Preplanned Studies

Hospital Strain and COVID-19 Fatality — England, April 2020–March 2022

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Summary

What is already known about this topic?

During the coronavirus disease 2019 (COVID-19) pandemic, tremendous efforts have been made in countries to suppress epidemic peaks and strengthen hospital services to avoid hospital strain and ultimately reduce the risk of death from COVID-19. However, there is limited empirical evidence that hospital strain increases COVID-19 deaths.

What is added by this report?

We found the risk of death from COVID-19 was linearly associated with the number of patients currently in hospitals, a measure of hospital strain, before the Omicron period. This risk could be increased by a maximum of 188.0%.

What are the implications for public health practice?

These findings suggest that any (additional) effort to reduce hospital strain would be beneficial during early large COVID-19 outbreaks and possibly also others alike. During an Omicron outbreak, vigilance remains necessary to prevent excess deaths caused by hospital strain as happened in Hong Kong Special Administrative Region, China.

Hospital capacity strain arises when the demand for care resources exceeds supply in hospitals. During the coronavirus disease 2019 (COVID-19) pandemic, tremendous efforts have been made in countries and regions to prevent hospital strain, but there is limited empirical evidence that hospital strain indeed increases COVID-19 deaths. Although a few small studies showed that shortage in intensive care was associated with an increased COVID-19 fatality (*1*–*3*), strain may occur in many areas (i.e., hospital beds, drugs, devices, and staff) in the entire healthcare system besides intensive care and they may all add up to increase the risk of death from COVID-19. As any new COVID-19 cases add service demand to normal healthcare capacities, the number of COVID-19 patients currently in hospitals (PIH) can be viewed as an approximate measure of the strain on the healthcare system. Therefore, we conducted this analysis of surveillance data and used the number of PIH as a measure of hospital strain to examine its effects on the risk of death from COVID-19 using data from England before March 11, 2022. We found that the risk of death from COVID-19 was linearly associated with the number of PIH before the Omicron period and could be increased due to hospital strain by a maximum of 188.0%. This suggests that any (additional) effort to reduce hospital strain would be beneficial during early large COVID-19 outbreaks and possibly also others alike. During an Omicron outbreak, vigilance remains necessary to prevent excess deaths caused by hospital strain as happened in Hong Kong Special Administrative Region (SAR), China.

This is an analysis of surveillance data on all 147,276 COVID-19 deaths and 601,084 hospitalized COVID-19 patients in England during the period between April 9, 2020 and March 11, 2022 extracted on a daily basis from the UK Health Security Agency (*4*). The daily number of COVID-19 PIH was used as a measure of hospital strain, and daily case fatality was expressed as the ratio of the daily number of deaths from COVID-19 to the daily number of COVID-19 PIH and used as a measure of the risk of death from COVID-19. The study was divided into four periods, i.e., the wild, Alpha, Delta, and Omicron waves. The hospital strain-fatality relation in the four different periods was presented separately with a scatter plot and compared using log-linear regressions, controlling for potential confounders including proxy indicators for vaccination effect, severity of illness, error in the number of deaths, variant of the virus, improvement in hospital care, and other factors that changed over the study period. All statistical analyses were performed using R (version 4.1.0, R Development Core Team, Vienna, Austria). Details on the methods are provided in Supplementary Materials (available in http://weekly.chinacdc.cn).

Summary data including the duration of the study period, the total and median daily number of new cases and deaths, median percentage of the population vaccinated with one, two and three doses, and median daily case fatality are presented according to the four periods of the epidemic in Table 1. Notably, the median daily number of new cases increased steadily from 1,425 cases per day in period 1 to 62,303 cases per day in period 4 (mostly Omicron), a 43.7-fold increase. However, the daily number of PIH did not increase proportionally to the daily new cases diagnosed and showed a maximum of only 1.9-fold difference in the 4 periods. The median daily number of deaths was highest during period 1, resulting in a declining daily case fatality during the 4 periods from the highest 3.4% in period 1 to the lowest 1.2% in period 4, a 64.7% decrease (P=0.0137). The decline in fatality could only partially be explained by vaccination, as there were no or only a few people who completed two doses of vaccines during the first two study periods.

The 7-day moving average of daily number of new cases, PIH, and deaths, daily case fatality during the 4 periods of the epidemic in relation to the progress of vaccination and changes in lockdowns, public health measures, and variants of the virus were shown graphically in Supplementary Figure S1 (available in http://weekly.chinacdc.cn). Patterns similar to those observations described above can be visually observed regarding daily new cases, PIH, deaths, and fatality.

Importantly, the association between the daily case fatality and number of PIH, a measure of hospital strain in this study, according to the 4 periods of the epidemic is shown in Figure 1. In periods 1, 2, and 3, the fatality was positively and linearly associated with the number of PIH with a correlation coefficient of 0.95, 0.55, and 0.58, respectively (all P values <0.0001). In period 4, the fatality was sharply divided into two parts. The first part was mostly Delta and the second was predominantly Omicron, in which the fatality was the lowest and remained stable regardless of the variations in the number of PIH. The same conclusions can be drawn when patients currently in ventilation beds were used as a measure of hospital

TABLE 1. The total number of new cases and death events, average of daily new cases, death events, cases in hospitals, percentage of first, second, and third dose of vaccination, and daily case fatality during the 4 periods of the coronavirus disease 2019 epidemic in England between April 9, 2020, and March 11, 2022.

