RSV vaccine recommendations and ACIP meeting recap with Sandra Fryhofer, MD [Podcast]

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AMA Update

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Who should get vaccinated for RSV? What are the side effects and safety concerns for RSV vaccines? Your vaccine questions answered by in-house expert Sandra Fryhofer, MD—the AMA ACIP liaison and AMA’s immediate past board chair. Dr. Fryhofer shares everything physicians need to know about the new recommendations from CDC’s Advisory Committee on Immunization Practices (ACIP) for both RSV vaccines. AMA Chief Experience Officer Todd Unger hosts.

Speaker

- Sandra Fryhofer, MD, AMA liaison, ACIP; immediate past board chair, AMA

Transcript

Unger: Hello and welcome to the AMA Update video and podcast. Today we're talking about new recommendations for RSV vaccines from ACIP, the CDC’s Advisory Committee on Immunization Practices. Here with us today is the AMA's in-house vaccine expert, our AMA ACIP liaison and the AMA's immediate past board chair Dr. Sandra Fryhofer. I'm Todd Unger, AMA's chief experience officer in Chicago. Dr. Fryhofer, thanks for joining us today.

Dr. Fryhofer: Well, Todd, thanks for having me back.

Unger: Sounds like you’ve been very busy first at VRBPAC where the FDA’s Independent Advisory Committee recommended strange changes to update the COVID vaccine. And now the ACIP met for three full days last week. What do we need to know?
Dr. Fryhofer: Well, Todd, it has been a vaccine update marathon. The biggest game changer was ACIP's new recommendation for RSV vaccines for adults. The first ever vaccines for RSV were FDA approved just last month in May 2023 for adults 60 and older. Both have now been recommended by ACIP for those 60 and older under shared clinical decision making, meaning you and your patient have to decide.

This was not the strongest recommendation that ACIP could have given for these shots. It was not a blanket recommendation that all adults in this age group should get the RSV vaccine. ACIP stopped short of saying that. But now these two RSV vaccines are available for those 60 and older.

Unger: Well, let's start by talking about the differences between the two available RSV vaccines.

Dr. Fryhofer: Well, both vaccines are referred to as RSV preF vaccines, which means they're based on the RSV fusion protein RSV F, which has been stabilized in a prefusion conformation. One by GSK called Arexvy contains a recombinant subunit prefusion RSV glycoprotein F antigen that's combined with GSK's proprietary ASO1 adjuvant. Now this is the same adjuvant that's in GSK's recombinant shingles vaccine Shingrix. But the amount of the average adjuvant in the RSV vaccine—it's only half as much.

The other RSV vaccine ABRYSVO is made by Pfizer. And it's also a prefusion RSV F vaccine. It does not contain an adjuvant, but it's bivalent, meaning it protects against two different RSV strains, RSV A and RSV B.

The study designs for each of the vaccines were different. So it's not possible to do a head-to-head comparison. However, both are extremely effective at preventing serious illness from RSV infection in older adults. The shared clinical decision-making vote for those 65 and older was a little surprising to me. The RSV vaccine workgroup had actually suggested a full recommendation for all adults 65 and older and suggested shared clinical decision making for the younger subset, those aged 60 to 64. However, the ACIP voting members disagreed.

Unger: Now you talked a little bit about the paradigm of shared decision making. Tell us a little bit more. What's that involved and how is it different from a full recommendation?

Dr. Fryhofer: Well, a full recommendation would mean that all adults in that age group should receive the vaccine. Shared clinical decision making is more complicated because you have to take into account the patient's individual characteristics, values and preferences, as well as the characteristics of the vaccine being considered.

Now understand that about 94% of adults hospitalized with RSV have underlying medical conditions. Nearly half of them, 48%, have three or more underlying medical conditions. The top three chronic medical conditions in adults hospitalized with RSV include heart disease, chronic lung disease and
diabetes. 28% of those hospitalized had congestive heart failure.

**Unger:** Now in addition to those, are there some other conditions that increase the risk of severe RSV?

**Dr. Fryhofer:** So risk of severe RSV disease is increased in those with chronic lung diseases such as COPD and asthma, heart problems like congestive heart failure and coronary artery disease, and also in those with kidney problems, liver disorders, blood disorders, neurological disorders and other endocrine problems, including diabetes. Data also show that medical risk factors can disproportionately affect certain racial and ethnic groups at earlier ages.

