

APSR RESPIRATORY UPDATES



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Inside this issue: Special Edition on COVID-19—one year on

A timeline of the COVID-19 pandemic

31 Dec 2019	Cases of viral pneumonia detected in Wuhan, China, were first reported to WHO
1 Jan 2020	China closes Huanan seafood market (Wuhan) after discovering that live wild animals sold there could be the source of virus
7 Jan 2020	Chinese authorities confirm the identity of the novel coronavirus virus, named 2019-nCov by WHO
9 Jan 2020	First death in Wuhan due to the viral pneumonia in a 61 year old Male
22 Jan 2020	N Korea closes its borders to all travelers, the first country in the world to do so
23 Jan 2020	China imposes a total lock down in Wuhan and a few neighboring cities
4 Feb 2020	Japan announces that 10 people on cruise ship (Diamond Princess) are sick with Covid19. In the subsequent days, a total of 712 (out of 3711 passengers) are affected with 13 fatalities
7 Feb 2020	Dr Li Wen Liang, a Wuhan doctor who tried to sound the alarm of the viral pneumonia epidemic on social media earlier in December dies of covid19
10 Feb 2020	New hospital for Covid19 is built in 10 days to help overwhelmed hospital resources in Wuhan
11 Feb 2020	WHO names the new disease Covid19
9 Mar 2020	Lockdown of Italy announced as Italy and many European countries have many cases, overwhelming its hospitals
11 Mar 2020	WHO announces that Covid19 is now a pandemic
27 Mar 2020	British PM tests positive for Covid19
4 Apr 2020	1 million cases worldwide is reached
8 Apr 2020	Lockdown of Wuhan is lifted after 76 days
29 Apr 2020	Gilead announces the results of trial with Remdesevir, suggesting that 5 days of the drug is just as good with 10 days of treatment
16 Jun 2020	Oxford University scientists announces positive result from Recovery Trial with Dexamethasone
11 Aug 2020	Russian President Putin announces approval of Covid19 vaccine, sputnik V
2 Oct 2020	US President Trump tests positive for Covid19
3 Dec 2020	UK announces approval of Pfizer vaccine
8 Dec 2020	First Covid19 vaccine given in UK to 90 year old Female
12 Dec 2020	US FDA approves FDA Pfizer vaccine
15 Dec 2020	Worldwide case count reaches 72 million affected and 1.2 million deaths

Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study.

Chen N, Zhou M, Dong X, et al.

Lancet. 2020 Feb 15;395(10223):507-513.

doi: 10.1016/S0140-6736(20)30211-7.

<https://pubmed.ncbi.nlm.nih.gov/32007143/>

Abstract

Background: In December, 2019, a pneumonia associated with the 2019 novel coronavirus (2019-nCoV) emerged in Wuhan, China. We aimed to further clarify the epidemiological and clinical characteristics of 2019-nCoV pneumonia.

Methods: In this retrospective, single-centre study, we included all confirmed cases of 2019-nCoV in Wuhan Jinyintan Hospital from Jan 1 to Jan 20, 2020. Cases were confirmed by real-time RT-PCR and were analysed for epidemiological, demographic, clinical, and radiological features and laboratory data. Outcomes were followed up until Jan 25, 2020.

Findings: Of the 99 patients with 2019-nCoV pneumonia, 49 (49%) had a history of exposure to the Huanan seafood market. The average age of the patients was 55.5 years (SD 13.1), including 67 men and 32 women. 2019-nCoV was detected in all patients by real-time RT-PCR. 50 (51%) patients had chronic diseases. Patients had clinical manifestations of fever (82 [83%] patients), cough (81 [82%] patients), shortness of breath (31 [31%] patients), muscle ache (11 [11%] patients), confusion (nine [9%] patients), headache (eight [8%] patients), sore throat (five [5%] patients), rhinorrhoea (four [4%] patients), chest pain (two [2%] patients), diarrhoea (two [2%] patients), and nausea and vomiting (one [1%] patient). According to imaging examination, 74 (75%) patients showed bilateral pneumonia, 14 (14%) patients showed multiple mottling and ground-glass opacity, and one (1%) patient had pneumothorax. 17 (17%) patients developed acute respiratory distress syndrome and, among them, 11 (11%) patients worsened in a short period of time and died of multiple organ failure.

