

Attributes and predictors of Long-COVID: analysis of COVID cases and their symptoms collected by the Covid Symptoms Study App

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Reports of “Long-COVID”, are rising but little is known about prevalence, risk factors, or whether it is possible to predict a protracted course early in the disease. We analysed data from 4182 incident cases of COVID-19 who logged their symptoms prospectively in the COVID Symptom Study app. 558 (13.3%) had symptoms lasting ≥ 28 days, 189 (4.5%) for ≥ 8 weeks

and 95 (2.3%) for ≥ 12 weeks. Long-COVID was characterised by symptoms of fatigue, headache, dyspnoea and anosmia and was more likely with increasing age, BMI and female sex. Experiencing more than five symptoms during the first week of illness was associated with Long-COVID, OR=3.53 [2.76;4.50]. A simple model to distinguish between short and long-COVID at 7 days (total sample 2149), which gained a ROC-AUC of 76%, was replicated in an independent sample of 2472 antibody positive individuals. This model could be used to identify individuals for clinical trials to reduce long-term symptoms and target education and rehabilitation services.

Introduction

COVID-19 can manifest a wide severity spectrum from asymptomatic to fatal forms¹. A further source of heterogeneity is the duration of symptoms, which could have considerable impact due to the huge scale of the pandemic. Hospitalised patients are well recognised to have lasting dyspnoea and fatigue in particular², yet such patients constitute the ‘tip of the iceberg’ of symptomatic SARS CoV2 disease³. Few studies capture symptoms prospectively in the general population to ascertain with accuracy the duration of illness and the prevalence of long-lasting symptoms.

Here we report a prospective observational cohort study of COVID-19 symptoms in a subset of 4182 users of the COVID Symptom Study app meeting inclusion criteria (see online methods)^{4,5}, compared to 4182 matched symptomatic test-negative controls **in terms of symptom duration**. Briefly, the cases comprised individuals who reported testing positive for SARS-CoV2 by swab

testing who started on the app “feeling physically normal” to be able to determine symptom onset.

We then compare cases with symptoms persisting over 28 days, LC28) and short duration (symptoms lasting less than 10 days, short-COVID). Our previous findings that clusters of symptoms predicted the need for acute care⁶ led us to hypothesize that persistent symptomatology in COVID-19 (Long-COVID) is associated with early symptom patterns which could be used to predict who might be affected.

Results

Duration and prevalence in comparison to matched negative controls

Figure 1 shows the duration of symptoms reported in COVID+ cases (orange) over-laid on age, sex and BMI matched negative-testing symptomatic controls (blue). For COVID-19 swab positive cases, the overall median symptom duration was 11 days (IQR[6;19]), and , 558 (13.3%) met the LC28 definition (Median 41, IQR[33,63]) of whom 189 (4.5%) met LC56, and 108 (2.6%) LC84. In contrast 1591 (38.0%) had short-COVID (median 6, IQR[4-8]). The proportions were comparable in three countries (LC28: GB 13.3%, USA 16.1%, Sweden 12.1% p=0.35; LC56: GB 4.7%, USA 5.5%, Sweden 2.5% p=0.07). For matched COVID-19 negatives the median duration of symptoms was 5 [3;9] with 2.4% reporting symptoms for more than 28 days.

Demographics of Long-Covid

Table 1 summarises the descriptive characteristics of the study population stratifying by symptom/disease duration. Age was significantly associated with LC28, rising from 9.9% in 18-49 year-olds to 21.9% in those aged ≥ 70 ($p < 0.0005$), with escalating OR by age decile (Figure 1b, Supplementary Table 2). LC28 disproportionately affected women (14.9%) compared to men (9.5%), although not in the older age-group. Long-COVID affected all socio-economic groups (assessed using Index of Multiple Deprivation), (Supplementary Figure 2). Individuals with Long-COVID were more likely to have required hospital assessment. Asthma was the only/unique pre-existing condition providing significant association with LC28 (OR=2.14 [1.55-2.96]).

Symptoms in LC28

Fatigue (97.7%) and headache (91.2%) were the most reported symptoms in those with LC28, followed by anosmia and lower respiratory symptoms, and headache was more often reported intermittently (Figure 2, supplementary Table s1). Free-text additional symptoms were more commonly reported in LC28 cases (81%) compared to Short-COVID (45%), with cardiac symptoms (palpitations, tachycardia) (LC28, 6.1%; short-COVID 0.5% $p < 0.0005$), concentration or memory issues (4.1% vs 0.2%, $p < 0.0005$), tinnitus and earache (3.6% vs 0.2% $p < 0.0005$) and peripheral neuropathy symptoms (pins and needles and numbness) (2% vs 0.5% $p = 0.004$) disproportionately reported in LC28. Most of these symptoms were reported for the first time 3-4 weeks post-symptom onset.