Variable	Four periods of the epidemic				Total (09/04/2020–11/03/2022)
	Period 1 (09/04/2020–11/07/2020)	Period 2 (12/07/2020–30/04/2021)	Period 3 (01/05/2021–26/11/2021)	Period 4 (27/11/2021–11/03/2022)	
No. of days in the period	94	293	210	105	702
Total No. of new cases, (%)	186,230 (1.1)	3,696,656 (22.4)	4,855,376 (29.4)	7,760,057 (47.0)	16,498,319 (100.0)
Total No. of deaths, (%)	36,335 (24.7)	83,400 (56.6)	14,554 (9.9)	12,987 (8.8)	147,276 (100.0)
Total No. of hospital admission, (%)	68,382 (11.4)	287,440 (47.8)	111,316 (18.5)	133,946 (22.3)	601,084 (100.0)
Median (quartiles) No. of new cases	1,425 (760, 3,125)	7,780 (2,224, 18,197)	25,598 (13,505, 31,601)	62,303 (39,223, 93,784)	15,156 (2,752, 31,327)
Median (quartiles) No. of deaths	240 (91, 583)	124 (28, 413)	78 (18, 106)	111 (94, 156)	102 (39, 224)
Median (quartiles) of the percentage of deaths outside hospitals (%)*	43.4 (41.2, 46.6)	29.5 (25.2, 34.2)	20.5 (17.9, 24.3)	30.2 (21.8, 32.3)	28.9 (21.7, 35.1)
Median (quartiles) No. of hospital admission	562 (300, 1,058)	528 (135, 1,467)	636 (196, 751)	1,220 (926, 1,604)	696 (218, 1,232)
Median (quartiles) No. of patients in hospital	7,360 (3,717, 12,265)	5,976 (1,378, 14,411)	5,032 (1,274, 6,066)	9,369 (7,114, 13,331)	5,996 (2,117, 11,585)
Median (quartiles) No. of patients in ventilation beds	764 (299, 1,832)	682 (178, 1,339)	683 (228, 810)	608 (355, 770)	674 (247, 910)
Percentage of population vaccinated (%)					
Median (quartiles) completed 1st dose	0.0 (0.0, 0.0)	0.0 (0.0, 27.7)	82.0 (75.3, 85.0)	90.6 (89.7, 91.3)	52.0 (0.0, 84.2)
Median (quartiles) completed 2nd dose	0.0 (0.0, 0.0)	0.0 (0.0, 1.0)	69.8 (55.4, 78.0)	83.3 (82.0, 84.6)	4.8 (0.0, 76.8)
Median (quartiles) completed 3rd dose	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 3.2)	63.3 (56.1, 65.2)	0.0 (0.0, 0.0)
Median (quartiles) daily case fatality (%)	3.4 (2.6, 4.9)	2.7 (2.1, 3.0)	1.6 (1.4, 1.8)	1.2 (1.0, 1.4)	1.9 (1.5, 2.8)

* Data were available on a weekly basis.

strain (Supplementary Figure S2, available in http://weekly.chinacdc.cn). After adjusting for vaccination score, admission rate, percentage of deaths outside hospitals, study period, and interaction term between PIH and study period, hospital strain remained statistically significantly associated with daily case fatality in the first 3 periods (all *P* values <0.0001 in study periods 1, 2, and 3, respectively) (Table 2, Supplementary Table S1, available in http://weekly.chinacdc.cn).

Finally, as the daily number of PIH increased from the lowest to the highest, the actual (or unadjusted) daily case fatality increased by 188.0% [95% confidence interval (*CI*): 165.9%, 211.6%], 69.9% (95% *CI*: 59.0%, 81.8%), and 58.2% (95% *CI*: 35.4%, 89.0%), respectively, in study periods 1, 2, and 3 (Supplementary Table S2, available in http://weekly.chinacdc.cn).

Results of additional analyses, including sensitivity analyses, are presented in the Supplementary Figures

