Impact of Non-Pharmaceutical Interventions on URIs and Influenza in Crowded, Urban Households

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SYNOPSIS

Objectives. We compared the impact of three household interventions—education, education with alcohol-based hand sanitizer, and education with hand sanitizer and face masks—on incidence and secondary transmission of upper respiratory infections (URIs) and influenza, knowledge of transmission of URIs, and vaccination rates.

Methods. A total of 509 primarily Hispanic households participated. Participants reported symptoms twice weekly, and nasal swabs were collected from those with an influenza-like illness (ILI). Households were followed for up to 19 months and home visits were made at least every two months.

Results. We recorded 5,034 URIs, of which 669 cases reported ILIs and 78 were laboratory-confirmed cases of influenza. Demographic factors significantly associated with infection rates included age, gender, birth location, education, and employment. The Hand Sanitizer group was significantly more likely to report that no household member had symptoms ($p<0.01$), but there were no significant differences in rates of infection by intervention group in multivariate analyses. Knowledge improved significantly more in the Hand Sanitizer group ($p<0.0001$). The proportion of households that reported ≥50% of members receiving influenza vaccine increased during the study ($p<0.001$). Despite the fact that compliance with mask wearing was poor, mask wearing as well as increased crowding, lower education levels of caretakers, and index cases 0–5 years of age (compared with adults) were associated with significantly lower secondary transmission rates (all $p<0.02$).

Conclusions. In this population, there was no detectable additional benefit of hand sanitizer or face masks over targeted education on overall rates of URIs, but mask wearing was associated with reduced secondary transmission and should be encouraged during outbreak situations. During the study period, community concern about methicillin-resistant *Staphylococcus aureus* was occurring, perhaps contributing to the use of hand sanitizer in the Education control group, and diluting the intervention's measurable impact.

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Viral upper respiratory infections (URIs), although not generally considered to be major causes of mortality, are among the most common causes of morbidity, and take a significant global economic and social toll in terms of missed work and school, use of health-care services, and costs of over-the-counter and prescribed treatments. The common cold is the most frequent and universal infection; most people have as many as 200 colds in a lifetime. Colds cause more illness in children than all other diseases combined and are responsible for up to 50% of school absenteeism. Colds account for approximately 25 million primary care visits, 1.6 million visits to the emergency department, and 42 million missed work or school days annually in the U.S.[1–5] The economic burden of non-influenza URI alone is about $40 billion annually.[6]

Prior to the current H1N1 outbreak, there were three influenza pandemics in the 20th century.[7] Even in non-epidemic years, more than 500,000 people in the U.S. are hospitalized annually with influenza-associated disease, and 20,000 to 40,000 die.[8,9] The 2007–2008 influenza season, although it was not a pandemic year, was particularly concerning because of a poor match between vaccine and circulating strains and because of increasing resistance to both types of approved antiviral drugs—neuroamindase inhibitors and adamantanes.[10] The recent H1N1 outbreak bodes poorly for the 2009–2010 season.

While influenza vaccination is clearly the most important prevention strategy available, non-pharmaceutical interventions may also be important in the absence of sufficient vaccine supply and to reduce transmission of other respiratory viruses (e.g., rhinoviruses), as the large number of immunotypes precludes the development of a vaccine.[11] Despite the economic and health implications of viral URI and influenza, data on effectiveness of non-pharmaceutical interventions are sparse and/or inconclusive, particularly in community settings.[12–15] Hence, the goal of this randomized clinical trial was to test the effectiveness of three household-level interventions—education, hand sanitizers, and hand sanitizers and face masks—on rates of symptoms and secondary transmission of URIs, incidence of virologically confirmed influenza, knowledge of prevention and treatment strategies for influenza and URIs, and rates of influenza vaccination.

METHODS

Sample and setting

We conducted the study in an upper Manhattan neighborhood with a predominantly immigrant Latino population of about 220,000. Inclusion criteria for the study included having at least three people living in the household, with at least one being a preschool or elementary school child; speaking English or Spanish; having a telephone; being willing to complete symptom assessments and having bimonthly home visits; and not routinely using alcohol-based hand sanitizer.

We used the following assumptions to calculate the sample size: a 73% rate of one or more symptoms per household per month based on a previous study conducted in the same neighborhood;[16] a within-household correlation coefficient of 0.2–0.3, as noted in two previous studies;[17,18] an alpha of $p<0.05$; and a power of 0.80. We predicted a 40% to 50% decrease in symptoms with the application of the alcohol-based hand sanitizer intervention, based on our literature review. Assuming a loss-to-follow-up rate comparable with that in our previous study,[16] we planned to recruit 150 households per intervention group. Sources used to identify and recruit potential subjects included local churches, preschools and elementary schools, clinics, and neighborhood referrals. Recruitment was by word of mouth, personal referral, and flyer. In addition, we met with the local community board and partnered with a not-for-profit community organization with close ties to the local Latino community.

Intervention groups

Households were block randomized into one of three groups: (*1*) the Education group, which received written Spanish- or English-language educational materials regarding the prevention and treatment of URIs and influenza; (*2*) the Hand Sanitizer group, which received the same educational materials and hand sanitizer (Purell®, Johnson & Johnson, Morris Plains, New Jersey), in large (8- and 4-ounce) and small (1-ounce) containers to be carried by individual household members to work or school; and (*3*) the Hand Sanitizer and Face Mask group, which received the same interventions as well as face masks (Procedure Face Masks for adults and children, Kimberly-Clark, Roswell, Georgia) with instructions for both the caretaker and the ill person to wear them when an influenza-like illness (ILI) occurred in any household member. The masks were regular surgical masks, not National Institute for Occupational Safety and Health-certified N95 respirators.

