Case Fatality Rates for Patients with COVID-19 Requiring Invasive Mechanical Ventilation
A Meta-analysis

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Abstract

Rationale: Initial reports of case fatality rates (CFRs) among adults with coronavirus disease (COVID-19) receiving invasive mechanical ventilation (IMV) are highly variable.

Objectives: To examine the CFR of patients with COVID-19 receiving IMV.

Methods: Two authors independently searched PubMed, Embase, medRxiv, bioRxiv, the COVID-19 living systematic review, and national registry databases. The primary outcome was the “reported CFR” for patients with confirmed COVID-19 requiring IMV. “Definitive hospital CFR” for patients with outcomes at hospital discharge was also investigated. Finally, CFR was analyzed by patient age, geographic region, and study quality on the basis of the Newcastle-Ottawa Scale.

Measurements and Results: Sixty-nine studies were included, describing 57,420 adult patients with COVID-19 who received IMV. Overall reported CFR was estimated as 45% (95% confidence interval [CI], 39–52%). Fifty-four of 69 studies stated whether hospital outcomes were available but provided a definitive hospital outcome on only 13,120 (22.8%) of the total IMV patient population. Among studies in which age-stratified CFR was available, pooled CFR estimates ranged from 47.9% (95% CI, 46.4–49.4%) in younger patients (age ≦ 40 yr) to 84.4% (95% CI, 83.3–85.4%) in older patients (age > 80 yr). CFR was also higher in early COVID-19 epicenters. Overall heterogeneity is high (I² > 90%), with nonsignificant Egger’s regression test suggesting no publication bias.

Conclusions: Almost half of patients with COVID-19 receiving IMV died based on the reported CFR, but variable CFR reporting methods resulted in a wide range of CFRs between studies. The reported CFR was higher in older patients and in early pandemic epicenters, which may be influenced by limited ICU resources. Reporting of definitive outcomes on all patients would facilitate comparisons between studies.

Systematic review registered with PROSPERO (CRD42020186997).

Keywords: COVID-19; SARS-CoV-2; case fatality rate; mortality; invasive mechanical ventilation

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The novel coronavirus disease (COVID-19) pandemic, which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has severely burdened healthcare system capacities in many parts of the world (1). The World Health Organization reports the global crude mortality rate to be 3.9% (2).

The care of critically ill patients with COVID-19 has been rapidly evolving (3). Although there have been promising therapies such as remdesivir (4) and dexamethasone (5), mechanical ventilation continues to be the mainstay of management of severe COVID-19 (6). Hypoxemia (PaO₂ <60 mm Hg) has been commonly reported in hospitalized patients with COVID-19 (7). Early invasive mechanical ventilation (IMV) was promoted early in the pandemic because of concerns of aerosol generation from noninvasive oxygenation therapies facilitating nosocomial viral transmission (8–10).

The case fatality rate (CFR) is defined as the proportion of a population with a disease that dies during a specific period (11). The reported CFRs of critically ill patients with COVID-19 receiving IMV have been observed to be highly variable (12). Causes of this inconsistency likely include the heterogeneity in the management of these patients and in the presentation of outcome data (12, 13). Addressing this knowledge gap will assist in intensive care resource planning and public health strategies.

The aim of this systematic review and meta-analysis was to report the CFR of critically ill adult patients with COVID-19 who received IMV based on the available evidence. The variability in CFR by patient age, geographic region, and study quality was also analyzed in this study.

Methods

This systematic review and meta-analysis was reported using the preferred reporting items for systematic reviews and meta-analyses framework (14) and has been registered on PROSPERO (CRD42020186997). The majority of patients receiving IMV are admitted to the ICU; however, not all ICU patients receive IMV. We therefore included studies explicitly reporting on patients receiving IMV to limit heterogeneity in illness severity. The review process is illustrated in a flow diagram (Figure 1).

Eligibility Criteria

Only studies reporting on consecutive adult patients (>18 yr of age) with laboratory-confirmed COVID-19 receiving IMV were included. Studies were excluded if 1) the sample size of the cohort was less than 10, 2) they did not report the results of original research, or 3) the cohort consisted only of deceased patients. Studies were also excluded if a significant overlap in patient cohorts was identified.

Search Strategy, Information Sources, and Study Selection

Two authors (Z.J.L. and A.S.) independently searched on the publicly available COVID-19 living systematic review. This dynamic systematic review contains a daily updated list of preprint and published articles relating to COVID-19 obtained from PubMed, EMBASE, medRxiv, and bioRxiv (15). The workflow for obtaining these articles is freely available and has been used previously during the Zika virus epidemic (16). This living platform has been recently validated against an Ovid search relating to COVID-19 (17). Two authors (Z.J.L. and M.P.R.) independently extracted the content of this living systematic review and national registry databases between January 1, 2020, and July 8, 2020. Conflicts in data extraction were resolved by discussion between the reviewers or adjudication by a third author (A.S.). Corresponding authors for all the selected papers were contacted by e-mail for outcome data for patients who were still in the hospital at the time the manuscript was published. The search terms “mortality,” “fatality,” “ICU,” “characteristic,” “invasive,” “mechanical,” “ventilation,” “death,” and “died” were used within the title and abstract columns of the systematic review list. The searching criteria were combined with the Boolean operator “OR.” All studies, including preprint and non-English language articles, were considered. A separate search for COVID-19 national registries was also conducted. Study period and location were analyzed as part of the data collection process.

Definitions

Reported CFR. “Reported CFR” was defined as the CFR among all patients who received IMV, before accounting for patients who were still receiving care in hospital.

Author Contributions: Z.J.L. conceived the project idea, conducted the systematic review and statistical analysis, assisted with data analysis, wrote the initial drafts of the manuscript, created tables and figures, and finalized the manuscript. A.S. conceived the project idea, conducted the systematic review, assisted with data analysis, wrote the initial drafts of the manuscript, and finalized the manuscript. M.K. analyzed the data, wrote the initial drafts of the manuscript, and finalized the manuscript. F.B. analyzed the data and edited the manuscript. J.R.C. provided oversight for analysis of the data and edited the manuscript. F.R. analyzed the data and edited the manuscript. All authors critically reviewed the manuscript and approved the final version before submission.

