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## Studies: Flu vaccine effectiveness waned over 2011-12 season

Robert Roos ■ News Editor

Jan 31, 2013 (CIDRAP News) – It's been more or less an article of faith that influenza vaccination in the fall will protect a person through the winter flu season, but three studies published today in *Eurosurveillance* are challenging that view.

All three studies suggest that during the 2011-12 flu season, the vaccine provided modest protection at first, but its effectiveness dropped sharply after 3 or 4 months.

A multicenter study by researchers in eight European countries indicated that overall vaccine effectiveness (VE) against influenza A/H3N2 in the first months of the season was 38%, but after mid-February it dropped to -1%.

Similarly, British researchers report that the vaccine had an overall effectiveness of 43% against H3N2 viruses from October 2011 to January 2012, but it dropped to 17% for February through April. And a study from Navarre, Spain, yielded similar findings, with overall VE of 61% against all flu types for the first 100 days after vaccination but zero effectiveness seen after 119 days.

"The concept that vaccine protection can be so short-lived provides a challenge for public health policy," says the British report. The authors say the findings raise the question of whether a second dose of seasonal vaccine might be needed for late-season outbreaks, and also point up "the pressing need for the development of influenza vaccines which provide better and longer-lasting protection."

The researchers say it's unclear how much of the drop in estimated VE was due to waning immunity and how much was attributable to late-season viral mutations (antigenic drift) or changes in the mix of circulating viruses.

### Multicenter study

All three studies used the test-negative case-control method, wherein patients with influenza-like illness (ILI) symptoms are tested for flu and asked whether or not they received a flu vaccine.

The multicenter study was part of the Influenza Monitoring Vaccine Effectiveness in Europe (I-MOVE) project, which has been assessing flu VE since 2008. It included 4,362 patients with ILI, of whom 2,084 tested positive for flu; about 85% had H3N2 infections.

After adjusting for various potential confounders, the researchers found that the whole-season, all-ages VE was 25% (95% confidence interval [CI], -6% to 47%), with a much higher 63% for those ages 15 to 59, but only 15% for those 60 and older.

Further, the authors found that overall effectiveness in the early part of the season, up to week 6 of 2012, was 38% (95% CI, -8% to 65%). After week 6, VE dropped to -1% (95% CI, -60%)

to 37%).

The report says there was some evidence of a suboptimal match between the 2011-12 vaccine and the H3N2 strains that circulated, and the mismatch might have increased during the season, possibly contributing to the lower VE seen late in the season.

But the researchers also note that it was a late flu season, causing a long delay between vaccination and peak flu activity. They say their data suggest that waning immunity may also be a plausible explanation of the late-season decline in VE.

"It is difficult to disentangle the respective roles of changes in the circulating viruses, possible waning immunity, and otherwise imperfect vaccine," they comment.

### **British and Spanish findings**

The British study included 3,869 patients, of whom 396 tested positive for H3N2 and 45 had influenza B. The researchers calculated that overall VE against H3N2 viruses was 23% (95% CI, 10% to 47%).

By time period, the estimated VE was 43% (95% CI, -34% to 75%) for the first 4 months of the season (October through January), but it dropped to 17% (95% CI, -24% to 45%) for the last 3 months.

When the researchers assessed VE according to the interval between vaccination and onset of ILI symptoms, they found it was 53% (95% CI, 0 to 78%) for those vaccinated less than 3 months and just 12% (95% CI, -31% to 41%) for those vaccinated more than 3 months.

The team also found that VE against influenza B was much higher than for H3N2: 92% (95% CI, 38% to 99%).

Besides suggesting that a second dose of vaccine might be needed in some cases, the British authors say their findings indicate that clinicians should suspect flu even in vaccinated patients and should have a lower threshold for prescribing antiviral drugs to prevent flu complications.

The Spanish study included 411 patients who tested positive for flu—93% for H3N2—and 346 controls who tested negative. The overall adjusted VE was 31% (95% CI, -21% to 60%), with 44% for those younger than 65 and 19% for those 65 and older.

By time period, VE was 61% (95% CI, 5% to 84%) in the first 100 days after vaccination, 42% (95% CI, -39% to 75%) between 100 and 119 days after vaccination, and zero after that. The waning protection occurred primarily in the elderly patients, the authors report.

"This finding could be explained by an immunosenescence phenomenon, aggravated by the long time between vaccination and virus circulation, which was longer than in most other seasons, and the limited match between vaccine and circulating strains," they write.

### **Breaking new ground**

Nicholas S. Kelley, PhD, a research associate at the University of Minnesota's Center for Infectious Disease Research and Policy (CIDRAP), which publishes CIDRAP News, said the three studies break new ground.

He said researchers have speculated about waning protection in one flu season, mainly on the basis of studies in seniors, adding, "This is the first real evidence that shows any reduction in how well the vaccine works over the duration of a season." Kelley is the co-author of a major report on flu vaccine effectiveness and related issues, released last October.

Kelley said the I-MOVE study suggests that the reported mismatch between the vaccine and circulating H3N2 strains "didn't really seem to have that much impact" and that the time between vaccination and ILI symptoms appeared to be more important. "Maybe the duration of immunity has a bigger role to play," he said.

He praised *Eurosurveillance* for publishing three studies that challenge the time-honored view that vaccine-induced protection lasts the whole flu season.

"It's still early data, but its commendable to publish something like that," he said. "It's never easy to publish something that doesn't fit with the things we like to say. It shows scientific integrity and a passion for the best data."

**Kissling E, Valenciano M, Larrauri A, et al.** Low and decreasing vaccine effectiveness against influenza A(H3) in 2011/12 among vaccination target groups in Europe: results from the I-MOVE multicentre case-control study. *Eurosurveillance* 2013 Jan 31;18(5) [[Full text](#)]

**Pebody RG, Andrews N, McMenamin J, et al.** Vaccine effectiveness of 2011/12 trivalent seasonal influenza vaccine in preventing laboratory-confirmed influenza in primary care in the United Kingdom: evidence of waning intra-seasonal protection. *Eurosurveillance* 2013 Jan 31;18(5) [[Full text](#)]

**Castilla J, Martinez-Baz I, Martinez-Artola V, et al.** Decline in influenza vaccine effectiveness with time after vaccination, Navarre, Spain, season 2011/12. *Eurosurveillance* 2013 Jan 31;18(5) [[Full text](#)]

#### See also:

Today's [CIDRAP News item](#) on this season's flu VE in Canada, UK thus far

Jan 11 CIDRAP News story "[CDC's early-season look finds flu vaccine 62% effective](#)"

Oct 15, 2012, CIDRAP News story "[Report: Complacency, misperception stymie quest for better flu vaccines](#)"