International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC)

A global federation of clinical research networks, providing a proficient, coordinated, and agile research response to outbreak-prone infectious diseases

COVID-19 Report: 06 May 2020

Summary

The results in this report have been produced using data from the ISARIC COVID-19 database. For information, or to contribute to the collaboration, please contact ncov@isaric.org.

We thank all of the data contributors for collecting standardised data during these extraordinary times. We plan to issue this report of aggregate data weekly for the duration of the SARS-CoV-2/COVID-19 pandemic.

Please note the following caveats. Information is incomplete for the many patients who are still being treated. Furthermore, it is likely that that we received more cases of severely ill individuals than those with relatively less severe illness; outcomes from these data, such as the proportion dying, must therefore not be used to infer outcomes for the entire population of people who might become infected. Some patients may be participants in clinical trials of experimental interventions. Many of the included cases are from the United Kingdom. Additional caveats are provided in the in the 'Caveats' section below.

Up to the date of this report, data have been entered for **35978** individuals from **336** sites across **35** countries.

The analysis detailed in this report only includes individuals:

1. for whom data collection commenced on or before 22 April 2020. (We have applied a 14-day rule to focus analysis on individuals who are more likely to have a recorded outcome. By excluding patients enrolled during the last 14 days, we aim to reduce the number of incomplete data records and thus improve the generalisability of the results and the accuracy of the outcomes. However, this limits our focus to a restricted cohort despite the much larger volumes of data held in the database.)

AND

2. who have laboratory-confirmed or clinically-diagnosed SARS-COV-2 infection.

The cohort satisfying the above criteria has 20276 cases.

The flow chart in Figure 1 gives an overview of the cohort and outcomes as of 06 May 2020.

Demographics and presenting features

Of these 20276 cases, 12088 are males and 8121 are females – sex is unreported for 67 cases. The minimum and maximum observed ages were 0 and 104 years respectively. The median age is 72 years.

The observed mean number of days from (first) symptom onset to hospital admission was 12.1, with a standard deviation (SD) of 7.6 days and a median of 5 days.

The observed mean duration for the number of days from hospital admission to outcome (death or discharge) was 9.5, with SD 8.8 days and a median of 7 days. These estimates are based on all cases which have complete records on length of hospital stay (N = 16079).

The symptoms on admission represent the policy for hospital admission and containment at that time plus, whatever the case definition was. As time passes for most countries these will change. The five most common symptoms at admission were history of fever, shortness of breath, cough, fatigue/malaise, and confusion. Frequencies of symptom prevalence vary with age.

Outcomes

Outcomes have been recorded for 15108 patients, consisting of 9712 recoveries and 5396 deaths. Follow-up is ongoing for 3950 patients. Outcome records are unavailable for 1218 patients.

ICU/HDU: A total of 3767 (19%) patients were admitted at some point of their illness into an intensive care unit (ICU) or high dependency unit (HDU). Of these, 1190 died, 1121 are still in hospital and 1108 have recovered and been discharged.

The observed mean and median durations (in days) from hospital admission to ICU/HDU admission were 3.3 and 1 respectively (SD: 6.5) – estimated from records on cases with complete date records on hospital admission and ICU/HDU entry (N = 3731).

The duration of stay in ICU/HDU had a mean of 8.7 days and a median of 6 (SD: 8.5 days) – estimated on only those cases with complete records for ICU/HDU duration or ICU/HDU start/end dates (N = 2552). Of these 3767 patients who were admitted into ICU/HDU, 1190 died, 1121 are still in hospital and 1108 have recovered and been discharged. Outcome records are unavailable for 348 cases.

Treatment

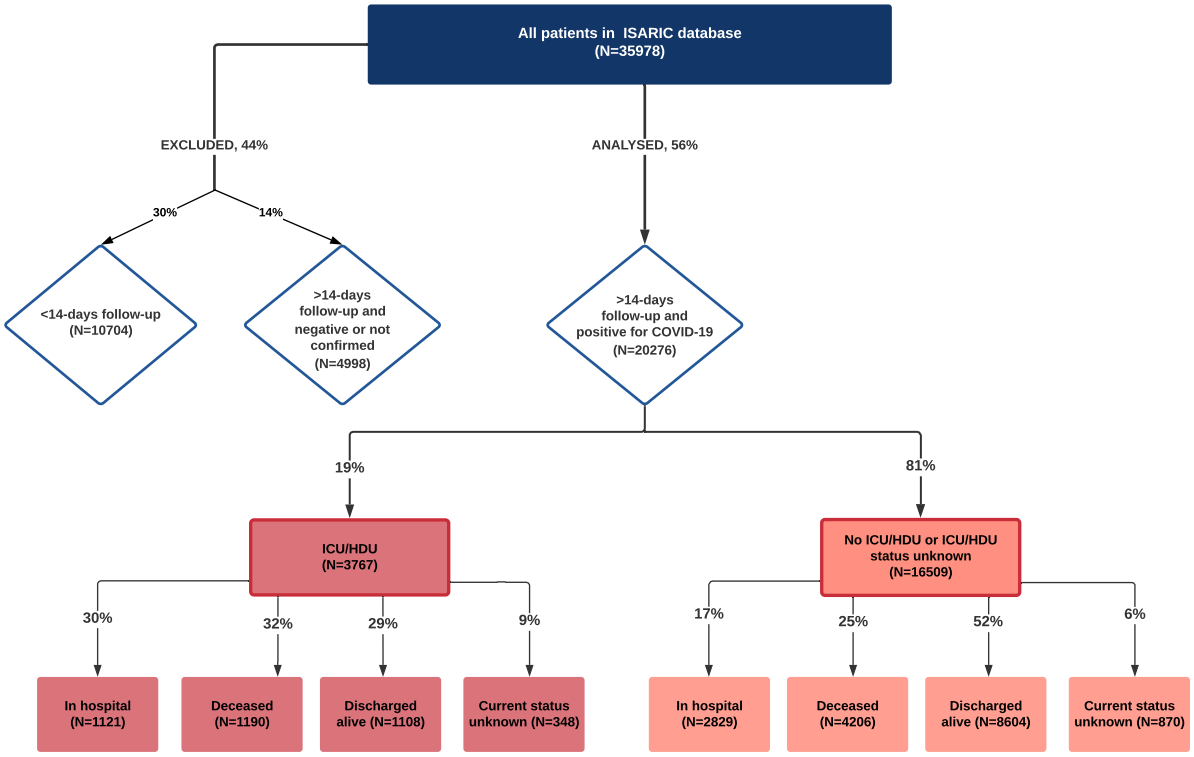
Antibiotics were received by 12406 / 14922 (83.1%) patients, and 1365 / 14399 (9.5%) received antivirals. These treatment categories are not mutually exclusive since some patients received multiple treatments. (The denominators differ due to data completeness.) 12875 / 19302 (66.7%) patients received some degree of oxygen supplementation: of these, 3039 / 12875 (23.6%) received NIV and 2286 / 12875 (17.8%) IMV.

Of the patients admitted into ICU/HDU, 2308 / 2530 (91.2%) received antibiotics and 1858 / 3716 (50%) antivirals. 3364 / 3690 (91.2%) received some degree of oxygen supplementation, of which, 1576 / 3364 (46.8%) received NIV and 2203 / 3364 (65.5%) IMV.

A total of 3039 patients received non-invasive mechanical ventilation (NIV). The mean and median durations from admission to receiving NIV were 4.5 days and 2 days respectively (SD: 8.6 days) – estimated from records on cases with complete records on dates of hospital admission and NIV onset (N = 2525). The mean and median durations for NIV were 2.2 days and 0.5 days respectively (SD: 3.7 days) – estimated based on only those cases which have complete NIV duration records (N = 1431).

A total of 2286 patients received invasive mechanical ventilation (IMV). The mean and median durations from admission to receiving IMV were 3.6 days and 2 days respectively (SD: 6.6 days) – estimated from records on cases with complete records on dates of hospital admission and IMV onset (N = 2150). The mean, median and SD for the duration of IMV – estimated based on all 1213 cases with complete records on IMV stays – were 10.3 days, 9 days and 7.3 days respectively.

Figure 1: Overview of cohort and outcomes as of 06 May 2020.



Patient Characteristics

Figure 2: Age and sex distribution of patients. Bar fills are outcome (death/discharge/ongoing care) at the time of report.

