

Quale insegnamento dai trial clinici e possibilità di un vaccino

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Disclosures

- AG received speaker's honoraria and fees for attending advisory boards from ViiV Healthcare, Gilead, Janssen-Cilag, Merck Sharp & Dohme, Bristol-Myers Squibb, Pfizer and Novartis and received research grants from ViiV, Bristol-Myers Squibb, and Gilead.





COVID-19....

NEW THERAPEUTIC PERSPECTIVES

Covid-2019: Treatment



Vaccine: not available



Active drugs: no effective treatment



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Covid-2019: Treatment



Vaccine: not available



Active drugs: no effective treatment



**Support therapy in severe forms:
marked improvement**



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Science & technology

The Economist May 9th 2020



How covid-19 is changing science

Reaping from the whirlwind



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MAJOR ARTICLE

Treatment With Lopinavir/Ritonavir or Interferon- β 1b Improves Outcome of MERS-CoV Infection in a Nonhuman Primate Model of Common Marmoset

Jasper Fuk-Woo Chan,^{1,2,3,4,a} Yanfeng Yao,^{5,a} Man-Lung Yeung,² Wei Deng,⁵ Linlin Bao,⁵ Lilong Jia,² Fengdi Li,⁵ Chong Xiao,⁵ Hong Gao,⁵ Pin Yu,⁵ Jian-Piao Cai,² Hin Chu,² Jie Zhou,² Honglin Chen,^{1,2,3,4} Chuan Qin,^{5,b} and Kwok-Yung Yuen^{1,2,3,4,b}

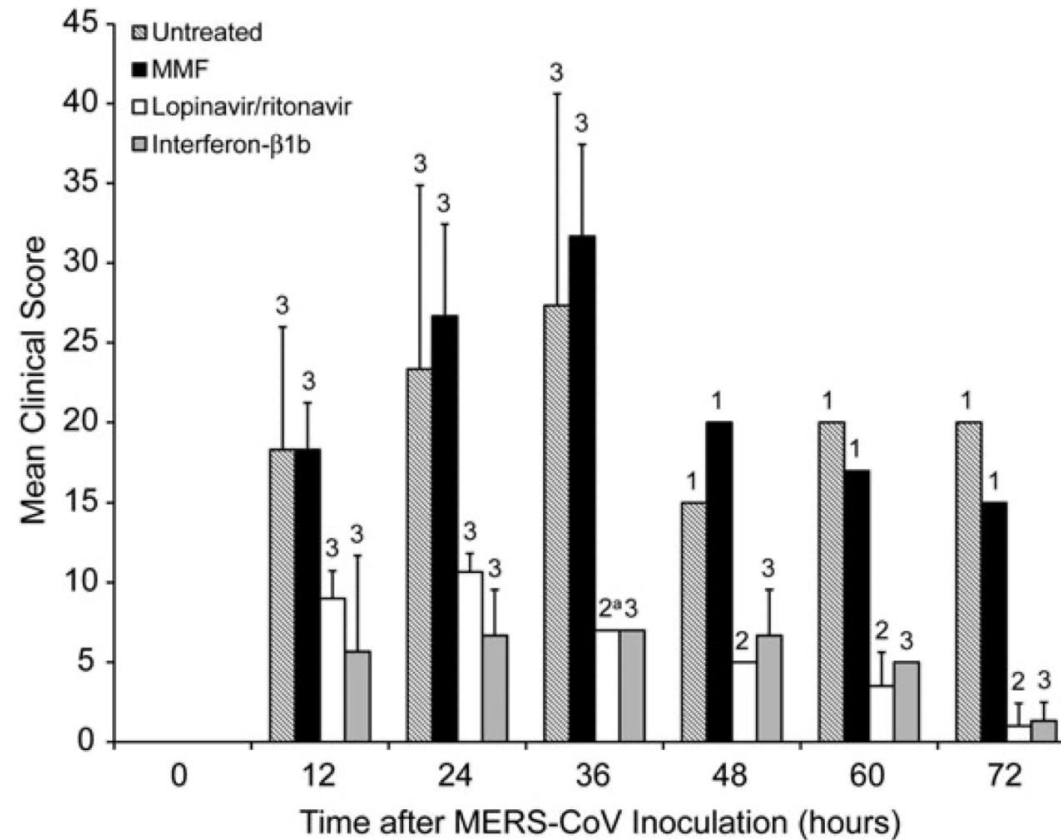
¹State Key Laboratory of Emerging Infectious Diseases, ²Department of Microbiology, ³Research Centre of Infection and Immunology, ⁴Carol Yu Centre for Infection, The University of Hong Kong, Hong Kong Special Administrative Region, and ⁵Institute of Laboratory Animal Sciences, Chinese Academy of Medical Sciences, Beijing, China

• JID 2015:212 (15 December) • Chan et al



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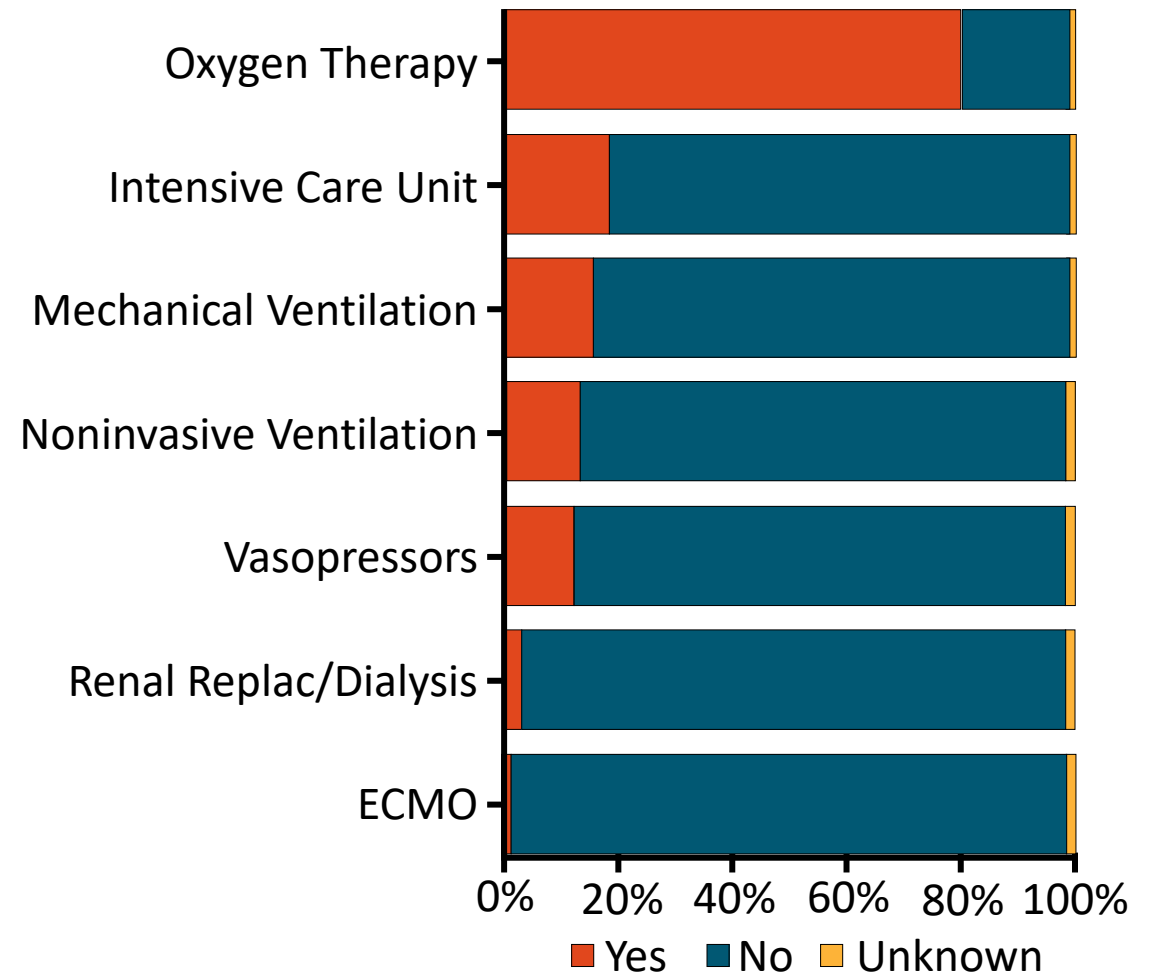
Mean clinical scores of MERS-CoV-infected common marmosets at different time points after virus inoculation



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Medications and Supportive Therapy Among COVID-19–Positive Hospitalized Patients in Spain

| Medication | Number/ With Data | % |
|---------------------|----------------------|------|
| Viral targeted | | |
| Lopinavir/ritonavir | 2820/4005 | 70.4 |
| Hydroxychloroquine | 2618/3995 | 65.5 |
| Azithromycin | 1499/3928 | 38.2 |
| Interferon-beta | 1153/3950 | 29.2 |
| Remdesivir | 48/3957 | 1.2 |
| Ribavirin | 1/3956 | 0.03 |
| Host targeted | | |
| Corticosteroids | 1109/3965 | 28.0 |
| Tocilizumab | 373/3951 | 9.4 |



ORIGINAL ARTICLE

ESTABLISHED IN 1812

MAY 7, 2020

VOL. 382 NO. 19

A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19

B. Cao, Y. Wang, D. Wen, W. Liu, Jingli Wang, G. Fan, L. Ruan, B. Song, Y. Cai, M. Wei, X. Li, J. Xia, N. Chen, J. Xiang, T. Yu, T. Bai, X. Xie, L. Zhang, C. Li, Y. Yuan, H. Chen, Huadong Li, H. Huang, S. Tu, F. Gong, Y. Liu, Y. Wei, C. Dong, F. Zhou, X. Gu, J. Xu, Z. Liu, Y. Zhang, Hui Li, L. Shang, K. Wang, K. Li, X. Zhou, X. Dong, Z. Qu, S. Lu, X. Hu, S. Ruan, S. Luo, J. Wu, L. Peng, F. Cheng, L. Pan, J. Zou, C. Jia, Juan Wang, X. Liu, S. Wang, X. Wu, Q. Ge, J. He, H. Zhan, F. Qiu, L. Guo, C. Huang, T. Jaki, F.G. Hayden, P.W. Horby, D. Zhang, and C. Wang

CONCLUSIONS

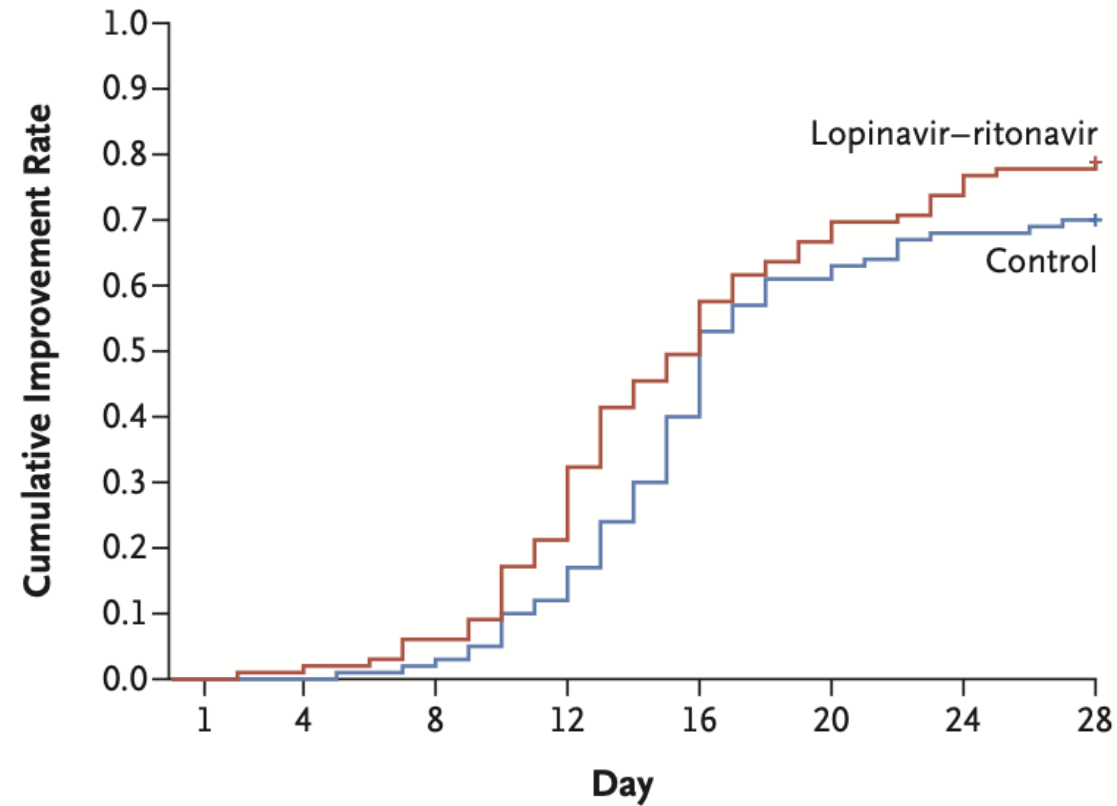
In hospitalized adult patients with severe Covid-19, no benefit was observed with lopinavir–ritonavir treatment beyond standard care. Future trials in patients with severe illness may help to confirm or exclude the possibility of a treatment benefit. (Funded by Major Projects of National Science and Technology on New Drug Creation and Development and others; Chinese Clinical Trial Register number, ChiCTR2000029308.)