We found two main patterns of symptomatology within LC28: those reporting exclusively fatigue, headache and upper respiratory complaints (shortness of breath, sore throat,

persistent cough and loss of smell) and those with additional multi-system complaints, including ongoing fever and gastroenterological symptoms (Supplementary figure 3). In the individuals with long duration (LC28), ongoing fever OR 2.16 [1.50;3.13] and skipped meals OR 2.52 [1.74;3.65] were associated with a hospital visit. Details of the frequency of symptoms persisting beyond 28 and 56 days after disease onset are provided in Supplementary table 3.

Individuals with LC28 were more likely to report relapses (16.0% vs 8.4%) ($p < 0.0005$). In comparison, in the matched group of SARS-CoV2 negative-tested individuals, relapse was reported in 11.5%, and relapse was longer in LC28 (median = 9 [5-18] vs 6 [4-10] days).

Risks to develop LC28

We explored how to estimate risk of LC28 among positive individuals from data available early in the disease course. Individuals reporting more than 5 symptoms in the first week (the median number reported) were significantly more likely to go on to experience LC28, (OR=3.95 [3.10;5.04]). This strongest risk factor was predictive in both sexes and all age groups (supplementary Figures 4, a-e).

The five symptoms experienced during the first week most predictive of LC28 in the positive individuals were: fatigue OR=2.83 [2.09;3.83], headache OR=2.62 [2.04;3.37], dyspnoea OR=2.36 [1.91;2.91], hoarse voice OR=2.33 [1.88;2.90] and myalgia OR=2.22 [1.80;2.73] (Figure 3). Similar patterns were observed in both genders. In adults aged over 70, loss of smell (which is less common) was the most predictive of long-COVID OR=7.35 [1.58;34.22] before fever

OR=5.51 [1.75;17.36] and hoarse voice OR=4.03[1.21;13.42] (Supplementary figures 4). Co-occurrence plots of symptoms in short-COVID versus LC28 further illustrate the importance of early multi-symptom involvement (Figure 3c).

Models of prediction

We created Random Forest Prediction models using a combination of the first week's symptom reporting, personal characteristics and comorbidities. Using all features, the average ROC AUC was 76.7% (SD=2.5) (Figure 3d) in the classification between short-COVID and LC28. The strongest predictor was age (29.2%) followed by the number of symptoms during the first week (16.3%). Feature importance was relatively similar across age-specific models. However, in the over 70s, early features such as fever, anosmia and comorbidities were important, and may be 'red flags' in older adults (Supplementary figure 6).

To create a model usable in healthcare settings, we simplified the prediction model to include only symptom number in the first week with age and sex in a logistic regression model, obtaining ROC AUC of 76.7% (SD 2.5) (Figure 3d), for which the calibration slope had a median of 0.99 [0.92;1.13]. When optimising the balance between false positives and false negatives, we obtained a specificity of 73.4% (SD 9.7) and a sensitivity of 68.7% (SD 9.9). Specificity, Sensitivity, PPV and NPV values at different thresholds are presented in Supplementary table 6. Comparison of decision analysis curves between other simple prediction models highlighted the superiority of this choice (Supplementary figure 7).

Key predictive findings of our analysis were validated in an independent dataset of 2412 individuals who reported testing antibody positive (but no positive PCR result) for SARS-CoV2 from 2 weeks after symptom onset where, again, the number of symptoms in the first week of illness was the strongest predictor, OR=4.60 [95% CI 3.28; 6.46]. The simple prediction model was similarly predictive of LC28 in the antibody group, with a ROC-AUC of 75.9% (SD=4.3%) and median calibration slope of 1.09 [0.85; 1.63] (Figure 3-e).

Discussion

While this study provides important insights into the disease presentation there are important limitations and any generalisation should be considered carefully. Our study was limited by being confined to app users, rather than a representative sample, who were disproportionately female and under-represented those >70years which could increase or decrease our estimate of the extent of Long-COVID respectively and caution is needed in interpreting associations found in smaller population subgroups. Swab test results were self-reported and were all assumed to be RT-PCR, as antigen tests were not available at the time. Applying a weighting following the UK population (see Supplementary Methods), the estimated proportion of people experiencing symptomatic COVID-19 going on to suffer Long-COVID were similar: 14.5%, 5.1% and 2.2% for 4, 8- and 12-weeks duration respectively. While estimates could be inflated because early PCR testing was restricted to those more severely unwell, or if regular logging or test results encouraged a systematic bias in symptom reporting, Long-COVID may here be underestimated if individuals with prolonged symptoms were more likely to stop logging symptoms on the app. Our participant selection criteria were chosen to confidently identify

