FluSAFE: Flu SMS Alerts to Freeze Exposure

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SPECIFIC AIMS

We propose to conduct a randomized controlled trial assess whether a scalable, text message-based educational intervention triggered by text message-based surveillance for influenza-like illness (ILI) in households with one or more children can decrease laboratory-confirmed influenza transmission.

Influenza infection results in an estimated 31 million outpatient visits, 55,000 to 974,200 hospitalizations (2014-15 estimate: 974,206), and 3000 to 49,000 deaths (2014-15 estimate: 49,006) annually.[1-3] Membership in a household in which someone else has influenza is the major risk factor for contracting influenza.[4-7] The household secondary attack rate (SAR) is as high as 19% based on laboratory-confirmed influenza and 30% based on symptoms.[6-14] Non-pharmaceutical preventive measures including education have been found to decrease influenza transmission.[15] For example, in one study during the 2009 influenza A H1N1 pandemic, having had a household discussion about preventing transmission was significantly associated with decreased SAR.[7] Most transmission occurs early in an illness,[7,10,13] and it has been demonstrated that non-pharmaceutical interventions are effective only if started within 36 hours of index case symptom onset.[16,17] Yet, most interventions are delayed because they are not initiated until care is sought.[16,17] In one study, less than 30% of households were identified within 36 hours when an index case was diagnosed at a medical visit.[16] We reasoned that use of home surveillance with text-message symptom reporting to trigger an educational intervention has the potential to overcome delays in implementing preventative behaviors.

In previous work, we demonstrated in one primarily Latino, urban sample, that text messaging by family members can be used to rapidly identify members with ILI/acute respiratory infections (ARI) early in an illness.[18] This approach to early identification would enable implementation of an educational intervention targeted to the 36-hour timeframe. Providing education within a text message is a proven successful strategy to influence behavior.[19-22] Using text message surveillance to trigger a novel educational intervention also allows inclusion of both medically and non-medically attended index cases, a key element in reducing influenza SAR since less than one-third of persons with laboratory-confirmed influenza seek medical care.[18] Text messaging itself is scalable, low-cost, and can be used in low literacy populations.[23] However, using text-message based surveillance to trigger a real-time text-message behavioral educational intervention to decrease household influenza transmission has not been assessed. In evaluating the impact of this intervention strategy, the primary outcome will be laboratory-confirmed influenza. The primary outcome will be determined using self-swabs among household members to detect SAR, including asymptomatic infection and medically- and non-medically attended illness. We have successfully piloted self-swab collection.

Aim: To assess the impact of an educational intervention delivered by text messaging on transmission of influenza within households

Primary Outcome Hypothesis: Educational text-messages will reduce laboratory-confirmed influenza household transmission from 12% to 5%

Secondary Outcome Hypothesis: Educational text-messages will reduce ILI transmission from 23% to 11%

Exploratory Aim: To compare the yield of text message ILI/ARI surveillance among subgroups in a diverse, community sample

Hypothesis: Response rates to text messages will be similar among different sociodemographic groups.

We will enroll and randomize 400 households (n=~1500 individuals) with ≥1 child recruited from four contiguous communities in New York City 1:1, stratified by community, to receive surveillance-only vs. surveillance plus text message educational intervention. We will have 88% power to detect a decrease in influenza SAR from 12% to 5%. These percentages are derived from the paper by Cowling *et al.,* reporting a reduction from 12% to 5% between hand hygiene and usual care arms in SAR for influenza when a non-text message-based behavioral intervention was started ≤36 hours of index illness onset.[16] For surveillance, households in both arms will receive text messages 3x/week during each influenza season (Nov-Mar) and report household members with ILI/ARI symptoms. For those in the educational intervention arm, when an ILI/ARI is reported, educational text messages will be sent targeted to decrease household transmission.