N ENGL J MED 382;19 NEJM.ORG MAY 7, 2020



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Time to Clinical Improvement in the Intention-to-Treat Population



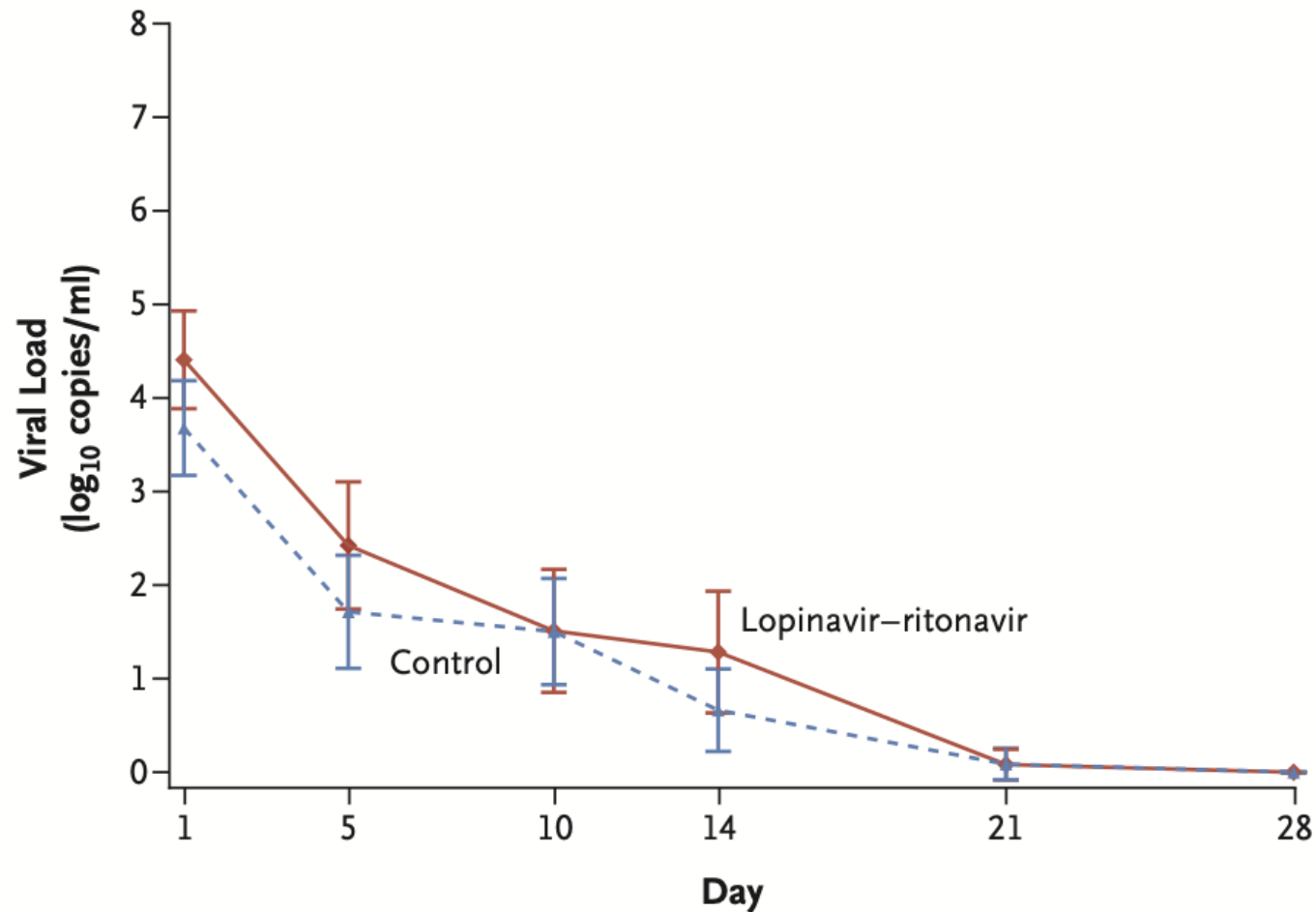
No. at Risk

| | | | | | | | | |
|---------------------|-----|-----|----|----|----|----|----|----|
| Lopinavir-ritonavir | 99 | 98 | 93 | 78 | 50 | 33 | 26 | 22 |
| Control | 100 | 100 | 98 | 88 | 60 | 39 | 32 | 30 |



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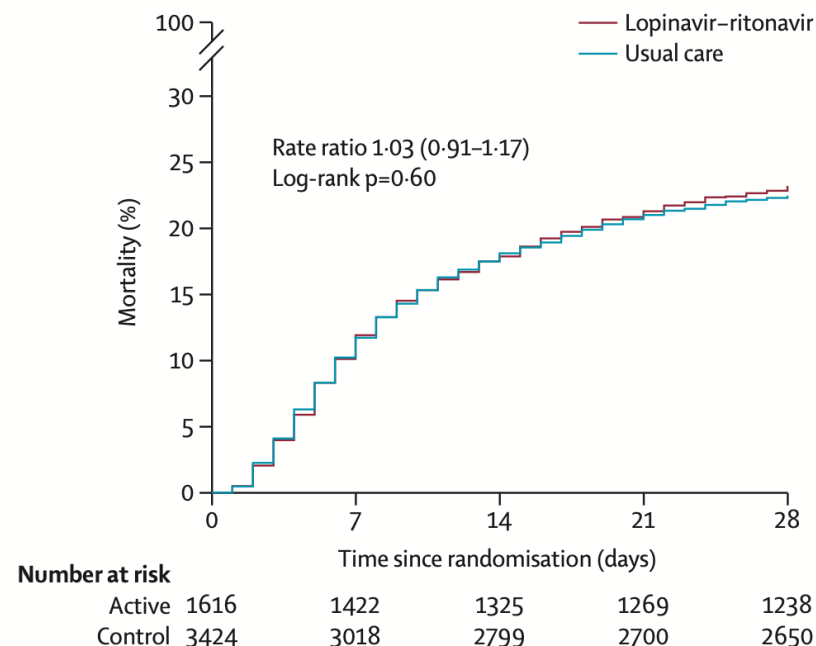
Mean Change from Baseline in SARS-CoV-2 Viral RNA Load by qPCR on Throat Swabs



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Lopinavir–ritonavir in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial

RECOVERY Collaborative Group*



Interpretation In patients admitted to hospital with COVID-19, lopinavir–ritonavir was not associated with reductions in 28-day mortality, duration of hospital stay, or risk of progressing to invasive mechanical ventilation or death. These findings do not support the use of lopinavir–ritonavir for treatment of patients admitted to hospital with COVID-19.



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This Issue

Views **15,479** | Citations **0** | Altmetric **199**



Clinical Trials Update

FREE



May 26, 2020

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No Benefit for Lopinavir-Ritonavir in Severe COVID-19

Anita Slomski

JAMA. 2020;323(20):1999. doi:10.1001/jama.2020.6793

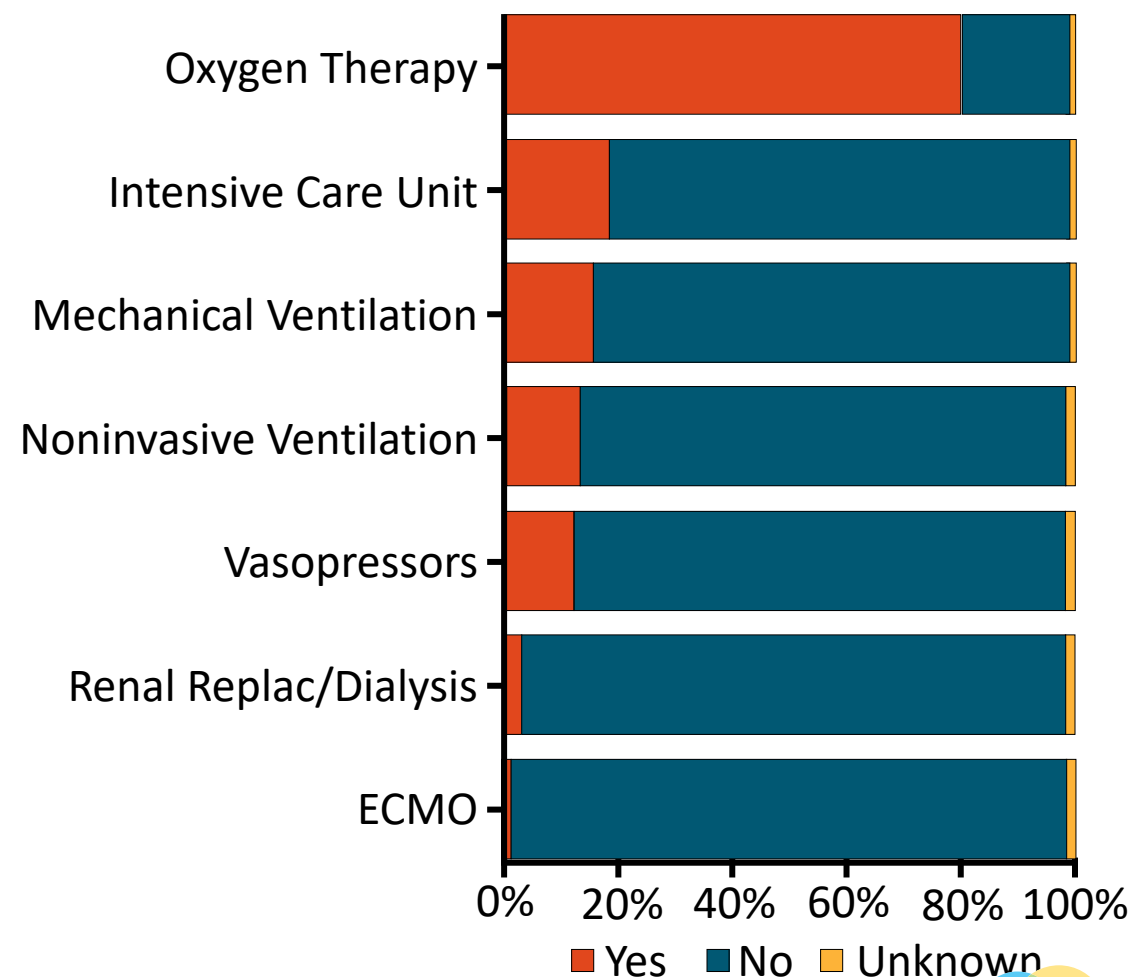
Treatment with the HIV combination drug lopinavir-ritonavir did not accelerate recovery or improve mortality rates among hospitalized patients with severe coronavirus disease 2019 (COVID-19), a **trial** in the *New England Journal of Medicine* reported.



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Medications and Supportive Therapy Among COVID-19–Positive Hospitalized Patients in Spain

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| Host targeted | | |
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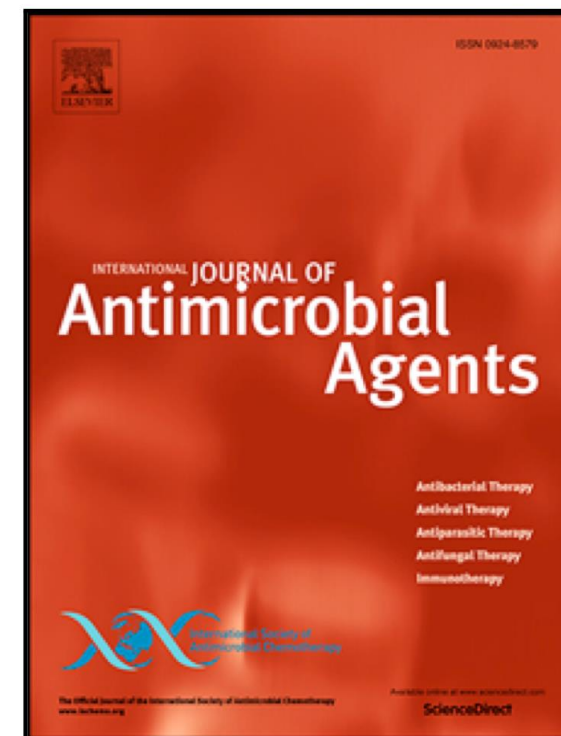


Berenguer. IAS COVID-19. Abstr 11569.

Journal Pre-proof

Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial

Philippe Gautret , Jean-Christophe Lagier , Philippe Parola ,
Van Thuan Hoang , Line Meddeb , Morgane Mailhe ,
Barbara Doudier , Johan Courjon , Valérie Giordanengo ,
Vera Esteves Vieira , Hervé Tissot Dupont , Stéphane Honoré ,
Philippe Colson , Eric Chabrière , Bernard La Scola ,
Jean-Marc Rolain , Philippe Brouqui , Didier Raoult



Background

Chloroquine and hydroxychloroquine have been found to be efficient on SARS-CoV-2, and reported to be efficient in Chinese COV-19 patients. We evaluate the role of hydroxychloroquine on respiratory viral loads.

