@Risk: The Last COVID Mile with Helen Branswell

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Jodi: Hey, I'm Jodi Butts. And welcome to @Risk, brought to you by Interac.

It's been a long risky year in large part due to COVID-19 and its sprawling health and economic consequences. Thanks to the development of effective vaccines, we can finally see some light at the end of the pandemic tunnel. Let's be buoyed by this over the holidays, but not get too ahead of ourselves either.

What about this last mile of our COVID-19 journey? What are the potential bottlenecks and stumbling points that we should be looking out for? What should we be considering to ensure we reach our zero COVID-19 destination?

To explore these questions I'm joined by Helen Branswell. Helen is Stat News's infectious diseases and global health reporter. She's Canadian and was introduced to epidemic reporting during Toronto's SARS outbreak in 2003. In the years since, she has written about bird flu, the H1N1 flu pandemic, Ebola, Zika, and now leads stats coverage of the coronavirus pandemic. Helen spent the summer of 2004 embedded at the US Centers for Disease Control and Prevention as a CDC knight fellow. In 2010 and 2011, she was a Neiman global health fellow at Harvard where she focused on polio eradication. Nobody covers the COVID-19 vaccine beat more thoughtfully or with more rigor than Helen.

Our journey to this point has been long. Let's not stumble now with the end in sight. Lucky for us, Helen Branswell has us covered.

Thank you for joining me Helen, and welcome to At Risk.

Helen: Thanks for having me.

Jodi: Helen you've written extensively about infectious diseases throughout your career, and as of late you've written volumes on the coronavirus pandemic and specifically the COVID-19 vaccine. About that vaccine you've said, "If we're not careful we could fail to take full advantage of the opportunity that scientists and governments and pharmaceutical companies and philanthropic foundations have created for us." What do we need to be most careful about?

Helen: Oh, lots of things. I think primarily there I was thinking about vaccine hesitancy, addressing what are legitimate concerns amongst people about new vaccine platforms, completely new vaccine platforms that could on the surface sound a bit scary. Ensuring that there's demand for vaccine, because at least in the United States there seems to be an assumption on the part of Operation Warp Speed, the government program to fast-track this work, that if they build it they will come. And I'm

not certain, and I think a lot of experts are not certain, that the demand is going to be massive at the beginning. We'll have to see.

But the other thing is obviously, and you probably want to unpack this a bit later because this is a lot, but there's the whole issue of how much we're going to get from vaccines in the near term and how much they're going to allow us to let down our guard and try to return to normal life.

I think people who think that we're going to instantly be able to doff our masks are going to be disappointed, and we're just going to have to be careful during the rollout, I think.

Jodi: Yeah, in many ways the name Operation Warp Speed really makes you cringe. Firstly it reminds you of fictional science from Star Trek, and secondly it kind of implies rushed.

Helen: Yeah, there are a lot of people who wish they hadn't chosen that name. It apparently came from Peter Marks, the director of the FDA's Center for Biologics Evaluation and Research, he came up with the idea of this fast tracking thing and he's apparently a Star Trek fan. So that's where Operation Warp Speed came from.

But people in public health and people who turn vaccine into vaccinations and know about the difficulty of doing that really did, like you, cringe when they heard that. Because the last thing you want to be doing is implying to the public that these vaccines are slapdash or that corners were cut.

Jodi: And you mentioned distrust of the vaccine, the need to build up demand. There's even hesitancy in health care workers, correct?

Helen: Yeah, that's not new. If you talk to any infection control person in any large hospital in Canada, they'll talk to you about the challenges of getting staff to get flu vaccines every winter. There are some health care workers who don't love getting vaccinations. And with this one, it's brand new. And I think they are people like everybody else, and they may have some concerns.

One of the things that we may have going for us on the hesitancy front is that the two vaccines that seem to be at the front of the pack have quite extraordinary early estimates of efficacy. I mean, way higher than anybody was expecting, 95 percent. That may help to assuage some of the hesitancy. Initially people were talking about the fact that these vaccines might not be that immunogenic, that they might not trigger such a strong immune response, that they might be sort of like flu shots. And a lot of people feel fairly indifferent to flu shots, I don't think they get enough bang for the buck. But if you're talking about a vaccine that is 95 effective, that may sway some people.