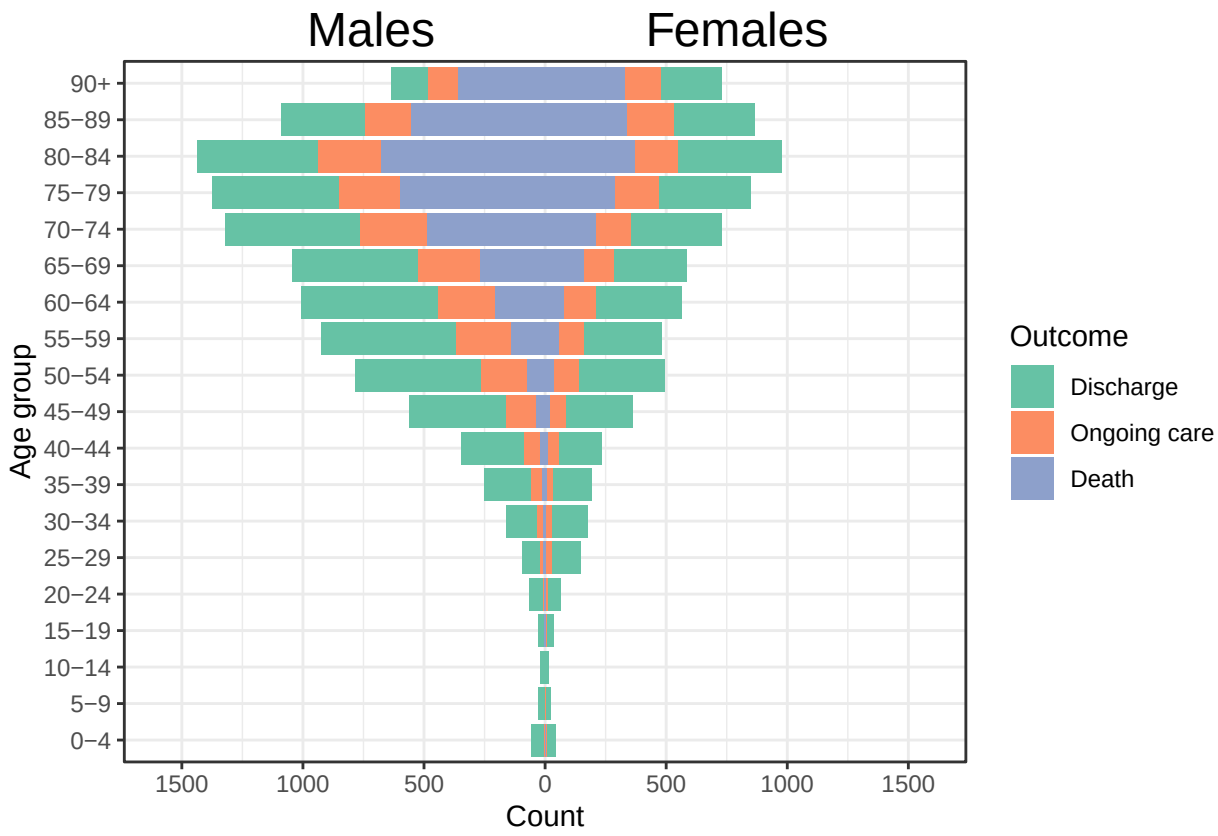
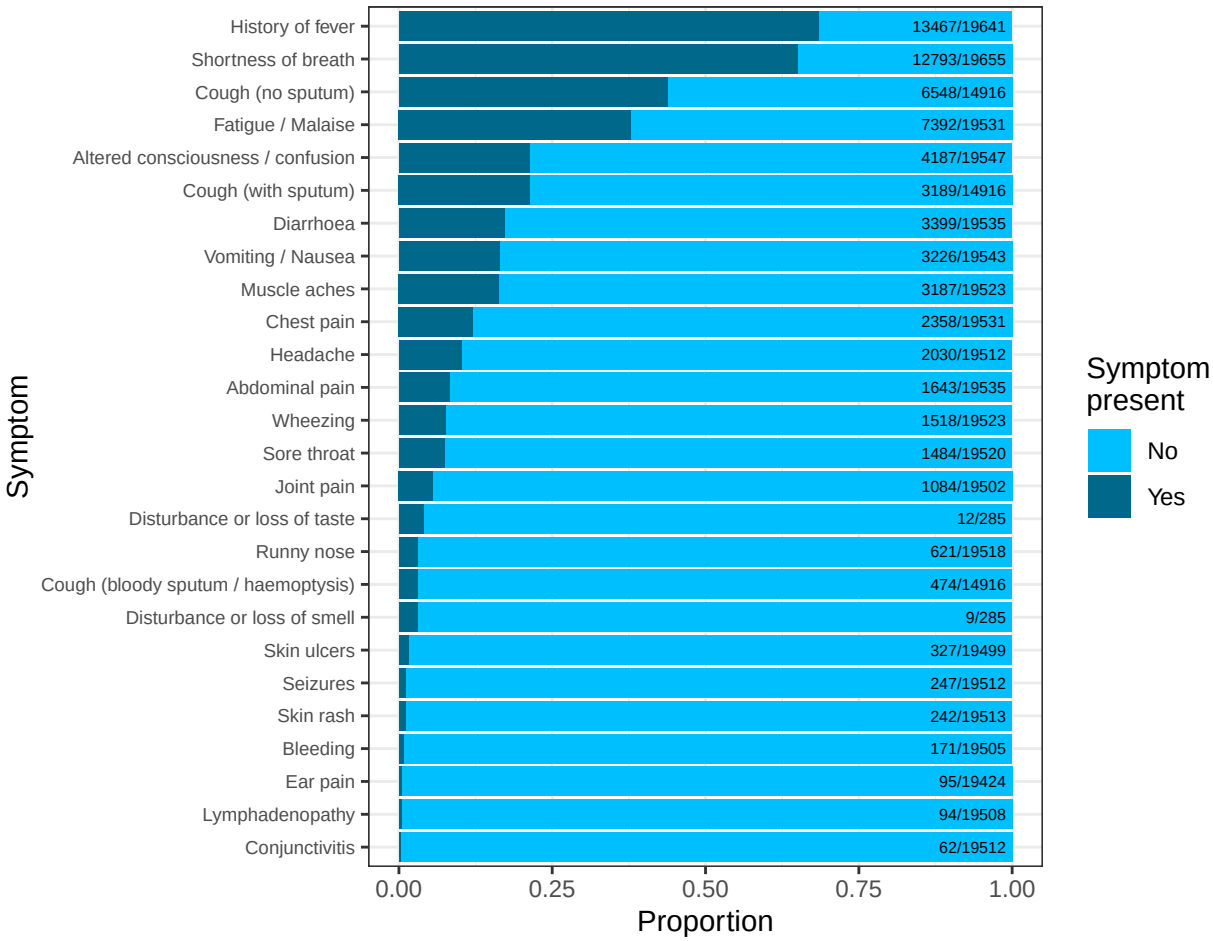
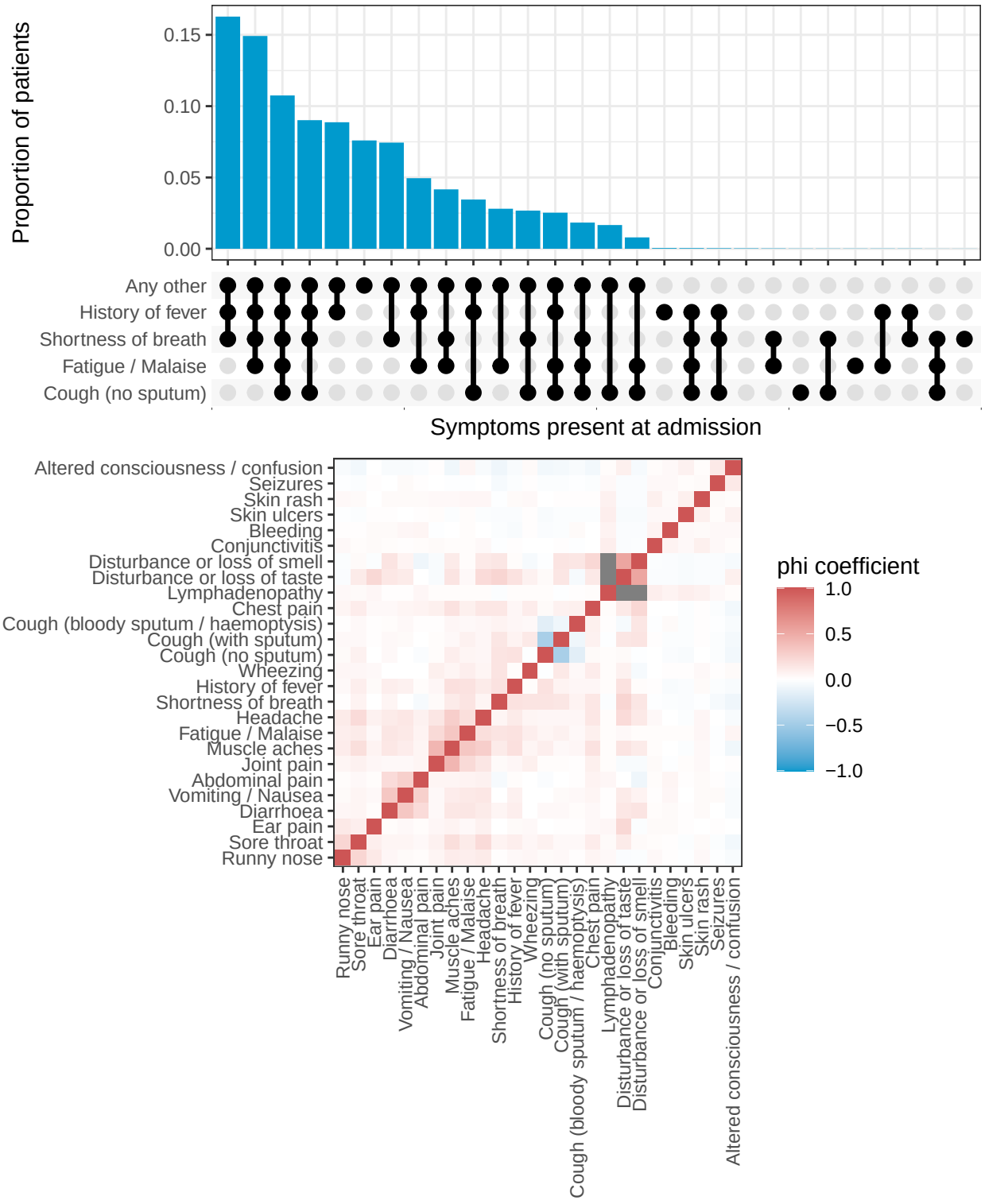


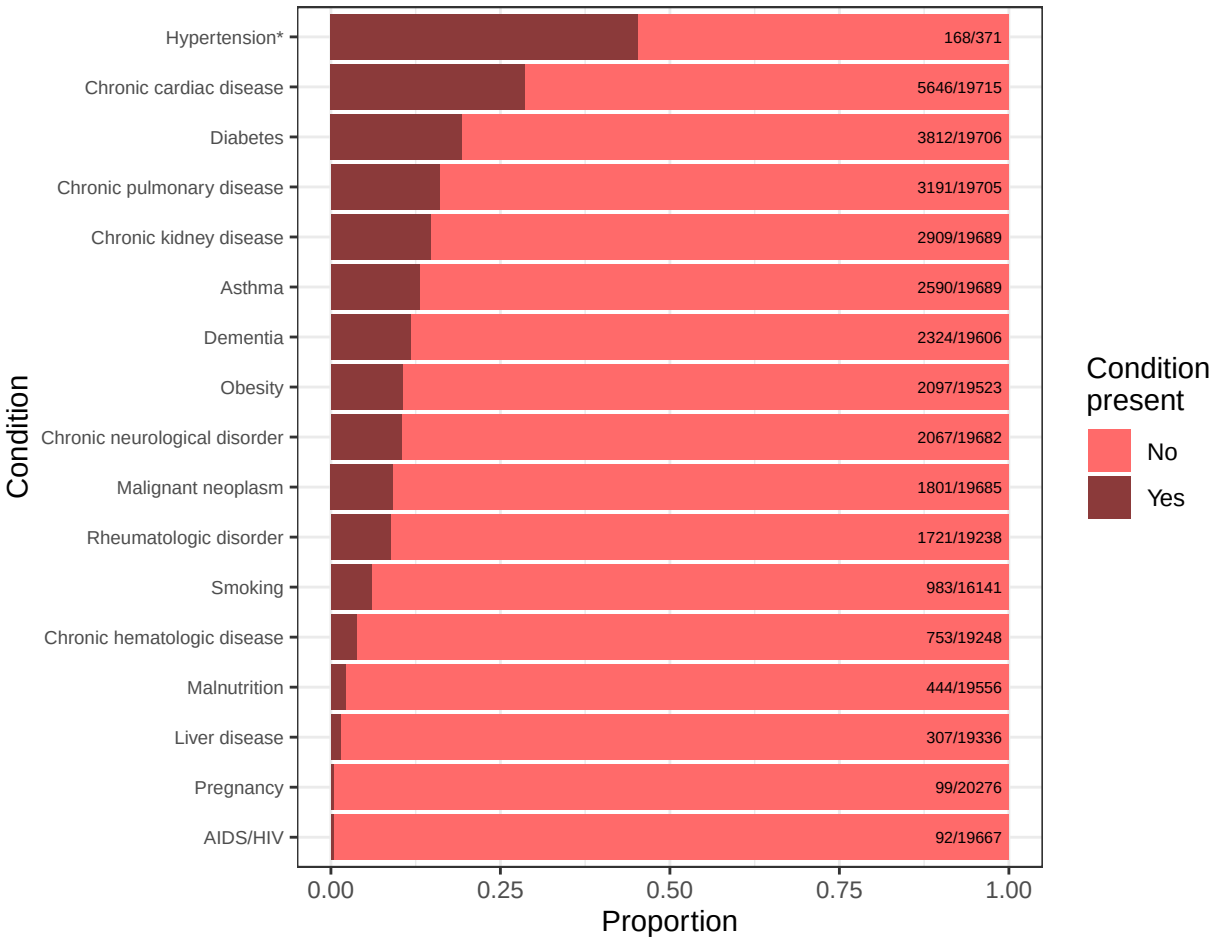
Figure 3: **Top**: Frequency of symptoms seen at admission amongst COVID-19 patients. Bars are annotated with a fraction representing the number of patients presenting with this symptom over the number of patients for whom presence or absence of this symptom was recorded. **Middle**: The distribution of combinations of the four most common symptoms, amongst all patients for whom these data were recorded. Filled and empty circles below the x-axis indicate the presence or absence of each comorbidity. The "Any other" category contains all remaining symptoms in the top plot. **Bottom**: Heatmap for correlation between symptoms. Fill colour is the phi correlation coefficient for each pair of symptoms, calculated amongst patients with recorded presence or absence of both.* Tiles appear grey where some combinations are entirely absent from the data, due to small numbers.



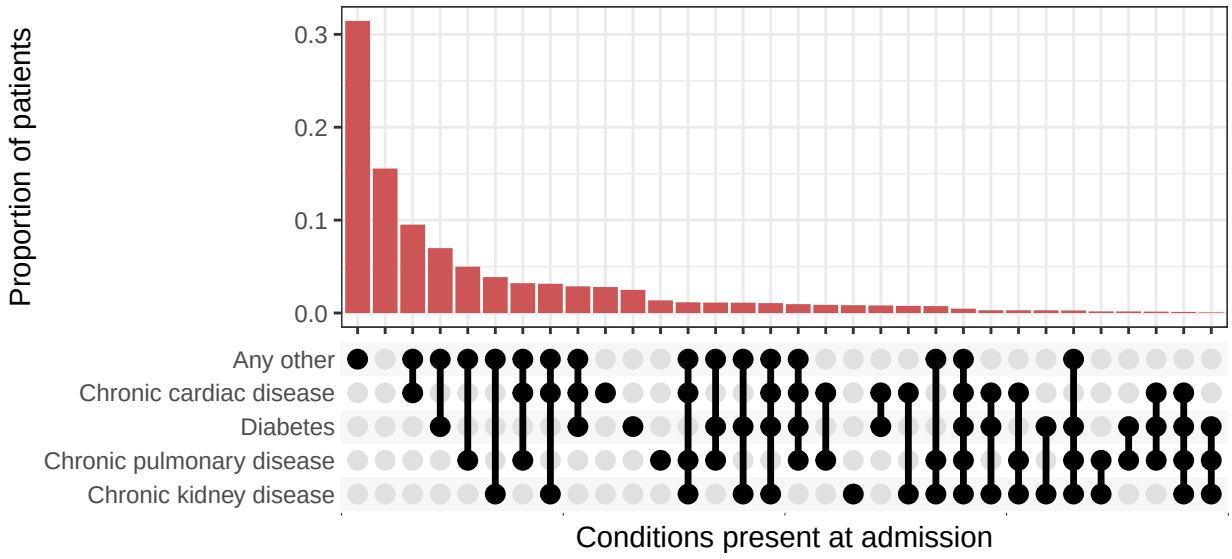


* We are working to gain a greater understanding of patients reported as having no presenting symptoms.