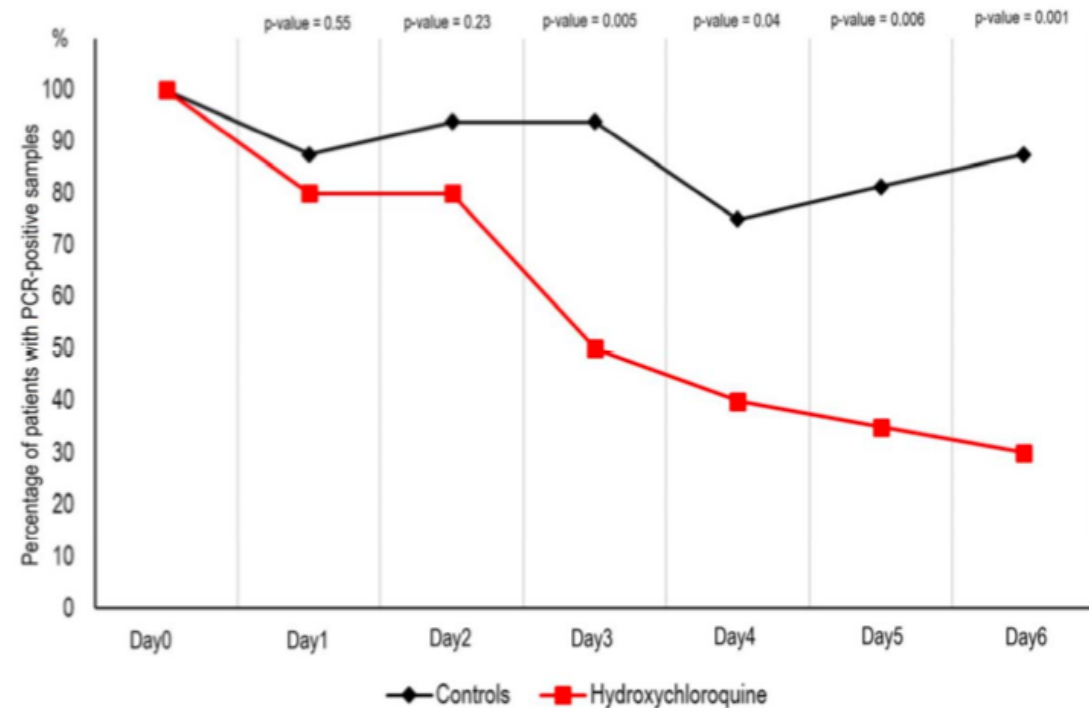
Conclusion

Despite its small sample size our survey shows that hydroxychloroquine treatment is significantly associated with viral load reduction/disappearance in COVID-19 patients and its effect is reinforced by azithromycin.

Cloroquina – evidenze cliniche

- Al giorno 6 post-inclusione il 70% dei pazienti trattati risultava virologicamente guarito (RT-PCR per SARS-CoV-2 negativa su tampone nasale) contro il 12.5% del gruppo controllo
- Differenza nella riduzione della carica già presente al giorno 3 post-trattamento

Figure 1. Percentage of patients with PCR-positive nasopharyngeal samples from inclusion to day6 post-inclusion in COVID-19 patients treated with hydroxychloroquine and in COVID-19 control patients.



P. Gautret et al., Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. JAA 2020

Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis

Mandeep R Mehra, Sapan S Desai, Frank Ruschitzka, Amit N Patel



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Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis



Mandeep R Mehra, Sapan S Desai, Frank Ruschitzka, Amit N Patel

Summary

Background Hydroxychloroquine or chloroquine, often in combination with a second-generation macrolide, are being widely used for treatment of COVID-19, despite no conclusive evidence of their benefit. Although generally safe when used for approved indications such as autoimmune disease or malaria, the safety and benefit of these treatment regimens are poorly evaluated in COVID-19.

Methods We did a multinational registry analysis of the use of hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19. The registry comprised data from 671 hospitals in 50 continents. We included patients hospitalised between Dec 20, 2019, and April 14, 2020, with a positive laboratory finding for SARS-CoV-2. Patients who received one of the treatments of interest within 48 h of diagnosis were included in one of four treatment groups (chloroquine alone, chloroquine with a macrolide, hydroxychloroquine alone, or hydroxychloroquine with a macrolide), and patients who received none of these treatments formed the control group. Patients for whom one of the treatments of interest was initiated more than 48 h after diagnosis or while they were on mechanical ventilation, as well as patients who received remdesivir, were excluded. The main outcomes of interest were in-hospital mortality and the occurrence of de-novo ventricular arrhythmias (as defined on the basis of sustained ventricular tachycardia or ventricular fibrillation).

Findings 96 032 patients (mean age 53·8 years, 46·3% women) with COVID-19 were hospitalised during the study period and met the inclusion criteria. Of these, 62 211 patients were in the treatment groups (1868 received chloroquine, 3783 received chloroquine with a macrolide, 3016 received hydroxychloroquine, and 6221 received hydroxychloroquine with a macrolide) and 33 821 patients were in the control group. 10 698 (11·1%) patients died in hospital. After controlling for multiple confounding factors (eg, sex, race or ethnicity, body-mass index, underlying cardiovascular disease and its risk factors, diabetes, underlying lung disease, smoking, immunosuppressed condition, and baseline disease severity), we compared with mortality in the control group (9·3%), hydroxychloroquine (18·0%; hazard ratio 1·335, 95% CI 1·220–1·457), hydroxychloroquine with a macrolide (23·8%; 1·447, 1·368–1·531), chloroquine (16·4%; 1·365, 1·218–1·531), chloroquine with a macrolide (22·2%; 1·368, 1·273–1·469) were each independently associated with an increased risk of in-hospital mortality. Compared with the control group (0·3%), hydroxychloroquine (6·6%; 2·360, 1·935–2·906), hydroxychloroquine with a macrolide (8·1%; 5·106, 4·106–5·983), chloroquine (4·3%; 1·551, 1·200–4·596), and chloroquine with a macrolide (6·5%; 4·011, 3·344–4·812) were independently associated with an increased risk of de-novo ventricular arrhythmia during hospitalisation.

Interpretation We were unable to confirm a benefit of hydroxychloroquine or chloroquine, when used alone or with a macrolide, on in-hospital outcomes for COVID-19. Each of these drug regimens was associated with decreased in-hospital mortality but with an increased frequency of ventricular arrhythmias when used for treatment of COVID-19.

Funding William Harvey Distinguished Chair in Advanced Cardiovascular Medicine at Brigham and Women's Hospital.

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Expression of concern: Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis



Important scientific questions have been raised about data reported in the paper by Mandeep Mehra et al—Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis¹—published in *The Lancet* on May 22, 2020. Although an independent audit of the provenance and validity of the data has been commissioned by the authors not affiliated with Surgisphere and is ongoing, with results expected very shortly, we are

issuing an Expression of Concern to alert readers to the fact that serious scientific questions have been brought to our attention. We will update this notice as soon as we have further information.

The Lancet Editors

The Lancet, London EC2Y 5AS, UK

- 1 Mehra MR, Desai SS, Ruschitzka F, Patel AN. Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis. *Lancet* 2020; published online May 22. [https://doi.org/10.1016/S0140-6736\(20\)31180-6](https://doi.org/10.1016/S0140-6736(20)31180-6).

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June 2, 2020
[https://doi.org/10.1016/S0140-6736\(20\)31290-3](https://doi.org/10.1016/S0140-6736(20)31290-3)

Chloroquine or hydroxychloroquine for COVID-19: why might they be hazardous?



The findings from Mehra and colleagues' study add to preliminary reports suggesting that regimens of chloroquine or hydroxychloroquine, alone or with azithromycin, are not useful and could be harmful in hospitalised patients with COVID-19.



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ORIGINAL ARTICLE

Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19

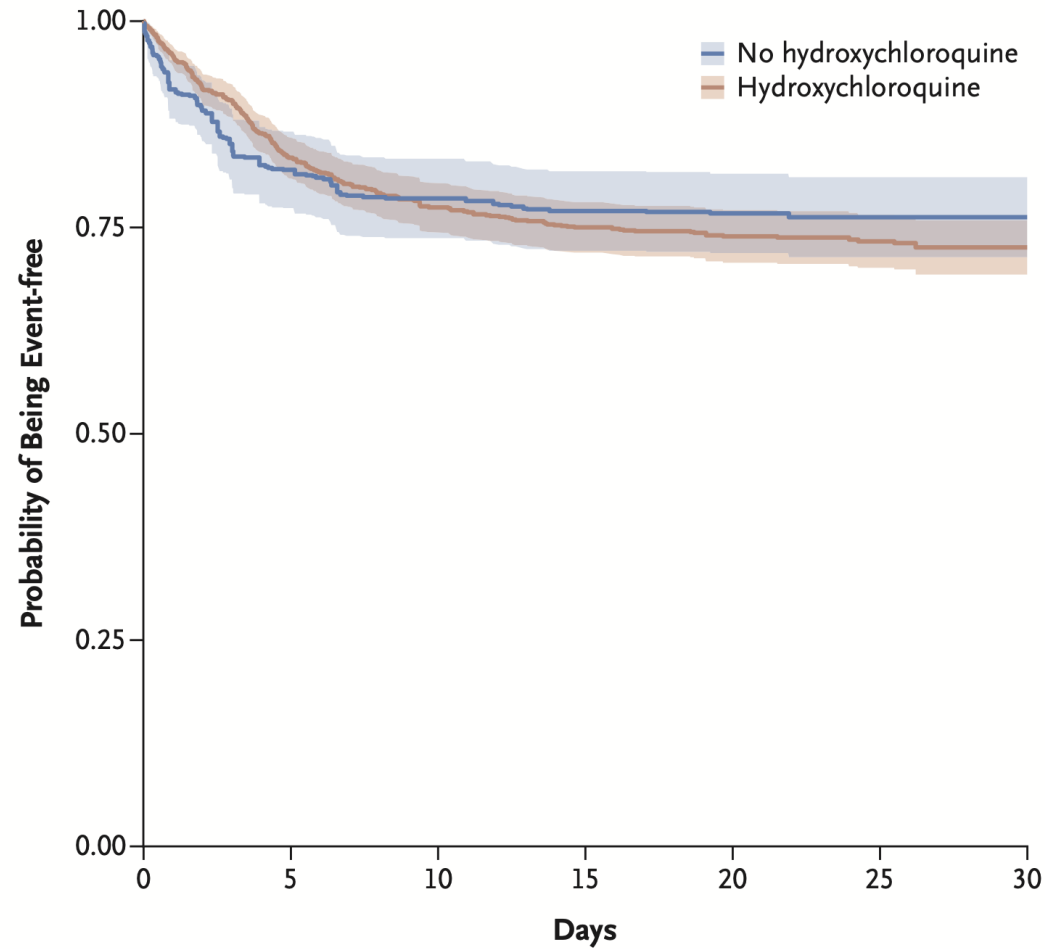
Joshua Geleris, M.D., Yifei Sun, Ph.D., Jonathan Platt, Ph.D., Jason Zucker, M.D., Matthew Baldwin, M.D., George Hripcsak, M.D., Angelena Labella, M.D., Daniel K. Manson, M.D., Christine Kubin, Pharm.D., R. Graham Barr, M.D., Dr.P.H., Magdalena E. Sobieszczyk, M.D., M.P.H., and Neil W. Schluger, M.D.

CONCLUSIONS

In this observational study involving patients with Covid-19 who had been admitted to the hospital, hydroxychloroquine administration was not associated with either a greatly lowered or an increased risk of the composite end point of intubation or death. Randomized, controlled trials of hydroxychloroquine in patients with Covid-19 are needed. (Funded by the National Institutes of Health.)



Freedom from Composite End Point of Intubation or Death

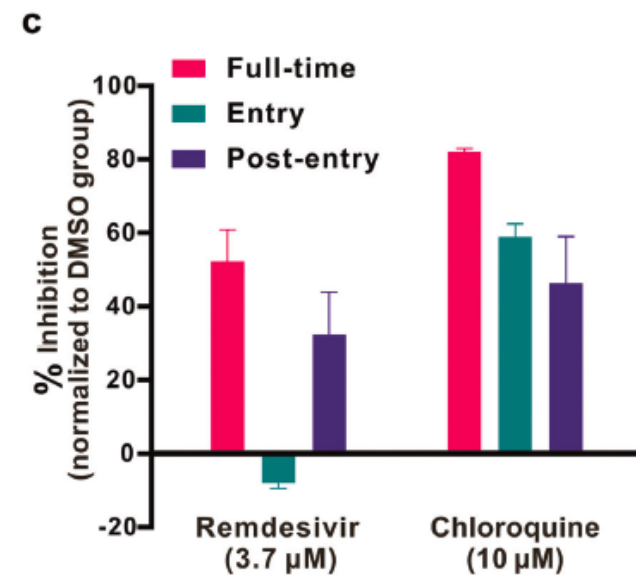
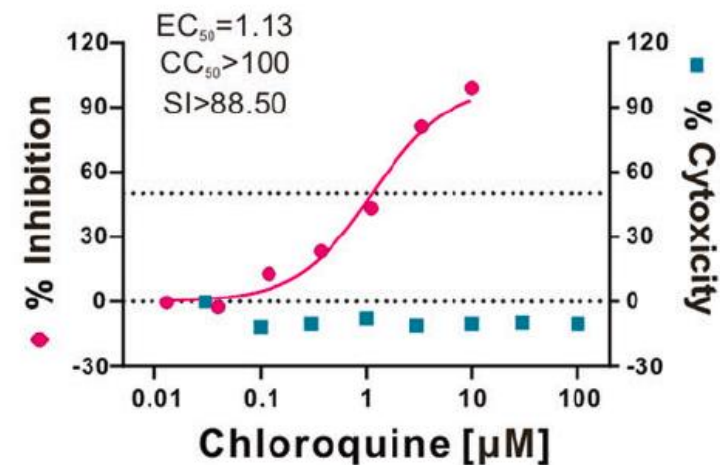


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Remdesivir – evidenze precliniche

- Evidenza in vitro di efficacia di inibizione della replicazione virale di SARS-CoV-2 a concentrazioni terapeutiche raggiungibili in vivo
- Attività antivirale in vitro nei confronti dei coronavirus umani endemici OC43 ed 229E
- Efficacia pre clinica in modelli murini nel ridurre la carica virale, nel migliorare la funzionalità polmonare e nel prevenire la patologia polmonare da MERS-CoV e SARS-CoV

1. M. Wang et al., Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus in vitro. Nature 2020
2. Brown et al., remdesivir inhibits human endemic and zoonotic deltacoronaviruses with highly divergent RNA dependent RNA polymerases. Antiviral research 2019
3. P. Timothy et al., Comparative therapeutic efficacy of remdesivir and LPV/r and IFN beta against MERS-CoV. Nature communications 2020



ORIGINAL ARTICLE

Compassionate Use of Remdesivir for Patients with Severe Covid-19

J. Grein, N. Ohmagari, D. Shin, G. Diaz, E. Asperges, A. Castagna, T. Feldt, G. Green, M.L. Green, F.-X. Lescure, E. Nicastri, R. Oda, K. Yo, E. Quiros-Roldan, A. Studemeister, J. Redinski, S. Ahmed, J. Bennett, D. Chelliah, D. Chen, S. Chihara, S.H. Cohen, J. Cunningham, A. D'Arminio Monforte, S. Ismail, H. Kato, G. Lapadula, E. L'Her, T. Maeno, S. Majumder, M. Massari, M. Mora-Rillo, Y. Mutoh, D. Nguyen, E. Verweij, A. Zoufaly, A.O. Osinusi, A. DeZure, Y. Zhao, L. Zhong, A. Chokkalingam, E. Elboudwarej, L. Telep, L. Timbs, I. Henne, S. Sellers, H. Cao, S.K. Tan, L. Winterbourne, P. Desai, R. Mera, A. Gaggar, R.P. Myers, D.M. Brainard, R. Childs, and T. Flanigan

CONCLUSIONS

In this cohort of patients hospitalized for severe Covid-19 who were treated with compassionate-use remdesivir, clinical improvement was observed in 36 of 53 patients (68%). Measurement of efficacy will require ongoing randomized, placebo-controlled trials of remdesivir therapy. (Funded by Gilead Sciences.)



