

eSupplement

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

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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 2019¹. 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 ≥ 80).

Body Mass Index (BMI): Based on the latest height and weight data available and was only calculated for the adult (≥ 16 years) study cohort. Normoweight was defined as a BMI of 18.5-24.9 kg/m², underweight < 18.5 kg/m², overweight 25-29.9 kg/m², obese ≥ 30 kg/m². 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, respectively²⁻⁴. The CCI and ECI scores were presented both as continuous and categorical variables (CCI: 0-1, 2-4, ≥ 5 and ECI: ≤ 0 , 1-10, ≥ 11) in comparisons between the different virus groups.

The specific comorbidities in the adult as well as the pediatric study cohort were defined according 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

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

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.

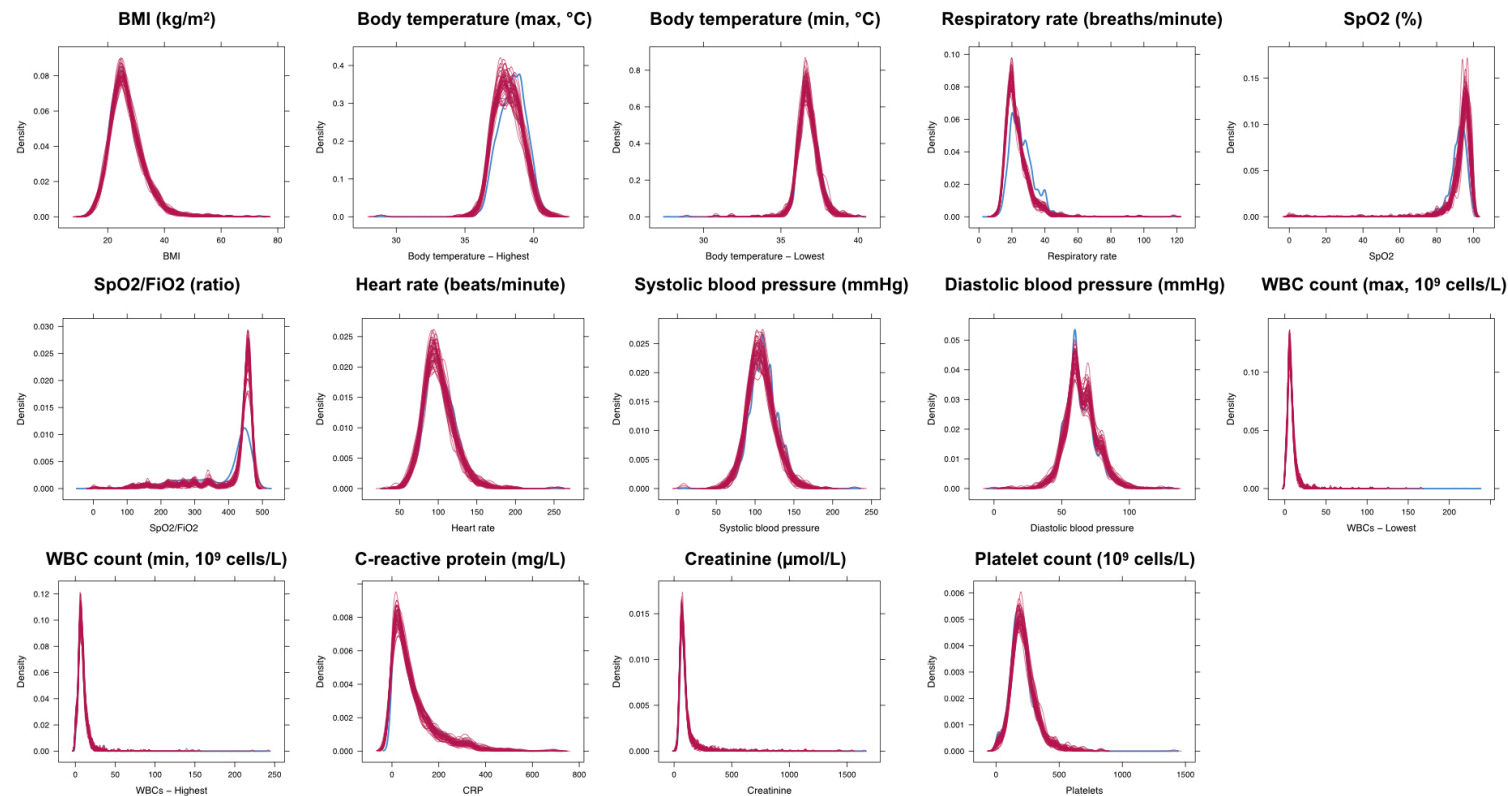
eMethods 3. Handling of missing data

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 ($\text{maxit} = 20$) 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)										P-value ^a
	SARS-CoV-2 (1721)	Influenza (2468)	RSV (624)	RV (682)	EV (30)	PIV (247)	MPV (211)	SCoV (183)	AdV (43)	BoV (30)	
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)	<0.001
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)	[[SEP]]
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)	[[SEP]]<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	38.7	38.4	38.2	38.0	38.4	38.5	38.3	38.6	38.0
	37.7-39.2	38.0-39.3	37.7-39.1	37.6-39.0	37.6-39.5	37.6-39.0	37.6-39.1	37.4-38.9	37.8-39.2	37.4-38.8