Jodi: Yes, I think that's right. Sometimes people really get tripped up on the numbers with the flu vaccine. They will hesitate because they worry that the particular strain of flu that they might be exposed to is not reflected in the flu vaccine that they may receive. But that's not an issue here thankfully.

Helen: Yeah, that's correct. That is absolutely not an issue. With flu, the various types of flu, the strains that are in the vaccine, they evolve very rapidly. And the flu shot can miss the target some years. But with COVID-19 there's just one virus, it's not multiple viruses. And while it is evolving, it doesn't evolve at the rate that flu does. And there's no reason at this point to think that it will be off target in the near future.

Jodi: Now, thinking about the rollout, and one of the things we have to be careful about, we've poured a lot of money into the development of these vaccines. Governments, philanthropic foundations, even the pharmaceutical companies themselves. But a lot of money is required to effectively roll these vaccines out. What do you see in the United States? Do local public health authorities feel like they have the funds to actually do this well?

Helen: No, they don't. I mean, there are a couple of groups here that are sort of the liaisons between government and the people who put vaccines into arms and they've been saying for a while now that it's going to cost about eight billion dollars to get this job done. But the money hasn't been forthcoming. Instead they've had several hundreds of millions of dollars. I'm not clear whether that's tied up in the impasse in congress about a stimulus package related to the COVID pandemic or what, exactly. Maybe there's just not an understanding that this is expensive work to do.

But the last mile of the vaccine project is critical. Like the part that takes the vaccine from the vials and puts it into arms is the point that tells you whether or not the project has been successful or not. And it feels at this point in the United States like it's underfunded, it's being rushed. The people who are doing this work are under tremendous pressure from the generals who run Operation Warp Speed to be able to put vaccines into arms within 24 hours of the CDC signing off on recommendations for who should get the vaccine.

And people feel like this is both an artificial deadline and something that could undermine the success of the rollout because they don't have information sheets yet on the vaccine, because it hasn't been clear how much vaccine was coming in, which vaccine was coming. I mean there are going to be two coming this month in small supplies, but some supplies in the United States. They both require a significant cold chain. One, the Pfizer vaccine, requires an ultra cold chain. Knowing which one you're gonna get, knowing where and when you're gonna get it, these are all things that are still up in the air in some locations.

And there's a lot of confusion at the ground level. It's going to be a real challenge and I think it's going to be messy. I really think it's going to be messy.

Jodi: Now we're not just vaccinating for vaccinations sake. We are really trying to work towards getting back to some sense of normal. And as I understand it, it's herd immunity that gets us there. Now you mentioned the high efficacy rates of the current vaccines that are going to be made available. What's the influence of the high efficacy rates on this vaccine project, and is that a source of hope?

Helen: Yeah, it is a source of hope for a number of reasons, both from an individual point of view. If you get it stand a good chance of being protected for some period of time. That's good news. But also from a sort of societal point of view, the more people who are protected the less transmission we'll have.

You and your listeners probably already know about this, but one of the big unanswered questions about these vaccines is whether they prevent infection or prevent an infection from progressing to illness and disease. The studies have all been set up to show the latter. They're looking only for whether or not people got sick with symptoms of COVID in their trial. They're not systematically swabbing everybody in their trials to see whether or not they had asymptomatic infections.

The reason that's important is if you can still get infected and but don't get sick, I mean you benefit from it but the societal benefit from vaccination that might not be as great. If you can get infected and have a virus replicating in your upper airways and you still transmit virus, what effectively could happen is the vaccines could be contributing to the number of people who are walking around as asymptomatic shutters of a virus. And so that might make it harder to get to herd immunity if vaccinated people are contributing to the onward transmission of the SARS-2 virus.

We won't know for a while whether that's true or not. What is thought, a lot of experts people like Tony Fauci and vaccinologists believe that what is likely to happen is if the vaccines don't completely block infection that they will shut down replication a lot quicker. So that even if people can pick up an infection, they won't transmit as much and if they transmit, they will transmit for a shorter period of time. So that may effectively help to cut how much transmission there is going on in the community.

Jodi: Yes, we've learned so much about this virus in such a truncated period of time. Yet there's still some things we don't know about transmission. If we knew just a little bit more about transmission, we might be able to be more targeted in our vaccine campaign. But because we still don't quite understand super spreader events and people who may act as super spreaders, we have to take this broader approach to immunizing as many adults as we possibly can.

