COVID-19 pandemic

AN UPDATE

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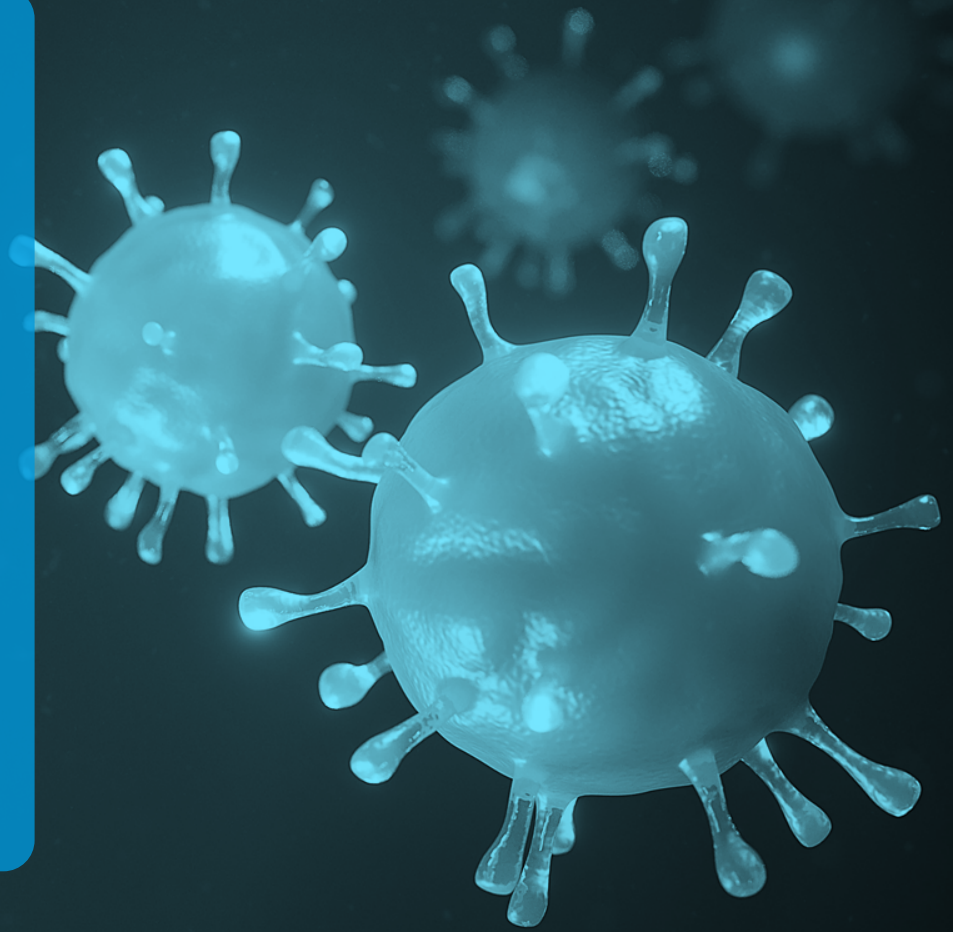
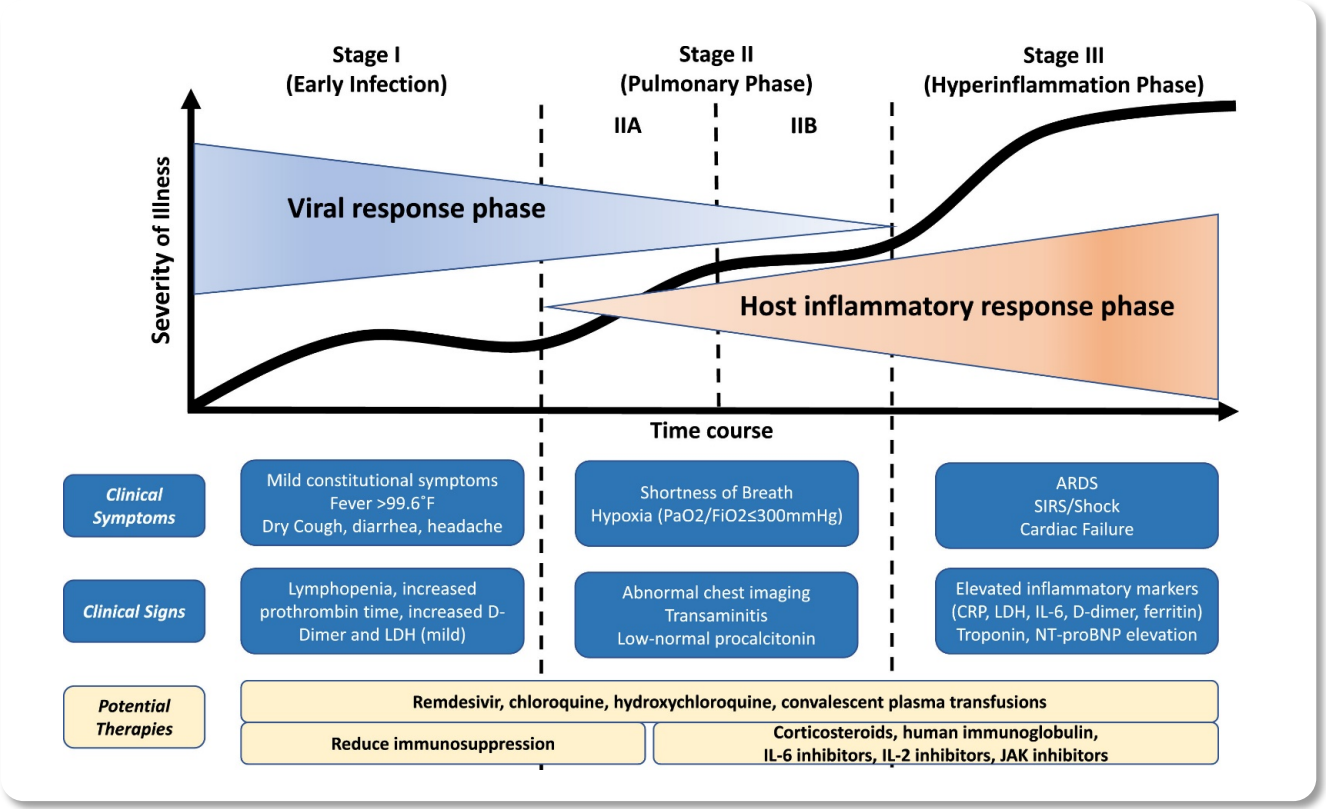


