

Original research

Patient outcomes following emergency admission to hospital for COVID-19 compared with influenza: retrospective cohort study

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ABSTRACT

Background We examine differences in posthospitalisation outcomes, and health system resource use, for patients hospitalised with COVID-19 during the UK's first pandemic wave in 2020, and influenza during 2018 and 2019.

Methods This retrospective cohort study used routinely collected primary and secondary care data. Outcomes, measured for 90 days follow-up after discharge were length of stay in hospital, mortality, emergency readmission and primary care activity.

Results The study included 5132 patients admitted to hospital as an emergency, with COVID-19 and influenza cohorts comprising 3799 and 1333 patients respectively. Patients in the COVID-19 cohort were more likely to stay in hospital longer than 10 days (OR 3.91, 95% CI 3.14 to 4.65); and more likely to die in hospital (OR 11.85, 95% CI 8.58 to 16.86) and within 90 days of discharge (OR 7.92, 95% CI 6.20 to 10.25). For those who survived, rates of emergency readmission within 90 days were comparable between COVID-19 and influenza cohorts (OR 1.07, 95% CI 0.89 to 1.29), while primary care activity was greater among the COVID-19 cohort (incidence rate ratio 1.30, 95% CI 1.23 to 1.37). Conclusions Patients admitted for COVID-19 were more likely to die, more likely to stay brings used for

more likely to die, more likely to stay in hospital for over 10 days and interact more with primary care after discharge, than patients admitted for influenza. However, readmission rates were similar for both groups. These findings, while situated in the context of the first wave of COVID-19, with the associated pressures on the health system, can inform health service planning for subsequent waves of COVID-19, and show that patients with COVID-19 interact more with healthcare services as well as having poorer outcomes than those with influenza.

INTRODUCTION

Health systems internationally have struggled to cope with high numbers of acutely ill patients through the first and subsequent peaks of the COVID-19 pandemic. As well as the risk of severe disease and death, there are long-term health impacts for some individuals surviving the acute illness phase of COVID-19, and increasing evidence on the impact of this on patients and health services. ¹²

Parallels have been drawn between COVID-19 and influenza due to assumed similarities in their

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Despite initial assumed similarities in clinical features of COVID-19 and influenza, they have different clinical manifestations and clinical outcomes; however, published evidence is bounded to Spring 2020 and mainly come from distinct medical centres.

WHAT THIS STUDY ADDS

- ⇒ This study is the first to quantify differences in both primary and secondary care outcomes for COVID-19 and influenza in a UK regional population.
- ⇒ Patients admitted for COVID-19 were more likely to die, and more likely to stay in hospital for over 10 days, than patients admitted for influenza.
- ⇒ There were also higher levels of primary care activity recorded following discharge for patients with COVID-19 compared with those with influenza.
- ⇒ Readmission rates were similar for both groups.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ Patients with COVID-19 interacted more with healthcare services and had poorer outcomes than those with influenza.
- ⇒ The findings could inform postdischarge care planning for individuals recovering from acute COVID-19, and primary and secondary care resource planning, for example, winter planning.
- ⇒ Quantification of the relative impact of COVID-19 may be relevant to future epidemics of viral respiratory infections.

clinical features. Initially, responses to the pandemic were based on planning for influenza epidemics. However, whereas influenza introduces a recurrent major challenge to healthcare systems and patient outcomes, the COVID-19 pandemic differs from recent seasonal influenza epidemics in its scale and global impact.³ The burden of the COVID-19 pandemic in terms of mortality, morbidity and the economic consequences, has been significantly greater than that associated with recent influenza epidemics.⁴⁻⁶ There are few studies examining differences in outcomes for patients and associated



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burden on health systems, accounting for differences in the demographic profiles of those with severe disease.⁷⁸

In a review, patients with COVID-19 and influenza had many differences in clinical manifestations and radiographic findings.9 Another review10 reported that COVID-19 has a higher mortality compared with influenza with case fatality rate almost 15 times greater than that of influenza. However, these reviews summarised studies reporting on COVID-19 and influenza separately. Only a few studies reported on outcomes of COVID-19 versus influenza directly. Patients with COVID-19 had worse outcomes⁷ 11 than patients with influenza, and had a higher mortality rate. 7 12 13 Patients with COVID-19 had worse respiratory outcomes, including longer duration of mechanical ventilation compared with those with influenza, 7 12 13 greater likelihood of stroke, ¹⁴ acute respiratory distress syndrome, systemic inflammatory response syndrome or acute kidney injury¹³; longer hospitalisation and were admitted to ICU more often than patients with influenza. 15

Patients with COVID-19 were more likely to be male, ¹² ¹³ ¹⁶ have a higher body mass index and have higher rates of chronic kidney disease and diabetes. ¹² They were typically younger, and healthier, with fewer comorbidities and lower medication use. ¹⁶ In children, there was no difference in hospitalisation rates, yet more patients with COVID-19 reported clinical symptoms at the time of diagnosis. ¹⁷

These studies provide evidence up to Spring 2020. Up to June 2020, the UK experienced some of the highest per capita mortality from COVID-19 of any country. 18 It is therefore important to identify differences in the clinical presentation, patient demographics and prognosis of these two diseases. In particular, health system planning for future waves of COVID-19, and for subsequent winters, requires accurate predictions of the impact of both COVID-19 and influenza on service utilisation. Official statistics reported that the mortality rate for COVID-19 is also significantly higher than influenza for both 2020 and the 5-year average, and that people infected with both influenza and COVID-19 are more than twice as likely to die as someone with COVID-19 alone. 19 Despite this, we are unaware of any peer-reviewed study that directly quantifies the difference between COVID-19 and influenza in patient outcomes and service utilisation for the two diseases in a UK population.

We therefore compared outcomes of patients admitted to hospital diagnosed with COVID-19 with patients admitted with a diagnosis of influenza in the previous 2 years, in the population of Northwest London.

