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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Canas LS, Molteni E, Deng J, et al. Profiling post-COVID-19 condition across different variants of SARS-CoV-2: a prospective longitudinal study in unvaccinated wild-type, unvaccinated alpha-variant, and vaccinated delta-variant populations. *Lancet Digit Health* 2023; published online May 16. https://doi.org/10.1016/ S2589-7500(23)00056-0.

Supplementary Material

App description and development

In this prospective cohort study, data were acquired from CSS, through a mobile application for iPhone® and Android® users launched jointly by ZOE Limited. and KCL on 24 March 2020. 15 The COVID Symptoms Study app was tested before its launch, as well as before the release of any new version; software for repeatable and consistent data extraction, curation, and analytics was also engineered.48

The app is concurrently available to be downloaded to Android and iOS, in both English and Swedish, and available in the UK, US, and Sweden. The app was widely publicised in these countries during the peak of the pandemic, and new functionalities were added when appropriate to address the needs of the population, such as the registration of side-effects of the vaccination. Additionally, to keep the users engaged with the study, daily and weekly updates regarding research conducted using the data collected via the app are provided to participants (with notification through the app, email alerts, and posted on the website of the ZOE COVID Study (joinzoe.com)).

Supplementary Methods

Table S1. List of symptom and comorbidity questions asked in the COVID Symptom Study application during the current study period.

Symptom	COVID Symptom Study app question	Date of addition to the app	Symptom group
Fever	Fever (at least 37.8C or 100F)	2020-03-29	Systemic/inflammatory
Persistent Cough	A persistent cough (coughing a lot for more than an hour or 3 or more coughing episodes in 24 hours)	2020-03-29	Cardiorespiratory
Fatigue	Unusual fatigue (no; mild fatigue; severe fatigue/ I struggle to get out of bed)	2020-03-29	Systemic/inflammatory
Dyspnoea	Shortness of breath or trouble breathing (no; yes mild symptoms/ slight shortness of breath during ordinary activity: yes significant symptoms/ breathing is comfortable only at rest; yes, severe symptoms/ breathing is difficult even at rest).	2020-03-29	Upper respiratory
Anosmia/Ageusia	Loss of smell/taste	2020-03-29	Central neurological
Hoarse Voice	Unusually hoarse voice	2020-03-29	Upper respiratory
Chest Pain	Unusual chest pain or tightness in your chest	2020-03-29	Cardiorespiratory
Abdominal Pain	Unusual abdominal pain or stomach-ache	2020-03-29	Abdominal
Diarrhoea	Diarrhoea	2020-03-29	Abdominal
Delirium	Confusion, disorientation or drowsiness	2020-03-29	Central neurological
Eye Soreness	Do your eyes have any unusual eye soreness or discomfort (e.g. light sensitivity, excessive tears, or pink/red eye)?	2020-04-29	Immune related/cutaneous

Low appetite (anorexia)	Skipping meals	2020-04-29	Systemic/inflammatory
Headache	Headache	2020-03-29	Central neurological
Nausea	Nausea or vomiting	2020-03-29	Systemic/inflammatory
Dizziness	Dizziness or light-headedness	2020-04-29	Systemic/inflammatory
Sore Throat	Sore or painful throat	2020-03-29	Upper respiratory
Myalgias	Unusual strong muscle pains or aches	2020-04-01	Systemic/inflammatory
Red Welts	Raised, red, itchy welts on the skin or sudden swelling of the face or lips	2020-11-03	Immune related/cutaneous
Blisters	Red/purple sores or blisters on your feet, including your toes	2020-04-29	Immune related/cutaneous
Rashes	Rash on your arms or torso	2020-11-03	Immune related/cutaneous
Sensitive Skin	Strange, unpleasant sensations in your skin like pins & needles or burning	2020-11-03	Immune related/cutaneous
Hair Loss	Unusual hair loss	2020-11-03	Immune related/cutaneous
Low mood (depression)	Feeling down, depressed, or hopeless	2020-11-03	Central neurological
Brain Fog	Loss of concentration or memory (brain fog)	2020-11-03	Central neurological
Dysosmia/Dysgeusia	Altered smell/taste (things smell or taste different to usual)	2020-11-03	Central neurological
Rhinorrhoea	Runny nose	2020-11-03	Upper respiratory
Sneezing	Sneezing more than usual	2020-11-03	Upper respiratory
Ear Pain	Earache	2020-11-03	Upper respiratory
Tinnitus	Ringing in your ears	2020-11-03	Upper respiratory
Lymphadenopathy	Swollen neck glands	2020-11-03	Systemic/inflammatory
Palpitations	Unusually fast or irregular heartbeat (palpitations)	2020-11-03	Cardiorespiratory
Comorbidities			
Diabetes	Do you have diabetes?	2020-06-05	N/A

Cancer	Are you living with cancer?	2020-06-05	N/A
Lung Disease	Do you have lung disease or asthma?	2020-06-05	N/A
Heart Disease	Do you have heart disease?	2020-06-05	N/A
Kidney Disease	Do you have kidney disease?	2020-06-05	N/A

Table S2. List of questions from CSSB Long-COVID questionnaire included in the study.

Outcome	Question	Answer	Answer Encoding
Early Medical help	Q.B.5 In the first 4 weeks of illness, did you look for any medical help for any symptoms you think may have been caused by COVID-19?	Yes - discussed symptoms with doctor/GP/practice nurse Yes - discussed symptoms with NHS 111 in England, Wales and Northern Ireland or NHS 24 in Scotland Yes - accessed online advice at NHS 111 in England, Wales and Northern Ireland or NHS 24 in Scotland Yes - visited pharmacist Yes - visited A&E or walk-in centre No	Yes (1-5) – encoded as 1 No (6) – encoded as 0
Delayed Medical help	Q.B.6 Did you look for any medical help for any symptoms you had more than 4 weeks after your symptoms began, that you think may have been caused by COVID-19?	Yes - discussed symptoms with doctor/GP/practice nurse Yes - discussed symptoms with NHS 111 in England, Wales and Northern Ireland or NHS 24 in Scotland Yes - accessed online advice at NHS 111 in England, Wales and Northern Ireland or NHS 24 in Scotland Yes - visited pharmacist Yes - visited A&E or walk-in centre No	Yes (1-5) – encoded as 1 No (6) – encoded as 0
Hospitalisation	Q.B.7 Have you ever had to stay in hospital because of COVID-19 symptoms?	Yes No	Yes (1) – encoded as 1 No (2) – encoded as 0
Re-infection	Q.B.8 Do you think you have caught COVID-19 more than once?	Yes, confirmed by a second positive test Yes, based on medical advice Yes, based on strong personal suspicion Unsure No	Yes (1 – 2) – encoded as 1 No (5) – encoded as 0 Excluded (3-4) for absence of clear answer
Severe impact on daily activities	Q.B.13 How many days were you or have you been so unwell that you stayed in bed or on the sofa?	None 1-3 days 4-6 days 7-13 days 2-3 weeks 4-12 weeks 12+ weeks	Yes (6-7) – encoded as 1, reflecting OCS and PCS No (1-5) – encoded as 0
Prolonged impact in daily activities	Q.B.16 Thinking of how you felt 12 weeks after your COVID-19 illness began, what did you need help with because of COVID-19?	Getting essential shopping - e.g., food or medication Preparing food and/or drink Washing and dressing Housework - e.g., laundry, cleaning or hoovering Managing household responsibilities - e.g., finances or paying bills Day to day work / study Childcare or other caring responsibilities Letting other people know about my illness (e.g. employer, university, family) Getting about (travel) - e.g., driving I have not needed any additional support	Yes (1 – 9) – encoded as 1 No (10) – encoded as 0

Figure S1. SARS-CoV-2 variants of concern in the UK by weeks, from 15th of March 2020 to 3rd of March 2022. Figure adapted from COG-UK/Mutation Explorer34. The variant periods are defined when the prevalence of the variant is higher than 80%. Variant sub-lineages are neglected and analysed as a single variant.

