ORIGINAL ARTICLE

Trends in Intensive Care for Patients with COVID-19 in England, Wales, and Northern Ireland

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Abstract

Rationale: By describing trends in intensive care for patients with coronavirus disease (COVID-19) we aim to support clinical learning, service planning, and hypothesis generation.

Objectives: To describe variation in ICU admission rates over time and by geography during the first wave of the epidemic in England, Wales, and Northern Ireland; to describe trends in patient characteristics on admission to ICU, first-24-hours physiology in ICU, processes of care in ICU and patient outcomes; and to explore deviations in trends during the peak period.

Methods: A cohort of 10,741 patients with COVID-19 in the Case Mix Program national clinical audit from February 1 to July 31, 2020, was used. Analyses were stratified by time period (prepeak, peak, and postpeak periods) and geographical region. Logistic regression was used to estimate adjusted differences in 28-day in-hospital mortality between periods.

Measurements and Main Results: Admissions to ICUs peaked almost simultaneously across regions but varied 4.6-fold in magnitude. Compared with patients admitted in the prepeak period, patients admitted in the postpeak period were slightly younger but with higher degrees of dependency and comorbidity on admission to ICUs and more deranged first-24-hours physiology. Despite this, receipt of invasive ventilation and renal replacement therapy decreased, and adjusted 28-day in-hospital mortality was reduced by 11.8% (95% confidence interval, 8.7%–15.0%). Many variables exhibited u-shaped or n-shaped curves during the peak.

Conclusions: The population of patients with COVID-19 admitted to ICUs, and the processes of care in ICUs, changed over the first wave of the epidemic. After adjustment for important risk factors, there was a substantial improvement in patient outcomes.

Keywords: COVID-19; intensive care; trends; United Kingdom; mortality

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Access to the Case Mix Program data underlying this paper can be requested by following the guidance here: https://www.icnarc.org/Our-Audit/Audits/Cmp/Reports/Access-Our-Data.

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This article has a related editorial.

This article has an online supplement, which is accessible from this issue's table of contents at www.atsjournals.org.

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At a Glance Commentary

Scientific Knowledge on the Subject: This study uses a high-quality clinical database with 100% coverage of adult general ICUs across England, Wales, and Northern Ireland. We present a comprehensive exploration of the evolution of trends in patient characteristics, first-24-hours physiology, processes of care, and outcomes in ICUs across the first wave of the coronavirus disease (COVID-19) epidemic.

What This Study Adds to the Field: Deviations in the trends during the peak of the epidemic wave were explored, defining the peak period by combining numbers of new ICU patients with the total numbers in ICUs to reflect the overall burden, or strain, of COVID-19 on ICUs. Despite increases in most risk factors exhibited by patients on admission to or during the first 24 hours in ICUs, we found that rates of organ support decreased and mortality improved over time. Improvement in mortality persisted even after sophisticated adjustment for important risk factors.

On March 11, 2020, the outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was declared a pandemic by the World Health Organization (1). After originating in Wuhan, China (2), coronavirus disease (COVID-19) spread across the globe. By November 16, 2020, 1,319,342 deaths across 191 countries had been identified as associated with COVID-19 and the United Kingdom has reported 52,026 COVID-19 associated deaths (3).

With reports of approximately 5% of patients with COVID-19 requiring critical care admission (4, 5), the United Kingdom undertook a number of measures to maximize its ICU capacity to deal with the potential increase in admissions. These measures included increasing the number of overall critical care beds through surge capacity, the building of new "Nightingale" hospitals (specially constructed COVID-19 hospitals), canceling elective surgery, and increasing numbers of available ventilators through redeployment and purchase. Critical care bed capacity in England was expanded from a prepandemic total of 4,122 critical care beds to 7,560 beds equipped for invasive ventilation and 3,405 beds equipped for noninvasive ventilation, an increase from 7.4 to 19.6 beds per 100,000 population.

Complete coverage by the Case Mix Program (CMP), the national clinical audit of National Health Service (NHS) ICUs in England, Wales, and Northern Ireland, provided a unique opportunity to examine trends in critical care for COVID-19 (6). Our aim was to learn from the changes over time during the first wave of the epidemic. Our objectives were to describe variation in ICU admission rates over time and by geography; to describe trends in patient characteristics, the first-24-hours physiology, processes of care, and outcomes; and to explore any deviations in trends during the peak period.

Some of the results of these studies have been previously reported in the form of a preprint (https://www.preprints.org/manuscript/202008.0267).

Methods

Ethics Approval and Consent

Processing of patient data without consent was approved by the Confidentiality Advisory Group of the Health Research Authority under Section 251 of the NHS Act of 2006 (formerly the Patient Information Advisory Group [PIAG 2-10[f]/20059]). Approval by a research ethics committee was not required, as the analysis was performed as a service evaluation.

Data Source

The CMP is the national clinical audit for adult critical care collecting, validating, and pooling case mix and outcome data for individual patient admissions and covering 100% of adult general ICUs (including both standalone and combined intensive/high-dependency care units) across England, Wales, and Northern Ireland. In response to the emerging epidemic, CMP data submission was accelerated, from monthly/quarterly, to daily for COVID-19 admissions. Data included patient characteristics and first-24-hours physiology, ICU, and acute hospital outcome, and type and duration of organ support in ICU.

Data

Data were extracted for all patients with confirmed COVID-19 who were first admitted to ICUs between February 1 and July 31, 2020, using all data submitted up to October 1, 2020. The elapsed period from July 31 to October 1 allowed for data validation and provided a comparable period of follow-up, of at least 60 days, for all patients. Testing for COVID-19 was mandated for all patients in all NHS critical care units with respiratory symptoms from March 2, 2020 (7). Variables were selected on clinical relevance in four areas: patient characteristics on admission to ICU; first-24-hours physiology from the first admission to ICU processes of care in ICU; and outcomes. When selected variables were nonbinary, they were categorized to illustrate variation over time (categories provided in parentheses, below).

