

Supplementary Table 1 List of HPV genetic instruments.

Exposure	CHR	POS	SNP	Effect allele	Other allele	Beta	SE	P-value	EAF	Sample	COVID-19 IV	Severe COVID-19 IV	Hospitalized COVID-19 IV	R ²	F
HPV-16	1	37479392	rs548661	T	G	-0.196	0.045	1.62E-05	0.38	997	rs548661	rs548661	rs548661	3.74E-05	18.775
HPV-16	1	71154117	rs1334997	T	C	0.192	0.046	3.39E-05	0.354	997	rs1334997	rs1334997	rs1334997	3.46E-05	17.347
HPV-16	1	194104179	rs6670046	T	C	0.443	0.097	5.15E-06	0.038	997	rs6670046	rs6670046	rs6670046	4.19E-05	21.013
HPV-16	1	242522042	rs2919024	A	G	-0.781	0.185	2.77E-05	0.013	997	rs2919024	rs2919024	rs2919024	3.54E-05	17.732
HPV-16	2	55970893	rs17047217	A	G	-0.715	0.175	4.72E-05	0.03	997	rs17047217	rs17047217	rs17047217	3.33E-05	16.703
HPV-16	2	60866057	rs6719607	G	A	0.245	0.059	3.55E-05	0.178	997	rs6719607	rs6719607	rs6719607	3.44E-05	17.256
HPV-16	2	179421694	rs9808377	A	G	-0.252	0.053	1.96E-06	0.25	997	rs9808377	rs9808377	rs9808377	4.57E-05	22.906
HPV-16	3	54264197	rs9830760	T	C	0.304	0.067	6.67E-06	0.135	997	rs9830760	rs9830760	rs9830760	4.09E-05	20.503
HPV-16	3	145529197	rs2864426	C	G	-0.237	0.057	3.69E-05	0.165	997	~	~	~	3.43E-05	17.181
HPV-16	5	27610789	rs7447521	C	A	0.374	0.091	4.18E-05	0.079	997	rs7447521	rs7447521	rs7447521	3.38E-05	16.941
HPV-16	6	24931083	rs216259	G	A	0.212	0.050	2.14E-05	0.284	997	rs216259	rs216259	rs216259	3.64E-05	18.241
HPV-16	6	65433784	rs985915	G	A	0.224	0.054	3.59E-05	0.201	997	rs985915	rs985915	rs985915	3.44E-05	17.231
HPV-16	6	81380831	rs2503718	A	G	0.560	0.126	9.99E-06	0.051	997	rs2503718	rs2503718	rs2503718	3.93E-05	19.714
HPV-16	9	1358244	rs682927	G	T	-0.205	0.046	8.34E-06	0.437	997	rs682927	rs682927	rs682927	4.00E-05	20.070
HPV-16	9	95589160	rs7850036	C	T	0.244	0.053	4.49E-06	0.203	997	rs7850036	rs7850036	rs7850036	4.24E-05	21.280
HPV-16	11	80884316	rs10897761	T	C	-0.441	0.094	3.55E-06	0.066	997	rs10897761	rs10897761	rs10897761	4.34E-05	21.743
HPV-16	13	48650492	rs41284209	A	G	0.295	0.066	9.84E-06	0.134	997	rs41284209	rs41284209	rs41284209	3.94E-05	19.749
HPV-16	13	50005050	rs28692644	A	G	0.351	0.085	3.60E-05	0.074	997	rs28692644	rs28692644	rs28692644	3.44E-05	17.231
HPV-16	13	109504132	rs7339361	T	C	0.341	0.078	1.34E-05	0.066	997	rs7339361	rs7339361	rs7339361	3.82E-05	19.141
HPV-16	14	87365603	rs8016986	C	T	-0.335	0.072	3.90E-06	0.115	997	rs8016986	rs8016986	rs8016986	4.30E-05	21.548
HPV-16	17	9713505	rs4791360	G	A	-0.201	0.046	1.56E-05	0.348	997	rs4791360	rs4791360	rs4791360	3.76E-05	18.853
HPV-16	18	37304602	rs1513688	C	T	0.229	0.054	2.46E-05	0.242	997	rs1513688	rs1513688	rs1513688	3.58E-05	17.961
HPV-16	18	44040660	rs17766830	T	C	0.211	0.050	2.44E-05	0.262	997	rs17766830	rs17766830	rs17766830	3.59E-05	17.978
HPV-18	1	75700632	rs12743566	A	G	0.332	0.081	4.90E-05	0.089	997	rs12743566	rs12743566	rs12743566	3.32E-05	16.630
HPV-18	1	168683476	rs35449613	C	T	0.393	0.092	2.34E-05	0.029752	997	rs35449613	rs35449613	rs35449613	3.60E-05	18.062
HPV-18	2	116955767	rs4849449	C	T	-0.195	0.044	1.07E-05	0.423	997	rs4849449	rs4849449	rs4849449	3.91E-05	19.581
HPV-18	4	58935390	rs930937	G	T	0.334	0.076	1.32E-05	0.09	997	rs930937	rs930937	rs930937	3.82E-05	19.176
HPV-18	5	6621031	rs4702371	A	G	-0.221	0.049	5.86E-06	0.327	997	rs4702371	rs4702371	rs4702371	4.14E-05	20.757

