Supplementary Online File

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Methods

Literature Search Strategy And Selection Criteria

On 8 April 2020, we used *PubMed* to conduct a literature review to obtain country-level ACE1 D-allele frequency estimates. Over 5000 publications were identified. These included a large number of systematic reviews of case control studies assessing the associations of various diseases with I/D polymorphism. These reviews typically tabulated the prevalence of the II, ID and DD genotypes in the control groups in all the studies included. To expedite the review process, we limited our search to systematic reviews that provided such tables and we extracted the prevalence of the D-allele in the control groups only. We used the following *MeSH* terms: 'ACE' OR 'angiotensin-converting enzyme' AND ('polymorphism' OR 'deletion' OR 'insertion') AND ('systematic review' OR ‘metanalysis’ OR 'meta-analysis’).

Inclusion and exclusion criteria

Studies were eligible for inclusion if they used systematic review methodology and reported at least the frequency of II genotype in groups of controls in more than one country. Only articles in English were considered eligible. The relevant data was extracted from each paper including frequency of II, ID and DD, country research was conducted in and year research was published. Only samples sizes of 50 or above were included. All duplicates were deleted.

Study flow and data synthesis

We identified 361 studies. A total of 52 systematic reviews that included results from more than one country were evaluated in detail. After excluding reviews that did not provide adequate data on ACE1 allele frequency, inadequately sized control groups and duplicates of other studies, we were left with 21 systematic reviews with useable data (Table S2). These reviews provided 223 unique ACE1 D-allele frequency estimates from 50 countries, including 31 high income countries. We used this data to calculate country level median frequency of the D-allele.

Definitions and sources of variables:

Mortality/capita. The COVID-19 attributable mortality per 100 000 inhabitants. This data was obtained from the World of Meters data repository on 8 April 2020: https://www.worldometers.info/coronavirus/

Cases/capita. The cumulative number of cases of COVID-19 infection per 100 000 inhabitants on 8 April 2020 per country. This data was obtained from the World of Meters data repository on 8 April 2020: https://www.worldometers.info/coronavirus/

Tests/capita. Cumulative number of nucleic acid amplification SARS CoV-2 tests conducted per country per 100 000 inhabitants up till 8 April 2020. This data was obtained from the World of Meters data repository on 8 April 2020: https://www.worldometers.info/coronavirus/

Age of epidemic. The date the first case of COVID-19 was diagnosed in each country. This was measured in days after the first COVID-19 case was officially reported in China (10 January 2020). This data was obtained from the ECDC data repository on 8 April 2020: https://www.ecdc.europa.eu/en/geographical-distribution-2019-ncov-cases

Regions: Countries were categorized into world regions according to the WHO world regions. https://www.who.int/healthinfo/global_burden_disease/definition_regions/en/. For the comparisons of European regions, we used the four European Regions as defined by the United Nations Geoscheme for Europe.
https://unstats.un.org/unsd/methodology/m49/

Income category: We used the World Bank income categorization schema. Countries are divided among income groups according to 2018 gross national income (GNI) per capita, calculated using the World Bank Atlas method. The groups are: low income, $1,025 or less; lower middle income, $1,026 - 3,995; upper middle income, $3,996 - 12,375; and high income, $12,375 or more. https://datahelpdesk.worldbank.org/

Data analysis

Multiple linear regression was used to analyze the association between the COVID-19 mortality rate/100 000 inhabitants and COVID-19 tests/capita (number of tests/100 000 inhabitants) controlling for the cumulative number of COVID-19 infections/100 000 inhabitants (cases/capita), the age of the epidemic (number of days between first case reported and 8 April), national health expenditure per capita and WHO world region. The most recent data available as of 8 April 2020 was used for all variables. Sensitivity analyses were conducted limiting the analysis to countries whose epidemics were older than 15 March 2020. A p-value of < 0.01 was considered statistically significant. The analyses were performed in STATA version 16 (Stata Corp, College Station, Tx).

Table S1. World Bank Income category (Income; 1=high- and 2=upper-middle-income), cumulative number of cases of COVID-19/100 000 inhabitants (Cum. Cases), cumulative number of deaths attributable to COVID-19/100 000 (Cum. Deaths), date first COVID-19 case reported (Age Epi.), prevalence (%) of D-allele of the angiotensin-converting enzyme gene (D-allele) and number tested for COVID-19/100 000 (Test Intensity), in 41 high- and upper-middle-income-countries.