Patient characteristics on admission to ICUs. Patient characteristics included, age (⩾75 yr); sex (male); ethnic group (Asian, Black, white, or other); prior dependency (any degree of assistance in daily activities); severe comorbidity (any from 16 defined; *see* table legends); deprivation (highest quintile), which was derived using residential postcode from the 2019 English (8) or Welsh Index of Multiple Deprivation (9) or from the 2017 Northern Ireland Multiple Deprivation Measure (10); body mass index (⩾30) was calculated from weight in kilograms divided by squared height in meters; cardiopulmonary resuscitation within 24 hours before admission to ICUs (received); and the duration of hospital stay before admission to ICUs (admitted to ICU on the same day).

First-24-hours physiology in ICUs. The first-24-hours physiology in ICUs derived from extreme (lowest/highest) physiological values collected during the first 24 hours included, a Pa_{O_2}/FI_{O_2} ratio (⩽200 mm Hg) derived from arterial blood gas with lowest Pa_{O_2} (11), acute kidney injury (stage 2 or 3) derived from Kidney Disease: Improving Global Outcomes (12), and an acute severity of illness (highest quartiles) derived from both the Acute Physiology and Chronic Health Evaluation II (APACHE II) acute physiology score and APACHE II total score.

Processes of care in ICUs. The processes of care in ICUs included the receipt of invasive ventilation (during first

24 h and at any point), the receipt of renal replacement (at any point), and the duration of each of these.

Outcomes. The outcomes included 28-day in-hospital mortality, duration of ICU stay, and time to in-hospital death.

Statistical Analysis

Multiple ICU admissions for the same patient were linked using the unique national identifier (NHS number), residential postcode, date of birth, and sex, and combined into a single patient record. In deriving the 28-day in-hospital mortality, patients discharged from the acute hospital before 28 days were up were assumed to have survived to 28 days. Durations of invasive ventilation, renal replacement, and ICU stay were capped and stratified by survivorship at 28 days. Using the date of a patient's first admission to the ICU with a diagnosis of COVID-19, ICU admission rates were derived and combined with estimates of population size reported by the Office for National Statistics (13). ICU admission rates were also stratified by geographical region (as defined by the NHS Commissioning Region for the treating hospital).

Trends were described continuously using linearly weighted moving averages, assigning a weight of one for the given date, and reducing to one-eighth at ±7 days. To further describe trends, the observation window was partitioned into three periods: the prepeak, peak, and postpeak periods. The primary analysis defined the peak period as 3 days before the observed peak in new ICU admissions to 3 days after the observed peak in the total number of patients in ICUs. Patient characteristics, 24-hour physiology, processes of care, and outcomes were summarized by these periods with differences estimated for the peak period versus the prepeak period and the postpeak period versus the prepeak period. Survival was further explored using a Kaplan-Meier curve, stratified by time period, censoring patients remaining in the hospital on the most recent date of update from the treating hospital and censoring patients discharged from hospital on October 1, 2020 (date of data extraction). Outcome data from subsequent readmissions to an ICU in a separate hospital stay were included.

To control for potential confounding, a logistic regression model was fitted for 28-day in-hospital mortality, with dummy variables for the time period, before and after controlling for a range of covariates recorded during the first 24 hours of the first admission to ICU. Covariate selection was informed by a previous analysis of independent predictors of death in ICU patients with COVID-19 (14). To support regression modeling, 10 sets of multiply imputed data were created using fully conditional specification using the same approach as described elsewhere (14). The unadjusted and adjusted outcomes were compared overall, for London and non-London regions combined.

The sensitivity analyses included redefining the peak period as either the peak in new ICU admissions ± 7 days or the peak in the total number of patients in ICUs ± 7 days and restricting the analysis to patients who received invasive ventilation.

All analyses were conducted using Stata 16 (StataCorp).

