The Central Presbyterian Church Reopening Task Force has been working hard since the beginning of the pandemic to help our church leadership determine how to safely reopen. The information below is shared so that those who are interested can learn more about how this group came to make their recommendations. We share it to also perhaps help some in our church family who want to know more about the science behind much of what has happened with the vaccine, CDC recommendations and more with COVID-19. If you have questions about the information shared below please reach out to Luanne Tilstra (tilstra@rose-hulman.edu).

How was it possible to develop a vaccine so quickly?

There are two principle reasons the COVID vaccine was developed so quickly.

1. ***The research community—pharmaceutical companies, academic research groups and federal research laboratories—all made it a priority. All other projects were put on hold so that time, energy and money focused on vaccine development.***

Scientists in research laboratories that had any capacity to work with viruses focused time, talent, and money (lots of money) on a wide variety of approaches. Not all of the approaches were successful, but some were.

Vaccine developments that were successful went through the same review and testing that all drugs and treatments go through. The federal agencies that conduct the reviews took all the same steps, however all work except COVID vaccine work was put on hold. The same number of reviewers read reports with the same degree of care. The difference is that all their energy was focused on reports related to COVID vaccine development. Review of other drugs under development was put on hold. Steps were not skipped, rather those involved ran up the steps rather than walking up the steps.

The difference between the existing authorization and full approval is that—once the clinical trial is complete—authorization requires 2 months observation and approval requires 6 months observation. As of now, there is no evidence that the additional 4 months of observation will result in anything other than full approval.

Despite the record-breaking rapidity by which this vaccine was developed and put into use, it is at least as safe to use as any other vaccine. The method by which it imparts immunity is more effective than most vaccines.

2. ***The technology used to create the COVID-19 vaccines has been decades in developing***

COVID vaccine development built on a foundation of knowledge, skills, and techniques that resulted from decades of basic research.

The first step of developing any vaccine is to determine the DNA sequence of the virus. In 1980, Sangar received the Nobel Prize in Chemistry for determining the sequence of a single, small virus. It took him 20 years to do so. Because of the human genome project in the 1980's, methods to determine DNA sequence have improved a bit. Once a virus is isolated, it now takes one day to determine its sequence. That's a bit quicker than 20 years.

Two of the vaccines (Moderna and Pfizer-BioNTech) are based on creating a specific messenger-RNA (mRNA); the mRNA delivers a message to cells that incites them to create a system that destroys the virus before it can do significant damage. Developing an mRNA vaccine requires working with RNA which requires a lot of skill and special tools. Bench biochemists are particularly persistent and—due in large part to the SARS outbreak in 2002—they have learned how to develop mRNA vaccines. Their routine, persnickety practices play a huge role in the success of the COVID-19 mRNA vaccine development.

COVID vaccine development is really a culmination of a centuries-long trend. Development of a safe and effective small pox vaccine took hundreds of years. Development of a safe and effective measles vaccine took decades. Development of a safe and effective Ebola vaccine took about five years, and development of a safe and effective COVID-19 vaccine took about 18 months. A miracle that has been at least 50 years in the making.

How safe is the vaccine, really?

Every time you get in your car, there is a chance that you will have an accident resulting in bodily injury or death. Throughout your lifetime, the odds that you will be in a fatal automobile accident are 1 in 107. (www.iii.org/fact-statistic/facts-statistics-mortality-risk) Most of us do not think about that; we've concluded that the convenience of being able to drive to where we want to go outweighs the risk of being injured. We also recognize, to varying degrees, that we can reduce the risk of injury by wearing seatbelts, driving defensively, and driving at a reasonable speed.

When you get the COVID vaccine, there's a chance that you will have a side effect that may result in poor health or death. With the Johnson & Johnson vaccine, women aged 18 – 49 have a 7 in 1 million chance of blood clot formation; the risk is 1 in 1 million for women outside that age range. No risk is reported for men. With the Moderna and Pfizer-BioNTech vaccines the odds of developing myocarditis (a temporary immune-response inflammation of the heart muscle) are 6 in one million. (www.cdc.gov/coronavirus/2019-ncov/vaccines) It is worth noting that in 2017 (before COVID), more than 400 cases of myocarditis were reported per one million people (worldwide). (www.myocarditisfoundation.org, and www.un.org) In short, the risk of negative side-effects from receiving any COVID-19 vaccine are significantly less than the risk of dying in a car accident.