Interpretation: The 2019-nCoV infection was of clustering onset, is more likely to affect older males with comorbidities, and can result in severe and even fatal respiratory diseases such as acute respiratory distress syndrome. In general, characteristics of patients who died were in line with the MuLBSTA score, an early warning model for predicting mortality in viral pneumonia. Further investigation is needed to explore the applicability of the MuLBSTA score in predicting the risk of mortality in 2019-nCoV infection.

Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19)

28 February 2020 | Report

[https://www.who.int/publications/i/item/report-of-the-who-china-joint-mission-on-coronavirus-disease-2019-\(covid-19\)](https://www.who.int/publications/i/item/report-of-the-who-china-joint-mission-on-coronavirus-disease-2019-(covid-19))

Overview

The overall goal of the Joint Mission was to rapidly inform national (China) and international planning on next steps in the response to the ongoing outbreak of the novel coronavirus disease (COVID-19) and on next steps in readiness and preparedness for geographic areas not yet affected.

The findings in this report are based on the Joint Mission's review of national and local governmental reports, discussions on control and prevention measures with national and local experts and response teams, and observations made and insights gained during site visits. The figures have been produced using information and data collected during site visits and with the agreement of the relevant groups. References are available for any information in this report that has already been published in journals.

The WHO-China joint mission of 25 national and international experts was held from 16-24 February 2020. It was led by Dr Bruce Aylward of WHO and Dr Wannian Liang of the People's Republic of China. Dr Aylward is currently a WHO Senior Advisor.

Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention

Wu Z, McGoogan JM

JAMA. 2020;323(13):1239–1242. doi:10.1001/jama.2020.2648

<https://jamanetwork.com/journals/jama/fullarticle/2762130>

Overview

The Chinese Center for Disease Control and Prevention recently published the largest case series to date of coronavirus disease 2019 (COVID-19) in mainland China (72 314 cases, updated through February 11, 2020). This Viewpoint summarizes key findings from this report and discusses emerging understanding of and lessons from the COVID-19 epidemic.

COVID-19 infection: the China and Italy perspectives.

Chen J, Lu H, Melino G, Boccia S, Piacentini M, Ricciardi W, Wang Y, Shi Y, Zhu T.

Cell Death Dis. 2020 Jun 8;11(6):438. doi: 10.1038/s41419-020-2603-0.

<https://www.nature.com/articles/s41419-020-2603-0>

Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the COVID-19 pandemic. Since its first report in December 2019, despite great efforts made in almost every country worldwide, this disease continues to spread globally, especially in most parts of Europe, Iran, and the United States. Here, we update the recent understanding in clinical characteristics, diagnosis strategies, as well as clinical management of COVID-19 in China as compared to Italy, with the purpose to integrate the China experience with the global efforts to outline references for prevention, basic research, treatment as well as final control of the disease. Being the first two countries we feel appropriate to evaluate the evolution of the disease as well as the early result of the treatment, in order to offer a different baseline to other countries. It is also interesting to compare two countries, with a very significant difference in population, where the morbidity and mortality has been so different, and unrelated to the size of the country.

Correlation of Chest CT and RT-PCR Testing for Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases.

Ai T, Yang Z, Hou H, et al.

Radiology. 2020 Aug;296(2):E32-E40. doi: 10.1148/radiol.2020200642.

<https://pubs.rsna.org/doi/10.1148/radiol.2020200642>

Abstract

Background Chest CT is used in the diagnosis of coronavirus disease 2019 (COVID-19) and is an important complement to reverse-transcription polymerase chain reaction (RT-PCR) tests. Purpose To investigate the diagnostic value and consistency of chest CT as compared with RT-PCR assay in COVID-19.

