

COVID-19, HI and the Vaccines

Update July 1, 2021

Chearing



C Literature Updates

- COVID-19 and Inner Ear
- HI in the pandemic

COVID-19 and Inner Ear

- Tinnitus surge since the start of the pandemic was <u>reported by British Tinnitus Association</u>.
 o recognized as a common symptom of COVID and LongCOVID by NIH
- <u>Professor Kevin Munro and PhD researcher Ibrahim Almufarrij</u> found 56 studies that identified an association between COVID-19 and auditory and vestibular problems. The pooled estimate of prevalence based primarily on retrospective recall of symptoms, was 7.6%, 14.8%, and 7.2%, for hearing loss, tinnitus and rotatory vertigo, respectively.

• these could be an over-estimate because the data primarily used self-reported questionnaires or medical records rather than hearing tests.

- Delta variant may cause hearing and balance issues especially in patients who already have tinnitus, according to <u>a study</u> led by Professor Colleen Le Prell from the University of Texas.
- <u>Incidence of sudden SNHL</u> occurring after COVID-19 vaccination does not exceed that of the general poluation



- <u>Prof H Monhammed</u> from UK reported reduced number of chldren who need AUD evaluation, with more delays on appointment. However,
 - The rate of failure to attend CI assessment was dropped (31.5% \rightarrow 0)
 - Average time from CI decision to surgery reduced (6.25 \rightarrow 3.9 weeks)
 - NONE of the 11 children undergone CI in pandemic developed COVID symptoms.
- Reduced performance on speech test in school-aged CI users was reported by <u>Karen</u> <u>A etc</u> from Ontario.
- Reduced speech recognition (CI) with "N95+face shield" reported by <u>Teresa G</u>.
 - No difference detected between uncovered and N95 mask

Share of people who received at least one dose of COVID-19 vaccine

Vaccine



Share of the total population that received at least one vaccine dose. This may not equal the share that are fully vaccinated if the vaccine requires two doses. This data is only available for countries which report the breakdown of doses administered by first and second doses.



23.4% of the world population has received at least one dose of a COVID-19 vaccine.3.04 billion doses have been administered globally, and 41.06 million are now administered each day.



- <u>A study</u> in more than 25,000 health-care workers in the UK found that a nature infection reduced the risk of catching the virus again by 84% for at least 7 months
 - vaccine-induced immunity will not be as durable as immunity from natural infection
 - a booster to be needed in about 8–12 months after the second dose of the Pfizer-BioNTech vaccine.
- Long term data source:
 - o Safety reports per regulatory requirement
 - o Ongoing studies
 - New studies (survey etc..)
 - o Real world data
 - o Modelling



Data background

•Israel data collected between January 17 and March 6, 2021 (B.1.1.7 is in place)

•Danish data 39040 residents vaccinated between Dec 27 – Feb 18

Effectiveness at a week after the second dose.

•(Israel) between 66%-85% effective at preventing infection and 87%-96% effective for preventing severe disease

•(Denmark) 64% effective in long-term-care residents with a median age of 84, and 90% effective in health-care workers

Pfizer news

97% effectiveness against symptomatic COVID-19 cases, hospitalizations, severe and critical hospitalizations94% effectiveness against asymptomatic SARS-CoV-2 infections

Reference

• https://www.pfizer.com/news/press-release/press-release-detail/real-world-evidence-confirms-high-effectiveness-pfizer

https://www.medrxiv.org/content/10.1101/2021.03.08.21252200v1



tudy design

• 3,975 participants completed weekly SARS-CoV-2 testing for 17 consecutive weeks (from December 13, 2020 to April 10, 2021) in eight U.S. locations.