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studies have reported the CFR among patients who have completed their hospital course. This variance in reporting methods therefore resulted in variance in the CFRs reported by authors. As a secondary outcome, we examined the “definitive hospital CFR” for the subgroup of studies for whom we were able to ascertain hospital discharge outcomes. For all studies, we also present a sensitivity analysis that includes all patients showing “lowest possible” CFR for each study (assuming all patients still hospitalized lived) and a “highest possible” CFR (assuming all patients still hospitalized died). Within the appendix, the definitive hospital CFR is calculated by excluding patients who were still hospitalized to report the CFR only among patients with a known hospital outcome. Studies were also stratified based on geographical location (continent), economy (based on United Nations classification 2020), mean age, and study quality.

Data Analysis and Data Collection Process
Statistical analyzes were performed using the statistical software package Stata, version 16.1 (StataCorp). Mean and SD were used for numerical data and proportion was used for categorical data. The random-effects model and the Hartung-Knapp-Sidik-Jonkman method for meta-analysis (19) were used for the pooled prevalence of CFR because these demonstrate better properties in the presence of heterogeneity, accounting for both within-study and between-study variances (20). Results were presented in forest plots. Heterogeneity was tested by using the $\chi^2$ test on Cochran’s $Q$ statistic, which was calculated by means of $H$ and $I^2$ indices. The $I^2$ index estimates the percentage of total variation across studies on the basis of true between-study differences rather than on chance. Conventionally, $I^2$ values of 0–25% indicate low heterogeneity, values of 26–75% indicate moderate heterogeneity, and values of 76–100% indicate substantial heterogeneity. Authors conducted subgroup analyzes to identify the possible causes of substantial heterogeneity (21). Univariable metaregression was used, symmetry of the funnel plots was evaluated, and the Egger’s regression test was used to examine for publication bias (22). Confidence interval (CI) was used to evaluate whether differences in CFRs were statistically significant. The 95% CI of prevalence

Range of estimates for CFR. We also provided a sensitivity analysis of the best possible and worse possible CFRs, assuming all remaining hospitalized patients either lived (lowest possible) or died (highest possible) in the subset of studies that reported the number of patients who received IMV who were still hospitalized at the time of study conclusion.

Definitive CFR. We examined the number of patients receiving IMV who died divided by the number of patients with a known hospital outcome (died or discharged alive) to calculate the definitive CFR.

Quality Assessment and Risk of Bias in Individual Studies
The Newcastle-Ottawa Scale (NOS) is a quality assessment tool used to evaluate nonrandomized studies on the basis of an eight-item score divided into three domains. The NOS has been selected for the purpose of this study because these domains assess selection, comparability, and ascertainment of the outcome of interest. The NOS is the most suitable for the purpose of comparing both reported and definitive CFR values. The NOS was used by the two reviewers (Z.J.L. and U.K.) to independently evaluate the quality of included studies and assess for risk of bias (18). The same set of decision rules was used by each reviewer to score the studies. Any discrepancies from the NOS were reviewed and resolved by two additional authors (A.S. and M.P.R.).

Study Outcomes
The primary outcome was the reported CFR for patients with COVID-19 receiving IMV based on the published studies. However, multiple methods of reporting CFR existed across different studies. Studies have reported the CFR of patients receiving IMV out of all patients receiving IMV, including those still hospitalized, whereas other
including 0.0% and 100% were calculated using the standard equation (23). As prevalence cannot fall below 0% or above 100%, the CI is trimmed at 0% and 100% (20).

**Additional Analyses**

We also examined the reported CFR based on age stratification for the subset of studies that reported outcomes by patient age. In addition, we compared the CFRs in studies from different geographic regions and examined difference between reports from cities with an early and dramatic pandemic outbreak, such as Hubei, China, and New York, United States, compared with studies from other cities in the same country.

**Results**

A total of 5,322 studies were obtained from the living systematic review with 662 unique studies assessed for eligibility via full-text screening (Figure 1). Sixty-nine studies across 23 countries with reported CFRs were included in the final analysis (13, 24–91), including publicly available national registry data from seven countries (29, 56, 59, 65, 66, 80, 90). A summary of the reported CFRs for adult patients receiving IMV in the hospital is outlined in Table 1. A total of 121,009 patients with confirmed COVID-19 were reported across 69 studies, with 89,405 patients (73.9%) from national registry data. Across 69 studies, 66,900 patients were male (55.3%). The patients’ mean age, as derived by the estimation formula to convert median to mean values (92), was 59.9 years. IMV was administered to 57,420 patients. Fifty-four of the 69 studies reported on the number of patients receiving IMV still hospitalized at the time of study conclusion.

**Primary Outcome: Reported CFR of Patients with Severe COVID-19 Receiving IMV**

The reported CFR across these studies was calculated at 45% (95% CI, 39–52%). Although a high heterogeneity was observed across all studies ($I^2 = 99.52$%), our Egger’s regression test for publication bias was 0.43 (nonsignificant). High heterogeneity was observed when studies were analyzed by continent ($I^2 >90$%). The reported CFRs varied between 36% (95% CI, 24–48%) and 52% (95% CI, 19–85%) among different continents, with no significant difference in CFRs. The forest plot is illustrated in Figure 2. Individual study NOS score is illustrated in Table E1 in the online supplement. There was no significant difference in CFR when studies were analyzed based on NOS score (Figure E1).

**Range of Estimates for CFR**

Fifty-four studies reported on the number of patients who were still hospitalized at the time of publication. Across these 54 studies, 15,064 of 35,880 patients (42.0%) received IMV. The sensitivity analysis comparing the “lowest possible” CFR (assuming all patients still hospitalized lived) with the “highest possible” CFR (assuming all patients still hospitalized died) ranged from 43% (95% CI, 36–51%) to 64% (95% CI, 56–72%) (Table E2).

