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TRANSCRIPT - GR 12 06 24 ***"Adult RSV Vaccination – The Time Has Come"*** guest speaker Ann R. Falsey MD, University of Rochester

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Internal Medicine Grand Rounds

- Welcome, everybody. Welcome to our friends on Zoom and colleagues as well. I'm Justin Mutter. I'm the director of the Medical Center hour, which is a program of our center for health Humanities and ethics. Here at Uva you all may know, and we have the privilege of partnering with medical grand rounds for some of our programs. And this is one. And we're excited to be here.
- Just want to thank there a lot of people that helped put this together today, and I won't name everybody by by name, but just want to thank all of our team at the center as well as all the administrative team and infectious diseases for helping us
- put today's event together.
- I am going to run through some of our Cme. Slides very quickly, as you all know, we are accredited to provide continuing education credit, and so we are required to kind of go through these very quickly. Here.
- I'm going to get to the most important ones.
- which is the credit one so, and they're also for those of you here in the room. There are flyers in the back that have the codes. So if you need to remember the really important to put your code in quickly, because it's only live for about 24 h, and the important one is 2, 4, 1, 7, 3 for today's event today.
- All right. So
- I am privileged to just briefly introduce Kosti Sifri, who is the Becton Dickinson, professor of infectious Diseases, wears a lot of hats here at Uva, and he will introduce our very distinguished speaker. Thank you, Kosti.
- Thank you. Thank you very much, Justin. And
- again, to reiterate, it's my pleasure to introduce today's speaker who is going to be our 12th Hayden and far lecture in virology and epidemiology.
- This, as Justin said, is the preeminent combined medical Grand Rounds and Medical Center Hour. That's on the topic of infectious diseases for Uva health. It's a lecture that is, in fact, named to honor the career of 2 of our distinguished faculty members, Dr. Fred Hayden, who's here in the front as well as the late epidemiologist, Dr. Barry Farr. It's made through generous support through Dr. Jack.
- All means. So thank you, Jack. So today it's my distinct pleasure to introduce Dr. Ann Falsley as the 2024 Hayden Farr lecturer. Dr. Falsley, is a professor of medicine at the University of Rochester School of Medicine. Her research focuses on clinical and translational studies related to respiratory viral infections in adults with a particular interest in respiratory syncytial virus rsv which is the subject of today's talk.
- She's also had research that's extended to influenza, human mendenumovirus, parainfluenza viruses and coronaviruses, of course, including most recently sars-cov-two and Covid-nineteen.

- Dr. Fallsley earned her Bachelor's of Science in Biology from Providence College, her Md. From Vanderbilt University completed Internal Medicine Training at Strong Memorial Hospital at the University of Rochester, and then completed id fellowship training at both Yale University and the University of Rochester.
- Her research has been focused on understanding the epidemiology and clinical impacts of Rsv infection in adult populations, and more recently, as I said, extended to investigating other respiratory viruses. As mentioned earlier, she's led numerous surveillance and vaccine studies across a wide range of populations in clinical settings, including outpatient clinics and older adults, nursing homes and senior daycare centers.
- She's highly experienced also in developing and evaluating diagnostic studies and serologic assays for respiratory viral infections. Currently, she serves as the co-pi of the University of Rochester vaccine treatment and evaluation unit a research that's supported by the Niaid and played a critical role in evaluating scientific investigations around Covid-nineteen and Sars-cov-two.
- So thank you, Dr. Falsey, for joining us today.
- Well, it's my pleasure to be here with you today. I'm happy to be here, actually in person, because the weather was conspiring yesterday to make that unlikely, and it's also my pleasure to be here for a name lecture for my friend Fred Hayden. So thank you. So I'm going to be talking about adult Rsv vaccine vaccination. The time has has come.
- These are my disclosures. And
- you know what I'm going to do is start with some background on Rsv. Not everybody is in the weeds as much about Rsv. What it is, how to diagnosis with the clinical before getting into the vaccine studies, which is really the focus. So you probably didn't know. Or maybe you did, that. It was initially named Chimpanzee Chorosa agent, because it was 1st discovered from a chimp with a runny nose at the Nih.
- and it's not a zoonosis. The poor chimp probably got it from the caregiver who gave it to the chimp, but it was shortly thereafter that it was renamed respiratory syncytial virus because of its characteristic in cell culture, that it fuses cells together and produces these syncytium. And then along came Dr. Chanik, who then linked it and found it in a young child with bronchiolitis, and it was very
- close after that that it became well known that Rsv. Was the major cause of bronchiolitis in in young kids, and even though they knew that it could infect adults, they really thought it was just a cold.
- So it really wasn't until around the 19 eighties that people started to take note and realize that Rsv could actually be a problem in older adults when there started to be outbreaks in nursing homes where older folks were getting sick, there were high attack rates, and sometimes very high pneumonia and death rates. So it really grabbed people's notice that oh, this could, in fact, be an adult disease.
- Now, it's also notable that only 5% of older people live in nursing homes, and so very little was known about what was going on in the community. And so around that time Ed Walsh and I, in Rochester, embarked on this very ambitious 4 year study with inpatients and outpatients, prospective cohorts to really try to define this disease, to see whether it was worth doing something about.
- And it turns out it was. And we wrote it up. And for a long time, though, we felt like people didn't believe our data like, Oh, that's just something that happens in Rochester. But it what? Maybe because it's snowy and it's cold. But since then