Pfizer and Moderna vaccines were 91% effective

- After partial vaccination, participants' risk of infection was reduced by 81 %.
- 60% lower risk of developing symptoms
- more likely to have a milder and shorter illness
- fully or partially vaccinated study participants had 40 percent less detectable virus in their nose (i.e., a lower viral load), and
- the virus was detected for six fewer days (i.e., viral shedding)

Reference

<u>https://www.cdc.gov/media/releases/2021/p0607-mrna-reduce-risks.html</u>



Real world data from Scottland

- 5.4 million people vaccinated with Pfizer and AstraZeneca
- The first dose of the BNT162b2 vaccine was associated with a vaccine effect of **85%** (95% confidence interval [CI] 76 to 91) for COVID-19 related hospitalisation at 28-34 days post-vaccination
- Vaccine effect at the same time interval for the ChAdOx1 vaccine was 94% (95% CI 73 to 99).

Safety

• ANSM (France) confirms a risk of rare thrombosis associated with AstraZeneca

Reference

- <u>https://www.astrazeneca.com/media-centre/articles/2021/first-real-world-study-of-covid-19-vaccine-astrazeneca-demonstrates-94-reduction-in-hospitalisations.html</u>
- https://www.ed.ac.uk/files/atoms/files/scotland_firstvaccinedata_preprint.pdf



lovavax

- estimated efficacy of 89.3% in phase 3 trial UK and
- 60% efficacy for the prevention of mild, moderate and severe COVID-19 disease in South Africa.

Iohnson & Johnson

- phase 3 trial shows **66%** effective overall in **preventing moderate to severe** COVID-19, 28 days after vaccination.
- 72% in the United States, 66% in Latin America and 57% in South Africa.

Russia's Sputnik V

- estimated 92% efficacy
- On Feb. 12, the director of the Gameleya center said that it would likely provide only **four to five months** of protection.

Developers	ers Vaccine / Vaccine type		Clinical Efficacy against Beta (B.1.351) (South Africa) / Neutralisation	Clinical Efficacy against Gamma (P.1) (Brazil) / Neutralisation	Clinical Efficacy against Delta (B.1.617.2) (India) / Neutralisation
Vaccines contracted or exploratory talks have concluded for EU					
Moderna + National Institute of Allergy and Infectious Diseases (NIAID)	COVID-19 Vaccine Moderna (mRNA -1273) / m RNA	Not yet available Decrease by 1.8x	Not yet available Decrease by ≤8.6x	Not yet available Decrease by 4.5x	Not yet available
AstraZeneca + University of Oxford	COVID-19 Vaccine AstraZeneca (ChAdOx1-S - (AZD1222) / Viral vector (Non-replicating)	70.4% against symptomatic COVID-19 Decrease by9x	10.4% against symptomatic COVID-19 Decrease by ≤86× to complete immune escape	Not yet available Decrease by 2.9x	Real word data: 60% effective at two weeks after the second dose; 33% effective against symptomatic disease three weeks after the first dose
BioNTech + Pfizer	Comirnaty (BNT162b2) / mRNA	Real-word data: 72% (95% CI 58-86) 21 days after first dose and 86% (95% CI 76- 97) seven days after two doses Decrease by 2x	100% in South Africa Decrease by ≤6.5x to 10.3x	Not yet available Decrease by 2.6X, 6.7x to 14x	Real word data: 88% effective, two weeks after the second dose; 33% effective against symptomatic disease three weeks after the first dose
Janssen Pharmaceutical/Johnson&Johnson	COVID-19 Vaccine Janssen (Ad26.COV2.S) / Viral vector (Non- replicating)	Not yet available	57% against moderate to severe COVID-19; 85% against severe COVID- 19 and hospitalisation Not yet available	68.1% against moderate to severe disease Not yet available	Not yet available
CureVac AG	CVnCoV / mRNA	Not yet available	Not yet available (Strong results variant when tested on mice; CureVac would expand a trial in Europe and Latin America to analyse the vaccine's efficacy against select variants)	Not yet available	Not yet available
Sanofi Pasteur + GSK	VAT00002; SARS-CoV-2 vaccine formulation 1 with adjuvant 1 (S protein (baculovirus production) / Protein subunit	Not yet available	Not yet available	Not yet available	Not yet available

Vaccine Effectiveness Against mutated variants



Seasonal Flu Vaccine Effectiveness



Flu Season



For community:

- •70-85% of the population would need to be vaccinated or immune to reach herd immunity
- Medical resource, finance loss, mental health, quality of life etc.. Need to be considered

For individuals:

- Effective to prevent from hospitalization, severe diease or death
- Medical history, lifestyle, possible side effects need to be considered

Mutation and future?

