Chapter 10
Household-Based Studies

10.1 Concepts of Household Studies

In Chapter 2 we introduced vaccine efficacy parameters that require conditioning on exposure to infection. Household studies were used as the basis for defining exposure to infection in vaccine studies as early as the 1930s in evaluating the efficacy of pertussis vaccines (Kendrick and Eldering 1939). In addition to evaluating vaccine efficacy, household studies have been used to learn about transmission and natural history of many infections. Aspects of the natural history studied in households include the transmissibility, the incubation and latent periods, the duration of infectiousness, and the serial interval between cases (Hope-Simpson 1952; Bailey 1957). Household studies have also been used to evaluate other interventions, such as post-exposure prophylaxis with influenza antiviral agents (Welliver et al 2001; Hayden et al 2004). Exposure to an infectious case within a household can be used as a natural challenge study, for example, when studying immunological correlates of protection (Storsaeter et al 1998). Longitudinal studies of pneumococcal carriage in households and schools have been used to estimate the acquisition and clearance rates for asymptomatic pneumococcal carriage.

The general idea of a transmission unit is that individuals make contact sufficient for transmission within it. Households are the most common form of transmission unit used in studies. It allows easy identification of contacts between a case and susceptibles, and families are convenient units of study. Many other settings are also used as transmission units in studies and analyses that condition on exposure to infection. These include sexual partnerships, classrooms, schools, school buses, airplanes, day care centers, and workplaces, among others. Here we talk mostly about household studies, but many of the study designs and analyses are applicable with possibly slight modification to other transmission units as well. The term household is much easier for exposition than is “transmission unit”.

Historically the use of household studies to evaluate vaccine effects focused on evaluating the protective effects of vaccination. The relative risk of developing illness in vaccinated compared to unvaccinated susceptibles exposed to cases in their
household was the basis of estimating the protective effects. In recent years, the vaccine effect on the ability to transmit the infection in vaccinated infected people compared to unvaccinated infected people, $VE_I$, has gained attention. In contrast to protective effects, $VE_I$ generally needs contact and exposure to infection information for its evaluation. An additional measure of interest is the overall reduction in transmission if both the infective person and the susceptible person who make contact are vaccinated compared to if neither is vaccinated, $VE_T$. The analysis is often based on the relative secondary attack rate (SAR), between the vaccinated and unvaccinated individuals of interest. The SAR is a special case of the transmission probability. The secondary attack rate is the probability that an individual infects another person during some period of time. The secondary attack rate can be estimated from the proportion of susceptibles who become infected when exposed to an infectious person. In the secondary attack rate, the contact between the infectious susceptible persons may be defined as occurring over some time period, such as the duration of infectiousness, or over the period of the study. For example, the household SAR is the probability that a susceptible individual living in the same household with an infectious person during his or her period of infectiousness will become infected (Fine et al 1988; Orenstein et al 1988).

Considering the estimates of VE based on the relative secondary attack rates, there are three main unstratified vaccine effects:

\[
VE_{S,1/0} = 1 - \frac{SAR_{1}}{SAR_{0}}, \quad VE_{I,1/0} = 1 - \frac{SAR_{1}}{SAR_{0}}, \quad VE_T = 1 - \frac{SAR_{11}}{SAR_{00}}. \tag{10.1}
\]

If one stratifies on the vaccine status of the infective person or the susceptible person, then there are four further stratified measures of $VE_S$ and $VE_I$:

\[
VE_{S,01/00} = 1 - \frac{SAR_{01}}{SAR_{00}}, \quad VE_{S,11/10} = 1 - \frac{SAR_{11}}{SAR_{10}}, \quad VE_{I,10/00} = 1 - \frac{SAR_{10}}{SAR_{00}}, \quad VE_{I,11/01} = 1 - \frac{SAR_{11}}{SAR_{01}}. \tag{10.2}
\]

Equations (10.1) and (10.2) give the three main unstratified and three stratified vaccine effects conditional on exposure to infection data, conditional on exposure to infection. The vaccine efficacies in (10.1) and (10.2) could also be defined in terms of the relative transmission probabilities or transmission rates.

Despite being widespread for some infections such as pertussis, household studies of vaccine effects have not generally been used for primary licensure efficacy trials. Household studies are sometimes nested within randomized controlled studies and provide secondary analyses. The primary analysis is generally based on one of the unconditional measures of vaccine efficacy, such as $VE_{S,IR}$ or $VE_{S,CI}$. When an exposure is determined to have occurred, for instance, when a sibling of a vaccine study participant has a case of pertussis, then the outcomes are evaluated in a secondary analysis. Household studies are also used in observational evaluation of