Figure 4: **Top**: Frequency of comorbidities or other concomitant conditions seen at admission amongst COVID-19 patients. Bars are annotated with a fraction representing the number of patients presenting with this comorbidity over the number of patients for whom presence or absence of this comorbidity was recorded. **Bottom**: The distribution of combinations of the four most common such conditions, amongst all patients for whom these data were recorded. Filled and empty circles below the x-axis indicate the presence or absence of each comorbidity. The "Any other" category contains all remaining conditions in the top plot, and any others recorded as free text by clinical staff.



*Caution when interpreting this result as the sample size is small due to it being a new variable in the dataset.


Proportion of patients
0.3
0.2
0.1
0.0
Any other
Chronic cardiac disease
Diabetes
Chronic pulmonary disease
Chronic kidney disease
Conditions present at admission

Variables by age

Figure 5: Comorbidities stratified by age group. Boxes show the proportion of individuals with each comorbidity, with error bars showing 95% confidence intervals. The size of each box is proportional to the number of individuals represented. N is the number of individuals included in the plot (this varies between plots due to data completeness).

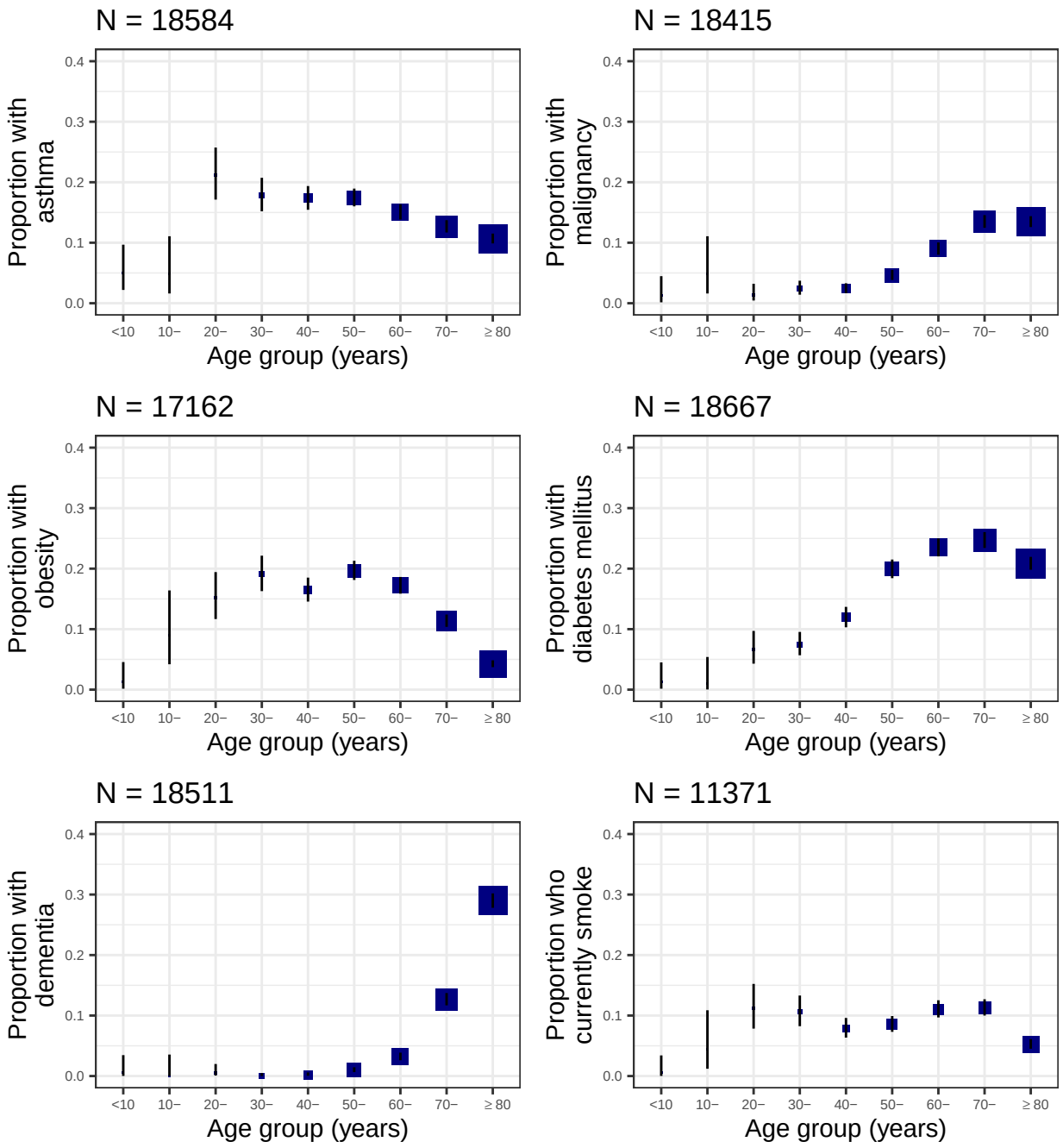


Figure 6: Symptoms recorded at hospital presentation stratified by age group. Boxes show the proportion of individuals with each symptom, with error bars showing 95% confidence intervals. The size of each box is proportional to the number of individuals represented. N is the number of individuals included in the plot (this varies between plots due to data completeness). The following symptoms are grouped: lower respiratory is either wheeze or shortness of breath; upper respiratory is any of runny nose, sore throat or ear pain; gastrointestinal is any of abdominal pain, vomiting or diarrhoea; neurological is either seizures or confusion; and constitutional is any of myalgia, joint pain, fatigue or headache.

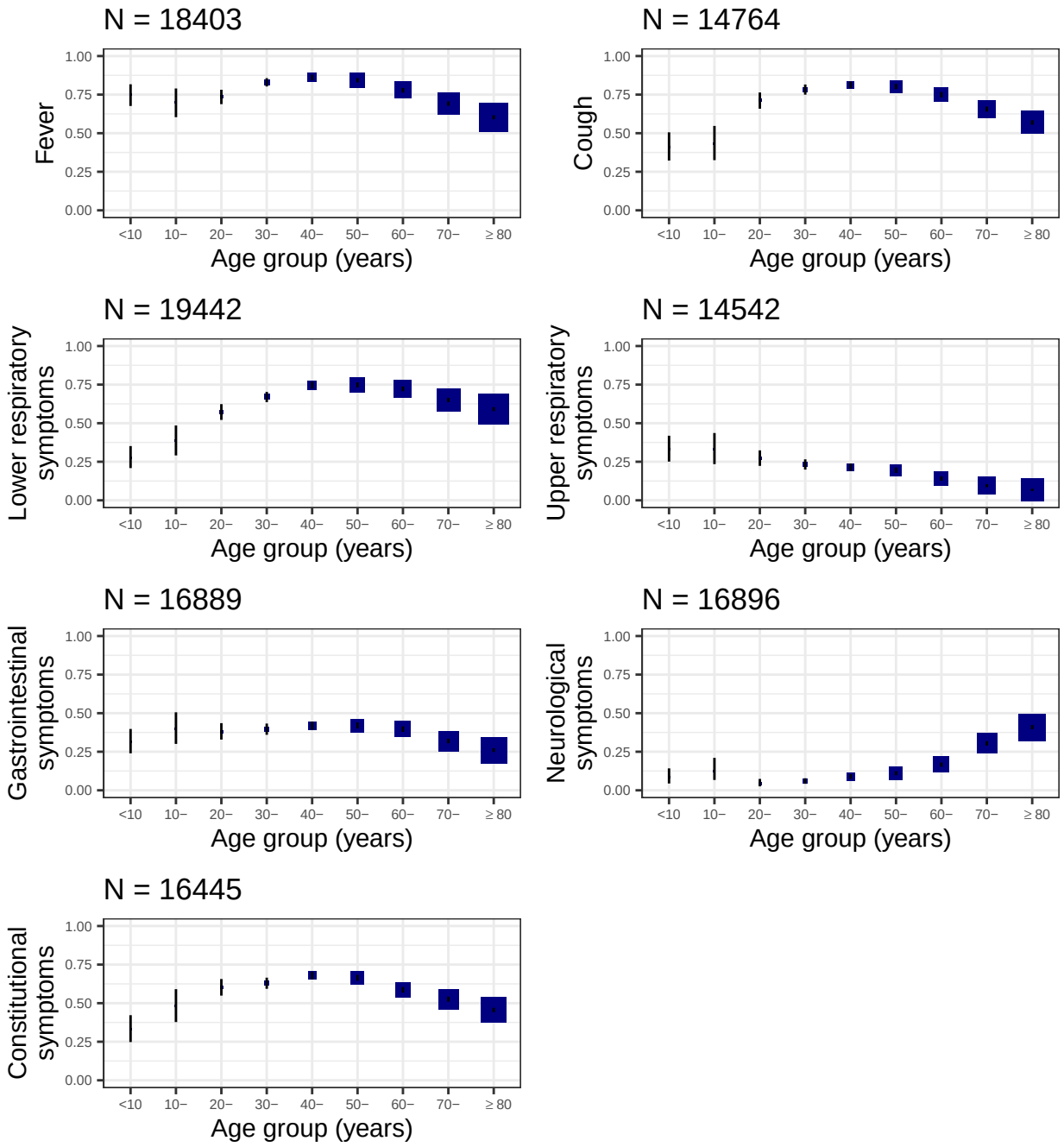


Figure 7: Box and whisker plots for observations at hospital presentation stratified by age group. Outliers are omitted. N is the number of individuals included in the plot (this varies between plots due to data completeness).