Country	Income	Cum. cases	Cum. Deaths	Age epi.	D-allele	Test intensity
Australia	1	23.6	.2	24jan2020	80.55	1252.4
Austria	1	143.2	3	24feb2020	80.8	1340.8
Belgium	1	201.9	19.3	03feb2020	81	726.9
Czech Republic	1	47	.8	29feb2020	76.05	921.5
Denmark	1	93	3.8	26feb2020	77	1008.6
Finland	1	44.9	.7	28jan2020	75.7	658.8
France	1	167.1	15.8	23jan2020	82	343.6
Germany	1	130.5	2.5	26jan2020	78.6	1096.2
Greece	1	18.1	.8	25feb2020	90.4	274.2
Hong Kong	1	12.8	.05	22jan2020	67.2	1290
Hungary	1	9.3	.6	03mar2020	75.5	266.5
Israel	1	108.6	.8	20feb2020	89.5	1355.7
Italy	1	224.3	28.3	29jan2020	86	1249.5
Japan	1	3.4	.07	14jan2020	59	43.7
Kuwait	1	20	.02	23feb2020	84.45	.
Latvia	1	30.6	.1	01mar2020	73.9	1274.3
Lithuania	1	33.5	.6	27feb2020	73.9	1106
Macao	1	6.9	0	21jan2020	66.15	306.8
Netherlands	1	119.9	13.1	26feb2020	80	505.3
Poland	1	13.2	.4	03mar2020	79.7	262.3
Portugal	1	128.9	3.7	01mar2020	84	1263
Singapore	1	27.7	.1	22jan2020	55	1111
Slovakia	1	12.5	.04	05mar2020	77.8	360.5
South Korea	1	20.3	.4	19jan2020	69.75	931
Spain	1	313.7	31.1	30jan2020	84.5	759.3
Sweden	1	83.4	6.8	30jan2020	73	541.6
Switzerland	1	263.3	9.9	24feb2020	70.9	1986.7
Taiwan	1	1.6	.02	20jan2020	45.5	170.9
United Arab Emirates	1	26.9	.1	28jan2020	94	5451.7
United Kingdom	1	81.4	9.1	30jan2020	76.7	392.9

Country	Income	Cum. cases	Cum. Deaths	Age epi.	D-allele	Test intensity
United States	1	122.1	3.9	20jan2020	80.05	636.7
Brazil	2	6.7	.3	24feb2020	72.3	25.8
China	2	5.7	.2	10jan2020	66.15	306.8
Iran	2	76.9	4.8	18feb2020	81	251.4
Jamaica	2	2.1	.1	09mar2020	82.6	18.2
Lebanon	2	8.4	.3	20feb2020	85.55	158.3
Malaysia	2	12.7	.2	24jan2020	55.5	179.9
Romania	2	24.7	1.1	25feb2020	80	245.4
Russian Federation	2	5.9	.04	30jan2020	77.4	623.7
South Africa	2	2.9	.02	04mar2020	80.15	98
Turkey	2	40.4	.9	09mar2020	81.8	264.3

Table S2. Data from 21 systematic reviews as regards ACE1 D/I frequencies in individual studies in 50 countries.

Country	First Author	Year	N	D-allele freq	I/I (N)	I/D (N)	D/D (N)	Systematic Review
Australia	Wong	1995	72	84.7	11	43	18	21
Australia	Gayagay	1998	118	83.1	20	58	36	7
Australia	Taylor	1999	685	78	151	336	199	7
Australia	Doolan	2004	200	76	48	94	58	5
Austria	Weger	2007	182	80.8	35	93	54	17
Belgium	Gu	1994	109	81	NA	NA	NA	1
Brazil	Sprovieri	2005	65	72.3	18	39	8	10
China	Iwai	1994	122	59	NA	NA	NA	1
China	Ohishi	1994	175	63	NA	NA	NA	1
China	Guan	1997	150	94	9	59	82	10
China	Young	1998	183	61	NA	NA	NA	1
China	Jianqing	1999	70	70	21	19	30	11
China	Wu	1999	70	70	21	19	30	3
China	Su	1999	116	79.3	24	40	52	6
China	Wong	1999	108	54.6	49	46	13	16
China	Dang	2000	107	83.2	18	36	53	6
China	Cai	2000	56	53.6	26	23	7	5
China	Gao	2000	61	49.2	31	18	12	5
China	Li	2001	63	55.6	28	23	12	5
China	Lee	2001	96	65.6	33	48	15	11
China	Lee	2001	177	72.9	48	15	114	3
China	Thomas	2001	119	67	NA	NA	NA	1
China	Lv	2002	116	79.3	24	40	52	10
China	Yang	2003	50	80	10	21	19	11
China	Zou	2003	53	47.2	28	20	5	5
China	Huijuan	2003	105	66.7	35	36	34	11
China	Wang	2003	105	66.7	35	36	34	3
China	Gu	2003	159	69.2	49	85	25	2
China	Chang	2003	116	48.3	60	42	14	16
China	Lu	2003	365	56.2	160	165	40	3
China	Ruan-jia	2004	79	79.7	16	35	28	11
China	Ye	2004	79	79.7	16	35	28	3
China	Liu	2005	60	63.3	22	28	10	20
China	Wang	2005	101	56.4	44	41	16	19
China	Chan	2005	123	60.2	49	61	13	9
China	Yan	2005	352	59	NA	NA	NA	1
China	Jerng	2006	210	51	103	90	17	9
China	Liu	2007	50	64	18	21	11	20
China	Meijun	2008	81	79	17	36	28	11
China	Shi	2008	81	79	17	36	28	3