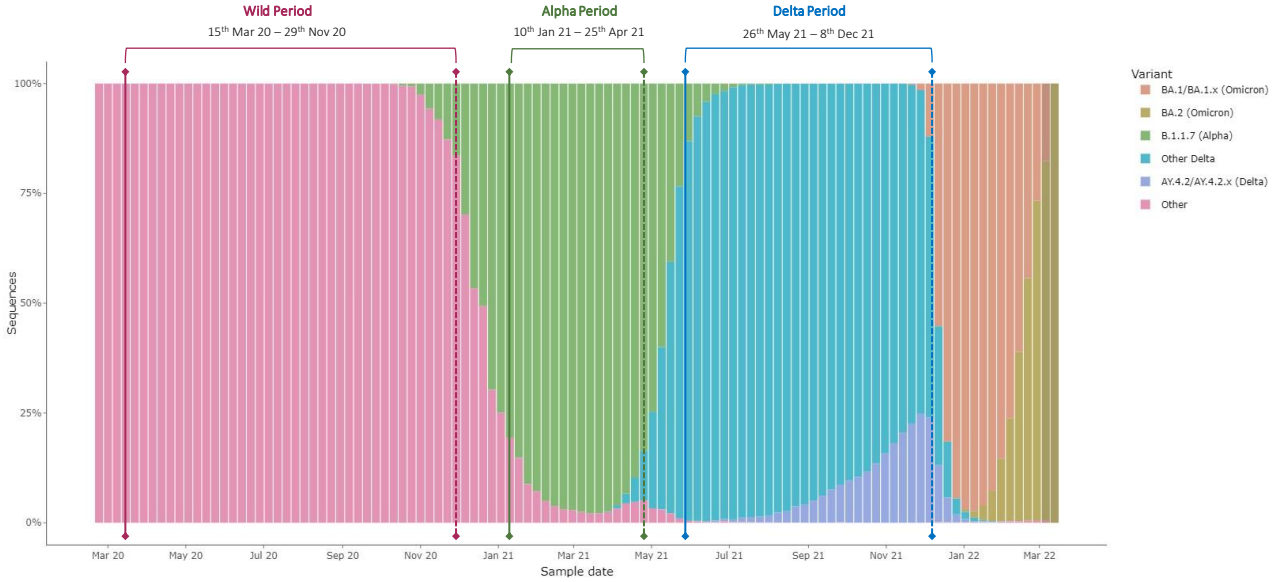


Figure S2. Flowchart of participants satisfying the inclusion and exclusion criteria for this study. The candidates were included the study if reporting a positive test following logging as healthy for at least 4 weeks (*). Individuals who reported symptom duration for at least 28 days were then retained according to inclusion/exclusion criteria. Individuals were further subdivided according to the timing of SARS-CoV-2 infection relative to vaccination: vaccinated (considered from at least one week after the first dose) and unvaccinated (infection prior to the first dose of vaccine). Parsing of individuals by variant type is defined by positive testing during time periods where the prevailing UK strain was >=80 % of circulating SARS-CoV-2, using UK-COG data (see text for details).CSSB: COVID Symptoms Study Biobank; PCS: post-COVID syndrome.

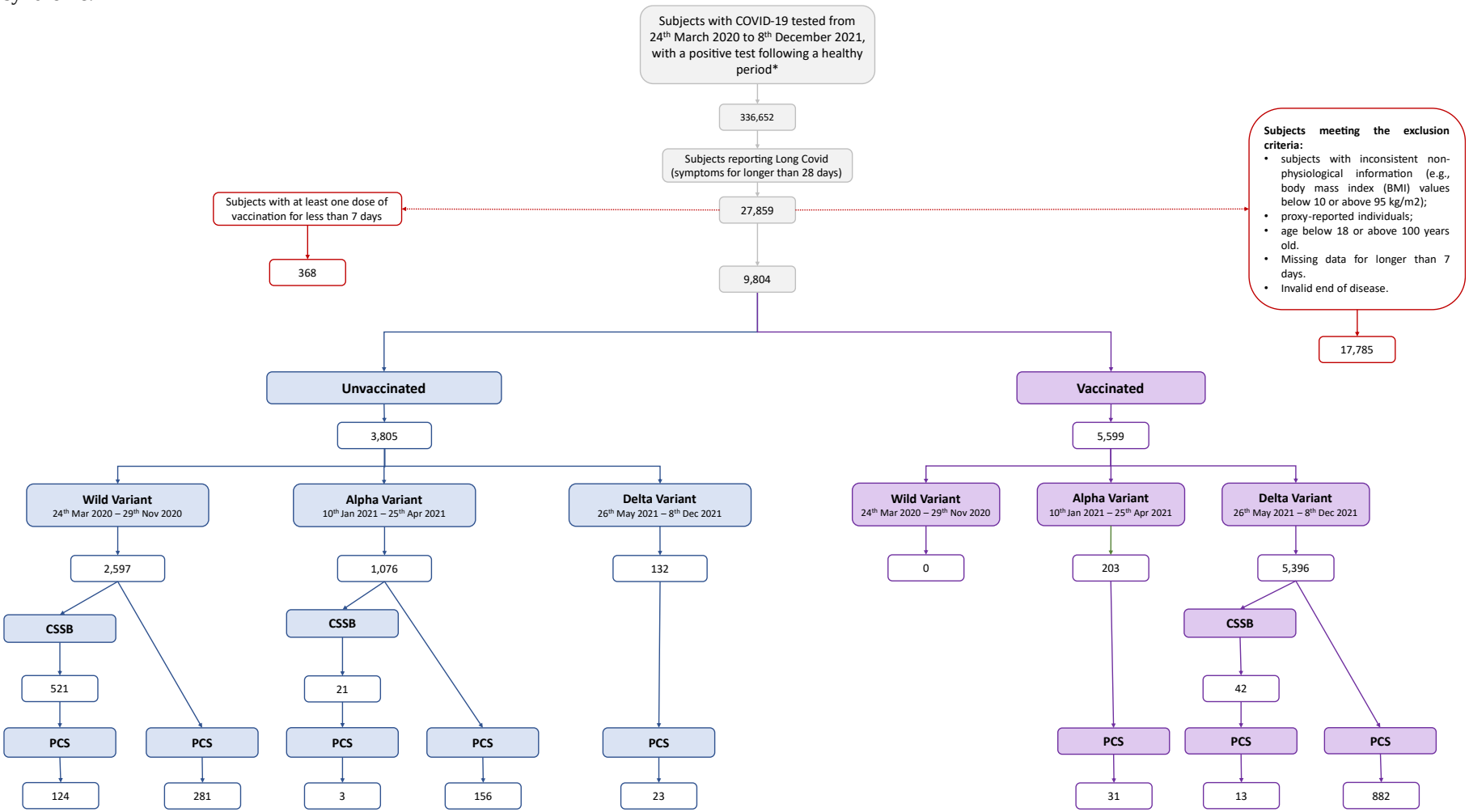
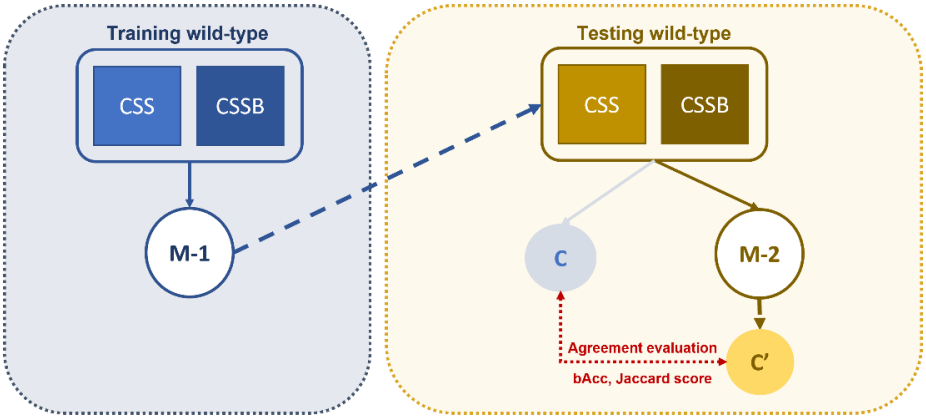


Figure S3. Framework to assess model robustness. The blue area represents the original training scheme, applied for cluster estimation per population and vaccination status. M-1 represents the optimised model from the training set. The yellow area encodes the re-trained model on the testing set – M-2. The predicted labels, C, for the testing set using the model M-1 are compared with labels predicted for the testing set using M-2, C'. CSS: COVID Symptoms Study. CSSB: COVID Symptoms Study Biobank. bACC: Balanced Accuracy.



Supplementary Results

Table S3. Description of the population with an invalid logging profile (not identifiable healthy status) and valid logging profile (with respect to the inclusion criteria).
Illness duration encodes the disease duration per patient from the self-reported symptoms. The illness duration and symptoms per week are presented with the median and interquartile range (IQR). Bold values encode statistical significance using the Mann-Whitney test between the invalid and valid logging within the same period, with * and ** encoding p-value<0.05 and p-value<0.01, respectively.

Illness duration 28-83 days														
Invalid logging								**Valid logging**						
	Number of subjects	Illness duration (weeks)	Proportion of reports during disease	Number of symptoms per week	Age (years)	BMI (kg/m^2)	Gender (proportion males)	Number of subjects	Illness duration (weeks)	Number of symptoms per week	Proportion of reports during disease	Age (years)	BMI (kg/m^2)	Gender (proportion males)
Wild type	142	5 [4; 6]	**0.52 [0.40; 0.63]***	5 [3; 8]	52.0 [41.0; 60.0]	27.8 [23.7; 32.8]	40 (0.28)	2,192	5 [4; 6]	3 [2; 6]	**0.57 [0.43; 0.71]***	54 [45; 62]	26.5 [23.4; 31.1]	586 (0.27)
Alpha	36	5 [4; 7]	**0.51 [0.37; 0.60]****	5 [3; 9]	54 [45; 59]	26.2 [24.1; 28.8]	12 (0.33)	917	5 [4; 6]	5 [2; 9]	**0.60 [0.44; 0.74]****	56 [49; 63]	26.1 [23.5; 29.9]	280 (0.31)
Delta	133	5 [4; 7]	**0.54 [0.43; 0.69]***	3 [5; 9]	55.0 [46.0; 61.0]	25.8 [23.6; 30.0]	44 (0.33)	4,501	5 [4; 7]	4 [2; 8]	**0.59 [0.42; 0.73]***	55 [48; 64]	26.0 [23.2; 29.9]	1475 (0.33)
Illness duration >= 84 days														
Invalid logging								**Valid logging**						
	Number of subjects	Illness duration (weeks)	Proportion of reports during disease	Number of symptoms per week	Age (years)	BMI (kg/m^2)	Gender (proportion males)	Number of subjects	Illness duration (weeks)	Number of symptoms per week	Proportion of reports during disease	Age (years)	BMI (kg/m^2)	Gender (proportion males)

Wild type	101	**73 [46; 76]****	**0.74 [0.62; 0.81]****	3 [1; 5]	56.0 [46.0; 65.0]	26.3 [24.2; 32.1]	33 (0.33)	405	**19 [14; 30]****	2 [1; 4]	**0.65 [0.54; 0.75]****	58 [50; 65]	26.3 [23.5; 31.8]	107 (0.26)
Alpha	53	**59 [39; 62]****	**0.75 [0.65; 0.83]***	4 [2; 8]	58 [52; 64]	27.6 [23.0; 30.5]	18 (0.34)	159	**16 [14; 20]****	4 [2; 6]	**0.68 [0.56; 0.80]***	58 [52; 65]	26.5 [23.1; 30.3]	46 (0.29)
Delta	457	**19 [23, 29]****	**0.69 [0.58; 0.78]***	4 [2; 7]	59.0 [52.0; 66.0]	26.0 [23.1; 29.9]	166 (0.36)	895	**15 [13; 18]****	3 [2; 7]	**0.67 [0.53; 0.78]***	59 [52; 66]	26.0 [23.1; 29.9]	300 (0.34)

Table S4. Symptoms prevalence for vaccinated and unvaccinated populations, per SARS-CoV-2 variant, for individuals with symptoms longer than 28 days (ongoing COVID, OCS, and post-COVID syndrome, PCS).

