Variant-specific symptoms of COVID-19 among 1,542,510 people in England

Matthew Whitaker[a,b*], Joshua Elliott[c,d*], Barbara Bodinier[a,b], Wendy Barclay,[d] Helen Ward[c,e,f], Graham Cooke[c,d,f], Christl A. Donnelly[a,e,g], Marc Chadeau-Hyam[a,b†], Paul Elliott[a,b,c,f,h,i†]

[a] School of Public Health, Imperial College London, UK
[b] MRC Centre for Environment and Health, Imperial College London, UK
[c] Imperial College Healthcare NHS Trust, UK
[d] Department of Infectious Disease, Imperial College London, London, UK
[e] MRC Centre for Global Infectious Disease Analysis and Jameel Institute, Imperial College London, UK
[f] National Institute for Health Research Imperial Biomedical Research Centre, UK
[g]Department of Statistics, University of Oxford, UK
[h] Health Data Research (HDR) UK London at Imperial College, UK
[i] UK Dementia Research Institute at Imperial College, UK

[*]Joint first author

[†]Equal contribution

Address for Correspondence:

Professor Paul Elliott, Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, St Mary's campus, London W2 1PG, UK

Email: p.elliott@imperial.ac.uk

Keywords

COVID-19, symptoms, SARS-CoV-2, Omicron, Delta, Alpha, wild-type

Abstract

Infection with SARS-CoV-2 virus is associated with a wide range of symptoms. The REal-time Assessment of Community Transmission -1 (REACT-1) study has been monitoring the spread and clinical manifestation of SARS-CoV-2 among random samples of the population in England from 1 May 2020 to 31 March 2022. We show changing symptom profiles associated with the different variants over that period, with lower reporting of loss of sense of smell and taste for Omicron compared to previous variants, and higher reporting of cold-like and influenza-like symptoms, controlling for vaccination status. Contrary to the perception that recent variants have become successively milder, Omicron BA.2 was associated with reporting more symptoms, with greater disruption to daily activities, than BA.1. With restrictions lifted and routine testing limited in many countries, monitoring the changing symptom profiles associated with SARS-CoV-2 infection and induced changes in daily activities will become increasingly important.

A meta-analysis of studies from the first wave of the pandemic identified 30 symptoms reported in multiple studies,[1] including common influenza-like symptoms (cough, fever, myalgia/fatigue, headache, sputum production), and less common but more specific symptoms including change or loss of sense of smell and taste.

Previous community-based studies have assessed the degree to which symptom data can predict polymerase chain reaction (PCR) positivity for SARS-CoV-2, and have used variable selection and ranking techniques to identify the most important (set of) symptoms for case identification.[2–4] Further studies have indicated that symptom profiles may differ between variants of SARS-CoV-2.[5–7]

The relationship between symptom profile and cycle threshold (Ct) value from PCR testing (an established proxy for viral load,[8–10] which in turn correlates with infectiousness[11,12]) has also yet to be fully investigated. Identifying individuals who are more likely to be i) infected, and ii) infectious on the basis of symptom profile would have clinical value as governments move away from mass testing programmes and mandatory isolation measures.

Here, we use regression modelling and variable selection models in the large community-based REal-time Assessment of Community Transmission -1 (REACT-1) study that was in the field approximately monthly from 1 May 2020 to 31 March 2022 to i) describe the symptom profiles of the main variants of SARS-CoV-2 that have been dominant in England and worldwide since May 2020, namely wild-type, Alpha, Delta and Omicron BA.1 and BA.2, and ii) identify the symptoms that are most predictive of high viral load, and hence infectiousness, for each variant.

Methods

Study population

The REACT-1 study has been tracking the prevalence of SARS-CoV-2 in the general population of England. The study protocol and methodology have been published in detail;[2,13] briefly, every 4–6 weeks, recruitment letters were sent to a random, nationally representative sample of people aged 5 years and over in England, using the National Health Service patient register. Participants then obtained self-administered throat and nasal swabs for SARS-CoV-2 PCR testing and completed an online or telephone questionnaire which included questions on demographic variables, behaviour, and recent symptoms. Questionnaires for each of the 19 completed rounds since May 2020 are available on the study website (https://www.imperial.ac.uk/medicine/research-and-impact/groups/react-study/for-researchers/react-1-study-materials/). Between 95,000 and 175,000 viable swabs and valid responses were gathered each round, with respondents unaware of their test result at the time of their response.

Participants were asked whether they experienced any of a list of 26 potential COVID-19 symptoms in the week prior to their test. These included loss or change of sense of smell or taste, respiratory/cardiac symptoms (new persistent cough, chest pain, tight chest, shortness of breath), cold-like symptoms (runny nose, blocked nose, sneezing, sore throat, hoarse voice, sore eyes), influenza-like symptoms (fever, chills, muscle aches, headache), gastrointestinal symptoms (nausea/vomiting, abdominal pain/belly ache, diarrhoea, appetite loss), fatigue-related symptoms (tiredness, severe fatigue, difficulty sleeping), and others (dizziness, heavy arms or legs, numbness/tingling).

We use data from 15 rounds of REACT-1 between 19 June 2020 and 31 March 2022 into distinct phases that correspond with the dominance of different SARS-CoV-2 variants in England: rounds 2–7 (at approximately monthly intervals between 19 June and 3 December 2020), when wild-type was dominant; rounds 8–10 (between 6 January and 29 March 2021), when Alpha (B.1.1.7) was dominant; rounds 13–15 (between 24 June and 5 November 2021), when Delta (B.1.617.2) was dominant; and rounds 17–19 (between 5 January and 31 March 2022), when Omicron (B.1.1.529) was dominant. In rounds 17–19 we use sequencing data to identify those participants who were infected with BA.1 or BA.2. Round 1 is excluded because the symptom questions asked were not consistent with subsequent rounds. Rounds 11, 12 and 16 are excluded from analysis because they occurred at times when two variants were competing for dominance in the population.[14]

Adults aged 18 years and over were included in the analysis. A total of 266,847 participants were excluded because of missing symptom data, and 38 were excluded because of missing age or sex data resulting in a final study population, after exclusions, of 1,542,510 participants.

Statistical analyses

We used univariable logistic regression models to estimate the risk of PCR swab-positivity for each variant conditional on experiencing each of the 26 symptoms. Models were adjusted on age group, sex, and self-reported vaccination status (coded as the number of vaccines received). Odds ratios and 95% confidence intervals are reported for each symptom and each variant.

Variable selection models were trained on 70% of the data set, with 30% held back for model performance evaluation (see **Supplementary Methods**). We used stability selection applied to least absolute shrinkage and selection operator (LASSO) penalised logistic regression, with swab positivity as the binary outcome variable, and the 26 symptoms as predictors. To adjust for age, sex and vaccination status, these were included in the models as unpenalised variables. The regression coefficients for selected symptoms were constrained to non-negative values. LASSO models were fit on 1000 random 50% subsamples of the 70% training data. The proportion of models in which each symptom was selected is taken as a measure of variable importance. The threshold in selection proportion for final variable selection was calibrated in conjunction with the LASSO penalty parameter using an internal stability score.[15]

BA.1 vs BA.2

Omicron BA.1 and BA.2 lineages were determined using viral genome sequencing on swab-positive swabs from rounds 17–19. We compared the symptom profiles in (BA.1 or BA.2) swab-positive individuals using logistic regression with BA.2 vs BA.1 as the binary outcome variable and each of the 26 symptoms as explanatory variables, adjusted on age group, sex, vaccination status and round. As a sensitivity analysis, we 1:1 matched swab-positive participants with BA.1 and BA.2 on age group (+/- 5 years), sex, vaccination status and round in rounds 17–19, and conducted conditional logistic regression with BA.2 vs BA.1 as the binary outcome variable.

Severity of symptoms

To assess whether there are differences in symptom severity between BA.1 and BA.2 independent of vaccination history we took a subset of swab-positive individuals with sequence-confirmed BA.1 or BA.2 who had received booster (third) vaccines at least two weeks before their PCR test. In this group, we compared the risk of reporting symptoms that affected their daily activities ‘a lot’ vs ‘a little’ or ‘not at all’ in people infected with BA.1 vs BA.2.
We adjusted for age, sex, days since booster (including a squared polynomial term), and round.

Ct values

Finally, we investigated the relationship between N-gene Ct value and symptom profile among swab positive individuals in rounds 17–19 (>95% Omicron), using linear regression models with Ct value as the outcome variable and each symptom separately as the independent variable. We

also compared Ct values between swab-positive individuals with BA.1 and BA.2 using an unpaired Wilcoxon test.

Results

Descriptive and univariable analysis

The characteristics of our study population are summarised in Figure 1 and Supplementary Tables 1 and 2. We included a total of 17,448 swab positive individuals: 2,971 (0.4% [0.4,0.4] unweighted prevalence) for wild,type; 2,275 (0.6% [0.6,0.7]) for Alpha; 1,493 (0.7% [0.6,0.7]) for Delta and 10,709 (4.4% [4.3,4.5]) for Omicron (Table S1).

The proportion of swab positive individuals reporting any of 26 symptoms was highest in those infected with BA.2 (75.9% [74.4,77.2], compared with 70% [68.3,71.6] in those with BA.1, 63.8% [61.3,66.2] in those with Delta, 54.7%, [52.7,56.8] in those with Alpha and 45% [43.3,46.8] in those with wild-type) (Table S2). Background prevalence of symptoms was also highest during January – March 2022, when Omicron dominated: 21.9%, [21.7,22.0] of all respondents reported one or more symptoms, compared with 13.5% [13.4,13.5] during the wild-type period (Table S1).

Those infected with BA.2 reported an average of 6.02 symptoms in the week prior to PCR testing, compared with 2.70, 3.38, 4.63 and 4.63 for wild-type, Alpha, Delta and BA.1 respectively (Table S2). A larger proportion of people with BA.2 reported that their symptoms had affected their ability to carry out day-to-day activities ‘a lot’ (17.6% [16.3,18.8]) compared with those infected with BA.1 (10.7% [9.6,11.9]) or Delta (10.5%, [9.1,12.2]) (Table S2).

All symptoms were positively associated with swab positivity for all variants (Figure 2, Table S3). The odds ratio for swab positivity of ‘any of 26 symptoms’ was highest for BA.2 (OR=12.9 [11.9,14.0], compared with 5.16 [4.79,5.55], 6.01 [5.12,7.06], 9.53 [8.55,10.6] and 9.61 [8.82,10.5] for wild-type, Alpha, Delta and BA.1, respectively) (Table S3, Figure 2).

Unlike for wild-type, Alpha, and Delta, where the highest odds ratios for swab positivity were for loss or change of sense of smell (ORs 49.7 [44.3,55.7], 37.8 [28.6,50.0] and 73.4 [64.2,83.9] respectively) or taste (ORs 35.9 [31.9,40.4], 38.9 [29.9,50.6] and 68.1 [59.4,78.0] respectively), for BA.1 and BA.2, influenza-like and cold-like symptoms were relatively more predictive of swab positivity, and loss or change of sense of smell or taste relatively less so. Within BA.1 and BA.2, the highest odds ratio of all symptoms was for fever: ORs were 18.4 [16.5,20.5] in BA.1 and 30.2 [27.7,33.0] in BA.2, compared with 12.9 [11.1,15.1] and 17.2 [15.1,19.5] respectively for loss or change of sense of smell and 16.0 [13.9,18.5] and 21.3 [18.9,24.0] respectively for loss or change of sense of taste (Figure 2, Table S3).

Multivariable analysis for variable selection

We used LASSO penalised logistic regression to identify parsimonious symptom sets selected as jointly and positively predictive of swab positivity for each variant (Figure 3); this method takes into account differences in symptom cooccurrence by variant (Figure S3). Loss or change of

sense of taste, new persistent cough, and fever were selected for each variant. Notably, cold-like symptoms of runny nose, sore throat, sneezing and hoarse voice were only selected for Omicron (BA.1 and BA.2).

Omicron (BA.1 and BA.2)

Comparing symptoms for BA.2 vs BA.1 using (adjusted and matched) logistic regression (see **Methods**), infection with BA.2 was positively associated with chest pain, severe fatigue, runny nose, muscle aches, sneezing, fever, chills, tiredness, blocked nose and headache (in both models); in unmatched analysis, infection with BA.2 is further associated with further associated with sore eyes, appetite loss and new persistent cough.

In a triple-vaccinated subgroup of 4,834 swab-positive individuals with BA.1 or BA.2, those infected with BA.2 were 64% more likely to report symptoms that interfered with their ability to carry out day-to-day activities ‘a lot’ (OR 1.64 [1.22, 2.19]) vs ‘a little’, ‘not at all’, or not reporting any symptoms, after adjustment for age group, sex, round, and time since third vaccine (Table 1). In the same models, men were 40% less likely than women to report symptoms that interfered with their ability to carry out day-to-day activities ‘a lot’ (OR 0.60, [0.51,0.72]).

Ct values

Ct values were lower for BA.2 than BA.1 (Figure S1). This may reflect the timing of the sampling with respect to the growth of the variant since more recent infections will tend to have lower Ct values (see Table S2 and Supplementary Figure S5, which show that mean time since symptom onset was lower in BA.2 than for BA.1). Symptomatic individuals had lower Ct values than asymptomatic people. In linear regression models among swab positive individuals in rounds 17–19, for each of the 26 surveyed symptoms, symptom reporting was associated with a lower Ct value. The lowest adjusted Ct values were for influenza-like or cold-like symptoms: fever, chills, sore throat, muscle aches, runny nose, sneezing and headache (Figure 4), which frequently co-occurred (Figure S3). With the exception of fever, these symptoms were also commonly reported as the first symptom among symptomatic swab positives (Figure S4, Table S2).

