Twitter Thread by Dr. Angela Rasmussen



Dr. Angela Rasmussen
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There's been a lot of discussion about how to communicate uncertainty about vaccines/transmission, guidance for vaccinated people, how to increase vaccine demand/address hesitancy, & what vaccines mean for the "end" of the pandemic.

Here are my thoughts. I call it "the well."

This pandemic has plunged us to the bottom of a very deep well. After recovering from the shock of a long, abrupt fall into cold, fetid water, we looked up and saw only darkness. But we did find a ladder leading upward.

We've been slowly climbing this ladder, sometimes slipping and falling down a few rungs, but we've endured and kept climbing. Our dedication was rewarded. We've developed very efficacious vaccines, and now as we look up, we can see a small circle of light at the top.

As we continue to climb, the circle will slowly expand. The hope of that circle, slowly growing as we climb ever closer to the top, keeps us going. Eventually we will emerge into the bright sun. Hopefully then we'll put a cover on the well so we can't fall in again.

Now that we have two very efficacious vaccines—that have exceeded our wildest expectations at protecting us against disease. That's a tremendous public health achievement. It should allow us to tighten our grip on the ladder and give us a second wind on the climb.

But there's still a lot we don't know about the vaccines. Will they prevent infection? Will they reduce transmission when enough people are vaccinated? We don't yet know. But this research is ongoing because it is so crucially important. https://t.co/9ZmDc92dE1

> Let\u2019s say (and we don\u2019t know this yet) the vaccines decrease asymptomatic transmission.
>
> Whether they achieve that by day 14, 28, or 42 is a matter of great importance and public safety.
>
> Whether/when they \u2935\ufe0f it by 50%, 75%, or >90% is also life-and-death matter.
>
> Too nuanced?

— Jeremy Faust MD MS (ER physician) (@jeremyfaust) January 17, 2021

My suspicion is that vaccines this good at preventing disease will have a substantial impact on protecting against infection altogether, and will likely reduce transmission. It's unlikely that these vaccines would have no effect on transmission. But we don't know that yet.

This is supported by pre-clinical data in non-human primates, as reviewed here by @florian_krammer.

Most of the vaccines under development or authorized at least partially protect against infection & reduce replication (see URT and LRT protection columns)
https://t.co/g8NrCISY7E

Company (ref.)	Vaccine candidate (type)	Dose range (route)	Neut. titre after prime	Neut. titre after boost	T cell response	Challenge dose (route)	URT protection	LRT protection	Species
Sinovac[34]	PiCoVacc (inactivated virion + aluminium hydroxide)	3–6 μg (i.m.)	None[a]	1:10 range[a] after first boost; 1:50 range[a] after second boost	ND	10^6 $TCID_{50}$ (i.t.)	Partial[b]	Partial (low dose)[b] Complete (high dose)	Rhesus macaques
Beijing Institute of Biological Products[33]	BBIBP-CorV (inactivated virion + aluminium hydroxide)	4–8 μg (i.m.)	1:100 range[a]	1:200 range[a]	ND	10^6 $TCID_{50}$ (i.t.)	Partial[b]	Complete[b]	Cynomolgus macaques
AstraZeneca[49]	ChAdOxnCoV-19 (non-replicating AdV)	2.4×10^{10} VP; 1× or 2× (i.m.)	1:5–1:40 range[a]	1:10–1:160 range[a]	Yes	2.6×10^6 $TCID_{50}$ (i.t., oral, i.n., ocular)	None (1×)[c] None (2×)[c]	Partial (1×)[c] Complete (2×)[c]	Rhesus macaques
Janssen[41]	Ad26COVS1 (non-replicating AdV)	1×10^{11} VP (i.m.)	1:100 range[d]	NA	Low	10^5 $TCID_{50}$ (i.n, i.t.)	Complete in S.PP group[c]	Complete in S.PP group[c]	Rhesus macaques
Moderna[57]	mRNA-1273 (mRNA via LNPs)	2× 10–100 μg (i.m.)	ND[e]	1:501–1:3,481 range[d]	Yes, CD4, T_{FH}	7.6×10^5 $TCID_{50}$ (i.n., i.t.)	None (10 μg)[c] Partial (100 μg)[c]	Partial (10 μg)[c] Complete (100 μg)[c]	Rhesus macaques
Novavax[79]	NVX CoV2373 (spike protein + Matrix-M)	2× 2.5–25 μg	Not reported	17,920–23,040 range[a]	ND	10^4 plaque-forming units (i.n., i.t.)	Partial (low dose)[c] Complete (higher doses)[c]	Complete[c]	Cynomolgus macaques

[a]Based on microneutralization assay with CPE as readout.
[b]Based on viral genome RNA copy number.
[c]Based on subgenomic RNA copy number.
[d]Based on microneutralization assay with a SARS-CoV-2 reporter virus; 50% reduction in relative light units as readout.
[e]Not assessed using authentic SARS-CoV-2.

But you can see that some of that protection was partial, and this was in monkeys anyway. Therefore we can't assume that vaccination alone will completely prevent transmission in the real world (though it likely will reduce it significantly!)

