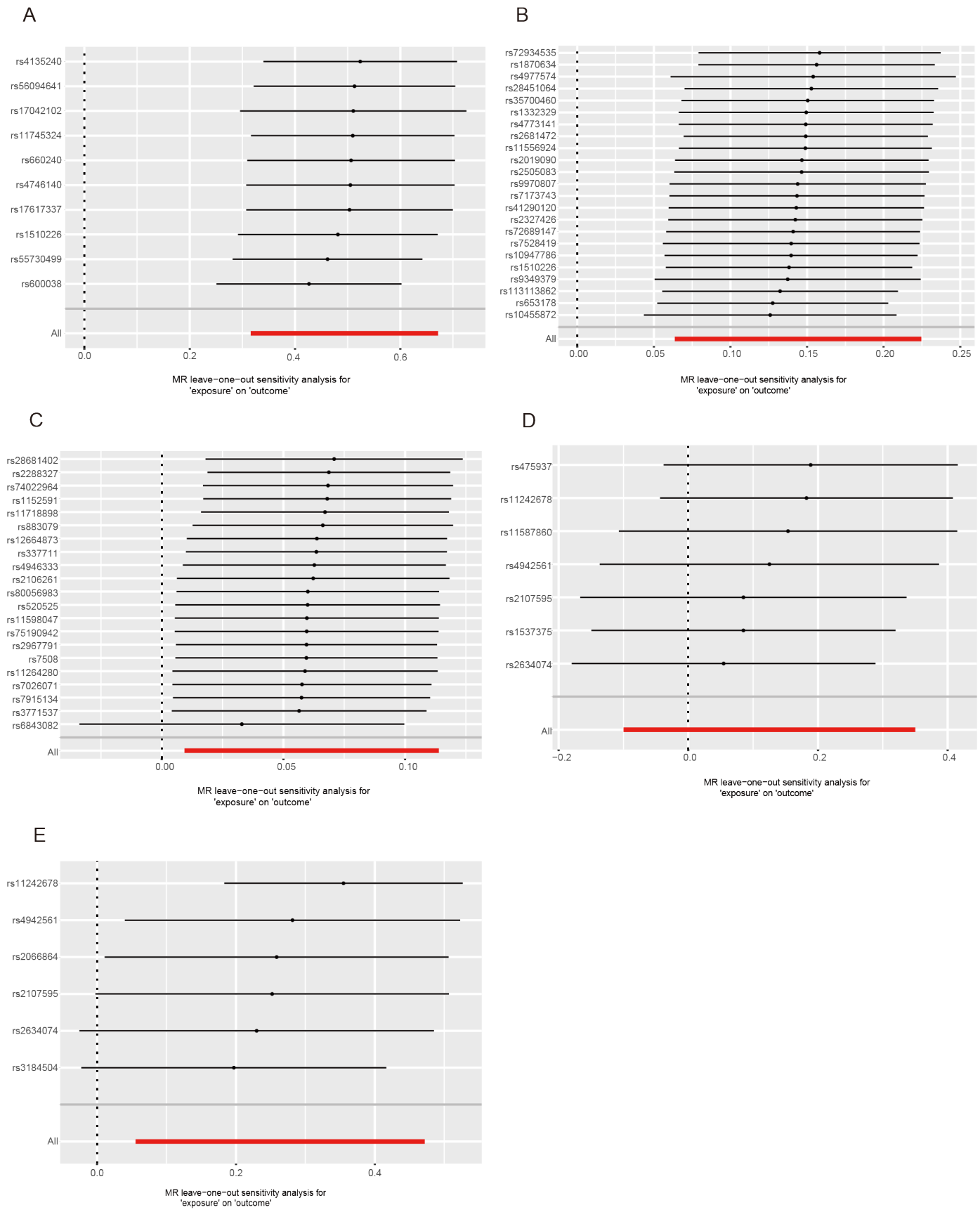

Figure S4 Leave-one-out sensitivity analysis in the Mendelian randomization analysis of cardiovascular disease and anemia in FinnGen study. (A) Heart failure and Anemia; (B) Coronary artery disease and Anemia; (C) Atrial fibrillation and Anemia; (D) Any stroke and Anemia, "rs10774624" was removed as outliers in the MR-PRESSO analysis; AIS*, any ischemic stroke; (E) Any ischemic stroke and Anemia, "rs2634074" and "rs4942561" was removed as outliers in the MR-PRESSO analysis.

