research

New York City covid-19 case series p 401

Risk factors for covid-19 admission and critical illness p 402

Covid-19 on the US west coast p 403

ORIGINAL RESEARCH Retrospective case series

FAST TRACK

Characterisation and clinical course of 1000 patients with coronavirus disease 2019 in New York

Argenziano MG, Bruce SL, Slater CL, et al

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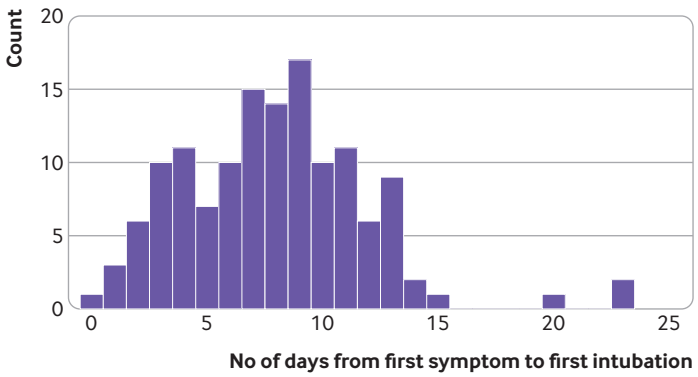
Study question What are the characteristics of patients with coronavirus disease 2019 (covid-19) presenting to a large New York City medical centre, and what is their clinical course across emergency departments, hospital wards, and intensive care units?

Methods This retrospective, manual review of medical records identified the first 1000 consecutive patients with laboratory confirmed covid-19 who first presented to the emergency department or were admitted to hospital at New York-Presbyterian/Columbia University Irving Medical Center between 1 March and 5 April 2020. Patient data were manually abstracted from electronic medical records and included personal characteristics, presenting symptoms, comorbidities on presentation, hospital course, time to intubation, complications, mortality, and disposition including discharge, transfer, or death.

Study answer and limitations Of the first 1000 patients, 150 presented to the emergency department, 614 were admitted to hospital (not intensive care units), and 236 were admitted or transferred to intensive care units. The most common presenting symptoms were cough (732/1000), fever (728/1000), and dyspnoea (631/1000). Patients in hospital, particularly those treated in intensive care units, often had baseline comorbidities, including hypertension, diabetes, and obesity. Patients admitted to intensive care units were older, predominantly male (158/236, 66.9%), and had long lengths of stay (median 23 days, interquartile range 12-32 days); 78.0% (184/236) developed acute kidney injury and 35.2% (83/236) needed dialysis. Only 4.4% (6/136) of patients who required mechanical ventilation were first intubated more than 14 days after symptom onset. Time to intubation from symptom onset had a bimodal distribution, with modes at three to four days and at nine days. As of 30 April 2020, 90 patients remained in hospital and 211 had died in hospital. This single centre study only included patient data documented in electronic medical records.

What this study adds Patients admitted to hospital with covid-19 at this medical centre, particularly those treated in intensive care units, faced major morbidity and mortality, prolonged intubations, and high rates of acute kidney injury and inpatient dialysis. Patients who required mechanical ventilation had a bimodal distribution in time to intubation from symptom onset, with most first intubated within 14 days.



Distribution of time from first symptom to intubation for 136 patients who had exact date of first symptom recorded. The time from first symptom to first intubation follows a bimodal distribution (P=0.004 for Hartigan's dip test), with modes at three to four days and at nine days

Funding, competing interests, and data sharing No support was received and no competing interests declared. Requests for the statistical code and dataset can be made to the corresponding author.