METHODS

Design and setting

We used a retrospective cohort study design to compare length of hospital stay, mortality, emergency readmission rate and interaction with primary care for patients admitted as an emergency with COVID-19 and influenza (table 1). The study took place in the geographical area of Northwest London. This area is covered by a National Health Service (NHS) Integrated Care System, comprising a single Clinical Commissioning Group, responsible for planning and commissioning health-care services for the eight boroughs of Northwest London; nine provider Trusts providing hospital, mental health and community services and six local authority councils, responsible for provision of social care services and local public health services. The population of Northwest London is 2.4 million, with similar age-sex distribution to the UK as a whole, and higher ethnic diversity.²⁰

Data

We used the Northwest London Discover dataset, a large population-based dataset covering the region. This dataset comprises linked data on primary, secondary and tertiary care, community and mental healthcare, emergency departments and social care. The Discover dataset contains data on 2.3 million residents currently registered with a general practitioner, as well as 1.1 million previously registered, and 208 000 previous residents now deceased. Fully linked records are available from January 2015 to January 2021 inclusive. Primary care data are sourced from general practice electronic record systems, whereas secondary care data are sourced from a Secondary Uses Service (SUS) dataset. In the service of the service of

Study population and definitions

The study consists of two cohorts: the COVID-19 cohort and the influenza cohort, both comprising adults registered with a general practitioner in Northwest London. Patients were assigned to the COVID-19 cohort if they were admitted to a Northwest London hospital at least once for COVID-19 during 1 February 2020 to 2 November 2020. Admission for COVID-19 was defined as a primary diagnosis International Classification of Diseases, Tenth Revision (ICD-10) code of U071. Patients were assigned to the influenza cohort if they were admitted to hospital at least once for influenza between 1 January 2018 and 31 December 2019, excluding those subsequently admitted for COVID-19. We chose the time period for the influenza cohort to be pre-COVID-19, since the epidemiology of influenza was affected by the COVID-19 pandemic. All emergency admissions to any acute hospital provider Trust in Northwest London were included. Influenza was defined as primary diagnosis ICD-10 codes [09, [10 or [11. For each patient, the index admission was defined as the first eligible admission. Patients with <90 days of follow-up available after index discharge were excluded; this comprised those whose index admission occurred <90 days prior to the end of the study.

Table 1 Outcome definitions				
Outcome	Definition			
Length of stay	Time difference in days between admission and discharge dates of the index admission. A binary variable was defined indicating patients whose index length of stay was in the upper quartile across both cohorts.			
Readmission	A subsequent emergency admission for any cause, within 90 days of the index discharge date.			
Mortality	For those who died outside hospital, we used the midpoint of their month of death as recorded in the Discover data. Binary outcome variables were defined for death in hospital, death prior to 30 and 90 days postdischarge (including in hospital).			
Primary care activity	For each patient, the number of days in which at least one clinical code was assigned to their record. Details of the process by which administrative codes were removed from the data, to leave only clinical codes, are provided in online supplemental file 2.			

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Demographic variables were age group at index admission, sex, ethnic group and an Index of Multiple Deprivation determined using the patient's lower super output area of residence.²²

Analysis

Patient characteristics and unadjusted outcomes were summarised. Differences between the cohorts were analysed using two-tailed Pearson's χ^2 tests, with significance level 0.05 and results expressed as p values and Cramer's V statistic, a measure of effect size. Unadjusted ORs were calculated comparing the cohorts on each binary outcome, and the incidence rate ratio (IRR) similarly for number of primary care activity. Multivariable logistic regression models were fitted for each binary outcome variable, on cohort and adjusting for demographic covariates selected based on clinical expertise, and within the constraints of the available data (age group, sex, ethnic group, Index of Multiple Deprivation quintile). A negative binomial model was fitted for number of primary care activity. Patients with missing ethnicity or Index of Multiple Deprivation data were excluded from regression models, no other variables had missing data. We conducted three sensitivity analyses: to evaluate impact of excluding patients with insufficient follow-up time, to assess any bias due to demographic differences in the cohorts and a survival analysis for length of stay. Results of regression analyses are stated as ORs and IRRs, respectively, with 95% CIs. R statistical software V.3.6.0 was used for all analyses. While we did not undertake power calculations a priori, we have included them for context (see online supplemental file 1).

Patient and public involvement

Lay members of the Northwest London Data Access Committee read the study synopsis and were part of a question-and-answer session before data access approval was granted. This work was also discussed with patient partners at a 'problem solving' session in May 2020. This work uses data provided by patients and collected by the NHS as part of their care and support.

Role of the funding source

The National Institute for Health and Care Research had no role in the design and conduct of the study; collection, analysis or interpretation of data; the writing of the manuscript or the decision to submit it for publication.

RESULTS

A total of 5132 patients met the inclusion criteria: 3799 (74.0%) in the COVID-19 cohort and 1333 (26.0%) in the influenza cohort (figure 1, table 2). This represents an annual incidence of 228 admissions per 100 000 population for COVID-19, 7.5 times that for influenza (30.3 per 100 000 population). The COVID-19 cohort were less likely than influenza admissions to be under 45 (9.7% vs 22.7%), corresponding to a small (V=0.19) but statistically significant difference in the overall age distribution (p<0.001). Patients with COVID-19 were more likely to be male than patients in the influenza cohort (61.4% vs 42.8%, p<0.001). While the difference in ethnicity between the cohorts was significant (p<0.001), with a higher proportion of the COVID-19 cohort of black ethnicity than in the influenza cohort (14.5% vs 9.5%), overall, the difference in ethnicities was small (V=0.07). There was no difference in the distribution of index of multiple deprivation between the cohorts (p=0.70, V = 0.02).