Deciding to get the vaccine means you have concluded that

- the convenience of being able to gather, in person, with friends and family outweighs the risk of negative side-effects.
- the risk of getting COVID-19, which has a 10% chance of long-term debilitating illness (www.sciencedaily.com), outweighs the risk of negative side-effects
- doing your part to prevent mutation of the virus outweighs the risk of negative side-effects. The potential for good outweighs the 1 in 3 million odds of something bad happening.

Why is it so important to get the vaccine? I know people who had COVID and it wasn't any big deal. I'm in an age bracket for which COVID isn't deadly. Why should I bother?

Every time someone becomes infected with any virus, their body becomes a vessel for mutation. The virus that we pass on to someone else is seldom (never?) the same as the virus that infected us. Someone who has only a mild fever with a few sniffles can be host to a major mutation. Someone who is severely ill for weeks may be host to a very small mutation. The magnitude of symptoms has no correlation with the degree of mutation.

Most mutations are small, but a large number of small mutations results in significant changes to the virus. The more people who are infected, the greater the degree of change. The Delta variant of COVID-19 is an example of a mutation that led to a more infectious, more deadly version of the disease. Of great concern is the possibility of a mutation that results in the existing vaccines becoming ineffective. The best way to assure the continued effectiveness of the existing vaccines is to reduce the number of mutations. The best way to reduce the number of mutations is to reduce the number of people who get infected. The best way to prevent infection is to get vaccinated.

How do the various vaccines differ from each other? Why do we need two doses of some but not all of these vaccines?

As you have most certainly heard by now, there are two main categories of vaccine. Both strive to introduce your body to harmless version of the virus, so that your body's immune system can build up a defense system to destroy the real virus if you happen to be exposed. In the case of COVID-19, the harmless piece is the spike protein found on the surface of the virus. The spike protein can't make you sick, but it helps your body build the machinery necessary to destroy the real virus.

The two categories of vaccine differ in how the picture is delivered. The Astrozenica and the Johnson & Johnson vaccines use a viral vector to deliver the picture. Inside this disabled virus there is a viral vector that gives our cells instructions to make the spike protein. The presence of these foreign proteins prompts our bodies to build machinery that will remember how to fight the virus if we are infected in the future. The CDC provides a wonderful pictorial summary. https://www.cdc.gov/coronavirus/2019-ncov/downloads/vaccines/COVID-19-viral-vector-infographic_D_FINAL-508_030621.pdf

Both Moderna and Pfizer-BioNTech vaccines use messenger RNA (mRNA) technology. The mRNA is enveloped in an oily shell so that it can make it through the battlefield that is your body to the interior of a cell. The envelope is opened inside the cell and the mRNA is read by the cell. The mRNA gives our cells instructions for how to make the spike protein. After our cells make copies of the protein, the mRNA is destroyed. Again, the presence of these foreign proteins prompts our bodies to build machinery that will remember how to fight the virus if we are infected in the future. The CDC provides a wonderful pictorial summary. https://www.cdc.gov/coronavirus/2019-ncov/downloads/vaccines/COVID-19-mRNA-infographic_G_508.pdf

On the wearing of masks to reduce the spread of COVID-19

Short version: In the absence of consistent and convincing evidence to support or refute effectiveness of mask-wearing to prevent the spread of COVID, the ReStart Task Force made recommendations about wearing masks in church spaces using an abundance of caution. These recommendations closely mapped recommendations made by the CDC. Recent publications reveal that the caution was merited; there is now significant data to support the value of wearing masks to reduce the risk of infection. The following paragraphs provide details.

Why did the CDC and we at CPC make the recommendations we made about wearing masks to help reduce the spread of COVID-19? There certainly have been a lot of conflicting reports about whether or not wearing a mask has any value, so how and why do folks think it's okay to require that people change how they behave when there is no solid proof it makes a difference? I think that's a very fair question. The answer is complicated and long.

Prevention is paramount: an abundance of caution

The first part of this response starts with an assumption about health-care professionals. The assumption is that healthcare workers' preference is to do all they can to prevent folks from getting sick. When they don't know exactly how to do that, they are likely to proceed with an abundance of caution. The challenge with the COVID-19 case was that folks didn't really know what would work. The response, then, was to take the most extreme measures to prevent spread of the virus until more was learned. The only way to totally prevent the spread of disease among a people is to isolate individuals, and so—based on what was known about the rapid spread and potential lethality of this disease—health care professionals recommended isolation.