Mann-Whitney two-sided test was used to assess the differences between the two groups, per variant of the virus. Alpha = 0.05, before multiple corrections. Bold encode significant differences, after multiple corrections (alpha corrected = 0.001).

	Alpha Variant				**Delta Variant**			
Symptoms	**Statistics (vaccinated)**	**p-value**	**Number vaccinated**	**Number unvaccinated**	**Statistics (vaccinated)**	**p-value**	**Number vaccinated**	**Number unvaccinated**
Persistent Cough	40111	0.331	118	720	177844	0.452	3798	98
Dizziness	33993	0.060	114	670	105051	0.977	2924	72
Palpitations	5503.5	0.995	44	250	9629.5	0.412	930	23
Dyspnoea	24284.5	0.661	85	555	60218	0.174	2318	58
Chest Pain	16781	0.037	82	478	63531.5	0.159	1914	60
Hoarse voice	22247.5	0.805	95	476	83509.5	0.953	2726	61
Sore throat	38185.5	0.030	126	690	157143	0.690	3485	88
Eyes soreness	18304	0.705	76	469	67597.5	0.514	2258	57
Rhinorrhoea	62384.5	0.020	176	798	261685	0.072	4737	100
Sneezing	48494	0.916	146	668	146331	0.360	4224	65
Earache	6696	0.905	48	276	18323.5	0.416	1493	27
Tinnitus	11606.5	0.291	63	340	26404.5	0.529	1764	28
Fatigue	103894.5	0.814	197	1066	354136	0.057	5076	127
Delirium	4378.5	0.240	39	254	18204.5	0.951	1145	32
Dysomnia	39057.5	0.091	116	746	179083	0.964	3741	96
Anosmia	24461	0.083	80	546	225144	0.718	4124	107
Headache	86060	0.487	179	994	290022.5	0.085	4730	112
Brain Fog	26892.5	0.327	100	573	86311.5	0.791	2775	61
Depression	16766	0.161	78	477	51245	0.350	1903	50
Diarrhoea	11917	0.258	61	429	38476	0.310	1606	44
Abdominal Pain	11516.5	0.931	61	375	28416.5	0.623	1488	40
Low appetite	18279	0.747	68	525	49685	0.741	1855	55
Nausea	11675	0.384	58	433	37538.5	0.860	1555	49
Fever	20896.5	0.054	81	594	84154.5	0.150	2519	74
Chills	29242	0.050	108	614	71373.5	0.323	2661	58

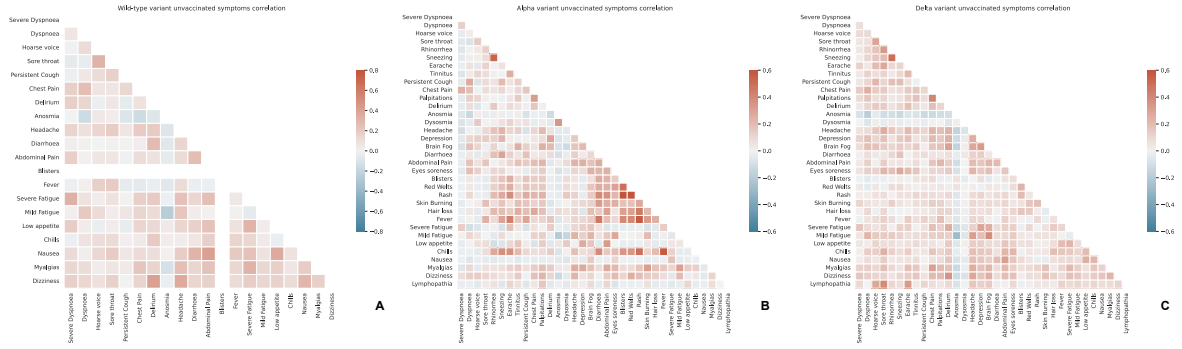
Blisters	84	0.139	8	32	77.5	0.095	118	3
Red Welts	504.5	0.549	9	100	1557.5	0.193	307	8
Lymphopathia	5496.5	0.103	46	281	22497	0.175	1398	37
Rash	1343.5	0.356	19	125	2637	0.992	351	15
Myalgias	24250	0.811	82	582	71218	0.348	2148	62
Skin Burning	4649.5	0.241	28	293	13268	0.227	866	27
Hair loss	277	0.765	10	59	1456.5	0.959	245	12

Table S5. Illness description for the post-COVID syndrome across clusters and variants. Clusters are labelled according to the profile found with the unsupervised algorithm. The number of individuals used to optimise the clusters within a variant (training sample) and the number of individuals classified with each cluster are presented. Median duration, in weeks, and interquartile range [IQR] presented per variant and optimised cluster. Main features and symptoms describe the highest ranked symptoms per cluster, based on z-scores values.

SARS-CoV-2 variant	Clusters	Number individuals	Duration (weeks)	Main features and symptoms	Classification
Wild	wild-A	138	24.0 [15.0; 40.8]	Symptoms groups: cardiorespiratory, central neurological (anosmia) and upper respiratory (dyspnoea). High prevalence of dysosmia. Persistent cough as the most relevant symptom (highest z-score).	Predominantly cardiorespiratory
	wild-B	60	27.5 [15.0; 48.3]	Symptoms groups: systemic/inflammatory, central neurological, upper respiratory, and immune-related/cutaneous. Severe symptoms, namely severe dyspnoea for longer than 12 weeks. High prevalence of systemic symptoms. Unique cluster with immune-related symptoms. Most heterogeneous cluster.	Systemic/inflammatory
	wild-C	38	15.0 [13.0; 30.8]	Symptoms groups: upper respiratory, central neurological and systemic/inflammatory. Hoarse voice as the most relevant symptom (highest z-score). High prevalence of anosmia, with almost neglectable z-score.	Predominantly respiratory
	wild-D	37	22.0 [15.0; 49.0]	Symptoms groups: upper respiratory, central neurological and abdominal. Diarrhoea and sore throat are the most relevant symptoms (highest z-score). High prevalence of neurological symptoms.	Predominantly central neurological with abdominal
	Overall	273	23.0 [15.0; 43.0]	Three main clusters: (1) with cardiorespiratory symptoms, (2) systemic/inflammatory and (3) central neurological. Abdominal and cutaneous symptoms isolated in singular clusters, with high relevance but lower prevalence.	---
Alpha	alpha-A	43	18.0 [14.0; 35.0]	Symptoms groups: upper respiratory, central neurological and cardiorespiratory. Anosmia is the most relevant symptom. High prevalence of central neurological symptoms.	Central neurological
	alpha-B	28	16.5 [14.0; 28.8]	Symptoms groups: upper respiratory, central neurological and cardiorespiratory. Persistent cough is the most relevant symptom, followed by dyspnoea. High prevalence of respiratory symptoms and persistent cough.	Predominantly upper respiratory with cardiorespiratory.
	alpha-C	23	22.0 [15.5; 55.0]	Symptoms groups: upper respiratory, central neurological, systemic/inflammatory and abdominal. Strong relevance of respiratory symptoms, followed by systemic symptoms. High prevalence of respiratory symptoms and persistent cough.	Predominantly upper respiratory with systemic.
	alpha-D	17	17.0 [14.0; 43.0]	Symptoms groups: upper respiratory, systemic/inflammatory and immune-related/cutaneous. Strong relevance of respiratory symptoms, followed by immune-related symptoms. High prevalence of systemic and immune-related symptoms.	Predominantly immune-related/cutaneous with systemic.
	alpha-E	16	23.0 [13.7; 41.0]	Symptoms groups: upper respiratory, systemic/inflammatory, immune-related/cutaneous, cardiorespiratory and central neurological. Strong relevance of immune-related symptoms, namely blisters.	Predominantly mild symptoms.