The Centers for Disease Control and Prevention (CDC) definition of ILI from the Sentinel Physicians' Network was used to determine when masks should be worn: "temperature of ≥37.8°C and cough and/or sore throat in the absence of a known cause other than influenza."[19] The household caretaker was instructed to wear a mask when he/she was within 3 feet of a person with an ILI for seven days or until symptoms disappeared, and to change the mask between interactions. If possible, the ill person was also encouraged to wear a mask within 3 feet of other household members. Children older than age 3 and adults in the household were trained in the appropriate technique for donning and removing masks and provided a demonstration of proper use. Phone calls were made on days one, three, and six following the onset of symptoms to reinforce mask use.

Procedures

The Columbia University Medical Center Institutional Review Board approved this study. Four bilingual research assistants (RAs) with a minimum of a baccalaureate degree and experience in longitudinal community-based research were trained in the research protocols; research team members role-played and practiced all study procedures with each other until interrater reliability and proficiency were demonstrated. Each RA obtained consent, made home visits, administered survey instruments, and obtained samples for virologic culture for a cohort of households.

At the first home visit, participants reviewed and signed the consent form, and the RA conducted an interview to obtain demographic information and baseline knowledge, attitudes, and practices (KAP) regarding URIs. Participants were oriented to their intervention strategies—those in the Hand Sanitizer and Hand Sanitizer and Face Mask groups received the appropriate products and written instructions for their use. The RA demonstrated use of the sanitizer and/or face mask, and participants did a return demonstration. Participants were provided with a two-month supply of hand sanitizer and/or face masks, and new supplies were delivered to the household at least once every two months. A dedicated phone line and the researchers' contact information were provided so that participants could contact the study team if needed. Participants were asked to keep the used hand sanitizer bottles and/or face masks (sealed plastic bags were provided for that purpose) so that we could monitor usage. Participants were also provided with disposable thermometers (3M™ Tempa•DOT™ single-use clinical thermometers, 3M, St. Paul, Minnesota) and demonstrated proficiency at taking a temperature to assure accurate reporting of fever.

The home visit to each household was made every two months to minimize study dropout, reinforce adherence to the assigned intervention, replenish product supplies and record use of supplies, answer questions, and correct ongoing misconceptions. At each visit, new educational materials regarding URI prevention and treatment and influenza vaccination were distributed. Throughout the 19-month data collection period, the Project Manager accompanied the RAs on random home visits and made random calls to household participants for ongoing quality monitoring.

Assessment of URI and influenza symptoms

Participants used electronic momentary assessment (EMA) to report at least twice weekly any symptoms of URI in any household member. Structured, automated telephone messages using a toll-free number allowed households to report the status of each member and provided reminder prompts when participants did not report. EMA has been used to minimize biases of repeated measures designs and to monitor a variety of conditions, symptoms, and behaviors.[20–25] Prompts to research staff were also generated when a household failed to report. When participants missed two reporting periods, members of the research team personally contacted them. At least six calls were made at varying times of the day and days of the week, and reminder letters were sent before the household was considered lost to follow-up. A payment of $20/month was provided for those who made at least 75% of the calls in the previous month.

Using the telephone EMA system, the presence or absence of six symptoms was reported for every household member at least twice weekly: rhinorrhea (runny nose), sore throat, cough, muscle aches, fever, and headache. When an ILI was reported, an alert was electronically sent to the project staff, who immediately contacted the reporting household. A member of the research team was then deployed to make a home visit within 24 to 48 hours to obtain a sample for laboratory testing for influenza.

To assess secondary transmission, an ill person was considered an index case if on the onset day of illness nobody else in the household had been symptomatic within the previous five days. For each episode, a secondary case was any member of the household who developed symptoms within five days following the index case, and the secondary attack rate was defined as the number of secondary cases recorded within five days of the onset of symptoms in the index case divided by the number of household members minus one. Many study subjects contributed more than one episode in which they were considered to be the index case.

Virologic procedures

Deep nasal swabs were obtained and tested in accordance with standard procedures (http://www.cdc

.gov/flu/professionals/diagnosis/labprocedures.htm). Samples were sent in 3 milliliters of viral transport medium[26] by overnight mail wrapped with cold packs to a commercial laboratory for confirmatory testing by culture or polymerase chain reaction (PCR). During the first year and the first half of the second flu season, Laboratory Corporation of America® (LabCorp®) was contracted to test for influenza types A and B as well as other common respiratory viruses by rapid culture (R-Mix®, Diagnostic Hybrids, Inc., Athens, Ohio).[27] During the second half of the second year, PCR and subtyping of the samples were performed by the Wadsworth Center, New York State Department of Health, Albany, New York.[28–30]

Data analysis

Initially, we used appropriate univariate statistics (e.g., Chi-square, Mann-Whitney, and t-tests) to examine differences in demographic characteristics among study groups and correlations among variables. To test for changes in knowledge, we calculated a score (range: 0–10) based on responses to 10 items, such as whether colds were caused by viruses or bacteria, whether antibiotics were appropriate to treat influenza, and whether URIs were spread by direct contact.

To test for differences in the number of episodes of URIs, ILIs, and influenza, adjusting for possible confounding factors, we applied multiple logistic or Poisson models. We used generalized estimating equation (GEE) techniques to account for the correlation among individuals within one household. Because several individuals had up to five episodes of ILI and up to 21 episodes of URI during the study period, we applied the Poisson GEE model to the ILI and URI outcomes. No individual had more than one laboratory-confirmed case of influenza during the study period; therefore, we applied the logistic GEE model to the influenza outcomes. We conducted initial analyses by year with adjustment of the possible seasonal effect (by including a categorical covariate with four levels to reflect four seasons). However, because the effects of intervention in each year were quite similar, we combined data across the entire two-year study period.

