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Original research

Clinical phenotypes and outcomes of SARS-CoV-2, influenza, RSV and seven other respiratory viruses: a retrospective study using complete hospital data

Pontus Hedberg ,[1,2] John Karlsson Valik,[2,3] Suzanne van der Werff,[2,3] Hideyuki Tanushi,[3] Ana Requena Mendez,[2,3] Fredrik Granath,[3] Max Bell,[4,5] Johan Mårtensson,[4,5] Robert Dyrdak,[1,6] Olof Hertting,[7,8] Anna Färnert,[2,3] Anders Ternhag,[2,3] Pontus Naucler[2,3]

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/thoraxjnl-2021-216949).

For numbered affiliations see end of article.

Correspondence to
Mr Pontus Hedberg, Microbiology, Tumor And Cell Biology, Karolinska Institute, 171 77 Stockholm, Sweden; Pontus.hedberg@ki.se

Received 25 January 2021
Accepted 25 May 2021
Published Online First 5 July 2021

ABSTRACT

Background An understanding of differences in clinical phenotypes and outcomes COVID-19 compared with other respiratory viral infections is important to optimise the management of patients and plan healthcare. Herein we sought to investigate such differences in patients positive for SARS-CoV-2 compared with influenza, respiratory syncytial virus (RSV) and other respiratory viruses.

Methods We performed a retrospective cohort study of hospitalised adults and children (≤15 years) who tested positive for SARS-CoV-2, influenza virus A/B, RSV, rhinovirus, enterovirus, parainfluenza viruses, metapneumovirus, seasonal coronaviruses, adenovirus or bocavirus in a respiratory sample at admission between 2011 and 2020.

Results A total of 6321 adult (1721 SARS-CoV-2) and 6379 paediatric (101 SARS-CoV-2) healthcare episodes were included in the study. In adults, SARS-CoV-2 positivity was independently associated with younger age, male sex, overweight/obesity, diabetes and hypertension, tachypnoea as well as better haemodynamic measurements, white cell count, platelet count and creatinine values. Furthermore, SARS-CoV-2 was associated with higher 30-day mortality as compared with influenza (adjusted HR (aHR) 4.43, 95% CI 3.51 to 5.59), RSV (aHR 3.81, 95% CI 2.72 to 5.34) and other respiratory viruses (aHR 3.46, 95% CI 2.61 to 4.60), as well as higher 90-day mortality, ICU admission, ICU mortality and pulmonary embolism in adults. In children, patients with SARS-CoV-2 were older and had lower prevalence of chronic cardiac and respiratory diseases compared with other viruses.

Conclusions SARS-CoV-2 is associated with more severe outcomes compared with other respiratory viruses, and although associated with specific patient and clinical characteristics at admission, a substantial overlap precludes discrimination based on these characteristics.

Key messages

What is the key question?

► What are the differences in clinical phenotypes and outcomes in patients with SARS-CoV-2 as compared with influenza, respiratory syncytial virus (RSV) and other respiratory viruses such as seasonal coronaviruses, rhinovirus and metapneumovirus?

What is the bottom line?

► Adult SARS-CoV-2 was associated with more severe outcomes compared with influenza, RSV and other respiratory viruses, and although associated with specific patient and clinical characteristics at admission, a substantial overlap precluded discrimination based on these characteristics.

Why read on?

► To our knowledge, this is the first extensive comparison of baseline characteristics, clinical presentation and patient outcomes in SARS-CoV-2 as compared with influenza and several other respiratory viruses.

INTRODUCTION

The clinical presentation of SARS-CoV-2 infected adults in hospitals includes fever, cough or dyspnoea, which are similar to those of other respiratory viruses.[1–3] Common characteristics of hospitalised patients with COVID-19 are male sex, cardiovascular disease, diabetes, hypertension or obesity.[4–6] A substantial portion of patients with COVID-19 require intensive care unit (ICU) admission and develop severe complications such as pulmonary embolism or acute kidney failure.[4 5 7 8] There is some evidence for lower susceptibility to SARS-CoV-2 infection in children, as well as more favourable disease outcome.[9–12] These observations are primarily based on case series and how these characteristics and outcomes compares in similar cohorts of patients infected with other respiratory infections is less well studied.

SARS-CoV-2 will likely remain endemic and cocirculate in the population together with influenza and other respiratory viruses.[13 14] To better understand the pathogenesis of SARS-CoV-2 and to optimise patient management and plan healthcare, it is important to understand variations in clinical phenotypes and outcomes associated with different respiratory viruses. In this study, the aim was to investigate differences in baseline characteristics, clinical presentation and outcomes for adult

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To cite: Hedberg P, Karlsson Valik J, van der Werff S, *et al*. *Thorax* 2022;**77**:1–10.

and paediatric patients with SARS-CoV-2 compared with other respiratory viruses.

METHODS

Patient population and study setting

We conducted a retrospective cohort study of hospitalised patients from October 2011 to September 2020 at Karolinska University Hospital, Stockholm, Sweden, an academic centre with 1100 beds divided between two sites and serving a population of 2.3 million inhabitants. Patients with the following PCR-confirmed infections from respiratory samples (nasopharyngeal, throat, sputum, tracheal or bronchoalveolar lavage samples) on admission were included: influenza A (H3N2 and H1N1), influenza B (FluB), adenovirus, bocavirus, seasonal coronaviruses species 229E, NL63, OC43 and HKU1, enterovirus, metapneumovirus, rhinovirus (RV), parainfluenza viruses type 1–4 (PIV), respiratory syncytial virus (RSV) and SARS-CoV-2 (see online supplemental eMethods 1 for additioal descriptions of PCR-methods). Samples collected within −24 hours to +48 hours from the hospital admission were included. Repeated positive tests within 90 days were excluded.

Data source and definitions

Data were obtained from a database of electronic health records of all patients admitted between January 2010 and September 2020, including demographics, International Classification of Diseases (ICD)-10 codes, body mass index (BMI), laboratory findings, vital signs, microbiology, intensive care and mortality. The study period start time of October 2011 was chosen to ensure at least 1.5 years of data on previous comorbidities and other variables. Specific individual comorbidities as well as Charlson Comorbidity Index (CCI) and Elixhauser Comorbidity Index (ECI) scores were based on ICD-10 codes recorded from 5 years before and up until admission.[15] BMI was based on the most updated height and weight available. For laboratory parameters and vital signs, the worst value −24 hours to +24 hours from admission was used. See online supplemental eMethods 1 for additional descriptions.

Outcomes

The primary outcome was 30-day mortality from hospital admission. Secondary outcomes were length of stay (LOS) at hospital, 90-day mortality, ICU admission (defined as units that provide inotropic and non-invasive or invasive respiratory treatment), LOS at ICU, mortality after ICU admission (calculated from ICU admission), acute kidney injury (AKI; based on the Kidney Disease: Improving Global Outcomes (KDIGO) criteria[16] but without urine volume measurements), pulmonary embolism (based on ICD-10 discharge code), acute myocardial injury (AMI; cardiac troponin T>50 ng/mL) and hospital-onset bacteraemia (HOB; significant findings in blood cultures taken >48 hours after admission).[17] See online supplemental eMethods 2 for detailed definitions. Patients were followed for 30 days for outcome measures, except for pulmonary embolism where patients were followed until discharge and 90-day mortality.

Statistical analysis

Children (≤15 years of age) and adults were analysed separately. Analyses were performed using 10 virus categories as well as four virus groups in adults—SARS-CoV-2, influenza, RSV and other viruses—to correspond to differential virus testing indications. Testing for other viruses is preferentially performed in patients with more severe disease, with immunosuppression and tested negative for other viruses. All analyses were restricted to patients positive for only one virus group, in order to distinguish clinical phenotypes and outcomes for each virus group. For rhinoviruses and enteroviruses, PCR cross-reactivity, preventing classification of 572 health care episodes (HCE) (82 adult and 490 paediatric) into virus-specific groups.[18] These 572 HCEs were excluded from virus-specific analyses, but adults were included in the other viruses group.

Multiple imputation with predictive mean matching was used to account for missing values for BMI, laboratory parameters and vital signs (proportion missing values 5%–13%) with other baseline characteristics and outcomes used as predictors (detailed description in online supplemental file).

Comparisons between all 10 virus groups were performed using χ^2 test for nominal and Kruskal-Wallis test for continuous variables. Sex- and age category adjusted logistic regression analyses were performed to compare baseline characteristics, laboratory parameters and vital signs in patients with SARS-CoV-2 compared with influenza, RSV and other respiratory viruses. To investigate overall differences in baseline characteristics and clinical presentation between SARS-CoV-2 and influenza, RSV and other respiratory viruses, three logistic regression models were used. Predictors in the first model were age category, sex and BMI category, the second also included specific comorbidities and the third included laboratory parameters and vital signs as well. Model performance was assessed using area under the receiver operating characteristics (AUROC).

Clinical outcomes were compared among different virus groups using regression analyses with adjustment for sex, age category, BMI category and individual comorbidities: Cox regression HRs for 30-day and 90-day mortality, ICU admission, AMI, AKI and HOB, logistic regression ORs for pulmonary embolism and negative binomial regression rate ratios for LOS. The proportional hazards assumption was checked by Schoenfeld residuals. Kaplan-Meier curves and standardised adjusted survival functions were calculated for 30-day and 90-day mortality.[15] In order to address potential time-related drifts in clinical management as well as more extensive testing of SARS-CoV-2 as compared with other viruses, predefined sensitivity analyses were performed for the outcomes mortality and ICU admission: (1) restriction to years 2015–2020, (2) restriction to patients with admission temperature ≥38°C, or oxygen saturation <95%, or respiratory rate >20, (3) stratification according to calendar time of SARS-CoV-2 positivity (February–April 2020 vs May–September 2020) and (4) restriction to the index HCE for each patient.

Statistical analyses were performed in R V.4.0.3.

RESULTS

In total, 782 345 inpatient admissions in 412 115 patients were registered between October 2011 and September 2020, of which 6700 adult and 8477 paediatric episodes tested positive for a respiratory virus at admission (figure 1). There were 661 episodes with repeated positive tests within 90 days. In the analysis, 12 700 episodes with one respiratory virus detected were included, 6321 adults (1721 SARS-CoV-2, 2468 influenza, 624 RSV and 1508 other viruses) and 6379 children (101 SARS-CoV-2, 871 influenza, 2425 RSV and 2982 other viruses).

Patient characteristics and clinical presentation of SARS-CoV-2 compared with other respiratory viruses among adults

Adult patients with SARS-CoV-2 were younger and more often male (median age 58 years (IQR 42–71), 59% male) compared

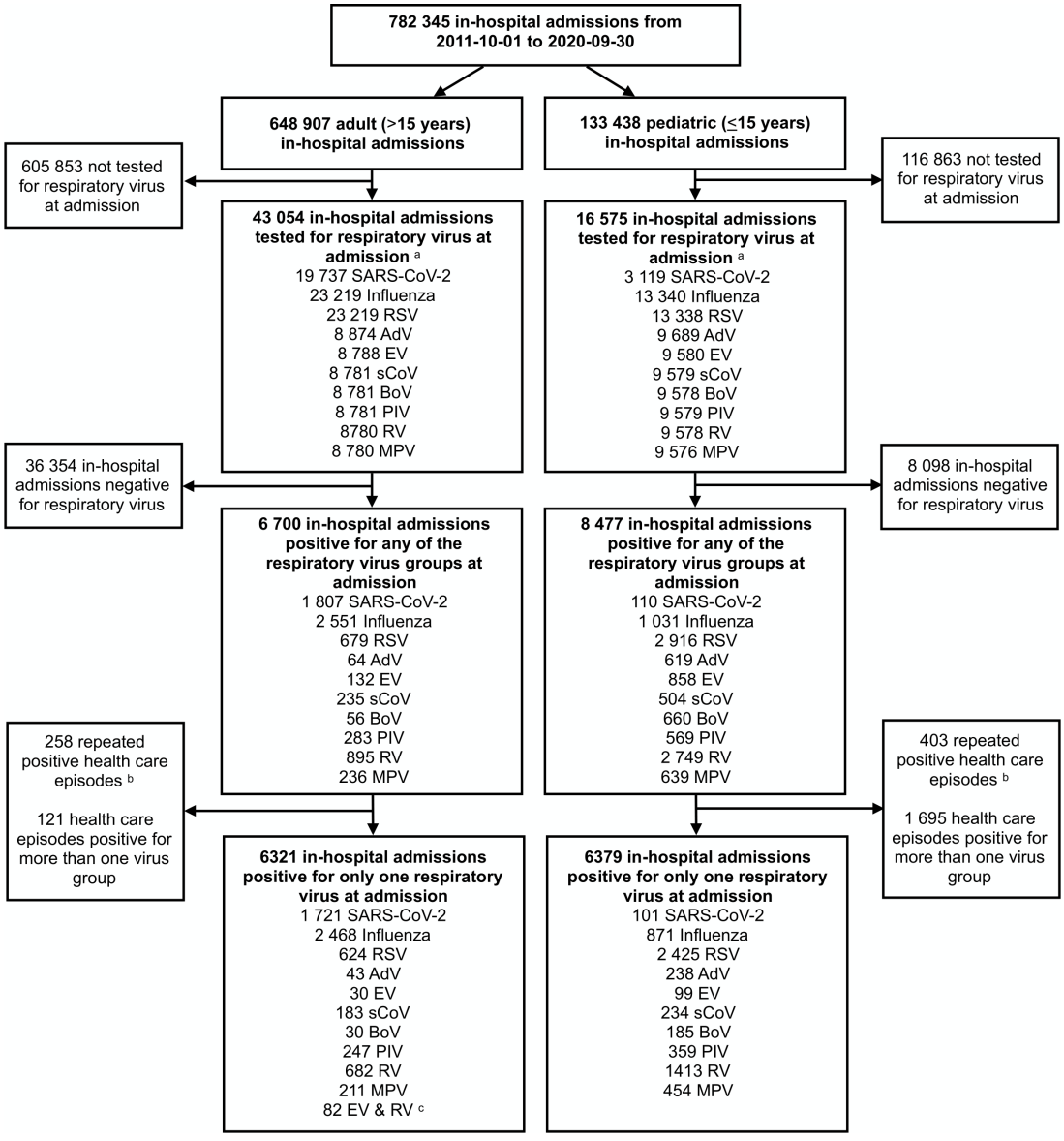

Figure 1 Flow chart of adult and paediatric healthcare episodes in the study. [a]Admission defined as −24 to +48 hours in relation to the admission time point. [b]Repeated positive for same respiratory virus in respiratory sample within 3 months. [c]Eighty-two adult healthcare episodes with PCR unable to discriminate between rhinoviruses and enteroviruses due to cross reactivity in the PCR assay. These cases were included in the other viruses group but excluded from virus group-specific analyses. AdV, adenovirus; BoV, bocavirus; EV, enterovirus; MPV, metapneumoviruses; PIV, parainfluenzaviruses; RSV, respiratory syncytial virus; RV, rhinovirus; sCoV, seasonal coronavirus.

with influenza (median age 68 years (IQR 51–79), 48% male), RSV (median age 71 years (IQR 60–81), 44% male) and other viruses (median age 61 years (IQR 40–72), 56% male) (p<0.001) (table 1 and online supplemental eTable 4). After adjustment for sex and age, SARS-CoV-2 admission was associated with overweight and obesity, as well as lower CCI and ECI compared with influenza, RSV and other viruses (table 1). The only comorbidities that were over-represented among patients with SARS-CoV-2 compared with influenza, RSV or other viruses were diabetes and hypertension.

Patients with SARS-CoV-2 more often presented with normal white cell count (WCC), platelet count and creatinine values (table 1, online supplemental eTable 5 and eFigure 2). In sex-adjusted and age-adjusted analyses, SARS-CoV-2 was associated with tachypnoea and less often hypotension or tachycardia, compared with all other virus groups, and less often fever (temperature >38°C) compared with influenza (online supplemental eTable 6 and eFigure 3). The prediction model that included age, sex, BMI, comorbidity, laboratory parameters and vital signs performed better compared with the simpler models, mean AUROC 0.74 for SARS-CoV-2 versus influenza, 0.83 for SARS-CoV-2 versus RSV and 0.82 for SARS-CoV-2 versus other viruses (online supplemental eFigure 4 and eTable 7).