HPV-18	5	79809658	rs249011	A	T	-0.193	0.043	1.00E-05	0.468	997	~	~	~	3.93E-05	19.714
HPV-18	5	118837658	rs257969	T	C	-0.193	0.046	3.31E-05	0.367	997	rs257969	rs257969	rs257969	3.47E-05	17.389
HPV-18	8	73443576	rs4738265	C	T	0.223	0.049	6.16E-06	0.277	997	rs4738265	rs4738265	rs4738265	4.12E-05	20.666
HPV-18	8	84495551	rs7820513	G	A	-0.239	0.054	1.09E-05	0.175	997	rs7820513	rs7820513	rs7820513	3.90E-05	19.545
HPV-18	10	59333071	rs2393316	A	G	0.577	0.138	3.12E-05	0.017	997	rs2393316	rs2393316	rs2393316	3.49E-05	17.506
HPV-18	11	73259543	rs11235802	A	C	-0.317	0.075	2.24E-05	0.091	997	rs11235802	rs11235802	rs11235802	3.62E-05	18.139
HPV-18	12	3818665	rs241993	T	C	-0.204	0.043	2.70E-06	0.498	997	rs241993	rs241993	rs241993	4.44E-05	22.288
HPV-18	16	8510914	rs3901280	T	C	0.179	0.044	4.63E-05	0.475	997	rs3901280	rs3901280	rs3901280	3.34E-05	16.744

Abbreviations: HPV-16: human papilloma virus E7 type 16; HPV-18: human papilloma virus E7 type 18; appendicular lean mass; CHR: chromosome; POS: position; SNP: single nucleotide polymorphism; SE:

standard error of beta; EAF: effect allele frequency; ~ palindrome SNP.

Supplementary Table 2 List of COVID-19 genetic instruments

Exposure	CHR	POS	SNP	Effect allele	Other allele	Beta	SE	P-value	EAF	Sample	HPV-16 IVs	HPV-18 IVs	R ²	F
COVID-19	1	155105882	rs4971066	G	T	-0.077	0.013	1.02E-08	0.1777	1,683,768	—	—	1.95E-05	32.81576
COVID-19	3	101433440	rs10936744	T	C	-0.063	0.010	3.51E-10	0.3588	1,683,768	rs34376498#	rs34376498#	2.34E-05	39.36792
COVID-19	3	45847241	rs17078348	G	A	0.092	0.016	1.20E-08	0.0997	1,683,768	—	—	1.93E-05	32.49434
COVID-19	3	45838013	rs2271616	T	G	0.156	0.015	3.61E-25	0.1181	1,683,768	—	—	6.38E-05	107.4253
COVID-19	9	136142355	rs643434	A	G	0.101	0.010	1.29E-23	0.371	1,683,768	rs643434	rs643434	5.96E-05	100.3165
COVID-19	12	113406945	rs757405	A	T	0.069	0.011	1.64E-10	0.7092	1,683,768	—	—	2.43E-05	40.85888
COVID-19	21	34611571	rs12482060	G	C	0.062	0.011	3.96E-09	0.3375	1,683,768	—	—	2.06E-05	34.64591
Hospitalized COVID-19	3	45889921	rs35081325	T	A	0.488	0.032	3.68E-54	0.08122	1,887,658	—	—	1.27E-04	240.1278
Hospitalized COVID-19	9	136149229	rs505922	C	T	0.112	0.019	4.42E-09	0.3501	1,887,658	rs505922	rs505922	1.82E-05	34.43301
Hospitalized COVID-19	12	113357442	rs2660	A	G	0.116	0.019	2.00E-09	0.6902	1,887,658	rs2660	rs2660	1.91E-05	35.97152
Hospitalized COVID-19	19	4719443	rs2109069	A	G	0.151	0.020	2.94E-14	0.3227	1,887,658	—	—	3.06E-05	57.77857
Hospitalized COVID-19	21	34615210	rs13050728	C	T	-0.168	0.020	7.44E-17	0.6528	1,887,658	—	—	3.68E-05	69.55039
Severe COVID-19	3	45889921	rs35081325	T	A	0.626	0.045	5.75E-45	0.07529	1,388,342	—	—	1.43E-04	197.9816
Severe COVID-19	6	31121232	rs111837807	C	T	0.295	0.043	5.66E-12	0.0996	1,388,342	rs17190776#	rs17190776#	3.42E-05	47.44419
Severe COVID-19	7	107607902	rs2237698	T	C	0.237	0.040	2.41E-09	0.08971	1,388,342	—	—	2.56E-05	35.60821
Severe COVID-19	12	113382977	rs2384074	T	C	0.198	0.028	2.10E-12	0.6756	1,388,342	rs2285932#	rs2285932#	3.56E-05	49.38281
Severe COVID-19	12	103014757	rs10860891	A	C	-0.239	0.040	1.64E-09	0.8855	1,388,342	—	—	2.62E-05	36.36407
Severe COVID-19	17	47940666	rs77534576	T	C	0.460	0.075	8.52E-10	0.03465	1,388,342	—	—	2.71E-05	37.63604
Severe COVID-19	19	4719443	rs2109069	A	G	0.257	0.028	6.12E-20	0.3287	1,388,342	—	—	6.02E-05	83.5852
Severe COVID-19	21	34615210	rs13050728	C	T	-0.200	0.029	2.44E-12	0.6627	1,388,342	—	—	3.54E-05	49.09655