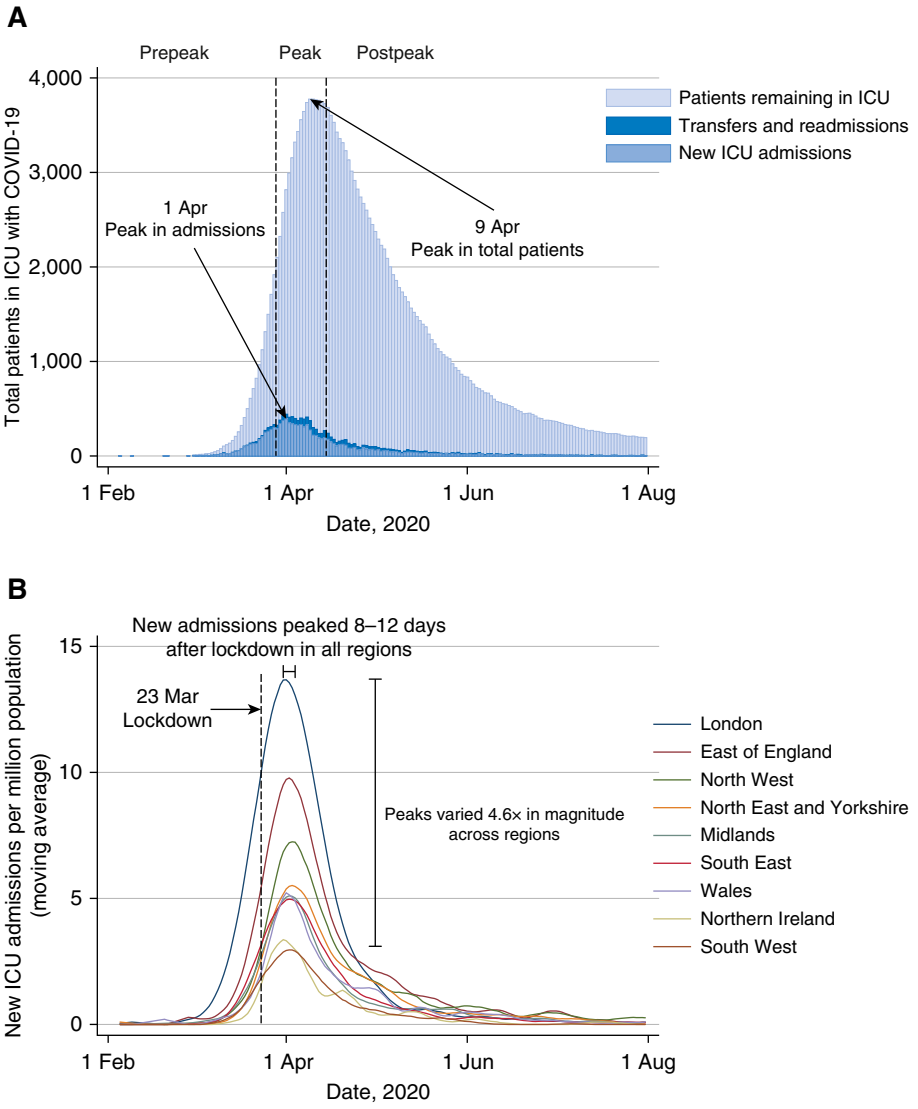

Figure 1. Coronavirus disease (COVID-19) critical care admission rates. (*A*) New ICU admissions, transfers and readmissions, and patients remaining in the ICU all contribute to the total number of patients in the ICU. (*B*) Regions are the National Health Service–commissioning regions, denominators are Office for National Statistics estimates of the mid-2019 regional population aged 15 years and over (13), and moving averages are linearly weighted averages ± 7 days.

Results

COVID-19 Cohort

By October 1, 13,896 admissions to 259 ICUs across 223 hospitals had been received for 10,741 patients with COVID-19 who were first admitted to ICUs between February 1 and July 31, 2020 (*see* Figure E1 in the online supplement). The COVID-19 cohort is summarized in Table E1 and has been reported in detail elsewhere (15). To support international comparisons, the COVID-19 cohort is also summarized by receipt of invasive ventilation in Table E2.

ICU Admission Rates over Time and by Geography

New ICU admissions peaked on April 1, 9 days after lockdown, and the total number of patients in ICUs peaked on April 9 (Figure 1A). We, therefore, defined the peak period of the first wave of the epidemic as being from March 29 (3 d before the peak in new admissions to ICUs) to April 12 (3 d after the peak in the total number of patients in ICUs). There were 2,451; 4,624; and 3,666 patients in the prepeak, peak, and postpeak periods, respectively.

Across regions, rates of new ICU admissions peaked approximately simultaneously but varied substantially in magnitude (4.6-fold population-adjusted difference between London and the South West of England) (Figure 1B).

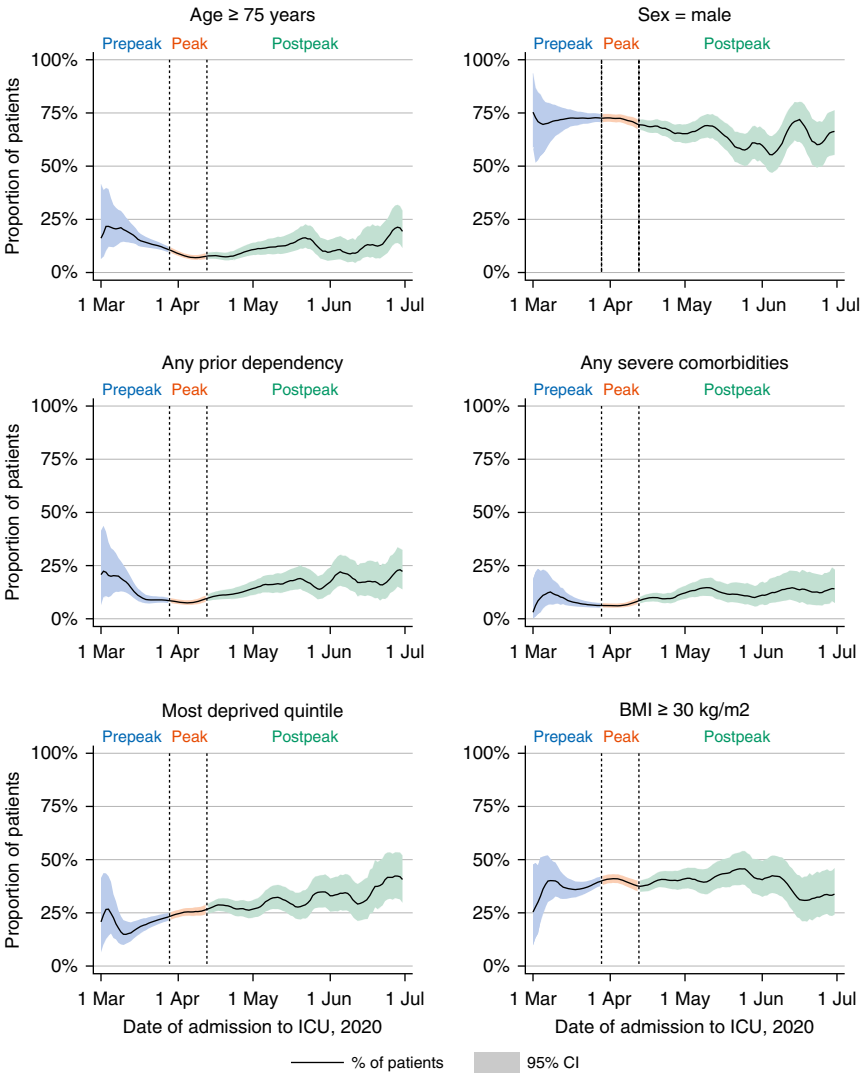

Figure 2. Trends in characteristics of patients with coronavirus disease (COVID-19) on admission to ICUs. The lines are the moving averages and linearly weighted averages ± 7 days. Patients first admitted during February or July are not presented because of the small numbers. BMI = body mass index; CI = confidence interval.