In addition to the primary predictor variable of intervention group, we included the following covariates in the initial GEE models: vaccination status, gender, age, place of birth (in or outside the U.S.), education level, number of hours spent outside the home per week (<10, 11–20, 21–40, >40), occupation (homemaker or unemployed vs. other employment), chronic respiratory illness such as asthma (yes/no), number of children in household, level of compliance with symptom reporting (≥75% or <75% of time), season (winter/summer), self-reported frequency of handwashing, and a crowding index calculated as the number of people in the household divided by the number of rooms. We applied a backward model selection procedure to select the best model that could explain the outcome variables. Only those variables that were statistically significant at $p<0.05$ were retained in the final models. We always kept the primary variable of interest—the intervention group—in the final models.

The goodness-of-fit tests suggested a good model fit for the logistic GEE on influenza and Poisson GEE on number of ILIs, but suggested a lack of model fit for Poisson GEE on the number of URIs. A possible explanation might be that URIs have a broad range of definitions and the causes may be multiple. Hence, there may have been factors that contributed to URIs that were not in our covariate list. We tested possible interactions in all three models, but none were significant. Therefore, our final models did not include interaction terms. We also confirmed that there was no collinearity in the variables included in the model to predict the outcomes.

To assess secondary attack rates, predictor variables examined included demographics and other characteristics of the index and secondary cases (e.g., gender, age group, whether or not born in the U.S., number of hours per week spent outside of the home, whether or not he/she had a chronic respiratory illness such as asthma, and influenza vaccination status). Other characteristics included household-level variables, such as crowding (defined as the number of household members divided by the number of rooms) and assigned intervention group (Education, Hand Sanitizer, and Hand Sanitizer and Face Mask). In addition, we included the education level of the index case or the caretaker (if the index case was a child younger than 18 years of age) as a covariate.

We conducted separate logistic regression analyses for (*1*) the total number of URI episodes (including influenza and ILI) and (*2*) the number of ILI episodes, including influenza but excluding non-ILI symptoms of URI. To account for correlations between different episodes of the same index case and between different index cases in the same household, we used the GEE method using SAS®.[31] We used backward elimination to arrive at a final model. We retained variables that were statistically significant at $p<0.05$ in the final model. We collected data during a 19-month period, from November 20, 2006, to June 20, 2008.

