

## **Supplementary material**

**Application of Mendelian randomization to explore the genetic association between drinking habits of different beverages and sleep disorder**

**Supplementary Table SI.** Five statistical methods with exposure and outcome

Exposure		Method	NSN	$\beta$	SE	<i>p</i>	OR (95% CI)
outcome			P				
		MR Egger		0.0410	0.04	0.3518	1.04 (0.96–1.13)
		Weighted median		0.0487	0.02	0.0286	1.05 (1.01–1.10)
ALI	INS	Inverse varianceweighted	34	0.0635	0.03	0.0175	1.07 (1.01–1.12)
		Simple mode		0.0248	0.05	0.5894	1.03 (0.94–1.12)
		Weighted mode		0.0457	0.02	0.0335	1.05 (1.01–1.09)
		MR Egger		−0.0196	0.04	0.6337	0.98 (0.91–1.06)
		Weighted median		0.0033	0.02	0.8352	1.00 (0.97–1.04)
ALI	IE	Inverse varianceweighted	34	−0.0254	0.02	0.3079	0.97 (0.93–1.02)
		Simple mode		−0.0630	0.05	0.1723	0.94 (0.86–1.03)
		Weighted mode		−0.0082	0.02	0.6051	0.99 (0.96–1.02)
		MR Egger		0.0673	0.07	0.3096	1.07 (0.94–1.22)
		Weighted median		0.0359	0.02	0.1142	1.04 (0.99–1.08)
ALI	SD	Inverse varianceweighted	34	0.0470	0.04	0.2399	1.05 (0.97–1.13)
		Simple mode		−0.0334	0.06	0.5894	0.97 (0.86–1.09)
		Weighted mode		0.0322	0.02	0.1785	1.03 (0.99–1.08)
		MR Egger		−0.0392	0.03	0.1627	0.96 (0.91–1.02)
		Weighted median		−0.0141	0.01	0.2446	0.99 (0.96–1.01)
ALF	INS	Inverse varianceweighted	96	0.0081	0.01	0.5213	1.01 (0.98–1.03)
		Simple mode		0.0179	0.04	0.6206	1.02 (0.95–1.09)
		Weighted mode		−0.0225	0.01	0.0991	0.98 (0.95–1.00)
		MR Egger		0.0180	0.02	0.3307	1.02 (0.98–1.06)
		Weighted median		0.0064	0.01	0.4267	1.01 (0.99–1.02)
ALF	IE	Inverse varianceweighted	96	0.0243	0.01	0.0028	1.02 (1.01–1.04)
		Simple mode		0.0218	0.02	0.3233	1.02 (0.98–1.07)
		Weighted mode		−0.0014	0.01	0.9023	1.00 (0.98–1.02)
		MR Egger		−0.0202	0.04	0.5873	0.98 (0.91–1.05)

		Weighted median		-0.0256	0.01	0.0803	0.97 (0.95–1.00)
ALF	SD	Inverse varianceweighted	96	-0.0400	0.02	0.0151	0.96 (0.93–0.99)
		Simple mode		-0.0034	0.03	0.9086	1.00 (0.94–1.06)
		Weighted mode		-0.0208	0.01	0.1515	0.98 (0.95–1.01)
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		MR Egger		-0.1987	0.49	0.6860	0.82 (0.32–2.13)
		Weighted median		-0.2559	0.05	0.0000	0.77 (0.70–0.86)
HAL	INS	Inverse varianceweighted	33	-0.2356	0.06	0.0002	0.79 (0.70–0.89)
		Simple mode		-0.2907	0.12	0.0191	0.75 (0.59–0.94)
		Weighted mode		-0.2907	0.1	0.0087	0.75 (0.61–0.92)
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		MR Egger		-0.1764	0.3	0.5602	0.84 (0.47–1.51)
		Weighted median		-0.0639	0.04	0.0706	0.94 (0.88–1.01)
HAL	IE	Inverse varianceweighted	33	-0.0781	0.04	0.0443	0.92 (0.86–1.00)
		Simple mode		-0.0834	0.08	0.2911	0.92 (0.79–1.07)
		Weighted mode		-0.0798	0.07	0.2635	0.92 (0.80–1.06)
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		MR Egger		-0.0632	0.55	0.9088	0.94 (0.32–2.74)
		Weighted median		0.1405	0.06	0.0170	1.15 (1.03–1.29)
HAL	SD	Inverse varianceweighted	33	0.2122	0.07	0.0028	1.24 (1.08–1.42)
		Simple mode		0.0957	0.14	0.4923	1.10 (0.84–1.44)
		Weighted mode		0.0780	0.12	0.5199	1.08 (0.85–1.37)
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		MR Egger		-0.0001	0.05	0.9991	1.00 (0.90–1.10)
		Weighted median		0.0212	0.02	0.3524	1.02 (0.98–1.07)
TEAI	INS	Inverse varianceweighted	40	-0.0060	0.02	0.7886	0.99 (0.95–1.04)
		Simple mode		0.0389	0.05	0.4820	1.04 (0.93–1.16)
		Weighted mode		0.0232	0.03	0.3696	1.02 (0.97–1.08)
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		MR Egger		-0.1070	0.04	0.0047	0.90 (0.84–0.96)
		Weighted median		-0.0838	0.02	0.0000	0.92 (0.89–0.95)
TEAI	IE	Inverse varianceweighted	40	-0.0518	0.02	0.0013	0.95 (0.92–0.98)
		Simple mode		-0.0507	0.03	0.1363	0.95 (0.89–1.01)
		Weighted mode		-0.0896	0.02	0.0000	0.91 (0.89–0.94)
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		MR Egger		0.0248	0.06	0.7010	1.03 (0.90–1.16)