Paediatric SARS-CoV-2 in relation to other respiratory viruses

Children with SARS-CoV-2 were older, while the sex distribution was similar compared with other respiratory viruses: SARS-CoV-2 median age 7 years (IQR 1–12), 55% male; influenza median age 2 years (IQR 0–5), 56% male; RSV median age 0 years (IQR 0–1), 56% male; and RV median age 1 year (IQR 0–3), 58% male (p<0.001 and 0.80) (table 2). The proportion of patients with at least one comorbidity differed between the viruses, being 20% (20/101) in SARS-CoV-2, 23% (198/871)

Table 1 Baseline characteristics in the different virus groups of the adult cohort

	Virus group (no. of healthcare episodes)				SARS-CoV-2 versus influenza		SARS-CoV-2 versus RSV		SARS-CoV-2 versus other viruses	
Variable	SARS-CoV-2	Influenza	RSV	Other viruses	OR (95% CI)	aOR (95% CI)*	OR (95% CI)	aOR (95% CI)*	OR (95% CI)	aOR (95% CI)*
Baseline characteristics										
Male sex, n (%)	1010 (59)	1194 (48)	275 (44)	840 (56)	**1.51 (1.34 to 1.71)**	–	**1.80 (1.50 to 2.17)**	–	**1.13 (0.98 to 1.30)**	–
Age, median (IQR), years	58 (42–71)	68 (51–79)	71 (60–81)	61 (40–72)	–	–	–	–	–	–
Age categories, n (%)										
16–39	377 (22)	401 (16)	36 (6)	376 (25)	0.89 (0.72 to 1.09)	–	**2.34 (1.54 to 3.56)**	–	**0.61 (0.49 to 0.76)**	–
40–49	212 (12)	186 (8)	33 (5)	146 (10)	1.07 (0.84 to 1.38)	–	1.43 (0.92 to 2.23)	–	0.88 (0.67 to 1.15)	–
50–59	345 (20)	325 (13)	77 (12)	209 (14)	1.0 (ref)	–	1.0 (ref)	–	1.0 (ref)	–
60–69	334 (19)	404 (16)	130 (21)	285 (19)	**0.78 (0.63 to 0.96)**	–	**0.57 (0.42 to 0.79)**	–	**0.71 (0.56 to 0.90)**	–
70–79	209 (12)	546 (22)	167 (27)	323 (21)	**0.36 (0.29 to 0.45)**	–	**0.28 (0.20 to 0.38)**	–	**0.39 (0.31 to 0.50)**	–
≥80	244 (14)	606 (25)	181 (29)	169 (11)	**0.38 (0.31 to 0.47)**	–	**0.30 (0.22 to 0.41)**	–	0.87 (0.67 to 1.14)	–
BMI, median (IQR), kg/m²§	27 (24–31)	25 (22–29)	25 (22–29)	24 (21–28)	–	–	–	–	–	–
BMI categories, n (%)										
Normoweight (18.5–24.9)†	529 (31)	1062 (43)	276 (44)	711 (47)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Underweight (<18.5)	44 (3)	137 (6)	39 (6)	128 (9)	**0.65 (0.44 to 0.96)**	0.67 (0.45 to 1.01)	**0.58 (0.35 to 0.94)**	0.59 (0.35 to 1.01)	**0.46 (0.31 to 0.69)**	**0.47 (0.31 to 0.69)**
Overweight (25–29.9)	638 (37)	772 (31)	176 (28)	412 (27)	**1.66 (1.42 to 1.95)**	**1.55 (1.31 to 1.83)**	**1.89 (1.50 to 2.38)**	**1.68 (1.31 to 2.15)**	**2.08 (1.74 to 2.49)**	**2.06 (1.71 to 2.47)**
Obese (≥30)	510 (30)	497 (20)	132 (21)	257 (17)	**2.06 (1.74 to 2.45)**	**1.91 (1.60 to 2.28)**	**2.01 (1.56 to 2.59)**	**1.67 (1.28 to 2.19)**	**2.67 (2.19 to 3.27)**	**2.66 (2.16 to 3.26)**
CCI, median (IQR), points	1 (0–2)	1 (0–3)	2 (1–4)	2 (1–3)	–	–	–	–	–	–
CCI categories, n (%)										
0–1	1199 (70)	1252 (51)	235 (38)	580 (38)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
2–4	386 (22)	890 (36)	284 (46)	675 (45)	**0.45 (0.39 to 0.52)**	**0.52 (0.45 to 0.61)**	**0.27 (0.22 to 0.33)**	**0.39 (0.31 to 0.49)**	**0.28 (0.24 to 0.32)**	**0.24 (0.20 to 0.28)**
≥5	136 (8)	326 (13)	105 (17)	253 (17)	**0.44 (0.35 to 0.54)**	**0.50 (0.40 to 0.62)**	**0.25 (0.19 to 0.34)**	**0.36 (0.27 to 0.49)**	**0.26 (0.21 to 0.33)**	**0.22 (0.17 to 0.28)**
ECI, median (IQR), points	0 (0–6)	5 (0–11)	9 (3–14)	7 (3–12)	–	–	–	–	–	–
ECI categories, n (%)										
≤0	947 (55)	809 (33)	104 (17)	352 (23)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
1–10	493 (29)	1005 (41)	255 (41)	613 (41)	**0.42 (0.36 to 0.48)**	**0.46 (0.40 to 0.54)**	**0.21 (0.16 to 0.27)**	**0.28 (0.21 to 0.36)**	**0.30 (0.25 to 0.35)**	**0.26 (0.21 to 0.31)**
≥11	281 (16)	654 (26)	265 (42)	543 (36)	**0.37 (0.31 to 0.43)**	**0.43 (0.36 to 0.52)**	**0.12 (0.09 to 0.15)**	**0.17 (0.13 to 0.23)**	**0.19 (0.16 to 0.23)**	**0.15 (0.12 to 0.18)**
Comorbidities, n (%)										
Diabetes mellitus‡	392 (23)	467 (19)	107 (17)	247 (16)	**1.26 (1.09 to 1.47)**	**1.46 (1.24 to 1.71)**	**1.43 (1.13 to 1.81)**	**1.87 (1.46 to 2.41)**	**1.51 (1.26 to 1.80)**	**1.54 (1.28 to 1.85)**

Continued

Table 1 Continued

Variable	Virus group (no. of healthcare episodes)				SARS-CoV-2 versus influenza		SARS-CoV-2 versus RSV		SARS-CoV-2 versus other viruses	
	SARS-CoV-2	Influenza	RSV	Other viruses	OR (95% CI)	aOR (95% CI)*	OR (95% CI)	aOR (95% CI)*	OR (95% CI)	aOR (95% CI)*
Hypertension‡	660 (38)	907 (37)	246 (39)	413 (27)	1.07 (0.94 to 1.22)	**1.68 (1.44 to 1.95)**	0.96 (0.79 to 1.15)	**2.10 (1.69 to 2.63)**	**1.65 (1.42 to 1.92)**	**1.95 (1.64 to 2.32)**
Cardiac disease‡	403 (23)	728 (29)	237 (38)	410 (27)	**0.73 (0.63 to 0.84)**	1.01 (0.86 to 1.18)	**0.50 (0.41 to 0.61)**	0.85 (0.68 to 1.06)	**0.82 (0.70 to 0.96)**	**0.80 (0.67 to 0.96)**
Chronic pulmonary disease‡	252 (15)	518 (21)	171 (27)	328 (22)	**0.65 (0.55 to 0.76)**	**0.79 (0.67 to 0.94)**	**0.45 (0.36 to 0.57)**	**0.66 (0.52 to 0.84)**	**0.62 (0.51 to 0.74)**	**0.63 (0.52 to 0.75)**
Chronic kidney failure‡	133 (8)	259 (10)	86 (14)	159 (11)	**0.71 (0.57 to 0.89)**	0.84 (0.67 to 1.05)	**0.52 (0.39 to 0.70)**	0.74 (0.54 to 1.00)	**0.71 (0.56 to 0.90)**	**0.70 (0.55 to 0.90)**
Malignancy‡	185 (11)	537 (22)	218 (35)	606 (40)	**0.43 (0.36 to 0.52)**	**0.46 (0.39 to 0.56)**	**0.22 (0.18 to 0.28)**	**0.27 (0.21 to 0.34)**	**0.18 (0.15 to 0.22)**	**0.17 (0.14 to 0.21)**
Immunosuppression‡	314 (18)	791 (32)	295 (47)	807 (54)	**0.47 (0.41 to 0.55)**	**0.50 (0.43 to 0.58)**	**0.25 (0.20 to 0.30)**	**0.30 (0.24 to 0.37)**	**0.19 (0.17 to 0.23)**	**0.18 (0.15 to 0.21)**
Any of the comorbidities above‡	1014 (59)	1754 (71)	513 (82)	1199 (80)	**0.58 (0.51 to 0.66)**	**0.72 (0.61 to 0.83)**	**0.31 (0.25 to 0.39)**	**0.54 (0.42 to 0.70)**	**0.37 (0.32 to 0.43)**	**0.27 (0.23 to 0.33)**

Bold values indicate statistical significance.
*Analyses were adjusted for age and sex.
†Nonweight defined as a BMI of 18.5–24.9, underweight <18.5, overweight 25–29.9, obese ≥30.
‡Based on ICD-10 codes from −5 years to +24 hours from admission time point. See list of ICD-10 codes for each comorbidity category in online supplemental table 1.
§Variable containing missing values, which were imputed using multiple imputation by chained equations by predictive mean modelling. Descriptive data were calculated for each of the 50 imputed datasets, and the mean of each descriptive statistics is presented.
aOR, adjusted OR; BMI, body mass index; CCI, Charlson Comorbidity Index; ECI, Elixhauser Comorbidity Index; RSV, respiratory syncytial virus.

in influenza and 16% (396/2425) in RSV, while it was higher (28%–43%) for the other viruses (p<0.001). Immunosuppression was the most prevalent comorbidity among patients with SARS-CoV-2 (10/101, 10%). Chronic respiratory disease, congenital malformations and chromosomal abnormalities were more prevalent in all nine other virus groups compared with SARS-CoV-2 (p<0.001). In the SARS-CoV-2 paediatric cohort, 41% presented with a temperature >38°C and 24% with increased respiratory rate or desaturation, which was lower than in all other virus groups (online supplemental eFigure 3). In children with SARS-CoV-2, the median LOS was 3 days (IQR 1–8), the 30-day and 90-day mortality were both 1% (1/101), 4% (4/101) were admitted to ICU and acute kidney injury based on modified KDIGO stage 1 criteria was detected in 8% (8/101).

Clinical outcomes in SARS-CoV-2 compared with other respiratory viruses among adults

The LOS in patients with SARS-CoV-2 was longer (6 days (IQR 3–11)) compared with influenza (4 days (IQR 2–7)), RSV (5 days (IQR 3–9)) and other viruses (4 days (IQR 2–8)). The 30-day mortality was 13% among patients with SARS-CoV-2 as compared with 5% for influenza, 7% for RSV and 5% for the other virus group (table 3 and figure 2). The adjusted 30-day mortality HR (aHR) for SARS-CoV-2 was 4.43 (95% CI 3.51 to 5.59), 3.81 (95% CI 2.72 to 5.34) and 3.46 (95% CI 2.61 to 4.60) compared with influenza, RSV and other viruses, respectively. This resulted in the following standardised 30-day survival probabilities: SARS-CoV-2 0.83 (95% CI 0.79 to 0.87), influenza 0.96 (95% CI 0.95 to 0.97), RSV 0.95 (95% CI 0.94 to 0.97) and other viruses 0.96 (95% CI 0.95 to 0.97) (figure 2). The SARS-CoV-2 30-day mortality was 16% (154/981) from February to April 2020 and 8% (62/740) from May to September 2020. For patients with SARS-CoV-2 admitted from May to September 2020, the 30-day mortality aHR compared with influenza, RSV and other viruses were 3.09 (95% CI 2.22 to 4.30), 3.00 (95% CI 1.95 to 4.62) and 2.60 (95% CI 1.79 to 3.80) (online supplemental eTable 8). In analyses stratified by age, the 30-day mortality aHR for patients aged 70 years or older was 5.41 (95% CI 4.17 to 7.00), 4.93 (95% CI 3.37 to 7.23) and 5.03 (95% CI 3.61 to 7.01) in patients with SARS-CoV-2 compared with influenza, RSV and other viruses, respectively (online supplemental eTable 9). The corresponding aHR for patients aged 50–69 years were 2.16 (95% CI 1.31 to 3.57), 1.71 (95% CI 0.81 to 3.60) and 2.07 (95% CI 1.13 to 3.79). The excess mortality in patients with SARS-CoV-2 occurred in the first 30 days, and in adjusted analyses, there was no significantly increased mortality risk among patients with SARS-CoV-2 compared with the other virus groups from day 31 to day 90 (online supplemental eFigure 5).

Patients with SARS-CoV-2 had an increased risk of ICU admission as compared with influenza and other viruses (table 3). The ICU LOS was longer, and the 30-day mortality after ICU admission was higher for patients with SARS-CoV-2 compared with all other virus groups. SARS-CoV-2 was associated with an increased risk of pulmonary embolism, adjusted ORs 5.26 (95% CI 3.34 to 8.28), 6.23 (95% CI 2.82 to 13.76) and 3.34 (95% CI 2.06 to 5.40) compared with influenza, RSV and other viruses, respectively, and also AMI compared with influenza and RSV, aHR 1.42 (95% CI 1.18 to 1.71) and 1.58 (95% CI 1.19 to 2.09), respectively. A decreased risk of AKI was observed for SARS-CoV-2 compared with influenza. For HOB, no significant risk differences were observed in adjusted analyses. The increased SARS-CoV-2 HR for mortality and ICU

Table 2 Baseline characteristics and outcomes of the paediatric cohort

Baseline characteristics	Virus group (no. of healthcare episodes)										
	SARS-CoV-2 (101)	Influenza (871)	RSV (2425)	RV (1413)	EV (99)	PIV (359)	MPV (454)	sCoV (234)	AdV (238)	BoV (185)	P value*
Male sex	55 (55)	484 (56)	1 362 (56)	824 (58)	57 (58)	196 (55)	267 (59)	138 (59)	141 (59)	109 (59)	0.80
Age at admission, median (IQR), years	7 (1–12)	2 (0–5)	0 (0–1)	1 (0–3)	1 (0–3)	1 (0–2)	2 (0–3)	1 (0–4)	1 (1–3)	1 (1–2)	<0.001
Age categories, n (%)											
<1	25 (25)	242 (28)	1 673 (69)	606 (43)	44 (44)	150 (42)	135 (30)	93 (40)	52 (22)	45 (24)	<0.001
1–4	20 (20)	377 (43)	689 (28)	535 (38)	38 (38)	159 (44)	242 (53)	92 (39)	151 (63)	125 (68)	<0.001
5–15	56 (55)	252 (29)	63 (3)	272 (19)	17 (17)	50 (14)	77 (17)	49 (21)	35 (15)	15 (8)	<0.001
Comorbidities, n (%)											
Prematurity and perinatal diseases†	3 (3)	61 (7)	201 (8)	168 (12)	3 (3)	45 (13)	59 (13)	36 (15)	27 (11)	25 (14)	<0.001
Chronic cardiac disease†	2 (2)	27 (3)	41 (2)	75 (5)	3 (3)	22 (6)	24 (5)	18 (8)	10 (4)	11 (6)	<0.001
Chronic respiratory disease†	7 (7)	170 (20)	512 (21)	414 (29)	18 (18)	101 (28)	161 (35)	70 (30)	53 (22)	63 (34)	<0.001
Congenital malformations and chromosomal abnormalities†	7 (7)	107 (12)	220 (9)	263 (19)	10 (10)	65 (18)	106 (23)	53 (23)	38 (16)	36 (19)	<0.001
Solid tumour†	4 (4)	16 (2)	17 (1)	64 (5)	3 (3)	10 (3)	8 (2)	13 (6)	6 (3)	6 (3)	<0.001
Haematological malignancy†	3 (3)	19 (2)	15 (1)	68 (5)	1 (1)	7 (2)	12 (3)	15 (6)	3 (1)	6 (3)	<0.001
Immunosuppression†	10 (10)	66 (8)	57 (2)	177 (13)	5 (5)	24 (7)	29 (6)	37 (16)	20 (8)	29 (16)	<0.001
Any of the comorbidities above†	20 (20)	198 (23)	396 (16)	494 (35)	16 (16)	110 (31)	157 (35)	100 (43)	66 (28)	68 (37)	<0.001
Outcomes											
Length of stay, median (IQR), days	3 (1–8)	3 (2–4)	4 (2–6)	3 (2–5)	3 (2–5)	3 (2–5)	4 (2–6)	3 (2–6)	3 (2–4)	3 (2–5)	<0.001
Mortality, n (%)											
30 days‡	1 (1)	6 (1)	3 (0)	15 (1)	0 (0)	2 (1)	0 (0)	6 (3)	2 (1)	4 (2)	<0.001
90 days§	1 (1)	6 (1)	4 (0)	24 (2)	0 (0)	3 (1)	2 (0)	7 (3)	4 (2)	6 (3)	<0.001
ICU											
ICU admitted, n (%)‡	4 (4)	32 (4)	146 (6)	61 (4)	4 (4)	21 (6)	35 (8)	19 (8)	16 (7)	16 (9)	0.009
Length of ICU stay, median (IQR), days§	6 (4–6)	1 (0–4)	1 (0–3)	1 (0–2)	0 (0–0)	0 (0–2)	1 (0–4)	1 (0–2)	0 (0–1)	1 (0–3)	0.102
Acute kidney injury, n (%)‡	8 (8)	49 (6)	43 (2)	102 (7)	3 (3)	9 (3)	20 (4)	24 (10)	12 (5)	14 (8)	<0.001
Hospital-onset bacteraemia, n (%)‡	2 (2)	11 (1)	14 (1)	29 (2)	0 (0)	3 (1)	6 (1)	9 (4)	6 (3)	2 (1)	<0.001

*Comparison of all virus groups using χ^2 test for nominal and Kruskal-Wallis test for continuous variables.
†Based on ICD-10 codes from −5 years to +24 hours from admission time point. See list of ICD-10 codes for each comorbidity category in online supplemental eTable 1.
‡Analysis restricted to patients with a minimum of 30-day follow-up time, that is, patients admitted until 1 September 2020. SARS-CoV-2 (99), influenza (871), RSV (2 425), RV (1380), EV (98), PIV (359), MPV (454), sCoV (234), AdV (238) and BoV (184).
§Analysis restricted to patients with a minimum of 90-day follow-up time, that, patients admitted until 1 July 2020. SARS-CoV-2 (81), influenza (871), RSV (2425), RV (1356), EV (98), PIV (359), MPV (454), sCoV (234), AdV (238) and BoV (183).
¶Analysis restricted to ICU-admitted patients. SARS-CoV-2 (4), influenza (32), RSV (146), RV (61), EV (4), PIV (21), MPV (35), sCoV (19), AdV (16) and BoV (16).
AdV, adenovirus; BoV, bocavirus; EV, enterovirus; ICU, intensive care unit; MPV, metapneumovirus; PIV, parainfluenzavirus; RSV, respiratory syncytial virus; RV, rhinovirus; sCoV, seasonal coronaviruses.

admission were consistent across sensitivity analyses (online supplemental eTable 8), but with more favourable outcomes for the SARS-CoV-2 cohort admitted from May to September 2020 as compared with February–April 2020. Adjusted mortality HRs were similar for analyses based on complete cases and multiple imputed data, and no significant difference was observed in 30-day mortality, 90-day mortality or ICU admission between 2015–2020 and 2011–2014 for influenza, RSV as well as other viruses (online supplemental eTable 10 and eFigure 6).

