hearing

COVID-19 and Hearing Implants

Vaccination

Status Report

(Dec 12, 2020 – Feb 15, 2021)

Yi Ge, MD.

Table of Contents

Vaccination / Treatment

[Vaccine Development Progress]

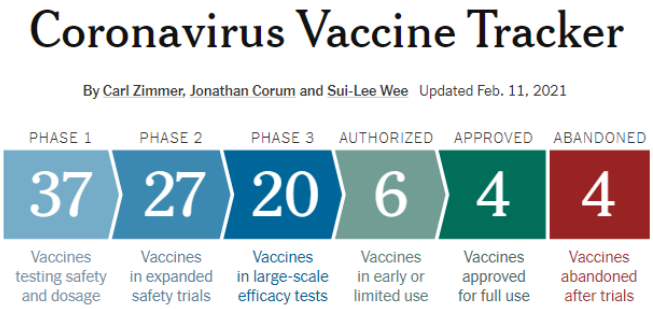

Figure 4: Coronavirus vaccine development status as of Feb 11

Leading vaccines

Developer	How It Works	Phase	Status
Pfizer-BioNTech	mRNA	2 3	Approved in several countries. Emergency use in U.S., E.U., other countries.
Moderna	mRNA	3	Approved in Switzerland. Emergency use in U.S., U.K., E.U., others.
Gamaleya	Ad26, Ad5	3	Early use in Russia. Emergency use in other countries.
Oxford-AstraZeneca	ChAdOx1	2 3	Emergency use in U.K., E.U., other countries.
CanSino	Ad5	3	Limited use in China.
Johnson & Johnson	Ad26	3	
Vector Institute	Protein	3	Early use in Russia.
Novavax	Protein	3	
Sinopharm	Inactivated	3	Approved in China, U.A.E., Bahrain. Emergency use in Egypt, other coutries.
Sinovac	Inactivated	3	Approved in China. Emergency use in Brazil, other countries.
Sinopharm-Wuhan	Inactivated	3	Limited use in China, U.A.E.
Bharat Biotech	Inactivated	3	Emergency use in India.

Figure 5: Development status of the leading vaccines, as of Feb 11

- As of February 12, 2021, EMA has given conditional approval to 3 vaccines:
  - BioNTech and Pfizer – Comirnaty® (vaccine efficacy 94.6%) on 21 December 2020, and
  - Moderna – COVID-19 Vaccine Moderna (vaccine efficacy 94.1%) on 6 January 2021, and
  - AstraZeneca - COVID-19 Vaccine AstraZeneca (vaccine efficacy around 60%) on 29 January 2021.

  And 3 more vaccines under "rolling review":
  - Janssen-Cilag International/ Johnson & Johnson N.V COVID-19 Ad26.COV2.S vaccine, a single-dose recombinant vector vaccine that uses a human adenovirus to express the SARS-CoV-2 spike protein in cells. On January 29, 2021 Johnson & Johnson announced efficacy and safety data from the phase 3 ENSEMBLE clinical trial, demonstrating that Janssen's COVID-19 vaccine candidate was 66% effective overall in preventing moderate to severe COVID-19, 28 days after vaccination. The onset of protection was observed as early as day 14. The level of protection against moderate to severe COVID-19 infection

was 72% in the United States, 66% in Latin America and 57% in South Africa. The vaccine candidate was 85% effective in preventing severe disease across all regions studied in all adults 18 years and older. The Janssen COVID-19 vaccine candidate demonstrated complete protection against COVID-related hospitalization and death, 28 days post-vaccination. Protection was generally consistent across race, age groups, including adults over 60 years of age (N= 13,610), and across all variants and regions studied, including South Africa where nearly all cases of COVID-19 (95%) were due to infection with a SARS-CoV-2 variant from the B.1.351 lineage.

