From Data to Decisions:
The Evidence Base for 2025 Fall/Winter Immunizations

Summary of Preliminary Findings

Key Findings

- Respiratory viruses, including influenza, COVID-19, and respiratory syncytial virus (RSV) pose a significant threat to the health of all populations studied in this review.
- This initial systematic review and meta-analysis reviewed the evidence for children, immunocompromised adults, and pregnancy, and searched for more than 15 severe adverse events of special interest.
- Immunizations are an effective tool to reduce health risks for all populations from flu, COVID, and RSV, and have a strong safety profile. The studies reviewed since the 2023/2024 Advisory Committee on Immunization Practices (ACIP) meeting found no significantly elevated safety risks from US-licensed immunizations for these conditions.

Background and Methods

As the respiratory virus season approaches, influenza, COVID-19, and RSV are expected to circulate concurrently. Healthcare providers and the public require clear, accurate, and trustworthy information to support informed decisions. Immunization remains one of the most effective tools to prevent severe illness and death, but its impact depends on public understanding of when vaccination is recommended, why it matters, and confidence in the guidance provided.

The Vaccine Integrity Project convened a nationwide team of experts in epidemiology, infectious diseases, and research methodology to conduct a comprehensive and independent analysis of vaccine safety and efficacy data for influenza, COVID-19, and RSV immunizations. The search strategy included studies assessing the epidemiology of each virus, as well as data on vaccine effectiveness (VE), safety, and co-administration for US-licensed vaccines. The timeframe for study inclusion was anchored to the 2023/24 ACIP respiratory vaccine meeting, focusing on relevant literature published since the evidence was last comprehensively reviewed and incorporated into official guidelines. This review screened over 17,000 scientific abstracts, reviewed 1,406 full articles, and extracted detailed data from 590 studies. Each article was reviewed by at least two experts. This work is guided by a research protocol that has been externally reviewed and registered with PROSPERO, a global registry that promotes transparency in systematic reviews. The data presented at this meeting includes results for three populations of interest: pregnancy, children, and immunocompromised adults.

Results

Pregnancy

There were no significant, new epidemiologic data published regarding COVID-19 and RSV in pregnancy. One new study supported the effectiveness of influenza vaccination in pregnancy to

reduce medically-attended infections. The literature again identified the known potential increased risk of preterm birth with RSVPreF, particularly if given early in pregnancy. Implementation of a later receipt of vaccination (32-36 weeks of gestation) as recommended by updated CDC guidelines demonstrated no concerns with preterm birth. RSV vaccines given during pregnancy was demonstrated to be highly effective at preventing infant hospitalization. For all other pregnancy outcomes examined, the risk of adverse outcomes with COVID-19, RSV, or influenza immunization in pregnancy was similar to or less than not receiving immunization during pregnancy. No safety concerns were found for COVID-19, RSV, or influenza vaccine use for miscarriage, stillbirth, small for gestational age, placental abruption, or congenital anomalies.

Children

There was a moderate volume of new data regarding the epidemiology of COVID-19, RSV, and influenza among children of all ages. Most notable were severe, sometimes fatal cases of influenza-associated encephalopathy in children, most of whom had not received age-appropriate vaccination. Multiple studies provided new data demonstrating a protective effect of RSV (nirsevimab) and influenza immunization against medically-attended events and hospitalization. The review included several studies providing new data regarding the possible associations between COVID-19 vaccination and Guillain-Barré Syndrome (GBS) and myocarditis among children; no elevated safety concerns were identified. Additional pediatric vaccine effectiveness, safety studies, and co-administration analyses are ongoing.

Immunocompromised Adults

The largest volume of recent literature on respiratory vaccines for immunocompromised adults fitting the search criteria was regarding the safety and VE of COVID-19 vaccines. For the overarching population of immunocompromised adults, VE for COVID-19 vaccines was comparable in effectiveness to that of immunocompetent individuals. RSV vaccination was relatively less effective in hematopoietic stem cell transplantation (HSCT) patients; however, the increased risk for severe outcomes from RSV infection in this population is substantial. Additionally, there was an increased risk of GBS in adults over 60 years of age with the Abrysvo RSV vaccine; however, the total magnitude of risk was very low (0.003%).

Conclusions

This provides clinicians, pharmacists, and the American people access to the latest safety and effectiveness data to make informed decisions and guide conversations about flu, COVID-19, and RSV immunizations this fall. The American Academy of Pediatrics announced guidelines for children on August 19th, and additional immunization guidelines from medical societies are expected soon. The recorded meeting and slides are available on the Vaccine Integrity Project website; additional analyses of these data, including for the healthy adults, will be made available on the website, and a detailed manuscript with all populations is forthcoming.