

Supplementary data

Table S1- Comorbidity categories used in the study

Category in source data	Study comorbidity category	Count in overall population
Diagnosis Asthma	Asthma	66041
Diagnosis COPD ²	COPD	18018
Diagnosis Cystic Fibrosis	Respiratory- other ¹	69
Diagnosis Diabetes	Diabetes	40803
Diagnosis Hypertension	Hypertension	107696
Diagnosis Ischemic Heart Disease	Ischemic Heart Disease	27511
Diagnosis Transplant	Immunosuppression	479
Diagnosis Lung Disease	Respiratory- other ¹	97401
Diagnosis Severe Lung Disease	Respiratory- other ¹	10098
Indication Transplant	Immunosuppression	1562
Indication Immuno	Immunosuppression	770
Indication Respiratory	Respiratory- other ¹	6103
Asthma Prescriptions: HS ICS ³ , ICS LABA ⁴ , LABA ⁵ , Montel, Prednisone	Asthma	30477
COPD Prescription: ICS, LABA ⁴ , LAMA ⁶ , Roflumilast	COPD	66517
Immuno Cortisol 5 or 20 Prescription	Immunosuppression	4365
Transplant DMARD Prescription	Immunosuppression	1562
Azithromycin Prescription	Respiratory- other ¹	1109
Immuno DMARD ⁷ Prescription	Immunosuppression	4247

¹only if patient was not found to also have asthma, COPD, or cystic fibrosis, ²Chronic obstructive pulmonary disease, ³High strength inhaled corticosteroid, ⁴Inhaled corticosteroid long-acting bronchodilator, ⁵Long-acting bronchodilator, ⁶Long-acting muscarinic antagonist, ⁷Disease modifying anti-rheumatic drugs

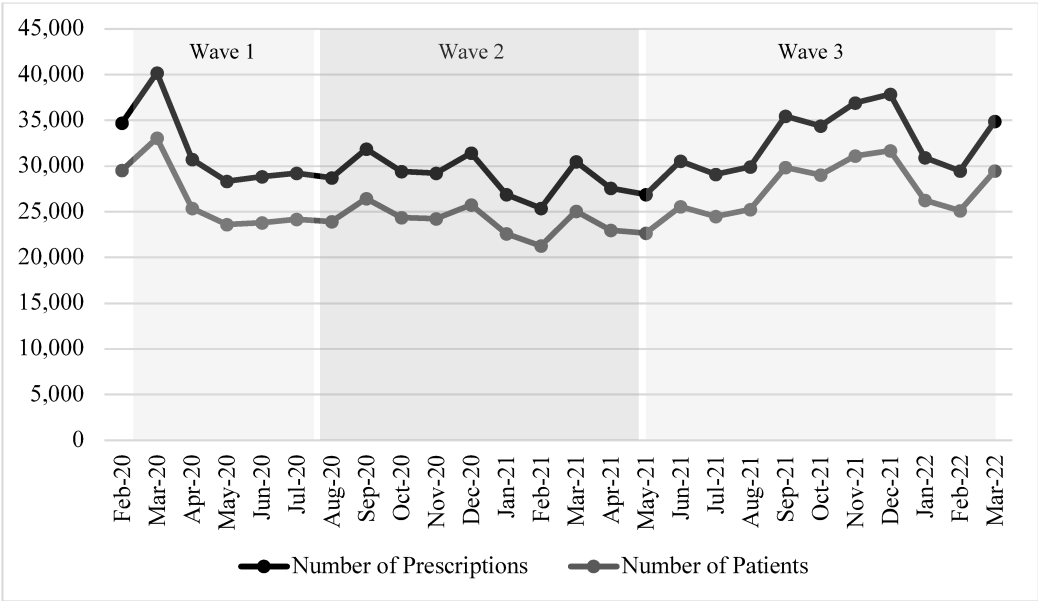
Table S2- Demographics of episodes with antibiotic prescriptions +/- 28 days by COVID-19 wave

