Facemasks and Hand Hygiene to Prevent Influenza Transmission in Households: A Cluster Randomized Trial

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Facemasks and Hand Hygiene to Prevent Influenza Transmission in Households

A Cluster Randomized Trial

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Background: Few data are available about the effectiveness of nonpharmaceutical interventions for preventing influenza virus transmission.

Objective: To investigate whether hand hygiene and use of facemasks prevents household transmission of influenza.

Design: Cluster randomized, controlled trial. Randomization was computer generated; allocation was concealed from treating physicians and clinics and implemented by study nurses at the time of the initial household visit. Participants and personnel administering the interventions were not blinded to group assignment. (ClinicalTrials.gov registration number: NCT00425893)

Setting: Households in Hong Kong.

Patients: 407 people presenting to outpatient clinics with influenza-like illness who were positive for influenza A or B virus by rapid testing (index patients) and 794 household members (contacts) in 259 households.

Intervention: Lifestyle education (control) (134 households), hand hygiene (136 households), or surgical facemasks plus hand hygiene (137 households) for all household members.

Measurements: Influenza virus infection in contacts, as confirmed by reverse-transcription polymerase chain reaction (RT-PCR) or diagnosed clinically after 7 days.

Results: Sixty (8%) contacts in the 259 households had RT-PCR–confirmed influenza virus infection in the 7 days after intervention. Hand hygiene with or without facemasks seemed to reduce influenza transmission, but the differences compared with the control group were not significant. In 154 households in which interventions were implemented within 36 hours of symptom onset in the index patient, transmission of RT-PCR–confirmed infection seemed reduced, an effect attributable to fewer infections among participants using facemasks plus hand hygiene (adjusted odds ratio, 0.33 [95% CI, 0.13 to 0.87]). Adherence to interventions varied.

Limitation: The delay from index patient symptom onset to intervention and variable adherence may have mitigated intervention effectiveness.

Conclusion: Hand hygiene and facemasks seemed to prevent household transmission of influenza virus when implemented within 36 hours of index patient symptom onset. These findings suggest that nonpharmaceutical interventions are important for mitigation of pandemic and interpandemic influenza.

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Interpandemic human influenza virus infects millions of people every year. Some infections are mild, but others—especially in young or elderly persons—can result in more severe illness requiring hospitalization. Influenza is associated with hundreds of thousands of deaths worldwide annually (1, 2). The 2009 swine-origin influenza A (H1N1) pandemic highlighted the importance of identifying public health measures to mitigate influenza virus transmission.

Many countries would use nonpharmaceutical interventions, including facemasks, improved hand hygiene, cough etiquette, isolation of sick and quarantine of exposed individuals, social distancing measures, and travel restrictions, as their primary means to mitigate an influenza pandemic, particularly at its beginning (3–10). However, data are scarce on the effectiveness of simple personal protective measures, such as facemasks and hand hygiene, against pandemic or interpandemic influenza and on the modes of influenza virus transmission among people (5, 11). After a pilot study in 2007 (12), we conducted a prospective cluster randomized trial to test whether improved hand hygiene or surgical facemasks reduce the transmission of interpandemic influenza in households. We used a cluster design with randomization to interventions at the household level to avoid difficulties in blinding and potential contamination of interventions.

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Context

Hand hygiene and use of facemasks are key elements of influenza pandemic preparedness plans, but their effects on preventing transmission of infection have not been demonstrated.

Contribution

In this cluster randomized trial, hand washing and facemasks seemed to prevent influenza transmission when healthy family members started using these measures within 36 hours of symptom onset in an infected family member.

Caution

Adherence to the interventions was low.

Implication

Hand hygiene and facemasks seem to reduce influenza virus transmission when implemented early after symptom onset.

—The Editors

METHODS

Design

From 45 outpatient clinics in the private and public sectors across Hong Kong, we enrolled persons who reported at least 2 symptoms of acute respiratory illness (temperature ≥37.8 °C, cough, headache, sore throat, or myalgia); had symptom onset within 48 hours; and lived in a household with at least 2 other people, none of whom had reported acute respiratory illness in the preceding 14 days. After participants gave informed consent, they provided nasal and throat swab specimens, which were combined and tested with the QuickVue Influenza A+B rapid diagnostic test (Quidel, San Diego, California). Participants with a positive rapid test result and their household contacts were randomly assigned to 1 of 3 study groups: control (lifestyle measures), control plus enhanced hand hygiene only, and control plus facemasks and enhanced hand hygiene. **Table 1** provides detailed descriptions of the interventions. Data on clinical signs and symptoms were collected for all participants. An additional nasal and throat swab specimen was collected for laboratory confirmation of influenza virus infection by reverse-transcription polymerase chain reaction (RT-PCR).

Randomization lists were prepared by a biostatistician. The households of eligible study index patients were allocated to 3 groups in a 1:1:1 ratio under a block randomization structure with randomly permuted block sizes of 18, 24, and 30 by using a random-number generator (R software, R Development Core Team, Vienna, Austria). Interventions were assigned to households by the study manager on the basis of the randomization sequence. The allocation to specific intervention groups was concealed to recruiting physicians and clinics throughout the study. Participants and people who administered the interventions were not blinded to the interventions, but participants were not informed of the specific nature of the interventions applied to other participating households.

After randomization, a home visit was scheduled within 2 days (ideally within 12 hours) to implement the intervention and to collect informed consent, baseline demographic data, and nasal and throat swab specimens from all household members 2 years of age or older. During the home visit, index patients and household contacts were instructed in the proper use of a tympanic thermometer. During the 6 days after the initial home visit, all household contacts were asked to keep daily symptom diaries. Further home visits were scheduled around 3 and 6 days after the

Table 1. **Study Interventions**

Control intervention

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).

Hand hygiene intervention

All household members (including the index patient) received education about the potential efficacy of proper hand hygiene in reducing transmission. All household members (including the index patient) were instructed to use the liquid soap provided instead of their usual soap after every washroom visit, after sneezing or coughing, and in general when their hands were soiled. They were instructed to use the alcohol hand rub when first retuning home and immediately after touching any potentially contaminated surfaces.

1. Provision of liquid hand soap for each kitchen and each bathroom (221 mL Ivory liquid hand soap [Proctor & Gamble, Cincinnati, Ohio]).
2. Provision of individual small bottles of alcohol hand rub to each participant (100 mL World Health Organization Recommended Formulation I, liquid content with 80% ethanol, 1.45% glycerol, and 0.125% hydrogen peroxide [Vickmans Laboratories, Hong Kong, China]).
3. Demonstration of proper hand washing and antisepsis.

Facemask intervention

Index cases and all household contacts received education about the potential efficacy of surgical facemasks in reducing disease spread to household contacts if all parties wear masks. Index patients and all household contacts were requested to wear masks as often as possible at home during the 7-day follow-up period (except when eating or sleeping) and also when the index patient was with the household members outside of the household.

1. Provision of a box of 50 surgical facemasks (Tecnol–The Lite One [Kimberly-Clark, Roswell, Georgia]) to each household member or a box of 75 pediatric masks for children aged 3 to 7 years.
2. Demonstration of proper facemask wearing and hygienic disposal.

baseline household visit to monitor adherence to interventions and to collect further nasal and throat swab specimens from all household members regardless of illness. During the final home visit, study nurses collected and reviewed symptom diaries, and they evaluated adherence to interventions by interview and by counting the number of surgical masks remaining and weighing the amount of soap and alcohol left in bottles and dispensers. Households were reimbursed for their participation with a supermarket coupon worth approximately U.S. $25.

All participants 18 years or older gave written informed consent. Proxy written consent from parents or legal guardians was obtained for persons 17 years or younger, with additional written assent from those 8 to 17 years of age. The study protocol was approved by the institutional review board of The University of Hong Kong and the Hospital Authority Hong Kong West Cluster.

Outcome Measures

The primary outcome measure was the secondary attack ratio at the individual level: the proportion of household contacts infected with influenza virus. We evaluated the secondary attack ratio by using a laboratory definition (a household contact with a nasal and throat swab specimen positive for influenza by RT-PCR) as the primary analysis and 2 clinical definitions of influenza based on self-reported data from the symptom diaries as secondary analyses (12). The first definition of clinical influenza was at least 2 of the following signs and symptoms: temperature 37.8 °C or greater, cough, headache, sore throat, and myalgia (13); the second was temperature 37.8 °C or greater plus cough or sore throat (14). An additional secondary outcome measure was the secondary attack ratio at the household (cluster) level: the proportion of households with 1 or more secondary case.

Laboratory Methods

Specimens collected from index patients at recruitment were stored in a refrigerator at 2 to 8 °C. Specimens collected during home visits were stored in an ice chest with at least 2 ice packs immediately after collection. Before the end of the day of a home visit, study nurses obtained samples to the nearest collection point for storage in a refrigerator at 2 to 8 °C. Samples stored at 2 to 8 °C in ice chests were delivered to the central testing laboratory at Queen Mary Hospital by courier. Samples were eluted and cryopreserved at −70 °C immediately after receipt. All specimens were tested by RT-PCR for influenza A and B viruses using standard methods (15–17). The **Appendix** (available at www.annals.org) provides additional details of the laboratory procedures that we used.

