

Supplementary file:

Antibiotic prescribing:

Tables S1.1 and S1.2 shows the monthly prescribing rate of azithromycin and doxycycline in 2019 and 2020. These data are used for Figure 1.

	2019 Azith. Px.	2020 Azith. Px.
Month	rate	rate
Jan	108.4	111.1
Feb	95.5	98.0
Mar	98.7	133.0
Apr	99.2	103.5
May	96.8	94.2
June	85.9	99.7
July	99.0	100.6
Aug	90.3	90.1
Sept	97.1	105.4
Oct	105.5	106.0
Nov	102.5	107.6
Dec	111.7	114.1

Table S1.1 Azithromycin prescription rate by month per 100,000 registered patients for 2019 and 2020

	2019 Doxy. Px.	2020 Doxy. Px.
Month	rate	rate
Jan	519.0	545.6
Feb	408.6	416.7
Mar	382.4	536.4
Apr	389.4	412.5
May	362.7	298.8
June	318.9	279.7
July	337.9	276.7
Aug	296.1	240.6
Sept	337.2	324.2
Oct	429.8	344.7
Nov	433.8	326.6
Dec	511.9	357.1

Table S1.2 Doxycycline prescription rate by month per 100,000 registered patients for 2019 and 2020

Monthly rates of respiratory tract infections (RTI) comparing 2019 with 2020:

These are the monthly rates of LRTI, URTI and ILI for 2019 and 2020, rates per 10,000 registered populations (Tables S2.1 to S2.3). These data were used to support Figure 2.

Month	2019 LRTI rate	2020 LRTI rate
Jan	359.4	299.4
Feb	296.1	226.7
Mar	248.4	137.9
Apr	211.7	65.1
May	194.4	51.5
June	167.8	48.0
July	159.2	50.3
Aug	143.9	53.8
Sept	223.1	93.7
Oct	294.4	86.3
Nov	350.2	71.7
Dec	405.0	80.3

Table S2.1: LRTI rates, monthly incidence comparing 2019 and 2020, per 10,000 registered patients

Month	2019 URTI rate	2020 URTI rate
Jan	747.2	624.4
Feb	618.5	560.3
Mar	595.7	341.7
Apr	397.4	151.3
May	413.9	97.6
June	369.9	88.9
July	340.6	106.6
Aug	275.5	107.8
Sept	445.0	243.0
Oct	559.9	176.2
Nov	700.0	156.5
Dec	751.0	154.0

Table S2.2: URTI rates, monthly incidence comparing 2019 and 2020, per 10,000 registered patients

Month	2019 ILI rate	2020 ILI rate
Jan	62.8	37.2
Feb	50.6	31.3
Mar	23.3	59.6
Apr	10.3	63.6
May	8.2	17.3
June	6.9	8.7
July	4.4	6.5
Aug	4.7	5.8
Sept	9.5	26.1
Oct	19.9	22.7
Nov	34.5	18.5
Dec	69.1	23.7

Table S2.3 ILI rates, monthly incidence comparing 2019 and 2020, per 10,000 registered patients

Change in respiratory infections 2020 compared to 2019:

We cross-tabulated the change in respiratory infections between 2020 and 2019, by RTI (Table S3.1).

Overall RTI reduced by over 50%, but there was a small rise in ILI.

Resp. Tract Infection Consultations in RSC			
	2019	2020	
LRTI	118,940	49,631	
URTI	241,997	110,230	
ILI	11,846	12,607	
Total	372,783	172,468	

Table S3.1: Respiratory tract infections recorded in the RSC 2019 and 2020.

We next show (Tables S3.2 and S3.3) the change in prescribing of azithromycin and doxycycline comparing the RTI consultations where these antibiotics were prescribed with those where they were not.

All RTI Consultations in RSC			
	2019	2020	<i>p</i> <0.0001
RTI no azithromycin Px	370,885	171,220	
RTI with azithromycin Px	1,898	1,248	
Total RTI consults.	372,783	172,468	

Table S3.2: Change in azithromycin prescribing (Px) in all RTI consultations

	2019	2020	<i>p</i> <0.0001
RTI no doxycycline Px	328,580	145,232	
RTI with doxycycline Px	44,203	27,236	
Total RTI consults.	372,783	172,468	

Table S3.3: Change in doxycycline prescribing (Px) in all RTI consultations

We next have compared the frequency of RTI consultations in RSC with antibiotic prescription by year and infection-type. (Table S3.4)

	RTIs in RSC prescribed azithromycin			RTIs in RSC prescribed doxycycline		
	2019	2020	<i>p</i> <0.0001	2019	2020	<i>p</i> <0.0001
LRTI	1,208	788		30,318	15,599	
URTI	659	399		13,357	10,148	
ILI	31	61		528	1489	
Total	1,898	1,248		44,203	27,236	

Table S3.4: Change in prescribing pattern 2019 and 2020 in consultations where an antibiotic was prescribed

These data allow us to report the change in the percentage of people with RTI prescribed our antibiotics of interest, azithromycin and doxycycline, and the change between years (Table S3.5).

Overall % RTI consultations	2019	2020	Risk difference
Prescribed azithromycin	0.51	0.72	0.214 (0.211,0.217)
Prescribed doxycycline	11.86	15.79	3.93 (3.73,4.14)

Table S3.5: Change in the proportion of RTI consultations in which our antibiotics of interest were prescribed

Negative Binomial Models for Doxycycline

These models compare 2019 prescribing with 2020 (Table S3.6) and then look at whether those with COVID-19 are more likely to be prescribed doxycycline (Table S3.7).