there's been lots and lots and lots and lots of studies that basically have confirmed what we found. It is a problem. It causes significant morbidity and mortality.

- And what you find also depends on how you what methods you use to diagnose it.
- And it's important both in the research realm and for clinical care. So it used to be back in the old days. The only way you could diagnose it was cell culture, viral culture which was super insensitive for Rsv. It's a much more fastidious virus than influenza. And so, if you were depending on viral culture, you would think nobody had no adult. Had Rsv kids have a huge amount of virus in their nose with a
- primary infection. So then, we started using serology and a well-timed, acute, and convalescent sample to look for antibody rise was quite useful. The rapid Antigen tests that we're all familiar with now with Covid don't work at all in adults with Rsv. It's a total waste of time.
- And then finally, along comes Pcr, particularly real-time. Pcr, and it's really made a difference in clinical care. You could now actually diagnose it with your adult. But it's also made a difference in research studies. It's
- important that we've now finally multiplexed a lot of Rsv
- testing with flu testing, because otherwise nobody really actually is testing to see if your patient has Rsv, they're usually looking for flu. And oh, gosh, look! They have. Rsv.
- but more recently, and this is data from some collaborators in Kentucky. We've started to question. Maybe a nasopharyngeal or a nasal swab is not the best sample. It is by convention. What we all do when we're testing for respiratory viruses, but particularly in the hospital, when people have been sick a little while, you can see these are the different types of samples that we were collecting in this study all at the same time.
- and a nasal swab was missing a fair amount and saliva, which pretty much everybody can spit in a cup
- was positive. In 25 people that were missed by nasal swab and sputum is great. It's the highest yield, but a lot of people can't cough it up. And then, if you look over at the other graph with the red oval
- serology is great, and it turns out when we moved from studies that were just doing serology to Pcr. We thought, Oh, my God, everybody's going to have Rsv, but it turns out serology was really quite good, and it didn't change the overall effects. But again, you need somebody to be alive to get the serum, so
- just to remember it may be evolved that saliva is a better sample, and people hate getting nasal swabs stuck up their nose. So these are the results of that 1st study that I showed from the New England journal shown in blue is our study. Where we had these prospective cohorts of older people. We use both Pcr. And Serology, and the
- infection rates were 4.8 to 6.5%, with about a 3rd of patients going to see their doctor. And because we enrolled a high risk population, people with heart and lung disease. We had a fair amount of hospitalizations, and even had some deaths. And then for many years nobody did anything like this, because it's very expensive to do these prospective studies. But along came Korsten et Al. In Europe.
- you know, 15 years later, use the same methodology, Pcr and serology, and found it basically the exact same thing. So we found that very rewarding that things really, this is what it is. This is the infection rate. They had similar office visits. They did not have as high a hospitalization
- and death rate because they did not enroll high risk patients.