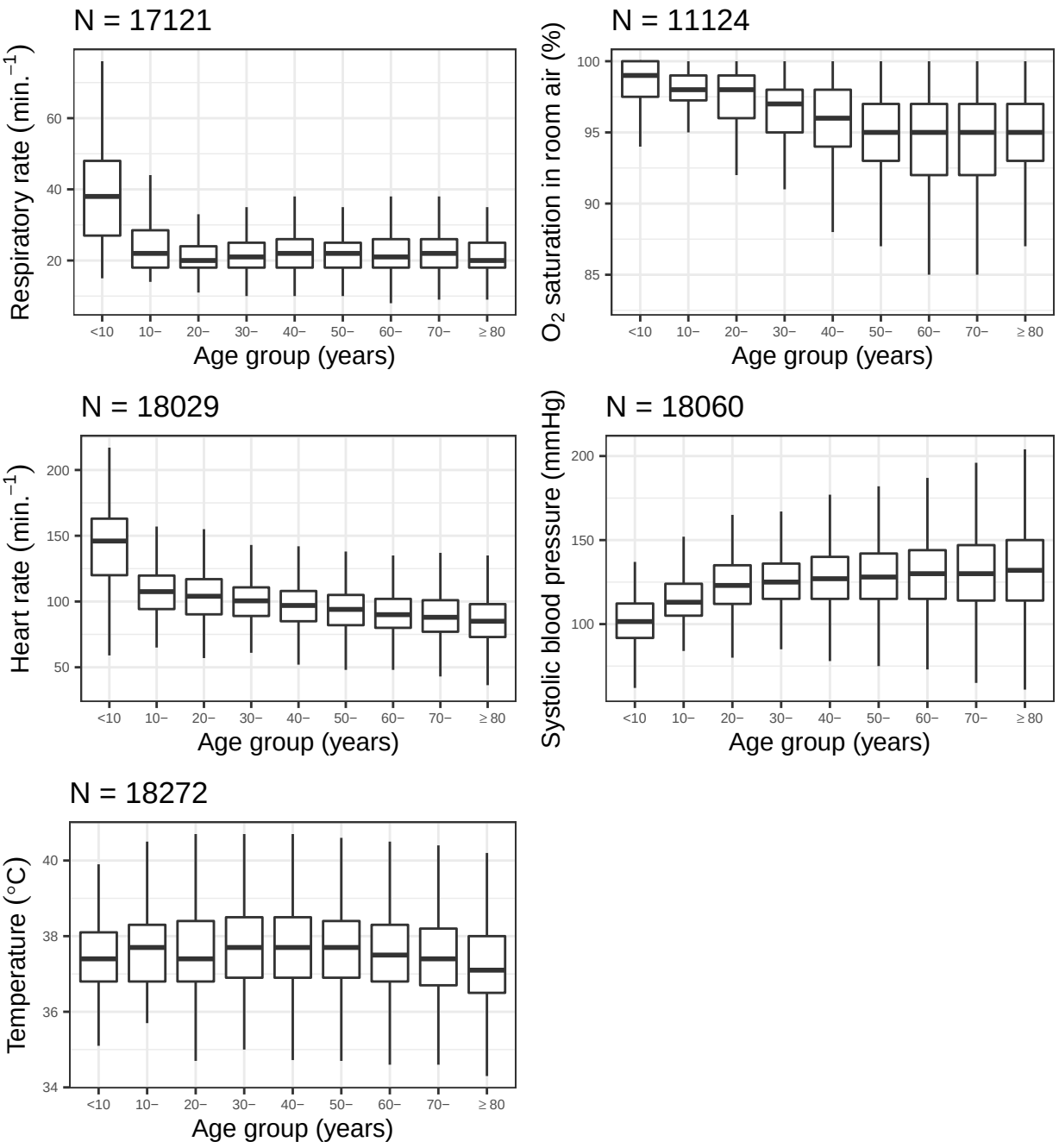
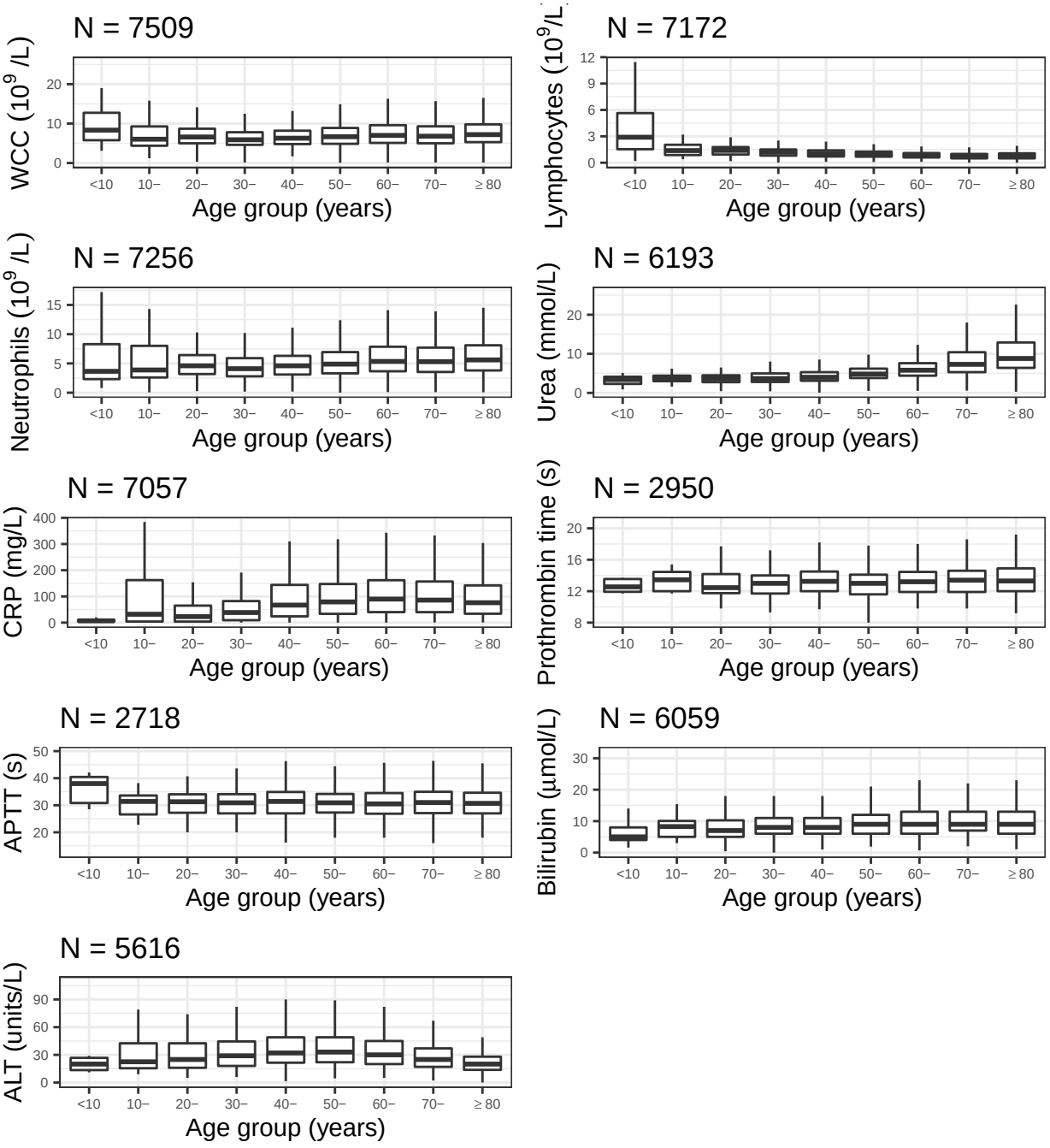


Figure 8: Box and whisker plots for laboratory results within 24 hours of hospital presentation stratified by age group. Outliers are omitted. N is the number of individuals included in the plot (this varies between plots due to data completeness). ALT, Alanine transaminase; APTT, Activated partial thromboplastin time; CRP, C-reactive protein; WCC, white cell count



Hospital stays and outcomes

Figure 9: Distribution of length of hospital stay, according to sex. This only includes cases with reported outcomes. The coloured areas indicate the kernel probability density of the observed data and the box plots show the median and interquartile range of the variable of interest. White dots are outliers.

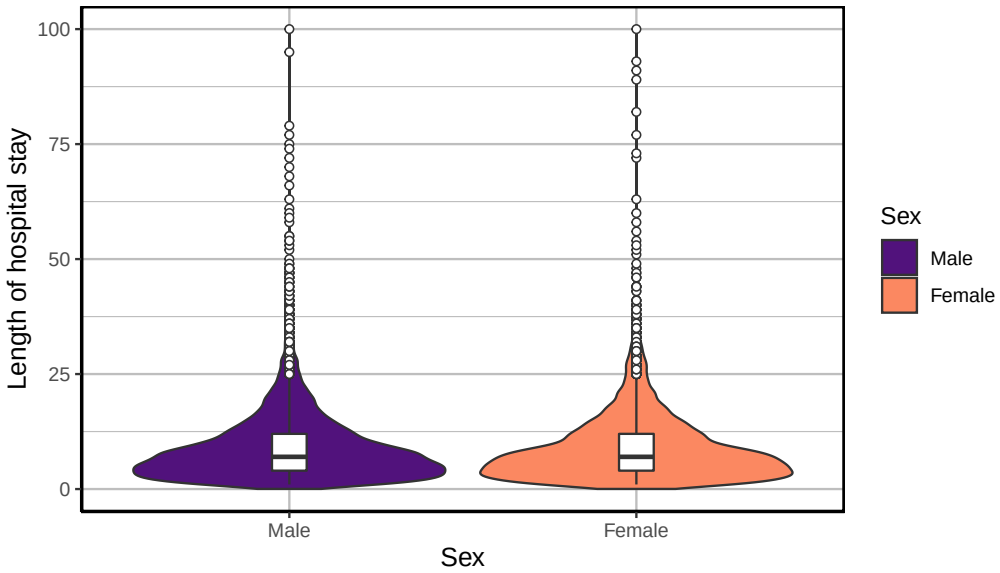
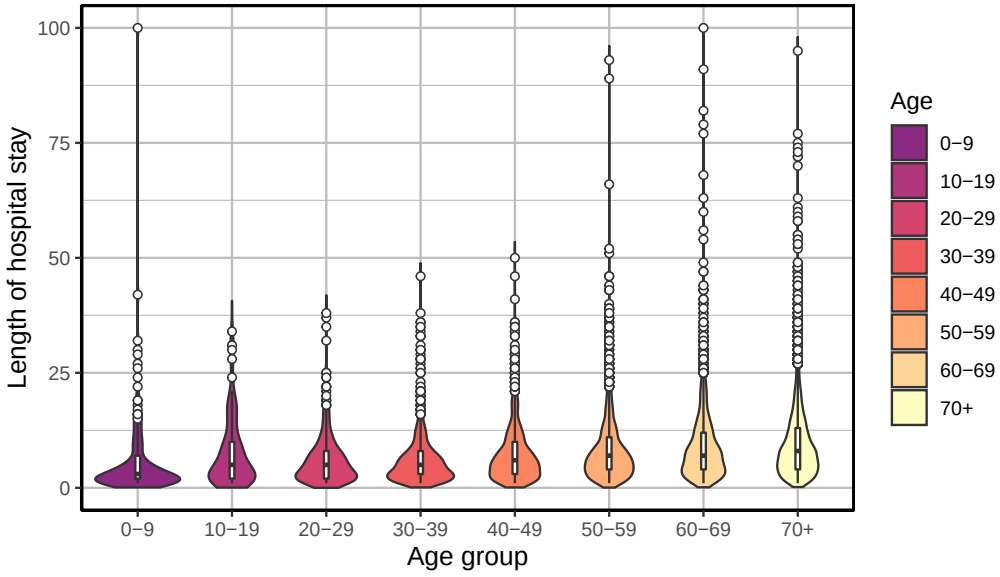


Figure 10: Distribution of length of hospital stay, according to patient age group. This only includes cases with reported outcomes. The coloured areas indicate the kernel probability density of the observed data and the box plots show the median and interquartile range of the variable of interest. White dots are outliers.*



* We are working to gain a greater understanding of the patient pathway for individuals recorded as having extremely long hospital stays.

Figure 11: The distribution of patient status by number of days after admission. Patients with "unknown" status have left the site at the time of report but have unknown outcomes due to missing data. Patients still on site at the time of report appear in the "ongoing care" category for days which are in the future at that time. (For example, a patient admitted 7 days before the date of report and still on site by the date of the report would be categorised as "ongoing care" for days 8 and later.) The black line marks the end of 14 days; due to the cut-off, only a small number of patients appear in the "ongoing care" category left of this line.

