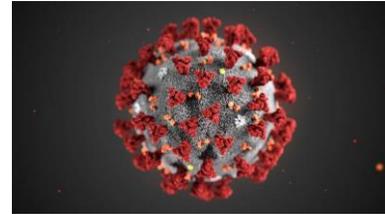


Facts on the Coronavirus

25 May 2021

The Virus

- COVID-19 (SARS-CoV) is one of several coronaviruses: 4 are known to cause the common cold, one was SARS (2004) and the other MERS (2012).
 - SARS is considered contained and MERS is restricted to the Arabian Peninsula; neither have a vaccine.
 - They are far less infectious but more fatal (10-50% fatality rate) than the current COVID-19.
- It's called a coronavirus because of the "crown" of protein spikes on the surface
- All coronaviruses are spread through aerosolization and mucus exposure.
- COVID-19 has been shown to last about 4 days on impermeable surfaces and about 2 days on permeable surfaces.
- The virus is a sack of fat with protein spikes on the outside and messenger RNA (mRNA) on the inside.
 - The virus itself is not alive, but the protein spikes attach to the cell it is infecting via the ACE2 (Angiotensin-Converting Enzyme 2) receptor.
 - The ACE2 receptor is a vasodilator that influences blood flow, making it a poor target for treatment or a vaccine.
 - The ACE2 receptor is found all over the body but is prevalent on lung cells lining air sacs, which is why this virus infection can cause pneumonia.
 - Once the virus attaches to the cell via the protein spike, it injects the mRNA into the cell which takes over cellular genetic reproduction, causing the cell to become a virus factory. Eventually the cell bursts and releases additional virus.
 - Variants have been found on the structure of the protein spike which make the virus more infectious (easier to spread) but not to date more virulent (doesn't cause more or more serious disease).
 - Genetic sequence completed 1/11/2020



Infectivity

- COVID-19 is 3 times more infectious than other respiratory viruses.
- The chances of being exposed depend on how many virus particles you are exposed to and the length of time you are exposed.
 - **Maximum exposure time is only 15 minutes.**
- All ages can be infected. The severity of the symptomatic response is correlated to age and the presence of other underlying medical conditions, but not exclusively.
- All ages are infectious.
 - **40% of those who are infected are asymptomatic**, but they are still infectious (they just don't know it and neither do you).
 - For those who are infected and will go on to develop symptoms, **they are infectious (more highly infectious) for up to 8 days before symptoms emerge** (so again they don't yet know they are infectious and neither do you- and that could be 2 Sundays).
 - A recent study of young children in the US showed that children – who are mostly asymptomatic – have up to **25 times** the amount of virus in the nasal passages than hospitalized adults. They can be significant vectors of community spread. At last count, testing has shown that 40-90% of children in spots are infected.

- Demonstrated cases of re-infection have been documented. It is not known whether the virus becomes latent (stays in the body and re-emerges, similar to chicken pox becoming shingles later in life). The re-infection appears to be a mutated version of the virus, and the second infection brings more significant symptomatology. This means the virus is endemic – it will always be with us – and that eventual vaccines may be annual.
- “exposure” is multiplicative – if you’ve met with 10 people during the day and they’ve each met with 10 people, you’ve been potentially exposed to 100 people