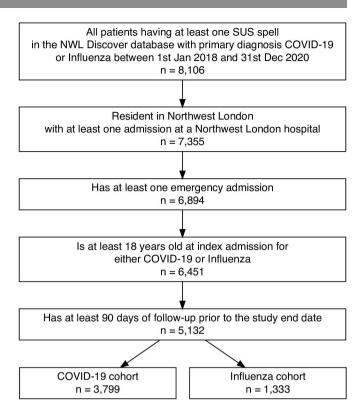


Figure 1 Study flow diagram. The Northwest London (NWL) Discover database contains all Secondary Uses Service (SUS) spells meeting either of the following criteria: (i) the patient is registered with a general practitioner in NWL or (ii) the SUS spell is for a hospital in NWL.

Multivariable regression results

Patients with missing ethnicity or Index of Multiple Deprivation were excluded from multivariate analysis, as their numbers were too small to include an 'unknown' level for these variables in the models. For the mortality models, 179 of the total 5132 patients were excluded. For the other models, 122 of the 3802 patients who did not die during follow-up were excluded. Duration of index admissions was more often longer than 10 days (the overall upper quartile) for COVID-19 than influenza (adjusted OR (AOR) 3.81, 95% CI 3.14 to 4.65) (table 3, figure 2). Patients in the COVID-19 cohort were more likely to die during the index admission (AOR 11.85, 95% CI 8.58 to 16.86), between admission and 30 days postdischarge (AOR 11.01, 95% CI 8.28 to 14.96) and between admission and 90-day postdischarge (AOR 7.92, 95% CI 6.20 to 10.25). Among patients who did not die during index admission or 90 days postdischarge, rates of emergency readmission to hospital within 90 days were comparable between the two cohorts (AOR 1.07, 95% CI 0.89 to 1.29). However, primary care activity within 90 days of discharge was greater among the COVID-19 cohort (adjusted IRR 1.30, 95%) CI 1.23 to 1.37). These relationships were qualitatively the same regardless of whether adjusted (table 3) or unadjusted (table 4) for patients' demographic characteristics. Results of the sensitivity analyses (online supplemental file 1) did not qualitatively alter these results.

DISCUSSION

Summary of main findings

Using a linked, population-level dataset, we found a 7.5 times higher incidence of acute hospital admission for COVID-19 during the first wave of infection in 2020 than for influenza during 2018–19. Those admitted for COVID-19 were more

Table 2 Demographic characteristics of patients with at least one emergency hospital admission for COVID-19 (1 February 2020–2 November 2020) or influenza (1 January 2018–31 December 2019)

Nation N		COVID-19: 3799	Influenza: 1333	Combined: 5132	χ² p value, Cramer's V
135-44 228 (6.0%) 133 (10.0%) 361 (7.0%) 45-54 537 (14.1%) 149 (11.2%) 686 (13.4%) 55-64 691 (18.1%) 209 (15.7%) 900 (17.5%) 55-64 691 (18.1%) 351 (26.3%) 1514 (29.5%) 55-64 1163 (30.6%) 351 (26.3%) 1514 (29.5%) 55-64 1039 (27.3%) 322 (24.2%) 1361 (26.5%) 70-001 70-001 70-016 70-001 70-016 70-001 70-016 70-001 70-016 70-001 70-016 70-001 70-016 70-001 70-016 70-001 70-016 70-001 70-	Age group (years) at index admission				
45-54 537 (14.1%) 149 (11.2%) 686 (13.4%) 55-64 691 (18.1%) 209 (15.7%) 900 (17.5%) 65-79 1163 (30.6%) 351 (26.3%) 1514 (29.5%) 80+ 1039 (27.3%) 322 (24.2%) 1361 (26.5%) Exex P<0.001 V=0.16	18–34	141 (3.7%)	169 (12.7%)	310 (6.0%)	
S5-64 691 (18.1%) 209 (15.7%) 900 (17.5%) 65-79 1163 (30.6%) 351 (26.3%) 1514 (29.5%) 65-79 1163 (90.6%) 322 (24.2%) 1361 (26.5%) 70.01	35–44	228 (6.0%)	133 (10.0%)	361 (7.0%)	
65-79 1163 (30.6%) 351 (26.3%) 1514 (29.5%) 80+ 1039 (27.3%) 322 (24.2%) 1361 (26.5%) 5ex P<0.001 V=0.16	45–54	537 (14.1%)	149 (11.2%)	686 (13.4%)	
80+ 1039 (27.3%) 322 (24.2%) 1361 (26.5%) Sex P<0.001 V=0.16 Male 2334 (61.4%) 570 (42.8%) 2904 (56.6%) Female 1465 (38.6%) 763 (57.2%) 2228 (43.4%) Ethnic group P<0.001 V=0.07 White 1435 (37.8%) 544 (40.8%) 1979 (38.6%) Asian 1308 (34.4%) 481 (36.1%) 1789 (34.9%) Black 551 (14.5%) 127 (9.5%) 678 (13.2%) Mixed 114 (3.0%) 46 (3.5%) 160 (3.1%) Other 371 (9.8%) 128 (9.6%) 499 (9.7%) Index of Multiple Deprivation quintile P=0.70 V=0.02 Index of Multiple Deprivation quintile P=0.70 V=0.02 1 (most deprived) 712 (18.7%) 270 (20.3%) 982 (19.1%) 2 1248 (32.9%) 434 (32.6%) 1682 (32.8%) 3 1029 (27.1%) 335 (25.1%) 1364 (26.6%) 4 490 (12.9%) 175 (13.1%) 665 (13.0%) 5 (least deprived) 210 (5.5%) 77 (5.8%) 287 (5.6%)	55–64	691 (18.1%)	209 (15.7%)	900 (17.5%)	
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Index of Multiple Deprivation quintile P=0.70 V=0.02 1 (most deprived) 712 (18.7%) 270 (20.3%) 982 (19.1%) 2 1248 (32.9%) 434 (32.6%) 1682 (32.8%) 3 1029 (27.1%) 335 (25.1%) 1364 (26.6%) 4 490 (12.9%) 175 (13.1%) 665 (13.0%) 5 (least deprived) 210 (5.5%) 77 (5.8%) 287 (5.6%)	Other	371 (9.8%)	128 (9.6%)	499 (9.7%)	
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4 490 (12.9%) 175 (13.1%) 665 (13.0%) 5 (least deprived) 210 (5.5%) 77 (5.8%) 287 (5.6%)	2	1248 (32.9%)	434 (32.6%)	1682 (32.8%)	
5 (least deprived) 210 (5.5%) 77 (5.8%) 287 (5.6%)	3	1029 (27.1%)	335 (25.1%)	1364 (26.6%)	
	4	490 (12.9%)	175 (13.1%)	665 (13.0%)	
Missing 110 (2.9%) 42 (3.2%) 152 (3.0%)	5 (least deprived)	210 (5.5%)	77 (5.8%)	287 (5.6%)	
	Missing	110 (2.9%)	42 (3.2%)	152 (3.0%)	