Materials and Methods This study included 1014 patients in Wuhan, China, who underwent both chest CT and RT-PCR tests between January 6 and February 6, 2020. With use of RT-PCR as the reference standard, the performance of chest CT in the diagnosis of COVID-19 was assessed. In addition, for patients with multiple RT-PCR assays, the dynamic conversion of RT-PCR results (negative to positive, positive to negative) was analyzed as compared with serial chest CT scans for those with a time interval between RT-PCR tests of 4 days or more.

Results Of the 1014 patients, 601 of 1014 (59%) had positive RT-PCR results and 888 of 1014 (88%) had positive chest CT scans. The sensitivity of chest CT in suggesting COVID-19 was 97%

(95% confidence interval: 95%, 98%; 580 of 601 patients) based on positive RT-PCR results. In the 413 patients with negative RT-PCR results, 308 of 413 (75%) had positive chest CT findings. Of those 308 patients, 48% (103 of 308) were considered as highly likely cases and 33% (103 of 308) as probable cases. At analysis of serial RT-PCR assays and CT scans, the mean interval between the initial negative to positive RT-PCR results was 5.1 days \pm 1.5; the mean interval between initial positive to subsequent negative RT-PCR results was 6.9 days \pm 2.3. Of the 1014 patients, 60% (34 of 57) to 93% (14 of 15) had initial positive CT scans consistent with COVID-19 before (or parallel to) the initial positive RT-PCR results. Twenty-four of 57 patients (42%) showed improvement on follow-up chest CT scans before the RT-PCR results turned negative.

Conclusion Chest CT has a high sensitivity for diagnosis of coronavirus disease 2019 (COVID-19). Chest CT may be considered as a primary tool for the current COVID-19 detection in epidemic areas.

Dexamethasone in Hospitalized Patients with Covid-19 - Preliminary Report.

RECOVERY Collaborative Group, Horby P, Lim WS, et al.

N Engl J Med. 2020 Jul 17:NEJMoa2021436. doi: 10.1056/NEJMoa2021436.

<https://pubmed.ncbi.nlm.nih.gov/32678530/>

Abstract

Background: Coronavirus disease 2019 (Covid-19) is associated with diffuse lung damage. Glucocorticoids may modulate inflammation-mediated lung injury and thereby reduce progression to respiratory failure and death.

Methods: In this controlled, open-label trial comparing a range of possible treatments in patients who were hospitalized with Covid-19, we randomly assigned patients to receive oral or intravenous dexamethasone (at a dose of 6 mg once daily) for up to 10 days or to receive usual care alone. The primary outcome was 28-day mortality. Here, we report the preliminary results of this comparison.

Results: A total of 2104 patients were assigned to receive dexamethasone and 4321 to receive usual care. Overall, 482 patients (22.9%) in the dexamethasone group and 1110 patients (25.7%) in the usual care group died within 28 days after randomization (age-adjusted rate ratio, 0.83; 95% confidence interval [CI], 0.75 to 0.93; $P < 0.001$). The proportional and absolute between-group differences in mortality varied considerably according to the level of respiratory support that the patients were receiving at the time of randomization. In the dexamethasone group, the incidence of death was lower than that in the usual care group among patients receiving invasive mechanical ventilation (29.3% vs. 41.4%; rate ratio, 0.64; 95% CI, 0.51 to 0.81) and among those receiving oxygen without invasive mechanical ventilation (23.3% vs. 26.2%; rate ratio, 0.82; 95% CI, 0.72 to 0.94) but not among those who were receiving no respiratory support at randomization (17.8% vs. 14.0%; rate ratio, 1.19; 95% CI, 0.91 to 1.55).

Conclusions: In patients hospitalized with Covid-19, the use of dexamethasone resulted in lower 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone at randomization but not among those receiving no respiratory support. (Funded by the Medical Research Council and National Institute for Health Research and others; RECOVERY ClinicalTrials.gov number, NCT04381936; ISRCTN number, 50189673.).