Doxy. Px Incidence Rates	IRR	Lower 95% CI	Upper 95% CI	p
Yr 2020 (ref level 2019)	1.012	0.994	1.030	0.199
Age Band (ref. level 0-15)				
16-64	12.34	11.86	12.85	<0.0001
65+	45.46	43.53	47.48	<0.0001
Gender (ref. level F)	0.79	0.78	0.81	<0.0001
IMD Quintile (ref. level Most Deprived)				
Q2	0.89	0.87	0.91	<0.0001
Q3	0.84	0.81	0.86	<0.0001
Q4	0.82	0.79	0.84	<0.0001
Q5 (least deprived)	0.71	0.69	0.73	<0.0001
NHS Region (Ref London)				
Midlands and East	1.71	1.66	1.75	<0.0001
North East and Yorkshire	1.55	1.50	1.60	<0.0001
North West	1.28	1.24	1.32	<0.0001
South East	1.11	1.08	1.14	<0.0001
South West	1.60	1.55	1.65	<0.0001
Resp. Disease				
LRTI Count	1.0061	1.0056	1.0066	<0.0001
URTI Count	1.0003	1.0000	1.0007	0.0477
ILI Count	1.0170	1.0148	1.0193	<0.0001

Table S3.6: Model reporting the incident rate ratio (IRR) comparing prescribing of doxycycline in 2020 with 2019. Taking the variables in the model into account there was no difference in prescribing

Doxycycline prescribing rate	IRR	Lower 95% CI	Upper 95% CI	p
Covid19 Confirmed Count	1.0003	1.0002	1.0005	0.0001
Age Band (ref. level 0-15)				
16-64	12.3	11.6	13.1	<0.0001
65+	43.6	41.0	46.4	<0.0001
Gender (ref. level F)	0.79	0.77	0.81	<0.0001
IMD Quintile (ref. level Most Deprived)				
Q2	0.88	0.85	0.92	<0.0001
Q3	0.84	0.81	0.88	<0.0001
Q4	0.82	0.79	0.85	<0.0001
Q5 (least deprived)	0.71	0.69	0.74	<0.0001
NHS Region (Ref London)				
Midlands and East	1.69	1.63	1.76	<0.0001
North East and Yorkshire	1.45	1.38	1.52	<0.0001
North West	1.23	1.18	1.28	<0.0001
South East	1.07	1.02	1.12	0.002
South West	1.52	1.46	1.59	<0.0001
Resp. Disease				
LRTI Count	1.0098	1.0088	1.0109	<0.0001
URTI Count	1.0002	0.9995	1.0009	0.551
ILI Count	1.021	1.017	1.024	<0.0001

Table S3.7: Doxycycline prescribing in cases of COVID-19, for each unit rise in COVID-19 cases there has been a non-clinically significant rise in prescribing. Age 65 years and older, female gender, being more deprived, northern regions LRTI or ILI infections are all associated with a higher rate of prescribing

Comparison with Open Prescribing:

We compared the differences in the rate of prescribing in OpenPrescribing between 2019 and 2020 with those in the RSC. The increase in azithromycin prescribing was almost identical. Both datasets showed a decrease in doxycycline prescribing however it was -2.31% in OpenPrescribing compared with -7.02% in the RSC (Table S4.1).

	2019 OpenPrescribing			2020 OpenPrescribing			2019 RCGP			2020 RCGP	
	Doxy	Azith		Doxy	Azith		Doxy	Azith		Doxy	Azith
01/01/2019	330019	67232	01/01/2020	357980	71487	01/01/2019	20059	4189	01/01/2020	21389	4356
01/02/2019	262533	60916	01/02/2020	273769	64557	01/02/2019	15827	3699	01/02/2020	16375	3852
01/03/2019	249507	64264	01/03/2020	321979	77963	01/03/2019	14818	3826	01/03/2020	21131	5240
01/04/2019	245028	61168	01/04/2020	276404	73153	01/04/2019	15120	3852	01/04/2020	16295	4087
01/05/2019	231681	63809	01/05/2020	197299	64352	01/05/2019	14095	3762	01/05/2020	11810	3723
01/06/2019	206910	58523	01/06/2020	178034	64237	01/06/2019	12412	3342	01/06/2020	11051	3938
01/07/2019	206731	59961	01/07/2020	175987	65058	01/07/2019	13156	3853	01/07/2020	10930	3975
01/08/2019	201024	62694	01/08/2020	156884	58762	01/08/2019	11553	3522	01/08/2020	9503	3560
01/09/2019	211819	61199	01/09/2020	205472	65440	01/09/2019	13160	3791	01/09/2020	12755	4145
01/10/2019	275028	68038	01/10/2020	220466	68308	01/10/2019	16807	4124	01/10/2020	13463	4140
Total 2019	2420280	627804	Total 2020	2364274	673317	01/11/2019	17008	4020	01/11/2020	12676	4177
N.B. Open prescribing data only available for 10months in 2020						01/12/2019	20079	4382	01/12/2020	13789	4405
						Total 2019	184094	46362	Total 2020	171167	49598
Difference between years				-5600.6	4551.3	Difference between years				-12927	3236
% Difference between years				-2.31	7.25	% Difference between years				-7.02	6.98

Table S4.1 Comparison of prescribing of azithromycin and doxycycline in 2019 and 2020 in OpenPrescribing (national dataset, but data only to October 2020) and RSC. In both azithromycin prescribing increased by 7%. In both doxycycline prescribing reduced, but by 2.31 in OpenPrescribing and 7% in the RSC