**Definitive CFR**

A total of 13,120 of 15,064 (87.1%) patients (22.8% of the total IMV cohort) completed their hospital stay. Among these patients, 6,643 of 13,120 patients died (49.5%). The adjusted CFR among these patients was 56% (95% CI, 47–65%) (Figure E2). Within this subset of patients, no statistically significant differences in definitive hospital CFRs were observed when analyzing studies by geographical location (continent), economy, mean age (studies with main age >70 yr had a statistically lower CFR; however, the number of patients who received IMV was small [$N = 10$]), or study quality (Figures E2–E5). Heterogeneity continued to remain high ($I^2 >90$%) across all analyses.

**Analysis of CFR Based on Patient Age and Studies from Early COVID-19 Epicenters**

Three studies and three national registries (39, 44, 58, 59, 80, 90) reported on 42,618 IMV patients, of whom 28,547 (67.0%) died, and stratified CFR by age. CFR was >70% among patients aged more than 60 years of age. CFR increased exponentially ($y = 0.429e^{0.116x}$) with increasing age (Figure 3). The analysis comparing CFR in Wuhan with that of studies from other regions of China, as well as New York versus other regions in the United States, is illustrated in Figures E6 and E7. The reported CFR across 17 studies (encompassing 640 patients receiving IMV) from China reported an overall CFR of 56% (95% CI, 39–74%). Studies from Wuhan reported a significantly higher CFR of 75% (95% CI, 63–87%) compared with studies from other regions of China (20%; 95% CI 0–45%). Among patients with a known hospital outcome ($N = 11$ studies), the CFR reported from Wuhan (87%; 95% CI 77–97%) was lower than the CFR reported from other regions in China (33%; 95% CI, 0–82%).

An overall reported CFR of 47% (95% CI, 36–57%) was reported across 21 studies encompassing 3,811 patients with COVID-19 receiving IMV in the United States. Studies from New York reported a CFR of 54% (95% CI, 36–72%) whereas other regions in the United States reported a CFR of 41% (95% CI, 30–53%). When considering definitive outcomes, the overall CFR across 21 studies from the United States was 61% (95% CI 50–72%), with eight studies from New York reporting a significantly higher CFR of 78% (95% CI, 68–88%) compared with other regions in United States (49%; 95% CI, 35–63%).

**Univariate and Multivariate Analysis**

A simple regression (univariate) analysis and multivariate regression analysis were conducted across the 46 studies with definitive hospital outcome (Table E3). Studies were analyzed by common variables, including geographical location (continent), study quality (NOS score), mean age, and economic status. Poor-quality studies reported significantly lower CFRs compared with good-quality studies ($P = 0.035$). Multivariate regression did not yield any further statistical significance in study quality. A univariate analysis of studies from earlier epicenters (Wuhan and New York) showed significantly higher CFRs within these epicenters compared with nonepicenter studies in the same country ($P = 0.010$ for Wuhan vs. other studies in China and $P = 0.002$ for New York vs. other studies in the United States).

**Discussion**

This is a large international systematic review and meta-analysis to examine global reports of CFRs for adult patients with COVID-19 receiving IMV. The reported CFR was 45% across all 69 studies, but this included patients still in the hospital. Among all 54 studies, lowest possible to best possible hospital CFR ranged from 43% to
Table 1. The 69 Studies Selected for the Systematic Review and Meta-analysis