TEAI	SD	Weighted median		0.0515	0.03	0.0426	1.05 (1.00–1.11)
		Inverse variance	40	0.0648	0.03	0.0219	1.07 (1.01–1.13)
		weighted					
		Simple mode		–0.0114	0.05	0.8304	0.99 (0.89–1.10)
		Weighted mode		0.0264	0.03	0.3249	1.03 (0.97–1.08)
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		MR Egger		0.0152	0.06	0.7989	1.02 (0.90–1.14)
COFI	INS	Weighted median		0.0258	0.03	0.3128	1.03 (0.98–1.08)
		Inverse variance	39	0.0035	0.03	0.9045	1.00 (0.95–1.06)
		weighted					
		Simple mode		0.0976	0.06	0.0901	1.10 (0.99–1.23)
		Weighted mode		0.0341	0.03	0.2066	1.03 (0.98–1.09)
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		MR Egger		–0.1304	0.04	0.0048	0.88 (0.81–0.96)
COFI	IE	Weighted median		–0.0991	0.02	0.0000	0.91 (0.87–0.94)
		Inverse variance	39	–0.0670	0.02	0.0025	0.94 (0.90–0.98)
		weighted					
		Simple mode		0.0443	0.07	0.5229	1.05 (0.91–1.20)
		Weighted mode		–0.1056	0.02	0.0000	0.90 (0.87–0.93)
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		MR Egger		–0.0165	0.08	0.8340	0.98 (0.84–1.15)
COFI	SD	Weighted median		0.0044	0.03	0.8783	1.00 (0.95–1.06)
		Inverse variance	39	–0.0127	0.04	0.7403	0.99 (0.92–1.06)
		weighted					
		Simple mode		0.0135	0.06	0.8094	1.01 (0.91–1.13)
		Weighted mode		0.0276	0.03	0.3235	1.03 (0.97–1.09)
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		MR Egger		0.2736	0.14	0.0708	1.31 (1.00–1.73)
RWI	INS	Weighted median		0.0042	0.04	0.9243	1.00 (0.92–1.09)
		Inverse variance	18	–0.0529	0.05	0.3088	0.95 (0.86–1.05)
		weighted					
		Simple mode		–0.0348	0.09	0.6891	0.97 (0.82–1.14)
		Weighted mode		0.0205	0.08	0.7968	1.02 (0.88–1.19)
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		MR Egger		0.0831	0.06	0.2156	1.09 (0.96–1.23)

		Weighted median		0.0226	0.02	0.3640	1.02 (0.97–1.07)
RWI	IE	Inverse variance	18	0.0084	0.02	0.6921	1.01 (0.97–1.05)
		weighted					
		Simple mode		0.0058	0.04	0.8885	1.01 (0.93–1.09)
		Weighted mode		0.0380	0.04	0.3175	1.04 (0.97–1.12)
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		MR Egger		-0.0080	0.19	0.9667	0.99 (0.68–1.44)
		Weighted median		-0.0297	0.05	0.5259	0.97 (0.89–1.06)
RWI	SD	Inverse variance	18	-0.0376	0.06	0.5278	0.96 (0.86–1.08)
		weighted					
		Simple mode		0.0920	0.08	0.2724	1.10 (0.94–1.29)
		Weighted mode		0.0858	0.08	0.2769	1.09 (0.94–1.27)
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Methods: MR Egger, weighted median, IVW, simple mode, weighted mode;  $\beta$  regression coefficient; SE: standard error; *p*-value; OR (95% CI) – odds ratio (95% confidence interval), the standard line is the line of “X = 1”.

