Supplementary Information

Aerosol transmission is an important mode of influenza A virus spread

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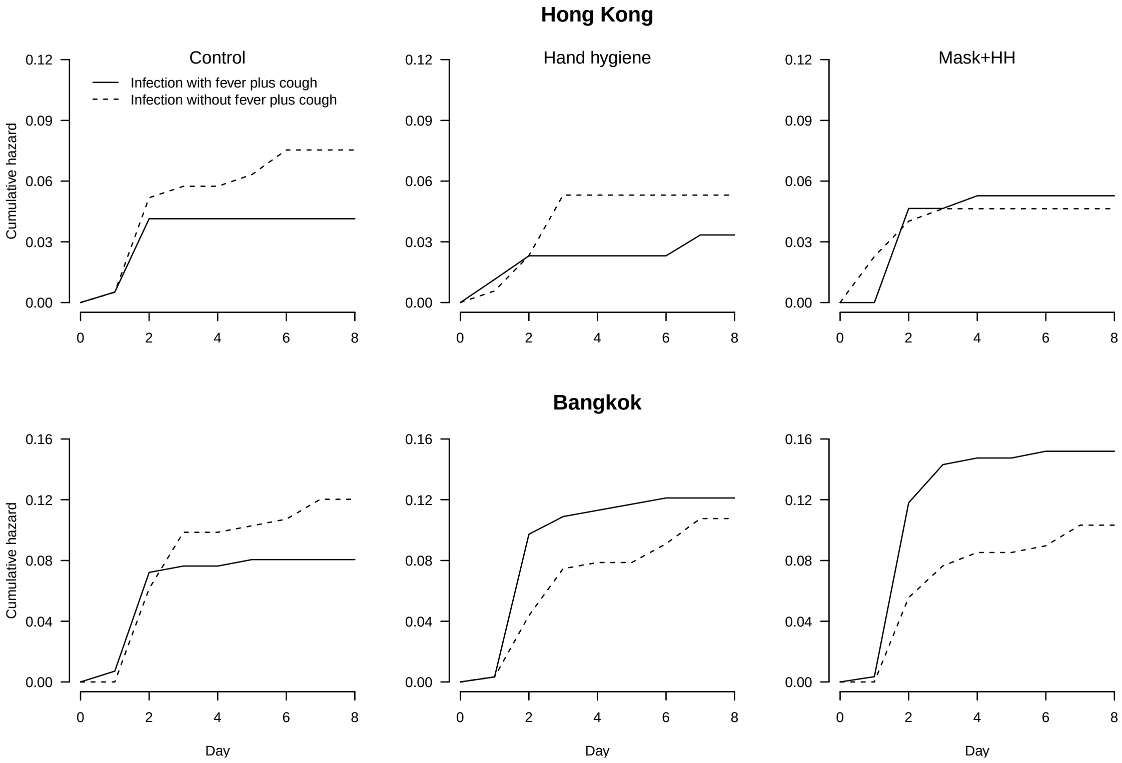
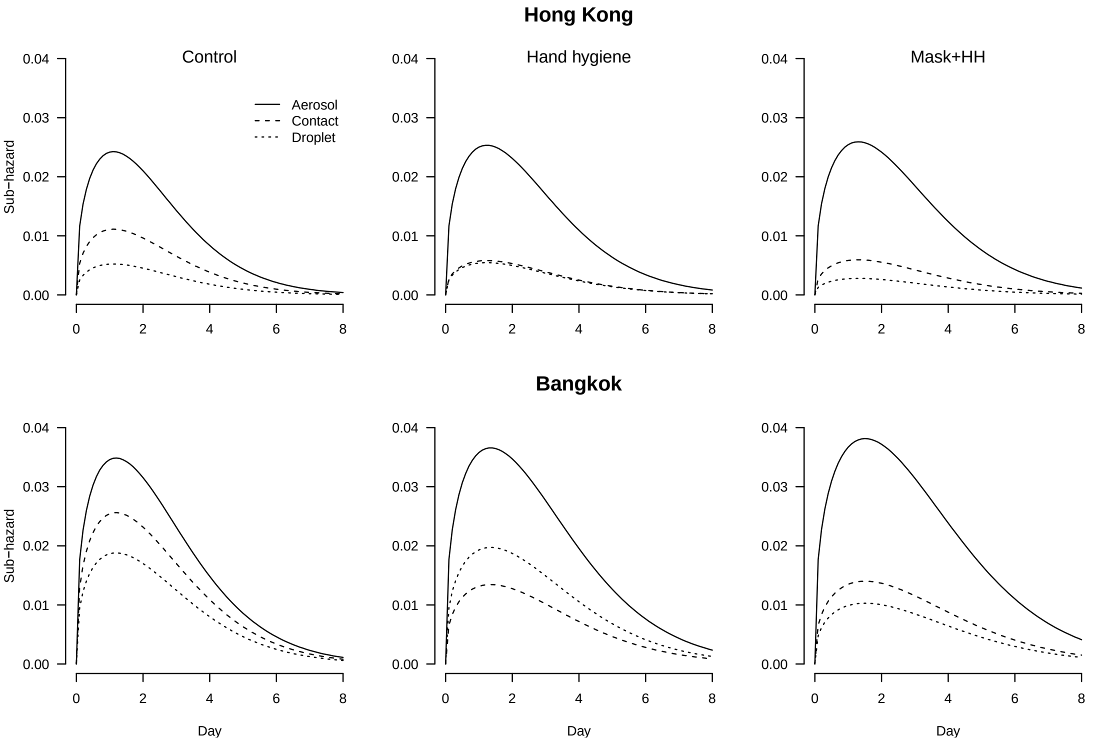
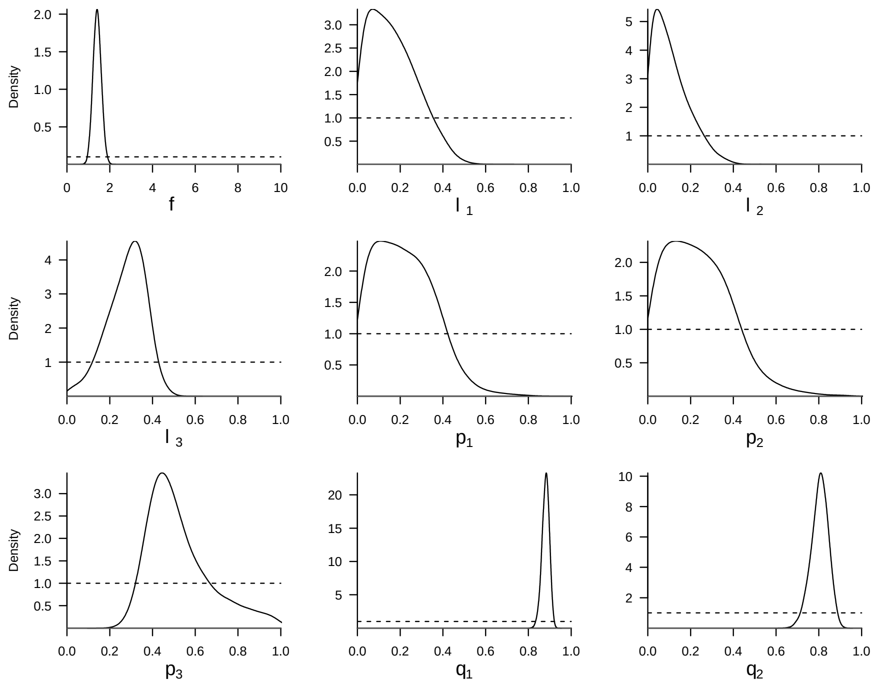
Supplementary Figures



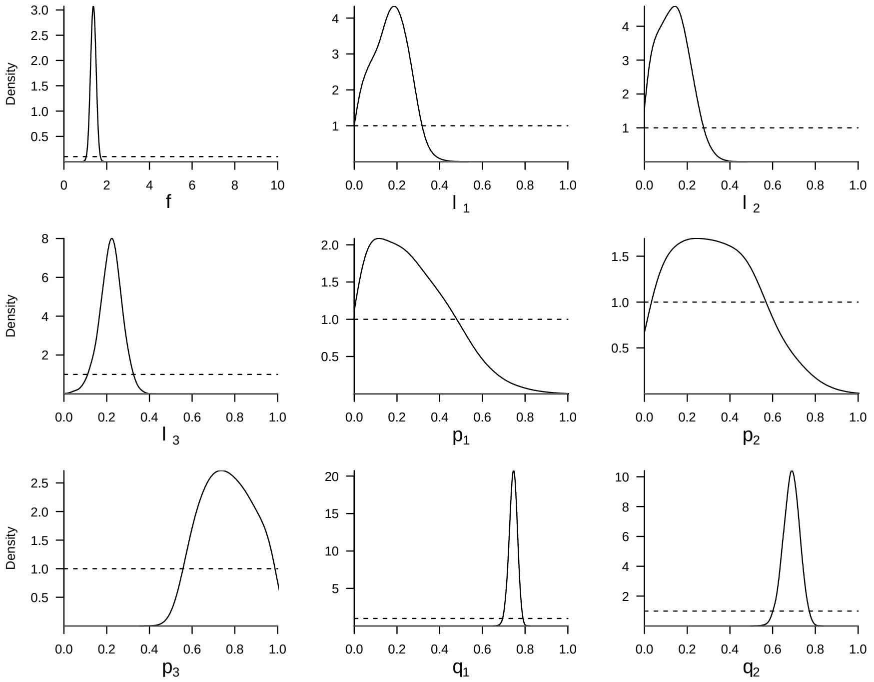
Supplementary Figure S1: **Risk of infection in a subset of household contacts.** Cumulative hazards of confirmed influenza A virus infection presenting with fever plus cough or not presenting with fever plus cough, in Hong Kong and Bangkok, based on the subset of households in which the intervention was applied within 36 hours of illness onset in the index case.