| Study                        | Location of Study | Sample Size (N) | Mean Age (yr) | Sex, M (n) | Received IMV (n) | IMV Patients Still Receiving Care (n) | Died after IMV (n) | IMV Patients with Definitive Hospital Outcome [n (%)] | Primary Outcome: CFR of Patients Requiring IMV by Reported Outcome [% (95% CI)] |
|------------------------------|-------------------|-----------------|---------------|------------|-----------------|--------------------------------------|-------------------|------------------------------------------------------|----------------------------------------------------------------------------------|
| Chen et al., May 2020 (24)   | Hubei, China      | 135 NR          | NR            | 78         | 9               | 0                                    | 6                 | 9 (100)                                               | 67 (40–93)                                                                      |
| Hu et al., May 2020 (25)     | Hubei, China      | 323 59.0        | 166           | 34         | NR              | 31                                   | NR                | 91 (80–100)                                          |                                                                                  |
| Hu and Li, May 2020 (26)     | Hubei, China      | 105 58.2        | 66            | 67         | NR              | 39                                   | NR                | 58 (47–70)                                           |                                                                                  |
| Hua et al., June 2020 (27)   | Hubei, China      | 469 68.0        | 76            | 113        | 0               | 104                                  | 113 (100)         | 92 (87–97)                                           |                                                                                  |
| Huang et al., June 2020 (28) | Changsha, China   | 238 45.0        | 117           | 4          | NR              | 2                                    | NR                | 50 (15–85)                                           |                                                                                  |
| Japan registry, July 2020 (29)| Japan             | 575 NR          | NR            | 575        | 67              | 133                                  | 508 (88)          | 23 (20–27)                                           |                                                                                  |
| Jung et al., May 2020 (30)   | South Korea       | 5,179 44.6      | 2,295         | 36         | NR              | 21                                   | NR                | 58 (43–74)                                           |                                                                                  |
| Liao et al., April 2020 (31) | Sichuan, China    | 81 51.3         | 66            | 10         | 7               | 3                                    | 3 (30)            | 30 (5–55)                                            |                                                                                  |
| Nasir et al., June 2020 (32) | Karachi, Pakistan | 30 62.5         | 25            | 10         | 0               | 5                                    | 5 (100)           | 50 (24–76)                                           |                                                                                  |
| Ratanarat et al., July 2020 (33) | Bangkok, Thailand | 13 58.0       | 8             | 5          | 0               | 0                                    | 0               | 5 (100)                                              | 0 (0–27)                                                                  |
| Ruan et al., March 2020 (34) | Hubei, China      | 150 NR          | 102           | 25         | 0               | 25                                   | 25 (100)          | 100 (91–100)                                         |                                                                                  |
| Shi et al., June 2020 (35)   | Hubei, China      | 671 61.7        | 322           | 36         | NR              | 29                                   | NR                | 81 (68–93)                                           |                                                                                  |
| Sirivongrangson et al., June 2020 (36) | Bangkok, Thailand | 19 52.0      | 15            | 10         | 2               | 0                                    | 8 (80)            | 0 (0–18)                                             |                                                                                  |
| Wang et al., April 2020 (37) | Anhui, China      | 125 38.8        | 71            | 4          | 3               | 0                                    | 1 (25)            | 0 (0–30)                                             |                                                                                  |
| Wang et al., June 2020 (38)  | Nationwide, China | 141 63.0        | 99            | 50         | 25              | 25                                   | 25 (50)           | 50 (37–63)                                           |                                                                                  |
| Wang et al., March 2020 (39) | Hubei, China      | 18 70.4         | 10            | 18         | 12              | 5                                    | 6 (33)            | 28 (8–47)                                            |                                                                                  |
| Yang et al., May 2020 (40)   | Hubei, China      | 59 66.1         | 40            | 59         | NR              | 36                                   | NR                | 61 (49–73)                                           |                                                                                  |
| Yang et al., May 2020 (41)   | Hubei, China      | 52 59.7         | 35            | 22         | 3               | 19                                   | 19 (86)           | 86 (71–100)                                          |                                                                                  |
| Ye et al., June 2020 (42)    | Zhejiang, China   | 856 46.0        | 439           | 29         | NR              | 1                                    | NR                | 3 (0–13)                                             |                                                                                  |
| Young et al., March 2020 (43) | Singapore         | 18 49.5         | 9             | 1          | 0               | 0                                    | 1 (100)           | 0 (0–44)                                             |                                                                                  |
| Yu et al., May 2020 (44)     | Hubei, China      | 226 63.0        | 139           | 121        | 6               | 79                                   | 115 (95)          | 65 (57–74)                                           |                                                                                  |
| Zhao et al., June 2020 (45)  | Henan, China      | 29 51.2         | 14            | 5          | 0               | 1                                    | 5 (100)           | 20 (0–51)                                            |                                                                                  |
| Zheng et al., May 2020 (46)  | Hangzhou, China   | 34 66.7         | 23            | 15         | 13              | 0                                    | 2 (13)            | 0 (0–14)                                             |                                                                                  |