Status

- Currently WHO reports more than **168 million** confirmed cases of COVID-19 globally with more than **3.5 million** reported deaths
 - 219 countries are involved
 - In the US, we have more than **34 million** confirmed cases and **605,000** deaths
 - more than all the US deaths from WWII, Vietnam and Korea combined: highest per capita in the world accounting for 20% of all global deaths and 26% of all global infections
 - It took 4 months to get to 100K deaths, 2 months, 3 months each to get to 200K and 300K, then 1 month each to get to 400 and 500K. Death rate is steady.
 - Nationally still seeing about 290,000 new cases per week (41,000/day)
 - Rates for infections and hospitalization are dropping
 - A person dies from COVID every 15 seconds (average globally, World Health Organization)
- **Current: infections rising in 7 states and plateauing in 18 other states**
- Significant variants have emerged (2021) – all are in the US
 - More than 4000 identified, some sequenced; some from US; CDC is warning that too early relaxation of mandates may result in a fourth spike even as vaccines are rolled out
 - Variants “of concern”:
 - New coronavirus variants found in Scotland, Japan, France, New York and California are more contagious than the original virus. Cases attributed to the New York variant (B.1.526) have risen more than 12 percent in the last two weeks, while the California variant (B.1427/B.1429) makes up more than half of the cases in 44 counties across the state.
 - **India variant a triple mutation (B.1.617) more highly infectious and may evade vaccines – WHO has declared a global threat; mRNA vaccines mostly effective to date**
 - UK variant B.1.1.7 is highly (more) infectious (about 50%), is more virulent and 2x more fatal especially in younger, and appears to be covered by the current mRNA vaccines albeit at slightly lower efficacy – doubling every 10 days in US – in all 50 states and 125 countries – is now the prevalent virus spreading. It is dominant in California and Florida. Scientists also believe it can prolong the infection, making those who have it infectious for a longer period of time.
 - South Africa variants B.1.351 also more infectious but appears to have mutated a critical part of the protein spike that makes it more refractive to mRNA vaccines, and may be more virulent (also 20% more fatal); one variant covered by existing vaccines but at reduced efficacy, one may not be covered by current vaccines; in 45 states and 75 countries
 - Brazil variant P1 is more highly infectious and virulent; not completely clear that vaccines will cover it; in 35 states and 41 countries
 - Variant in California is causing significant spikes there; now in 18 states and 8 countries; other US and global variants emerging – also more infectious and virulent

- Variant from NYC (B.1.526) has a unique set of spike variants, which scientists at Columbia University say "could threaten the efficacy of current antibody therapies and vaccines."
- Variants have arisen in 14 other states of note
- Additional variant from Brazil does not appear to be covered by vaccines
- This is to be expected – viruses make incomplete copies when they replicate so opportunistically variants that are at an advantage for spread will take over
- Coronaviruses still mutate more slowly than the flu virus

Fatality, Co-Morbidity and Long-Term Sequelae

- COVID-19 is **10 times more fatal than the flu** (COVID-19 has an overall 1% fatality rate; the flu is about 0.1%)
- A 1% fatality rate in the US is 3.3 Million people
- Currently in the US 1 person dies about every 70 seconds from COVID; in the EU it's about 1 every 17 seconds
- **Currently more people have died in the US from coronavirus in one year than all soldiers died in WWII, Korea and Vietnam combined**
- The fatality rate is generally correlated to age and underlying medical conditions
 - Fatality is 30.5/1000 for 85 years of age and above (3%)
 - Fatality is 6/1000 for 65-84, 4/1000 for 50-64, 1/900 18-29, 0.3/1000 5-17
- The virus affects the respiratory system but also the heart, liver, kidneys, GI tract, central nervous system, pancreas (causing diabetes), thyroid (affecting metabolism), and causes significant clotting in small blood vessels
- The **long-term consequences** are far more significant than other viruses: for every 1 fatality there will be:
 - 19 hospitalizations (62 million)
 - 18 who develop permanent heart damage (in one study, 80% of those who recovered showed heart damage by MRI) (59 million)
 - 10 who develop permanent lung scarring and damage (32 million)
 - 3 who develop permanent kidney damage (10 million)
 - 3 strokes (10 million)
 - 2 permanent neurological defects (up to and including psychoses, especially in younger population) (6.5 million)
 - 2 significant cognitive dysfunctions (6.5 million)
 - Long-lasting nerve damage, affecting everything from smell to walking
 - **People younger than 21 account for about one-quarter of the population in the United States, but they make up less than 1 percent of deaths from Covid-19. Still, about 2 percent of children who get Covid-19 require hospital care, and at least 227 children in the United States have died of the disease.**

Symptoms

- Early cardinal symptoms include loss of taste and smell, fatigue, shortness of breath, fever, dry cough, joint pain, heaviness in the chest; Progressive symptoms include acute respiratory failure, sepsis, intravascular coagulation (blood clots), and multi-organ failure
- Symptoms are long-lasting – 3 months' post recovery only about 12% are symptom-free, and symptoms can recur after abating
- Stillbirths with infection have been reported to be as high as 80% of pregnancies