DISCUSSION

This observational study of 12 700 adult and paediatric admissions to a University Hospital in Stockholm, Sweden, showed that although SARS-CoV-2 was associated with younger age in adults and an overall lower comorbidity burden, there was a marked increased risk of 30-day mortality, ICU admission, ICU mortality and pulmonary embolism compared with other respiratory viruses. The mortality increase was most pronounced among the elderly and was attenuated during the later part of the study period, possibly due to improved management of patients with SARS-CoV-2. These findings were consistent across sensitivity analyses, considering potential change over time in diagnostic procedures, patient management and clinical presentation at admission, which highlights important differences in healthcare demands between SARS-CoV-2 and other respiratory viruses.

Combined with data from others studies, our results indicate substantial differences in outcomes for patients with SARS-CoV-2 compared with other respiratory viruses. In a study from Denmark where SARS-CoV-2 positive patients were compared with influenza, the unadjusted 30-day mortality was three times higher for patients with SARS-CoV-2, and a study from the UK

Table 3 Outcomes for SARS-CoV-2 versus influenza, RSV and other viruses in the adult cohort

	Virus group (no. of healthcare episodes)				SARS-CoV-2 versus influenza		SARS-CoV-2 versus RSV		SARS-CoV-2 vs other viruses	
Outcome variable	**SARS-CoV-2 (1721)**	**Influenza (2468)**	**RSV (624)**	**Other viruses (1508)**	**Unadjusted ratio (95% CI)**	**Adjusted ratio (95% CI)***	**Unadjusted ratio (95% CI)**	**Adjusted ratio (95% CI)***	**Unadjusted ratio (95% CI)**	**Adjusted ratio (95% CI)***
Length of stay, median (IQR)†	6 (3–11)	4 (2–7)	5 (3–9)	4 (2–8)	**1.53 (1.43 to 1.64)**	**1.47 (1.37 to 1.58)**	**1.38 (1.25 to 1.53)**	**1.37 (1.22 to 1.53)**	**1.35 (1.25 to 1.46)**	**1.30 (1.19 to 1.41)**
Mortality										
Days 0–30, n (%)§¶	216 (13)	121 (5)	45 (7)	76 (5)	**2.73 (2.18 to 3.41)**	**4.43 (3.51 to 5.59)**	**1.83 (1.33 to 2.53)**	**3.81 (2.72 to 5.34)**	**2.62 (2.02 to 3.40)**	**3.46 (2.61 to 4.60)‡**
Days 0–90, n (%)§**	235 (15)	192 (8)	65 (10)	148 (10)	**2.02 (1.67 to 2.44)‡**	**3.34 (2.73 to 4.08)‡**	**1.48 (1.13 to 1.95)‡**	**3.13 (2.34 to 4.18)‡**	**1.56 (1.27 to 1.92)‡**	**2.28 (1.82 to 2.86)‡**
Days 31–90, n (%)§††	24 (2)	71 (3)	20 (4)	73 (5)	**0.57 (0.36 to 0.91)‡**	0.98 (0.60 to 1.59)	**0.50 (0.28 to 0.91)**	1.14 (0.59 to 2.19)	**0.33 (0.21 to 0.52)‡**	0.62 (0.37 to 1.03)
Intensive care										
ICU admission, n (%)§¶	294 (17)	244 (10)	72 (12)	167 (11)	**1.70 (1.43 to 2.01)‡**	**1.46 (1.22 to 1.75)‡**	**1.52 (1.18 to 1.97)‡**	**1.28 (0.96 to 1.69)‡**	**1.53 (1.27 to 1.85)‡**	**1.32 (1.07 to 1.64)‡**
ICU length of stay, median (IQR)†††	4 (1–11)	1 (0–3)	1 (0–4)	1 (0–4)	**2.17 (1.64 to 2.85)**	**2.24 (1.68 to 3.00)**	**2.48 (1.70 to 3.56)**	**1.99 (1.32 to 3.00)**	**3.22 (2.42 to 4.26)**	**2.80 (2.02 to 3.87)**
30-day mortality in ICU-admitted cohort, n (%)§††	77 (26)	47 (19)	18 (25)	23 (14)	1.42 (0.98 to 2.03)	**2.40 (1.58 to 3.64)**	1.04 (0.62 to 1.74)	**2.87 (1.55 to 5.33)**	**2.07 (1.30 to 3.30)**	**3.75 (2.15 to 6.54)**
Acute myocardial injury, n (%)§¶	253 (15)	250 (10)	71 (11)	151 (10)	**1.25 (1.05 to 1.49)‡**	**1.42 (1.18 to 1.71)‡**	1.14 (0.88 to 1.49)‡	**1.58 (1.19 to 2.09)‡**	**1.34 (1.09 to 1.63)‡**	1.17 (0.94 to 1.46)‡
Acute kidney injury, n (%)§¶	286 (17)	333 (14)	82 (13)	228 (15)	0.93 (0.80 to 1.09)	**0.77 (0.65 to 0.91)‡**	1.14 (0.89 to 1.46)‡	1.11 (0.85 to 1.45)‡	**0.94 (0.79 to 1.11)**	0.86 (0.70 to 1.05)‡
Pulmonary embolism, n (%)‡‡§§	83 (5)	32 (1)	8 (1)	35 (2)	**3.93 (2.63 to 6.01)**	**5.26 (3.34 to 8.28)**	**3.97 (2.03 to 8.96)**	**6.23 (2.82 to 13.76)**	**2.14 (1.45 to 3.24)**	**3.34 (2.06 to 5.40)**
Hospital-onset bacteraemia, n (%)§¶	92 (5)	46 (2)	16 (3)	52 (3)	**1.86 (1.30 to 2.65)**	1.43 (0.98 to 2.09)	1.55 (0.91 to 2.64)	1.27 (0.70 to 2.31)‡	1.14 (0.81 to 1.61)	1.10 (0.73 to 1.64)

Bold values indicate statistical significance.
*The regression models were adjusted for age, sex, BMI, diabetes, hypertension, chronic cardiac disease, chronic respiratory disease, chronic kidney disease, malignancy and immunosuppression.
†Analysed by a negative binomial regression model.
‡Violation of proportional hazards assumption (Schoenfeld individual test, p value <0.05).
§Analysed by a Cox regression model.
¶Analysis restricted to patients with a minimum of 30-day follow-up time, that is, patients admitted until 1 September 2020. SARS-CoV-2 (1692), influenza (2 468), RSV (624) and other viruses (1490).
**Analysis restricted to patients with a minimum of 90-day follow-up time, that is, patients admitted until 1 July 2020. SARS-CoV-2 (1 588), influenza (2 465), RSV (624) and other viruses (1478).
††Analysis restricted to ICU-admitted patients. SARS-CoV-2 (294), influenza (244), RSV (72) and other viruses (167).
‡‡Analysed by a logistic regression model.
§§Analysis restricted to the current healthcare episode, with only finished episodes included. SARS-CoV-2 (1719), influenza (2468), RSV (624) and other viruses (1508).
BMI, body mass index; ICU, intensive care unit; RSV, respiratory syncytial virus.

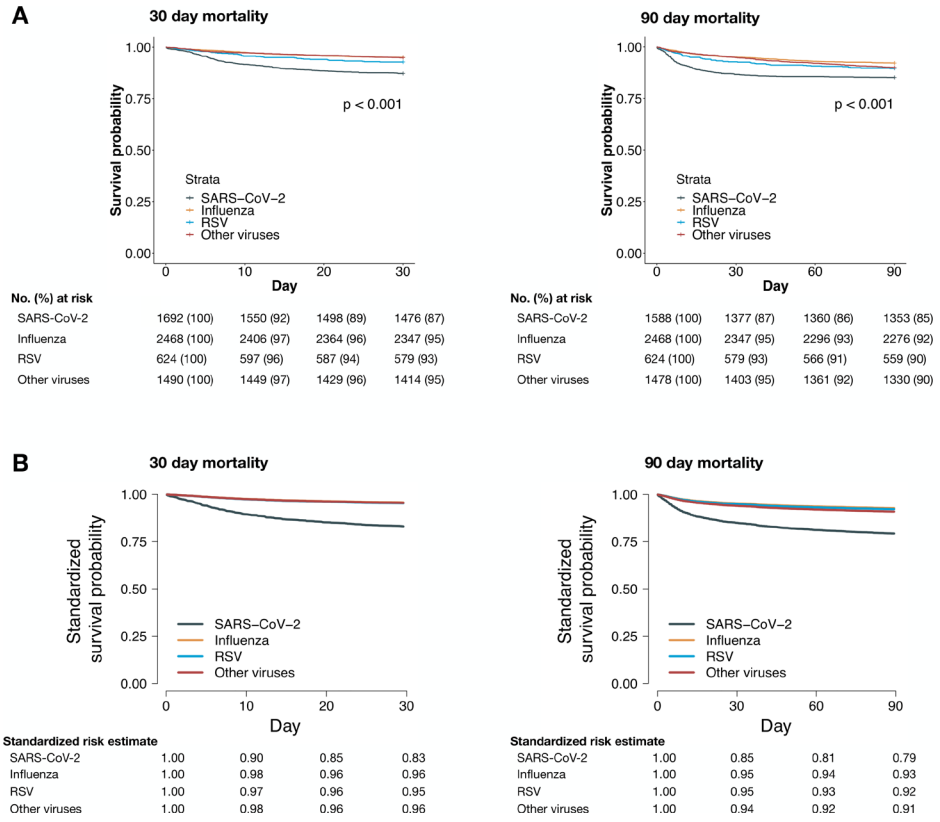

Figure 2 Unadjusted Kaplan-Meier curves (A) and standardised survival function curves (B) for mortality by virus group. (A) Unadjusted Kaplan-Meier curves and risk tables for 30-day (left) and 90-day (right) mortality. P value represents result of significance testing using log-rank tests. The 30-day mortality Kaplan-Meier curves for the influenza and other viruses groups overlap. (B) Complete case-based standardised survival functions for 30-day (left) and 90-day (right) mortality. For 30-day mortality, complete data were available for 1272 SARS-CoV-2, 2220 influenza, 591 RSV and 1386 other viruses healthcare episodes. For 90-day mortality, complete data were available for 1194 SARS-CoV-2, 2118 influenza, 555 RSV and 1315 other viruses healthcare episodes. The survival functions were all standardised and adjusted for sex, age, BMI category, diabetes, hypertension, cardiac disease, respiratory disease, chronic kidney disease and malignancy as presented in table 1. The 30-day mortality curves for the influenza, RSV and other viruses groups overlap. AdV, adenovirus; BMI, body mass index; BoV, bocavirus; EV, enterovirus; MPV, metapneumoviruses; PIV, parainfluenzaviruses; RSV, respiratory syncytial virus; RV, rhinovirus; sCoV, seasonal coronavirus.

comparing two cohorts of ICU patients admitted with diagnostic codes of COVID-19 and other respiratory viruses reported an almost doubled mortality in the COVID-19 cohort.[19 20] A French study based on diagnostic codes reported a three times increased in-hospital mortality in 89 530 patients with COVID-19 compared with 45 819 patients with influenza, with the risk increase being more pronounced for patients aged ≥60 years.[21]

A study based on data from the US Department of Veterans Affairs healthcare system, with 95% of patients being male, reported a five times higher mortality in patients with COVID-19 compared with influenza.[22] These studies corroborate our findings of a threefold and fourfold increased 90-day and 30-day mortality in patients with SARS-CoV-2 compared with patients hospitalised with influenza or RSV.

Previous case series have demonstrated cardiac and circulatory complications in COVID-19, with reported acute myocardial injury incidence between 7% and 40% in hospitalised patients and 2%–9% developing pulmonary embolism.[23–27] However, acute cardiovascular events have also been associated with influenza and RSV, and previous studies based on diagnostic codes reported higher proportion of influenza patients developing cardiovascular complications as compared with patients with COVID-19.[21 28–30] In our study, SARS-CoV-2 was associated with an increased risk of troponin-defined acute myocardial injury compared with influenza and RSV, and there was a 3–5 fold increased risk of pulmonary embolism in patients with SARS-CoV-2 compared with the other virus groups. This is concordant with studies from Denmark, France and the USA that reported an increased risk of thromboembolic events in patients with SARS-CoV-2 compared with influenza.[19 21 30] Yet, retrospective studies comparing thromboembolic and cardiac events in patients with COVID-19 compared with other viruses might suffer from bias since they rely on ICD-10 discharge codes as well as likely differential testing strategies in patients with COVID-19. In our study, troponin T was assessed in 65% of SARS-CoV-2 compared with 27% and 29% in influenza and RSV patients. Also, elevated troponin might indicate myocarditis that has been associated with COVID-19, rather than ischaemic heart disease.[21]

Male sex, overweight, obesity, diabetes and hypertension were more common in patients with SARS-CoV-2 compared with the other respiratory viruses, which strengthen evidence that these are risk factors for hospitalisation with COVID-19.[5 6 31 32] Yet, the overall comorbidity burden of patients with SARS-CoV-2, as measured by CCI and ECI scores, were lower. Patients with SARS-CoV-2 in our study were somewhat younger than reported from other cohorts, which was adjusted for in the analyses.[19 30] The younger age distribution could partly be explained by differences in the affected patient populations and hospitalisation patterns during the SARS-CoV-2 pandemic.

Few studies have directly compared with what extent clinical presentation at admission can be used to differentiate SARS-CoV-2 from other respiratory viruses, and current evidence is based on studies of small sample sizes.[4 5 33 34] Patients with SARS-CoV-2 more often presented with normal haemodynamic measurements, WCC, platelet count and creatinine values and were more often tachypnoeic. No clear difference was observed for saturation, measured as worst peripheral capillary oxygen saturation (SpO2), or when accounting for oxygen treatment using the SpO2/fraction of inspired oxygen (FiO2) ratio. Prediction models of increased complexity, although increasing in performance, demonstrated limited virus discriminating capability, for example, model 3 resulted in 60% sensitivity and 80% specificity to differentiate between SARS-CoV-2 and influenza. Future prospective studies should assess if symptoms and laboratory tests such as ferritin and interleukin-6 are associated with SARS-CoV-2 compared with other viruses.[35]

Among children, no difference in sex distribution was observed, whereas patients with SARS-CoV-2 were older compared with other respiratory viruses in line with a previous study that reported patients with COVID-19 to be older compared with patients with influenza.[21] Paediatric patients with SARS-CoV-2 were more likely to present without an increased body temperature and dyspnoea, possibly due to more frequent screening of SARS-CoV-2 compared with other respiratory viruses. Paediatric patients with SARS-CoV-2 had a lower prevalence of chronic respiratory diseases and congenital malformations compared with other viruses. Severe outcomes were rare in the paediatric cohort.

Strengths of our study include the large study size, similar strict inclusion criteria regardless of viral infections and ample access to clinical data that enabled thorough analyses of clinical phenotype as well as adjustment for confounding. The strict virological inclusion criteria increased the internal validity of the study and reduced the risk of including patients transferred from other hospitals to the Karolinska University Hospital, which was more common during the SARS-CoV-2 epidemic. Even though the study population comprised a large portion of consecutively admitted patients with viral infections in the Stockholm region during a 9-year period, to verify generalisability, confirmation of the findings is warranted in patients from other geographical regions and hospitals. Data were collected from patient records, which depends on correct entry by healthcare staff. Yet, the risk of misclassification is likely independent of type of respiratory infections, and we restricted our analysis to routinely collected data. To increase internal validity, we restricted the analyses to episodes positive for only one virus, which might hamper the generalisability to all patients positive with respiratory virus. Yet, this would have minor impact on the results among adults since we only excluded 1.8% of admissions. Indications for SARS-CoV-2 testing might have differed compared with other respiratory viruses. Yet, the results were robust in sensitivity analyses restricting the study population to patients with fever, reduced oxygen saturation or increased respiratory rate at admission. However, the results for other viruses than SARS-CoV-2, influenza and RSV need to be interpreted with caution due to differential testing indications. Finally, due to the pandemic, hospitalisation patterns in different age groups, length of stay and ICU admission criteria might differ compared with the earlier study period.