Healthcare professionals also know that wearing a mask is an excellent way to reduce (not prevent) the probability that an individual will pass an airborne virus to another individual. This is why medical offices offer masks to patients who come in with symptoms of cold and flu. This is also why surgeons, nurses, anesthesiologists and all the folks doing the work in a surgery theater wear masks. The goal is to reduce the probability that something they exhale will cause an infection in the patient. The practice of wearing a face mask to reduce the possibility that the individual wearing the mask will pass a disease to someone else is called **source-control** masking. Wearing a mask to protect the wearer from infection even if no one else is wearing a mask is known as **wearer-protection**.

Evidence of effectiveness

Folks who found the wearing of a mask to be inconvenient and/or strongly objected to being told what to do felt that unless there was proof that wearing a mask would prevent the spread of COVID, they should not be asked or expected to do so. Folks who were (are) terrified of acquiring COVID huddled in their houses and—when they had to go out—stared in terror at those who were not wearing a mask. Most of us, I suspect, were somewhere in between. How can we know that our behavior is based on reality and not on either bravado or fear?

The first issue to address is the fact that there is not, nor will there ever be proof that wearing a mask completely prevents the spread of COVID or any other airborne virus. Masks can reduce the possibility of passing and receiving a viral infection, but they cannot prevent it.

To the specific question of how effective wearing a mask is at reducing the spread of this specific coronavirus, the actual answer—in March 2020—was "We don't know." The number of science-based studies that could either support or refute claims with respect to the effectiveness of mask wearing for reduction of spread of airborne viruses was remarkably small. Most of the evidence provided was extrapolations of somewhat related studies and rapid analysis of anecdotal evidence. What most of us heard was a series of confusing and contradicting reports. How could we judge what to believe?

In the absence of solid evidence, folks at the CDC (and the leadership at CPC) chose to follow the path of abundant caution. Isolation (virtual church and no in-person meetings) was recommended when the COVID case count in the community was high. As the case count fell, the desire to reduce risk led to a recommendation that re-starting church be accompanied with structures to support a physical distance between family units and a requirement that all in attendance wear masks. Rigorous cleaning practices were implemented, and air filtration methods were updated and improved.

At the time that decision was made, there was very little numerical data to support the efficacy of masking at reducing the spread of viral infections. Some folks argued that—in the absence of hard (numerical) data—we cannot claim that wearing a mask is effective (and therefore wearing a mask should not be required). Others noted that anecdotal evidence was sufficient to support the use of masks. This apparent discrepancy provides a wonderful opportunity to remind some and introduce others to how scientific discovery works.

The nature of science; how scientific discovery works.

All major developments in science begin with observation of the world around us. Folks with a penchant for noting details begin to see patterns in these observations. Over time, recurrence of these patterns inspires great minds to propose why these patterns exist; the result is a scientific theory or model. A core element of the scientific method is the proposal of a hypothesis from a theory or model. A hypothesis is—at its core—a prediction of whether or not the pattern will repeat itself under controlled conditions. After making a hypothesis, the scientist designs an experiment to test the hypothesis; a well-designed experiment includes controls, the identity of the controls is informed by the theory or model upon which the hypothesis is based. The scientist collects data. If the results of the experiment differ from what is predicted (the hypothesis), the theory is modified. Please notice, the results are not modified, the theory is. When reality (results or observations) and theory disagree, it is NOT the reality that is wrong.

Also, please note that all of this takes a great deal of time.

For the current discussion, the relevant reality was this: in communities in which isolation and mask wearing was strongly enforced, the rate of COVID transmittance dropped significantly. I invite you to recall your own observations of the world around you. Think of all the people who talked about how few colds and flus their family had last winter. The combination of isolating at home and wearing masks in public had the real effect of reducing the spread of all kinds of airborne pathogens, not just COVID. This anecdotal evidence is no less real just because it isn't documented in a research scientist's notebook. This real result does not attempt to explain why there were fewer illnesses. Being unable to explain why something happens does not mean it didn't happen. When reality and theory disagree, it is time to examine the theory. In the following pages, I summarize two recent studies.

Recent realization 1. Discrepancies in results of experiments assessing the efficacy of masking disappear when the correct model is used to analyze the data. Masking always reduces how much virus is inhaled. Masking alone can only prevent infection when the viral load is low. When the viral count is high, isolation is the only prevention.

