

Supplementary material

Table 1. Excluded symptoms from the analysis

	Excluded symptoms
Creation in the model	
	<i>lump on the lower extremity</i>
	<i>pustule in the armpit</i>
	<i>indurated skin of the armpit</i>
	<i>indurated skin of the groin</i>
	<i>scarring in the groin</i>
	<i>scarring in the armpit</i>
	<i>pruritic armpit</i>
	<i>erythema of the armpit</i>
	<i>proctitis on examination</i>
	<i>recurrent candidiasis in females</i>
	<i>recurrent candidiasis in males</i>
	<i>ear abscess</i>
	<i>penile discharge foreskin</i>
	<i>hyphema</i>
	<i>raised bumps on the glans penis</i>
	<i>raised bumps on the penis shaft</i>
	<i>spot on the glans penis</i>
	<i>spot on the penis shaft</i>
Deletion from the model	
	<i>recurrent candidiasis</i>
	<i>severe acute respiratory syndrome associated coronavirus</i>
Modification in associated terms	
	<i>alopecia</i>
	<i>thinning hair</i>
	<i>spot on the penis</i>

Table 2. Relative difference (log2 fold change values) in the proportions of Ada users' reported symptoms with statistically significant differences between the Baseline and COVID-19 Measures periods in Germany

ICD-10 groups & symptoms	Baseline (%)	Measures (%)	log2 fold change	P value^a
Cognition, perception, emotional state, and behaviour				
<i>diminished sense of taste^b</i>	.10	.48	2.26	<.001
<i>hyposmia^b</i>	.05	.24	2.20	<.001
<i>bad taste in mouth</i>	.27	.41	.62	.002
<i>depressed mood^b</i>	2.71	2.02	-.42	<.001
<i>loss of motivation</i>	.94	.59	-.67	<.001
<i>inability to manage constant stress and demands at work^b</i>	.43	.21	-1.07	<.001
<i>impaired concentration^b</i>	1.24	.91	-.46	<.001
<i>dizziness</i>	8.53	7.75	-.14	<.001
<i>memory difficulty^b</i>	.57	.39	-.56	<.001
<i>teeth grinding</i>	.09	.04	-1.26	.033
<i>aggressive behavior</i>	.36	.25	-.51	.046
Nervous system				
<i>excessive daytime sleepiness^b</i>	2.74	1.9	-.53	<.001
General symptoms and signs				
<i>lowered temperature of the foot^b</i>	.34	.55	.71	<.001
<i>body temperature decreased</i>	.06	.14	1.12	.005
<i>malaise^b</i>	2.53	1.25	-1.02	<.001
<i>fatigue^b</i>	9.24	7.35	-.33	<.001
<i>chills^b</i>	3.88	2.78	-.48	<.001
<i>fever</i>	6.32	4.95	-.35	<.001
<i>headache</i>	19.90	17.90	-.16	<.001
<i>reduced performance</i>	1.96	1.51	-.37	<.001
<i>abulia</i>	.66	.45	-.56	<.001
<i>tenderness head</i>	1.24	.97	-.36	.001
<i>hyperhidrosis generalized</i>	1.98	1.70	-.23	.015
Musculoskeletal system				
<i>mark from bug bite</i>	.04	.17	2.12	<.001
<i>myalgia^b</i>	4.11	2.52	-.71	<.001
<i>muscle cramps in the lower extremity</i>	.38	.26	-.57	.014
<i>feeling of heavy limbs</i>	.11	.05	-1.10	.029
<i>feeling of unstable knee</i>	.08	.04	-1.25	.047
Digestive system and abdomen				
<i>odynophagia^b</i>	3.99	2.33	-.77	<.001
<i>vomiting^b</i>	2.62	1.83	-.51	<.001
<i>nausea^b</i>	10.90	10.00	-.13	<.001
<i>diarrhea^b</i>	5.90	5.37	-.14	.007