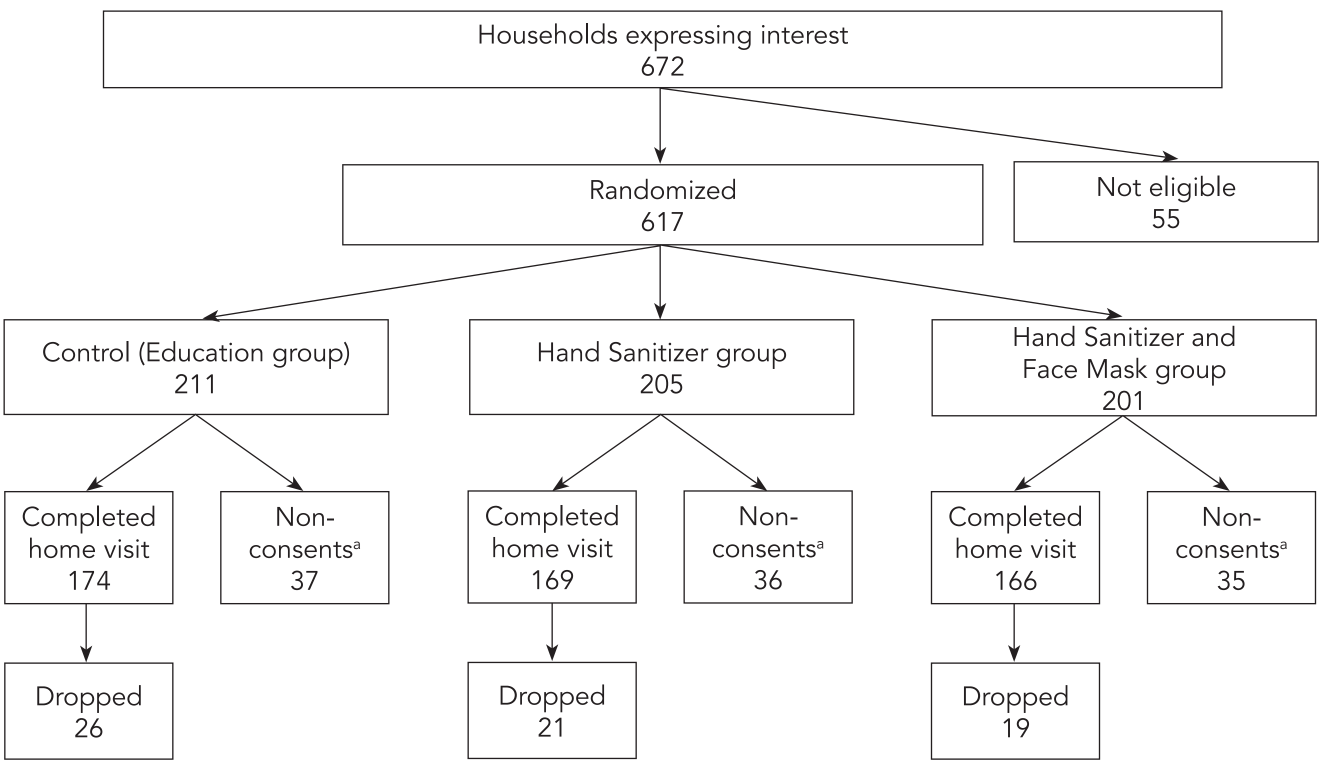
RESULTS

Participant characteristics

Overall, 91.8% (617/672) of households that expressed interest in participation met eligibility criteria; 82.5% (509/617) were reachable and completed the initial home visit. The mean duration of the households in the study was 55.5 weeks with a 13.0% (66/509) dropout rate. The 509 participating households included a total of 2,788 members (Figure). The majority of household members were Latino (96.2%, 2,682/2,788), born outside the U.S. (54.0%, 1,500/2,776), and 18 years of age or older (52.7%, 1,456/2,763). Most (90.4%, 2,448/2,708) reported having no chronic respiratory disease. The mean household size was 4.5 people per one-bedroom apartment. Households randomized to the Education (n=174), Hand Sanitizer (n=169), or Hand Sanitizer and Face Mask (n=166) group were comparable in terms of mean household size (five members, range: 3–14), gender, ages, and proportion born outside the U.S.

About one-third of working individuals were either homemakers or unemployed, 28.3% were employed in service industries (e.g., food preparation, health care, education, and childcare), and 38.3% were employed in other settings (e.g., construction, transportation, or sales). Overall, 44.6% of the children attended a public or private school, 31.5% were routinely cared for at home, and others were in some form of daycare. The Education group included significantly more household members of Latino descent (98.1%) than the other two groups (94.2% for the Hand Sanitizer group and 96.4% for the Hand Sanitizer and Face Mask group) (p<0.005), as well as members who had not completed high school (54.6% vs. 44.7% in the Hand Sanitizer group and 39.8% in the Hand Sanitizer and Face Mask group (p<0.005). Significantly more individuals spent at least 40 hours per week outside the home in the Hand Sanitizer and Face Mask group (42.6%) as compared with the Education (33.8%) or Hand Sanitizer (32.3%) groups (p<0.005) (Table 1).

Figure. Number of households contacted, recruited, and randomized in a clinical trial of non-pharmaceutical interventions for URIs, New York, November 2006 to July 2008



[a]Non-consents consisted of those who were randomized but never participated because they could not be located after randomization or were no longer interested in participating.

URI = upper respiratory infection

Table 1. Summary of characteristics of household member participants in a study of non-pharmaceutical interventions for URIs, by intervention group, New York, November 2006 to July 2008

	Education group		Hand Sanitizer group		Hand Sanitizer and Face Mask group		Total		
Characteristics	N	*(percent)*	N	*(percent)*	N	*(percent)*	N	*(percent)*	P-value[a]
Gender (n=2,788)									0.31
Male	422	(46.7)	474	(50.1)	446	(47.5)	1,342	(48.0)	
Female	482	(53.3)	472	(49.9)	492	(52.2)	1,446	(52.0)	
Age (in years) (n=2,763)									0.28
0–5	262	(29.2)	259	(27.6)	287	(30.9)	808	(29.2)	
6–11	95	(10.6)	106	(11.3)	105	(11.3)	306	(11.1)	
12–17	70	(7.8)	60	(6.4)	63	(6.8)	193	(7.0)	
18–40	357	(39.8)	392	(41.8)	375	(40.4)	1,124	(40.7)	
41–64	103	(11.5)	101	(10.8)	93	(10.0)	297	(10.7)	
≥65	10	(1.1)	19	(2.0)	6	(0.6)	35	(1.3)	
Ethnicity (n=2,788)									<0.005
Hispanic	887	(98.1)	891	(94.2)	904	(96.4)	2,682	(96.2)	
Other	17	(1.9)	55	(5.8)	34	(3.6)	106	(3.8)	
Occupation (n=1,463)									0.011
Homemaker/unemployed (primarily stays at home)	181	(39.1)	151	(29.3)	156	(32.2)	488	(33.4)	
Service industry	129	(27.9)	146	(28.3)	139	(28.7)	414	(28.3)	
Other	153	(33.0)	219	(42.4)	189	(39.0)	561	(38.3)	
Education level for adults (n=1,379)									<0.005
<High school	253	(54.6)	205	(44.7)	182	(39.8)	640	(46.4)	
High school diploma or GED	117	(25.3)	123	(26.8)	154	(33.7)	394	(28.6)	
>High school	69	(14.9)	92	(20.0)	78	(17.1)	239	(17.3)	
College graduate	24	(5.2)	39	(8.5)	43	(9.4)	106	(7.7)	
Child attending (n=1,300)									0.90
Public or private school	194	(46.0)	173	(40.8)	213	(46.9)	580	(44.6)	
Daycare center, pre-nursery, or Headstart	70	(16.6)	103	(24.3)	77	(17.0)	250	(19.2)	
Daycare in private home	21	(5.0)	19	(4.5)	20	(4.4)	60	(4.6)	
No routine care outside home or not attending school and working	137	(32.4)	129	(30.4)	144	(31.7)	410	(31.5)	
Location of birth (n=2,776)									0.99
U.S.	417	(46.1)	432	(45.8)	427	(46.0)	1,276	(46.0)	
Outside U.S.	487	(53.9)	512	(54.2)	501	(54.0)	1,500	(54.0)	
Number of hours spent outside of home/week (n=2,785)									<0.005
<10	160	(17.7)	243	(25.8)	248	(26.4)	651	(23.4)	
11–20	187	(20.7)	118	(12.5)	91	(9.7)	396	(14.2)	
21–40	251	(27.8)	277	(29.4)	199	(21.2)	727	(26.1)	
>40	306	(33.8)	305	(32.3)	400	(42.6)	1,011	(36.3)	
Respiratory diseases (n=2,708)									0.24
Yes	93	(10.6)	91	(9.9)	76	(8.3)	260	(9.6)	
No	784	(89.4)	826	(90.1)	838	(91.7)	2,448	(90.4)	