		Wave 1		Wave 2		Wave 3	
		Total Episodes	Total Episodes with an Antibiotic (%)	Total Episodes	Total Episodes with an Antibiotic (%)	Total Episodes	Total Episodes with an Antibiotic (%)
Total		2432	496 (20.4%)	4330	765 (17.7%)	9478	1134 (12.0%)
Age group	<25	81	6 (7.4%)	386	24 (6.2%)	2185	154 (7.0%)
	25-44	537	66 (12.3%)	940	110 (11.7%)	2481	230 (9.3%)
	45-64	850	121 (14.2%)	1224	162 (13.2%)	2320	256 (11.0%)
	65-74	229	44 (19.2%)	428	80 (18.7%)	774	126 (16.3%)
	75+	735	259 (35.2%)	1352	389 (28.8%)	1718	368 (21.4%)
Sex	Male	898	198 (22.0%)	1550	277 (17.9%)	4141	389 (9.4%)
	Female	1534	298 (19.4%)	2780	488 (17.6%)	5327	745 (14.0%)
Any high-risk comorbidity	No	1454	229 (15.7%)	2405	309 (12.8%)	6249	552 (8.8%)
	Yes	978	267 (27.3%)	1925	456 (23.7%)	3229	582 (18.0%)
Hospital admission +/-28 days	No	1771	317 (17.9%)	3145	470 (14.9%)	8131	830 (10.2%)
	Yes	661	179 (27.1%)	1185	295 (24.9%)	1347	304 (22.6%)
Health board of residence	A	780	147 (18.8%)	1667	289 (17.3%)	4496	517 (11.5%)
	B	1652	349 (21.1%)	2663	476 (17.9%)	4982	617 (12.4%)
Scottish Index of Multiple Deprivation (SIMD) quintile	1	426	74 (17.4%)	888	147 (16.6%)	1936	262 (13.5%)
	2	374	59 (15.8%)	878	144 (16.4%)	1612	160 (9.9%)
	3	447	88 (19.7%)	747	147 (19.7%)	1655	216 (13.1%)
	4	650	162 (24.9%)	936	166 (17.7%)	2018	239 (11.8%)
	5	318	50 (15.7%)	601	115 (19.1%)	1422	163 (11.5%)
	Missing Data	217	63 (39.0%)	279	46 (16.5%)	835	94 (11.3%)

Table S3- Proportion of common antibiotics prescribed in COVID-19 episodes by wave

Name	Proportion of all antibiotic prescriptions per wave		
	Wave 1	Wave 2	Wave 3
Amoxicillin	29.1%	26.6%	26.3%
Doxycycline	17.8%	13.9%	16.4%
Nitrofurantoin	11.8%	13.9%	9.7%
Trimethoprim	8.8%	10.3%	10.3%
Flucloxacillin	7.2%	7.5%	7.7%
Co-amoxiclav	5.3%	5.6%	5.1%
Clarithromycin	4.1%	4.0%	2.6%
Azithromycin	3.1%	1.3%	2.0%
Ciprofloxacin	1.2%	0.8%	1.3%

20 **Figure S1- Overall community antibiotic prescribing in study health boards, February**
21 **2020-March 2022**



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24 **Figure S2- Proportion of COVID-19 episodes with antibiotic prescriptions per wave by**
25 **age and gender**