Both arms will obtain one self-swab of the index case, and self-swabs of all other household members on days 3 and 5 from index onset.[7,10,13,24] Swabs will be returned via postage-paid envelope and analyzed using an FDA-approved reverse-transcriptase multiplex PCR assay to identify influenza, including sub-types, as well as other viral respiratory pathogens, e.g., parainfluenza etc. We will also collect symptom reports from all household members. The primary outcome will be SAR of laboratory-confirmed influenza. Secondarily, we will assess SAR based on ILI/ARI symptoms, and of non-influenza viruses. Response rates will be compared between arms and by demographic factors (age, education, race/ethnicity). Trial results could provide support for text-based strategies to reduce influenza transmission.

B. RESEARCH STRATEGY

SIGNIFICANCE

Impact of Influenza: Influenza infection results in an estimated 31 million outpatient visits, 55,000 to 974,200 hospitalizations (2014-15 estimate: 974,206), and 3000 to 49,000 deaths (2014-15 estimate: 49,006) annually.[1-3] The burden of influenza also includes high cost from direct medical expenses, days lost from work or school,[25] and inappropriate use of antibiotics.[26] Children and adolescents 6 months-18 years old are at increased risk of influenza morbidity and mortality, and influenza is one of the most common causes of hospitalization for the pediatric population.[1] School-aged children and adolescents also serve as an important reservoir, transmitting influenza to household members.[1,27]

Household Transmission of Influenza. Membership in a household in which someone else has influenza is the major risk factor for contracting influenza.[4-7] The secondary attack rate of influenza in a household is as high as 19% based on laboratory-confirmed seasonal and pandemic influenza, and as high as 30% based on symptoms for ILI/ARI.[6-14] Non-pharmaceutical preventive measures including education have been found to reduce household transmission.[15] One study conducted during the 2009 H1N1 pandemic found that having had a household discussion about how to prevent transmission was the only household-level factor significantly associated with decreased secondary attack rates.[7] However, since most transmission occurs in the first few days of illness,[7,10,13] it is important that the intervention occur as soon as possible after onset of symptoms in the index case. Cowling *et al.* demonstrated an effect of non-pharmaceutical intervention (hand hygiene alone and hand hygiene plus face mask) only when initiated within 36 hours of symptom onset in the index case.[16] Seuss *et al.* also found an impact of mask or mask plus hand hygiene only in households for which the intervention was also started within 36 hours.[17] Interventions will be delayed when they depend on the index case seeking care.[16,17] In Cowling's study, less than 30% of households were identified within 36 hours of onset based on identifying index cases at a medical visit. During the 2009 H1N1 influenza A pandemic, surveillance based on medical visits for ILI was not completely useful for detecting or monitoring the outbreak due in part to the lack of timeliness of visits.[28] These failures to capture cases within 36 hours arise from two factors: time between onset of ILI and seeing a medical provider, and cases that are not medically attended at all. We reported that less than one-third of persons with laboratory-confirmed influenza in a community surveillance study sought medical care.[18] Influenza cases have the potential to transmit infection to household members during the first 36 hours of symptoms; the earlier in this period and the higher the proportion with ILI who receive an educational intervention, the greater the potential to reduce transmission.

Text Messaging and Community-based ILI/ARI Surveillance. To address the limitations of rapid identification of cases based on medical attendance, several studies have had people report via an automated telephone system,[29] but this strategy depends on participants actively remembering to initiate the report. Others have used email, but use may differ by demographics and may not be feasible in diverse populations.[30] While others have used Internet surveillance,[31] or other sources like Google Flu Trends, Twitter [32-34] or crowdsourcing,[35] these data are only available in aggregate. Furthermore, they cannot be verified, be used to measure transmission, nor determine an infectious etiology since respiratory samples are not taken. In addition, internet-based communications may have HIPAA limitations.[36]

Text messaging, however, could facilitate rapid surveillance and data collection from large numbers of participants from diverse populations by using a personalized, patient-centered approach. Text-messaging is not internet-based and does not have internet-related HIPAA limitations. Currently, 90% of adults in the U.S. own a cell phone, with high rates in both minority and non-minority populations (90% White, 90% Black, 92% Latino).[23] Smart phone use, although increasing, is lower (64%).[23] Text messaging can also accommodate different languages, and messages can be tailored to each participant by using response algorithms. Text-messaging can be used effectively in low-literacy populations.[18-22] Another advantage of text messaging is its scalability. After the initial investment to develop the platform, the cost of each additional message is negligible, allowing large numbers of participants to be monitored simultaneously and serially over time. Text messaging can also be centralized and standardized across large geographic areas, allowing surveillance and assessment of distinct demographic subgroups or geographic areas while still maintaining the economy of centralized data collection, management, and analysis. Finally, it allows captured of both medically-attended and non-medically attended disease.

