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Help Protect Your Older Patients This Flu Season: Examining Real-World Data

Announcer:
Welcome to ReachMD. This medical industry feature, titled “Help Protect Your Older Patients This Flu Season: Examining Real-World Data,” is sponsored by CSL Seqirus. Here’s your host, Dr. Charles Turck.

Dr. Turck:
This is ReachMD, and I’m Dr. Charles Turck. Joining me for our conversation today is Dr. Stephen Pelton, who’s an author of a real-world study comparing the relative vaccine effectiveness of the adjuvanted trivalent influenza vaccine and the high-dose trivalent influenza vaccine in preventing test-confirmed influenza hospitalizations over three influenza seasons.

Dr. Pelton is a Professor of Pediatrics at the Boston University Chobanian and Avedisian School of Medicine and the former Director of Pediatrics Infectious Diseases at Boston Medical Center.

Dr. Pelton, welcome to the program.

Dr. Pelton:
Thanks for inviting me, Dr Turck.

Dr. Turck:
Well, to kick things off, Dr. Pelton, this study looked at real-world data. Can you tell us more about real-world evidence?

Dr. Pelton:
Sure. Real-world evidence uses data collected outside of randomized trials to develop clinical evidence about a medical intervention[1,2]

Real-world data can be collected prospectively from observational studies or retrospectively from electronic health records, large claims databases, or patient/disease registries.[2]

And so real-world evidence isn’t intended to replace clinical trial data in assessing the safety and efficacy of therapies, but rather they complement the evidence from randomized, controlled trials.

The randomized controlled trial data for adjuvanted influenza vaccine has shown that:[3]

- This vaccine met immunogenicity non-inferiority criteria compared to a non-adjuvanted, standard-dose influenza vaccine.
- And has a demonstrated safety profile. The most common local and systemic adverse reactions in adults 65 years of age and older were
    - injection site pain in 25 percent
    - injection site tenderness in 21 percent
    - myalgia in 15 percent
    - fatigue in 13 percent
    - and headache in 13 percent.

Each resolved over several days.

Dr. Turck:

Thanks for that context, Dr. Pelton. Now turning to the real-world study, could you give us a brief overview of the study's objectives and the rationale for this analysis?

Dr. Pelton:
This real-world study compared the relative effectiveness of adjuvanted influenza vaccine versus high-dose vaccine in preventing test-confirmed influenza hospitalizations in adults aged 65 years and older. As the severity of Influenza varies season to season, our study looked at data from three influenza seasons: 2017-2018, 2018-2019, and 2019-2020.[4]

Now, before we move onto the study details, I'd like to take a moment to discuss why studying this question in this population is so important.

Influenza disproportionately affects adults 65 years and older due to the decline in the vigor of the immune system, known as immunosenescence. This age group also has an increased frequency of comorbidities, thus a higher-risk population for complications from influenza.[5]

For example, influenza can exacerbate underlying chronic medical conditions, such as congestive heart failure and chronic obstructive pulmonary disease. And in high-risk groups, influenza infection is linked to neurologic, cardiovascular, and respiratory complications.[5]

In fact, taking a look at the last two pre-pandemic seasons—or the 2018-2019 and the 2019-2020 seasons—approximately half of hospitalizations and between two-thirds and three-quarters of the deaths from influenza in the US were in adults 65 years and older.[5,6]

In June of 2022, the US Advisory Committee on Immunization Practices recommended that adults aged 65 years and older receive adjuvanted or higher-dose influenza vaccines due to their enhanced immunogenicity and effectiveness.[7]

Previous studies generally showed no difference in effectiveness between adjuvanted and high-dose vaccines, and these studies relied mainly on clinical diagnostic codes used for billing. Such clinical diagnostic codes aren't always precise and can vary depending on physician practices.[8,9]

We took a different approach for this retrospective study to address the gap in evidence. We used test-confirmed influenza diagnoses as the outcome rather than clinical diagnostic codes. By focusing on test-confirmed cases, the outcomes are more accurately attributable to influenza and can provide a more precise comparison of vaccine effectiveness in order to offer valuable insights for the development of vaccine policy and clinical practice.[4]

Dr. Turck:
Now since multiple influenza seasons were studied, how might they have influenced the results?