Oxygen-Support Status at Baseline and after Treatment

Improvement (blue cells), no change (beige) and worsening (gray) in oxygen-support status are shown

| | | No. of Patients in Oxygen-Support Group at Baseline (%) | | | |
|--|-----------------|---|----------------------|---------------------------|----------------------|
| | | Invasive (N=34) | Noninvasive (N=7) | Low-flow oxygen (N=10) | Ambient air (N=2) |
| Category on ordinal scale → | | 5 | 4 | 3 | 2 |
| No. of Patients in Oxygen-Support Group after Treatment (%) | Death | 6 (18) | 1 (14) | 0 | 0 |
| | Invasive | 9 (26) | 1 (14) | 0 | 0 |
| | Noninvasive | 3 (9) | 0 | 0 | 0 |
| | Low-flow oxygen | 0 | 0 | 0 | 0 |
| | Ambient air | 8 (24) | 0 | 0 | 0 |
| | Discharged | 8 (24) | 5 (71) | 10 (100) | 2 (100) |
| Improvement | | 19 (56) | 5 (71) | 10 (100) | 2 (100) |
| Category on ordinal scale ↑ | | | | | |

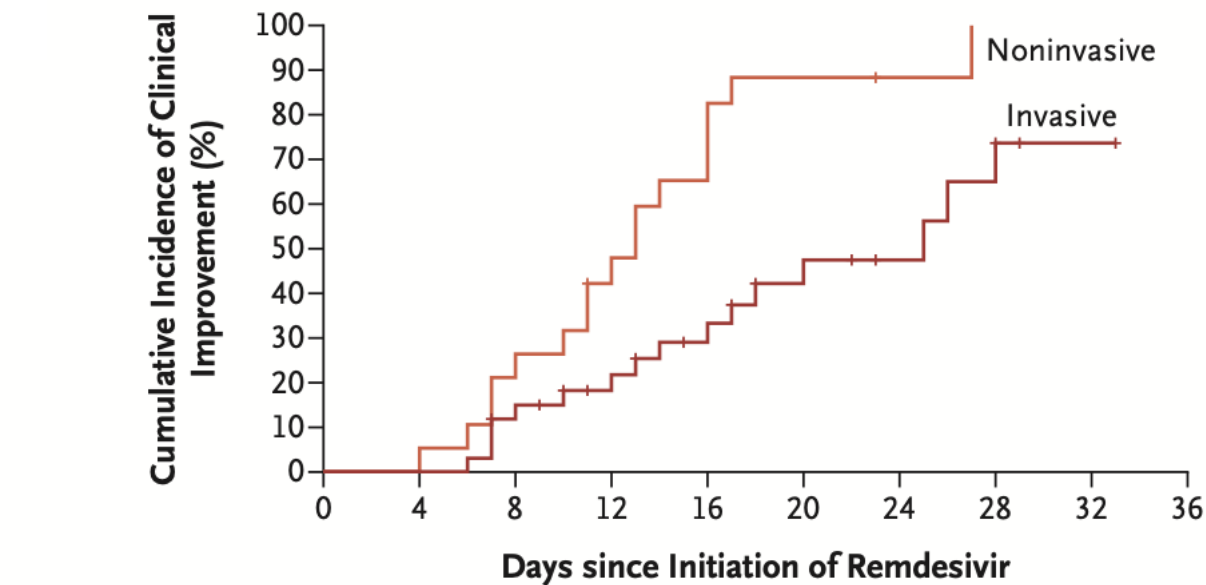


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Cumulative Incidence of Clinical Improvement from Baseline to Day 36

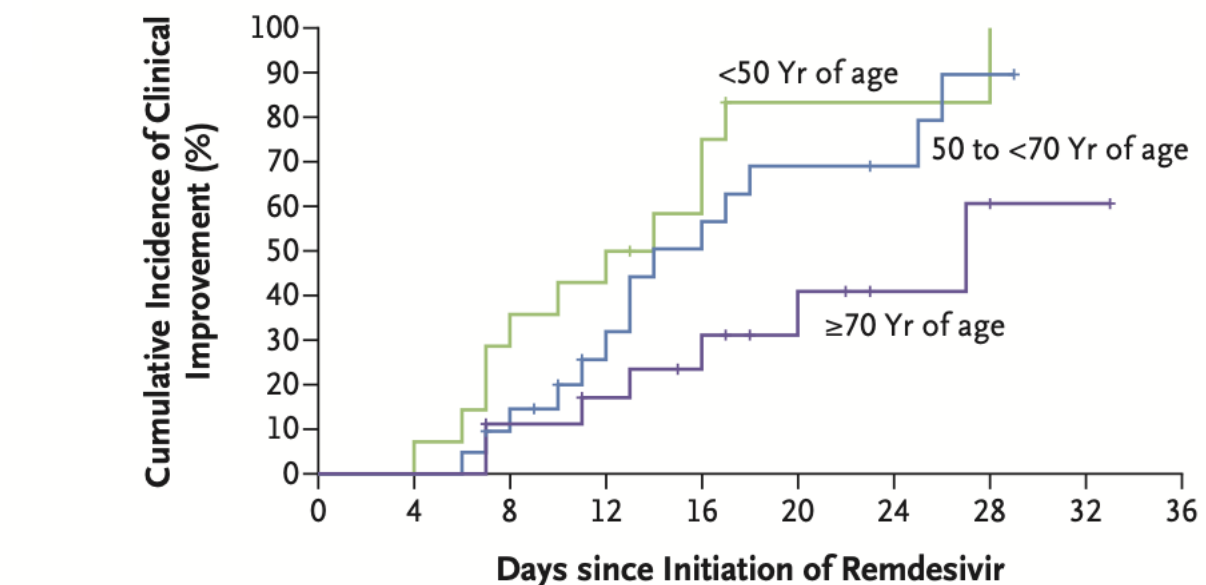
Clinical improvement is shown in the full cohort, in the cohort stratified according to ventilation status at baseline, and in the cohort stratified by age

D Baseline Oxygen Support



| No. at Risk | | | | | | | | | | | |
|-------------|----|----|----|----|----|----|---|---|---|---|--|
| Noninvasive | 19 | 19 | 15 | 10 | 6 | 2 | 1 | 0 | | | |
| Invasive | 34 | 34 | 28 | 23 | 17 | 11 | 6 | 4 | 1 | 0 | |

C Age



| No. at Risk | | | | | | | | | | | |
|---------------------|----|----|----|----|----|---|---|---|---|---|--|
| <50 Yr of age | 14 | 14 | 10 | 8 | 5 | 1 | 1 | 1 | | | |
| 50 to <70 Yr of age | 21 | 21 | 18 | 12 | 8 | 5 | 3 | 1 | 0 | | |
| ≥70 Yr of age | 18 | 18 | 15 | 13 | 10 | 7 | 3 | 2 | 1 | 0 | |

Summary of Adverse Events

| Event | Invasive Ventilation (N=34) | Noninvasive Oxygen Support (N=19) | Total (N=53) |
|--|-----------------------------------|---|-----------------|
| <i>number of patients (percent)</i> | | | |
| Any adverse event | 22 (65) | 10 (53) | 32 (60) |
| Adverse events occurring in 2 or more patients | | | |
| Hepatic enzyme increased* | 8 (24) | 4 (21) | 12 (23) |
| Diarrhea | 1 (3) | 4 (21) | 5 (9) |
| Rash | 3 (9) | 1 (5) | 4 (8) |
| Renal impairment | 4 (12) | 0 | 4 (8) |
| Hypotension | 3 (9) | 1 (5) | 4 (8) |
| Acute kidney injury | 2 (6) | 1 (5) | 3 (6) |
| Atrial fibrillation | 2 (6) | 1 (5) | 3 (6) |
| Multiple-organ-dysfunction syndrome | 3 (9) | 0 | 3 (6) |
| Hypernatremia | 3 (9) | 0 | 3 (6) |
| Deep-vein thrombosis | 3 (9) | 0 | 3 (6) |
| Acute respiratory distress syndrome | 1 (3) | 1 (5) | 2 (4) |
| Pneumothorax | 2 (6) | 0 | 2 (4) |
| Hematuria | 2 (6) | 0 | 2 (4) |
| Delirium | 1 (3) | 1 (5) | 2 (4) |
| Septic shock | 2 (6) | 0 | 2 (4) |
| Pyrexia | 1 (3) | 1 (5) | 2 (4) |
| Any serious adverse event | 9 (26) | 3 (16) | 12 (23) |
| Serious events occurring in 2 or more patients | | | |
| Multiple-organ-dysfunction syndrome | 2 (6) | 0 | 2 (4) |
| Septic shock | 2 (6) | 0 | 2 (4) |
| Acute kidney injury | 2 (6) | 0 | 2 (4) |
| Hypotension | 2 (6) | 0 | 2 (4) |



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ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Preliminary Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*

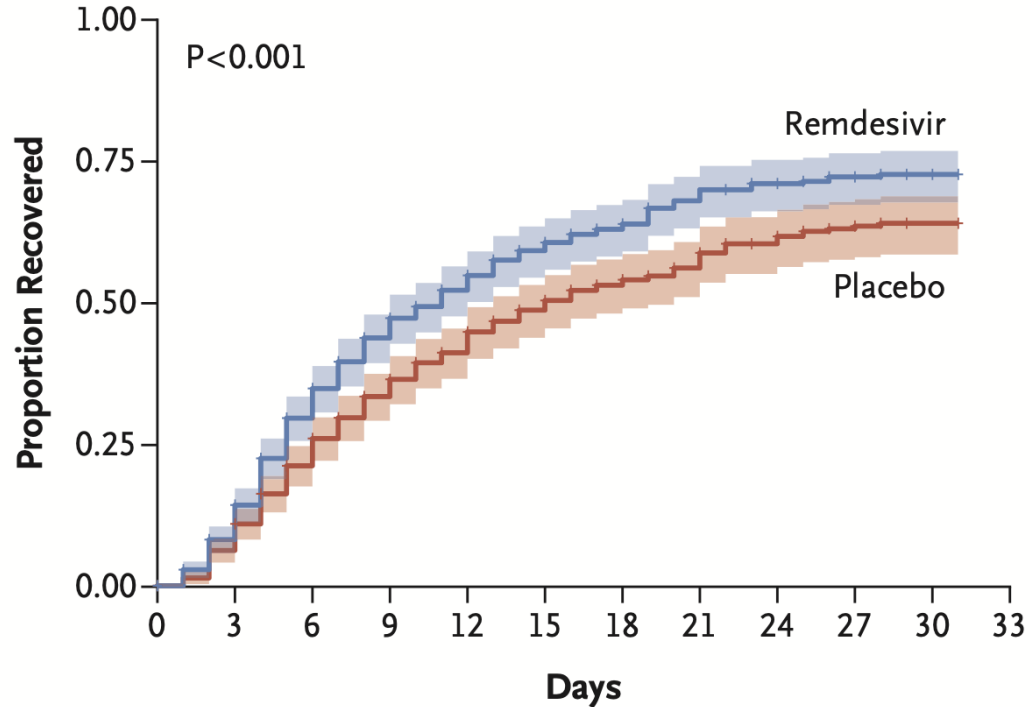
CONCLUSIONS

Remdesivir was superior to placebo in shortening the time to recovery in adults hospitalized with Covid-19 and evidence of lower respiratory tract infection. (Funded by the National Institute of Allergy and Infectious Diseases and others; ACTT-1 ClinicalTrials.gov number, NCT04280705.)