Trends in Patient Characteristics, First-24-Hours Physiology, Processes of Care, and Outcomes

Trends are presented in Figures 2–4 and E2 and summarized by time period in Table 1. With respect to patient characteristics on admission to the ICU, comparing postpeak with prepeak periods showed that proportions of patients aged ⩾75 years or who were male or of the black ethnic group were lower in the postpeak period. Conversely, the proportions who were of the Asian or white ethnic groups, had any prior dependency or any severe comorbidities, or were from the most deprived quintile were higher in the postpeak period. The proportion of patients admitted to ICUs on the same day as hospital admission decreased, in the postpeak period, with a corresponding increase in the mean duration of hospital stay before ICU admission. With respect to the first-24-hours physiology in the ICU, the proportion with Pa_{O_2}/FI_{O_2} ratios ⩽ 200 mm Hg reduced slightly in the postpeak period, but the proportion with APACHE II acute physiology scores ⩾ 14 or total APACHE II scores ⩾ 18 increased in the postpeak period. Comparing processes of care in ICUs for postpeak to prepeak periods, receipt of invasive ventilation reduced markedly both within the first 24 hours (32.7% reduction; 95% confidence interval [95% CI], 30.3–35.1%) and at any point during the ICU stay (23.9% reduction; 95% CI, 21.8–26.0%). The duration of ventilation increased slightly among survivors but not among nonsurvivors in the postpeak period. The receipt of renal replacement was also reduced in the postpeak period.

With respect to outcomes, the overall 28-day in-hospital mortality decreased from 43.6% (95% CI, 41.6–45.6%) in the prepeak period to 33.6% (95% CI, 32.0–35.1%) in the postpeak period. The difference seen in the 28-day in-hospital mortality was sustained to 90 days (Figure E3) and, after adjustment for important covariates, the estimated reduction in the overall 28-day in-hospital mortality postpeak period versus the prepeak period was 11.8% (95% CI, 8.7–15.0%; odds ratio, 0.62; 95% CI, 0.54–0.70) (Figure 5 and Table E3). The

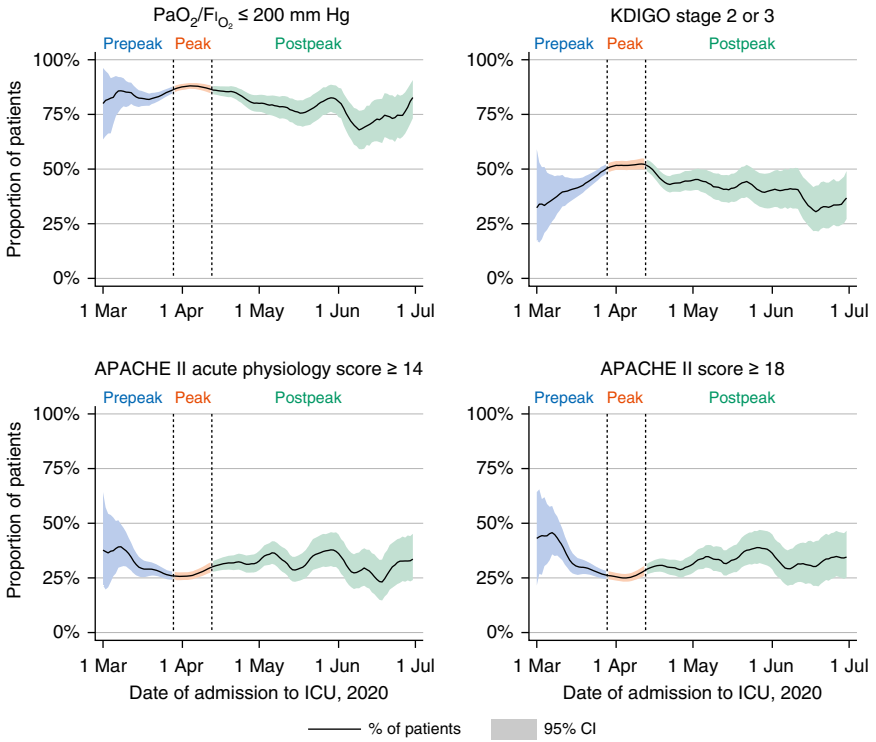

Figure 3. Trends in patients with coronavirus disease (COVID-19) first-24-hours physiology in ICUs. The lines are the moving averages and linearly weighted averages ± 7 days. Patients first admitted during February or July are not presented because of the small numbers. APACHE II = Acute Physiology and Chronic Health Evaluation; CI = confidence interval; KDIGO = Kidney Disease: Improving Global Outcomes.

duration of the ICU stay reduced in the postpeak period both overall and among survivors but remained stable among nonsurvivors (Figure 4 and Table 1).

Missing data are summarized in Table E4 and multiple imputations and regression outputs are detailed in Tables E5 and E6.

Deviations in Trends during the Peak Period

Some trends revealed deviations during the peak period, indicated by u-shaped or n-shaped curves (Figures 2–4) and inconsistent differences between periods (Table 1). The proportions of patients aged ⩾75 years or with any prior dependency was lower during the peak period. The proportion of patients with APACHE II scores ⩾ 18 decreased during the peak period despite a long-term increasing trend, and the proportions with Pa_{O_2}/FI_{O_2} ratio ⩽ 200 mm Hg or Kidney Disease: Improving Global Outcomes stage 2 or stage 3 kidney injury increased during the peak period despite long-term downwards trends.

