Appendix 1 (as submitted by the authors): Supplementary information

Data Quality and Availability

Manual validation of data collected by GEMINI have previously demonstrated high accuracy, compared to data held in electronic medical records.[1] We note several issues with data availability.

First, in 3% of hospitalizations, no provincial health insurance number was recorded. These patients could not be linked across encounters and were therefore excluded from analyses of readmission.

Second, in 6% of hospitalizations, postal code was not available or was for residence in locations that could not be linked to census information. In regression models, we assumed these individuals to be in the middle quintile (Q3) for neighborhood-level measures.

Third, we were unable to electronically collect any vital signs data from Sunnybrook hospital. For patients with COVID-19 at that hospital, we manually abstracted the first vital sign reading between ED triage and up to 24 hours after admission by reviewing nurse and physician documentation. Vital signs were also missing from electronic clinical data in approximately 15% of COVID-19 patients, mainly because vital signs data are typically recorded on paper charts in the emergency department and ICU, so would be missing for patients transferred directly from ED to ICU. We manually collected these vital signs data for patients with COVID-19, to facilitate validation of risk scores, using the same approach as was used for Sunnybrook. This could bias the comparisons between COVID-19 and influenza, as we did not manually abstract data for patients with influenza. Given that it was typically ICU patients with missing electronic vitals data, this could bias COVID-19 vital signs toward appearing more abnormal. We did not include presenting vital signs in regression models comparing COVID-19 and influenza, so this would not bias comparisons for any of the clinical outcomes.

Fourth, diagnostic imaging and laboratory test data was missing from the emergency department portion of patient visits at Sunnybrook. For COVID-19 patients, we collected this data manually, but were unable to do so for influenza patients, and this could underestimate thoracic CT use or some laboratory test use in influenza patients. Manually adding this missing data changed the estimate of thoracic CT use in COVID-19 from 19.7% to 20.4%, so is unlikely to have a major effect on the estimates for influenza.

Finally, data regarding patient mental/neurological status (eg. Confusion Assessment Method or Glasgow Coma Scale) was available only in the COVID-19 patients for whom we manually collected data or electronically in some patients from two hospitals (St. Michael's Hospital and Mount Sinai Hospital). Two risk prediction models required this data (NEWS2 and ISARIC-4C), thus performance of those models was reported only in patients for whom these data were available.

Respiratory-acting antibiotics

We report the use of antibiotics with action against respiratory bacterial pathogens, as described in clinical practice guidelines and prior literature.[2–4]

Antibiotic classes included
Third Generation Cephalosporin
Macrolide
Fluoroquinolone
Penicillin-derived beta-lactams/beta-lactamase
Other
Action against methicillin-resistant S. aureus
Simple Penicillins
Ceftazidime
Tetracyclines
Carbapenem (with and without pseudomonas coverage)
Clindamycin

Specific antibiotics included

Third generation cephalosporin=Ceftriaxone, cefotaxime, cefepime, cefdinir, cefditoren, cefpoxidime, ceftaroline. Macrolide=Azithromycin, clarithromycin, erythromycin, streptomycin. Fluoroquinolone=levofloxacin, moxifloxacin, ciprofloxacin, gemifloxicin. Tetracyclines=doxycycline. Penicillin-derived beta-lactam/beta-lactamases=amoxicillin-clavulinic acid, ampicillin-sulbactam, ticarcillin-clavulanate, piperacillin-tazobactam. Carbapenems=meropenem, imipenem, impenem+cilastatin. ertapenem. Action against methicillin-resistant S. aureus =vancomycin, linezolid. Simple Penicillins=Penicillin G, amoxicillin, ticarcillin, flucloxacillin, ampicillin, piperacillin. Other=aztreonam, colistin, gentamicin, trimethoprim-sulfamethoxazole, first and second generation cephalosporins (cefazolin, cefprozil, cefuroxime, cephalexin).

Measuring neighbourhood-level variables

Individual patient-level data regarding income and ethnicity were not available. To obtain neighbourhood-level variables, we linked 6-character patient postal codes to Census Dissemination Areas using Statistics Canada's Postal Code Conversion File Plus (version 7c; postal codes current up to November 2019).[5] We use data from the 2016 Census to report neighbourhood-level income (using neighbourhood after-tax income per single person equivalent) and visible minority concentration, defined as the percentage of residents who self-identified as belonging to a visible minority.[6] We derived quintile category boundaries for both income and visible minority status based on all dissemination areas in the Toronto Census Metropolitan Area and assigned each hospital admission to a quintile. Q1 to Q5 represented lowest to highest income and visible minority status concentration, respectively.

Implementing mortality prediction scores for COVID-19

Mortality risk for COVID-19 hospitalizations was estimated using 7 externally developed risk scores, designed to predict short-term mortality. Risk scores were identified based on a living systematic review[7] and we selected the 4 best performing models in a UK-based external validation study[8] (AUROC > 0.7): Lu[9], Hu[10], Xie[11] and NEWS2[12]. We also predicted mortality using the modified APACHE (mAPACHE) score[13], the critical illness severity scoring system (CISSS)[14] and ISARIC-4C score[15].