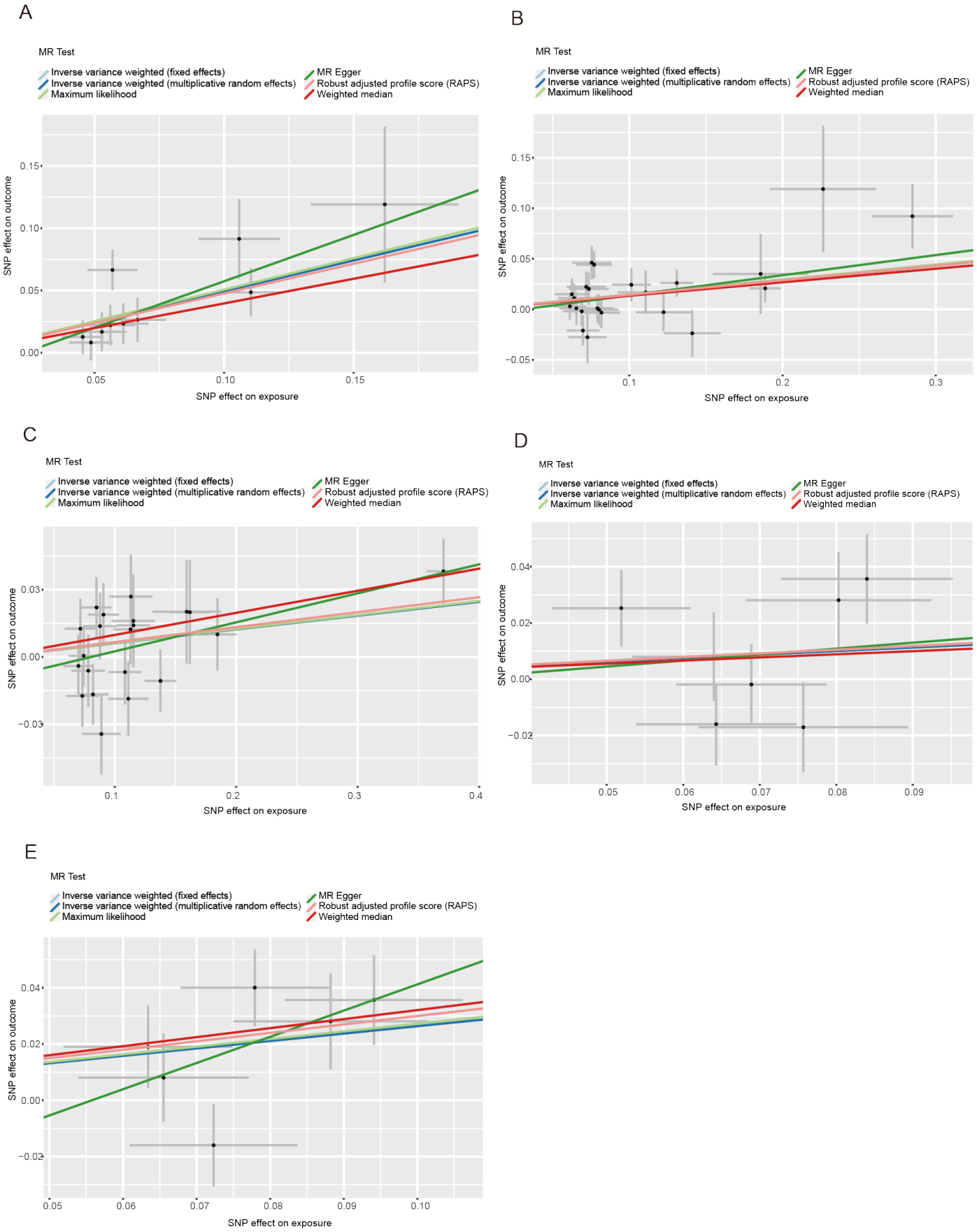

Figure S5 Scatter_plot in the Mendelian randomization analysis of cardiovascular disease and anemia in FinnGen study. (A) Heart failure and Anemia; (B) Coronary artery disease and Anemia; (C) Atrial fibrillation and Anemia; (D) Any stroke and Anemia, "rs10774624" was removed as outliers in the MR-PRESSO analysis; AIS*, any ischemic stroke; (E) Any ischemic stroke and Anemia, "rs2634074" and "rs4942561" was removed as outliers in the MR-PRESSO analysis.