• Possible booster shot in the future

Effectiveness of a booster shot

- Moderna has released <u>preliminary results</u> showing that a booster vaccine using a spike-protein sequence from the B.1.351 variant increased the concentration of antibodies that neutralize SARS-CoV-2, and particularly the B.1.351 variant
- On 19 May, the UK government announced that it had funded a study
 - 7 different COVID-19 vaccines given as boosters at least 10–12 weeks after the second dose of an initial vaccine.
 - Early findings are expected in September
- NIH launched a <u>small trial (May 28)</u>
 - 150 adults, who have received one of the three vaccines. All will be given one dose of the <u>Moderna vaccine</u> 12 to 20 weeks after fully vaccinated.

https://www.nih.gov/news-events/news-releases/nih-clinical-trial-evaluating-mixed-covid-19-vaccine-schedules-begins

https://www.nature.com/articles/d41586-021-01505-x



- EMA granted Pfizer vaccine for 12-15 y on May 28
- No real world data yet
- Clinical trials are currently under way to test the Pfizer, Moderna, Oxfor dAstraZeneca, Jansenn/Johnson&Johns on and Sinovac vaccines in children.
- Pfizer-BioNTech (BNT162b2)<u>study</u>:
 - o 100% effective on 12-15ys of age
 - o 93% effective for 12-17ys of age
 - \circ Study on ≥5 to <12 ys of age just started



Developers	Vaccine / Vaccine type					
Moderna + National Institute of Allergy and Infectious Diseases (NIAID)	COVID-19 Vaccine Moderna (mRNA - 1273) / m RNA	NCT04796896 (KidCOVE) Phase 2/3 RCT in 6,750 children ages 6 months through 11 years in U.S. and Canada				
		Two parts:				
		1. Part 1: open label, dose-escalation, age de-escalation study. 2 yo – up to 12 yo: each participant may receive either 50 µg or 100 µg dose of the vaccine.				
		6 mo – up to 2 yo: each participant may receive either 25 μg, 50 μg, or 100 μg dose.				
		2. Part 2 randomised, observer-blind, placebo-controlled expansion study based on the preliminary evaluation of the Part 1 results. The participants will receive two doses of the vaccine 28 days apart. To evaluate the medicine's safety, tolerability, reactogenicity and effectiveness, the company will observe the participants for 12 months after the second jab.				
		NCT 04649151 (TeenCOVE) Phase 2/3 RCT, to evaluate the safety, reactogenicity, and effectiveness of mRNA-1273 SARS CoV 2 vaccine in 3000 healthy adolescents 12 to <18 years of age in US. See Press Release from 15 May 2021, on results related to primary endpoint below.				
		On June 08, 2021 EMA has started evaluating an application to extend the use of the COVID-19 Vaccine Moderna to include young people aged 12 to 17.				
AstraZeneca + University of Oxford	COVID-19 Vaccine AstraZeneca (ChAdOx1-S - (AZD1222) / Viral vector	Phase 2 RCT in 300 children aged 6-17, in UK Currently has been paused while the EMA investigates the link between the shot and rare blood clots				
BioNTech + Pfizer	Comirnaty (BNT162b2) / mRNA	NCT 04368728 Phase 2/3 RCT in 2200 volunteers ages 12 to 15				
		On March 31, 2021 announced adolescent trials have shown efficacy of 100% in protecting adolescents ages 12-15, with no significant safety concerns. About 2,260 adolescents ages 12-15 years participated in the trial, with roughly half receiving the vaccine and half receiving a placebo. There were 18 cases of COVID-19 reported, all within the placebo group. One month after a second dose, the vaccine elicited SARS-CoV-2-neutralizing antibody geometric mean titers of 1,239.5 in a				