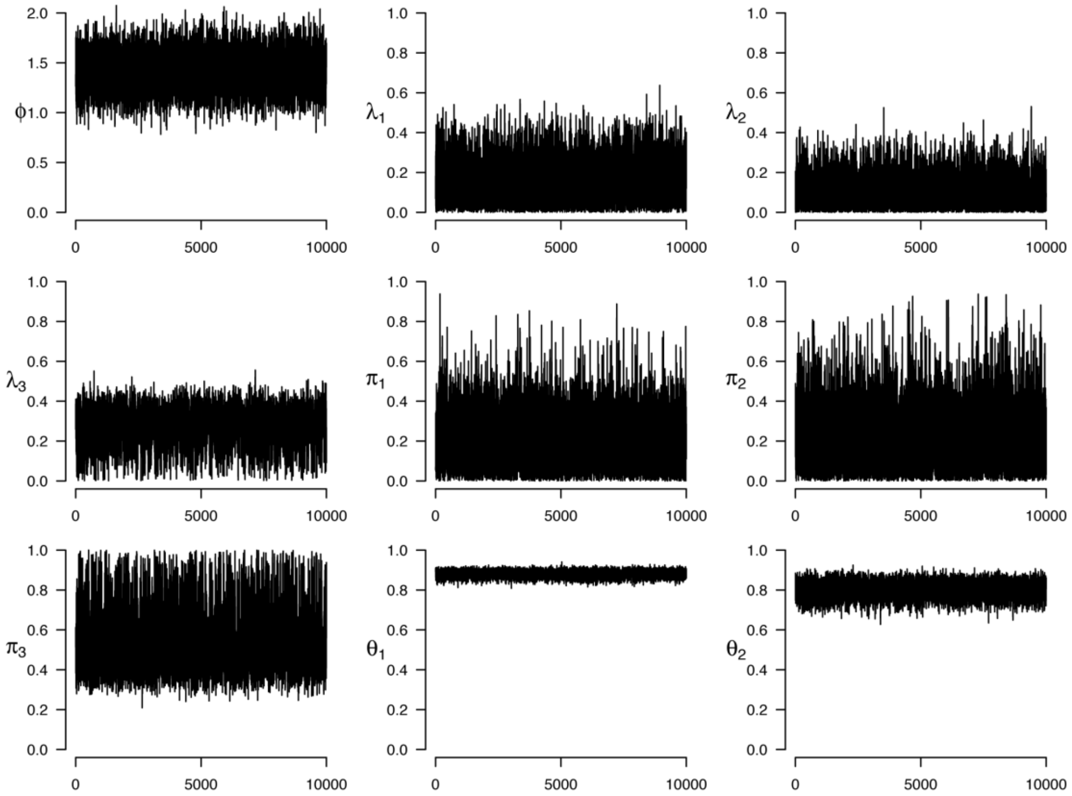
Supplementary Figure S2: **Sub-hazards for each mode of transmission.** Estimated sub-hazard functions for each mode of influenza transmission in three intervention groups, based on Hong Kong and Bangkok data respectively.



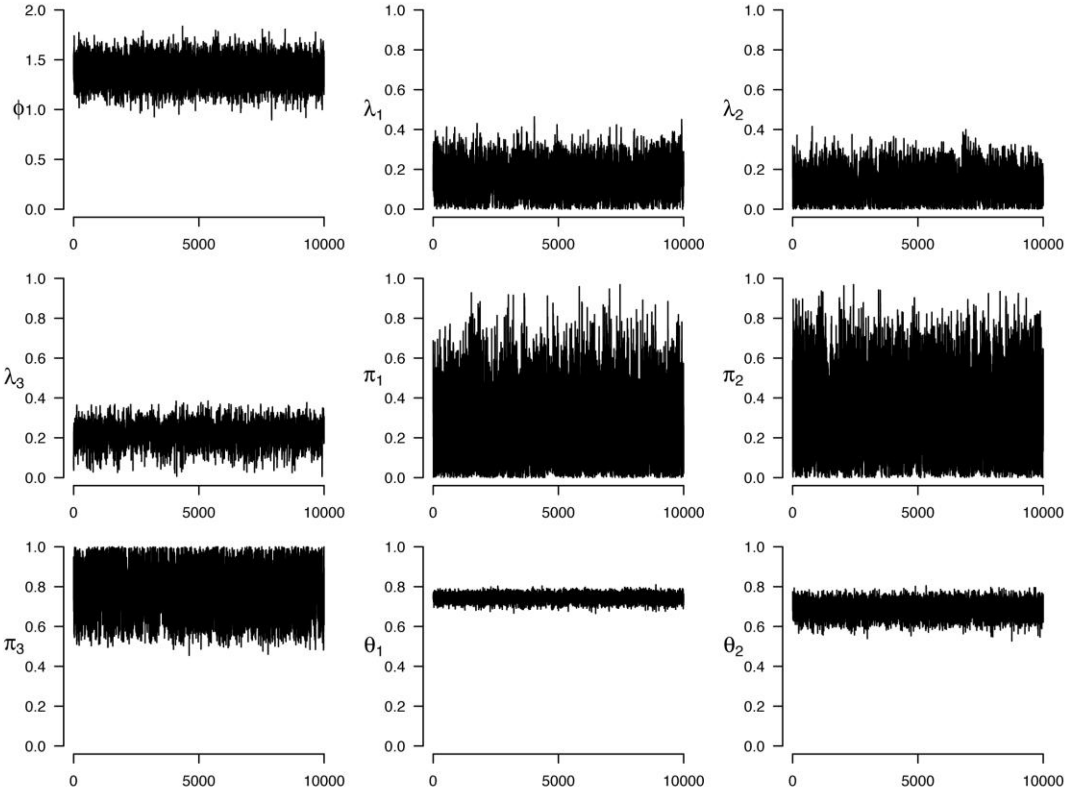
Supplementary Figure S3: **Fitted priors and posteriors (Hong Kong).** Prior distributions (dashed lines) and posterior distributions (solid lines) for the parameter estimates under the model fitted to data from households in Hong Kong.



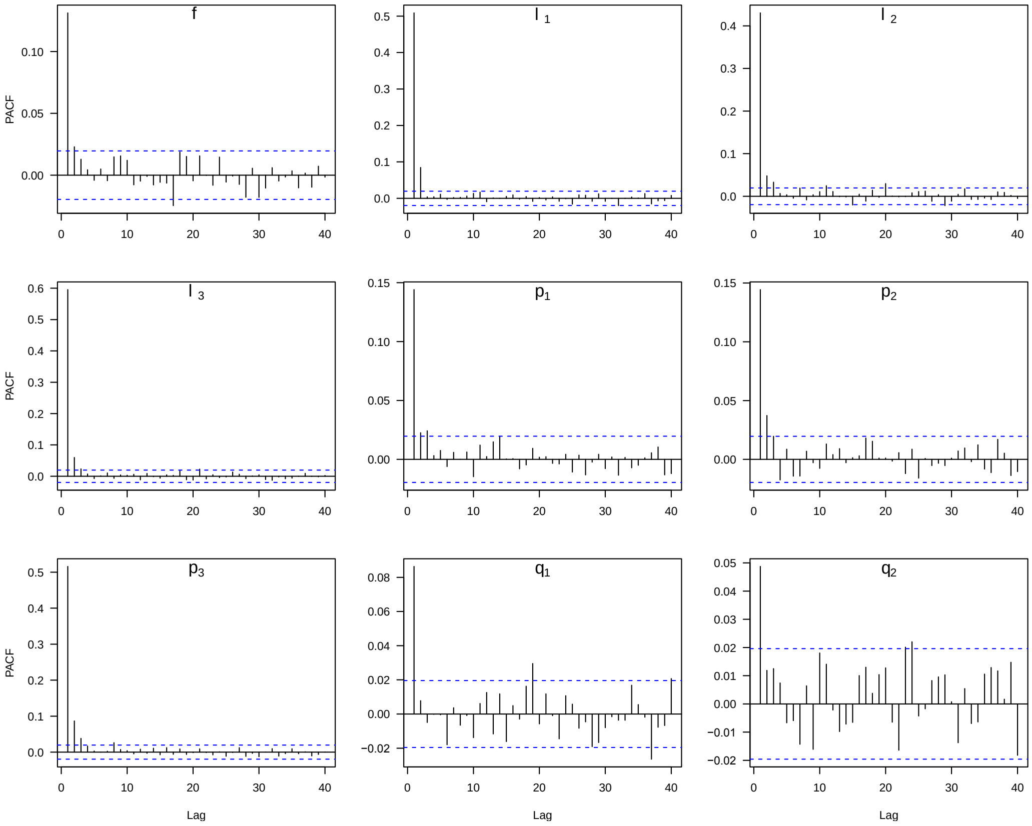
Supplementary Figure S4: **Fitted priors and posteriors (Bangkok).**Prior distributions (dashed lines) and posterior distributions (solid lines) for the parameter estimates under the model fitted to data from households in Bangkok.