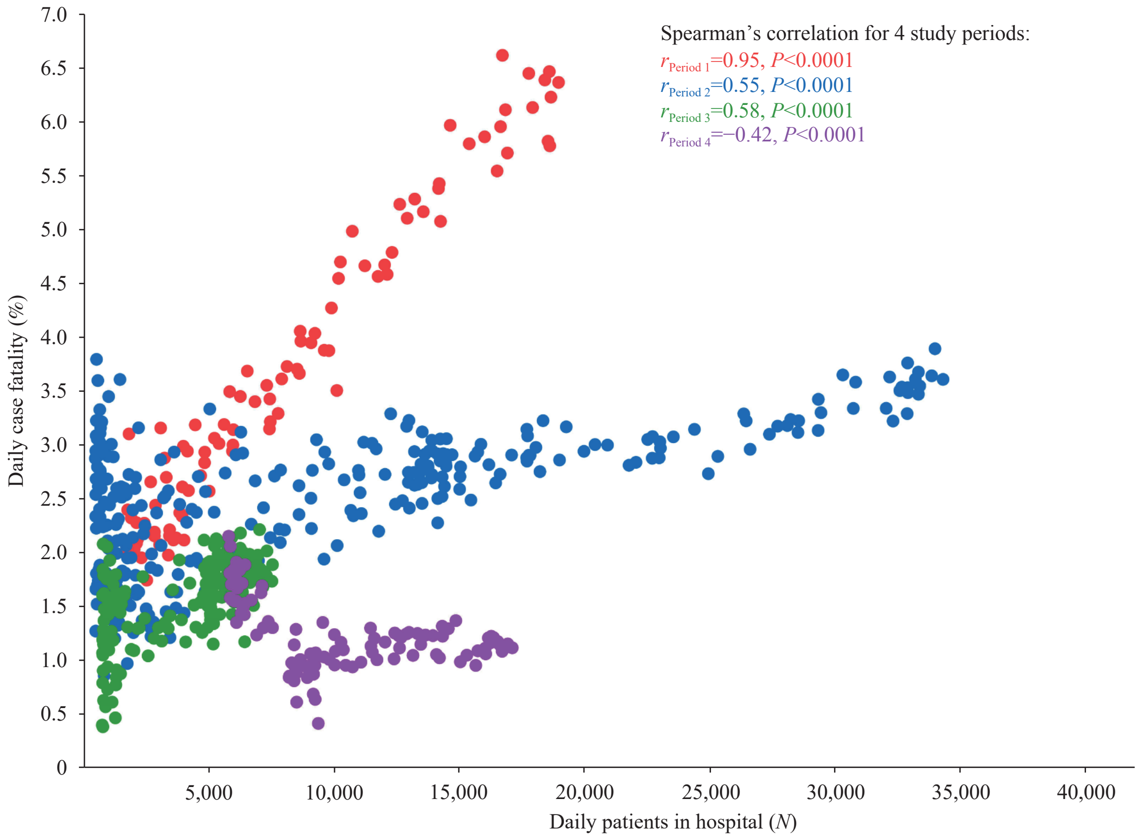

FIGURE 1. Scatter plot and Spearman's correlation between daily case fatality and daily number of patients in hospitals according to the 4 periods of epidemic in England between April 9, 2020, and March 11, 2022.

TABLE 2. Relative increase in daily case fatality for a 1,000-increase in daily number of patients in hospitals according to study period and adjusted for potential confounders.

Study period	Regression coefficients (95% *CI*)*	Relative increase (95% *CI*)*	*P*-value
Period 1	0.062 (0.057, 0.066)	1.063 (1.059, 1.068)	<0.0001
Period 2	0.014 (0.013, 0.015)	1.014 (1.013, 1.015)	<0.0001
Period 3	0.120 (0.102, 0.137)	1.127 (1.108, 1.147)	<0.0001
Period 4	−0.005 (−0.014, 0.003)	0.995 (0.986, 1.003)	0.2306

Abbreviation: *CI*=confidence interval.

* Log-linear multivariable regression was used to estimate the regression coefficients (i.e., the effect of daily number of patients in hospital on daily case fatality) and relative increase (exponential of the regression coefficient) for each period. The regression coefficients and relative increases were adjusted for vaccination score, study period, interaction term between daily number of patients in hospital and study period, admission rate, and percentage of deaths outside hospitals, and weighted by the number of patients in hospital (detailed results in Supplementary Table S1, available in https://weekly.chinacdc.cn/).

S3–S4 (available in http://weekly.chinacdc.cn), and related methods were described in Supplementary Materials.

DISCUSSION

By using authoritative English national data over 2 years of the epidemic, we found that the daily number of COVID-19 PIH as an indicator of overall hospital strain caused by the epidemic was linearly associated with the risk of death from COVID-19, except in the Omicron period, which confirmed findings from several previous studies (*1–3*). The largest difference in the risk of death from COVID-19 observed during an outbreak in England was 2.88-fold, suggesting that a maximum of 65.3% death risk reduction could be achieved theoretically by reducing COVID-19 PIH. However, the linear relation suggests that any (additional) effort to reduce COVID-19 PIH is related to a reduction in the risk of death and is worthwhile regardless of the total number of hospital beds available and their occupancy percentage. Our findings provide strong evidence to support efforts to ease hospital strain in order to reduce deaths during early COVID-19 outbreaks and have important implications for future infectious disease outbreaks similar to early COVID-19 variants and possibly for current Omicron outbreaks as well.

The number of COVID-19 PIH is a composite indicator for overall hospital strain, which can be caused by many complex and interrelated factors within and outside hospitals. Hospital factors include staff, facilities, equipment, drugs, ventilation beds, and preparedness. Non-pharmacological interventions (NPIs) and vaccination are major efforts that can be mobilized outside hospitals to suppress outbreak peaks and reduce hospital strain (*5*). In addition, factors such as the variant of the virus and patients' care-seeking behaviors also affect hospital strain. For example, a shortage in intensive care resources was shown to be associated with an increased risk of death from COVID-19 in the early stage of the pandemic in various countries (*2–3*). Our analyses with a much larger dataset also showed that the number of ventilation beds occupied by COVID-19 patients had a similar effect on fatality. However, studies on these individual determinants of hospital strain may underrate the effect of overall hospital strain on COVID-19 fatality because these studies are restricted to a small fraction of all patients who may die (*2–3*).