Country	First Author	Year	N	D-allele freq	I/I (N)	I/D (N)	D/D (N)	Systematic Review
China	Zhang	2008	57	64.9	20	28	9	2
China	Xiao-Hong	2008	98	75.5	24	48	26	11
China	Tang	2009	98	75.5	24	48	26	3
China	Shi	2011	198	66.7	66	100	32	4
China	Liu	2011	299	68.2	95	158	46	3
China	Wang	2012	151	60.3	60	71	20	3
China	Su	2013	63	73	17	19	27	4
China	Yang	2014	668	54.5	304	299	65	17
China	Wang	2016	74	64.9	26	33	15	16
China	Huang	2017	256	53.5	119	111	26	17
China	Liu	2018	189	76.7	44	71	74	21
Czech Republic	Vasku	1999	208	78.4	45	104	59	17
Czech Republic	McGrath	2001	179	73.7	47	94	38	13
Denmark	Bladbjerg	1999	199	77	NA	NA	NA	1
Egypt	Saber-Ayad	2010	50	80	10	34	6	6
Egypt	Naglaa	2012	93	82.8	16	52	25	8
Finland	Pietinalho	1999	70	75.7	17	34	19	13
France	Kreft-Jais	1994	71	78.9	15	29	27	3
France	Girerd	1998	340	83	NA	NA	NA	1
France	Blanche	2001	560	82	NA	NA	NA	1
Germany	Schunkert	1994	290	83.4	48	170	72	21
Germany	Pfeufer	1996	50	28	36		14	5
Germany	Schmidt	1997	256	78.9	54	119	83	16
Germany	Ringel	1997	259	78	57	134	68	16
Germany	Filler	2001	200	82	NA	NA	NA	1
Germany	Bucholz	2003	127	79.5	26	71	30	14
Germany	Ebert	2005	144	77.8	32	72	40	4
Germany	Kolsch	2005	348	81.3	65	185	98	20
Germany	Ebert	2005	145	77	NA	NA	NA	1
Germany	Adamzik	2007	200	80.5	39	106	55	9
Germany	Rocken	2007	189	78.3	41	95	53	3
Germany	Pabst	2009	158	75.3	39	69	50	2
Greece	Nikiteas	2007	102	94.1	6	44	52	3
Greece	Papadimitriou	2009	181	86.7	24	100	57	7
Hong Kong	Thomas	2001	119	67.2	39	61	19	16
Hungary	Barkai	2005	120	73	NA	NA	NA	1
Hungary	Zsom	2011	200	78	44	110	46	16
India	Ahsan	2004	66	65.2	23	33	10	2
India	Patil	2005	300	74	NA	NA	NA	1
India	Rai	2008	164	71.3	47	87	30	5
India	Vettriselvi	2008	120	54.2	55	38	27	14
India	Shenoy	2010	101	74.3	26	54	21	7
Indonesia	Sasongko	2005	68	91.2	6	21	41	6

Country	First Author	Year	N	D-allele freq	I/I (N)	I/D (N)	D/D (N)	Systematic Review
Iran	Bagheri	2010	63	81	12	27	24	15
Iran	Aarabi	2011	94	76.6	22	47	25	14
Iran	Poursadegh	2013	50	86	7	28	15	15
Iran	Bahramali	2016	88	71.6	25	43	20	21
Iran	Tanhapour	2018	100	92	8	50	42	17
Israel	Frishberg	1998	216	61.1	84	110	22	6
Israel	Amir	2007	56	85.7	8	28	20	7
Israel	Amir	2007	191	90.6	18	87	86	7
Israel	Amir	2007	247	89.5	26	115	106	7
Israel	Eynon	2009	240	90	24	110	106	7
Italy	Margaglione	1996	109	84.4	17	49	43	18
Italy	Scacchi	1998	153	86.9	20	73	60	20
Italy	Perticone	1999	104	87.5	13	56	35	21
Italy	Fatin	2000	70	71.4	20	30	20	14
Italy	Zuliani	2001	54	85.2	8	30	16	20
Italy	Scanavini	2002	152	87.5	19	66	67	7
Italy	Panza	2002	252	87	NA	NA	NA	1
Italy	Di Pasquale	2005	684	82	NA	NA	NA	1
Italy	Sessa	2011	61	83.6	10	23	28	7
Italy	Massidda	2012	106	86.8	14	38	54	7
Jamaica	Scott	2010	304	82.6	53	143	108	7
Japan	Furuya	1994	71	64.8	25	35	11	11
Japan	Iwai	1994	72	52.8	34	31	7	21
Japan	Ishigami	1995	87	49	NA	NA	NA	1
Japan	Kario	1996	104	60.6	41	55	8	18
Japan	Yoshida	1996	96	55.2	43	46	7	16
Japan	Maguchi	1996	84	52	NA	NA	NA	1
Japan	Yamada	1997	122	59	50	55	17	5
Japan	Odawara	1997	248	58	NA	NA	NA	1
Japan	Sato	1998	100	85	15	50	35	10
Japan	Akai	1999	100	85	15	50	35	10
Japan	Hori	2001	130	90.8	12	62	56	6
Japan	Okumura	2001	54	64.8	19	31	4	3
Japan	Gohda	2001	621	56.4	271	259	91	16
Japan	Mannami	2001	3657	57	NA	NA	NA	1
Japan	Mukae	2002	120	76.7	28	73	19	3
Japan	Ogimoto	2002	205	59.5	83	95	27	5
Japan	Kawaguchi	2003	88	51.1	43	28	17	5
Japan	Goto	2005	452	54.2	207	189	56	4
Japan	Katoh	2005	270	59	NA	NA	NA	1
Japan	Sugimoto	2006	524	63.4	192	260	72	4
Japan	Tobina	2010	335	53.7	155	146	34	7
Japan	Hibi	2011	1740	57.2	745	791	204	4