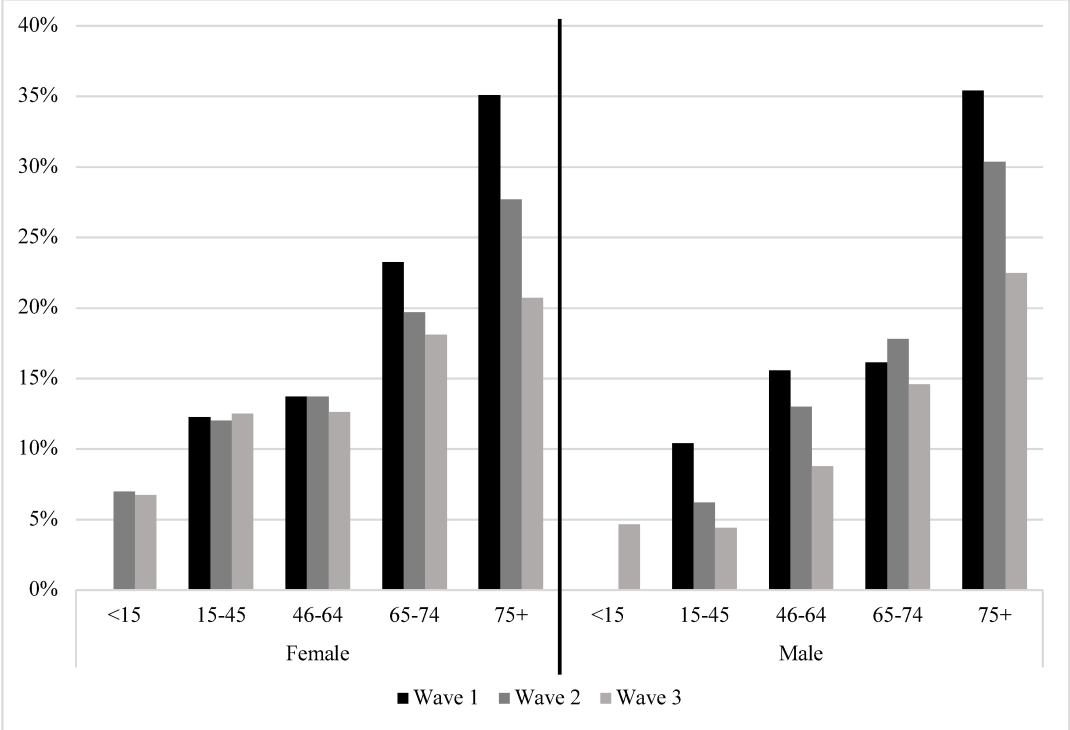


Table S4- Deaths following COVID-19 episodes by pandemic wave

	Wave 1	Wave 2	Wave 3
Total patients with a COVID-19 episode	2430	4324	9434
Deaths within 28 days of positive test (% of all episodes)	334 (13.7%)	499 (11.5%)	267 (2.8%)
Deaths with COVID-19 as underlying cause (% of deaths within 28 days)	304 (91.0%)	414 (83.0%)	166 (62.2%)

Table S5: Associations between demographic and healthcare factors and the odds of a community antibiotic prescription within 14 days for COVID-19 episodes, from binary logistic regression (sensitivity analysis)

Variable	Category	Frequency	Univariate OR (95% CI)	p-value	Multivariate OR (95% CI)	p-value
Age group	<25	2652	REF	-	-	-
	25-44	3958	1.79 (1.42, 2.29)	<0.001	1.46 (1.15, 1.91)	0.003
	45-64	4394	2.28 (1.82, 2.88)	<0.001	1.74 (1.37, 2.24)	<0.001
	65-74	1431	3.61 (2.80, 4.68)	<0.001	2.39 (1.81, 3.18)	<0.001
	75+	3805	6.05 (4.89, 7.56)	<0.001	3.59 (2.82, 4.62)	<0.001
Sex	Male	6599	REF	-	-	-
	Female	9641	1.23 (1.11, 1.38)	<0.001	1.26 (1.13, 1.42)	<0.001
Any high-risk comorbidity	No	10108	REF	-	-	-
	Yes	6132	2.38 (2.14, 2.64)	<0.001	1.50 (1.33, 1.70)	<0.001
Hospital admission +/-28 days	No	13047	REF	-	-	-
	Yes	3193	2.06 (1.84, 2.30)	<0.001	1.35 (1.18, 1.53)	<0.001
Health board of residence	A	6943	REF	-	-	-
	B	9297	1.16 (1.04, 1.29)	0.007	1.16 (1.03, 1.31)	0.01
Scottish Index of Multiple Deprivation (SIMD) quintile	1 (most deprived)	3251	REF	-	-	-
	2	2864	0.84 (0.71, 1.00)	0.06	0.82 (0.69, 0.99)	0.03
	3	2849	1.10 (0.94, 1.30)	0.24	1.01 (0.85, 1.19)	0.92
	4	3604	1.04 (0.89, 1.22)	0.62	0.83 (0.70, 0.98)	0.02
	5 (least deprived)	2341	0.94 (0.79, 1.13)	0.54	0.84 (0.70, 1.01)	0.07
COVID wave	1	2432	REF	-	-	-
	2	4330	0.76 (0.65, 0.88)	<0.001	0.75 (0.64, 0.88)	<0.001
	3	9478	0.49 (0.43, 0.56)	<0.001	0.63 (0.54, 0.73)	<0.001