- So who is at risk. Not all older people are at risk, I mean, you know, if you're 65, and out running marathons and biking 20 miles a day. You're probably not at high risk.
- But age is important. And this is some modeling data from Europe, from the Uk. And a guy named Douglas Fleming has been studying Rsv. For many years, and what this shows on the top is hospitalization rates per 100,000. On the bottom is death rates per 100,000, and you can see the purple line is much higher than all the other lines, and that is people over the age of 75. The green line are people 65 to 74, you know, kind of what we traditionally think is senior.
- But the big jump really occurs at 75. Now this is a modeling study. And so we like to do data-driven studies. And so this is a collaboration
- upstate with us and downstate with Columbia. It was 3 years of data, and we actually diagnosed Rsv. By Pcr.
- And the 3 different years are shown in the different shades of blue
- and the overall incidence per 100,000 was 8 to 12 per 100,000 people, 18 to 49, which goes up to 137 to 256 in people over the age of 65. So yes, if you're older, you're at risk.
- And then really, this is that 75 year old kind of cut mark. And you can see that in our study, too, the rates really increase over the age of 75. The hash lines are New York City, and I'm really not sure why their rates were higher than our rates. It may have to do with different ways. They live multi-generational families. We have yet to analyze that so clearly the
- presence of underlying medical conditions is hugely important and shown here is that same study, but broken down by different conditions. Blue is without orange is with, and you can see the huge rises in rates of Copd and Chf. But also diabetes, coronary, artery, disease, and even asthma and obesity.
- So these things don't occur in isolation. They occur together. You can have a overweight diabetic, or somebody with both Copd and heart failure. And so this was a study doing multivariate analysis. Looking at what's independently predictive
- of hospitalization in people with Rsv and the light blue balls are those things that were significant. And again, we see the effect of age with over 75 being important, but also Copd congestive heart failure, hemologic malignancies, prior history of stroke and chronic kidney disease. I think chronic kidney disease is important. And we're just starting to understand that.
- So it turns out, you know, there's probably about 3.4 million acute respiratory illnesses each year in the Us. Leading to about 1.7 million outpatient visits
- somewhere between 108 and 177,000 hospitalizations and 8 to 14,000 deaths. And this is probably an underestimate due to selection bias in studies and under testing
- so briefly. What does Rsv look like before we're starting to vaccine this lovely lady, Betty Braun had Copd. She was in one of our studies, and she said we could use our picture.
- I like to tell people that Rsv. Is a very phlegmy, snotty, wheezy infection.
- and if you can see here where we compared flu and Rsv.
- they were statistically, significantly more common with Rsv. And in flu you get higher rates of fever. But the reality is, there's a lot of overlap, and you need a test. You need to do a Pcr. If you really need to know. The other thing is is that, unlike Covid. The pneumonia is
- patchy, it's wispy. So this was a lady in one of our studies. She actually came into the hospital. We knew she had Rsv. She was culture positive.