Abbreviations: HPV-16: human papilloma virus E7 type 16; HPV-18: human papilloma virus E7 type 18; appendicular lean mass; CHR: chromosome; POS: position; SNP: single nucleotide polymorphism;

SE: standard error of beta; EAF: effect allele frequency; # proxy SNP; —SNP cannot be found in outcome GWAS data.

Supplementary Table 3 MR estimate results of HPV on outcomes

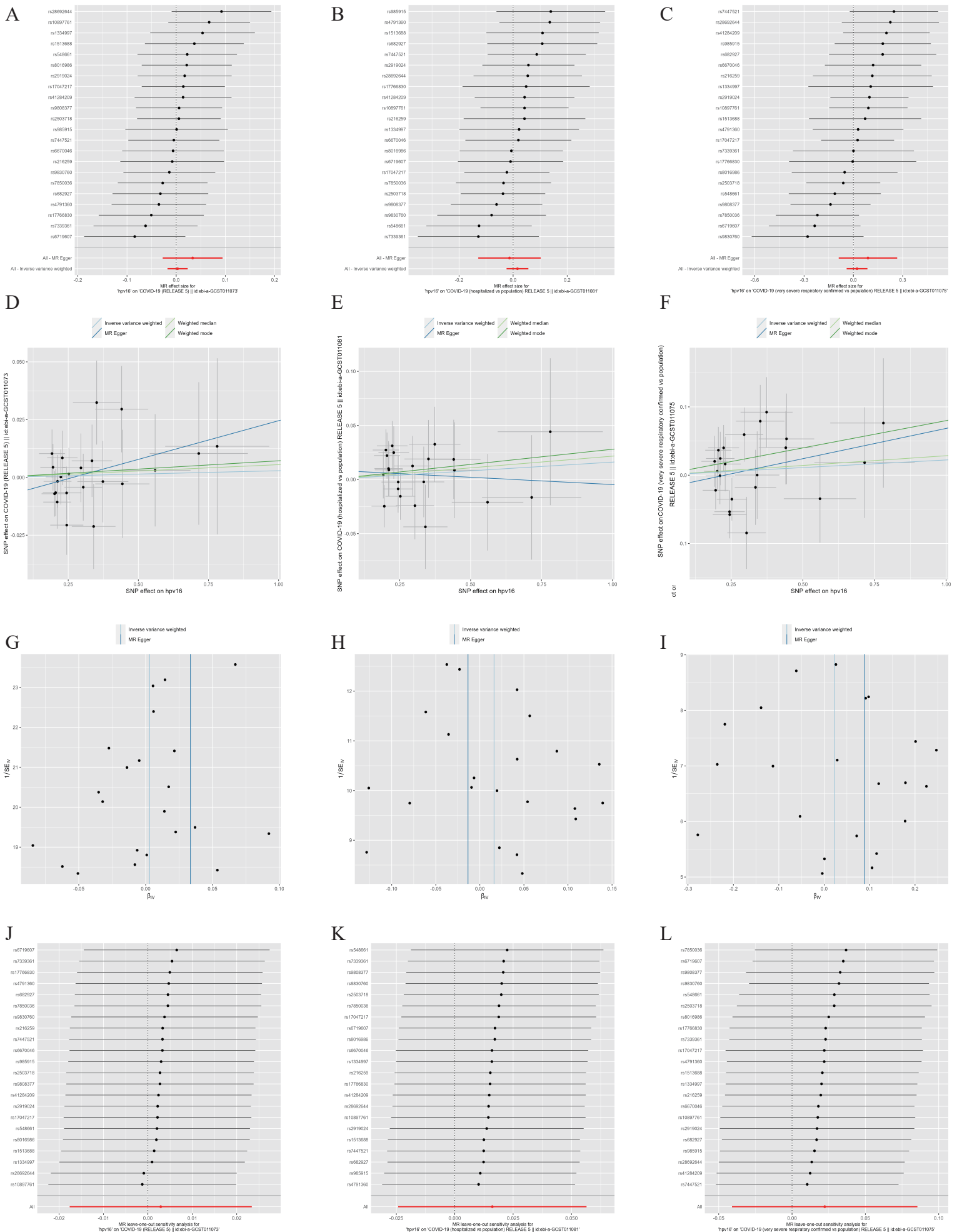
Exposure	Outcome	Methods	Nsnp	Beta	SE	P value	OR	or_lci95	or_uci95	Horizontal pleiotropy					Heterogeneity	
										MR-Egger regression			MR-PRESSO		Cochran's <i>Q</i>	P value
										Egger intercept	SE	P value	Global test P value	Pleiotropic SNP		
HPV-16	COVID-19 infection	Weighted median	22	0.006	0.014	0.690	1.006	0.979	1.033	-0.009	0.009	0.308	18.622	0.757	14.023	0.869
		MR Egger	22	0.033	0.031	0.294	1.034	0.973	1.099							
		Weighted mode	22	0.007	0.024	0.772	1.007	0.960	1.057							
		IVW	22	0.003	0.010	0.782	1.003	0.983	1.024							
HPV-16	Hospitalized COVID-19	Weighted median	22	0.022	0.027	0.423	1.022	0.969	1.077	0.009	0.016	0.599	14.089	0.934	12.279	0.932
		MR Egger	22	-0.013	0.059	0.822	0.987	0.879	1.108							
		Weighted mode	22	0.028	0.051	0.588	1.028	0.931	1.136							
		IVW	22	0.016	0.021	0.434	1.016	0.976	1.058							