				High prevalence of mild fatigue. Highly heterogeneous cluster.	
	alpha-F	15	18.0 [14.5; 37.5]	Symptoms groups: upper respiratory, systemic/inflammatory, abdominal and central neurological. Strong relevance of systemic/inflammatory followed by neurological. High prevalence of central neurological and systemic symptoms.	Predominantly central neurological with systemic/inflammatory.
	alpha-G	13	21.0 [15.0; 44.0]	Symptoms groups: upper respiratory, systemic/inflammatory, immune-related, abdominal and cardiorespiratory. Strong relevance of cardiorespiratory, followed by immune-related symptoms. High prevalence of cardiorespiratory symptoms.	Multi-systemic with the predominance of cardiorespiratory symptoms.
	Overall	159	18.0 [14.0; 43.5]	Three main clusters: (1) with cardiorespiratory symptoms, (2) systemic/inflammatory and immune-related and (3) central neurological. Abdominal symptoms influence mostly the smaller cluster and immune-related symptoms are highly prevalent in clusters with systemic symptoms.	---
Delta	v-delta-A	431	18.0 [14.0; 24.0]	Symptoms groups: central neurological. Strong relevance of anosmia with high prevalence.	Central neurological
	v-delta-B	142	19.0 [14.0; 23.8]	Symptoms groups: upper respiratory, systemic/inflammatory, immune-related, and central neurological. Strong relevance immune-related symptoms, namely blisters. High prevalence of upper respiratory and central neurological symptoms.	Predominantly upper respiratory with central neurological.
	v-delta-C	123	18.0 [14.0; 23.0]	Symptoms groups: upper respiratory, systemic/inflammatory, central neurological and cardiorespiratory. Strong relevance of upper respiratory, followed by cardiorespiratory. High prevalence of mild fatigue.	Multi-systemic with a predominance of mild fatigue, upper respiratory and headache.
	v-delta-D	107	20.0 [16.0; 25.0]	Symptoms groups: upper respiratory, systemic/inflammatory, central neurological and immune-related/cutaneous. Strong relevance of immune-related, followed by systemic/inflammatory. High prevalence of mild fatigue and neurological symptoms.	Predominantly immune-related with central neurological and systemic.
	v-delta-E	80	20.0 [16.8; 28.3]	Symptoms groups: upper respiratory, systemic/inflammatory, immune-related/cutaneous, abdominal and cardiorespiratory. Strong influence of cardiorespiratory symptoms and severe dyspnoea. High prevalence of mild fatigue and neurological symptoms.	Severe symptoms
All population	Overall	883	19.0 [15.0; 24.0]	Three main clusters: (1) with cardiorespiratory symptoms – severe symptoms, (2) systemic/inflammatory and immune-related and (3) central neurological. Abdominal symptoms influence mostly the smaller cluster and immune-related symptoms are highly prevalent in clusters with systemic symptoms.	---

Figure S4. Spearman correlation matrix self-reported symptoms. The correlation matrix was computed using the aggregated symptoms (sum of symptoms per week, for each individual) for wild-type unvaccinated subjects (A), alpha variant unvaccinated individuals (B) and delta variant vaccinated individuals (C). Red encodes positive correlations, and blue corresponds to negative correlations.



Most of the symptoms introduced later in the app, used to characterise the alpha and delta variants, are positively correlated with symptoms included in the initial list. Examples of that are palpitations highly correlated with chest pain, brain fog highly correlated with central neurological, and immune-related symptoms such as rashes correlated with blisters for both the latest variants of the virus. Note that such symptoms also belong to the same group of symptoms. Other new symptoms are also correlated with initially existing ones, suggesting that new symptoms only added more granularity to the initial 20 symptoms.

Figure S5. Symptom prevalence and duration for subjects reporting PCS. Median duration of symptoms, in weeks, for subjects reporting infection before vaccination (unvaccinated – hollowed bars; subsequently vaccinated – filled bars; interquartile range (IQR) represented by the black lines; green: wild-type variant; yellow: alpha variant; red: delta variant).

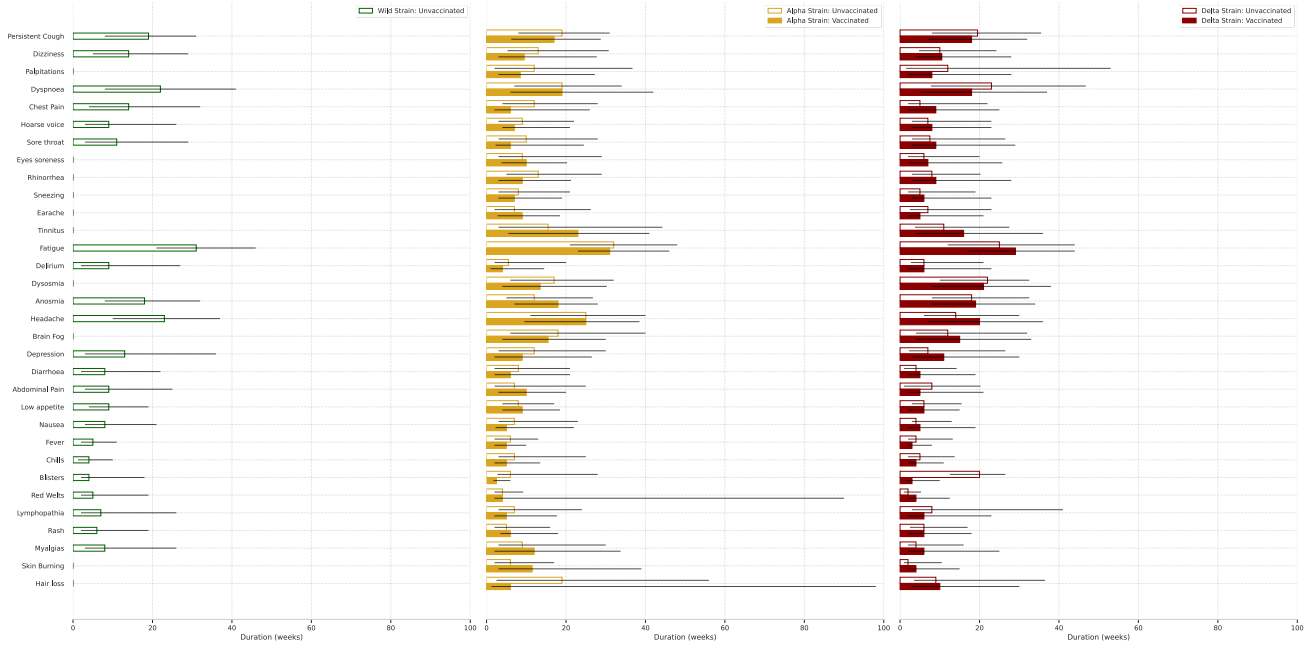


Figure S6. Optimisation of BIC to select the best number of clusters per SARS-CoV-2 variant. A: Bootstrapping analysis for 50 randomly selected populations for training and testing set, for wild-type variant. B: Bootstrapping analysis for 20 randomly selected populations for training for alpha (left panel) and delta (right panel) variants. Panel B assesses the robustness of the optimised number of clusters. Given early convergence and a smaller sample to bootstrap (small sample size of CSSB sample with both alpha- and delta variants), only 20 runs were performed. No formal testing was performed for these samples.

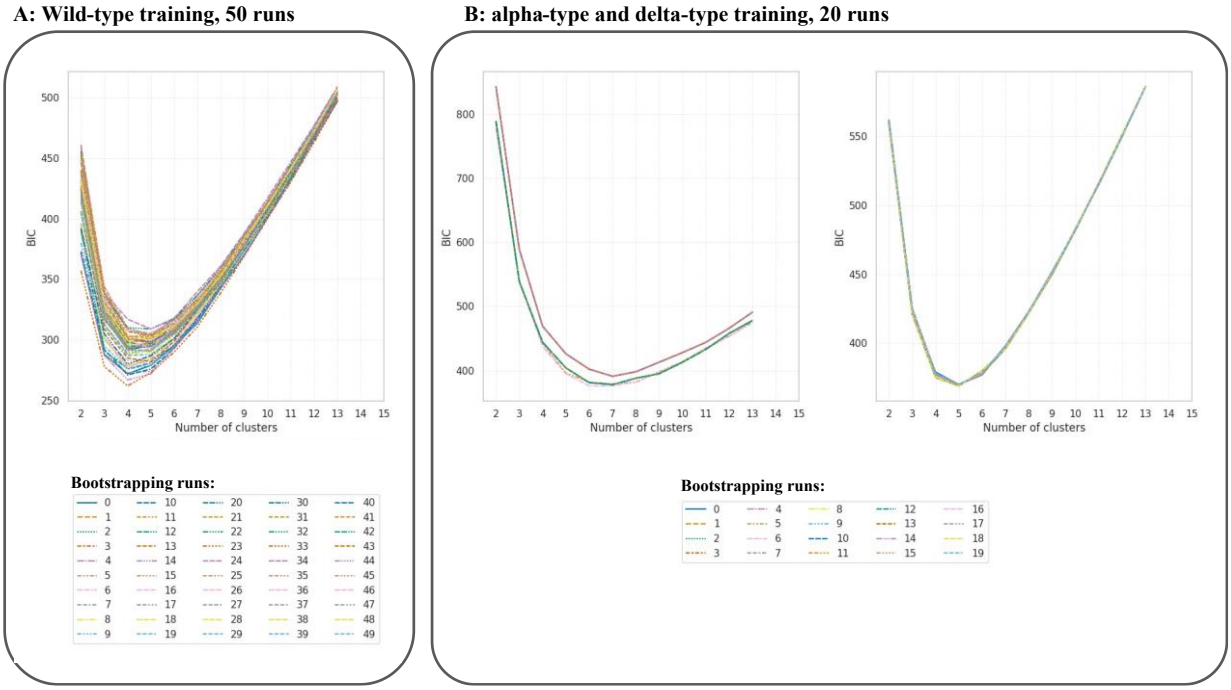


Figure S7. Significance analysis of symptoms profiles per cluster for the wild-type variant of the virus, for symptomatic disease longer than 12 weeks.