[a]Chi-square test comparing Education, Hand Sanitizer, and Hand Sanitizer and Face Mask groups

URI = upper respiratory infection

GED = general educational development

Incidence of URIs, ILIs, and confirmed influenza

A total of 5,034 URI symptoms were reported, most commonly rhinorrhea or cough. About 83.3% (424/509) of households had at least one member with one or more symptoms, but 48.6% (1,355/2,788) of members had no reported symptoms. Households in the Hand Sanitizer group included significantly more members without any reported symptoms (57.6% as compared with 49.4% in the Education group and 38.7% in the Hand Sanitizer and Face Mask group, p<0.01). Table 2

Table 2. Outcomes of household members in a study of non-pharmaceutical interventions for URIs, New York, November 2006 to July 2008

	Intervention group			
Outcome	*Education*	*Hand Sanitizer*	*Hand Sanitizer and Face Mask*	*P-value*
Percentage of household members with no reported symptoms (*N*)	49.4 (447/904)	57.6 (545/946)	38.7 (363/938)	<0.01
URI rate/1,000 person-weeks (*N*)	35.38 (1,646/46,526)	29.06 (1,416/48,731)	38.91 (1,972/50,676)	
ILI rate/1,000 person-weeks (*N*)	2.26 (105/46,526)	1.93 (94/48,731)	1.56 (79/50,676)	
Influenza rate/1,000 person-weeks (*N*)	0.52 (24/46,526)	0.60 (29/48,731)	0.49 (25/50,676)	
Mean KAP change score	0.63	1.76	1.29	<0.0001
Reporting compliance rate (percent)	65.5	75.7	80.7	0.005

URI = upper respiratory infection

ILI = influenza-like illness

KAP = knowledge, attitudes, and practices

summarizes unadjusted rates of household members with no reported symptoms; URI, ILI, and influenza; change scores on the KAP survey; and compliance with symptom reporting ($\geq$75% of required time) by intervention group.

Households reported 669 episodes of ILI (0–5 per individual). Of the 234 deep nasal swabs obtained, 33.3% (n=78) tested positive for influenza; 43.6% (n=34) were influenza A and 56.4% (n=44) were influenza B. Among the 66.7% who tested negative for influenza, 30.8% (48/156) tested positive for other viruses: seven for respiratory syncytial virus, nine for parainfluenza, 11 for enterovirus, 10 for rhinovirus, six for adenovirus, and five for metapneumovirus. Swabs were not obtained from the remaining 435 reported ILI episodes for the following reasons: 72.0% (n=313) did not meet the CDC definition of an ILI and were therefore included in the URI symptom count, 21.4% of episodes (n=93) were reported after 48 hours of ILI onset or the participant refused to be swabbed, and the research staff were unable to reach the participant in 6.7% of episodes (n=29).

Based on the Poisson GEE analysis, people born in the U.S. had approximately 1.5 more URI episodes than those born outside the U.S. (mean of 2.3 and 1.4 episodes per person, respectively, p=0.004), younger age was significantly associated with higher rates (p<0.001, data not shown), and those with chronic respiratory illness had about 1.4 times more URI episodes than those without respiratory problems (2.5 and 1.8 episodes per person, respectively, p=0.009). Men were significantly less likely to have both URIs and ILIs than women. The odds of getting influenza were 5.16 times higher for college graduates than for those with less than a high school education, even when adjusting for the number of hours each week spent outside the home. The odds of getting influenza were 2.56 times higher for homemakers and those who were unemployed vs. those working in other professions. However, there were no significant differences in rates of URI, ILI, or influenza by intervention group (Table 3).

Secondary attack rates

We used a total of 3,463 episodes of URI, ILI, or influenza with complete data for this analysis, yielding a total of 1,751 secondary cases. Table 4 presents the means and standard deviations of the secondary attack rate in each of the three intervention groups. The mean secondary attack rates were 0.137 for the Education group, 0.144 for the Hand Sanitizer group, and 0.124 for the Hand Sanitizer and Face Mask group. There were 323 episodes of ILI and influenza, resulting in 29 secondary cases. The mean secondary attack rates for the Education, Hand Sanitizer, and Hand Sanitizer and Face Mask groups were 0.023, 0.020, and 0.018, respectively.

Regarding URI, ILI, and influenza episodes, there was a significant decrease in secondary attack rates in the Hand Sanitizer and Face Mask group when compared with the Education group. Regarding the other significant explanatory variables, crowding had a negative association with the secondary attack rate

($p<0.0001$) (i.e., more crowded households had less transmission). To confirm that the significant effect of crowding was not a result of confounding, we ran the logistic regression model on the data from all URI, ILI, and influenza episodes with all the covariates listed in the Methods section. We found that the effect of crowding was still significant ($p<0.0001$), with an odds ratio of 0.80 (95% confidence interval 0.72, 0.89). In addition, secondary attack rates were significantly lower when the index case was 0–5 years of age and significantly higher when the index case was 6–17 years of age when compared with adult index cases. For the

Table 3. Regression coefficients and *p*-values for outcomes from GEE logistic models (for influenza) and GEE Poisson models (for ILI and URIs) in a study of non-pharmaceutical interventions for URIs, New York, November 2006 to July 2008

