

Twin Research and Human Genetics

Supplementary Tables: Self-Reported Symptoms of COVID-19, Including Symptoms Most Predictive of SARS-CoV-2 Infection, are Heritable

Frances M. K. Williams¹, Maxim B. Freidin¹, Massimo Mangino^{1,2}, Simon Couvreur¹, Alessia Visconti¹, Ruth C. E. Bowyer¹, Caroline I. Le Roy¹, Mario Falchi¹, Olatz Mompeó¹, Carole Sudre³, Richard Davies⁴, Christopher Hammond¹, Cristina Menni¹, Claire J. Steves¹, Tim D. Spector¹

¹Department of Twin Research and Genetic Epidemiology, School of Life Course Sciences, King's College London, London, UK, ²NIHR Biomedical Research Centre at Guy's and St Thomas' Foundation Trust, London, UK, ³Department of Biomedical Engineering, School of Biomedical Engineering and Imaging Sciences, King's College London, London, UK, ⁴ZOE Global Ltd, London, UK

Supplementary Table 1 – Biometric modelling for covid-19 symptoms in TwinsUK adjusting for distance between households

Trait	Model	Variance components			Model fit			Model comparison			
		A	C	E	es	minus2LL	AIC	χ^2	df	p	base
Feeling unhealthy	Saturated	-	-	-	14	2045.96	-1086.04	-	-	-	-
	ACE	0 [0-0]	0.35 [0.08-0.45]	0.65 [0.55-0.76]	9	2053.03	-1092.97	7.07	7	0.421	Saturated
	AE	0.36 [0.24-0.48]	-	0.64 [0.52-0.76]	8	2058.65	-1089.35	5.62	1	0.018	ACE
	CE	-	0.35 [0.24-0.45]	0.65 [0.55-0.76]	8	2053.03	-1094.97	0.00	1	1.000	ACE
	E	-	-	1.00 [1.00-1.00]	7	2091.48	-1058.52	38.45	1	5.6E-10	CE
Abdominal pain	Saturated	-	-	-	14	1274.80	-1857.20	-	-	-	-
	ACE	0 [0-0]	0.27 [0-0.41]	0.73 [0.57-0.89]	9	1282.21	-1863.79	7.40	7	0.388	Saturated
	AE	0.29 [0.12-0.38]	-	0.71 [0.55-0.88]	8	1282.99	-1865.01	0.78	1	0.377	ACE
	CE	-	0.27 [0.11-0.41]	0.73 [0.59-0.89]	8	1282.21	-1865.79	0.00	1	1.000	ACE
	E	-	-	1.00 [1.00-1.00]	7	1293.71	-1856.29	11.51	1	0.001	CE
Chest pain	Saturated	-	-	-	14	1279.26	-1852.74	-	-	-	-
	ACE	0 [0-0]	0.29 [0-0.43]	0.71 [0.57-0.86]	9	1285.45	-1860.55	6.19	7	0.518	Saturated
	AE	0.3 [0.13-0.45]	-	0.7 [0.55-0.87]	8	1287.46	-1860.54	2.01	1	0.156	ACE
	CE	-	0.29 [0.14-0.43]	0.71 [0.57-0.86]	8	1285.45	-1862.55	0.00	1	1.000	ACE
	E	-	-	1.00 [1.00-1.00]	7	1299.61	-1850.39	14.16	1	0.000	CE
Delirium	Saturated	-	-	-	14	842.86	-2289.14	-	-	-	-
	ACE	0.44 [0-0.62]	0 [0-0]	0.56 [0.38-0.76]	9	855.63	-2290.37	12.77	7	0.078	Saturated
	AE	0.44 [0.24-0.62]	-	0.56 [0.38-0.76]	8	855.63	-2292.37	0.00	1	1.000	ACE
	CE	-	0.38 [0.19-0.55]	0.62 [0.45-0.81]	8	858.24	-2289.76	2.61	1	0.106	ACE
	E	-	-	1.00 [1.00-1.00]	7	873.32	-2276.68	17.69	1	2.6E-05	AE
Diarrhoea	Saturated	-	-	-	14	1316.76	-1815.24	-	-	-	-
	ACE	0.36 [0-0.5]	0 [0-0]	0.64 [0.5-0.8]	9	1325.01	-1820.99	8.25	7	0.311	Saturated
	AE	0.36 [0.2-0.5]	-	0.64 [0.5-0.8]	8	1325.01	-1822.99	0.00	1	1.000	ACE
	CE	-	0.31 [0.17-0.45]	0.69 [0.55-0.83]	8	1326.65	-1821.35	1.64	1	0.200	ACE
	E	-	-	1.00 [1.00-1.00]	7	1344.34	-1805.66	19.34	1	1.1E-05	AE
Fatigue	Saturated	-	-	-	14	667.58	-2464.42	-	-	-	-
	ACE	0.29 [0-0.52]	0 [0-0]	0.71 [0.48-0.98]	9	673.82	-2472.18	6.23	7	0.513	Saturated