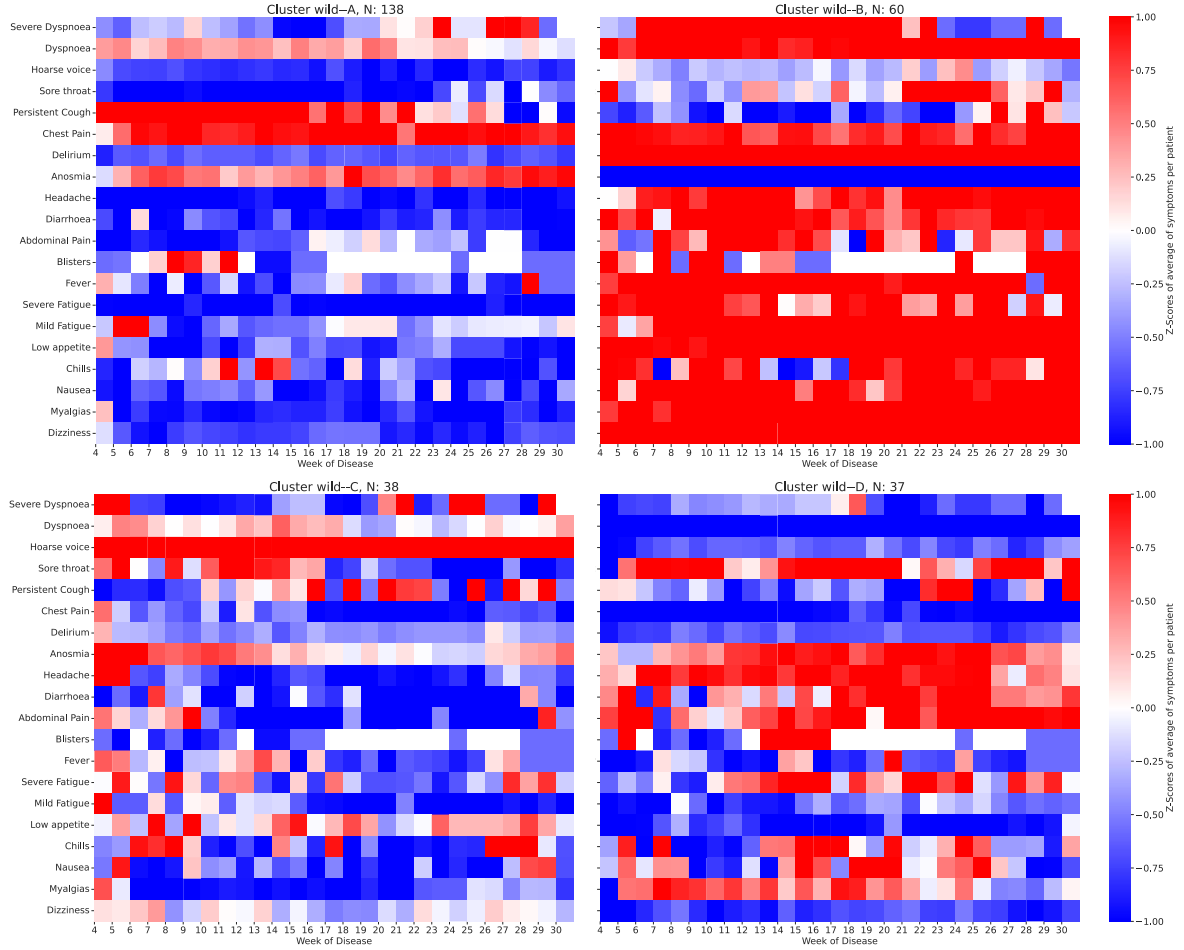


Figure S8. Demographic profile per cluster for the wild-type variant of the virus, for symptomatic disease longer than 12 weeks. A: Body Mass Index (BMI) in kg/m^2; B: Age in years. The diamond (♦) encodes outliers. Mann-Whitney test was conducted to assess statistical differences, alpha = 0.05.

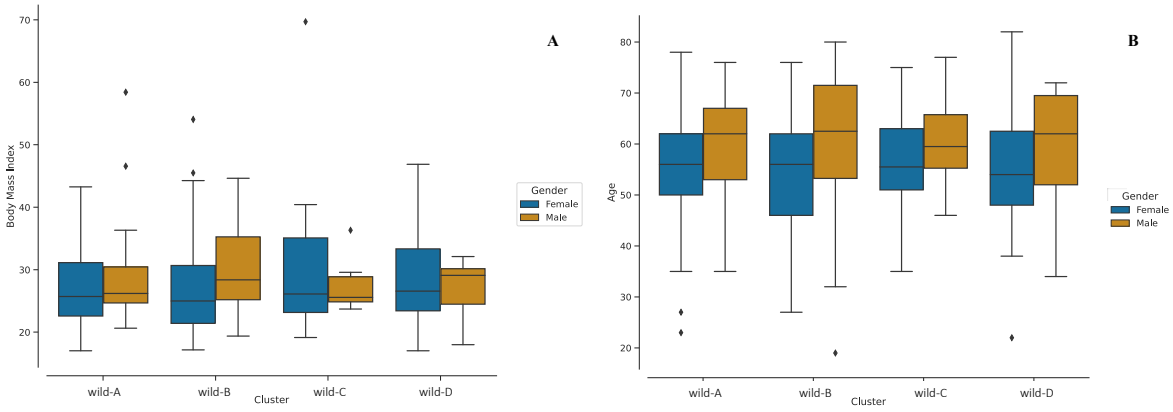


Figure S9. Individual profile for the clusters optimised for the wild-type variant for subjects with the symptomatic disease for longer than 12 weeks. The duration of each symptom is presented by the colour bar. The grey dots encode the average duration of each symptom for the population labelled with each cluster. The gradient colours encode the prevalence of the symptoms per week – darker encodes a higher prevalence of the symptom. Median prevalence across weeks is used to encode the symptom prevalence.

Figure S10. Symptom prevalence profile for PCS clusters for unvaccinated subjects infected with the alpha variant. The proportion of subjects reporting each symptom (ratio) per week is encoded by the colourmap (darker represents a higher ratio).

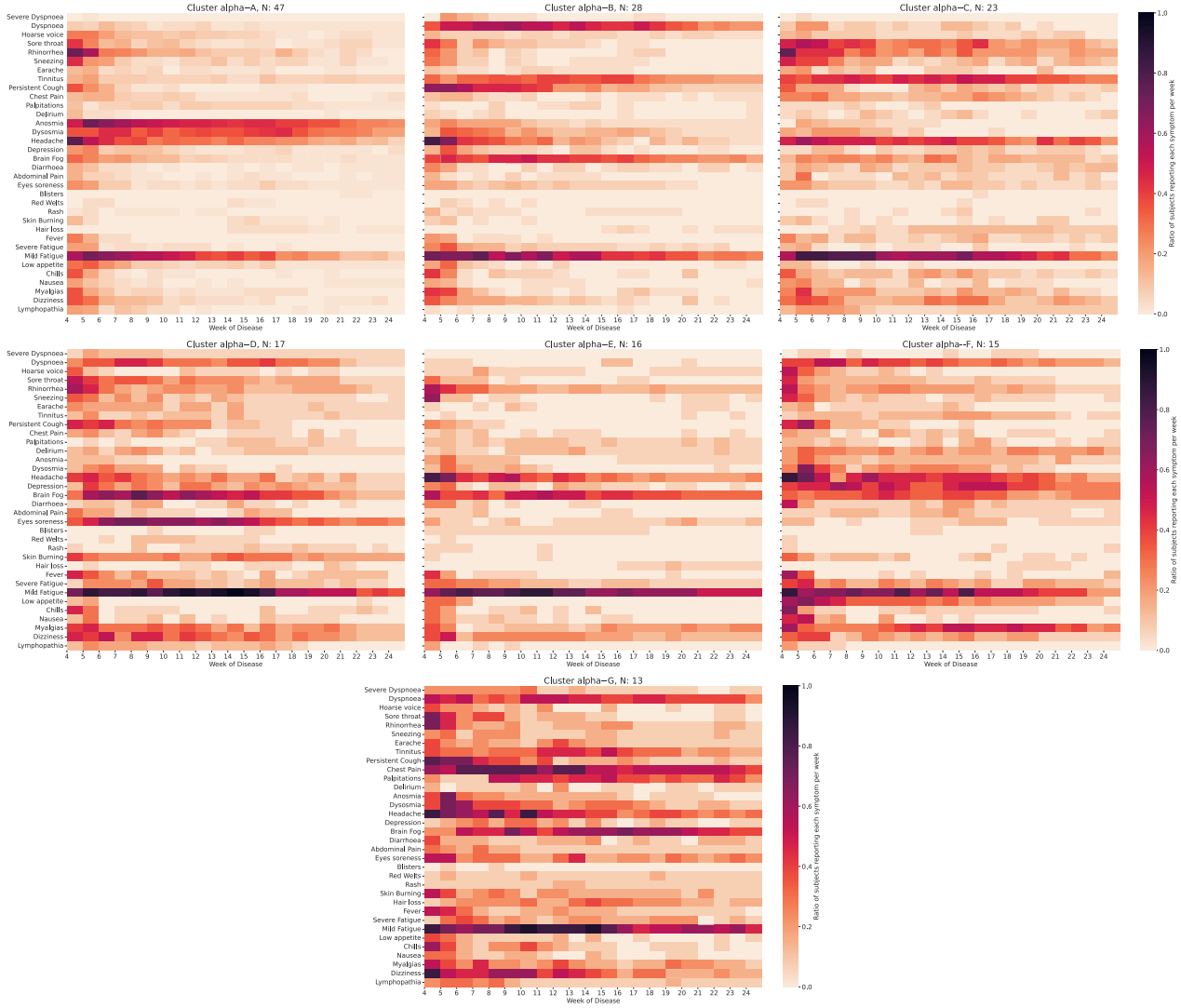


Figure S11. Significance analysis of symptoms profiles per cluster for the alpha variant of the virus, for symptomatic disease longer than 12 weeks.