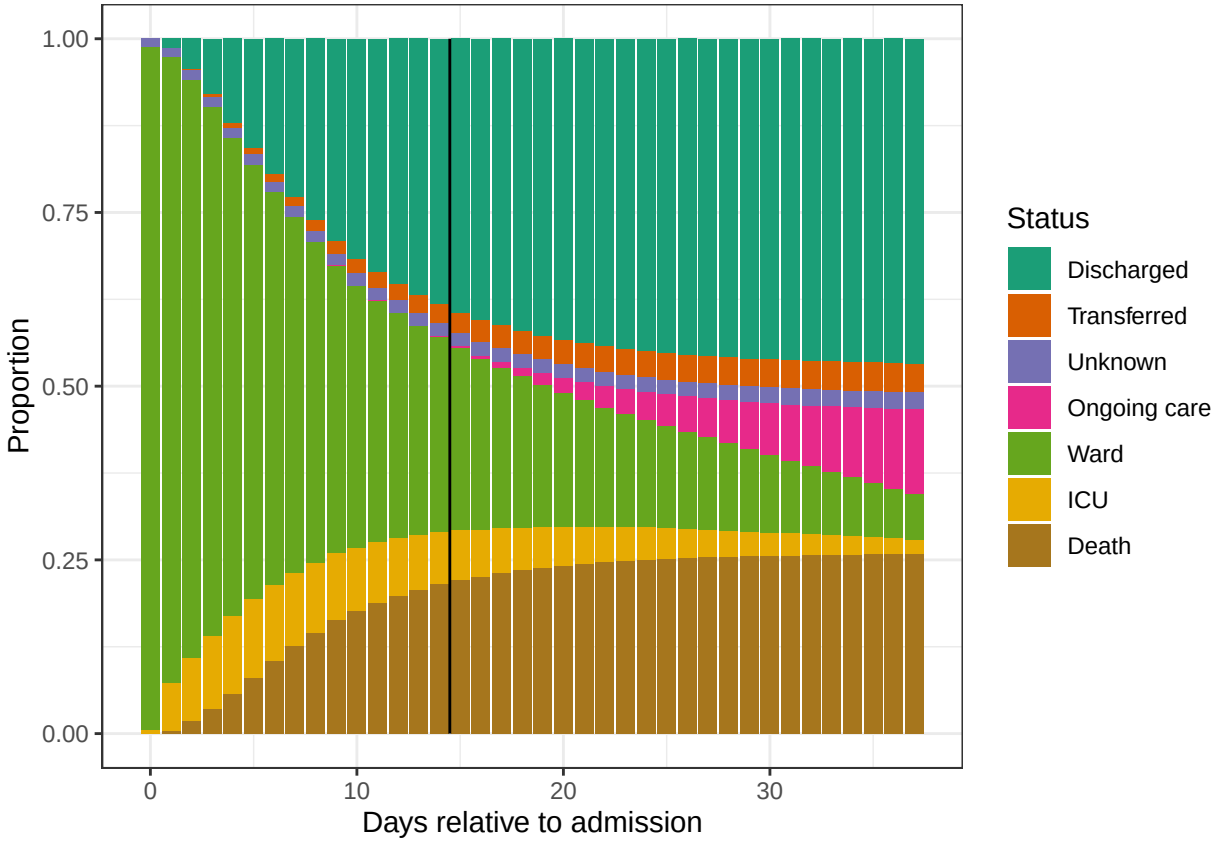
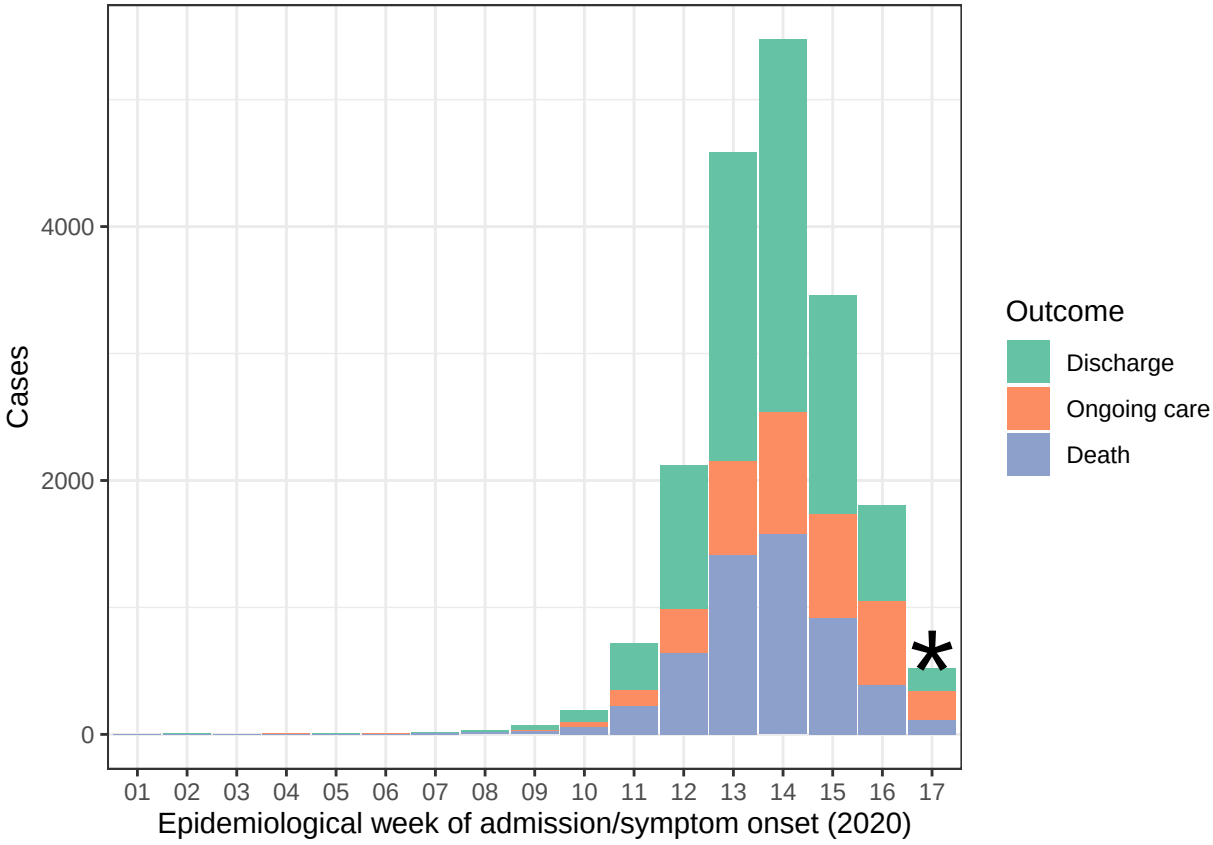
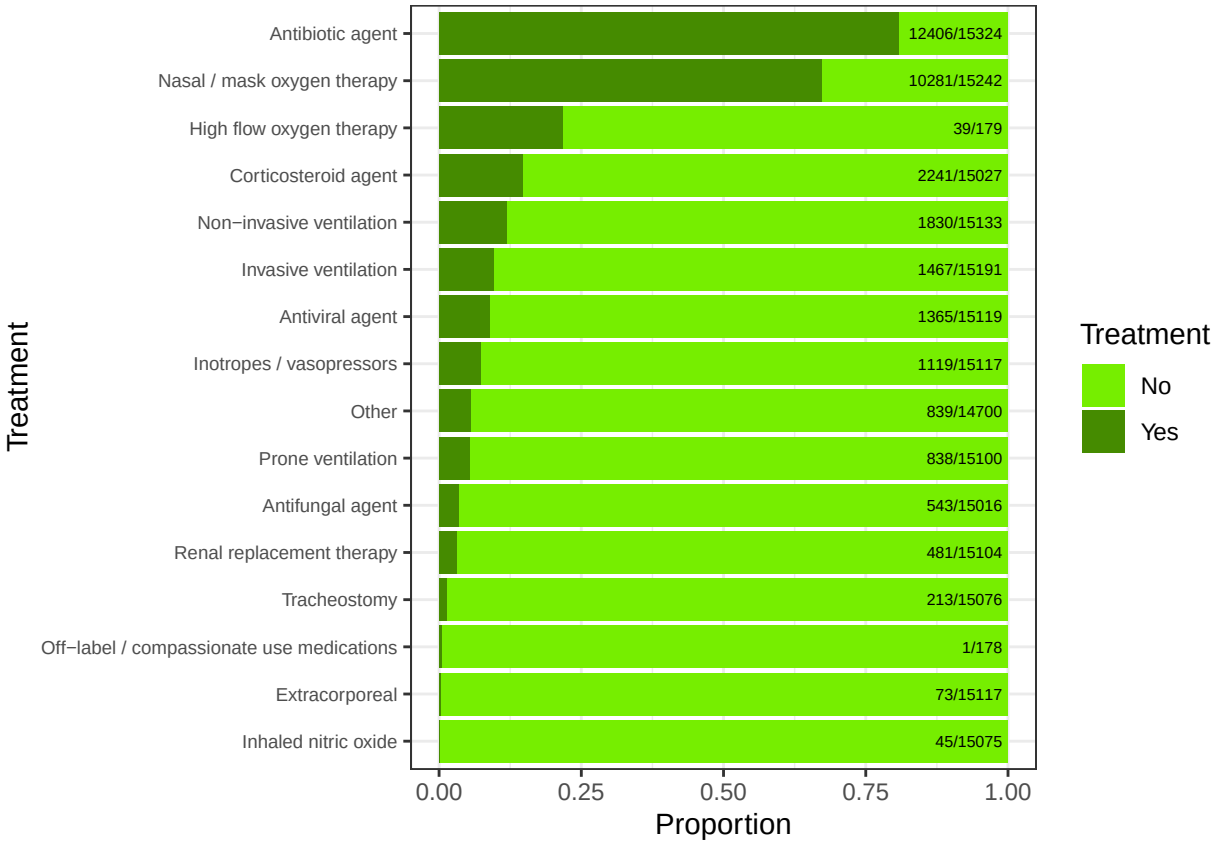


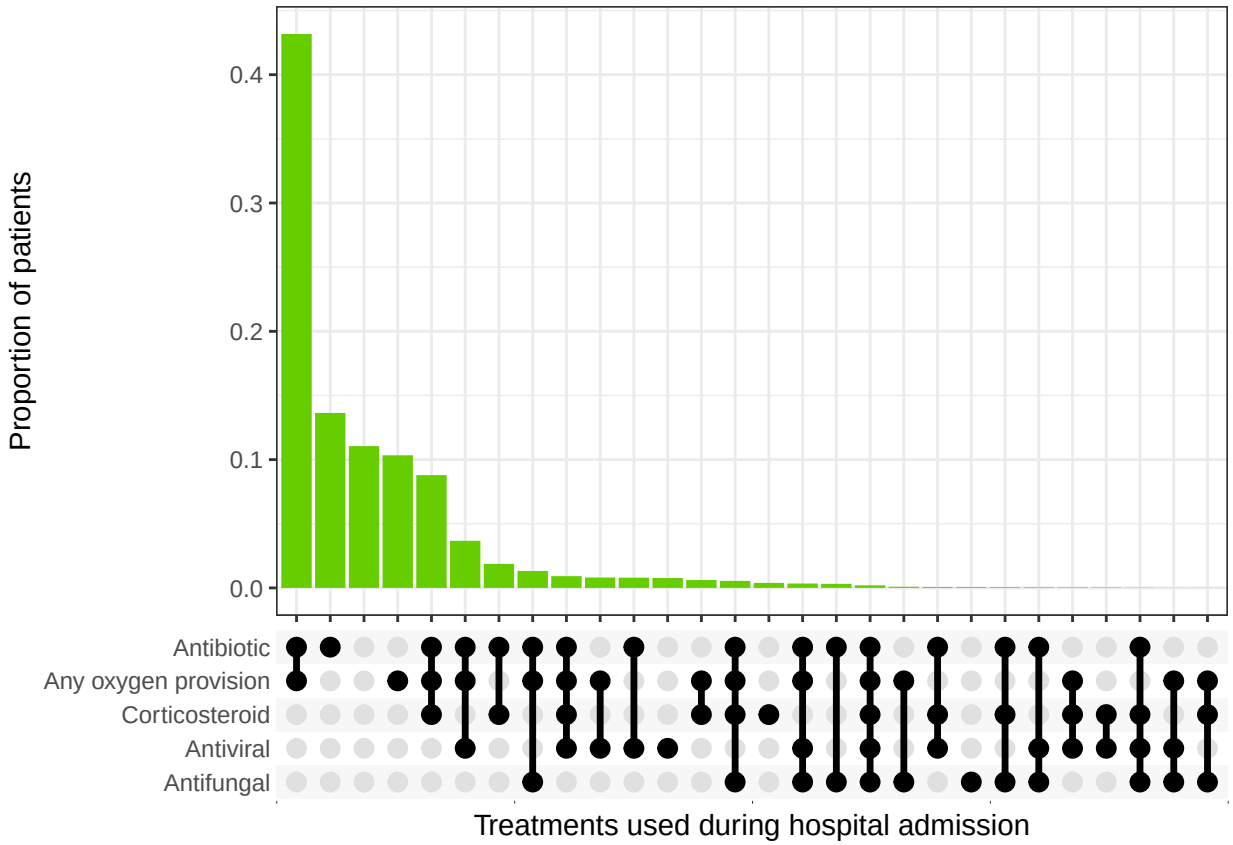
Figure 12: Patient numbers and outcomes by epidemiological week (of 2020) of admission (or, for patients infected in hospital, of symptom onset). The rightmost bar, marked with an asterisk, represents an incomplete week (due to the 14-day cutoff).



Treatment

Figure 13: **Top**: Treatments used. This only includes patients for whom this information was recorded. **Bottom**: The distribution of combinations of antimicrobial treatments and steroids administered during hospital stay, across all patients with completed hospital stay and recorded treatment data. Filled and empty circles below the x-axis indicate treatments that were and were not administered.