Furthermore, these factors may work together to cause difficulties for patients with severe COVID-19 and those with other diseases to be admitted to hospitals, infections in hospital staff, and inpatient cross-infections, which in turn may further increase COVID-19 fatality (*6–7*). Importantly, most of these factors and their interactions in each place or setting would change dynamically over time. Thus, different profiles of hospital strain determinants in a place during different periods of the epidemic may explain the different patterns of the hospital strain-fatality relation found in our study. For example, hospitals were least prepared at the beginning of the pandemic and as a result, the highest fatality was observed during period 1 in our study. As hospitals gained more experience and became more prepared, the hospital strain-fatality relation gradually became less evident. During the last period of our study, the Omicron variant caused the least severe infections, the majority of people had been vaccinated, almost all patients in the UK hospitals had been routinely tested for antigens, and hospitals, care management, and NPIs had become most prepared and efficient (*8*). Consequently, the number of PIH during this period was maintained at a relatively low level, and below it, hospital strain was not shown to be related to fatality.

Besides NPIs, including vaccination, measures can also be taken regarding or within hospitals to reduce hospital strain. For example, in the UK measures including the construction of temporary facilities (e.g. the Nightingale hospitals), the cancellation of elective admissions of patients with other diseases, and stricter triage of admissions and management of mild or moderate COVID-19 cases in communities have been implemented to ease hospital strain (*9*). Our study also showed how the relationship between hospital strain and case fatality varied with different viral variants, providing further implications for policymaking.

Having said all that, we would like to emphasize, importantly, that England's experiences with Omicron may not apply to Omicron outbreaks in all other places. If NPIs were not mobilized quickly and sufficiently, outbreaks of Omicron variants could still raise the number of patients in hospitals to a level that is high enough to cause hospital strain and increase the risk of death from COVID-19, as happened in early 2022 in Hong Kong SAR, which experienced one of the highest fatality rates from Omicron outbreaks in the world (*10*).

The study has some limitations. First, it is possible that more severe patients were admitted when the numbers of PIH were larger. Therefore, the hospital strain-fatality relation may be a result of severity of patients admitted. Second, we used the daily numbers of PIH as the denominator of the daily case fatality, which may not be completely comparable in their severity as they may have different amalgamations of patients at different stages of disease. Third, the numerator of the daily case fatality included death events that occurred outside of hospitals, which may lead to an overestimation of the fatality at the peaks of outbreaks when a larger proportion of patients could not be admitted to hospitals and some of them died. Finally, the variant of the virus, the number of ventilation beds available and vaccination rate could all change over time and caused confounding bias in the relation between the number of PIH and fatality. However, we did sensitivity analyses and believed these limitations were unlikely to change the conclusions of this study (Supplementary Materials).

In conclusion, hospital strain is linearly associated with the risk of death from COVID-19 during early COVID-19 outbreaks, suggesting that any (additional) efforts to ease hospital strain would be beneficial in early COVID-19 outbreaks and possibly others alike. NPIs, vaccination, and hospital preparedness should be used in concert to reduce hospital strain and ultimately minimize deaths.

Conflicts of interest: No conflicts of interest.