- and she was so hypoxic that in the emergency room they looked at her chest. X-ray shown here a little bit of effusions. They thought, maybe she has a pulmonary embolus. So I got a Ct. And you can see these wispy sort of infiltrates. And that's pretty characteristic. So there's a lot of airway reactivity as pathogenesis. Unlike the diffuse pneumonia that we see with Covid.
- So this is the virus that I think is the basis on which we will talk about vaccines. It's an Rna virus. It's enveloped. It has 2 major surface proteins, the F protein and the g protein. There's 2 subgroups A and B, and most of the antigenic diversity is in the g protein.
- and therefore because the f protein is pretty well conserved, that has been the focus of vaccine efforts, so that you don't have to have 2 different vaccines and neutralizing antibody are directed against both of these proteins.
- and I always think, before talking about vaccine development in Rsv. It's always important to acknowledge the disastrous formalin inactivated Rsv vaccine. That was done in the 19 sixties at the Nih unfortunately, it was done in disadvantaged children.
- and 2 kids died. So when they formalin inactivated the virus, the whole virus. It led to enhanced disease, unnatural infection. And if you're interested. This is a really great article on Undarc, very fair and balanced, and it just really goes through what happened. But, so needless to say, vaccine development in young children has been slow and careful as it should be.
- So I'll just leave that there. If you want to take a picture.
- Really really good article.
- So this is the pathway to success. We now have vaccines for adults and and products for children. And, as I said, we started in 1956, when they discovered the virus, and I like to highlight the discovery of the fusion. Protein. The 1st person who identified isolated the protein was Ed Walsh in Rochester, who was a co-resident with Fred Hayden.
- and also showed that early in animal studies that if you immunize mice with the f protein, they would be protective. But you know, mice are not people, and so early on we embarked in a variety of vaccine trials in older adults, basically using purified fusion. Protein, with a variety of manufacturers, as you can see here. And you know it just wasn't
- that immunogenic maybe induced about a 2 to 4 fold increase in neutralizing antibody, and the latter 2 studies failed to show efficacy.
- So it really wasn't until some super smart people at the Nih figured out that the F protein
- actually existed in 2 different States, and that the prefusion state before the virus starts to fuse to the cells is unstable. It just doesn't stay in that state very long. So the sort of round structure is prefusion, and the more linear structure is post fusion.
- and they outlined here in colors. The different epitopes
- and red and orange induce the most potent neutralizing antibodies, and you can see, as it moves from prefusion to post-fusion, you lose those antigenic sites. So this was important to figure out that the protein was doing this. And in the old study, as we
- purified that protein, we were basically purifying post fusion. F, which isn't that it's not immunogenic. It's just not as good. And then they figured out to introduce some stabilizing mutations that would keep

- prefusion. F in that particular state. So now we had a great antigen to serve as the basis for a vaccine.
- So this is some data from one of our early Pfizer studies, and it shows highlighted in the red box. Given 120 micrograms of prefusion. F. We were now inducing twelve-fold increases in antibody so much different than that previous 2 to 4 fold, and it would it would last over a year.
- So onward. And you know, in all the vaccines, Gsk and Moderna, they all kind of look the same. So on to the efficacy trials, the efficacy trials were conducted in people over the age of 60, with a primary outcome of Rsv. Documented lower respiratory tract disease.
- There were 2 protein-based vaccines, Gsk, now called Orexv, and it has an adjuvant the same adjuvant used in Shingrix and Pfizer, which is a little different. They have a bivalent vaccine that incorporates protein from both A and B, and then we have one Rna vaccine made by Moderna.
- and in the interest of time I'll just show you the data from the Gsk trial. They were 1st out of the box, and this is their efficacy to prevent 3 or more symptoms of lower respiratory tract disease placebo in blue, the vaccine in orange, and you can see a big difference. They met their primary outcome. The vaccine efficacy was estimated to be 82.6 and 94.1 for a severe subset, and, you know, think about flu vaccine. This is pretty darn good.
- And so at the time all the studies were starting to report their endpoints, and Pfizer, you can see here was 85.7. Moderna was 82.4, and they even had efficacy against any Ari.
- and we were very encouraged that all of the studies were coming in around the same level, because, due to the pandemic, we're doing these studies at the worst possible time. They were done kind of. As the pandemic was winding down, and there were low event rates because it suppressed viral activity for all the other viruses. So there were low event rates. So, despite this, we need to think about safety. All the vaccines were associated with some mild injection site.
- and they were mild and transient. But there were some safety signals. There were 2 cases of Guillain-barre and Pfizer, and one in an earlier trial of Gsk. There was an imbalance in atrial fibrillation, and so far no safety signals from Moderna.
- And you know, when the FDA approved the vaccines in the fall or the summer of 2,003. And then the acip met, and they came out with these sort of anemic recommendations that somebody who is
- labored in this field, you know, kind of made my head want to explode. So they said
- that a adult over 60 could receive a single dose of the Rsv vaccine using shared clinical decision making, and the pediatricians laugh about shared clinical decision making. This is where vaccines go to die. So the problem they had was that there were too few people enrolled in the trial with high risk conditions over 80,
- few frail nobody, almost nobody from a nursing home.
- and not enough events to prove efficacy against hospitalization and death, which is very unfair, because no big pivotal vaccine study ever does any of these things. They just change the criteria.
- And you know, I just felt that that was unfair. They did show in the trials that they were quite effective at preventing medically attended disease. So in what universe would it not translate into hospitalization. They did have legitimate concerns about adverse events, and they had questions about durability
- and cost.