Treatments

- There are very few significantly effective treatments for COVID-19
- Normal flu treatments (neuraminidase and endonuclease inhibitors) do not work on COVID-19
- Early in the infection treatment with an anti-viral (Remdesivir) showed some promise; later (smaller studies) have called that into question. Remdesivir just approved by FDA for COVID (10/20); the only approved treatment
- Later in the infection, to stem a hyper-immune response and cytokine storm (causing significant inflammation in the body, the cause of some of the long-term consequences), anti-inflammatory agents (Dexamethasone, a steroid) have been shown to be marginally useful
- Convalescent plasma has also shown some promise but has not been sufficiently tested to demonstrate proof. FDA has not approved convalescent plasma for treatment.
- Some physical manipulation, such as lying the patient on their stomach instead of their back, has provided some relief of lung damage
- Studies with monoclonal antibodies for treatment and potentially prevention are underway (this approach has been shown to be effective for Ebola)
 - In November 2020, the FDA granted emergency use authorization to two monoclonal antibody treatments (bamlanivimab, made by Eli Lilly; and a combination of casirivimab and imdevimab, made by Regeneron). Both treatments have been approved for non-hospitalized adults and children over age 12 with mild to moderate COVID-19 symptoms who are at risk for developing severe COVID-19 or being hospitalized for it. In these patients, the approved treatments can reduce the risk of hospitalization and emergency room visits. These therapies must be given intravenously (by IV) soon after developing symptoms.

Immunity

- The native immune response to COVID-19 has generally been shown to be weak and short-lived
- T-cell response (one of the types of normal immune cells in the body) to the virus may be a more important measure of long-duration immunity than antibody formation and duration, however, tests for antibody are quick and inexpensive, whereas testing for T-cell response is difficult and expensive
- Currently there have been antibodies demonstrated 3-4 months after infection and at least 8 months after vaccination
- Documented re-infections show that native immunity is too specific to cover variants

Vaccines

- There are currently vaccines in various stages of testing; 3 have been approved in US for Emergency Authorization to date with at least two more coming
- 41% US population have received both doses; 56% have received at least one dose. J&J one-dose vaccine is re-established by FDA.
 - “Herd” immunity (80-90% immune) – announced 5/3/21 not likely to be achieved this year as vaccination rates continue to decline and vaccines for children/adolescents not yet approved. Virus is endemic –will become a constant but manageable threat globally for several more years. Variants developing too quickly for herd immunity to be reasonably expected.
 - Vaccines are not as effective in immunocompromised patients
- Twenty vaccine candidates are currently in Phase III (large-scale human) testing
- In the US, 3 vaccines are approved by FDA for Emergency Use – this IS AN APPROVAL
 - Two utilize an mRNA technology, using snippets of the coronavirus mRNA that will infect but not cause disease, to prime the immune system into recognizing the virus and providing early immunity (Moderna and Pfizer)
 - **The mRNA of the vaccine does not affect the human DNA or fertility at all!**
 - both vaccines have been shown to be highly effective (95%)