cases, and demographics of excluded groups as well upper and lower bounds for estimates given each exclusion criteria are presented in Supplementary Table 4 and 5. Symptom reporting rates through the study period for all users are also presented in Supplementary Table 6. Taken together, these data suggest that our estimates may be conservative. We had insufficient numbers to explore risk factors for disease over 2 months and were unable to analyse the impact of ethnicity due to incomplete data. A further limitation is that, due to the need for very regular assessment, we could not use any other external dataset for external validation. In addition, the list of symptoms on the app is necessarily non-exhaustive, although analysis of the free-text responses allowed us to highlight other symptoms present in Long-COVID, such as cardiac and neurological manifestations. With emerging evidence of ongoing myocardial inflammation^{8,9} associated with COVID-19, this calls for specific studies of cardiac and neurological longer-term sequelae of COVID-19.

At the population level, it is critical to quantify the burden of Long-COVID to better assess its impact on the healthcare system and appropriately distribute resources. In our study, prospective logging of a wide range of symptoms allowed us to conclude that the proportion of people with symptomatic COVID-19 who experience prolonged symptoms is considerable, and relatively stable across three countries with different cultures. Whether looking at a four-week or an eight-week threshold for defining long duration, those experiencing Long-COVID were consistently older, more likely to be female and to require hospital assessment than in the group reporting symptoms for a short period of time. Those going on to experience LC28 had multi-system disease from the start, supporting the need for holistic support¹⁰. While asthma

was not reported as a factor of risk for hospitalisation in¹¹, its association with Long-COVID (LC28) warrants further investigation. **Analysis of the pathophysiological drivers underlying the risk factors for Long-COVID identified here is a critical next step.**

We found early disease features were predictive of duration. With only three features - number of symptoms in the first week, age and sex, **we built a model designed to separate short (<10 days) and long duration individuals (>=28 days)** Importantly, the model generalised **with same performance** to the population reporting antibody testing. This important information could feature in highly needed targeted education material for both patients and healthcare providers and we present typical nomograms for use in clinical settings in Supplementary Figure **8 with model results at different thresholds depending on whether high sensitivity, specificity or a balanced model is required (Supplementary table 7)**. Moreover, the method could help determine at-risk groups and could be used to target early intervention trials and clinical service developments to support rehabilitation in primary and specialist care¹⁴ to alleviate Long-COVID and facilitate timely recovery.

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Author contribution

Competing interests

Zoe Global Limited co-developed the app *pro bono* for non-commercial purposes. Investigators received support from the Wellcome Trust, the MRC/BHF, EU, NIHR, CDRF, and the NIHR-funded BioResource, Clinical Research Facility and BRC based at GSTT NHS Foundation Trust in partnership with KCL. RD, JW, JCP, AM and SG work for Zoe Global Limited and TDS and PWF are consultants to Zoe Global Limited. LHN, DAD, JM, PWF and ATC previously participated as investigators on a diet study unrelated to this work that was supported by Zoe Global Ltd.

Ethics: In the UK, the App Ethics has been approved by KCL ethics Committee REMAS ID 18210, review reference LRS-19/20-18210 and all subscribers provided consent. In Sweden, ethics approval for the study was provided by the central ethics committee (DNR 2020-01803). Zoe Global Limited co-developed the app *pro bono* for non-commercial purposes. Investigators received support from the Wellcome Trust, the MRC/BHF, EU, NIHR, CDRF, and the NIHR-funded BioResource, Clinical Research Facility and BRC based at GSTT NHS Foundation Trust in partnership with KCL. RD, JW, JCP, AM and SG work for Zoe Global Limited and TDS and PWF are consultants to Zoe Global Limited. LHN, DAD, JM, PWF and ATC previously participated as investigators on a diet study unrelated to this work that was supported by Zoe Global Ltd.

Data and materials availability: Code for data extraction can be found at : <https://github.com/KCL-BMEIS/ExeTera>. Data used in this study is available to bona fide researchers through UK Health Data Research using the following link

<https://web.www.healthdatagateway.org/dataset/fddcb382-3051-4394-8436-b92295f14259>

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Methods

Ethics: In the UK, the App Ethics have been approved by KCL ethics Committee REMAS ID 18210, review reference LRS-19/20-18210 and all subscribers provided consent. In Sweden, ethics approval for the study was provided by the central ethics committee (DNR 2020-01803). In USA, **this study was approved by the Partners Human Research Committee (Protocol 2020P000909).**

Dataset:

Data used in this study were acquired through the COVID 19 Symptom Study app, a mobile health application developed by Zoe Global Limited with input from physicians and scientists at King’s College London, Massachusetts General Hospital, Lund and Uppsala Universities¹⁵. The app, which collects data on personal characteristics and enables prospective logging of symptoms, was launched in the UK, the US and Sweden between 24 March 2020 (UK) and 30 April 2020 (Sweden), and rapidly reached over 4 million users from the community. App users are asked to report their health status daily, and any incident COVID-test (both undertaking of the test and its result). Questions on the app are appended below. The current study focuses on 4182 users who reported testing positive to SARS-CoV2 by PCR swab test with symptom onset between 25 March 2020 and 30 June 2020, for whom the date of symptom onset

matched clinically with the date of test and in whom duration of symptoms could be estimated (Supplementary Figure 1 presents a flowchart of study inclusion). We repeated the analyses in an independent subgroup of 2412 app users who reported positive testing for antibodies against SARS-CoV2 at least two weeks after symptom onset, but without swab test results (Supplementary Figure 1).

To understand how the duration and relapse rate compared to a comparable population not suffering from COVID-19, we selected an additional matched sample from all app users meeting study inclusion criteria but who tested negative by PCR swab test, choosing for each COVID+ case the individual from the negative group with the smallest Euclidean distance based on sex, age, and BMI ¹⁶.

Definitions

Symptoms considered when determining disease duration are abdominal pain, chest pain, sore throat, shortness of breath, fatigue, hoarse voice, delirium, diarrhoea, skipped meals, fever, persistent cough, unusual muscle pains, loss of smell and headache

Onset of disease was defined as the first day of reporting at least one symptom and a sum of symptoms being non-zero for more than one day.

Disease end was defined as the last day of symptom reporting before reporting as healthy for the next consecutive seven days; or the last day of reporting with fewer than 5 symptoms before ceasing using the app. For included participants who had ceased using the app whose cumulative number of symptoms were fewer than 5, disease end was considered as the last log.

Relapse was defined as two or more days of symptoms (minimum 1 symptom) within a 7-day window after one week of healthy logging, if initial symptoms were temporally close to a positive swab test.

Long-COVID was defined as symptoms persisting for more than 4 weeks (28 days, LC28), more than 8 weeks (56 days, LC56) or more than 12 weeks (LC84) between symptom onset and end, while short duration was defined as the interval between symptom onset and end of less than 10 days, without a subsequent relapse (Short-COVID).

Inclusion/Exclusion criteria

To be included in the subsequent analysis, users of the COVID Symptoms Study app were selected based on the following criteria:

Inclusion criteria: Age ≥ 18 years; BMI greater than 15 and less than 55, a positive SARS-CoV-2 swab test (PCR) confirming the diagnosis of COVID-19; disease onset between 14 days before and 7 days after the test date, and before the 30 June 2020 (to limit right censoring).

Exclusion criteria: individuals who started app reporting when already unwell; users reporting as exclusively healthy throughout the study period; users with gaps of more than seven days after an unhealthy report who did not report any hospital visit (to allow for gaps due to hospitalisation). In addition, individuals reporting for fewer than 28 days but who reported more than five symptoms at their last log were excluded, as symptom duration could not be ascertained.

Inclusion and exclusion criteria were similar for the matched negative-tested sample, which differed only on the result of their RT-PCR test.

In order to assess the impact of the different exclusion criteria on rates of LC28, Supplementary Table 4 presents the lower and upper bounds of these proportions according to lower and upper bounds assumptions on duration. This table also includes the estimation of proportion of LC28 when accounting for a possible rate of false negatives ranging from 2 to 30% based on the distribution estimated from the matched negative sample. Table 5 reflects the demographics of the different excluded groups.

Statistical testing and modelling

Data collected prospectively until 02 September were included, to allow sufficient time to ascertain duration. Univariable and multivariable logistic regression was used to assess symptoms associated with short- and long-COVID respectively, adjusting for sex and age, using Statsmodels v0.11.1 Python3.7. Separate models were fitted to subgroups stratified by sex and age (18-49; 50-69; >70 years). For analysis of relapse, existence and duration of relapse were compared between the LC28 group and the whole control sample, using a Mann Whitney U test.

We used a K-mode clustering analysis to investigate whether there was evidence of different sub-types of long-COVID, using the kmode package v0.10.2. Number of ideal symptom clusters was obtained via a silhouette analysis with dice distance metrics. Differences between LC28 and short-COVID were visualised using a co-occurrence network (networkx for visualisation), applying a 10% threshold to remove rare edges to aid visualisation.