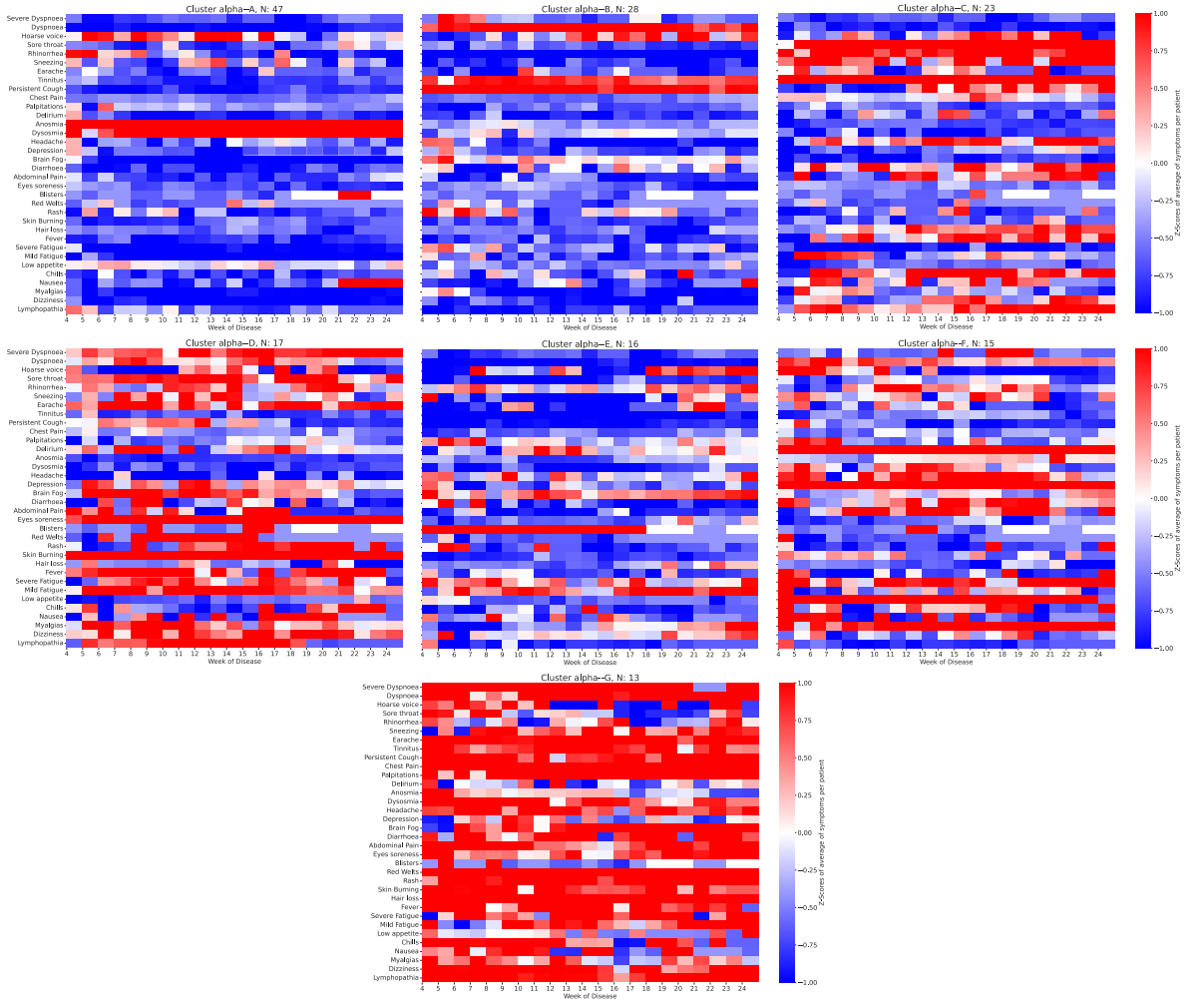


Figure S12. Individual profile for the clusters optimised for the unvaccinated alpha variant for subjects with the symptomatic disease for longer than 12 weeks. The duration of each symptom is presented by the colour bar. The grey dots encode the average duration of each symptom for the population labelled with each cluster. The gradient colours encode the prevalence of the symptoms per week – darker encodes a higher prevalence of the symptom. Median prevalence across weeks is used to encode the symptom prevalence.

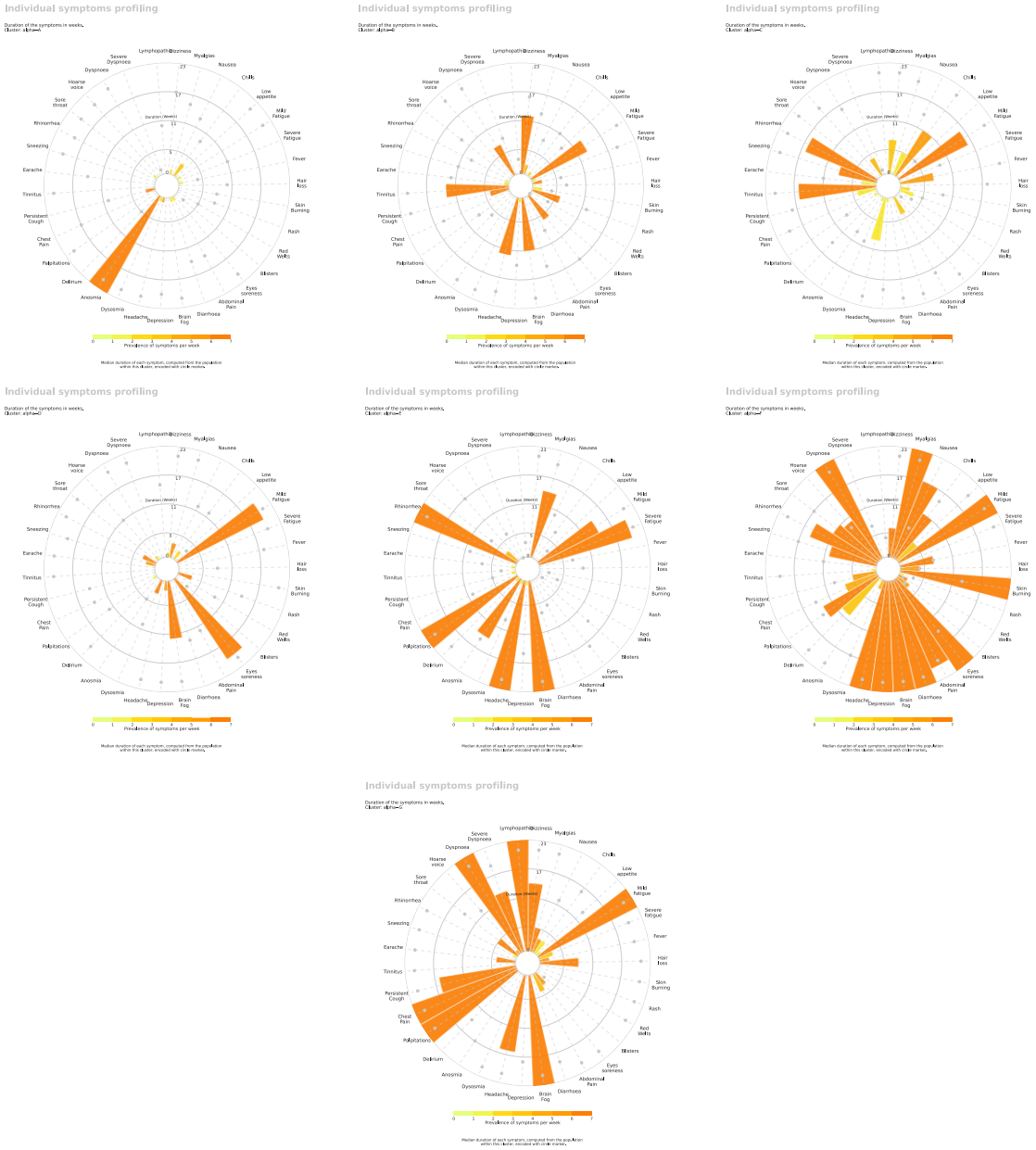


Figure S13. Demographic profile per cluster for the unvaccinated alpha variant of the virus, for symptomatic disease longer than 12 weeks. A: Body Max Index (BMI) in kg/m^2; B: Age in years. The diamond (♦) encodes outliers. Mann-Whitney test was conducted to assess statistical differences, alpha = 0.05.

