INCREASING UNDERSTANDING OF ENHANCED INFLUENZA VACCINE PRODUCTS IN LONG-TERM CARE SETTINGS

Real-World Evidence: What It Says About Enhanced Influenza Vaccine Products

Key Points

Real-world evidence is derived from the analysis of data from electronic medical records, medical claims and billing data, information from product and disease registries, patient-generated data, and data gathered by personal devices and health applications.

Data collected for real-world evidence, which often come from clinical practice and medical records, are useful for verifying the safety and efficacy of enhanced influenza vaccine products. Real-world evidence also provides insights and expands understanding of how these products affect health at the population level.

When medications and biological agents such as vaccines reach the market, the U.S. Food and Drug Administration has already reviewed efficacy and safety data and approved the products for general use. Yet many of the studies used to obtain this approval exclude older adults and, more specifically, residents of long-term care facilities.

To compensate for this exclusion, researchers use data-mining techniques to study the real-world use of vaccines and other agents. Large databases contain electronic medical records, medical claims and billing data, information from product and disease registries, patient-generated data (sometimes from home settings), and data gathered by personal devices and health applications. Studies can be randomized trials (e.g., large simple trials, pragmatic clinical trials) or observational studies, conducted either retrospectively or prospectively.[1-3]

Identifying Real-World Data on Enhanced Influenza Vaccines

Bias is a primary threat to the validity of real-world studies. In vaccine studies, it is difficult to identify groups of patients and compare them because people who have chosen not to be vaccinated may also be less likely to present for medical care when they are ill. This creates selection bias. If comparisons are made with patients who have other conditions requiring routine medical care, they cannot be assumed to be "similar" to those with influenza. Patients presenting with influenza-like illness (ILI) who have pathogens other than the influenza virus often recover on their own and can be lost to follow-up thereby increasing the bias in results.

The test-negative case–control study was adopted for vaccine effectiveness research in recent years to overcome many of these concerns. As depicted in Figure 1 on the next page, eligibility for study inclusion is simply presentation with ILI. This assures similarity among those included in the analysis. All patients presenting with ILI and agreeing to be in the study are tested for influenza. Those testing positive become the "cases," while those with negative test results become the "controls."

Through patient interviews, reviews of medical records, or searches in immunization information systems, researchers determine who received the seasonal influenza vaccine for that year, when those patients were vaccinated, and which vaccine they received. No one is lost to follow-up because all data are collected at the incident visit. Percentages are calculated to determine vaccine effectiveness and statistical tests are used to assess significance and determine confidence intervals.[4]

The Centers for Disease Control and Prevention (CDC) uses a test-negative design in several networks to estimate vaccine effectiveness, including the U.S. Flu Vaccine Effectiveness Network and the Hospitalized Adult Influenza Vaccine Effectiveness Network (HAIVEN). Sites across the country participate in these networks through contracts with CDC, and many of these sites also participate in industry-sponsored research.

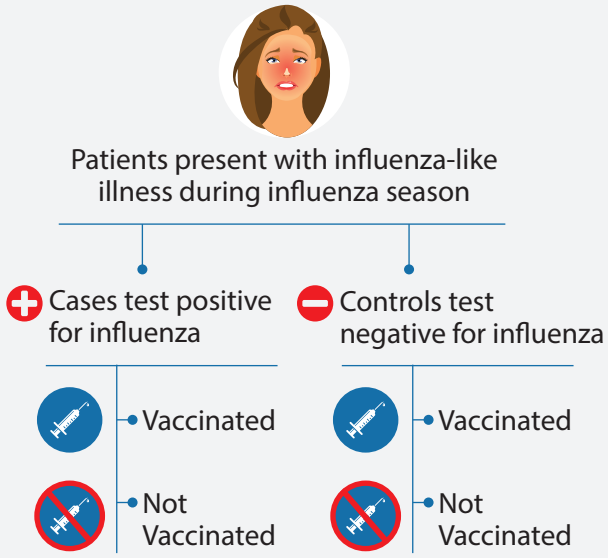
Real-World Evidence: Evaluating Enhanced Influenza Vaccines

Several studies illustrate other ways in which real-world evidence is used to compare effectiveness of enhanced influenza vaccines with standard formulations. When research on influenza is conducted in long-term care facilities, a cluster-randomized design is often used to clearly identify the effects of different vaccines on the individual as well as "herd" effects, such as reduced person-to-person spread.

Real-world studies of enhanced influenza vaccines include the following:

- The trivalent version of the high-dose enhanced influenza vaccine produced significantly higher antibody levels and better protection against laboratory-confirmed influenza illness, compared with the standard-dose trivalent vaccine, in a randomized, double-blind, active-controlled trial of 31,989 adults aged 65 years or older.[5]
- The high-dose enhanced influenza vaccine reduced respiratory-related hospital admissions compared with the standard-dose product during the 2013–14 influenza season. The study included residents aged 65 years or older in 823 nursing homes cluster-randomized to either the high-dose or standard-dose vaccine.[6]
- During the 2016–17 influenza season, an enhanced vaccine lowered all-cause hospitalizations by 6% and hospitalizations for influenza and pneumonia by 20% among 50,012 nursing home residents aged 65 years or older, compared with a standard trivalent influenza vaccine, in a cluster-randomized study.[7]

Figure 1. Test-Negative Design for Evaluating Influenza Vaccine Effectiveness



Resources

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