- mRNA vaccines had never been commercialized in the US and require extreme transport and storage conditions (up to -70° F), making them difficult to use and requiring some additional safety information for review and approval; Pfizer has completed additional testing and the vaccine can safely be stored in a normal freezer
- both have been approved by FDA and the EU board of health for emergency approval and are rolled out per CDC guidelines (approved only for ages 16 and up)
- initial side effects are generally mild flu-like symptoms; anaphylaxis is rare but under evaluation
- takes 2-4 weeks for immunity to develop – can still be infected during that time and can still pass the virus after immunization
- boosters 3-4 weeks apart to get to full immunity potential
- If you have had COVID wait 90 days before getting the vaccine to avoid competing with natural antibodies
- These manufacturers have made all safety data available to consumers
- Pfizer and Moderna vaccines safely tested in more than 20,000 pregnant women.
- These are showing results similar or better to the antibody and T-cell responses after recovery from the virus (similar to the body's response)
- Vaccine data shows that the vaccine appears as effective in older patients as in younger (not true for all vaccines).
- Testing combinations of vaccine and different booster, as well as testing boosters for key variants
- Pfizer/Moderna vaccines in Phase III for children 12+
- Pfizer has applied for dosing 12+; approval likely by end of summer
- Moderna Phase II/III for 6 months and up
- Approvals in younger children possibly available fall 2021 to 1Q 2022
- Moderna announced that it has shipped doses of its booster vaccine for the South Africa variant to the National Institutes of Health for clinical study.
- Other vaccines are using traditional vaccine manufacture processes, similar to the vaccines on the market today
 - These will be easier to manufacture/transport/store globally – no extreme refrigeration required
 - Emergency Use Approval for Janssen (1 shot) granted in March 2021.
 - Reports of reduced effectiveness for Janssen due to timing of trials (likely included more patients infected with variant): 72% effective in US and 57% effective in SA (but not yet tested on UK and other variants) – single dose; adenovirus carrier
 - Astra-Zeneca and Novovax have completed Phase III and will soon petition FDA for EUA; AZ vaccine is approved in the UK. AZ shown to be significantly less effective than first thought esp. for 65 yoa+; distribution stopped in South Africa and UK for possible side effects
 - Novovax early results look good even against variants
 - These are showing results similar to the antibody and T-cell responses after recovery from the virus (similar or slightly better than the body's response)
- Many manufacturers are taking a risk and beginning to produce stockpiles of the vaccines before approval to be ready as early as possible
- Manufacturers and scientists are also engaged in an unprecedented open-source data share
- Vaccine rollout is slower than anticipated in the US but getting better
 - Pfizer increased production speed and tested to say extreme refrigeration not needed

- The majority of the population will not likely be vaccinated before the middle 2021 (June-August)
- Vaccines for adolescents (12+) may be available this fall; vaccines for elementary school children in Phase 3 testing and unlikely to be available until 2022
- Current surveys show that 30% of Americans say they will NOT get the vaccine
- **Only vaccinations will protect – simply having the vaccine and expecting others to be vaccinated will not provide epidemiologic protection sufficient to stop virus spread – will need to stay masked and distanced through fall.**
- Need for booster vaccines and/or annual shots likely

What Can I do with a Vaccine?

- A vaccination is not a magic cape
 - Even 95% efficacy means that statistically 19 out of 20 people are effectively covered by the vaccine but 1 in 20 is not
 - Vaccines are less effective against variants
 - Being vaccinated means it's unlikely YOU will become seriously ill, but there is still a chance you can catch a variant and/or be infectious (be a virus carrier)
- CDC recommends that masks and distancing remain in effect until the average number of new cases in the US drops below 10,000/day – the last time that happened was March 2020. We are currently at 70,000 new cases per day.
- Herd immunity is defined as 70-90% of the entire population vaccinated (not just your congregation)
 - 20% of the population is below 18 and therefore not eligible for vaccination yet (current vaccines are for 16 and above)
 - Statistically that means even if all who are eligible are vaccinated, >25% is not covered until vaccines are approved for 4 and above
 - Herd immunity won't really come until 2022
- Latest CDC recos for vaccinated individuals:
 - Individuals who are fully vaccinated (at least two weeks past last shot) may safely gather unmasked **but only with family and small group (<10) who are not at risk**
 - Fully vaccinated people must still wear masks, socially distance and avoid larger gatherings
- Globally 3.5% received two doses, 7.7% at least first dose, 14% vaccination rate
- **Breakthrough infection after full vaccination is about 0.008% - miniscule but likely under-reported.**
 - Unvaccinated people who are infected will carry the virus at a much higher level than vaccinated people
 - About 30% of those infected after full vaccination are still asymptomatic
 - More than 50% are in those 60+
 - Variant breakthrough is only one possible reason people can be infected after full vaccination, but it is possible variants will emerge that are not covered by the current vaccines
 - Other reasons – all being investigated at this point:
 - Exposure level to virus/variant
 - Other medications that lessened the vaccine effect
 - Other lifestyle or underlying medical issues
 - If you get symptoms even after full vaccination, insist on a COVID test

BOTTOM LINE – Get Vaccinated!! Continue to distance and wear a mask in a crowd!