likely to be older and male than those admitted for influenza. A greater proportion of patients were of black ethnicity in the COVID-19 cohort. After adjusting for demographics, patients admitted with COVID-19 were much more likely to die in hospital or to stay in hospital for over 10 days, and to die within 30 or 90 days of discharge, compared with those admitted for influenza. Patients who did not die were equally likely to be readmitted to hospital within 90 days of discharge for the two diseases, but the COVID-19 cohort interacted with primary care services more than the influenza cohort.

Correspondence with current literature

This study offers new direct evidence of longer hospital stays for COVID-19 admissions compared with influenza. Our findings of greater activity by primary care services among the COVID-19 cohort, but no difference in emergency readmission rates, are new. The higher mortality rates seen among patients admitted with COVID-19 compared with influenza are in accordance with existing evidence from France and the USA. Moreover, our study adds to the growing body of knowledge internationally concerning the impact of severe COVID-19 infection for patients and for health service providers, including primary care as well as specialist providers.

Our study confirms that COVID-19 has a bigger impact on health outcomes and service use than influenza at both an individual and a population level. Factors contributing to this include the likely higher potential of COVID-19 for respiratory pathogenicity, leading to more respiratory complications, greater risk of ischaemic stroke and higher mortality. This reinforces the need for effective prevention measures to limit the spread and impact of COVID-19, including non-pharmaceutical interventions, as well as vaccination.

Policy implications

Our findings have implications for enhanced pandemic response planning, in terms of understanding patient and service outcomes in relation to influenza, a disease that is currently better understood than COVID-19 and which health services have years of experience dealing with. First, the results on service use both for secondary and primary care during the COVID-19 pandemic have implications for care planning for individuals being discharged from hospital having recovered from acute COVID-19. For example, many patients will need ongoing support in primary care after discharge. Second, our findings provide data for improved service planning, for primary care and perhaps most significantly for secondary care resource planning, for example, in NHS winter planning. Existing scenarios based on influenza epidemic planning may be adapted, taking into account the relative scale of service use for COVID-19 identified in this study. As well as providing an evidence base for such planning

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Table 3 Multivariable regression analysis results of various outcomes for patients admitted to hospital as an emergency for COVID-19 or influenza

	Model 1: length of stay in upper quartile (>10 days)*† N=3680	Model 2: died in hospital N=4953		Model 4: died in hospital/ in 90 days of discharge N=4953	Model 5: readmitted within 90 days of discharge* N=3680	Model 6: primary care activity* N=3680
Model outcome	Logistic regression mode	ls OR (95% CI), p value				Negative binomial model IRR (95% CI), p value
Cohort (influenza rc.)						
COVID-19	3.81 (3.14 to 4.65), p<0.001	11.85 (8.58 to 16.86), p<0.001	11.01 (8.28 to 14.96), p<0.001	7.92 (6.20 to 10.25), p<0.001	1.07 (0.89 to 1.29), p=0.48	1.30 (1.23 to 1.37), p<0.001
Age (18–54 rc.)						
55–64	1.63 (1.29 to 2.06), p<0.001	2.85 (2.07 to 3.97), p<0.001	3.07 (2.29 to 4.15), p<0.001	3.10 (2.34 to 4.15), p<0.001	1.48 (1.13 to 1.93), p=0.0045	1.29 (1.20 to 1.38), p<0.001
65–79	2.27 (1.84 to 2.81), p<0.001	6.90 (5.21 to 9.26), p<0.001	6.82 (5.27 to 8.94), p<0.001	6.67 (5.19 to 8.66), p<0.001	2.12 (1.68 to 2.69), p<0.001	1.47 (1.38 to 1.56), p<0.001
80+	4.40 (3.52 to 5.52), p<0.001	11.75 (8.86 to 15.82), p<0.001	12.26 (9.43 to 16.12), p<0.001	13.05 (10.11 to 17.02), p<0.001	2.75 (2.15 to 3.54), p<0.001	1.50 (1.41 to 1.61), p<0.001
Sex (male rc.)						
Female	0.94 (0.80 to 1.10), p=0.43	0.83 (0.71 to 0.97), p=0.022	0.79 (0.68 to 0.92), p=0.002	0.79 (0.68 to 0.91), p=0.0012	0.86 (0.72 to 1.02), p=0.090	1.07 (1.02 to 1.12), p=0.010
Ethnicity (white rc.)						
Asian	0.70 (0.59 to 0.85), p=0.00020	1.07 (0.89 to 1.28), p=0.47	1.08 (0.91 to 1.28), p=0.40	1.08 (0.91 to 1.28), p=0.38	0.96 (0.79 to 1.18), p=0.71	1.02 (0.96 to 1.08), p=0.49
Black	0.88 (0.68 to 1.12), p=0.30	1.11 (0.87 to 1.41), p=0.40	1.11 (0.88 to 1.40), p=0.38	1.08 (0.86 to 1.36), p=0.50	0.95 (0.72 to 1.25), p=0.72	1.01 (0.93 to 1.09), p=0.82
Mixed	0.76 (0.47 to 1.19), p=0.24	0.95 (0.57 to 1.54), p=0.85	0.98 (0.61 to 1.55), p=0.94	1.04 (0.65 to 1.61), p=0.87	0.57 (0.30 to 0.99), p=0.062	0.93 (0.81 to 1.07), p=0.28
Other	0.81 (0.61 to 1.07), p=0.14	1.10 (0.82 to 1.45), p=0.52	0.984 (0.748 to 1.29), p=0.91	0.98 (0.75 to 1.27), p=0.87	0.76 (0.55 to 1.05), p=0.10	0.92 (0.85 to 1.00), p=0.06
IMD quintile (1—most o	deprived rc.)					
2	0.92 (0.74 to 1.15), p=0.47	1.04 (0.84 to 1.29), p=0.72	1.07 (0.87 to 1.32), p=0.54	1.06 (0.87 to 1.31), p=0.56	0.97 (0.76 to 1.23), p=0.77	0.96 (0.90 to 1.03), p=0.30
3	0.96 (0.76 to 1.20), p=0.71	0.76 (0.61 to 0.96), p=0.022	0.87 (0.70 to 1.08), p=0.21	0.88 (0.71 to 1.09), p=0.25	0.84 (0.65 to 1.08), p=0.17	0.96 (0.90 to 1.03), p=0.28
4	0.83 (0.63 to 1.10), p=0.19	0.85 (0.64 to 1.11), p=0.23	0.90 (0.69 to 1.17), p=0.43	0.84 (0.65 to 1.09) p=0.19	0.79 (0.58 to 1.08), p=0.14	0.97 (0.89 to 1.06), p=0.48
5—least deprived	1.07 (0.74 to 1.54), p=0.72	0.92 (0.64 to 1.30), p=0.63	1.01 (0.72 to 1.42), p=0.94	1.04 (0.75 to 1.45), p=0.81	0.58 (0.36 to 0.90), p=0.018	0.96 (0.86 to 1.08), p=0.51