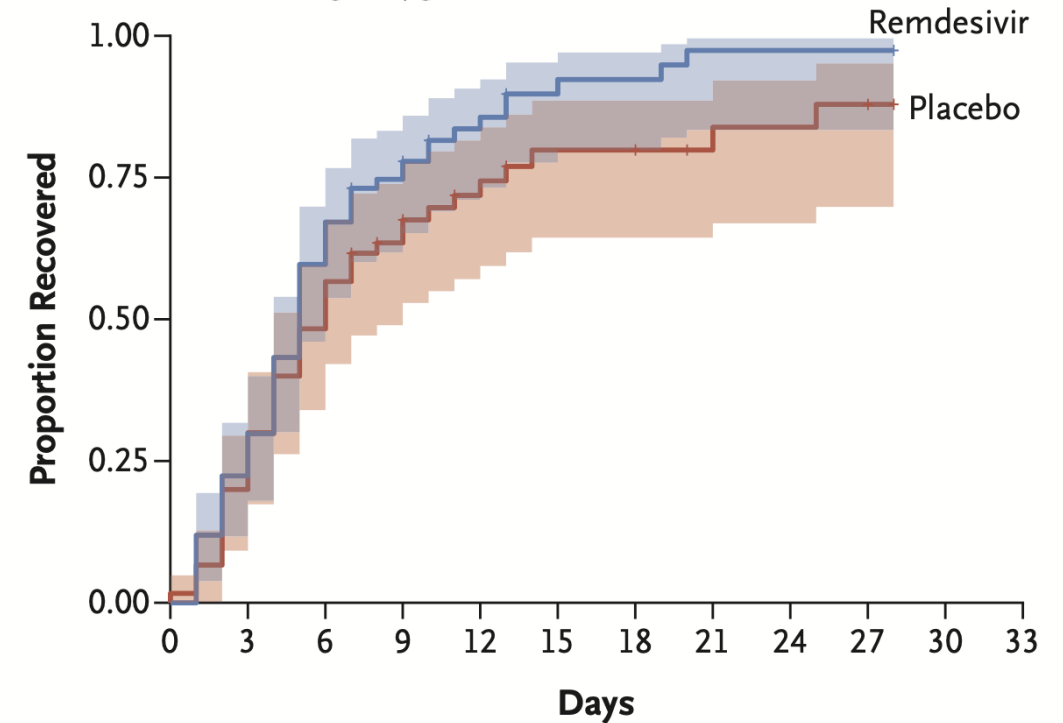


Kaplan–Meier Estimates of Cumulative Recoveries

A Overall



B Patients Not Receiving Oxygen



No. at Risk

| | | | | | | | | | | | | |
|------------|-----|-----|-----|-----|-----|-----|-----|-----|----|----|---|---|
| Remdesivir | 538 | 481 | 363 | 274 | 183 | 142 | 121 | 98 | 78 | 65 | 3 | 0 |
| Placebo | 521 | 481 | 392 | 307 | 224 | 180 | 149 | 115 | 91 | 78 | 2 | 0 |

No. at Risk

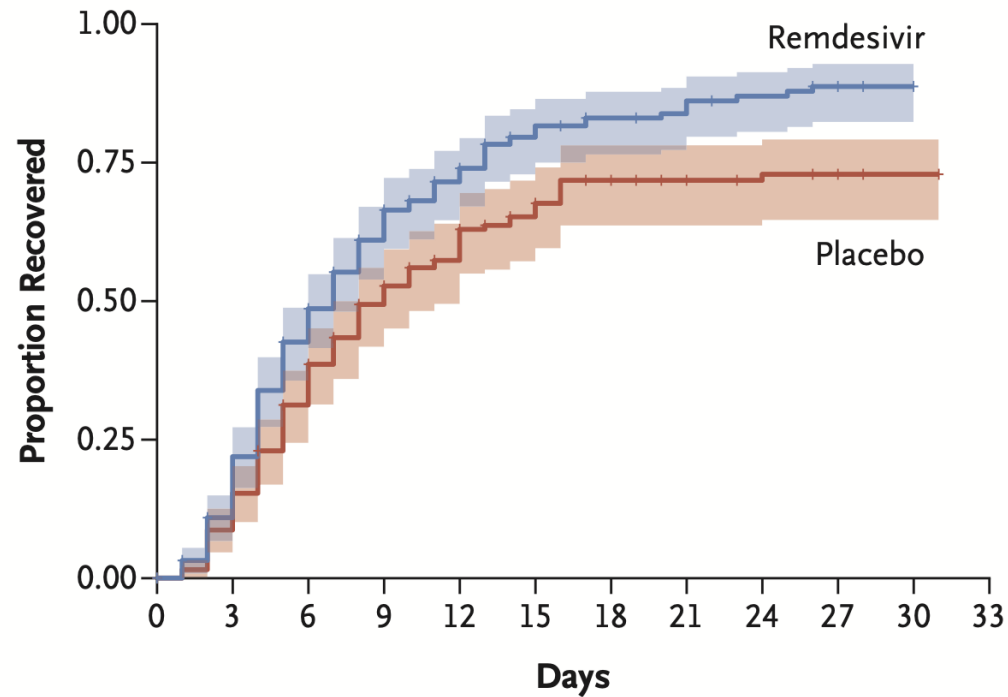
| | | | | | | | | | | | | |
|------------|----|----|----|----|----|---|---|---|---|---|---|---|
| Remdesivir | 67 | 52 | 27 | 16 | 8 | 4 | 3 | 1 | 1 | 1 | 0 | 0 |
| Placebo | 60 | 48 | 31 | 18 | 11 | 7 | 7 | 5 | 4 | 3 | 0 | 0 |



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Kaplan–Meier Estimates of Cumulative Recoveries

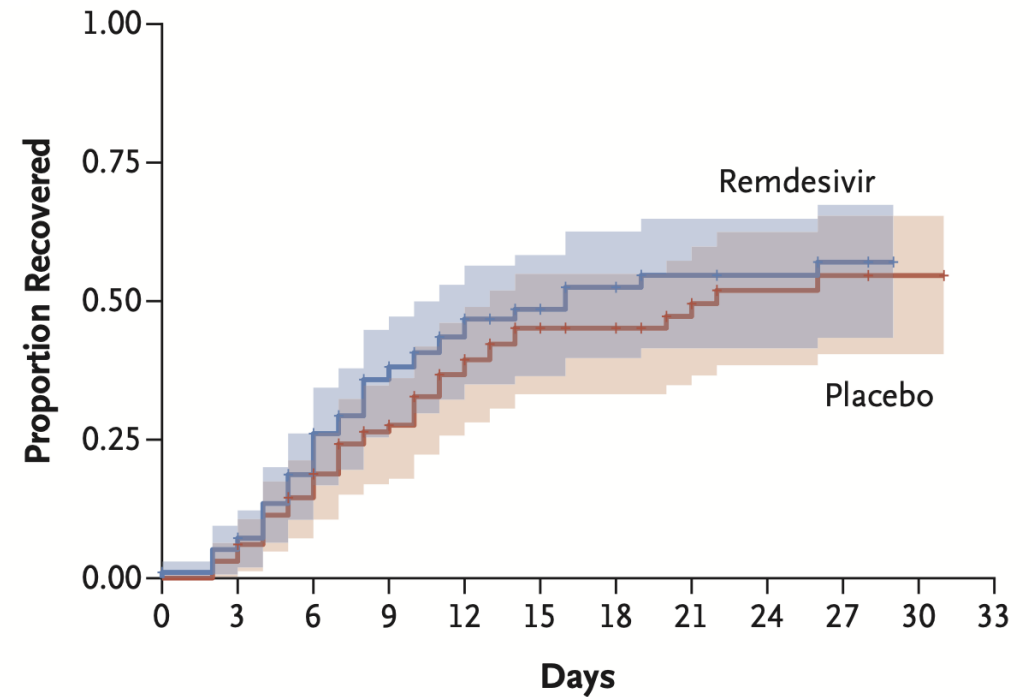
C Patients Receiving Oxygen



No. at Risk

| | | | | | | | | | | | | |
|------------|-----|-----|-----|----|----|----|----|----|----|----|---|---|
| Remdesivir | 222 | 194 | 124 | 79 | 47 | 30 | 23 | 21 | 15 | 12 | 2 | 0 |
| Placebo | 199 | 179 | 131 | 91 | 61 | 43 | 33 | 29 | 26 | 23 | 1 | 0 |

D Patients Receiving High-Flow Oxygen or Noninvasive Mechanical Ventilation

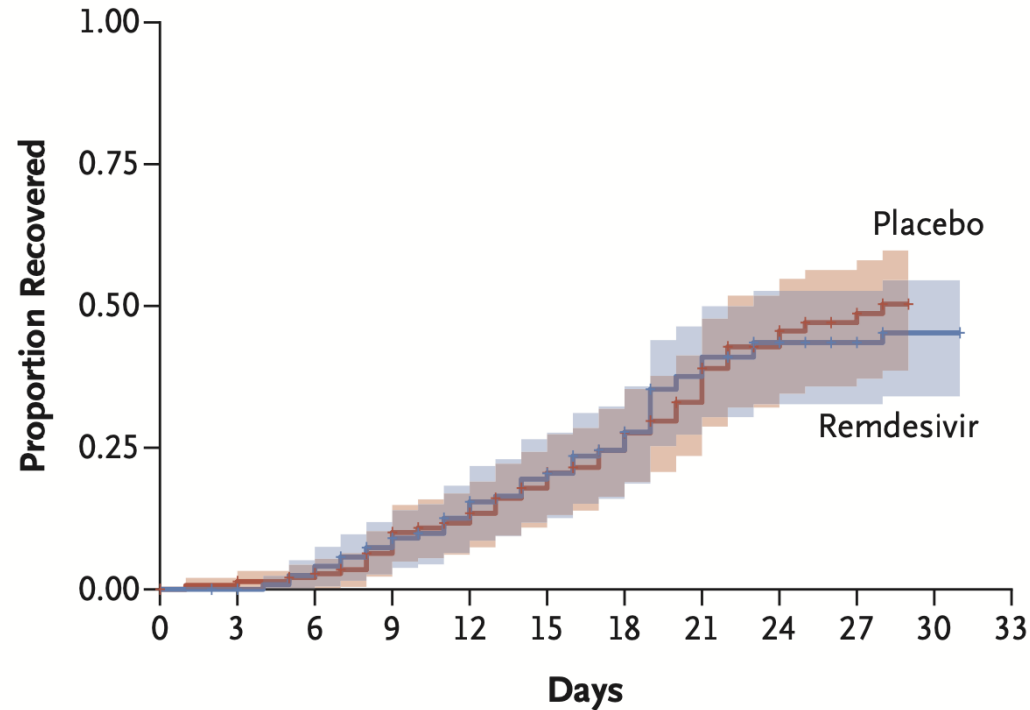


No. at Risk

| | | | | | | | | | | | | |
|------------|----|----|----|----|----|----|----|----|----|----|---|---|
| Remdesivir | 98 | 92 | 77 | 56 | 35 | 27 | 23 | 20 | 19 | 17 | 0 | 0 |
| Placebo | 99 | 96 | 80 | 62 | 47 | 37 | 34 | 23 | 18 | 17 | 1 | 0 |

Kaplan–Meier Estimates of Cumulative Recoveries

E Patients Receiving Mechanical Ventilation or ECMO



No. at Risk

| | | | | | | | | | | | | |
|------------|-----|-----|-----|-----|-----|----|----|----|----|----|---|---|
| Remdesivir | 125 | 124 | 120 | 111 | 91 | 80 | 71 | 55 | 42 | 34 | 1 | 0 |
| Placebo | 147 | 145 | 141 | 127 | 102 | 91 | 73 | 56 | 41 | 33 | 0 | 0 |



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MedRxiv (October 15) version