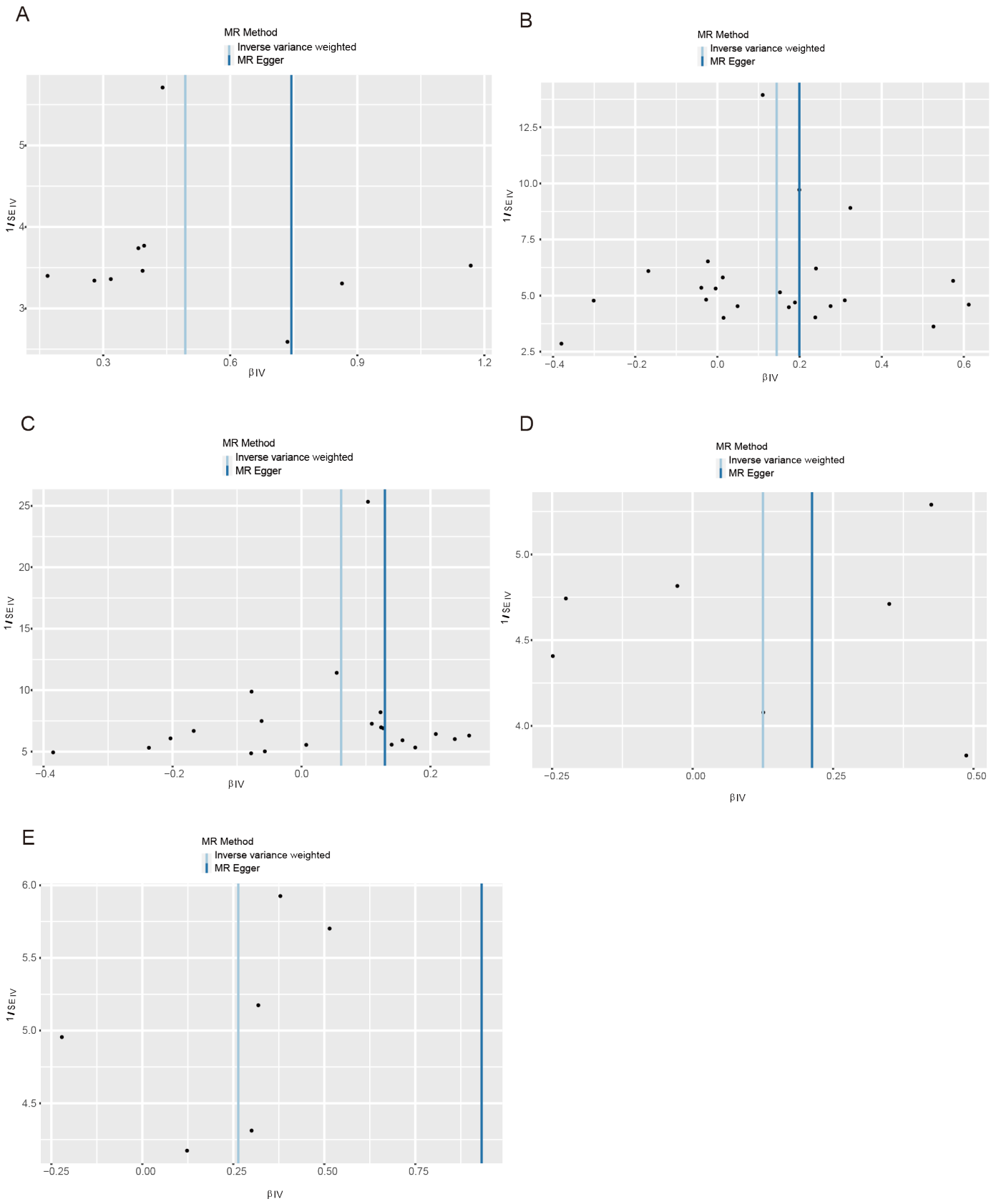

Figure S6 Funnel_plot in the Mendelian randomization analysis of cardiovascular disease and anemia in FinnGen study. (A) Heart failure and Anemia; (B) Coronary artery disease and Anemia; (C) Atrial fibrillation and Anemia; (D) Any stroke and Anemia, "rs10774624" was removed as outliers in the MR-PRESSO analysis; AIS*, any ischemic stroke; (E) Any ischemic stroke and Anemia, "rs2634074" and "rs4942561" was removed as outliers in the MR-PRESSO analysis.