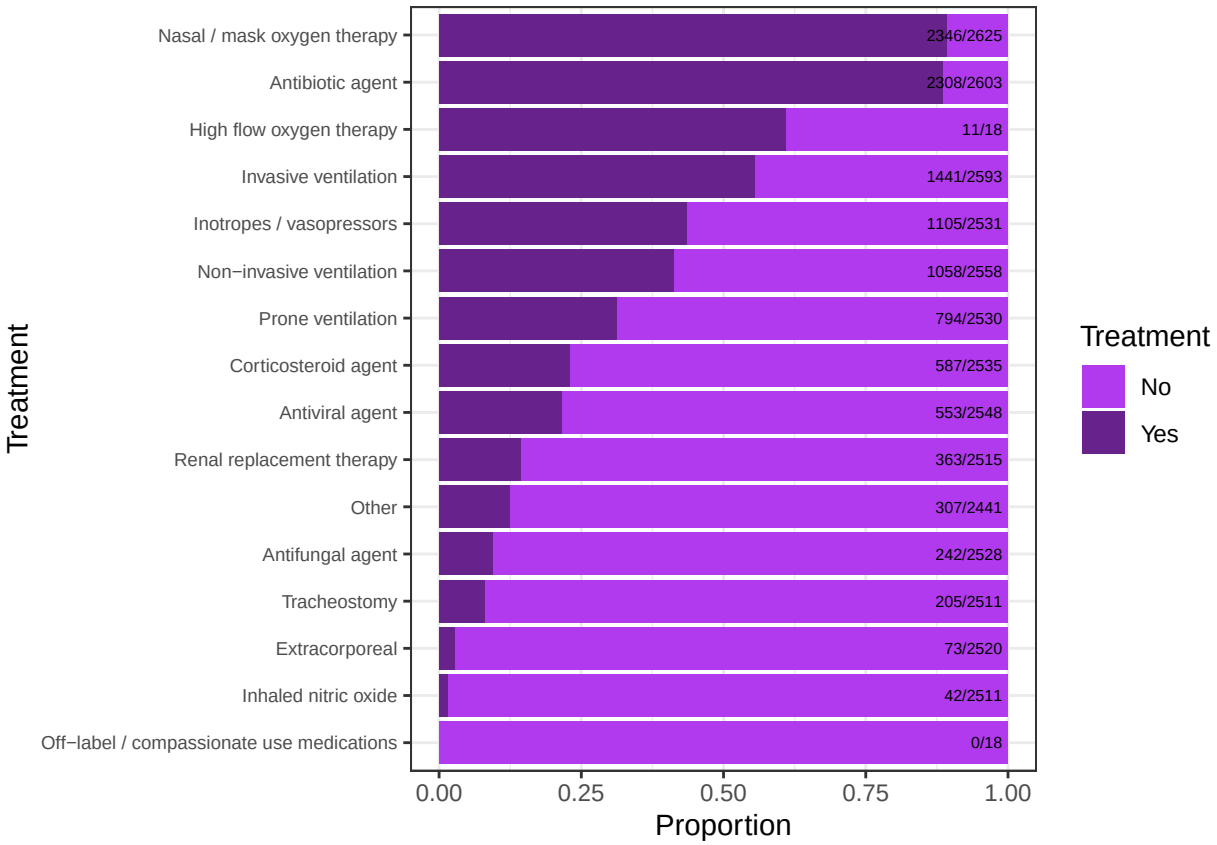


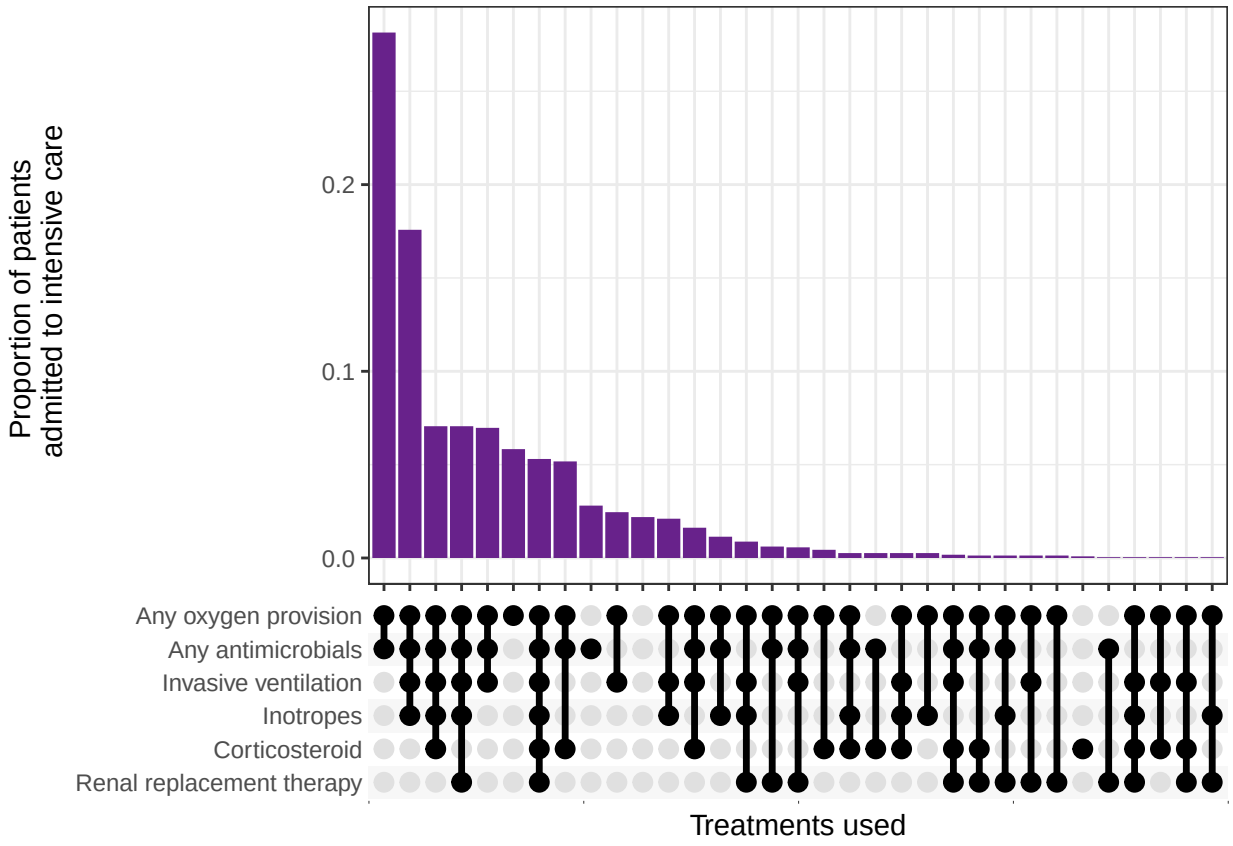

Proportion of patients
0.4
0.3
0.2
0.1
0.0
Antibiotic
Any oxygen provision
Corticosteroid
Antiviral
Antifungal
Treatments used during hospital admission

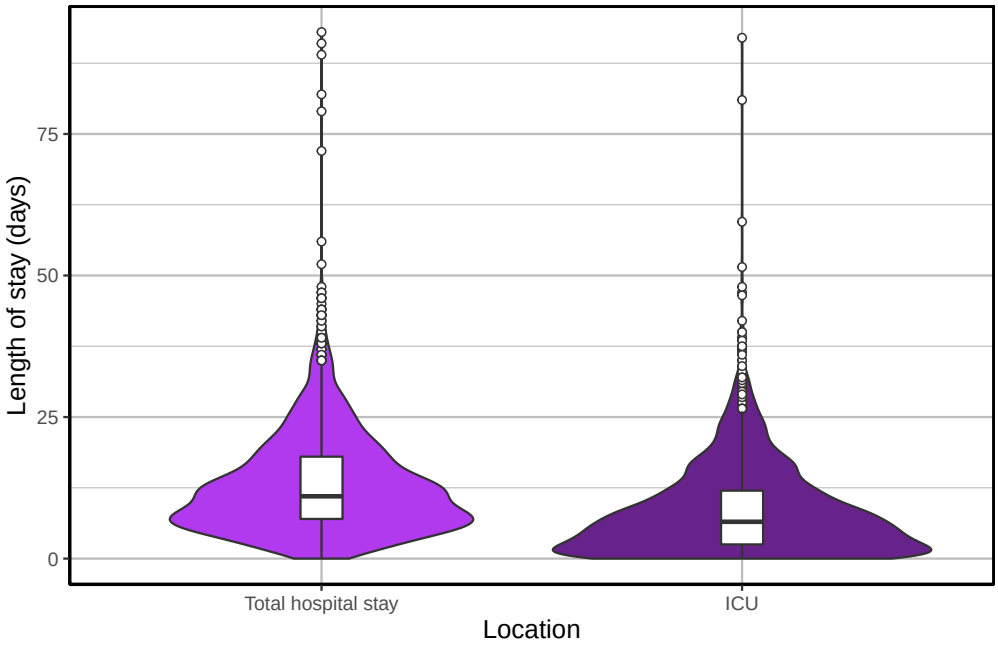
Intensive Care and High Dependency Unit Treatments

Figure 14: **Top**: Treatments used amongst patients admitted to the ICU. This only includes patients for whom this information was recorded. **Middle**: The distribution of combinations of treatments administered during ICU/HDU stay. Filled and empty circles below the x-axis indicate treatments that were and were not administered respectively.* **Bottom**: Distribution of lengths of stay for patients who were admitted to ICU/HDU: total length of stay for this group and length of stay within intensive care. This only includes cases with reported completed stays. The coloured areas indicate the kernel probability density of the observed data and the box plots show the median and interquartile range of the variable of interest.

* We are working to gain a greater understanding of patients reported as having been admitted to ICU/HDU but having no intensive treatments recorded.




Proportion of patients admitted to intensive care
0.2
0.1
0.0
Any oxygen provision
Any antimicrobials
Invasive ventilation
Inotropes
Corticosteroid
Renal replacement therapy
Treatments used


Length of stay (days)
75
50
25
0
Total hospital stay
ICU
Location

Statistical Analysis

Figure 15: Distribution of time from symptom onset to admission. The blue curve is the Gamma distribution fit to the data. The black dashed line indicates the position of the expected mean. The expected mean estimate here differs from the observed mean indicated in the summary text due to the differences in estimation: the mean shown in the figure below is the mean of the fitted Gamma distribution whereas the observed mean (in the summary text) is the arithmetic mean.

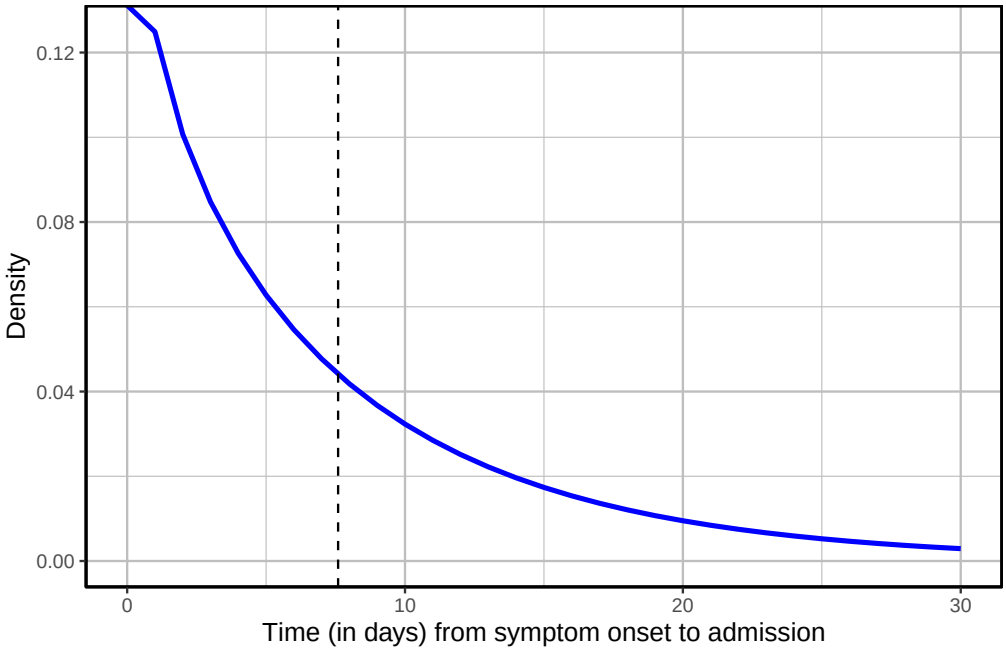


Figure 16: Distribution of time from admission to an outcome - either death or recovery (discharge). The blue curve is the Gamma distribution fit to the data. The black dashed line indicates the position of the expected mean. The expected mean differs from the observed mean in that it accounts for unobserved outcomes.