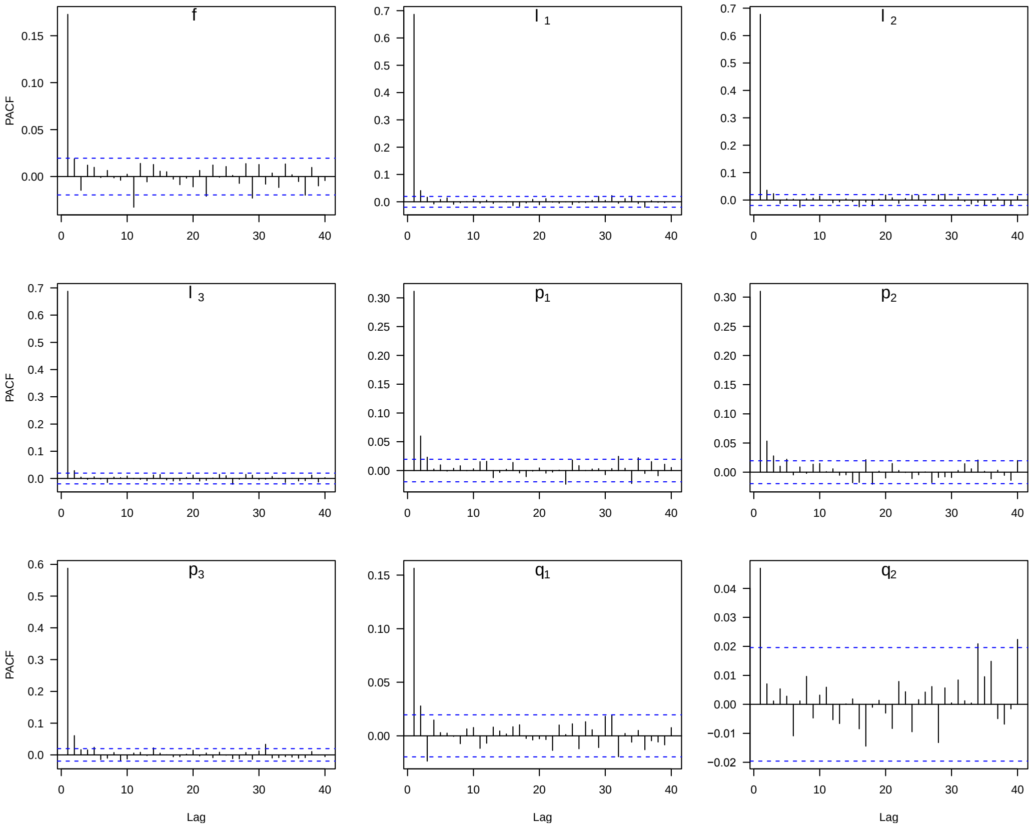
Supplementary Figure S5: **Model diagnostics – trace plots (Hong Kong).** MCMC trace plots for the parameter estimates under the model fitted to data from households in Hong Kong.



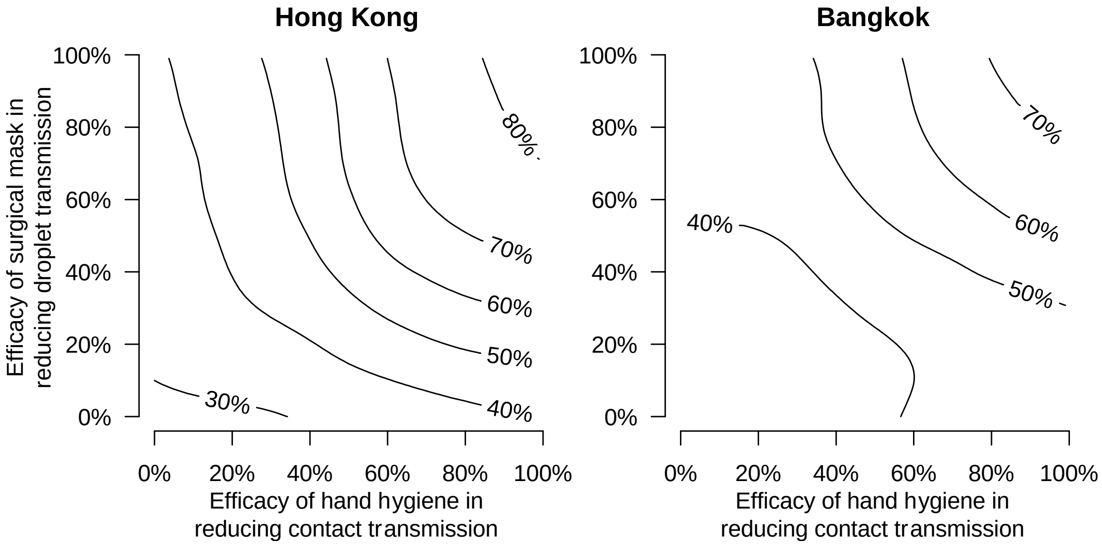
Supplementary Figure S6: **Model diagnostics – trace plots (Bangkok).** MCMC trace plots for the parameter estimates under the model fitted to data from households in Bangkok.



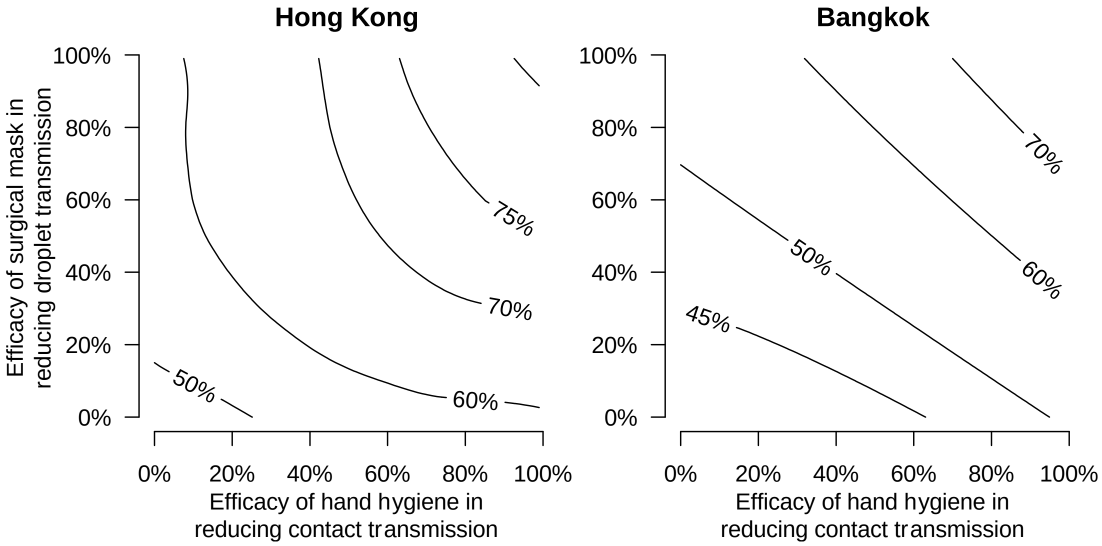
Supplementary Figure S7: **Model diagnostics – ACF plots (Hong Kong).** Partial auto-correlation plot for the parameter estimates under the model fitted to data from households in Hong Kong.



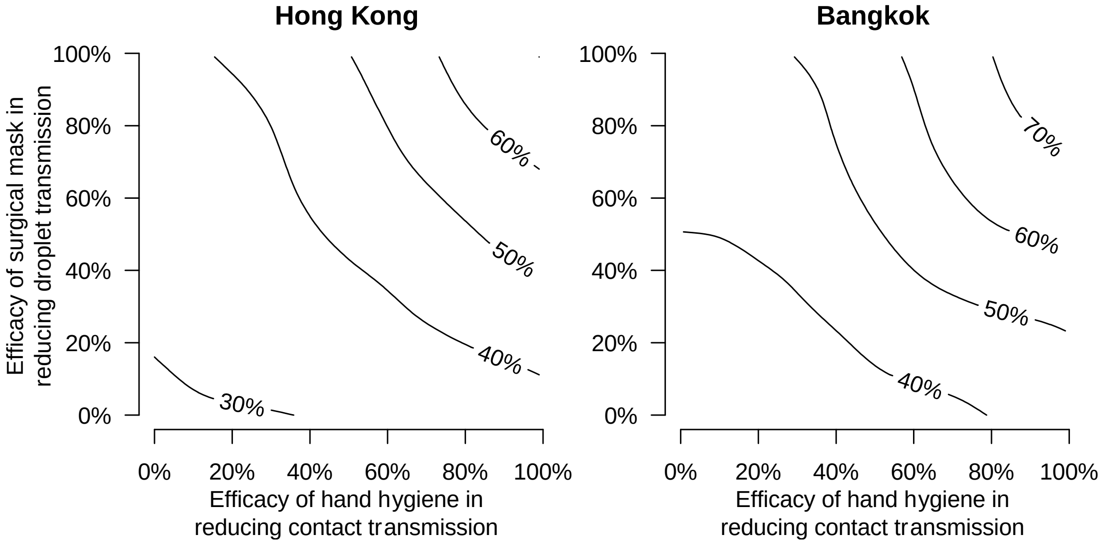
Supplementary Figure S8: **Model diagnostics – ACF plots (Bangkok).** Partial auto-correlation plot for the parameter estimates under the model fitted to data from households in Bangkok.



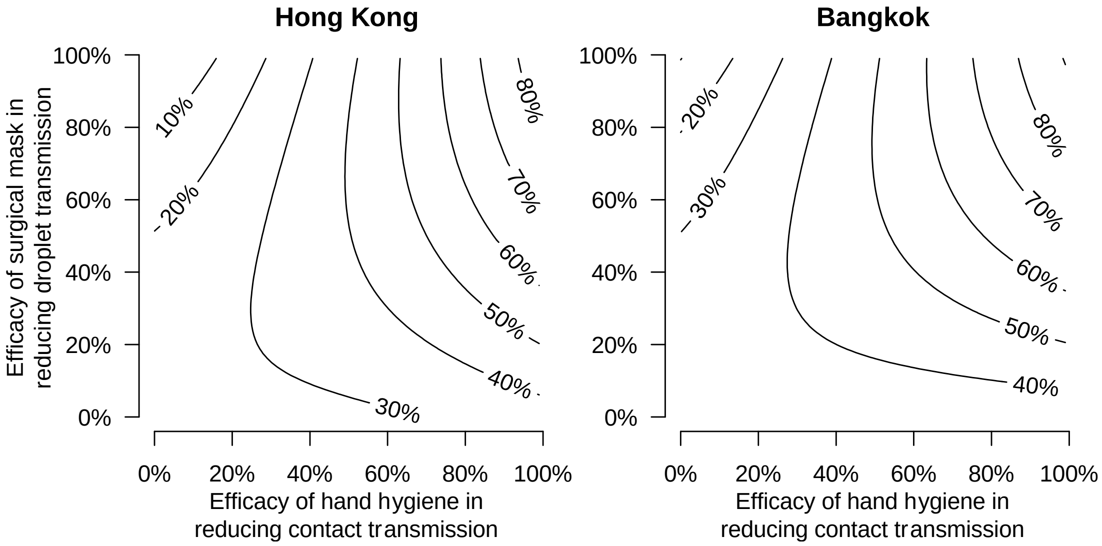
Supplementary Figure S9: **Results of sensitivity analysis 1.** The relative importance of aerosol transmission in the absence of control measures in households in Hong Kong and Bangkok, quantified in terms of the cause-specific probability of aerosol transmission. The contour lines show the proportion of secondary infections attributed to aerosol transmission in the absence of interventions, under varying assumptions about the efficacy of randomization to the hand hygiene and surgical mask interventions in reducing contact and droplet transmission respectively.