CONCLUSION

SARS-CoV-2 is associated with an increased risk of mortality, ICU admission and pulmonary embolism in hospitalised patients compared with influenza, RSV and other respiratory viruses. Although SARS-CoV-2 is associated with specific patient and clinical characteristics at admission compared with other respiratory viruses, substantial overlap precludes discrimination based on these characteristics.

Author affiliations
[1]Department of Microbiology, Tumor and Cell Biology, Karolinska Institute, Stockholm, Sweden
[2]Department of Infectious Diseases, Karolinska University Hospital, Stockholm, Sweden
[3]Department of Medicine Solna, Karolinska Institute, Stockholm, Sweden
[4]Department of Physiology and Pharmacology, Karolinska Institute, Stockholm, Sweden
[5]Department of Perioperative Medicine and Intensive Care, Karolinska University Hospital, Stockholm, Sweden
[6]Department of Clinical Microbiology, Karolinska University Hospital, Stockholm, Sweden
[7]Department of Women's and Children's Health, Karolinska Institute, Stockholm, Sweden
[8]Department of Paediatric Infectious Diseases, Astrid Lindgren's Hospital, Karolinska University Hospital, Stockholm, Sweden

Contributors PH, HT and SvdW had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: PH, AF, MB, AT and PN. Acquisition, analysis or interpretation of data: PH, JKV, SvdW, HT, ARM, JM, RD and OH. Drafting of the manuscript: PH nd PN. Critical revision of the manuscript for important intellectual content: all authors. Statistical analysis: PH and FG. Additional contributions: none.

Funding The work was supported by grants from the Swedish Innovation Agency (Vinnova) and Region Stockholm. PH was supported by Karolinska Institutet (combined clinical studies and PhD training programme). JKV was supported by Region Stockholm (combined clinical residency and PhD training programme).

Disclaimer The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review or approval of the manuscript; and decision to submit the manuscript for publication.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study was approved by the Regional Ethical Review Board in Stockholm (Dnr 2018/1030-31, COVID-19 research amendment Dnr 2020–01385).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available. Data from deidentified electronic health records are not freely available due to protection of the personal integrity of the participants.

ORCID iD
Pontus Hedberg http://orcid.org/0000-0003-3153-098X

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eSupplement

Clinical phenotypes and outcomes of SARS-CoV-2, influenza, RSV and seven other respiratory viruses: a retrospective study using complete hospital data

eMethods 1. Data collection and variable definition

PCR methodology: Diagnostics for a narrow respiratory virus panel including influenza A virus (IAV), influenza B virus (IBV), and respiratory syncytial virus (RSV) were performed using in-house realtime PCR assays until 14 September 2014 when they were replaced by the Simplexa Flu A/B \& RSV Kit (Focus Diagnostics Inc., Cypress (CA, USA)), which were in turn replaced by the Xpert Flu/RSV ((Cepheid, Solna, Sweden) from 15 May 2019 [1]. An extended respiratory virus panel, which included the four seasonal CoVs (229E, NL63, OC43, and HKU1) as well as adenovirus (AdV), enterovirus (EV), human bocavirus (BoV), human metapneumovirus (MPV), parainfluenza virus (PIV) 1, 2, and 3, and rhinovirus (RV), was performed using in-house realtime PCR assays (Tiveljung-Lindell) until 5 November 2017 when they were replaced by the Allplex Respiratory Panels 2 and 3 (Seegene Inc., Seoul (South Korea)). The Allplex assay does not discriminate between the *Betacoronaviruses* OC43 and HKU1 but includes PIV4.

Age on admission: Approximated by the available data on year and month of birth, with the 1st of each month set as a fictional day of birth. In total, 200 individuals were excluded from the final analysis due to missing information on age. In all analyses adjusted for age, age was treated as a categorical variable (16-39, 40-49, 50-59, 60-69, 70-79 and $\geq$80).

Body Mass Index (BMI): Based on the latest height and weight data available and was only calculated for the adult ($\geq$16 years) study cohort. Normoweight was defined as a BMI of 18.5-24.9 kg/m^2, underweight <18.5 kg/m^2, overweight 25-29.9 kg/m^2, obese $\geq$30 kg/m^2. In all analyses adjusted for BMI, BMI was treated as a categorical variable (underweight, normoweight, overweight and obese).

Charlson Comorbidity Index (CCI) score and Elixhauser Comorbidity Index (ECI): Charlson Comorbidity Index (CCI) score and Elixhauser Comorbidity Index (ECI) score were calculated using the comorbidity package in R based on the Quan et al. and van Walraven version, respectively [2–4]. The CCI and ECI scores were presented both as continuous and categorical variables (CCI: 0-1, 2-4, $\geq$5 and ECI: $\leq$0, 1-10, $\geq$11) in comparisons between the different virus groups.

The specific comorbidities in the adult as well as the pediatric study cohort were defined accoirding to supplemental table 1 and 2. Each comorbidity category was defined as having any of the comorbidity specific ICD-10 codes recorded from five years before until 24 hours after the admission time point.

For laboratory parameters and vital signs, the worst value (either highest or lowest) -24 hours to +24 hours from admission was used. Cut-offs for body temperature, respiratory rate, heart rate, blood pressure and WBC count were based on the Systemic Inflammatory Response Syndrome (SIRS) and Confusion-Respiration-Blood pressure-age 65 (CRB 65) scoring systems. For respiratory rate, the highest respiratory rate was recorded for each healthcare episode, irrespective of oxygen supplementation or not. **The lowest**

peripheral saturation, SpO2, was recorded for each healthcare episode, irrespective of oxygen supplementation or not and the worst SpO2/FiO2 was calculated by extracting the level of oxygen supplementation (L/min) and using the same FiO2 assumptions as in Valik et al.[5] SpO2/FiO2 ratio cutoffs were based on SpO2/FiO2 ratios corresponding to a previously published conversion equation.[6]

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eTable 1. ICD-10 codes for adult comorbidities

Comorbidity category	ICD-10 codes [a]
Diabetes mellitus	E10-E14
Hypertension	I10-I15
Cardiac disease	I11, I13, I2, I42, I50, I6
Chronic pulmonary disease	J40-J47
Chronic kidney failure	N18-N19
Malignancy	C
Immunosuppression	C0, C1, C2, C30-C34, C37-C39, C4, C5, C6, C7, C80, D70-D72, D73.0, D80, D81 D83, D84, Z94.0, Z94.1, Z94.2, Z94.3, Z94.4, Z94.6, Z94.8, Z94.9, B2, Z21, N18

[a] The shortest text-pattern for identification of included ICD-10 codes are listed

eTable 2. ICD-10 codes for pediatric comorbidities

Comorbidity category	ICD-10 codes [a]
Prematurity and perinatal diseases	P07, P27, P29
Chronic cardiac diseases	I05-I08, I20-I22, I24-I28, I34-I37, I42, I44-I50
Chronic respiratory diseases	J43-J47, J6, J7, J80-J84, J92-J96, J98-J99
Congenital malformations and chromosomal abnormalities	Q0, Q2, Q30-Q34, Q60-Q64, Q9
Solid tumor	C0-C7, C80
Haematooncological malignancy	C81-C96
Immunosuppression	D70-D72, D73.0, D80, D81 D83, D84, Z51.0, Z51.1, Z94.0, Z94.1, Z94.2, Z94.3, Z94.4, Z94.6, Z94.8, Z94.9, B2, Z21

[a] The shortest text-pattern for identification of included ICD-10 codes are listed

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eMethods 2. Definition of patient outcomes

Length of stay (LOS) was defined as the time from first admission time point (either emergency department arrival or direct hospital admission) until discharge time point. LOS was compared between the virus groups using a negative binomial regression model, with ratios presented as rate ratios with 95% confidence interval.

30-day mortality *was defined as all-cause mortality from the admission time point and 30 days forward, irrespective of discharge status. 30-day mortality was analyzed as a time-to-event outcome. Complete outcome ascertainment was possible as data on mortality in the electronic health records is continuously updated based on the Swedish population register. Persons with a follow-up time less than 30 days were excluded from the analysis. Ratios were presented as hazard ratios with 95% confidence interval.*

90-day mortality *was defined as all-cause mortality from the admission time point and 90 days forward, irrespective of discharge status. 90-day mortality was analyzed as a time-to-event outcome. Complete outcome ascertainment was possible as data on mortality in the electronic health records is continuously updated based on the Swedish population register. Persons with a follow-up time less than 90 days were excluded from the analysis. Ratios were presented as hazard ratios with 95% confidence interval.*

31-90-day mortality was defined as all-cause mortality from 30 days after the admission time point and 60 days forward, irrespective of discharge status. 31-*90-day mortality was analyzed as a time-to-event outcome. Complete outcome ascertainment was possible as data on mortality in the electronic health records is continuously updated based on the Swedish population register. Persons with a follow-up time less than 90 days were excluded from the analysis. Ratios were presented as hazard ratios with 95% confidence interval.*

ICU-admission *was defined as care units able to provide inotropic and non-invasive or invasive respiratory treatment, including an intensive care unit (ICU), intermediate care unit (IMU) or extracorporeal membrane oxygenation (ECMO) unit. The IMU can provide noninvasive ventilation, invasive/non-invasive monitoring and have higher nurse staffing compared to general wards, but less compared to the ICU. ICU-admission was analyzed as a time-to-event outcome with 30 days follow-up time, and patients were censored upon hospital discharge or death. Persons with a follow-up time less than 30 days were excluded from the analysis. Ratios were presented as hazard ratios with 95% confidence interval.*

LOS at ICU was defined as the time from ICU admission time point until ICU discharge time point. If several ICU-admissions during the same healthcare episode were recorded the total time only in the ICU was calculated. LOS at ICU was compared between the virus groups using a negative binomial regression model, with ratios presented as rate ratios with 95% confidence interval.

30-day mortality in ICU-admitted cohort was defined as all-cause mortality from the first ICU admission time point and 30 days forward, irrespective of discharge status. ICU *30-day mortality was analyzed as a time-to-event outcome. Complete outcome ascertainment was possible as data on mortality in the electronic health records is continuously updated based on the Swedish population register. Persons with a follow-up time less than 30 days were excluded from the analysis. Ratios were presented as hazard ratios with 95% confidence interval.*

Acute Myocardial Injury (AMI) was defined as cardiac Troponin T > 50 ng/ml within 30 days after admission time point. AMI was analyzed as a time-to-event outcome with 30 days follow-up time, and patients were censored upon hospital discharge or death. Persons with a follow-up time less than 30 days were excluded from the analysis. Ratios were presented as hazard ratios with 95% confidence interval.

Acute Kidney Injury (AKI) was based on the KDIGO criteria but without the urine volume measurements due to inconsistent recording in the EHR system. No staging of the AKI was done, thus the criteria used for AKI was >1.5 times baseline within the last 7 days or an increase in serum creatinine by 26.5 µmol/L more within the last 48 hours. The baseline creatinine was defined as the best reported value reported within 90 days prior to the admission time point and if no such value was reported prior to hospital admission, the first creatinine measurement was used. AKI was analyzed as a time-to-event outcome with 30 days follow-up time, and patients were censored upon hospital discharge or death. Persons with a follow-up time less than 30 days were excluded from the analysis. Ratios were presented as hazard ratios with 95% confidence interval.

Pulmonary embolism (PE) was defined as an I26 ICD-10 code registered within the healthcare episode, irrespective of length of the health care episode. PE was analyzed using a logistic regression model and ratios were presented as odds ratios with 95% confidence interval.

Hospital Onset Bacteremia (HOB) was defined as significant findings in blood cultures taken >48 hours after hospital admission, with the same definition of significant bloodstream infections as described by Valik et al.[5] HOB was analyzed as a time-to-event outcome with 30 days follow-up time, and patients were censored upon hospital discharge or death. Persons with a follow-up time less than 30 days were excluded from the analysis. Ratios were presented as hazard ratios with 95% confidence interval.

eMethods 3. Handling of missing data

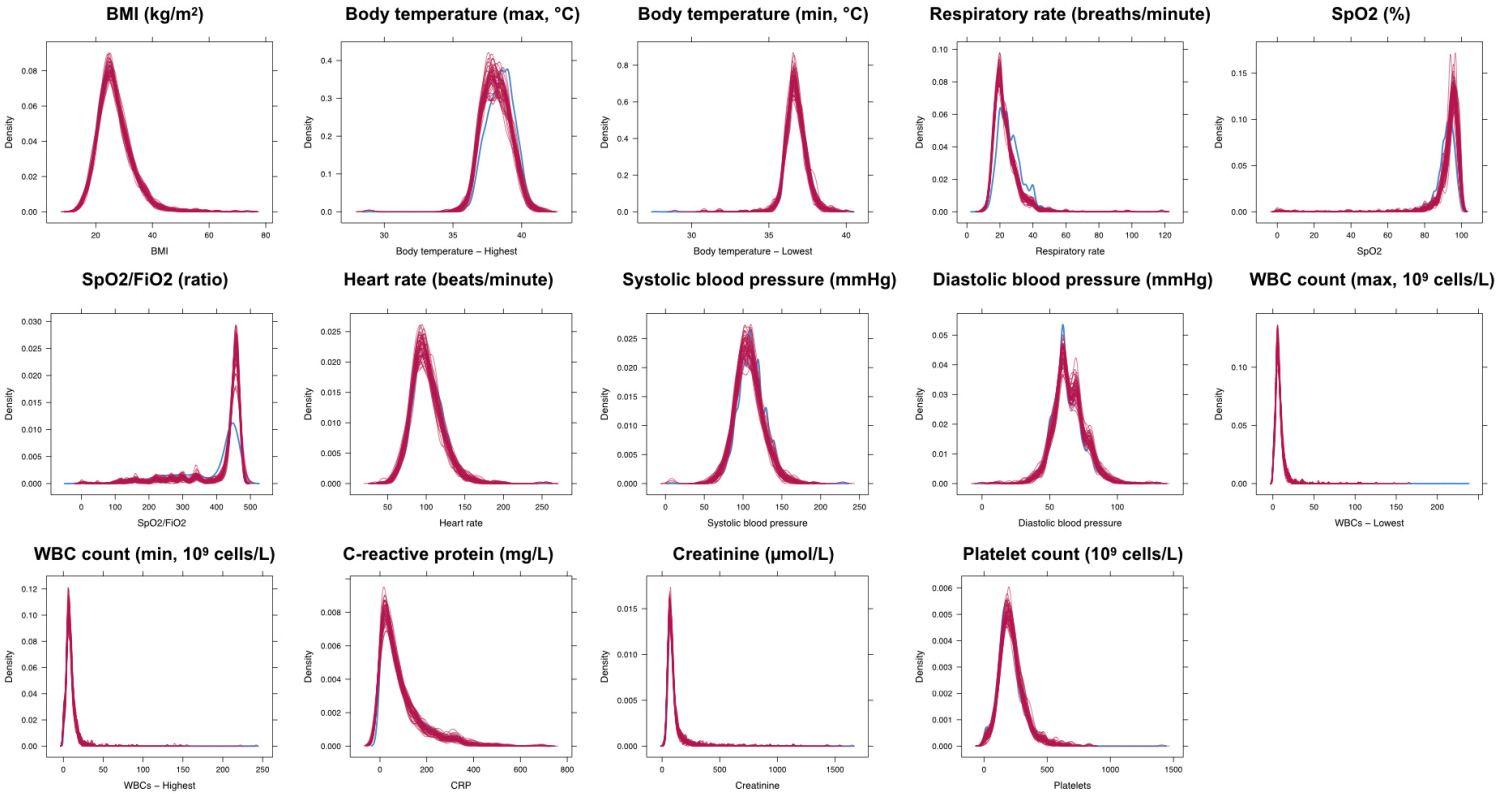
Missing data for BMI, body temperature, respiratory rate, SpO2, SpO2/FiO2, Heart rate, systolic and diastolic blood pressure, WBC count, CRP, creatinine value and platelet count at admission were considered missing at random (MAR) and multiple imputation by chained equations (MICE) were used with predictive mean matching in the mice R-package.[7] All other baseline characteristic and outcome variables were used as predictor variables. Fifty imputed datasets (m = 50) were created with 20 iterations (maxit = 20) and the final estimates in the analyses were obtained using Rubin's rules.[8] The number and proportions of missing data points per variable are available in eTable 3. The density distributions of the 50 imputed datasets compared to the complete case data are found in eFigure 1.

eTable 3. Number and proportion of missing data per variable in the adult study cohort

Variable	Number of (%) missing values
BMI	813 (13)
Body temperature	292 (5)
Respiratory rate	463 (7)
SpO2	300 (5)
SpO2/FiO2	306 (5)
Heart rate	300 (5)
Systolic blood pressure	324 (5)
Diastolic blood pressure	337 (5)
WBC count	360 (6)
C-reactive protein	375 (6)
Creatinine	453 (7)
Platelet count	386 (6)

Abbreviations: BMI: Body Mass Index, SpO2: Peripheral capillary oxygen saturation, FiO2: Fraction of inspired oxygen, WBC: White blood cells

eFigure 1. Density distributions after multiple imputation by chained equations



Note: Distribution of 50 imputed dataset variables (magenta lines) compared to complete case dataset (blue line). All variables were imputed using predictive mean matching (PMM) and 20 iterations were performed for each imputed dataset.