Helen: Yeah, that's absolutely true. I was talking… I asked Mike Ryan of the WHO, the head of their emergencies program, about herd immunity recently and that's exactly what he said. That to get to hurt immunity we're probably going to need to know more about transmission dynamics. Why super spreading events, why some people manage

to trigger super spreading events. Who is doing the most spreading of the disease, and maybe target them?

With flu, it's known that kids really are the ones who amplify transmission of flu. And if you think about it in the fall, you start to hear about kids getting sick in schools. And then as the weather gets colder, parents start to get sick and grandparents start to get sick and flu moves through the community. It doesn't seem like kids are the major vectors of COVID-19, but we're not clear who is playing that role in this pandemic. And knowing that could help you try to figure out how to most effectively use vaccine.

Jodi: So fascinating. Now, it may take us a little bit longer than anybody would like for us to get to herd immunity. But before that, when will things start to just feel better? What have you been hearing from the experts on that score?

Helen: I'm almost hesitant to make too many predictions because this is all predicated on vaccine, and the production and distribution of vaccine is such a difficult and unpredictable business. Last evening I was up late writing a story about the fact that Sanofi Pasteur, which is one of the major vaccine production companies of the world, has had a setback in its COVID-19 vaccine production. In their efforts to try to speed up production of their vaccine, they used some commercial reagents to assess how much antigen they had in their vaccine vials, and they got the wrong reading. So they ended up giving people in their clinical trial too little vaccine and saw some disappointing results in seniors.

When they were trying to figure out why the vaccine didn't appear to be working in that group, which is of course the pivotal group for COVID vaccines, they discovered this problem with the reagents. And so they're having to step back, redo some work, and re-estimate when they're going to be able to get vaccine to market. They're now looking at potentially the second quarter or, excuse me, the second half of 2021.

These are people who were projecting being able to make a billion doses of vaccine in 2021. If their vaccine doesn't start to roll out until towards the end of the year, that's going to affect how much vaccine there is available in the world to get the job done.

I don't want to be a doomsayer. I had been thinking that by next summer or next fall things would be getting to the point where we would feel more normal. But it could be that it might take a little longer than that. And I think we need to sort of build that into our expectations.

We have tools with which to deal with this thing, if we would choose to use them effectively. We're not helpless, but it may take a while to get enough vaccine to vaccinate a substantial portion of our populations.

Jodi: Yes, I think if there's any lesson of 2020 it's that the future is hard to predict. But 2020 also contained some mini lessons. And certainly one of them was the difficulties associated with supply chains.

Helen: Yes, that's absolutely true. I mean, people who have been working in the pandemic preparedness sphere have been predicting this for years. From interviews I've done over the years, I was fully expecting there to be supply chain problems. I wasn't anticipating how quickly they would start to manifest themselves. I mean, the fact that the United States was running out of PPE for healthcare workers in like February and early March really stunned me. I guess we need to be thinking more about that as we go forward.

Jodi: Yes, absolutely. And speaking of supply chain challenges, I must say, well look. I'm not a clinician. I worked at Mount Sinai hospital for a number of years, but that doesn't make me an expert by any stretch. But when I sit back and think about the public policy challenges, the logistical challenges, communication challenges, and acceptance challenges, it's hard for me to imagine that a two-dose vaccine that has such stringent cold chain requirements is going to be the pathway to herd immunity for us. Are there any other vaccines on the horizon? Are we going to have more tools in our toolbox, or are these the two that we're going to have to focus on and rely on during our pathway to a better future?

Helen: So for the globe, I share your skepticism that the mRNA vaccines as they are currently formulated can be the global answer. People point to the fact that the Ebola vaccine, the Ebola vaccine that was designed at the lab in Winnipeg, that Merck has been able to get that vaccine which requires ultra cold chain to very low resource settings in DRC and in west Africa to vaccinate in Ebola outbreaks.

But you're talking there about a precise event involving some tens, or at minimum some hundreds of thousands of people for a short period of time. It's a whole different thing to try to think about how to operationalize that across the entire globe. It does feel like that can't be the best answer there is. It would be very resource intensive and not practical, I think.