It is not possible to separate the effect of isolation and masking retroactively. It is, however, possible to re-examine the models and theories used to create hypotheses and design early experiments that reported on the effect of mask wearing on reducing the spread of airborne pathogens. That's what began to happen in 2020. In a recent article published by the American Chemical Society (*Biomaterial Science & Engineering*, 2021, 7, 2791 - 2802), 30 of the 46 references were published ***after*** March 2020. That is an unusually high number of recent citations.

A report in the 20 May 2021 edition of *Science* (Y. Cheng, *et al., Science* 10.1126/science.abg6296 (2021)) directly addresses and explains the source of variations in results of studies on the effectiveness of face masks. The authors present a new model to predict the probability of infection (P_{inf}). The key result of their study is that changes in the probability of infection due to changing numbers of viral particles is ***highly nonlinear***. In other words, a ten-percentage decrease in N_V (the number of viruses to which an individual is likely to be exposed) will result in a greater decrease in the probability of infection when N_V is small than when N_V is large.

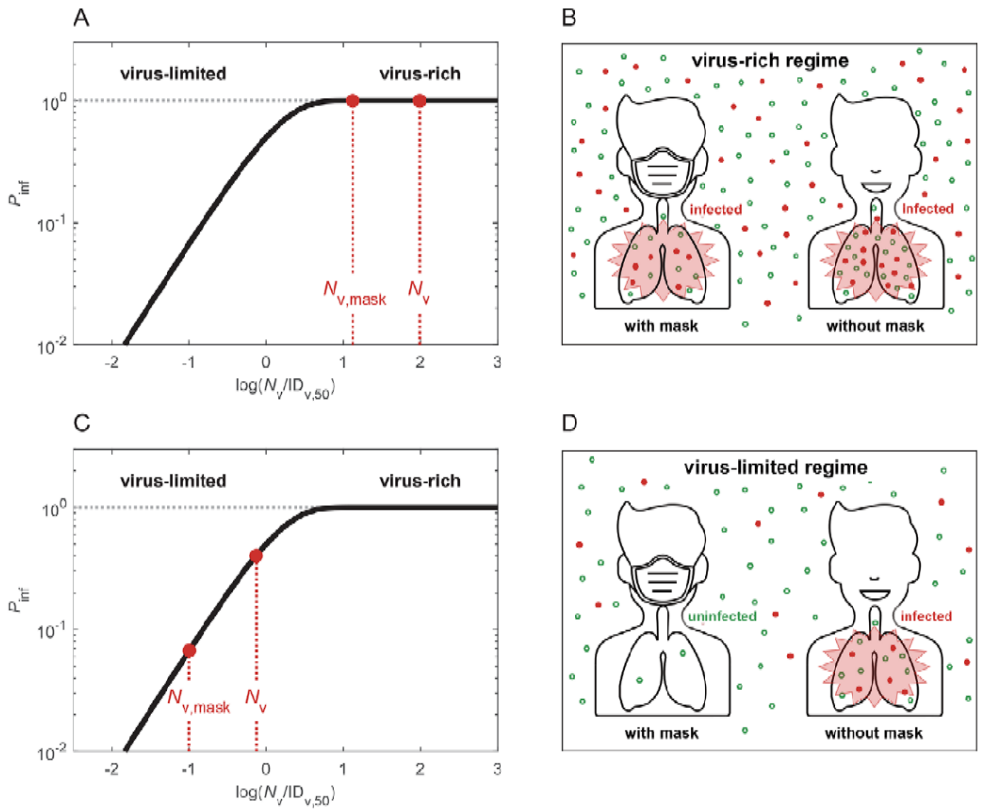

Figure 1. In panels A and C, N_V reflects the number of viral particles inhaled. In panels B and D, the red dots represent respiratory particles containing viruses, and the green circles represent respiratory particles without viruses. (Taken from: Y. Cheng, *et al., Science* 10.1126/science.abg6296 (2021))

Consider **Figure 1**. If you speak math, please note that parts A and C are log-log plots. If you prefer diagrams, look at parts B & D; the red dots represent respiratory particles containing viruses, and the green circles represent respiratory particles without viruses. Wearing a mask DOES prevent a percentage of viral particles from entering your lungs. When there is a lot of virus around, the reduction is not sufficient to prevent infection. When there is less virus around, the reduction is sufficient to prevent infection.