Admissions were to hospitals in Northwest London, between 1 February 2020 and 2 November 2020 for the COVID-19 cohort and between 1 January 2018 and 31 December 2019 for the influenza cohort. Regression model output is shown as ORs for binary outcomes, and IRRs for primary care activity, with 95% CI and p value. The reference category for each covariate is denoted by rc. Ratios for all terms in the regression models are reported in this table. No interaction terms were included.

in the near future, this quantification of the relative impact of COVID-19 may be of use in responding to future epidemics of viral respiratory infections.

Similar 90-day emergency readmission rates for the two diseases may indicate that learning from interventions used to avoid hospital admissions during the COVID-19 pandemic could potentially be applied to future seasonal influenza epidemics.

Strengths and limitations

This study directly compared patient and service use outcomes following admission to hospital for COVID-19 and influenza. Unlike comparisons made with the general population, this offers insights into differences between disease trajectories independently of other factors associated with hospital admission. We used hospital diagnoses, rather than test results, to define the cohorts, thus avoiding bias due to less comprehensive testing for influenza than COVID-19 during the study period. The diverse population-wide scope of the Discover data virtually eliminated the risk of selection bias due to data coverage, and the routinely collected nature of the data meant that data were available for every patient admitted and coded for

the two diseases over the study period. The only exceptions to this were hospital admissions occurring outside of Northwest London, but this was the same for both cohorts so is not likely to have affected the findings. The datasets used have been found to have good face validity compared with established research datasets.²⁰ Although generalisations from these study findings to other populations should be made with caution, previous research has shown that the study population matches the overall age-sex and chronic disease prevalence distribution of the UK well, while being more ethnically diverse. The SUS data, and the derived hospital episode statistics, are a well-established source of data for observational studies in England.²⁴ A systematic review found that the accuracy of clinical coding used in such databases is sufficiently robust for research purposes.²⁵ Taken together, these features convey significant advantages in terms of the validity of this study, strengthening the potential for our results to inform policy.

The main limitations of this study are common among similar studies based on routinely collected data. The quality of data recorded was dependent on healthcare provider practices in relation to diagnosis and clinical coding. Date of death was only available to

^{*}Readmissions, length of stay and primary care activity are evaluated only for patients who did not die in hospital or within 90 days of discharge.

[†]Comparison for length of stay is Q4 vs Q1-3.

IMD, Index of Multiple Deprivation; IRR, incidence rate ratio.

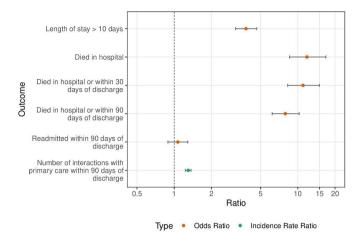


Figure 2 Outcomes for patients admitted to hospital as an emergency for COVID-19 (1 February 2020–2 November 2020) compared with influenza (1 January 2018–31 December 2019) in Northwest London. Each OR was derived from a multivariable logistic regression model for the respective outcome. The incidence rate ratio for primary care activity within 90 days of discharge was derived from a multivariable negative binomial regression model. All ratios are for COVID-19 cohort in comparison with the reference category influenza cohort, adjusted for age, sex, ethnic group and socioeconomic deprivation.

the nearest month for deaths outside of hospital, this was the same for both cohorts. Data on consultations with general practitioners were not available, so we instead considered clinically read-coded interactions with primary care as a proxy for primary care activity. While this likely overestimated actual use of services by patients, this approach was also the same across both cohorts. We cannot rule out systematic changes in coding between the two cohorts however, and future research should seek to explore the nature and extent of primary care use among people discharged from hospital following an acute episode of COVID-19. The covariates included in our

models were chosen to account for the difference in demographic profiles of both incidence and disease severity for COVID-19 and influenza, however, we did not have data on infection severity and so could not adjust for this independently. The Index of Multiple Deprivation is established at a local geography level, each area covering between 1000 and 3000 individuals. While this is not as precise as an individual level measure of socioeconomic deprivation, this was the most precise measure available in the data and is commonly used in observational studies. While other potential sources of confounding exist, such as prior disease history, there were not enough admissions to include these variables in our regression models. Similarly, there were insufficient admissions in these data to explore interaction effects between demographics and the disease cohort. Future research should explore this relationship, especially from the perspective of health inequalities.