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SUPPLEMENTARY MATERIALS

Detailed Methods of the Study

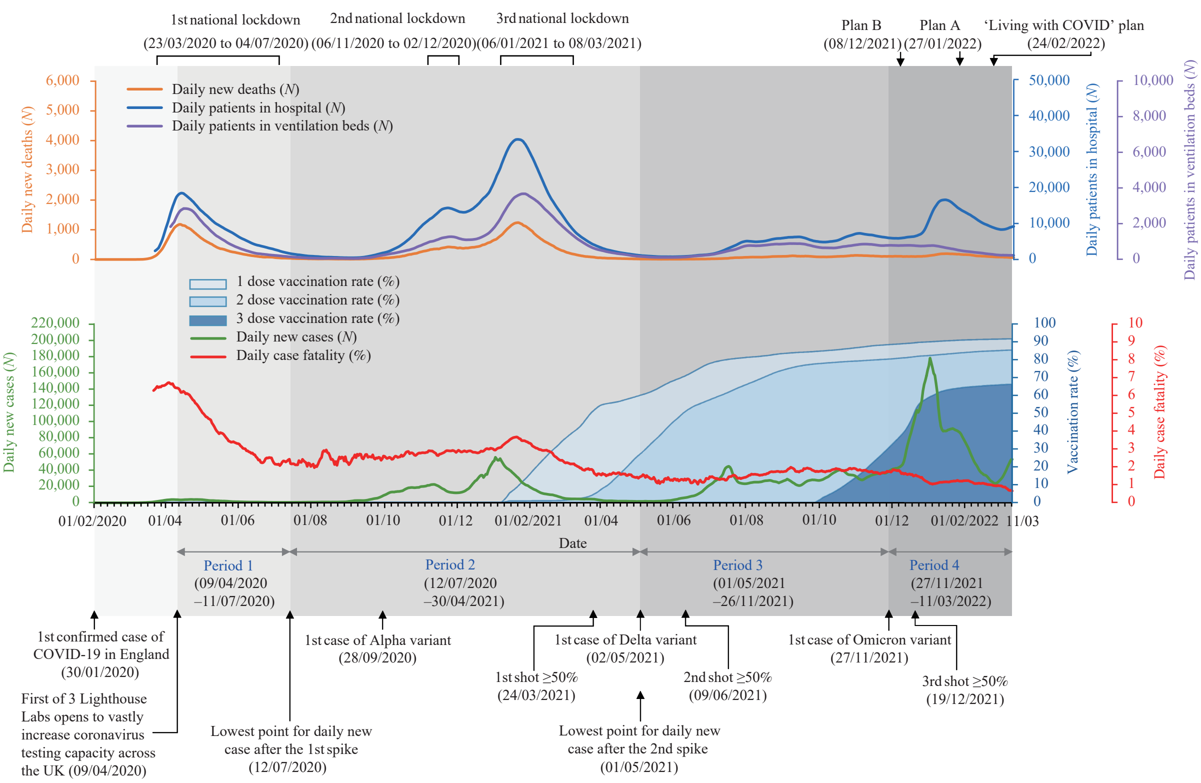
Study Design and Data Sources

This is an analysis of surveillance data extracted on a daily basis from the UK Health Security Agency (UKHSA) (*1*), the most comprehensive and authoritative source of data on coronavirus disease 2019 (COVID-19) in the country (*2*). As mentioned by the UKHSA, these COVID-19 statistics are presented in line with the Code of Practice for Statistics (the standards that producers of official statistics should commit to) (*3*) to ensure high public value, quality, and trustworthiness of the data (*4*). The baseline data included the daily number of newly diagnosed COVID-19 cases, patients currently in hospitals (PIH), patients currently in ventilation beds, and cumulative vaccination rates of 1, 2, and 3 doses in people aged 12 or above. Diagnosis of cases was confirmed by nucleic acid testing, and the date of reporting was that of sampling for the testing. The outcome of interest was those who died with COVID-19 on the same day.

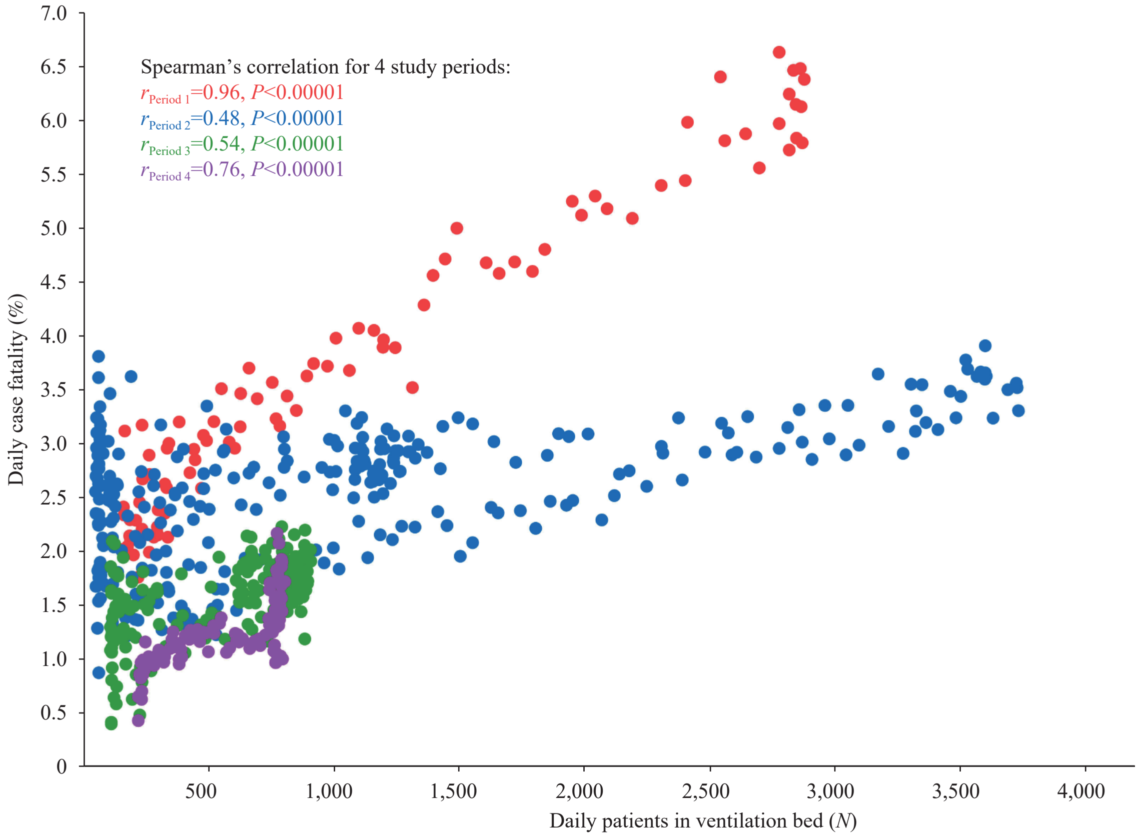
Definitions

Fatality: Daily case fatality was defined as the ratio of the daily number of deaths from COVID-19 over the daily number of COVID-19 PIH (*5–6*). The problem with this definition is that the number of deaths included death events that occurred outside of hospitals. This issue was addressed by examining the correlation between the percentage of deaths outside hospitals and the number of PIH, and considering the percentage of deaths outside hospitals as a potential confounder in the multiple regression analyses assessing the hospital strain-fatality relation (see the statistical analysis section).