		0.29 [0.02-0.52]	-	0.71 [0.48-0.98]	8	673.82	-2474.18	0.00	1	1.000	ACE
	AE	-	0.25 [0.01-0.47]	0.75 [0.53-0.99]	8	674.31	-2473.69	0.49	1	0.484	ACE
	CE	-	-	1.00 [1.00-1.00]	7	678.39	-2471.61	4.57	1	0.032	AE
Fever	Saturated	-	-	-	14	907.75	-2224.25	-	-	-	
	ACE	0 [0-0]	0.13 [0-0.33]	0.87 [0.66-1]	9	911.86	-2234.14	4.11	7	0.767	Saturated
	AE	0.12 [0-0.36]	-	0.88 [0.64-1]	8	912.42	-2235.58	0.56	1	0.453	ACE
	CE	-	0.13 [0-0.27]	0.87 [0.67-0.87]	8	911.86	-2236.14	0.00	1	1.000	ACE
	E	-	-	1.00 [1.00-1.00]	7	913.30	-2236.70	1.44	1	0.229	CE
Hoarse voice	Saturated	-	-	-	14	1093.02	-2038.98	-	-	-	
	ACE	0 [0-0]	0.13 [0-0.31]	0.87 [0.69-1]	9	1105.01	-2040.99	11.99	7	0.101	Saturated
	AE	0.09 [0-0.29]	-	0.91 [0.71-1]	8	1106.31	-2041.69	1.29	1	0.256	ACE
	CE	-	0.13 [0-0.31]	0.87 [0.69-1]	8	1105.01	-2042.99	0.00	1	1.000	ACE
	E	-	-	1.00 [1.00-1.00]	7	1107.09	-2042.91	2.08	1	0.150	CE
Loss of smell	Saturated	-	-	-	14	840.19	-2291.81	-	-	-	
	ACE	0.11 [0-0.11]	0 [0-0]	0.89 [0.71-0.9]	9	846.15	-2299.85	5.95	7	0.545	Saturated
	AE	0.11 [0-0.34]	-	0.89 [0.66-1]	8	846.15	-2301.85	0.00	1	1.000	ACE
	CE	-	0.05 [0-0.27]	0.95 [0.73-1]	8	846.65	-2301.35	0.50	1	0.479	ACE
	E	-	-	1.00 [1.00-1.00]	7	846.86	-2303.14	0.71	1	0.398	AE
Persistent cough	Saturated	-	-	-	14	1265.28	-1866.72	-	-	-	
	ACE	0 [0-0]	0.34 [0-0.47]	0.66 [0.52-0.81]	9	1273.08	-1872.92	7.80	7	0.351	Saturated
	AE	0.35 [0.19-0.5]	-	0.65 [0.5-0.81]	8	1275.24	-1872.76	2.16	1	0.142	ACE
	CE	-	0.34 [0.19-0.47]	0.66 [0.53-0.81]	8	1273.08	-1874.92	0.00	1	1.000	ACE
	E	-	-	1.00 [1.00-1.00]	7	1292.15	-1857.85	19.07	1	1.3E-05	CE
Predicted COVID	Saturated	-	-	-	12	816.55	-2319.45	-	-	-	
	ACE	0.25 [0-0.47]	0 [0-0]	0.75 [0.53-0.99]	7	822.83	-2327.17	6.28	7	0.507	Saturated
	AE	0.25 [0.01-0.47]	-	0.75 [0.53-0.99]	6	822.83	-2329.17	0.00	1	1.000	ACE
	CE	-	0.19 [0-0.4]	0.81 [0.6-1]	6	824.14	-2327.86	1.31	1	0.252	ACE
	E	-	-	1.00 [1.00-1.00]	5	827.06	-2326.94	4.23	1	0.040	AE
Shortness of breath	Saturated	-	-	-	14	320.40	-2811.60	-	-	-	
	ACE	0 [0-0.78]	0.54 [0-0.77]	0.46 [0.21-0.79]	9	324.91	-2821.09	4.51	7	0.720	Saturated
	AE	0.56 [0.21-0.8]	-	0.44 [0.2-0.79]	8	325.66	-2822.34	0.748	1	0.387	ACE

