ACCSCIENCE PUBLISHING

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ORIGINAL RESEARCH ARTICLE

Causal relationships between mitochondrial DNA copy number and hypertensive disorders in pregnancy: A Mendelian randomization study

Supplementary Files

Table S1. Genetic variants used as IVs for mtDNA copy number

SNP	Affected base	Substituted base	Beta	SE	*p*-value
rs114694170	C	T	0.0331	0.0045	3.04E−13
rs2304693	A	G	0.0181	0.0028	5.11E−11
rs9494142	C	T	0.018	0.0024	1.93E−13
rs74750282	C	T	0.038	0.0038	4.29E−24
rs1065853	T	G	0.0388	0.0039	1.59E−23
rs4698839	T	C	0.0124	0.0022	9.47E−09
rs11064074	T	C	0.0197	0.0021	4.87E−20
rs11553699	G	A	0.0445	0.0032	1.45E−43
rs12148	G	T	−0.0139	0.0022	1.32E−10
rs6959832	A	G	−0.021	0.0021	2.10E−23
rs2263663	T	C	0.02	0.0024	1.97E−16
rs12247015	G	A	0.0337	0.0021	1.28E−55
rs1613662	A	G	−0.0167	0.0028	3.90E−09
rs1569419	C	T	0.0189	0.0025	6.87E−14
rs289713	A	T	−0.0149	0.0027	4.14E−08
rs10835540	A	T	0.0184	0.0023	5.74E−16
rs11085147	T	C	0.0756	0.0036	1.54E−95
rs10749636	A	G	0.0155	0.0025	5.43E−10
rs77261872	T	C	0.0262	0.0032	2.28E−16
rs56069439	A	C	−0.0274	0.0023	2.30E−32
rs701834	T	C	−0.0254	0.0026	1.12E−22
rs12426673	T	G	−0.0141	0.0021	4.03E−11
rs2038480	T	A	0.0162	0.0027	1.39E−09
rs4284061	A	T	−0.0186	0.0022	2.97E−17
rs74874677	G	A	−0.0819	0.0071	3.62E−31
rs342293	G	C	0.0283	0.0021	1.05E−40
rs17850455	G	C	0.091	0.0104	1.81E−18
rs36009521	TA	T	0.0181	0.0031	6.27E−09
rs12052715	G	C	−0.0133	0.0024	1.72E−08
rs4814776	A	C	−0.03	0.0023	2.00E−40
rs72660908	G	C	0.0457	0.0021	8.25E−101
rs4841132	G	A	−0.0212	0.0037	7.46E-09
rs7896518	G	A	−0.0456	0.0022	9.53E−99
rs5745582	T	C	0.021	0.0028	3.46E−14
rs13088724	A	G	0.0175	0.0026	7.70E−12
rs1967556	G	T	0.0175	0.0021	1.97E−16
rs1354034	C	T	−0.0268	0.0022	2.05E−35
rs1127787	A	G	−0.0159	0.0028	1.49E−08
rs11764390	A	G	−0.0122	0.0022	1.55E−08
rs11064881	A	G	0.0255	0.004	2.58E−10
rs2977608	C	A	0.0236	0.0025	2.58E−21
rs1760940	C	A	0.0263	0.0024	5.20E−27
rs3766744	A	G	−0.0179	0.0021	2.91E−17
rs2274319	C	T	−0.0139	0.0022	4.09E−10
rs182346769	A	G	0.0213	0.0027	7.87E−15
rs5012419	G	A	0.0247	0.0022	2.66E−29
rs2290507	A	G	0.0223	0.0031	3.64E−13
rs28665408	C	A	0.0157	0.0021	2.11E−13
rs6105852	A	G	0.0221	0.0021	1.41E−25
rs212930	G	A	0.0149	0.0025	3.18E−09
rs2245946	A	G	0.0317	0.0023	9.38E−45
rs4807780	C	T	−0.0191	0.0022	1.61E−17
rs34778241	TG	T	0.014	0.0023	2.02E−09
rs143989240	TTG	T	0.0127	0.0023	2.61E−08
rs2322718	G	T	0.0136	0.0021	1.53E−10
rs6511720	T	G	0.0192	0.0033	4.08E−09
rs62641680	A	G	−0.0903	0.0063	4.63E−47
rs78909033	A	G	−0.021	0.0031	1.00E−11
rs72698722	T	C	−0.0192	0.0027	1.25E−12
rs156355	C	T	0.0214	0.0022	6.41E−23
rs385893	C	T	0.0153	0.0021	5.96E−13
rs57066921	G	T	−0.1081	0.0081	8.98E−41
rs3961455	A	G	0.0142	0.0024	4.31E−09
rs445	T	C	0.0207	0.0036	8.85E−09
rs7705526	A	C	0.0178	0.0023	6.46E−15
rs8176645	A	T	−0.0145	0.0026	3.06E−08

Abbreviations: IVs: Instrumental variables; mtDNA: Mitochondrial DNA; SE: Standard error; SNPs: Single nucleotide polymorphisms.