- NVX-CoV2373, a COVID-19 vaccine being developed by Novavax CZ AS (a subsidiary of Novavax, Inc.) and sponsored by CEPI is a recombinant protein nanoparticle technology platform that is to generate antigens derived from the Spike protein. On January 28, 2021 Novavax, Inc. announced that NVX-CoV2373, its protein-based COVID-19 vaccine candidate, met the primary endpoint, with a vaccine efficacy of 89.3%, in its phase 3 clinical trial conducted in the United Kingdom. Novavax also announced successful results of its phase 2b study conducted in South Africa in which approximately 90% of COVID-19 cases attributed to South Africa escape variant: 60% efficacy for the prevention of mild, moderate and severe COVID-19 disease was observed.
- CVnCoV, a COVID-19 vaccine being developed by CureVac AG, is a protaminecomplexed mRNA-based vaccine expressing undisclosed SARS-CoV-2 protein(s). The preliminary results fromm Phase I study showed that two doses of CVnCoV, administerd 28 days apart were safe. No other data available so far.

All of these six vaccines are investigated in phase 3 RCTs and contracted for EU. Besides, the 7th contracted vaccine is from Sanofi-GSK (Protein Subunit vaccine, with adjuvant 1 vaccine), in phase ½.

- On February 5, 2021 EMA released its first safety update on a COVID-19 vaccine — Moderna, a vaccine produced by Moderna Biotech Spain, S.L. This update presents the assessment of an investigation of reports of suspected severe allergic reaction coming from a single vaccination site in the United States. The assessment of these reports has not identified new aspects regarding the nature of this known side effect. The benefits of COVID-19 Vaccine Moderna in preventing COVID-19 continue to outweigh any risks, and there are no recommended changes regarding the use of the vaccine. On February 10, 2021 EMA stated that it is developing guidance for manufacturers planning changes to the existing COVID-19 vaccines to tackle the new virus variants. In order to consider options for additional testing and development of vaccines that are effective against new virus mutations, the Agency has requested all vaccine developers to investigate if their vaccine can offer protection against any new variants, e.g., those identified in the United Kingdom - variant called B.1.1.7, South Africa - B.1.351 and Brazil - variant called P.1, and submit relevant data.
- Russia's Sputnik V vaccine (Viral Vector Vaccines: based on 20 cases of Covid-19 among the trial participants, Russian scientists estimated that the Sputnik V vaccine demonstrated 92% efficacy. On Feb. 12, the director of the Gameleya center said in a television interview that it would likely provide only four to five months of protection.
- Current worldwide vaccination status (Figure 6):