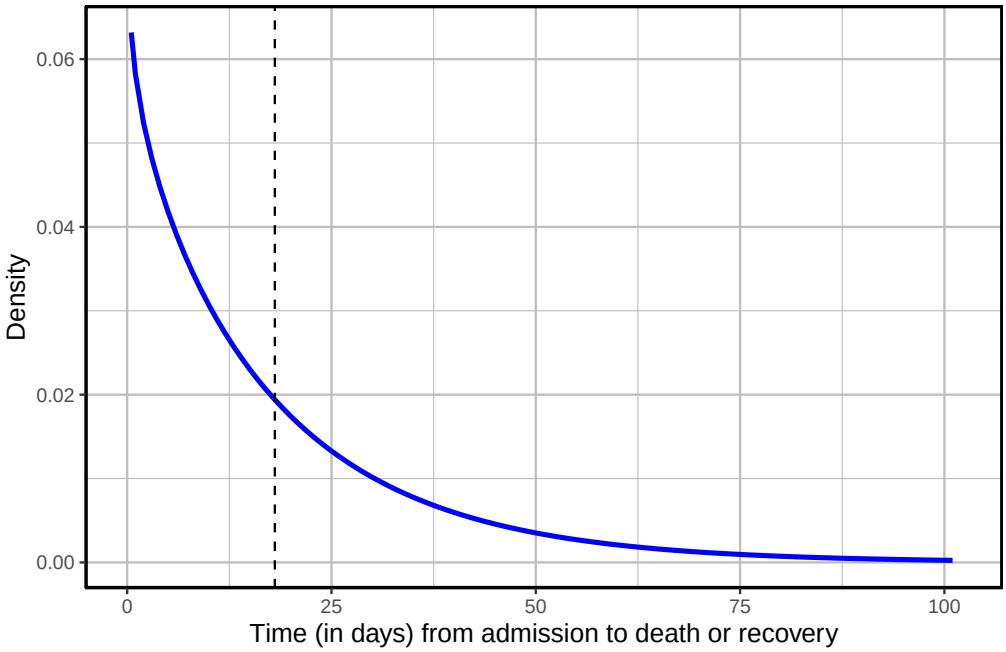
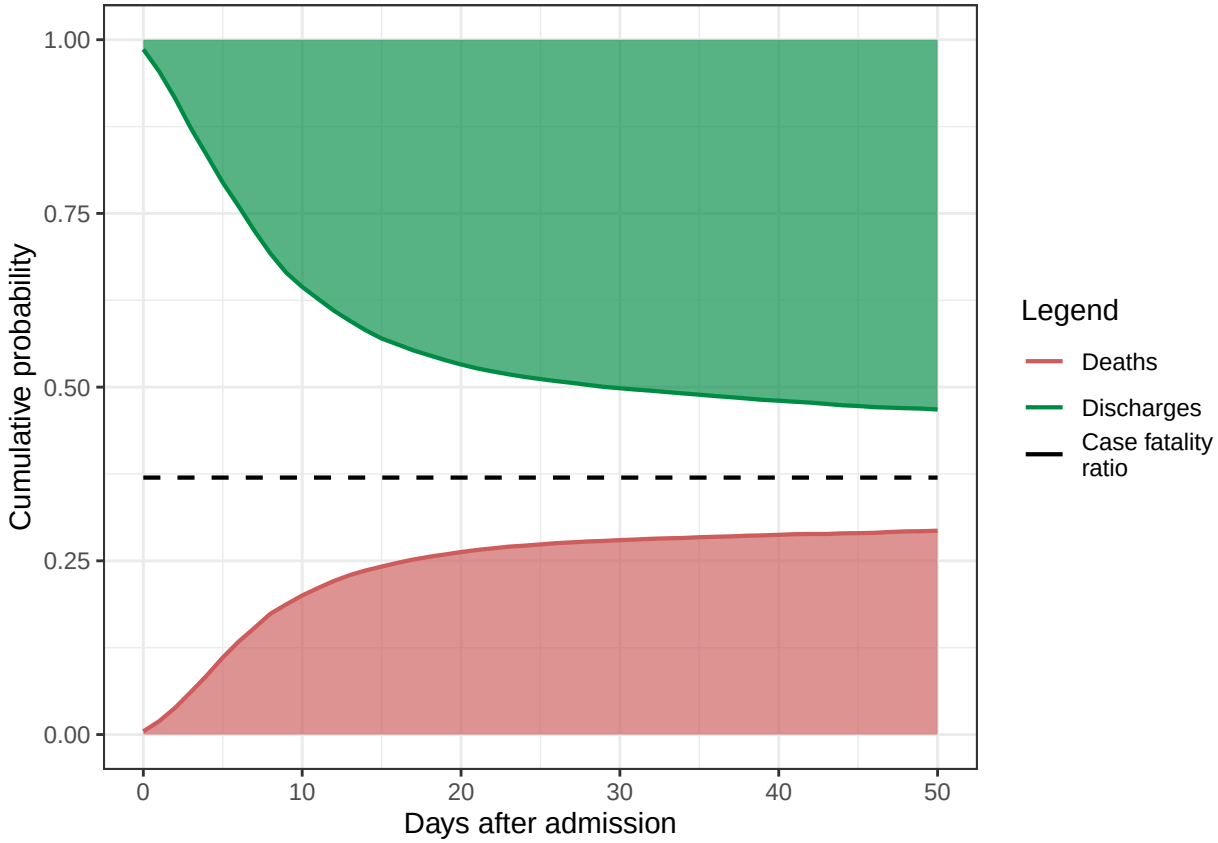


Figure 17: Probabilities of death (red curve) and recovery (green curve) over time. The black line indicates the case fatality ratio (CFR). The method used here considers all cases, irrespective of whether an outcome has been observed. For a completed epidemic, the curves for death and recovery meet. Estimates were derived using a nonparametric Kaplan-Meier–based method proposed by Ghani *et al.* (2005). The point estimate of the CFR is 0.37.



Country Comparisons

Figure 18: Number of sites per country.

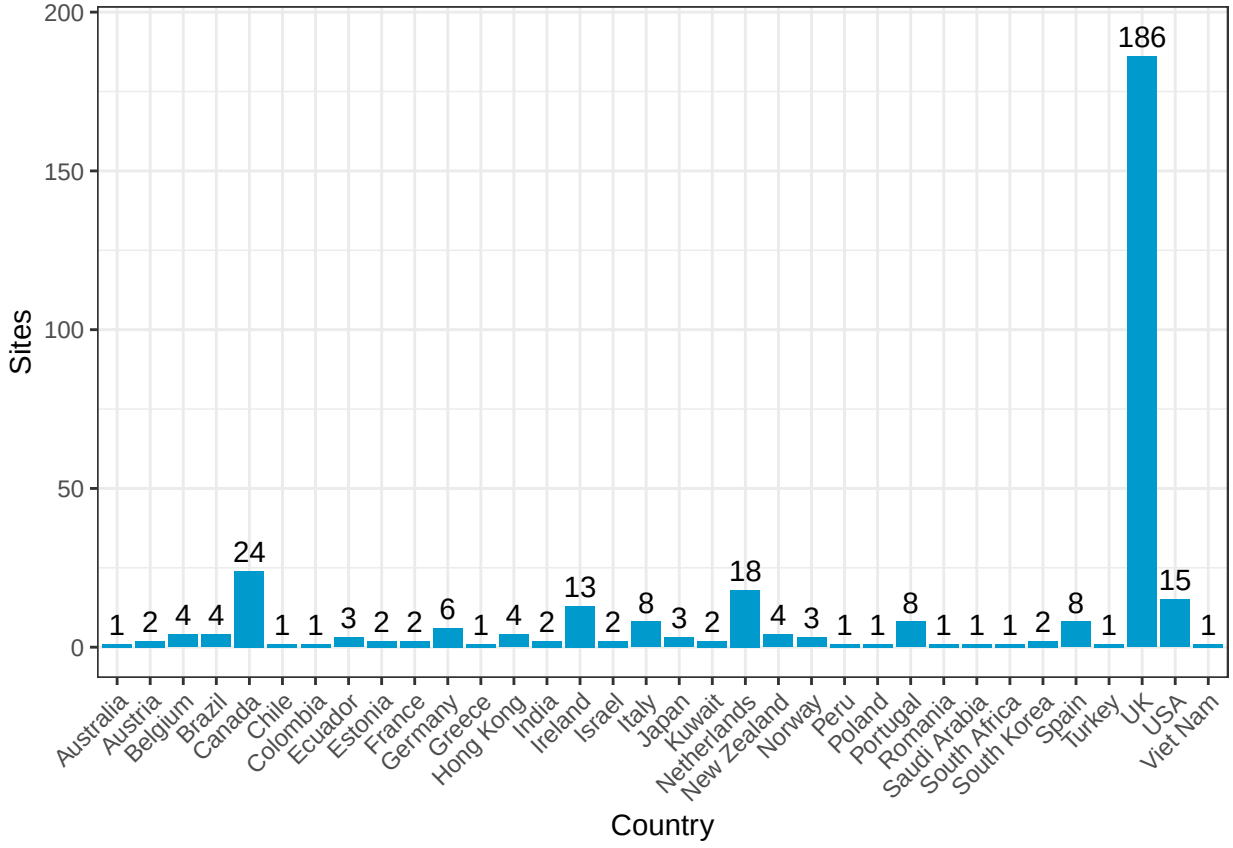
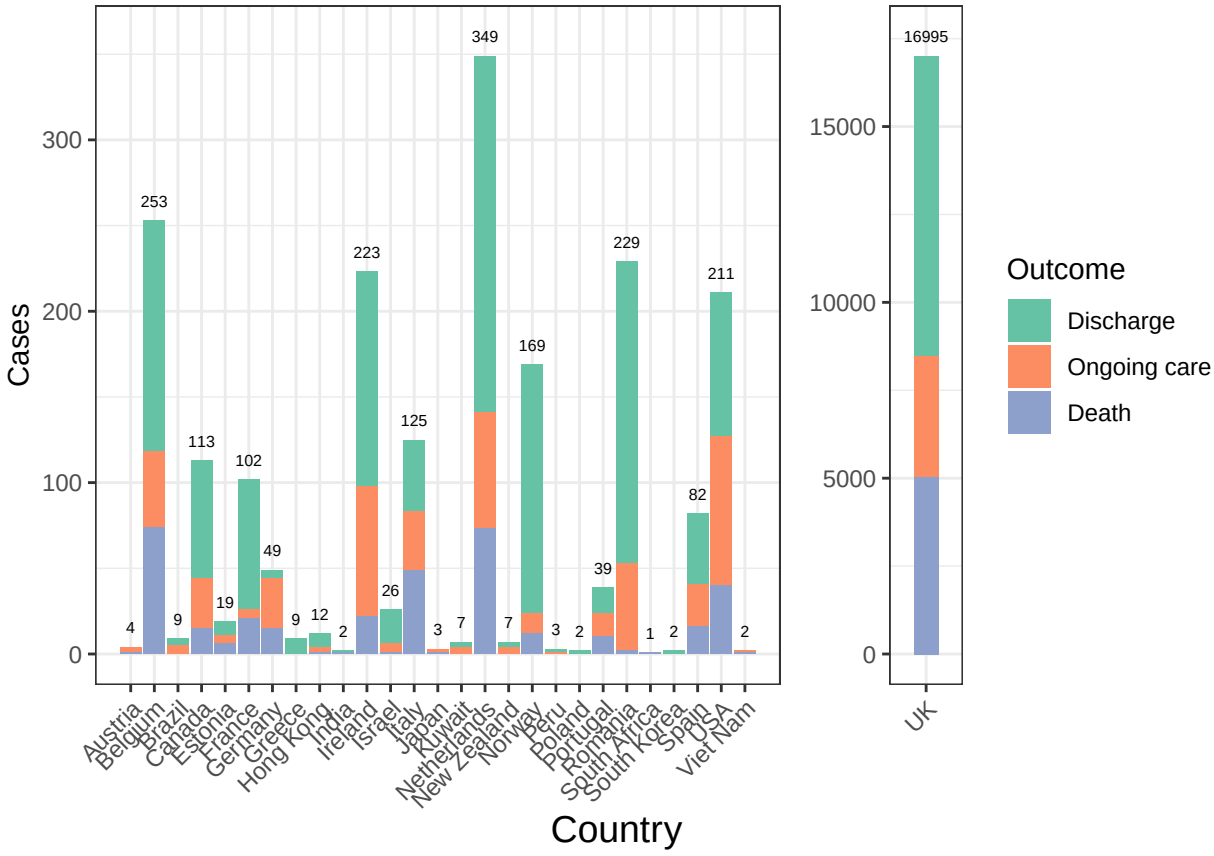


Figure 19: Distribution of patients by country and outcome.