The study period did not include winter admissions for COVID-19, so it was not possible to adjust for seasonality in the models. Influenza is highly variable in pathogenicity year on year, and the years chosen (2018 and 2019) may be atypically mild or severe. The COVID-19 pandemic placed huge stress on health service provision during the study period (in 2020), which was not present to the same degree in the years used for comparison with influenza. COVID-19 outcomes have, overall, improved as the pandemic has progressed, therefore the reported comparisons may differ for subsequent waves and variants of COVID-19. In this study, we focused on straightforward binary and count outcomes within a fixed follow-up period posthospital discharge. We excluded patients who died during follow-up from analyses of the other outcomes, providing a perspective on postdischarge service use given survival, rather than an assessment of these outcomes with death as a competing risk.

CONCLUSIONS

Patients admitted to hospital as an emergency for COVID-19 are more likely to die in hospital and within 90 days of discharge from hospital, more likely to stay in hospital for >10 days and interact more with primary care after discharge than patients admitted for

 Table 4
 Univariate and descriptive analysis of various outcomes for patients admitted to hospital as an emergency for COVID-19 or influenza

	COVID-19	Influenza	Combined	Unadjusted OR/IRR (95% CI), p value: COVID-19 compared with influenza
Length of stay in days*	N=2546	N=1256	N=3802	
Median: (LQ-UQ)	7 (3–12)	3 (1–6)	5 (2–10)	
Quartile: n (%)				
Q1: <2	479 (18.8%)	513 (40.8%)	992 (26.1%)	
Q2: 3–5	605 (23.8%)	369 (29.4%)	974 (25.6%)	
Q3: 6–10	699 (27.5%)	238 (18.9%)	937 (24.6%)	
Q4: >10	763 (30.0%)	136 (10.8%)	899 (23.6%)	3.52 (2.89 to 4.32)†
Mortality:	N=3799	N=1333	N=5132	
Died in hospital	1025 (27.0%)	39 (2.9%)	1064 (20.7%)	12.26 (8.84 to 17.46), p<0.001
Died in hospital or within 30 days of discharge	1196 (31.5%)	52 (3.9%)	1248 (24.3%)	11.32 (8.50 to 15.36), p<0.001
Died in hospital or within 90 days of discharge	1253 (33.0%)	77 (5.8%)	1330 (25.9%)	8.03 (6.31 to 10.34), p<0.001
Readmission*: n (%)	N=2546	N=1256	N=3802	
Readmitted within 90 days of discharge	459 (18.0%)	209 (16.6%)	668 (17.6%)	1.10 (0.92 to 1.33), p=0.29
Primary care activity*	N=2546	N=1256	N=3802	
Primary care activity: number of distinct days with clinical coding	27 256 (mean 10.7 per patient)	10 466 (mean 8.3 per patient)	37 722 (mean 9.9 per patient)	IRR 1.28 (1.26 to 1.31), p<0.001

Admissions were to hospitals in Northwest London, between 1 February 2020 and 2 November 2020 for the COVID-19 cohort and between 1 January 2018 and 31 December 2019 for the influenza cohort. Univariate comparison results are ORs for binary outcomes, and IRRs for primary care activity, with 95% CIs and p values.

†Comparison for length of stay is Q4 vs Q1–3. IRR. incidence rate ratio.

^{*}Readmissions, length of stay and primary care activity are evaluated only for patients who did not die in hospital or within 90 days of discharge.

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influenza. However, readmission rates within 90 days are similar for the two diseases among those who survive. These findings provide insight into COVID-19 outcomes in comparison to influenza, a more familiar disease. Health service commissioners and providers should draw on the findings of this study, specifically the impact of increased length of stay and primary care activity, in planning and providing services during the pandemic, during winter and in future epidemics. This is likely to be particularly important should COVID-19 become endemic and seasonal, like influenza.

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Data supplement 1

1 Statistical Power

We did not undertake a power calculation in advance for this study. However, for context we include here power calculations performed after the study was complete.

We performed power calculations for logistic regression based on one covariate, cohort.(1) All power calculations use a type I error rate of 5%. For the logistic regression models, we have not used the effect sizes observed in this study, since this simply yields a one-to-one function of the reported p-value, but rather have drawn on a priori literature where available to derive minimum detectable effect sizes.(2) Baseline odds were derived from the observed outcomes for influenza however, as was the cohort balance.

We used the odds ratio for in hospital mortality from Piroth et al. as the minimum detectable effect size for all mortality outcomes.(3) For readmissions we used the readmission rate for COVID-19 from Donnelly et al.(4) For long length of stay we used odds ratios of 2 and 1.5, as no literature was available a priori for this outcome. For the primary care events outcome, we calculated power for negative binomial regression using the observed data from this study, since no comparable literature was available a priori. For this we used the maximum likelihood approach.(5) The resulting minimum sample sizes to achieve power of 80% are shown in the table below.