Discussion

In this study of more than 1.5 million people randomly selected from the population in England, we show a change in symptom reporting associated with Omicron compared with previous variants, and within Omicron for BA.2 vs BA.1. This may reflect changes in the underlying pathophysiology associated with different variants, affecting receptor binding, cell entry and host response, against a background of varying levels of population immunity (both from natural infection and vaccine-induced).[16–18]

We found that loss or change of sense of smell and taste were less predictive of swab positivity for Omicron than for other variants, and that cold-like symptoms were more predictive for Omicron than for previous variants. Both these findings were consistent with previous research.[5,19,20] It is of interest that infections with Omicron variants are not as strongly associated with anosmia. The loss of sense of smell and taste following infection with early variants of SARS-CoV-2 results from the downregulated expression of olfactory receptors.[21] It is likely that changes in the sequence of viral genes that regulate host responses in Omicron do not result in this effect. Detailed transcriptomic studies in animal models and humans may help to pinpoint the mechanisms involved.

Comparing Omicron BA.2 with BA.1, we found that those with BA.2 were more likely to be symptomatic, reported more symptoms on average, were more likely to report a number of influenza-like and cold-like symptoms, and were more likely to report that their symptoms affected their day-to-day activities 'a lot'. This last finding was robust to adjustment for time since third vaccine dose and is therefore unlikely to be explained by waning immunity from vaccination.

From 1 April 2022 the UK government moved to a policy of 'living with COVID'.[22] With the lifting of restrictions and access to free testing limited, identifying individuals who are particularly likely to be infectious on the basis of symptoms alone may help reduce ongoing transmission of SARS-CoV-2. We showed that reporting fever, chills, sore throat, muscle aches, runny nose, sneezing and headache was associated with the lowest adjusted Ct values and therefore most likely to be indicative of higher viral load and increased infectiousness.

Our study has limitations. Response rates varied between 11.7% and 26.5% for rounds 2–19, so the samples may not be fully representative of, or results fully generalisible to, the population. Nevertheless, our random community sampling procedure included individuals from all of the 315 lower tier local authority areas in England in each round, ensuring wide geographical coverage and socio-economic and demographic diversity. Of those who provided valid swabs and consented to linkage in rounds 1–19 of REACT-1 (2,191,597 people in total), approximately 3% (65,915 people) participated in more than one round. On this basis, a correction factor of

1.015 could therefore be applied to the standard error estimates. We are not able to definitively identify instances of participation in more than one round among those who did not consent to linkage. However, because the consent-based estimate of the correction factor is so close to one, we feel confident reporting uncorrected SEs and confidence intervals. The symptoms surveyed were not exhaustive but, while not specific to COVID-19, were all shown to be predictive of SARS-CoV-2 swab positivity. Our analysis covers a period of 22 months, during which time background levels of natural and vaccine-acquired immunity varied substantially, making it difficult to differentiate the effect of viral mutations from the impact of vaccines and prior infection.[18] As REACT-1 data collection was non-continuous, we may have captured different stages of epidemic growth across variants, which may have differentially affected symptom reporting at different times.

In summary, we have detected changes in symptom profiles reported during nearly two years of the epidemic in England, reflecting the emergence of different variants over that period. Most recently, infection with Omicron is associated with lower reporting of loss or change of sense of smell and taste, and higher reporting of cold-like and influenza-like symptoms. Sequence-confirmed BA.2 was associated with reporting of more symptoms and greater disruption to daily activity compared with BA.1. As routine testing becomes more limited in many countries, and as new variants emerge, understanding the symptom profiles which can identify individuals with a higher risk of transmission will become increasingly important.

Funding

The study was funded by the Department of Health and Social Care in England. The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of this manuscript. PE is Director of the Medical Research Council (MRC) Centre for Environment and Health (MR/L01341X/1, MR/S019669/1). PE acknowledges support from Health Data Research UK (HDR UK); the National Institute for Health Research (NIHR) Imperial Biomedical Research Centre; NIHR Health Protection Research Units in Chemical and Radiation Threats and Hazards, and Environmental Exposures and Health; the British Heart Foundation Centre for Research Excellence at Imperial College London (RE/18/4/34215); and the UK Dementia Research Institute at Imperial College London (MC_PC_17114). HW acknowledges support from an NIHR Senior Investigator Award, the Wellcome Trust (205456/Z/16/Z), and the NIHR Applied Research Collaboration (ARC) North West London. JE is an NIHR academic clinical fellow in infectious diseases. GC is supported by an NIHR Professorship. CAD acknowledges support from the MRC Centre for Global Infectious Disease Analysis, the NIHR Health Protection Research Unit in Emerging and Zoonotic Infections and the NIHR-funded Vaccine Efficacy Evaluation for Priority Emerging Diseases (PR-OD-1017-20007). MC-H and BB acknowledge support from Cancer Research UK, Population Research Committee Project grant 'Mechanomics' (grant No 22184 to MC-H). MC-H acknowledges support from the H2020-EXPANSE (Horizon 2020 grant No 874627) and H2020-LongITools (Horizon 2020 grant No 874739).

Ethics

We obtained research ethics approval from the South Central-Berkshire B Research Ethics Committee (IRAS ID: 283787). Notification of favorable opinion and brief summary of the protocol are available here: https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/react1-covid-19-uph/

Public involvement

A Public Advisory Panel provides input into the design, conduct, and dissemination of the REACT research program.

Data availability

Access to REACT-1 individual-level data is restricted to protect participants' anonymity. Summary statistics, descriptive tables, and code from the current REACT-1 study are available at https://github.com/mrc-ide/reactidd (doi 10.5281/zenodo.6550327). REACT-1 study materials are available for each round at

https://www.imperial.ac.uk/medicine/research-and-impact/groups/react-study/react-1-study-materials/

Sequence read data are available without restriction from the European Nucleotide Archive at https://www.ebi.ac.uk/ena/browser/view/PRJEB37886, and consensus genome sequences are available from the Global initiative on sharing all influenza data (GISAID)[23].

Figures and tables

Figure 1 Study population flow-chart. Variant prevalence data in bottom panel is from GISAID[23]

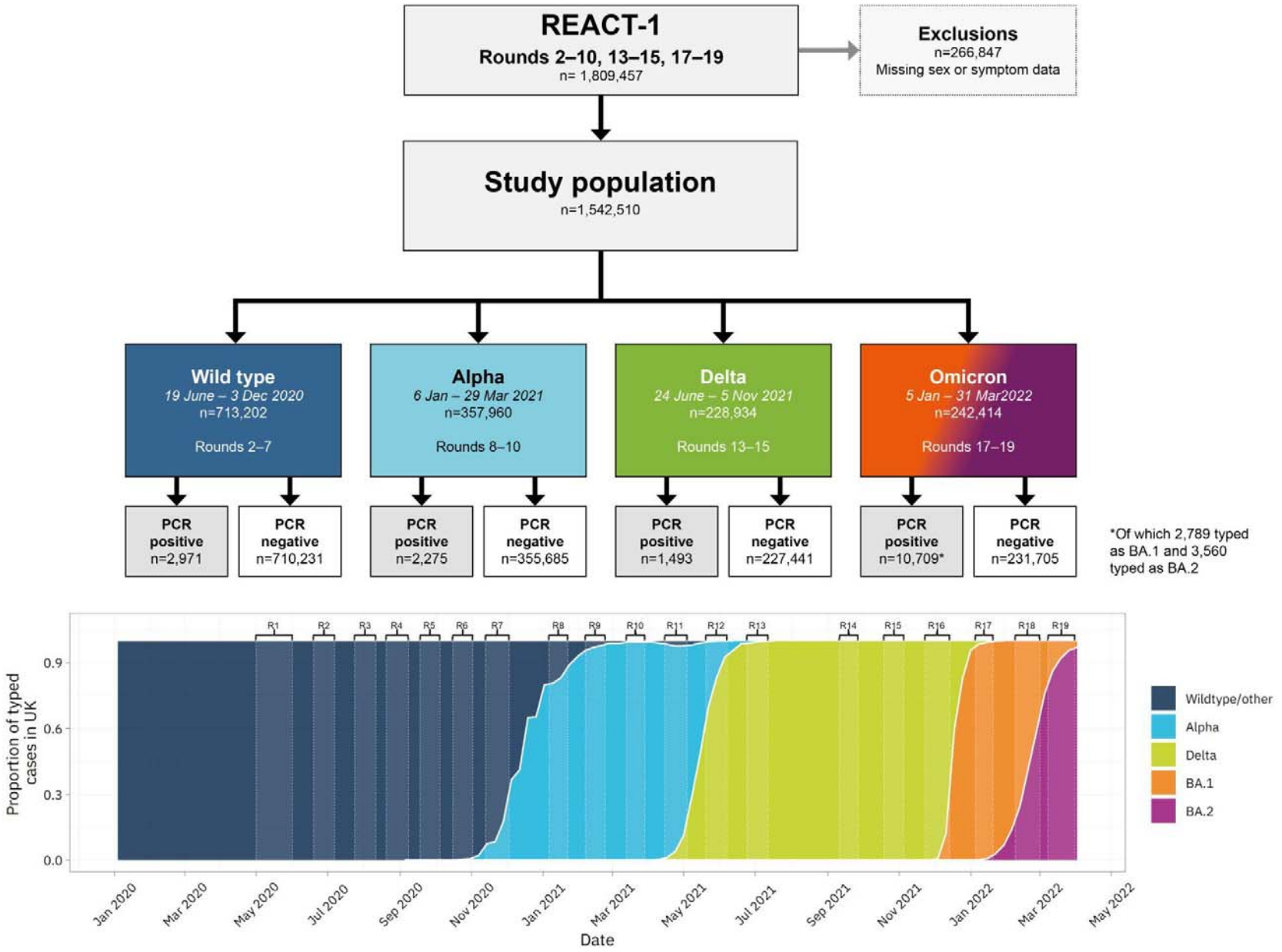


Figure 2 Comparison of ORs for swab positivity based on presence or absence of any of 26 symptoms surveyed across five variant-phases of REACT-1. ORs are derived from logistic regression models with swab positive (1/0) as the outcome variable, adjusted on age, sex and vaccination status. Bars show 95% confidence intervals. ORs are higher in BA.2 than BA.1 for all symptoms. Fever and cough have the highest ORs for BA.1 and BA.2, while loss of smell and taste have the highest ORs in all previous variants.

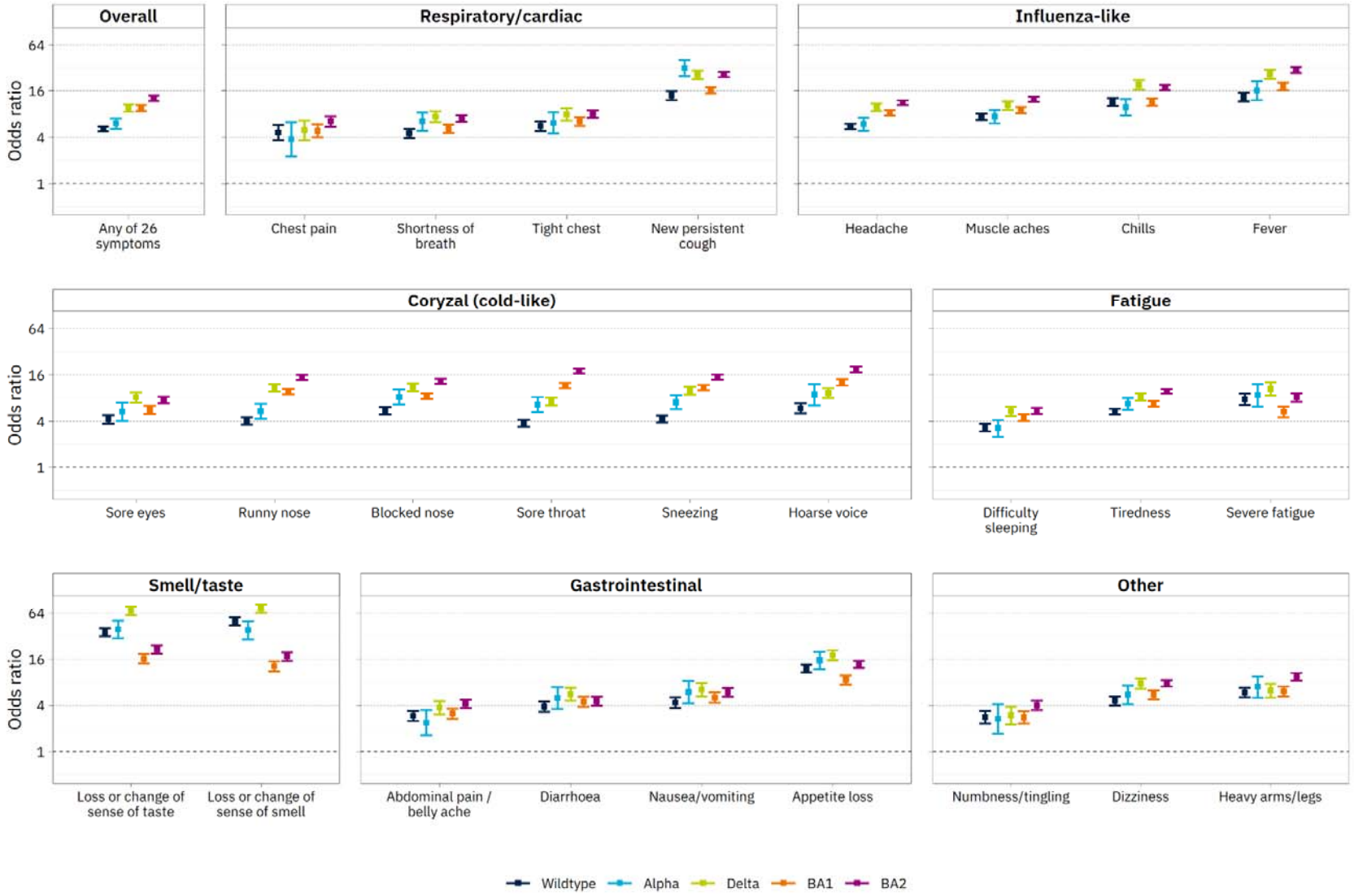


Figure 3 Results of LASSO stability selection proportions with swab positive/negative as the binary outcome variable and each of 26 symptoms as predictors, in five SARS-CoV-2 variants in England. Age, sex and, where appropriate, vaccination status are forced into the models as unpenalised variables; regression coefficients for the symptoms are constrained to be positive. The selection proportion indicates the proportion of LASSO models, trained on subsamples of the data, in which each symptom was selected as a predictor.