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Remdesivir for the Treatment of Covid-19 - Final Report.

Beigel JH, Tomashek KM, Dodd LE, Mehta et al. ACTT-1 Study Group Members. N Engl J Med. 2020 Nov 5;383(19):1813-1826. doi: 10.1056/NEJMoa2007764. <https://www.nejm.org/doi/10.1056/NEJMoa2007764>

Abstract

Background: Although several therapeutic agents have been evaluated for the treatment of coronavirus disease 2019 (Covid-19), no antiviral agents have yet been shown to be efficacious.

Methods: We conducted a double-blind, randomized, placebo-controlled trial of intravenous remdesivir in adults who were hospitalized with Covid-19 and had evidence of lower respiratory tract infection. Patients were randomly assigned to receive either remdesivir (200 mg loading dose on day 1, followed by 100 mg daily for up to 9 additional days) or placebo for up to 10 days. The primary outcome was the time to recovery, defined by either discharge from the hospital or hospitalization for infection-control purposes only.

Results: A total of 1062 patients underwent randomization (with 541 assigned to remdesivir and 521 to placebo). Those who received remdesivir had a median recovery time of 10 days (95% confidence interval [CI], 9 to 11), as compared with 15 days (95% CI, 13 to 18) among those who received placebo (rate ratio for recovery, 1.29; 95% CI, 1.12 to 1.49; $P < 0.001$, by a log-rank test). In an analysis that used a proportional-odds model with an eight-category ordinal scale, the patients who received remdesivir were found to be more likely than those who received placebo to have clinical improvement at day 15 (odds ratio, 1.5; 95% CI, 1.2 to 1.9, after adjustment for actual disease severity). The Kaplan-Meier estimates of mortality were 6.7% with remdesivir and 11.9% with placebo by day 15 and 11.4% with remdesivir and 15.2% with placebo by day 29 (hazard ratio, 0.73; 95% CI, 0.52 to 1.03). Serious adverse events were reported in 131 of the 532 patients who received remdesivir (24.6%) and in 163 of the 516 patients who received placebo (31.6%).

Conclusions: Our data show that remdesivir was superior to placebo in shortening the time to recovery in adults who were hospitalized with Covid-19 and had evidence of lower respiratory tract infection. (Funded by the National Institute of Allergy and Infectious Diseases and others; ACTT-1 ClinicalTrials.gov number, [NCT04280705](https://clinicaltrials.gov/ct2/show/study/NCT04280705).)

High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study.

Helms J, Tacquard C, Severac F, et al. CRICS TRIGGERSEP Group (Clinical Research in Intensive Care and Sepsis Trial Group for Global Evaluation and Research in Sepsis). Intensive Care Med. 2020 Jun;46(6):1089-1098. doi: 10.1007/s00134-020-06062-x. <https://pubmed.ncbi.nlm.nih.gov/32367170/>

Abstract

Purpose: Little evidence of increased thrombotic risk is available in COVID-19 patients. Our purpose was to assess thrombotic risk in severe forms of SARS-CoV-2 infection.

Methods: All patients referred to 4 intensive care units (ICUs) from two centers of a French tertiary hospital for acute respiratory distress syndrome (ARDS) due to COVID-19 between March 3rd and 31st 2020 were included. Medical history, symptoms, biological data and imaging were prospectively collected. Propensity score matching was performed to analyze the occurrence of thromboembolic events between non-COVID-19 ARDS and COVID-19 ARDS patients.