HPV-16	Severe COVID-19	Weighted median	22	0.028	0.046	0.534	1.029	0.941	1.126	-0.020	0.026	0.442	25.355	0.426	23.026	0.343
		MR Egger	22	0.089	0.091	0.340	1.093	0.915	1.305							
		Weighted mode	22	0.080	0.084	0.351	1.083	0.919	1.276							
		IVW	22	0.022	0.032	0.490	1.023	0.960	1.089							
HPV-18	COVID-19 infection	Weighted median	12	-0.027	0.021	0.192	0.973	0.935	1.014	0.004	0.015	0.772	15.134	0.388	12.947	0.297
		MR Egger	12	-0.040	0.062	0.534	0.961	0.850	1.085							
		Weighted mode	12	-0.024	0.037	0.527	0.976	0.908	1.049							
		IVW	12	-0.022	0.016	0.164	0.978	0.948	1.009							
HPV-18	Hospitalized COVID-19	Weighted median	12	-0.057	0.042	0.174	0.945	0.871	1.025	0.030	0.027	0.292	13.039	0.554	10.957	0.447
		MR Egger	12	-0.155	0.112	0.197	0.856	0.687	1.067							
		Weighted mode	12	-0.067	0.068	0.348	0.935	0.818	1.069							
		IVW	12	-0.035	0.029	0.237	0.966	0.912	1.023							
HPV-18	Severe COVID-19	Weighted median	12	-0.037	0.057	0.512	0.963	0.862	1.077	0.018	0.040	0.668	6.024	0.959	4.647	0.947
		MR Egger	12	-0.122	0.169	0.486	0.885	0.636	1.232							
		Weighted mode	12	0.005	0.088	0.951	1.005	0.847	1.194							
		IVW	12	-0.050	0.044	0.251	0.951	0.873	1.036							

Abbreviations: HPV-16: human papilloma virus E7 type 16; HPV-18: human papilloma virus E7 type 18; SE: standard error of beta; IVW: inverse variance weighted.

