

HOUSEHOLD AND COMMUNITY TRANSMISSION OF THE ASIAN INFLUENZA A (H2N2) AND INFLUENZA B VIRUSES IN 1957 AND 1961

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Abstract. This study analyzed the distribution of the number of cases in households of various sizes, reconsidering previous survey data from the Asian influenza A (H2N2) pandemic in 1957 and the influenza B epidemic in 1961. The final size distributions for the number of household cases were extracted from four different data sources ($n = 547, 671, 92$ and 263 households), and a probability model was applied to estimate the community probability of infection (CPI) and household secondary attack rate (SAR). For the 1957 Asian influenza pandemic, the CPI and household SAR were estimated to be 0.42 [95% confidence intervals (CI): $0.37, 0.47$] and 7.06% (95% CI: $4.73, 9.44$), respectively, using data from Tokyo. The figures for the same pandemic using data from Osaka were 0.21 (95% CI: $0.19, 0.22$) and 9.07% (95% CI: $6.73, 11.53$), respectively. Similarly, the CPI and household SAR for two different datasets of influenza B epidemics in Osaka in 1961 were estimated as 0.37 (95% CI: $0.30, 0.44$) and 18.41% (95% CI: $11.37, 25.95$) and 0.20 (95% CI: $0.13, 0.28$) and 10.51% (95% CI: $8.01, 13.15$), respectively. Community transmission was more frequent than household transmission, both for the Asian influenza pandemic and the influenza B epidemic, implying that community-based countermeasures (eg, area quarantine and social distancing) may play key roles in influenza interventions.

INTRODUCTION

The world experienced three major influenza pandemics during the 20th century. These occurred in 1918, 1957 and 1968, and were caused by different antigenic subtypes of influenza A virus: H1N1, H2N2 and H3N2, respectively. These pandemics have been referred to as the Spanish, Asian and Hong Kong influenza pandemics, respectively, based on informally identified origins (Kilbourne, 2006).

It is generally acknowledged that the Spanish flu pandemic was the most serious (Crosby, 2003). Although the next pandemic strain could potentially be different from the three that have gone before, the recent emergence and spread of avian influenza virus H5N1 has raised considerable public health concern. To prepare for the next pandemic with effective controls and tight management, an understanding of the epidemiological patterns of previous pandemics is crucial. However, many questions remain in regard to influenza epidemiology (Taubenberger and Morens, 2006).

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Previous epidemiological data has been particularly useful for quantifying transmission potential. The basic reproduction number, R_0 , defined as the average number of secondary

cases arising from the introduction of a single primary case into an otherwise fully-susceptible population, has been estimated, in various recent studies from around the world, to lie in the range of 1-3 for the 1918-1919 influenza pandemic (Mills *et al*, 2004; Chowell *et al*, 2006, 2007; Ferguson *et al*, 2006). Such estimates have been useful in the formulation of pandemic planning using recently-developed mathematical models. However, despite extensive studies on R_0 , the heterogeneous patterns of influenza transmission have hardly been investigated, and thus, remain to be clarified. For example, since historical data tend to provide only limited information (*eg*, temporal distributions of deaths or cases only), it is still unclear as to how community and household transmission probabilities characterize influenza epidemics. Since epidemiological methods matured during the mid- and late-20th century, records from the later Asian and Hong Kong influenza pandemics offer more detailed information than those from the Spanish influenza pandemic, allowing further clarification of transmission patterns. To date, community and household transmission parameters of Asian influenza have been inferred based only on one epidemiological study in Japan (Sugiyama, 1960, 1961; Longini and Koopman, 1982) and the subsequent works have had to rely on seasonal influenza data, mainly due to the lack of detail of pandemic data (Longini *et al*, 1982, 1988).

Given that the estimates are directly applied in simulation studies for pandemic planning, there should be some benefit in analyzing other datasets and examining whether the estimates differ by place and time. Extracting key information from historical records would be useful for policy making and thus, of public health importance (Nishiura, 2006a,b,c). The aim of this study was to reanalyze the distributions of the number of household cases, which were observed during the Asian influenza A (H2N2) pandemic in 1957 and the in-

fluenza B epidemic in 1961, and to investigate community and household transmission patterns.