Statistical Analysis

On the basis of data collected in our pilot study (12) and other studies with similar design (18, 19), we assumed that 10% to 15% of household contacts in the control group would develop RT-PCR–confirmed influenza, with an average household size of 3.8 and an intracluster correlation coefficient of 0.29. Specifying 80% power and a significance level of 5%, we aimed to follow 300 households in each intervention group to allow us to detect differences in secondary attack ratios of 35% to 45%, depending on the actual secondary attack ratios in the control group (15% or 10%, respectively). Recruiting 100 or 200 households to each group would allow 80% power to detect 55% to 70% and 45% to 55% differences in secondary attack ratios, assuming a secondary attack ratio of 10% to 15% in the control group.

To evaluate and compare secondary attack ratios by intervention group, we estimated 95% CIs by using a cluster bootstrap technique with 1000 resamples (20) and chi-square tests and multivariable logistic regression models adjusting for potential within-household correlation (21, 22). We estimated the intracluster correlation coefficient from the mean squared errors in the secondary attack ratio between and within households (21). For the multivariable logistic regression models, we used forced-entry methods to include plausible confounders, including the intervention allocated, the age and sex of the household contacts and their corresponding index patients, vaccination status of the household contacts, and antiviral use in corresponding index patients, whereas missing data on the exact age of 14 household contacts were imputed by comparison with their relationship with the index patient or occupation. Participants were analyzed in the group to which they were randomly assigned, regardless of adherence to the intervention or use of hand washing or facemasks in groups not assigned that intervention.

Our protocol specified that households with more than 1 member with RT-PCR–confirmed influenza virus infection at baseline (co–index patients) or index patients in whom influenza virus infection could not be confirmed by RT-PCR would be excluded from analyses. We excluded from analyses participants who dropped out before receiving the intervention and the few participants who dropped out after the intervention but before data on the primary outcome measure were collected (23). In sensitivity analyses, we analyzed all households in which the intervention was applied, using multiple imputation for unobserved outcomes (24) and including an additional explanatory variable for households with more than 1 index patient. Statistical analyses were conducted in R, version 2.7.1 (R Development Core Team).

Role of the Funding Source

The study was funded by the Centers for Disease Control and Prevention; the Research Fund for the Control of Infectious Disease, Food and Health Bureau, Government of the Hong Kong SAR; and the Area of Excellence Scheme of the Hong Kong University Grants Committee. The sponsors had no role in data collection and analysis, or the decision to publish, but the Centers for Disease Control and Prevention were involved in study design and preparation of the manuscript.

RESULTS

We recruited 2750 potential index patients from 2 January through 30 September 2008; recruitment increased during periods of peak influenza activity in February and March and July and August (**Appendix Figure 1**, available at www.annals.org).

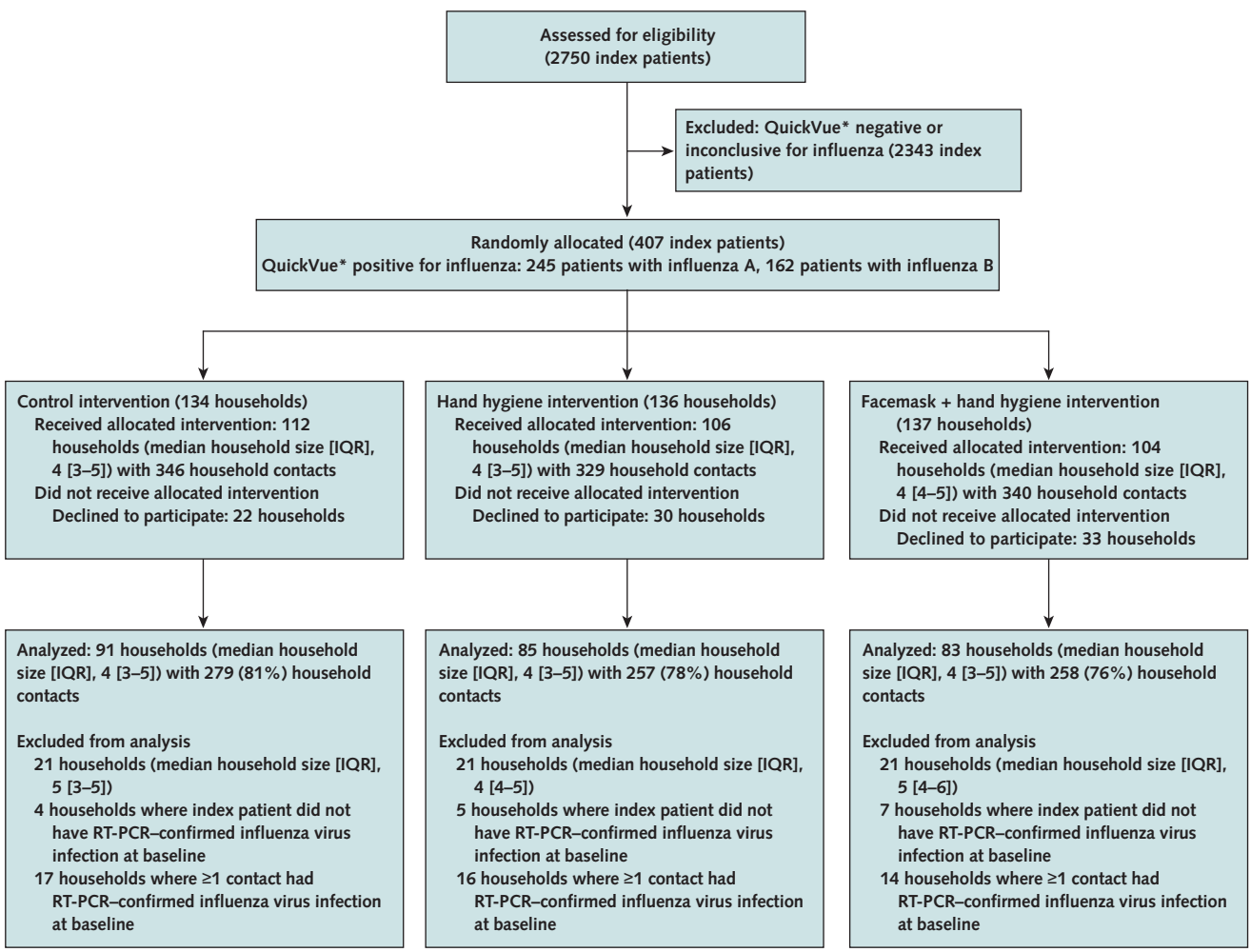
The **Figure** shows the study flow. Of the 2750 potential index patients, 407 (14.8%) had influenza A or B virus infection according to the rapid test; these persons and their households were randomly allocated. In an unintentional deviation from that protocol, 49 of the 407 persons had a household contact with influenza symptoms at recruitment (a potential co–index patient). We also randomly assigned 6 of 407 persons who had symptoms for slightly more than 48 hours.

After random assignment, 76 (19%) of the households declined home visits or could not be contacted after numerous repeated attempts. We implemented the interventions in 331 households. After initial home visits, 9 households declined further participation and were excluded from analyses. Thus, 322 (97%) households completed follow-up. Influenza could not be confirmed by RT-PCR in 16 of 322 index patients in these households at baseline, and those 16 households were excluded (**Figure 1**). A further 47 households were excluded because 1 or more contacts had RT-PCR–confirmed influenza virus infection at baseline. Three household contacts declined to participate and were excluded from analyses. We evaluated and compared secondary attack ratios in the remaining 259 (64%) households, which included 794 household contacts. One hundred sixty (62%) index patients had influenza A virus infection, and 99 (38%) had influenza B virus infection.

Participants

Table 2 shows the characteristics of all randomly assigned index patients and of the index patients and house-

Figure. **Study flow diagram.**



IQR = interquartile range; RT-PCR = reverse-transcription polymerase chain reaction.
* QuickVue Influenza A+B rapid diagnostic test (Quidel, San Diego, California).