Finally, to create a predictive model for Long-COVID LC28, we used sklearn v0.22.2.post1 package, training random forest classifiers with stratified repeated cross-validation (10 times, 5 folds) with hyperparameter grid search including, as features, information available during the first week of illness, reported comorbidities (asthma, lung disease, heart disease, kidney disease and diabetes) and personal characteristics (BMI, age, sex). In addition to a global consideration of the studied sample population, separate models stratified by age were also entrained using a similar cross-validation setting (hyperparameter search and stratified sampling). After running the cross-validation for each model structure (50 times), the feature importance was averaged across the different repeated folds. To create a simplified linear model, we applied a Lasso least angular regression information criterion with Bayesian information criterion was used for feature selection. This resulted in a model that included only age, gender, and the number of symptoms experienced during the first week.

Using only these three features, a logistic regression model was then assessed using the same stratification and cross-validation.

To assess performance on the test dataset (antibody positive), cross-validation was also performed to obtain an indication of the variability in performance using models that were trained on the whole PCR-positive sample.

For the reduced logistic regression model, the score was given by the following formula:

$S = 0.259503 * \text{NumberSymptoms} + 0.055457 * \text{Age} - 0.633310 * \text{Sex} - 3.20$ (where sex is encoded as 1 – Female / 2 – Male)

Where NumberSymptoms corresponds to the sum of different symptoms experienced over the first week among the list of 14 symptoms reported on daily reports. This score was then transformed as probability following the formula $1/(1+\exp(-\text{score}))$

Matching with negative sample:

The selected negative cases followed the same inclusion rules and were matched to the positive samples using the minimum Euclidean distance between the vectors of features created by age, BMI, and sex applying an Hungarian matching algorithm. Sex feature was multiplied by 100 to ensure balance between feature strength.

In order to assess the impact of possible false negatives in the estimate of prevalence of LC28, for both extremes of the expected proportion of false negative results (2% and 29%) we randomly sampled 100 times individuals from the matched sample and adjusted the estimate of LC28 according to the mean proportion of LC28 obtained during the random sampling

Rebalancing to UK population demographics

Lastly, the rebalancing with respect to the UK population was performed by reweighting the age/sex proportions of LC28 in the studied sample by that of the UK population based on census data from 2018. The weighting per age group is described in the Supplementary table 8:

Ascertainment of parameters

The wording of the questions on the app when registering and when later describing symptom presentation is described in supplementary table 9. Specific comments regarding changes and interpretation are in square brackets.

Index of multiple deprivation deciles (IMD), were calculated within each country in the UK as an indicator of area-based socio-economic status using the post-code of the app contributors. The IMD was downloaded from the relevant government websites as below, and the most recent IMD available at time of analysis was used:

English (2019): <https://www.gov.uk/government/statistics/english-indices-of-deprivation>

2019

Scottish (2016): <https://www2.gov.scot/Topics/Statistics/SIMD>

Welsh (2019): <https://statswales.gov.wales/Catalogue/Community-Safety-and-Social-Inclusion/Welsh-Index-of-Multiple-Deprivation/WIMD-2019>

Table 1. Characteristics of Individuals with COVID-19 by duration of symptoms, compared to matched sample testing negative for COVID-19. In statistical comparison, the short COVID group is the reference.

	Positive PCR test					Matched Negative sample
	Short (<10 days)	LC28 (>=28 days) (including LC56)	LC56 (>=56 days)	In between - >=10 days < 28 days	Overall	
Number	1591	558	189	1915	4182	4182
GB/SE/US [numbers, %]	1365 / 139 / 87 85.8 / 8.7 / 5.5	466/57/35 83.5 / 10.2 / 6.3	165/12/12 87.3 / 6.3 / 6.3	1558/271/86 81.4/14.2/4.5	3491 / 473 / 218 83.5 / 11.3 / 5.2	3882/131/169 92.8/3.1/4.1
Male (%)	32.7	20.3***	16.9*	27.9	28.5	28.5