	91	97	98	97	100	98	98	98	100	100
Respiratory rate, breaths/min ^b	26	24	25	24	22	24	25	24	21	24
	22-31	20-30	20-30	20-30	20-24	20-30	22-32	20-30	20-28	20-30
	90	94	95	92	100	92	94	92	93	93
SpO₂, % ^{c, d}	92	92	92	93	94	93	92	94	95	93
	90-95	89-95	88-94	90-96	92-95	89-95	89-94	91-96	93-97	89-95
	91	97	98	97	100	97	97	98	100	100
SpO₂/FiO₂, ratio ^c	433	429	419	438	443	433	429	445	452	443
	297-448	310-448	297-448	339-452	(431-452)	308-448	281-448	349-457	438-460	298-452
	91	96	98	97	100	97	97	98	100	93
Heart rate, beats/min ^b	98	102	105	105	106	104	105	100	107	105
	87-109	90-117	90-120	91-120	89-115	94-119	93-120	91-115	98-120	87-118
	91	97	98	97	100	97	97	98	100	100
Systolic BP, mm Hg ^c	110	110	112	108	107	110	110	110	110	109
	102-122	100-122	100-127	97-120	99-120	100-121	100-125	99-120	100-116	100-120
	90	96	98	96	100	98	97	99	91	100
Diastolic BP, mm Hg ^c	63	60	60	60	61	60	60	60	60	60
	58-70	55-70	56-70	55-70	56-70	55-70	56-70	56-70	58-70	53-70
	90	96	98	95	100	98	96	99	91	100
Laboratory parameters ^a										
Highest WBC count, 10⁹ cells/L	6.9	7.7	9.1	10.1	10.4	8.8	8.6	10.0	9.4	11.5
	5.2-9.4	5.5-10.5	6.5-12.2	5.9-14.4	5.8-14.6	5.4-12.6	5.9-13	6.2-13.8	6.2-13.4	8.2-15.9
	89	96	97	96	97	97	96	97	98	97
Lowest WBC count, 10⁹ cells/L	6.3	6.7	8.1	8.4	10.4	7.1	7.2	8.2	7.3	9.9
	4.6-8.6	4.7-9.1	5.4-10.6	5.0-12.5	5.5-13.2	4.5-10.3	4.9-10.5	4.8-11.6	5.5-12.1	6.3-11.7
	89	96	97	96	97	97	96	97	98	97
C-reactive protein, mg/L ^b	65	64	65	73	77	57	69	63	95	131
	27-133	28-125	28-133	34-149	17-123	25-143	33-144	20-131	43-162	64-241
	87	97	97	96	97	98	96	97	98	93

Variable	SARS-CoV-2 (1721)	Influenza (2468)	RSV (624)	RV (682)	EV (30)	PIV (247)	MPV (211)	S-CoV (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