Table S2. Genetic variants used as IVs for hypertensive disorders in pregnancy in the reverse MR analyses

SNP	Affected base	Substituted base	EAF	Beta	SE	*p*-value	Traits
rs10059884	A	C	0.586198	0.105327	0.0152063	4.31E−12	GH
rs10857147	T	A	0.312712	0.111231	0.0159815	3.40E−12	GH
rs10882397	A	C	0.598799	0.0838888	0.0152757	3.98E−08	GH
rs167479	G	T	0.574759	0.0970364	0.0151621	1.55E−10	GH
rs2011946	A	C	0.64508	0.0948055	0.0157425	1.72E−09	GH
rs2208589	G	A	0.889831	0.194577	0.0253088	1.49E−14	GH
rs2293289	A	G	0.0762611	0.15056	0.0273761	3.80E−08	GH
rs236717	A	G	0.826334	−0.128051	0.0191828	2.47E−11	GH
rs552528831	C	G	0.0743545	−0.191378	0.0295573	9.49E−11	GH
rs7139122	A	G	0.0202325	0.303492	0.0474184	1.55E−10	GH
rs9855086	T	A	0.462845	−0.0999967	0.0150147	2.74E−11	GH
rs12509595	C	T	0.311814	0.269542	0.0296688	1.04E−19	EH
rs167479	G	T	0.574216	0.168725	0.0288624	5.04E−09	EH
rs6015445	C	G	0.162092	0.232339	0.0363186	1.58E−10	EH
rs6026578	G	C	0.649056	0.164927	0.0301802	4.64E−08	EH
rs10857147	T	A	0.31271	0.120527	0.0179746	2.01E−11	PE
rs12567119	T	C	0.145102	−0.136704	0.0247174	3.19E−08	PE
rs167479	G	T	0.574543	0.0996315	0.0171214	5.92E−09	PE
rs915665	A	G	0.110303	0.144863	0.026137	2.98E−08	PE
rs12509595	C	T	0.312093	0.0012	0.0173201	3.07E−13	POE
rs12567119	T	C	0.145056	0.0099	0.0238158	5.54E−09	POE
rs167479	G	T	0.574598	0.0011	0.0164943	2.03E−09	POE
rs73412716	T	G	0.108084	−0.0051	0.0272793	1.79E−08	POE
rs9265628	C	T	0.248956	−0.0049	0.0184438	9.38E−09	POE

Abbreviations: EAF: Effect allele frequency; EH: Pre-existing hypertension complicating pregnancy; GH: Gestational hypertension; IVs: Instrumental variables; MR: Mendelian randomization; PE: Pre-eclampsia; POE: Pre-eclampsia or eclampsia; SE, Standard error; SNPs, Single nucleotide polymorphisms.