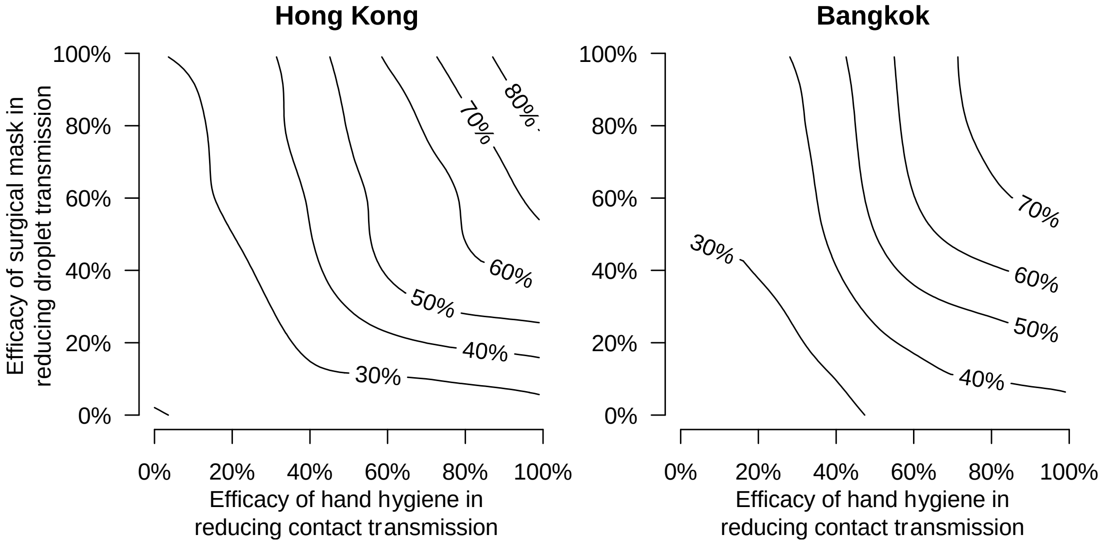
Supplementary Figure S10: **Results of sensitivity analysis 2.** The relative importance of aerosol transmission in the absence of control measures in households in Hong Kong and Bangkok, quantified in terms of the cause-specific probability of aerosol transmission. The contour lines show the proportion of secondary infections attributed to aerosol transmission in the absence of interventions, under varying assumptions about the efficacy of randomization to the hand hygiene and surgical mask interventions in reducing contact and droplet transmission respectively.



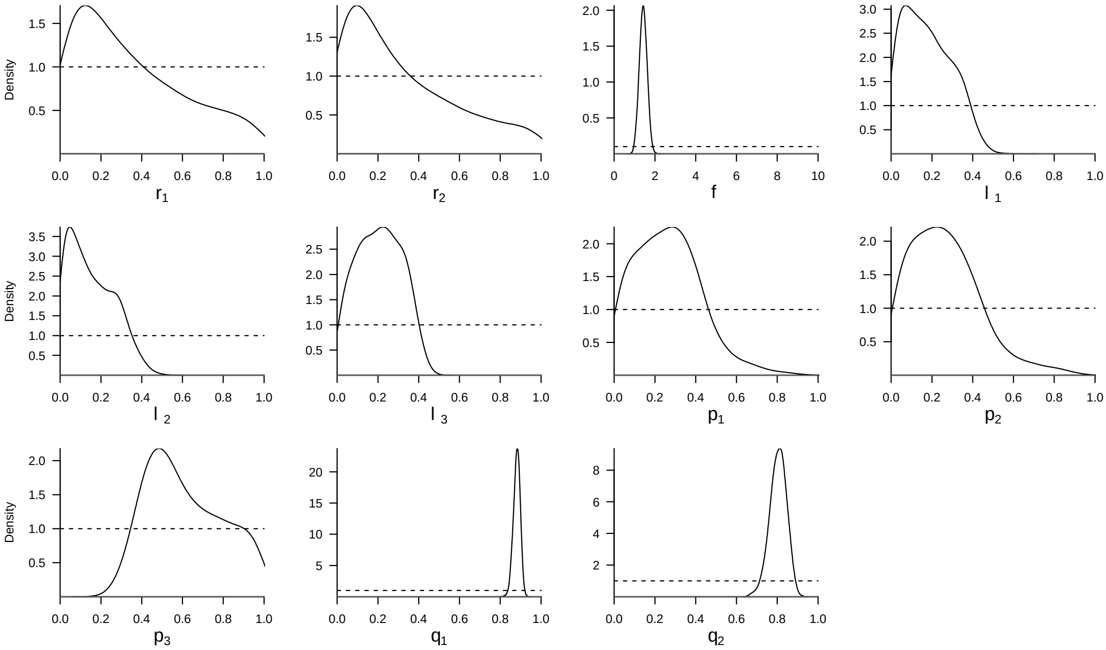
Supplementary Figure S11: **Results of sensitivity analysis 3.** The relative importance of aerosol transmission in the absence of control measures in households in Hong Kong and Bangkok, quantified in terms of the cause-specific probability of aerosol transmission. The contour lines show the proportion of secondary infections attributed to aerosol transmission in the absence of interventions, under varying assumptions about the efficacy of randomization to the hand hygiene and surgical mask interventions in reducing contact and droplet transmission respectively. This sensitivity analysis was based on a subset of households with intervention applied within 36 hours of illness onset in the index case in the household.



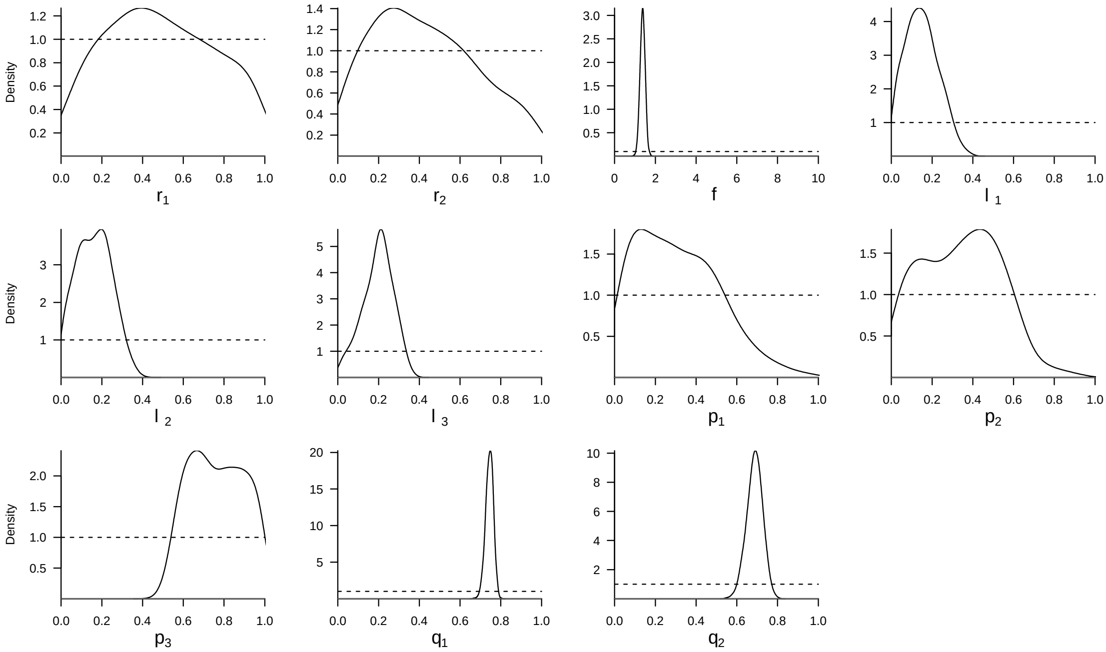
Supplementary Figure S12: **Results of sensitivity analysis 4.** The relative importance of aerosol transmission in the absence of control measures in households in Hong Kong and Bangkok, quantified in terms of the cause-specific probability of aerosol transmission. The contour lines show the proportion of secondary infections attributed to aerosol transmission in the absence of interventions, under varying assumptions about the efficacy of randomization to the hand hygiene intervention in reducing contact transmission, and the efficacy of randomization to the hand hygiene plus face mask intervention in reducing contact, droplet and aerosol transmission. In the latter intervention the efficacy against aerosol transmission is assumed to be half of the efficacy against droplet transmission.



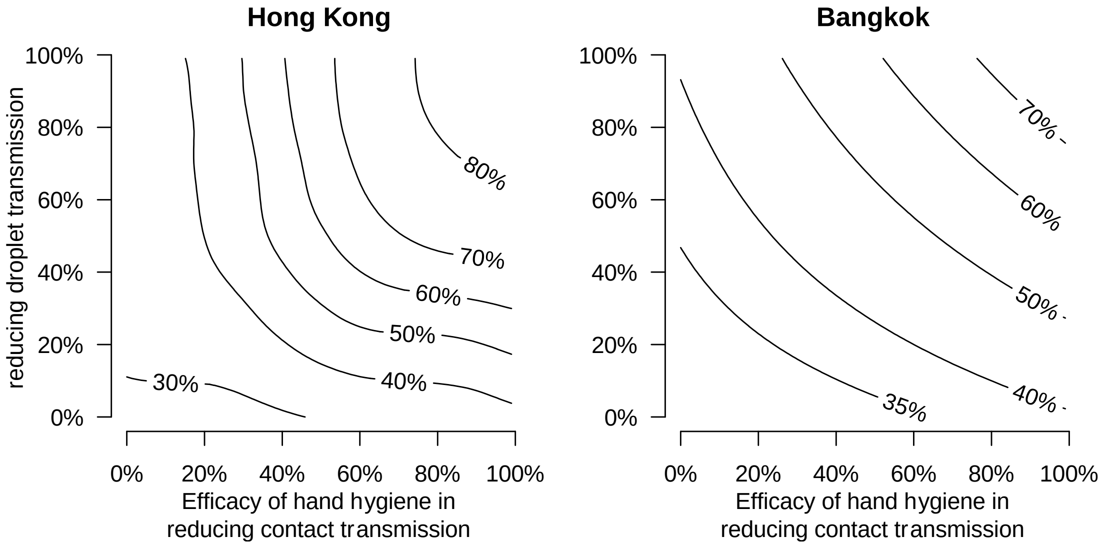
Supplementary Figure S13: **Results of sensitivity analysis 5.** The relative importance of aerosol transmission in the absence of control measures in households in Hong Kong and Bangkok, quantified in terms of the cause-specific probability of aerosol transmission. The contour lines show the proportion of secondary infections attributed to aerosol transmission in the absence of interventions, under varying assumptions about the efficacy of randomization to the hand hygiene and surgical mask interventions in reducing contact and droplet transmission respectively. In this sensitivity analysis it was assumed that all household contacts with ARI had influenza virus infection.