(Continued)
| Study                          | Location of Study | Sample Size (N) | Mean Age (yr) | Sex, M (n) | Received IMV (n) | IMV Patients Still Receiving Care (n) | Died after IMV (n) | IMV Patients with Definitive Hospital Outcome [n (%)] | Primary Outcome: CFR of Patients Requiring IMV by Reported Outcome [% (95% CI)] |
|-------------------------------|-------------------|----------------|--------------|------------|----------------|-----------------------------------|-------------------|---------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|
| Zhu et al., June 2020 (47)    | Hubei, China      | 102            | 65.2         | 59         | 29             | 0                                 | 25                | 29 (100)                                          | 86 (73–99)                                                          |
| Almezadeti et al., May 2020 (48) | South Surra, Kuwait | 1,096         | 41           | 888        | 31             | 16                                | 13                | 15 (48)                                           | 42 (26–58)                                                          |
| Goshayeshi et al., May 2020 (49) | Mashhad, Iran     | 1,067          | 56.9         | 663        | 231            | 32                                | 81                | 199 (86)                                          | 35 (29–41)                                                          |
| Khamis et al., July 2020 (50) | Oman              | 63             | 48.0         | 53         | 16             | NR                                | NR                | 5                                               | 31 (10–52)                                                          |
| Rinott et al., June 2020 (51) | Israel            | 403            | 44.0         | 220        | 17             | NR                                | 12                | NR                                               | 71 (50–91)                                                          |
| Shahriarirad et al., June 2020 (52) | South Iran, Iran   | 113            | 53.8         | 71         | 2              | 0                                 | 2                 | 2 (100)                                           | 100 (62–100)                                                       |
| Almezadeti et al., May 2020 (53) | Modena, Italy     | 307            | 65.2         | 219        | 53             | 14                                | 17                | 39 (74)                                           | 32 (20–44)                                                          |
| Busetto et al., May 2020 (54) | Veneto, Italy     | 92             | 70.5         | 57         | 9              | 0                                 | 0                 | 9 (100)                                           | 0 (0–20)                                                            |
| Ceruti et al., May 2020 (55)  | Lugano, Switzerland | 41            | 64.0         | 35         | 34             | 4                                 | 7                 | 30 (88)                                           | 21 (7–34)                                                           |
| France registry, June 2020 (56) | France            | 4,007          | 65.0         | 2,925      | 2,357          | NR                                | 480               | NR                                               | 20 (19–22)                                                          |
| Giacomelli et al., May 2020 (57) | Lombardy, Italy  | 233            | 61.0         | 72         | 8              | 0                                 | 7                 | 8 (100)                                           | 88 (63–100)                                                        |
| Grasselli et al., April 2020 (58) | Lombardy, Italy  | 1,591          | 63.0         | 1,304      | 1,150          | NR                                | 329               | NR                                               | 29 (26–31)                                                          |
| ICNARC, 10 July 2020 (59)     | United Kingdom    | 10,421         | 58.8         | 320        | 7,185          | 426                               | 3,479             | 6,759 (94)                                        | 48 (47–50)                                                          |
| Israelsen et al., May 2020 (60) | Hvidovre, Denmark | 175            | 69.0         | 85         | 27             | 8                                 | 17                | 19 (70)                                           | 63 (46–80)                                                          |
| Pavoni et al., May, 2020 (61) | Tuscany, Italy    | 40             | 61.0         | 24         | 4              | 1                                 | 3                 | 3 (75)                                            | 75 (41–100)                                                         |
| Pedersen et al., April 2020 (62) | Zealand, Denmark | 17             | 69.8         | 12         | 17             | 6                                 | 7                 | 11 (65)                                           | 41 (20–62)                                                          |
| Piano et al., June 2020 (63)   | Northern Italy, Italy | 584           | 66.0         | 357        | 62             | 10                                | 18                | 52 (84)                                           | 29 (18–40)                                                          |
| Regina et al., May 2020 (64)   | Lausanne, Switzerland | 200           | 66.0         | 120        | 38             | NR                                | 11                | NR                                               | 29 (15–43)                                                          |
| Spain registry, July 2020 (65) | Spain             | 7,695          | 60.3         | 5,344      | 3,867          | NR                                | 1,943             | NR                                               | 50 (49–52)                                                          |
| Sweden registry July, 2020 (66) | Sweden            | 3,437          | 59.2         | 2,530      | 2,412          | 58                                | 455               | 2,354 (98)                                        | 19 (17–20)                                                          |
| Zangrillo et al., April 2020 (67) | Lombardy, Italy  | 73             | 61.3         | 61         | 73             | 33                                | 17                | 40 (55)                                           | 23 (14–33)                                                          |
| Aggarwal et al., May 2020 (68) | Iowa, United States | 16            | 65.5         | 12         | 5              | 0                                 | 0                 | 5 (100)                                           | 0 (0–27)                                                            |
| Arentz et al., March 2020 (69) | Washington/Seattle, United States | 21          | 70           | 11         | 15             | 3                                 | 10                | 12 (80)                                           | 67 (45–88)                                                          |
| Argenziano et al., May 2020 (70) | New York, United States | 1,000        | 62.7         | 596        | 233            | 86                                | 111               | 147 (63)                                          | 48 (41–54)                                                          |
| Study                          | Location of Study                      | Sample Size (N) | Mean Age (yr) | Sex, M (n) | Received IMV (n) | IMV Patients Still Receiving Care (n) | Died after IMV (n) | IMV Patients with Definitive Hospital Outcome [n (%)] | Primary Outcome: CFR of Patients Requiring IMV by Reported Outcome [% (95% CI)] |
|-------------------------------|----------------------------------------|-----------------|--------------|------------|-----------------|--------------------------------------|------------------|----------------------------------------------------|-----------------------------------------------------------------------------|
| Auld et al., May 2020 (71)    | Georgia, United States                 | 217             | 63.7         | 119        | 165             | 11                                   | 56               | 154 (93)                                           | 34 (27–41)                                                          |
| Bhatraju et al., March 2020   | Washington/Seattle, United States      | 24              | 64.0         | 15         | 18              | 3                                    | 9                | 15 (83)                                            | 50 (29–71)                                                          |
| Buckner et al., May 2020      | Washington/Seattle, United States      | 105             | 64.5         | 53         | 19              | 0                                    | 10               | 19 (100)                                           | 53 (32–73)                                                          |
| Ferguson et al., July 2020    | California, United States              | 72              | 58.1         | 38         | 13              | 4                                    | 3                | 9 (69)                                             | 23 (1–45)                                                           |
| Garibaldi et al., May 2020    | Maryland, United States                | 832             | 60.4         | 443        | 70              | 24                                   | 24               | 46 (66)                                            | 34 (23–45)                                                          |
| Gold et al., May 2020 (76)    | Georgia, United States                 | 305             | 58.8         | 151        | 92              | 6                                    | 38               | 86 (93)                                            | 41 (31–51)                                                          |
| Goyal et al., April 2020      | New York, United States                | 393             | 61.5         | 238        | 130             | 88                                   | 19               | 42 (32)                                            | 15 (8–21)                                                           |
| Klang et al., May 2020 (77)   | New York, United States                | 3,406           | NR           | 1,961      | 809             | 0                                    | 682              | 809 (100)                                          | 84 (82–87)                                                          |
| Mani et al., June 2020 (79)   | New York, United States                | 184             | 64.7         | 111        | 30              | 17                                   | 13               | 13 (43)                                            | 43 (27–60)                                                          |
| Mexico registry, May 2020     | Mexico                                 | 6,898           | NR           | 4,665      | NR              | 6,898                                | NR               | 4,724                                              | NR                                                                |
| Mitra et al., June 2020 (81)  | Vancouver, Canada                      | 117             | 68.0         | 79         | 74              | 25                                   | 15               | 49 (66)                                            | 20 (11–29)                                                          |
| Palaiodimos et al., July 2020 | New York, United States                | 200             | 62.5         | 98         | 42              | 0                                    | 32               | 42 (100)                                           | 76 (63–89)                                                          |
| Petrilli et al., May 2020     | New York, United States                | 2,721           | 62.7         | 98         | 42              | 0                                    | 32               | 42 (100)                                           | 76 (63–89)                                                          |
| Reyes Gil et al., May 2020    | New York, United States                | 217             | NR           | 126        | 55              | 0                                    | 45               | 55 (100)                                           | 82 (72–92)                                                          |
| Richardson et al., April 2020 | New York, United States                | 5,700           | 60.9         | 3,437      | 1,151           | 831                                  | 282              | 320 (28)                                           | 25 (22–27)                                                          |
| Salacup et al., July 2020     | Philadelphia, United States            | 242             | 66.0         | 123        | 54              | 0                                    | 38               | 54 (100)                                           | 70 (58–82)                                                          |
| Shekhar et al., May 2020      | New Mexico, United States              | 50              | 54.0         | 23         | 22              | 6                                    | 12               | 16 (73)                                            | 55 (35–74)                                                          |
| Shi et al., July 2020 (88)    | Michigan, United States                | 172             | 61.5         | 97         | 61              | 2                                    | 16               | 59 (97)                                            | 26 (15–37)                                                          |
| Suleyman et al., June 2020    | Michigan, United States                | 355             | 57.5         | 204        | 114             | 6                                    | 91               | 108 (95)                                           | 80 (45–100)                                                         |
| Ziehr et al., June 2020 (13)  | Massachusetts, United States           | 66              | 56.5         | 43         | 66              | 0                                    | 11               | 66 (100)                                           | 17 (8–26)                                                           |
| Brazil registry, July 2020    | Brazil                                 | 56,372          | 68.2         | 32,940     | 27,748          | NR                                   | 19,935           | NR                                                 | 72 (71–72)                                                          |
| Olivares et al., June 2020    | Valdivia, Chile                        | 21              | 58.9         | 5          | 9               | 0                                    | 2                | 9 (100)                                            | 22 (0–47)                                                           |