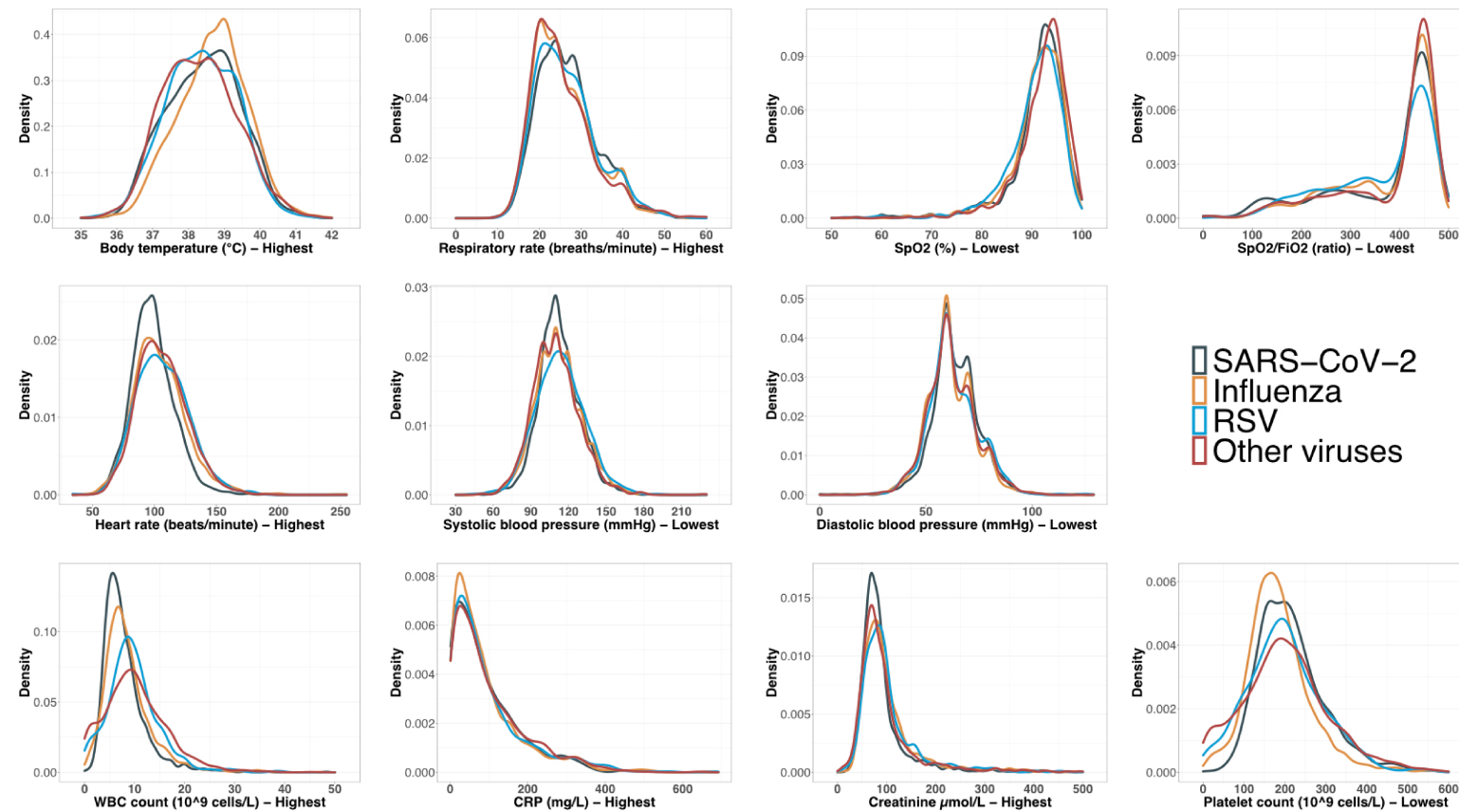
a Worst value -24 to +24 hours from admission time point for each parameter. Analysis based on complete case analysis.