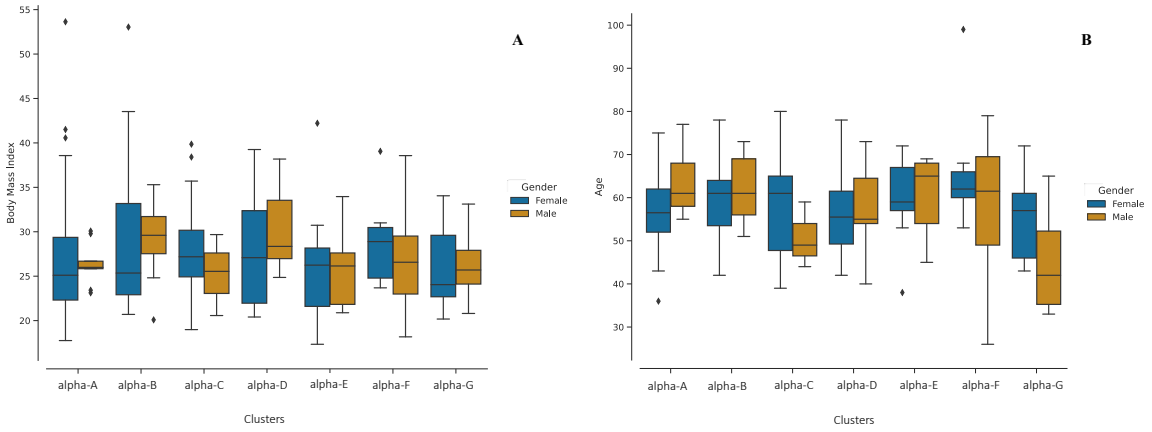


Figure S14. Symptom prevalence profile for PCS clusters for vaccinated individuals infected with the delta variant. The proportion of subjects reporting each symptom (ratio) per week is encoded by the colourmap (darker represents a higher ratio).

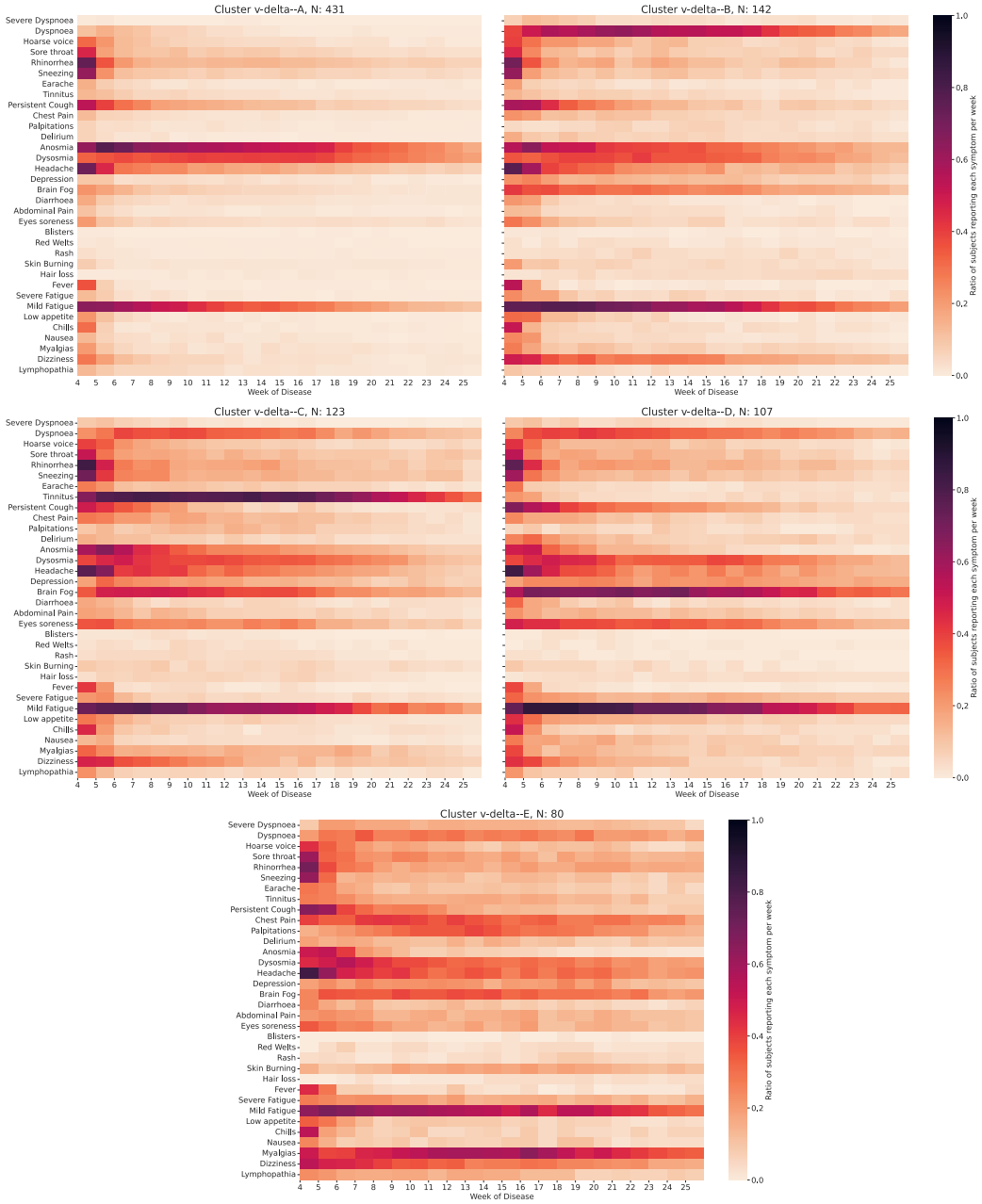


Figure S15. Significance analysis of symptoms profiles per cluster for the vaccinated delta variant of the virus, for symptomatic disease longer than 12 weeks, for vaccinated subjects.

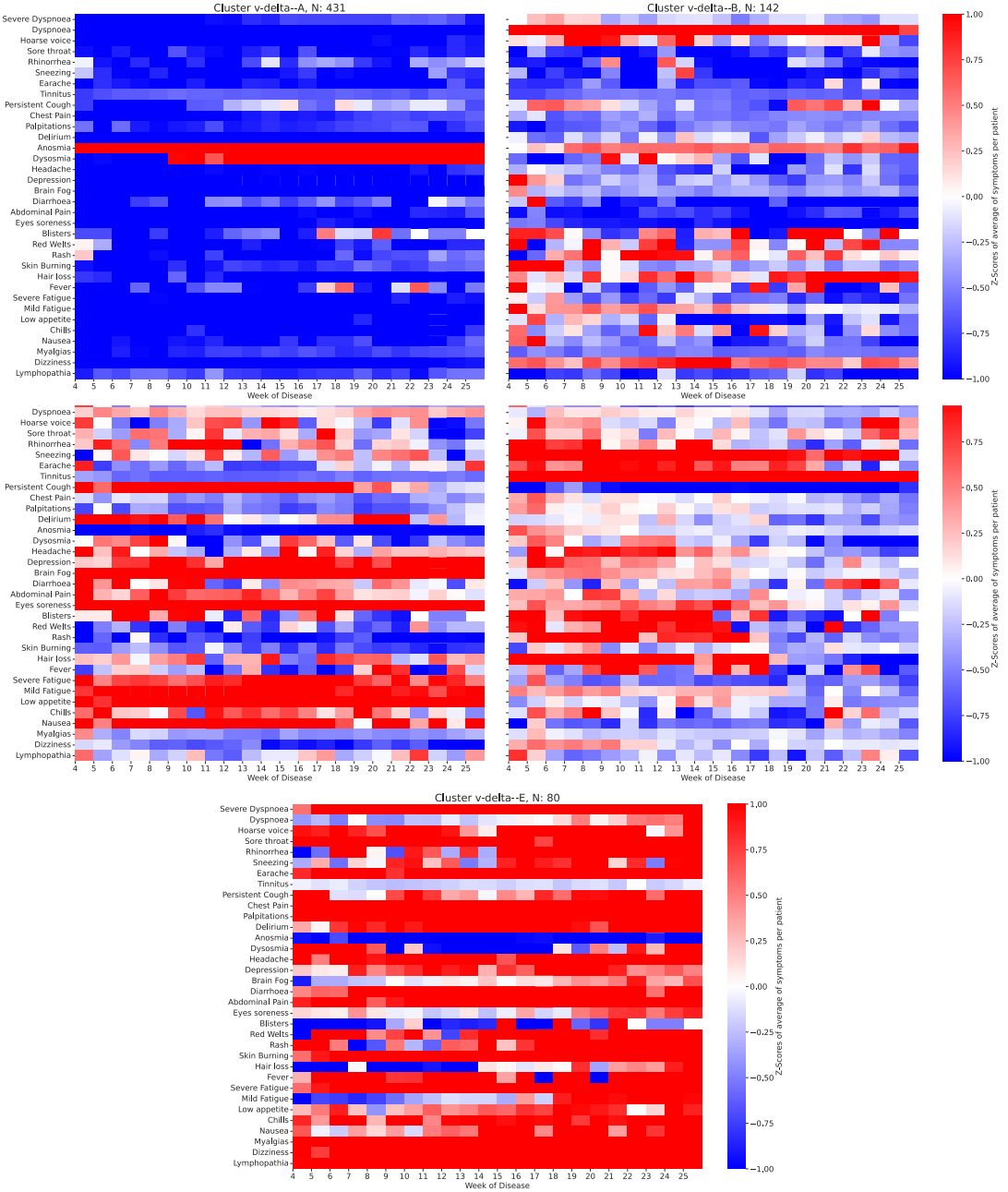


Figure S16. Individual profile for the clusters optimised for vaccinated delta variant for subjects, who were infected after vaccination, with symptomatic lasting for longer than 12 weeks. The duration of each symptom is presented by the coloured bar. The grey dots encode the average duration of each symptom for the population labelled with each cluster. The gradient colours encode the prevalence of the symptoms per week – darker encodes a higher prevalence of the symptom. Median prevalence across weeks is used to encode the symptom prevalence.