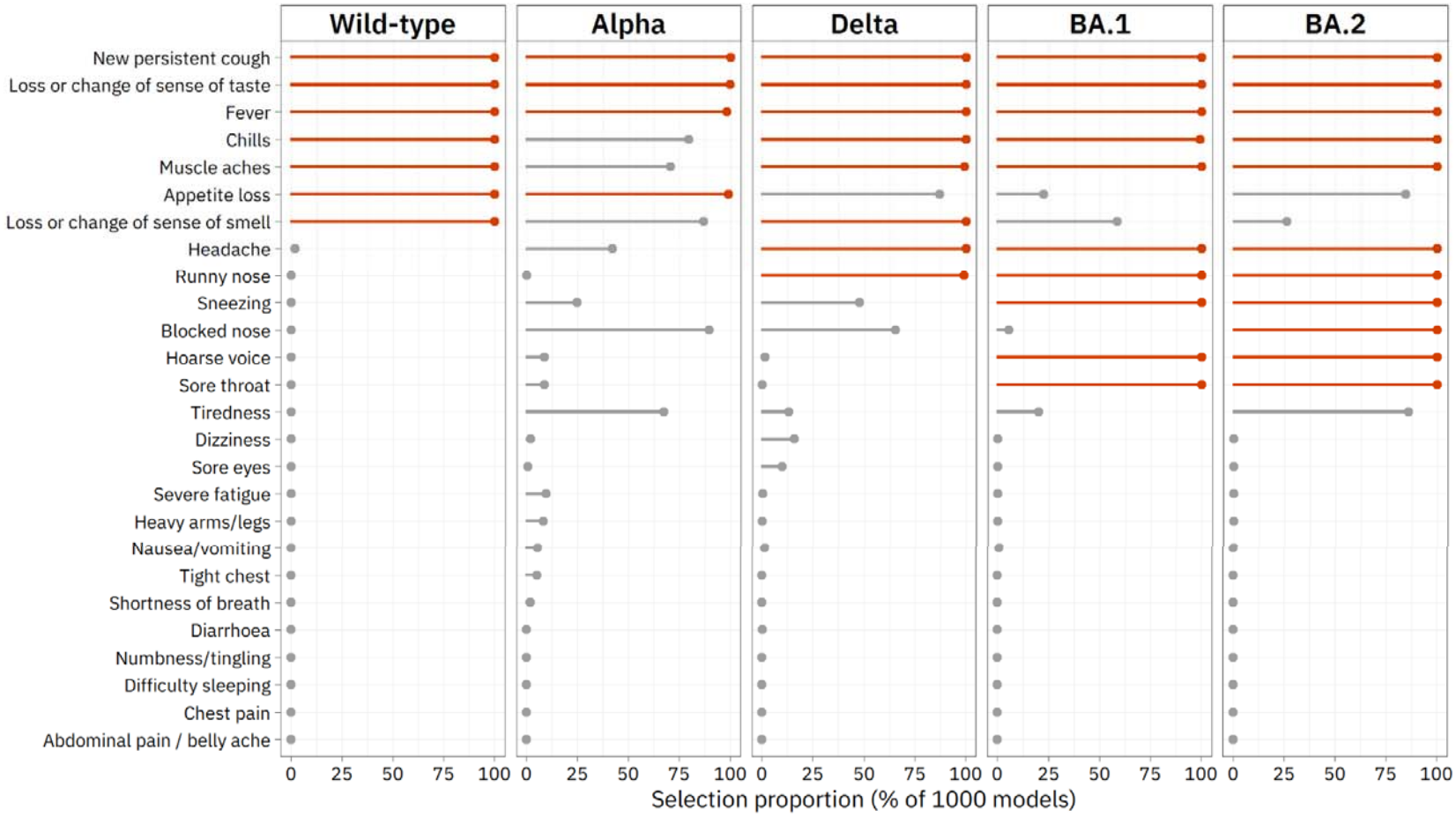


Figure 4 Results of linear regression models with N-gene Ct values as the outcome variable and symptoms as individual predictors, adjusted for age, sex and, where appropriate, vaccination status, among swab-positive respondents in rounds 17–19. Fever, chills, and sore throat are the symptoms with the strongest negative association with Ct value, each associated with approximately a tenfold decrease in viral load (3 Ct ~ 10x Δ).

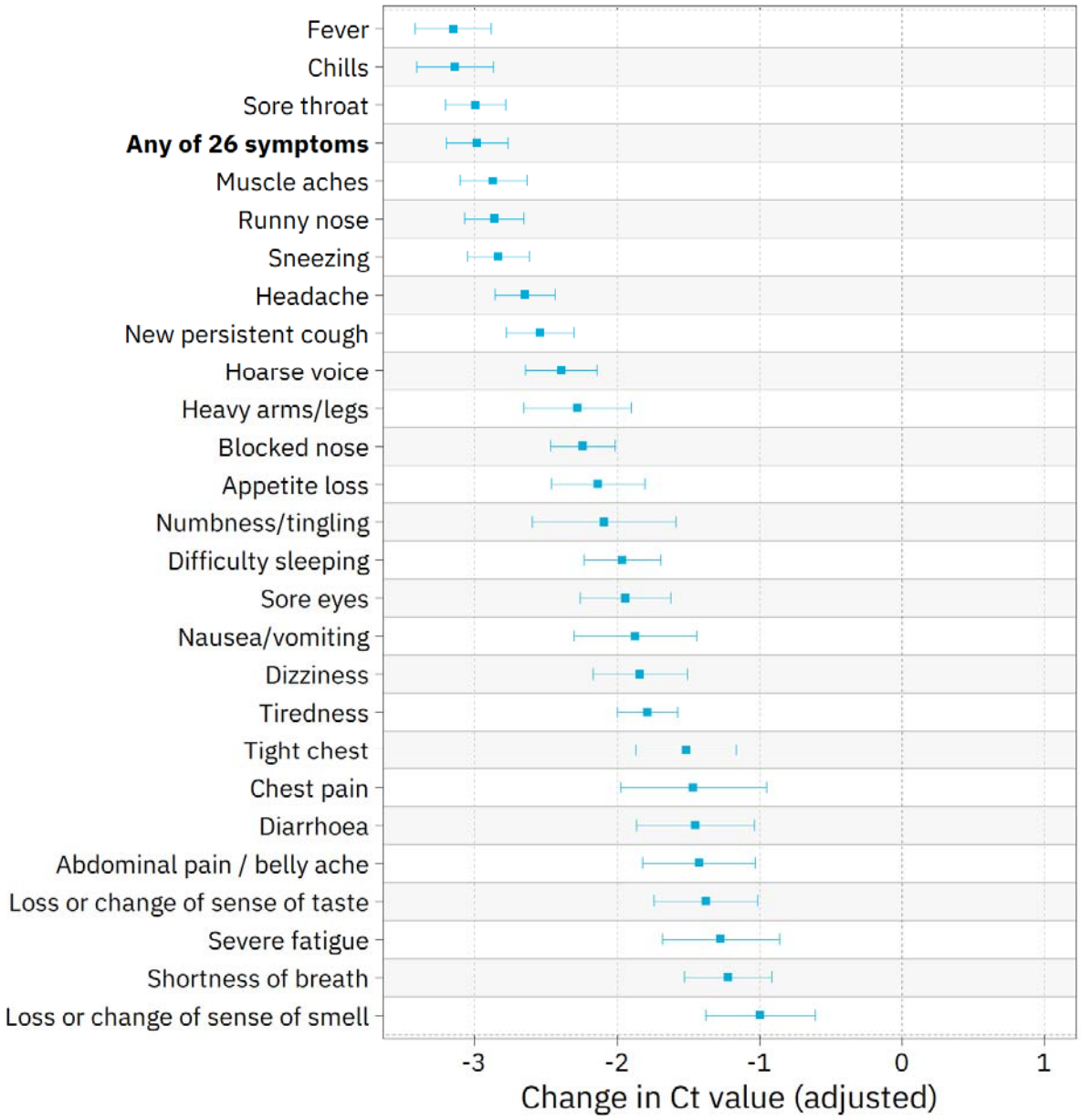


Figure 5 ORs for infection with BA.2 vs BA.1 among swab-positive respondents. ORs are derived from (i) logistic regression models with BA.2 vs BA.1 as the binary outcome variable, and presence or absence of any of 26 symptoms as explanatory variables, adjusted on age group, sex, round and vaccination status, among 5,598 swab-positive individuals with either BA.2 or BA.1 in rounds 17–19; and (ii) conditional logistic regression models with BA.2 vs BA.1 as the outcome variable among 1,510 swab-positive individuals with either the BA.2 or BA.1 variant in rounds 17–19, matched 1:1 on age (+/- 5 years), sex, vacination status and round. In left panel, bars show 95% confidence intervals, and symptoms are ordered by mean OR across both models. Right panel directly plots the ORs from the two models for comparison. In both analyses, infection with BA.2 (vs BA.1) is positively associated with chest pain, severe fatigue, runny nose, muscle aches, sneezing, fever, chills, tiredness, blocked nose and headache; in unmatched analysis, infection with BA.2 is further associated with sore eyes, appetite loss and new persistent cough.

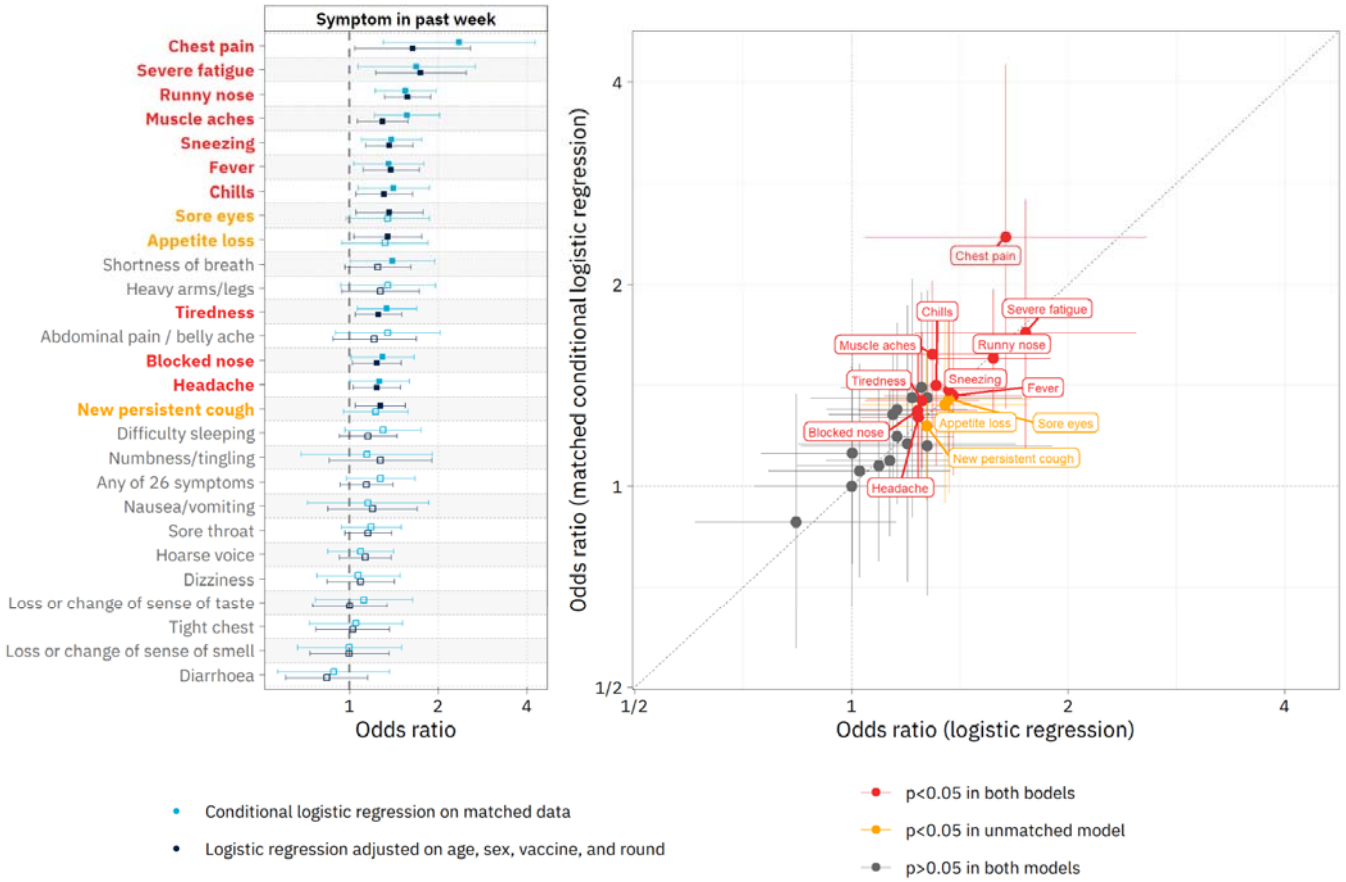


Table 1 Results from logistic regression modelling of the response to the question "How much, if at all, do the symptoms your/your child have/has had in the last 7 days reduce your/their ability to carry out day-to-day activities?" as a function of BA.1 / BA.2 infection, age, sex group, days since booster, and round, among 4,834 triple-vaccinated swab-positive individuals with either BA.1 or BA.2 lineage. The outcome variable is a binary 1/0 indicating where 1 indicates that the individual responded "A lot" and 0 indicates that the individual responded "A little" or "Not at all", or reported that they were asymptomatic. Those who responded "Prefer not to say" or "Don't know" were excluded from modelling.