Covid-19 related hospital admissions in the US

ORIGINAL RESEARCH Prospective cohort study

FAST TRACK

Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City

Petrilli CM, Jones SA, Yang J, et al

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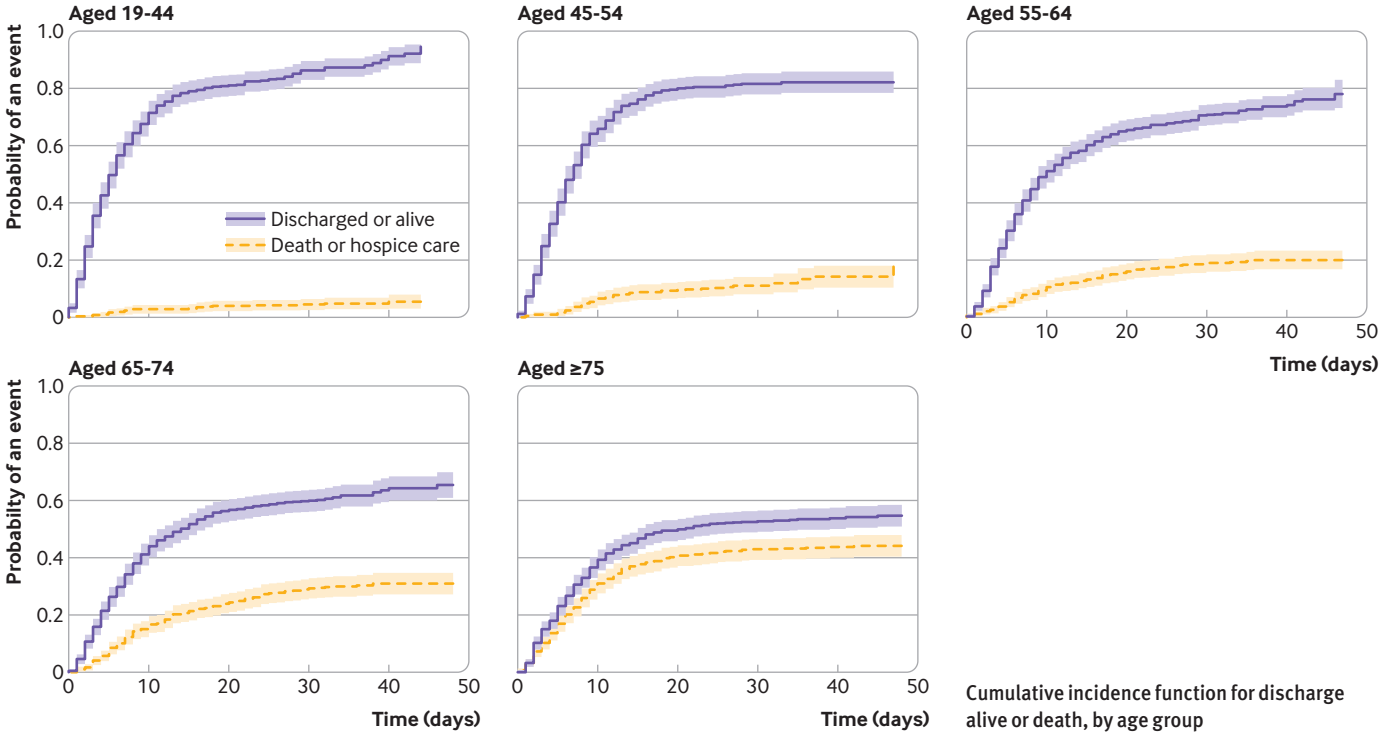
Study question What are the outcomes for people admitted to hospital with coronavirus disease 2019 (covid-19) in the United States, and what are the clinical and laboratory characteristics associated with severity of illness?

Methods Cross sectional analysis of all people with laboratory confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection at an academic medical centre in New York City between 1 March 2020 and 8 April 2020. Follow-up was to 5 May 2020. Outcomes were hospital admission, critical illness (intensive care, mechanical ventilation, and discharge to hospice care or death), and discharge to hospice care or death. Predictors included patient characteristics, medical history, vital signs, and laboratory test results. A multivariable logistic regression identified risk factors for adverse outcomes, and competing risk survival analysis was used for mortality.