Abbreviations: BMI: Body Mass Index, SpO2: Peripheral capillary oxygen saturation, FiO2: Fraction of inspired oxygen, WBC: White blood cells

eTable 4. Baseline characteristics for all ten virus groups of the adult cohort (Complete case analysis)

Variable	Virus group (No. health care episodes)										
	SARS-CoV-2 (1721)	**Influenza (2468)**	**RSV (624)**	**RV (682)**	**EV (30)**	**PIV (247)**	**MPV (211)**	**SCoV (183)**	**AdV (43)**	**BoV (30)**	***P*-value [a]**
Male sex, n (%)	1010 (59)	1194 (48)	275 (44)	406 (60)	16 (53)	137 (56)	100 (47)	99 (54)	24 (56)	15 (50)	<0.001
Age, median (IQR), years	58 (42-71)	68 (51-79)	71 (60-81)	58 (37-71)	55 (35-67)	65 (50-75)	66 (51-75)	60 (39-73)	42 (27-60)	64 (50-75)	<0.001
16-39, n (%)	377 (22)	401 (16)	36 (6)	198 (29)	12 (40)	37 (15)	28 (13)	47 (26)	21 (49)	4 (13)	
40-49, n (%)	212 (12)	186 (8)	33 (5)	61 (9)	2 (7)	24 (10)	19 (9)	21 (11)	5 (12)	4 (13)	
50-59, n (%)	345 (20)	325 (13)	77 (12)	96 (14)	3 (10)	36 (15)	35 (17)	22 (12)	5 (12)	3 (10)	
60-69, n (%)	334 (19)	404 (16)	130 (21)	123 (18)	7 (23)	56 (23)	42 (20)	28 (15)	8 (19)	7 (23)	<0.001
70-79, n (%)	209 (12)	546 (22)	167 (27)	140 (21)	4 (13)	57 (23)	53 (25)	42 (23)	3 (7)	10 (33)	
≥80, n (%)	244 (14)	606 (25)	181 (29)	64 (9)	2 (7)	37 (15)	34 (16)	23 (13)	1 (2)	2 (7)	
BMI, median (IQR), kg/m²	27 (24-31)	25 (22-29)	25 (22-29)	24 (21-28)	24 (21-27)	24 (21-28)	26 (22-30)	25 (22-28)	25 (23-28)	24 (20-28)	<0.001
Normoweight, n (%)	393 (30)	955 (43)	261 (44)	316 (51)	14 (50)	106 (45)	82 (41)	69 (39)	18 (46)	14 (52)	
Underweight, n (%)	29 (2)	122 (5)	37 (6)	61 (10)	2 (7)	25 (11)	9 (5)	13 (7)	2 (5)	2 (7)	
Overweight, n (%)	490 (38)	695 (31)	166 (28)	151 (24)	7 (25)	71 (30)	55 (28)	61 (35)	10 (26)	6 (22)	<0.001
Obese, n (%)	380 (29)	450 (20)	127 (21)	97 (16)	5 (18)	32 (14)	53 (27)	32 (18)	9 (23)	5 (19)	
N/A, n (%)	429 (25)	246 (10)	33 (5)	57 (8)	2 (7)	13 (5)	12 (6)	8 (4)	4 (9)	3 (10)	
CCI-score, median (IQR), points	1 (0-2)	1 (0-3)	2 (1-4)	2 (1-3)	2 (0-3)	2 (1-3)	2 (1-4)	2 (1-3)	0 (0-2)	3 (2-6)	<0.001
0-1, n (%)	1199 (70)	1252 (51)	235 (38)	261 (38)	13 (43	96 (39)	68 (32)	71 (39)	31 (72)	5 (17)	<0.001

Variable	SARS-CoV-2 (1721)	Influenza (2468)	RSV (624)	RV (682)	EV (30)	PIV (247)	MPV (211)	SCoV (183)	AdV (43)	BoV (30)	*P*-value [a]
2-4, n (%)	386 (22)	890 (36)	284 (46)	305 (45)	11 (37)	115 (47)	104 (49)	77 (42)	9 (21)	16 (53)	
≥5, n (%)	136 (8)	326 (13)	105 (17)	116 (17)	6 (20)	36 (15)	39 (18)	35 (19)	3 (7)	9 (30)	<0.001
ECI-score, median (IQR), points	0 (0-6)	5 (0-11)	9 (3-14)	7 (3-12)	3 (0-12)	7 (3-12)	9 (3-13)	6 (3-12)	0 (0-6)	10 (5-16)	<0.001
≤0, n (%)	947 (55)	809 (33)	104 (17)	158 (23)	12 (40)	50 (20)	45 (21)	37 (20)	27 (63)	2 (7)	
1-10, n (%)	493 (29)	1005 (41)	255 (41)	264 (39)	8 (27)	113 (46)	82 (39)	87 (48)	10 (23)	13 (43)	<0.001
≥11, n (%)	281 (16)	654 (26)	265 (42)	260 (38)	10 (33)	84 (34)	84 (40)	59 (32)	6 (14)	15 (50)	
Diabetes mellitus, n (%) [b]	392 (23)	467 (19)	107 (17)	105 (15)	3 (10)	37 (15)	55 (26)	27 (15)	2 (5)	8 (27)	<0.001
Hypertension, n (%) [b]	660 (38)	907 (37)	246 (39)	170 (25)	6 (20)	75 (30)	87 (41)	49 (27)	1 (2)	11 (37)	<0.001
Cardiac disease, n (%) [b]	403 (23)	728 (29)	237 (38)	178 (26)	6 (20)	69 (28)	73 (35)	52 (28)	5 (12)	9 (30)	<0.001
Chronic pulmonary disease, n (%) [b]	252 (15)	518 (21)	171 (27)	146 (21)	5 (17)	49 (20)	55 (26)	42 (23)	2 (5)	7 (23)	<0.001
Chronic kidney failure, n (%) [b]	133 (8)	259 (10)	86 (14)	73 (11)	3 (10)	21 (9)	30 (14)	20 (11)	1 (2)	5 (17)	<0.001
Malignancy, n (%) [b]	185 (11)	537 (22)	218 (35)	282 (41)	11 (37)	110 (45)	75 (36)	64 (35)	11 (26)	18 (60)	<0.001
Immunosuppression, n (%) [b]	314 (18)	791 (32)	295 (47)	366 (54)	14 (47)	135 (55)	105 (50)	103 (56)	17 (40)	21 (70)	<0.001
Any of the comorbidities above, n (%) [b]	1014 (59)	1754 (71)	513 (82)	541 (79)	21 (70)	204 (83)	177 (84)	151 (83)	17 (40)	27 (90)	<0.001

a Comparison of all virus groups using Chi-square test for nominal and Kruskal-Wallis test for continuous variables
b See eTable 1 for corresponding ICD-10 codes for each comorbidity category.

Abbreviations: SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, RSV: Respiratory syncytial virus, RV: Rhinovirus, EV: Enterovirus, PIV: Parainfluenzaviruses, MPV: Metapneumoviruses, sCoV: Seasonal coronavirus, AdV: Adenovirus, BoV: Bocavirus, CCI: Charlson Comorbidity Index, ECI: Elixhauser Comorbidity Index

eTable 5. Vital signs and laboratory parameters at admission for the adult study cohort (Complete case analysis)

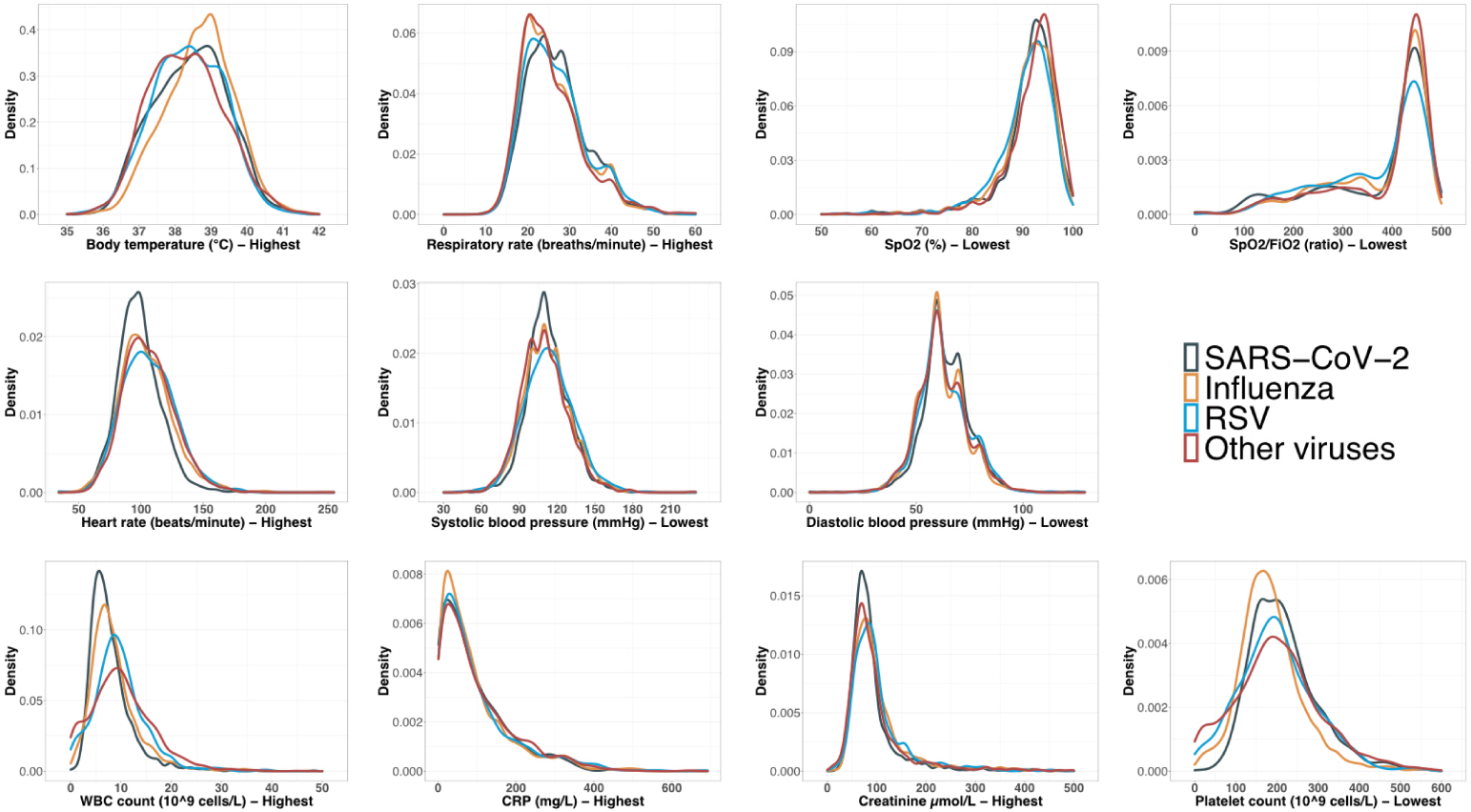
Variable	Virus group (No. health care episodes)									
	SARS-CoV-2 (1721)	**Influenza (2468)**	**RSV (624)**	**RV (682)**	**EV (30)**	**PIV (247)**	**MPV (211)**	**SCoV (183)**	**AdV (43)**	**BoV (30)**
Vital signs [a]					**median** IQR prop. (%) tested					
Temperature, °C [b]	**38.5** 37.7-39.2 *91*	**38.7** 38.0-39.3 *97*	**38.4** 37.7-39.1 *98*	**38.2** 37.6-39.0 *97*	**38.0** 37.6-39.5 *100*	**38.4** 37.6-39.0 *98*	**38.5** 37.6-39.1 *98*	**38.3** 37.4-38.9 *98*	**38.6** 37.8-39.2 *100*	**38.0** 37.4-38.8 *100*
Respiratory rate, breaths/min [b]	**26** 22-31 *90*	**24** 20-30 *94*	**25** 20-30 *95*	**24** 20-30 *92*	**22** 20-24 *100*	**24** 20-30 *92*	**25** 22-32 *94*	**24** 20-30 *92*	**21** 20-28 *93*	**24** 20-30 *93*
SpO2, % [c, d]	**92** 90-95 *91*	**92** 89-95 *97*	**92** 88-94 *98*	**93** 90-96 *97*	**94** 92-95 *100*	**93** 89-95 *97*	**92** 89-94 *97*	**94** 91-96 *98*	**95** 93-97 *100*	**93** 89-95 *100*
SpO2/FiO2, ratio [c]	**433** 297-448 *91*	**429** 310-448 *96*	**419** 297-448 *98*	**438** 339-452 *97*	**443** (431-452) *100*	**433** 308-448 *97*	**429** 281-448 *97*	**445** 349-457 *98*	**452** 438-460 *100*	**443** 298-452 *93*
Heart rate, beats/min [b]	**98** 87-109 *91*	**102** 90-117 *97*	**105** 90-120 *98*	**105** 91-120 *97*	**106** 89-115 *100*	**104** 94-119 *97*	**105** 93-120 *97*	**100** 91-115 *98*	**107** 98-120 *100*	**105** 87-118 *100*
Systolic BP, mm Hg [c]	**110** 102-122 *90*	**110** 100-122 *96*	**112** 100-127 *98*	**108** 97-120 *96*	**107** 99-120 *100*	**110** 100-121 *98*	**110** 100-125 *97*	**110** 99-120 *99*	**110** 100-116 *91*	**109** 100-120 *100*
Diastolic BP, mm Hg [c]	**63** 58-70 *90*	**60** 55-70 *96*	**60** 56-70 *98*	**60** 55-70 *95*	**61** 56-70 *100*	**60** 55-70 *98*	**60** 56-70 *96*	**60** 56-70 *99*	**60** 58-70 *91*	**60** 53-70 *100*
Laboratory parameters [a]										
Highest WBC count, 10^9 cells/L	**6.9** 5.2-9.4 *89*	**7.7** 5.5-10.5 *96*	**9.1** 6.5-12.2 *97*	**10.1** 5.9-14.4 *96*	**10.4** 5.8-14.6 *97*	**8.8** 5.4-12.6 *97*	**8.6** 5.9-13 *96*	**10.0** 6.2-13.8 *97*	**9.4** 6.2-13.4 *98*	**11.5** 8.2-15.9 *97*
Lowest WBC count, 10^9 cells/L	**6.3** 4.6-8.6 *89*	**6.7** 4.7-9.1 *96*	**8.1** 5.4-10.6 *97*	**8.4** 5.0-12.5 *96*	**10.4** 5.5-13.2 *97*	**7.1** 4.5-10.3 *97*	**7.2** 4.9-10.5 *96*	**8.2** 4.8-11.6 *97*	**7.3** 5.5-12.1 *98*	**9.9** 6.3-11.7 *97*
C-reactive protein, mg/L [b]	**65** 27-133 *87*	**64** 28-125 *97*	**65** 28-133 *97*	**73** 34-149 *96*	**77** 17-123 *97*	**57** 25-143 *98*	**69** 33-144 *96*	**63** 20-131 *97*	**95** 43-162 *98*	**131** 64-241 *93*

Variable	SARS-CoV-2 (1721)	Influenza (2468)	RSV (624)	RV (682)	EV (30)	PIV (247)	MPV (211)	SCoV (183)	AdV (43)	BoV (30)
Creatinine, µmol/L [b]	**78** 63-97 *87*	**86** 67-118 *95*	**88** 68-117 *96*	**79** 62-105 *93*	**79** 64-105 *97*	**83** 67-105 *96*	**84** 67-121 *94*	**79** 62-105 *95*	**84** 63-95 *88*	**68** 51-115 *93*
Platelet count, 10^9 cells/L [b]	**204** 158-260 *89*	**176** 137-224 *95*	**195** 138-257 *97*	**201** 123-270 *96*	**218** 175-278 *93*	**184** 133-240 *97*	**189** 147-240 *96*	**206** 141-275 *97*	**214** 156-291 *98*	**181** 123-298 *97*

a Worst value -24 to +24 hours from admission time point for each parameter. Analysis based on complete case analysis.
b Highest reported value per healthcare episode
c Lowest reported value per healthcare episode
d Irrespective of oxygen supplementation status

Abbreviations: SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, RSV: Respiratory syncytial virus, RV: Rhinovirus, EV: Enterovirus, PIV: Parainfluenzaviruses, MPV: Metapneumoviruses, sCoV: Seasonal coronavirus, AdV: Adenovirus, BoV: Bocavirus, SpO2: Peripheral capillary oxygen saturation, FiO2: Fraction of inspired oxygen, BP: Blood pressure, WBC: White blood cells

eFigure 2. Density curves for vital signs and laboratory parameters



Note: Kernel density estimates of the laboratory parameter and vital sign distributions in the different virus groups per age category. Data based on complete case analysis.

