Trends in Microbiology

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Review

Household Transmission of Influenza Virus

Tim K. Tsang,[1] Lincoln L.H. Lau,[2] Simon Cauchemez,[3,4] and
Benjamin J. Cowling[1,4,*]

Human influenza viruses cause regular epidemics and occasional pandemics with a substantial public health burden. Household transmission studies have provided valuable information on the dynamics of influenza transmission. We reviewed published studies and found that once one household member is infected with influenza, the risk of infection in a household contact can be up to 38%, and the delay between onset in index and secondary cases is around 3 days. Younger age was associated with higher susceptibility. In the future, household transmission studies will provide information on transmission dynamics, including the correlation of virus shedding and symptoms with transmission, and the correlation of new measures of immunity with protection against infection.

Trends

Historically, household cohort studies have provided valuable information on the incidence of respiratory infections and risk factors for infection. However, these studies require substantial resources and can provide limited information on transmission dynamics.

Household transmission studies provide an efficient approach to describing the risk of influenza transmission and factors affecting transmission. In these studies, households with at least one member infected by influenza are eligible and are followed intensively for 1–2 weeks to observe secondary transmission within the household.

Transmission studies also provide a model for evaluation of interventions in randomized controlled trials, and have been used to determine the efficacy of antiviral drugs for treatment and prophylaxis, and nonpharmaceutical interventions such as face masks and hand hygiene.

Transmission of Human Influenza Viruses

Human influenza viruses cause regular epidemics and occasional pandemics. During influenza epidemics, high attack rates of generally mild and self-limiting illnesses cause a substantial public health burden, and a small fraction of infections are severe, requiring hospitalization [1]. Community-based studies of influenza virus infection and transmission have provided detailed information on influenza epidemiology since the 1920s [2], with a series of seminal studies in the 1950s, 1960s, and 1970s, the most comprehensive of which was the 10-year Tecumseh study of acute respiratory infections in households [3,4]. These studies conducted serologic and virologic testing of participants to determine the frequency of acute respiratory illnesses and identified the etiologic agents responsible. By enrolling entire households, these studies also examined transmission of respiratory pathogens, including influenza virus, identifying, for example, the importance of school-age children in introducing infections to the household [5].

More recently, an efficient study design known as the household transmission study has been increasingly used to study influenza virus transmission. During the 2009 influenza pandemic, this design was used to provide early estimates of transmission dynamics of the novel H1N1pdm09 strain, including the risk of infection among household contacts and the serial interval, defined as the time from symptom onset in the index case to the secondary case, and the severity of illnesses [6]. This review describes the methodology used in these transmission studies, the main findings of the studies on the transmission dynamics of human influenza viruses in households, and the potential for further research using this study design to provide answers to important outstanding questions on influenza.

Household Cohort Studies and Transmission Studies

Household cohort studies have been used to study influenza epidemiology for many years [4] and continue to provide useful insights on influenza epidemiology [7–17]. In a household cohort study, households are recruited prospectively from a sampling frame that typically includes the entire community, and some studies exclude households with one person. Participants in the

[1] WHO Collaborating Centre for Infectious Disease Epidemiology and Control, School of Public Health, Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong Special Administrative Region, China
[2] Dalla Lana School of Public Health, University of Toronto, Toronto, Canada
[3] Mathematical Modelling of Infectious Diseases Unit, Institut Pasteur, Paris, France
[4] These authors are joint senior authors.

*Correspondence: bcowling@hku.hk (B.J. Cowling).

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study are then followed up prospectively across one or more influenza epidemic, or influenza season, to identify infections and illnesses. In many cohort studies, sera will be collected from participants before and after influenza epidemics, to permit identification of infections by, for example, the proportion of individuals with a 4-fold or greater rise in antibody titer against a particular strain across an epidemic of that strain [18,19]. During an influenza epidemic, or in some cases throughout follow-up regardless of influenza activity, participants may keep symptom diaries to permit estimation of the incidence of acute respiratory illnesses. Collection of nasal swabs or other respiratory specimens from ill participants, or at regular intervals from all participants regardless of illness [20], can permit virologic identification of specific pathogens causing those illnesses, including influenza viruses.

An advantage of household studies is the efficiency of simultaneously following up multiple individuals in households rather than separately following up the same number of people independently selected from the population. Compared with other types of close contacts, household contacts are easier to identify and follow up, and they provide a well-defined number of susceptible people that are likely to have been exposed to infection, compared with other settings such as schools, offices, or hospitals. Household cohort studies can also permit inference on the transmission dynamics of influenza in households, providing valuable data on transmission in the broader community because a substantial fraction of influenza virus transmission events do occur in households [21,22]. However, in many cohort studies infections are ascertained by serologic analysis, which can have imperfect sensitivity and specificity, and only provides what is known as final size data in which the number of infected and uninfected household members is known at the end of each epidemic [5]. Specialized methods have been developed to permit inference on transmission dynamics (who was infected by whom) based on final size data, allowing for the risks of acquiring infection from outside or inside the household [5,23,24]. It can be challenging to explore heterogeneities in transmission dynamics due to individual characteristics, for example age, when only final size data are available [7]. In addition, it is not possible to estimate the serial interval based on final size data, although this epidemiologic parameter, measuring the average time between illness onset in an infected person and a secondary case infected by that person, is an important parameter for mechanistic models (also called mathematical models) of influenza epidemics that are often used for policy planning [22,25]. Some of these limitations can be ameliorated by careful collection of respiratory specimens from ill individuals, although intense follow up for illnesses over a prolonged period is challenging and demands considerable resources [26,27].

While cohort studies can provide valuable data on influenza and other acute respiratory illnesses, there are a number of limitations, the greatest of which is the substantial resources required to establish and follow up a cohort of hundreds or typically thousands of participants over a series of influenza epidemics. Furthermore, in areas where influenza seasons are difficult to predict, for example in tropical and subtropical regions, collecting well-timed pre-epidemic and post-epidemic sera can be difficult [7–9,28–32], leading to difficulties in interpreting serological data. Cohort studies were established to determine the cumulative incidence of H1N1pdm09 infections in 2009, but most such studies could not be established quickly enough to collect baseline pre-epidemic sera [30]. Finally, as mentioned above, it is difficult to characterize heterogeneity in transmission dynamics using cohort studies.

One particular study design that has been introduced to characterize the risk of transmission and heterogeneity in transmission risk is the household transmission study, also known as the case ascertained study [6,33]. In a household transmission study of influenza, in contrast to a traditional cohort study as described above, households are eligible for enrolment only after at least one household member has been identified as having an acute influenza virus infection [34]. This case can be referred to as the index case, and the other members as household