MATERIALS AND METHODS

Data: historical observations of the number of household cases

This study used the final size distribution of the number of influenza cases per household as key information. The final size refers to the proportion of influenza cases arising from the total number of susceptible individuals at the end of a given epidemic period. Although the distribution of Asian influenza cases in households in Japan with three members was published in English (Sugiyama, 1960, 1961) and has been previously analyzed (Longini and Koopman, 1982), other Japanese epidemiologists have examined the relevant distributions in households of various sizes. Specifically, this study investigated the field survey results of the Asian influenza A (H2N2) pandemic of 1957 in Tokyo (Yamaguchi, 1957) and Osaka (Yamamoto, 1959) and the influenza B epidemic of 1961 in two different locations in Osaka (Horiuchi *et al*, 1964, 1965). From the Asian influenza study in Tokyo, the distributions of the number of cases in households with two, three and four members were extracted (547 households). In the Asian influenza study in Osaka (671 households) and the initial study of the influenza B epidemic in Osaka (92 households), the distribution was given for households with three members. The later study of the influenza B epidemic yielded the distribution for households with four members (263 households). The case definition during the Asian influenza pandemic was documented in detail and the survey was conducted by governmental health officers in Tokyo and Osaka (Public Health Bureau, Osaka City, 1957; Japanese Public Health Association, 1960). When differential diagnosis was needed among those exhibiting flu-like symp-

toms (*ie*, fever, shivering, chills, malaise, dry cough etc), the officers tentatively confirmed the infection, either by serological (*ie*, hemagglutinin inhibition test) or epidemiological methods (*ie*, contact investigations). Unfortunately, studies during the influenza B epidemic in 1961 were not accompanied by explicit documentation of the case definition, and thus, were based on syndromic surveys. During the Asian influenza pandemic, vaccination was not carried out on the public and was only tested in trials (*eg*, a trial limited to those working at the Transportation Bureau of Tokyo Metropolitan Government; Yamaguchi, 1957). Vaccination against the influenza B virus was not carried out before the period of the survey.

Statistical model

This study used a probability model for the final size distribution for the number of household cases, initially proposed by Longini and Koopman (1982). The model permits estimation of probabilities of transmission in the community and the household separately.

Let B denote the probability that a susceptible individual was not infected from the community during the course of the epidemic. Further, let Q represent the probability that a susceptible person escaped infection from a single infected household member. For a household with s initially susceptible individuals, the probability that k individuals will become infected is given by:

$$P(k|s) = \binom{s}{k} P(k|k) B^{s-k} Q^{k(s-k)} \quad \text{for } k = 0, 1, \dots, s-1; \quad (1-1)$$

$$P(s|s) = 1 - \sum_{k=0}^{s-1} P(k|s) \quad (1-2)$$

Fig 1 illustrates the use of equations (1-1) and (1-2) for households with three members. For households with three members, there are four possible outcomes at the end of the epi-

demical period, *ie* $k = 0, 1, 2$ or 3 . Since the studies of the Asian influenza pandemic in Tokyo and the later study of the influenza B epidemic in Osaka did not include a zero-class (*ie*, households without any cases were not surveyed), a zero-truncated distribution was needed, and thus, we used the following probability density function for these two datasets instead of equation (1-1):

$$P(k|s) = \binom{s}{k} \frac{P(k|k) B^{s-k} Q^{k(s-k)}}{1 - B^s} \quad (2)$$

where B^s is the expected frequency for the zero-class. The equations (1-1) and (1-2) can be reduced to simple formulae in the extreme case. When there is no transmission within the household (*ie*, $Q = 1$), equations (1-1) and (1-2) reduce to a binomial distribution (Haber *et al*, 1988):

$$P(k|s) = \binom{s}{k} (1 - B)^k B^{s-k} \quad (3)$$

for $k \leq s$. Thus, the expected number of cases, theoretically assuming that transmission occurs only in the community, is given by:

$$ns(1 - \hat{B}) \quad (4)$$

where n is the total number of observed households. In contrast, if there is transmission only within the household (*ie*, $B = 1$), this reduces to the final size distribution of the Reed-Frost model (Becker, 1989). The likelihood of estimating the parameters, B and Q , using equations (1) or (2), is given by:

$$L(Q, B) = \prod_s \prod_k P(k|s)^{a_{ks}} \quad (5)$$

where a_{ks} is the observed numbers of households with k cases among s susceptible individuals ($s = 1, 2, \dots, S$ and $k = 0, 1, \dots, s$).