Age (years) [median, IQR]	38 [29;49]	50 [39;57]***	52 [43;59]***	43 [33-53]	42 [32;53]	42 [32;53]
Age group (18-49/50-69/>70)	1122/331/38 75.3 / 22.2 / 2.5	259/262/24 47.5 / 48.1 / 4.4	69/96/11 39.2 / 54.5 / 6.3	1293/594/28 67.5/31.0/1.5	2627/1195/96 62.8 / 28.6 / 2.3	2821 / 1264/97 67.5 / 30.2 / 2.3
Obese (%)	23.8	27.6*	26.5	27.7***	26.3	26.4
BMI (kg/m ²) [median, IQR]	25.5 [22.7;29.7]	26.1 [23.3;30.5]	25.9[23.3;30.5]	26.2 [23.2;30.7]***	25.9[23.3;30.3]	25.9 [23.0;30.3]
Asthma (%)	7.7	15.8***	18.0***	10.0*	10.0	13.7
Lung disease (%)	12.8	16.5**	15.9	13.3	13.6	13.7
Diabetes (%)	3.0	3.9	5.8*	2.6	2.9	2.8
Heart (%)	1.7	3.2**	4.8**	1.6	1.9	1.7
Kidney (%)	0.5	0.9	0.5	0.4	0.6	0.6
IMD (median decile - IQR)	7 [4;9]	7 [5;9]	7 [5;9]	7 [4;9]*	7 [4;9]	7[5;9]***
IMD quintiles [‡]	64/75/334/132/63 4 5.2/6.1/27.0/10.7/ 51.2	23/23/86/49/240 5.5/5.5/20.4/11.6/ 57.0	10/9/26/18/88 6.6/6.0/17.2/11.9/ 58.3	155/246/310/334/39 7 10.7/17.1/21.5/23.2/ 27.5	158 / 194 /830/363 /1653 4.9 /6.1/26.0/11.4/ 51.7	118/193/895/376/ 2057 3.2/5.3/24.6/10.3/ 56.5
Visit to hospital (%)	7.0	31.5***	43.9***	14.3***	13.9	4.1
Number of symptom sin the first week [median [IQR]]	5 [3;7]	7 [5-9]***	7 [5;9]***	6[4;8]***	6 [4;8]	3 [2;4]***

* indicates p <0.1 ** <0.05 ***<0.01 when comparing to short covid. Comparison are performed with respect to the “short duration” within the positive group. Matched Negatives are compared to the overall positive population Mann Whitney U tests are performed for continuous variables and chi square tests are performed when comparing proportions.

‡ Index of Multiple Deprivation (IMD) information is only available for app users from the UK who have entered a complete post code

Acronyms: GB – Great Britain / SE – Sweden / US – United States / IMD – Index of multiple deprivation

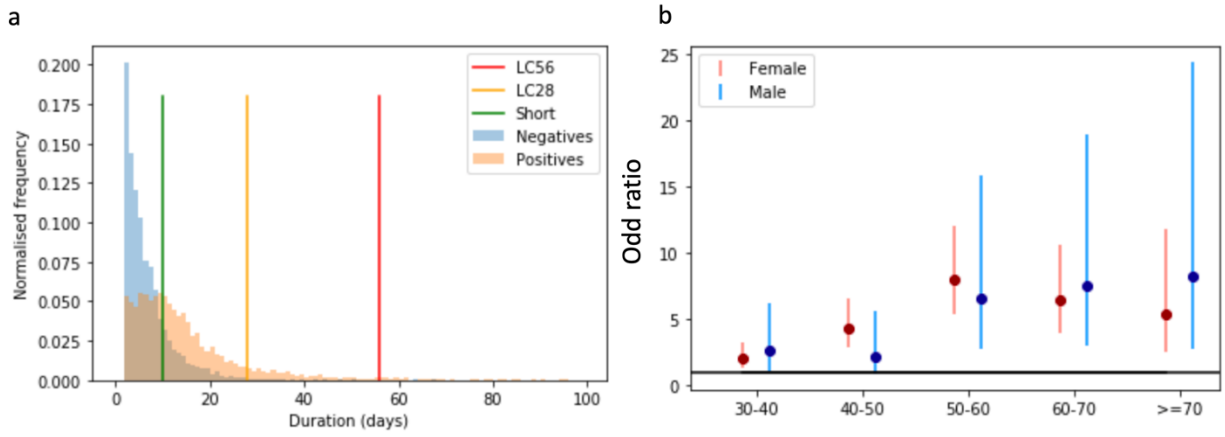


Figure 1. a) Distribution of duration of symptoms in COVID-19 – The coloured bars indicate the limits to define short, LC28 and LC56. The y-axis reports the normalised frequency of duration of symptoms. 2.4% of negative controls reported symptoms for more than 28 days and 13.3% in the case of positive cases b) OR and 95% CI of LC28 with each successive decile compared to 20-30-year-olds. For males 20-30 years old, proportion of LC28 was 4.5% for female in same age range 5.6%