Abbreviations: SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, RSV: Respiratory syncytial virus, SpO2: Peripheral capillary oxygen saturation, FiO2: Fraction of inspired oxygen, WBC: White blood cells, CRP: C-reactive protein

eTable 6. Laboratory parameters and vital signs in the different virus groups of the adult cohort

Variable	Virus group (No. healthcare episodes)				SARS-CoV-2 vs Influenza		SARS-CoV-2 vs RSV		SARS-CoV-2 vs other viruses	
	SARS-CoV-2	Influenza	RSV	Other viruses	OR (95% CI)	aOR (95% CI) [a]	OR (95% CI)	aOR (95% CI) [a]	OR (95% CI)	aOR (95% CI) [a]
Vital signs										
Body temperature, median (IQR), °C [b]	38.4 (37.7-39.1)	38.7 (38.0-39.3)	38.4 (37.7-39.1)	38.3 (37.5-39.0)	-	-	-	-	-	-
Body temperature categories, n (%)										
<36	103 (6)	95 (4)	26 (4)	77 (5)	1.14 (0.83-1.56)	1.26 (0.91-1.75)	1.55 (0.97-2.48)	**1.84 (1.13-2.99)**	1.38 (1.00-1.92)	1.40 (1.00-1.96)
36-38	575 (33)	605 (25)	224 (36)	599 (39)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
>38	1043 (61)	1768 (72)	374 (60)	832 (55)	**0.62 (0.54-0.72)**	**0.56 (0.48-0.65)**	1.09 (0.89-1.32)	1.01 (0.82-1.25)	**1.31 (1.12-1.52)**	**1.28 (1.09-1.50)**
Systolic blood pressure, median (IQR), mm Hg [b]	110 (101-121)	110 (100-122)	111 (100-126)	110 (98-120)	-	-	-	-	-	-
Diastolic blood pressure, median (IQR), mm Hg [b]	63 (58-70)	60 (55-70)	60 (56-70)	60 (55-70)	-	-	-	-	-	-
SBP/DBP categories, n (%)										
SBP <90 mm Hg or DBP ≤60 mm Hg	761 (44)	1390 (56)	337 (54)	812 (54)	**0.61 (0.54-0.70)**	**0.71 (0.62-0.81)**	**0.68 (0.56-0.82)**	0.86 (0.70-1.05)	**0.68 (0.59-0.78)**	**0.71 (0.61-0.82)**
Heart rate, median (IQR), beats/min [b]	97 (87-109)	102 (90-117)	105 (90-120)	105 (92-120)	-	-	-	-	-	-
Heart rate categories, n (%)										
>90	1134 (66)	1786 (72)	465 (75)	1156 (77)	**0.74 (0.64-0.85)**	**0.66 (0.58-0.77)**	**0.66 (0.53-0.81)**	**0.58 (0.44-0.72)**	**0.59 (0.50-0.69)**	**0.58 (0.49-0.68)**
Respiratory rate, median (IQR), breaths/min [b]	25 (21-30)	24 (20-30)	25 (20-30)	24 (20-30)	-	-	-	-	-	-
Respiratory rate categories, n (%)										
≤20	415 (24)	753 (31)	167 (27)	495 (33)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
21-29	783 (46)	1034 (42)	265 (43)	622 (41)	**1.37 (1.17-1.61)**	**1.53 (1.30-1.81)**	1.19 (0.94-1.50)	**1.57 (1.22-2.03)**	**1.50 (1.26-1.79)**	**1.51 (1.26-1.81)**
≥30	524 (30)	680 (28)	191 (31)	390 (26)	**1.40 (1.18-1.66)**	**1.64 (1.37-1.97)**	1.11 (0.86-1.42)	**1.52 (1.16-2.00)**	**1.60 (1.32-1.94)**	**1.60 (1.31-1.95)**
SpO2, median (IQR), % [b]	93 (90-95)	92 (89-95)	92 (88-94)	93 (90-95)	-	-	-	-	-	-
SpO2 categories, n (%)										
<90	401 (23)	670 (27)	204 (33)	340 (23)	**0.81 (0.67-0.97)**	1.04 (0.85-1.28)	**0.51 (0.39-0.67)**	0.83 (0.62-1.11)	1.19 (0.97-1.47)	1.23 (0.99-1.54)
90-94	811 (47)	1109 (45)	288 (46)	654 (43)	0.99 (0.83-1.18)	1.19 (0.99-1.45)	**0.73 (0.57-0.95)**	1.04 (0.80-1.36)	1.25 (1.04-1.51)	**1.28 (1.04-1.57)**

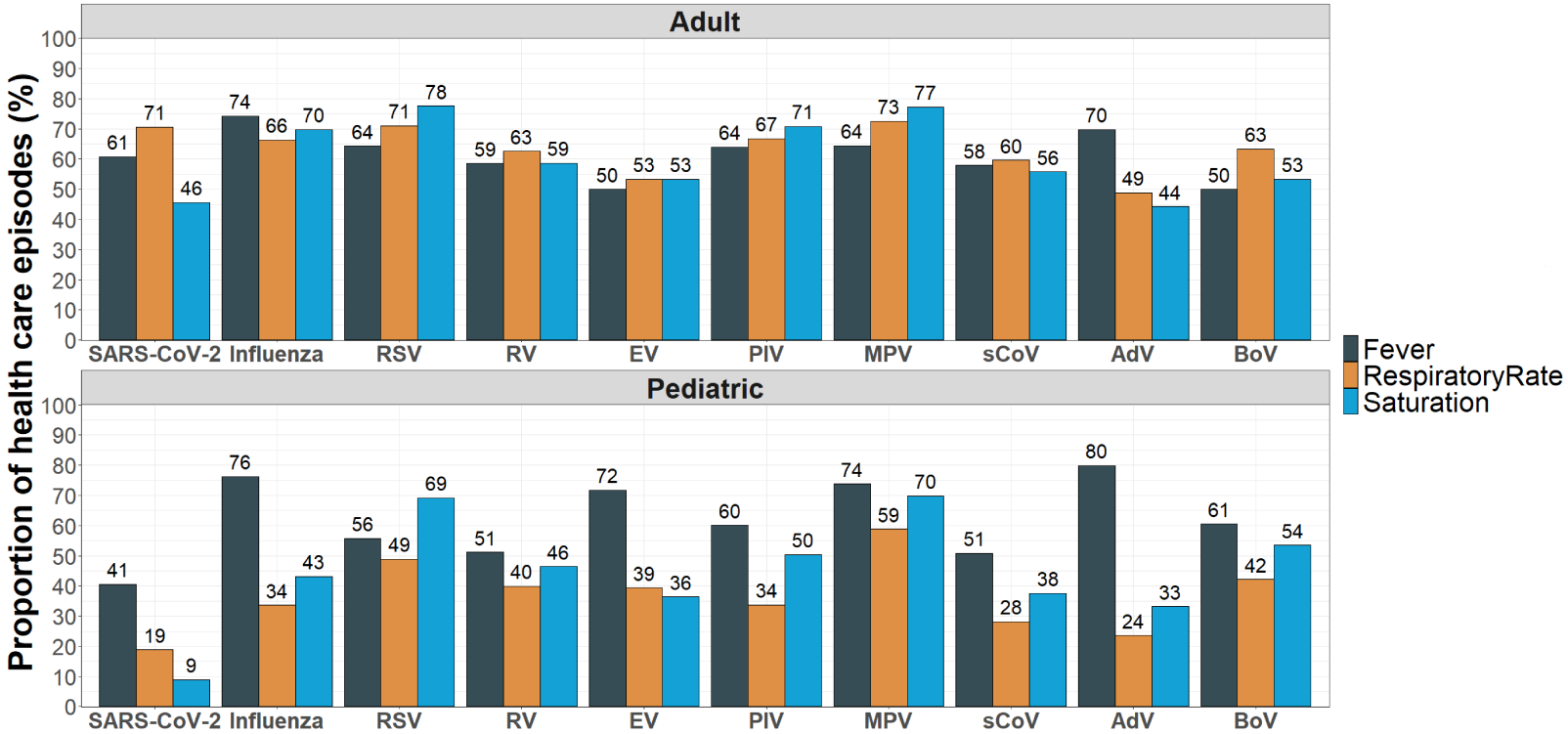
	Virus group (No. healthcare episodes)				SARS-CoV-2 vs Influenza		SARS-CoV-2 vs RSV		SARS-CoV-2 vs other viruses	
Variable	**SARS-CoV-2**	**Influenza**	**RSV**	**Other viruses**	**OR (95% CI)**	**aOR (95% CI) [a]**	**OR (95% CI)**	**aOR (95% CI) [a]**	**OR (95% CI)**	**aOR (95% CI) [a]**
≥95	509 (30)	688 (28)	132 (21)	515 (34)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
SpO2/FiO2, median (IQR), ratio [b]	438 (304-452)	432 (311-452)	419 (297-448)	438 (328-452)	-	-	-	-	-	-
SpO2/FiO2 categories, n (%)										
<235	241 (14)	287 (12)	95 (15)	189 (13)	**1.22 (1.01-1.47)**	**1.38 (1.13-1.68)**	0.88 (0.68-1.15)	1.02 (0.77-1.35)	1.15 (0.94-1.42)	1.14 (0.92-1.41)
235-315	213 (12)	332 (14)	82 (13)	169 (11)	0.93 (0.77-1.13)	1.03 (0.85-1.26)	0.91 (0.69-1.20)	1.06 (0.79-1.43)	1.15 (0.92-1.43)	1.14 (0.91-1.43)
>315	1267 (74)	1848 (75)	446 (71)	1150 (76)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Laboratory parameters										
CRP, median (IQR), mg/L [b]	63 (25-130)	64 (28-125)	65 (28-134)	68 (29-144)	-	-	-	-	-	-
CRP categories, n (%)										
<50	722 (42)	1004 (41)	259 (42)	562 (37)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
50-99	418 (24)	652 (26)	147 (24)	377 (25)	0.89 (0.76-1.05)	0.88 (0.75-1.04)	1.02 (0.80-1.30)	1.01 (0.78-1.30)	0.86 (0.72-1.04)	0.86 (0.72-1.04)
100-149	242 (14)	310 (13)	88 (14)	214 (14)	1.09 (0.89-1.33)	1.07 (0.86-1.32)	0.99 (0.74-1.33)	0.97 (0.71-1.32)	0.88 (0.71-1.10)	0.86 (0.68-1.08)
150-199	146 (8)	195 (8)	41 (6)	128 (9)	1.04 (0.81-1.32)	1.00 (0.78-1.28)	1.29 (0.88-1.90)	1.35 (0.90-2.02)	0.89 (0.68-1.16)	0.86 (0.65-1.12)
≥200	194 (11)	308 (13)	89 (14)	227 (15)	0.88 (0.71-1.09)	**0.78 (0.62-0.97)**	0.78 (0.58-1.05)	**0.69 (0.50-0.95)**	**0.67 (0.53-0.84)**	**0.65 (0.51-0.83)**
WBC count, median (IQR), 10^9 cells/L [b]	6.9 (5.1-9.5)	7.7 (5.5-10.5)	9.0 (6.5-12.2)	9.6 (5.9-13.7)	-	-	-	-	-	-
WBC count catgories, n (%)										
<4.0	179 (10)	258 (11)	75 (12)	228 (15)	0.85 (0.69-1.06)	0.80 (0.64-1.01)	**0.52 (0.38-0.71)**	**0.46 (0.33-0.65)**	**0.34 (0.27-0.33)**	**0.35 (0.28-0.44)**
4.0-8.8	1028 (60)	1265 (51)	222 (36)	447 (30)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
8.9-12.0	302 (18)	505 (21)	169 (27)	337 (22)	**0.74 (0.62-0.88)**	**0.76 (0.64-0.91)**	**0.38 (0.30-0.49)**	**0.39 (0.30-0.51)**	**0.39 (0.32-0.48)**	**0.39 (0.32-0.48)**
>12	212 (12)	440 (18)	158 (25)	496 (33)	**0.59 (0.49-0.72)**	**0.61 (0.50-0.74)**	**0.29 (0.22-0.37)**	**0.30 (0.22-0.39)**	**0.19 (0.15-0.23)**	**0.19 (0.16-0.24)**
Platelet count, median (IQR), 10^9 cells/L [b]	206 (159-262)	176 (137-224)	195 (139-257)	196 (133-261)	-	-	-	-	-	-
Platelet count categories, n (%)										
<150	333 (19)	814 (33)	178 (29)	459 (31)	**0.49 (0.42-0.57)**	**0.46 (0.39-0.54)**	**0.60 (0.48-0.74)**	**0.57 (0.45-0.72)**	**0.55 (0.46-0.65)**	**0.55 (0.46-0.65)**
Creatinine categories, n (%)										
>100	378 (22)	883 (36)	223 (36)	448 (30)	**0.50 (0.44-0.58)**	**0.53 (0.46-0.63)**	**0.51 (0.41-0.62)**	**0.69 (0.55-0.87)**	**0.66 (0.56-0.78)**	**0.63 (0.53-0.75)**

a Analyses were adjusted for age and sex
b Variable containing missing values, which were imputed using multiple imputation by chained equations (MICE) by Predictive Mean Modelling (PMM). Descriptive data were calculated for each of the 50 imputed datasets and the mean of each descriptive statistics is presented.

Abbreviations: SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, RSV: Respiratory syncytial virus, CI; Confidence Interval, OR: Odds Ratio, aOR: Adjusted Odds Ratio, BMI: Body Mass Index, CCI: Charlson Comorbidity Index, ECI: Elixhauser Comorbidity Index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SpO2: Peripheral capillary oxygen saturation, FiO2: Fraction of inspired oxygen, CRP: C-reactive protein, WBC: White blood cells

Hedberg P, *et al. Thorax* 2021;0:1–10. doi: 10.1136/thoraxjnl-2021-216949

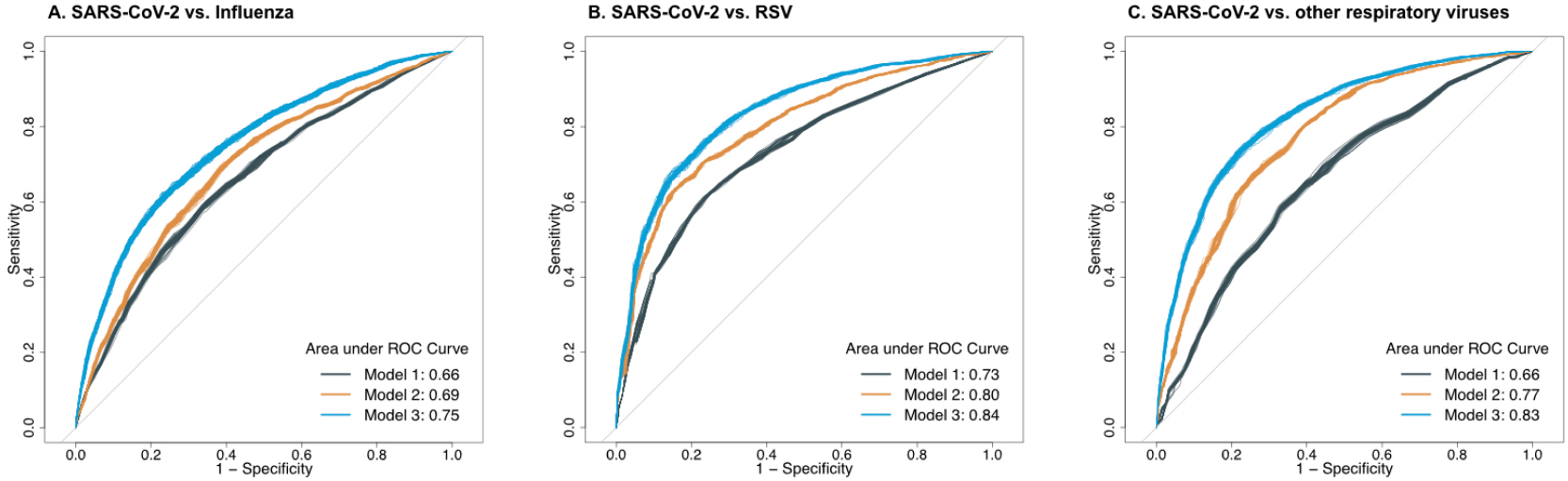
eFigure 3. Presence of fever and dyspnea at admission in the adult and pediatric study cohort by virus group



Note: Fever was defined as a body temperature of ≥38 °C on admission. Increased respiratory rate was defined as respiratory rate depending on age as follows: >60 for <12 months old, >40 for 1-3 year old, >34 for 4-5 year old, >30 for 6-12 year old, and >20 for >12 year old, on admission. Decreased Saturation was defined as a peripheral oxygen saturation of <95% on admission.