All scores were calculated based on the first valid laboratory and vital signs data that were available within 24 hours of hospital admission. Where comorbidity data was needed, we used discharge diagnoses for chronic conditions. ISARIC-4C used the number of Charlson comorbidities, which we were able to compute, and also clinician-defined obesity, which we were unable to include. Both ISARIC-4C and NEWS2 require assessment of patient mental/neurological status. ISARIC-4C assigns points for GCS <15 whereas NEWS2 assigns points for "confusion". We calculated these scores only in encounters for which patient mental/neurological status was measured using either GCS or the Confusion Assessment Method (CAM). We considered a positive CAM screen or GCS < 15 to represent altered mental status for both scores.

We report results for encounters for which we have complete data, and after the mean imputation of missing laboratory test result values, based on the assumption that if a laboratory test result was not ordered by a clinician, it was more likely to be normal. The missing data in numeric variables was imputed by taking the COVID-population mean value. We did not include patients in risk calculations with missing vital signs data in the observation window (which may have occurred for example because patients were considered palliative). We did not think it was fair to assume these values would be normal. We considered a patient to have surgery for the purpose of risk scores if they had a surgical procedure code during their hospitalization. Finally, because administrative codes for mechanical ventilation did not reliably report the timing of the intervention, we considered a patient to be ventilated in the first 24 hours of admission if they had an invasive mechanical ventilation code and the first day of their ICU admission was within 24 hours of their hospital admission time.

Table S1. Unadjusted outcomes stratified by age

Outcome	COVID-19	Influenza	p
Age <50 years – N	218	141	
Death – N (%)	11 (5.1)	<6 (<4.3)*	0.020
30-day Readmission – N (%)	14 (9.2)	12 (9.0)	0.50
ICU – N (%)	65 (29.8)	27 (19.2)	0.017
Hospital LOS, days – median (IQR)	5.6 (2.5, 12.9)	3.5 (1.5, 8.2)	<0.001
Age 50-75 years – N	480	390	
Death – N (%)	65 (13.5)	19 (4.9)	<0.001
30-day Readmission – N (%)	33 (9.9)	30 (8.3)	0.57
ICU – N (%)	169 (35.2)	83 (21.3)	<0.001
Hospital LOS, days – median (IQR)	8.8 (3.6, 20.8)	4.2 (2.0, 8.8)	<0.001
Age >75 years – N	329	252	
Death – N (%)	128 (38.9)	26 (10.3)	<0.001
30-day Readmission – N (%)	11 (7.9)	27 (12.2)	0.38
ICU – N (%)	37 (11.3)	31 (12.3)	<0.001
Hospital LOS, days – median (IQR)	11.9 (4.8, 25.1)	6.4 (3.7, 11.9)	<0.001

Table S1 Legend. 30-day unplanned readmission to a medical service or medical-surgical ICU at any participating hospital is reported after excluding patients who died and those discharged in the last 30 days of the study period. ICU: Intensive Care Unit. LOS: Length-of-stay. *All counts less than 6 are suppressed to reduce risk of patient reidentification.

Table S2. Characteristics, clinical outcomes, resource use, and clinical care of ICU patients with COVID-19 and Influenza

Variable	COVID-19	Influenza	P	SD
Number of admissions	271	141		
Age - median (IQR)	59 (51, 70)	64 (54, 74)	N/A	0.3
Age Group – N (%)			N/A	0.23
<50	65 (24.0)	27 (19.1)		
50-75	169 (62.4)	83 (58.9)		
>75	37 (13.7)	31 (22.0)		
Male Gender – N (%)	174 (64.2)	80 (56.7)	N/A	0.15
Charlson Score – N (%)			N/A	0.61
0	157 (57.9)	46 (32.6)		
1	59 (21.8)	30 (21.3)		
2+	55 (20.3)	65 (46.1)		
Neighborhood Income Quintile – N (%)			N/A	0.24
1	95 (35)	56 (40)		
2	53 (20)	23 (16)		
3	36 (13)	15 (11)		
4	36 (13)	22 (16)		
5	26 (10)	18 (13)		
Neighborhood Visible Minority Quintile – N (%)			N/A	0.4
1	22 (8)	24 (17)		
2	38 (14)	23 (16)		
3	54 (20)	32 (23)		
4	51 (19)	29 (21)		
5	81 (30)	24 (17)		
Long-Term Care Resident – N (%)	10 (3.7)	<6 (<4.3)*	N/A	0.008
Transfer from Acute Care Hospital – N (%)	84 (31.0)	19 (13.5)	N/A	0.43
Death – N (%)	69 (25.5)	28 (19.9)	0.25	0.13
7-day Readmission – N (%)	<6 (<2.2)*	<6 (<4.3)*	1.0**	0.03
30-day Readmission – N (%)	7 (4.7)	16 (14.8)	0.009	0.35
Hospital LOS, days – median (IQR)	16.8 (10.6, 27.3)	14.1 (6.8, 30.9)	0.24	0.20
ED LOS, hours – median (IQR)	7.1 (4.6, 9.8)	12.5 (7.2, 24.4)	<0.001**	0.77
ICU LOS, days – median (IQR)	10.9 (4.0, 17.8)	6.0 (2.3, 13.0)	<0.001	0.03
Invasive mechanical ventilation – N (%)	188 (69.4)	73 (51.8)	0.034**	0.37
GI Endoscopy – N (%)	7 (2.6)	13 (9.2)	0.33**	0.28
Bronchoscopy – N (%)	19 (7.0)	33 (23.4)	<0.001**	0.47
Renal Replacement Therapy – N (%)	52 (19.2)	18 (12.8)	1**	0.18
CT Thorax – N (%)	79 (29.2)	53 (37.6)	1**	0.18
Antibiotic – N (%)	244 (90.7)	128 (92.1)	1**	0.05
Corticosteroid – N (%)	89 (33.1)	69 (49.6)	0.09**	0.34
Warfarin or DOAC – N (%)	47 (17.5)	34 (24.5)	1**	0.17