Repurposed antiviral drugs for COVID-19 –interim WHO SOLIDARITY trial results

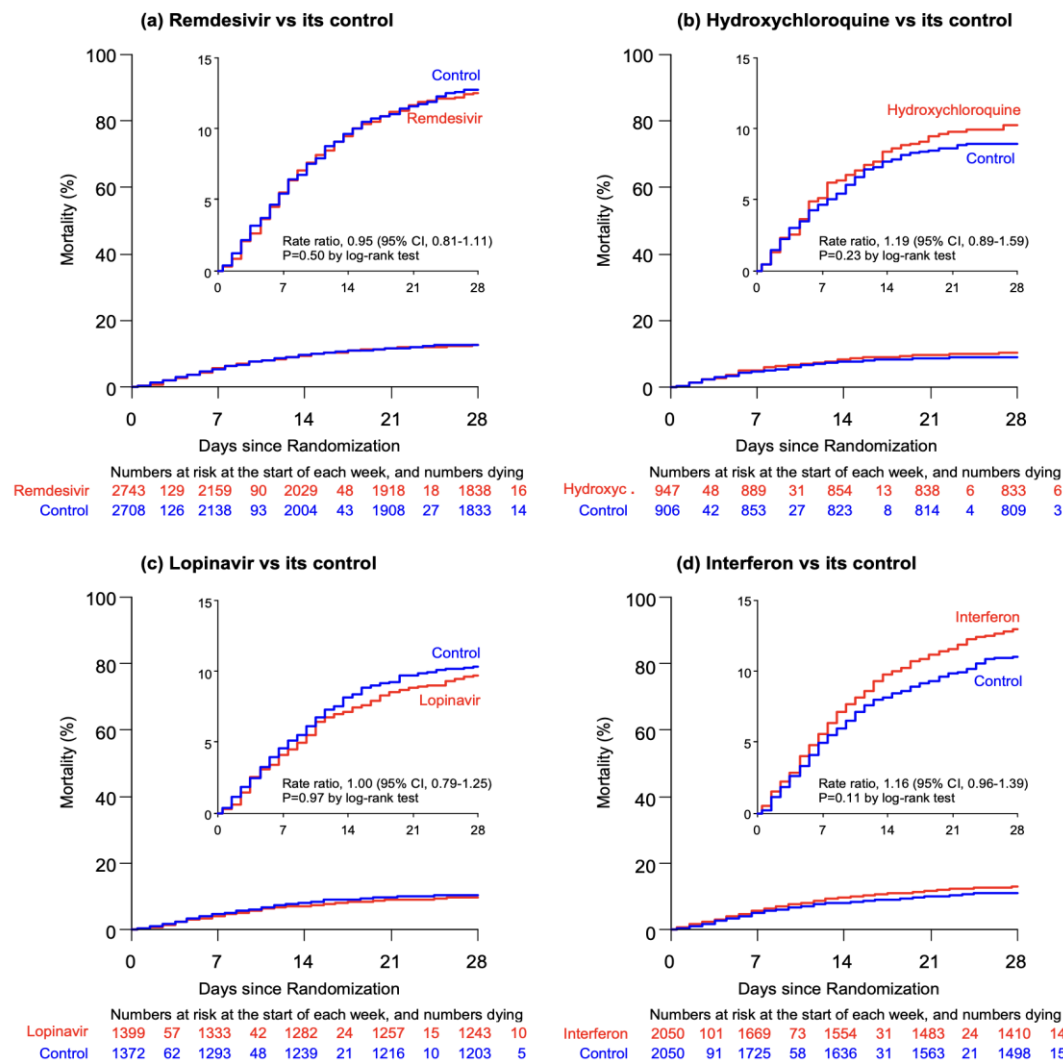
WHO Solidarity trial consortium*

CONCLUSIONS

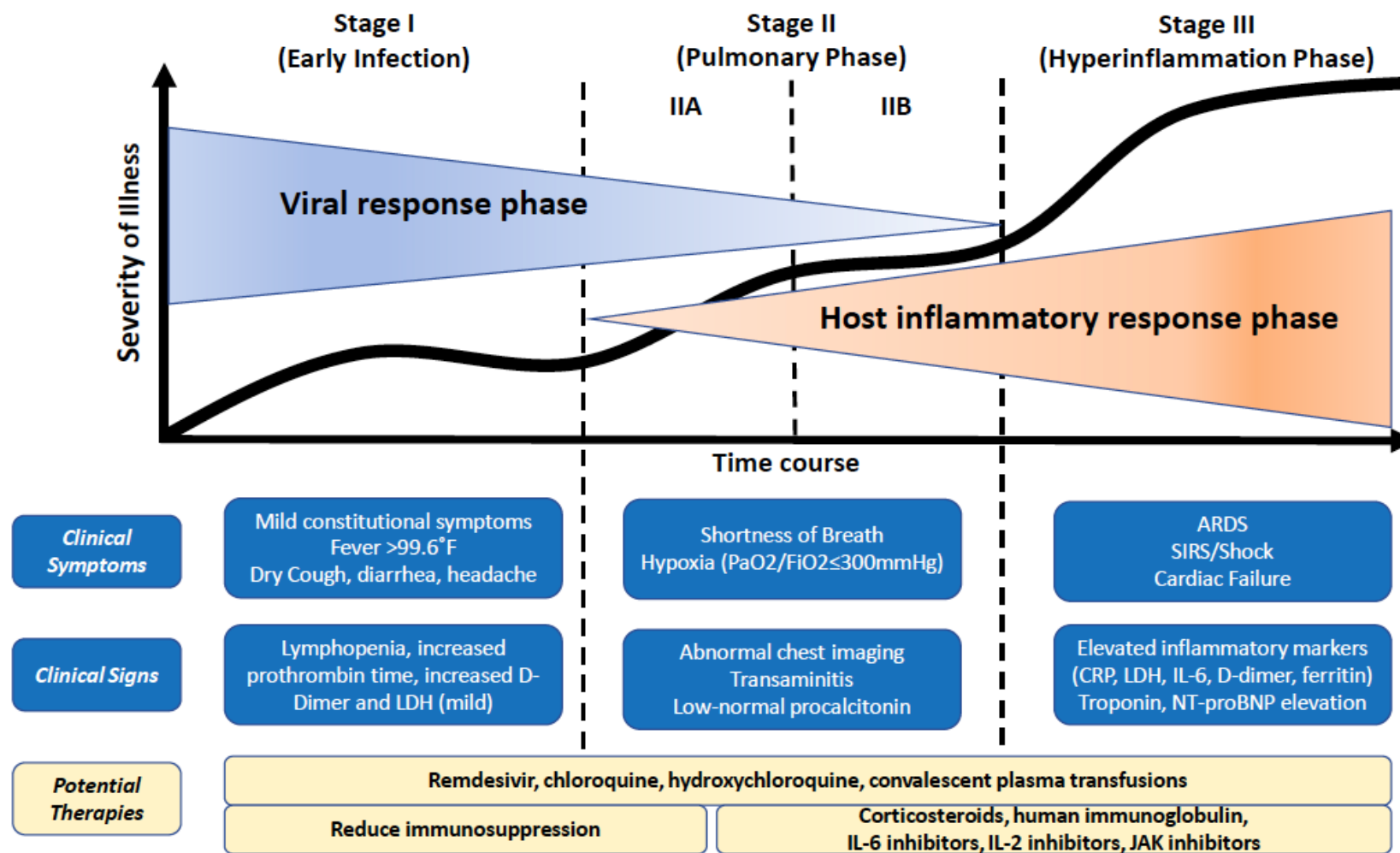
These Remdesivir, Hydroxychloroquine, Lopinavir and Interferon regimens appeared to have little or no effect on hospitalized COVID-19, as indicated by overall mortality, initiation of ventilation and duration of hospital stay. The mortality findings contain most of the randomized evidence on Remdesivir and Interferon, and are consistent with meta-analyses of mortality in all major trials. (Funding: WHO. Registration: ISRCTN83971151, NCT04315948)



Effects of (a) Remdesivir, (b) Hydroxychloroquine, (c) Lopinavir, and (d) Interferon on 28-day mortality

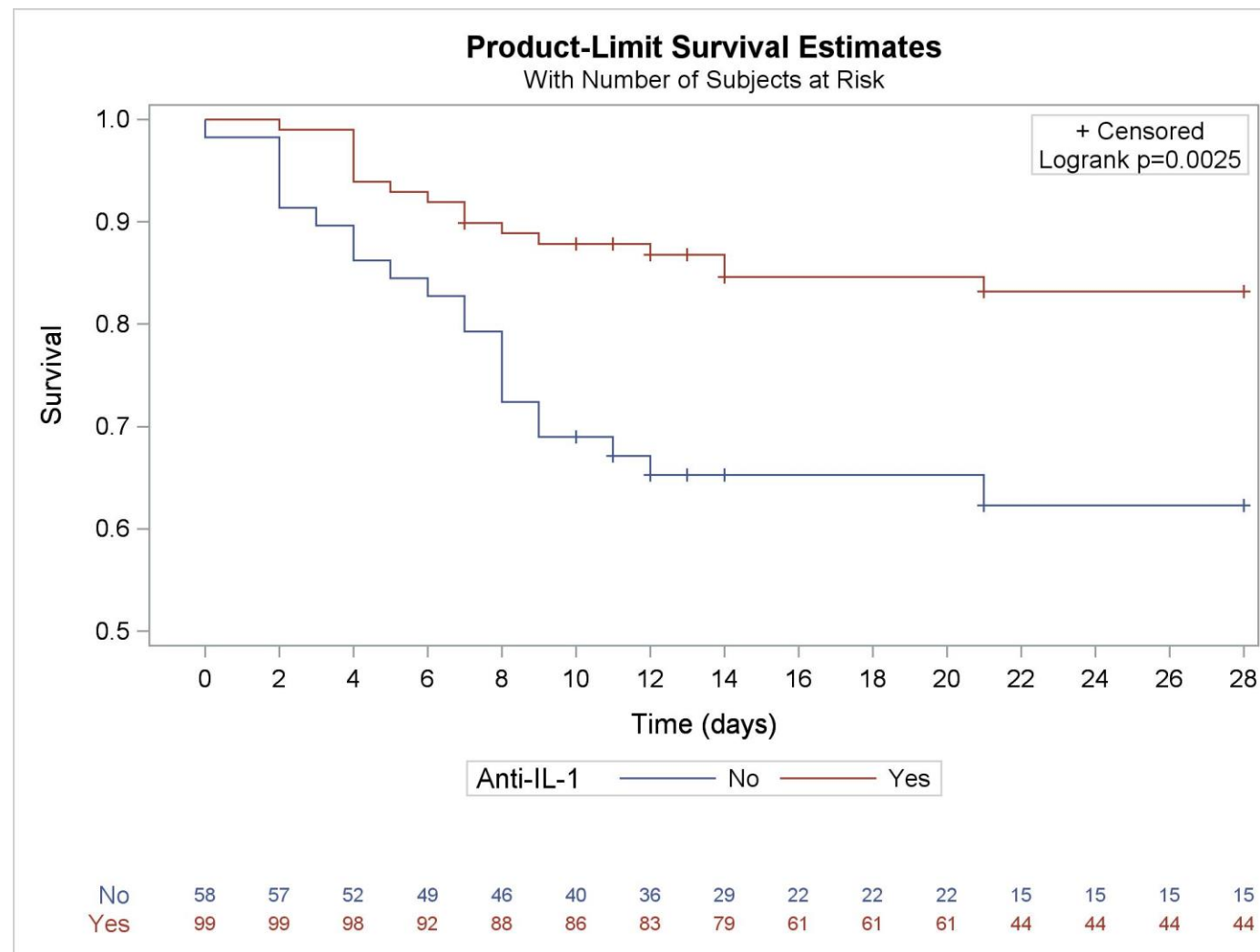


COVID-19: Le fasi di malattia



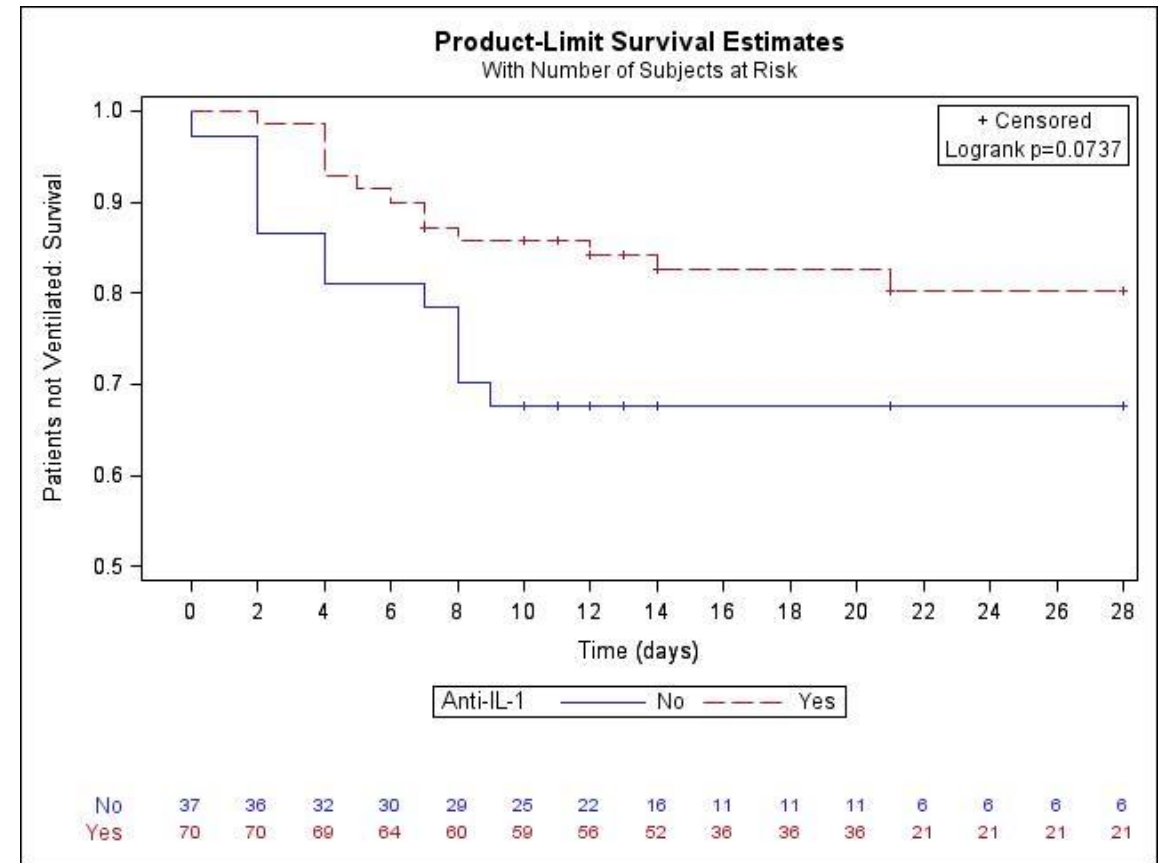
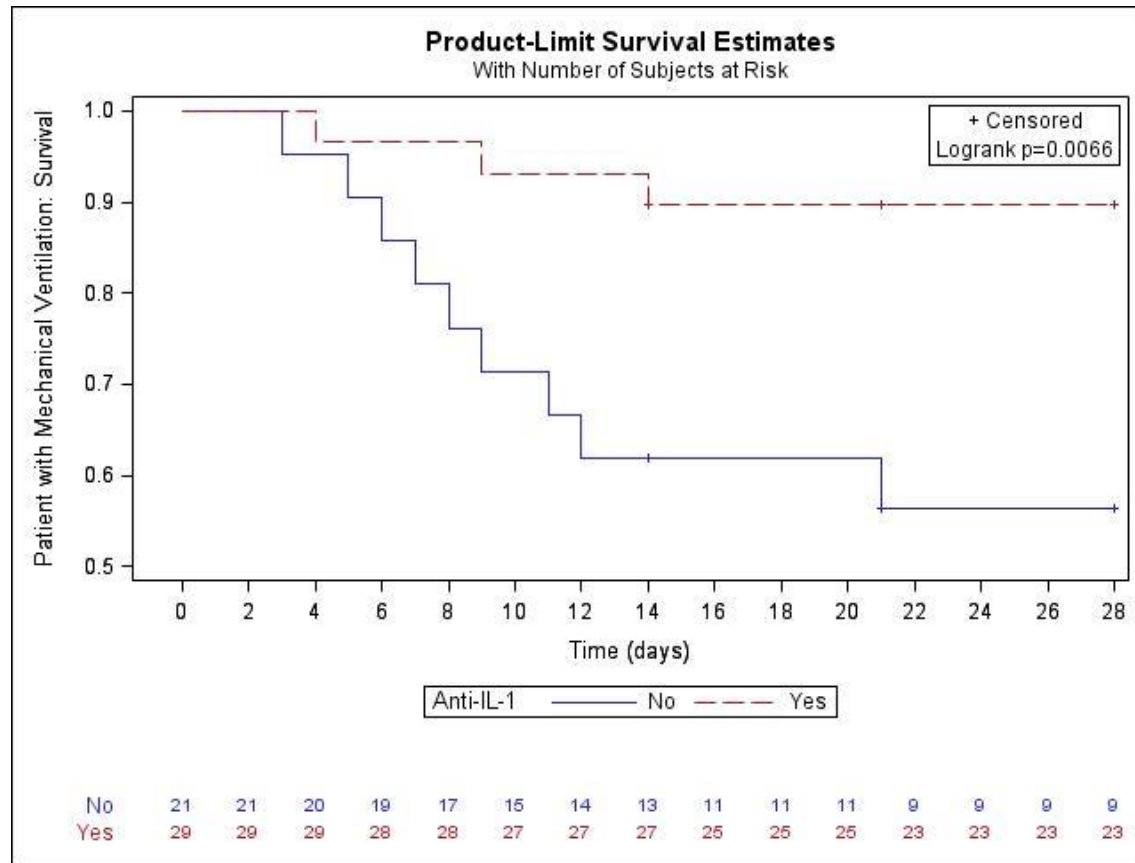
H.K. Siddiqi et. Al, COVID-19 illness in native and immunosuppressed states: a clinical-therapeutic staging proposal. J of heart and lung transp