**Supplementary Table SII.** The selected effective gene loci

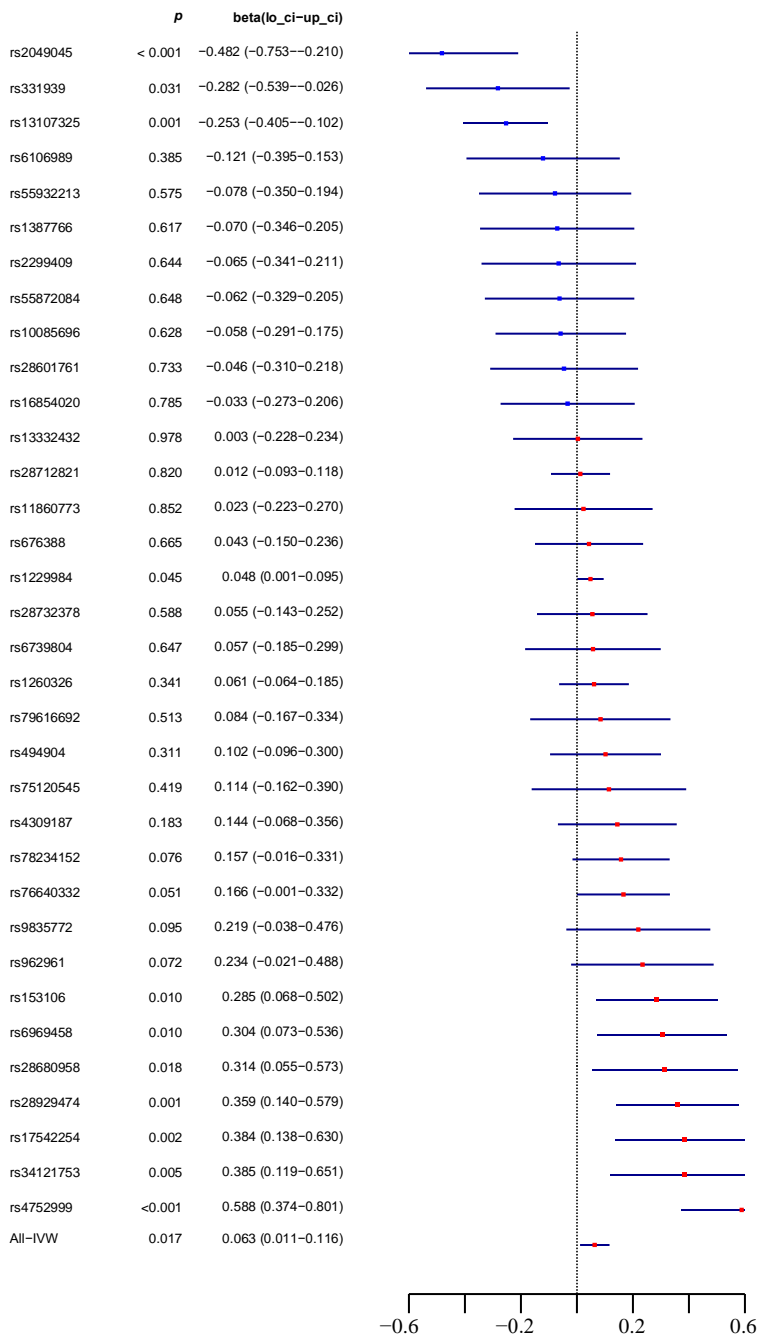
Sequence	Exposure	Outcome	SNP	$\beta$	$p$	lo_ci	up_ci
1			rs1229984	0.0481	0.0448	0.0011	0.095
2			rs28680958	0.314	0.0176	0.0547	0.573
3			rs153106	0.2851	0.0099	0.0684	0.502
4			rs6969458	0.3042	0.0101	0.0725	0.536
5	ALI	INS	rs34121753	0.385	0.0046	0.1187	0.651
6			rs17542254	0.3842	0.0022	0.1382	0.63
7			rs28929474	0.3591	0.0013	0.1397	0.579
8			rs4752999	0.5878	0.0000	0.3743	0.801
1			rs2411453	0.0611	0.0414	0.0024	0.12
2			rs34811474	0.1226	0.0430	0.0039	0.241
3			rs35105141	0.0868	0.0295	0.0086	0.165
4			rs650558	0.1252	0.0296	0.0124	0.238
5			rs1937522	0.1386	0.0232	0.019	0.258
6			rs62466318	0.1287	0.0106	0.03	0.227
7			rs61873510	0.1469	0.0077	0.0388	0.255
8	ALF	IE	rs2043677	0.1696	0.0026	0.0591	0.28
9			rs58905411	0.1364	0.0005	0.0593	0.213
10			rs7610856	0.1478	0.0007	0.062	0.234
11			rs9958320	0.1903	0.0011	0.0757	0.305
12			rs1228589	0.19	0.0009	0.0783	0.302
13			rs780094	0.1296	0.0000	0.089	0.17
14			rs780569	0.2324	0.0001	0.1191	0.346
15			rs13135092	0.229	0.0000	0.1453	0.313
1			rs2717063	-0.623	0.0000	-0.78	-0.47
2			rs1421085	-0.546	0.0000	-0.706	-0.39
3			rs13135092	-0.489	0.0000	-0.619	-0.36
4			rs73050128	-0.433	0.0000	-0.596	-0.27
5			rs8043563	-0.366	0.0000	-0.52	-0.21
6			rs2924321	-0.366	0.0000	-0.528	-0.2
7			rs17690703	-0.338	0.0000	-0.48	-0.2
8			rs2160935	-0.345	0.0001	-0.516	-0.17
9			rs58905411	-0.281	0.0000	-0.4	-0.16
10	ALF	SD	rs28768122	-0.334	0.0002	-0.512	-0.16
11			rs186347	-0.328	0.0003	-0.503	-0.15
12			rs12153855	-0.265	0.0027	-0.439	-0.09
13			rs8614	-0.24	0.0041	-0.404	-0.08
14			rs1515591	-0.223	0.0134	-0.4	-0.05
15			rs28622224	-0.225	0.0184	-0.413	-0.04
16			rs1228589	-0.197	0.0259	-0.37	-0.02
17			rs550942	-0.203	0.0305	-0.388	-0.02