Abbreviations: SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, RSV: Respiratory syncytial virus, RV: Rhinovirus, EV: Enterovirus, PIV: Parainfluenzaviruses, MPV: Metapneumoviruses, sCoV: Seasonal coronavirus, AdV: Adenovirus, BoV: Bocavirus

eFigure 4. Virus prediction models for SARS-CoV-2 compared to influenza (A), RSV (B) and other respiratory viruses (C)



Note: Receiver operator characteristic (ROC) curves for model 1-3 in SARS-CoV-2 vs. Influenza (Panel A), SARS-CoV-2 vs. RSV (Panel B) and SARS-CoV-2 vs. other respiratory viruses (Panel C). Results from each of the 50 imputed datasets are shown as individual ROC-curves. The area under ROC curve estimate represents the mean of all 50 imputed datasets per model and virus group comparison. **Model 1:** Adjusted for age, sex and BMI. **Model 2:** Adjusted for age, sex BMI, diabetes, hypertension, chronic cardiac disease, chronic respiratory disease, chronic kidney disease, malignancy and immunosuppression. **Model 3:** Adjusted for age, sex, BMI, diabetes, hypertension, chronic cardiac disease, chronic respiratory disease, chronic kidney disease, malignancy, immunosuppression, CRP value, WBC count, platelet count, creatinine value, respiratory rate, SpO2/FiO2-ratio, body temperature, blood pressure and heart rate.

Abbreviations: SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, RSV: Respiratory syncytial virus, ROC: Receiver operator characteristic.

eTable 7. Logistic regression estimates for the virus prediction models

	SARS-CoV-2 vs. Influenza			SARS-CoV-2 vs. RSV			SARS-CoV-2 vs. other viruses		
	aOR (95% CI)			aOR (95% CI)			aOR (95% CI)		
Variable	**Model 1 [a]**	**Model 2 [b]**	**Model 3 [c]**	**Model 1 [a]**	**Model 2 [b]**	**Model 3 [c]**	**Model 1 [a]**	**Model 2 [b]**	**Model 3 [c]**
Baseline characteristics									
Male sex	**1.48 (1.30-1.69)**	**1.49 (1.30-1.70)**	**1.76 (1.52-2.04)**	**1.93 (1.58-2.36)**	**1.98 (1.59-2.46)**	**2.02 (1.59-2.55)**	1.13 (0.97-1.31)	1.14 (0.97-1.35)	1.11 (0.93-1.34)
Age at admission, years									
16-39	1.07 (0.86-1.32)	1.05 (0.84-1.31)	1.19 (0.94-1.51)	**3.03 (1.97-4.67)**	**2.91 (1.86-4.56)**	**3.82 (2.37-6.17)**	**0.74 (0.59-0.94)**	**0.58 (0.44-0.75)**	**0.73 (0.55-0.97)**
40-49	1.09 (0.84-1.40)	1.09 (0.84-1.41)	1.11 (0.84-1.46)	1.45 (0.92-2.27)	1.48 (0.92-2.37)	1.61 (0.98-2.65)	0.91 (0.69-1.21)	0.80 (0.59-1.10)	0.91 (0.65-1.28)
50-59	*1.0 (ref)*	*1.0 (ref)*	*1.0 (ref)*	*1.0 (ref)*	*1.0 (ref)*	*1.0 (ref)*	*1.0 (ref)*	*1.0 (ref)*	*1.0 (ref)*
60-69	**0.78 (0.63-0.97)**	**0.76 (0.61-0.95)**	**0.75 (0.60-0.95)**	**0.58 (0.42-0.81)**	**0.57 (0.40-0.81)**	**0.56 (0.39-0.81)**	**0.72 (0.57-0.92)**	**0.74 (0.56-0.96)**	0.78 (0.58-1.04)
70-79	**0.39 (0.31-0.49)**	**0.37 (0.29-0.46)**	**0.37 (0.29-0.47)**	**0.31 (0.22-0.43)**	**0.30 (0.21-0.43)**	**0.30 (0.20-0.44)**	**0.45 (0.35-0.58)**	**0.50 (0.38-0.67)**	**0.62 (0.45-0.85)**
≥80	**0.46 (0.37-0.57)**	**0.41 (0.32-0.52)**	**0.40 (0.31-0.52)**	**0.39 (0.28-0.54)**	**0.35 (0.24-0.50)**	**0.34 (0.23-0.51)**	1.12 (0.86-1.48)	1.03 (0.75-1.41)	1.19 (0.84-1.67)
BMI, kg/m^2 [d]									
Normoweight	*1.0 (ref)*	*1.0 (ref)*	*1.0 (ref)*	*1.0 (ref)*	*1.0 (ref)*	*1.0 (ref)*	*1.0 (ref)*	*1.0 (ref)*	*1.0 (ref)*
Underweight	0.67 (0.45-1.01)	0.69 (0.46-1.04)	0.68 (0.45-1.04)	0.59 (0.35-1.01)	0.61 (0.35-1.05)	**0.54 (0.30-0.94)**	**0.47 (0.31-0.69)**	**0.47 (0.31-0.71)**	**0.51 (0.33-0.78)**
Overweight	**1.55 (1.31-1.83)**	**1.41 (1.19-1.67)**	**1.44 (1.21-1.72)**	**1.68 (1.31-2.15)**	**1.32 (1.02-1.72)**	1.25 (0.94-1.66)	**2.06 (1.71-2.47)**	**1.74 (1.42-2.14)**	**1.68 (1.34-2.09)**
Obese	**1.91 (1.60-2.28)**	**1.68 (1.40-2.02)**	**1.62 (1.33-1.97)**	**1.67 (1.28-2.19)**	1.28 (0.96-1.71)	1.17 (0.86-1.61)	**2.66 (2.16-3.26)**	**2.01 (1.60-2.52)**	**1.77 (1.38-2.27)**
Comorbidities									
Diabetes mellitus [e]	-	**1.23 (1.03-1.46)**	**1.19 (0.99-1.43)**	-	**1.60 (1.20-2.13)**	**1.53 (1.13-2.06)**	-	**1.29 (1.03-1.61)**	**1.34 (1.06-1.70)**
Hypertension [e]	-	**1.60 (1.36-1.89)**	**1.65 (1.39-1.97)**	-	**2.12 (1.64-2.73)**	**2.31 (1.77-3.03)**	-	**1.86 (1.51-2.29)**	**1.78 (1.43-2.23)**
Cardiac disease [e]	-	0.89 (0.75-1.05)	0.90 (0.75-1.07)	-	**0.69 (0.54-0.89)**	**0.75 (0.57-0.98)**	-	**0.68 (0.55-0.83)**	**0.76 (0.61-0.95)**

	SARS-CoV-2 vs. Influenza			SARS-CoV-2 vs. RSV			SARS-CoV-2 vs. other viruses		
	aOR (95% CI)			aOR (95% CI)			aOR (95% CI)		
Variable	**Model 1 [a]**	**Model 2 [b]**	**Model 3 [c]**	**Model 1 [a]**	**Model 2 [b]**	**Model 3 [c]**	**Model 1 [a]**	**Model 2 [b]**	**Model 3 [c]**
Chronic pulmonary disease [e]	-	**0.72 (0.60-0.86)**	**0.70 (0.58-0.84)**	-	**0.60 (0.47-0.77)**	**0.61 (0.46-0.80)**	-	**0.50 (0.40-0.61)**	**0.51 (0.41-0.64)**
Chronic Kidney failure [e]	-	1.32 (0.93-1.88)	**1.88 (1.28-2.75)**	-	1.46 (0.91-2.34)	**1.93 (1.16-3.22)**	-	**1.85 (1.28-2.67)**	**2.25 (1.48-3.40)**
Malignancy [e]	-	0.98 (0.69-1.39)	1.03 (0.71-1.49)	-	0.83 (0.52-1.33)	0.76 (0.46-1.24)	-	0.77 (0.54-1.10)	0.70 (0.48-1.02)
Immunosuppression [e]	-	**0.45 (0.31-0.63)**	**0.48 (0.33-0.69)**	-	**0.28 (0.17-0.45)**	**0.28 (0.17-0.46)**	-	**0.17 (0.12-0.25)**	**0.18 (0.12-0.26)**
Vital signs									
Body temperature, °C [d]									
<36	-	-	**1.55 (1.09-2.22)**	-	-	**2.67 (1.53-4.68)**	-	-	**1.99 (1.33-2.99)**
36-38	-	-	*1.0 (ref)*	-	-	*1.0 (ref)*	-	-	*1.0 (ref)*
>38	-	-	**0.53 (0.44-0.62)**	-	-	0.95 (0.73-1.23)	-	-	**1.50 (1.22-1.84)**
Blood pressure SBP ≤90 or DBP ≤60, mmHg [d]	-	-	**0.82 (0.71-0.96)**	-	-	0.97 (0.77-1.23)	-	-	**0.80 (0.66-0.96)**
Heart rate >90, beats/min [d]	-	-	**0.65 (0.55-0.76)**	-	-	**0.57 (0.44-0.74)**	-	-	**0.52 (0.43-0.65)**
Respiratory rate, breaths/min [d]									
≤20	-	-	*1.0 (ref)*	-	-	*1.0 (ref)*	-	-	*1.0 (ref)*
21-29	-	-	**1.87 (1.55-2.26)**	-	-	**1.62 (1.20-2.18)**	-	-	**1.45 (1.15-1.83)**
≥30	-	-	**2.02 (1.55-2.26)**	-	-	**1.72 (1.21-2.45)**	-	-	**1.59 (1.20-2.10)**

	SARS-CoV-2 vs. Influenza			SARS-CoV-2 vs. RSV			SARS-CoV-2 vs. other viruses		
	aOR (95% CI)			aOR (95% CI)			aOR (95% CI)		
Variable	**Model 1 [a]**	**Model 2 [b]**	**Model 3 [c]**	**Model 1 [a]**	**Model 2 [b]**	**Model 3 [c]**	**Model 1 [a]**	**Model 2 [b]**	**Model 3 [c]**
SpO2/FiO2, % [d]									
<235	-	-	**1.40 (1.10-1.77)**	-	-	1.00 (0.71-1.41)	-	-	1.07 (0.80-1.42)
235-315	-	-	0.97 (0.76-1.18)	-	-	0.94 (0.66-1.33)	-	-	0.92 (0.69-1.22)
>315	-	-	*1.0 (ref)*	-	-	*1.0 (ref)*	-	-	*1.0 (ref)*
Laboratory parameters									
CRP, mg/L [d]									
<50	-	-	*1.0 (ref)*	-	-	*1.0 (ref)*	-	-	*1.0 (ref)*
50-99	-	-	1.04 (0.87-1.25)	-	-	1.19 (0.88-1.61)	-	-	0.87 (0.69-1.10)
100-149	-	-	**1.28 (1.01-1.62)**	-	-	1.13 (0.79-1.62)	-	-	1.01 (0.76-1.35)
150-199	-	-	1.29 (0.97-1.72)	-	-	**2.02 (1.26-3.26)**	-	-	1.15 (0.82-1.62)
≥200	-	-	1.02 (0.79-1.34)	-	-	1.18 (0.79-1.76)	-	-	0.95 (0.70-1.29)
WBC count, 10^9 cells/L [d]									
<4.0	-	-	1.26 (0.98-1.62)	-	-	0.81 (0.55-1.19)	-	-	0.81 (0.60-1.09)
4.0-8.8	-	-	*1.0 (ref)*	-	-	*1.0 (ref)*	-	-	*1.0 (ref)*
8.9-12.0	-	-	**0.66 (0.54-0.80)**	-	-	**0.30 (0.22-0.40)**	-	-	**0.33 (0.26-0.42)**
>12	-	-	**0.57 (0.45-0.72)**	-	-	**0.23 (0.17-0.32)**	-	-	**0.19 (0.15-0.24)**
Platelet count < 150, 10^9 cells/L [d]	-	-	**0.49 (0.41-0.59)**	-	-	**0.62 (0.47-0.83)**	-	-	**0.67 (0.53-0.85)**
Creatinine > 100, umol/L [d]	-	-	**0.50 (0.41-0.61)**	-	-	**0.67 (0.50-0.90)**	-	-	**0.69 (0.54-0.89)**

a Adjusted for age, sex and BMI
b Adjusted for age, sex BMI, diabetes, hypertension, chronic cardiac disease, chronic respiratory disease, chronic kidney disease, malignancy and

immunosuppression. Due to missing values for BMI, pooled estimates and confidence intervals from 50 multiple imputed datasets are shown.
c Adjusted for age, sex BMI, diabetes, hypertension, chronic cardiac disease, chronic respiratory disease, chronic kidney disease, malignancy, immunosuppression, CRP, WBCs, platelets, creatinine, respiratory rate, saturation, body temperature, blood pressure and heart rate. Due to missing values for BMI, CRP, WBCs, platelets, creatinine, respiratory rate, saturation, body temperature, blood pressure and heart rate, pooled estimates and confidence intervals from 50 multiple imputed datasets are shown.
d Variable containing missing values, which were imputed using multiple imputation by chained equations (MICE) by Predictive Mean Modelling (PMM) (See eMethods 3 for more detailed information).
e Based on ICD-10 codes from -5 years to +24 hours from admission time point. See list of ICD-10 codes for each comorbidity category in E table 1.

Abbreviations: SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, RSV: Respiratory syncytial virus, aOR: Adjusted Odds Ratio, CI; Confidence Interval, BMI: Body Mass Index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SpO2: Peripheral capillary oxygen saturation, FiO2: Fraction of inspired oxygen, CRP: C-reactive protein, WBC: White blood cells

eTable 8. Sensitivity analyses for mortality and ICU-admission outcomes in the adult cohort

Outcome variable	SARS-CoV-2	Influenza	RSV	Other viruses	SARS-CoV-2 vs. Influenza		SARS-CoV-2 vs. RSV		SARS-CoV-2 vs. other viruses	
					HR (95% CI)	aHR (95% CI) [a]	HR (95% CI)	aHR (95% CI) [a]	HR (95% CI)	aHR (95% CI) [a]
	number (percent)	*number (percent)*	*number (percent)*	*number (percent)*						
30-day mortality	216 (13)	121 (5)	45 (7)	76 (5)	**2.73 (2.18-3.41)**	**4.43 (3.51-5.59)**	**1.83 (1.33-2.53)**	**3.81 (2.72-5.34)**	**2.62 (2.02-3.40)**	**3.46 (2.61-4.60)**
2015-2020	216 (13)	96 (5)	35 (8)	62 (5)	**2.60 (2.05-3.31)**	**4.79 (3.72-6.15)**	**1.72 (1.21-2.46)**	**4.02 (2.76-5.83)**	**2.66 (2.01-3.53)**	**3.85 (2.84-5.22)**
Symptomatic cohort [b]	204 (15)	105 (5)	43 (7)	62 (5)	**3.47 (2.74-4.39)**	**5.48 (4.29-7.01)**	**2.13 (1.53-2.96)**	**4.17 (2.95-5.89)**	**3.36 (2.53-4.46)**	**4.50 (3.30-6.12)**
SARS-CoV-2, February-April 2020	154 (16)	121 (5)	45 (7)	76 (5)	**3.41 (2.69-4.33)**	**5.79 (4.49-7.46)**	**2.29 (1.64-3.19)**	**4.87 (3.42-6.94)**	**3.27 (2.48-4.30)**	**4.63 (3.41-6.29)**
SARS-CoV-2, May-September 2020	62 (8)	121 (5)	45 (7)	76 (5)	**1.82 (1.34-2.48)**	**3.09 (2.22-4.30)**	1.22 (0.83-1.80)	**3.00 (1.95-4.62)**	**1.75 (1.25-2.45)**	**2.60 (1.79-3.80)**
Patient index HCEs [c]	202 (12)	115 (5)	44 (8)	67 (5)	**2.64 (2.10-3.31)**	**4.39 (3.46-5.58)**	**1.65 (1.19-2.29)**	**3.47 (2.46-4.90)**	**2.50 (1.90-3.29)**	**3.30 (2.45-4.45)**
90-day mortality	235 (15)	192 (8)	65 (10)	148 (10)	**2.02 (1.67-2.44)**	**3.34 (2.73-4.08)**	**1.48 (1.13-1.95)**	**3.13 (2.34-4.18)**	**1.56 (1.27-1.92)**	**2.28 (1.82-2.86)**
2015-2020	235 (15)	152 (8)	50 (11)	126 (10)	**1.93 (1.57-2.36)**	**3.45 (2.78-4.27)**	**1.41 (1.04-1.91)**	**3.16 (2.29-4.35)**	**1.52 (1.22-1.89)**	**2.30 (1.81-2.91)**
Symptomatic cohort [b]	223 (17)	167 (7)	62 (11)	123 (10)	**2.51 (2.05-3.07)**	**3.96 (3.21-4.89)**	**1.69 (1.27-2.24)**	**3.28 (2.43-4.41)**	**1.93 (1.55-2.41)**	**2.79 (2.19-3.55)**
SARS-CoV-2, February-April 2020	167 (17)	192 (8)	65 (10)	148 (10)	**2.36 (1.92-2.90)**	**4.00 (3.20-4.99)**	**1.73 (1.30-2.30)**	**3.70 (2.71-5.04)**	**1.83 (1.46-2.28)**	**2.80 (2.18-3.60)**
SARS-CoV-2, May-September 2020	68 (11)	192 (8)	65 (10)	148 (10)	**1.49 (1.13-1.97)**	**2.36 (1.77-3.16)**	1.10 (0.78-1.54)	**2.42 (1.66-3.53)**	1.16 (0.87-1.54)	**1.77 (1.29-2.42)**
Patient index HCEs [c]	220 (14)	182 (8)	61 (11)	129 (10)	**1.95 (1.60-2.37)**	**3.31 (2.69-4.07)**	**1.39 (1.05-1.85)**	**2.97 (2.20-4.02)**	**1.51 (1.21-1.87)**	**2.18 (1.72-2.77)**
ICU-admission	294 (17)	244 (10)	72 (12)	167 (11)	**1.70 (1.43-2.01)**	**1.46 (1.22-1.75)**	**1.52 (1.18-1.97)**	**1.28 (0.96-1.69)**	**1.53 (1.27-1.85)**	**1.32 (1.07-1.64)**
2015-2020	294 (17)	175 (9)	52 (11)	135 (11)	**1.82 (1.51-2.20)**	**1.59 (1.30-1.95)**	**1.56 (1.16-2.10)**	1.32 (0.96-1.81)	**1.58 (1.29-1.94)**	**1.33 (1.06-1.68)**
Symptomatic cohort [b]	294 (22)	244 (11)	72 (12)	167 (13)	**1.88 (1.59-2.24)**	**1.57 (1.30-1.88)**	**1.71 (1.32-2.22)**	**1.36 (1.03-1.80)**	**1.62 (1.34-1.96)**	**1.39 (1.12-1.73)**