Table S2 Legend. Unplanned readmission to a medical service or medical-surgical ICU at any participating hospital is reported, after excluding patients who died or were discharged in last 7- or 30-days of study period, respectively (denominator for COVID-19: 185 and 150 for 7- and 30-day, respectively and for influenza: 110 and 108 for 7- and 30-day respectively). For hospital resources and clinical care, we report the number of patients receiving at least one of the item described. ICU: Intensive Care Unit. LOS: Length-of-stay. GI: Gastrointestinal. Renal replacement therapy included hemodialysis and peritoneal dialysis and included both chronic use and new starts. CT: Computed tomography. Antibiotic: we report the use of respiratory-acting antibiotics (see Appendix). DOAC: direct-acting oral anticoagulant. *Exact number suppressed to reduce risk of patient reidentification. **p-values were adjusted using Bonferroni correction.

Table S3. Discriminative accuracy of mortality prediction models in COVID-19 hospitalizations with complete data

Measure	Sensitivity	Specificity	PPV	NPV
lu_index_2+	0.98 (0.92, 1.00)	0.15 (0.11, 0.19)	0.19 (0.15, 0.24)	0.98 (0.89, 1.00)
lu_index_3+	0.77 (0.65, 0.87)	0.62 (0.57, 0.68)	0.29 (0.23, 0.37)	0.93 (0.89, 0.96)
hu_index_0.1+	0.97 (0.86, 1.00)	0.36 (0.30, 0.44)	0.23 (0.17, 0.31)	0.99 (0.92, 1.00)
hu_index_0.2+	0.84 (0.69, 0.94)	0.52 (0.45, 0.59)	0.26 (0.18, 0.34)	0.94 (0.88, 0.98)
hu_index_0.3+	0.76 (0.60, 0.89)	0.61 (0.54, 0.68)	0.28 (0.20, 0.38)	0.93 (0.87, 0.97)
hu_index_0.4+	0.66 (0.49, 0.80)	0.72 (0.65, 0.79)	0.32 (0.22, 0.44)	0.91 (0.86, 0.95)
hu_index_0.5+	0.61 (0.43, 0.76)	0.80 (0.73, 0.85)	0.37 (0.25, 0.50)	0.91 (0.86, 0.95)
hu_index_0.6+	0.55 (0.38, 0.71)	0.86 (0.80, 0.91)	0.44 (0.29, 0.59)	0.91 (0.85, 0.94)
hu_index_0.7+	0.42 (0.26, 0.59)	0.91 (0.86, 0.95)	0.48 (0.31, 0.66)	0.89 (0.84, 0.93)
hu_index_0.8+	0.21 (0.10, 0.37)	0.95 (0.91, 0.98)	0.47 (0.23, 0.72)	0.86 (0.81, 0.90)
hu_index_0.9+	0.11 (0.03, 0.25)	0.98 (0.95, 0.99)	0.50 (0.16, 0.84)	0.85 (0.79, 0.89)
xie_index_0.1+	0.92 (0.85, 0.97)	0.44 (0.39, 0.49)	0.28 (0.23, 0.34)	0.96 (0.92, 0.98)
xie_index_0.2+	0.81 (0.71, 0.89)	0.69 (0.64, 0.74)	0.39 (0.32, 0.46)	0.94 (0.90, 0.96)
xie_index_0.3+	0.57 (0.46, 0.67)	0.83 (0.79, 0.87)	0.45 (0.35, 0.54)	0.89 (0.85, 0.92)
xie_index_0.4+	0.37 (0.27, 0.47)	0.90 (0.86, 0.93)	0.46 (0.34, 0.58)	0.86 (0.82, 0.89)
xie_index_0.5+	0.24 (0.16, 0.35)	0.95 (0.92, 0.97)	0.54 (0.37, 0.69)	0.84 (0.80, 0.87)
xie_index_0.6+	0.10 (0.05, 0.18)	0.97 (0.95, 0.98)	0.43 (0.22, 0.66)	0.82 (0.78, 0.85)
xie_index_0.7+	0.07 (0.02, 0.14)	0.98 (0.97, 0.99)	0.50 (0.21, 0.79)	0.82 (0.78, 0.85)
xie_index_0.8+	0.01 (0.00, 0.06)	0.99 (0.98, 1.00)	0.25 (0.01, 0.81)	0.81 (0.77, 0.84)
xie_index_0.9+	0.00 (0.00, 0.04)	0.99 (0.98, 1.00)	0.00 (0.00, 0.84)	0.81 (0.77, 0.84)
mapache_index_15+	1.00 (0.96, 1.00)	0.30 (0.24, 0.35)	0.32 (0.27, 0.38)	1.00 (0.95, 1.00)
mapache_index_40+	0.43 (0.32, 0.54)	0.96 (0.93, 0.98)	0.79 (0.64, 0.89)	0.83 (0.79, 0.87)
mapache_index_50+	0.13 (0.06, 0.21)	1.00 (0.99, 1.00)	1.00 (0.72, 1.00)	0.77 (0.73, 0.82)
mapache_index_60+	0.06 (0.02, 0.13)	1.00 (0.99, 1.00)	1.00 (0.48, 1.00)	0.76 (0.71, 0.81)
cisss_index_0.1+	0.42 (0.31, 0.54)	0.93 (0.90, 0.96)	0.62 (0.47, 0.75)	0.86 (0.82, 0.90)
cisss_index_0.2+	0.12 (0.06, 0.22)	0.98 (0.95, 0.99)	0.60 (0.32, 0.84)	0.81 (0.76, 0.85)
cisss_index_0.3+	0.08 (0.03, 0.17)	0.99 (0.97, 1.00)	0.75 (0.35, 0.97)	0.81 (0.76, 0.85)
cisss_index_0.4+	0.05 (0.01, 0.13)	1.00 (0.98, 1.00)	0.80 (0.28, 0.99)	0.80 (0.76, 0.84)
cisss_index_0.5+	0.04 (0.01, 0.11)	1.00 (0.99, 1.00)	1.00 (0.29, 1.00)	0.80 (0.75, 0.84)
cisss_index_0.6+	0.01 (0.00, 0.07)	1.00 (0.99, 1.00)	1.00 (0.03, 1.00)	0.79 (0.75, 0.84)
news2_index_5+	0.83 (0.68, 0.93)	0.53 (0.46, 0.60)	0.26 (0.19, 0.35)	0.94 (0.88, 0.97)
news2_index_7+	0.68 (0.52, 0.82)	0.64 (0.57, 0.71)	0.28 (0.19, 0.38)	0.91 (0.85, 0.95)

