Flu shot does not reduce risk of death

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The widely-held perception that the influenza vaccination reduces overall mortality risk in the elderly does not withstand careful scrutiny, according to researchers in Alberta. The vaccine does confer protection against specific strains of influenza, but its overall benefit appears to have been exaggerated by a number of observational studies that found a very large reduction in all-cause mortality among elderly patients who had been vaccinated.

The results will appear in the first issue for September of the *American Journal of Respiratory and Critical Care Medicine,* a publication of the American Thoracic Society.

The study included more than 700 matched elderly subjects, half of whom had taken the vaccine and half of whom had not. After controlling for a wealth of variables that were largely not considered or simply not available in previous studies that reported the mortality benefit, the researchers concluded that any such benefit "if present at all, was very small and statistically non-significant and may simply be a healthy-user artifact that they were unable to identify."

"While such a reduction in all-cause mortality would have been impressive, these mortality benefits are likely implausible. Previous studies were likely measuring a benefit not directly attributable to the vaccine itself, but something specific to the individuals who were vaccinated—a healthy-user benefit or frailty bias," said Dean T. Eurich,Ph.D. clinical epidemiologist and assistant professor at the School of Public Health at the University of Alberta. "Over the last two

decades in the United Sates, even while vaccination rates among the elderly have increased from 15 to 65 percent, there has been no commensurate decrease in hospital admissions or all-cause mortality. Further, only about 10 percent of winter-time deaths in the United States are attributable to influenza, thus to suggest that the vaccine can reduce 50 percent of deaths from all causes is implausible in our opinion."

Dr. Eurich and colleagues hypothesized that if the healthy-user effect was responsible for the mortality benefit associated with influenza vaccination seen in observational studies, there should also be a significant mortality benefit present during the "off-season".

To determine whether the observed mortality benefits were actually an effect of the flu vaccine, therefore, they analyzed clinical data from records of all six hospitals in the Capital Health region in Alberta. In total, they analyzed data from 704 patients 65 years of age and older who were admitted to the hospital for community-acquired pneumonia during non-flu season, half of whom had been vaccinated, and half of whom had not. Each vaccinated patient was matched to a non-vaccinated patient with similar demographics, medical conditions, functional status, smoking status and current prescription medications.

In examining in-hospital mortality, they found that 12 percent of the patients died overall, with a median length of stay of approximately eight days. While analysis with a model similar to that employed by past observational studies indeed showed that patients who were vaccinated were about half as likely to die as unvaccinated patients, a finding consistent with other studies, they found a striking difference after adjusting for detailed clinical information, such as the need for an advanced directive, pneumococcal immunizations, socioeconomic status, as well as sex, smoking, functional status and severity of disease. Controlling for those variables reduced the relative risk of death to a statistically non-significant 19 percent.

Further analyses that included more than 3,400 patients from the same cohort did not significantly alter the relative risk. The researchers concluded that there was a difficult to capture healthy-user effect among vaccinated patients.

"The healthy-user effect is seen in what doctors often refer to as their 'good' patients— patients who are well-informed about their health, who exercise regularly, do not smoke or have quit, drink only in moderation, watch what they eat, come in regularly for health maintenance visits and disease screenings, take their medications exactly as prescribed— and quite religiously get vaccinated each year so as to stay healthy. Such attributes are almost impossible to capture in large scale studies using administrative databases," said principal investigator Sumit Majumdar, M.D., M.P.H., associate professor in the Faculty of Medicine & Dentistry at the University of Alberta.

The finding has broad implications:

-- For patients: People with chronic diseases such as chronic respiratory diseases such as chronic obstructive pulmonary disease, immuno-compromised patients, healthcare workers, family members or friends who take care of elderly patients and others with greater exposure or susceptibility to the influenza virus should still be vaccinated. "But you also need to take care of yourself. Everyone can reduce their risk by taking simple precautions," says Dr. Majumdar. "Wash your hands, avoid sick kids and hospitals during flu season, consider antiviral agents for prophylaxis and tell your doctor as soon as you feel unwell because there is still a chance to decrease symptoms and prevent hospitalization if you get sick— because flu vaccine is not as effective as people have been thinking it is."

-- For vaccine developers: Previously reported mortality reductions are clearly inflated and erroneous–this may have stifled efforts at developing

newer and better vaccines especially for use in the elderly.

-- For policy makers: Efforts directed at "improving quality of care" are better directed at where the evidence is, such as hand-washing, vaccinating children and vaccinating healthcare workers.

Finally, Dr. Majumder said, the findings are a reminder to researchers that "the healthy-user effect is everywhere you don't want it to be."

Source: American Thoracic Society