Definition of abbreviations: CFR = case fatality rate; CI = confidence interval; ICNARC = Intensive Care National Audit and Research Centre; IMV = invasive mechanical ventilation; NR = not reported.
**Figure 2.** Forest plot of the reported case fatality rates (N=69 studies) for patients receiving invasive mechanical ventilation stratified by continent. CFR = case fatality rate; CI = confidence interval; ICNARC = Intensive Care National Audit and Research Centre; REML = restricted maximum likelihood.

67%. Among patients with a known hospital outcome, the definitive hospital CFR was 56%. We observed no statistical difference between continents. Older patients had a higher CFR, and the CFR was higher in the early COVID-19 epicenters of Wuhan and New York compared with that of other studies from the same country.

The CFR observed in this review of patients with COVID-19 is similar to that of previous outbreaks of severe respiratory infections. Studies from SARS-CoV in 2003 reported a CFR of 45–48% in patients receiving IMV (93, 94), and more recent studies from the Middle East respiratory syndrome reported a 60–74% CFR in critically ill patients (95, 96). In contrast, the CFR is lower in critically ill patients suffering from H1N1 influenza A, in which the CFR of patients receiving IMV was 24.2–26.5% (97). The reported CFR from severe acute respiratory distress syndrome before COVID-19 was lower at 45% (98, 99) when compared with the definitive CFR from COVID-19.

The CFR of patients receiving IMV among studies from Wuhan and New York was significantly higher than that of studies from other regions in China and the United States, respectively. This finding may reflect the significant challenges faced in the initial stages of the COVID-19 outbreak (100, 101). Reports suggest that prone positioning was infrequent in the initial phase (41), with one Wuhan study reporting only 12% of patients receiving IMV were managed with prone positioning. Variable provider:patient ratios may also have contributed to higher CFR (102–104).

Several factors may account for the large variance in CFRs between studies. ICUs outside of outbreak epicenters may have had the opportunity of time to obtain equipment and consolidate resources before the pandemic (71). This has enabled ICUs to continue at standard patient:provider ratios (71). Closer monitoring and early intensive care for critically ill patients potentially improved patient prognosis (31). Differences in hospital facilities, patient preferences (for which limitations of care may have been in place), and indications for IMV may have also influenced the CFR (12). Finally, the change in triage process considering comorbidities, age, and frailty status in allocating ICU beds and ventilators during the pandemic.
Despite stratifying studies on the basis of location and NOS score, high heterogeneity continued to exist across our meta-analysis. This has been reported in other meta-analyses studying COVID-19 mortality (109–113). Heterogeneity was the lowest at 83.4% among definitive outcomes from Wuhan (Figure E6). Although the reasons for this are not clear, we believe that studies originating from the same geographical location may provide a less heterogeneous cohort, and hence, the F² value was lower. Other potential factors influencing heterogeneity could be differences in illness severity, thresholds for IMV, admission criteria to the ICU, and regional differences in ICU care.

As demonstrated in a recent editorial, the CFR is substantially higher among older patients, with more than 70% of patients over 60 years of age receiving IMV dying (12). It has also been reported that the CFR for patients in their 80s and 90s receiving IMV with comorbidities has been higher (114). Our findings also suggest that older patients receiving IMV had significantly higher mortality.

There are several limitations to this systematic review. First, most of the included studies had very small numbers of patients; only 17 of 69 studies reported on more than 100 patients receiving IMV. Given the available evidence, we conducted a meta-analysis to account for this variability in sample size. Second, multiple studies may have covered similar patient cohorts. However, each study’s time period, hospital, and location were considered in the final inclusion of studies to minimize overlap in patient cohorts. Third, 14 studies were not peer reviewed, as they were prepublication articles. However, these studies still provided meaningful data on the CFR of the subgroup of patients with COVID-19 who receive IMV. Fourth, the overall heterogeneity was very high (F² >90%), which may preclude a valid conclusion from pooled results. Although we performed various sensitivity and metaregression analyses, the heterogeneity could not be minimized. This is most likely due to the case mix and the structure of age within included populations. Finally, we were unable to examine the influence of timing in the pandemic because timing and region were highly correlated.

**Conclusions**

The reported CFR for existing studies of adult patients with COVID-19 receiving...
IMV was 45%, but many of these reports included patients still in the hospital at the time of publication. Accounting for patients still in the hospital, we found a best possible CFR of 43% and a worst possible CFR of 64%. The CFR increased exponentially in both regions, with other regions in the same country.

Additional studies examining long-term CFRs beyond hospital discharge are needed.

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**References**

1. Remuzzi A, Remuzzi G. COVID-19 and Italy: what next? Lancet 2020; 395:1225–1228.

2. World Health Organization. Coronavirus disease (COVID-19) situation reports. Geneva, Switzerland: World Health Organization; 2020 [accessed 2020 Jul 30]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports.

3. Lin L, Lu L, Cao W, Li T. Hypothesis for potential pathogenesis of SARS-CoV-2 infection—a review of immune changes in patients with viral pneumonia. Emerg Microbes Infect 2020;9:727–732.

4. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, et al.; ACTT-1 Study Group Members. Remdesivir for the treatment of COVID-19: final report. N Engl J Med [online ahead of print] 8 Oct 2020; DOI: 10.1056/NEJMoa2007764.

5. Horby P, Lim WS, Emberson JR, Mathers M, Bell JL, Linsell L, et al.; RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with COVID-19: preliminary report. N Engl J Med [online ahead of print] 17 Jul 2020; DOI: 10.1056/NEJMoa21436.

6. Sanders JM, Monogue ML, Jodawski TZ, Cutrell JB. Pharmacologic treatments for coronavirus disease 2019 (COVID-19): a review. JAMA 2020;323:1824–1836.

7. COVID-19 Treatment Guidelines Panel. Coronavirus disease 2019 (COVID-19) treatment guidelines. Bethesda, MD: National Institutes of Health; 2020 [accessed 2020 May 28]. Available from: https://www.covid19treatmentguidelines.nih.gov/.

8. Phua J, Weng L, Ling L, Egi M, Lim CM, Divatia JV, et al.; Asian Critical Care Clinical Trials Group. Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. Lancet Respir Med 2020;8:506–517.

9. McGain F, Humphries RS, Lee JH, Schofield R, French C, Keywood MD, et al. Aerosol generation related to respiratory interventions and the effectiveness of a personal ventilation hood. Anesth Analg 2020;131:351–364.

10. Porta M, editor. A dictionary of epidemiology. Oxford, United Kingdom: Oxford University Press; 2014.

11. Wunsch H. Mechanical ventilation in COVID-19: interpreting the current epidemiology. Am J Respir Crit Care Med 2020;202:1–4.

12. Ziehr DR, Alladina J, Petri CR, Maley JH, Moskowitz A, Medoff BD, et al. Respiratory pathophysiology of mechanically ventilated patients with COVID-19: a cohort study. Am J Respir Crit Care Med 2020;201:1560–1564.

13. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009;339:b2535.

14. Couto et al. COVID-19 Case Fatality after Invasive Ventilation
77. Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A, Gold JAW, Wong KK, Szablewski CM, Patel PR, Rossow J, da Silva J, Garibaldi BT, Fiksel J, Muschelli J, Robinson ML, Rouhizadeh M, Nagy Buckner FS, McCulloch DJ, Atluri V, Blain M, McGuffin SA, et al. Characterization and clinical course of 1000 patients with coronavirus disease 2019 in New York: retrospective case series. BMJ 2020;369:m1996.

78. Mitra AR, Fergusson NA, Lloyd-Smith E, Wormsbecker A, Foster D, Petrilli CM, Jones SA, Yang J, Rajagopalan H, O Palaiodimos L, Kokkinidis DG, Li W, Karamanis D, Ognibene J, Arora S, Pal, Karpov A, Sethi A, Nall A K, Walbridge SL, Baran M, McCulloch DJ, Atluri V, Blain M, McGuffin SA, et al. Clinical characteristics and outcomes of COVID-19 in Saudi Arabia. Int J Infect Dis 2020;90:246–253.

79. Mani VR, Kalabin A, Valdivieso SC, Murray-Ramcharan M, Donaldson B. New York inner city hospital COVID-19 experience and current data: retrospective analysis at the epicenter of the American coronavirus outbreak. J Med Internet Res 2020;22:e20548.

80. La Secretaria de Salud. Información referente a casos COVID-19 en México. Gobierno de México: La Secretaría de Salud; 2020 [accessed 2020 Jul 1]. Available from: https://datos.gob.mx/busca/dataset/informacion-referente-a-casos-covid-19-en-mexico

81. Mitra AR, Fergusson NA, Lloyd-Smith E, Wormsbecker A, Foster D, Karpov A, et al. Baseline characteristics and outcomes of patients with COVID-19 admitted to intensive care units in Vancouver, Canada: a case series. CMAJ 2020;192:E694–E701.

82. Palacio-Díaz L, Kokkinis DG, Li W, Karamanis D, Ognibene J, Arora S, et al. Severe obesity, increasing age and male sex are independently associated with worse in-hospital outcomes, and higher in-hospital mortality, in a cohort of patients with COVID-19 in the Bronx, New York. Metabolism 2020;108:154262.

83. Petrelli RM, Jones SA, Yang J, Rajagopalan H, O’Donnell L, Chernyak Y, et al. Factors associated with hospital admission and clinical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. BMJ 2020;369:m1986.

84. Petrelli RM, Gonzalez-Lugo JD, Rahmat T, Sughoy S, Burgio M, Szymanski J, Ikemura K, et al. Correlation of coagulation parameters with clinical outcomes in Coronavirus-19 affected minorities in United States: observational cohort [preprint]. medRxiv 2020;10.1101/2020.05.01.20087392v1.

85. Riederer S, Hirsch J, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al.; the Northwell COVID-19 Research Consortium. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York city area. JAMA 2020;323:2052–2059.

86. Salacup G, Lo KB, Gul F, Peterson E, De Jooy R, Bhargav R, et al. Characteristics and clinical outcomes of COVID-19 patients in an underserved inner city population: a single tertiary center cohort. J Med Virol [online ahead of print] 3 Jul 2020; DOI: 10.1002/jmv.26252.

87. Shekhar R, Upadhyay S, Sheikh A, Atencio J, Kapuria D. Early experience with COVID-19 patients at tertiary care teaching hospital in southwestern United States [preprint]. medRxiv 2020 [accessed 2020 May 18]. Available from: https://www.medrxiv.org/content/10.1101/2020.05.01.20049284v1.

88. Shi H, Zuo Y, Yalavarthi S, Gockman K, Zuo M, Madison JA, et al. Neutrophil calprotectin identifies severe pulmonary edema in COVID-19 [preprint]; medRxiv 2020 [accessed 2020 Jul 15]. Available from: https://www.medrxiv.org/content/10.1101/2020.05.06.20093703v3.