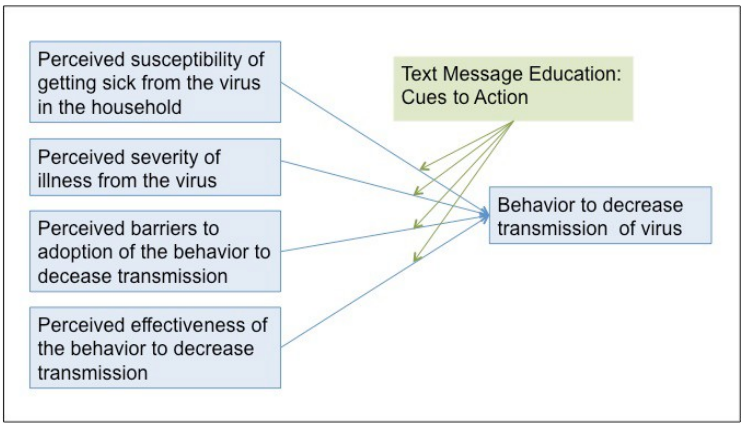
As part of an ongoing community-based study funded by CDC, we have demonstrated the feasibility of using text messaging to conduct ILI/ARI surveillance in one primarily Latino, urban neighborhood community.[18] During the first three years of the study, 62,650 text messages were sent to households and responses were received for 48,308 (77.1%). The response rate did not decrease over time. The majority (88.9%) of responses

were received within 4 hours of messages being sent and 96.2% responses were received within 12 hours (section- preliminary studies). Based on our community study, the CDC has now included the use of text message surveillance as part of their pandemic influenza research plans.[37]

Text Message Reporting and Real-time Behavioral Intervention to Reduce Transmission. While text messaging surveillance can rapidly assess if someone in a household is ill, one potential benefit of this type of surveillance that has not yet been studied is the ability to trigger a real-time educational intervention to decrease transmission by exploiting this rapid identification in order to decrease transmission from both medically-attended and non-attended index cases. Providing education within a text message is a proven successful strategy to influence behavior. We have demonstrated the impact of text message educational reminders to improve influenza vaccination as well as other vaccinations.[19-22] Text messaging has also been used for other behavioral interventions such as smoking cessation.[38]

The **Health Belief Model** provides a conceptual basis for the intervention we are proposing to test.[39,40] According to this model, four main factors affect health-related behaviors: perceived susceptibility of contracting the disease; perceived severity of the disease; perceived barriers to adoption of a behavior to avoid the disease; and the perceived effectiveness of the behavior. While the model is usually focused on an individual's behavior to protect him/herself from developing a disease, for infection transmission, the model can also include behaviors to protect oneself and other household members. Lastly, a cue to action must be present to trigger the behavior.

Figure 1: Health Belief Model and Behavioral Intervention to Decrease Respiratory Virus Transmission (modified from Rosenstock et al)



This conceptual framework will be used to design educational information to be sent within text messages (cue to action) (Figure 1). First, messages will include information explaining that an ill individual can transmit the viral respiratory illness to their household members, and that transmission could be harmful to their household members. Next, messages will include easy to implement behavioral suggestions, and finally will include information regarding the effectiveness of these behaviors. We will also include an interactive component, thereby allowing users to gain further information and enhance engagement.[20,41] Consistent with **health communication theory**, these messages will come from a credible source (e.g. the family's health care provider), be in easily understood language, and will recommend behaviors that can be immediately and easily implemented.[42,43]