Independent variable	Odds ratio with CI	P-value
Intercept	0.04, [0.02,0.07]	<0.01*
Age group: 25-34	1.70, [0.98,2.94]	0.06
Age group: 35-44	2.39, [1.41,4.07]	<0.01*
Age group: 45-54	2.91, [1.71,4.96]	<0.01*
Age group: 55-64	3.11, [1.83,5.28]	<0.01*
Age group: 65-74	1.75, [1.01,3.04]	0.05*
Age group: 74+	1.89, [1.02,3.49]	0.04*
Sex: male	0.60, [0.51,0.72]	<0.01*
BA.2	**1.64, [1.24,2.19]**	**<0.01***
Days since booster vaccine	1.00, [1.00,1.01]	0.13
[Days since booster vaccine]^2	1.00, [1.00,1.01]	0.22
Round 18	1.26, [0.90,1.75]	0.18
Round 19	1.23, [0.81,1.86]	0.33

Supplementary material

Table S1 Characteristics of study population

Variable	Category	Rounds 2-7 (Wild type)	Rounds 8-10 (Alpha)	Rounds 13-15 (Delta)	Rounds 17-19 (Omicron)	Sum / mean(SD)
All participants	All participants	713,202 (100%, [100-100])	357,960 (100%, [100-100])	228,934 (100%, [100-100])	242,414 (100%, [100-100])	1,542,510
Sex	Female	402,121 (56.4%, [56.3-56.5])	201,126 (56.2%, [56-56.3])	129,652 (56.6%, [56.4-56.8])	139,341 (57.5%, [57.3-57.7])	872,240
	Male	311,081 (43.6%, [43.5-43.7])	156,834 (43.8%, [43.7-44])	99,282 (43.4%, [43.2-43.6])	103,073 (42.5%, [42.3-42.7])	670,270
Age group	18-24	32,298 (4.5%, [4.5-4.6])	15,805 (4.4%, [4.3-4.5])	7,268 (3.2%, [3.1-3.2])	15,662 (6.5%, [6.4-6.6])	71,033
	25-34	73,352 (10.3%, [10.2-10.4])	35,260 (9.9%, [9.8-9.9])	19,691 (8.6%, [8.5-8.7])	34,242 (14.1%, [14-14.3])	162,545
	35-44	103,317 (14.5%, [14.4-14.6])	51,269 (14.3%, [14.2-14.4])	30,996 (13.5%, [13.4-13.7])	37,425 (15.4%, [15.3-15.6])	223,007
	45-54	137,175 (19.2%, [19.1-19.3])	68,057 (19%, [18.9-19.1])	43,205 (18.9%, [18.7-19])	37,937 (15.6%, [15.5-15.8])	286,374
	55-64	157,180 (22%, [21.9-22.1])	80,550 (22.5%, [22.4-22.6])	53,663 (23.4%, [23.3-23.6])	48,896 (20.2%, [20-20.3])	340,289
	65-74	144,612 (20.3%, [20.2-20.4])	74,535 (20.8%, [20.7-21])	50,980 (22.3%, [22.1-22.4])	45,876 (18.9%, [18.8-19.1])	316,003
	74+	65,268 (9.2%, [9.1-9.2])	32,484 (9.1%, [9-9.2])	23,131 (10.1%, [10-10.2])	22,376 (9.2%, [9.1-9.3])	143,259
Ethnicity	Asian	25,317 (3.6%, [3.6-3.6])	11,665 (3.3%, [3.3-3.4])	10,202 (4.6%, [4.5-4.6])	13,192 (5.6%, [5.5-5.7])	60,376
	Black	6,736 (1%, [0.9-1])	3,497 (1%, [1-1])	3,441 (1.5%, [1.5-1.6])	3,820 (1.6%, [1.6-1.7])	17,494
	Mixed	8,206 (1.2%, [1.1-1.2])	4,141 (1.2%, [1.1-1.2])	2,886 (1.3%, [1.2-1.3])	3,554 (1.5%, [1.5-1.6])	18,787
	Other	5,066 (0.7%, [0.7-0.7])	2,382 (0.7%, [0.7-0.7])	2,082 (0.9%, [0.9-1])	2,232 (0.9%, [0.9-1])	11,762
	White	658,752 (93.6%, [93.5-93.6])	330,027 (93.8%, [93.8-93.9])	205,368 (91.7%, [91.6-91.8])	213,938 (90.4%, [90.3-90.5])	1,408,085
PCR positive at time of survey	No	710,231 (99.6%, [99.6-99.6])	355,685 (99.4%, [99.3-99.4])	227,441 (99.3%, [99.3-99.4])	231,705 (95.6%, [95.5-95.7])	1,525,062
	Yes	2,971 (0.4%, [0.4-0.4])	2,275 (0.6%, [0.6-0.7])	1,493 (0.7%, [0.6-0.7])	10,709 (4.4%, [4.3-4.5])	17,448
Prior COVID-19 infection	No previous infection	604,198 (84.7%, [84.6-84.8])	301,856 (84.3%, [84.2-84.4])	189,854 (82.9%, [82.8-83.1])	165,113 (68.1%, [67.9-68.3])	1,261,021
	Previous infection greater than 28 days	3,308 (0.5%, [0.4-0.5])	10,374 (2.9%, [2.8-3])	14,428 (6.3%, [6.2-6.4])	42,367 (17.5%, [17.3-17.6])	70,477
	Previous infection with unknow time	26 (0%, [0-0])	56 (0%, [0-0])	34 (0%, [0-0])	67 (0%, [0-0])	183
	Previous infection within 28 days	1,276 (0.2%, [0.2-0.2])	1,906 (0.5%, [0.5-0.6])	1,659 (0.7%, [0.7-0.8])	13,349 (5.5%, [5.4-5.6])	18,190
	Suspected previous infection	103,703 (14.5%, [14.5-14.6])	43,483 (12.1%, [12-12.3])	22,805 (10%, [9.8-10.1])	21,333 (8.8%, [8.7-8.9])	191,324
	Unknown	691 (0.1%, [0.1-0.1])	285 (0.1%, [0.1-0.1])	154 (0.1%, [0.1-0.1])	185 (0.1%, [0.1-0.1])	1,315

Vaccination status	NA	-	-	912 (1.2%, [1.1-1.2])	2,882 (1.2%, [1.1-1.2])	3,794
	Not vaccinated	-	-	3,650 (4.6%, [4.5-4.8])	9,030 (3.7%, [3.7-3.8])	12,680
	One does	-	-	519 (0.7%, [0.6-0.7])	1,496 (0.6%, [0.6-0.6])	2,015
	Three does	-	-	14,388 (18.2%, [17.9-18.5])	198,035 (81.7%, [81.5-81.8])	212,423
	Two does	-	-	56,135 (71%, [70.7-71.3])	20,246 (8.4%, [8.2-8.5])	76,381
	Unknown does	-	-	3,433 (4.3%, [4.2-4.5])	10,725 (4.4%, [4.3-4.5])	14,158
Symptoms	Symptomatic	95,973 (13.5%, [13.4-13.5])	49,228 (13.8%, [13.6-13.9])	36,687 (16%, [15.9-16.2])	52,983 (21.9%, [21.7-22])	234,871
Number of reported symptoms	Mean (SD)	0.52 (1.66)	0.5 (1.63)	0.61 (1.84)	0.91 (2.34)	0.6 (1.83)
Sought medical attention for symptoms	No	87,252 (89.5%, [89.3-89.7])	43,636 (88.9%, [88.6-89.2])	31,933 (87.2%, [86.8-87.5])	47,231 (89.2%, [89-89.5])	210,052
	Yes	10,203 (10.5%, [10.3-10.7])	5,457 (11.1%, [10.8-11.4])	4,701 (12.8%, [12.5-13.2])	5,698 (10.8%, [10.5-11])	26,059
Symptoms affecting day-to-day activities	A lot	-	-	2,291 (1%, [1-1])	4,931 (2%, [2-2.1])	7,222
	A little	-	-	7,849 (3.4%, [3.4-3.5])	15,314 (6.3%, [6.2-6.4])	23,163
	Not at all	-	-	4,938 (2.2%, [2.1-2.2])	9,270 (3.8%, [3.7-3.9])	14,208
	Don't know / PNA / Non-reponse	-	-	21,609 (9.4%, [9.3-9.6])	23,468 (9.7%, [9.6-9.8])	190,278
	No symptoms reported	-	-	192,247 (84%, [83.8-84.1])	189,431 (78.1%, [78-78.3])	1,307,639
Days since onset of first symptom	Mean (SD)	7.93 (3.28)	8.09 (3.28)	7.89 (3.32)	7.97 (3.29)	7.95 (3.29)
Symptom in past 7 days	Loss or change of sense of smell	2,453 (0.3%, [0.3-0.4])	1,392 (0.4%, [0.4-0.4])	1,460 (0.6%, [0.6-0.7])	2,273 (0.9%, [0.9-1])	7,578
	Loss or change of sense of taste	2,876 (0.4%, [0.4-0.4])	1,551 (0.4%, [0.4-0.5])	1,420 (0.6%, [0.6-0.7])	2,362 (1%, [0.9-1])	8,209
	New persistent cough	4,710 (0.7%, [0.6-0.7])	2,120 (0.6%, [0.6-0.6])	3,599 (1.6%, [1.5-1.6])	7,212 (3%, [2.9-3])	17,641
	Fever	5,666 (0.8%, [0.8-0.8])	2,515 (0.7%, [0.7-0.7])	2,619 (1.1%, [1.1-1.2])	4,450 (1.8%, [1.8-1.9])	15,250
	Runny nose	24,262 (3.4%, [3.4-3.4])	12,008 (3.4%, [3.3-3.4])	11,105 (4.9%, [4.8-4.9])	19,335 (8%, [7.9-8.1])	66,710
	Sneezing	24,496 (3.4%, [3.4-3.5])	10,909 (3%, [3-3.1])	9,673 (4.2%, [4.1-4.3])	15,087 (6.2%, [6.1-6.3])	60,165
	Blocked nose	17,806 (2.5%, [2.5-2.5])	8,504 (2.4%, [2.3-2.4])	8,067 (3.5%, [3.4-3.6])	13,507 (5.6%, [5.5-5.7])	47,884
	Sore eyes	14,341 (2%, [2-2])	6,777 (1.9%, [1.8-1.9])	4,628 (2%, [2-2.1])	7,038 (2.9%, [2.8-3])	32,784

Sore throat	27,295 (3.8%, [3.8-3.9])	10,259 (2.9%, [2.8-2.9])	10,410 (4.5%, [4.5-4.6])	15,571 (6.4%, [6.3-6.5])	63,535
Hoarse voice	8,322 (1.2%, [1.1-1.2])	3,292 (0.9%, [0.9-1])	4,509 (2%, [1.9-2])	7,247 (3%, [2.9-3.1])	23,370
Headache	39,332 (5.5%, [5.5-5.6])	20,835 (5.8%, [5.7-5.9])	13,727 (6%, [5.9-6.1])	21,475 (8.9%, [8.7-9])	95,369
Dizziness	12,857 (1.8%, [1.8-1.8])	6,128 (1.7%, [1.7-1.8])	4,372 (1.9%, [1.9-2])	6,307 (2.6%, [2.5-2.7])	29,664
Appetite loss	6,676 (0.9%, [0.9-1])	3,318 (0.9%, [0.9-1])	2,736 (1.2%, [1.2-1.2])	4,296 (1.8%, [1.7-1.8])	17,026
Nausea/vomiting	8,185 (1.1%, [1.1-1.2])	3,884 (1.1%, [1.1-1.1])	2,825 (1.2%, [1.2-1.3])	3,948 (1.6%, [1.6-1.7])	18,842
Diarrhoea	11,107 (1.6%, [1.5-1.6])	4,799 (1.3%, [1.3-1.4])	3,573 (1.6%, [1.5-1.6])	4,741 (2%, [1.9-2])	24,220
Abdominal pain / belly ache	14,707 (2.1%, [2-2.1])	6,934 (1.9%, [1.9-2])	4,619 (2%, [2-2.1])	6,096 (2.5%, [2.5-2.6])	32,356
Shortness of breath	12,907 (1.8%, [1.8-1.8])	6,634 (1.9%, [1.8-1.9])	4,587 (2%, [1.9-2.1])	7,647 (3.2%, [3.1-3.2])	31,775
Tight chest	8,977 (1.3%, [1.2-1.3])	4,514 (1.3%, [1.2-1.3])	2,969 (1.3%, [1.3-1.3])	4,736 (2%, [1.9-2])	21,196
Chest pain	4,158 (0.6%, [0.6-0.6])	2,279 (0.6%, [0.6-0.7])	1,529 (0.7%, [0.6-0.7])	2,494 (1%, [1-1.1])	10,460
Chills	7,077 (1%, [1-1])	5,429 (1.5%, [1.5-1.6])	2,652 (1.2%, [1.1-1.2])	5,955 (2.5%, [2.4-2.5])	21,113
Difficulty sleeping	26,551 (3.7%, [3.7-3.8])	14,043 (3.9%, [3.9-4])	8,956 (3.9%, [3.8-4])	13,035 (5.4%, [5.3-5.5])	62,585
Tiredness	39,897 (5.6%, [5.5-5.6])	19,756 (5.5%, [5.4-5.6])	14,813 (6.5%, [6.4-6.6])	23,072 (9.5%, [9.4-9.6])	97,538
Severe fatigue	4,677 (0.7%, [0.6-0.7])	2,715 (0.8%, [0.7-0.8])	2,063 (0.9%, [0.9-0.9])	3,482 (1.4%, [1.4-1.5])	12,937
Numbness/tingling	9,748 (1.4%, [1.3-1.4])	4,725 (1.3%, [1.3-1.4])	3,214 (1.4%, [1.4-1.5])	4,295 (1.8%, [1.7-1.8])	21,982
Heavy arms/legs	8,527 (1.2%, [1.2-1.2])	4,017 (1.1%, [1.1-1.2])	2,707 (1.2%, [1.1-1.2])	4,080 (1.7%, [1.6-1.7])	19,331
Muscle aches	21,342 (3%, [3-3])	11,069 (3.1%, [3-3.1])	7,488 (3.3%, [3.2-3.3])	11,866 (4.9%, [4.8-5])	51,765