- So we can now answer some of these questions, because another year has gone by.
- And this is Pfizer data, showing that at the end of the 1st season the efficacy was actually 88.9 it dropped to 77.8 in the second season for cumulative efficacy of 81.5. So this is over 2 years.
- This is Gsk. They didn't show their efficacy in the second year, which actually dropped to 58%. But cumulatively, it was 73 to 80%. So lasting at least 2 years.
- What was interesting is when they looked at boosting. And this is data from Gsk. The green line shows, if you just did nothing. These are antibody titers over a year.
- and then they decided they would boost people at one year, and the orange line shows that it boosts. But it doesn't go up to nearly the level it did initially with the 1st vaccination. So it's against A and B, and these are CD 4 T. Cells at the end.
- which boosted very nicely. So I don't understand that. And then they waited another year. And this is more recent data that again, if you look at Green. That's no reboosting. If you look at the purple line that's boosting at one year, and if you look at the pink line that's waiting 2 years and boosting at 2 years. So the lower it goes, the longer you wait, the more boostable it probably is, and probably
- the efficacy is going to last about 3 to 4 years, so the the boosting, we assume, will be better at that point.
- Now, if we look at the Moderna vaccine their efficacy in the second year was lower than the protein vaccines. It was down around 50%, and they calculated that they were losing efficacy of about 2.4% each month.
- which I, you know, talking to these people on these advisor boards kind of bumming them out. But the other thing is that when they did their boosting study at a year, boosted right back up to the same level. So you know, it might be that this would be a yearly vaccine. It would be easier for the poor practitioners to keep track of you. Get your flu vaccine you get. They're just going to have to cut the price in half. But that's not my business.
- So another question came in. That natural infection is not very
- good for Rsv, we keep getting reinfected. So this is data just hot off the press, comparing the antibody response to natural infection compared to vaccination. And we look at the binding antibodies, and then the neutralizing antibodies and Rsv. Infection
- is shown in orange with the vaccine shown in blue, and it was significantly better for both binding antibody and neutralizing antibody with the vaccination. So there is a hope that this vaccine is so highly immunogenic that it will be somewhat better than natural infection.
- The other thing we did, because you know, the the nursing Home directors made me crazy because they just didn't want to endorse the vaccine.
- and it's it's unethical now to do a randomized placebo-controlled trial in a nursing home. It works.
- we just did immunobridging. And so we took a group of older people in the community and people in nursing homes. We vaccinated them with both Pfizer and Gsk. And if you look at the red bars, those are people in nursing home, and these were sick people, or even a couple of people on ventilators. Their antibody responses were just as good as the people in the community. So we have every reason to be optimistic that it will be quite effective.
- So one of the gripes