Outcome	*Variable*	*Variable*	*Beta*	*P-value*
Influenza	Intervention (Ref. = Education group)	Hand Sanitizer group	0.648	0.199
		Hand Sanitizer and Face Mask group	0.082	0.893
	Caretaker education (Ref.= <high school)	Caretaker: high school graduate	−0.274	0.689
		Caretaker: some college	−0.397	0.564
		Caretaker: college graduate	1.642	0.003
	Occupation (Ref. = other)	Homemaker/unemployed (primarily stays at home)	0.941	0.044
		Service industry (e.g., health care, restaurant)	−0.063	0.925
ILI	Intervention (Ref. = Education group)	Hand Sanitizer group	0.271	0.455
		Hand Sanitizer and Face Mask group	−0.185	0.61
	Gender (Ref. = female)	Male	−1.01	0.0006
URI	Intervention (Ref. = Education group)	Hand Sanitizer group	−0.199	0.138
		Hand Sanitizer and Face Mask group	0.152	0.194
	Caretaker education (Ref. = <high school)	Caretaker: high school graduate	0.068	0.598
		Caretaker: some college	0.425	0.001
		Caretaker: college graduate	0.283	0.11
	Born outside U.S. (Ref. = no)	Yes	−0.389	0.004
	Gender (Ref. = female)	Male	−0.591	<0.0001
		Age	−0.014	<0.0001
	Respiratory illness (Ref. = no)	Yes	0.359	0.009
	Occupation (Ref. = other)	Homemaker/unemployed (primarily stays at home)	0.276	0.009
		Service industry (e.g., health care, restaurant)	0.06	0.514

GEE = generalized estimating equation
ILI = influenza-like illness
URI = upper respiratory infection
Ref. = reference group

Table 4. Secondary attack rates of influenza, ILI, and URIs among participants in a study of non-pharmaceutical interventions for URIs, by intervention group (unadjusted), New York, November 2006 to July 2008

Symptom/group	*Total number of episodes*	*Secondary attack rates Mean (standard deviation)*
Influenza/ILI/URI		
Education	1,131	0.137 (0.223)
Hand Sanitizer	955	0.144 (0.232)
Hand Sanitizer and Face Mask	1,377	0.124 (0.218)
Influenza/ILI		
Education	115	0.023 (0.079)
Hand Sanitizer	111	0.020 (0.068)
Hand Sanitizer and Face Mask	97	0.018 (0.075)

ILI = influenza-like illness

URI = upper respiratory infection

ILI and influenza episodes, secondary attack rates were again significantly lower when the index case was 0–5 years of age as compared with episodes in which the index case was at least 18 years of age (Table 5).

Adherence to study protocols

The Hand Sanitizer and Face Mask group was more compliant with weekly reporting of symptoms (80.7%) as compared with the Hand Sanitizer (75.7%) and Education (65.5%) groups (p=0.005) (Table 2). Members of the Hand Sanitizer group used a mean of 12.1 ounces/month and the Hand Sanitizer and Face Mask group used a mean of 11.6 ounces/month (including counted empty bottles and self-reports) (p=0.36). At the exit survey, 44.2% (65/147) of households from the Education group reported using hand sanitizer occasionally at some point during the study, and 56.9% of these (37/65) reported using hand sanitizer one to two times within the previous 24 hours. Compliance with mask use was poor. Although households were instructed about mask use, and reinforcement by the RA and Project Manager occurred frequently, only half (22/44) of the households with an ILI reported using

Table 5. Final logistic regression models summarizing significant predictors of secondary attack rates for influenza, ILI, and URIs among participants in a study of non-pharmaceutical interventions for URIs, New York, November 2006 to July 2008

Symptom	*Variable*	*Percent of episodes*	*N*	*Odds ratio*	*95% confidence interval*	P-*value*
ILI/influenza	Age of index case (in years)					0.035
(n=322 episodes)	0–5	58.7	189	0.30	0.12, 0.72	
	6–17	12.7	41	0.74	0.23, 2.36	
	≥18	28.6	92	Ref.	Ref.	
URI/ILI/influenza	Age of index case (in years)					<0.0001
(n=3,408 episodes)	0–5	47.2	1,608	0.81	0.70, 0.94	
	6–17	13.1	448	1.39	1.15, 1.68	
	≥18	39.7	1,352	Ref.	Ref.	
	Education of caretaker					0.006
	<High school	38.6	1,315	0.79	0.61, 1.03	
	High school	27.7	944	0.83	0.64, 1.09	
	Some college	23.9	815	1.09	0.83, 1.42	
	College graduate	9.8	334	Ref.	Ref.	
	Intervention group					0.02
	Education	32.7	1,116	Ref.	Ref.	
	Hand Sanitizer	27.5	938	1.01	0.85, 1.21	
	Hand Sanitizer and Face Mask	39.7	1,354	0.82	0.70, 0.97	
	Crowding index[a]	NA	NA	0.80	0.72, 0.89	<0.0001

[a]The crowding index is the ratio of the number of people in the household divided by the number of rooms. The odds ratio corresponds to the decrease in odds of a secondary case when crowding is increased by 1.

ILI = influenza-like illness

URI = upper respiratory infection

Ref. = reference group

NA = not applicable

masks within 48 hours of episode onset. Those who used masks at all reported a mean of only two masks/day/ILI episode (range: 0–9).

Respondent knowledge of prevention and treatment strategies

A total of 441 households completed both a baseline and exit interview. The KAP scores at baseline were generally low (the mean in each of the three intervention groups was slightly more than 50% correct out of 10 items), but improved significantly in all groups by the end of the study (5.12 to 5.75 in the Education group, 5.48 to 7.24 in the Hand Sanitizer group, and 5.11 to 6.40 in the Hand Sanitizer and Face Mask group). The change in KAP scores was significantly greater for the Hand Sanitizer group as compared with the other two groups ($p<0.0001$). There were no significant interaction effects among covariates such as education, occupation, and group on KAP scores.