Results: 150 COVID-19 patients were included (122 men, median age 63 [53; 71] years, SAPSII 49 [37; 64] points). Sixty-four clinically relevant thrombotic complications were diagnosed in 150 patients, mainly pulmonary embolisms (16.7%). 28/29 patients (96.6%) receiving continuous renal replacement therapy experienced circuit clotting. Three thrombotic occlusions (in 2 patients) of centrifugal pump occurred in 12 patients (8%) supported by ECMO. Most patients (> 95%) had elevated D-dimer and fibrinogen. No patient developed disseminated intravascular coagulation. Von Willebrand (vWF) activity, vWF antigen and FVIII were considerably increased, and 50/57 tested patients (87.7%) had positive lupus anticoagulant. Comparison with non-COVID-19 ARDS patients

(n = 145) confirmed that COVID-19 ARDS patients (n = 77) developed significantly more thrombotic complications, mainly pulmonary embolisms (11.7 vs. 2.1%, p < 0.008). Coagulation parameters significantly differed between the two groups.

Conclusion: Despite anticoagulation, a high number of patients with ARDS secondary to COVID-19 developed life-threatening thrombotic complications. Higher anticoagulation targets than in usual critically ill patients should therefore probably be suggested.

Guidance for prone positioning of the conscious COVID-19 patient 2020 Intensive Care Society

Bamford P, Bentley A, Dean J et al.

Full guide download:

<https://emcrit.org/wp-content/uploads/2020/04/2020-04-12-Guidance-for-conscious-proning.pdf>

High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure

Frat JP, Thille AW, Mercat A et al.

N Engl J Med 2015; 372: 2185-2196, DOI: 10.1056/NEJMoa1503326

<https://www.nejm.org/doi/10.1056/NEJMoa1503326>

Abstract

BACKGROUND Whether noninvasive ventilation should be administered in patients with acute hypoxemic respiratory failure is debated. Therapy with high-flow oxygen through a nasal cannula may offer an alternative in patients with hypoxemia.

METHODS We performed a multicenter, open-label trial in which we randomly assigned patients without hypercapnia who had acute hypoxemic respiratory failure and a ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen of 300 mm Hg or less to high-flow oxygen therapy, standard oxygen therapy delivered through a face mask, or noninvasive positive-pressure ventilation. The primary outcome was the proportion of patients intubated at day 28; secondary outcomes included all-cause mortality in the intensive care unit and at 90 days and the number of ventilator-free days at day 28.

RESULTS A total of 310 patients were included in the analyses. The intubation rate (primary outcome) was 38% (40 of 106 patients) in the high-flow–oxygen group, 47% (44 of 94) in the standard group, and 50% (55 of 110) in the noninvasive-ventilation group (P=0.18 for all comparisons). The number of ventilator-free days at day 28 was significantly higher in the high-flow–oxygen group (24±8 days, vs. 22±10 in the standard-oxygen group and 19±12 in the noninvasive-ventilation group; P=0.02 for all comparisons). The hazard ratio for death at 90 days was 2.01 (95% confidence interval [CI], 1.01 to 3.99) with standard oxygen versus high-flow oxygen (P=0.046) and 2.50 (95% CI, 1.31 to 4.78) with noninvasive ventilation versus high-flow oxygen (P=0.006).

CONCLUSIONS In patients with nonhypercapnic acute hypoxemic respiratory failure, treatment with high-flow oxygen, standard oxygen, or noninvasive ventilation did not result in significantly different intubation rates. There was a significant difference in favor of high-flow oxygen in 90-day mortality. (Funded by the Programme Hospitalier de Recherche Clinique Interrégional 2010 of the French Ministry of Health; FLORALI ClinicalTrials.gov number, [NCT01320384](https://clinicaltrials.gov/ct2/show/study/NCT01320384).)

SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19.

Chen P, Nirula A, Heller B, et al. BLAZE-1 Investigators.
N Engl J Med. 2020 Oct 28;NEJMoa2029849. doi: 10.1056/NEJMoa2029849.
<https://www.nejm.org/doi/10.1056/NEJMoa2029849>

Abstract

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (Covid-19), which is most frequently mild yet can be severe and life-threatening. Virus-neutralizing monoclonal antibodies are predicted to reduce viral load, ameliorate symptoms, and prevent hospitalization.