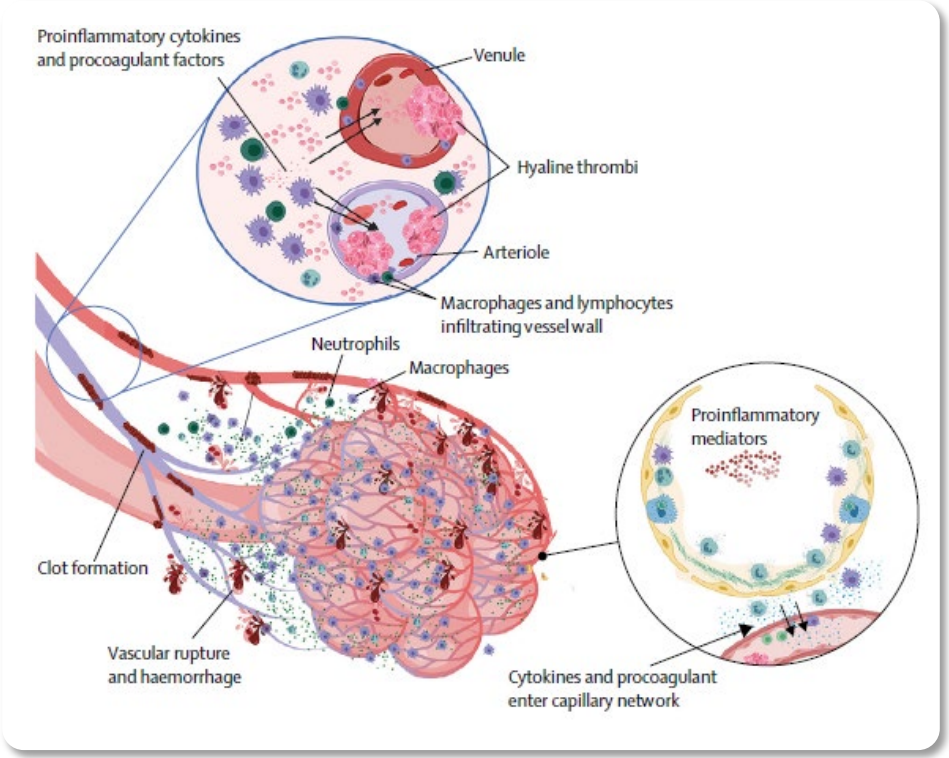
Therapeutic approaches



Siddiqi, *J Heart Lung Transpl* 2020

Therapeutic approaches

THE ROLE OF PULMONARY INTRAVASCULAR COAGULOPATHY IN COVID-19 PNEUMONIA



Source: *McGonagle, et al, Lancet Rheumatol 2020*

therapeutics

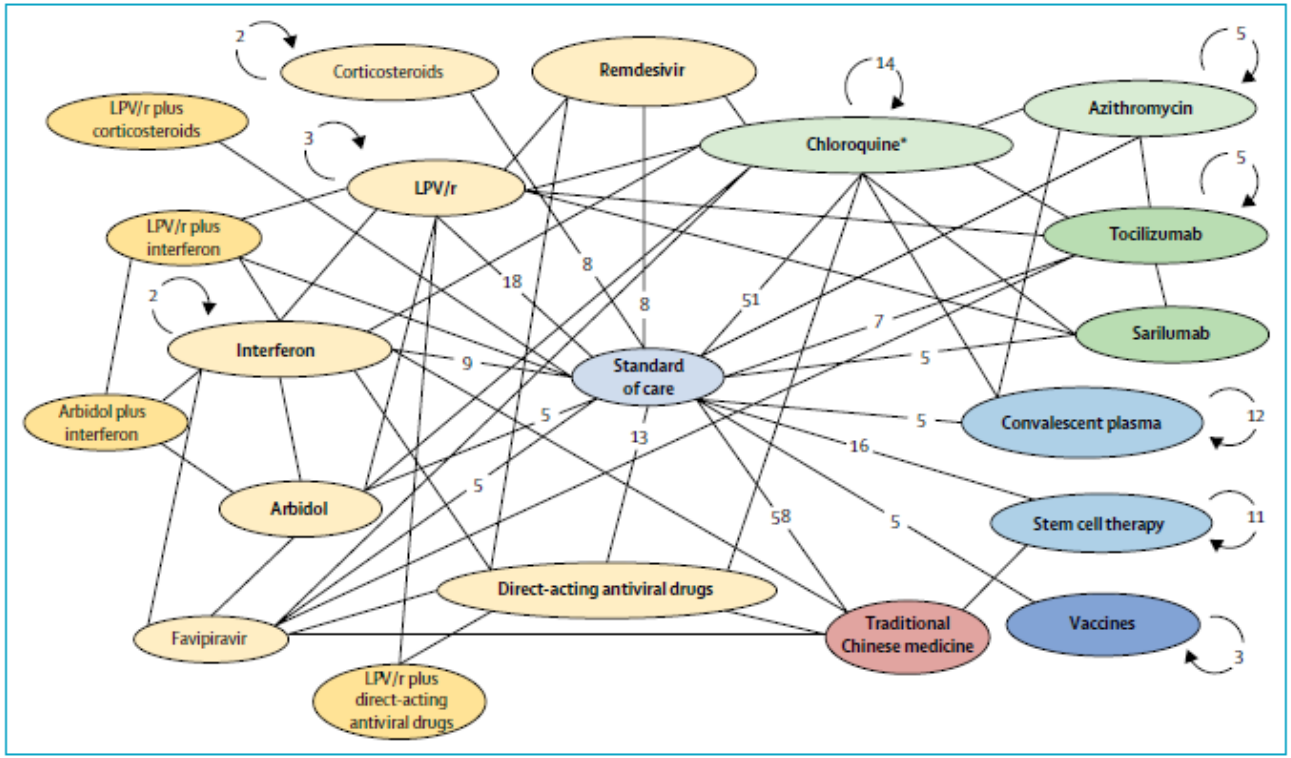


Figure: **Evidence network of COVID-19 clinical trials of top 15 interventions**
Circles (node) represent interventions or intervention groups (categories). Lines between two circles indicate comparisons in clinical trials. The numbers on the lines are the number of clinical trials making the specific comparison. Circular arrows and numbers indicate the number of non-comparative clinical trials in which that intervention is included. A few trials examining combination therapies are excluded from the figure due to space limitations. COVID-19=coronavirus disease 2019. LPV/r (lopinivir-ritonavir). *Includes trials on hydroxychloroquine and chloroquine.

Thorlund et al, Lancet 2020

ONGOING LARGE CLINICAL TRIALS

DISCOVERY: 750 patients have been included where most patients are from France, and one has been enrolled in Luxemburg. Are currently working on including additional patients from Germany and Portugal. DSMB looked at the results from the first 600 patients enrolled in the study.

SOLIDARITY: WHO's trial investigating safety and efficacy of different SARS-CoV-2 therapies. Due to the increased focus on toxicity of hydroxychloroquine, many have refrained from participating. More than 2500 patients enrolled globally.