The parameters of interest, Q and B , were

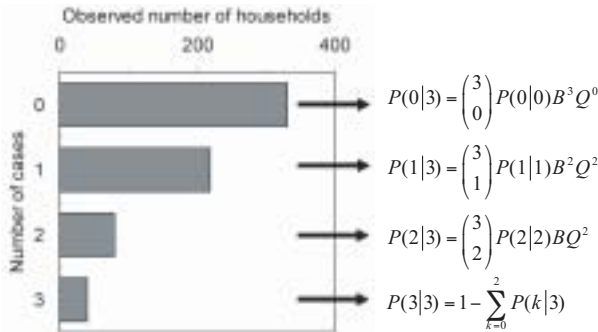


Fig 1—Household transmission model. The distribution of the number of cases in the households with three members is shown. In such households, there are 4 possible outcomes at the end of an epidemic period: there could be 0, 1, 2 or 3 cases in a household. For each frequency of the cases, a probabilistic model [see equation (1)] is applied. The probabilities, B and Q , which maximize the likelihood, would be the estimates of the community and household transmission parameters.

estimated by minimizing the negative logarithm of equation (5). The corresponding 95% confidence intervals (CI) were derived from the profile likelihood. By definition, community probability of infection (CPI) is given by $1-B$ which represents the community involvement in disease transmission. The expected number of cases arising from community transmission only, using equation (4), was calculated for completely observed data alone (*ie*, the Asian influenza in Osaka and the initial study of the influenza B epidemic). The probability, $1-Q$, indicates the probability of secondary transmission within households, where $100 \times (1-Q)$ provides an explicit measure of the household secondary attack rate (SAR). Supposing that β is the daily probability of transmission within the household, and let t_0 , t_1 and t_m be the times of infection, start and end of the infectious period, respectively, the following condition is given:

$$\begin{aligned} \beta &= 0 \text{ for } t_0 \leq t < t_1 \\ \beta &> 0 \text{ for } t_1 \leq t < t_m \end{aligned} \tag{6}$$

Assuming that $t_1 - t_0$ (latent period) and $t_m - t_1$ (infectious period) are 2 and 4 days (Kilbourne, 1975), respectively, β was estimated using the relationship between Q and β , applying equation (6):

$$Q = \prod_{t=t_0}^{t_m} (1-\beta) = (1-\beta)^4 \tag{7}$$

All statistical data were analyzed using the statistical software JMP IN version 5.1 (SAS Institute Inc, Cary, NC).

Summary of assumptions

In the above process, we made the following assumptions.

1. A person could become infected no more than once during the epidemic.
2. All individuals in the households were susceptible at the beginning of epidemic, since the new pandemic strain (H2N2) and influenza B viruses had not circulated extensively before the epidemics (this point is discussed later).
3. All subjects were members of a closed community. Each individual belonged to a single household.
4. Sources of influenza transmission were homogeneously distributed in the community. Household members mixed randomly within the household.
5. When the subjects were infected, this infection occurred either in the community or in the household. The probability of community transmission was independent of the number of infected members in the household the subject belonged to.

RESULTS

Table 1 compares the observed and expected frequencies of cases for households with two, three and four members, from the Asian influenza pandemic in Tokyo in 1957. The χ^2 goodness-of-fit test revealed no sig-

Table 1
Observed and expected frequencies of cases on a household level from the Asian influenza A (H2N2) pandemic (1957) in Tokyo, Japan.