38 **Table S6: Interactions between wave and demographic characteristics on the odds of**
39 **antibiotic prescription within 28 days of a positive COVID-19 test**

Variable	Wave 2*		Wave 3*	
	OR for interaction term (95% CI)	p-value	OR for interaction term (95% CI)	p-value
Age	0.92 (0.83, 1.03)	0.14	0.84 (0.76, 0.93)	<0.001
Sex	1.15 (0.89, 1.49)	0.30	1.84 (1.45, 2.35)	<0.001
Any high-risk comorbidity	1.05 (0.81, 1.35)	0.72	1.13 (0.89, 1.43)	0.31
Hospital admission +/-28 days	1.11 (0.85, 1.45)	0.45	1.51 (1.17, 1.95)	0.002
Health board of residence	0.90 (0.69, 1.18)	0.44	0.94 (0.73, 1.21)	0.64
Scottish Index of Multiple Deprivation (SIMD) quintile	0.98 (0.88, 1.08)	0.62	0.91 (0.83, 1.00)	0.04

40 *With wave 1 as the comparator

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42 **Table S7: Associations between demographic and healthcare factors and the odds of a**
43 **community antibiotic prescription within 28 days for COVID-19 episodes, by wave**
44 **from univariate binary logistic regression**

Variable	Category	Wave 1		Wave 2		Wave 3	
		Univariate OR (95% CI)	p-value	Univariate OR (95% CI)	p-value	Univariate OR (95% CI)	p-value
Age group	<25	REF	-	-	-	-	-
	25-44	1.75 (0.79, 4.64)	0.21	2.00 (1.29, 3.23)	0.003	1.35 (1.09, 1.67)	0.006
	45-64	2.07 (0.96, 5.44)	0.09	2.30 (1.50, 3.67)	<0.001	1.64 (1.33, 2.02)	<0.001
	65-74	2.97 (1.30, 8.04)	0.02	3.47 (2.18, 5.71)	<0.001	2.56 (1.99, 2.30)	<0.001
	75+	6.80 (3.17, 17.71)	<0.001	6.09 (4.05, 9.60)	<0.001	3.60 (2.95, 4.40)	<0.001
Sex	Male	REF	-	-	-	-	-
	Female	0.85 (0.70, 1.04)	0.12	0.98 (0.83, 1.15)	0.79	1.57 (1.38, 1.79)	<0.001
Any high-risk comorbidity	No	REF	-	-	-	-	-
	Yes	2.01 (1.66, 2.45)	<0.001	2.11 (1.80, 2.47)	<0.001	2.27 (2.00, 2.57)	<0.001
Hospital admission +/-28 days	No	REF	-	-	-	-	-
	Yes	1.70 (1.38, 2.1)	<0.001	1.89 (1.60, 2.22)	<0.001	2.56 (2.21, 2.97)	<0.001
Health board of residence	A	REF	-	-	-	-	-
	B	1.15 (0.93, 1.43)	0.19	1.04 (0.88, 1.22)	0.65	1.09 (0.96, 1.23)	0.18
Scottish Index of Multiple Deprivation (SIMD) quintile	1 (most deprived)	REF	-	-	-	-	-
	2	0.89 (0.61, 1.29)	0.55	0.99 (0.77, 1.27)	0.94	0.70 (0.57, 0.87)	<0.001
	3	1.17 (0.83, 1.64)	0.38	1.24 (0.96, 1.59)	0.10	0.96 (0.79, 1.16)	0.67
	4	1.58 (1.17, 2.16)	0.004	1.09 (0.85, 1.39)	0.50	0.86 (0.71, 1.04)	0.11
	5	0.89 (0.60, 1.31)	0.55	1.19 (0.91, 1.56)	0.20	0.83 (0.67, 1.02)	0.07