Study answer and limitations 2741 of 5279 (51.9%) people with laboratory confirmed SARS-CoV-2 infection were admitted to hospital. 1904 (69.5%) were discharged alive and 665 (24.3%) were discharged to hospice care or died. The strongest risk for hospital admission was associated with age (all age groups >44 years: odds ratio >2; ages ≥75 years 37.9, 95% confidence interval 26.1 to 56.0). Other risks were heart failure (4.4, 2.6 to 8.0), male sex (2.8, 2.4 to 3.2), chronic kidney disease (2.6, 1.9 to 3.6), and any increase in body mass index (BMI) (eg, for BMI >40: 2.5, 1.8 to 3.4). The strongest risks for critical illness besides age were associated with heart failure (1.9, 1.4 to 2.5), BMI >40 (1.5, 1.0 to 2.2), and male sex (1.5, 1.3 to 1.8). Admission oxygen saturation of <88% (3.7, 2.8 to 4.8), troponin level >1 (4.8, 2.1 to 10.9), C reactive protein level >200 (5.1, 2.8 to 9.2), and D-dimer level >2500 (3.9, 2.6 to 6.0) were, however, more strongly associated with critical illness than age or comorbidities. Limitations were a single centre and testing restricted largely to those with severe covid-19.

What this study adds Age and comorbidities were found to be strong predictors of hospital admission and to a lesser extent of critical illness and mortality in people with covid-19; however, impairment of oxygen on admission and inflammatory markers were most strongly associated with critical illness and mortality.

Funding, competing interests, and data sharing Funded in part by the Kenneth Griffin Charitable Fund. No competing interests. Individual data not available.



Cumulative incidence function for discharge alive or death, by age group

Incidence, clinical outcomes, and transmission dynamics of severe coronavirus disease 2019 in California and Washington

Lewnard JA, Liu VX, Jackson ML, et al

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Find this at: http://dx.doi.org/10.1136/bmj.m1923

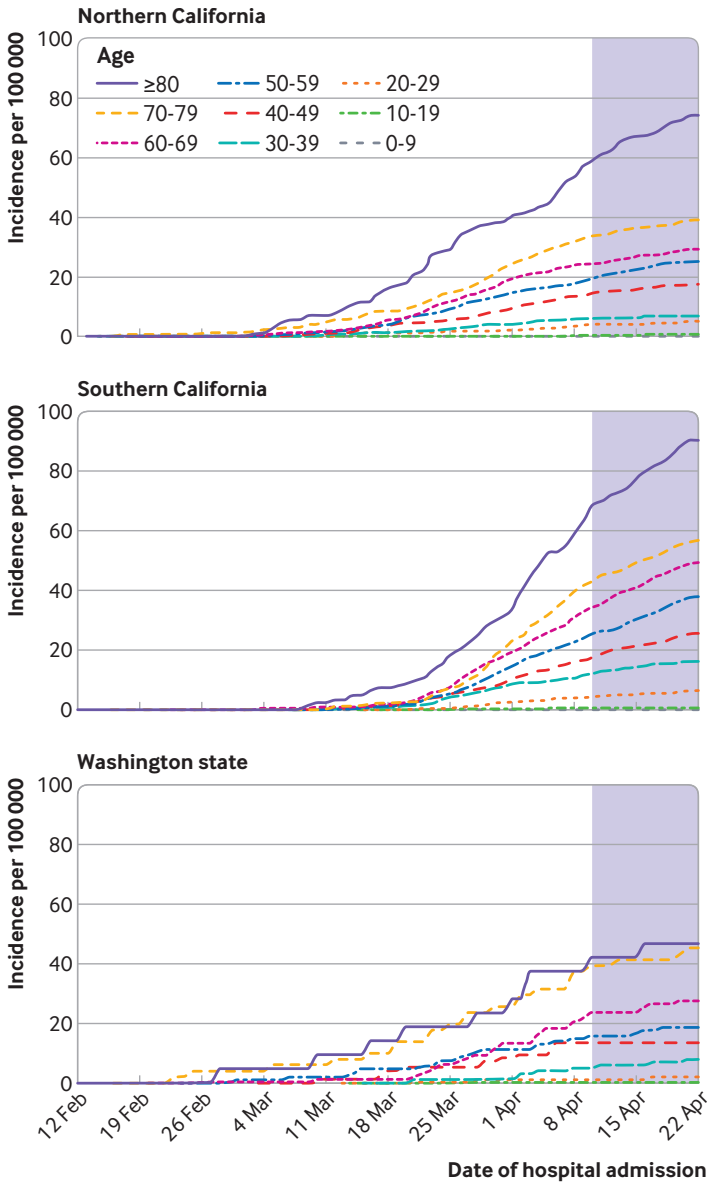
Study question What are the epidemiological features of acute inpatient admissions for coronavirus disease 2019 (covid-19) among enrollees in Kaiser Permanente healthcare plans in California and Washington state, United States?