Session Responsibilities

Spiritual

- Session Elders are spiritual leaders of the church, so if people are feeling disconnected, part of your role is to keep in touch and make sure they know they are still beloved and in prayers. This is not just the responsibility of the pastor!
- Consider creating an Elder-in-Touch list by dividing up congregational members amongst Elders so there's always a primary contact for each person. Cards (especially with holidays coming up), calls, emails, are all great and easy ways to stay in touch.

Administrative and Worship

- Session is responsible for the use and conditions of use for the building, and for decisions around that.
 - Because of that Session is also then responsible to monitor and enforce any conditions of use of the building you establish. This is NOT the responsibility of the pastor.
 - Whatever conditions of use you establish must be enforced both for the congregation, committees, and outside groups.
- Create a decision tree that takes into consideration the COVID status, vulnerable populations, the building itself, and vulnerability (if any) of your pastor, as well as the ability of the church to conduct virtual worship.
- Pick a CREDIBLE data source on which to base decisions (hint – Facebook isn't it).
 - In Ohio, use the Ohio government color-coded system – it's made up of 7 medically-relevant and medical system utilization data points that are objective and unbiased. Presbytery STRONGLY urges churches to meet virtually if your county is red or purple.
 - In other states, use the system at www.covidactnow.org - it's made up of 5 medically-relevant and medical system utilization data points that are objective and unbiased. Presbytery STRONGLY urges churches to meet virtually if your county is orange or red.
 - CDC also has a county-by-county search tool and is very credible, objective and unbiased.
- Pick ONE data source and stick to that – you will drive yourself crazy if you try to reconcile data from multiple sources, as reports are compiled at different times.
- Presbytery STRONGLY urges churches to stay virtual right now or consider outdoor worship as the weather gets nicer
- Presbytery STRONGLY urges churches that elect to go back to in-person worship to do the following:
 - Masks are mandatory and to be worn at all times.
 - Session members should plan to either provide masks for people who have signed up in advance (see below) and don't have one, or turn them away
 - Singing only if masked. Better to not sing at all; there are ways to have hymns played on the piano (maybe words on a screen if you have one).
 - Nothing that blows air around during worship – if your air conditioning or heater blows air over the congregation, pre-AC or -heat the room, turn the blower off during the service (encourage coats and sweaters if you must). Open windows and door to provide fresh air ventilation is great!
 - Special filters, foggers, UV etc., only cleans the air until that air blows over someone who is infected – then the air is dirty and infectious – and remember, 40% never show

symptoms but are still infectious, and a person who will go on to develop symptoms can be infectious and asymptomatic for up to 8 days

- More than 6 feet physical distancing between family groups – estimate in advance how many people your sanctuary can realistically hold with at least 6 feet distance - **Reduction for distancing to 3 feet is really only for children – not for adults!**
 - Limit anything that is passed around or touched by multiple people.
 - Leave collection plates in the back for people to put offerings in
 - Leave communion elements in the back for them to pick up in advance or have them bring their own
 - Have a sign up sheet before the service so you can estimate how many people want to come (and cut off the sign up when you've reached your calculated maximum).
 - If people try to come in who have not signed up in advance, Session members need to be at the door to tell them no
 - Have a sign up sheet before service in case you need to do contact tracing should there be an exposure
 - If there is an exposure, contact the local Board of Health immediately and shut the building and in-person meeting down for 2 weeks
 - Exclude use of bathrooms or any other part of the building (or limit bathrooms to one person at a time and provide alcohol wipes for them to clean surfaces they've touched)
- Understand your personal and church liability if someone is exposed during a church service

Vaccine Types

Platform	Attributes	Doses	Vaccine (Manufacturer)	Candidate
mRNA	Fast development speed; low-to-medium manufacturing scale	2	BNT-162b2 (Pfizer, BioNTech); mRNA-1273 (Moderna)	
DNA	Fast development speed; medium manufacturing scale	2	INO-4800 (Inovio)	
Viral vector with DNA	Medium development; high manufacturing scale	1 or 2	AZA-1222 (AstraZeneca; University); Ad26.COVS.2.S (Johnson & Johnson)	Ad5-CoV Oxford
Protein subunit	Medium- to-fast development; high manufacturing scale	2	NVX-CoV2373 (Novavax)	