Certainly there's been a ton of hope that the vaccine that Oxford University designed and that's being developed by AstraZeneca, who has promised to make it available on a no-profit basis, there's been a ton of hope that that vaccine which doesn't require ultra cold chain could be both produced in multiple parts of the world and distributed more easily in low resource settings. That vaccine is further behind than its manufacturers expected it to be at this point, and it's not clear yet how efficacious it is. They had some unusual results showing 62 percent efficacy in people who got two full doses which is quite a disappointment given that the mRNA vaccines are coming in around 95 percent. And some people by accident got a half dose for their first vaccine and a full dose for their booster shot, and there they saw much higher efficacy. But the number of people in that arm of the trial was very small and it's not clear that those results are statistically solid.

So that vaccine I think will play a role, but it's not yet clear how quickly it's going to be rolled out and how efficacious it's going to be in comparison to some of the others. Johnson & Johnson is developing a vaccine that it hopes could be delivered in a one-dose regimen, which would be much easier to operationalize. And it is also one that can be stored at fridge temperature, it doesn't require ultra cold chain. I think they're about at the point where their US trial has finished or will finish in a few days enrolling the full 40,000 people that they were trying to enroll. And then it will just be a case of accruing enough cases to be able to determine if the vaccine works. So we should know I think in January or so whether that vaccine is going to work in a one-dose formulation. They're testing it in two doses in Europe, so that vaccine will probably contribute if it's successful.

And one would hope Sanofi will have success in reformulating its vaccine and testing it and getting it out, but that's going to take a while. That's a vaccine that it's anticipated that it would require two doses, and it is a vaccine that only requires fridge temperature storage. So that could be quite useful.

I'm listing off a lot of things. I mean, obviously there are vaccines that China has produced. China's produce quite a lot of them and they are exercising vaccine diplomacy. They're making their vaccines available to parts of the world where they want to have influence. So that will contribute to curbing the pandemic as well.

Jodi: Now, this has been quite the month. December 2020 has been so significant in terms of the approval of emergency use authorizations of the COVID vaccine. But there have been some challenges as well within these approvals. And you were following closely the vaccines and related biological products advisory committee that was meeting to review the Pfizer BioNTech vaccine approval, and there were some dissenters in that approval process. What does that mean, Helen?

Helen: Well to be a hundred percent clear, we don't know what that means. Sometimes at the end of the VRBPAC meetings people, they'll go around and poll people who have voted against approval to ask them the reasons for their votes. That didn't happen yesterday, so it's not super clear at this moment why all the people who voted no voted no. There were four negative votes and one abstention.

At least one of the people who voted no has made clear that he did it because he didn't agree with the age… He's made clear he did it because he didn't agree with the notion that the vaccine should be used in people 16 and up. There's very little data for 16 and 17 year-olds. Most of the data is on people 18 and older, and he would have preferred that they'd taken the 16 and 17 year-olds out, but they did not. The debate about whether or not to include 16 and 17 year-olds came up very late in the day at the VRPPAC meeting, and several people expressed the view that they were uncomfortable with the notion that the emergency use authorization could extend to 16

and 17 year-olds. They would have preferred it would be taken out. So that might explain some of the negative votes.

Jodi: Yes, it's too bad that they didn't actually pull the abstention and the four negative votes and that really tells me two things. I think one, it was a really long meeting and I think fatigue might have played a role in not polling the negative votes and the abstention. And the fatigue across the healthcare system is very real at this point in the pandemic, no doubt.

And the second thing is communication is just so important and there's so little margin for error on good communicating.

Helen: Yeah, it is. You're entirely correct, and it's going to be so important going forward. I mean one of the issues that came up in that VRBPAC meeting was the news out of the UK where they started to vaccinate this week, and almost instantly they had two cases of anaphylaxis among two nurses who were vaccinated. Both of whom had allergies, severe allergies to I'm not sure what. But they both carry EpiPens, so they clearly have severe allergies, and they developed anaphylaxis. And this is something that now people have to sort of try to tease out what does that mean? Does it mean that people who have egg allergies or shellfish allergies or other significant allergies can't be vaccinated? That seems to be what the Brits are suggesting, but that's a lot of people. And you'd really want to get some precision about that before issuing that kind of a blanket warning.

But the news of this has sort of gotten out ahead of any kind of official messaging about it. It's going to be it's going to be a challenge. People are not going to know what to do.