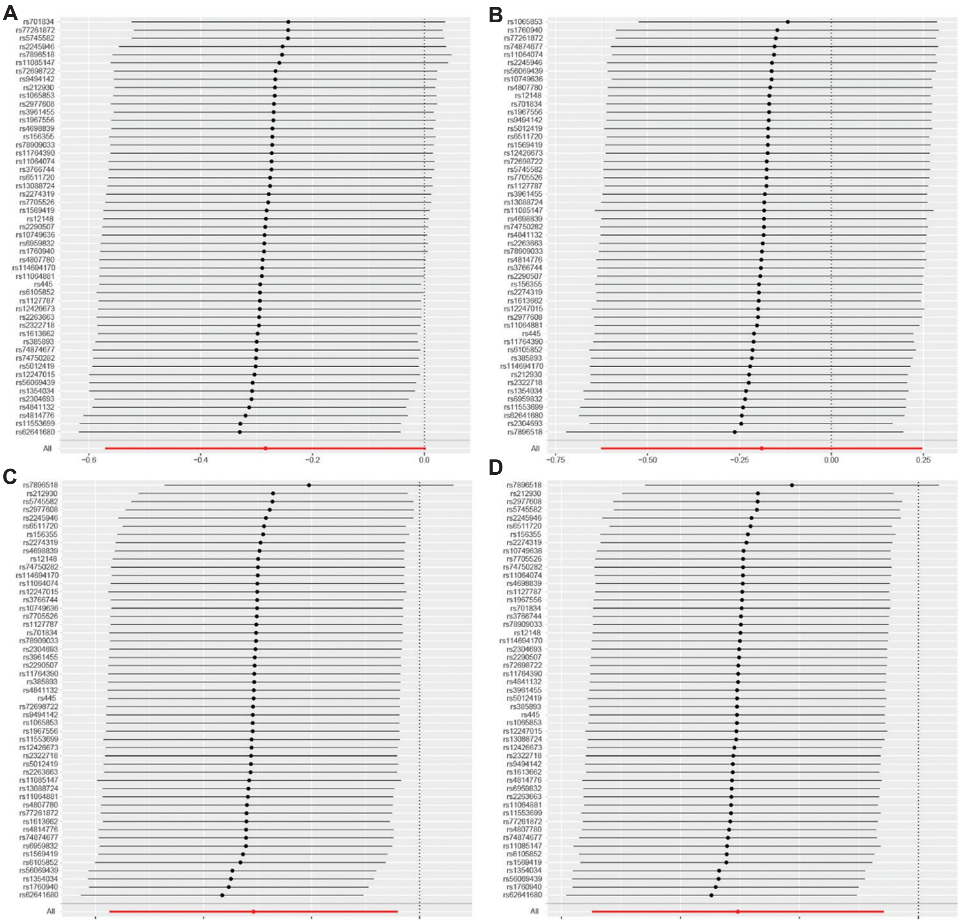

Figure S1. "Leave-one-out" sensitivity analyses for forward MR estimates assessing the causal effect of mtDNA copy number on the risk of hypertensive disorders in pregnancy. Results are shown for GH (A), EH (B), PE (C), and POE (D). The horizontal lines in the figure represent beta value and its 95% CI of causal inference, reflecting the robustness and potential influence of each SNP on hypertensive disorders in pregnancy Abbreviations: CI: Confidence interval; EH: pre-existing hypertension complicating pregnancy; MR: Mendelian randomization; mtDNA: Mitochondrial DNA; PE: pre-eclampsia; POE: pre-eclampsia or eclampsia; SNPs: single nucleotide polymorphisms; GH: gestational hypertension.

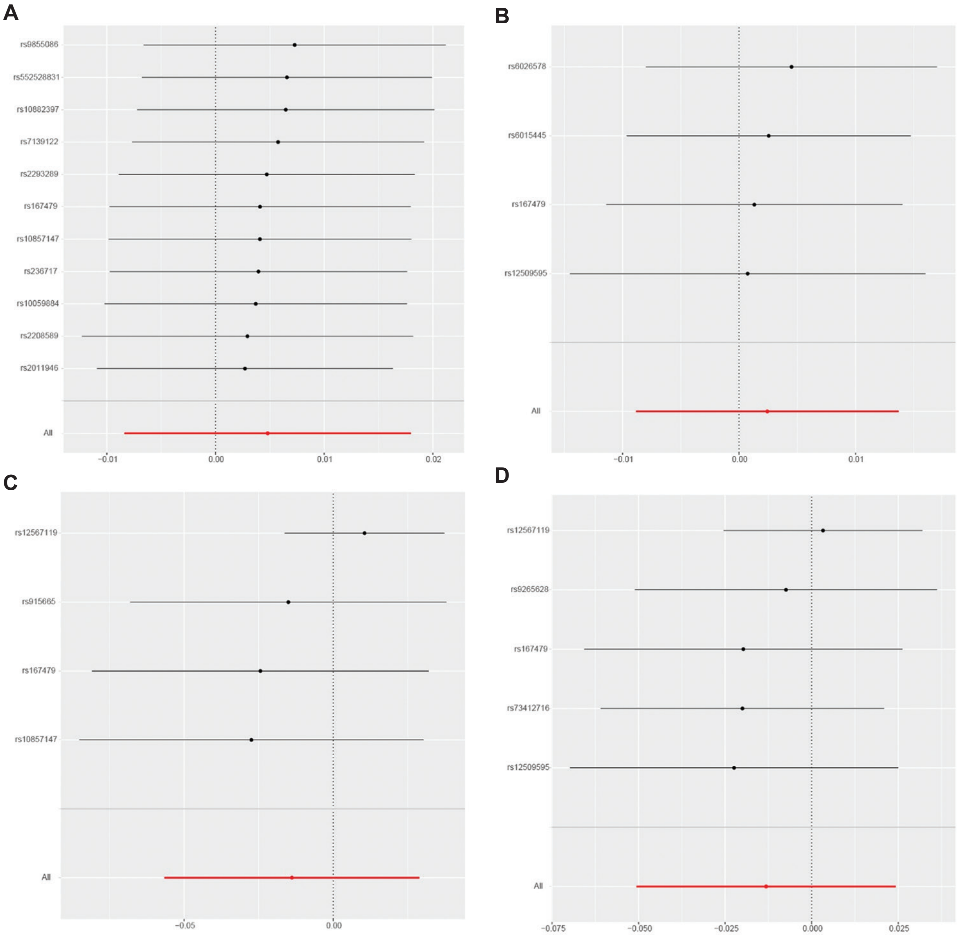

Figure S2. "Leave-one-out" sensitivity analyses for reverse MR estimates assessing the casual effect of hypertensive disorders in pregnancy on mtDNA copy number. Results are shown for GH (A), EH (B), PE (C), and POE (D). The horizontal lines in the figure represent beta value and its 95% CI of causal inference, reflecting the robustness and potential influence of each SNP on hypertensive disorders in pregnancy Abbreviations: EH: Pre-existing hypertension complicating pregnancy; GH; Gestational hypertension; MR: Mendelian randomization; mtDNA: Mitochondrial DNA; PE: Pre-eclampsia; POE: Pre-eclampsia or eclampsia; SNPs: Single nucleotide polymorphisms.