Table S2 Characteristics of swab positives in study population

Variable	Category	Rounds 2-7 (Wild type)	Rounds 8-10 (Alpha)	Rounds 12-15 (Delta)	BA.1 (Omicron)	BA.2 (Omicron)	Total
All participants	All participants	2,971 (100%, [99.9-100])	2,275 (100%, [99.9-100])	1,493 (100%, [99.8-100])	2,835 (100%, [99.9-100])	3,560 (100%, [99.9-100])	13,134
Sex	Female	1,683 (56.6%, [54.9-58.4])	1,283 (56.4%, [54.3-58.4])	809 (54.2%, [51.7-56.7])	1,617 (57%, [55.2-58.8])	2,043 (57.4%, [55.8-59])	7,435
	Male	1,288 (43.4%, [41.6-45.1])	992 (43.6%, [41.6-45.7])	684 (45.8%, [43.3-48.3])	1,218 (43%, [41.2-44.8])	1,517 (42.6%, [41-44.2])	5,699
Age group	18-24	239 (8%, [7.1-9.1])	178 (7.8%, [6.8-9])	60 (4%, [3.1-5.1])	153 (5.4%, [4.6-6.3])	235 (6.6%, [5.8-7.5])	865
	25-34	401 (13.5%, [12.3-14.8])	289 (12.7%, [11.4-14.1])	125 (8.4%, [7.1-9.9])	389 (13.7%, [12.5-15])	665 (18.7%, [17.4-20])	1,869
	35-44	475 (16%, [14.7-17.3])	401 (17.6%, [16.1-19.2])	298 (20%, [18-22.1])	484 (17.1%, [15.7-18.5])	688 (19.3%, [18.1-20.7])	2,346
	45-54	642 (21.6%, [20.2-23.1])	493 (21.7%, [20-23.4])	371 (24.8%, [22.7-27.1])	541 (19.1%, [17.7-20.6])	555 (15.6%, [14.4-16.8])	2,602
	55-64	618 (20.8%, [19.4-22.3])	510 (22.4%, [20.8-24.2])	307 (20.6%, [18.6-22.7])	618 (21.8%, [20.3-23.4])	646 (18.1%, [16.9-19.4])	2,699
	65-74	429 (14.4%, [13.2-15.7])	299 (13.1%, [11.8-14.6])	247 (16.5%, [14.7-18.5])	471 (16.6%, [15.3-18])	554 (15.6%, [14.4-16.8])	2,000
	74+	167 (5.6%, [4.8-6.5])	105 (4.6%, [3.8-5.6])	85 (5.7%, [4.6-7])	179 (6.3%, [5.5-7.3])	217 (6.1%, [5.4-6.9])	753
Ethnicity	Asian	158 (5.4%, [4.6-6.3])	137 (6.1%, [5.2-7.2])	84 (5.7%, [4.6-7])	137 (4.9%, [4.2-5.8])	173 (5%, [4.3-5.7])	689
	Black	40 (1.4%, [1-1.9])	42 (1.9%, [1.4-2.5])	31 (2.1%, [1.5-3])	49 (1.8%, [1.3-2.3])	45 (1.3%, [1-1.7])	207
	Mixed	26 (0.9%, [0.6-1.3])	30 (1.3%, [0.9-1.9])	14 (1%, [0.6-1.6])	50 (1.8%, [1.4-2.4])	73 (2.1%, [1.7-2.6])	193
	Other	23 (0.8%, [0.5-1.2])	20 (0.9%, [0.6-1.4])	19 (1.3%, [0.8-2])	26 (0.9%, [0.6-1.4])	37 (1.1%, [0.8-1.5])	125
	White	2,676 (91.5%, [90.5-92.5])	2,002 (89.7%, [88.4-90.9])	1,319 (89.9%, [88.3-91.3])	2,510 (90.5%, [89.4-91.6])	3,149 (90.6%, [89.5-91.5])	11,656
PCR positive at time of survey	Yes	2,971 (100%, [99.9-100])	2,275 (100%, [99.9-100])	1,493 (100%, [99.8-100])	2,835 (100%, [99.9-100])	3,560 (100%, [99.9-100])	13,134
Prior COVID-19 infection	No previous infection	1,840 (61.9%, [60.2-63.7])	1,011 (44.4%, [42.4-46.5])	563 (37.7%, [35.3-40.2])	816 (28.8%, [27.1-30.5])	877 (24.6%, [23.2-26.1])	5,107
	Previous infection greater than 28 days	35 (1.2%, [0.8-1.6])	86 (3.8%, [3.1-4.6])	51 (3.4%, [2.6-4.5])	148 (5.2%, [4.5-6.1])	198 (5.6%, [4.9-6.4])	518
	Previous infection with unknow time	3 (0.1%, [0-0.3])	4 (0.2%, [0.1-0.5])	0 (0%, [0-0.2])	2 (0.1%, [0-0.3])	1 (0%, [0-0.2])	10
	Previous infection within 28 days	586 (19.7%, [18.3-21.2])	766 (33.7%, [31.8-35.6])	722 (48.4%, [45.8-50.9])	1,665 (58.7%, [56.9-60.5])	2,188 (61.5%, [59.9-63])	5,927
	Suspected previous infection	500 (16.8%, [15.5-18.2])	403 (17.7%, [16.2-19.3])	152 (10.2%, [8.7-11.8])	200 (7.1%, [6.2-8.1])	291 (8.2%, [7.3-9.1])	1,546
	Unknown	7 (0.2%, [0.1-0.5])	5 (0.2%, [0.1-0.5])	5 (0.3%, [0.1-0.8])	4 (0.1%, [0.1-0.4])	5 (0.1%, [0.1-0.3])	26

Vaccination status	NA	-	-	11 (1.5%, [0.8-2.7])	36 (1.3%, [0.9-1.8])	33 (0.9%, [0.7-1.3])	80
	Not vaccinated	-	-	28 (3.8%, [2.6-5.4])	77 (2.7%, [2.2-3.4])	106 (3%, [2.5-3.6])	211
	One does	-	-	11 (1.5%, [0.8-2.7])	15 (0.5%, [0.3-0.9])	23 (0.6%, [0.4-1])	49
	Three does	-	-	73 (9.9%, [8-12.3])	2,276 (80.3%, [78.8-81.7])	2,925 (82.2%, [80.9-83.4])	5,274
	Two does	-	-	579 (78.6%, [75.5-81.4])	284 (10%, [9-11.2])	265 (7.4%, [6.6-8.4])	1,128
	Unknown does	-	-	35 (4.7%, [3.4-6.5])	147 (5.2%, [4.4-6.1])	208 (5.8%, [5.1-6.7])	390
Symptoms	Symptomatic	1,338 (45%, [43.3-46.8])	1,245 (54.7%, [52.7-56.8])	952 (63.8%, [61.3-66.2])	1,984 (70%, [68.3-71.6])	2,701 (75.9%, [74.4-77.2])	8,220
Number of reported symptoms	Mean (SD)	2.7 (4.1)	3.38 (4.5)	4.63 (5.21)	4.63 (4.72)	6.02 (5.26)	4.15 (4.83)
Sought medical attention for symptoms	No	1,187 (88.7%, [86.9-90.3])	1,091 (87.7%, [85.8-89.4])	850 (89.5%, [87.4-91.3])	1,865 (94.1%, [93-95.1])	2,522 (93.4%, [92.4-94.3])	7,515
	Yes	151 (11.3%, [9.7-13.1])	153 (12.3%, [10.6-14.2])	100 (10.5%, [8.7-12.6])	117 (5.9%, [4.9-7])	179 (6.6%, [5.7-7.6])	700
Symptoms affecting day-to-day activities	A lot	-	-	157 (10.5%, [9.1-12.2])	303 (10.7%, [9.6-11.9])	625 (17.6%, [16.3-18.8])	1,085
	A little	-	-	283 (19%, [17-21])	650 (22.9%, [21.4-24.5])	948 (26.6%, [25.2-28.1])	1,881
	Not at all	-	-	83 (5.6%, [4.5-6.8])	282 (9.9%, [8.9-11.1])	266 (7.5%, [6.7-8.4])	631
	Don't know / PNA / Non-reponse	-	-	429 (28.7%, [26.5-31.1])	749 (26.4%, [24.8-28.1])	862 (24.2%, [22.8-25.6])	4,623
	No symptoms reported	-	-	541 (36.2%, [33.8-38.7])	851 (30%, [28.4-31.7])	859 (24.1%, [22.8-25.6])	4,914
Days since onset of first symptom	Mean (SD)	7.08 (3.19)	7.58 (3.14)	6.85 (3.19)	6.62 (3.04)	6.06 (2.94)	7.06 (3.16)
Symptom in past 7 days	Loss or change of sense of smell	399 (13.4%, [12.3-14.7])	323 (14.2%, [12.8-15.7])	367 (24.6%, [22.5-26.8])	214 (7.5%, [6.6-8.6])	349 (9.8%, [8.9-10.8])	1,652
	Loss or change of sense of taste	355 (11.9%, [10.8-13.2])	329 (14.5%, [13.1-16])	340 (22.8%, [20.7-25])	258 (9.1%, [8.1-10.2])	408 (11.5%, [10.5-12.5])	1,690
	New persistent cough	260 (8.8%, [7.8-9.8])	326 (14.3%, [12.9-15.8])	380 (25.5%, [23.3-27.7])	703 (24.8%, [23.2-26.4])	1,249 (35.1%, [33.5-36.7])	2,918
	Fever	292 (9.8%, [8.8-11])	262 (11.5%, [10.3-12.9])	305 (20.4%, [18.5-22.5])	498 (17.6%, [16.2-19])	922 (25.9%, [24.5-27.4])	2,279
	Runny nose	389 (13.1%, [11.9-14.4])	384 (16.9%, [15.4-18.5])	505 (33.8%, [31.5-36.3])	1,146 (40.4%, [38.6-42.2])	1,825 (51.3%, [49.6-52.9])	4,249
	Sneezing	411 (13.8%, [12.6-15.1])	404 (17.8%, [16.2-19.4])	436 (29.2%, [27-31.6])	1,017 (35.9%, [34.1-37.7])	1,572 (44.2%, [42.5-45.8])	3,840