Survival according to treatment with Anti-IL-1



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Survival according to treatment with Anti-IL-1, in patients with MV and without MV at inclusion




Published Online: 3 December, 2018 | Supp Info: <http://doi.org/10.1084/jem.20182160>

Downloaded from jem.rupress.org on January 30, 2019



VIEWPOINT

Vaccines: An achievement of civilization, a human right, our health insurance for the future

Rino Rappuoli^{1,2}, Angela Santoni³, and Alberto Mantovani^{4,5,6} 

Vaccines have made a key, cost-effective contribution to the prolongation of life expectancy and quality. Here we summarize challenges facing vaccinology and immunology at the level of society, scientific innovation, and technology in a global health perspective. We argue that vaccines represent a safety belt and life insurance for humankind.



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The New York Times

Opinion

How Long Will a Vaccine Really Take?

By Stuart A. Thompson

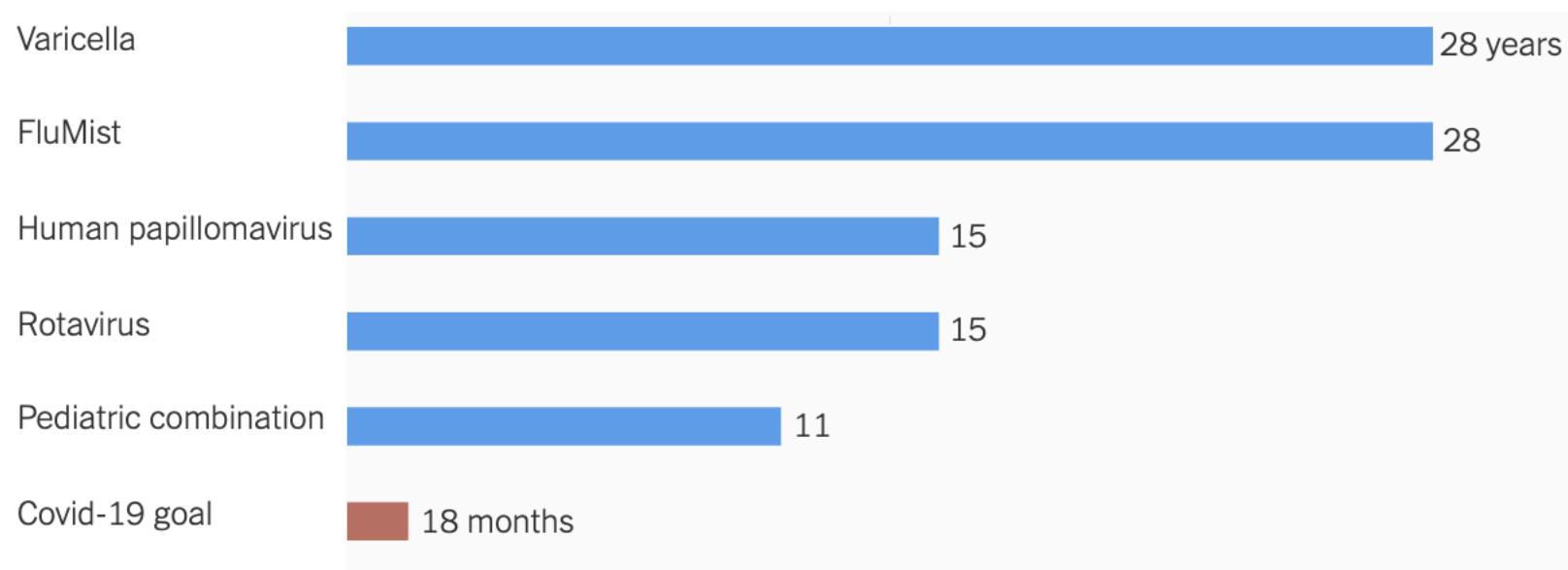
APRIL 30, 2020



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Years and years, at minimum

The vaccine development process has typically taken a decade or longer.



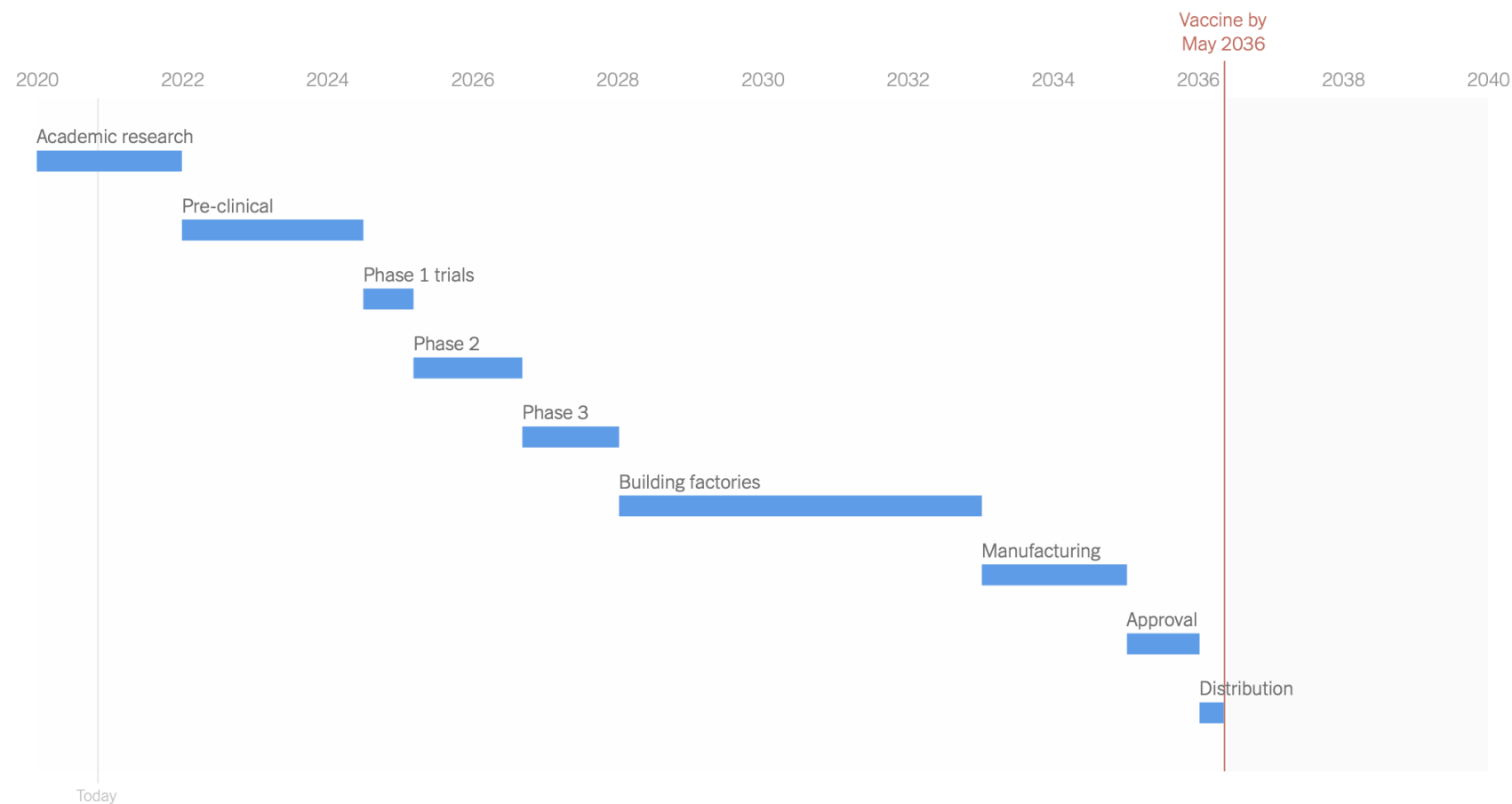
Note: Rotavirus and HPV vaccines include time from filing of the first investigational new drug to approval.

Source: "Plotkin's Vaccines" (7th edition)



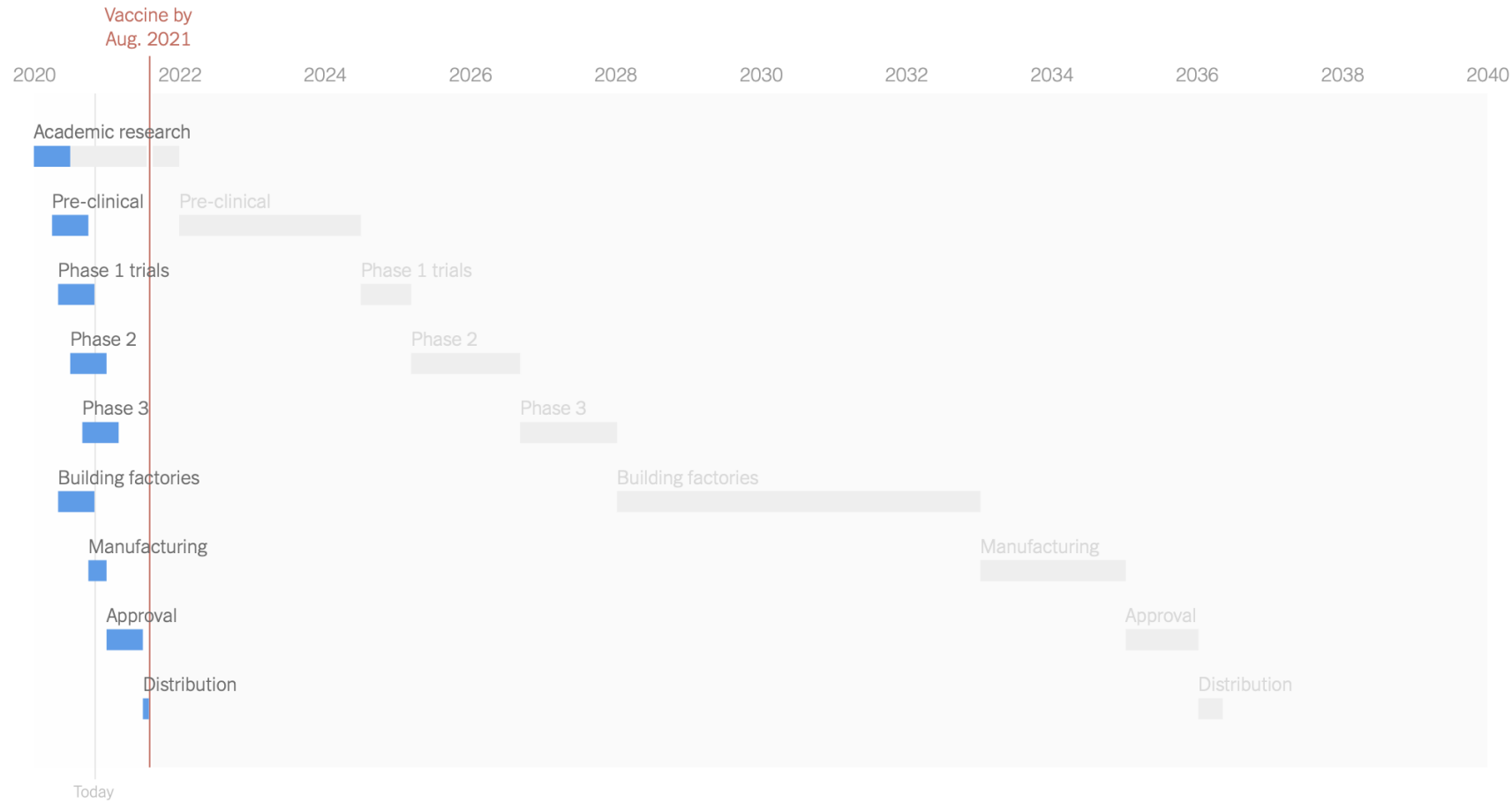
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A vaccine would be the ultimate weapon against the coronavirus and the best route back to normal life