Table S3 Legend. Mortality risk scores[9-15] were calculated based on first valid measurement between ED triage and 24 hours after admission. We report model performance based on hospitalizations with complete data for all inputs.

Table S4. Discriminative accuracy of mortality prediction models in COVID-19 hospitalizations after mean imputation of missing laboratory values

Measure	Sensitivity	Specificity	PPV	NPV
lu_index_2+	1.00 (0.97, 1.00)	0.06 (0.04, 0.08)	0.21 (0.18, 0.23)	0.98 (0.89, 1.00)
lu_index_3+	0.84 (0.79, 0.89)	0.50 (0.47, 0.54)	0.30 (0.26, 0.33)	0.93 (0.90, 0.95)
hu_index_0.1+	0.92 (0.87, 0.95)	0.34 (0.31, 0.37)	0.26 (0.22, 0.29)	0.94 (0.91, 0.97)
hu_index_0.2+	0.82 (0.76, 0.87)	0.48 (0.44, 0.51)	0.28 (0.25, 0.32)	0.92 (0.89, 0.94)
hu_index_0.3+	0.72 (0.65, 0.78)	0.59 (0.56, 0.63)	0.30 (0.26, 0.35)	0.89 (0.86, 0.92)
hu_index_0.4+	0.61 (0.54, 0.68)	0.70 (0.67, 0.73)	0.34 (0.29, 0.39)	0.88 (0.85, 0.90)
hu_index_0.5+	0.55 (0.48, 0.62)	0.78 (0.75, 0.81)	0.39 (0.33, 0.45)	0.88 (0.85, 0.90)
hu_index_0.6+	0.46 (0.39, 0.53)	0.86 (0.83, 0.88)	0.45 (0.38, 0.52)	0.87 (0.84, 0.89)
hu_index_0.7+	0.34 (0.27, 0.41)	0.91 (0.89, 0.93)	0.48 (0.40, 0.57)	0.85 (0.82, 0.87)
hu_index_0.8+	0.16 (0.11, 0.21)	0.96 (0.94, 0.97)	0.47 (0.35, 0.60)	0.82 (0.79, 0.84)
hu_index_0.9+	0.06 (0.03, 0.10)	0.99 (0.98, 0.99)	0.52 (0.31, 0.73)	0.81 (0.78, 0.83)
xie_index_0.1+	0.88 (0.82, 0.92)	0.45 (0.41, 0.48)	0.28 (0.24, 0.32)	0.94 (0.91, 0.96)
xie_index_0.2+	0.66 (0.59, 0.73)	0.71 (0.68, 0.74)	0.36 (0.31, 0.41)	0.90 (0.87, 0.92)
xie_index_0.3+	0.46 (0.39, 0.53)	0.86 (0.84, 0.89)	0.45 (0.38, 0.53)	0.87 (0.84, 0.89)
xie_index_0.4+	0.30 (0.24, 0.37)	0.92 (0.90, 0.94)	0.50 (0.40, 0.59)	0.84 (0.82, 0.87)
xie_index_0.5+	0.17 (0.12, 0.23)	0.97 (0.95, 0.98)	0.56 (0.42, 0.69)	0.83 (0.80, 0.85)
xie_index_0.6+	0.07 (0.04, 0.11)	0.98 (0.97, 0.99)	0.45 (0.26, 0.64)	0.81 (0.78, 0.84)
xie_index_0.7+	0.04 (0.01, 0.07)	0.99 (0.98, 1.00)	0.47 (0.21, 0.73)	0.81 (0.78, 0.83)
xie_index_0.8+	0.01 (0.00, 0.03)	0.99 (0.99, 1.00)	0.17 (0.00, 0.64)	0.80 (0.78, 0.83)
xie_index_0.9+	0.00 (0.00, 0.02)	1.00 (0.99, 1.00)	0.00 (0.00, 0.71)	0.80 (0.78, 0.83)
isaric_index_6+	1.00 (0.91, 1.00)	0.17 (0.12, 0.23)	0.20 (0.15, 0.26)	1.00 (0.90, 1.00)
isaric_index_9+	0.90 (0.77, 0.97)	0.43 (0.36, 0.50)	0.24 (0.18, 0.32)	0.96 (0.89, 0.99)
isaric_index_12+	0.56 (0.40, 0.72)	0.83 (0.77, 0.88)	0.40 (0.27, 0.53)	0.90 (0.85, 0.94)
mapache_index_15+	0.99 (0.96, 1.00)	0.18 (0.16, 0.21)	0.23 (0.20, 0.26)	0.99 (0.95, 1.00)
mapache_index_40+	0.38 (0.31, 0.46)	0.94 (0.92, 0.95)	0.59 (0.50, 0.68)	0.86 (0.84, 0.88)
mapache_index_50+	0.12 (0.07, 0.17)	0.99 (0.98, 1.00)	0.76 (0.56, 0.90)	0.82 (0.80, 0.85)
mapache_index_60+	0.05 (0.02, 0.09)	1.00 (1.00, 1.00)	1.00 (0.66, 1.00)	0.81 (0.79, 0.84)
cisss_index_0.1+	0.32 (0.25, 0.39)	0.95 (0.93, 0.96)	0.60 (0.50, 0.69)	0.85 (0.83, 0.87)
cisss_index_0.2+	0.09 (0.06, 0.14)	0.99 (0.98, 1.00)	0.69 (0.48, 0.86)	0.82 (0.79, 0.84)
cisss_index_0.3+	0.06 (0.03, 0.11)	1.00 (0.99, 1.00)	0.80 (0.52, 0.96)	0.81 (0.79, 0.84)
cisss_index_0.4+	0.03 (0.01, 0.06)	1.00 (0.99, 1.00)	0.83 (0.36, 1.00)	0.81 (0.78, 0.83)
cisss_index_0.5+	0.02 (0.00, 0.05)	1.00 (1.00, 1.00)	1.00 (0.29, 1.00)	0.81 (0.78, 0.83)
cisss_index_0.6+	0.01 (0.00, 0.03)	1.00 (1.00, 1.00)	1.00 (0.03, 1.00)	0.81 (0.78, 0.83)
news2_index_5+	0.83 (0.68, 0.93)	0.53 (0.46, 0.60)	0.26 (0.19, 0.35)	0.94 (0.88, 0.97)
news2_index_7+	0.68 (0.52, 0.82)	0.64 (0.57, 0.71)	0.28 (0.19, 0.38)	0.91 (0.85, 0.95)

Table S4 Legend. Mortality risk scores[9-15] were calculated based on first valid measurement between ED triage and 24 hours after admission. We report model performance based on hospitalizations with complete data for vital signs and mental/neurological status and mean imputation for missing laboratory test results.