RECOVERY: 10,000 patients have been enrolled with two levels of randomization in the UK. Work is ongoing as planned, and this study conducts a weekly follow-up to monitor progress.

Source: *McGonagle, et al, Lancet Rheumatol 2020*

- **EU "ERAvsCORONA" ACTION PLAN:**

  Action on "Extending and supporting large EU wide clinical trials for clinical management of COVID-19 patients", aiming at gathering additional funding to extend and support the implementation of large-scale, multi-centric clinical trials across Europe.

- It is essential to avoid fragmentation of study initiatives: studies need to enrol a sufficient number of patients, and use standardised and agreed upon protocols to reach robust results on safety and efficacy of treatments.

- Political, ethical, administrative, regulatory and logistical (PEARL) hurdles that may hamper the rapid implementation or adaptation of clinical trials need to be overcome.

- The innovative concept of a " EU network for Adaptive Platform Trials" is proposed as an answer to these challenges.

Remdesivir: First Antiviral to show efficacy

NIH Clinical Trial Shows Remdesivir Accelerates Recovery from Advanced COVID-19

April 29, 2020

Hospitalized patients with advanced COVID-19 and lung involvement who received remdesivir recovered faster than similar patients who received placebo, according to a preliminary data analysis from a randomized, controlled trial involving 1063 patients, which began on February 21. The trial (known as the Adaptive COVID-19 Treatment Trial, or ACTT), sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, is the first clinical trial launched in the United States to evaluate an experimental treatment for COVID-19.