	CE	-	0.54 [0.21-0.77]	0.46 [0.23-0.79]	8	324.91	-2823.09	0.000	1	1.000	ACE
	E	-	-	1.00 [1.00-1.00]	7	334.59	-2815.41	9.67	1	0.002	CE
Skipped meals	Saturated	-	-	-	14	1107.06	-2024.94	-	-	-	-
	ACE	0.47 [0-0.61]	0 [0-0]	0.53 [0.39-0.71]	9	1116.58	-2029.42	9.52	7	0.217	Saturated
	AE	0.47 [0.3-0.61]	-	0.53 [0.39-0.7]	8	1116.58	-2031.42	0.00	1	1.000	ACE
	CE	-	0.4 [0.25-0.4]	0.6 [0.6-0.75]	8	1118.88	-2029.12	2.30	1	0.129	ACE
	E	-	-	1.00 [1.00-1.00]	7	1142.95	-2007.05	26.37	1	2.8E-07	AE

Legend to Supplementary 1: Biometric modelling was carried out using OpenMx package for R as detailed in the main text. Twins living together have been excluded and adjustments were done for age, sex, BMI, and distance between households for all traits except Predicted COVID for which no adjustment for age and sex was done. es, number of estimated parameters in the model; minus2LL, log-likelihood for the model multiplied by -2; AIC, Akaike Information Criteria; χ^2 , test statistics for models comparison; df, degrees of freedom for χ^2 ; p-value, corresponding p-value; base, model against which the comparison was done.

Supplementary Table 2 – Biometric modelling for covid-19 symptoms in TwinsUK adjusting for index of multiple deprivation