Methods: In this ongoing phase 2 trial involving outpatients with recently diagnosed mild or moderate Covid-19, we randomly assigned 452 patients to receive a single intravenous infusion of neutralizing antibody LY-CoV555 in one of three doses (700 mg, 2800 mg, or 7000 mg) or placebo and evaluated the quantitative virologic end points and clinical outcomes. The primary outcome was the change from baseline in the viral load at day 11. The results of a preplanned interim analysis as of September 5, 2020, are reported here.

Results: At the time of the interim analysis, the observed mean decrease from baseline in the log viral load for the entire population was -3.81, for an elimination of more than 99.97% of viral RNA. For patients who received the 2800-mg dose of LY-CoV555, the difference from placebo in the decrease from baseline was -0.53 (95% confidence interval [CI], -0.98 to -0.08; P = 0.02), for a viral load that was lower by a factor of 3.4. Smaller differences from placebo in the change from baseline were observed among the patients who received the 700-mg dose (-0.20; 95% CI, -0.66 to 0.25; P = 0.38) or the 7000-mg dose (0.09; 95% CI, -0.37 to 0.55; P = 0.70). On days 2 to 6, the patients who received LY-CoV555 had a slightly lower severity of symptoms than those who received placebo. The percentage of patients who had a Covid-19-related hospitalization or visit to an emergency department was 1.6% in the LY-CoV555 group and 6.3% in the placebo group.

Conclusions: In this interim analysis of a phase 2 trial, one of three doses of neutralizing antibody LY-CoV555 appeared to accelerate the natural decline in viral load over time, whereas the other doses had not by day 11. (Funded by Eli Lilly; BLAZE-1 ClinicalTrials.gov number, NCT04427501.).

Prevalence of Asymptomatic SARS-CoV-2 Infection: A Narrative Review

Oran DP and Topol EJ
Ann Intern Med. 2020 Jun 3 : M20-3012. doi: 10.7326/M20-3012
<https://www.acpjournals.org/doi/10.7326/M20-3012>

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread rapidly throughout the world since the first cases of coronavirus disease 2019 (COVID-19) were observed in December 2019 in Wuhan, China. It has been suspected that infected persons who remain asymptomatic play a significant role in the ongoing pandemic, but their relative number and effect have been uncertain. The authors sought to review and synthesize the available evidence on asymptomatic SARS-CoV-2 infection. Asymptomatic persons seem to account for approximately 40% to 45% of SARS-CoV-2 infections, and they can transmit the virus to others for an extended period, perhaps longer than 14 days. Asymptomatic infection may be associated with subclinical lung abnormalities, as detected by computed tomography. Because of the high risk for silent spread by asymptomatic persons, it is imperative that testing programs include those without symptoms. To supplement conventional diagnostic testing, which is constrained by capacity, cost, and its one-off nature, innovative tactics for public health surveillance, such as crowdsourcing digital wearable data and monitoring sewage sludge, might be helpful.

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

Polack FP, Thomas SJ, Kitchin N et al. for the C4591001 Clinical Trial Group
N Engl J Med., December 10, 2020, DOI: 10.1056/NEJMoa2034577
<https://www.nejm.org/doi/full/10.1056/NEJMoa2034577>

Abstract

BACKGROUND Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and the resulting coronavirus disease 2019 (Covid-19) have afflicted tens of millions of people in a worldwide pandemic. Safe and effective vaccines are needed urgently.

METHODS In an ongoing multinational, placebo-controlled, observer-blinded, pivotal efficacy trial, we randomly assigned persons 16 years of age or older in a 1:1 ratio to receive two doses, 21 days apart, of either placebo or the BNT162b2 vaccine candidate (30 µg per dose). BNT162b2 is a lipid nanoparticle–formulated, nucleoside-modified RNA vaccine that encodes a prefusion stabilized, membrane-anchored SARS-CoV-2 full-length spike protein. The primary end points were efficacy of the vaccine against laboratory-confirmed Covid-19 and safety.