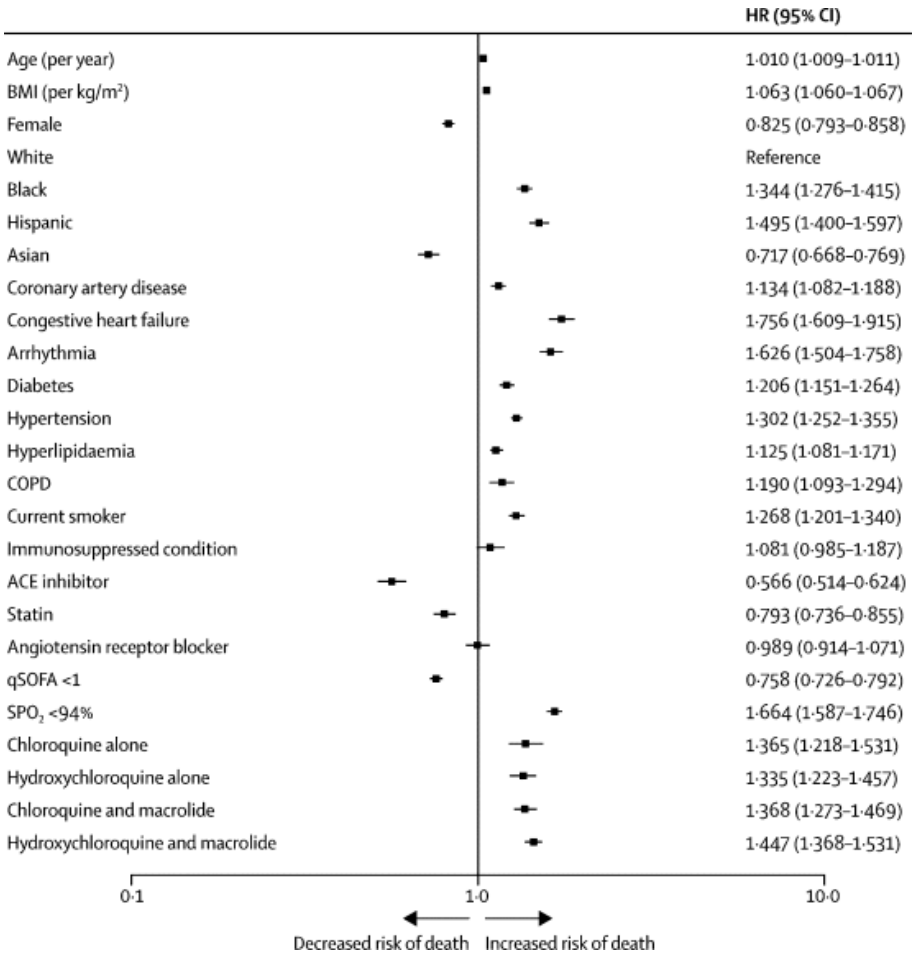
An independent data and safety monitoring board (DSMB) overseeing the trial met on April 27 to review data and shared their interim analysis with the study team. Based upon their review of the data, they noted that remdesivir was better than placebo from the perspective of the primary endpoint, time to recovery, a metric often used in influenza trials. Recovery in this study was defined as being well enough for hospital discharge or returning to normal activity level.

Preliminary results indicate that patients who received remdesivir had a 31% faster time to recovery than those who received placebo ($p<0.001$). Specifically, the median time to recovery was 11 days for patients treated with remdesivir compared with 15 days for those who received placebo. Results also suggested a survival benefit, with a mortality rate of 8.0% for the group receiving remdesivir versus 11.6% for the placebo group ($p=0.059$).

https://www.nih.gov/news-events/news-releases/nih-clinical-trial-shows-remdesivir-accelerates-recovery-advanced-covid-19