45 **Table S8: Associations between demographic and healthcare factors and the odds of a**
46 **community antibiotic prescription within 28 days for COVID-19 episodes, by wave**
47 **from multivariate binary logistic regression**

		Wave 1		Wave 2		Wave 3	
Variable	Category	Multivariate OR (95% CI)	p-value	Multivariate OR (95% CI)	p-value	Multivariate OR (95% CI)	p-value
Age group	<25	REF	-	-	-	-	-
	25-44	2.30 (0.90, 7.78)	0.12	1.76 (1.10, 2.92)	0.02	1.27 (1.01, 1.60)	0.04
	45-64	2.70 (1.08, 9.04)	0.06	2.11 (1.35, 3.45)	0.002	1.38 (1.10, 1.74)	0.005
	65-74	3.52 (1.33, 12.20)	0.02	2.51 (1.52, 4.29)	<0.001	1.79 (1.35, 2.37)	<0.001
	75+	6.70 (2.67, 22.49)	<0.001	4.62 (2.96, 7.56)	<0.001	2.25 (1.78, 2.88)	<0.001
Sex	Male	REF	-	-	-	-	-
	Female	1.04 (0.83, 1.32)	0.72	1.14 (0.95, 1.36)	0.15	1.59 (1.38, 1.83)	<0.001
Any high-risk comorbidity	No	REF	-	-	-	-	-
	Yes	1.42 (1.13, 1.79)	0.003	1.31 (1.09, 1.58)	0.004	1.60 (1.38, 1.87)	<0.001
Hospital admission +/-28 days	No	REF	-	-	-	-	-
	Yes	1.28 (0.99, 1.65)	0.05	1.39 (1.15, 1.67)	<0.001	1.93 (1.64, 2.27)	<0.001
Health board of residence	A	REF	-	-	-	-	-
	B	1.61 (1.25, 2.09)	<0.001	1.14 (0.96, 1.36)	0.14	1.03 (0.90, 1.18)	0.68
Scottish Index of Multiple Deprivation (SIMD) quintile	1 (most deprived)	REF	-	-	-	-	-
	2	1.01 (0.68, 1.48)	0.97	0.93 (0.72, 1.20)	0.57	0.69 (0.55, 0.85)	<0.001
	3	1.15 (0.81, 1.64)	0.44	1.08 (0.83, 1.41)	0.54	0.91 (0.75, 1.11)	0.37
	4	1.28 (0.92, 1.77)	0.14	0.88 (0.68, 1.13)	0.32	0.75 (0.62, 0.91)	0.004
	5	0.85 (0.56, 1.27)	0.43	0.99 (0.74, 1.30)	0.92	0.77 (0.62, 0.96)	0.02

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50 **Table S9: Associations between demographic and healthcare factors and the odds of a**
51 **community antibiotic prescription within 14 days for COVID-19 episodes, by wave**
52 **from univariate binary logistic regression (sensitivity analysis)**

		Wave 1		Wave 2		Wave 3	
Variable	Category	Univariate OR (95% CI)	p-value	Univariate OR (95% CI)	p-value	Univariate OR (95% CI)	p-value
Age group	<25	REF	-	-	-	-	-
	25-44	2.15 (0.76, 9.03)	0.21	2.59 (1.44, 5.06)	0.003	1.54 (1.17, 2.04)	0.002
	45-64	3.04 (1.11, 12.58)	0.06	2.53 (1.43, 4.92)	0.003	2.03 (1.56, 2.66)	<0.001
	65-74	4.53 (1.57, 19.21)	0.01	4.69 (2.56, 9.31)	<0.001	3.08 (2.25, 4.23)	<0.001
	75+	9.13 (3.36, 37.53)	<0.001	7.81 (4.53, 14.89)	<0.001	4.14 (3.43, 5.73)	<0.001
Sex	Male	REF	-	-	-	-	-
	Female	0.84 (0.67, 1.05)	0.13	1.04 (0.86, 1.27)	0.69	1.51 (1.29, 1.77)	<0.001