Trait	Model	Variance components			Model fit			Model comparison			
		A	C	E	es	minus2LL	AIC	χ^2	df	p	base
Feeling unhealthy	Saturated	-	-	-	14	2374.62	-1293.38	-	-	-	-
	ACE	0 [0-0]	0.35 [0.09-0.44]	0.65 [0.56-0.75]	9	2386.14	-1295.86	11.52	7	0.118	Saturated
	AE	0.37 [0.25-0.47]	-	0.63 [0.53-0.75]	8	2392.18	-1291.82	6.04	1	0.014	ACE
	CE	-	0.35 [0.34-0.36]	0.65 [0.64-0.66]	8	2386.14	-1297.86	0.00	1	1.000	ACE
	E	-	-	1.00 [1.00-1.00]	7	2430.76	-1255.24	44.62	1	2.4E-11	CE
Abdominal pain	Saturated	-	-	-	14	1485.08	-2182.92	-	-	-	-
	ACE	0 [0-0]	0.27 [0-0.4]	0.73 [0.59-0.87]	9	1497.12	-2184.88	12.04	7	0.099	Saturated
	AE	0.29 [0.13-0.29]	-	0.71 [0.71-0.87]	8	1498.63	-2185.37	1.51	1	0.219	ACE
	CE	-	0.27 [0.13-0.4]	0.73 [0.6-0.87]	8	1497.12	-2186.88	0.00	1	1.000	ACE
	E	-	-	1.00 [1.00-1.00]	7	1511.00	-2175.00	13.88	1	2.0E-04	CE
Chest pain	Saturated	-	-	-	14	1514.02	-2153.98	-	-	-	-
	ACE	0 [0-0]	0.3 [0-0.43]	0.7 [0.55-0.83]	9	1518.37	-2163.63	4.35	7	0.739	Saturated
	AE	0.32 [0.17-0.34]	-	0.68 [0.66-0.69]	8	1519.59	-2164.41	1.22	1	0.270	ACE
	CE	-	0.3 [0.17-0.43]	0.7 [0.57-0.83]	8	1518.37	-2165.63	0.00	1	1.000	ACE
	E	-	-	1.00 [1.00-1.00]	7	1536.71	-2149.29	18.34	1	1.9E-05	CE
Delirium	Saturated	-	-	-	14	1018.34	-2649.66	-	-	-	-
	ACE	0.49 [0-0.64]	0 [0-0]	0.51 [0.36-0.68]	9	1027.83	-2654.17	9.49	7	0.219	Saturated
	AE	0.49 [0.32-0.64]	-	0.51 [0.36-0.68]	8	1027.83	-2656.17	0.00	1	1.000	ACE
	CE	-	0.44 [0.43-0.58]	0.56 [0.42-0.72]	8	1029.91	-2654.09	2.08	1	0.149	ACE
	E	-	-	1.00 [1.00-1.00]	7	1055.89	-2630.11	28.06	1	1.2E-07	AE
Diarrhoea	Saturated	-	-	-	14	1583.89	-2084.11	-	-	-	-
	ACE	0.31 [0-0.45]	0 [0-0]	0.69 [0.55-0.83]	9	1594.49	-2087.51	10.60	7	0.157	Saturated
	AE	0.31 [0.17-0.45]	-	0.69 [0.55-0.83]	8	1594.49	-2089.51	0.00	1	1.000	ACE
	CE	-	0.28 [0.15-0.4]	0.72 [0.6-0.85]	8	1595.59	-2088.41	1.10	1	0.295	ACE
	E	-	-	1.00 [1.00-1.00]	7	1612.01	-2073.99	17.52	1	2.8E-05	AE
Fatigue	Saturated	-	-	-	14	793.07	-2874.93	-	-	-	-
	ACE	0.3 [0-0.51]	0 [0-0.46]	0.7 [0.49-0.94]	9	799.01	-2882.99	5.94	7	0.546	Saturated
	AE	0.3 [0.07-0.51]	-	0.7 [0.49-0.93]	8	799.01	-2884.99	0.00	1	1.000	ACE
	CE	-	0.27 [0.05-0.47]	0.73 [0.53-0.95]	8	799.49	-2884.51	0.48	1	0.489	ACE