RESULTS A total of 43,548 participants underwent randomization, of whom 43,448 received injections: 21,720 with BNT162b2 and 21,728 with placebo. There were 8 cases of Covid-19 with onset at least 7 days after the second dose among participants assigned to receive BNT162b2 and 162 cases among those assigned to placebo; BNT162b2 was 95% effective in preventing Covid-19 (95% credible interval, 90.3 to 97.6). Similar vaccine efficacy (generally 90 to 100%) was observed across subgroups defined by age, sex, race, ethnicity, baseline body-mass index, and the presence of coexisting conditions. Among 10 cases of severe Covid-19 with onset after the first dose, 9 occurred in placebo recipients and 1 in a BNT162b2 recipient. The safety profile of BNT162b2 was characterized by short-term, mild-to-moderate pain at the injection site, fatigue, and headache. The incidence of serious adverse events was low and was similar in the vaccine and placebo groups.

CONCLUSIONS A two-dose regimen of BNT162b2 conferred 95% protection against Covid-19 in persons 16 years of age or older. Safety over a median of 2 months was similar to that of other viral vaccines. (Funded by BioNTech and Pfizer; ClinicalTrials.gov number, [NCT04368728](https://clinicaltrials.gov/ct2/show/study/NCT04368728)).

Repurposed Antiviral Drugs for Covid-19 - Interim WHO Solidarity Trial Results.

WHO Solidarity Trial Consortium, Pan H, Peto R, Henao-Restrepo AM, Preziosi MP, et al.
N Engl J Med. 2020 Dec 2;NEJMoa2023184. doi: 10.1056/NEJMoa2023184.
<https://www.nejm.org/doi/full/10.1056/NEJMoa2023184>

Abstract

Background: World Health Organization expert groups recommended mortality trials of four repurposed antiviral drugs - remdesivir, hydroxychloroquine, lopinavir, and interferon beta-1a - in patients hospitalized with coronavirus disease 2019 (Covid-19).

Methods: We randomly assigned inpatients with Covid-19 equally between one of the trial drug regimens that was locally available and open control (up to five options, four active and the local standard of care). The intention-to-treat primary analyses examined in-hospital mortality in the four pairwise comparisons of each trial drug and its control (drug available but patient assigned to the same care without that drug). Rate ratios for death were calculated with stratification according to age and status regarding mechanical ventilation at trial entry.

Results: At 405 hospitals in 30 countries, 11,330 adults underwent randomization; 2750 were assigned to receive remdesivir, 954 to hydroxychloroquine, 1411 to lopinavir (without interferon), 2063 to interferon (including 651 to interferon plus lopinavir), and 4088 to no trial drug. Adherence was 94 to 96% midway through treatment, with 2 to 6% crossover. In total, 1253 deaths were reported (median day of death, day 8; interquartile range, 4 to 14). The Kaplan-Meier 28-day mortality was 11.8% (39.0% if the patient was already receiving ventilation at randomization and 9.5% otherwise). Death occurred in 301 of 2743 patients receiving remdesivir and in 303 of 2708

receiving its control (rate ratio, 0.95; 95% confidence interval [CI], 0.81 to 1.11; P = 0.50), in 104 of 947 patients receiving hydroxychloroquine and in 84 of 906 receiving its control (rate ratio, 1.19; 95% CI, 0.89 to 1.59; P = 0.23), in 148 of 1399 patients receiving lopinavir and in 146 of 1372 receiving its control (rate ratio, 1.00; 95% CI, 0.79 to 1.25; P = 0.97), and in 243 of 2050 patients receiving interferon and in 216 of 2050 receiving its control (rate ratio, 1.16; 95% CI, 0.96 to 1.39; P = 0.11). No drug definitely reduced mortality, overall or in any subgroup, or reduced initiation of ventilation or hospitalization duration.