Table 2. **Participant Characteristics***

Characteristic	Control Group		Hand Hygiene Group		Facemask Plus Hand Hygiene Group	
	Randomly Assigned (*n* = 134)	Analyzed (*n* = 91)	Randomly Assigned (*n* = 136)	Analyzed (*n* = 85)	Randomly Assigned (*n* = 137)	Analyzed (*n* = 83)
Index patients						
Age group						
≤5 y	26 (19)	20 (22)	19 (14)	10 (12)	25 (18)	14 (17)
6–15 y	70 (52)	54 (59)	66 (49)	46 (54)	67 (49)	45 (54)
16–30 y	17 (13)	5 (5)	24 (18)	12 (14)	22 (16)	11 (13)
31–50 y	15 (11)	11 (12)	23 (17)	15 (18)	18 (13)	9 (11)
>50 y	6 (4)	1 (1)	4 (3)	2 (2)	5 (4)	4 (5)
Median age (IQR), y	10 (6–18)	9 (6–12)	12 (7–28)	11 (8–28)	10 (6–22)	10 (6–20)
Men	63 (47)	44 (48)	76 (56)	41 (48)	62 (45)	33 (40)
Symptoms						
Temperature ≥37.8 °C	111 (83)	75 (82)	110 (81)	75 (88)	104 (76)	66 (80)
Headache	75 (56)	48 (53)	74 (54)	46 (54)	66 (48)	38 (46)
Sore throat	73 (54)	50 (55)	82 (60)	51 (60)	95 (69)	56 (67)
Cough	112 (84)	75 (82)	108 (79)	67 (79)	119 (87)	71 (86)
Myalgia	68 (51)	46 (51)	59 (43)	40 (47)	63 (46)	36 (43)
Runny nose	122 (91)	82 (90)	116 (85)	73 (86)	121 (88)	76 (92)
Phlegm	85 (63)	56 (62)	85 (62)	55 (65)	92 (67)	56 (67)
Symptom onset to randomization interval						
0–12 h	22 (16)	16 (18)	31 (23)	15 (18)	29 (21)	20 (24)
12–24 h	72 (54)	54 (59)	60 (44)	44 (52)	61 (45)	38 (46)
24–36 h	12 (9)	8 (9)	15 (11)	9 (11)	10 (7)	3 (4)
36–48 h	27 (20)	13 (14)	28 (21)	16 (19)	34 (25)	21 (25)
48–60 h	1 (1)	0 (0)	2 (1)	1 (1)	3 (2)	1 (1)
Randomization to intervention interval						
0–12 h	–	74 (81)	–	65 (76)	–	74 (89)
12–24 h	–	8 (9)	–	7 (8)	–	3 (4)
24–36 h	–	8 (9)	–	12 (14)	–	6 (7)
36–48 h	–	1 (1)	–	1 (1)	–	0 (0)
Prescribed antiviral						
Oseltamivir	–	22 (24)	–	19 (22)	–	23 (28)
Amantadine	–	0 (0)	–	0 (0)	–	0 (0)
Zanamivir	–	1 (1)	–	0 (0)	–	1 (1)
Ribavirin	–	1 (1)	–	0 (0)	–	0 (0)
Median household size, *n*		4		4		4
Household contacts†						
Age group						
≤5 y	–	20 (7)	–	9 (4)	–	15 (6)
6–15 y	–	29 (10)	–	32 (12)	–	25 (10)
16–30 y	–	37 (13)	–	27 (11)	–	36 (14)
31–50 y	–	157 (56)	–	125 (49)	–	131 (51)
>50 y	–	34 (12)	–	53 (21)	–	50 (19)
Unknown	–	2 (1)	–	11 (4)	–	1 (0)
Median age (IQR)	–	38 (26–45)	–	40 (28–49)	–	38 (27–48)
Men	–	105 (38)	–	103 (40)	–	98 (38)
Received influenza vaccination in the previous 12 mo	–	30 (11)	–	32 (12)	–	44 (17)

IQR = interquartile range.

* Data are the number (percentage) of participants, unless otherwise indicated. We excluded 85 households that dropped out, 16 households in which the index patients did not have reverse-transcription polymerase chain reaction–confirmed influenza virus infection at baseline, and 47 households in which ≥1 household contacts had reverse transcription polymerase chain reaction–confirmed influenza virus infection at baseline (a co–index patient).

† 279 patients in the control group, 257 in the hand hygiene group, and 258 in the facemask plus hand hygiene group.

hold members that were retained in the main analysis. In general, the groups were similar. Around two thirds of index patients were children.

The median household size was 4 persons (interquartile range, 3 to 5 persons). A median of 1 child (interquartile range, 1 to 2 children) lived in the analyzed households in each intervention group. The median size of a household's apartment was 700 square feet (interquartile range, 581 to 1000 square feet), and the mean residential density index, defined as the number of household members divided by the household size, was 0.6 (SD, 0.3) persons per 100 square feet; this did not differ substantially or significantly between intervention groups.

Table 3. **Secondary Attack Ratios of RT-PCR–Confirmed Influenza Virus Infection and Clinical Influenza**

Interval Between Symptom Onset and Intervention	Determination of Influenza*	Control Group (n = 279)		Hand Hygiene Group (n = 257)		Facemask Plus Hand Hygiene (n = 258)		P Value†
		Cases, n	SAR (95% CI), %‡	Cases, n	SAR (95% CI), %‡	Cases, n	SAR (95% CI), %‡	
Any	RT-PCR confirmed	28	10 (6–14)	14	5 (3–9)	18	7 (4–11)	0.22
	Clinical definition 1	53	19 (14–24)	42	16 (12–21)	55	21 (16–27)	0.40
	Clinical definition 2	14	5 (2–8)	9	4 (2–6)	18	7 (4–11)	0.28
≤36 h§	RT-PCR confirmed	22	12 (7–18)	7	5 (1–11)	6	4 (1–7)	0.040
	Clinical definition 1	42	23 (16–30)	14	11 (5–17)	27	18 (12–24)	0.032
	Clinical definition 2	12	7 (3–11)	5	4 (1–7)	11	7 (3–12)	0.52

RT-PCR = reverse-transcription polymerase chain reaction; SAR = secondary attack ratio.
* "Clinical definition 1" is at least 2 of the following: temperature ≥37.8 °C, cough, headache, sore throat, and myalgia. "Clinical definition 2" is temperature ≥37.8 °C, plus cough or sore throat.
† For difference among the 3 groups by the Pearson chi-square test, adjusted for within-household correlations of 0.12 for the RT-PCR–confirmed secondary attack ratios and 0.04 and 0.07 for the clinical influenza secondary attack ratios.
‡ The secondary attack ratio at the individual level was defined as the proportion of household contacts of an index case that subsequently became infected with influenza. The CIs were calculated by using a cluster bootstrap method (20).
§ Based on 183 patients in the control group, 130 in the hand hygiene group, and 149 in the facemask plus hand hygiene group.

Most of the initial home visits were completed within 12 hours of recruitment (**Appendix Table 1**, available at www.annals.org). The interval between symptom onset and intervention did not significantly differ between the intervention groups (data not shown).

Influenza Transmission

Overall, 60 (8%) household contacts in 49 (19%) households developed RT-PCR–confirmed influenza virus infection during the follow-up period, including 7 households with 2 secondary cases and 2 households with 3 secondary cases; 150 (19%) and 41 (5%) contacts met the 2 definitions of clinical influenza. There were no significant differences between intervention groups in contact infections when any of the influenza definitions were used (**Table 3**). Among 597 household contacts of 188 index patients who were children 15 years or younger, there were 54 (9%) secondary cases (17 siblings [secondary attack ratio, 15%], 26 parents (8%), 10 live-in domestic helpers (9%), and 1 aunt (2%). Among 197 household contacts of 71 adult index patients, there were 6 (3%) secondary cases (2 children [secondary attack ratio, 4%]) and 1 spouse [4%]). Secondary attack ratios did not significantly differ at the household level (24% in the control group, 14% in the hand hygiene group, and 18% in the facemask plus hand hygiene group; $P = 0.37$).

Table 4 shows the adjusted odds ratios of RT-PCR–confirmed influenza virus infection or clinical influenza in household contacts by intervention group, allowing for within-household correlation. The risk of RT-PCR–confirmed influenza virus infection did not differ significantly between intervention groups, but it was significantly higher for children 6 to 15 years of age, and there was a nonsignificant higher risk for influenza virus infection for contacts in households in which the index patient was a child.

In a subgroup analysis planned before study implementation (12), we found a significant reduction in RT-PCR–confirmed influenza virus infections in the household contacts in 154 households in which the intervention was applied within 36 hours of symptom onset in the index patient (**Table 3**). The significant difference between the treatment groups was also observed for the first definition of clinical influenza and seemed to be attributable to fewer infections in the facemask plus hand hygiene group (adjusted odds ratio, 0.33 [95% CI 0.13 to 0.87]) (**Table 5**). No significant difference was found between the facemask plus hand hygiene group and the hand hygiene group in RT-PCR–confirmed influenza virus infections in household contacts (odds ratio, 0.72 [CI, 0.21 to 2.48]). In an exploratory analysis, we found a borderline nonsignificant difference between intervention groups in RT-PCR–confirmed influenza virus infections among household contacts in which the intervention was applied within 48 hours of symptom onset in the index patient (**Appendix Table 2**, available at www.annals.org).

Consistent results were found in separate analyses of household contacts of index patients with influenza A or B virus infection (**Appendix Tables 3** and **4**, available at www.annals.org). The reductions were not statistically significant in the smaller number of household contacts of index patients with influenza B virus infection.