Background

In response to the emergence of novel coronavirus (COVID-19), ISARIC launched a portfolio of resources to accelerate outbreak research and response. These include data collection, analysis and presentation tools which are freely available to all sites which have requested access to these resources. All data collection tools are designed to address the most critical public health questions, have undergone extensive review by international clinical experts, and are free for all to use. Resources are available on the ISARIC website.

The ISARIC-WHO COVID-19 Case Record Form (CRF) enables the collection of standardised clinical data to inform patient management and public health response. These forms should be used to collect data on suspected or confirmed cases of COVID-19. The CRF is available in multiple languages and is now in use across dozens of countries and research consortia, who are contributing data to these reports.

To support researchers to retain control of the data and samples they collect, ISARIC also hosts a data platform, where data can be entered to a web-based REDCap data management system, securely stored, and used to produce regular reports on their sites as above. Data contributors are invited to input on the methods and contents of the reports, and can also contribute to the aggregated data platform which aggregates site-specific data from all other sites across the world who are using this system. For more information, visit the ISARIC website.

All decisions regarding data use are made by the institutions that enter the data. ISARIC keeps contributors informed of any plans and welcomes their input to promote the best science and the interests of patients, institutions and public health authorities. Feedback and suggestions are welcome at ncov@isaric.org.

Methods

Patient details were submitted electronically by participating sites to the ISARIC database. Relevant background and presenting symptoms were recorded on the day of study recruitment. Daily follow-up was then completed until recovery or death. A final form was completed with details of treatments received and outcomes. All categories that represent fewer than five individuals have been suppressed to avoid the potential for identification of participants.

Graphs have been used to represent the age distribution of patients by sex and status (dead, recovered & still in hospital), the prevalence of individual symptoms on admission, comorbidities on admission, the length of hospital stay by sex and age group and the distribution of patient statuses by time since admission. In addition, the number of cases recruited by country and site, as well as the case count by status, has been represented.

Using a non-parametric Kaplan-Meier-based method (Ghani *et al.*, 2005), the case- fatality ratio (CFR) was estimated, as well as probabilities for death and recovery. This method estimates the CFR with the formula $a/(a+b)$, where a and b are the values of the cumulative incidence function for deaths and recoveries respectively, estimated at the last observed time point. In a competing risk context (i.e. where there are multiple endpoints), the cumulative incidence function for an endpoint is equal to the product of the hazard function for that endpoint and the survival function assuming a composite endpoint. It is worth noting that this method assumes that future deaths and recoveries will occur with the same relative probabilities as have been observed so far. Binomial confidence intervals for the CFR were obtained by a normal approximation (See Ghani *et al.*, (2005)).

To obtain estimates for the distributions of time from symptom onset to hospital admission and the time from admission to outcome (death or recovery), Gamma distributions were fitted to the observed data, accounting for unobserved outcomes. Parameters were estimated by a maximum likelihood procedure and confidence intervals for the means and variances were obtained by bootstrap.

All analysis were performed using the R statistical software (R Core Team, 2019).

Caveats

Patient data are collected and uploaded from start of admission, however a complete patient data set is not available until the episode of care is complete. This causes a predictable lag in available data influenced by the duration of admission which is greatest for the sickest patients, and accentuated during the up-phase of the outbreak.

These reports provide regular outputs from the ISARIC COVID-19 database. We urge caution in interpreting unexpected results. We have noted some unexpected results in the report, and are working with sites that submitted data to gain a greater understanding of these.

Summary Tables

Proportions are presented in parantheses. Proportions have been rounded to two decimal places.

Table 1: Patient Characteristics

Description	**Value**
Size of cohort	20276
By sex	
Male	12088 (0.6)
Female	8121 (0.4)
Unknown	67 (0)
By outcome status	
Dead	5396 (0.27)
Recovered (discharged alive)	9712 (0.48)
Still in hospital	3950 (0.19)
Tranferred to another facility	910 (0.04)
Unknown	308 (0.02)
By age group	
0-9	160 (0.01)
10-19	105 (0.01)
20-29	380 (0.02)
30-39	818 (0.04)
40-49	1564 (0.08)
50-59	2838 (0.14)
60-69	3410 (0.17)
70+	10783 (0.53)
Unknown	218 (0.01)
Admitted to ICU/HDU?	
Yes	3767 (19)
No/Unknown	16509 (81)

Table 2: Outcome by age and sex.

Variable	**Still in hospital**	**Death**	**Discharge**	**Transferred**	**Unknown**
Age					
0-9	19 (0)	1 (0)	135 (0.01)	3 (0)	2 (0.01)
10-19	10 (0)	3 (0)	84 (0.01)	6 (0.01)	2 (0.01)
20-29	59 (0.01)	10 (0)	300 (0.03)	8 (0.01)	3 (0.01)
30-39	133 (0.03)	28 (0.01)	626 (0.06)	19 (0.02)	12 (0.04)
40-49	311 (0.08)	87 (0.02)	1108 (0.11)	43 (0.05)	15 (0.05)
50-59	635 (0.16)	308 (0.06)	1749 (0.18)	94 (0.1)	52 (0.17)
60-69	761 (0.19)	711 (0.13)	1743 (0.18)	142 (0.16)	53 (0.17)
70+	1984 (0.5)	4210 (0.78)	3842 (0.4)	589 (0.65)	158 (0.51)
Sex					
Male	2377 (0.6)	3459 (0.64)	5522 (0.57)	547 (0.6)	183 (0.59)
Female	1556 (0.39)	1921 (0.36)	4158 (0.43)	363 (0.4)	123 (0.4)
Unknown	5 (0)	9 (0)	20 (0)	0 (0)	1 (0)

Table 3: Prevalence of Symptoms

Symptoms	**Present**	**Absent**	**Unknown**
History of fever	13467 (0.66)	5140 (0.25)	1669 (0.08)
Shortness of breath	12793 (0.63)	6854 (0.34)	629 (0.03)
Cough	10211 (0.5)	4705 (0.23)	5360 (0.26)
Fatigue / Malaise	7392 (0.36)	8051 (0.4)	4833 (0.24)
Altered consciousness / confusion	4187 (0.21)	12531 (0.62)	3558 (0.18)
Diarrhoea	3399 (0.17)	12892 (0.64)	3985 (0.2)
Vomiting / Nausea	3226 (0.16)	13085 (0.65)	3965 (0.2)
Muscle aches	3187 (0.16)	11211 (0.55)	5878 (0.29)
Chest pain	2358 (0.12)	13380 (0.66)	4538 (0.22)
Headache	2030 (0.1)	12269 (0.61)	5977 (0.29)
Abdominal pain	1643 (0.08)	14074 (0.69)	4559 (0.22)
Wheezing	1518 (0.07)	13371 (0.66)	5387 (0.27)
Sore throat	1484 (0.07)	12546 (0.62)	6246 (0.31)
Joint pain	1084 (0.05)	12657 (0.62)	6535 (0.32)
Runny nose	621 (0.03)	13114 (0.65)	6541 (0.32)
Skin ulcers	327 (0.02)	14592 (0.72)	5357 (0.26)
Seizures	247 (0.01)	15593 (0.77)	4436 (0.22)
Skin rash	242 (0.01)	14692 (0.72)	5342 (0.26)
Bleeding	171 (0.01)	15440 (0.76)	4665 (0.23)
Ear pain	95 (0)	13514 (0.67)	6667 (0.33)
Lymphadenopathy	94 (0)	14487 (0.71)	5695 (0.28)
Conjunctivitis	62 (0)	14538 (0.72)	5676 (0.28)

Table 4: Prevalence of Comorbidities

Comorbidities	Present	Absent	Unknown
Chronic cardiac disease	5646 (0.28)	13286 (0.66)	1344 (0.07)
Diabetes	3812 (0.19)	15051 (0.74)	1413 (0.07)
Chronic pulmonary disease	3191 (0.16)	15666 (0.77)	1419 (0.07)
Chronic kidney disease	2909 (0.14)	15852 (0.78)	1515 (0.07)
Asthma	2590 (0.13)	16192 (0.8)	1494 (0.07)
Dementia	2324 (0.11)	16311 (0.8)	1641 (0.08)
Obesity	2097 (0.1)	15176 (0.75)	3003 (0.15)
Chronic neurological disorder	2067 (0.1)	16581 (0.82)	1628 (0.08)
Malignant neoplasm	1801 (0.09)	16807 (0.83)	1668 (0.08)
Rheumatologic disorder	1721 (0.08)	16426 (0.81)	2129 (0.11)
Smoking	983 (0.05)	9911 (0.49)	9382 (0.46)
Chronic hematologic disease	753 (0.04)	17412 (0.86)	2111 (0.1)
Malnutrition	444 (0.02)	17420 (0.86)	2412 (0.12)
Liver disease	307 (0.02)	17939 (0.88)	2030 (0.1)
Hypertension	168 (0.01)	175 (0.01)	19933 (0.98)
Pregnancy	99 (0)	19708 (0.97)	469 (0.02)

Table 5: Prevalence of Treatments

The counts presented for treatments include all cases, not only cases with complete details of treatments (as expressed in the summary).

Treatments	Present	Absent	Unknown
Oxygen therapy	12875 (0.63)	6427 (0.32)	974 (0.05)
Antibiotic agent	12406 (0.61)	2516 (0.12)	5354 (0.26)
Nasal / mask oxygen therapy	10281 (0.51)	4381 (0.22)	5614 (0.28)
Non-invasive ventilation	3039 (0.15)	16117 (0.79)	1120 (0.06)
Invasive ventilation	2286 (0.11)	16920 (0.83)	1070 (0.05)
Corticosteroid agent	2241 (0.11)	12064 (0.59)	5971 (0.29)
Antiviral agent	1365 (0.07)	13034 (0.64)	5877 (0.29)
Inotropes / vasopressors	1119 (0.06)	13091 (0.65)	6066 (0.3)
Other	839 (0.04)	12569 (0.62)	6868 (0.34)
Prone ventilation	838 (0.04)	13257 (0.65)	6181 (0.3)
Antifungal agent	543 (0.03)	13755 (0.68)	5978 (0.29)
Renal replacement therapy	481 (0.02)	13738 (0.68)	6057 (0.3)
Extracorporeal membrane oxygenation (ECMO)	226 (0.01)	18937 (0.93)	1113 (0.05)
Tracheostomy	213 (0.01)	13898 (0.69)	6165 (0.3)

Table 6: Key time variables.

Unlike the observed mean, the estimation process of the **expected mean** accounts for all cases, irrespective of whether an outcome has been observed. The expected mean is 'NA' for those variables for which parameter estimation could not be performed, due to the high proportion of unobserved end dates. The interquartile range is abbreviated 'IQR'.

Time (in days)	Mean (observed)	SD (observed)	Median (observed)	IQR (observed)	Expected mean (95% CI)
Length of hospital stay	9.5	8.8	7	8	18.1 (17.1, 19.4)
Symptom onset to admission	12.1	7.6	5	8	7.6 (7.3, 8.4)
Admission to ICU entry	3.3	6.5	1	2.5	3.5 (3.3, 3.8)
Duration of ICU	8.7	8.5	6	10.5	NA
Admission to IMV	3.6	6.6	2	3.5	3.6 (3.4, 3.9)
Duration of IMV	10.3	7.3	9	9	NA
Admission to NIV	4.5	8.6	2	4.5	4.7 (4.3, 5.1)
Duration of NIV	2.2	3.7	0.5	4.5	NA

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