Although the overall trend in 28-day in-hospital mortality was decreasing, when London (with the highest critical care admission rate) was compared with non-London (all other regions combined), an n-shaped curve was observed for London but the confidence intervals for London/non-London overlapped (Figure 5 and Table E3).

In each sensitivity analysis, results were similar but attenuated (Tables E7–E9).

Discussion

New ICU admissions for COVID-19 peaked nine days after lockdown and the total number of patients in ICUs peaked eight days later. Across geographical regions, COVID-19 ICU admission rates peaked almost simultaneously but varied considerably in magnitude (4.6–fold). COVID-19 testing was mandated in ICUs from March 2 onward and because ICU admission is intrinsically tied to the need for organ support, specifically invasive ventilation, ICU admission rates provide a reasonably consistent indicator of the disease burden over time. By reporting these relative to a population census rather than to community or hospitalized COVID-19 cases (for which available national data are inconsistent and incomplete), we minimized confounding by changes in testing over time. The ICU admission rates therefore strongly suggested that lockdown was effective at preventing—or, at least, postponing—infections.

Clearly, cities such as London with major national and international transport hubs will have had higher numbers of people traveling into, out of, and within them, which may help to explain why admission rates in London began climbing earliest. Although regions with higher proportions of people from nonwhite ethnic groups living in more deprived areas and greater levels of obesity may have been disproportionately affected by COVID-19 (16), other factors may also have contributed to the observed differences between regions, such as population density, household size, and the proportion of essential workers (17–20).

Over the first wave of the epidemic, the population of patients admitted to ICUs with COVID-19 became slightly younger individuals from more deprived areas and with higher degrees of preexisting dependency/comorbidity. These changes in age and deprivation were consistent with regional and demographic changes reported in infection surveillance reports (21) and could be due to the changing geographical spread of the first wave and/or reflect access to ICU care. Securing population-based data on age and deprivation, over time, for all those with COVID-19 would allow further exploration as to whether the patterns seen for ICU admissions reflected those for the total population and/or reflected access to ICU care.

Over time, the population of patients admitted to ICU with COVID-19 became more acutely ill. Despite a lower median of Pa_{O_2}/FI_{O_2} ratios (which may represent more permissive management of "happy hypoxemia") (22), the use of invasive ventilation reduced and, if used, shifted toward later commencement in ICUs. The reduction in invasive ventilation was associated with an equivalent reduction in the use of renal replacement therapy, which may reflect an indirect benefit. The changes in first-24-hours physiology and processes of care in the ICU may reflect an

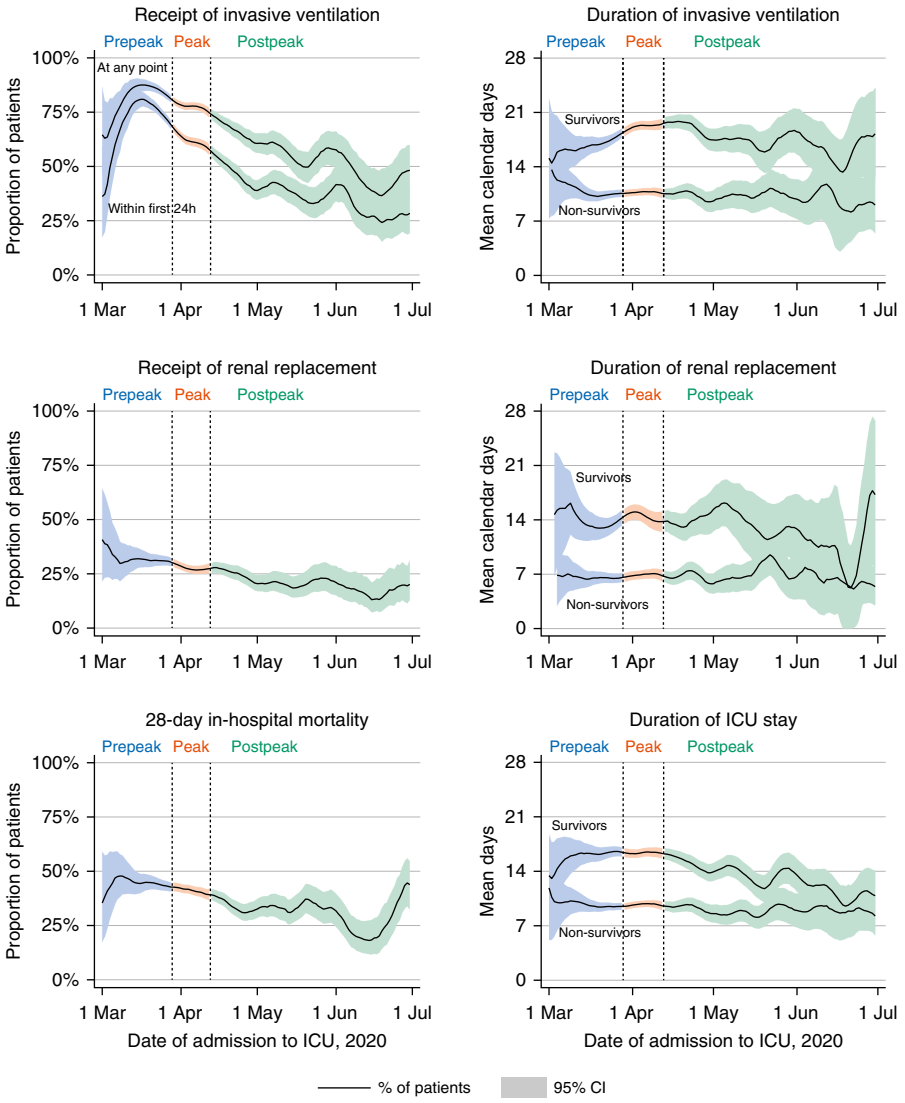

Figure 4. Trends in the coronavirus disease (COVID-19) processes of care in ICUs and outcomes. The lines are moving averages and linearly weighted averages ± 7 days. Patients first admitted during February or July were not shown because of the small numbers. The durations are capped and stratified by survivorship at 28 days. CI = confidence interval.

evolution in the management of patients with mild to moderate COVID-19 outside the ICU, which is also indicated by longer-duration hospital stays before ICU admission toward the end of the first wave of the epidemic. Another possible explanation for the trends observed in processes of care in ICU is earlier recognition and diagnosis leading to earlier admission to ICU, later in the epidemic wave, such that, patients did not require intubation on arrival to ICU (23, 24). Our measures of respiratory impairment in the first 24 hours in ICUs, however, do not support this interpretation.