89. Singapore G, Fadel RA, Malette KM, Hammond C, Abdullah H, Entz A, et al. Clinical characteristics and morbidity associated with coronavirus disease 2019 in a series of patients in metropolitan Detroit. JAMA Netw Open 2020;3:e2012270.

90. Ministerio de la Salud. SRAG 2020 - Banco de Dados de Síndrome Respiratoria Aguda Grave - incluido dados da COVID-19. Datasus: Ministerio de la Salud; 2020 [accessed 2020 Jul 7]. Available from: https://opendatasus.saude.gov.br/dataset/bd-srag-2020.

91. Olvides F, Munoz D, Fica A, Delama I, Alvarez I, Navarrete M, et al. Covid-19 in Chile: the experience of a regional reference center. Preliminary report. medRxiv 2020 [accessed 2020 Jun 16]. Available from: https://www.medrxiv.org/content/10.1101/2020.06.14.20130989v1.

92. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol 2014;14:135.

93. Fowler RA, Lapinsky SE, Hallett D, Detsky AS, Sibbald WJ, Slutsky AS, et al.; Toronto SARS Critical Care Group. Critically ill patients with severe acute respiratory syndrome. JAMA 2003;289:367–373.

94. Comas P, Vázquez-Prado S, García-Valverde E, Valdés-Vázquez E, Vázquez-Pascual A, et al. Severe obesity, increasing age and male sex are independently associated with worse in-hospital outcomes, and higher in-hospital mortality, in a cohort of patients with COVID-19 in the Bronx, New York. Metabolism 2020;108:154262.

95. Marín JG, Gattinoni L. Management of COVID-19 respiratory distress. JAMA 2020;323:2329–2330.

96. Du RH, Liu LM, Yin W, Wang W, Guan LL, Yuan ML, et al. Hospitalization and critical care of 109 decedents with COVID-19 in China: the experience in Saudi Arabia. Int J Infect Dis 2014;29:301–306.

97. Mascalzón JR, Pérez M, Almirall J, Lorente L, Marquéz A, Socias L, et al. Early non-invasive ventilation treatment for severe influenza pneumonia. Clin Microbiol Infect 2013;19:249–256.

98. Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, et al.; ARDS Definition Task Force. Acute respiratory distress syndrome: the Berlin definition. JAMA 2012;307:252–262.

99. Marín JG, Gattinoni L. Management of COVID-19 respiratory distress. JAMA 2020;323:2329–2330.

100. Du RH, Liu LM, Yin W, Wang W, Guan LL, Yuan ML, et al. Hospitalization and critical care of 109 decedents with COVID-19 pneumonia in Wuhan, China. Ann Am Thorac Soc 2020;17:839–846.

101. Zhang H-F, Bo L, Lin Y, Li-F X, Sun S, Lin H-B, et al. Response of Chinese anaesthesiologists to the COVID-19 outbreak. Anaesthesia 2020;132:1333–1338.
102. Wang H, Feng J, Shao L, Wei J, Wang X, Xu X, et al. Contingency management strategies of the nursing department in centralized rescue of patients with coronavirus disease 2019. *Int J Nurs Sci* 2020;7:139–142.

103. Lee A, Cheung YSL, Joynt GM, Leung CCH, Wong WT, Gomersall CD. Are high nurse workload/staffing ratios associated with decreased survival in critically ill patients? A cohort study. *Ann Intensive Care* 2017;7:46.

104. European Society of Intensive Care Medicine. COVID-19: ICU nursing capacity and workload. 2020 [accessed 2020 Apr 7]. Available from: https://www.medscape.com/viewarticle/928162.

105. Rosenbaum L. Facing COVID-19 in Italy - ethics, logistics, and therapeutics on the epidemic’s front line. *N Engl J Med* 2020;382:1873–1875.

106. White DB, Lo B. A framework for rationing ventilators and critical care beds during the COVID-19 pandemic. *JAMA* 2020;323:1773–1774.

107. National Institute for Health and Care Excellence. COVID-19 rapid guideline: critical care in adults. London, United Kingdom: National Institute for Health and Care Excellence; 2020. Available from: https://www.nice.org.uk/guidance/ng159.

108. Sprung CL, Joynt GM, Christian MD, Truog RD, Rello J, Nates JL. Adult ICU triage during the coronavirus disease 2019 pandemic: who will live and who will die? Recommendations to improve survival. *Crit Care Med* 2020;48:1196–1202.

109. Meyerowitz-Katz G, Merone L. A systematic review and meta-analysis of published research data on COVID-19 infection-fatality rates. *medRxiv*; 2020 [accessed 2020 Jul 7]. Available from: https://www.medrxiv.org/content/10.1101/2020.05.03.2008954v4.

110. Nasiri MJ, Haddadi S, Tahvildari A, Farsi Y, Arbabi M, Hasanzadeh S, et al. COVID-19 clinical characteristics, and sex-specific risk of mortality: systematic review and meta-analysis. *medRxiv*; 2020 [accessed 2020 Mar 26]. Available from: https://www.medrxiv.org/content/10.1101/2020.03.24.20042903v1.

111. Cohen JF, Korevaar DA, Matczak S, Brice J, Chalumeau M, Toubiana J. COVID-19-related mortality by age groups in Europe: A meta-analysis. *medRxiv*; 2020 [accessed 2020 Apr 16]. Available from: https://www.medrxiv.org/content/10.1101/2020.04.11.20061721v1.

112. Armstrong RA, Kane AD, Cook TM. Outcomes from intensive care in patients with COVID-19: a systematic review and meta-analysis of observational studies. *Anaesthesia* 2020;75:1340–1349.

113. Quah P, Li A, Phua J. Mortality rates of patients with COVID-19 in the intensive care unit: a systematic review of the emerging literature. *Crit Care* 2020;24:285.

114. Wunsch H, Linde-Zwirble WT, Angus DC, Hartman ME, Milbrandt EB, Kahn JM. The epidemiology of mechanical ventilation use in the United States. *Crit Care Med* 2010;38:1947–1953.