18			rs7610856	-0.149	0.0281	-0.282	-0.02
19			rs13102973	-0.179	0.0353	-0.345	-
							0.01
1			rs1515591	-0.223	0.0134	-0.4	-0.05
2			rs28622224	-0.225	0.0184	-0.413	-0.04
3			rs1228589	-0.197	0.0259	-0.37	-0.02
4			rs550942	-0.203	0.0305	-0.388	-0.02
5			rs7610856	-0.149	0.0281	-0.282	-0.02
6			rs13102973	-0.179	0.0353	-0.345	-0.01
7	HAL	INS	rs1515591	-0.223	0.0134	-0.4	-0.05
8			rs28622224	-0.225	0.0184	-0.413	-0.04
9			rs1228589	-0.197	0.0259	-0.37	-0.02
10			rs550942	-0.203	0.0305	-0.388	-0.02
11			rs7610856	-0.149	0.0281	-0.282	-0.02
12			rs13102973	-0.179	0.0353	-0.345	-0.01
13			rs1515591	-0.223	0.0134	-0.4	-0.05
1			rs2820309	-0.866	0.0000	-1.136	-0.59
2			rs1291836	-0.382	0.0077	-0.662	-0.1
3			rs13246732	-0.301	0.0101	-0.53	-0.07
4	HAL	IE	rs72720396	-0.289	0.0095	-0.507	-0.07
5			rs6805189	-0.284	0.0223	-0.527	-0.04
6			rs1714081	-0.249	0.0260	-0.469	-0.03
7			rs58734839	-0.258	0.0315	-0.493	-0.02
1			rs1714081	0.3441	0.0478	0.0034	0.685
2			rs58734839	0.3822	0.0401	0.0173	0.747
3			rs1526912	0.4551	0.0218	0.0661	0.844
4			rs2016975	0.5334	0.0138	0.109	0.958
5			rs6805189	0.4936	0.0104	0.1161	0.871
6	HAL	SD	rs2860872	0.5609	0.0093	0.1385	0.983
7			rs11783227	0.6084	0.0028	0.2094	1.008
8			rs72720396	0.6811	0.0001	0.3422	1.02
9			rs13246732	0.8589	0.0000	0.5033	1.214
10			rs2820309	1.1158	0.0000	0.6958	1.536
11			rs4636654	1.2843	0.0000	0.8504	1.718
1			rs72797284	-0.243	0.0003	-0.376	-0.11
2			rs10764990	-0.26	0.0027	-0.429	-0.09
3			rs2472297	-0.105	0.0000	-0.148	-0.06
4	TEAI	IE	rs17685	-0.148	0.0030	-0.245	-0.05
5			rs2645929	-0.217	0.0141	-0.39	-0.04
6			rs4410790	-0.093	0.0004	-0.145	-0.04
7			rs10741694	-0.154	0.0304	-0.293	-
							0.01
1			rs1481012	0.1928	0.0458	0.0036	0.382

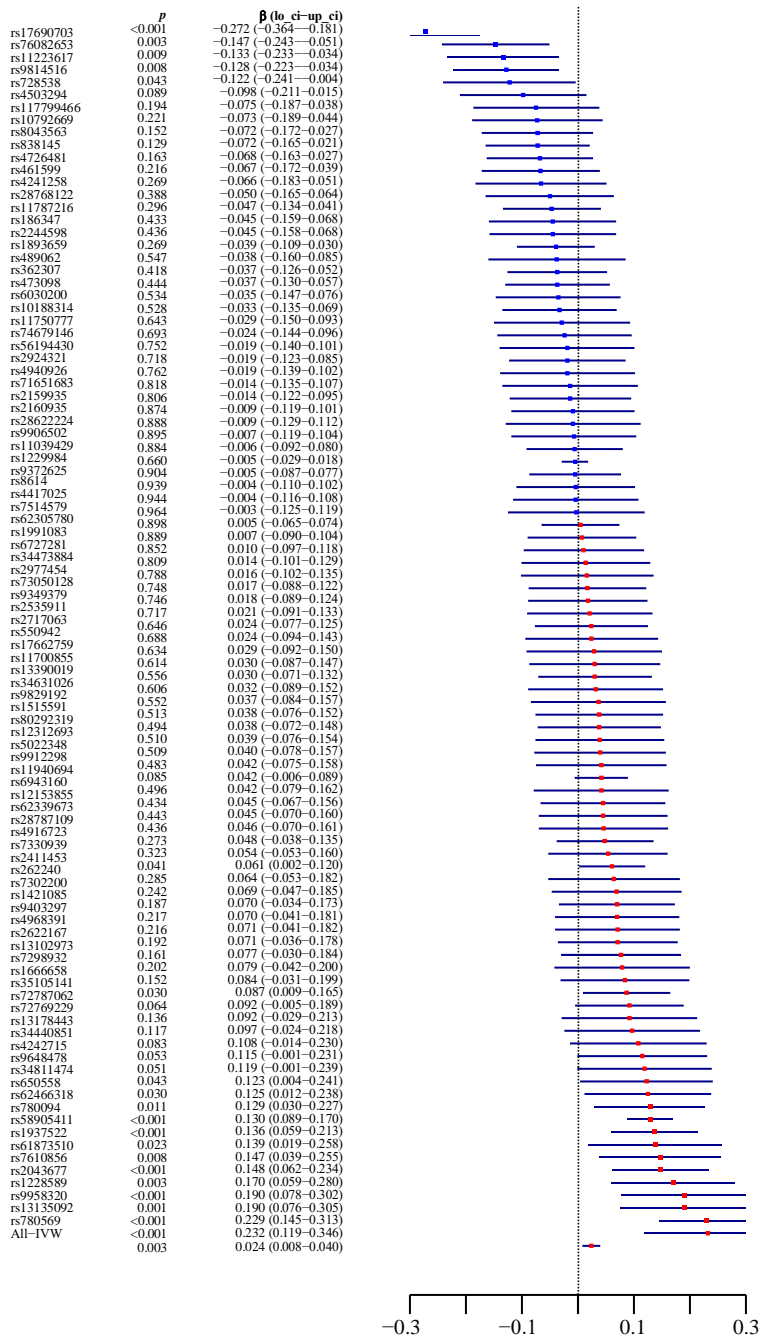
2			rs9624470	0.1553	0.0162	0.0287	0.282
3			rs9302428	0.302	0.0261	0.036	0.568
4	TEAI	SD	rs13282783	0.3072	0.0188	0.0508	0.564
5			rs132904	0.3301	0.0045	0.1026	0.558
6			rs72797284	0.4685	0.0000	0.2624	0.675
7			rs2645929	0.5362	0.0001	0.2678	0.805
8			rs9937354	0.8017	0.0000	0.5768	1.027
<b>1</b>			rs780093	-0.496	0.0000	-0.652	-0.34
2			rs12989746	-0.441	0.0001	-0.666	-0.22
3			rs13054099	-0.299	0.0060	-0.512	-0.09
4	COFI	IE	rs2472297	-0.121	0.0000	-0.17	-0.07
5			rs6469262	-0.279	0.0139	-0.502	-0.06
6			rs1057868	-0.159	0.0053	-0.271	-0.05
7			rs4410790	-0.097	0.0004	-0.15	-0.04
8			rs6063085	-0.244	0.0173	-0.444	-0.04