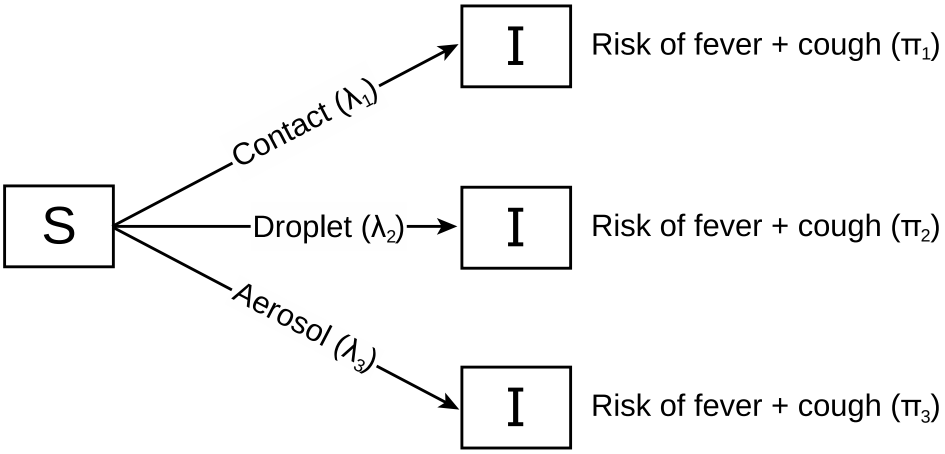
Supplementary Figure S14: **Results of sensitivity analysis 6 (Hong Kong).** Priors (dashed lines) and posteriors (solid lines) for the parameter estimates under the model fitted to data from households in Hong Kong.



Supplementary Figure S15: **Results of sensitivity analysis 6 (Bangkok).** Priors (dashed lines) and posteriors (solid lines) for the parameter estimates under the model fitted to data from households in Bangkok.



Supplementary Figure S16: **Results of sensitivity analysis 7.** The relative importance of aerosol transmission in the absence of control measures in households in Hong Kong and Bangkok, quantified in terms of the cause-specific probability of aerosol transmission. The contour lines show the proportion of secondary infections attributed to aerosol transmission in the absence of interventions, under varying assumptions about the efficacy of randomization to the hand hygiene and surgical mask interventions in reducing contact and droplet transmission respectively. This sensitivity analysis was based on the assumption of a constant 2-day incubation period.



Supplementary Figure S17: **Diagram of competing modes of transmission in households.**

Supplementary Tables

Supplementary Table S1: **Subject characteristics in Hong Kong.** Characteristics of index cases with confirmed influenza A and their household contacts in Hong Kong

Characteristics	Control		Hand hygiene		Face mask + hand hygiene	
	n	(%)	n	(%)	n	(%)
Index cases	95		86		94	
Age group						
≤5 y	25	(26%)	14	(16%)	20	(21%)
6-15 y	49	(52%)	44	(51%)	47	(50%)
16-30 y	8	(8%)	11	(13%)	16	(17%)
31-50 y	11	(12%)	11	(13%)	6	(6%)
>50 y	2	(2%)	6	(7%)	5	(5%)
Men	54	(57%)	42	(49%)	46	(49%)
Median household size (IQR)	4	(3, 4)	4	(3, 5)	4	(3, 5)
Influenza A subtype						
Seasonal H1N1	46	(48%)	48	(56%)	51	(54%)
Seasonal H3N2	17	(18%)	12	(14%)	19	(20%)
Not subtyped	32	(34%)	26	(30%)	24	(26%)
Household contacts	278		265		279	
Age group						
≤5 y	17	(6%)	16	(6%)	15	(5%)
6-15 y	34	(12%)	28	(11%)	31	(11%)
16-30 y	27	(10%)	23	(9%)	33	(12%)
31-50 y	167	(60%)	152	(57%)	154	(55%)
>50 y	33	(12%)	46	(17%)	46	(16%)
Men	107	(38%)	105	(40%)	98	(35%)
Received seasonal influenza vaccine in the previous 12 month	28	(10%)	37	(14%)	40	(14%)

Supplementary Table S2: **Subject characteristics in Bangkok.** Characteristics of index cases with confirmed influenza A and their household contacts in Bangkok

Characteristics	Control		Hand hygiene		Face mask + hand hygiene	
	n	(%)	n	(%)	n	(%)
Index cases	175		166		166	
Age group						
≤5 y	94	(52%)	93	(56%)	81	(49%)
6-15 y	84	(48%)	73	(44%)	85	(51%)
Men	104	(59%)	84	(51%)	86	(52%)
Median household size (IQR)	3	(2, 4)	3	(2, 4)	3	(2, 4)
Influenza A subtype						
A(H1N1)pdm09	86	(13%)	84	(14%)	79	(13%)
Seasonal H1N1	23	(38%)	24	(35%)	22	(39%)
Seasonal H3N2	66	(49%)	58	(51%)	65	(48%)
Household contacts	439		409		418	
Age group						
≤5 y	22	(5%)	19	(5%)	21	(5%)
6-15 y	46	(10%)	43	(11%)	49	(12%)
16-30 y	102	(23%)	96	(23%)	84	(20%)
31-50 y	225	(51%)	198	(48%)	219	(52%)
>50 y	44	(10%)	53	(13%)	45	(11%)
Men	185	(42%)	162	(40%)	176	(42%)
Received seasonal influenza vaccine in the previous 12 month	0	(0%)	0	(0%)	0	(0%)

Supplementary Table S3: **Risks of infection and illness in household contacts.** Risk of confirmed infection with influenza A virus among household contacts of index cases with influenza A virus infection confirmed by RT-PCR in Hong Kong and Bangkok, and the proportion of confirmed secondary cases presenting with fever and cough.

	Hong Kong (275 households)				Bangkok (507 households)			
	Control	Hand hygiene	Face mask + hand hygiene	p-value	Control	Hand hygiene	Face mask + hand hygiene	p-value
Confirmed secondary infections	27/278 (10%)	21/265 (8%)	27/279 (10%)	0.71	74/439 (17%)	81/409 (20%)	89/418 (21%)	0.24
Fever among confirmed secondary infections	9 (33%)	11 (52%)	11 (41%)	0.41	37 (50%)	49 (60%)	56 (63%)	0.22
Cough among confirmed secondary infections	20 (74%)	13 (62%)	24 (89%)	0.09	52 (70%)	57 (70%)	70 (79%)	0.37
Fever + cough among confirmed secondary infections	9 (33%)	8 (38%)	11 (41%)	0.85	32 (43%)	45 (56%)	53 (60%)	0.10

Supplementary Table S4: **Results of sensitivity analysis 1.** Point estimates and 95% credible intervals of model parameters, assuming that randomization to hand hygiene and face masks reduce contact and droplet transmission respectively by 50% from the time of application of those interventions.

Parameters	Hong Kong (275 households with 822 contacts)		Bangkok (507 households with 1266 contacts)	
	Estimate	(95% CI)	Estimate	(95% CI)
ϕ Shape of the Weibull distribution	1.41	(1.05, 1.77)	1.38	(1.14, 1.63)
λ_1 Force of contact transmission*	0.19	(0.01, 0.41)	0.17	(0.01, 0.33)
λ_2 Force of droplet transmission*	0.10	(0.00, 0.27)	0.13	(0.01, 0.30)
λ_3 Force of aerosol transmission*	0.28	(0.08, 0.42)	0.22	(0.09, 0.32)
π_1 Risk of fever plus cough for infections by contact route	22%	(1%, 50%)	31%	(2%, 70%)
π_2 Risk of fever plus cough for infections by droplet route	28%	(2%, 69%)	39%	(2%, 79%)
π_3 Risk of fever plus cough for infections by aerosol route	58%	(37%, 95%)	80%	(59%, 98%)
θ_1 Proportion of household adults immune/not exposed	88%	(84%, 91%)	74%	(71%, 78%)
θ_2 Proportion of household children immune/not exposed	80%	(71%, 88%)	69%	(61%, 76%)

Supplementary Table S5: **Results of sensitivity analysis 2.** Point estimates and 95% credible intervals of model parameters, assuming that randomization to hand hygiene and face masks reduce contact and droplet transmission respectively by 50% from the time of application of those interventions.