		subset of adolescents, compared to 705.1 in an earlier group of 16- to 25-year-olds, according to the news release. Scientific publication in NEJM [28], see details below.
		On May 10, 2021 FDA authorised Pfizer/BionTech COVID-19 vaccine for emergency use in adolescents 12-15 years old. On May 28, 2021 EMA's CHMP recommended granting an extension of indication for the COVID-19 vaccine Comirnaty to include children aged 12 to 15.
		NCT 04816643. Phase 1/2/3 Study in 4644 children 6 months to 11 years old in US
		Evaluating the safety, tolerability, and immunogenicity of the Pfizer-BioNTech COVID-19 vaccine on a two-dose schedule (approximately 21 days apart) in three age groups: children aged 5 to 11 years, 2 to 5 years, and 6 months to 2 years. The 5 to 11 year-old cohort started dosing last week and the companies plan to initiate the 2 to 5 year-old cohort next week.
		https://www.pfizer.com/news/press-release/press-release-detail/pfizer-biontech-announce-positive-topline-results- pivotal?linkId=114996658
Janssen	COVID-19 Vaccine Janssen	RCT, phase 2a
Pharmaceutical/Johnson&Johnson	(Ad26.COV2.S) / Viral vector	Has begun in April 2021 testing its Covid-19 vaccine in 1700 adolescents aged 12; Initially will be tested in a small number of adolescents aged 16-17 years (following the review of initial data in this phase 2a trial, the study will be expanded to a larger group of younger adolescents in a stepwise approach).
		Currently enrolling participants in Spain and the United Kingdom; enrollment will commence shortly in the United States, the Netherlands and Canada, with Brazil and Argentina to follow
		https://www.wsj.com/articles/j-j-starts-testing-covid-19-vaccine-in-adolescents-11617379165
CureVac AG	CVnCoV / mRNA	Not available
Sanofi Pasteur + GSK	VAT00002; SARS-CoV-2 vaccine formulation 1 with adjuvant 1 (S protein (baculovirus production) / Protein subunit	Not available
Novavax	NVX-CoV2373 / Protein subunit	Pediatric and adolescent arms of the trials expected to initiate later in the second quarter 2021 https://www.marketwatch.com/story/novavax-to-expand-covid-19-vaccine-trials-to-children-teens-2021-04-05
Valneva	VLA2001 / Inactivated virus	Not available
Sinovac Biotech	CoronaVac; SARS-CoV-2 vaccine (inactivated) / Inactivated virus	RCT on 500 children in China ages 3 to 17; preliminary results from phase ½ trials announced safe and could induce immune responses among children and adolescents; The lower dose of the vaccine could induce favourable antibody responses in children aged three to 11 years while the medium dose worked well for those aged 12 to 17 years. https://www.clinicaltrialsarena.com/news/sinovac-vaccine-immune-responses-children/

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Treatment Update



As of June 23, there are 19 recommendations from IDSA:

- Dexamethosone
- Neutralizing antibodies
- Convalescent plasma
- Remdesivir (anti virus)
- Ivermectin (anti parasite)
- Bamlanivimab with etesevimab (monoclonal antibody)
- Tocilizumab (immunosuppressive)