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

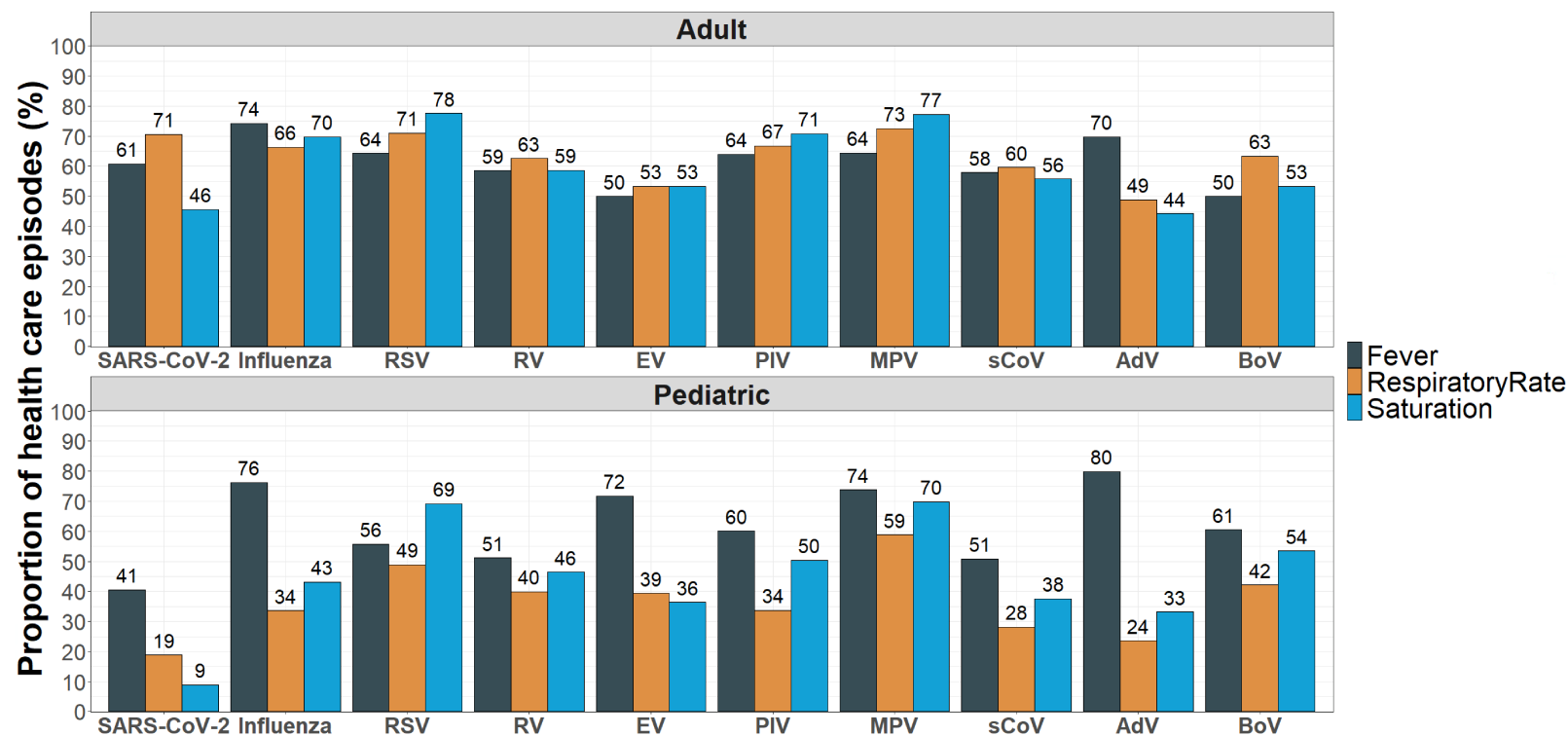
Variable	Virus group (No. healthcare episodes)				SARS-CoV-2 vs Influenza		SARS-CoV-2 vs RSV		SARS-CoV-2 vs other viruses	
	SARS-CoV-2	Influenza	RSV	Other viruses	OR (95% CI)	aOR (95% CI) ^a	OR (95% CI)	aOR (95% CI) ^a	OR (95% CI)	aOR (95% CI) ^a
Vital signs										
Body temperature, median (IQR), °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)	-	-	-	-	-	-
SpO ₂ 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)

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
>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)	-	-	-	-	-	-
SpO ₂ /FiO ₂ 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), 10⁹ 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 categories, 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), 10⁹ 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.