	E	-	-	1.00 [1.00-1.00]	7	805.30	-2880.70	6.29	1	0.012	AE
Fever	Saturated	-	-	-	14	1083.68	-2584.32	-	-	-	-
	ACE	0 [0-0.34]	0.18 [0-0.36]	0.82 [0.64-1]	9	1088.26	-2593.74	4.58	7	0.711	Saturated
	AE	0.17 [0-0.38]	-	0.83 [0.62-1]	8	1089.55	-2594.45	1.29	1	0.256	ACE
	CE	-	0.18 [0-0.36]	0.82 [0.64-1]	8	1088.26	-2595.74	0.00	1	1.000	ACE
	E	-	-	1.00 [1.00-1.00]	7	1091.83	-2594.17	3.57	1	0.059	CE
Hoarse voice	Saturated	-	-	-	14	1296.50	-2371.50	-	-	-	-
	ACE	0 [0-0]	0.16 [0-0.32]	0.84 [0.68-1]	9	1311.93	-2370.07	15.43	7	0.031	Saturated
	AE	0.13 [0-0.3]	-	0.87 [0.7-1]	8	1313.45	-2370.55	1.52	1	0.217	ACE
	CE	-	0.16 [0-0.32]	0.84 [0.68-1]	8	1311.93	-2372.07	0.00	1	1.000	ACE
	E	-	-	1.00 [1.00-1.00]	7	1315.51	-2370.49	3.59	1	0.058	CE
Loss of smell	Saturated	-	-	-	14	1019.97	-2648.03	-	-	-	-
	ACE	0.17 [0-0.37]	0 [0-0]	0.83 [0.63-1]	9	1025.88	-2656.12	5.91	7	0.550	Saturated
	AE	0.17 [0-0.37]	-	0.83 [0.63-1]	8	1025.88	-2658.12	0.00	1	1.000	ACE
	CE	-	0.12 [0-0.31]	0.88 [0.69-1]	8	1026.82	-2657.18	0.94	1	0.332	ACE
	E	-	-	1.00 [1.00-1.00]	7	1028.25	-2657.75	2.37	1	0.124	AE
Persistent cough	Saturated	-	-	-	14	1479.88	-2188.12	-	-	-	-
	ACE	0 [0-0]	0.37 [0-0.49]	0.63 [0.5-0.77]	9	1487.92	-2194.08	8.04	7	0.329	Saturated
	AE	0.39 [0.24-0.52]	-	0.61 [0.48-0.76]	8	1489.79	-2194.21	1.87	1	0.171	ACE
	CE	-	0.37 [0.23-0.49]	0.63 [0.51-0.77]	8	1487.92	-2196.08	0.00	1	1.000	ACE
	E	-	-	1.00 [1.00-1.00]	7	1515.08	-2170.92	27.16	1	1.9E-07	CE
Predicted COVID	Saturated	-	-	-	12	997.60	-2674.40	-	-	-	-
	ACE	0.29 [0-0.48]	0 [0-0]	0.71 [0.52-0.91]	7	1005.72	-2680.28	8.12	7	0.322	Saturated
	AE	0.29 [0.09-0.48]	-	0.71 [0.52-0.91]	6	1005.72	-2682.28	0.00	1	1.000	ACE
	CE	-	0.25 [0.06-0.43]	0.75 [0.57-0.94]	6	1007.28	-2680.72	1.56	1	0.212	ACE
	E	-	-	1.00 [1.00-1.00]	5	1013.62	-2676.38	7.90	1	0.005	AE
Shortness of breath	Saturated	-	-	-	14	352.37	-3315.63	-	-	-	-
	ACE	0 [0-0]	0.46 [0-0.72]	0.54 [0.27-0.88]	9	358.54	-3323.46	6.17	7	0.520	Saturated
	AE	0.47 [0.09-0.75]	-	0.53 [0.25-0.91]	8	359.79	-3324.21	1.25	1	0.264	ACE
	CE	-	0.46 [0.12-0.72]	0.54 [0.28-0.88]	8	358.54	-3325.46	0.00	1	1.000	ACE
	E	-	-	1.00 [1.00-1.00]	7	365.48	-3320.52	6.94	1	0.008	CE
Skipped meals	Saturated	-	-	-	14	1292.73	-2375.27	-	-	-	-
	ACE	0.47 [0-0.61]	0 [0-0]	0.53 [0.39-0.69]	9	1301.05	-2380.95	8.31	7	0.306	Saturated

AE	0.47 [0.31-0.61]	-	0.53 [0.39-0.69]	8	1301.05	-2382.95	0.00	1	1.000	ACE
CE	-	0.39 [0.25-0.53]	0.61 [0.47-0.75]	8	1304.91	-2379.09	3.87	1	0.049	ACE
E	-	-	1.00 [1.00-1.00]	7	1331.76	-2354.24	30.71	1	3.0E-08	AE

Legend to Supplementary 2: Biometric modelling was carried out using OpenMx package for R as detailed in the main text. Adjustments were done for age, sex, BMI, and index of multiple deprivation for all traits except Predicted COVID for which no adjustment for age and sex was done. es, number of estimated parameters in the model; minus2LL, log-likelihood for the model multiplied by -2; AIC, Akaike Information Criteria; χ^2 , test statistics for models comparison; df, degrees of freedom for χ^2 ; p-value, corresponding p-value; base, model against which the comparison was done.