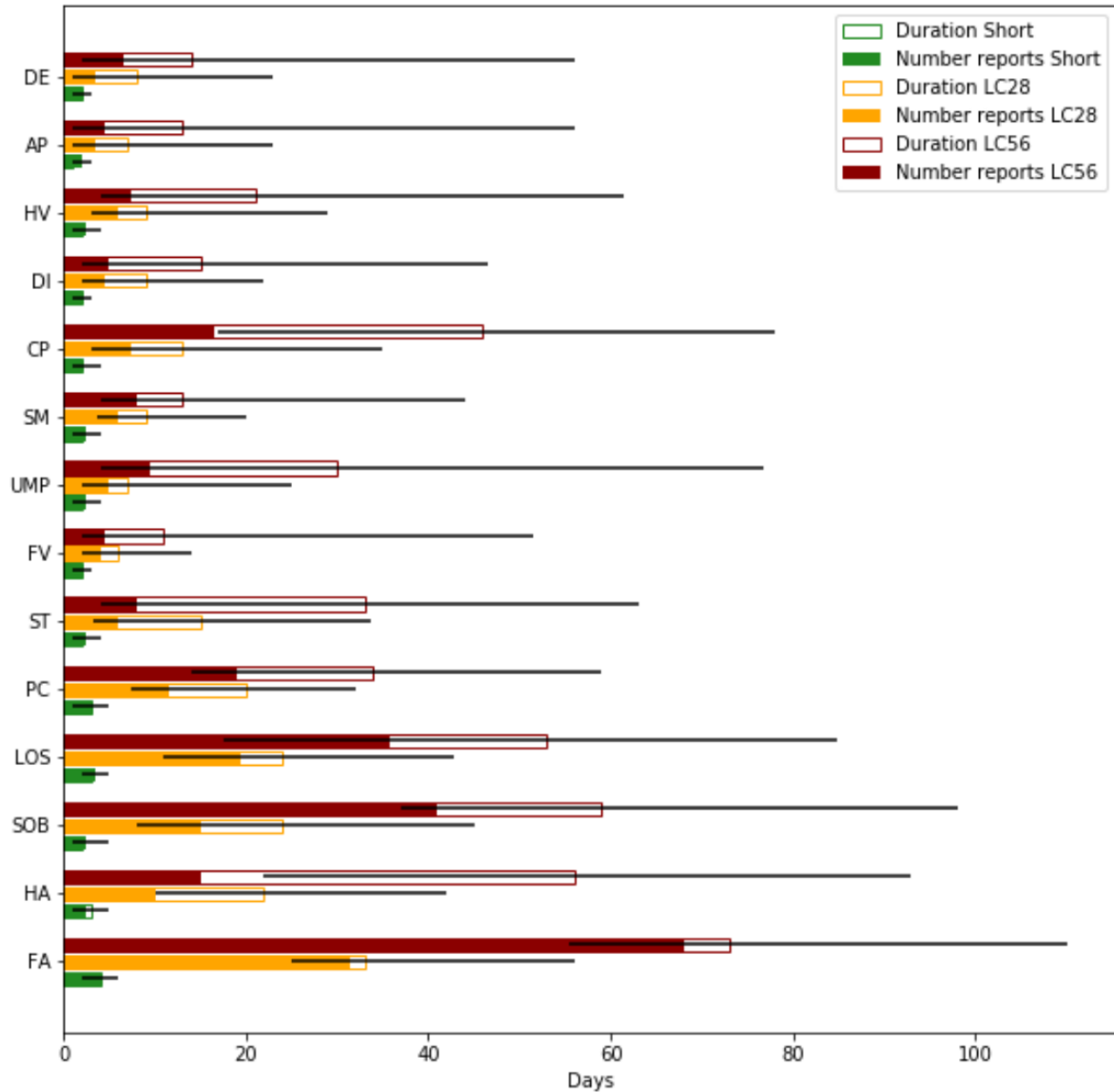


Figure 2 : Symptoms by duration. For each symptom (ordered from top to bottom by increasing frequency of occurrence) the median duration of report is presented by the total (hollowed) bar height, with associated interquartile range represented by the black line, for the short, LC28 and LC56 durations. The filled bars represent the number of times a report has been given. For both duration and number of reported days of symptoms, the x axis reflects the number of days. This highlights the differences in the symptoms in terms of their intermittence throughout the course of the disease. (Abbreviations DE – delirium, AP – Abdominal Pain, HV – Hoarse Voice, DI – Diarrhoea, CP – Chest Pain, SM – skipped meals, UMP – Unusual Muscle pains, FV – Fever, ST – Sore Throat, PC – Persistent Cough, LOS – Loss of smell, SOB – Shortness of breath, HA – Headache, FA – Fatigue)