Speech and voice				
<i>hoarseness</i> ^b	.77	.36	-1.10	<.001
<i>odynophonia</i> ^b	.37	.24	-.64	.004
<i>aphonia</i> ^b	.06	.02	-1.64	.047
Eye and adnexa				
<i>otalgia</i> ^b	2.93	1.93	-.61	<.001
<i>inability to clear the ear with changing barometric pressure</i> ^b	.52	.31	-.77	<.001
<i>aural fullness</i> ^b	.85	.60	-.51	<.001
<i>post orbital pain</i>	1.92	1.59	-.27	.003
<i>hearing deficit</i>	.47	.34	-.49	.017
<i>ocular discharge</i>	.15	.08	-.87	.046
Circulatory and respiratory systems				
<i>dyspnea</i> ^b	3.67	5.38	.55	<.001
<i>sneezing</i>	.69	1.31	.93	<.001
<i>chest pain</i> ^b	7.11	8.34	.23	<.001
<i>tragal tenderness</i>	.05	.19	1.84	<.001
<i>throat tightness</i>	1.11	1.47	.40	<.001
<i>sternal pain</i>	.18	.28	.69	.009
<i>dry throat</i>	.59	.77	.39	.011
<i>throat clearing</i> ^b	.16	.26	.71	.011
<i>nasal discharge</i> ^b	7.20	4.75	-.60	<.001
<i>sore throat</i> ^b	8.44	6.14	-.46	<.001
<i>cough</i> ^b	12.90	10.20	-.34	<.001
<i>sinus pain</i> ^b	.71	.43	-.73	<.001
<i>nasal congestion</i> ^b	3.32	2.71	-.29	<.001
<i>recurrent respiratory tract infections</i>	.64	.39	-.73	<.001
Skin and subcutaneous tissue				
<i>pruritic eyes</i> ^b	.38	.81	1.10	<.001
<i>dry skin of the hands</i> ^b	.20	.46	1.21	<.001
<i>skin rash of the hand</i>	.27	.52	.97	<.001
<i>skin rash of the upper extremity</i>	.27	.46	.76	<.001
<i>spot on the upper extremity</i> ^b	.15	.30	.98	<.001
<i>pruritic nasal cavity</i> ^b	.16	.30	.94	<.001
<i>pruritic hand</i>	.13	.23	.90	.001
<i>scaling skin of the intertriginous areas</i>	.01	.05	2.51	.003
<i>indurated skin of the foot</i>	.00	.04	3.27	.011
<i>skin rash of the antecubital fossa</i>	.02	.07	1.61	.011
<i>spot on the hand</i>	.05	.11	1.11	.023
<i>pruritic penis</i>	.16	.08	-.92	.021
Genitourinary system				
<i>breast tenderness</i>	1.13	1.48	.39	<.001
<i>pustule on the male genital</i>	.07	.03	-1.40	.048

^a Pearson chi-square test for differences between Baseline and Measures. *P* values were adjusted for multiple testing using the false discovery rate method.

^b symptoms were also found to be significantly different between the Baseline and the Measures period in the United Kingdom

Table 3. Relative difference (log2 fold change values) in the proportions of Ada users' reported symptoms with statistically significant differences between the Baseline and COVID-19 Measures periods in the United Kingdom

ICD-10 groups & symptoms	Baseline (%)	Measures (%)	log2 fold change	P value^a
Cognition, perception, emotional state, and behaviour				
<i>hyposmia^b</i>	.07	.96	3.74	<.001
<i>diminished sense of taste^b</i>	.09	.98	3.38	<.001
<i>olfactory hallucination</i>	.04	.11	1.49	.023
<i>depressed mood^b</i>	4.11	2.49	−.72	<.001
<i>anxiety</i>	2.72	1.71	−.67	<.001
<i>social phobia</i>	.66	.31	−1.08	<.001
<i>inability to manage constant stress and demands at work^b</i>	.35	.13	−1.43	<.001
<i>impaired concentration^b</i>	1.71	1.18	−.53	<.001
<i>memory difficulty^b</i>	.72	.43	−.73	<.001
<i>previous depressive episode</i>	.40	.21	−.94	<.001
<i>suicidal tendencies</i>	.79	.52	−.61	<.001
<i>crying</i>	.77	.52	−.57	.001
<i>mood lability</i>	1.39	1.08	−.35	.009
<i>excessive worry</i>	.51	.33	−.61	.010
<i>extreme fear of situations with difficulty to escape or to get help</i>	.16	.07	−1.26	.010
Nervous system				
<i>excessive daytime sleepiness^b</i>	2.10	1.57	−.43	<.001
<i>poorly restorative sleep</i>	.62	.43	−.53	.015
General symptoms and signs				
<i>lowered temperature of the foot^b</i>	.37	.56	.60	.006
<i>fatigue^b</i>	12.70	10.10	−.33	<.001
<i>malaise^b</i>	3.54	2.31	−.61	<.001
<i>chills^b</i>	4.21	3.36	−.33	<.001
<i>binge eating</i>	.46	.24	−.91	<.001
<i>cervical lymphadenopathy</i>	1.25	.92	−.44	.001
<i>weight gain</i>	.66	.43	−.61	.002
<i>irritability pediatric patient</i>	.17	.07	−1.26	.007
<i>weight loss</i>	.59	.42	−.51	.025
Musculoskeletal system				
<i>generalized arthralgia</i>	1.04	.75	−.48	.001
<i>hip pain</i>	1.18	.93	−.34	.027
<i>imbalance</i>	.32	.20	−.69	.037
<i>myalgia^b</i>	3.86	3.42	−.17	.037
Digestive system and abdomen				

