



Vaccine effectiveness

Informing decision-makers
with real-world evidence

Dr. Katia Bruxvoort, Dr. Hung Fu Tseng, and Lina Sy take a break outside of the offices in Pasadena.

Rreal-world evidence could be a critical component in creating federal policies and regulations about vaccines, but it hasn't always been considered. Scientists at Kaiser Permanente Southern California's Department of Research & Evaluation provide an example that shows the important role of real-world evidence in regulatory decision-making.

Real-world evidence is information obtained from real-life clinical settings. It provides insight into the potential risks and benefits of medical treatments. One way R&E researchers collect real-world evidence is through the electronic health records of our large and diverse patient population.

In this study, researchers examined the effectiveness of giving the live shingles vaccine at the same time as the pneumonia vaccine. Their aim was not only to confirm previous research, but also to show the importance of real-world evidence in light of legislation that requires the U.S. Food and Drug Administration to consider real-world evidence to support regulatory decision-making.

We asked the study authors Katia Bruxvoort, PhD, MPH; Lina S. Sy, MPH; Yi Luo, PhD, MS; and senior author Hung Fu Tseng, PhD, MPH, about the research they conducted, its findings and implications.

Why is this topic of real-world evidence for regulatory decision-making important now?

Evidence generated from randomized controlled trials has always been the gold standard when vaccines and drugs are being considered for licensure. The results of these trials are usually included in the product label.

Recently, there has been a greater interest in trying to use non-clinical trial data, such as real-world evidence, to expand or revise the label for new indications, new populations, new dosing modifications, potential drug interactions, or new safety concerns. Some drivers come from the fact that more and better real-world data are being collected from a variety of sources, including electronic health records.

Most important, recent legislation in the 21st Century Cures Act and the 6th Prescription Drug User Fee Act (PDUFA VI) calls for the FDA to utilize real-world data and to evaluate the use of real-world evidence in informing regulatory decisions.

What are some potential benefits for regulatory decision-making?

Real-world evidence from carefully designed and analyzed studies can fill in the evidence gaps that are not typically addressed with traditional randomized controlled trials. For example, real-world evidence can reflect the actual use of products in patients with multiple illnesses or rare diseases, who are often not included in clinical trials. It also can be used to evaluate long-term outcomes, which are often not assessed in clinical trials of modest duration. Real-world evidence may significantly reduce the time and cost of developing evidence for regulatory decisions.

Can you give us some background about your study?

A previous randomized controlled trial looked at people who received the shingles (live zoster) vaccine and the pneumonia (pneumococcal polysaccharide) vaccine at the same time and compared them to people receiving the vaccines 4 weeks apart. That study found patients who received the vaccines at the same time had lower levels of antibodies against the virus that causes shingles. Based on that, the FDA required changes to the vaccine labels to state that these vaccines should be given at least 4 weeks apart. However, studies have shown that antibodies are not a good marker of vaccine protection against shingles.

Can you give us some details about your study?

We conducted a study using almost 10 years of electronic health records from over 35,000 KPSC members who received the live shingles vaccine, and followed them electronically to see if they developed shingles. We found there was no difference in the risk of shingles between people who received the live shingles vaccine and pneumonia vaccine at the same time and those who received the vaccines at least a month apart.

Why does it matter whether people get the shots at the same time?

If we tell people to get their shots a month apart, fewer might get the vaccine because some may not return for the other shot. Allowing people to get both shots at the same time removes barriers for patients and helps to improve the vaccination rate.

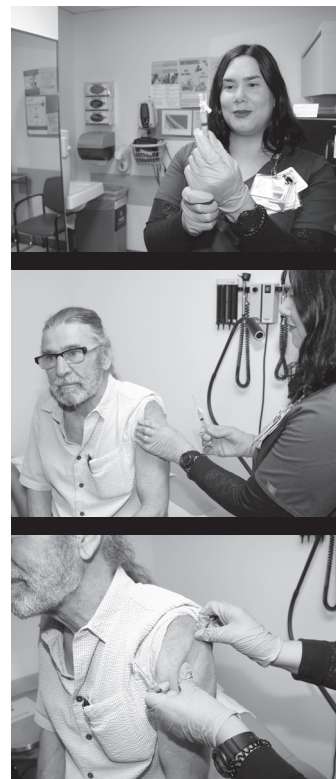
Why is this study a test case for regulatory decision-making?

Historically, the FDA relied on randomized controlled trial data for regulatory decision-making. This research is part of changing that paradigm. Using real-world evidence gives regulators a better idea of how vaccines will be used in actual clinical practice, rather than an ideal randomized controlled trial setting. This research, published in the *American Journal of Epidemiology* in early 2018, highlights how these findings from our integrated system can potentially be used to revise product labels and remove barriers to concomitant vaccination.

How can real-world evidence continue to shape regulatory decision-making for vaccines?

Real-world evidence will be even more critical in the evaluation of the safety and effectiveness of the new shingles vaccine (zoster vaccine recombinant, adjuvanted, or Shingrix). Randomized controlled trials show the new vaccine to be safe and effective, but limited data are available about its long-term outcomes, effects on high-risk populations, and potential interactions with other vaccines. The new vaccine is being used in the elderly, so it will be critical to monitor its safety and the effect of giving it at the same time as other vaccines. It also will be important to monitor compliance with the 2-dose schedule. We plan to study both the safety and the effectiveness of the new vaccine to address these evidence gaps.

The knowledge gained from the research conducted within Kaiser Permanente's integrated health care system can inform not just the care we give to our members, but can also shape national regulations and policies around immunization practices.



A patient receives a shingles vaccine at Los Angeles Medical Center.