Hospital strain: Hospital strain was measured by the total number of PIH in a day.



SUPPLEMENTARY FIGURE S1. Daily number of coronavirus disease 2019 (COVID-19) new cases, cases in hospital, death events, and daily case fatality during the 4 periods of the COVID-19 epidemic and in relation to the progress of vaccination in England between April 9, 2020 and March 11, 2022.



SUPPLEMENTARY FIGURE S2. Scatter plot and Spearman's correlation between daily coronavirus disease 2019 (COVID-19) fatality and daily number of patients currently in ventilation beds according to 4 periods of epidemic in England between April 9, 2020 and March 11, 2022.

Study periods: As the variant of the virus, vaccination coverage, and hospital strain differed considerably over time, we divided the study into four different periods and examined the effect of hospital strain on fatality separately. The first three periods were defined and divided according to the lowest numbers of cases between two major epidemic periods in England, while period 4 started from the reporting of the first Omicron case in the UK. The epidemic period before April 9, 2020 was excluded from the analyses as there was no sufficient nucleic acid testing capacity for diagnosing all infections during the period (*7*) and fatality estimates were likely biased.

Vaccination score: The vaccination rates of 1, 2, and 3 doses were converted into a single vaccination score as a measure of overall protection effect by vaccinations. Let P_1= percentage of people having received 1 dose of vaccine, P_2 for 2 doses, and P_3 for 3 doses. Then the vaccination score = $(P_1 - P_2) + 2(P_2 - P_3) + 3P_3$, which assumes that 1 dose and 2 doses give a protection approximately 1/3 and 2/3 of that of 3 doses according to current available evidence on the protection rate of vaccination (*8*).

Statistical Analysis

The 7-day moving average of daily number of new cases, PIH, deaths, vaccination rate, and daily case fatality were described chronologically in a line chart. Summary results of these variables for the 4 periods were described in a table.

The relation of hospital strain and fatality was examined graphically by scatter plots and by log-linear multivariable regression analyses weighted according to the daily number of PIH. Potential confounders adjusted included the vaccination score, admission rate (as an approximate measure of the severity of illness of patients upon hospital admission), the percentage of deaths outside hospitals (as an approximate quantification of the size of error in the number of deaths for estimating fatalities), study period (as an approximate measure of the total effect of the variants of the virus, improvements in hospital care for COVID-19 patients and other unmeasured potential confounders that differed or changed over the four study periods), and the interaction between PIH and study period (to model different associations between PIH and fatality across four study periods). Data on the percentage of deaths outside hospitals were available on a weekly basis and acquired from the Office for National Statistics website (*9*). Additionally, we are aware that PIH acts as both the independent variable and the denominator for estimating the dependent variable (the fatality). A spurious negative association can, in theory, arise between them. As a result, a positive PIH-fatality association will be underestimated and stronger than that thus observed.

The daily case fatality was also compared for the times when hospitals were least and most strained (namely at the lowest and highest number of PIH) by using the simple regression of fatality against the number of PIH. The relative increase in fatality from the least to most strained time point was estimated and used to reflect the actual maximum increase in fatality due to hospital strain during a study period.

All analyses were conducted separately for the four study periods. P value ≤ 0.05 was considered statistically significant for all significance tests and 95% confidence intervals were constructed for all estimates. All statistical analyses and scatter plots were performed by using R software (Version 4.1.0, R Development Core Team, Vienna, Austria). The epidemic curves were drawn with OriginPro software (version 9.9.0.225, OriginLab Corporation, Northampton, USA).