Country	First Author	Year	N	D-allele freq	I/I (N)	I/D (N)	D/D (N)	Systematic Review
Japan	Kikuchi	2012	333	70.6	98	150	85	7
Kenya	Scott	2005	85	85.9	12	41	32	7
Kuwait	Al-Awadhi	2007	100	86	14	45	41	17
Kuwait	Shehab	2008	111	82.9	19	18	74	17
Latvia	Kupcinskas	2011	238	73.9	62	110	66	3
Lebanon	Saab	2007	570	93	NA	NA	NA	1
Lebanon	Fawwaz	2017	64	78.1	14	29	21	16
Lithuania	Kupcinskas	2011	238	73.9	62	110	66	3
Malaysia	Jayapalan	2010	137	55.5	61	56	20	16
Morocco	Mansouri	2017	85	92.9	6	32	47	16
Netherlands	Hosoi	1996	61	80	NA	NA	NA	1
Netherlands	vanSuylen	1999	95	82.1	17	50	28	2
Netherlands	Vander	2008	6015	77.9	1332	3006	1677	3
Nigeria	Mary	2014	400	85.7	57	190	153	8
Pakistan	Saeed	2005	79	82.3	14	38	27	10
Pakistan	Rabbani	2008	79	65.8	27	38	14	12
Pakistan	Hussain	2010	61	62.3	23	32	6	10
Pakistan	Shaikh	2014	115	71.3	33	41	41	16
Pakistan	Munir	2016	571	84.6	88	299	184	17
Pakistan	Agha	2018	263	65.8	90	122	51	17
Palestine	Al Sallout	2010	100	88	12	34	54	15
Poland	Buraczynska	2006	520	78.5	112	268	140	16
Poland	Cieszczyk	2009	115	80.9	22	58	36	7
Portugal	Costa	2009	100	84	16	45	39	7
Romania	Toma	2008	150	80	30	73	47	3
Russian Federation	Moiseev	1997	168	80.4	33	55	80	5
Russian Federation	Nazarov	2001	180	73.9	47	88	45	7
Russian Federation	Nazarov	2001	269	78.1	59	145	65	7
Russian Federation	Nazarov	2001	449	76.6	105	235	109	7
Singapore	Wong	2010	110	55	50	47	13	10
Slovakia	Pullmann	1999	148	70.9	43	68	37	10
Slovakia	Tk´aˇcov´a	2005	118	83.9	19	68	31	2
Slovakia	Hrukovicova	2006	252	77.8	56	126	70	7
South Africa	Collins	2004	199	82.4	35	99	65	7
South Africa	Moholisa	2013	77	77.9	17	34	26	3
South Korea	Lee	1997	61	85.2	9	25	27	6
South Korea	Hyeong	1999	402	85.8	57	55	290	11
South Korea	Kim	1999	302	81.1	57	55	190	3
South Korea	Uhm	2002	114	84.2	18	57	39	10
South Korea	Ryu	2002	167	66	NA	NA	NA	1
South Korea	Ha	2003	200	71.5	57	105	38	16
South Korea	Um	2003	613	63	NA	NA	NA	1