Figure S1. Calibration plots for mortality prediction models in COVID-19 hospitalizations
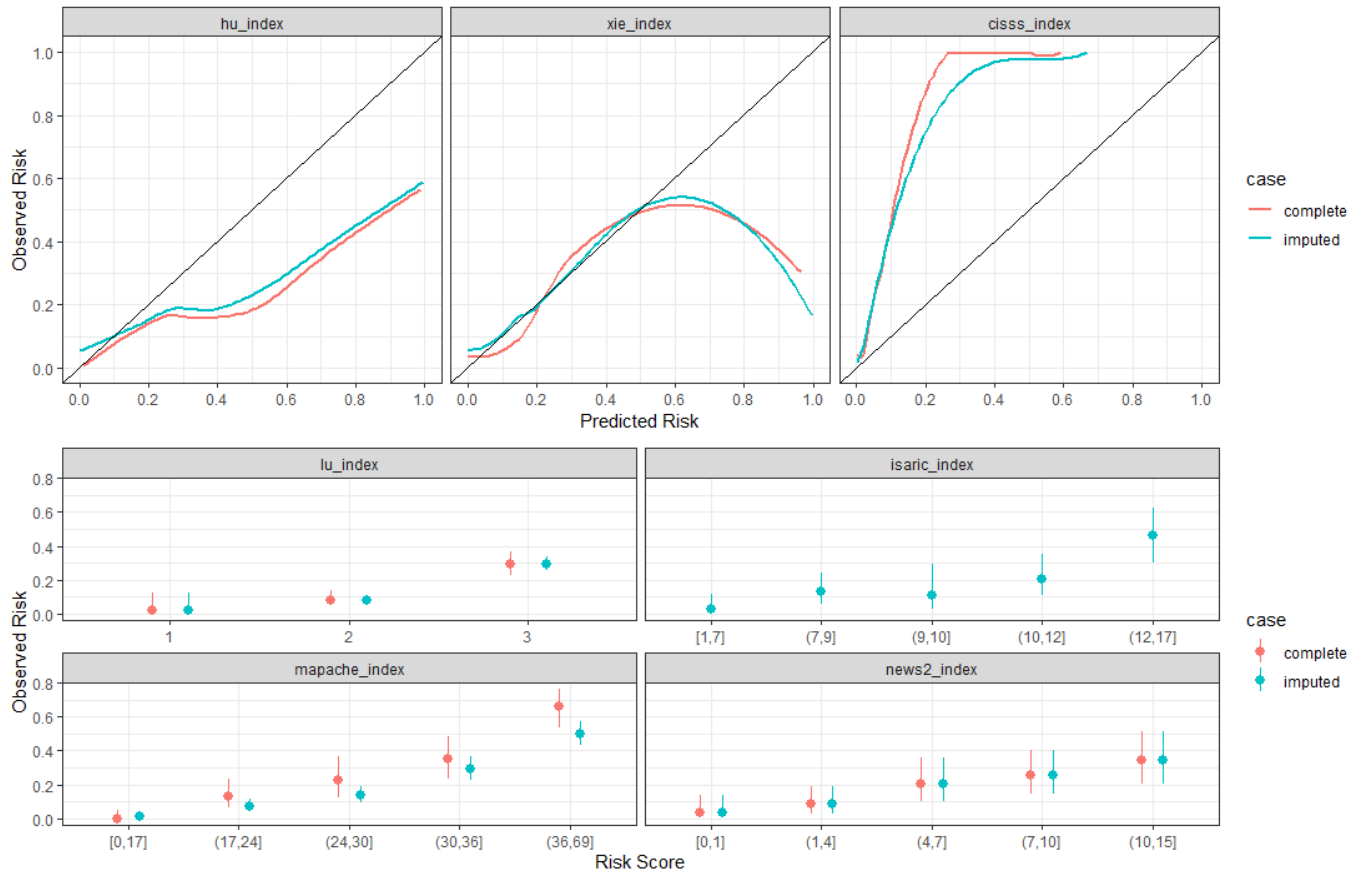
Figure S1 Legend. We report model calibration visually, by plotting model scores versus observed outcome proportions for points-based systems and Loess-smoothed calibration plots comparing observed to predicted probabilities for probability score-based systems.

Sensitivity Analyses

Our findings were materially unchanged after excluding the 79 COVID-19 admissions without laboratory confirmation of virus infection (data not shown).

ED admissions accounted for 73.3% of COVID-19 and 86.0% of influenza admissions. Findings were generally similar after excluding non-ED admissions (Tables S5-9), except differences in hospital length-of-stay and ICU use were somewhat attenuated.

When ICU and death were treated as a composite outcome to account for competing risks, COVID-19 remained more severe than influenza (aRR 1.99, 95% CI: 1.70, 2.34, Table S10). Results were not meaningfully changed after including only one admission per patient to account for clustering (data not shown).

Table S5. Characteristics of hospitalizations for COVID-19 and influenza, among patients admitted from the emergency department