In sensitivity analyses, we compared secondary attack ratios by using combinations of RT-PCR or clinical influenza outcomes in household contacts, by intervention group (**Appendix Tables 5**, **6**, and **7**, available at www.annals.org). When the intervention was applied within 36 hours of symptom onset of the index patient, we found significant differences between groups in influenza infections that were both RT-PCR confirmed and met the first clinical definition. We also found significant differences in influenza virus infections that were either RT-PCR confirmed or met the first clinical definition, or both. In additional sensitivity analyses on all 331 households in which the intervention was applied, results were similar to the

main findings (**Appendix Tables 8** and **9**, available at www.annals.org).

Adherence

At the final home visit, the intervention groups reported higher adherence to the interventions than the control group. Self-reported data were consistent with measurements of the amount of soap, alcohol hand rub, and facemasks used (**Table 6**). As part of their symptom diaries, participants in the intervention groups reported daily adherence to the respective interventions; improved hand hygiene was maintained throughout follow-up and was similar among index patients and contacts (**Appendix Figure 2**, available at www.annals.org). Adherence to the hand hygiene intervention was slightly higher in the hand hygiene group than the facemask plus hand hygiene group (**Appendix Table 10**, available at www.annals.org). Index patients reported greater use of facemasks than household contacts, particularly during the first few days of follow-up (**Appendix Figure 2**, available at www.annals.org). Adherence was similar in the subgroup of households in which the intervention was applied within 36 hours of symptom onset in the index patient (**Appendix Table 10**, available at www.annals.org).

DISCUSSION

We report the largest study to date of the efficacy of facemasks and hand hygiene to prevent influenza virus transmission in households. Overall, the interventions did not lead to statistically significant reductions in household transmission, although we did observe statistically significant reductions where interventions were applied early after symptom onset in the index patient. The strengths of our study include laboratory confirmation of secondary influenza virus infections and the community setting with outpatient-based recruitment, which allows broad generalizability.

Our study design resulted in delays between symptom onset in the index patient and application of the interventions; thus, although adherence was incomplete, we have probably underestimated the true effectiveness of these simple interventions. Our results suggest that substantial clinically significant reductions in household infections could result if the interventions are applied

Table 4. **Risk for Influenza Virus Infection in Included Households***

Characteristic	Participants, *n*	Odds Ratio (95% CI)†		
		RT-PCR–Confirmed Influenza	Clinical Influenza‡	
			Definition 1	Definition 2
Study group				
Control	279	1.00 (reference)	1.00 (reference)	1.00 (reference)
Hand hygiene	257	0.57 (0.26–1.22)	0.92 (0.57–1.48)	0.81 (0.33–2.00)
Facemask plus hand hygiene	258	0.77 (0.38–1.55)	1.25 (0.79–1.98)	1.68 (0.68–4.15)
Contact characteristics				
Age				
Adult (>16 y)	662	1.00 (reference)	1.00 (reference)	1.00 (reference)
Child (6–15 y)	88	2.87 (1.42–5.78)	1.71 (0.99–2.96)	6.64 (3.01–14.7)
Child (≤5 y)	44	1.91 (0.69–5.30)	1.27 (0.59–2.72)	6.75 (2.45–18.6)
Sex				
Female	488	1.00 (reference)	1.00 (reference)	1.00 (reference)
Male	306	0.71 (0.41–1.24)	0.69 (0.47–1.01)	0.46 (0.21–1.02)
Vaccination status				
No influenza vaccination in the past 12 mo	688	1.00 (reference)	1.00 (reference)	1.00 (reference)
Influenza vaccination in the past 12 mo	106	0.33 (0.12–0.91)	1.19 (0.71–2.01)	1.50 (0.57–3.93)
Index patient characteristics				
Age				
Adult (>16 y)	71	1.00 (reference)	1.00 (reference)	1.00 (reference)
Child (6–15 y)	144	2.74 (0.95–7.90)	1.75 (1.01–3.01)	1.85 (0.55–6.17)
Child (≤5 y)	44	2.82 (0.87–9.14)	2.22 (1.19–4.14)	3.89 (0.98–15.4)
Sex				
Female	140	1.00 (reference)	1.00 (reference)	1.00 (reference)
Male	119	1.11 (0.61–2.04)	0.99 (0.67–1.44)	0.47 (0.23–0.99)
Antiviral status				
Not prescribed antiviral	191	1.00 (reference)	1.00 (reference)	1.00 (reference)
Prescribed antiviral	68	0.70 (0.33–1.45)	0.71 (0.45–1.12)	0.70 (0.28–1.78)

RT-PCR = reverse-transcription polymerase chain reaction.
* Based on 794 household contacts in 259 analyzed households.
† Adjusted for intervention group; age, sex, and vaccination history of the contact; and age, sex, and antiviral use of the index patient.
‡ "Clinical definition 1" is at least 2 of the following: temperature ≥37.8 °C, cough, headache, sore throat, and myalgia. "Clinical definition 2" is temperature ≥37.8 °C, plus cough or sore throat.

soon after symptom onset (**Tables 3** and **5**), which is plausible given that infectiousness may be highest soon after symptom onset (25–27). Although our results suggest a benefit of hand hygiene and facemasks in combination if applied early, our study cannot precisely distinguish the relative contributions of the 2 interventions. A recent prospective trial of 143 households reported a protective effect of facemasks against a clinical outcome measure in the per-protocol (as-treated) analysis, although no evidence of efficacy was found by intention-to-treat analysis or in laboratory-confirmed respiratory virus infections (28).

In addition to statistically significant differences between the intervention groups in the primary outcome measure of RT-PCR–confirmed infections, we observed statistically significant differences between groups when we used the first definition of clinical influenza but not the second definition (**Table 3**). Symptom-based outcomes can lack specificity for influenza virus infections (12, 29), and the interventions in our study aimed to reduce influenza virus transmission within households and may not have been effective in preventing other respiratory infections outside the home. Another possible explanation is that our study lacked statistical power to identify differences in the second clinical definition, with few patients meeting the stricter criteria of fever plus cough or sore throat.

As in our pilot study (12), adherence to the interventions varied. We observed contamination between groups, because both interventions were practiced to some degree in the control group. Only half of the index patients in the facemask plus hand hygiene group reported regular use of a surgical mask during follow-up. Facemask adherence among household contacts was lower. Adherence to the hand hygiene intervention seemed low compared with rates recommended in health care settings but was similar to rates in previous community studies (30–32). In addition, effects in our study may tend toward a lower bound on the effects that might be observed in a pandemic with heightened public awareness (28). It is important to find ways of improving adherence for future studies.

Limitations of our study design include the potential bias from recruiting symptomatic persons, which

Table 5. **Risk for Influenza Virus Infection When the Intervention Was Applied Within 36 Hours of Symptom Onset in the Index Patient***

Characteristic	Participants, *n*	Odds Ratio (95% CI)†		
		RT-PCR–Confirmed Influenza	Clinical Influenza‡	
			Definition 1	Definition 2
Study group				
Control	183	1.00 (reference)	1.00 (reference)	1.00 (reference)
Hand hygiene	130	0.46 (0.15–1.43)	0.46 (0.22–0.96)	0.64 (0.20–2.02)
Facemask plus hand hygiene	149	0.33 (0.13–0.87)	0.86 (0.48–1.53)	1.45 (0.49–4.24)
Contact characteristics				
Age				
Adult (≥16 y)	386	1.00 (reference)	1.00 (reference)	1.00 (reference)
Child (6–15 y)	51	3.02 (1.16–7.85)	2.09 (1.01–4.32)	7.57 (2.79–20.6)
Child (≤5 y)	25	2.45 (0.75–8.01)	2.16 (0.87–5.34)	7.20 (1.92–27.0)
Sex				
Female	283	1.00 (reference)	1.00 (reference)	1.00 (reference)
Male	179	0.68 (0.30–1.53)	0.40 (0.23–0.70)	0.36 (0.12–1.06)
Vaccination status				
No influenza vaccination in the past 12 mo	401	1.00 (reference)	1.00 (reference)	1.00 (reference)
Influenza vaccination in the past 12 mo	61	0.40 (0.12–1.33)	1.33 (0.71–2.49)	1.10 (0.31–3.91)
Index patient characteristics				
Age				
Adult (≥16 y)	39	1.00 (reference)	1.00 (reference)	1.00 (reference)
Child (6–15 y)	85	1.17 (0.33–4.23)	1.57 (0.66–3.74)	0.79 (0.20–3.19)
Child (≤5 y)	30	1.55 (0.37–6.45)	2.26 (0.86–5.95)	2.36 (0.46–12.3)
Sex				
Female	82	1.00 (reference)	1.00 (reference)	1.00 (reference)
Male	72	0.97 (0.44–2.14)	1.18 (0.71–1.98)	0.56 (0.24–1.30)
Antiviral status				
Not prescribed antiviral	109	1.00 (reference)	1.00 (reference)	1.00 (reference)
Prescribed antiviral	45	0.81 (0.32–2.04)	0.76 (0.42–1.38)	0.66 (0.21–2.06)

RT-PCR = reverse-transcription polymerase chain reaction.
* Based on 462 household contacts in 154 analyzed households.
† Adjusted for intervention group; age, sex, and vaccination history of the contact; and age, sex, and antiviral use of the index patient.
‡ "Clinical definition 1" is at least 2 of the following: temperature ≥37.8 °C, cough, headache, sore throat, and myalgia. "Clinical definition 2" is temperature ≥37.8 °C, plus cough or sore throat.

