

Estimation of influenza vaccine effectiveness (VE) using the test-negative case-control design

The seasonal influenza vaccine typically contains three inactivated viruses: two influenza A viruses and one influenza B virus.

It is the end of January 2013 and the influenza season 2012/13 has been very tough with a high influenza-activity and excess mortality among the elderly. In Denmark an influenza A (H3N2) virus has been dominant, comprising more than 95% of all influenza A viruses subtyped. A similar virus was in the seasonal flu vaccine, but the virologists at SSI claim that the virus circulating in Denmark has undergone genetic changes.

In February 2013 the WHO will decide which viruses that should be included in the next seasons influenza vaccine for the Northern hemisphere. This decision is based on virological and epidemiological information on the vaccine effectiveness (VE) from countries on the Northern Hemisphere in the current season.

SSI has access to information on all influenza tests taken in the country from the microbiologic database, as well as information on all vaccinations given to elderly above 65 y. You decide to estimate the VE against influenza A and B in a test-negative case-control design. Cases will be persons who test positive for influenza A or B and controls will be those who test negative for both influenza A and B.

A total of 1,443 patients aged ≥ 65 years were tested for influenza from 1 October 2012 to 27 January 2013. A total of 364 and 35 elderly tested positive for influenza A and B respectively. Among the 364 influenza A cases 165 were vaccinated and 199 were not vaccinated. Among the 35 influenza B cases 7 were vaccinated and 28 were not vaccinated. Among the 1044 elderly who tested negative for influenza, a total of 428 were vaccinated and 616 were not vaccinated. In the background population the vaccination coverage among the elderly is 44%.

The VE can be calculated from this formula $VE = (1 - OR) \times 100\%$

1. Try to make two by two tables to calculate:

VE against influenza A:

VE against influenza B:

2. What do the results indicate? Could the results be biased?

3. Would it be possible to estimate the flu VE in an observational cohort study? How could such a study be designed? And what kind of biases may be introduced in a cohort study?