Parameters	Hong Kong (275 households with 822 contacts)		Bangkok (507 households with 1266 contacts)	
	Estimate	(95% CI)	Estimate	(95% CI)
ϕ Shape of the Weibull distribution	1.41	(1.04, 1.77)	1.39	(1.14, 1.62)
λ_1 Force of contact transmission*	0.11	(0.01, 0.31)	0.10	(0.01, 0.26)
λ_2 Force of droplet transmission*	0.10	(0.00, 0.25)	0.13	(0.01, 0.28)
λ_3 Force of aerosol transmission*	0.32	(0.17, 0.43)	0.26	(0.15, 0.34)
π_1 Risk of fever plus cough for infections by contact route	46%	(3%, 87%)	47%	(3%, 88%)
π_2 Risk of fever plus cough for infections by droplet route	39%	(2%, 82%)	42%	(3%, 78%)
π_3 Risk of fever plus cough for infections by aerosol route	87%	(71%, 99%)	87%	(73%, 99%)
θ_1 Proportion of household adults immune/not exposed	88%	(84%, 91%)	75%	(71%, 78%)
θ_2 Proportion of household children immune/not exposed	80%	(72%, 87%)	69%	(61%, 76%)

Supplementary Table S6: **Results of sensitivity analysis 3.** Point estimates and 95% credible intervals of model parameters, assuming that randomization to hand hygiene and face masks reduce contact and droplet transmission respectively by 50% from the time of application of those interventions

Parameters	Hong Kong (183 households with 546 contacts)		Bangkok (348 households with 868 contacts)	
	Estimate	(95% CI)	Estimate	(95% CI)
ϕ Shape of the Weibull distribution	1.20	(0.82, 1.60)	1.51	(1.24, 1.78)
λ_1 Force of contact transmission*	0.17	(0.01, 0.41)	0.20	(0.02, 0.35)
λ_2 Force of droplet transmission*	0.13	(0.01, 0.34)	0.12	(0.01, 0.28)
λ_3 Force of aerosol transmission*	0.20	(0.02, 0.39)	0.25	(0.13, 0.35)
π_1 Risk of fever plus cough for infections by contact route	27%	(1%, 67%)	25%	(1%, 64%)
π_2 Risk of fever plus cough for infections by droplet route	26%	(1%, 63%)	32%	(2%, 75%)
π_3 Risk of fever plus cough for infections by aerosol route	64%	(38%, 97%)	76%	(55%, 98%)
θ_1 Proportion of household adults immune/not exposed	88%	(84%, 92%)	75%	(71%, 79%)
θ_2 Proportion of household children immune/not exposed	76%	(64%, 85%)	70%	(62%, 78%)

Supplementary Table S7: **Results of sensitivity analysis 4.** Point estimates and 95% credible intervals of model parameters, assuming that randomization to hand hygiene reduced contact transmission by 50%, and randomization to hand hygiene plus face masks reduced contact and droplet transmission by 50% as well as reducing aerosol transmission by 25% from the time of application of those interventions.

Parameters	Hong Kong (275 households with 822 contacts)		Bangkok (507 households with 1266 contacts)	
	Estimate	(95% CI)	Estimate	(95% CI)
ϕ Shape of the Weibull distribution	1.34	(1.00, 1.73)	1.37	(1.13, 1.62)
λ_1 Force of contact transmission*	0.21	(0.01, 0.45)	0.16	(0.01, 0.33)
λ_2 Force of droplet transmission*	0.14	(0.01, 0.36)	0.13	(0.01, 0.30)
λ_3 Force of aerosol transmission*	0.22	(0.02, 0.43)	0.23	(0.08, 0.36)
π_1 Risk of fever plus cough for infections by contact route	24%	(2%, 60%)	29%	(1%, 71%)
π_2 Risk of fever plus cough for infections by droplet route	27%	(1%, 68%)	32%	(1%, 72%)
π_3 Risk of fever plus cough for infections by aerosol route	61%	(35%, 97%)	77%	(54%, 99%)
θ_1 Proportion of household adults immune/not exposed	88%	(84%, 91%)	74%	(71%, 78%)
θ_2 Proportion of household children immune/not exposed	80%	(72%, 87%)	69%	(61%, 76%)

Supplementary Table S8: **Results of sensitivity analysis 5.** Point estimates and 95% credible intervals of model parameters, assuming that randomization to hand hygiene and face masks reduce contact and droplet transmission respectively by 50% from the time of application of those interventions, and that all household contacts with ARI had influenza virus infection.

Parameters	Hong Kong (275 households with 822 contacts)		Bangkok (507 households with 1266 contacts)	
	Estimate	(95% CI)	Estimate	(95% CI)
ϕ Shape of the Weibull distribution	1.75	(1.55, 1.96)	1.39	(1.22, 1.55)
λ_1 Force of contact transmission*	0.21	(0.02, 0.42)	0.19	(0.03, 0.32)
λ_2 Force of droplet transmission*	0.10	(0.00, 0.26)	0.09	(0.00, 0.22)
λ_3 Force of aerosol transmission*	0.32	(0.19, 0.41)	0.23	(0.13, 0.31)
π_1 Risk of fever plus cough for infections by contact route	9%	(0%, 21%)	12%	(0%, 35%)
π_2 Risk of fever plus cough for infections by droplet route	11%	(0%, 30%)	22%	(1%, 52%)
π_3 Risk of fever plus cough for infections by aerosol route	26%	(17%, 50%)	54%	(37%, 86%)
θ_1 Proportion of household adults immune/not exposed	57%	(52%, 61%)	50%	(46%, 54%)
θ_2 Proportion of household children immune/not exposed	50%	(41%, 58%)	41%	(34%, 49%)

Supplementary Table S9: **Results of sensitivity analysis 6.** Point estimates and 95% credible intervals of model parameters, jointly estimating the efficacy of the interventions along with the other parameters.

Parameters	Hong Kong (275 households with 822 contacts)		Bangkok (507 households with 1266 contacts)	
	Estimate	(95% CI)	Estimate	(95% CI)
r_1 Relative risk reduction in contact transmission by hand hygiene	35%	(1%, 94%)	49%	(4%, 97%)
r_2 Relative risk reduction in droplet transmission by face mask	32%	(1%, 94%)	43%	(3%, 94%)
ϕ Shape of the Weibull distribution	1.43	(1.06, 1.79)	1.37	(1.13, 1.61)
λ_1 Force of contact transmission*	0.18	(0.01, 0.41)	0.15	(0.01, 0.31)
λ_2 Force of droplet transmission*	0.15	(0.01, 0.38)	0.16	(0.01, 0.32)
λ_3 Force of aerosol transmission*	0.21	(0.02, 0.40)	0.20	(0.03, 0.33)
π_1 Risk of fever plus cough for infections by contact route	26%	(1%, 64%)	31%	(2%, 76%)
π_2 Risk of fever plus cough for infections by droplet route	26%	(2%, 69%)	34%	(2%, 71%)
π_3 Risk of fever plus cough for infections by aerosol route	61%	(33%, 97%)	76%	(54%, 99%)
θ_1 Proportion of household adults immune/not exposed	88%	(85%, 91%)	74%	(70%, 78%)
θ_2 Proportion of household children immune/not exposed	80%	(72%, 88%)	69%	(61%, 76%)

Supplementary Table S10: **Results of sensitivity analysis 7.** Point estimates and 95% credible intervals of model parameters, assuming that randomization to hand hygiene and face masks reduce contact and droplet transmission respectively by 50% from the time of application of those interventions.

Parameters	Hong Kong (275 households with 822 contacts)		Bangkok (507 households with 1266 contacts)	
	Estimate	(95% CI)	Estimate	(95% CI)
ϕ Shape of the Weibull distribution	1.61	(1.25, 1.97)	1.49	(1.27, 1.71)
λ_1 Force of contact transmission*	0.19	(0.01, 0.44)	0.20	(0.02, 0.38)
λ_2 Force of droplet transmission*	0.13	(0.01, 0.36)	0.16	(0.01, 0.32)
λ_3 Force of aerosol transmission*	0.33	(0.13, 0.46)	0.27	(0.16, 0.37)
π_1 Risk of fever plus cough for infections by contact route	21%	(1%, 51%)	26%	(1%, 65%)
π_2 Risk of fever plus cough for infections by droplet route	23%	(1%, 56%)	32%	(2%, 71%)
π_3 Risk of fever plus cough for infections by aerosol route	52%	(33%, 91%)	76%	(55%, 98%)
θ_1 Proportion of household adults immune/not exposed	88%	(85%, 91%)	74%	(70%, 77%)
θ_2 Proportion of household children immune/not exposed	81%	(72%, 88%)	68%	(60%, 75%)

Supplementary Table S11: **Study design features**. Minor differences between the study designs in Hong Kong and Bangkok.

Study component	**Hong Kong**	**Bangkok**
Recruitment locations	45 public and private outpatient clinics across Hong Kong Special Administrative Region (population 7 million).	Outpatient department of a large pediatric public hospital in Bangkok (population 8 million).
Study period	January 2008 through June 2009	April 2008 through February 2011
Age of index cases	Any age	Children 1 month up to15 years of age
Eligibility of index case (symptoms)	Presenting with at least two of: fever, cough, sore throat, headache, runny nose, phlegm, and myalgia; living with at least two other people.	<2 years: fever >38 degrees Celsius *and* one or more of the following symptoms; nasal congestion, cough, conjunctivitis, respiratory distress, sore throat, new seizure > 2 years: Presenting with ILI (fever plus cough or sore throat); living with at least two other people.
Exclusion criteria	Recent (within 2w) URTI in any household member	Recent (within 1w) ILI in any household member; recent (within 12m) influenza vaccination in any household member.
Measurement of body temperature	All households were provided and instructed in the use of a free tympanic thermometer and asked to record their body temperature daily.	Thermometers were not provided to households, and participants recorded either measured body temperature or 'feverishness'.

Supplementary Table S12: **Description of study interventions**

Intervention	Hong Kong	Bangkok
Control	Education about the importance of a healthy diet and lifestyle, both in terms of illness prevention (for household contacts) and symptom alleviation (for the index case).	Education on nutrition, increasing physical activity and smoking cessation for illness prevention for household contacts and symptom alleviation for the index case.
Hand Hygiene	All household members including the index case received education about the potential efficacy of proper hand hygiene in reducing transmission. Household members were taught to use the liquid hand soap provided in place of their regular soap after every washroom visit and in general when their hands were soiled or after sneezing or coughing, while they should use the alcohol hand rub provided when first returning home and immediately after touching any potentially contaminated surfaces. 1. Distribution of liquid hand soap for each kitchen and washroom (Ivory liquid hand soap, Procter & Gamble, Cincinnati, OH). 2. Distribution of a small bottle of alcohol hand rub to each participant (221ml WHO recommended formulation I, liquid content with 80% ethanol, 1.45% glycerol, 0.125% hydrogen peroxide, Vickmans Labs Ltd., Hong Kong). 3. Demonstration and return demonstration of proper hand washing and hand antisepsis.	All household members including the index case received education about the potential efficacy of proper hand hygiene in reducing transmission. Household members were taught to use the provided liquid hand soap provided in a clear plastic graduated dispenser for measurement of consumption after every washroom visit, before and after meals and when their hands were soiled or after sneezing or coughing. 1. Distribution of common liquid hand soap (not antibacterial) for each kitchen and washroom (Teepol Pure, Sherwood Chemicals Public Company Limited, Bangkok). 2. Demonstration and return demonstration of proper hand washing technique.