Disadvantaged Populations and Households with Children are at Higher Risk for Influenza. The study population will include disadvantaged and other high-risk populations. Understanding the impact of an intervention to decrease influenza household transmission in a low-income, urban population may be particularly important as they may be at higher risk for infection and transmission due to overcrowding.[44,45] In addition, they are at greater risk of having non-medically attended disease as being low-income, Latino, publicly insured, foreign born and having a lower education level are factors associated with lower likelihood of having a primary health care provider and seeking care for illness.[18,46] Also, each household will have at least one child which potentially can lead to higher infection risk.[27] Thus, the risk and impact may be greater, and strategies that work in such populations – such as text messaging – need to be tested.

Thus, the significance of our proposed trial arises from the high secondary attack rate of influenza in households with children, the high morbidity and cost of influenza, and the use of new HIPAA-compliant communications technology, specifically text messaging, that is low cost, scalable, and usable in high-risk populations, to implement home surveillance-linked text-message based educational and behavioral intervention. No trials of this approach have been reported or are being conducted to our knowledge.

INNOVATION

This study is innovative in four ways. (1) It will assess the effectiveness of delivering a real-time text-message-based behavioral intervention to decrease influenza transmission within households. (2) It will also determine if the intervention decreases transmission of other respiratory viruses. (3) It will use text messaging for large-scale ILI/ARI surveillance among varied sociodemographic groups and assess group-specific response rates. (4) It will obtain self-swabs from participants with ILI/ARI to detect respiratory pathogens.

First, while we have previously demonstrated the effective use of text messaging surveillance for ILI, we have not assessed coupling an educational intervention targeted at decreasing influenza transmission to this approach to surveillance. We are not aware of any trials of this strategy for reducing influenza SAR.

Second, while the primary target for most surveillance efforts is influenza, because of the affordability and availability of commercially available multiplex PCR kits, we will be able to assess the impact of the intervention on other non-influenza respiratory pathogens, which are more common than influenza.[18] Thus, the use of text messaging to provide a real-time health behavioral intervention during respiratory illness could provide new insights into prevention strategies for non-influenza viral pathogens. This is also novel.

Third, while we are successfully using text messaging for ILI/ARI surveillance in a predominately Latino community, it is not known if it will be as effective in other populations included in this study-- African-Americans and White, non-Latinos of varying sociodemographic status. In addition, in our ongoing MoSAIC study, families are very closely followed, which may decrease the generalizability of their text response rates. In this proposed study, we will also assess the feasibility of using text messaging in a more diverse and geographically widespread population with less frequent contact with research staff to demonstrate its feasibility, effectiveness, and potential scalability.

Finally, the feasibility of collecting respiratory tract specimens is limited by the time and effort required for an ill individual to come to a central site to have a sample taken, as done in some studies,[10] or the time and expense required for staff to go to an ill person's home to obtain a sample as done in our ongoing study. We and others have shown that self-swabs can be used to identify respiratory pathogens during acute illness, (section preliminary studies).[47-50] However, a study coupling text message ILI/ARI surveillance with self-swabs as the mode of data collection has not, to our knowledge, been conducted among participants from varied socio-demographic populations.

APPROACH

PROJECT TEAM: This interdisciplinary research team has expertise and experience in all key study aspects including community-based sample recruitment and retention, community ILI/ARI surveillance, text message surveillance, using multiplex reverse-transcriptase polymerase chain reaction (RT-PCR), and text messaging-based behavioral interventions. The investigators also have a long history of collaborative work.

Dr. Melissa Stockwell, the contact PI, has expertise in monitoring ILI/ARI in a community household sample. She is PI of a CDC funded grant, the MoSAIC study (U01P000618), which includes community-based surveillance for ARI/ILI using text messages.[18,47,51] Additionally, she has provided expertise to the CDC on pandemic influenza planning including community surveillance and conducted two studies of the 2009 influenza A H1N1 pandemic.[52,53] She was PI on an NIH funded grant, the ACURI study (RC1 MD004109), an educational intervention to improve care for ARI,[54] and is experienced with the use of text messages for vaccine adverse event surveillance, and for other behavioral interventions including promoting vaccination,[18-22] including serving as PI on four grants (R01HS022677, R40MC17169, U01IP000313, U01IP000618).