Outcome variable	SARS-CoV-2	Influenza	RSV	Other viruses	SARS-CoV-2 vs. Influenza		SARS-CoV-2 vs. RSV		SARS-CoV-2 vs. other viruses	
					HR (95% CI)	aHR (95% CI) [a]	HR (95% CI)	aHR (95% CI) [a]	HR (95% CI)	aHR (95% CI) [a]
SARS-CoV-2, February-April 2020	197 (20)	244 (10)	72 (12)	167 (11)	**1.96 (1.63-2.37)**	**1.63 (1.33-1.99)**	**1.78 (1.34-2.30)**	**1.31 (0.97-1.78)**	**1.77 (1.44-2.18)**	**1.45 (1.14-1.83)**
SARS-CoV-2, May-September 2020	97 (14)	244 (10)	72 (12)	167 (11)	**1.34 (1.06-1.70)**	**1.41 (1.10-1.80)**	1.19 (0.88-1.61)	1.41 (1.001.99)	1.20 (0.94-1.55)	1.31 (0.99-1.74)
Patient index HCEs [c]	286 (17)	236 (10)	67 (12)	149 (11)	**1.68 (1.41-2.00)**	**1.45 (1.20-1.74)**	**1.51 (1.15-1.96)**	1.28 (0.95-1.71)	**1.50 (1.23-1.83)**	**1.27 (1.02-1.59)**
30-day mortality in the ICU-cohort	77 (26)	47 (19)	18 (25)	23 (14)	1.42 (0.98-2.03)	**2.40 (1.58-3.64)**	1.04 (0.62-1.74)	**2.87 (1.55-5.33)**	**2.07 (1.30-3.30)**	**3.75 (2.15-6.54)**
2015-2020	77 (26)	34 (19)	13 (25)	16 (12)	1.40 (0.94-2.10)	**2.27 (1.43-3.62)**	1.02 (0.57-1.84)	**2.78 (1.39-5.52)**	**2.41 (1.41-4.14)**	**4.28 (2.30-7.96)**
Symptomatic cohort [b]	77 (26)	47 (19)	18 (25)	23 (14)	1.42 (0.98-2.03)	**2.40 (1.58-3.65)**	1.04 (0.62-1.74)	**2.95 (1.58-5.50)**	**2.07 (1.30-3.30)**	**3.78 (2.15-6.63)**
SARS-CoV-2, February-April 2020	52 (26)	47 (19)	18 (25)	23 (14)	1.43 (0.96-2.12)	**2.66 (1.64-4.32)**	1.06 (0.62-1.81)	**3.22 (1.60-6.51)**	**2.09 (1.28-3.42)**	**4.49 (2.44-9.02)**
SARS-CoV-2, May-September 2020	25 (26)	47 (19)	18 (25)	23 (14)	1.38 (0.85-2.24)	**1.85 (1.07-3.19)**	1.01 (0.55-1.86)	2.01 (0.96-4.23)	**2.03 (1.15-3.58)**	**2.96 (1.52-5.76)**
Patient index HCEs [c]	73 (26)	46 (19)	18 (27)	18 (12)	1.38 (0.96-1.99)	**2.35 (1.55-3.58)**	0.99 (0.59-1.65)	**2.74 (1.47-5.10)**	**2.10 (1.31-3.38)**	**3.81 (2.17-6.72)**

a The regression models were adjusted for age, sex, BMI, diabetes, hypertension, chronic cardiac disease, chronic respiratory disease, chronic kidney disease, malignancy and immunosuppression Due to missing values for BMI, pooled estimates and confidence intervals from 50 multiple imputed datasets are shown.
b Symptomatic cohort defined as patients with admission temperature ≥38°C, or oxygen saturation <95%, or respiratory rate >20
c For each patient, only the first HCE was included for analysis

Abbreviations: SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, RSV: Respiratory syncytial virus, HR: Hazard ratio, aHR: Adjusted hazard ratio, CI; Confidence Interval

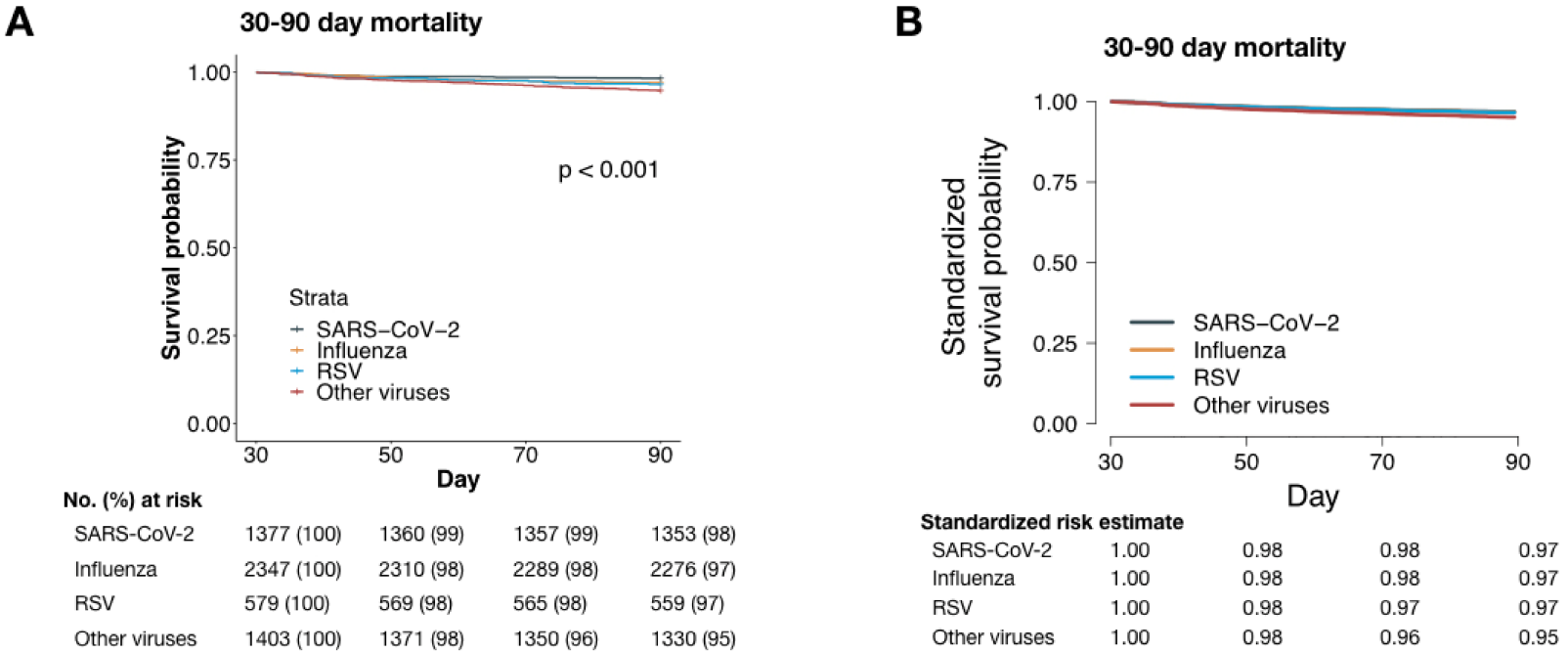
eTable 9. Age stratified logistic regression analysis of 30-day mortality in the adult cohort

					SARS-CoV-2 vs. Influenza		SARS-CoV-2 vs. RSV		SARS-CoV-2 vs. other viruses	
Outcome variable	**SARS-CoV-2**	**Influenza**	**RSV**	**Other viruses**	**HR (95% CI)**	**aHR (95% CI) [a]**	**HR (95% CI)**	**aHR (95% CI) [a]**	**HR (95% CI)**	**aHR (95% CI) [a]**
30-day mortality	216/1692 (13)	121/2468 (5)	45/624 (7)	76/1490 (5)	**2.73 (2.18-3.41)**	**4.43 (3.51-5.59) [b]**	**1.83 (1.33-2.53)**	**3.81 (2.72-5.34) [b]**	**2.62 (2.02-3.40)**	**3.46 (2.61-4.60) [b]**
16-49 years	8/579 (1)	4/587 (1)	3/69 (4)	12/511 (2)	2.03 (0.61-6.75)	**3.53 (1.01-12.40) [c]**	0.31 (0.08-1.18)	1.27 (0.29-5.47) [c]	0.59 (0.24-1.44)	1.22 (0.44-3.34) [c]
50-69 years	48/668 (7)	26/729 (4)	10/207 (5)	18/491 (4)	**2.05 (1.27-3.30)**	**2.16 (1.31-3.57) [c]**	1.51 (0.76-2.98)	1.71 (0.81-3.60) [c]	**2.00 (1.16-3.44)**	**2.07 (1.13-3.79) [c]**
≥70 years	160/445 (36)	91/1152 (8)	32/348 (9)	46/488 (9)	**5.51 (4.26-7.13)**	**5.41 (4.17-7.00) [c]**	**4.67 (3.19-6.82)**	**4.93 (3.37-7.23) [c]**	**4.49 (3.23-6.23)**	**5.03 (3.61-7.01) [c]**

a Due to missing values for BMI, pooled estimates and confidence intervals from 50 multiple imputed datasets are shown.
b The regression models were adjusted for age, sex, BMI and Elixhauser Comorbidity Index Score
c The regression models were adjusted for sex, BMI and Elixhauser Comorbidity Index Score

Abbreviations: SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, RSV: Respiratory syncytial virus, HR: Hazard ratio, aHR: Adjusted hazard ratio, CI; Confidence Interval

eFigure 5. Unadjusted Kaplan Meier curve (A) and standardized survival function curve (B) for 30-90 day mortality in the adult study cohort



No. (%) at risk				
SARS-CoV-2	1377 (100)	1360 (99)	1357 (99)	1353 (98)
Influenza	2347 (100)	2310 (98)	2289 (98)	2276 (97)
RSV	579 (100)	569 (98)	565 (98)	559 (97)
Other viruses	1403 (100)	1371 (98)	1350 (96)	1330 (95)

Standardized risk estimate				
SARS-CoV-2	1.00	0.98	0.98	0.97
Influenza	1.00	0.98	0.98	0.97
RSV	1.00	0.98	0.97	0.97
Other viruses	1.00	0.98	0.96	0.95

Note: A. Unadjusted Kaplan Meier curve and risk table for 30-90-day mortality. *P*-value represents result of significance testing using log-rank tests. B. Complete case-based standardised survival function for 30-90-day mortality. Complete data were available for 1024 SARS-CoV-2, 2220 influenza virus, 591 RSV and 1377 other viruses healthcare episodes. The survival function was standardized and adjusted for sex, age, BMI-category, diabetes, hypertension, cardiac disease, respiratory disease, chronic kidney disease and malignancy.

Abbreviations:
SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, RSV: Respiratory syncytial virus, AdV: Adenovirus, RV: Rhinovirus, EV: Enterovirus, sCoV: Seasonal coronavirus, BoV: Bocavirus, PIV: Parainfluenzaviruses, MPV: Metapneumoviruses

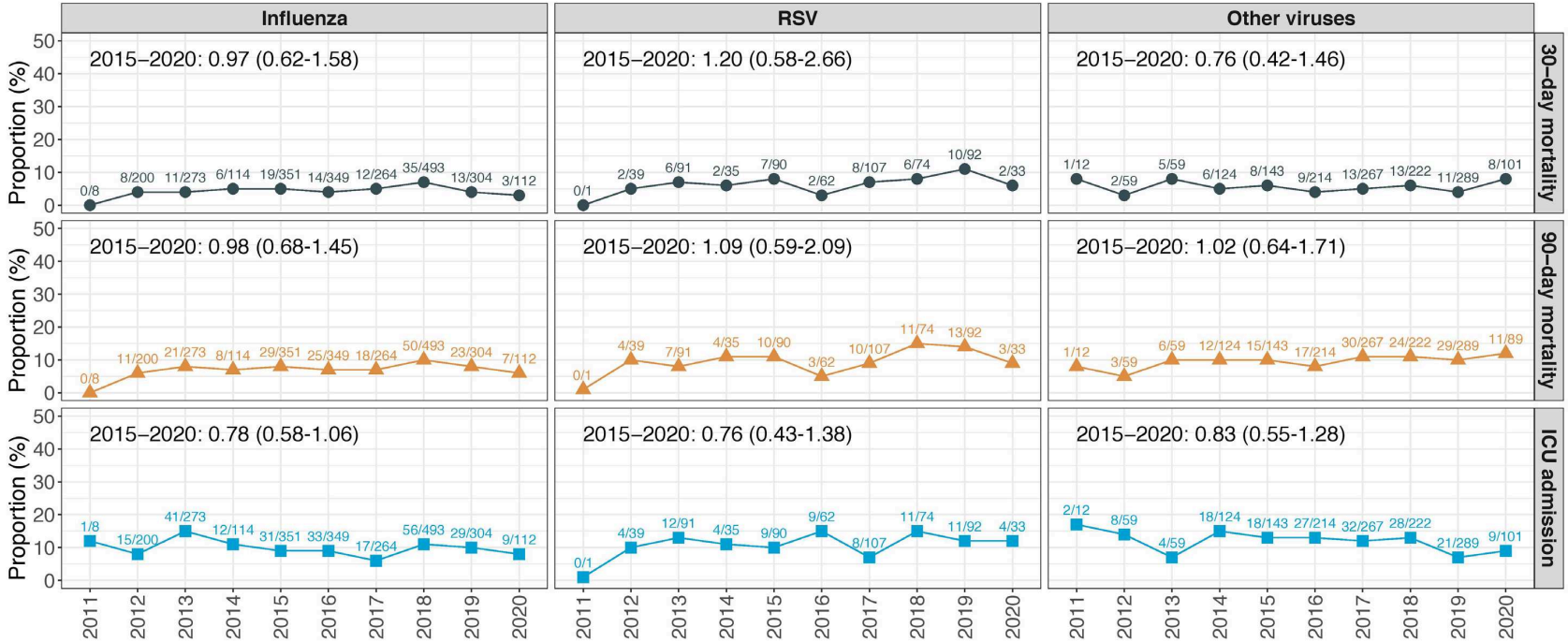
eTable 10. Comparison of mortality hazard ratios for complete case and multiple imputed analysis in the adult cohort

	SARS-CoV-2 vs. Influenza aHR (95% CI) [a]	SARS-CoV-2 vs. RSV aHR (95% CI) [a]	SARS-CoV-2 vs. Other viruses aHR (95% CI) [a]
Mortality			
Day 0-30			
Multiple Imputed data	**4.43 (3.51-5.59)**	**3.81 (2.72-5.34)**	**3.46 (2.61-4.60)**
Complete case	**4.84 (3.75-6.24)**	**4.47 (3.07-6.50)**	**3.99 (2.92-5.45)**
Day 0-90			
Multiple Imputed data	**3.34 (2.73-4.08)**	**3.13 (2.34-4.18)**	**2.28 (1.82-2.86)**
Complete case	**3.55 (2.85-4.42)**	**3.42 (2.50-4.69)**	**2.54 (1.98-3.24)**
Day 31-90			
Multiple Imputed data	0.98 (0.60-1.59)	1.14 (0.59-2.19)	0.62 (0.37-1.03)
Complete case	0.93 (0.54-1.61)	1.00 (0.50-2.01)	0.61 (0.35-1.08)

a The regression models were adjusted for age, sex, BMI, diabetes, hypertension, chronic cardiac disease, chronic respiratory disease, chronic kidney disease,
malignancy and immunosuppression

Abbreviations: SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, RSV: Respiratory syncytial virus, HR: Hazard ratio, aHR: Adjusted hazard ratio, CI; Confidence Interval

eFigure 6. Comparison of 30-day mortality, 90-day mortality and ICU-admission per calendar year in the adult influenza, RSV and other viruses groups



Note: The 30-day mortality, 90-day mortality and ICU-admission rates per calendar year in the adult influenza, RSV and other viruses groups. The numbers above each point indicates the number of events and the total number of health care episodes per unique calendar year. The age-category, sex, diabetes, hypertension, chronic cardiac disease, chronic respiratory disease, chronic kidney disease, malignancy and immunosuppression-adjusted odds ratio (95% CI) for 2015-2020 as compared to 2011-2014 for each outcome measure and virus group is presented in the top-left of each facet.

Abbreviations: RSV: Respiratory syncytial virus

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