CBS's National Health Interview Survey looked at differences and prevalence of multiple chronic conditions by age and race/ethnicity. For those aged 60 to 65, there was a 10% difference in prevalence of multiple chronic medical conditions between Black adults as compared to those who are white. So for this reason, having the vaccine available to this younger age group can increase equity, especially for those with chronic underlying medical conditions.

**Unger:** Now I was just thinking back to the beginning of the pandemic when we had a great deal of folks who were in nursing homes at risk wondering if this is the same. Are patients in nursing homes at higher risk for RSV?

**Dr. Fryhofer:** Yes, residents of nursing homes and other long-term care facilities are also at extremely high risk and are very vulnerable to RSV outbreaks and serious illness as are patients with immunocompromising conditions, especially those who've had lung transplants, hematopoietic cell transplants, and those getting chemotherapy for lymphoma and leukemia. But, unfortunately, patients with immunocompromising conditions were not included in the clinical trials for these vaccines.

So how well these vaccines work in this population is unknown. Also, the studies did not include many older adults aged 75 to 80 and older. And this is an age group at highest risk of severe RSV complications. And these gaps in the vaccine clinical trial design were a source of angst in ACIP discussions.

**Unger:** I'm curious. What were some of the other discussion points at ACIP?

**Dr. Fryhofer:** Well, safety and price. And it was sort of odd. Neither company would disclose the final price of the vaccine. This lack of transparency about vaccine costs was surprising and somewhat frustrating.

In fact, one of the ACIP voting members even complained that none of us would buy a car before knowing how much it would cost. GSK finally did confirm a price range of $200 to $295 a dose. During the meeting, the Pfizer representative remained vague and said the company had not set the final list
price and left it at that. But the bottom line is this is an expensive vaccine.

**Unger:** And in that regard, is it a single dose, multiple doses? How many are recommended?

**Dr. Fryhofer:** Well, for now at least only a single dose is recommended. Protection from the GSK vaccine Arexvy did seem a bit more durable. RSV protection after the single GSK vaccine dose dropped in the second RSV season, but not quite as much. And for reasons that are unclear, a second shot booster didn't seem to help, which was sort of a conundrum. Both companies are doing studies looking at giving boosters after two years. And I am quite certain the companies will let us know if and when a booster is indicated.

**Unger:** Any background on side effects, safety?

**Dr. Fryhofer:** Well, there was a lot of discussion about that as well. Expected side effects include fatigue, headache, muscle aches and joint aches. There's an important safety concern that needs a closer look. And that's risk of GBS, Guillain-Barre Syndrome. GBS is a rare autoimmune neurological disorder characterized by ascending weakness and paralysis.

And FDA is actually requiring postmarketing surveillance for GBS for both manufacturers. There were a total of six patients with inflammatory neurologic events within 42 days of vaccination among the nearly 40,000 adults given one of these two RSV vaccines. Three cases were reported in studies for each of the RSV vaccine types. And at least two of these cases are likely GBS.

**Unger:** Now how common is GBS and what is the background incidence of GBS among older adults in this age group to begin with?

**Dr. Fryhofer:** Baseline GBS risk in the general population ranges from 0.4 to 2 cases per 100,000 in the U.S. The risk of Guillain-Barre increases with age. A meta-analysis of 13 studies that was presented to ACIP showed GBS risk range from 1.85 per 100,000 population for those in their 60s and increased up to 2.66 per 100,000 population for those in their 80s.

GBS is also more common in males. An analysis from CDC's vaccine safety data link looked at sex-based differences between GBS risk. For those 65 and older, the annual rate was 4.69 per 100,000 for females and 7.06 per 100,000 for males.

**Unger:** So how does that compare to GBS risk with other vaccines?

**Dr. Fryhofer:** Well, what we know so far is at least two of the GBS cases in the nearly 40,000 people who received RSV vaccine. And you may recall that GSK's Shingrix vaccine also carries an FDA warning about an increased risk of GBS, an extra three cases of GBS for every million Shingrix doses given. But there are six excess cases per million first Shingrix doses and no increased risk after the
second dose.