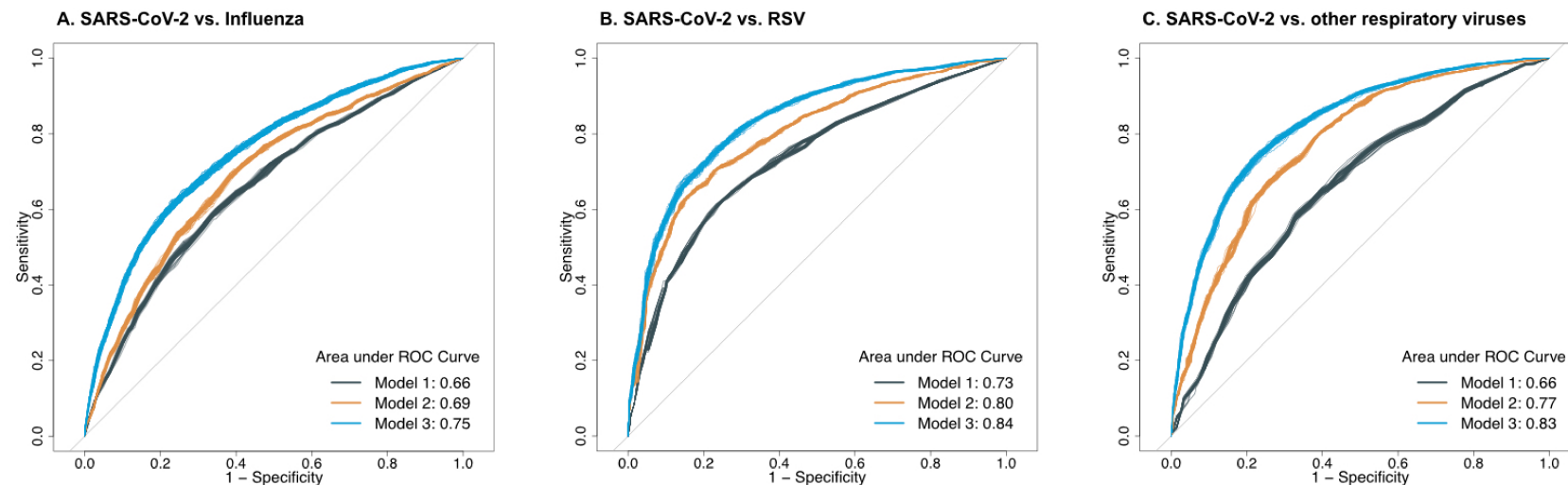
Abbreviations: SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, RSV: Respiratory syncytial virus, CI: Confidence Interval, OR: Odds Ratio, aOR: Adjusted Odds Ratio, BMI: Body Mass Index, CCI: Charlson Comorbidity Index, ECI: Elixhauser Comorbidity Index, SBP: Systolic blood pressure, DBP: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

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

Variable	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)		
	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)

Variable	SARS-CoV-2 vs. Influenza			SARS-CoV-2 vs. RSV			SARS-CoV-2 vs. other viruses		
	Model 1 ^a	aOR (95% CI)		Model 1 ^a	aOR (95% CI)		Model 1 ^a	aOR (95% CI)	
		Model 2 ^b	Model 3 ^c		Model 2 ^b	Model 3 ^c		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)

Variable	SARS-CoV-2 vs. Influenza			SARS-CoV-2 vs. RSV			SARS-CoV-2 vs. other viruses		
	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
SpO ₂ /FiO ₂ , % ^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
30-day mortality	<i>number (percent)</i> 216 (13)	<i>number (percent)</i> 121 (5)	<i>number (percent)</i> 45 (7)	<i>number (percent)</i> 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 _{SEP} (2.02-3.40)	3.46 _{SEP} (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 _{SEP} (2.74-4.39)	5.48 (4.29-7.01)	2.13 _{SEP} (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 _{SEP} (1.67-2.44)	3.34 _{SEP} (2.73-4.08)	1.48 _{SEP} (1.13-1.95)	3.13 _{SEP} (2.34-4.18)	1.56 _{SEP} (1.27-1.92)	2.28 _{SEP} (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 _{SEP} (1.43-2.01)	1.46 _{SEP} (1.22-1.75)	1.52 _{SEP} (1.18-1.97)	1.28 _{SEP} (0.96-1.69)	1.53 _{SEP} (1.27-1.85)	1.32 _{SEP} (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 (1.00-1.99)	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										
2015-2020	77 (26)	47 (19)	18 (25)	23 (14)	1.42 ^[SEP] (0.98-2.03)	2.40 (1.58-3.64)	1.04 ^[SEP] (0.62-1.74)	2.87 (1.55-5.33)	2.07 ^[SEP] (1.30-3.30)	3.75 (2.15-6.54)
Symptomatic cohort ^b	77 (26)	47 (19)	18 (25)	23 (14)	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)
SARS-CoV-2, February-April 2020	52 (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, May-September 2020	25 (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)
Patient index HCEs ^c	73 (26)	46 (19)	18 (27)	18 (12)	1.38 (0.96-1.99)	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)
					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 $\geq 38^{\circ}\text{C}$, 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