Conclusions: These remdesivir, hydroxychloroquine, lopinavir, and interferon regimens had little or no effect on hospitalized patients with Covid-19, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay. (Funded by the World Health Organization; ISRCTN Registry number, ISRCTN83971151; ClinicalTrials.gov number, [NCT04315948](https://clinicaltrials.gov/ct2/show/study/NCT04315948)).

World Health Organization Best Practices for the Naming of New Human Infectious Diseases

May 2015

<https://www.who.int/news/item/08-05-2015-who-issues-best-practices-for-naming-new-human-infectious-diseases>

APSR Publications



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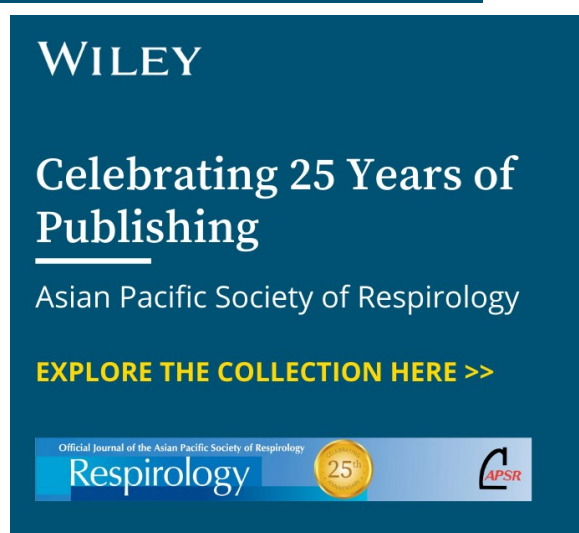
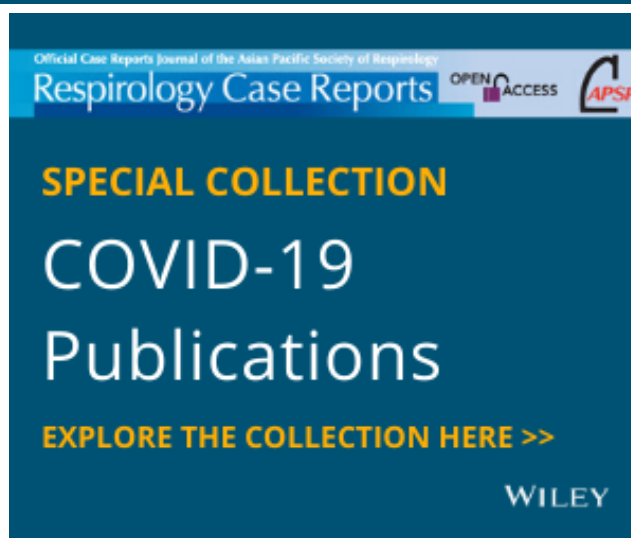
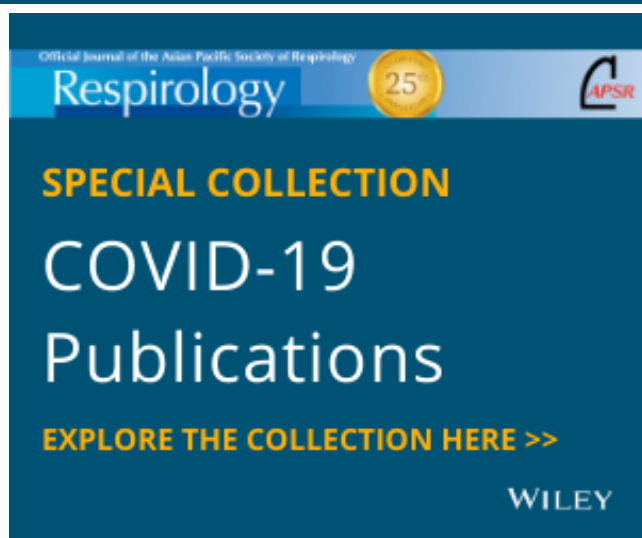


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