<i>gingival swelling</i>	.09	.18	.95	.049
<i>vomiting</i> ^b	3.11	2.15	-.53	<.001
<i>odynophagia</i> ^b	1.29	.75	-.78	<.001
<i>nausea</i> ^b	12.50	11.40	-.14	<.001
<i>diarrhea</i> ^b	5.81	5.10	-.19	.001
<i>abdominal pain</i>	18.10	17.00	-.09	.005
<i>flatulence</i>	1.69	1.38	-.30	.018
<i>change in stool color</i>	.64	0.47	-.45	.046
Speech and voice				
<i>aphonia</i> ^b	.26	.07	-1.87	<.001
<i>odynophonia</i> ^b	.47	.21	-1.17	<.001
<i>hoarseness</i> ^b	.37	.23	-.68	.020
Eye and adnexa				
<i>inability to clear the ear with changing barometric pressure</i> ^b	.37	.21	-.85	.002
<i>aural fullness</i> ^b	1.03	.77	-.42	.008
<i>otalgia</i> ^b	3.00	2.62	-.20	.040
Circulatory and respiratory systems				
<i>chest pain</i> ^b	7.85	9.59	.29	<.001
<i>pruritic throat</i>	.49	.74	.59	.001
<i>dyspnea</i> ^b	5.71	6.45	.18	.001
<i>throat clearing</i> ^b	.15	.28	.90	.006
<i>nasal pain</i>	.41	.58	.49	.036
<i>muscular tenseness of the chest muscles</i>	.17	.28	.72	.047
<i>sore throat</i> ^b	10.50	7.20	-.55	<.001
<i>nasal discharge</i> ^b	5.63	3.31	-.77	<.001
<i>nasal congestion</i> ^b	5.16	3.61	-.51	<.001
<i>sinus pain</i> ^b	2.66	2.14	-.31	<.001
<i>cough</i> ^b	13.60	12.60	-.11	.005
<i>tonsillopharyngeal exudate</i>	.46	.31	-.59	.023
<i>tonsillar enlargement</i>	.43	.28	-.61	.026
Skin and subcutaneous tissue				
<i>pruritic eyes</i> ^b	.44	.89	1.02	<.001
<i>pruritic nasal cavity</i> ^b	.10	.28	1.52	<.001
<i>urticaria</i>	.18	.33	.86	.004
<i>dry skin of the hands</i> ^b	.14	.28	.96	.004
<i>scaling skin of the face</i>	.05	.13	1.38	.015
<i>spot on the upper extremity</i> ^b	.18	.30	.72	.037
<i>scrotal pruritus</i>	.16	.06	-1.27	.011
Genitourinary system				
<i>vaginal pain</i>	.62	.44	-.51	.019

^a Pearson chi-square test for differences between Baseline and Measures. *P* values were adjusted for multiple testing using the false discovery rate method.

^b symptoms were also found to be significantly different between the Baseline and the Measures period in Germany

Table 4. Relative difference (log2 fold change values) in the proportions of Ada users' reported symptoms with statistically significant differences between the same period as the Baseline and COVID-19 Measures periods in 2019 in Germany

ICD-10 groups & symptoms	Baseline (%)	Measures (%)	log2 fold change	P value ^a
General symptoms and signs				
<i>malaise</i>	2.57	1.82	-.50	<.001
<i>fatigue</i>	8.97	7.98	-.17	.014
<i>chills</i>	4.01	2.61	-.62	<.001
<i>fever</i>	5.67	3.65	-.64	<.001
<i>headache</i>	21.1	17.6	-.26	<.001
Musculoskeletal system				
<i>myalgia</i>	4.03	2.76	-.55	<.001
Circulatory and respiratory systems				
<i>nasal discharge</i>	8.15	6.24	-.39	<.001
<i>sore throat</i>	8.53	7.12	-.26	<.001
<i>cough</i>	11.3	8.8	-.37	<.001
<i>sinus pain</i>	.84	.56	-.59	.029

^a Pearson chi-square test for differences between Baseline and Measures. P values were adjusted for multiple testing using the false discovery rate method.