- was, well, you didn't have sick people. You didn't have, you know, serious endpoints, and you can only do real world effectiveness now, and some of that data is starting to come in as well. And so in these observational studies, although there's always a little bit of bias
- you can get in people who are very frail, who are from nursing homes, and you can start to look at hospitalization and er and critical illness. And the most common way we do this is with the test negative
- test design. And so what you have is, let's say you got. You're looking at people who come into a hospital. You've got people who have respiratory illness. Some of them test positive for Rsv. Those are the cases you have people that test negative for Rsv, and then you compare the ratio of vaccination to non vaccination.
- and you can get a real world efficacy study. This is probably too small for anybody to read, and I apologize that this was just published in the Lancet in October, and it's from the Vision Network.
- and they looked at hospitalization and
- compared to unvaccinated the real world effectiveness was 80% to prevent hospitalization. It held true for the different age groups, and it even held true for immunocompromised individuals.
- And then there's a number of other studies shown here. They're shown the top. The blue is the randomized clinical trials. The bottom is Rsv hospitalization in these real world effectiveness studies. This is from the acip. Some of this data is not yet published, but they're really coming in around the same range of between 70 and 85% effective to prevent hospitalization, which I think is pretty good.
- We do know that there are people less than age 60 that are also high risk.
- And this is some data that looks at the Cdc network, and they estimate 10 to 20,000 people a year between the ages of 50 and 59 are hospitalized with Rsv. These are all people with underlying medical conditions. So the companies are starting to do immunobridging in that age group. So the FDA has now approved the vaccine for these younger people. But the acip has not yet recommended
- so a word about safety, because I do think that was driving some of the acips concern. There's a data safety data link. This is one
- project. It's between the Cdc. And 13 different sites. They have 13 million persons a year in this surveillance, and honestly, I read the statistics, and I don't understand it. But they
- they did look at safety signals, and they looked at all of these conditions and for atrial fibrillation there's nothing. So you can just dismiss the concern about atrial fibrillation. They also did not see a signal for guillain-bre, and weirdly they saw this immune
- the itp with the Gsk vaccine, which everybody thinks is a little bit spurious.
- They've also been doing studies the FDA called the Self-controlled Case Series, and this is where you use a person as their own control. So shown here is the vaccination occurs on day 0, and you consider the period of risk
- to be days, one to 48, 42, and then they have. The rest of the year is a non-risk period, because we know the incidence of guillain-barre goes up with age. So the the incidence is somewhere between 5 to 7 per 100,000 in just your general population of older people. So how do you figure out what's due to the vaccine? And what is just chance.
- So they looked at these results just again, just real. Recently in October, they compared Gsk and Pfizer. There are now about 3 million vaccinees that they could

look at the cases in the risk interval were 24 for Gsk. 18 with Pref. And then less than that in the control period 11 to less than 11,

- so they concluded that these results are kind of consistent with what they were seeing prelicensure, that the Gbs risk following vaccination is rare
- less than 10 cases per 1 million. But there's probably a real association, but it's real, but rare.
- and there was no difference between getting a common vaccine, and not
- so, because there's a real but rare risk you have to do risk benefit to see whether you feel comfortable recommending that vaccine.
- So they also did a really nice job of looking at what
- per 1 million doses, how many hospitalizations, icu admissions and deaths would be prevented with the vaccine shown in green are people over 75,
- shown in purple are individuals 60 to 74 with a risk factor. And you can clearly see that even if they and they chose attributable risk of Gbs, which is probably not more than 10, they said, well, we should say 0 to 18, just to give the full span. Clearly the benefit outweighs the risk in these groups
- when they looked at. Oh, so the avertible cases of deaths and hospitalizations is much greater than the potential risk of Gbs in people over 75, and people 60 to 74, and the magnitude of avertible deaths was
- less. But still there, for people 60 to 74 without risk factors and 50 to 59 with risk factors. So they haven't yet recommended. It's approved. The vaccine is licensed, but they haven't recommended it there.
- So the current recommendations by the acip is that people over 75 should receive a single dose of Rsv. And they've done away with shared decision, making same thing for people 60 to 74 with a risk factor, and that people 60 to 74 without risk. Factors for severe Rsv. Disease are no longer recommended to receive Rsv vaccination.
- so you could go out and do it. But it's possible your insurance company might not pay for it.
- These are the risk factors that they've deemed
- important. You can see diabetes with end organ damage and severe obesity over 40, and I asked them like, where did you come up with that? And they
- kind of admitted. Maybe they just sort of made it up.
- And then they do now include residents in a nursing home frailty. And then there's a fudge factor. Other factors determined to be important for risk of severe disease. And you know, I worry that people will not want to do it because they're worried. They'll get a vaccine, and then they'll be stuck with a $250 bill for the vaccine.
- It's also important to remember that
- people of color are hospitalized at younger age range or ages than the white non-hispanic population. So this is some data that we haven't published yet.
- but shown in Orange, I'll just highlight. The orange is the African immunic African American persons admitted with Rsv.
- And in that 45 to 64 year old range. It's 152.4 per 100,000
- compared to 36.3 for the white community. And there's probably a lot of different reasons for that that I won't go into. But I think the current recommendations potentially widen disparity in health care even worse. I'll just finish by saying, you know, Rsv. Still has an identity crisis. Everybody knows about flu. They now know about Covid. You know, we're doing better with Rsv.