Jodi: Yeah, and who gets the vaccine is just so complicated. We were mentioning earlier 16 and 17 year-olds, that's an age group where there isn't a lot of data. And yet they're on that cusp of being transmitters of the virus, more so than let's say elementary school-aged children. So obviously that's why people are wanting to include them in that group of people to be vaccinated.

Pregnant women, you've written about this, the challenge of women of child-bearing age. There just isn't a lot of data out there on that, right?

Helen: There's no data on that. To my mind it's a tragedy. People have been writing for years about the fact that there's a sort of, I don't even know how to describe it, it's almost like a paternalism. When people are developing drugs and vaccines, they want to they test them first in healthy young adults because that's the population in which they think they could do the least damage if anything goes wrong. And they only get around to testing in vulnerable populations, and we think about pregnant people and children as really vulnerable populations, they only do that last after they have evidence

from healthy adults that this new drug or this new vaccine is safe, it appears to be safe in healthy adults.

There have been people arguing for years that this does a disservice to women who are pregnant and women who like are lactating because, well, what happens is the research doesn't really get done. And then something comes forward, it's approved, and there are no data on which to gauge whether or not it's safe for pregnant and lactating people to use the drug or the vaccine.

The same researchers who've been warning about this for a long time started warning about this last February, arguing that when vaccine trials started, they needed to include people who were pregnant. It hasn't happened. And at yesterday's VRBPAC meeting, Pfizer said that it is in the process of completing animal trials that are called dart trials. That stands for developmental and reproductive toxicity trials. Those trials are precursor to human trials. You need to effectively get animal data to look for any evidence that a vaccine might cause damage to a developing fetus before you start to test in people. But they they're just doing that work now.

And meanwhile in the United States, the vaccine could be started. They could start to administer this within 48 hours. And so they won't have an answer when vaccine becomes available. And there will be pregnant women who are standing there trying to figure out, on their own, should I try to get this vaccine?

Jodi: Yes, it's so difficult. And of course, pregnant women and lactating women they are teachers, they are health care workers. They cut across many of the groups that we consider to be priority groups.

Helen: Yeah, that's correct. I mean the CDC estimates that at any one time there are about 330,000 pregnant people among healthcare workers in the United States.

Jodi: It's a big number.

Helen: It is a big number, and they are at the front of the vaccine line and there are no data on which to gauge whether or not these vaccines are safe for them.

Jodi: Even on the topic of kids, so if your child is otherwise a healthy child you can feel pretty good about them either not being vaccinated until they get older or sort of being at the end of the line once more studies can take place. But if your child has another type of disease challenge that makes them particularly vulnerable to this virus, it's a pretty horrible situation as a parent just to basically be told that you're not at the front of the line.

Helen: I don't disagree, but I don't think that's the reason why they're not a priority. Because the rate of serious illness in young children in particular is so much slower than it is amongst older adults, young kids were always going to be at the back of the

line for this vaccine. When supplies are scarce, they're just not the priority because they don't need it as much.

And so in some senses that's a benefit because it gives people time to do the studies. I mean, Pfizer has a little bit of data in 16 and 17 year-olds, and it recently started to vaccinate down to 12. 12 is sort of a tipping point. Below that they have to do what are called dose de-escalation studies. They have to figure out whether or not they need to give smaller doses to younger kids. So they would start with 11 year-olds and test the dose in them, and then go down to 10 year-olds to try to sort of hit the sweet spot for how much antigen to give to be protective but also not to be too reactogenic not to generate too many side effects.

That work will take some time, but there is time. Because when supplies are scarce, kids are not going to be vaccinated. And so those data can be generated. But to your point about parents of children who have other health concerns, I mean that's another layer of anxiety still. And I don't know how quickly people are going to be able to generate data that will tell you that yes, if your child, not only do we know that this is a safe and effective vaccine for your child, for a healthy child, but it's also something that your child can take safely as well.

Jodi: Now, we need to study the impact of the vaccine in real world conditions. Trials focus on safety, and we should all feel confident in the data coming out of those trials. But we also need to study the vaccine and how it works in real world conditions and across the general population. When you're speaking with experts in the United States, do we feel like we're ready to do this research? What are you hearing?