Vaccines Approved or in Development

Vaccine	Clinical Trials	Results	Regulatory Status
<p>BNT-162b2 (2 injections) Pfizer (nucleoside-modified messenger RNA (modRNA) vaccine that encodes an optimized SARS-CoV-2 receptor-binding domain (RBD) antigen)</p>	<p>Phase 3 trial completed in individuals 43000+ 16 y and older, 40% diverse; 40%>55yoa</p> <p>In mid-October 2020, company allowed by FDA to expand phase 3 trial to adolescents 12 y and older – completed, data not yet released; no plans announced for trials in younger children</p>	<p>Primary efficacy analysis: 95% effective against clinically evident COVID-19 infection 28 d after 1st dose across all subgroups ^[9] Well tolerated across all populations ^[9] 170 confirmed cases (placebo group, 162; vaccine group, 8) 10 severe cases after 1st dose (placebo group, 9; vaccine group, 1) ^[9] Efficacy consistent across age, sex, race, and ethnicity ^[9] Not evaluated for asymptomatic infection/carriage ^[9]</p>	<p>First approved in United Kingdom on December 2, 2020 Approved in early December 2020 by Bahrain and Canada Emergency use authorized by FDA on December 11, 2020.</p>
<p>mRNA-1273 (2 injections) Moderna (encodes the S-2P antigen)</p>	<p>US phase 3 trial (COVE) completed 30000+, 18yr +; 40% diverse Phase 2/3 trial began in adolescents 12-17 yr in December 2020 and ongoing</p>	<p>Primary efficacy analysis: Efficacy rate 94.1% 196 confirmed cases (placebo group, 185; vaccine group, 11) Only severe illness (30 cases) was in placebo group, including 1 death ^[13] 90 d after 2nd dose (30 participants): high levels of binding and neutralizing antibodies that fell but remained elevated Well tolerated ^[10]</p>	<p>Emergency use authorized by FDA on December 18, 2020.</p>

Vaccine	Clinical Trials	Results	Regulatory Status
<p>AZA-1222 (2 injections) AZ-Oxford (replication-deficient chimpanzee adenoviral vector vaccine containing the surface glycoprotein antigen (spike protein) gene. This vaccine primes the immune system by eliciting antibodies to attack the SARS-CoV-2 virus)</p>	<p>Phase 3 trials ongoing. One dosing regimen (n = 2741) showed vaccine efficacy of 90% when given as a half dose, followed by a full dose at least 1 month later. Another dosing regimen (n = 8895) showed 62% efficacy when given as 2 full doses at least 1 month apart. The combined analysis from both dosing regimens (N = 11,636) resulted in an average efficacy of 70.4%. All results were statistically significant (p< .0001). [15] Concerns about the clinical trial implementation and data analysis have emerged because the half-dose regimen was not in the approved study design. [16, 17]</p>	<p>Participant in United Kingdom diagnosed with transverse myelitis, triggering temporary hold on trial. Interim analysis of phase 3 clinical trial in United Kingdom, Brazil, and South Africa: Efficacy 90%, depending on dosage; average efficacy of 70.4% in combined analysis of 2 dosing regimens. 131 COVID-19 cases: from 21 d after 1st dose, 10 hospitalizations, all in placebo group (2 classified as severe; 1 death)</p>	<p>Approved in United Kingdom December 29, 2020. Submitted to FDA.</p>
<p>Ad26.COVS.2 (1 injection) Janssen adenovirus serotype 26 (Ad26) recombinant vector-based vaccine)</p>	<p>Phase 3 trial (ENSEMBLE) ongoing Second phase 3 trial (EMSEMBLE 2) announced November 15, 2020, to study effects of 2 doses</p>	<p>Phase 1/2a study: antibodies to SARS-CoV-2 observed after a single injection 99% were positive for neutralizing antibodies against SARS-CoV-2 at day 29: strong T-cell responses and a T_H1 response were also noted [11]</p>	<p>Emergency use authorized by FDA on 2 March 2021</p>