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Officials like Dr. Anthony S. Fauci, the top infectious disease expert on the Trump administration's coronavirus task force, estimate a vaccine could arrive in at least 12 to 18 months



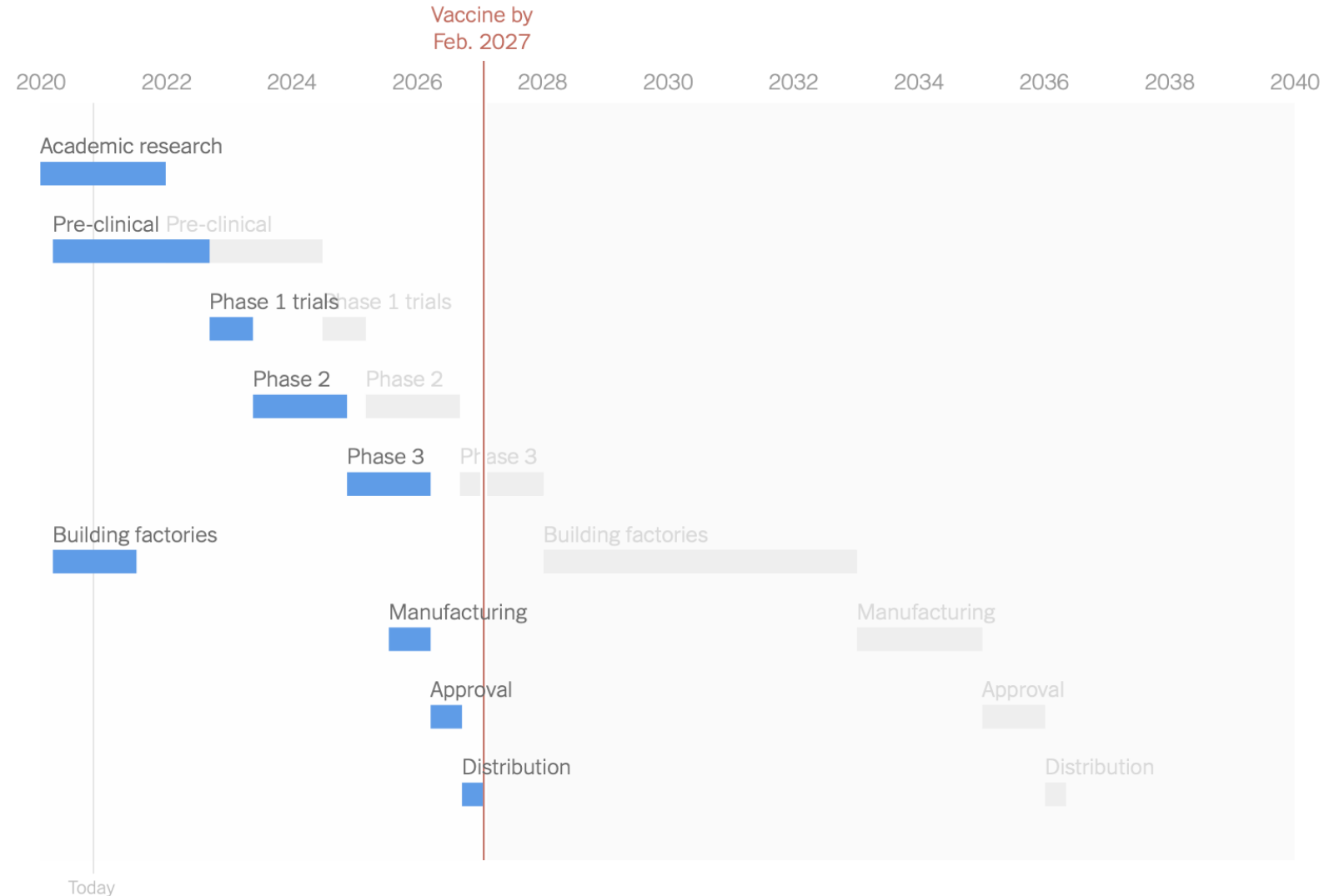
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Don't wait for academic research

- Skip to clinical phases using what we know about the coronavirus so far

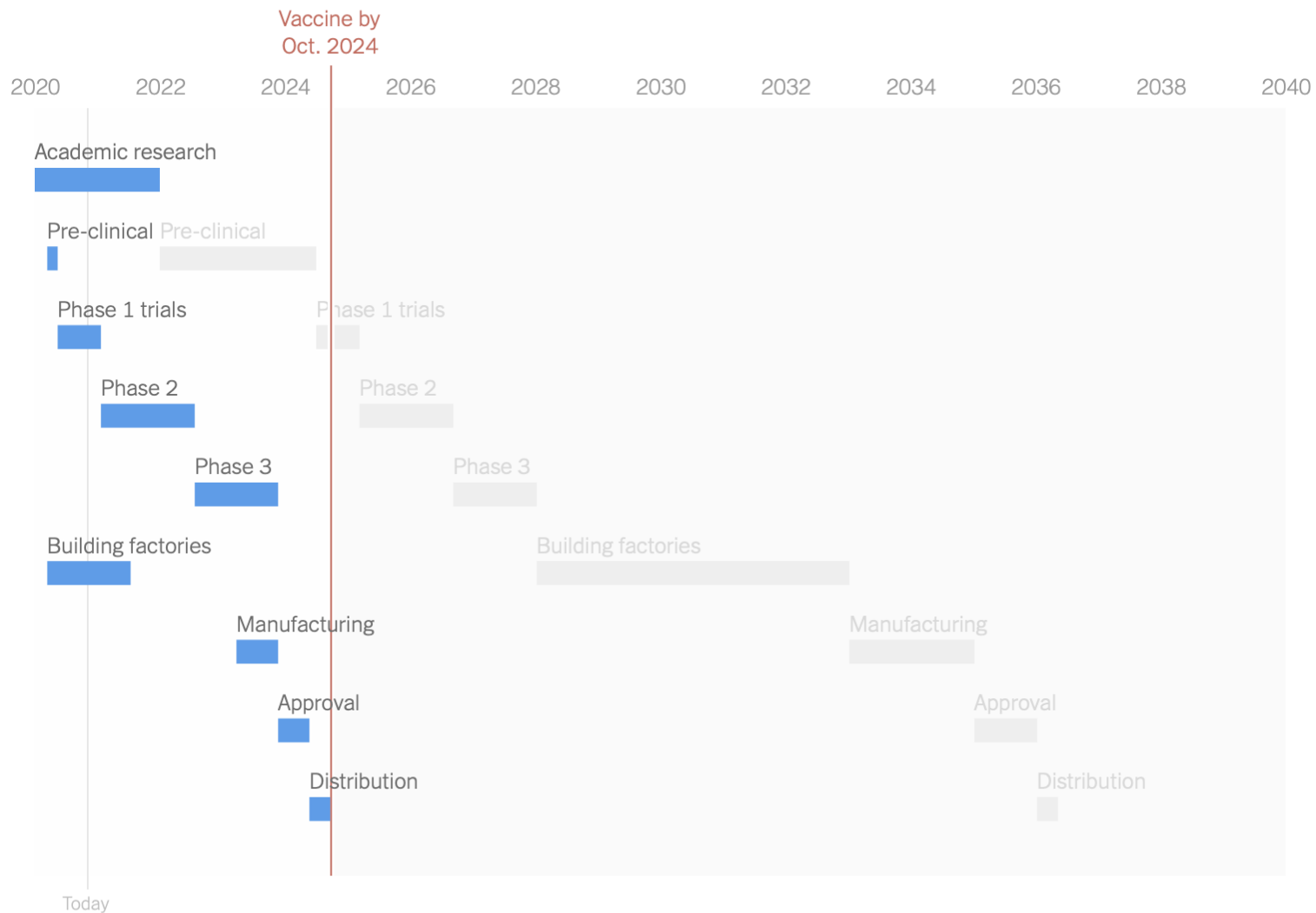
Start trials early

- Rely on work from studying SARS and MERS to shorten preparations before clinical trials



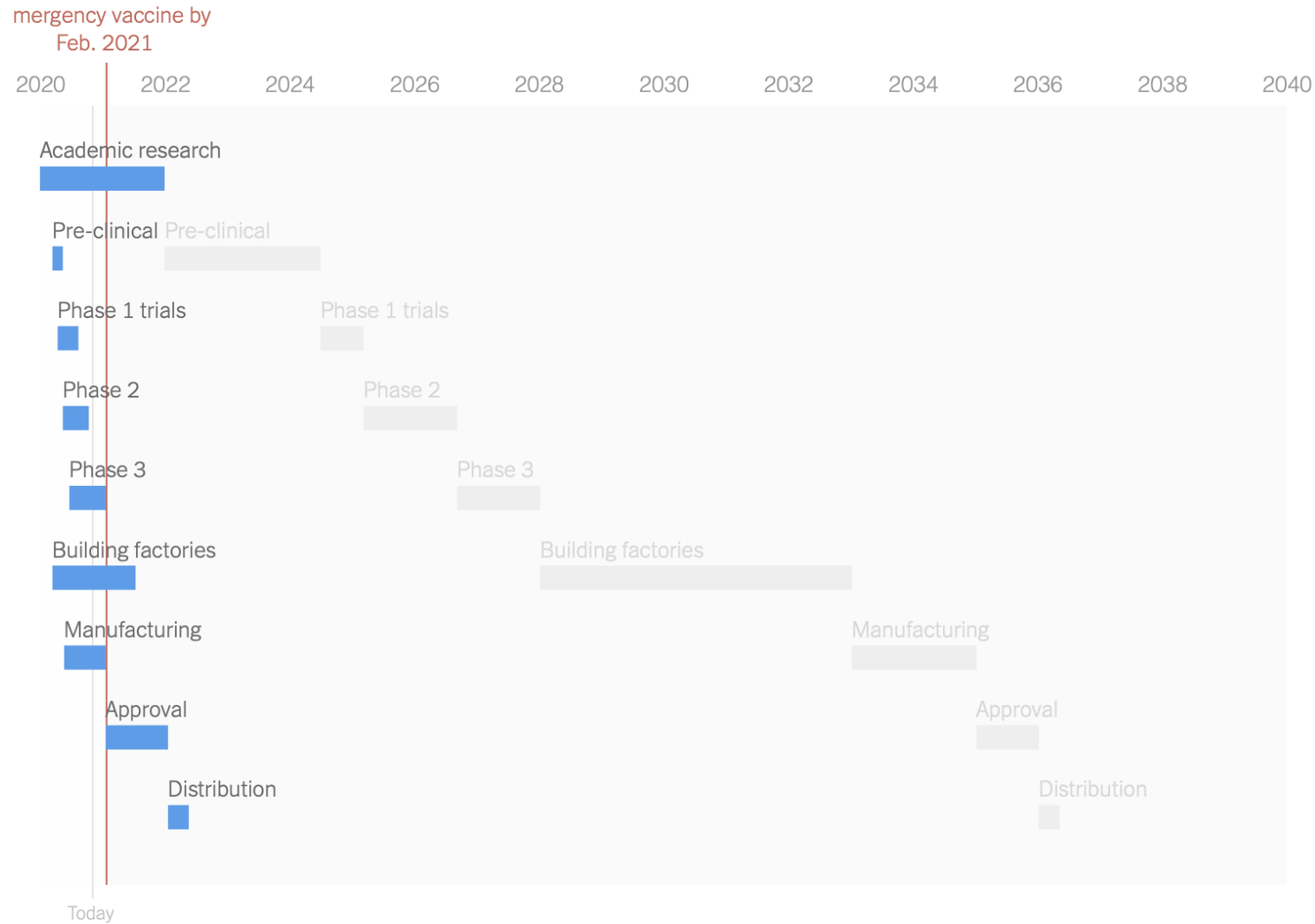
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Move at 'Pandemic Speed' Through Trials



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Start Preparing Factories Now



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The Bill and Melinda Gates Foundation says it will build factories for seven different vaccines

“Even though we’ll end up picking at most two of them, we’re going to fund factories for all seven, just so that we don’t waste time”



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A personal take on science and society

World view

Don't rush to deploy
COVID-19 vaccines and drugs



By Shibo Jiang

**Safety testing must be paramount in measures
to tackle the new coronavirus.**

“
**It is
important
not to cut
corners.”**



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VIEWPOINT

Finding Effective Treatments for COVID-19

Scientific Integrity and Public Confidence in a Time of Crisis

Jesse L. Goodman, MD, MPH
Georgetown University,
Washington, DC.

Luciana Borio, MD
In-Q-Tel, Arlington
County, Virginia.

As learned from the Ebola outbreak,
mortality can be reduced through
identifying best practices.



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EDITORIAL · 11 FEBRUARY 2020

As coronavirus spreads, the time to think about the next epidemic is now



Philanthropist Bill Gates (left) has pledged \$100 million for coronavirus-response efforts. Tedros Adhanom Ghebreyesus (right), director-general of the World Health Organization, is calling for urgent support to bolster weak health systems. Credit: Mustafa Yalcin/Anadolu Agency/Getty



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Virginia Caccialanza

Aliana Chitani

MACH

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Mario Raviglione



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Ospedale Maggiore Policlinico

Sistema Socio Sanitario



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Lombardia



UNIVERSITÀ DEGLI STUDI DI MILANO
DIPARTIMENTO DI FISIOPATOLOGIA
MEDICO-CHIRURGICA E DEI TRAPIANTI



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