Overall, 28-day in-hospital mortality improved substantially even after adjustment for important risk factors. This could reflect rapid learning from a large number of informal, information-sharing networks (national/international), leading to avoidance of potentially harmful interventions (e.g., early intubation) and/or adoption of potentially beneficial treatments. The use of steroids (e.g., dexamethasone), however, is unlikely to explain the improvement in 28-day in-hospital mortality, as the RECOVERY (Randomized Evaluation of COVID-19 Therapy) trial released their preliminary results to the press on June 16 (25), with few patients admitted to ICUs after this date being included in our study. Our finding of reducing mortality over the first wave of the epidemic is consistent with a single-center study from Italy (26) and with an analysis of surveillance data from England with lower coverage (77%) and less sophisticated adjustment for important risk factors (27).

Deviations in some trends were apparent during the peak period. Patients admitted during the peak period were slightly younger (less likely to be aged ⩾75 yr), less likely to have any prior dependency, and more likely to have moderate or severe respiratory dysfunction or renal dysfunction, despite overall downward trends for these during the first wave of the epidemic. Processes of care in ICUs, however, did not deviate and mortality only slightly improved during the peak period. Examining London, the region with the highest burden of COVID-19 admissions, there was some indication (nonsignificant) of an increase in the adjusted 28-day in-hospital mortality during the peak period. Taken together, these observations might suggest conservation of ICU resources (i.e., caring for less severe critically ill patients outside of the ICU) and/or rationing of care during the peak period. However, at the peak of the epidemic, critical care bed capacity in England was expanded from a total of 4,122 critical care beds before the pandemic (7.4 beds per 100,000 population) to 7,560 beds equipped for invasive ventilation and 3,405 beds equipped for noninvasive ventilation (19.6 beds per 100,000 population). The reported occupancy of these expanded beds never exceeded 60%. The degree to which ICU capacity played a role in the trends seen will require data on all admissions to ICU, both COVID-19 and non-COVID-19 cases.

The study benefited from a rapid response to the emerging epidemic through the existence of the CMP (a platform able to adapt quickly), a well-defined and unchanged dataset, an established mechanism for the collection of prospective data, and a network of trained data collectors across ICUs who submitted high-quality clinical data daily. This response was informed by lessons learned during the H1N1 pandemic (28, 29). By examining and combining both new ICU admissions and the total number of patients