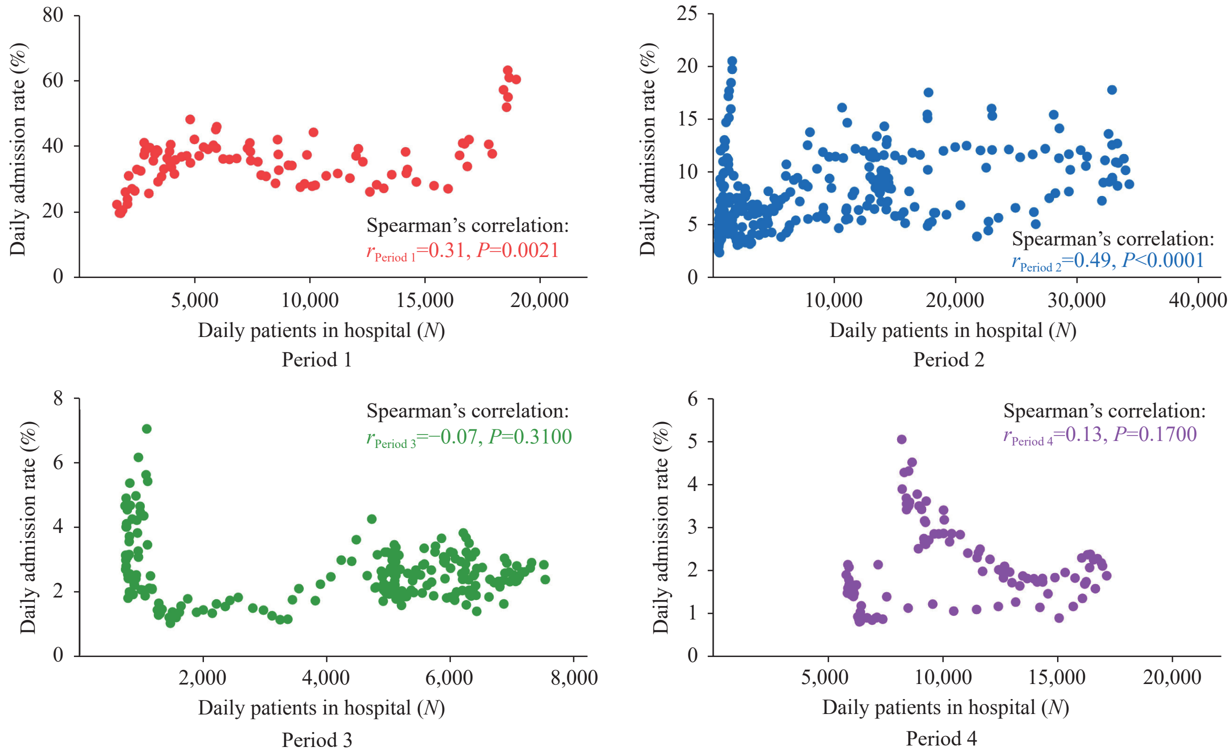
Limitations of the Study

Our study is based on a large amount of high-quality data from England on COVID-19, related deaths, and other relevant factors. Although we have made tremendous efforts to reduce biases and control for confounding, the hospital strain-fatality relation may still be fully or partly explained by residual biases and confounding. We observed that the fatality was higher when the numbers of PIH were larger. Understandably, as the total number of hospital beds was relatively stable during the period of an outbreak, only a fixed number of patients could be admitted. It is therefore possible that more severe patients were admitted when a large number of patients needed to be admitted. Consequently, the number of PIH would be positively related to the severity of patients, causing a false relation between hospital strain and fatality. The admission rate of all COVID-19 patients can be used as an indicator for the severity of patients admitted, and it indeed varied considerably, ranging from 0.8% to 63.4% during the four study periods. We found that the admission rate was not adversely associated with the number of PIH within the study periods (Supplementary Figure S3). Moreover, the hospital strain-fatality relation was affected little when admission rate was included in multiple regression analyses. Thus, we believe that the hospital strain-fatality relation is unlikely a result of the severity of patients admitted.

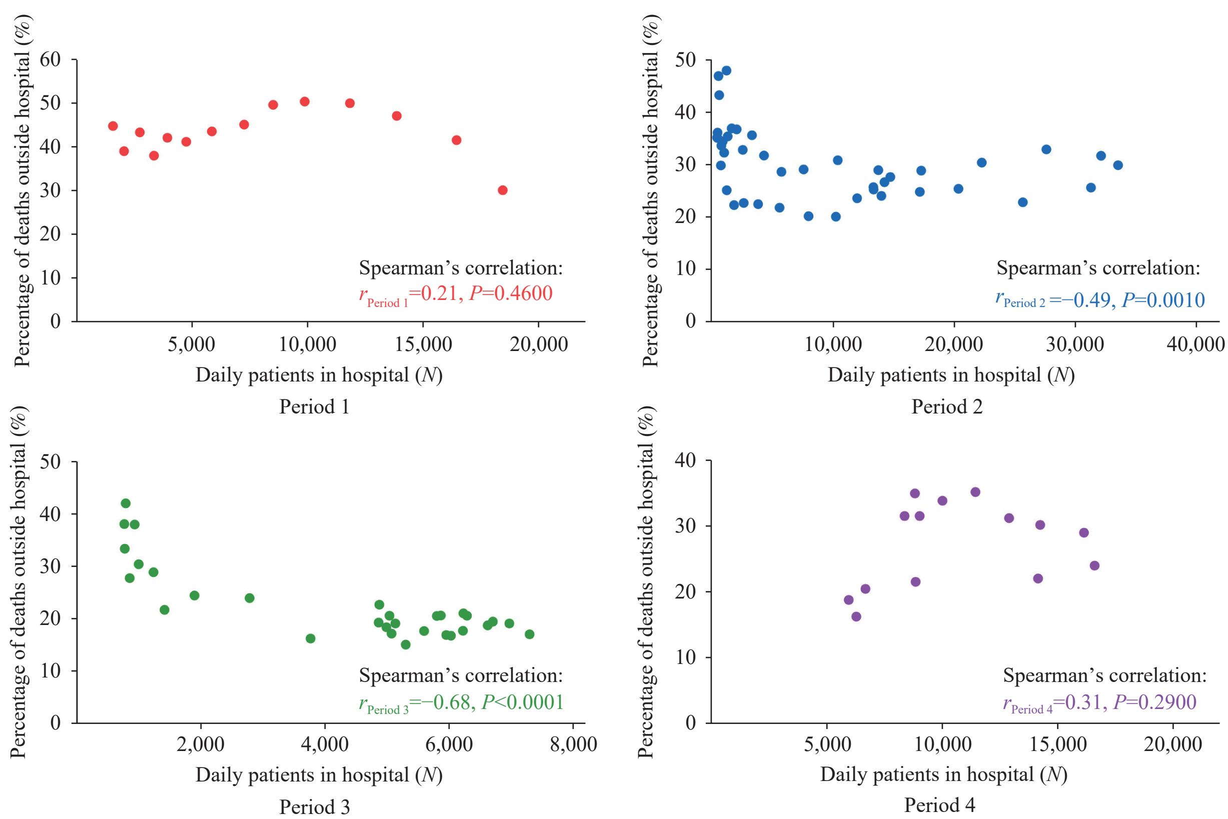
Second, our main analyses used the daily number of deaths divided by the number of PIH as the risk of death. However, the daily numbers of PIH may not be completely comparable in their severity, as they may have different amalgamations of patients at different stages of disease. It is likely that the percentage of patients admitted in earlier days and stayed on in hospitals was relatively smaller when a large number of patients need to be admitted in recent days. As patients admitted in earlier days and stayed on in hospitals were likely more severe than those admitted in recent days (*10*), the hospital strain-fatality relation in our study would have been underestimated as a result.