Table 6. **Summary Measures of Adherence to Interventions During the 7-Day Follow-up Period**

Characteristic	Control Group		Hand Hygiene Group		Facemask Plus Hand Hygiene Group	
	Index Patient	Contact	Index Patient	Contact	Index Patient	Contact
Using liquid soap, %*	70	77	68	71	77	78
Using alcohol hand rub, %*	7	6	36	28	33	24
Practicing good hand hygiene, %†	44	46	62	54	61	56
Median amount of liquid hand soap used by household (IQR), *g*	–	–	85.7 (42.9–155.2)		78.9 (37.9–120.1)	
Median amount of alcohol hand rub used by individuals (IQR), *g*	–	–	2.7 (0.6–6.0)	1.4 (0.3–5.3)	1.6 (0.5–5.4)	1.4 (0.3–4.7)
Wearing surgical mask, %‡	15	7	31	5	49	26
Median number of masks used (IQR)	–	–	–	–	9 (3.0–16.3)	4 (0–9)

IQR = interquartile range.
* Proportion of individuals who reported washing their hands with liquid hand soap or using alcohol hand rub often or always (rather than sometimes or never) during the follow-up period.
† Proportion of individuals who reported washing their hands often or always (rather than sometimes or never) after sneezing, coughing, or blowing their nose during the follow-up period.
‡ Proportion of individuals who reported wearing a surgical facemask often or always (rather than sometimes or never) during the follow-up period.

has 3 effects. First, by using a point-of-care rapid test to detect influenza virus infection, we might preferentially have included index patients with higher viral shedding (33). However, statistical power would generally be increased if index patients were more infectious, because we might observe more household transmission; the limitation thus relates more to generalizability. Second, our study design resulted in an unavoidable delay between onset of symptoms in the index patient and the application of interventions; this may have led to underestimation of their true effects, as suggested by our statistically significant finding of reduced infection when interventions were implemented within 36 hours. Our household sample may have been biased toward including household contacts with preexisting immunity, because in households in which all contacts were susceptible, there might have been more possibility of secondary cases being observed before the index patient presented to a primary care provider (12). Our primary outcome measure is based on laboratory confirmation of influenza by RT-PCR, with specimens collected from home visits at 3-day intervals, and some infections may have been missed if peak viral shedding in the respiratory tract occurred between home visits. We may have missed secondary infections that occurred 7 days or more after illness onset in the index patient. In addition, collection of poor-quality specimens or degeneration during transport or freezing could have reduced RT-PCR sensitivity. Finally, we did not evaluate other facemasks or respirators, such as P2 or N95 masks; these might be more effective than surgical facemasks, although fit testing is usually required and adherence could be difficult to maintain (28).

Several issues should be considered when planning further studies of nonpharmaceutical interventions. We recruited index patients from outpatient clinics, and recruitment was therefore driven by influenza incidence (**Appendix Figure 1**, available at www.annals.org). This could be problematic in temperate locations with shorter and more intense influenza seasons, where delays between recruitment and intervention may dilute effects. An alternative approach would be to recruit a cohort of uninfected households before an influenza season. However, a much larger sample would be needed, given the low attack rate of influenza. Studies over multiple influenza seasons are useful to allow for variability in incidence rates from year to year. It is challenging to obtain longitudinal laboratory specimens from participants with repeated home visits, but relying on clinical symptoms to guide testing may not yield results specific for influenza. Paired serology could be compared to determine influenza infections during follow-up; this was not feasible in our study.

In conclusion, our results suggest that hand hygiene and facemasks can reduce influenza virus transmission if implemented early after symptom onset in an index patient. During a pandemic, resources may not be available to isolate all infected individuals, and home isolation of some patients may be required. Our results directly inform the personal protective measures that should be taken in such a scenario and support the use of these nonpharmaceutical interventions in public health control measures against interpandemic influenza in annual epidemics.

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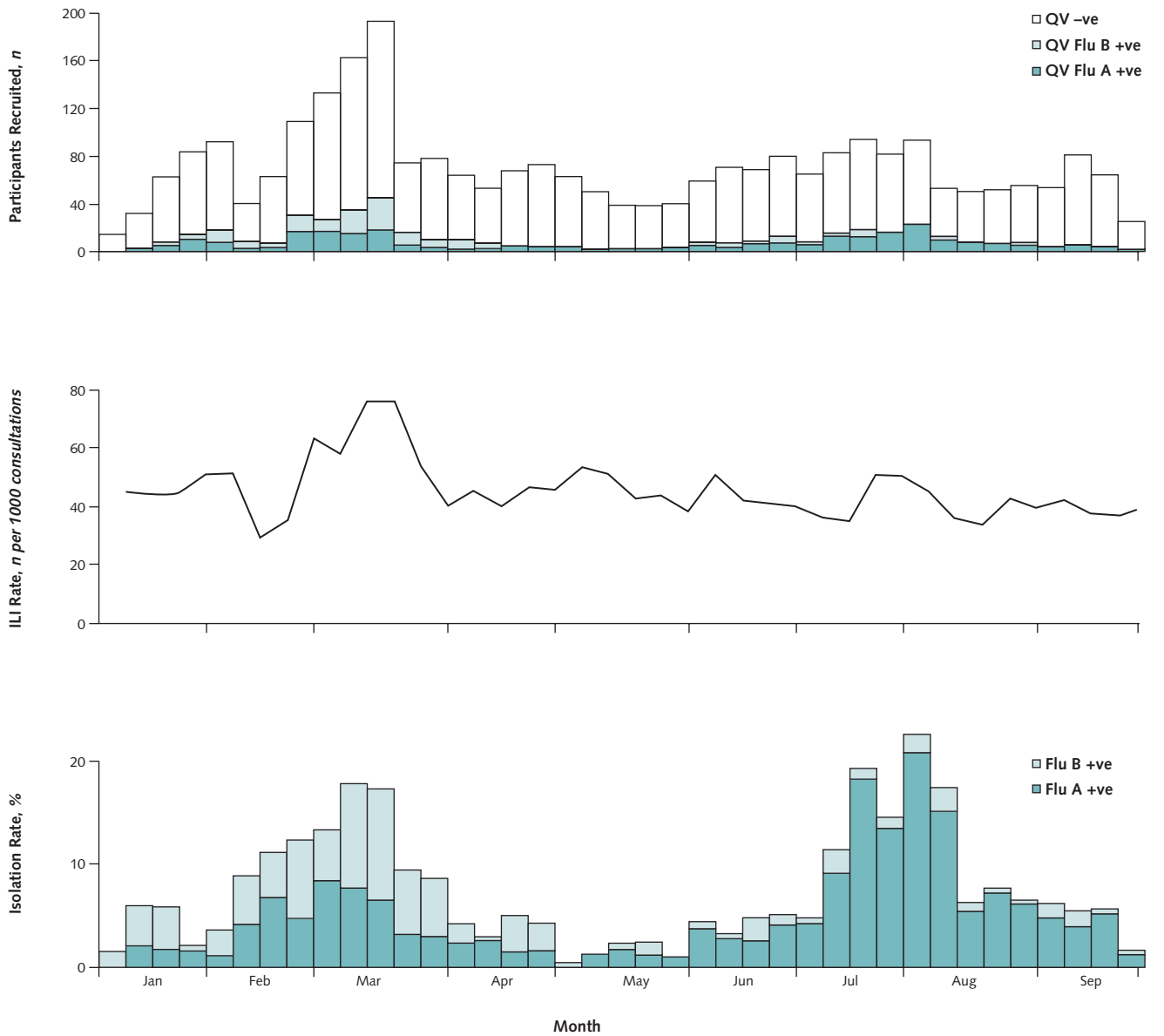
Appendix: Additional Details of RT-PCR Methods

Total nucleic acid was extracted from specimens by using the NucliSens easyMAG extraction system (bioMérieux, Boxtel, the Netherlands) according to the manufacturer's instructions. Twelve microliters of extracted nucleic acid was used to prepare complementary DNA (cDNA) by using an Invitrogen Superscript III kit (Invitrogen, San Diego, California) with random, primer, as described elsewhere (16).