Methods This prospective cohort study measured the cumulative incidence of first acute inpatient admission for confirmed covid-19 among people enrolled in comprehensive, integrated healthcare plans from Kaiser Permanente in northern and southern California and Washington state. Among patients admitted to hospital, this study estimated probabilities of admission to an intensive care unit (ICU) and mortality, as well as duration of hospital admission and ICU stay.

Study answer and limitations Among 9 596 321 enrollees of Kaiser Permanente healthcare plans, 1840 patients experienced a first acute inpatient admission for confirmed covid-19 by 22 April 2020. Cumulative incidences of a first acute hospital admission for covid-19 per 100 000 cohort members were 15.6 in northern California, 23.3 in southern California, and 14.7 in Washington. Accounting for censoring of incomplete hospital admissions among those admitted by 9 April 2020 (n=1328), the estimated median duration of stay was 9.3 days among survivors (with 95% staying 0.8 to 32.9 days) and 12.7 days among non-survivors (1.6 to 37.7 days). The censoring adjusted probability of ICU admission for male patients was 48.5% (95% confidence interval 41.8% to 56.3%) and for female patients was 32.0% (26.6% to 38.4%). For patients requiring critical care, the median duration of ICU stay was 10.6 days (with 95% staying 1.3 to 30.8 days). The censoring adjusted case fatality ratio was 23.5% (19.6% to 28.2%) among male inpatients and 14.9% (11.8% to 18.6%) among female inpatients; mortality risk increased with age for both male and female patients. Because all people under investigation for covid-19 might not have been tested during early phases of the outbreak, the estimates of disease incidence should be interpreted as lower bounds.

What this study adds Among residents of California and Washington enrolled in Kaiser Permanente healthcare plans who were admitted to hospital with covid-19, the probabilities of ICU admission, long hospital stay, and mortality were identified to be high. The incidence of new hospital admissions has stabilised or declined in conjunction with implementation of social distancing interventions.

Funding, competing interests, and data sharing This study was funded by Kaiser Permanente. VXL was supported by grant R35GM128672 from the US National Institutes of Health (NIH). See bmj.com for details of Kaiser Permanente employees and recipients of honorariums from Kaiser Permanente. VXL was supported by grant R35GM128672 from NIH. No additional data available.



Age specific cumulative incidence of first inpatient admissions in 2020 with confirmed coronavirus disease 2019 among all participants with Kaiser Permanente health plans. Shaded regions (10 April onwards) indicate admission dates when participants were excluded from analyses of clinical outcomes (duration of hospital stay, admission to intensive care unit, and case fatality risk) owing to limited follow-up duration

Cohort studies and case series of patients with coronavirus disease 2019 (covid-19) have spread almost as quickly as the virus,[1-5] with inadequate methodological quality sometimes hampering thoughtful interpretation. For example, one New York cohort study initially reported a mortality of 88% for patients requiring mechanical ventilation before readers' responses led to a correction clarifying that the rate was 25% and would grow to an uncertain extent because 72% of patients were still in hospital.[4] In contrast, the two cohort studies from the United States in this issue provide rigorous outcome ascertainment and adjustment for case mix.[6 7] By delaying publication until most enrolled patients had confirmed outcomes and by using modern survival analysis methods these authors have greatly enhanced our understanding of the epidemiology of covid-19.