Face Mask	Index cases and all household contacts received education about the potential efficacy of masks in reducing disease spread to household contacts if all parties wear masks. Household members were taught to wear the surgical masks provided as often as possible at home (except when eating or sleeping) and also when the index was with the household members outside of the household. 1. Distribution of a box of 50 surgical masks (Tecnol – The Lite One, Kimberly Clark, Roswell, GA) for each household member, or a box of 75 pediatric masks for children aged 3-7 years. 2. Demonstration and return demonstration of proper face mask wearing and hygienic disposal	Index cases and all household contacts received education about the potential efficacy of masks in reducing influenza spread to other household contacts. Household members were taught to wear the provided surgical masks as often as possible at home (except when eating or sleeping). 1. Distribution of a box of 50 paper surgical masks for each household member (Face Mask, Med-Con (Thailand) Co. Ltd.) and pediatric masks for children aged 3-7 years. 2. Demonstration and return demonstration of proper face mask use and hygienic disposal.

Supplementary Table S13: **General notation used in the model description.**

Notation	Explanation
i	Index for individual subject
j	Index for the route of transmission
n	Number of subjects analyzed
S	Survivor function of infection
S_u	Survivor function of infection among susceptible & exposed group
f	Probability density function of infection
f_u	Probability density function of infection among the susceptible & exposed group
h_{uj}	The sub-hazards for contact/droplet/aerosol transmission, j

Supplementary Table S14: **Variables involved in the statistical analysis**

Variable	Explanation
T_i	Time of infection in individual *i*
δ_i	Kronecker delta to represent if T_i was observed (=1) or right censored (=0) in individual *i*
T_{0i}	Time of left truncation (i.e. time of recruitment) of individual *i*
X_{hi}	Dichotomous variable representing the hand hygiene intervention (=1) or not (=0) in individual *i*
X_{mi}	Dichotomous variable representing the surgical mask intervention (=1) or not (=0) in individual *i*
M_i	Dichotomous variable representing if the infected subject *i* presented fever plus cough or not in individual *i*
C_i	Dichotomous variable representing if the subject *i* was younger than 16 years old or not

Supplementary Table S15: **Parameters involved in the statistical model.**

Parameter	Explanation
r_1	Relative risk reduction in contact transmission by hand hygiene
r_2	Relative risk reduction in droplet transmission by face mask
ϕ	Shape of the Weibull distributions
λ_1	Scale of the Weibull distribution for contact transmission
λ_2	Scale of the Weibull distribution for droplet transmission
λ_3	Scale of the Weibull distribution for aerosol transmission
π_1	Risk of fever plus cough for infections by contact route
π_2	Risk of fever plus cough for infections by droplet route
π_3	Risk of fever plus cough for infections by aerosol route
θ_1	Proportion of adult household contacts immune
θ_2	Proportion of child household contacts immune

Supplementary Methods

Statistical model for modes of transmission

To estimate the relative importance of modes of influenza A virus transmission, we decompose the hazard of infection into the three different modes of transmission (Supplementary Figure S17). We construct a mathematical model to explicitly describe how the risk of influenza virus infection for household contacts relates to the competing risks of infection through different modes of transmission. For this objective, we use a household transmission model in which the multiple chains of transmission are mathematically described. Our model allows for multiple chains of influenza virus transmission within a household. We did not consider household contacts to be infected from outside the household after illness onset in the index case, because our observations of household transmission were truncated after a relatively short period of time since illness onset was observed in each index case (around 7 days), and because virus sequence data has shown this to be rare in similar studies (*37, 38*).

The general notation for the model is described in Supplementary Table S13, Supplementary Table S14 and Supplementary Table S15.

We assume there are three distinct modes of influenza virus transmission – contact, droplet, and aerosol, respectively indexed by $j \in \{1, 2, 3\}$. Since we only observed that a subject was infected or not instead of the exact mode of getting infected, we base our analysis on a fully masked competing risk model. We adopt Weibull sub-hazards for each route of transmission and assume that the time and cause of infection are independent (i.e., sharing an identical shape parameter, ϕ). To allow a certain proportion of subjects to be immune or not exposed, we use a cure rate model (i.e. a mixture model). The following tables list the variables and notation that is used in our statistical model.

The mixture model of the probability of being immune for an individual *i* is modeled as

$$\theta_i = \theta_1 (1 - C_i) + \theta_2 C_i \qquad (1)$$

The fraction θ_i would not experience infection, and thus, the survivorship is scaled as

$$S(T_i) = \theta_i + (1 - \theta_i) S_u(T_i) \qquad (2)$$

and, similarly, the density of infection is described as

$$f(T_i) = (1 - \theta_i) f_u(T_i) \qquad (3)$$

The Weibull sub-hazards for modes of transmission, *j*= 1, 2 and 3 are written as follows:

$$
\begin{aligned}
&h_{u1}\left(T_i, X_{hi}, X_{mi}\right) = \phi\lambda_1^{\phi} T_i^{\phi-1} \exp\left(\beta_1 X_{hi}\right) \qquad \textit{where}\ \beta_1 = \log\left(1-r_1\right) \\
&h_{u2}\left(T_i, X_{hi}, X_{mi}\right) = \phi\lambda_2^{\phi} T_i^{\phi-1} \exp\left(\beta_2 X_{mi}\right) \qquad \textit{where}\ \beta_2 = \log\left(1-r_2\right) \\
&h_{u3}\left(T_i, X_{hi}, X_{mi}\right) = \phi\lambda_3^{\phi} T_i^{\phi-1}.
\end{aligned} \tag{4}
$$

Interactions between three different modes of transmission are regulated by the common shape parameter only. Otherwise, we do not address the interactions due to an absence of additional biological information on which interactions could be based. Alternatively, one could adopt a stochastic process of a particular form, e.g. a multivariate Gaussian stochastic process with linear transitions of viral particles from aerosols to environment and indoor air dynamics accounting for the production and removal of virus particles in the environment (*39*). Using our model, we could have slightly overestimated the hazard of aerosol transmission, if there is a strong positive correlation with droplet transmission.

It should be noted that the abovementioned hazards for contact and droplet infections incorporate the efficacy of randomization to the hand-hygiene and face mask interventions within the exponential term. Since these competing hazards are assumed to have independently acted on susceptible individuals in households, the survivor function of infection is written as

$$
S_u\left(T_i, X_{hi}, X_{mi}\right) = \exp\left\{-\left(\lambda_1 T_i\right)^{\phi} \exp\left(\beta_1 X_{hi}\right) - \left(\lambda_2 T_i\right)^{\phi} \exp\left(\beta_2 X_{mi}\right) - \left(\lambda_3 T_i\right)^{\phi}\right\}. \tag{5}
$$

With only the abovementioned competing risk model, one cannot identify the contribution of each mode of transmission to overall risk of household secondary transmission event. Thus, we accounted for the protective effect of personal hygiene. Moreover, we additionally use the risk of developing fever and cough upon infection, which differs for infections from the different modes. We assume that the risk of fever plus cough caused by infections follows a Bernoulli distribution, i.e., $M_i \sim \text{Bernoulli}\left(\pi_j\right),\ j = 1,2,3$.

Provided that the mode of transmission *j* was known, the likelihood function would read:

$$
L = \prod_{i=1}^{n} \left\{(1-\theta_i) h_{uj}\left(T_i, X_{hi}, X_{mi}\right) S_u\left(T_i, X_{hi}, X_{mi}\right) \pi_j^{\ M_i} (1-\pi_j)^{1-M_i}\right\}^{\delta_i} \frac{\left(\theta_i + (1-\theta_i) S_u\left(T_i, X_{hi}, X_{mi}\right)\right)^{1-\delta_i}}{\theta_i + (1-\theta_i) S_u\left(T_{0i}, X_{hi}, X_{mi}\right)}. \tag{6}
$$

However, the cause *j* is not directly observable, and given the underlying model, each mode is equally likely. Thus, the full likelihood function becomes

$$
\prod_{i=1}^{n} \left\{ \sum_{j=1,2,3} (1-\theta_i) h_{uj}\left(T_i, X_{hi}, X_{mi}\right) S_u\left(T_i, X_{hi}, X_{mi}\right) \pi_j^{\ M_i} (1-\pi_j)^{1-M_i} \right\}^{\delta_i} \frac{\left(\theta_i + (1-\theta_i) S_u\left(T_i, X_{hi}, X_{mi}\right)\right)^{1-\delta_i}}{\theta_i + (1-\theta_i) S_u\left(T_{0i}, X_{hi}, X_{mi}\right)}. \tag{7}
$$

To simplify the computation, we assume that the incubation period is a constant (1 day), and assume that we know the exact time of infection based on the time of illness onset. When there are two or more household transmission events, we consider each pair of cases and their times of infection, T^1 and T^2, respectively. If $T^1 = T^2$, then we regard that both acquired infection from index case and the likelihood function remains the same as before. If $T^1 < T^2$, then the tertiary case could be infected by either the index case or the secondary case. Hence the likelihood contribution for this subject is

$$L_i = \sum_{j=1,2,3} (1-\theta_i) h_{uj}^D S_u^D \pi_j^{M_i} (1-\pi_j)^{1-M_i}, \quad where$$
$$h_{uj}^D \left(T^2, X_{hi}, X_{mi}\right) = h_{uj}\left(T^2, X_{hi}, X_{mi}\right) + h_{uj}\left(T^2 - T^1, X_{hi}, X_{mi}\right), \quad and \qquad (8)$$
$$S_u^D \left(T^2, X_{hi}, X_{mi}\right) = S_u\left(T^2, X_{hi}, X_{mi}\right) \times S_u\left(T^2 - T^1, X_{hi}, X_{mi}\right).$$

For households in which we observed three or more transmission events, we apply exactly the same arguments to account for multiple chains of transmission.