Influenza vaccination rates

There was an increase between the baseline and exit interview in all three groups that reported ≥50% of members receiving influenza vaccine (pre- vs. post-intervention for each group: 21.1% and 40.8% in the Education group, 19.0% and 57.1% in the Hand Sanitizer group, and 22.4% and 43.5% in the Hand Sanitizer and Face Mask group ($p<0.001$). Additionally, those in the Hand Sanitizer group reported a significantly greater increase than the other two groups, controlling for baseline rates ($p=0.002$).

DISCUSSION

Impact of interventions on rates of URI and influenza

Until very recently, there has been a dearth of information regarding the effectiveness of non-pharmaceutical interventions to reduce transmission of respiratory infections.[32,33] The severe acute respiratory syndrome (SARS) outbreak, however, offered an opportunity to examine the impact of barriers on the transmission of respiratory viruses, and a meta-analysis of six case-control studies suggested that hand hygiene and mask wearing were highly effective in preventing spread.[12,13]

A second meta-analysis of studies published in English regarding the impact of hand hygiene on URI in the community demonstrated reductions in gastrointestinal (GI) infection with less dramatic reductions in URI.[15] Sandora et al. randomized 292 families with children in daycare to receive hand sanitizer and hand hygiene education or not, and reported significant reductions in GI illness and marginal but not statistically significant reductions in respiratory infections.[4] In a second study, their team randomized 285 elementary school children to hand sanitizer use and surface disinfection in classrooms, again demonstrating a reduction in absenteeism associated with GI illness but not URI.[5] In the more controlled setting of a military camp, Mott and colleagues reported 40% less respiratory illness ($p<0.001$) and 48% less GI illness among battalions randomized to hand sanitizer use.[36]

Consistent with our findings, Cowling et al.[37] found a modest but nonsignificant impact of hand hygiene on viral respiratory transmission. Grayson and colleagues recently reported that soap and water as well as alcohol sanitizers were effective at reducing influenza A on hands that were artificially contaminated.[38] In fact, after a short period of air drying, there was an immediate, large reduction in viral counts, with 30% of hands (6/20) being negative for virus even before hand hygiene. Additional studies with natural infection would be needed to confirm the effectiveness of hand hygiene products at reducing viral loads.

Despite several demographic differences among the groups (e.g., more individuals who spent >40 hours/week outside the home in the Hand Sanitizer and Face Mask group and more adults in the Education group who had not completed high school), these factors were not predictors of infection in the multivariate analyses. However, several other reasons may explain why there were minimal differences in rates of URI among intervention groups. The study did not include a "no intervention" group because the necessary home visits and symptom reporting were in themselves an intervention. Because a "no intervention" group was not possible, we decided to provide some passive education to each group. Hence, the comparison is between education alone vs. education and additional interventions.

Secondly, compliance with mask wearing was poor. Thirdly, during the course of the study period, use of hand sanitizers became widespread in the community and households randomized to the Education group reported at least occasional use of hand sanitizer. Finally, the Education group had lower rates of reporting than the other two intervention groups. It is possible, therefore, that some or all of the interventions, even in the comparison/Education group, served to reduce URI rates, making it difficult to find differences among groups.

Impact of interventions on secondary transmission

Current understanding of the transmission dynamics of URIs has been facilitated first by the classic work of Gwaltney and colleagues with rhinovirus[39–42] beginning in the 1970s, and then by the study of the spread of SARS during this decade in hospital and household settings.[18,43–45] The relative contribution of airborne, aerosol, and contact transmission routes for rhinovirus have been characterized, demonstrating that efficient fomite transmission can occur when nasal secretions are fresh, but the transmission chain from environmental surfaces is likely to be tenuous and short-lived.[40,46–48] Secondary transmission of SARS within households has been shown to be low (6% to 15%), with increasing transmission associated with more time spent at home by the index case.[43,45,49] In a recent review article, Weber and Stilianakis noted that even if the influenza virus dies quickly on human skin, "The transfer of virus to hands appears to be a critical bottleneck for contact transmission." They also noted that there could be considerable risk of transmission of the virus through frequently used surfaces, even if the virus did not survive long.[50] In fact, the influenza virus artificially inoculated onto banknotes survived more than two weeks when mixed with respiratory secretions.[51]

With regard to seasonal influenza transmission, estimates of secondary transmission are widely variable. Using data from the 1918 pandemic in San Francisco, for example, Chowell and colleagues estimated reproduction numbers (R_0, the number of cases among fully susceptible individuals after an index case) from two to three, depending upon model assumptions used.[52] Yang et al. estimated rates of human-to-human transmission of avian influenza (H5N1) in Sumatra to be 29%, but there was no evidence of transmission in Turkey.[53] Using a probability model of household transmission from 1957 and 1961 data, Nishiura and Chowell[54] reported secondary attack rates of 7% to 9% for influenza A and 10% to 18% for influenza B, whereas Viboud et al.[55] reported 24.1% of secondary cases among 543 household contacts in France.

Our data are not directly comparable with previous reports because we examined household secondary attack rates for URIs and ILIs as well as for laboratory-confirmed influenza. The rationale for this approach was that the transmission dynamics for most viral URIs are likely to be similar, and we were interested in the overall public health burden of household transmission of these infections and predictors of such transmission. Nevertheless, secondary transmission rates in this study (0.018–0.023 for ILI and influenza) were generally lower than those previously reported, perhaps because participants received home visits and various reminders to adhere to their assigned interventions (i.e., it is possible that all of the intervention groups had lower transmission rates than would be expected without intervention).