Vaccine	Clinical Trials	Results	Regulatory Status
<p>NVX-CoV2373 Novovax (recombinant nanoparticle technology from SARS-CoV-2 genetic sequence to generate an antigen derived from the coronavirus spike protein. This is combined with an adjuvant (Matrix-M). Results of preclinical studies showed that it binds efficiently with human receptors targeted by the virus)</p>	<p>Phase 3 trial in United Kingdom concluded enrollment at end of November 2020. US and Mexico phase 3 trial began December 2020.</p>	<p>Phase 1 data showed the adjuvanted vaccine induced neutralization titers in healthy volunteers that exceeded responses in convalescent serum from mostly symptomatic patients with COVID-19. [12]</p>	<p>Phase 3</p>

Other Vaccines in Development

Vaccine	Comments
<p>INO-4800 (Inovio Pharmaceuticals) ^[19]</p> <p>DNA-based, 2-dose vaccine</p>	<p>Stable at room temperature for more than 1 y; frozen shipment not needed; interim results from phase 1 human trial (n = 40): favorable safety and immunogenicity; expanded to include older participants. ^[46]</p> <p>Phase 2/3 trial (INNOVATE) ongoing; phase 2 to evaluate 2-dose regimen (1 mg or 2 mg) vs placebo in 400 participants.</p> <p>Grant from Bill and Melinda Gates Foundation to speed testing and scale up a smart device (Celectra 3PSP) for large-scale intradermal vaccine delivery; company has also received funds from the US Department of Defense.</p>
<p>CVnCoV (CureVac) ^[20]</p> <p>mRNA, 2-dose vaccine</p>	<p>Preliminary data from phase 1 dose-escalating trial: 12-μg dose provided IgG antibody levels similar to convalescent plasma. phase 2b/3 trial enrollment (goal, 35,000 in Europe and Latin America) ongoing.</p>
<p>COVID-19 S-Trimer (GlaxoSmithKline [GSK]) ^[22]</p>	<p>Partnering with multiple companies using GSK's adjuvants (compounds that enhance vaccine efficacy).</p>
<p>CpG 1018 adjuvant vaccine (Dynavax) ^[23]</p>	<p>Under development with Sanofi's S-protein COVID-19 antigen and GSK's adjuvant technology that stimulates the immune system; phase 1/2 trial ongoing.</p>
<p>UB-612 multipeptide-based vaccine (COVAXX [division of United Biomedical, Inc]) ^[24]</p>	<p>Comprises SARS-CoV-2 amino acid sequences of the receptor binding domain; further formulated with designer Th and CTL epitope peptides derived from the S2 subunit, membrane, and nucleoprotein regions of SARS-CoV-2 structural proteins for induction of memory recall, T-cell activation, and effector functions against SARS-CoV-2.</p> <p>Company partnering with University of Nebraska Medical Center in the United States; phase 1, open-label, dose escalation study ongoing in Taiwan.</p>
<p>HaloVax (Hoth Therapeutics; Voltron Therapeutics) ^[25]</p>	<p>Collaboration with the Vaccine and Immunotherapy Center at Massachusetts General Hospital; use of VaxCelerate self-</p>

Vaccine	Comments
	assembling vaccine platform offers 1 fixed immune adjuvant and 1 variable immune target to allow rapid development.
Nanoparticle SARS-CoV-2 vaccine (Ufovax) ^[26]	Vaccine prototype development utilizing self-assembling protein nanoparticle (1c-SapNP) vaccine platform technology.
PDA0203 (PDS Biotechnology Corp) ^[27]	Utilizes Versamune T-cell-activating platform for vaccine development.
CoVLP recombinant coronavirus virus-like particles (Medicago and GlaxoSmithKline) ^[28]	Combines Medicago's recombinant coronavirus virus-like particles (rCoVLP) with GSK's adjuvant system; phase 2/3 trial ongoing.
AS03-adjuvanted SCB-2019 (Clover Pharmaceuticals) ^[44] Subunit vaccine containing SARS-CoV-2 spike (S) protein	Phase 1 trial results reported in December 2020 showed high level of antibodies. Phase 2/3 trial launching by end of 2020 using GSK adjuvant with goal of 34,000 volunteers.
Covaxin (Bharat Biotech and Ocugen) ^[45] Whole-virion inactivated vaccine	Developed and manufactured in Bharat Biotech's bio-safety level 3 biocontainment facility. Co-development with Ocugen announced for the US market. Elicited strong IgG responses against spike (S1) protein, receptor-binding domain (RBD) and the nucleocapsid (N) protein of SARS-CoV-2 along with strong cellular responses in Phase 1 and 2 clinical trials (n ~1000). Phase 3 trial is in progress in India that involves 26,000 volunteers.
Recombinant adenovirus type-5-vectored vaccine	Approved in China and Saudi Arabia; preliminary data: 86% efficacy; phase 2 trial: seroconversion of neutralizing antibodies