Dr. Pelton:
Good question. So each season had distinct characteristics for adults 65 years and older:[10–13]

- The 2017-2018 season was highly severe with a peak in January and February and an absolute vaccine effectiveness of 17 percent
- The 2018-2019 season was longer, peaking in mid-February with a vaccine effectiveness of 12 percent
- And the 2019-2020 season was cut short by the COVID-19 pandemic, with a vaccine effectiveness of 39 percent.

These variations underscore the importance of analyzing each season individually to understand their specific impacts on vaccine effectiveness, as the severity and length of the influenza season could influence vaccine performance and study outcomes. This is why we perform both an analysis over the three years, as well as season-specific analysis; however, the season specific results were exploratory for single seasons due to limited statistical power.[4]

Dr. Turck:
I see. And when analyzing real-world data, confounders and biases may be introduced that a randomized controlled trial is more able to mitigate. So, Dr. Pelton, could you elaborate on how the researchers addressed potential biases to ensure the validity and reliability of the findings using these data?

Dr. Pelton:
Certainly. To start, the study used a test-negative design in which participants who sought care and were tested for influenza were categorized as either cases if they tested positive for influenza or controls if they tested negative. This design helps to ensure that the cases and controls are comparable in terms of their healthcare-seeking behavior to mitigate confounding related to seeking medical care.[4,14,15]

We analyzed data from the US Optum integrated dataset, which includes electronic health records and administrative claims from over 90 million patients. For this study, we focused on individuals aged 65 years and older who received either an adjuvanted or high-dose vaccine and had an influenza test within seven days of an emergency department visit or inpatient admission due to acute respiratory or febrile illness.[4]

Because we're examining real-world data and not data from a randomized controlled trial, we used robust statistical approaches to adjust for potential bias in this study. We combined two techniques—inverse probability of treatment weighting and logistic regression—to help balance out any differences between the treatment groups like age, location, the timing of testing, how likely individuals were to get tested. Using both methods can help reduce bias when comparing the vaccines. We also conducted sensitivity analyses, which are important to help validate the study results.[4,16,17]

Dr. Turck:
For those just tuning in, you're listening to ReachMD. I'm Dr. Charles Turck, and today I'm speaking with Dr. Stephen Pelton about a real-world study of the relative effectiveness of adjuvanted trivalent vaccine versus high-dose trivalent vaccine in preventing test-confirmed influenza hospitalizations among older adults.

So, Dr. Pelton, what were the main findings regarding the relative vaccine effectiveness of adjuvanted influenza vaccine versus high-dose influenza vaccine in this study population?

Dr. Pelton:
We found, in the pooled 3 season analysis, we generally saw no difference in effectiveness between the adjuvanted vaccine and high-dose vaccine in preventing test-confirmed influenza. For inpatient admission and/or emergency department visits, the relative vaccine effectiveness was a negative 2.5 percent, and for inpatient admissions only, it was a negative 1.6 percent. In both instances, the confidence intervals included zero, indicating no statistically significant difference in effectiveness between the vaccines.[4]

And the sensitivity analyses confirmed the robustness of the main findings. After adjusting for peak season and propensity to be tested, we demonstrated similar results, with confidence intervals crossing the null, further indicating no significant differences between the vaccines. This consistency suggests that the findings are reliable despite potential residual confounding.[4]

And although the season-specific analyses were exploratory, they provided valuable insights. In the 2017-2018 season, which was particularly severe, the relative vaccine effectiveness for inpatient admissions or emergency department visits was 1.6 percent, indicating that both vaccines performed similarly well under high influenza activity conditions. The 2018-2019 season showed a similar relative vaccine effectiveness of 1.6 percent, reinforcing the consistency of the findings across different seasons.[4]

The 2019-2020 season, with a point estimate of negative 15.2 percent, presented a different picture, likely due to the abrupt end of the season caused by the COVID-19 pandemic. This reduction in sample size and statistical power might have influenced the results. These variations highlight the importance of considering seasonal factors when interpreting the results. But even so, the overall trend across seasons generally suggested no difference in effectiveness between adjuvanted vaccine and high-dose vaccine.[4]

Dr. Turck:
Thanks for walking us through the results, Dr. Pelton. Now as we are discussing real-world data, what were the key strengths and limitations of this study?