Country	First Author	Year	N	D-allele freq	I/I (N)	I/D (N)	D/D (N)	Systematic Review
South Korea	Park	2005	88	65.9	30	51	7	16
South Korea	Kim	2006	207	63.8	75	100	32	20
South Korea	Woo	2009	60	60	24	31	5	3
South Korea	Kim	2010	693	68	222	352	119	7
South Korea	Choi	2011	126	72.2	35	50	41	14
Spain	Lopez-Haldon	1999	269	87.7	33	125	111	5
Spain	Alvarez	2000	400	84.5	62	182	156	7
Spain	Arpa	2003	103	83.5	17	57	29	20
Spain	Coll	2003	133	85	NA	NA	NA	1
Spain	Alia	2005	104	81.7	19	51	34	13
Spain	Busquets	2007	77	85.7	11	53	13	2
Spain	Villar	2008	92	81.5	17	40	35	9
Spain	Coto-Segura	2009	272	87.5	34	145	93	17
Spain	Muniesa	2010	123	65	43	57	24	7
Spain	Ruiz	2010	100	56	44	43	13	7
Spain	Coto	2010	300	84.7	46	135	119	5
Sweden	Papadopoulos	2000	107	79.4	22	58	27	13
Sweden	Kurland	2001	59	73	NA	NA	NA	1
Sweden	Planck	2002	65	70.8	19	32	14	13
Switzerland	Sasse	2006	199	70.9	58	91	50	6
Taiwan	Lee	2002	750	53	NA	NA	NA	1
Taiwan	Ku	2006	66	45.5	36	27	3	19
Taiwan	Lue	2006	102	45.1	56	42	4	19
Taiwan	Wang	2006	161	42.2	93	59	9	20
Taiwan	Chang	2007	615	53.3	287	265	63	17
Tunisia	Hayet	2013	425	90.6	40	180	205	8
Turkey	Bedir	1999	143	87	NA	NA	NA	1
Turkey	Karaali	2004	67	82.1	12	29	26	21
Turkey	Oktem	2004	76	82.9	13	53	10	6
Turkey	Ozkur	2004	154	81.8	28	69	57	17
Turkey	Serdaroglu	2005	287	65.5	99	124	64	6
Turkey	Tanriverdi	2005	102	76	NA	NA	NA	1
Turkey	Ozdemir	2012	106	68.9	33	54	19	15
Turkey	Ayada	2014	64	87.5	8	28	28	2
United Arab Emirates	Saeed	2005	130	94	NA	NA	NA	1
United Kingdom	Sharma	1994	100	80	20	47	33	18
United Kingdom	Chadwick	1994	221	73.8	58	97	66	3
United Kingdom	Markus	1995	101	82.2	18	47	36	18
United Kingdom	Ueda	1995	488	81.6	90	271	127	18
United Kingdom	Cato	1996	215	76.7	50	102	63	18
United Kingdom	Myerson	1999	1906	76	457	953	496	7
United Kingdom	Kehoe	1999	386	77	NA	NA	NA	1
United Kingdom	Narain	2000	342	82	NA	NA	NA	1

Country	First Author	Year	N	D-allele freq	I/I (N)	I/D (N)	D/D (N)	Systematic Review
United Kingdom	Steeds	2001	507	78	NA	NA	NA	1
United Kingdom	Ortlep	2002	100	72	28	43	29	21
United Kingdom	Marshall	2002	88	64.8	31	36	21	9
United Kingdom	Marshall	2002	1906	75.9	459	949	498	9
United Kingdom	Hopkinson	2008	101	72.3	28	49	24	2
United States	Marian	1993	106	79.2	22	46	38	5
United States	Lindpaintner	1996	2086	80.9	399	1074	613	21
United States	Zee	1998	70	82.9	12	37	21	3
United States	Tassiulas	1998	200	56	88	90	22	10
United States	Kaufman	2001	465	69.5	142	228	95	10
United States	Douglas	2004	271	67.2	89	127	55	10
United States	Scott	2010	190	83.2	32	99	59	7