Table 1. COVID-19 Cohort by Time Period

Characteristic*	Median (IQR) or *n/N* (%)			Unadjusted Difference (95% CI)*	
	Prepeak Period from February 1 to March 28	Peak Period from March 29 to April 12	Postpeak Period from April 13 to July 31	Peak vs. Prepeak Periods	Postpeak vs. Prepeak Periods
N	2,451	4,624	3,666	—	—
Mean new admissions/d per hospital, median (IQR)	0.3 (0.1 to 0.6)	1.1 (0.6 to 1.9)	0.1 (0.1 to 0.2)	**0.8 (0.6 to 1.0)**	−0.1 (−0.2 to −0.1)
Patient characteristics on admission to ICU					
Age					
Median (IQR)	61 (51 to 70)	59 (51 to 67)	59 (50 to 68)	**−2.0 (−2.7 to −1.3)**	**−2.0 (−2.7 to −1.3)**
⩾75 yr, *n/N* (%)	329/2,451 (13.4%)	372/4,624 (8.0%)	381/3,666 (10.4%)	**−5.4% (−6.9% to −3.8%)**	**−3.0% (−.7% to −1.4%)**
Sex, M, *n/N* (%)	1,778/2,449 (72.6%)	3,321/4,621 (71.9%)	2,432/3,665 (66.4%)	−0.7% (−2.9% to 1.5%)	**−6.2% (−8.6% to −3.9%)**
Ethnic group, *n/N* (%)					
Asian	312/2,347 (13.3%)	729/4,461 (16.3%)	587/3,530 (16.6%)	**3.0% (1.3% to 4.8%)**	**3.3% (1.5% to 5.2%)**
Black	303/2,347 (12.9%)	427/4,461 (9.6%)	258/3,530 (7.3%)	**−3.3% (−4.9% to −1.7%)**	**−5.6% (−7.2% to −4.0%)**
White	1,532/2,347 (65.3%)	2,895/4,461 (64.9%)	2,420/3,530 (68.6%)	−0.4% (−2.8% to 2.0%)	**3.3% (0.8% to 5.7%)**
Other	200/2,347 (8.5%)	410/4,461 (9.2%)	265/3,530 (7.5%)	0.7% (−0.7% to 2.1%)	−1.0% (−2.4% to 0.4%)
Any prior dependency, *n/N* (%)	242/2,436 (9.9%)	360/4,568 (7.9%)	516/3,634 (14.2%)	**−2.1% (−3.5% to −0.6%)**	**4.3% (2.6% to 5.9%)**
Any severe comorbidities, *n/N* (%)†	168/2,437 (6.9%)	302/4,568 (6.6%)	408/3,638 (11.2%)	−0.3% (−1.5% to 1.0%)	**4.3% (2.9% to 5.8%)**
Most deprived quintile, *n/N* (%)	498/2,419 (20.6%)	1,154/4,563 (25.3%)	1,071/3,611 (29.7%)	**4.7% (2.7% to 6.7%)**	**9.1% (6.9% to 11.3%)**
Body mass index, kg/m^2					
Median (IQR)	28.0 (24.8 to 32.7)	28.4 (25.0 to 32.9)	28.1 (24.6 to 33.3)	**0.4 (0.0 to 0.8)**	0.1 (−0.3 to 0.5)
⩾30, *n/N* (%)	887/2,358 (37.6%)	1,758/4,371 (40.2%)	1,374/3,472 (39.6%)	**2.6% (0.2% to 5.0%)**	2.0% (−0.6% to 4.5%)
CPR within or before 24 h, *n/N* (%)	24/2,451 (1.0%)	47/4,621 (1.0%)	53/3,665 (1.4%)	0.0% (−0.4% to 0.5%)	0.5% (−0.1% to 1.0%)
Hospital stay before ICU admission					
Duration (calendar days), mean (SD)	1.8 (6.2)	1.9 (3.8)	3.6 (8.1)	0.1 (−0.1 to 0.4)	**1.8 (1.4 to 2.2)**
Admitted to ICU on same day as hospital, *n/N* (%)	1,162/2,451 (47.4%)	1,909/4,624 (41.3%)	1,297/3,666 (35.4%)	**−6.1% (−8.6% to −3.7%)**	**−12.0% (−14.5% to −9.5%)**
First-24-h physiology in ICU					
Pa_{O_2}/FI_{O_2} ratio, mm Hg					
Median (IQR)	126.0 (87.9 to 173.6)	115.5 (84.6 to 159.0)	116.7 (82.5 to 173.6)	**−10.5 (−14.3 to −6.7)**	**−9.3 (−13.3 to −5.3)**
⩽200 mm Hg, *n/N* (%)	1,972/2,367 (83.3%)	3,829/4,353 (88.0%)	2,746/3,389 (81.0%)	**4.7% (2.9% to 6.4%)**	**−2.3% (−4.3% to −0.3%)**
Acute renal failure (KDIGO stage 2 or 3), *n/N* (%)	1,082/2,416 (44.8%)	2,356/4,518 (52.1%)	1,563/3,578 (43.7%)	**7.4% (4.9% to 9.8%)**	−1.1% (−3.7% to 1.5%)
APACHE II score					
Acute physiology score, median (IQR)	11 (9, 14)	11 (8, 14)	11 (9, 14)	0.0 (0.0 to 0.0)	0.0 (−0.5 to 0.5)
Acute physiology score ⩾ 14, *n/N* (%)‡	686/2,441 (28.1%)	1,225/4,589 (26.7%)	1,166/3,645 (32.0%)	−1.4% (−3.6% to 0.8%)	**3.9% (1.5% to 6.2%)**
APACHE II score, median (IQR)	15 (12 to 18)	14 (11 to 18)	15 (12 to 19)	**−1.0 (−1.5 to −0.5)**	0.0 (−0.5 to 0.5)
APACHE II score ⩾ 18, *n/N* (%)‡	706/2,441 (28.9%)	1,182/4,588 (25.8%)	1,161/3,645 (31.9%)	**−3.2% (−5.4% to −1.0%)**	**2.9% (0.6% to 5.3%)**
Processes of care in ICU					
Invasive ventilation					
During first 24 h, *n/N* (%)	1,825/2,423 (75.3%)	2,839/4,560 (62.3%)	1,541/3,616 (42.6%)	**−13.1% (−15.3% to −10.8%)**	**−32.7% (−35.1% to −30.3%)**
At any point, *n/N* (%)	2,083/2,451 (85.0%)	3,591/4,623 (77.7%)	2,238/3,662 (61.1%)	**−7.3% (−9.2% to −5.5%)**	**−23.9% (−26.0% to −21.8%)**
Duration (calendar days) among survivors, mean (SD)§	17.3 (9.1)	19.2 (8.9)	18.4 (9.4)	**1.9 (1.2 to 2.5)**	**1.1 (0.3 to 1.8)**

(Continued)

Table 1. (*Continued*)

Characteristic*	Median (IQR) or *n/N* (%)			Unadjusted Difference (95% CI)*	
	Prepeak Period from February 1 to March 28	Peak Period from March 29 to April 12	Postpeak Period from April 13 to July 31	Peak vs. Prepeak Periods	Postpeak vs. Prepeak Periods
Duration (calendar days) among nonsurvivors, mean (SD)§	10.6 (6.1)	10.7 (6.6)	10.3 (7.1)	0.1 (−0.4 to 0.6)	−0.3 (−0.9 to 0.3)
Renal replacement					
At any point, *n/N* (%)	771/2,451 (31.5%)	1,269/4,622 (27.5%)	844/3,660 (23.1%)	**−4.0% (−6.2% to −1.8%)**	**−8.4% (−10.7% to −6.1%)**
Duration (calendar days) among survivors, mean (SD)§	13.4 (8.3)	14.5 (9.2)	13.5 (9.7)	1.1 (0.0 to 2.2)	0.1 (−1.2 to 1.3)
Duration (calendar days) among nonsurvivors, mean (SD)§	6.5 (4.8)	6.9 (5.3)	6.7 (5.1)	0.4 (−0.2 to 1.1)	0.2 (−0.5 to 0.9)
Outcomes					
28-d in-hospital mortality, *n/N* (%)	1,068/2,450 (43.6%)	1,911/4,620 (41.4%)	1,227/3,649 (33.6%)	−2.2% (−4.7% to 0.2%)	**−10.0% (−12.5% to −7.5%)**
ICU stay					
Duration (calendar days) overall, mean (SD)§	13.5 (9.2)	13.6 (9.6)	12.4 (9.7)	0.1 (−0.4 to 0.6)	**−1.1 (−1.6 to −0.6)**
Duration (calendar days) among survivors, mean (SD)§	16.5 (9.9)	16.3 (10.4)	14.1 (10.4)	−0.2 (−0.8 to 0.5)	**−2.4 (−3.1 to −1.8)**
Duration (calendar days) among nonsurvivors, mean (SD)§	9.6 (6.3)	9.7 (6.6)	9.2 (7.1)	0.1 (−0.4 to 0.6)	−0.4 (−1.0 to 0.1)