Variable	COVID-19	Influenza	SD[a]
Number of admissions	753	673	
Number of unique patients	727 (96.5)	660 (98.1)	0.094
Age - median (IQR)	66.00 [53.00, 80.00]	69.00 [56.00, 81.00]	0.088
Age Group – N (%)			0.139
<50	166 (22.0)	115 (17.1)	
50-75	333 (44.2)	335 (49.8)	
>75	254 (33.7)	223 (33.1)	
Male Gender – N (%)	437 (58.0)	339 (50.4)	0.154
Charlson Score – N (%)			0.314
0	406 (53.9)	259 (38.5)	
1	126 (16.7)	146 (21.7)	
2+	221 (29.3)	268 (39.8)	
Neighbourhood Income Quintile – N (%)			0.148
1	265 (35.2)	225 (33.4)	
2	118 (15.7)	117 (17.4)	
3	117 (15.5)	107 (15.9)	
4	120 (15.9)	120 (17.8)	
5	83 (11.0)	79 (11.7)	
Neighbourhood Visible Minority Quintile – N(%)			0.167
1	73 (9.7)	81 (12.0)	
2	165 (21.9)	157 (23.3)	
3	210 (27.9)	157 (23.3)	
4	127 (16.9)	136 (20.2)	
5	125 (16.6)	109 (16.2)	
Long-Term Care Resident – N (%)	108 (14.3)	33 (4.9)	0.32
Hypertension - N (%)	257 (34.1)	222 (33.0)	0.024
Diabetes Mellitus - N (%)	206 (27.4)	194 (28.8)	0.033
Renal failure - N (%)	139 (18.5)	136 (20.2)	0.044
Neurocognitive disorders - N (%)	122 (16.2)	92 (13.7)	0.071
Coronary heart disease - N (%)	55 (7.3)	52 (7.7)	0.016
Heart failure - N (%)	48 (6.4)	82 (12.2)	0.201
COPD - N (%)	47 (6.2)	80 (11.9)	0.198