Code	**Systematic Review**
1	Saab, Y. B., P. R. Gard and A. D. Overall (2007). "The geographic distribution of the ACE II genotype: a novel finding." Genet Res 89(4): 259-267.
2	Kang, S. W., S. K. Kim, J. H. Chung, H. J. Jung, K. I. Kim, J. Kim and J. Y. Ban (2016). "Genetic Polymorphism of Angiotensin-Converting Enzyme and Chronic Obstructive Pulmonary Disease Risk: An Updated Meta-Analysis." Biomed Res Int **2016**: 7636123.
3	Mu, G., Q. Xiang, S. Zhou, Q. Xie, Z. Liu, Z. Zhang and Y. Cui (2019). "Association between genetic polymorphisms and angiotensin-converting enzyme inhibitor-induced cough: a systematic review and meta-analysis." Pharmacogenomics **20**(03): 189-212.
4	Gan, L., X. Liu, Z. Wu, M. Huang, X. Zhang and W. Guo (2015). "Angiotensin-converting enzyme insertion/deletion polymorphism and gastric cancer: a systematic review and meta-analysis." International journal of clinical and experimental medicine **8**(4): 5788.
5	Yuan, Y., L. Meng, Y. Zhou and N. Lu (2017). "Genetic polymorphism of angiotensin-converting enzyme and hypertrophic cardiomyopathy risk: A systematic review and meta-analysis." Medicine (Baltimore) 96(48): e8639.
6	Zhou, T. B., Y. H. Qin, L. N. Su, F. Y. Lei, W. F. Huang, Y. J. Zhao, Y. S. Pang and K. P. Yang (2011). "The association between angiotensin-converting enzyme insertion/deletion gene variant and risk of focal segmental glomerulosclerosis: a systematic review and meta-analysis." J Renin Angiotensin Aldosterone Syst 12(4): 624-633.
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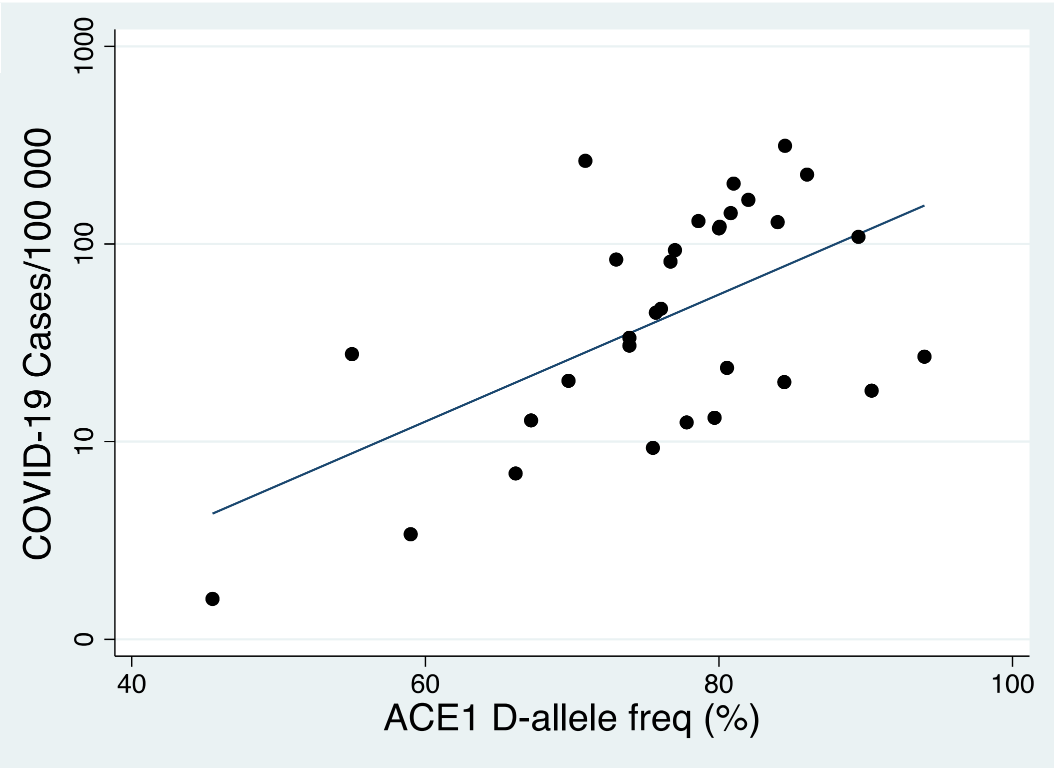
Table S3. Sensitivity analysis including high- and upper-middle-income countries. Multiple linear regression assessing the country-level association between COVID-19 cumulative incidence (log number of cases/100 000 inhabitants)/COVID-19 cumulative mortality (log number of deaths/100 000) and the prevalence of the D-allele of the ACE gene, the age of the COVID-19 epidemic and testing intensity (tests conducted/100 000).

	Cumulative Cases			**Cumulative Deaths**		
	Coef.	95% CI	P-value	Coef.	95% CI	P-value
N	40			40		
D-allele prevalence (%)	0.067	0.016- 0.119	0.012	0.119	0.043- 0.196	0.003
Age of epidemic	-0.013	-0.040- 0.013	0.319	-0.030	-0.069-0.010	0.134
Testing intensity	0.000	0.000- 0.001	0.346	0.000	-0.001-0.000	0.254

Figure S1. Association between COVID-19 cumulative incidence/100 000 (a), COVID-19 cumulative mortality/100 000 (b) and the frequency of the D-allele of the angiotensin-converting enzyme 1 (ACE1) gene for 30 high income countries.