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
30-day mortality	216/1692 (13)	121/2468 (5)	45/62 (7)	76/1490 (5)	2.73 ^[1] (2.18-3.41)	4.43 ^[1] (3.51-5.59) ^b	1.83 ^[1] (1.33-2.53)	3.81 ^[1] (2.72-5.34) ^b	2.62 ^[1] (2.02-3.40)	3.46 ^[1] (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)	10/20 (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)	32/34 (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

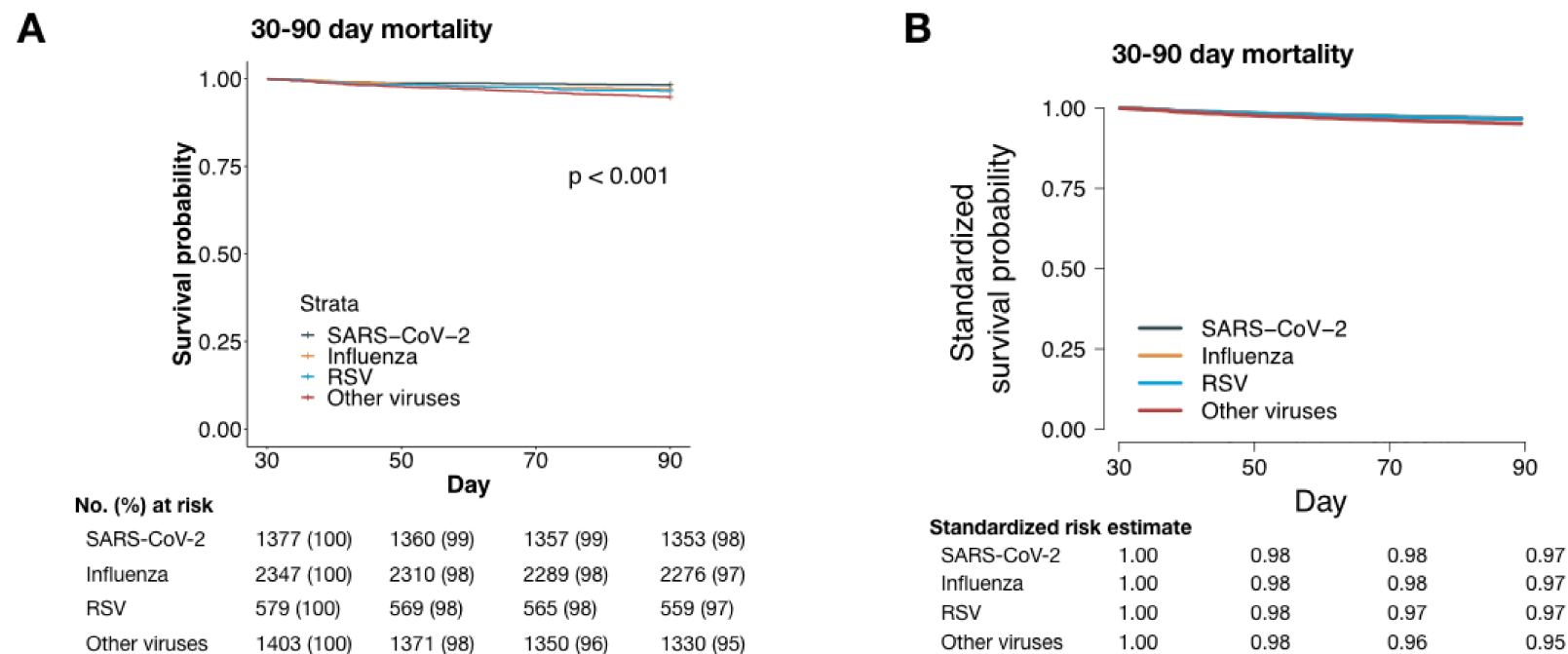
a Due to missing values for BMI, pooled estimates and confidence intervals from 50 multiple imputed datasets are shown.