Dr. Pelton:
Key strengths include the use of a large, real-world dataset, a robust test-negative design, comprehensive adjustment for biases, and data from three different influenza seasons.[4]

Specifically, the study's use of the US Optum integrated dataset provided a comprehensive view of influenza vaccine effectiveness in a real-world setting. By using a large dataset with extensive electronic health records and administrative claims data, we could adjust for a wide range of confounders, enhancing the robustness of the findings.[4]

Also, the inclusion of multiple influenza seasons helped to account for seasonal variability in influenza activity and vaccine performance, which enhanced the generalizability of the findings.[4]

The test-negative design is particularly powerful in vaccine effectiveness studies because it controls for healthcare-seeking behavior, ensuring that both cases and controls are comparable in this respect. Also, using test-confirmed influenza outcomes minimizes the risk of misclassifying influenza status.[4,14,15]

However, there are some limitations. The truncated 2019-2020 season due to the COVID-19 pandemic led to a smaller sample size and

broader confidence intervals, which could impact the statistical power of the findings, especially for season-specific analyses. Additionally, despite achieving good balance post-weighting, there could still be residual confounding due to unmeasured factors. Geographic differences in vaccine distribution could also introduce biases that might not be fully accounted for, even with extensive adjustments. Moreover, the broad definition of acute respiratory or febrile illness might have included cases that weren't directly comparable, potentially affecting the precision of the relative vaccine effectiveness estimates.[4]

Future vaccine could benefit from longer study periods to capture more influenza seasons, including those with varying severities and characteristics. Additionally, incorporating more granular data on patient demographics and comorbidities could help to further refine the adjustments for confounding factors. And finally, expanding the geographic scope of the study may help to address potential biases related to vaccine distribution and healthcare access.

Dr. Turck:
Now to wrap up, Dr. Pelton, can you give us an overview of the main takeaways from this study for healthcare providers and policymakers?

Dr. Pelton:
The study reinforces that there generally is no difference in effectiveness of adjuvanted vaccine and high-dose vaccine in preventing test-confirmed influenza hospitalizations among older adults. This evidence supports the current CDC Advisory Committee on Immunization Practices recommendations and provides valuable information for healthcare providers and policymakers when considering influenza vaccination strategies for older adults.[4,7]

The findings also confirm that both vaccines are viable options for protecting older adults against influenza, which offers flexibility in vaccine choice based on availability and patient preferences.[4]

Dr. Turck:
Those are great key takeaways as we end our discussion today. And I want to thank my guest, Dr. Stephen Pelton, for his insights on a real-world study of the relative effectiveness of adjuvanted trivalent influenza vaccine versus high-dose trivalent influenza vaccine in preventing test-confirmed influenza hospitalizations among older adults. Dr. Pelton, it was great speaking with you today.

Dr. Pelton:
It's been my pleasure, Dr. Turck

Dr. Charles Turck:
I'm Dr. Charles Turck.

Please stay tuned to hear some Important Safety Information.

Announcer:
FLUAD® (Influenza Vaccine, Adjuvanted)

INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION AND USAGE
FLUAD is a vaccine indicated for active immunization for the prevention of influenza disease caused by influenza virus subtypes A and type B contained in the vaccine. FLUAD is approved for use in adults 65 years of age and older.

This indication is approved under accelerated approval based on the immune response elicited by FLUAD. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS
Do not administer FLUAD to anyone with a history of a severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine, including egg protein, or to a previous influenza vaccine.

WARNINGS AND PRECAUTIONS
If Guillain-Barré Syndrome (GBS) has occurred within six weeks of previous influenza vaccination, the decision to give FLUAD should be based on careful consideration of the potential benefits and risks.

Appropriate medical treatment must be immediately available to manage potential anaphylactic reactions following administration of FLUAD.

Syncope (fainting) may occur in association with administration of injectable vaccines including FLUAD. Procedures should be in place to avoid injury from fainting.

The immune response to FLUAD in immunocompromised persons, including individuals receiving immunosuppressive therapy, may be lower than in immunocompetent individuals.

Vaccination with FLUAD may not protect all vaccine recipients against influenza disease.

ADVERSE REACTIONS
The most common (≥10%) local and systemic adverse reactions in adults 65 years of age and older who received FLUAD were injection site pain (25%), injection site tenderness (21%), myalgia (15%), fatigue (13%) and headache (13%).

Other adverse events may occur.

To report SUSPECTED ADVERSE REACTIONS, contact CSL Seqirus at 1-855-358-8966 or VAERS at 1-800-822-7967 and www.vaers.hhs.gov.

Before administration, please see the full US Prescribing Information for FLUAD.

This medical industry feature was sponsored by CSL Seqirus. If you missed any part of this discussion, visit Industry Features on ReachMD.com, where you can Be Part of the Knowledge.

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