	Blocked nose	387 (13%, [11.9-14.3])	401 (17.6%, [16.1-19.2])	402 (26.9%, [24.7-29.2])	804 (28.4%, [26.7-30])	1,383 (38.8%, [37.3-40.5])	3,377
	Sore eyes	240 (8.1%, [7.2-9.1])	215 (9.5%, [8.3-10.7])	199 (13.3%, [11.7-15.1])	358 (12.6%, [11.5-13.9])	568 (16%, [14.8-17.2])	1,580
	Sore throat	409 (13.8%, [12.6-15.1])	386 (17%, [15.5-18.6])	374 (25.1%, [22.9-27.3])	1,073 (37.8%, [36.1-39.6])	1,734 (48.7%, [47.1-50.4])	3,976
	Hoarse voice	194 (6.5%, [5.7-7.5])	184 (8.1%, [7-9.3])	221 (14.8%, [13.1-16.7])	631 (22.3%, [20.8-23.8])	1,043 (29.3%, [27.8-30.8])	2,273
	Headache	740 (24.9%, [23.4-26.5])	670 (29.5%, [27.6-31.4])	553 (37%, [34.6-39.5])	1,130 (39.9%, [38.1-41.7])	1,684 (47.3%, [45.7-48.9])	4,777
	Dizziness	237 (8%, [7.1-9])	223 (9.8%, [8.6-11.1])	187 (12.5%, [10.9-14.3])	309 (10.9%, [9.8-12.1])	536 (15.1%, [13.9-16.3])	1,492
	Appetite loss	308 (10.4%, [9.3-11.5])	319 (14%, [12.7-15.5])	238 (15.9%, [14.2-17.9])	292 (10.3%, [9.2-11.5])	562 (15.8%, [14.6-17])	1,719
	Nausea/vomiting	153 (5.1%, [4.4-6])	141 (6.2%, [5.3-7.3])	107 (7.2%, [6-8.6])	185 (6.5%, [5.7-7.5])	289 (8.1%, [7.3-9.1])	875
	Diarrhoea	180 (6.1%, [5.3-7])	171 (7.5%, [6.5-8.7])	122 (8.2%, [6.9-9.7])	209 (7.4%, [6.5-8.4])	280 (7.9%, [7-8.8])	962
	Abdominal pain / belly ache	180 (6.1%, [5.3-7])	165 (7.3%, [6.3-8.4])	103 (6.9%, [5.7-8.3])	192 (6.8%, [5.9-7.8])	328 (9.2%, [8.3-10.2])	968
	Shortness of breath	223 (7.5%, [6.6-8.5])	232 (10.2%, [9-11.5])	185 (12.4%, [10.8-14.2])	353 (12.5%, [11.3-13.7])	575 (16.2%, [15-17.4])	1,568
	Tight chest	204 (6.9%, [6-7.8])	203 (8.9%, [7.8-10.2])	139 (9.3%, [7.9-10.9])	270 (9.5%, [8.5-10.7])	423 (11.9%, [10.9-13])	1,239
	Chest pain	83 (2.8%, [2.3-3.4])	87 (3.8%, [3.1-4.7])	50 (3.3%, [2.5-4.4])	119 (4.2%, [3.5-5])	202 (5.7%, [5-6.5])	541
	Chills	309 (10.4%, [9.4-11.5])	330 (14.5%, [13.1-16])	252 (16.9%, [15.1-18.9])	495 (17.5%, [16.1-18.9])	880 (24.7%, [23.3-26.2])	2,266
	Difficulty sleeping	349 (11.7%, [10.6-13])	323 (14.2%, [12.8-15.7])	263 (17.6%, [15.8-19.6])	520 (18.3%, [17-19.8])	788 (22.1%, [20.8-23.5])	2,243
	Tiredness	727 (24.5%, [23-26])	700 (30.8%, [28.9-32.7])	534 (35.8%, [33.4-38.2])	1,073 (37.8%, [36.1-39.6])	1,658 (46.6%, [44.9-48.2])	4,692
	Severe fatigue	149 (5%, [4.3-5.9])	167 (7.3%, [6.3-8.5])	118 (7.9%, [6.6-9.4])	168 (5.9%, [5.1-6.9])	331 (9.3%, [8.4-10.3])	933
	Numbness/tingling	110 (3.7%, [3.1-4.4])	90 (4%, [3.2-4.8])	58 (3.9%, [3-5])	126 (4.4%, [3.7-5.3])	214 (6%, [5.3-6.8])	598
	Heavy arms/legs	196 (6.6%, [5.8-7.5])	193 (8.5%, [7.4-9.7])	100 (6.7%, [5.5-8.1])	228 (8%, [7.1-9.1])	419 (11.8%, [10.8-12.9])	1,136
	Muscle aches	549 (18.5%, [17.1-19.9])	463 (20.4%, [18.7-22.1])	372 (24.9%, [22.8-27.2])	766 (27%, [25.4-28.7])	1,198 (33.7%, [32.1-35.2])	3,348
First reported symptoms	Loss or change of sense of smell	109 (3.7%, [3.1-4.4])	82 (3.6%, [2.9-4.5])	73 (4.9%, [3.9-6.1])	36 (1.3%, [0.9-1.8])	46 (1.3%, [1-1.7])	346
	Loss or change of sense of taste	96 (3.2%, [2.7-3.9])	83 (3.6%, [3-4.5])	66 (4.4%, [3.5-5.6])	38 (1.3%, [1-1.8])	59 (1.7%, [1.3-2.1])	342
	New persistent cough	125 (4.2%, [3.5-5])	148 (6.5%, [5.6-7.6])	168 (11.3%, [9.7-13])	255 (9%, [8-10.1])	375 (10.5%, [9.6-11.6])	1,071
	Fever	112 (3.8%, [3.1-4.5])	104 (4.6%, [3.8-5.5])	83 (5.6%, [4.5-6.8])	133 (4.7%, [4-5.5])	232 (6.5%, [5.8-7.4])	664
	Runny nose	129 (4.3%, [3.7-5.1])	110 (4.8%, [4-5.8])	176 (11.8%, [10.2-13.5])	363 (12.8%, [11.6-14.1])	561 (15.8%, [14.6-17])	1,339
	Sneezing	125 (4.2%, [3.5-5])	122 (5.4%, [4.5-6.4])	146 (9.8%, [8.4-11.4])	304 (10.7%, [9.6-11.9])	442 (12.4%, [11.4-13.5])	1,139

	Blocked nose	120 (4%, [3.4-4.8])	138 (6.1%, [5.2-7.1])	98 (6.6%, [5.4-7.9])	203 (7.2%, [6.3-8.2])	304 (8.5%, [7.7-9.5])	863
	Sore eyes	77 (2.6%, [2.1-3.2])	65 (2.9%, [2.2-3.6])	42 (2.8%, [2.1-3.8])	91 (3.2%, [2.6-3.9])	147 (4.1%, [3.5-4.8])	422
	Sore throat	206 (6.9%, [6.1-7.9])	183 (8%, [7-9.2])	186 (12.5%, [10.9-14.2])	620 (21.9%, [20.4-23.4])	1,084 (30.4%, [29-32])	2,279
	Hoarse voice	50 (1.7%, [1.3-2.2])	38 (1.7%, [1.2-2.3])	59 (4%, [3.1-5.1])	159 (5.6%, [4.8-6.5])	212 (6%, [5.2-6.8])	518
	Headache	384 (12.9%, [11.8-14.2])	340 (14.9%, [13.5-16.5])	250 (16.7%, [14.9-18.7])	508 (17.9%, [16.6-19.4])	716 (20.1%, [18.8-21.5])	2,198
	Dizziness	76 (2.6%, [2-3.2])	65 (2.9%, [2.2-3.6])	41 (2.7%, [2-3.7])	64 (2.3%, [1.8-2.9])	116 (3.3%, [2.7-3.9])	362
	Appetite loss	69 (2.3%, [1.8-2.9])	78 (3.4%, [2.8-4.3])	48 (3.2%, [2.4-4.2])	49 (1.7%, [1.3-2.3])	85 (2.4%, [1.9-2.9])	329
	Nausea/vomiting	38 (1.3%, [0.9-1.8])	30 (1.3%, [0.9-1.9])	28 (1.9%, [1.3-2.7])	44 (1.6%, [1.2-2.1])	81 (2.3%, [1.8-2.8])	221
	Diarrhoea	47 (1.6%, [1.2-2.1])	46 (2%, [1.5-2.7])	30 (2%, [1.4-2.9])	46 (1.6%, [1.2-2.2])	69 (1.9%, [1.5-2.4])	238
	Abdominal pain / belly ache	58 (2%, [1.5-2.5])	44 (1.9%, [1.4-2.6])	18 (1.2%, [0.8-1.9])	43 (1.5%, [1.1-2])	70 (2%, [1.6-2.5])	233
	Shortness of breath	69 (2.3%, [1.8-2.9])	67 (2.9%, [2.3-3.7])	32 (2.1%, [1.5-3])	77 (2.7%, [2.2-3.4])	109 (3.1%, [2.5-3.7])	354
	Tight chest	45 (1.5%, [1.1-2])	48 (2.1%, [1.6-2.8])	31 (2.1%, [1.5-2.9])	51 (1.8%, [1.4-2.4])	77 (2.2%, [1.7-2.7])	252
	Chest pain	19 (0.6%, [0.4-1])	11 (0.5%, [0.3-0.9])	10 (0.7%, [0.4-1.2])	20 (0.7%, [0.5-1.1])	36 (1%, [0.7-1.4])	96
	Chills	103 (3.5%, [2.9-4.2])	131 (5.8%, [4.9-6.8])	60 (4%, [3.1-5.1])	139 (4.9%, [4.2-5.8])	271 (7.6%, [6.8-8.5])	704
	Difficulty sleeping	114 (3.8%, [3.2-4.6])	104 (4.6%, [3.8-5.5])	77 (5.2%, [4.1-6.4])	118 (4.2%, [3.5-5])	184 (5.2%, [4.5-5.9])	597
	Tiredness	314 (10.6%, [9.5-11.7])	264 (11.6%, [10.4-13])	202 (13.5%, [11.9-15.4])	385 (13.6%, [12.4-14.9])	602 (16.9%, [15.7-18.2])	1,767
	Severe fatigue	57 (1.9%, [1.5-2.5])	49 (2.2%, [1.6-2.8])	35 (2.3%, [1.7-3.2])	48 (1.7%, [1.3-2.2])	93 (2.6%, [2.1-3.2])	282
	Numbness/tingling	30 (1%, [0.7-1.4])	25 (1.1%, [0.7-1.6])	12 (0.8%, [0.5-1.4])	31 (1.1%, [0.8-1.5])	37 (1%, [0.8-1.4])	135
	Heavy arms/legs	58 (2%, [1.5-2.5])	53 (2.3%, [1.8-3])	21 (1.4%, [0.9-2.1])	44 (1.6%, [1.2-2.1])	86 (2.4%, [2-3])	262
	Muscle aches	249 (8.4%, [7.4-9.4])	197 (8.7%, [7.6-9.9])	121 (8.1%, [6.8-9.6])	261 (9.2%, [8.2-10.3])	378 (10.6%, [9.6-11.7])	1,206

Table S3 Odds ratios for swab positivity based on presence or absence of any of 26 symptoms surveyed across selected rounds of REACT-1. ORs are derived from logistic regression models with swab positive (1/0) as the outcome variable, adjusted on age, sex and vaccination status. 95% confidence intervals are shown.

Symptom	Wild-type Rounds 2-7	Alpha Rounds 8-10	Delta Rounds 13–15	BA.1 Rounds 17–19	BA.2 Rounds 17–19
	June – Dec 2020	*Jan – Mar 2021*	*June – Nov 2021*	*Jan–Mar 2022*	*Jan–Mar 2022*
Any of 26 symptoms	5.16 (4.79,5.55)	6.01 (5.12,7.06)	9.53 (8.55,10.6)	9.61 (8.82,10.5)	12.9 (11.9,14.0)
Loss or change of sense of smell	49.7 (44.3,55.7)	37.8 (28.6,50.0)	73.4 (64.2,83.9)	12.9 (11.1,15.1)	17.2 (15.1,19.5)
Loss or change of sense of taste	35.9 (31.9,40.4)	38.9 (29.9,50.6)	68.1 (59.4,78.0)	16.0 (13.9,18.5)	21.3 (18.9,24.0)
New persistent cough	13.9 (12.2,15.8)	31.9 (24.9,40.9)	25.9 (22.9,29.3)	16.4 (14.9,18.0)	26.2 (24.2,28.3)
Fever	13.3 (11.7,15.0)	16.2 (12.2,21.4)	26.3 (23.0,30.1)	18.4 (16.5,20.5)	30.2 (27.7,33.0)
Appetite loss	12.0 (10.6,13.6)	15.2 (11.8,19.7)	17.8 (15.4,20.7)	8.56 (7.50,9.77)	13.6 (12.3,15.1)
Chills	11.5 (10.2,13.0)	9.79 (7.62,12.6)	19.3 (16.7,22.2)	11.5 (10.4,12.8)	17.9 (16.4,19.4)
Severe fatigue	7.70 (6.51,9.11)	8.74 (6.28,12.1)	10.5 (8.69,12.7)	5.30 (4.49,6.26)	8.16 (7.21,9.25)
Muscle aches	7.32 (6.66,8.04)	7.44 (6.06,9.15)	10.3 (9.16,11.7)	9.02 (8.25,9.87)	12.5 (11.6,13.5)
Hoarse voice	5.88 (5.07,6.81)	8.80 (6.40,12.1)	9.28 (8.00,10.8)	12.8 (11.7,14.2)	18.9 (17.4,20.5)
Heavy arms/legs	5.87 (5.07,6.80)	6.96 (5.06,9.56)	6.19 (5.04,7.61)	6.07 (5.25,7.02)	9.47 (8.46,10.6)
Tight chest	5.57 (4.82,6.44)	6.13 (4.45,8.45)	7.91 (6.59,9.51)	6.40 (5.59,7.31)	7.96 (7.12,8.90)
Headache	5.49 (5.04,5.98)	5.88 (4.90,7.07)	9.83 (8.80,11.0)	8.28 (7.62,8.98)	11.2 (10.5,12.1)
Blocked nose	5.45 (4.89,6.08)	8.26 (6.63,10.3)	11.1 (9.85,12.5)	8.47 (7.75,9.25)	13.2 (12.3,14.3)
Tiredness	5.33 (4.89,5.80)	6.75 (5.64,8.07)	8.27 (7.41,9.23)	6.78 (6.25,7.36)	9.76 (9.09,10.5)
Chest pain	4.59 (3.68,5.72)	3.75 (2.24,6.28)	4.93 (3.67,6.62)	4.86 (3.99,5.91)	6.40 (5.48,7.47)
Dizziness	4.58 (4.00,5.24)	5.46 (4.10,7.28)	7.65 (6.53,8.96)	5.46 (4.82,6.19)	7.76 (7.02,8.57)
Shortness of breath	4.45 (3.88,5.11)	6.39 (4.90,8.34)	7.40 (6.31,8.66)	5.16 (4.58,5.80)	7.02 (6.38,7.73)
Nausea/vomiting	4.34 (3.68,5.12)	5.95 (4.26,8.31)	6.40 (5.23,7.84)	5.05 (4.32,5.91)	5.90 (5.18,6.72)
Sneezing	4.28 (3.85,4.76)	7.06 (5.70,8.76)	10.0 (8.92,11.3)	10.9 (10.0,11.8)	15.0 (14.0,16.1)
Sore eyes	4.22 (3.69,4.82)	5.32 (4.03,7.02)	8.15 (7.00,9.49)	5.63 (5.00,6.34)	7.53 (6.83,8.29)
Runny nose	4.04 (3.62,4.50)	5.36 (4.28,6.72)	10.8 (9.67,12.1)	9.81 (9.05,10.6)	14.9 (13.9,16.0)
Diarrhoea	3.84 (3.30,4.48)	4.96 (3.57,6.88)	5.62 (4.64,6.81)	4.44 (3.82,5.15)	4.52 (3.96,5.16)
Sore throat	3.76 (3.38,4.19)	6.56 (5.24,8.20)	7.22 (6.38,8.18)	11.6 (10.7,12.6)	18.0 (16.8,19.4)
Difficulty sleeping	3.30 (2.95,3.70)	3.23 (2.51,4.15)	5.39 (4.70,6.18)	4.48 (4.05,4.95)	5.45 (5.01,5.94)
Abdominal pain / belly ache	2.89 (2.48,3.37)	2.37 (1.62,3.47)	3.74 (3.06,4.58)	3.13 (2.68,3.65)	4.17 (3.70,4.71)
Numbness/tingling	2.80 (2.31,3.39)	2.66 (1.72,4.12)	2.95 (2.27,3.84)	2.78 (2.30,3.35)	4.00 (3.46,4.63)

Figure S1 Comparison of Ct values in swab-positive respondents with Omicron BA.1 and BA.2 variants in REACT-1 rounds 17–19, stratified by symptom status (presence of any of 26 surveyed symptoms). Ct values are lower in BA.2, in both asymptomatic and symptomatic respondents.