For detection of influenza A virus, 2 μL of cDNA was amplified in a LightCycler 2.0 (Roche Diagnostics, Penzberg, Germany) with a total reaction-mix volume of 20 μL reaction containing FastStart DNA Master SYBR Green I Mix reagent kit (Roche Diagnostics), 4.0 mM $MgCl_2$ and 0.5mM of each primer. The forward primer (5′-CTTCTAACCGAGGTCGAAACG-3′) and the reverse primer (5′-GGCATTTTGGACAAAKCGTCTA-3′) were used for amplification of the matrix gene of influenza A virus [15]. Cycling conditions were as follows: initial denaturation at 95 °C for 10 minutes, followed by 40 cycles of 95 °C for 10 seconds, 60 °C for 3 seconds, and 72 °C for 12 seconds, with ramp rates of 20 °C/s. At the end of the assay, PCR products were subjected to a melting-curve analysis to determine the specificity of the assay.

For detection of influenza B virus, forward (5′-GCATCTTTTGTTTTTTATCCATTCC) and reverse (5′-CACAATTGCCTACCTGCTTTCA) primers and 5′ nuclease probe (Fam-TGCTAGTTCTGCTTTGCCTTCTCCATCTTCT-TAMRA) were used for amplification of the matrix gene [17]. Testing was performed by using the TagMan EZ RT-PCR Core reagent kit (Applied Biosystems, Hammonton, New Jersey), with 0.8 μmol/L of forward and reverse primers and 0.2 μmol/L of probe in a total reaction volume of 25 μL, comprising 4 μL of nucleic acid extract. Amplification and detection was performed on an ABI StepOneTM Real-Time PCR System (Applied Biosystems) under the following conditions: initial hold at 50 °C for 20 minutes and 95 °C for 15 minutes, followed by 45 cycles at 95 °C for 15 seconds and 60 °C for 1 minute.

Appendix Figure 1. **Study recruitment and local influenza activity.**



ILI = influenza-like illness; QV −ve = negative result by QuickVue Influenza A+B test; QV Flu A +ve = positive result for influenza A by QuickVue Influenza A+B test; QV Flu B +ve = positive result for influenza B by QuickVue Influenza A+B test.
Top. Weekly recruitment rates, stratified by rapid test result. **Middle.** Local surveillance data on the weekly rate of ILI consultations per 1000 consultations among sentinel general practitioners reporting to the Centre for Health Protection. **Bottom.** Weekly rate of positive influenza A and B virus isolations among specimens submitted to the World Health Organization reference laboratory of Queen Mary Hospital, Hong Kong.

Appendix Table 1. **Interval Between Symptom Onset in Index Patients, Random Assignment, and Application of the Intervention***

Delay	Symptom Onset to Random Assignment, *n* (%)	Random Assignment to Intervention, *n* (%)	Symptom Onset to Intervention, *n* (%)
0–12 h	51 (20)	213 (82)	0 (0)
12–24 h	136 (53)	18 (7)	44 (17)
24–36 h	20 (8)	26 (10)	110 (42)
36–48 h	50 (19)	2 (1)	30 (12)
48–60 h	2 (1)	0 (0)	65 (25)
60–72 h	–	–	6 (2)
72–84 h	–	–	3 (1)
84–96 h	–	–	1 (0)

* Based on 259 index patients.

Appendix Table 2. **Secondary Attack Ratios for RT-PCR–Confirmed and Clinical Influenza When the Intervention Was Applied Within 48 Hours of Symptom Onset in the Index Patient***

Interval Between Symptom Onset and Intervention	Determination of Influenza†	Secondary Attack Ratio (95% CI), %‡			*P* Value§
		Control Group (*n* = 214)	Hand Hygiene Group (*n* = 167)	Facemask Plus Hand Hygiene Group (*n* = 171)	
≤48 h	RT-PCR confirmed	11 (6–16)	6 (2–10)	4 (2–7)	0.077
	Clinical definition 1	20 (14–26)	13 (7–18)	19 (13–25)	0.182
	Clinical definition 2	6 (2–10)	3 (1–6)	8 (4–12)	0.24

RT-PCR = reverse-transcription polymerase chain reaction.
* Based on 552 household contacts in 184 analyzed households.
† "Clinical definition 1" is at least 2 of the following: temperature ≥37.8 °C, cough, headache, sore throat, and myalgia. "Clinical definition 2" is temperature ≥37.8 °C, plus cough or sore throat.
‡ The CIs were calculated by using a cluster bootstrap method (20).
§ For the difference among the 3 groups by the Pearson chi-square test, adjusted for within-household correlation.

Appendix Table 3. **Secondary Attack Ratios for RT-PCR–Confirmed and Clinical Influenza A Virus Infection**

Interval Between Symptom Onset and Intervention	Determination of Influenza*	Secondary Attack Ratio (95% CI), %†			*P* Value‡
		Control Group	Hand Hygiene Group	Facemask Plus Hand Hygiene Group	
Any§	RT-PCR confirmed	10 (5–16)	4 (1–7)	5 (2–9)	0.117
	Clinical definition 1	20 (13–27)	13 (8–18)	21 (14–28)	0.162
	Clinical definition 2	5 (2–9)	3 (1–6)	8 (3–14)	0.173
≤36 h‖	RT-PCR confirmed	12 (5–20)	3 (0–10)	4 (1–8)	0.083
	Clinical definition 1	23 (15–31)	8 (3–14)	20 (12–29)	0.031
	Clinical definition 2	7 (2–12)	3 (0–8)	9 (4–15)	0.30

RT-PCR = reverse-transcription polymerase chain reaction.
* "Clinical definition 1" is at least 2 of the following: temperature ≥37.8 °C, cough, headache, sore throat, and myalgia. "Clinical definition 2" is temperature ≥37.8 °C, plus cough or sore throat.
† The CIs were calculated by using a cluster bootstrap method (20).
‡ For the difference among the 3 groups by the Pearson chi-square test, adjusted for within-household correlation.
§ Based on 175 persons in the control group, 158 in the hand hygiene group, and 154 in the facemask plus hand hygiene group.
‖ Based on 123 persons in the control group, 87 in the hand hygiene group, and 99 in the facemask plus hand hygiene group.

Appendix Table 4. Secondary Attack Ratios for RT-PCR–Confirmed and Clinical Influenza B Virus Infection

Interval Between Symptom Onset and Intervention	Determination of Influenza*	Secondary Attack Ratio (95% CI), %†			*P* Value‡
		Control Group	Hand Hygiene Group	Facemask Plus Hand Hygiene Group	
Any§	RT-PCR confirmed	10 (5–16)	8 (3–15)	10 (4–17)	0.93
	Clinical definition 1	17 (10–25)	22 (14–30)	22 (15–30)	0.62
	Clinical definition 2	5 (0–11)	4 (1–8)	5 (1–8)	0.97
≤36 h‖	RT-PCR confirmed	12 (5–20)	09 (2–20)	4 (0–11)	0.32
	Clinical definition 1	23 (12–34)	16 (5–28)	14 (6–22)	0.42
	Clinical definition 2	7 (0–16)	5 (0–11)	4 (0–11)	0.90

RT-PCR = reverse-transcription polymerase chain reaction.
* "Clinical definition 1" is at least 2 of the following: temperature ≥37.8 °C, cough, headache, sore throat, and myalgia. "Clinical definition 2" is temperature ≥37.8 °C, plus cough or sore throat.
† The CIs were calculated by using a cluster bootstrap method (20).
‡ For the difference among the 3 groups by the Pearson chi-square test, adjusted for within-household correlation.
§ Based on 104 persons in the control group, 99 in the hand hygiene group, and 104 in the facemask plus hand hygiene group.
‖ Based on 60 persons in the control group, 43 in the hand hygiene group, and 50 in the facemask plus hand hygiene group.

Appendix Table 5. Secondary Attack Ratios for RT-PCR–Confirmed and Clinical Influenza Virus Infection When Composite Definitions Are Used*

Interval Between Symptom Onset and Intervention	Determination of Influenza†	Secondary Attack Ratio (95% CI), %‡			*P* Value§
		Control Group	Hand Hygiene Group	Facemask Plus Hand Hygiene Group	
Any‖	RT-PCR confirmed or clinical definition 1	22 (17–28)	19 (14–24)	23 (18–28)	0.55
	RT-PCR confirmed and clinical definition 1	7 (4–10)	3 (1–6)	5 (3–9)	0.178
	RT-PCR confirmed or clinical definition 2	11 (8–16)	7 (4–10)	11 (7–15)	0.23
	RT-PCR confirmed and clinical definition 2	4 (2–6)	2 (1–5)	3 (1–6)	0.71
≤36 hours¶	RT-PCR confirmed or clinical definition 1	26 (20–33)	13 (8–20)	19 (13–26)	0.040
	RT-PCR confirmed and clinical definition 1	9 (5–14)	3 (1–8)	3 (1–8)	0.051
	RT-PCR confirmed or clinical definition 2	13 (9–19)	7 (3–13)	9 (5–14)	0.31
	RT-PCR confirmed and clinical definition 2	5 (3–10)	2 (0–7)	3 (1–7)	0.26

RT-PCR = reverse-transcription polymerase chain reaction.
* Based on 794 household contacts in 259 analyzed households.
† "Clinical definition 1" is at least 2 of the following: temperature ≥37.8 °C, cough, headache, sore throat, and myalgia. "Clinical definition 2" is temperature ≥37.8 °C, plus cough or sore throat.
‡ The CIs were calculated by using a cluster bootstrap method (20).
§ For the difference among the 3 groups by the Pearson chi-square test, adjusted for within-household correlation.
‖ Based on 279 persons in the control group, 257 in the hand hygiene group, and 258 in the facemask plus hand hygiene group.
¶ Based on 183 persons in the control group, 130 in the hand hygiene group, and 149 in the facemask plus hand hygiene group.