Helen: There are tons of things that need to be studied, and there's really important questions that can only be answered when vaccines are used broadly. Clinical trials are never going to give you all of the answers. So things like how long it will be protective, we'll only know that after they've been in use for a while.

And we talked before about transmission. Will people who get vaccinated still be able to be infected and transmit the virus but just not have symptoms? Once the vaccines are in broad use studies will show us that.

Yes, people are starting to look at the trials that need to be done. Yesterday at the VRBPAC meeting, Nancy Messonnier from the CDC was talking about some of the trials they're setting up already to try to gauge real world effectiveness of the vaccines in healthcare workers, for instance. It's clear from previous vaccine rollouts that the efficacy that you see in a clinical trial and the effectiveness you see in the real world are not always the same. That typically the real world performance of a vaccine will not be as high as the clinical trial efficacy because clinical trials typically enroll mostly healthy people, even though these ones had to make a point of including older adults and people who had some of the health conditions that put you at high risk of bad disease

with COVID. They were still probably in the main a healthier population than the population at large.

And so when you start to give the vaccine to millions, tens of millions and more people, it would probably turn out that the Pfizer vaccine isn't 95 percent effective. What percent effective it is, those kinds of trials that you were talking about will tell us.

Jodi: So much to be proud of and so much to be learned at the same time.

Helen: These vaccines by the time they reach average people will have been tested in tens of thousands of people. It's also true that that there can be things that are rare side effects, something that happens at a rate of a one in a million doses given. You're never going to see those until you start to use vaccines very broadly. And so there are also lots of efforts underway to try to ensure that any kind of safety signal that might arise will be spotted quickly, and a lot of effort will go into trying to study whether or not what's being seen is something that's being caused by the vaccine or something that happened on its own and it was only temporarily associated with vaccine receipt, it looks like they might be linked because it happened at the same time but is really not caused by vaccine.

Jodi: Yeah, it's definitely a lot to tease out and there's still much to be learned during this pandemic. You've written that vaccine production has been forever changed by this experience and really, that's good news. Right?

Helen: Yeah, I mean what I wrote was that pandemic vaccine production has been forever changed. It may be true that vaccine production in general has been too. But for years people have been trying to figure out how the world could respond quickly to a pandemic that would require a vaccine, and it's never been clear that the process of developing a vaccine from scratch and producing it at scale could be done as quickly as it has been done. It’s really a remarkable accomplishment.

Jodi: Last question before I let you go, Helen. You've covered SARS, bird flu, Ebola, Zika and now COVID-19. And frankly, you've done this heroically given how long and difficult a haul it's been. What has been your biggest surprise or two of 2020?

Helen: I have been astonished to see what the impact of layering politics onto a pandemic would be. It never occurred to me that people who were in the midst of a pandemic, whose communities were being affected, who were losing neighbors, it never occurred to me that people would choose to believe that the threat that was being described to them was a hoax because of their political beliefs. That never occurred to me. I’m still trying to figure out how to make sense of the way politics has undermined the response, at least in this country, to the pandemic. That has been a huge surprise.

The other surprise is a good one. I have been warning people for months now that we needed to temper our expectations of how well these vaccines would work, because

typically vaccines that target respiratory pathogens don't work all that well. And I also was telling people that we needed to be very careful because vaccines are very hard to make. And you would have more failures than successes. And in fact I think there's an estimate that only like 17 percent of vaccines that start in clinical trials come through the end of the pipeline.

Currently we haven't had any failures. The first vaccine reported out at an astonishing level of efficacy. Even people like Tony Fauci were stunned. And that's been like a very pleasant surprise. Yeah, I wasn't expecting it but I'll take it.

Jodi: Absolutely, there's been too few of those in 2020. Helen Branswell, thank you so much for joining me and thank you for your careful and enriching reporting that you do on infectious diseases, particularly during this year of pandemic. Thank you so much.

Helen: Oh, thank you.

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Jodi: This is our last episode of @Risk for the year 2020, and I want to thank you all for tuning in and for giving me the opportunity to have these conversations. Your feedback is appreciated and welcome, so please rate and review the show on iTunes and follow us on Twitter at 2020 Network if you haven't done that already.

We'll be back in January with a new episode. Until then, these holidays will be very different and more lonely for many of us. Please stay safe, and remember. There's little risk in being kind to one another. Happy holidays.