SNP – single nucleotide polymorphism,  $\beta$  – risk index, SE – standard error; lo\_ci – the lower limit of risk index, up\_ci – the upper limit of risk index, the standard line is the line of “X = 0”.

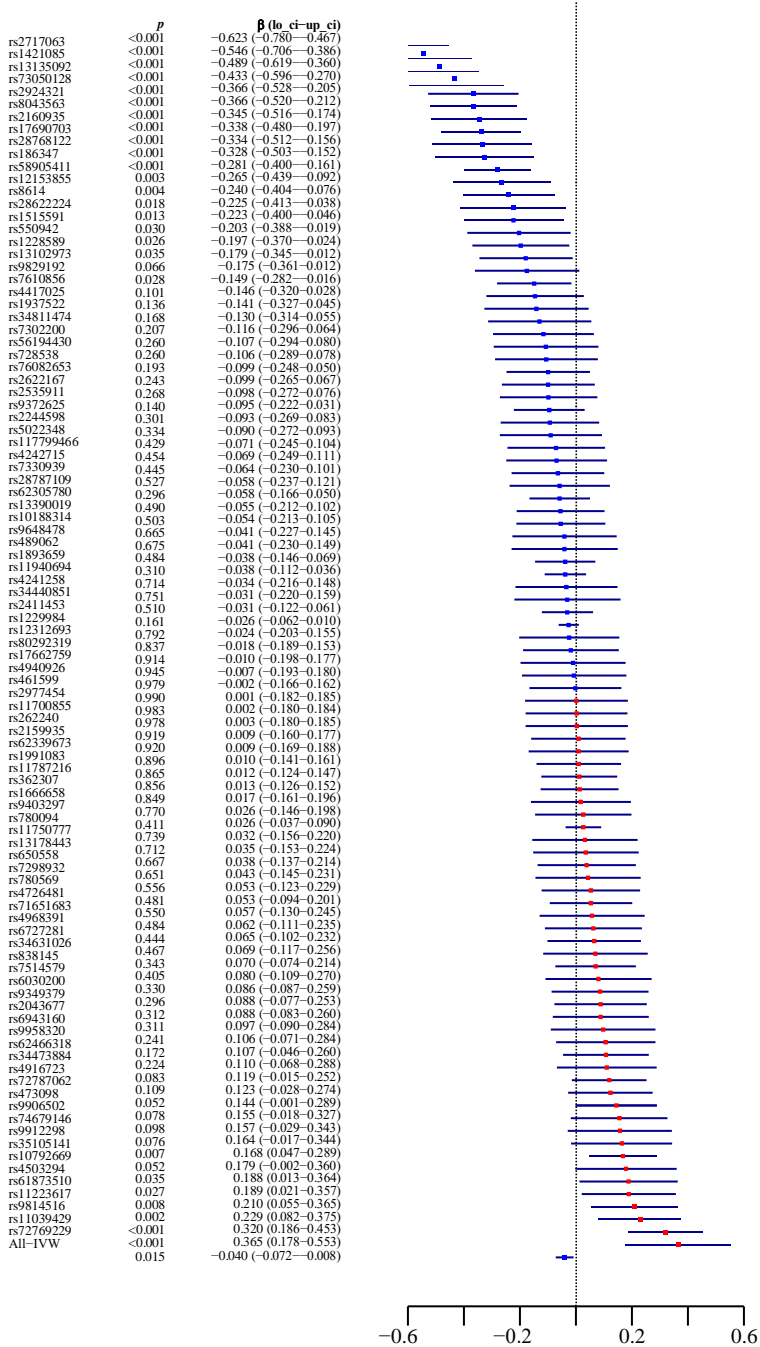
### Supplementary Figure S1. SNPs with ALI as the exposure, INS as the outcome