Outcome	Sources	Baseline (influenza) proportion/rate	Proportion/rate (COVID-19 minimum detectable)	Minimum detectable Odds/Rate Ratio	Cohort Balance (% COVID- 19)	Required sample size
In-hospital mortality	Piroth et al.	2.9%	20.7%	8.72	74%	297
30 day mortality	Piroth et al.	3.9%	26.1%	8.72	74%	226
90 day mortality	Piroth et al.	5.8%	34.9%	8.72	74%	158
90 day readmission	Donnelly et al.	16%	25.0%	1.75	67%	912
Long length of stay	-	10.8%	19.5%	2	67%	802
Long length of stay	-	10.8%	15.4%	1.5	67%	2,348
Primary care events	This study	8.3	10.6	1.28	67%	374

We also computed the power that would be achieved for these effect sizes, with the actual number of observations in this study, shown in the table below.

Outcome	Sources	Baseline (influenza) proportio n/rate	Proportio n/rate (COVID- 19 minimum detectable	Minimum detectable Odds/Rat e Ratio	Cohort Balance (% COVID- 19)	Actual sample size	Power
In- hospital mortality	Huang et al.	2.9%	20.7%	8.72	74%	5,132	99.9%
30 day mortality	Huang et al.	3.9%	26.1%	8.72	74%	5,132	99.9%
90 day mortality	Huang et al.	5.8%	34.9%	8.72	74%	5,132	99.9%
90 day readmissi on	Donnelly et al.	16%	25.0%	1.75	67%	3,802	99.9%
Long length of stay	-	10.8%	19.5%	2	67%	3,802	99.9%
Long length of stay	-	10.8%	15.4%	1.5	67%	3,802	94.9%
Primary care events	This study	8.3	10.6	1.28	67%	3,802	99.9%

These calculations give some reassurance that the study was powered to detect differences between the influenza and COVID-19 on the level described in the literature, and indeed on the level identified in this study.

2 Sensitivity Analyses

2.1 Sensitivity analysis 1: follow-up time

Aim of sensitivity analysis

To understand the potential impact of any bias introduced through excluding patients with less than 90 days of follow-up

Methods

The 1,319 patients excluded through insufficient follow-up time were those whose index admission date was less than 90 days prior to the study end date (2nd November 2020). To emulate the impact of this exclusion, we re-ran the main regression analyses on a subset of the study population formed by setting the study end date to an earlier date, such that as close as possible to 1,319 were further excluded. This end date for the sensitivity analysis was 11th July 2020, resulting in exclusion of a further 1,262 patients from the COVID-19 cohort.

Results

The influenza cohort was unchanged from the main analysis, comprising the same 1,333 patients. The COVID-19 comprised 2,537 patients, compared with 3,799 in the main analysis. Of the total 3,870 patients included in the sensitivity analysis, 136 had missing ethnicity or IMD data and were excluded from the regression models, as in the main analysis. Of the 2,841 patients who did not die during the follow up period, and were hence included in the length of stay, readmission and primary care interaction models, there were 88 excluded due to missing data. Odds ratios of each outcome for COVID-19 compared with Influenza are shown in supplementary table 1.

Outcome		Full Study (as per table 4	Sensitivity Analysis
		in main manuscript)	
Model 1: Length of		3.81 (3.14 to 4.65)	4.31 (3.496 - 5.34)
stay in upper quartile		p < 0.001	p < 0.001
(> 10 days)		N = 3,680	N = 2,753
Model 2: Died in	[0]	11.85 (8.58 to 16.86)	15.4 (11.1 - 22.0)
hospital	gist (p < 0.001	p < 0.001
	tic r OR	N = 4,953	N = 3,734
Model 3: Died in	(9:	11.01 (8.28 to 15.0)	14.2 (10.6 - 19.4)
hospital / in 30d of	egres:	p < 0.001	p < 0.001
discharge	sion CI),	N = 4,953	N = 3,734
Model 4: Died in	Logistic regression models OR (95% C1), p	7.92 (6.20 to 10.25)	10.0 (7.81 - 13.1)
hospital / in 90 days of	100	p < 0.001	p < 0.001
discharge	lels	N = 4,953	N = 3,734
Model 5: Readmitted	•	1.07 (0.89 to 1.29)	0.976 (0.792 - 1.21)
within 90 days of		p = 0.48	p = 0.82
discharge		N = 3,680	N = 2,753
Model 6: Number of	Negative	1.30 (1.23 to 1.37)	1.26 (1.19 - 1.33)
interactions with	binomial	p < 0.001	p < 0.001
primary care	IRR (95%	N = 3,680	N = 2,753
	CI), p		

2.2 Sensitivity analysis 2: differences between cohorts

Aim of sensitivity analysis

To assess the extent to which the main findings might be biased by differences in demographics between the two cohorts

Methods

We conducted sensitivity analyses by creating matched cohorts of influenza and COVID-19 patients, using exact matching on all covariates in the main analyses; namely age band, sex, ethnic group, and index of multiple deprivation quintile. For each outcome measure we then fitted a weighted univariate regression model, of the same type as for the main analysis, with weights derived from the matching procedure. Model results are provided as marginal odds ratios or incidence rate ratios for the COVID-19 cohort compared with the influenza cohort. 95% confidence intervals were calculated using cluster-robust standard errors.

Results

After matching there were 4,864 patients eligible for inclusion in the mortality analyses, and 3,620 in the other analyses. The results were very similar to those of the main analyses, with all effects in the same direction, of the same statistical significance, and of comparable magnitudes. These results provide reassurance that the main findings are not adversely affected by differences in the observed demographics of the two cohorts.