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



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

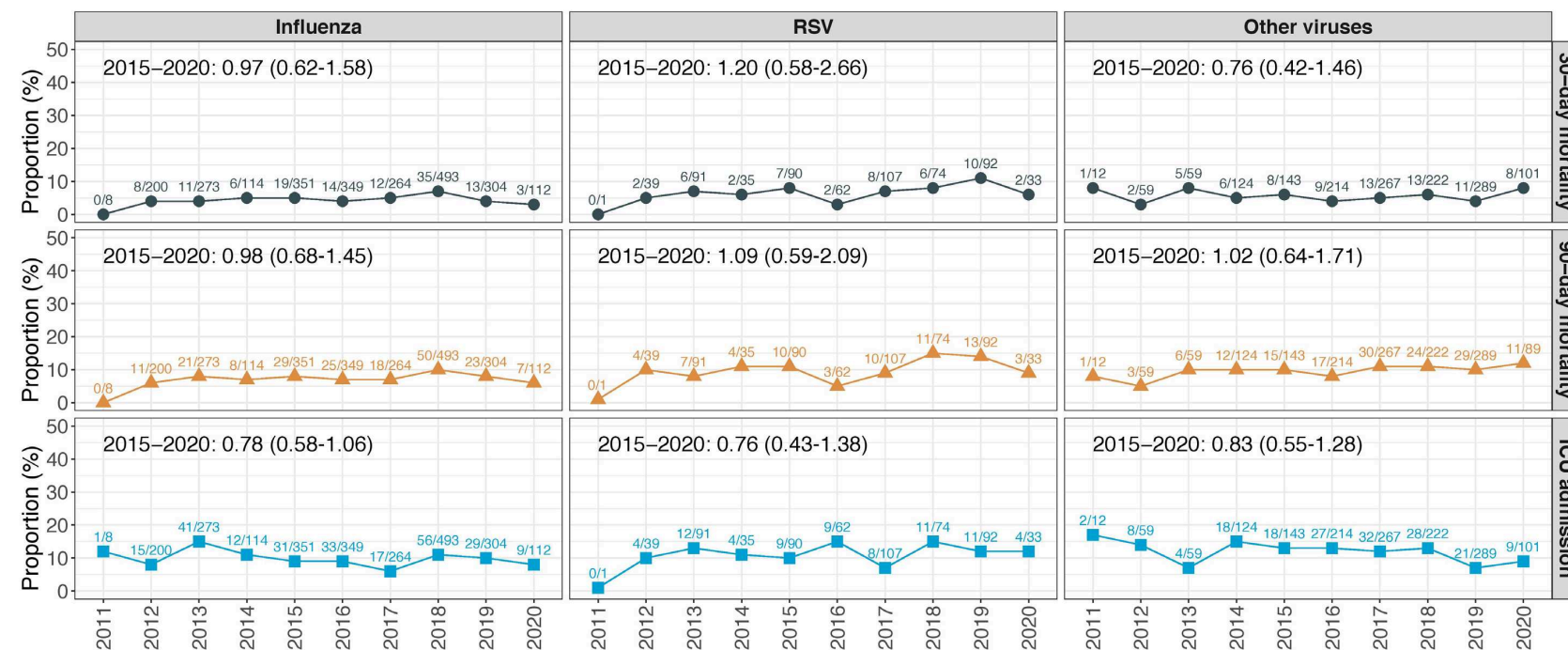
eTable 10. Comparison of mortality hazard ratios for complete case and multiple imputed analysis in the adult cohort

	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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