Appendix Table 6. **Risk for Influenza Virus Infection in the Overall Sample, Using a Composite Definition of Infection***

Characteristic	Participants, *n*	Odds Ratio (95% CI)†			
		RT-PCR–Confirmed Influenza or Clinical Influenza (Definition 1)‡	RT-PCR–Confirmed Influenza and Clinical Influenza (Definition 1)‡	RT-PCR–Confirmed Influenza or Clinical Influenza (Definition 2)‡	RT-PCR–Confirmed Influenza and Clinical Influenza (Definition 2)‡
Study group					
Control	279	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Hand hygiene	257	0.90 (0.56–1.45)	0.46 (0.17–1.21)	0.60 (0.30–1.22)	0.75 (0.26–2.15)
Facemask plus hand hygiene	258	1.14 (0.72–1.79)	0.91 (0.41–1.99)	1.03 (0.55–1.95)	1.09 (0.37–3.25)
Contact characteristics					
Age					
Adult (≥16 y)	662	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Child (6–15 y)	88	1.59 (0.95–2.68)	4.46 (1.93–10.3)	3.01 (1.60–5.66)	9.72 (3.70–25.5)
Child (≤5 y)	44	1.05 (0.50–2.23)	3.34 (1.09–10.3)	2.29 (0.94–5.55)	8.74 (2.57–29.8)
Sex					
Female	488	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Male	306	0.72 (0.51–1.03)	0.56 (0.29–1.10)	0.60 (0.36–1.01)	0.59 (0.23–1.51)
Vaccination status					
No influenza vaccination in the past 12 mo	688	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Influenza vaccination in the past 12 mo	106	1.00 (0.59–1.68)	0.56 (0.19–1.60)	0.69 (0.30–1.60)	0.86 (0.22–3.39)
Index patient characteristics					
Age					
Adult (≥16 y)	71	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Child (6–15 y)	144	2.06 (1.22–3.48)	1.83 (0.51–6.50)	2.50 (0.97–6.42)	1.79 (0.41–7.78)
Child (≤5 y)	44	2.24 (1.20–4.18)	2.86 (0.72–11.4)	2.93 (1.03–8.37)	4.03 (0.78–20.7)
Sex					
Female	140	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Male	119	1.05 (0.72–1.53)	0.92 (0.44–1.95)	0.83 (0.48–1.44)	0.72 (0.28–1.83)
Antiviral status					
Not prescribed antiviral	191	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Prescribed antiviral	68	0.79 (0.52–1.21)	0.41 (0.13–1.30)	0.77 (0.40–1.48)	0.46 (0.13–1.69)

RT-PCR = reverse-transcription polymerase chain reaction.
* Based on 794 household contacts in 259 households.
† Adjusted for intervention group; age, sex, and vaccination history of the contact; and age, sex, and antiviral use of the index patient.
‡ "Clinical definition 1" is at least 2 of the following: temperature ≥37.8 °C, cough, headache, sore throat, and myalgia. "Clinical definition 2" is temperature ≥37.8 °C, plus cough or sore throat.

Appendix Table 7. **Risk for Influenza Virus Infection When the Intervention Was Applied Within 36 Hours of Symptom Onset in the Index Patient, Using a Composite Definition of Infection***

Characteristic	Participants, *n*	Odds Ratio (95% CI)†			
		RT-PCR–Confirmed Influenza or Clinical Influenza (Definition 1)‡	RT-PCR–Confirmed Influenza and Clinical Influenza (Definition 1)‡	RT-PCR–Confirmed Influenza or Clinical Influenza (Definition 2)‡	RT-PCR–Confirmed Influenza and Clinical Influenza (Definition 2)‡
Study group					
Control	183	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Hand hygiene	130	0.50 (0.25–1.01)	0.34 (0.08–1.34)	0.54 (0.20–1.51)	0.43 (0.11–1.65)
Facemask plus hand hygiene	149	0.75 (0.43–1.34)	0.40 (0.13–1.24)	0.70 (0.31–1.57)	0.64 (0.17–2.40)
Contact characteristics					
Age					
Adult (≥16 y)	386	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Child (6–15 y)	51	1.65 (0.82–3.34)	6.31 (2.13–18.8)	3.18 (1.38–7.36)	11.1 (3.08–40.1)
Child (≤5 y)	25	1.62 (0.68–3.87)	5.19 (1.44–18.8)	2.64 (0.85–8.13)	9.44 (2.29–39.0)
Sex					
Female	283	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Male	179	0.50 (0.30–0.84)	0.37 (0.13–1.03)	0.54 (0.26–1.11)	0.48 (0.13–1.74)
Vaccination status					
No influenza vaccination in the past 12 mo	401	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Influenza vaccination in the past 12 mo	61	1.10 (0.58–2.06)	0.65 (0.19–2.26)	0.72 (0.27–1.89)	0.46 (0.05–4.15)
Index patient characteristics					
Age					
Adult (≥16 y)	39	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Child (6–15 y)	85	1.76 (0.78–3.96)	0.79 (0.16–3.83)	1.19 (0.36–3.87)	0.58 (0.12–2.81)
Child (≤5 y)	30	2.12 (0.84–5.35)	1.73 (0.29–10.4)	1.81 (0.48–6.77)	1.92 (0.31–11.9)
Sex					
Female	82	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Male	72	1.26 (0.76–2.10)	0.72 (0.29–1.81)	0.73 (0.36–1.51)	0.88 (0.31–2.46)
Antiviral status					
Not prescribed antiviral	109	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Prescribed antiviral	45	0.82 (0.47–1.41)	0.69 (0.20–2.32)	0.75 (0.32–1.75)	0.65 (0.16–2.59)

RT-PCR = reverse-transcription polymerase chain reaction.
* Based on 462 household contacts in 154 households.
† Adjusted for intervention group; age, sex, and vaccination history of the contact; and age, sex, and antiviral use of the index patient.
‡ "Clinical definition 1" is at least 2 of the following: temperature ≥37.8 °C, cough, headache, sore throat, and myalgia. "Clinical definition 2" is temperature ≥37.8 °C, plus cough or sore throat.

Appendix Table 8. **Risk for Influenza Virus Infection in All Households That Received the Intervention***

Characteristic	Participants, *n*	Odds Ratio (95% CI)†		
		RT-PCR–Confirmed Influenza	Clinical Influenza‡	
			Definition 1	Definition 2
Study group				
Control	331	1.00 (reference)	1.00 (reference)	1.00 (reference)
Hand hygiene	317	0.73 (0.38–1.38)	1.43 (0.91–2.22)	1.60 (0.73–3.49)
Facemask plus hand hygiene	336	0.89 (0.46–1.73)	1.47 (0.94–2.29)	1.89 (0.85–4.18)
Contact characteristics				
Age				
Adult (≥16 y)	820	1.00 (reference)	1.00 (reference)	1.00 (reference)
Child (6–15 y)	109	3.20 (1.74–5.89)	2.16 (1.34–3.46)	4.64 (2.36–9.12)
Child (≤5 y)	56	1.81 (0.78–4.19)	1.72 (0.95–3.11)	8.37 (3.85–18.2)
Sex				
Female	609	1.00 (reference)	1.00 (reference)	1.00 (reference)
Male	375	0.81 (0.52–1.28)	0.78 (0.57–1.08)	0.68 (0.38–1.23)
Vaccination status				
No influenza vaccination in the past 12 mo	848	1.00 (reference)	1.00 (reference)	1.00 (reference)
Influenza vaccination in the past 12 mo	136	0.50 (0.24–1.05)	1.03 (0.65–1.64)	1.16 (0.53–2.55)
Index patient characteristics				
Age				
Adult (≥16 y)	93	1.00 (reference)	1.00 (reference)	1.00 (reference)
Child (6–15 y)	177	3.71 (1.41–9.77)	2.02 (1.26–3.24)	3.10 (1.07–8.99)
Child (≤5 y)	61	3.76 (1.25–11.3)	2.48 (1.41–4.36)	4.23 (1.27–14.1)
Sex				
Female	171	1.00 (reference)	1.00 (reference)	1.00 (reference)
Male	160	1.20 (0.71–2.05)	1.02 (0.72–1.44)	0.69 (0.38–1.26)
Antiviral status				
Not prescribed antiviral	246	1.00 (reference)	1.00 (reference)	1.00 (reference)
Prescribed antiviral	85	0.73 (0.39–1.37)	0.78 (0.53–1.14)	0.87 (0.43–1.77)
Household characteristics				
No co–index patients	282	1.00 (reference)	1.00 (reference)	1.00 (reference)
Co–index patients	49	1.99 (0.98–4.05)	1.33 (0.83–2.12)	2.28 (1.12–4.63)