Thus, we must be cautious, especially when not many people have been vaccinated. It doesn't mean we'll be wearing masks and distancing indefinitely or that we release the ladder in despair. It means we grip the ladder tighter, fix our gaze on the light, and keep climbing.

So right now, when people get vaccinated, they should continue taking precautions until we know more. Be reassured that studies are ongoing to get more information on transmission and asymptomatic infection, and we'll know more very soon (in a month or two).

But as we gaze at the light at the top of the well, and it drives us forward, we also can't forget that we aren't there yet. If we look around, we are still surrounded by the cold, dark stones lining the well.
https://t.co/qQjID1s9yz

> \U0001f6a8A reality check\U0001f6a8
>
> If you are becoming complacent and if #COVID19 fatigue is setting in, remind yourself of these numbers. It is in our hands to curb the spread of #SARSCoV2.\U0001f637
>
> > 95 MILLION cases
>
> >2 MILLION deaths. pic.twitter.com/hfnKHaR48Y
>
> — Dr. Arinjay Banerjee, PhD (@sci_questions) January 18, 2021

Right now in many places, including the US, the situation is very grim. More transmission=more cases=more hospitalization=more deaths. We can't become complacent. We can't become so fixated on the light that we forget to climb towards it. We MUST reduce transmission.

That means increasing vigilance on measures to reduce our own exposure risk:
-Avoid gatherings outside your household
-Stay home if sick
-Avoid crowded spaces
-Avoid enclosed spaces
-Ventilate if possible
-Masks
-Distancing
-Wash hands
-Disinfect high-touch surfaces

It also means advocating for public health policies that serve this goal:
-Increase test/trace capacity
-Increase surveillance (genomic, wastewater, etc)
-Economic support to help people comply with the risk reduction measures above
-Create vaccine demand
-Counter misinformation

The good news that's often lost is that if we reduce overall transmission & vaccinate more people, the effect will be synergistic. Less transmission + more vaccines = faster progress to fewer restrictions. It will feel like the climb is getting faster. Hope will be more tangible.

There have also been a lot of alarming statements about the herd immunity threshold, as in "it's much higher than we thought". Maybe, but if we can reduce transmission, we don't need to get all the way to 80-90% vaccination uptake before we can relax restrictions. Here's why.

Viruses are obligate parasites and can't exist without a host. They are driven by evolution to find a susceptible host (in this case, a person) & thus spread in populations. Herd immunity threshold is the & of immune people at which a virus can no longer spread in a population.

When a virus hits an immunized host, it's a dead end. Even if immunized people can become asymptomatically infected and shed virus to infect unvaccinated people, it's very unlikely this would result in transmission to another vaccinated person. This is not typical virus behavior.

Furthermore, we know from non-human primate vaccine and convalescent rechallenge studies that this doesn't happen in monkeys. So it would be very unusual, and I'd go so far as to say it's probably not going to happen in people either.

If everyone is susceptible and/or if virus transmission is rampant, it's not hard for the virus to find a new host. But if there's more people immunized, there are fewer susceptible hosts. If there's less virus spreading around, that decreases opportunity for spread further.

So back to the well, as we keep climbing, more people are going to be vaccinated. If we reduce transmission too, then we're going to increase the pace at which we climb this ladder. The circle of light at the top will expand faster as we get closer and closer.

The challenge now is to keep climbing. To not lose our grip because we are tired and this climb has already been so long and so arduous. We are exhausted, physically and mentally. Our health has suffered. We are tired of being in the dark.

So keep your eyes on the circle of light. Have hope that though each step up the ladder feels like a herculean effort, the circle is expanding. If we can summon the reserves to make it through this final climb, we'll step into the light, possibly by summer. It all depends on us.

Vaccines work and we have great ones. Risk reduction works if we can stay the course. Get vaccinated as soon as you can. Be cautious but know that this is in our power and the end is in sight, even though things are still hard. Let's just keep climbing towards it.

Also just adding here the things that will set us back:
-Overstating or outright lying about vaccine efficacy
-Equating guidance intended to address a short-term problem as telling people to abandon hope
-Stating that education/nuance=telling people restrictions are eternal

Here's a great perspective from @notdred about vaccines being undersold. We need to create vaccine demand. We should do so by being honest and direct about what we know and what we don't.
https://t.co/L2ROwFqvZB

> Since the conversation today is about whether vaccines are being undersold, let me hype you up once again with my thread about how all the current vaccines look great and you should get whichever one you can as soon as you can https://t.co/HBd4NQ41xl
>
> — Ed MD (@notdred) January 18, 2021

Finally, my predictions for when we will "step into the light". If we can get vaccination > 40% and rising by May/June while simultaneously reducing transmission, we can probably start to relax. Travel and in-person holidays in 2021 will be totally feasible for vaccinated people.

So bottom line: take precautions now. Get the vaccines when you can. I certainly will be first in line when my number is called for either Pfizer or Moderna (and J&J or Novavax if the data is similar). Vaccines work, are safe, and yes, they are the long-term solution!