Table S5 Legend. Comparison of patients hospitalized with COVID-19, influenza, and all other conditions. a) SD = standardized difference. SD>0.1 reflects imbalance between groups. Comorbidities were categorized from ICD-10-CA discharge diagnoses using the CCSR tool. COPD: Chronic Obstructive Pulmonary Disease.

Table S6. Unadjusted clinical outcomes, resource use, and clinical care of patients with COVID-19, influenza, and other conditions, among patients admitted from the emergency department

Variable	COVID-19	Influenza	p
Number of Admissions	753	673	
Death – N (%)	154 (20.5)	37 (5.5)	<0.001
7-day Readmission – N (%)[a]	28 (5.2)	21 (3.4)	1**
30-day Readmission – N (%)[b]	47 (10.3)	59 (9.5)	0.72
ICU – N (%)	137 (18.2)	101 (15.0)	0.124
Hospital LOS, days – median (IQR)	6.8 (3.0, 16.2)	4.7 (2.2, 9.5)	<0.001
ED LOS, hours – median (IQR)	8.7 (6.1, 13.2)	21.1 (12.0, 32.2)	<0.001**
ICU LOS, days – median (IQR)	7.9 (2.7, 15.4)	6.3 (2.8, 13.3)	0.60
Invasive mechanical ventilation – N (%)	79 (10.5)	50 (7.4)	1**
GI Endoscopy – N (%)	16 (2.1)	23 (3.4)	1**
Bronchoscopy – N (%)	<6 (<0.8)*	32 (4.8)	<0.001**
Renal Replacement Therapy – N (%)	29 (3.9)	37 (5.5)	1**
CT Thorax – N (%)	159 (21.1)	147 (21.8)	1**
Respiratory Antibiotic – N (%)	518 (69.4)	505 (75.5)	0.685**
Corticosteroid – N (%)	104 (13.9)	243 (36.3)	<0.001**
Warfarin or DOAC – N (%)	111 (14.9)	133 (19.9)	0.816**

Table S5 Legend. Readmission to a medical service or medical-surgical ICU at any participating hospital is reported. For hospital resources and clinical care, we report the number of patients receiving at least one of the items described. ICU: Intensive Care Unit. a) After excluding patients who died and those discharged in the last 7 days of the study period, the denominator was 538 admissions for COVID-19 and 625 for influenza. b) After excluding patients who died and those discharged in the last 30 days of the study period, the denominator was 456 admissions for COVID-19 and 624 for influenza. LOS: Length-of-stay. GI: Gastrointestinal. Renal replacement therapy included hemodialysis and peritoneal dialysis and included both chronic use and new starts. CT: Computed tomography. Antibiotic: we report the use of respiratory-acting antibiotics (see Appendix). DOAC: direct-acting oral anticoagulant. *All counts less than 6 suppressed to reduce risk of patient reidentification. **p-values were adjusted using Bonferroni correction for the secondary outcomes.

Table S7. Clinical outcomes in patients with COVID-19 compared to influenza before and after multivariable adjustment, among patients admitted from the emergency department

Outcome	Unadjusted		Adjusted	
	Effect (95% CI)	p	Effect (95% CI)	p
Death	3.72 (2.64, 5.25)	<0.001	3.96 (2.80, 5.59)	<0.001
ICU	1.21 (0.96, 1.53)	0.11	1.28 (1.00, 1.64)	0.048
Readmission	1.09 (0.76, 1.57)	0.64	1.19 (0.82, 1.73)	0.36
Hospital LOS	1.19 (0.96, 1.47)	0.12	1.22 (1.03, 1.45)	0.02
ICU LOS	0.64 (0.35, 1.17)	0.15	0.79 (0.54, 1.17)	0.24

Table S7 Legend. Poisson regression models were fit for death, ICU, and readmission (effect: adjusted relative risk) and negative binomial regression models were fit for hospital LOS and ICU LOS (effect: adjusted rate ratio). Models were adjusted for patient age, sex, long-term care residence, Charlson comorbidity index score, admitting hospital, neighbourhood-level income and visible minority concentration quintiles. Outcomes reported are: in-hospital death, admission to ICU at any point during hospitalization, readmission to a medical service or medical-surgical ICU at any participating hospital within 30-days of discharge, hospital LOS, and ICU LOS. ICU: intensive care unit. LOS: length-of-stay.