Data on GBS risk and seasonal flu vaccine is variable and inconsistent across flu seasons. The excess risk, if any, is about one to two additional cases per million doses of flu vaccine administered. The importance of determining if there is a link between RSV vaccine and GBS was highlighted by several ACIP members. And, again, both companies are conducting post-marketing surveillance for Guillain-Barre and also for supraventricular arrhythmias. There were 10 patients who received GSK’s Arexvy that had atrial fibrillation.

**Unger:** Now we think about where we are in the year. Believe it or not, the fall is not that far away and thinking about other vaccines. What are the guidelines regarding co-administration of RSV vaccines with other vaccines?

**Dr. Fryhofer:** Well, CDC says in accordance with CDC’s general best practices guidelines, it's OK to give RSV vaccines with other vaccines. But there is some concern that doing so could decrease immune response. A study looking at co-administration of RSV and flu vaccine did show antibody titers for both were somewhat lower with co-administration.

Coadministration can also magnify vaccine side effects. Remember that the GSK version of RSV contains the same adjuvant as shingles vaccine Shingrix. Shingrix is associated with some severe side effects for some. So it may be best not to give those two together. Post-marketing licensure safety monitoring of giving RSV vaccines with other vaccines is needed, and it will be very helpful.

**Unger:** When we think about the best time to get an RSV vaccine, is it kind of seasonal like flu, which means getting it in the fall?

**Dr. Fryhofer:** Well, in general, just like flu, RSV is seasonal with outbreaks typically starting in the fall and peaking in winter. But the timing of both the onset and peak of RSV can vary. RSV seasonality during the COVID pandemic deviated from prior seasons.

For example, in 2021, RSV started in the spring and peaked in July. This past year we had that tripledemic of flu, COVID and RSV in December. And that was terrible. The recommendation for now is vaccinated as soon as vaccine is available. But the reality is we probably won't have any RSV vaccine available until the fall.

**Unger:** So there are still some questions about safety, co administration and whether a second booster is going to be needed. Do you think that patients will agree to get it?

**Dr. Fryhofer:** Well, this vaccine will be life-saving for some, especially for those with multiple chronic medical conditions. However, many older patients and many primary care physicians may be unaware of the risk of RSV because we typically don't test for it. RSV is highly contagious. And just about every
child will have had it by the time they hit two years old.

For most of us, it causes just a nasty cold. But for the very young and the fairly and very old, bronchiolitis from RSV can lead to hospitalization, life-threatening pneumonia and even death. CDC says RSV is to blame for as many as 60,000 to 160,000 hospitalizations in those 65 and older each year. And anywhere from 6 to 10,000 of those people die.

We're also dealing with booster fatigue. And the thought of getting three different shots, RSV, flu and COVID all at the same time of year but not necessarily being able to get them all at the same time is somewhat daunting and may be difficult to implement.

Unger: Understandable. What about Pfizer's RSV vaccine for maternal vaccination? Can you tell us where things stand with that?

Dr. Fryhofer: Sure. RSV kills between 100 and 300 children under the age of five in the U.S. each year. Most infants, 68%, are infected and their very first year of life. And 79% of children less than two years old who get RSV had no underlying medical conditions. So this means that all young infants are at risk of RSV.

ACIP was presented with updates on studies of Pfizer's maternal RSV vaccine given between 24 and 36 weeks so protective antibodies against RSV could be passed on to the developing baby to protect the baby during their first few months of life. VRBPAC, FDA's Advisory Committee, had already reviewed these studies and voted 14 to 0 that the data supported effectiveness but voted only 10 to 4 that the data supported safety.

The big safety concern is possible increase in preterm births linked to vaccination. RSV is only FDA approved at this time for those age 60 and older. Also, a new monoclonal antibody niservimab to prevent RSV in infants was also discussed. Now it's also not FDA approved yet.

Unger: And I think this sounds like a teaser for a future AMA Update, Dr. Fryhofer. Thank you as usual for this thorough update and for all your work as AMA's liaison to ACIP. We'll have you back again soon when there's more news.

Dr. Fryhofer: Well, I would love to come back. And thank you so much again for having me, Todd.

Unger: Well, that wraps up today's episode. We'll be back soon with another AMA Update. You can find all our videos and podcasts at ama-assn.org/podcasts. Thanks for joining us today. Please take care.

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