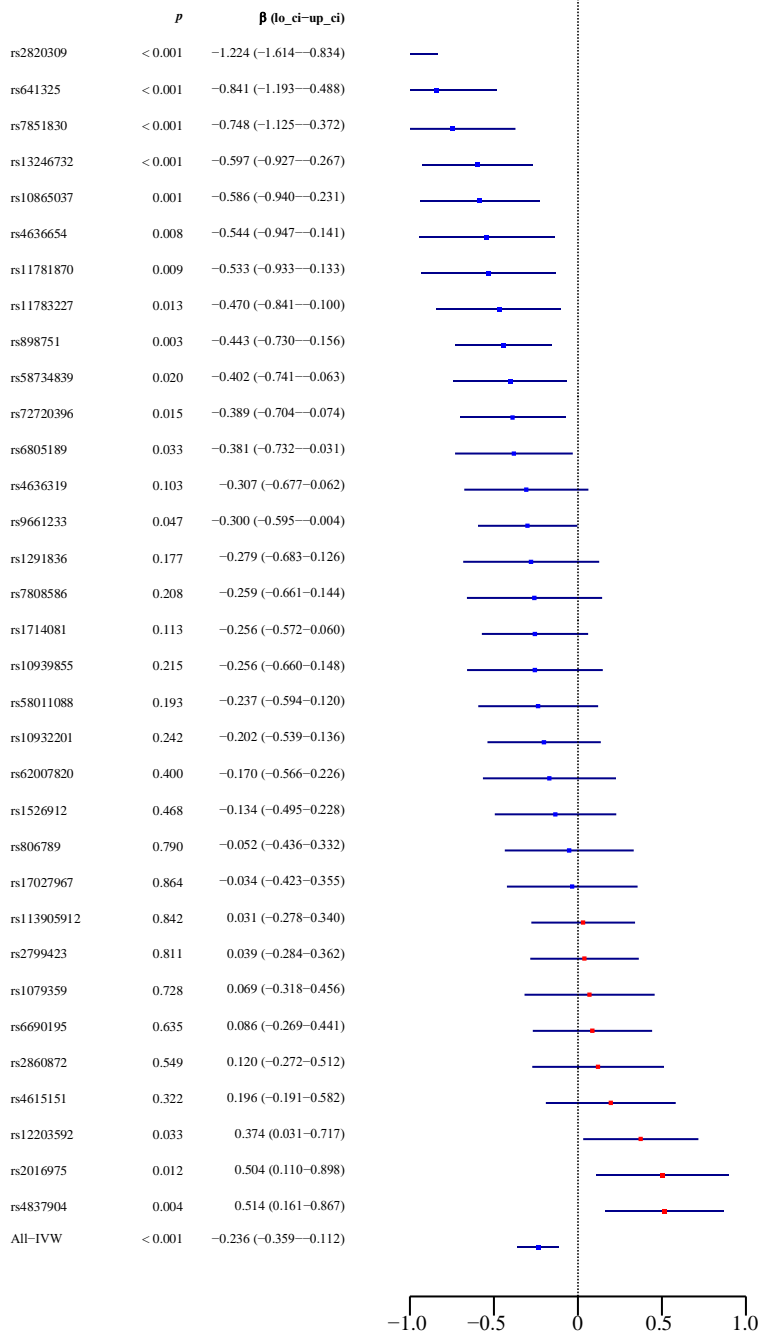
## Supplementary Figure S2. SNPs with ALF as the exposure, IE as the outcome



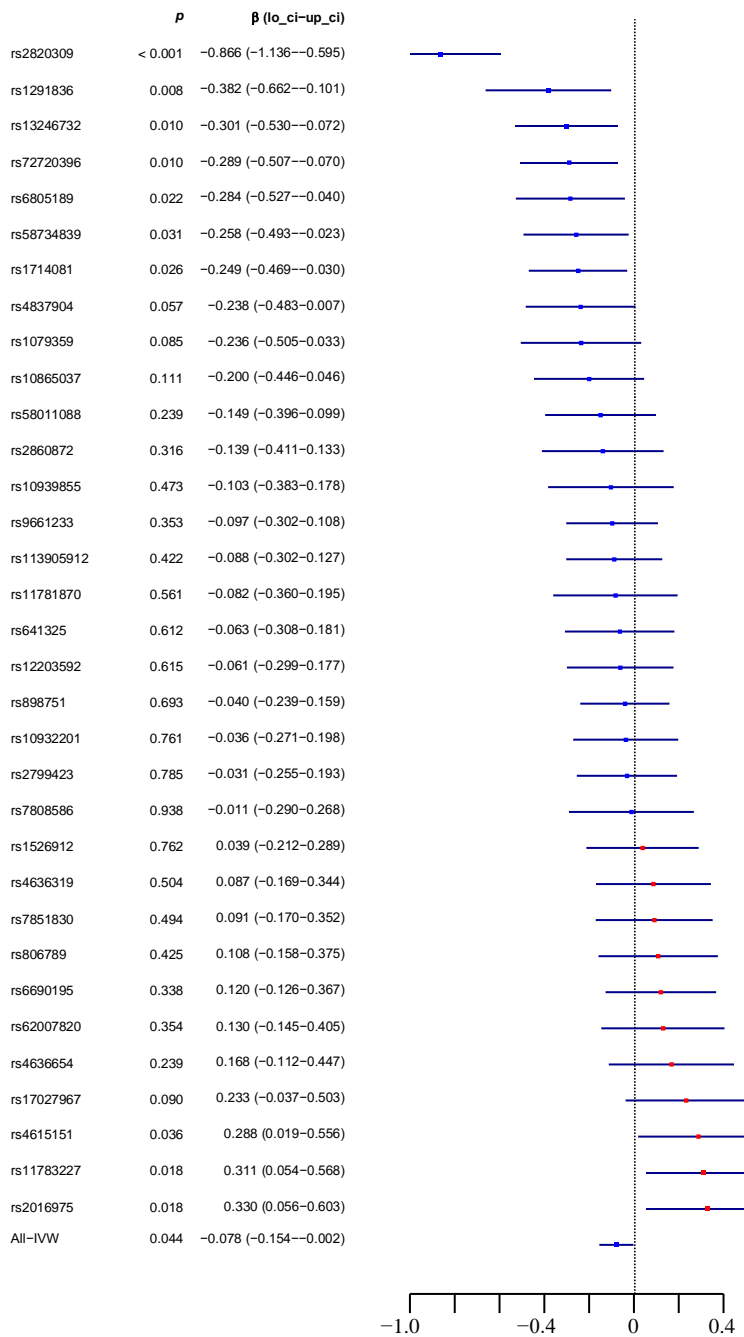
Supplementary Figure S3. SNPs with ALF as the exposure, SD as the outcome