Third, the numerator of the daily case fatality included an average of 28.7% of deaths outside hospitals. This may lead to overestimation of the fatality at the peaks of outbreaks when a larger proportion of patients could not be admitted to hospitals and some of them died, causing a false hospital strain-fatality relation. However, the hospital strain-fatality relation was unlikely biased by the deaths outside hospitals. First, the percentage of deaths outside hospitals was not positively associated with the number of PIH, implying that it was similar regardless of the number of PIH and could not have caused a bias on the hospital strain-fatality relation (Supplementary Figure S4). In addition, the result of the hospital strain-fatality relation was not changed after the percentage of deaths outside hospitals was included in multiple regression analyses.

Finally, the variant of the virus, the number of ventilation beds available, and vaccination rate could all change over time and cause confounding bias in the relation between the number of PIH and fatality. However, we believed that by dividing into four study periods, confounding effects by the variant of the virus and the number of ventilation beds available have been reduced to a minimum as they had either not changed or changed only slightly within a study period. The confounding effect of vaccination rate was ruled out by including it in multiple regression analyses.



SUPPLEMENTARY FIGURE S3. Scatter plot and Spearman's correlation between daily admission rate and patients currently in hospital during the 4 study periods.



SUPPLEMENTARY FIGURE S4. Scatter plot and Spearman's correlation between the percentage of deaths outside hospitals and daily patients currently in hospital during the 4 study periods (on a weekly basis).

SUPPLEMENTARY TABLE S1. Regression coefficients and relative increase in daily case fatality for each predictor in the multivariable log-linear regression model in Table 2.

Variable	Regression coefficients (95% *CI*)	Relative increase (95% *CI*)	*P*-value
Study periods			
Period 1	−0.005 (−0.113, 0.103)	0.995 (0.893, 1.108)	0.9262
Period 2	Ref (0.000)	Ref (1.000)	NA
Period 3	−0.180 (−0.284, −0.076)	0.835 (0.753, 0.927)	0.0007
Period 4	0.544 (0.347, 0.741)	1.723 (1.414, 2.098)	<0.0001
Daily number of patients in hospital (per 1,000 increase) in period 2	0.014 (0.013, 0.015)	1.014 (1.013, 1.015)	<0.0001
Interaction term between daily number of patients in hospital (per 1,000 increase) and study periods			
Period 1	0.047 (0.043 ,0.052)	NA	<0.0001
Period 2	Ref (0.000)	NA	NA
Period 3	0.106 (0.088, 0.123)	NA	<0.0001
Period 4	−0.019 (−0.028, −0.011)	NA	<0.0001
Vaccination score (per 10% increase)	−0.051 (−0.059, −0.044)	0.950 (0.943, 0.957)	<0.0001
Admission rate (per 10% increase)	−0.019 (−0.040, 0.002)	0.981 (0.961, 1.002)	0.0826
Percentage of deaths outside hospital (per 10% increase)	−0.018 (−0.045, 0.009)	0.982 (0.956, 1.009)	0.1914

Note: NA=not applicable.
Abbreviation: *CI*=confidence interval.

SUPPLEMENTARY TABLE S2. Percentage increase in daily case fatality when the actual daily number of patients in hospital increased from the lowest to the highest in each of the 4 study periods.

Study period	Daily number of patients in hospitals (*N*)		Estimated daily case fatality (%)*		
	Lowest	Highest	At the lowest number patients in hospital (a)	At the highest number patients in hospital (b)	Percentage increase (b−a)/a†
Period 1	1,640	18,974	2.39 (2.29, 2.49)	6.87 (6.65, 7.10)	188.0 (165.9, 211.6)
Period 2	451	34,336	2.15 (2.09, 2.21)	3.65 (3.56, 3.74)	69.9 (59.0, 81.8)
Period 3	730	7,535	1.22 (1.14, 1.30)	1.93 (1.86, 2.00)	58.2 (35.4, 89.0)
Period 4	5,784	17,120	1.25 (1.15, 1.36)	1.08 (1.00, 1.17)	−13.5 (−24.0, 0.5)

* Estimated by using simple linear regression of log daily case fatality against daily number of patients in hospitals, weighted by daily number of patients in hospitals.
† 95% confidence interval (*CI*) was estimated by using the bootstrapping method to generate 10, 000 resampling pairs of estimated daily case fatality at the lowest and highest number patients in hospital within 95% *CI*.

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