HCQ B/R

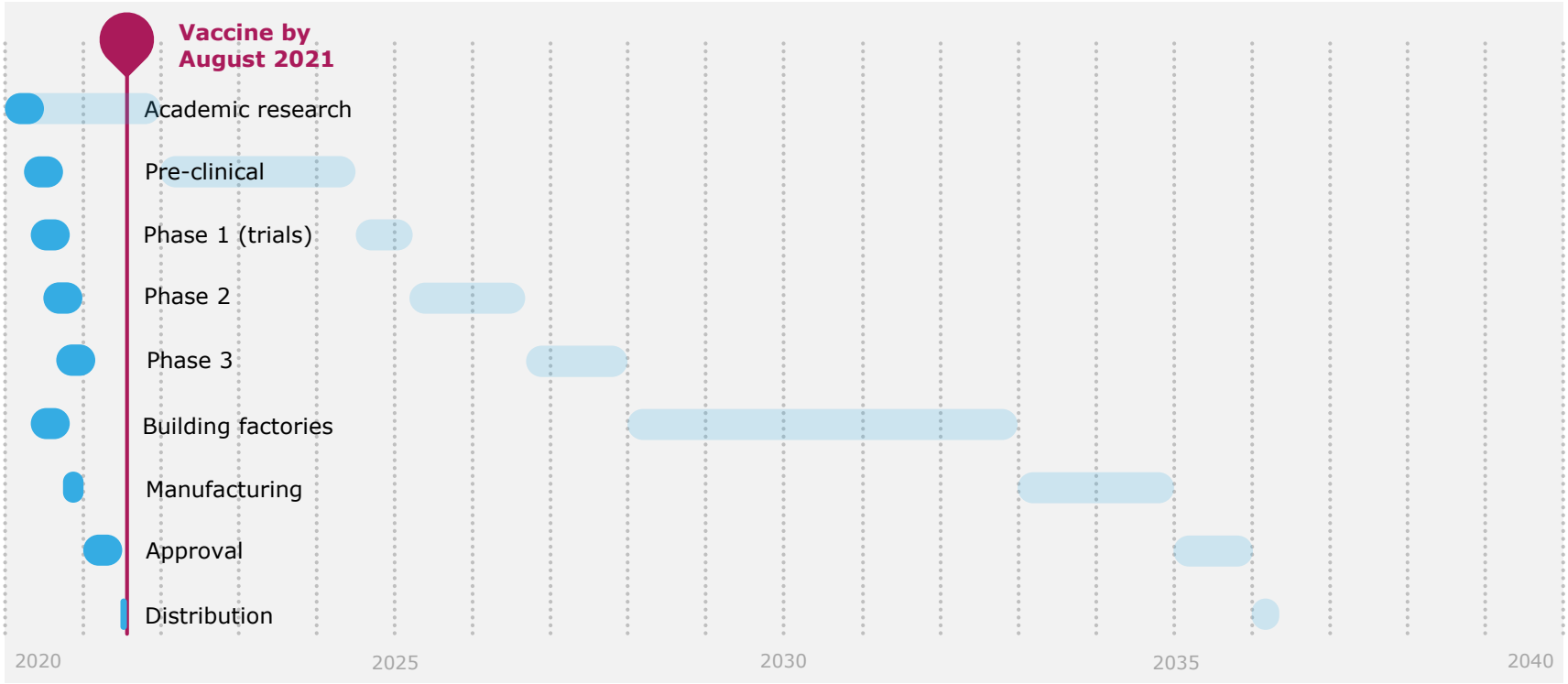
- Lancet publication triggered actions by sponsors of clinical trials and regulatory agencies
- Deleterious impact on ongoing trials for PEP/PrEP with HCQ
- Doubts raised on the quality of the data published on the Lancet https://zenodo.org/record/3864691
- Cochrane review did not identify mortality risk https://www.who.int/who-documents-detail/targeted-update-safety-and-efficacy-of-hydroxychloroquine-or-chloroquine-for-treatment-of-covid-19



