Estimating vaccine effectiveness when there are sub-clinical infections

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The possibility of sub-clinical infections is an ever present problem when assessing the effectiveness of a vaccine. It may be that the vaccine provides partial protection against clinical symptoms, but does little to reduce transmission of the infection. This concern must be addressed when contemplating possible inclusion of the vaccine in an immunisation schedule. A model is formulated to describe the transmission of an infection in which some infected individuals meet the case definition, while others do not and may even be asymptomatic. The two settings considered are a community of uniformly mixing individuals and a community of households. The size of the epidemic and the size of household outbreaks are quantified. We explore the estimation of model parameters for three types of data:

(i) observe which participants of a vaccine trial acquire a serologically detected infection,
(ii) observe only which participants acquire an infection meeting the clinical case definition, or
(iii) observe who acquires an infection and whether the infection meets the case definition.

We consider measures of vaccine efficacy for

(a) protecting against infection,
(b) protecting against clinical symptoms, and
(c) reducing transmission.

Estimation of these measures is best from a study of household outbreaks in which all infections are observed and cases that meet the case definition are identified. Studies that observe only clinical cases can estimate the measures of vaccine efficacy, but generally require too many households to be practical.