Outcome	Model 1: Length of stay in upper quartile (> 10 days)	Model 2: Died in hospital	Model 3: Died in hospital / in 30d of discharge	Model 4: Died in hospital / in 90 days of discharge	Model 5: Readmitted within 90 days of discharge	Model 6: Number of interactions with primary care
N (before matching)	3,680	4,953	4,953	4,953	3,680	3,680
n (after matching)	3,620	4,864	4,864	4,864	3,620	3,620
	Log	Negative binomial regression model IRR (95% CI), p- value				
Cohort (Influenza rc.) COVID-19	3.38 (2.81 to 4.09), p < 0.001	9.19 (6.22 to 13.56), p < 0.001	8.88 (6.28 to 12.55), p < 0.001	6.67 (5.33 to 8.44), p < 0.001	1.11 (0.90 to 1.36), p = 0.26	1.26 (1.19 to 1.32), p < 0.001

2.3 Sensitivity Analysis 3: Survival analysis for length of stay in hospital

Aim of sensitivity analysis

Survival analysis offers an alternative, and potentially more sensitive, approach to comparing length of stay for COVID-19 and influenza, and as such we conducted a sensitivity analyses, censoring deaths before successful hospital discharge, as an additional check of the robustness of the main findings for this outcome.

Methods

Using the same inclusion and exclusion criteria as for the main regression models, we first fitted a Cox proportional hazard model, and assessed compliance with the proportional hazards assumption graphically and using Schoenfeld residuals. Where the proportional hazards assumption did not hold we fitted accelerated failure time models, for a range of different distributions, and assessed the accelerated failure assumption graphically. We also fitted Cox models with time-varying coefficients where indicated.

Results

There were n = 4,953 patients included in the analysis. The proportional hazards assumption did not hold (overall Schoenfeld test p < 0.001), being violated for the main variable of interest, namely cohort, and for age band. Stratification by age band still left proportional hazards violated for cohort (p < 0.001). Model assumptions were also violated for all accelerated failure time models fitted (exponential, Weibull, lognormal and log-logistic distributions), and for Cox models with time-varying coefficients for cohort and age band.

The table shows the hazard ratios and p-values for the Cox proportional hazard model stratified by age band; it should be noted that since the proportional hazards assumption is violated here, the hazard ratio for cohort may only be interpreted as an average effect over the timepoints observed in the data.(6) The average hazard ratio for cohort (0.44, 95% CI 0.41 to 0.47) is consistent with the main analysis results of longer lengths of stay in the COVID-19 cohort on average.

Variable	Hazard Ratio (95% CI)	p-value
COVID-19	0.46 (0.43 to 0.50)	p < 0.001
Sex (Male rc.)		
Female	1.09 (1.02 to 1.16)	p = 0.011
Ethnic Group (White rc.)		
Asian	1.14 (1.06 to 1.23)	p < 0.001
Black	1.06 (0.95 to 1.17)	p = 0.307
Mixed	1.21 (1.01 to 1.45)	p = 0.037
Other	1.13 (1.01 to 1.27)	p = 0.032
IMD Quintile (1 – most		
deprived rc.)		
2	1.03 (0.94 to 1.13)	p = 0.503
3	1.08 (0.98 to 1.18)	p = 0.122
4	1.15 (1.03 to 1.29)	p = 0.014
5 – least deprived	1.05 (0.90 to 1.22)	p = 0.565

References

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- 3. Piroth L, Cottenet J, Mariet AS, Bonniaud P, Blot M, Tubert-Bitter P, et al. Comparison of the characteristics, morbidity, and mortality of COVID-19 and seasonal influenza: a nationwide, population-based retrospective cohort study. The Lancet Respiratory Medicine. 2021 Mar;9(3):251–9.
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Data supplement 2

Read codes excluded from patient records when counting distinct days on which primary care clinical activity was recorded.

As a proxy for primary care activity in relation to patients in this study, we counted the number of days in a 90 day period following discharge from hospital. To avoid counting days on which only administrative activity occurred, we used the clinical codes table provided by the Discover database, which first removes any Read CTV2 codes from the data that pertain to purely administrative functions.

The full detail of this process is provided by the SQL code below.

```
Select ReadCodeV2 collate
SQL Latin1 General CP1 CS AS, ReadCodePreferredTerm30
          From
          DimReadCodeV2
          where
          (ReadCodeV2 like '9%' -- Remove for Admin activity
from costing DZ 08/2017
               and not ReadCodeV2 collate
SQL Latin1 General CP1 CS AS in (
     '9b0m.','9b0n.','9bE5.','9k27.','9l0..','9m40.','9m42.','
9m43.','9N2q.',
     '9N2R.','9N2r.','9N2s.','9N2S.','9N2T.','9N2t.','9N2u.','
9N2U.', '9N2V.', '9N2v.',
     '9N2w.','9N2W.','9N2X.','9N2x.','9N2Y.','9N2y.','9N2z.','
9N3..','9N31.','9N311',
     '9N34.','9N3A.','9N3F.','9N45.','9N46.','9N4P.','9N5..','
9N58.', '9N5B.', '9N79.',
     '9N7A.','9N7E.','9N7F.','9N7G.','9Na1.','9NzF.','9OX50','
90X51','90X52','90X54',
     '90X55','90X56','90X57','9Ed..','9H9..','9H90.','9H91.','
9H92.')) -- Phase 2 bringing back some read codes
         or ReadCodeV2 collate SQL Latin1 General CP1 CS AS
in ('9N2..', '9N2Z.')
          or ReadCodeV2 collate SQL Latin1 General CP1 CS AS
     '4141.','4142.','4143.','4144.','4145.','4146.','4147.','
4149.
     '4214.','4411.','4615.','0....','134..','414..','419..','
     '41B10','41B2.','41C1.','44H1.','44I1.','44O1.','46D1.','
     '4J41.','4JF5.','4JJ1.','4JJ2.','4JJ3.','4K11.','4K12.','
67DJ.',
```

```
'681C.','685M.','8B3h.','8B3U.','8B4..','8B41.','8BM8.','8BMA.',

'8BMC.','8BME.','8BMG.','8C1B.','8CE5.','8H2..','8HE..','

8MD..',

'ZV68.','ZV681','38Gt0')
```