Definition of abbreviations: APACHE II = Acute Physiology and Chronic Health Evaluation; CI = confidence interval; COVID-19 = coronavirus disease; CPR = cardiopulmonary resuscitation; IQR = interquartile range; KDIGO = Kidney Disease: Improving Global Outcomes.

The 95% CIs were calculated using an exact formula for the difference in proportions, *t*-statistics for the difference in means, and the Bonett-Price formula for the difference in medians. The bold indicates $P < 0.05$. Analyses were based on observed data (not imputed).

*See text for definitions.

†Any severe comorbidities are defined as cardiovascular (symptoms of fatigue, claudication, dyspnea, or angina at rest), respiratory (shortness of breath with light activity or home ventilation), renal (receipt of renal replacement therapy for end-stage renal disease), liver-related (biopsy-proven cirrhosis, portal hypertension, or hepatic encephalopathy), metastatic disease–related (distant metastases), hematological malignancy–related (acute or chronic leukemia, multiple myeloma, or lymphoma), and immunocompromise–related (receipt of chemotherapy, radiotherapy, or daily high-dose steroid treatment in previous 6 months, HIV/AIDS, or a congenital immune deficiency).

‡Seventy-fifth percentile selected to illustrate changes in distribution over time.

§Survivorship was calculated, and durations were capped at 28 days.

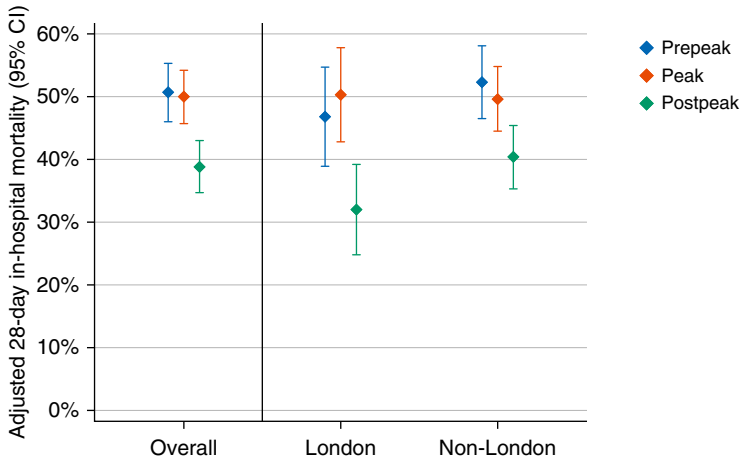

Figure 5. Adjusted 28-day in-hospital mortality, by time period and geography. The estimates represent the average marginal predicted risk of 28-day mortality for a patient with the mean values for all covariates, fitted after a multiple logistic regression. The results were adjusted for age, sex, ethnicity, quintile of deprivation, body mass index, any dependency before hospital admission, immunocompromised, sedated for entire of first 24 hours, highest temperature, lowest systolic blood pressure, highest heart rate, highest respiratory rate, Pa_{O_2}/F_{IO_2} ratio, highest blood lactate concentration, highest serum creatinine, highest serum urea, lowest Hb concentration, and lowest platelet count. CI = confidence interval.

in ICUs to define our peak period, we better reflected the potential burden of COVID-19 cases on ICUs. Using the CMP ensured high coverage, reducing potential selection bias. Although the burden of COVID-19 cases on ICU resources could have affected case ascertainment and accuracy of data submitted during the peak (i.e., coverage, completeness, validity, and reliability), ongoing further checking of case coverage and data accuracy continued beyond the peak and postpeak periods.

Although there was 100% coverage of ICUs and patients with COVID-19 admitted to ICUs, not all critically ill patients treated solely outside of ICUs (e.g., in surge areas) were captured. Although testing in ICUs was established after the start of the prepeak period, only 11 patients (0.4%) were admitted before mandatory testing was introduced and, of these, only 2 (0.1%) completed their ICU stay before March 2. Accurate data on testing for community or hospitalized COVID-19 cases, or how such testing strategies evolved over time, were not available. However, the institution of broader testing during the pandemic led to the increasing inclusion of critically ill patients with COVID-19 coded as the secondary reason for admission to ICUs (2.8%, 2.4%, and 8.8% in the prepeak, peak, and postpeak periods, respectively). However, these patients had comparable rates of invasive ventilation and 28-day in-hospital mortality (57.2% and 31.1%, respectively), so this could not explain the lower observed mortality in the postpeak period.

Although data completeness was high, the amount of missing data for Pa_{O_2}/F_{IO_2} ratio was 5.9% and correlated with the use of invasive ventilation during the first 24 hours. The amount of missing data for the Pa_{O_2}/F_{IO_2} ratio could not explain the trends observed. This is a descriptive observational study, and we recognize that there may be other potential explanations for many of the observed trends. Finally, we report the COVID-19 experience for the NHS, and generalizability to other healthcare systems must be considered.

In conclusion, this study highlights changes over the first wave of the epidemic, in terms of patient characteristics on admission to ICU, first-24-hours physiology in ICU, processes of care in ICU, and outcomes. After adjustment for important risk factors, there was a substantial improvement in 28-day in-hospital mortality over the course of the first wave of the epidemic. ■

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