		Setting and severity of illness							
		Ambulatory care: mid-to- mederate disease in the second se							
1	Hydraxy- chloroquine (HCQ)*	NA	Recommend against use ⊕⊕⊕⊖	commend against use 0⊕⊕⊖ 0					
2	HCQ*+ azithromycin	NA	Recommend against use Recommend against use ⊕⊕⊖⊖○ ⊕⊕⊖⊖○		Recommend against use ⊕⊕⊖⊖				
3	Lopinsvir + ritonavir	NA	Recommend against use ⊕⊕⊕⊖	Recommend against use ⊕⊕⊕⊖	Recommend against use ⊕⊕⊕⊖				
46	Corticosteroids	NA	Suggest against use	Suggest use The II dexamethasone is unavailable, equivalent total daily doses of alternative glacocorticoids may be used.**	Recommend use The same set of the same set of				
7	Tooltrumob	MA	NA	Suggest use $\bigoplus \bigoplus \bigcirc \bigcirc$ $\bigoplus \bigoplus \bigcirc \bigcirc$ \bigoplus B Putterns, particularly those who response to steroids avoiding possible adverse exects of frontiannub and a low value on the users tain mostally relative, would reasonably decline torolinumah, ortexine of forolinumah, contening for systems: inflammation was defined as CPP 273 mg/t.	Suggest use $\bigoplus \bigoplus \bigoplus$				
8-9	Convalescent plasma	Recommended only in the context of a clinical trial (knowledge gap)	Suggest against use ⊕⊕⊖⊖	Suggest against use ⊕⊕⊖⊖	Suggest against use ⊕⊕⊖⊖				
10- 12	Remdesivir	NA.	Suggest against rootine use Suggest use ⊕ ⊖ ⊖ ⊖ G drop ⊕ ⊖ Suggest root of the suggest		Routine initiation of remdesivit: Suggest against use ⊕				
13	Famotidine	NA	Suggests against use except in a clinical trial ⊕○○○	Suggests against use except in a clinical trial \oplus \bigcirc \bigcirc \bigcirc	Suggests against use except in a clinical trial ⊕○○○				
14	Bamlaniutmað + éteseinnað <u>OR</u> casinninnab + imdevinnab <u>OR</u> Sotrovinnab	suggest use $\Theta \Theta \Theta \Theta$. Repared to the set of the set of the set of the set of progression to a moderate (COV-2) who are at the high mix of progression to a the set of progression to a set of the set of the set of the set of the COV-2-10 may also reselve the constraints of the set of the set or units. It is the the set of the set of the set of the set of the set of the set of the set of the set of the set of the set of the set of the set of the set of the set of the set of the set of th	NA	NA	на				
15	Bomlenivimab monotherapy	NA	NA	Recommend against use	NA				
16	Baricitinib + Remdesivir	NA	NA	Suggest use ⊕⊕⊕⊖ R: Barrichnib 4 mg por day up to 34 days or until discharge from hospital. R: Barrichinib apprars to demostrate the most benefit in those with severe G2010-19 on high-flow avgen/non- invasive ventilation at baseline.					
17	Banicitinib + remdesivir + corticosteroids	NA.	NA	Suggest use **** ⊕ ⊕ ○ ○ R: Barictimb 4 mg daily dowe for 14 days or multi hospital discharge. The benefits of barictimb plus rendesive for persons on mechanical ventilation are uncertain.	NA.				
18- 19	hermectin	Suggests against use except in a clinical trial \oplus	NA	Suggests against use except in a clinical trial	NA				