Figure S17. Demographic profile per cluster for the vaccinated delta variant of the virus, for symptomatic disease longer than 12 weeks. A: Body Max Index (BMI) in kg/m^2; B: Age in years. The diamond (♦) encodes outliers. Mann-Whitney test was conducted to assess statistical differences, alpha = 0.05. Asterisk (*) denotes statistical significance.

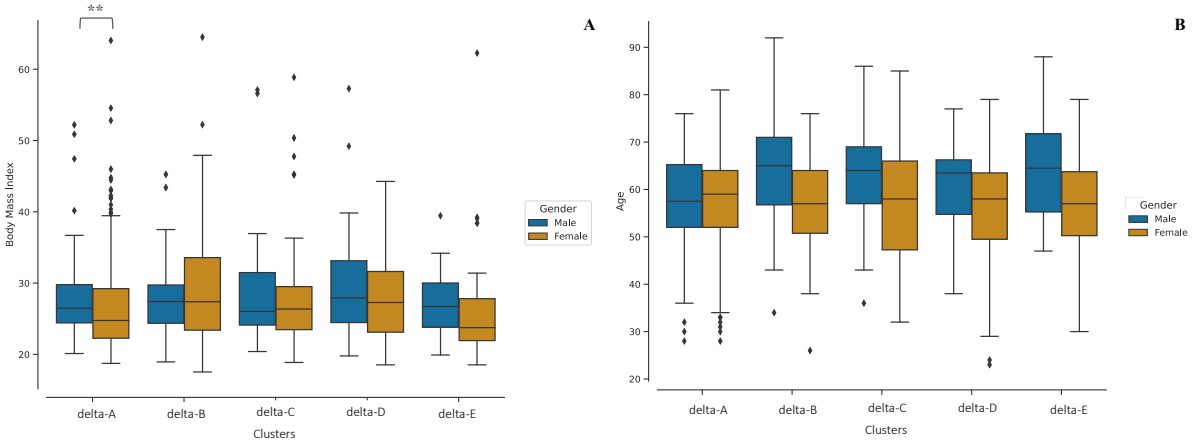


Figure S18. Comorbidity profile per cluster for the three variants of the virus, for symptomatic disease longer than 12 weeks.

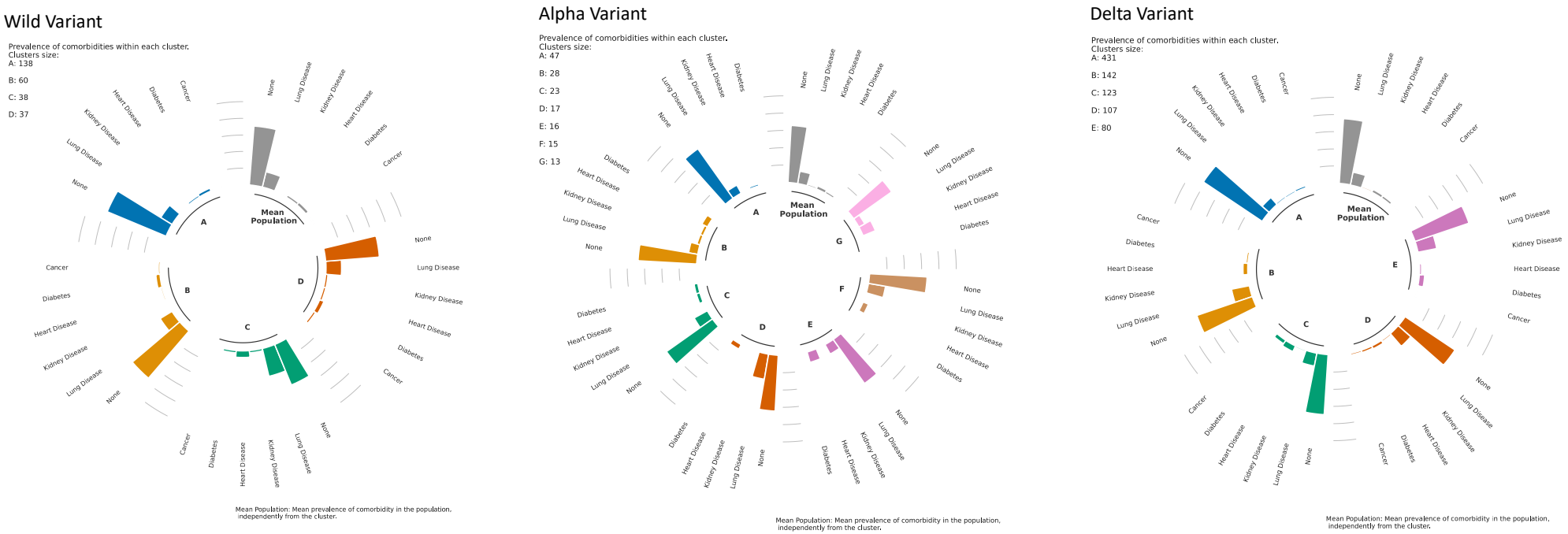


Figure S19. Symptom prevalence profile for the cluster prediction for the independent sample composed unvaccinated individuals infected by the wild-type variant with symptomatic illness for longer than 12 weeks. The proportion of subjects reporting each symptom (ratio) per week is encoded by the colourmap (darker represents higher ratio).

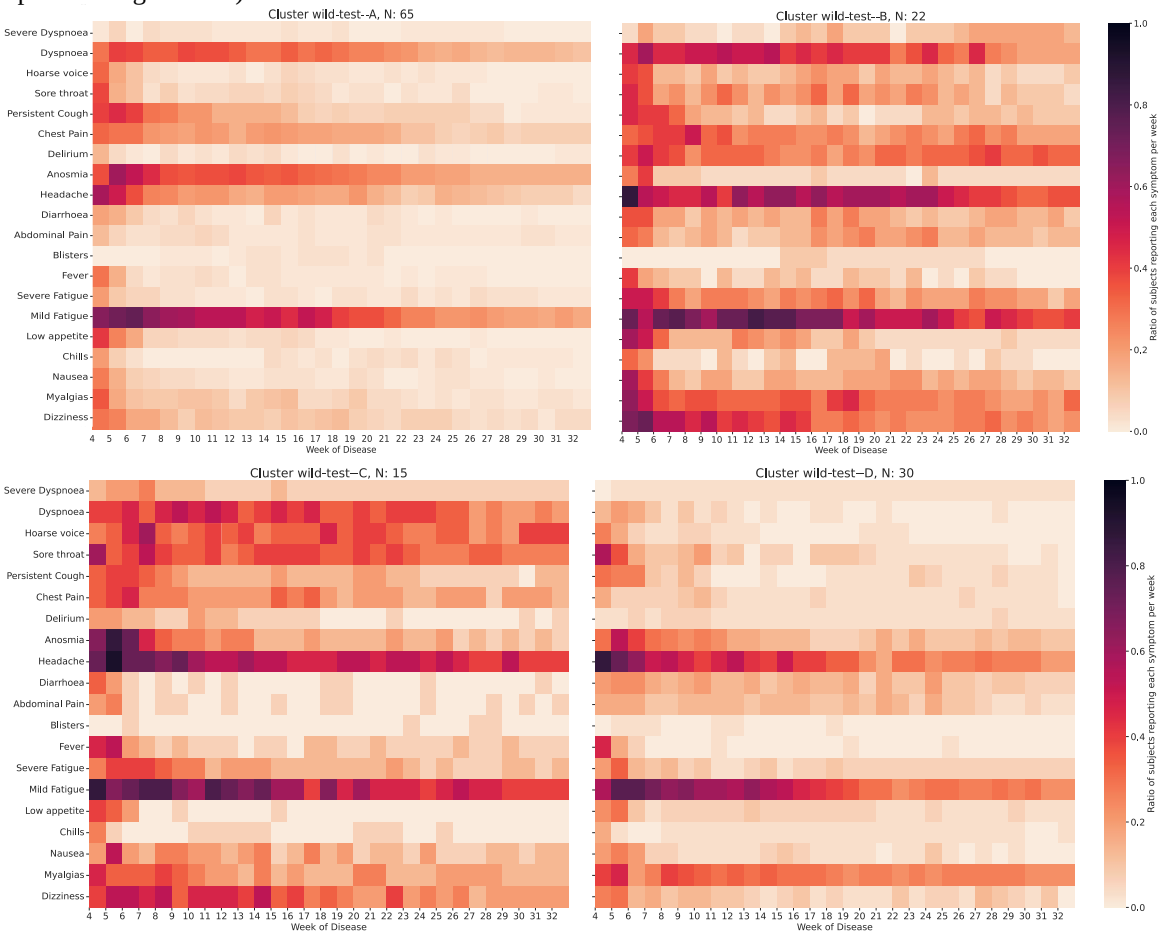


Figure S20. Robustness evaluation of the clusters for wild-type. A: Confusion matrix between the predicted labels of the testing set using the model trained on the training set (wild-type), and the re-trained model on the testing set. The predicted cluster refers to the re-trained model on the testing set, while the actual cluster refers to the labels predicted with the originally trained model. B: Similarity matrix between the symptom profile of the predicted clusters (wild-type variant) and the symptom profile of the training set (wild-type variant). Median ratio of individuals reporting a symptom across illness is used to identify the top symptoms per cluster in the testing set (right column). The Euclidian distance between the top four (20%) symptom profile per testing cluster and equivalent symptom profile per training cluster is computed as similarity measure. Small differences identify the best matching symptom profile during the illness.