Table S8. Unadjusted outcomes stratified by age, among patients admitted from the emergency department

Outcome	COVID-19	Influenza	p
Age <50 years – N	166	115	
Death – N (%)	<6 (<3.6)*	<6 (<5.2)*	0.623
30-day Readmission – N (%)	12 (9.8)	7 (6.4)	0.034
ICU – N (%)	28 (16.9)	15 (13.0)	0.370
Hospital LOS, days – median (IQR)	4.7 (1.8, 9.0)	3.2 (1.3, 6.7)	0.003
Age 50-75 years – N	333	335	
Death – N (%)	42 (12.6)	13 (3.9)	<0.001
30-day Readmission – N (%)	28 (11.8)	27 (8.5)	0.052
ICU – N (%)	83 (24.9)	60 (17.9)	0.024
Hospital LOS, days – median (IQR)	6.7 (2.9, 16.4)	4.4 (1.9, 8.4)	<0.001
Age >75 years – N	254	223	
Death – N (%)	108 (42.5)	23 (10.3)	<0.001
30-day Readmission – N (%)	7 (7.4)	25 (12.6)	0.40
ICU – N (%)	26 (10.2)	26 (11.7)	0.209
Hospital LOS, days – median (IQR)	10.6 (4.5, 24.0)	6.0 (3.7, 11.7)	<0.001

Table S8 Legend. Readmission to a medical service or medical-surgical ICU at any participating hospital is reported. ICU: Intensive Care Unit. LOS: Length-of-stay. *All counts less than 6 suppressed to reduce risk of patient reidentification.

Table S9. Characteristics, clinical outcomes, resource use, and clinical care of ICU patients, among patients admitted from the emergency department

Variable	COVID-19	Influenza	p
Number of admissions	137	101	
Age - median (IQR)	62 (52, 73)	67 (56, 77)	1**
Age Group – N (%)			1**
<50	28 (20.4)	15 (14.9)	
50-75	83 (60.6)	60 (59.4)	
>75	26 (19.0)	26 (25.7)	
Male Gender – N (%)	78 (56.9)	56 (55.4)	1**
Charlson Score – N (%)			0.01**
0	73 (53.3)	30 (29.7)	
1	31 (22.6)	23 (22.8)	
2+	33 (24.1)	48 (47.5)	
Long-Term Care Resident – N (%)	8 (5.8)	<6 (<6.0)*	1**
Death – N (%)	41 (29.9)	19 (18.8)	0.07
30-day Readmission – N (%)	6 (8.2)	10 (12.3)	0.57
Hospital LOS, days – median (IQR)	15.9 (9.7, 26.5)	15.0 (7.3, 32.6)	0.81
ED LOS, hours – median (IQR)	7.1 (4.6, 9.8)	12.5 (7.2, 24.4)	<0.001**
ICU LOS, days – median (IQR)	7.9 (2.7, 15.4)	6.3 (2.8, 13.3)	0.60
Invasive mechanical ventilation – N (%)	77 (56.2)	50 (49.5)	1**
GI Endoscopy – N (%)	<6 (<4.4)*	11 (10.9)	1**
Bronchoscopy – N (%)	<6 (<4.4)*	22 (21.8)	0.001**
Renal Replacement Therapy – N (%)	19 (13.9)	13 (12.9)	1**
CT Thorax – N (%)	45 (32.8)	41 (40.6)	1**
Antibiotic – N (%)	119 (88.1)	94 (94.0)	1**
Corticosteroid – N (%)	40 (29.6)	48 (48.0)	0.32**
Warfarin or DOAC – N (%)	24 (17.8)	25 (25.0)	1**

Table S9 Legend. Readmission to a medical service or medical-surgical ICU at any participating hospital is reported. For hospital resources and clinical care, we report the number of patients receiving at least one of the items described. ICU: Intensive Care Unit. LOS: Length-of-stay. GI: Gastrointestinal. Renal replacement therapy included hemodialysis and peritoneal dialysis and included both chronic use and new starts. CT: Computed tomography. Antibiotic: we report the use of respiratory-acting antibiotics (see Appendix). DOAC: direct-acting oral anticoagulant. *Exact number suppressed to reduce risk of patient reidentification. **p-values were adjusted using Bonferroni correction, by multiplying with the number of comparisons presented in this study except main outcomes (Death, 30-day Readmission, ICU, ICU Length of Stay and Hospital Length of Stay).

Table S10. Analysis of death and ICU transfers as a composite outcome

Outcome	COVID-19	Influenza	p-value
Number of Admissions	1027	783	N/A
ICU or Death – N (%)	406 (39.5)	161 (20.6)	<0.001
Unadjusted Regression (ICU or Death) – RR (95%CI)	1.92 (1.64, 2.25)	Referent	<0.001
Adjusted Regression (ICU or Death) – aRR (95%CI)	1.99 (1.70, 2.34)	Referent	<0.001

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