Overview of IDSA COVID-19 Treatment Guidelines

Version 4.4.0 - June 22, 2021



https://www.bmj.com/content/370/bmj.m2980

- Corticosteroids
- Cochicine
- IL-6
- JAKi



	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	Ventila free days:
Standard care*	130 per 1000	116 per 1000	9 per 1000	51 per 1000	500 per 1000	13 days	13 days	15 days	11 days	7 days	12 day
ACEI/ARB	-4 (-59 to 83)	-16 (-55 to 44)	8 (-5 to 58)†			-1.9 (-5.7 to 1.8)					
Anakinra		21 (-52 to 155)									
Anticoagulants	-2 (-33 to 34)										
Azithromycin	-4 (-25 to 21)	-6 (-33 to 28)				-0.9 (-1.7 to 0.3)†					-1.2 (-4 to 2.0
Colchicine	-78 (-110 to -9)	-57 (-90 to 3)		-11 (-34 to 42)		-1.7 (-2.8 to -0.7)†					
Corticosteroids	-20 (-36 to -3)	-25 (-44 to -1)			-82 (-269 to 111)	-0.3 (-1.7 to 1.3)		-1.4 (-3.4 to 0.7)			2.6 (0 to 5.0
Doxycycline + ivermectin	-130 (-130 to -123)		34 (-7 to 547)†								
Favipiravir	-41 (-113 to 207)	-14 (-74 to 120)	2 (-7 to 47)†		50 (-96 to 193)	-1.3 (-2.4 to -0.1)†			-4.3 (-5.9 to -2.14)	-0.6 (-3.2 to 4.2)	
Hydroxy- chloroquine	10 (-8 to 30)	15 (-9 to 45)	8 (-1 to 27)†	-10 (-31 to 26)	2 (-93 to 109)	0.1 (-1.8 to 2.0)			-1.5 (-3.0 to 0.2)	-0.9 (-2.9 to 2.1)	-1.4 (-4 to 2.2
Hydroxy- chloroquine + azithromycin	-42 (-96 to 53)	54 (-22 to 174)	9 (-5 to 60)	-1 (-35 to 83)	-35 (-211 to 154)	0.4 (-1.4 to 2.1)†					
IL-6i	-15 (-30 to 6)	-30 (-46 to -10)	-4 (-9 to 67)†			-4.3 (-8.1 to -0.5)†			-0.7 (-2.7 to 1.7)		1.6 (-0 to 3.3
Interferon beta	2 (-34 to 28)	-7(-40 to 32)				-0.4 (-1.9 to 1.0)†			-1.8 (-4.0 to 1.0)		
Interferon gamma					419 (41 to 497)						
Interferon kappa + treefoil factor 2					284 (-54 to 451)						
lvermectin	-103 (-117 to -78)	-54 (-100 to 80)	26 (-2 to 187)	-32 (-47 to 23)	118 (-13 to 241)	-0.5 (-1.7 to 1.1)†			-0.4 (-3.7 to 3.5)	-2.0 (-4.4 to 2.4)	
JAKi	-50 (-84 to 0)	-46 (-74 to -5)				-1.5 (-3.0 to 0.1)†		-3.8 (-7.5 to -0.1)†	-1.0 (-3.8 to 2.8)		
Lopinavir- ritonavir	3 (-17 to 25)	10 (-16 to 41)	46 (9 to 197)	-17 (-39 to 37)	-20 (-165 to 98)	0.7 (-1.1 to 2.7)†			0.1 (-2.5 to 3.5)		
Lopinavir- ritonavir + interferon b1a	62 (-20 to 176)	41 (-17 to 125)	136 (31 to 506)		-93 (-296 to 143)	5.0 (3.7 to 6.3)†			1.2 (-2.8 to 6.9)		
Nitazoxanide			63 (-3 to 725)	0 (-39 to 151)	159 (-97 to 350)						
Peginterferon lambda					206 (-142 to 418)						
Proxalutimide	-130 (-130 to -118)	-116 (-116 to -111)		-50 (-51 to -38)†							
rhG-CSF	-102 (-124 to -43)	-96 (-107 to -76)				-0.7 (-1.8 to 0.5)†			-0.8 (-4.6 to 5.2)		
Remdesivir	-11 (-33 to 12)	-26(-51 to -2)	1 (-6 to 26)		13(-242 to 262)	0.4 (-0.1 to 1.4)†		-1.3 (-4.3 to 1.5)	-2.0 (-4.1 to 0.7)		
Sulodexide	-78 (-119 to 50)	-62 (-105 to 81)	3 (-7 to 65)	-24 (-41 to 20)							
Umifenovir	794 (-130 to 870)										
Vitamin C	-50 (-89 to 22)	17 (-41 to 110)				-1.6 (-3.3 to 1.3)†					
Vitamin D	-11 (-86 to 150)	-63 (-96 to 7)				0 (-1.2 to 1.2)†					

High/moderate certainty Low certainty Very low certainty

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This report is based on facts and data

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