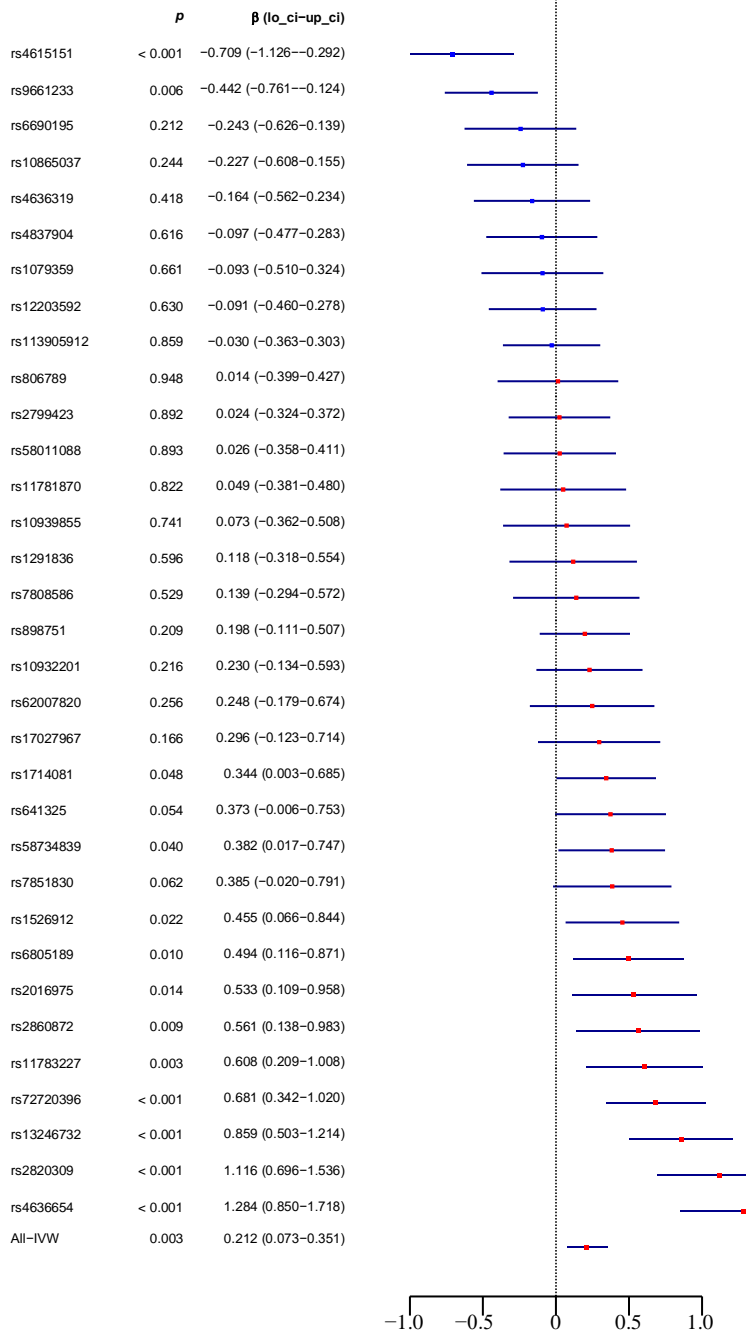
### Supplementary Figure S4. HAL as the exposure, INS as the outcome