There is evidence that mask wearing decreases exposure to respiratory viruses and may disrupt transmission.[56–59] Two recent clinical trials have demonstrated a protective effect of masks, despite the fact that in both studies, consistent with our findings, there was low adherence.[37,60] Even in Hong Kong, where mask wearing is a more accepted part of the culture,[61] poor adherence to mask wearing was noted.[62] Factors associated with measures such as mask wearing include perceived efficacy of preventive strategies, risk of an outbreak, and risk of contracting influenza.[61,63] Among 183 elementary school children who received education about avian influenza using fear or humor, the fear-related program was more effective at improving perceptions of risk and prevention behaviors.[64] Hence, it is less likely that mask wearing will be a viable intervention unless the level of fear in the community is heightened, with a concomitant increase in adherence.

Surprisingly, in our study, more crowded households and households in which the caretaker had less education were also associated with significantly lower rates of transmission. Several possible factors might have contributed to this finding. In our home visits, we found that the apartments, although crowded, were extremely clean. The majority of the primary caretakers in the household were full-time homemakers. Many were recent immigrants who spent little time outside the household, were less likely to have health insurance, and were, therefore, concerned about keeping the family well and committed to taking care of the family. For these reasons, they may have been more likely to use precautions when they or another member of their household fell ill. Further, all participants received extensive education about prevention of URIs as part of this study, and social distancing was emphasized as an important strategy for prevention of cross-transmission. It is possible that those in more crowded environments were even more careful. There was a rather narrow range of "crowdedness," as the mean household size was 4.5 people in a one-bedroom apartment, and there were few households that could be classified as uncrowded (e.g., two or fewer people/bedroom).

Finally, some households had boarders who rented a room but had little contact with the family; this would have increased the crowding index without increasing the interactions among members of the household. This finding suggests that it is possible to minimize URI transmission, even in crowded settings. On the other hand, when an index case was a school-age child, there was significantly greater secondary transmission, indicating that schoolchildren are major contributors to transmission.

Knowledge of prevention and treatment strategies

For all respondents, knowledge regarding URIs was relatively low, with only about half of the questions answered correctly at baseline—a score similar to that reported among 400 adult patients surveyed in an internal medicine clinic.[65] As expected, all groups had significant improvements in their KAP scores between the baseline and exit interview. In addition, the Hand Sanitizer and Hand Sanitizer and Face Mask groups had higher scores than the Education group, despite the fact that all three groups received identical educational materials. There are several possible explanations. First, it is possible that the three RAs varied in their skill or presentation of the material. However, this scenario seems unlikely because the messages were highly structured, and quality monitoring was ongoing to assure standardization and consistency of interventions. The lower education level of the Education group is unlikely to explain the differences, as education level was not significant in the regression models. It seems more likely that the presence of the sanitizer and masks served as a prompt or booster that reinforced the educational messages. Such an explanation is congruent with cognitive dissonance theory (i.e., the educational material introduced new understandings about prevention and control of URIs that differed from their previously held knowledge and beliefs). This could create dissonance, which could be reduced or resolved by adding new behaviors as well as new information.[66]

Influenza vaccination rates

In this study, influenza vaccination rates were not associated with rates of URI, ILI, or influenza. It is possible that the rates were overreported by household informants, and/or that even though the rates were significantly higher at the end of the study, the mean rates were still less than 50%. Further, there was a poor match between vaccine strains and circulating strains of influenza during the 2007–2008 season.[67] It is interesting that the Hand Sanitizer and the Hand Sanitizer and Face Mask groups reported higher vaccination rates than the Education group, perhaps again as a result of a booster/prompting effect of the products in the home.

Limitations

This study had several limitations. Because the 2006–2007 influenza season was milder than anticipated and there may also have been some underreporting of symptoms by participants, our projected sample size was not attained for laboratory-confirmed influenza cases. Hence, the power of the study to detect differences among groups for influenza was limited. During the 2007–2008 influenza season, considerable media attention was devoted to community-associated methicillin-resistant *Staphylococcus aureus*. As a result, a number of households in the Education group reported that they began to use hand sanitizers, resulting in some crossover of the hand sanitizer intervention to the Education group. Compliance was extremely low for the Hand Sanitizer and Face Mask group. Additionally, because face mask and hand sanitizer use was measured in part by self-report, compliance may have been even lower than reported. Hence, it was not possible to determine whether the interventions might have been more effective if they had been more consistently practiced. It is also possible that reports of runny nose might have been allergic rhinitis rather than a symptom of infection, although in cases confirmed by home visit this was not the case.

CONCLUSIONS

Non-pharmaceutical interventions are likely to continue as one important component of a national/global strategy to minimize the impact of seasonal or pandemic influenza. Hence, their relative efficacy and effectiveness in the community must be assessed. Based on previous data and our finding that there were significantly more people in the Hand Sanitizer group who reported no symptoms at all during the course of this study, it is possible that alcohol-based hand hygiene may offer some protection against URIs in the community. However, the relatively small number of individuals studied to date has not been adequate to provide an estimate of effect size and, overall, there were no differences in infection rates among the intervention groups. Mask wearing is a promising non-pharmaceutical intervention to reduce risk of secondary transmission of viral URI, but it is likely that adherence to mask wearing would occur only if there was a major pandemic that resulted in a heightened level of community concern and fear.

This study was funded by grant #1 U01 CI000442-01, "Stopping URIs and Flu in the Family: The Stuffy Trial."

The authors thank the following research coordinators: Maria Alvarez-Cid, Angela Barrett, and Maria Gonzalez; external advisors: Sara Beatrice, Adolfo Garcia-Sastre, and Arthur Stone; and Centers for Disease Control and Prevention liaisons: Lyn Finelli, Daniel Fishbein, and Andrew Plummer. The hand sanitizer product was supplied by Johnson & Johnson, Morristown, New Jersey.

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