- Because the manufacturers are marketing pretty aggressively with their commercials. But a lot of people still don't know about it, and this was a small study looking at providers about what they knew about Rsv, and I just highlighted in red.
- How often do you see adults with Rsv, and it was 33%, sometimes 37% rarely and 20% never. So clearly, those people are just missing the boat.
- And they they admitted that a lot of their facilities just don't test. And even more disturbingly, 85% could not name the major risk factors for doing poorly with Rsv. So we have some work to do
- so. I think the more we test.
- which you know some of the hospital administrators don't like, because
- well, what are you going to do differently? It doesn't change your management. But until we start making that diagnosis in our own patients, and, like primary care, doctors see their beloved Mrs. Jones, who ended up in the Icu with Rsv. It doesn't mean the same thing as reading a bunch of papers, and so I have
- personalizing
- so clearly for Barbara.
- It was not a minor cold, and so I think the more we can make an Rsv diagnosis in older people the more people will accept sort of that risk benefit ratio. They'll understand it's an important disease. So I'll conclude with, you know, Rsv is common in older adults. People over the age of 75, and those with high risk conditions are at the greatest risk, and I think the acip recognize that
- Rsv vaccines are now available. You can go to your Cvs. They are safe and effective. There's this lingering concern about Gbs. But remember, it's rare. And so, you know, if you've got somebody at high risk, they're much higher risk for ending up in the hospital and doing poorly
- the durability and boosting issue we're still working on. It's good for at least 2 years, probably 3, maybe 4. Well, at least the protein ones and the Rsv. I didn't talk about. But another common question is, can you give it with flu and Covid vaccines, and you can.
- So I will finish with this slide. I always like to end with this slide. This is my 101 year old Daddy, who in November of 2,023, I was really pleased to be able to take him to the drugstore and get him his Rsv vaccine.
- So I'll stop there and see if anybody has any questions.
- I don't. I don't know how I would see questions online.
- Does anybody know how to monitor the. Oh, okay, okay, thank you for that. I did have a question about these vaccines, and I'm saying it from the perspective of my daughter who's 5 months old, and when we were at Clinic they talked about the Bay fortis vaccine, which is the monoclonal antibody vaccine against Rsv. For infants and toddlers. So just wanted to ask if you could weigh in on.
- If there's studies around that as well for older adults, and why?
- The thought for monoclonal antibody, passive immunization for infants and toddlers has been
- has been favored over just like immunity overall.
- So you know that it's it's a long history that begins with that formalin, inactivated vaccine.
- the the naive, immune system of a young child. Everybody is very reticent to do active vaccination in that group, and if they ever get to it it would be alive, attenuated.

- vaccine, so that you set the immune system in the proper way, and they haven't been able to get the attenuation right like it's not like these vaccines are so virulent, but you know you make a 2 week old or one month old. Have a runny nose they can't feed. And so the reason that the vaccines have evolved in young children to vaccinate the mom with the Pfizer vaccine, which is the exact same one that's given to the older adults or Bay fortis. The monoclonal antibody
- is for that reason, and the reason we now do it, and you know they had palavizumab which you had to give each month. It was very expensive. It was based based on weight and
- They monkeyed with the Fc. Receptor of the antibody. And now it lasts for a whole season. So it's basically a passive vaccine for young kids. We're trying to figure out if there's 1 preferred over another, it may be.
- you know, you don't want to have a vaccine, 2 different products for 1st world and then low and middle income countries. But the reality is that the monoclone currently priced
- is probably too expensive for those countries to use, and the vaccine works, you know, maternal vaccine. Why don't we consider that for adults, you know Bayfortis or a monoclone? And when we did with Covid there are certain groups of adults in whom the companies are thinking about that. So you can imagine a
- stem cell transplant. They're never going to react to any vaccine.
- A monoclon may be useful. But you know, again, they're based on weight. And so
- they have to figure that out.
- Thanks very much. A couple of questions. Could you just comment on where we stand currently in the Us. With coverage, both in the older adult population, but also in pregnant women with the vaccines.
- I can't comment on the pregnant women, because I actually don't know. But for adults it was at the end of last season. It was about 25%.
- How much it's been accepted this season. The data are still rolling in, you know. I think, that the covid pandemic damaged the acceptance of all vaccines. So even flu vaccine rates are down.
- Covid vaccine is, I don't know 17%.
- It's a little better. In older adults. Flu vaccine. We do. Okay, maybe 50% of older adults get flu vaccine, and Rsv is significantly below that still
- and then separate, but related in terms of your point about multiple vaccines. At the same time, where we stand with the multivalent Mrna vaccines. They're working on it. They're definitely working on it. I think that the obvious choice
- would be Mrna.
- And the the problem with Mrna is, it's a little more reactogenic. And so you you mix Rsv
- flu metapneumovirus. And the other thing is that some things change and some things don't.
- And so, you know, marrying Rsv, which hopefully won't change to flu vaccine, which every year you have to update. It is a problem. Rna is adaptable. So we have to. We have to deal with. And they're working on ways to make it less reactogenic. So it would be more acceptable
- to people. But people are working on it, you know. My, my! The Holy Grail is resp of ax, you know you. You go in in October, you get shot up. You get protected for all this winter time. Crud, so
- the other