Number of cases	Number of susceptible individuals per household					
	2		3		4	
	Observed	Expected	Observed	Expected	Observed	Expected
0	-	66.52 ^a	-	44.35 ^a	-	28.52 ^a
1	81	90.48	85	84.08	73	66.98
2	52	42.52	60	63.40	66	70.41
3	-	-	41	38.52	53	51.19
4	-	-	-	-	36	39.41
Total	133	133.00	186	186.00	228	228.00

^a Not included in the total. The χ^2 goodness-of-fit test revealed no significant deviation between observed and expected frequencies ($\chi^2_6 = 4.64$, $p = 0.59$).

Table 2
Observed and expected distributions of influenza cases in the households with three members in the Asian influenza A (H2N2) pandemic (1957) in Osaka city and influenza B epidemic (1961) in Temnouji, Osaka, Japan.

Number of cases	Influenza A (H2N2) in Osaka city, 1957		Influenza B in Temnouji, Osaka, 1961	
	Observed	Expected	Observed	Expected
	0	331	332.85	22
1	219	217.37	30	26.99
2	80	79.91	15	17.14
3	41	40.87	25	24.80
Total	671	671.00	92	92.00

The χ^2 goodness-of-fit tests revealed no significant deviation between observed and expected frequencies ($\chi^2_1 = 0.02$, $p = 0.89$ and $\chi^2_1 = 0.65$, $p = 0.42$, respectively).

nificant deviation between the observed and expected data ($p = 0.59$). The maximum likelihood estimates of B and Q were 0.58 (95% CI: 0.53, 0.63) and 0.93 (95% CI: 0.91, 0.95), respectively. Consequently, CPI and household SAR were estimated to be 0.42 (95% CI: 0.37, 0.47) and 7.06% (95% CI: 4.73, 9.44), respectively.

Table 2 documents the distributions of cases in households with three members from the Asian influenza pandemic in Osaka, 1957,

and the initial study of the influenza B epidemic in Osaka in 1961. The probabilities, B and Q , were 0.79 (95% CI: 0.78, 0.81) and 0.91 (95% CI: 0.88, 0.93), respectively, for the Asian influenza A pandemic, and consequently, CPI and household SAR were estimated to be 0.21 (95% CI: 0.19, 0.22) and 9.07% (95% CI: 6.73, 11.53), respectively. Analysis of influenza B epidemic data demonstrates that B and Q were 0.63 (95% CI: 0.63, 0.70) and 0.82 (95% CI: 0.74, 0.89), and thus, the CPI and house-

Table 3

Observed and expected distributions of cases in the households with four members in the influenza B epidemic (1961) in Toyonaka and Osaka cities, Japan.

Number of cases	Observed	Expected
0	-	175.09 ^a
1	129	129.36
2	65	65.06
3	36	35.65
4	33	32.92
Total	263	263.00

^a Not included in the total. The χ^2 goodness-of-fit test revealed no significant deviation between observed and expected frequencies ($\chi^2_1 < 0.005$, $p = 0.95$).

hold SAR were 0.37 (95% CI: 0.30, 0.44) and 18.41% (95% CI: 11.37, 25.95), respectively. No significant deviation was found between the observed and expected data for either distribution ($p = 0.89$ and 0.42 for the Asian influenza pandemic and the influenza B epidemic, respectively).

Table 3 shows the zero-truncated distribution for households with four members from the later study of the influenza B epidemic in Osaka in 1961. The χ^2 goodness-of-fit test revealed no significant deviation between observed and expected data ($p = 0.95$). The maximum likelihood estimates of B and Q were 0.80 (95% CI: 0.72, 0.87) and 0.89 (95% CI: 0.87, 0.92), respectively. Thus, CPI and household SAR were estimated to be 0.20 (95% CI: 0.13, 0.28) and 10.51% (95% CI: 8.01, 13.15), respectively.