Any high-risk comorbidity	No	REF	-	-	-	-	-
	Yes	2.00 (1.59, 2.51)	<0.001	2.18 (1.80, 2.64)	<0.001	2.53 (2.18, 2.95)	<0.001
Hospital admission +/-28 days	No	REF	-	-	-	-	-
	Yes	1.59 (1.25, 2.01)	<0.001	1.58 (1.30, 1.92)	<0.001	2.41 (2.02, 2.87)	<0.001
Health board of residence	A	REF	-	-	-	-	-
	B	1.26 (0.98, 1.62)	0.07	1.02 (0.84, 1.23)	0.87	1.06 (0.91, 1.23)	0.48
Scottish Index of Multiple Deprivation (SIMD) quintile	1 (most deprived)	REF	-	-	-	-	-
	2	0.92 (0.60, 1.40)	0.69	1.01 (0.75, 1.37)	0.93	0.70 (0.54, 0.90)	0.006
	3	1.17 (0.80, 1.73)	0.42	1.28 (0.95, 1.72)	0.11	0.97 (0.77, 1.22)	0.80
	4	1.51 (1.07, 2.16)	0.02	1.03 (0.77, 1.39)	0.83	0.82 (0.65, 1.03)	0.08
	5	0.99 (0.64, 1.53)	0.97	1.20 (0.87, 1.65)	0.27	0.81 (0.63, 1.04)	0.11

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55 **Table S10: Associations between demographic and healthcare factors and the odds of a**
56 **community antibiotic prescription within 14 days for COVID-19 episodes, by wave**
57 **from multivariate binary logistic regression (sensitivity analysis)**

Variable	Category	Wave 1		Wave 2		Wave 3	
		Multivariate OR (95% CI)	p-value	Multivariate OR (95% CI)	p-value	Multivariate OR (95% CI)	p-value
Age group	<25	REF	-	-	-	-	-
	25-44	2.00 (0.70, 8.48)	0.26	1.99 (1.09, 3.94)	0.03	1.39 (1.04, 1.87)	0.03
	45-64	2.77 (0.99, 11.51)	0.09	2.20 (1.23, 4.29)	0.01	1.65 (1.24, 2.21)	<0.001
	65-74	3.92 (1.32, 16.88)	0.03	3.64 (1.94, 7.36)	<0.001	2.02 (1.42, 2.86)	<0.001
	75+	6.58 (2.35, 27.51)	0.002	5.87 (3.32, 11.39)	<0.001	2.57 (1.91, 3.49)	<0.001
Sex	Male	REF	-	-	-	-	-
	Female	1.03 (0.79, 1.33)	0.84	1.17 (0.95, 1.45)	0.14	1.48 (1.25, 1.75)	<0.001
Any high-risk comorbidity	No	REF	-	-	-	-	-
	Yes	1.35 (1.04, 1.75)	0.02	1.35 (1.08, 1.69)	0.009	1.75 (1.46, 2.10)	<0.001
Hospital admission +/-28 days	No	REF	-	-	-	-	-
	Yes	1.13 (0.85, 1.50)	0.40	1.07 (0.86, 1.34)	0.53	1.78 (1.46, 2.15)	<0.001
Health board of residence	A	REF	-	-	-	-	-
	B	1.94 (1.44, 2.63)	<0.001	1.14 (0.93, 1.41)	0.20	1.00 (0.85, 1.18)	0.99
Scottish Index of Multiple Deprivation (SIMD) quintile	1 (most deprived)	REF	-	-	-	-	-
	2	1.06 (0.68, 1.64)	0.79	0.94 (0.69, 1.28)	0.69	0.68 (0.53, 0.88)	0.004
	3	1.15 (0.77, 1.72)	0.48	1.10 (0.81, 1.50)	0.55	0.92 (0.72, 1.16)	0.48
	4	1.17 (0.81, 1.69)	0.41	0.81 (0.60, 1.10)	0.18	0.71 (0.56, 0.90)	0.004
	5	0.96 (0.61, 1.50)	0.86	0.95 (0.68, 1.33)	0.79	0.75 (0.58, 0.98)	0.03

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