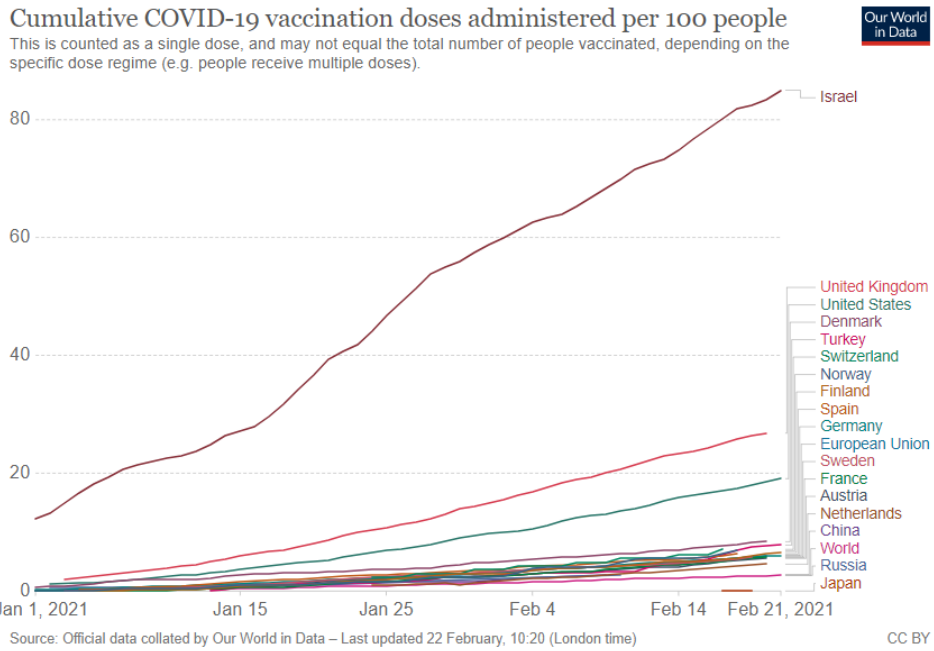

Figure 6: Cumulative vaccination data from Ourworldindata, as of Feb 21

Other relevant information

- The real-world data from Israel suggested that the Pfizer-BioNTech vaccine is between 66%-85% effective at preventing infection and 87%-96% effective for preventing severe disease, a week after the second dose.
- Elisabeth reported (Elisabeth Mahase Feb 4, BMJ) based on Israel vaccination experience, that a single dose of the Pfizer vaccine was 51% effective 13-24 days post vaccination. Meanwhile, researchers from the University of East Anglia reanalysed the same data and said that efficacy was "pretty much zero at day 14, but then rose to about 90% at day 21 before levelling off.
- Who to get vaccines first? Kate M's team used a mathematical model to compare five age-stratified prioritization strategies. They found that in most scenarios, giving the jabs to people older than 60 before those in other age groups saved the greatest number of lives. But to prevent as many people as possible from getting infected, countries should prioritize younger age groups, according to the analysis.
- When many rumors around, it is important to see some fact check:
    - (fact check) Vaccines did not cause COVID-19 outbreak in New York nursing home
    - (fact check) Clarifying claims around Pfizer vaccine deaths and side effects

Treatment

This living systematic review by Siemieniuk and colleagues (BMJ 2020;370:m2980) was first published on July 30 2020. The effects of current treatment are summarized in the table below:

	Mortality	Mechanical ventilation	Adverse events	Admission to hospital	Viral clearance at 7 days	Duration of hospital stay	ICU length of stay	Duration of mechanical ventilation	Time to symptom resolution	Time to viral clearance	Ventilator free days
Standard care*	130 per 1000	116 per 1000	15 per 1000	43 per 1000	484 per 1000	13 days	13 days	15 days	11 days	10 days	11 days
Azithromycin	6 (-40 to 62)	1 (-60 to 90)				0.4 (-2.9 to 3.9)					-1.7 (-5.1 to 1.8)
Colchicine	-106 (-129 to 42)					-1.6 (-2.8 to -0.3)**					
Corticosteroids	-17 (-34 to 1)	-29 (-54 to 1)			5 (-426 to 458)	-0.9 (-3.4 to 1.7)	-3.8 (-5.9 to -1.8)	-1.4 (-3.4 to 0.62)			2.6 (0.2 to 5.0)
Favipiravir	63 (-113 to 773)				81 (-301 to 399)						
Hydroxy-chloroquine	11 (-11 to 38)	20 (-18 to 76)	16 (-11 to 192)**	-26 (-38 to 12)**	18 (-293 to 334)	0.1 (-1.9 to 2.0)			-2.0 (-4.0 to 0.1)	-0.7 (-4.3 to 4.8)**	
Hydroxy-chloroquine + azithromycin	-48 (-103 to 66)	58 (-32 to 216)				0.6 (-1.2 to 2.4)**					
Interferon beta	2 (-35 to 35)	-13 (-60 to 45)									
Interferon gamma					436 (-215 to 516)						
Interferon kappa+ treefoil factor 2					290 (-334 to 503)						
Lopinavir-ritonavir	-12 (-31 to 10)	10 (-31 to 60)			-235 (-449 to 164)	-0.4 (-1.7 to 0.6)**			-1.0 (-4.1 to 3.2)		
Nitazoxanide											
rhG-CSF	-102 (-124 to -41)	-96 (-108 to -68)				-0.7 (-2.3 to 1.0)**			-0.8 (-4.5 to 4.6)		
Remdesivir	-12 (-35 to 14)	-33 (-65 to 1)	0 (-9 to 40)		14 (-429 to 460)	-0.2 (-1.9 to 1.2)**		-1.3 (-4.1 to 1.5)	-2.0 (-4.2 to 0.9)		
Tocilizumab	5 (-46 to 81)	-35 (-80 to 54)	-8 (-15 to 300)**			-2.5 (-6.9 to 1.8)	-4.5 (-13.8 to 4.9)		-1.8 (-5.0 to 3.4)		4.7 (-4.2 to 13.9)
Umifenovir	-130 (-130 to 870)										

*The expected risk of each outcome with standard care is reported in the grey row. Numbers in the coloured cells are the estimated risk differences (95% CI) per 1000 patients or mean difference (95% CI) in days when compared to standard care
** The best estimate of effect was obtained from direct evidence
Empty cells: there was no evidence for the specific intervention
rSG-CSF: Recombinant human granulocyte colony-stimulating factor

Figure 7: Summary on current treatment