Supplementary Table 4 MR estimate results of COVID-19 on outcomes

Exposure	Outcome	Methods	Nsnp	Beta	SE	P value	OR	or_lci95	or_uci95	Heterogeneity	
										Cochran's <i>Q</i>	P value
COVID-19 infection	HPV-16	IVW	2	0.314	0.486	0.519	1.368	0.528	3.549	1.574	0.210
Hospitalized COVID-19	HPV-16	IVW	2	0.250	0.379	0.510	1.284	0.611	2.698	1.727	0.189
Severe COVID-19	HPV-16	IVW	2	0.161	0.172	0.349	1.175	0.838	1.647	0.092	0.762
COVID-19 infection	HPV-18	IVW	2	-0.158	0.387	0.683	0.854	0.400	1.823	0.031	0.860
Hospitalized COVID-19	HPV-18	IVW	2	-0.550	0.635	0.386	0.577	0.166	2.002	4.881	0.027
Severe COVID-19	HPV-18	IVW	2	0.224	0.221	0.312	1.251	0.810	1.931	1.660	0.198

Abbreviations: HPV-16: human papilloma virus E7 type 16; HPV-18: human papilloma virus E7 type 18; SE: standard error of beta; IVW: inverse variance weighted.



Supplementary Figure 1. MR estimate results of HPV-16 on outcomes

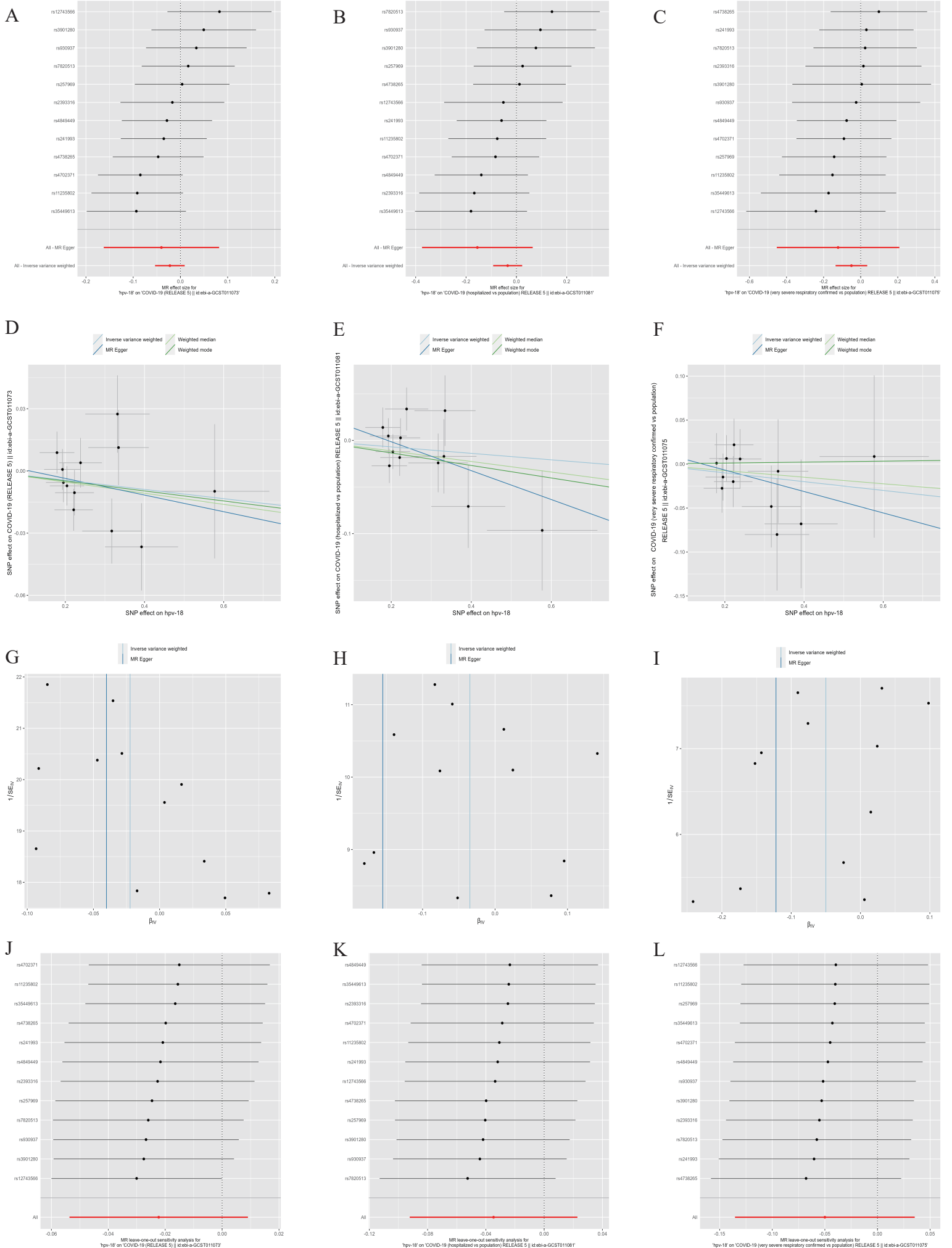
Note: A: Forest plot of HPV-16 on COVID-19; B: Forest plot of HPV-16 on hospitalized COVID-19; C: Forest plot of HPV-16 on severe COVID-19;