Using the above-estimated probabilities, Q , obtained from each dataset, the daily probability of infection within the household was estimated to be 0.018 (95% CI: 0.012, 0.024), 0.023 (95% CI: 0.017, 0.030), 0.049 (95% CI: 0.030, 0.072), and 0.027 (95% CI: 0.021,

0.034), respectively, for the Asian influenza A pandemics in Tokyo and Osaka and two studies on the influenza B epidemic in Osaka. For the Asian influenza pandemic in Osaka ($n = 671$) and the initial study of the influenza epidemic B in Osaka ($n = 92$), the theoretically expected number of cases allowing community transmission only would have been 419.5 ($= 671 \times 3 \times 0.208$) and 101.9 ($= 92 \times 3 \times 0.369$), respectively. These exceeded the observed number of cases (*ie*, 340 and 70 cases) in both studies.

DISCUSSION

This study analyzed the distribution of influenza cases observed in households of various sizes to investigate the community and household transmission probabilities. Relatively unknown data from the Asian influenza A pandemic of 1957, and the influenza B epidemic of 1961, were used to extract the key information. The simple model was adequately and successfully fitted to all the household-level influenza datasets. The model indicated that community transmission played a more important role than household transmission for both the Asian influenza pandemic and the influenza B epidemic. The transmission probability within households was estimated to be small.

To date, the community and household transmission parameters for pandemic influenza have only been estimated by Longini and Koopman (1982) and the remaining relevant estimates have been derived from seasonal influenza data (Longini *et al*, 1982, 1988). In a previous study of Asian influenza, the CPI and household SAR were suggested to be 0.114 and 17.6%, respectively, which are broadly consistent with our findings. For both influenza A and B viruses, our results indicate the importance of community transmission, and moreover, our estimates also suggest that within-household transmission is slightly less

important than previous estimates have suggested (Longini and Koopman, 1982). Although a recent household study using different assumptions and datasets (*ie*, time series data of seasonal influenza) claimed a relatively smaller CPI (Cauchemez *et al*, 2004), we were only able to apply the estimation framework (and associated assumptions) of Longini and Koopman (1982) for the historical data used in the present study, and our results were consistent with previous findings reported for the Asian influenza pandemic. In practical terms, our findings imply that community-based interventions (*eg*, area quarantine and social distancing measures) may play key roles in determining the effectiveness of pandemic countermeasures. This agrees with the results of recent mathematical studies which have suggested that hospital and community transmission control measures alone may be highly effective in reducing the impact of a potential influenza pandemic (Ferguson *et al*, 2006; Nuno *et al*, 2007).

Two technical issues have to be discussed in relation to the fact that the expected number of cases resulting from community transmission alone exceeded the observed total number of cases. The first and most likely reason for this relates to error when calculating the secondary attack rate using household data. Since the actual transmission process involves some reduction in susceptible individuals due to spread within households, the use of *ns* in equation (4) may lead to overestimation of the expected number of cases following community transmission. The second is concerned with the possible background immunity in the population due to previous exposure to the influenza virus. A slight overestimation may have resulted from the presence of immune individuals (Kemper, 1978, 1980), since the subtypes of influenza A virus, H2N2, and influenza B virus were known to have circulated before the pandemic (epidemic) period (Masurel and Marine, 1973). As observed

in the Hong Kong pandemic (H3N2) in 1968, elderly individuals in the household may have been partially immune (Fukumi, 1969). However, considering that the pandemic strain probably underwent an antigenic shift involving genetic reassortment shortly before 1957, and given the extremely small proportion of immune individuals, our general conclusion, suggesting the importance of community transmission, is still valid. The influenza B virus is also not documented to have caused large epidemics before 1961. Despite this trivial limitation, our study was motivated by a critical need to estimate community and household transmission parameters from existing data to aid public health policy formulation.

In summary, this study estimated the community and household transmission parameters of influenza using household datasets from the Asian influenza pandemic of 1957, and the influenza B epidemic of 1961, and showed that the probability of infection via community transmission was relatively high. Because of differences in estimates according to time and place, and because the validity of the assumptions needs to be explicitly explored with additional data, further clarification of this point is the subject of our ongoing work. Because little is known about the intrinsic dynamics (*ie*, natural history and mechanism of spread) of influenza, we believe that this study partially satisfies a need for more epidemiological evidence on community and household transmission patterns.

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