Prior to 2021, models assumed a linear dependence of infection probability (P_{inf}) on the number of viral particles (N_V). The model in this 2021 *Science* article predicts results that agree with both extremes. The studies that demonstrate masks to be ineffective were done in a virus-rich environment; this model predicts results that masks are ineffective a virus-rich environment. The studies that demonstrate masks to be effective were done in a low-virus environment; this model predicts results that masks are highly effective in a low-virus environment.

Most of you will have heard that masks are most effective when used as a **source-control**; i.e., I wear a mask to reduce the chance that I will pass COVID to you. It is reasonable to question if wearing a mask can protect the wearer from infection even if no one else is wearing a mask; this is known as **wearer-protection**. The answer is yes, but not as well as when everyone is wearing a mask; (**universal protection**).

According to the 2021 Science article, the greater the number of folks in the community who are currently infected, the less effective is wearer-protection. Specific numbers demonstrate the point. When the number of folks in the community who are currently infected means that the probability of becoming infected is 5%, then wearing a mask reduces that probability to 3.5% (about two-thirds the original risk). When the viral count is low enough that that probability of infection is 1%, wearing a mask protects the wearer by reducing the probability of infection to 0.35% (about one-third the original risk). In both cases, the larger numbers (5% and 1%) assume no one is wearing a mask and the smaller numbers (3.5% and 0.35%) assume only the uninfected person is wearing a mask.

What this study tells us is that when the viral count is high, isolation is the only prevention. However, when viral count is low enough, wearing a mask is a very effective prevention against infection. The article also provides a means to determine how low is 'low enough.' A recent, informal poll of members of CPC revealed that close to 80% of our membership is fully vaccinated. That means that the viral count among gatherings of CPC member is likely to be very low. If you are not vaccinated or not confident in the efficacy of the vaccine, please know that—in the setting of CPC—wearing a mask to protect yourself will be highly effective.

Recent Realization 2. When made of the appropriate fibers and worn properly, cloth masks are very effective.

There has been some question about the effectiveness of cloth masks vs surgical masks. An article in the American Chemical Society journal *Biomaterials Science & Engineering* (Bhattacharjee, et al., pp 2791 – 2802, July 2021), presents evidence that clearly supports that while surgical masks outperform single-layer cloth masks, cloth masks with 2 or 3 layers are better at blocking respiratory droplets than a surgical mask when the fabric of the cloth masks is either cotton or cotton/polyester blends. Airborne viruses are carried in respiratory droplets; if the droplets are captured the virus is captured. The paper

also reports that the masks ability to block respiratory droplets persists or improves when the masks are laundered. This article really digs into the relationship between the composition of the fibric (cotton, linen, silk, blends) and how well it absorbs or repels water. Breathability is also addressed. (The authors of this article also comment on the importance of good fit and the reality that wearer-protection is significantly more impacted by the fit of the mask than source-control.)

Should I continue to wear a mask even though I'm fully vaccinated.

In the state of Indiana, only 38% of the population is fully vaccinated. That means that when you go to your favorite grocery store or medical office, you should assume that 6 out of 10 of the people you see are not vaccinated and could be carrying the COVID virus. If you are fully vaccinated, you are well-protected; wearing a mask in these settings will have little to no impact on your risk of becoming infected.

There is some evidence of vaccinated individuals becoming infected with COVID. Their symptoms are much milder than the symptoms of those who have not been vaccinated. The difference is even more profound when discussing the Delta variant of COVID-19. Wearing a mask as an added precaution to protect yourself from the Delta variant is not foolish. If it makes you more confident to go out and about, by all means wear a mask.

I confess here that I continue to wear a mask in public settings (shopping and running other errands). I do this both because of the higher probability of COVID being present in settings where 60% of the population is not vaccinated. I also wear a mask as a quiet way to remind the people around me that the COVID virus is still around.

Finally, recognize the value of hanging on to your masks. Consider wearing a mask if you suspect you have a cold, flu, or other viral infection. Mask-wearing is most effective when it is used to control the emission of virus-containing droplets at the source, i.e., an infected individual. If wearing a mask becomes a symbol of showing love for our neighbors, that would be a positive outcome of a difficult year. At the very least, it would be nice to have another cold/flu season with minimal cases.