Source: *Mehra et al, Lancet 2020*

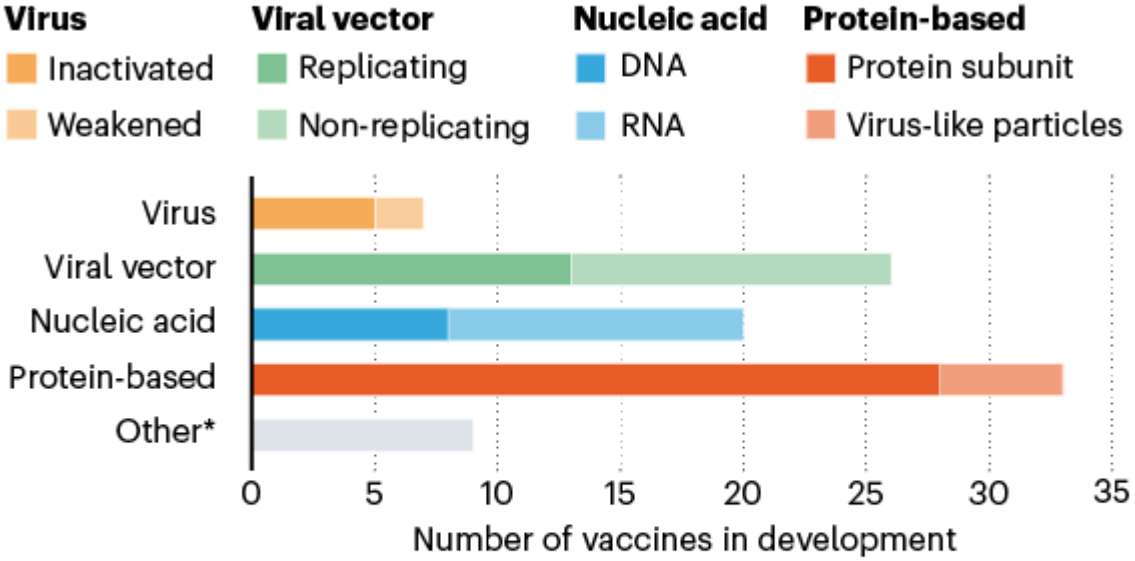
How Long Will a Vaccine Really Take?

DESIRABLE SCENARIO – FROM RESEARCH TO DISTRIBUTION



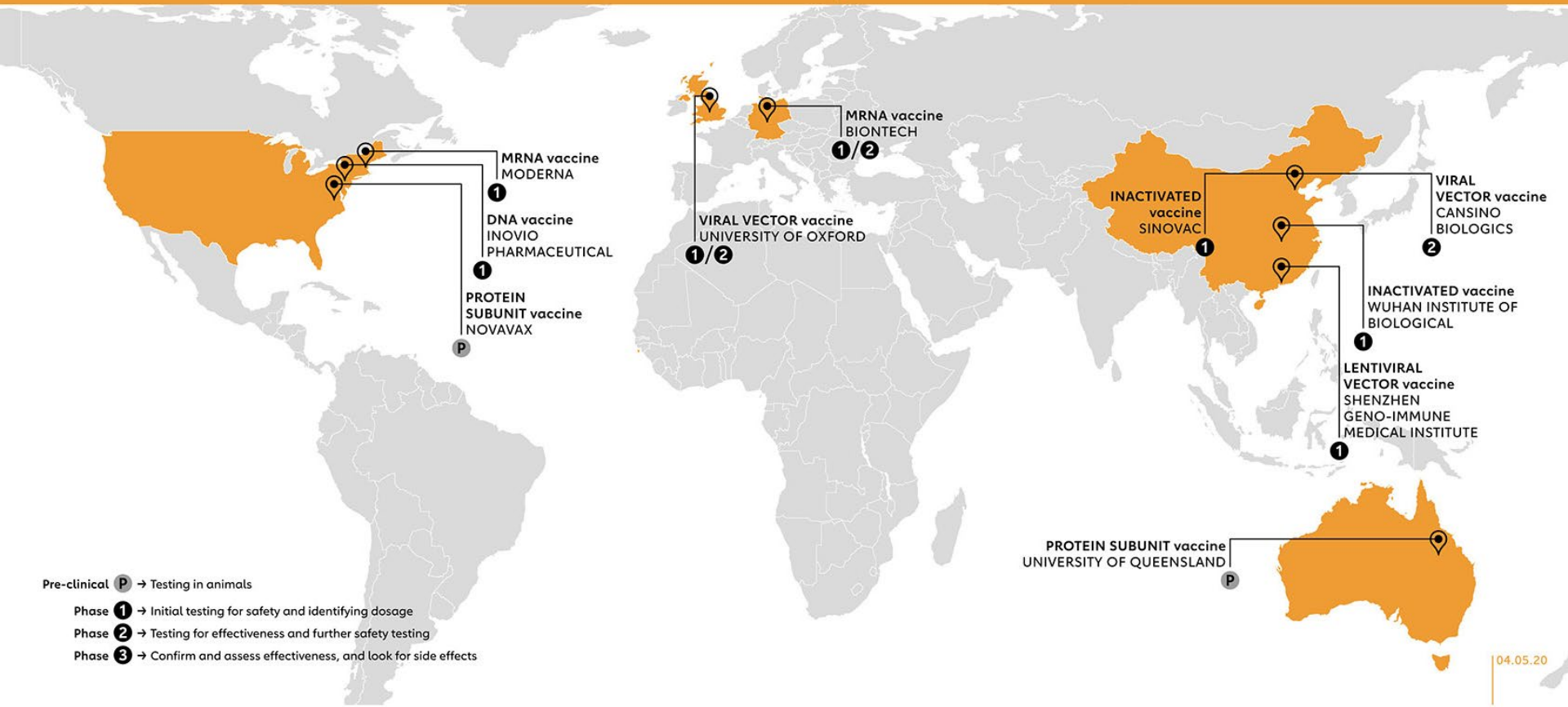
Source: https://www.nytimes.com/interactive/2020/04/30/opinion/coronavirus-covid-vaccine.html