Dr. Stockwell has worked closely over the last six years with Dr. Elaine Larson, a PI on the proposed study, who is a Co-I on the MoSAIC project[18,47,51] and was Co-PI on the ACURI study.[54] Dr. Stockwell is a member of the Steering Committee of the Columbia Center for Interdisciplinary Research to Reduce Infections (CIRI) directed by Dr. Larson. Dr. Larson is an expert in antimicrobial resistance, infection prevention, epidemiology, and clinical and nursing research. She was a chair of the CDC's Healthcare Infection Control Practices Advisory Committee. Dr. Larson also has expertise in monitoring households for ILI as PI of CDC and NIH- funded trials related to household transmission of ARI/ILI.[29,55](R01 NR05251; U01CI000442).

Dr. Stockwell also works closely with Dr. Lisa Saiman, a PI on this proposed study and a Co-I on MoSAIC.[18,47,51] They have also collaborated on follow-up of exposed children after measles cases at Columbia University Medical Center (CUMC), and an assessment of measles and influenza vaccination status in children admitted to the pediatric ED.[56] Drs. Larson and Saiman have a long-standing collaborative relationship over 13 years, including being co-authors on 35 publications, as well as serving as Co-PI's and Co-I's on related grants (R01 NR010821)(R01HS021470) and on an NINR-funded T32 "Interdisciplinary Research to Prevent Infections". Dr. Saiman is also on the Steering Committee of CIRI, is the hospital epidemiologist at Morgan Stanley Children's Hospital and has expertise in healthcare-associated infections, and outbreak investigations of bacterial and viral pathogens. Dr. Saiman has had a long-standing interest in infections of the respiratory tract and has performed a household study of nasal carriage of methicillin-resistant *Staphylococcus aureus* in which self-swabs were successfully obtained in adults and children and mailed to her laboratory.[57] She has

also performed epidemiologic studies of the impact of the 2009 influenza A H1N1 pandemic at CUMC.[58-60] She oversees the laboratory component of the MoSAIC study.

Drs. Stockwell, Saiman and Larson have also worked closely with Dr. Haomiao Jia, the statistician for this study and for the MoSAIC project. Additionally, Dr. Jia collaborated with Dr. Larson on a project assessing predictors of influenza.[61] His work with Dr. Saiman has included analysis of knowledge, attitude and practice surveys, epidemiology studies, and interventional studies. Dr. Stockwell also has a history of collaboration with Dr. Philip LaRussa, a co-investigator, as they co-direct a CDC-funded research program to assess adverse events post-vaccination using text messaging surveillance.[62-64] Dr. Saiman works with Dr. LaRussa who helps oversee the laboratory component of the MoSAIC study. Drs. Stockwell and Larson collaborated with Dr. Dodi Meyer on the NIH-funded ACURI study.[54] Dr. Meyer is the Director of Columbia University's Community Pediatrics program and an expert in cultural competency and health literacy. Dr. Stockwell has worked previously with Dr. Elizabeth Cohn, an advisor; they both serve on the Steering Committee of Columbia University's Patient-Centered Outcomes Research Initiative. Dr. Larson has a long-standing relationship with Dr. Cohn, including 8 publications. Dr. Cohn is a founding member of the Communities of Harlem Health Revival, a coalition of 72 community and faith-based organizations that seeks to improve the health of urban residents in upper Manhattan, and will aid recruitment.

OVERVIEW: We propose to conduct a randomized controlled trial of real-time text message-based educational intervention to reduce transmission of laboratory-confirmed influenza in 400 households sampled from four diverse, contiguous urban communities in New York City. The primary outcome is household transmission of laboratory-confirmed influenza. The secondary outcome is household transmission of symptomatic ILI/ARI and of non-influenza respiratory viruses among household contacts of index cases.