Reduction in transmission rates

Lewnard and colleagues report on 1840 people with covid-19 at Kaiser Permanente system hospitals in California and Washington state.[6] Median age was 61 years, with 25% aged 48 years or younger. The study reported incidence of hospital admission (15-23 episodes per 100 000 cohort members in their insured populations), hospital length of stay (median 10.1 days), probability of intensive care unit (ICU) admission (41%), length of stay among ICU patients (median 10.6 days), and mortality. Mortality among all patients with completed hospital stays and outcomes was 18%.

The study also estimated dynamic changes in infection transmission rates by calculating the effective reproduction number (R_E). The authors estimated a high R_E ranging from 1.31 to 2.49 for those acquiring infection on 1 March 2020 in the different regions covered by the study and lower R_E ranging from 0.78 to 0.90 for those acquiring infection on 1 April 2020. This strong evidence of decreased transmission over time corresponds with enactment of social distancing policies.

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Risk of critical illness

Petrilli and colleagues report on 5279 patients with covid-19 at an academic medical center in New York City.[7] The cohort included patients testing positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in any outpatient or emergency department setting. Median age of patients admitted to hospital was 62 years, with 25% aged 51 years or younger.

The study outcomes included inpatient hospital stay (52%) and critical illness among those admitted to hospital (36%), representing a composite of ICU admission, mechanical ventilation, and hospital mortality or discharge to hospice care. Mortality among patients receiving mechanical ventilation was 60%. Of the 990 patients who developed critical illness, 399 (40%) were younger than 65 years, with 91 (9%) patients being younger than 45 years.

Several patient characteristics in the New York study, including age, male sex, obesity, and heart failure were risks for more severe illness, mirroring earlier reports.[1-5] The authors also provide compelling evidence confirming the predictive value of reduced oxygen saturation and increases in troponin, C reactive protein, and D-dimer levels near admission.

Importantly, although emerging data show rates of covid-19 cases, hospital admissions, and deaths among African-American and Latino populations have been worse than among white populations,[8 9] the authors did not find evidence of racial or ethnic disparities in critical illness or death once patients had been admitted to hospitals in their health system.

Perhaps the most intriguing finding from the New York cohort was that risk of critical illness declined progressively over the study period, with a suggestion of declining mortality as well, without changes in risk of hospital admission. Several potential explanations worthy of future investigation include the influence of strain in hospital capacity on quality of care, allocation of resources, and disposition decisions in the emergency department[10 11]; changes in care delivery over time, such as proning in awake, non-intubated patients to avoid intubation[12] or better adherence to lung protective mechanical ventilation strategies; and changes in targeted therapy that might be beneficial (remdesivir[13] and anticoagulation[14]) or harmful (hydroxychloroquine[15]).

The burden of severe covid-19 illness is clearly borne across the lifespan

Valuable lessons for clinical practice

These studies provide the strongest evidence to date that for every covid-19 related hospital death in the US there have been four times as many survivors, typically requiring one to two weeks in hospital, and often in the ICU.

The studies also provide rigorous confirmation of risk factors for poor outcomes that had been suggested in early reports. While older age is the greatest risk factor for adverse outcomes, including death, the burden of severe covid-19 illness is clearly borne across the lifespan, as most hospital admissions (53%[7] to 60%[6]) occurred in patients younger than 65 years. Early reports with incomplete follow-up are liable to considerable errors in reporting absolute event rates but often provide reasonable estimates of relative risks.

These lessons will inform the transition to handling long term debility among hundreds of thousands of hospital survivors, deciding which patients can be managed safely at home, understanding risks for readmission, and developing effective strategies for long term care.

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