

Influenza Vaccine Less Effective on Elderly Than Thought

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February 27, 2012 — The benefits of influenza vaccination in the elderly may have been overestimated, a new analysis suggests.

In a survey of nearly 13 million older Canadians across 9 influenza seasons, lead author Kenny Wong, MPH, from the Institute for Clinical Evaluative Sciences and the Dalla Lana School of Public Health, University of Toronto, Ontario, Canada, and colleagues found that vaccination was associated with reductions in hospitalization for pneumonia and influenza (P&I) and a modest decrease in all-cause mortality during the influenza season, but not at other times of the year. These observations run counter to the findings of some earlier studies, in which vaccination was associated with large reductions in all-cause mortality even during non-influenza seasons.

These results were obtained through a technique known as instrumental variable (IV) analysis, which is designed to eliminate bias by controlling for unmeasured confounding. IV is "highly correlated with treatment and does not independently affect the outcome, so it is not associated with measured or unmeasured patient health status," the authors explain in their article, [published online](#) February 27 in the *Archives of Internal Medicine*.

In this study, the IV was census subdivision (CSD)-specific vaccine coverage, defined as the percentage of people aged 65 years or older living in a specific CSD in Ontario who received an influenza vaccine in a given influenza season. "Rather than compare patients with respect to whether they received influenza vaccination, IV analysis compares groups of patients that differ in the likelihood of receiving influenza vaccination," write Wong and coauthors.

This approach allowed the authors to control for possible unobserved biases that might not be accounted for with traditional randomization or standard regression modeling. For example, simply comparing outcomes among people who either did or did not get the vaccine would not account for other differences in health-related behaviors between the groups that could affect their morbidity and mortality.

Recent studies showing an association between influenza vaccination and mortality reduction among the elderly, even in non-influenza seasons, "suggest potential bias in such studies" and prompted the use of the IV method, the authors explain.

Data Collected Over the Course of 9 Influenza Seasons

To perform the study, they used information from health administrative databases in Ontario from the 9 influenza seasons from 2000-2001 through 2008-2009. The analysis included everyone older than 65 years who was living in the designated CSDs.

Overall, data were gathered on 12,621,806 individuals, of whom 7,345,891 (58.2%) had been vaccinated. There were 130,532 deaths and 62,913 P&I hospitalizations during the influenza seasons.

With standard regression modeling, vaccination was associated with a 33% reduction in mortality during influenza season (adjusted odds ratio [OR] .67; 95% confidence interval [CI], .62 - .72), and a 15% reduction after the influenza season (adjusted OR, .85; 95% CI, .83 - .86).

On IV analysis, the vaccination was associated with a 6% reduction in mortality during the influenza season (adjusted OR, .94; 95% CI, .84 - 1.03), which was insignificant. IV analysis also showed no association between the vaccination and any reduction in mortality after the influenza season (OR, 1.13; 95% CI, 1.07 - 1.19).

Data were adjusted for demographics, comorbidities, previous use of healthcare services, prescription medication use, and receipt of specific medical procedures.

For the composite outcome of P&I hospitalization or death, regression modeling showed a 26% reduction associated with the vaccine during influenza season (adjusted OR, .74; 95% CI, .70 - .78) and a smaller, yet still significant,

reduction afterward (adjusted OR, .88, 95% CI, .87 - .90). IV analysis showed a 14% reduction during the season (adjusted OR, .86; 95% CI, .79 - .92), but no reduction during non-influenza seasons (adjusted OR, 1.02; 95% CI, .97 - 1.06).

"The association between influenza vaccination and outcomes during non-influenza seasons is evidence that previous observational studies are biased," the authors write.

"With IV analysis, influenza vaccination was found not to be associated with reductions in post-influenza season P&I hospitalization or death."

Protective Effect Smaller Than Once Thought

These findings suggest that "the protective effect of the vaccine is much smaller than previously thought," M. Alan Brookhart, PhD, and Leah McGrath, MS, from the Department of Epidemiology, University of North Carolina Gillings School of Global Public Health, Chapel Hill, write in an editorial accompanying the study. The 6% reduction observed in this study may be close to "the maximum attainable benefit" of the influenza vaccine in this population.

Still, "current guidelines recommending annual vaccination against influenza for elderly individuals should remain in place until more definitive evidence has been amassed," Wong and colleagues conclude.

"[E]ven small reductions in outcomes during influenza season as a result of influenza vaccination would be worthwhile because it is a generally safe and relatively low-cost intervention."

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