Vaccine	Comments
(Ad5-vectored vaccine; Sinopharm [China]) ^[29]	seen in 59% and 47% of those in 2-dose groups; seroconversion of binding antibody seen in 96-97% of participants; Positive specific T-cell responses seen in 88-90% of participants.
CoronaVac (Ad5-vectored vaccine; Sinovac [China]) ^[47]	Limited use in China. Interim phase 3 efficacy reports vary widely from several trials. A trial in Brazil reports efficacy of 50-90%. However, a Turkish trial reports 91.25% efficacy (n = 7,371; data analysis based on 1322 participants – 752 vaccine and 570 placebo).
rAD26 (frozen) and rAd5 vector-based (lyophilized) formulations (Sputnik V; Moscow Gamaleya Institute) ^[30]	Phase 1/2 trial complete; approved in Russia; both vaccines safe and well tolerated with mostly mild adverse events and no serious adverse events; all participants produced anti-spike protein and neutralizing antibodies after second dose, and generated CD4+ and CD8+ responses.
hAd5 -COVID-19 (ImmunityBio) ^[31]	Phase 1 trial ongoing; vaccine targets inner nucleocapsid (N) and outer spike (S) protein, which have been engineered to activate T cells and antibodies against SARS-CoV-2, respectively. These dual constructs offer the possibility for the vaccine candidate to provide durable, long-term cell-mediated immunity with potent antibody stimulation to patients against both the S and N proteins.
MRT5500 (Sanofi and Translate Bio) ^[32]	mRNA-based vaccine candidate; preclinical evaluation demonstrated favorable ability to elicit neutralizing antibodies using a 2-dose schedule administered 3 wk apart; phase 1/2 trial anticipated to start in Q4 2020.
AG0302-COVID19 (AnGes and Brickell Biotech) ^[33]	Adjuvanted DNA vaccine in phase 1/2 study in Japan; data readouts expected in Q1 2021; intent to follow with phase 3 trials in United States and South America.

Non-Injectable Vaccines in Development

Noninjectable Vaccine	Comments
Intranasal COVID-19 vaccine (AdCOVID; Altimmune, Inc) ^[34]	Single-dose vaccine; preclinical results completed at University of Alabama Birmingham showed stimulation of antigen-specific CD4+ and

Noninjectable Vaccine	Comments
	CD8+ T-cells in mildly affected lungs as early as 10 d; phase 1 safety and immunogenicity study expected to begin in Q4 2020.
ChAdOx1 nCov-19 inhaled (University of Oxford) [35]	Dose-ranging trial for orally inhaled vaccine beginning phase 1 trials in 30 volunteers in Fall 2020.
saRNA inhaled (Imperial College of London) [35]	Dose-ranging trial for orally inhaled vaccine beginning phase 1 trials in 30 volunteers in Fall 2020.
VXA-CoV2-1 oral vaccine (Vaxart) [36]	Recombinant adenovirus vector type 5 (Ad5) expressing coronavirus antigen and a toll-like receptor 3 (TLR3) agonist as an adjuvant; theorized to confer superior protection compared with injection owing to activation of mucosal immunity; room temperature-stable vaccine tablet entering phase 1 trial in September 2020.
PittCoVacc (University of Pittsburgh School of Medicine) [37]	Vaccine candidate using transdermal microneedle for COVID-19; testing in mice produced antibodies over a 2-wk period; microneedles are made of sugar, making it easy to mass-produce and store without refrigeration.