- sort of missing part of the management strategy is, that is an effective antiviral. Yes, and I didn't. Where do we stand? I mean, I know about some of the data with the, you know, fusion and nuclear protein and polymerase inhibitors. But so far nothing is really
- stood out dramatically, except perhaps for the rest of your, if you believe those data.
- yeah, that well, that didn't work in adults. There was something made by Arc that is, in from China that seemed very promising in children. One of the problems with antivirals in adults is.
- it takes some
- 5 or 6 days to get sick enough to come to the hospital, which is generally, you know, it makes the job of an antiviral more difficult flu. People come in a little sooner, because they have a high fever and they feel terrible. So you have a shot at it.
- and we definitely need them particularly for immunocompromised populations, and there will always be vaccine failures. And one of my issues with the whole antiviral film field is they keep doing challenge studies to show they work and they do the wrong challenge. Studies they like. Give them the drug
- when they're Pcr positive before they have any symptoms like, well, that doesn't mean anything. I mean, you're not going to treat somebody before they know they have an infection. So there's a lot of issues that need, but I think we need them. But we're not very far along.
- Thanks, Ann. Just wondering what's the reservoir for? Rsv. Is it younger children? Primarily in terms of for the elderly population like we don't think of it circulating in
- adults. Regular, healthy adults, you know the way covid and flu.
- you know, is kind of the general population, and it can spread. Just wondering if what was known about the reservoir. Rsv. I mean, I think that the main perpetrators are school age kids.
- the school age child, you know, in Karen Hall in Rochester, did a lot of these studies, brings it into the home, and then gives it to the vulnerable baby and to the old people where it's circulating in the summer, like, you know, I think it's probably the same as for flu and other respiratory viruses, that there are rare infections that people don't know. If you do these year round. Surveillance studies, you know. It's like amazing. You'll find flu in the summer. It's like.
- well, I didn't think that happened, but it does. And you know, particularly immunocompromised hosts who shed it for a long time. It's in that population there's no animal reservoir. It's not that poor chimp. The poor chimp got it from the handler.
- Yeah. And so, following up on Eric's question,
- and maybe sort of apropos with the chimp question, if there is a circulation that goes from kids, maybe to adults, and then we bring it into nursing homes. What does that suggest is potentially like interventions thinking about? Would this be a vaccine that we should be thinking about potentially if there are data for healthcare workers to prevent outbreaks in nursing homes. It's always been generally difficult to vaccinate one population. If you don't think that population has a benefit
- to benefit another population, and we know from flu vaccine. They showed nicely in
- vaccinating Japanese school children that the rates in elderly people went down. We know from nursing homes, that if you vaccinate the staff it does better than vaccinating the residents themselves, because they didn't have a very good response. So your point is well taken.

- but unless there's a real benefit to that group, you're vaccinating. People are not generally not anxious to do it, and we'll still have that lingering guillain-barre like, do you really want to vaccinate a healthy 40 year old with a vaccine? They don't really need to protect
- grandma. So we're we're not sure yet.
- Okay, thank you.