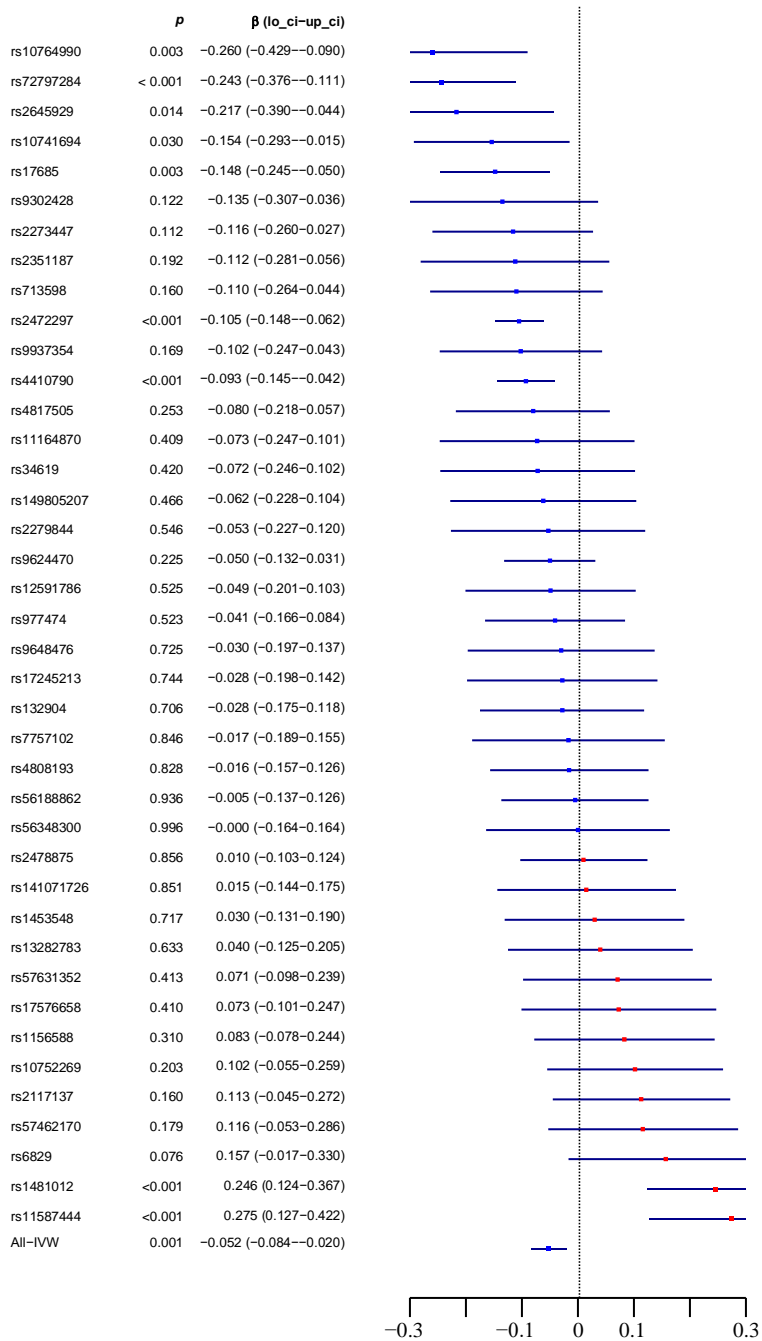
### Supplementary Figure S5. SNPs with HAL as the exposure, IE as the outcome



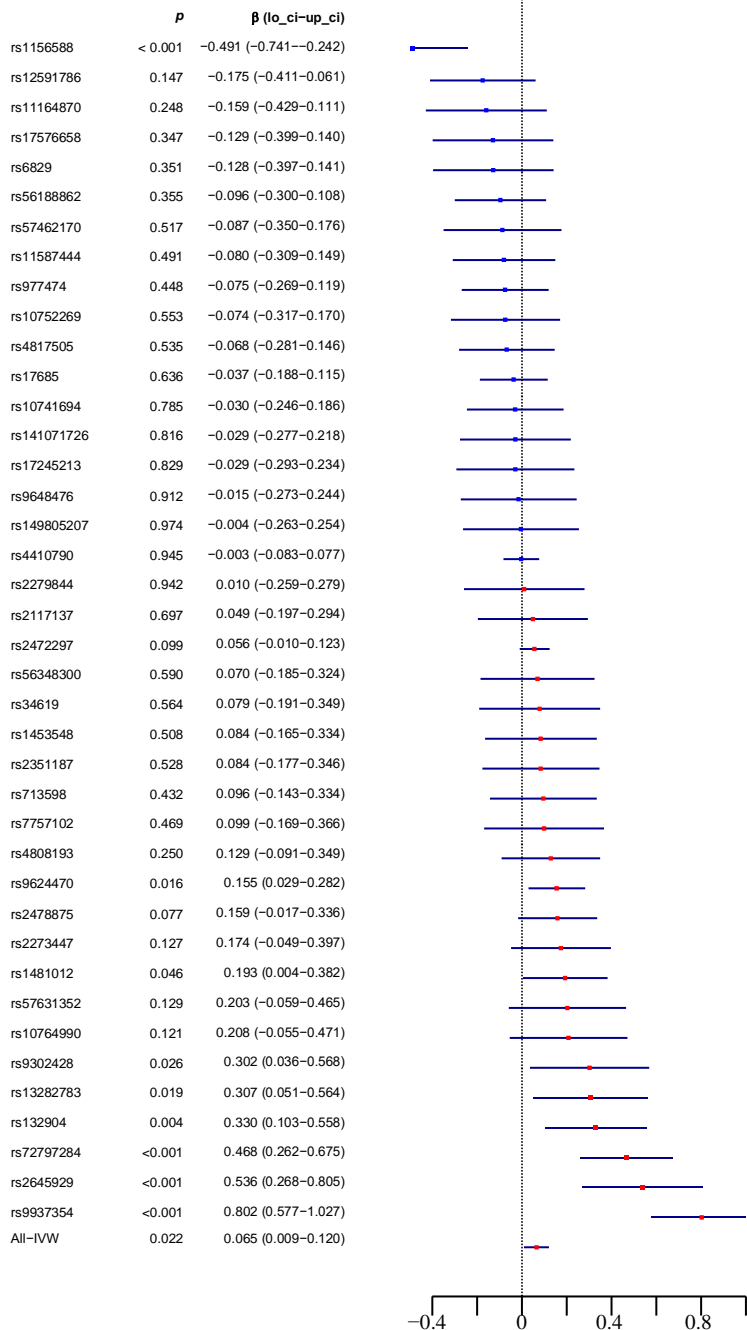
### Supplementary Figure S6. SNPs with HAL as the exposure, SD as the outcome



### Supplementary Figure S7. SNPs with TEAI as the exposure, IE as the outcome



### Supplementary Figure S8. SNPs with TEAI as the exposure, SD as the outcome



### Supplementary Figure S9. SNPs with COFI as the exposure, IE as the outcome