Table 5. Relative difference (log2 fold change values) in the proportions of Ada users' reported symptoms with statistically significant differences between the same period as the Baseline and COVID-19 Measures periods in 2019 in the United Kingdom

ICD-10 groups & symptoms	Baseline (%)	Measures (%)	log2 fold change	P value ^a
Genitourinary system				
<i>breast tenderness</i>	2.59	1.85	-.49	<.001

^a Pearson chi-square test for differences between Baseline and Measures. P values were adjusted for multiple testing using the false discovery rate method.

Table 6. Correlation between the significantly different symptoms in Germany and three weather variables (temperature, precipitation, and sunshine)

Symptoms	Temperature		Precipitation		Sunshine	
	ρ	<i>P</i> value ^a	ρ	<i>P</i> value ^a	ρ	<i>P</i> value ^a
<i>dyspnea</i>	.08	.825	.02	.964	.25	.458
<i>diminished sense of taste</i>	-.46	.145	.05	.964	-.25	.458
<i>pruritic eyes</i>	.50	.116	-.37	.964	.76	.023
<i>hyposmia</i>	-.34	.301	-.04	.964	-.14	.700
<i>chest pain</i>	-.80	.007	.09	.964	-.67	.061
<i>dry skin of the hands</i>	-.51	.104	-.37	.964	-.09	.773
<i>lowered temperature of the foot</i>	-.86	.003	.09	.964	-.79	.023
<i>spot on the upper extremity</i>	.80	.007	-.09	.964	.75	.023
<i>pruritic nasal cavity</i>	.49	.116	-.49	.917	.77	.023
<i>throat clearing</i>	.03	.917	-.06	.964	.26	.458
<i>nasal discharge</i>	-.60	.052	-.02	.964	-.41	.243
<i>odynophagia</i>	-.68	.027	-.04	.964	-.60	.070
<i>malaise</i>	-.64	.040	.17	.964	-.59	.070
<i>myalgia</i>	-.74	.012	.05	.964	-.62	.070
<i>sore throat</i>	-.53	.104	.02	.964	-.33	.349
<i>cough</i>	-.75	.011	.06	.964	-.60	.070
<i>fatigue</i>	-.41	.196	.05	.964	-.28	.456
<i>otalgia</i>	-.73	.014	.08	.964	-.58	.071
<i>chills</i>	-.77	.010	.03	.964	-.64	.070
<i>excessive daytime sleepiness</i>	.17	.638	.23	.964	.05	.856
<i>hoarseness</i>	-.61	.052	.29	.964	-.58	.071
<i>vomiting</i>	-.64	.040	-.12	.964	-.65	.070
<i>depressed mood</i>	-.52	.104	.32	.964	-.61	.070
<i>inability to manage constant stress and demands at work</i>	-.20	.572	.50	.917	-.55	.092
<i>sinus pain</i>	-.76	.010	.15	.964	-.72	.033
<i>nasal congestion</i>	-.60	.052	-.19	.964	-.34	.349
<i>inability to clear the ear with changing barometric pressure</i>	-.44	.169	.23	.964	-.46	.181
<i>impaired concentration</i>	-.37	.256	.18	.964	-.42	.240
<i>aural fullness</i>	-.52	.104	.44	.964	-.60	.070
<i>nausea</i>	.05	.890	.28	.964	-.17	.627
<i>memory difficulty</i>	-.15	.669	.22	.964	-.27	.456
<i>odynophonia</i>	-.55	.088	.03	.964	-.34	.349
<i>diarrhea</i>	.66	.035	.15	.964	.49	.147
<i>aphonia</i>	-.23	.519	-.49	.917	-.10	.773

^a Pearson chi-square test for differences between Baseline and Measures. *P* values were adjusted for multiple testing using the false discovery rate method.

Figure 1. Correlation between the significantly different symptoms in Germany and three weather variables (temperature, precipitation, and sunshine)