D: Scatter plot of HPV-16 on COVID-19; E: Scatter plot of HPV-16 on hospitalized COVID-19; F: Scatter plot of HPV-16 on severe COVID-19;

G: Funnel plot of HPV-16 on COVID-19; H: Funnel plot of HPV-16 on hospitalized COVID-19; I: Funnel plot of HPV-16 on severe COVID-19;

J: Leave-one-out plot of HPV-16 on COVID-19; K: Leave-one-out plot of HPV-16 on hospitalized COVID-19; L: Leave-one-out plot of HPV-16 on severe COVID-19;

MR: Mendelian randomization; HPV-16: human papillomavirus type 16; COVID-19: coronavirus disease 2019.



Supplementary Figure 2. MR estimate results of HPV-18 on outcomes

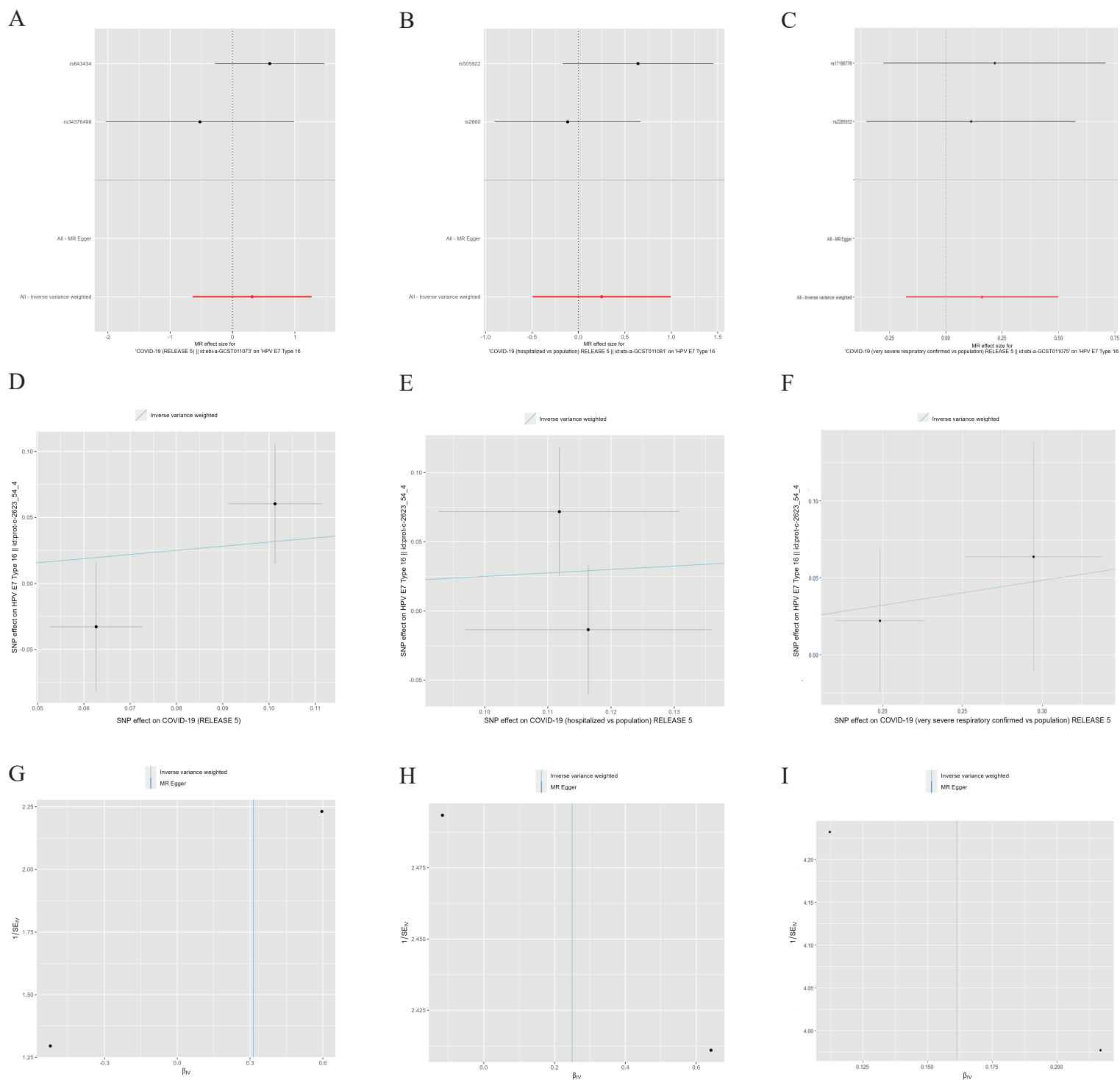
Note: A: Forest plot of HPV-18 on COVID-19; B: Forest plot of HPV-18 on hospitalized COVID-19; C: Forest plot of HPV-18 on severe COVID-19;