We employ Markov chain Monte Carlo (MCMC) within a Bayesian framework, deriving parameter estimates from the posterior distributions. For each MCMC chain, we ran 120,000 iterations with a thinning parameter 10 and the first 20,000 iterations were used as burn-in period and discarded from posterior distribution. Due to the absence of prior information from empirical studies, we set non-informative priors for each of the parameters as shown below, and impose the restrictions $\pi_1 < \pi_3$ and $\pi_2 < \pi_3$.

$$r_1 \sim U(0,1), r_2 \sim U(0,1),$$
$$\lambda_1 \sim U(0,1), \lambda_2 \sim U(0,1), \lambda_3 \sim U(0,1),$$
$$\phi \sim U(0,10), \theta_1 \sim U(0,1), \theta_2 \sim U(0,1),$$
$$\pi_1 \sim U(0,1), \pi_2 \sim U(0,1), \pi_3 \sim U(0,1).$$

The overall density of infection at time *t* since infection in index cases is

$$f_u(t) = S_u(t) \sum_{j=1}^{3} h_{uj}(t) \qquad (9)$$

in which the hazard h_{uj} is free from interventions. We directly estimate the relative importance of aerosol transmission by employing two different statistical measures. First, in natural settings without interventions, multiple modes of transmission compete with each other to infect a susceptible individual, and one may wish to quantify the overall probability of transmission due to aerosol transmission in some interval *A* by

$$\int_A h_{u3}(t) S_u(t) dt, \qquad (10)$$

i.e., the subject is infected due to aerosol and the subject escapes infection due to all modes of transmission up to time *t* since infection in index case. This is referred to as the crude cause-specific probability.

Second, because we fully quantify h_{uj} for all *j*, the same probability if only a route *j* was operating can be calculated as

$$\int_A h_{uj}(t) \exp\left\{-\int_0^t h_{uj}(s) ds\right\} dt \qquad (11)$$

expressed as the product of the probability of being infected by route *j* and the survival probability of escaping infection due to mode *j* up to time *t* since infection in index case. This has been referred to as the net probability, representing the theoretical relative contribution of route *j* to the transmission in the absence of all other routes. The crude probability is useful for understanding the relative contribution of each mode of transmission to actual infection in "natural settings", whereas the net probability is extremely useful for understanding an expected risk reduction of infection if a specific mode is eliminated from the population dynamics. That is, the net probability is regarded as "cause-deleted" measure that can be used to estimate the effect of a specific intervention (e.g. hand hygiene or wearing a mask) on reducing the risk of infection in susceptible contacts.

Let $A = (0, \infty)$ and we could simplify the above function of crude probability due to aerosol transmission in natural settings. The relative contribution of aerosol transmission is calculated as:

$$\begin{aligned}
&\int_0^\infty h_{u3}(t) S_u(t)\,dt \\
&= \int_0^\infty \phi \lambda_3^\phi t^{\phi-1} \exp\left\{-(\lambda_1 t)^\phi - (\lambda_2 t)^\phi - (\lambda_3 t)^\phi\right\} dt \\
&= -\frac{\lambda_3^\phi}{\lambda_1^\phi + \lambda_2^\phi + \lambda_3^\phi} \exp\left\{-(\lambda_1 t)^\phi - (\lambda_2 t)^\phi - (\lambda_3 t)^\phi\right\}\Bigg|_{t=0}^{t=\infty} \\
&= \frac{\lambda_3^\phi}{\lambda_1^\phi + \lambda_2^\phi + \lambda_3^\phi}
\end{aligned} \tag{12}$$

Analysis of data from the studies in Hong Kong and Bangkok

Descriptive summary

In total, the studies in Hong Kong and Bangkok included successful follow-up of 275 and 507 index cases with confirmed influenza A, respectively. Their characteristics are summarized in Supplementary Table S1 and Supplementary Table S2, respectively. There was no significant difference between study arms in the risk of confirmed secondary influenza A virus infection (Supplementary Table S3). In both studies, household contacts with confirmed influenza A virus infection had slightly higher but non-significant risk of fever plus cough in the intervention arms compared to the control arm.

However when the cumulative incidence of confirmed influenza infections were plotted for household contacts, we identified a change in the risk of fever plus cough that was particularly apparent in the households in Bangkok, although not so apparent in the households in Hong (Figure 1 in the main text). In an analysis restricted to the subset of households in which the intervention was applied within 36 hours of illness onset in the index case, among which the intervention effect should be most apparent, because the intervention covers a greater part of the infectious period of the index case (*11*), we also identified a change in the risk of fever plus cough in the hand hygiene plus face mask group in Hong Kong (Supplementary Figure S1).

Fitted model for competing modes of transmission

The parameter estimates for the fitted model are shown in Table 1, under the assumptions that the hand hygiene and face mask interventions reduced contact and droplet transmission by 50% respectively, from the time of application of those interventions. The cause-specific probability of aerosol transmission in the control arm for the full range of assumed efficacies of hand hygiene and face masks are shown in Figure 1 in the main text. In both Hong Kong and Bangkok, aerosol transmission was associated with the greatest cause-specific hazard, and we estimated that around half of all transmission could be attributed to this mode in the control group.

The priors and posteriors for the fitted model are shown in Supplementary Figure S3 and Supplementary Figure S4, corresponding to the parameter estimates shown in Table 1 in the main text. The MCMC traces for each parameter are shown in Supplementary Figure S5 and Supplementary Figure S6, for the Hong Kong and Bangkok data respectively, and plots of the autocorrelation in the posterior samples are shown in Supplementary Figure S7 and Supplementary Figure S8.

We plotted the sub-hazard function h_j for each mode of influenza transmission in three intervention groups based on Hong Kong and Bangkok data, separately, in Supplementary Figure S2.

Sensitivity analyses

Sensitivity analysis 1. Using fever instead of fever+cough as the indicator discriminating between modes of transmission

We identified increases in both fever and cough in the intervention arms of the studies in Hong Kong and Bangkok. Whereas in the main analysis we used the combination of fever plus cough as the proxy measure to distinguish the mode of transmission, in this sensitivity analysis we use fever alone as the indicator. The parameter estimates are shown in Supplementary Table S4 and Supplementary Figure S9, and are similar to the results from the main analysis shown in the main text.

Sensitivity analysis 2. Using cough instead of fever+cough as the indicator discriminating between modes of transmission

We identified increases in both fever and cough in the intervention arms of the studies in Hong Kong and Bangkok. Whereas in the main analysis we used the combination of fever plus cough as the proxy measure to distinguish the mode of transmission, in this sensitivity analysis we use cough alone as the indicator. The parameter estimates are shown in Supplementary Table S5 and Supplementary

Figure S10, and are similar to the results from the main analysis shown in the main text.

Sensitivity analysis 3. A subset of data with intervention applied within 36 hours from index symptom onset.

Any intervention effects should be strongest among those households in which the intervention was applied within 36 hours of illness onset in the index case, because the interventions would then cover a greater portion of the infectious period of the index case (*11*). We therefore conducted a sensitivity analysis restricting the data to only households in which the intervention was applied within 36 hours of illness onset in the index case. The parameter estimates are shown in Supplementary Table S6 and Supplementary Figure S11, and are similar to the results from the main analysis shown in the main text as would be expected.

Although we only analyzed a subset of the data in which the intervention would be expected to have a greater effect, our model accounts for the time of application of the intervention, and in Supplementary Figure S11 we present the estimates of the contribution of aerosol transmission in the control arms in Hong Kong and Bangkok which would be unaffected by the time at which any intervention was applied (because no intervention was applied in the control arms).

Sensitivity analysis 4. Assuming face masks reduced aerosol transmission

In the main analysis, we assumed that randomization to the hand hygiene intervention led to reductions in contact transmission, and randomization to the hand hygiene plus face masks intervention led to reductions in droplet transmission. It is possible that randomization to the face mask intervention also led to reductions in aerosol transmission (*17*). In this sensitivity analysis we assumed that randomization to the face mask intervention led to half as much reduction in aerosol transmission as in droplet transmission. For example, we assumed that if face masks reduced droplet transmission by 50% they would also reduce aerosol transmission by 25%.

The results are shown in Supplementary Table S7 and Supplementary Figure S12, and it is noted that the conclusions regarding aerosol transmission are similar to those in the main text.

Sensitivity analysis 5. Assuming some influenza infections in household contacts were not identified

Households were visited at 3-day intervals to collect nose and throat swabs from all household members regardless of illness, and all swabs were tested for influenza by RT-PCR. However it is possible that some influenza virus infections among household contacts could not be confirmed for various reasons (*11, 12*). Approximately 27% and 21% of household contacts in Hong Kong and Bangkok, respectively, reported an acute respiratory illness (at least two of fever, cough, sore throat, headache, myalgia, runny nose, and phlegm) during follow-up but were not confirmed to have influenza by RT-PCR. In this sensitivity analysis, we made the assumption that all subjects with acute respiratory illness were infected with influenza virus despite lack of laboratory confirmation.

The results are shown in Supplementary Table S8 and Supplementary Figure S13, and it is noted that the conclusions regarding aerosol transmission are similar to those in the main text.

Sensitivity analysis 6. Jointly estimating the efficacy of the hand hygiene and face mask interventions

Because of the strong correlation between the assumed efficacy of the interventions and the risk of fever plus cough associated with each mode, it is difficult to robustly estimate both of these groups of parameters and in the main analysis we fixed the assumed efficacy of the interventions. In this sensitivity analysis we demonstrate the joint estimation of all parameters. The results are shown in Supplementary Table S9. The conclusions regarding aerosol transmission are similar to those in the main text. However the posterior densities are plotted in Supplementary Figure S14 and Supplementary Figure S15 for Hong Kong and Bangkok respectively, and one can see the lack of precision for the efficacy parameters r_1, r_2 and the risk of fever plus cough for each mode π_j.

Sensitivity analysis 7. Assuming the incubation period as 2 days

In the main analysis we assumed a constant 1-day incubation period, while in this sensitivity analysis we assumed a constant 2-day incubation period. The parameter estimates are shown in Supplementary Table S10 and Supplementary Figure S16, and are similar to the results from the main analysis shown in the main text.

Supplementary References

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