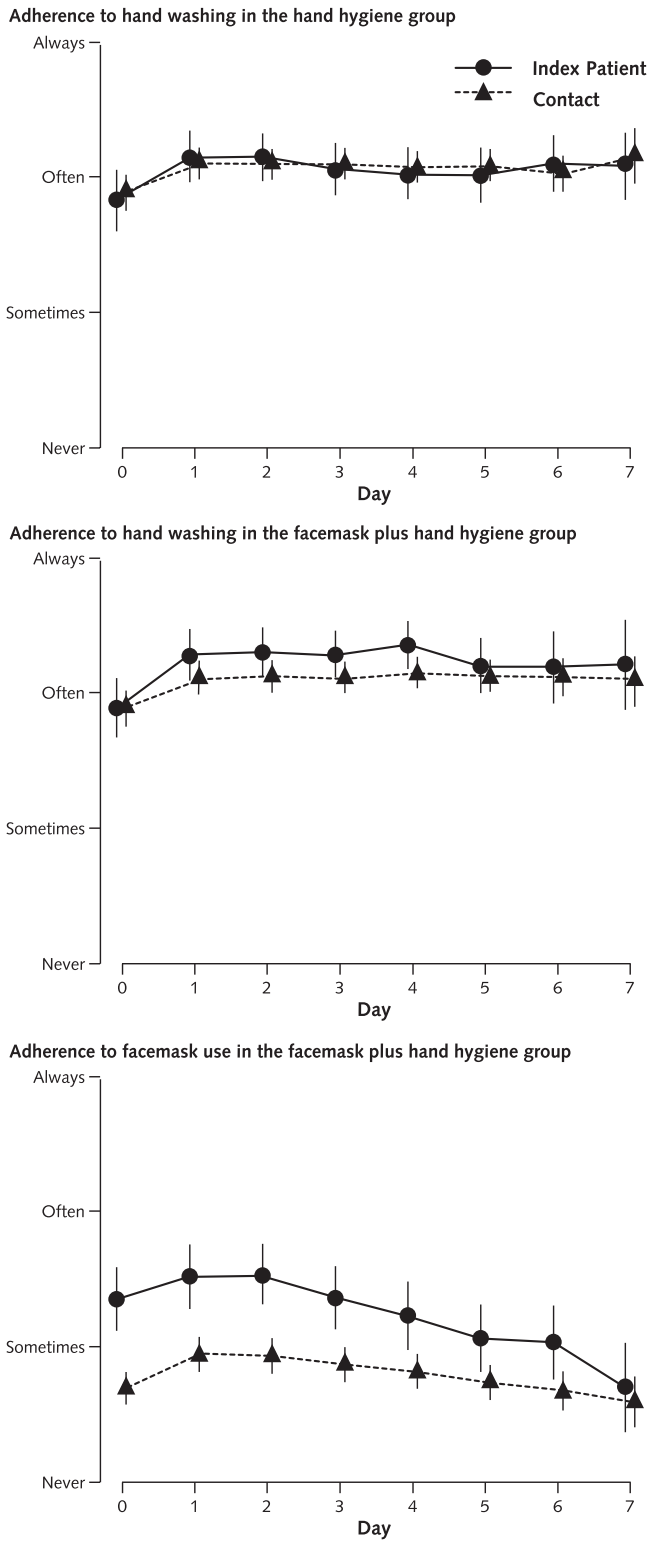
RT-PCR = reverse-transcription polymerase chain reaction.
* Based on 984 household contacts in 331 households.
† Adjusted for intervention group; age, sex, and vaccination history of the contact; and age, sex, and antiviral use of the index patient.
‡ "Clinical definition 1" is at least 2 of the following: temperature ≥37.8 °C, cough, headache, sore throat, and myalgia. "Clinical definition 2" is temperature ≥37.8 °C, plus cough or sore throat.

Appendix Table 9. **Risk for Influenza Virus Infection When the Intervention Was Applied Within 36 Hours of Symptom Onset in the Index Patient***

Characteristic	Participants, *n*	Odds Ratio (95% CI)†		
		RT-PCR–Confirmed Influenza	Clinical Influenza‡	
			Definition 1	Definition 2
Study group				
Control	212	1.00 (reference)	1.00 (reference)	1.00 (reference)
Hand hygiene	158	0.54 (0.22–1.33)	0.97 (0.53–1.78)	1.43 (0.52–3.95)
Facemask plus hand hygiene	191	0.46 (0.19–1.08)	1.14 (0.67–1.96)	1.83 (0.70–4.78)
Contact characteristics				
Age				
Adult (≥16 y)	469	1.00 (reference)	1.00 (reference)	1.00 (reference)
Child (6–15 y)	60	4.30 (1.94–9.55)	3.11 (1.68–5.74)	6.19 (2.63–14.6)
Child (≤5 y)	32	2.16 (0.86–5.39)	2.24 (1.10–4.58)	6.92 (2.52–19.0)
Sex				
Female	349	1.00 (reference)	1.00 (reference)	1.00 (reference)
Male	212	0.89 (0.47–1.68)	0.56 (0.36–0.86)	0.64 (0.28–1.44)
Vaccination status				
No influenza vaccination in the past 12 mo	490	1.00 (reference)	1.00 (reference)	1.00 (reference)
Influenza vaccination in the past 12 mo	71	0.43 (0.16–1.15)	1.03 (0.57–1.87)	0.63 (0.18–2.24)
Index patient characteristics				
Age				
Adult (≥16 y)	49	1.00 (reference)	1.00 (reference)	1.00 (reference)
Child (6–15 y)	104	2.13 (0.61–7.44)	1.93 (0.94–3.96)	1.88 (0.48–7.45)
Child (≤5 y)	39	2.36 (0.59–9.48)	2.74 (1.18–6.38)	4.10 (0.84–19.9)
Sex				
Female	101	1.00 (reference)	1.00 (reference)	1.00 (reference)
Male	91	0.92 (0.44–1.89)	1.02 (0.64–1.62)	0.68 (0.32–1.45)
Antiviral status				
Not prescribed antiviral	136	1.00 (reference)	1.00 (reference)	1.00 (reference)
Prescribed antiviral	56	0.76 (0.35–1.66)	0.84 (0.51–1.37)	0.85 (0.36–1.98)
Household characteristics				
No co–index patients	162	1.00 (reference)	1.00 (reference)	1.00 (reference)
Co–index patients	30	1.51 (0.61–3.78)	1.40 (0.77–2.56)	1.76 (0.71–4.33)

RT-PCR = reverse-transcription polymerase chain reaction.
* Based on 561 household contacts in 192 households.
† Adjusted for intervention group; age, sex, and vaccination history of the contact; and age, sex, and antiviral use of the index patient.
‡ "Clinical definition 1" is at least 2 of the following: temperature ≥37.8 °C, cough, headache, sore throat, and myalgia. "Clinical definition 2" is temperature ≥37.8 °C, plus cough or sore throat.

Appendix Figure 2. **Daily reported adherence to hand hygiene and facemask interventions.**



Data are presented as means (95% CIs).

Appendix Table 10. **Summary Measures of Adherence to Interventions During the 7-Day Follow-up Period in Households in Which the Intervention Was Applied Within 36 Hours of Symptom Onset in the Index Patient**

Characteristic	Control Group		Hand Hygiene Group		Facemask Plus Hand Hygiene Group	
	Index Patient	Contact	Index Patient	Contact	Index Patient	Contact
Using liquid soap, %*	69	79	66	72	69	74
Using alcohol hand rub, %*	7	7	41	30	29	30
Practicing good hand hygiene, %†	42	48	68	60	63	55
Median amount of liquid hand soap used by household (IQR), *g*	–	–	77.6 (42.4–162.6)		78.9 (35.2–114.2)	
Median amount of alcohol hand rub used by individuals (IQR), *g*	–	–	3.2 (1.1–9.7)	1.5 (0.3–5.3)	1.6 (0.7–5.1)	1.5 (0.3–3.8)
Wearing surgical mask, %‡	19	8	32	8	47	27
Median number of masks used (IQR)	–	–	–	–	10 (2–16)	3 (0–9)

IQR = interquartile range.
* Proportion of individuals who reported washing their hands with liquid hand soap or using alcohol hand rub often or always (rather than sometimes or never) during the follow-up period.
† Proportion of individuals who reported washing their hands often or always (rather than sometimes or never) after sneezing, coughing, or blowing their nose during the follow-up period.
‡ Proportion of individuals who reported wearing a surgical facemask often or always (rather than sometimes or never) during the follow-up period.