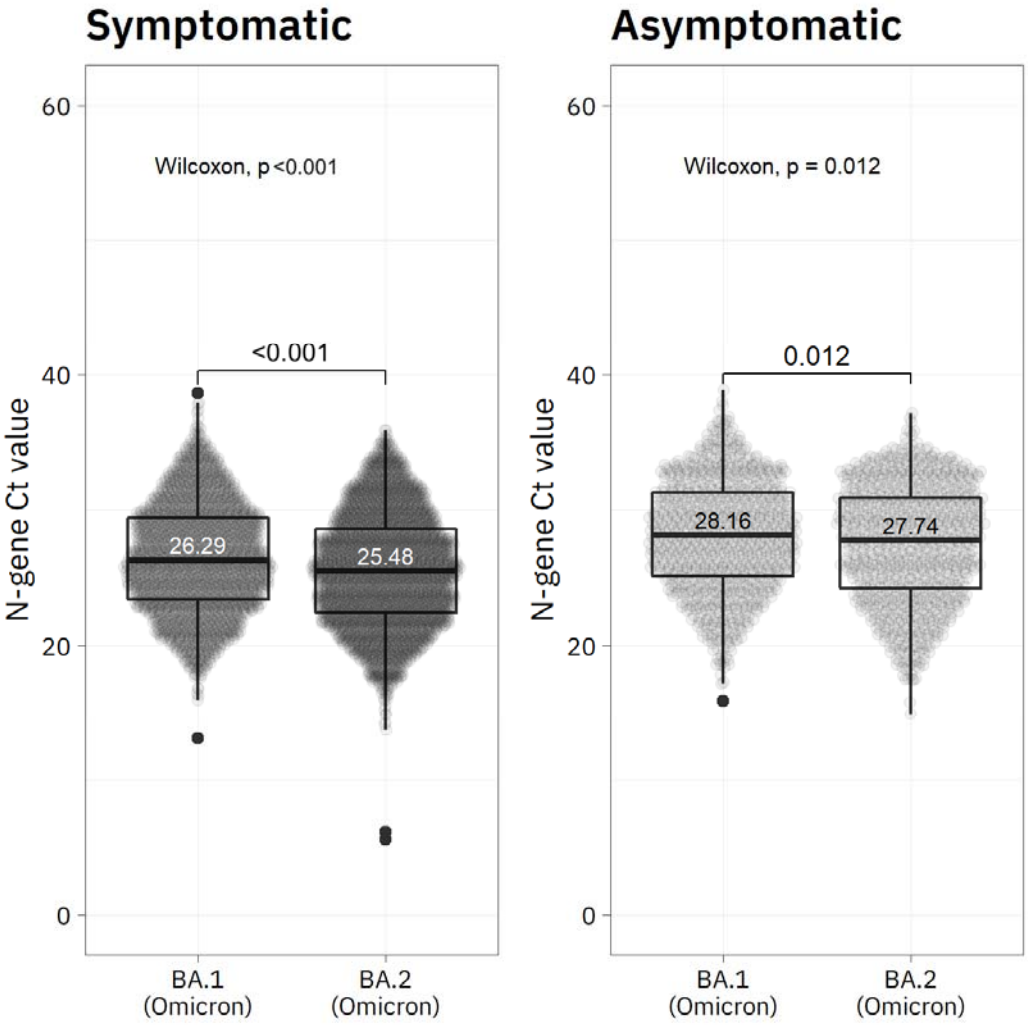


Figure S2 Results of LASSO stability selection with swab positive/negative as the binary outcome variable and each of 26 symptoms as predictors, in four phases of REACT-1 corresponding to periods of dominance of four SARS-CoV-2 variants in England. Age, sex and, where appropriate, vaccination status are forced into the models as unpenalised variables; regression coefficients for the symptoms are constrained to be positive. The median, 5th and 95th percentiles of AUCs are obtained from unpenalised models adding each symptom incrementally (from top to bottom) applied on un-seen holdout data. with regression coefficients for symptoms constrained to be non-negative.

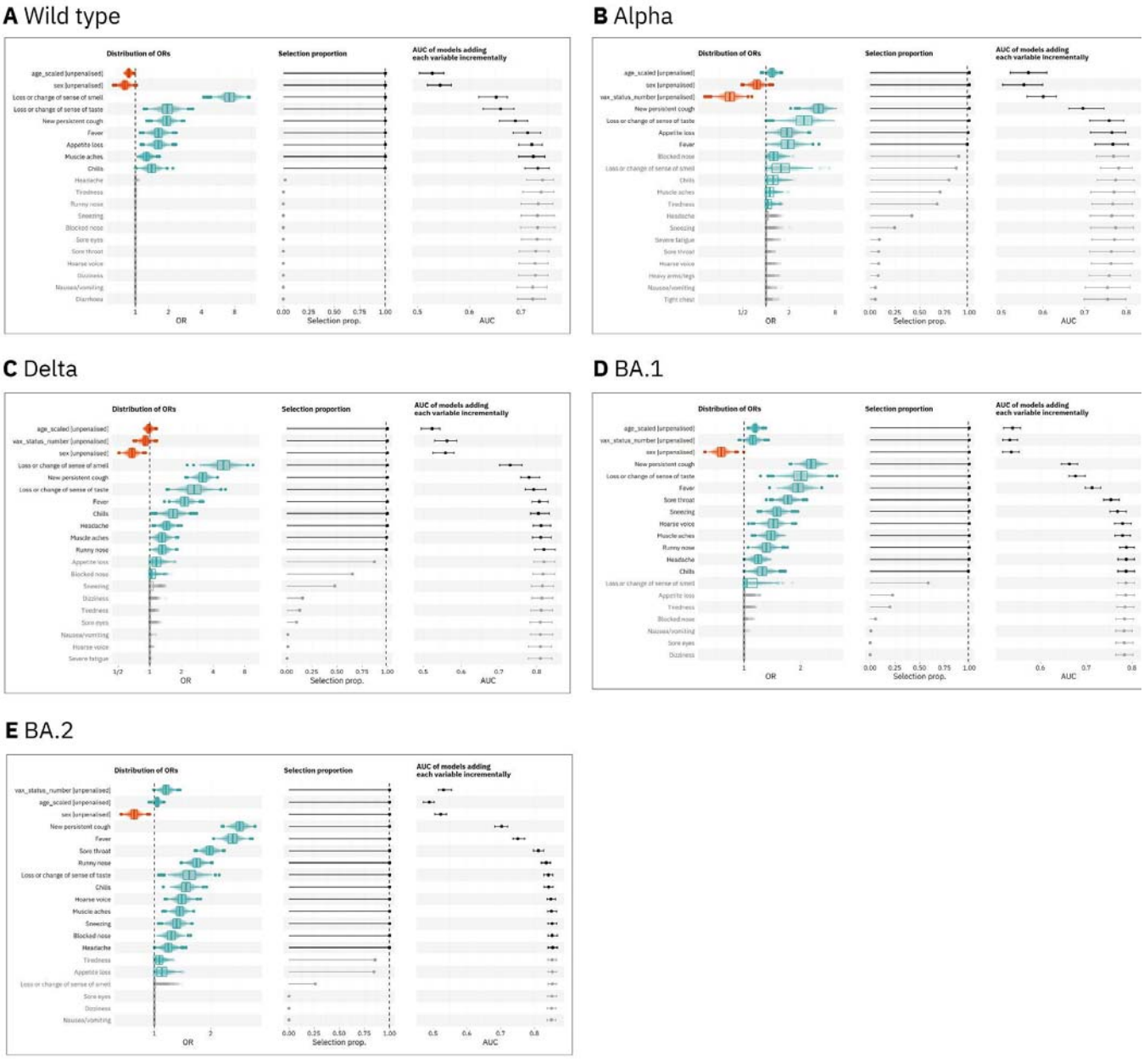


Figure S3 Heatmaps showing co-occurrence of symptoms across variants among swab-positive individuals. Denominators for percentages are the number of swab positive individuals with each variant.

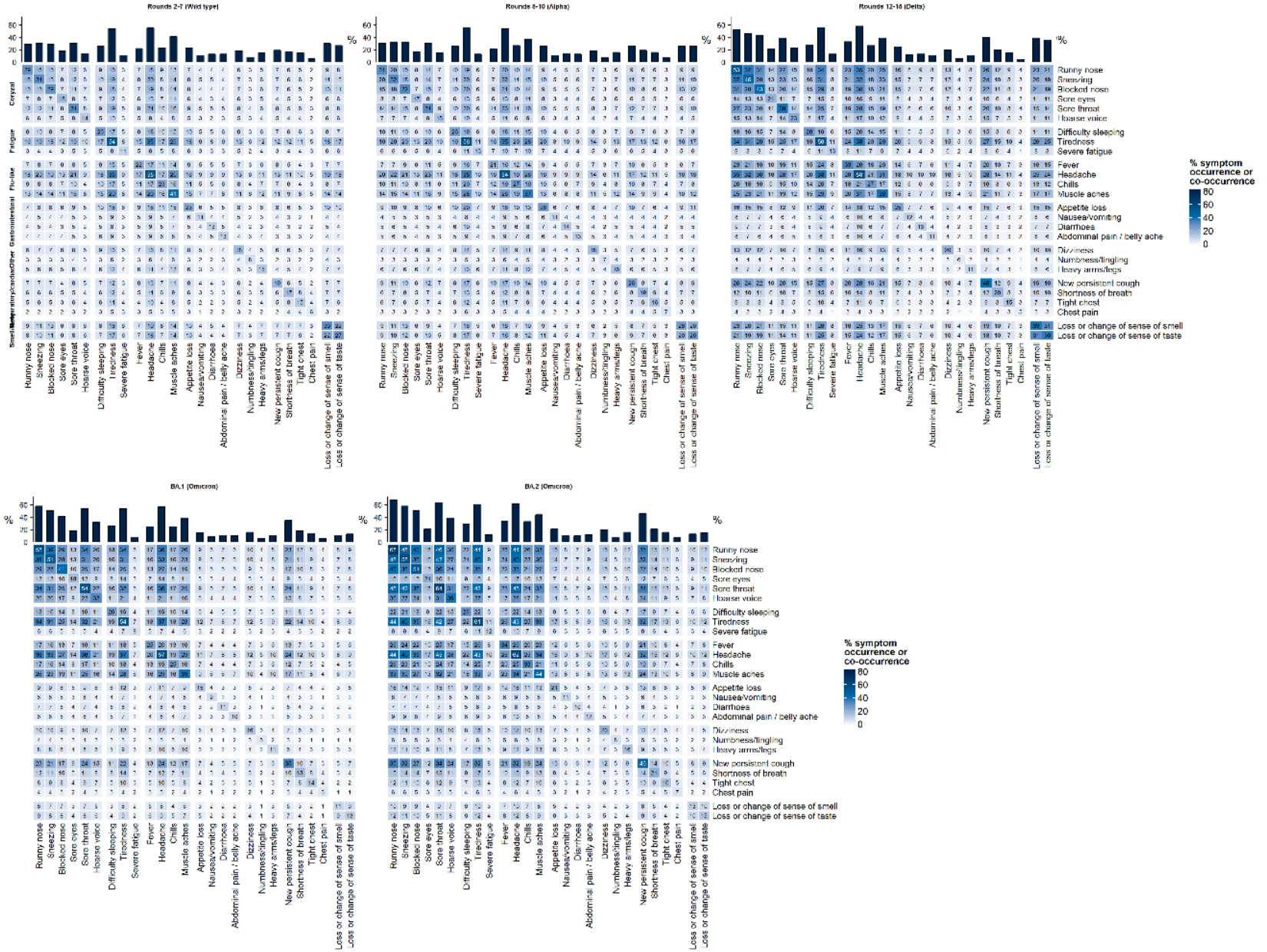


Figure S4 Heatmap showing co-occurence of first symptoms among swab positive individuals in rounds 17–19, when Omicron was dominant. The denominator for percentages is the number of swab positive individuals who reported experiencing one or more of 26 symptoms in the week prior to testing in rounds 17–19 (n=7,176). Sore throat, headache, and tiredness are the most common first symptoms, are are the most commonly co-occurring pairs of first symptoms.