D: Scatter plot of HPV-18 on COVID-19; E: Scatter plot of HPV-18 on hospitalized COVID-19; F: Scatter plot of HPV-18 on severe COVID-19;

G: Funnel plot of HPV-18 on COVID-19; H: Funnel plot of HPV-18 on hospitalized COVID-19; I: Funnel plot of HPV-18 on severe COVID-19;

J: Leave-one-out plot of HPV-18 on COVID-19; K: Leave-one-out plot of HPV-18 on hospitalized COVID-19; L: Leave-one-out plot of HPV-18 on severe COVID-19;

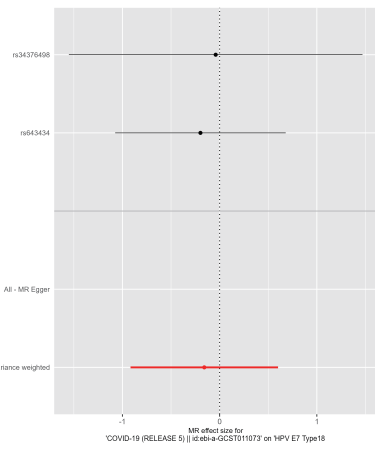
MR: Mendelian randomization; HPV-18: human papillomavirus type 18; COVID-19: coronavirus disease 2019.



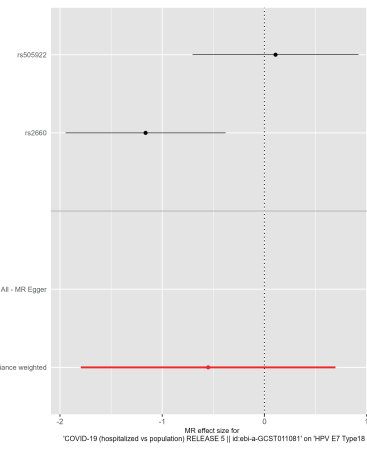
Supplementary Figure 3. MR estimate results of COVID-19 on HPV-16

Note: A: Forest plot of COVID-19 on HPV-16; B: Forest plot of hospitalized COVID-19 on HPV-16; C: Forest plot of severe COVID-19 on HPV-16; D: Scatter plot of COVID-19 on HPV-16; E: Scatter plot of hospitalized COVID-19 on HPV-16; F: Scatter plot of severe COVID-19 on HPV-16; G: Funnel plot of COVID-19 on HPV-16; H: Funnel plot of hospitalized COVID-19 on HPV-16; I: Funnel plot of severe COVID-19 on HPV-16; MR: Mendelian randomization; HPV-16: human papillomavirus type 16; COVID-19: coronavirus disease 2019.