a



b

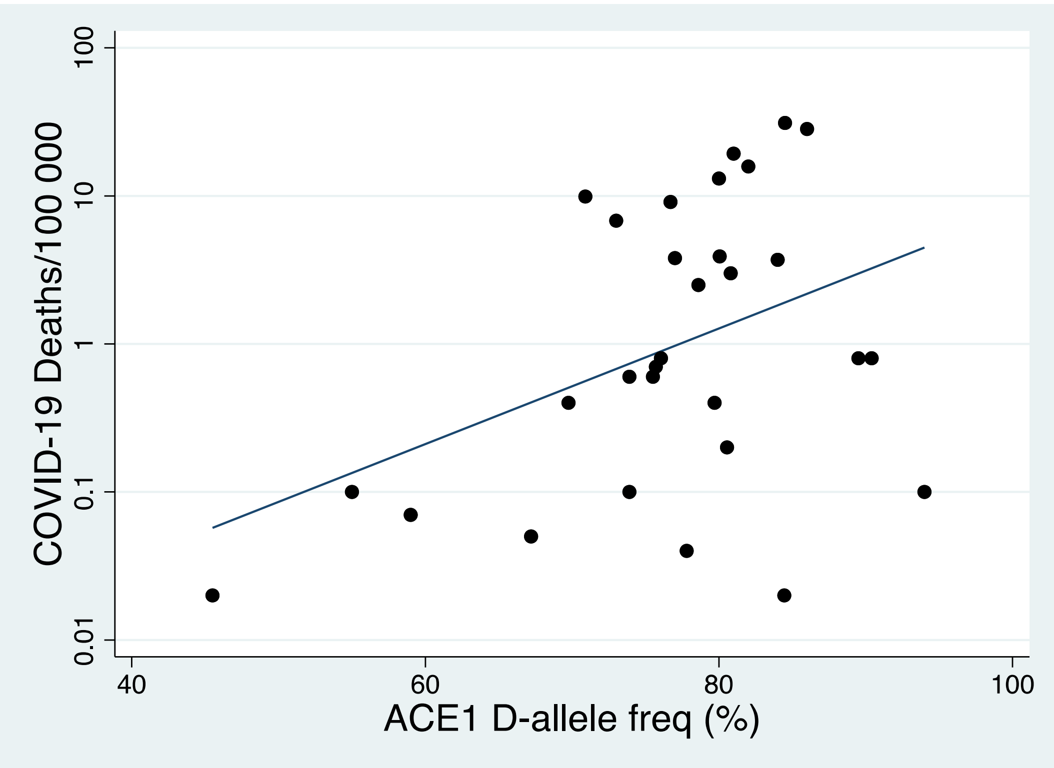
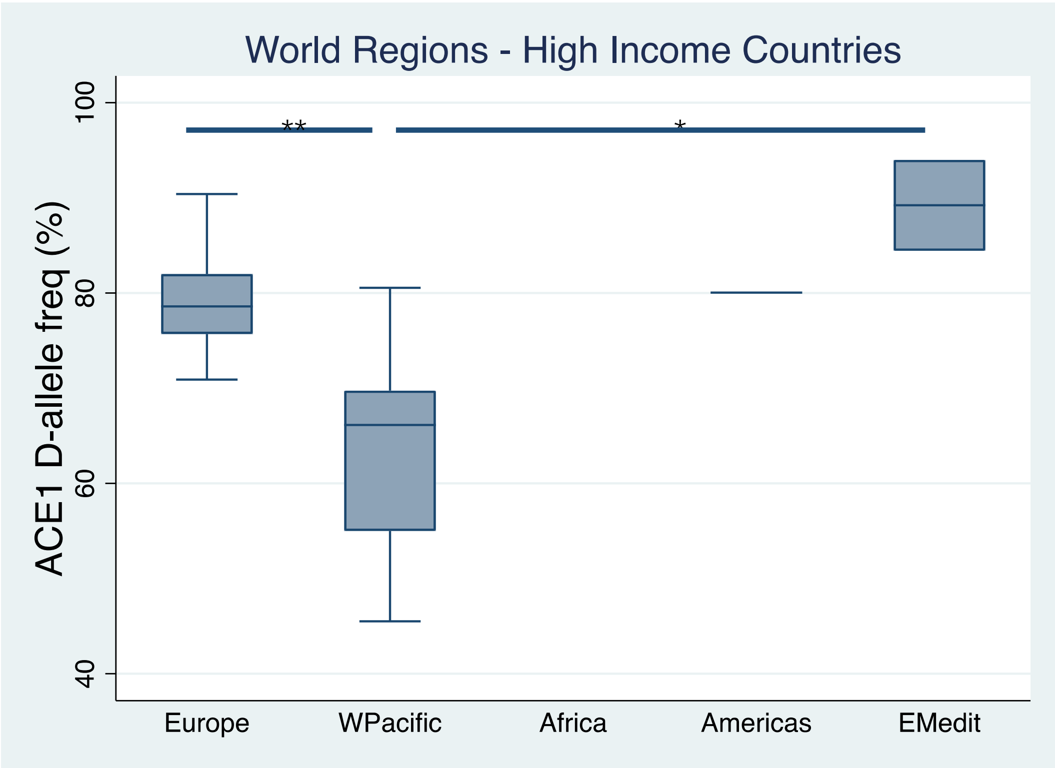
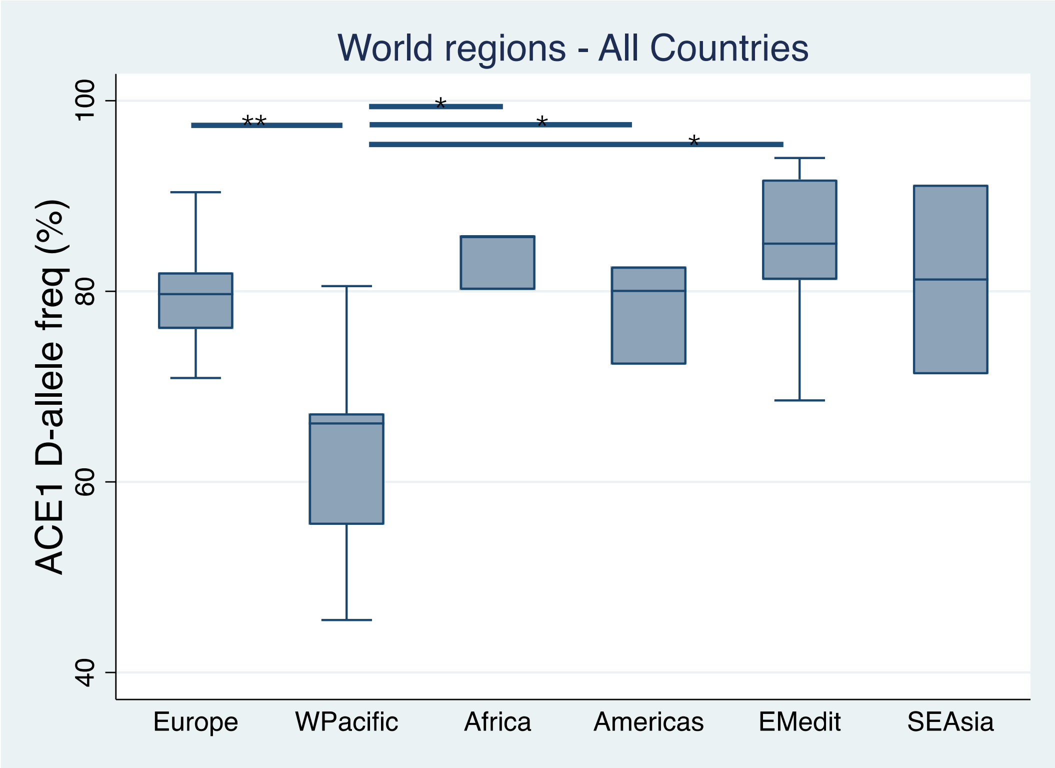