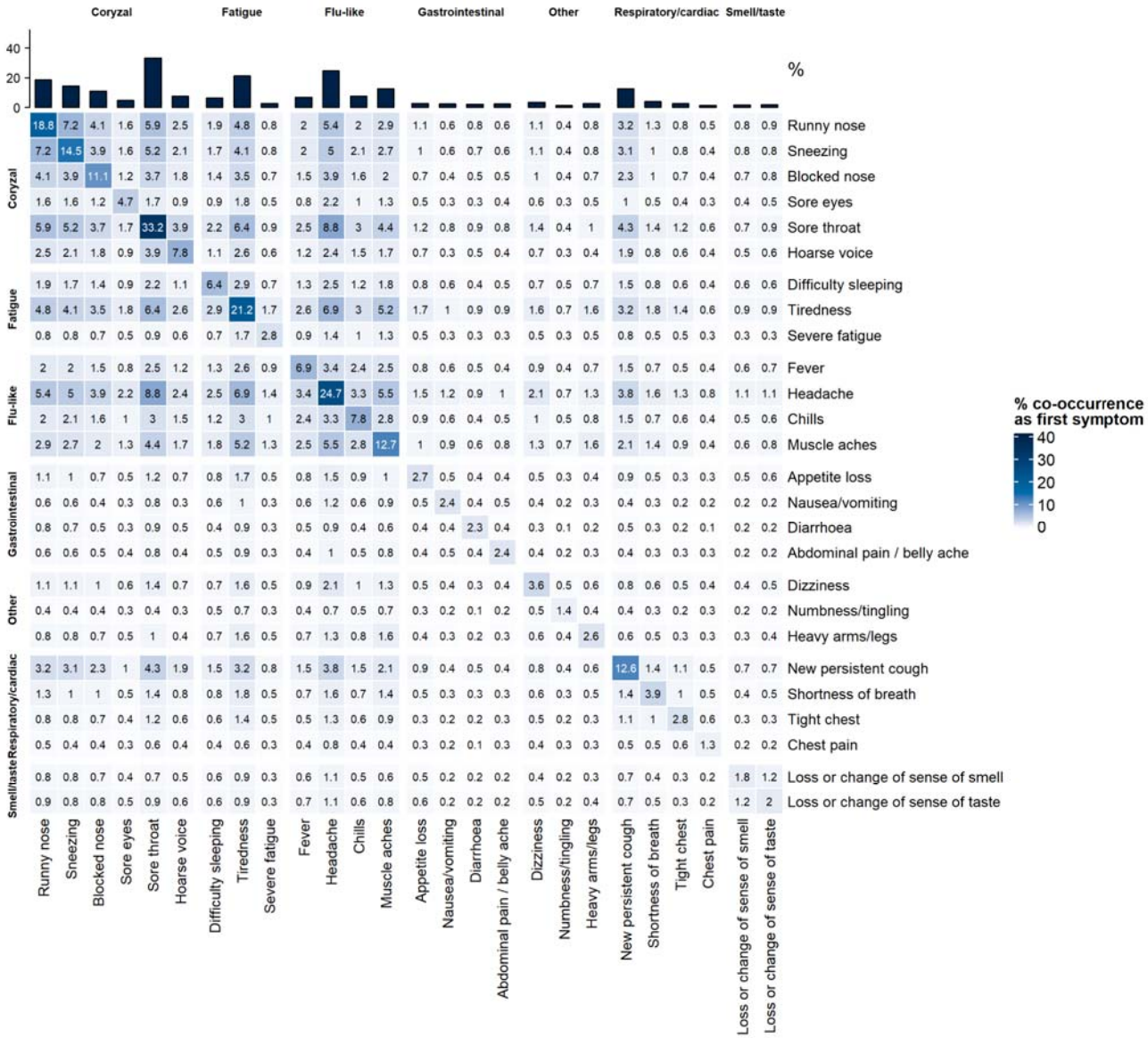
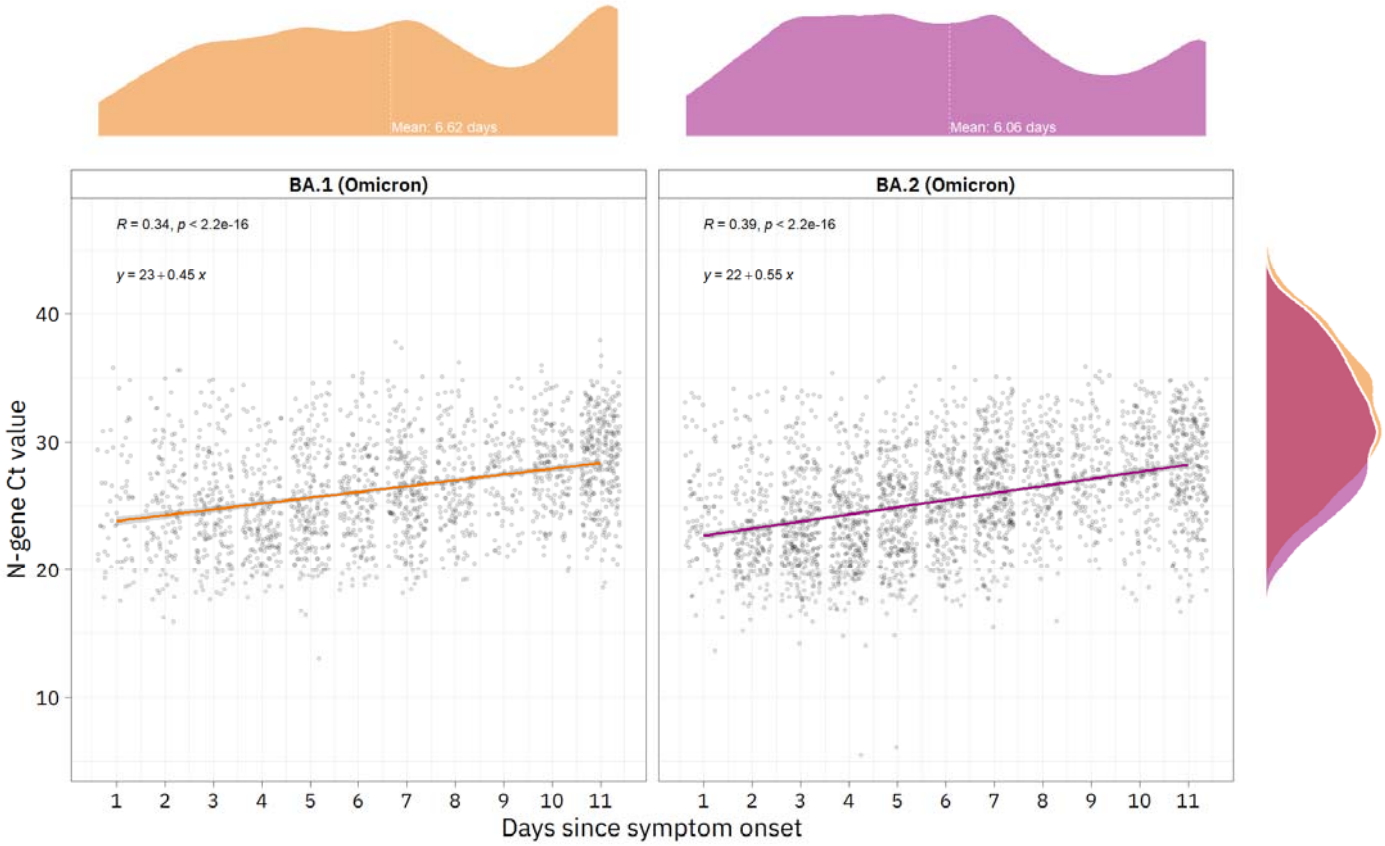


Figure S5 Scatter plot showing N-gene Ct values among symptomatic swab-positive individuals plotted against time (in days) since symptom onset, by BA.1/BA.2. Within each variant, a linear regression model is fitted with Ct value as the dependent variable and days since symptom onset (between 1 and 11 or more). In BA.2, there is a more even spread of time-since-symptom onset. In both variants there is a positive association between time since symptom onset and Ct value.



Supplementary methods

Assessing model performance in variable selection

To quantify the gain in predictive accuracy conferred by each selected symptom, un-penalised logistic models were successively re-fit on 80% subsamples of the holdout data, adding each symptom in order of decreasing selection proportion, and evaluated on the remainder of the holdout data (20%). Age, sex and vaccination status were forced in as predictors in all models. For each set of predictors, the procedure was repeated 100 times with different splits of the holdout data. As in the variable selection, regression coefficients were constrained to non-negativity in the re-fit models.

References

1. Grant, M. C. *et al.* The prevalence of symptoms in 24,410 adults infected by the novel coronavirus (SARS-CoV-2; COVID-19): A systematic review and meta-analysis of 148 studies from 9 countries. *PLoS One* **15**, e0234765 (2020).
2. Elliott, J. *et al.* Predictive symptoms for COVID-19 in the community: REACT-1 study of over 1 million people. *PLoS Med.* **18**, e1003777 (2021).
3. Antonelli, M. *et al.* Optimal symptom combinations to aid COVID-19 case identification: Analysis from a community-based, prospective, observational cohort. *J. Infect.* **82**, 384–390 (2021).
4. Zens, M., Brammertz, A., Herpich, J., Südkamp, N. & Hinterseer, M. App-Based Tracking of Self-Reported COVID-19 Symptoms: Analysis of Questionnaire Data. *J. Med. Internet Res.* **22**, e21956 (2020).
5. Graham, M. S. *et al.* Changes in symptomatology, reinfection, and transmissibility associated with the SARS-CoV-2 variant B.1.1.7: an ecological study. *Lancet Public Health* **6**, e335–e345 (2021).
6. Mahase, E. Covid-19: Sore throat, fatigue, and myalgia are more common with new UK variant. *BMJ* **372**, n288 (2021).
7. Menni, C. *et al.* Symptom prevalence, duration, and risk of hospital admission in individuals infected with SARS-CoV-2 during periods of omicron and delta variant dominance: a prospective observational study from the ZOE COVID Study. *Lancet* **399**, 1618–1624 (2022).
8. Mishra, B. *et al.* High proportion of low cycle threshold value as an early indicator of COVID-19 surge. *J. Med. Virol.* **94**, 240–245 (2022).
9. Jefferson, T., Spencer, E. A., Brassey, J. & Heneghan, C. Viral Cultures for Coronavirus Disease 2019 Infectivity Assessment: A Systematic Review. *Clin. Infect. Dis.* **73**, e3884–e3899 (2021).
10. Walker, A. S. *et al.* Ct threshold values, a proxy for viral load in community SARS-CoV-2 cases, demonstrate wide variation across populations and over time. *Elife* **10**, e64683 (2021).
11. Marc, A. *et al.* Quantifying the relationship between SARS-CoV-2 viral load and infectiousness. *Elife* **10**, (2021).
12. Kawasuji, H. *et al.* Transmissibility of COVID-19 depends on the viral load around onset in adult

and symptomatic patients. *PLoS One* **15**, e0243597 (2020).

13. Riley, S. *et al.* REal-time Assessment of Community Transmission (REACT) of SARS-CoV-2 virus: Study protocol. *Wellcome Open Res* **5**, 200 (2020).
14. Elliott, P. *et al.* Twin peaks: the Omicron SARS-CoV-2 BA.1 and BA.2 epidemics in England. (2022).
15. Bodinier, B., Filippi, S., Nost, T. H., Chiquet, J. & Chadeau-Hyam, M. Automated calibration for stability selection in penalised regression and graphical models: a multi-OMICs network application exploring the molecular response to tobacco smoking. *arXiv [stat.ME]* (2021).
16. Lauring, A. S. & Hodcroft, E. B. Genetic Variants of SARS-CoV-2-What Do They Mean? *JAMA* **325**, 529–531 (2021).
17. Hui, K. P. Y. *et al.* SARS-CoV-2 Omicron variant replication in human bronchus and lung ex vivo. *Nature* (2022) doi:10.1038/s41586-022-04479-6.
18. Bhattacharyya, R. P. & Hanage, W. P. Challenges in Inferring Intrinsic Severity of the SARS-CoV-2 Omicron Variant. *N. Engl. J. Med.* **386**, e14 (2022).
19. Latest insights team. Coronavirus (COVID-19) latest insights - Office for National Statistics. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19latestinsights/infections (2022).
20. Butowt, R., Bilińska, K. & von Bartheld, C. Why Does the Omicron Variant Largely Spare Olfactory Function? Implications for the Pathogenesis of Anosmia in Coronavirus Disease 2019. *The Journal of Infectious Diseases* (2022) doi:10.1093/infdis/jiac113.
21. Zazhytska, M. *et al.* Non-cell-autonomous disruption of nuclear architecture as a potential cause of COVID-19-induced anosmia. *Cell* **185**, 1052–1064.e12 (2022).
22. Cabinet Office. COVID-19 response: Living with COVID-19. *GOV.UK* https://www.gov.uk/government/publications/covid-19-response-living-with-covid-19 (2022).
23. GISAID - initiative. https://www.gisaid.org/.