AN ARRAY OF VACCINES



* Other efforts include testing whether existing vaccines against poliovirus or tuberculosis could help to fight SARS-CoV-2 by eliciting a general immune response (rather than specific adaptive immunity), or whether certain immune cells could be genetically modified to target the virus.

COVID-19 vaccines in development around the world



Source: https://www.gavi.org/sites/default/files/maps/Corona-Vaccine-race-01_h1.jpg

An international randomised trial of candidate vaccines against COVID-19
19 April 2020

R&DBlueprint
Powering research to prevent epidemics

The trial will individually randomize very large numbers of adult participants in many different populations. Each participant will be contacted weekly for information as to whether any potentially relevant symptoms have arisen, with laboratory testing triggered if the report suggests COVID-19. By using a shared placebo/control group and a common Core protocol to evaluate multiple candidate vaccines in the trial, resources allocated to the evaluation of each candidate vaccine are judiciously saved while a high standard of scientific rigor and efficiency is ensured.

The primary objective is to evaluate the effect of each vaccine on the rate of virologically confirmed COVID-19 disease, regardless of severity

Vaccines production

This is the Achilles' heel of the vaccine problem, no one has the capacity to meet global demand. Building new factories takes years, existing capacities need to be maximised to respond this crisis. Manufacturing platforms not interchangeable across different technologies.

MERCK

"We are tasked with creating a new vaccine in a 10th of the time and must manufacture at 1,000 times the scale"

SANOFI

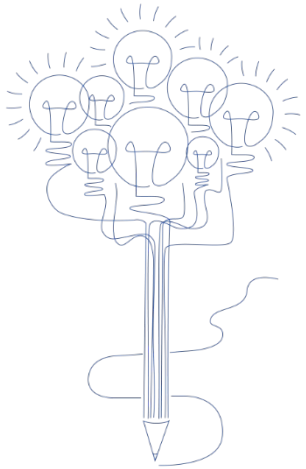
"There is less concern about finding a successful vaccine than there is about making the volumes needed […] The biggest untold story in Europe right now is the one about number of doses, not number of vaccines."

ARCTURUS therapeutics

" It is the greatest demand for a pharmaceutical product ever, way more demand than the iPhone ."

Source: EC

Summary of activities



115 therapeutics in discussion with EMA

33 vaccines identified for interaction

Rapid scientific advice proceeding for advanced vaccines and therapeutics

Remdesivir ongoing discussion at ETF, CHMP and PDCO – no centralised Emergency Use Authorisation in the EU

Chloroquine/hydroxychloroquine continuous B/R evaluation using EMA internal competences and in cooperation with ETF, PRAC and CHMP

Intense international and EU collaboration: EC, ICMRA, WHO, FDA

Any questions?

Further information

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