Figure S2. Box plots of country median ACE1 D-allele frequency grouped by a) WHO world regions limited to high income countries only (a) and all countries (b) and limited to the four subregions of Europe. Abbreviations: WPacific – Western Pacific/East Asia, EMedit – Eastern Mediterranean, SEAsia – South East Asia. * P<0.05, ** P<0.005.

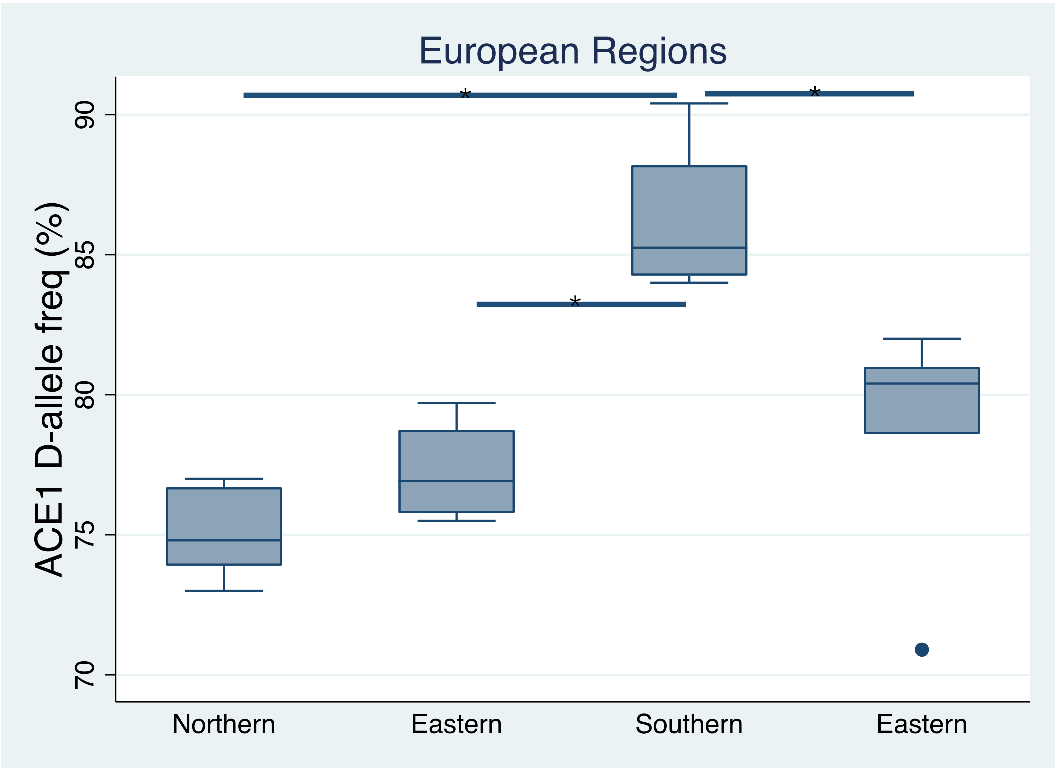
a



b


World regions - All Countries
ACE1 D-allele freq (%)
100
80
60
40
**
*
*
*
Europe
WPacific
Africa
Americas
EMedit
SEAsia

c


European Regions
ACE1 D-allele freq (%)
90
85
80
75
70
*
*
*
Northern
Eastern
Southern
Eastern