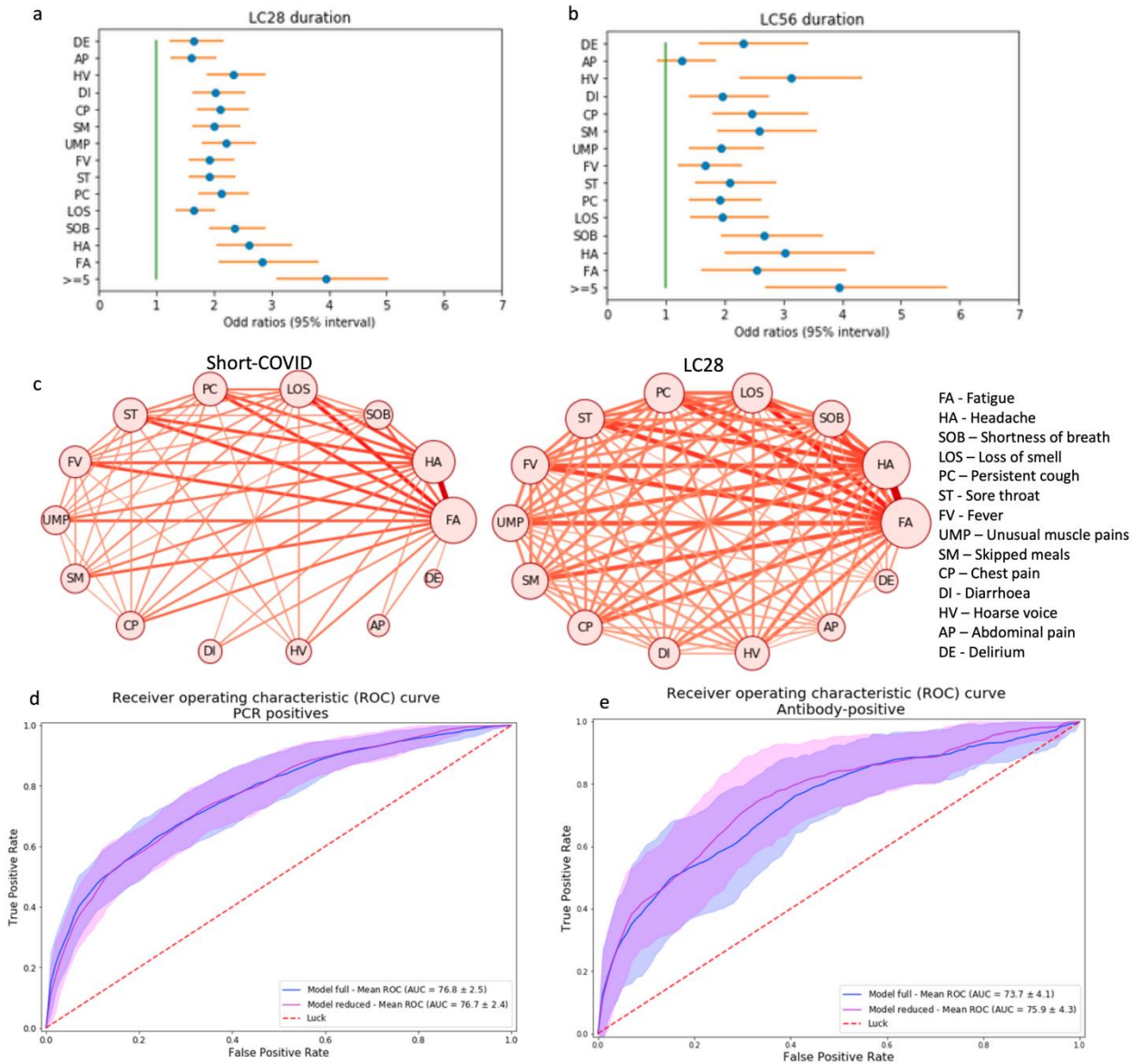


Figure 3: Symptom correlates of long-COVID for LC28 (a) and LC56 (b) with correction for age and gender. c) Co-occurrence network of symptom pairs with the frequency of symptom report as the size of the node and the likelihood of symptom pair co-occurrence by the weight of the edge linking them. Edges representing a co-occurrence of less than 10% were removed. d) – Receiver Operating Characteristic (ROC) curve of the cross-validated full and reduced models on the PCR cohort. e)– ROC curve when training on the whole PCR cohort and testing on the antibody-positive cohort for the full (blue) and reduced (magenta) model. Random predictive probability is indicated in both panels as a dashed red line. (Abbreviations DE – delirium, AP – Abdominal Pain, HV – Hoarse Voice, DI – Diarrhoea, CP – Chest Pain, SM – skipped meals, UMP – Unusual Muscle pains, FV – Fever, ST – Sore Throat, PC – Persistent Cough, LOS – Loss of smell, SOB – Shortness of breath, HA – Headache, FA – Fatigue)