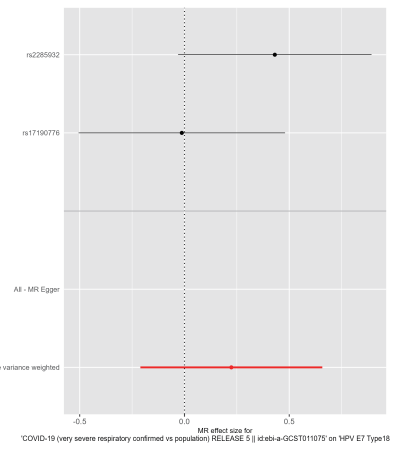
A



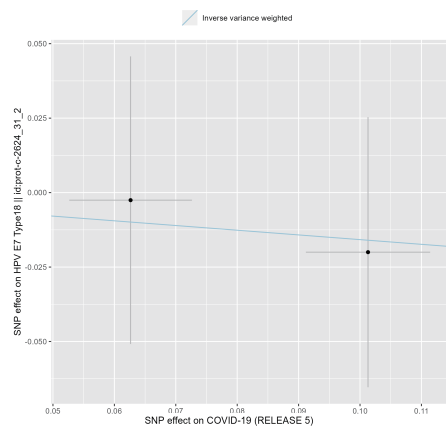
B



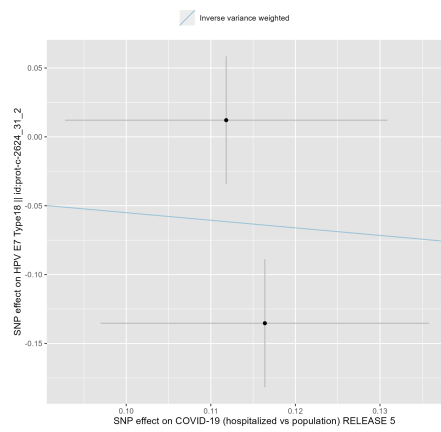
C



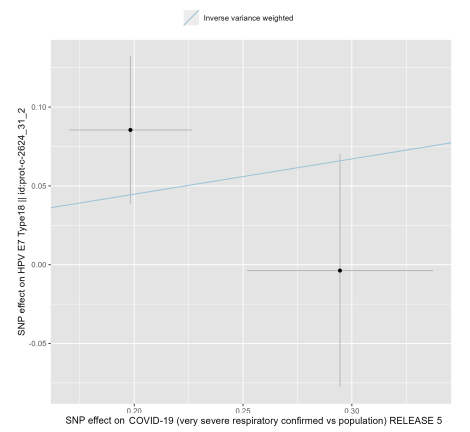
D



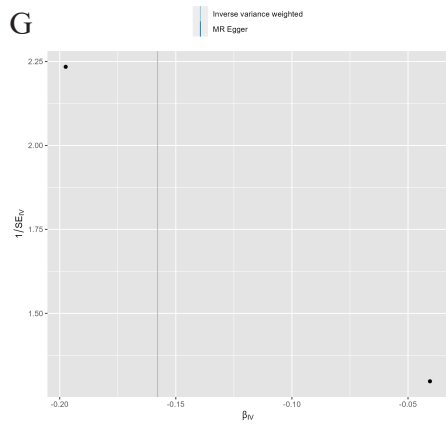
E



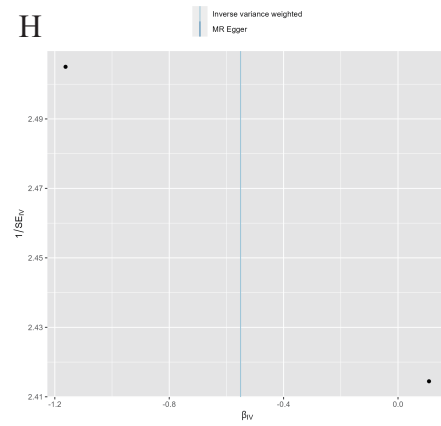
F



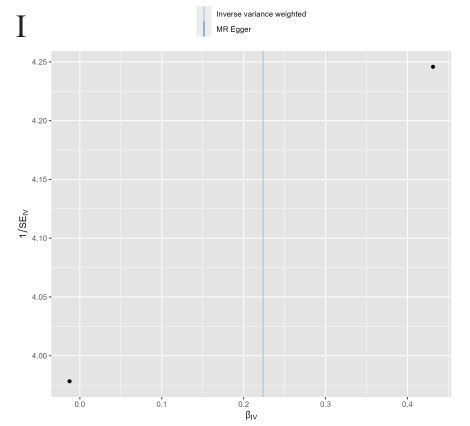
G



H



I



Supplementary Figure 4. MR estimate results of COVID-19 on HPV-18

Note: A: Forest plot of COVID-19 on HPV-18; B: Forest plot of hospitalized COVID-19 on HPV-18; C: Forest plot of severe COVID-19 on HPV-18; D: Scatter plot of COVID-19 on HPV-18; E: Scatter plot of hospitalized COVID-19 on HPV-18; F: Scatter plot of severe COVID-19 on HPV-18; G: Funnel plot of COVID-19 on HPV-18; H: Funnel plot of hospitalized COVID-19 on HPV-18; I: Funnel plot of severe COVID-19 on HPV-18; MR: Mendelian randomization; HPV-18: human papillomavirus type 18; COVID-19: coronavirus disease 2019.