PRELIMINARY STUDIES

1.***Recruitment of Participants to Clinical Studies Including Trials in Our Setting.***

1.1 MoSAIC: MObile Surveillance for ARI/ILI in the Community (U01 IP000618):[18] Drs. Stockwell, Saiman and Larson recruited 158 households (84.5% of 187 households approached) in year 1 and 175 additional households in subsequent years 2-4 from one of the communities proposed in this study. The current surveillance population is over 1200 people. Many households recruited in year 1 are still in the study in year 4. Near all (99%) of the study population are Latino, and 72% are Spanish-speaking.

1.2 Appropriate Care of URIs in Children of Latino Immigrants: The ACURI Project (RC1MD004109):[54] Drs. Stockwell and Larson recruited 355 households, including 1460 individuals, from one of the communities in this proposed study. The mean number of people per household was 4 (range, 2 to 8 members) and nearly all (94%) households were retained through an 8-month study period. Near all (92%) of the study population are Latino, and 87% were Spanish-speaking.

1.3 Impact of Non-Pharmaceutical Interventions on URIs and Influenza in Crowded, Urban Households (U01 CI000442):[29] Dr. Larson recruited 509 households, including 2788 individuals. The mean number of household members was 4.5, and mean duration of participation was 55.5 weeks with an 87% retention rate. Most (96%) individuals were Latino.

1.4 Effect of Antibacterial Home Cleaning and Handwashing Products on Infectious Disease Symptoms (R01NR05251):[55] Dr. Larson recruited 238 households, including 1178 persons. The mean number of household members was 5 (range, 3 to 13 members). Retention rates through the 48-week study were 94.1%. Most (98%) individuals were Latino.

2.***ARI/ILI Surveillance in a Community-Based Sample and Text Messaging Surveillance***

2.1 MoSAIC: MObile Surveillance for ARI/ILI in the Community:[18] Drs. Stockwell, Saiman, and Larson have used text messaging to conduct surveillance for ARI/ILI. During the first three years of the study, 62,650 text messages were sent to households; responses were received for 48,308 (77.1%). The response rate has not decreased over time. The majority (88.9%) of households who responded did so within 4 hours of messages being sent; 96.2% responded within 12 hours. The median time from symptom onset to research-assistant obtained nasal swab is 2 days; 75-80% of specimens were collected within the optimal 48-72 hour window.[18]

2.2 Appropriate Care of URI in Children of Latino Immigrants: The ACURI Project:[54] Drs. Stockwell and Larson conducted illness surveillance in household using weekly telephone reporting. There were 1,829 illnesses reported. Research staff conducted home visits on a random sample of participants with telephone reports of medication use and the telephone reports were 93.7% accurate (95% CI 86.9%-97.4%).

2.3 Effect of Antibacterial Home Cleaning and Hand Washing Products on Infectious Disease Symptoms:[55] Dr. Larson conducted ARI/ILI surveillance in households using weekly telephone reporting. Research staff determined the sensitivity (93%) and specificity (97%) of the first 100 self-reports of symptoms through an in-person assessment conducted during a home visit. During 26.2%, 23.3% and 10.2% of household-months at least one household member had a runny nose, cough, and/or sore throat.

2.4 Impact of Non-Pharmaceutical Interventions on URIs and Influenza in Households:[29] Dr. Larson and colleagues used twice weekly structured, automated telephone messages using a toll-free number to detect symptoms of ARI/ILI in household members. There were 5,034 ARIs reported, of which 669 cases were consistent with ILI and 78 (11%) were laboratory-confirmed cases of influenza.

2.5 Text Messaging and Vaccine Safety Surveillance:[62-64] Drs. Stockwell and LaRussa have also successfully demonstrated text message vaccine adverse event surveillance in pediatric and obstetric patients.

3.***Identifying Etiology of ARI/ILI***

3.1 MoSAIC: MObile Surveillance for ARI/ILI in the Community:[18] In this study, 59.5% of 1677 samples were positive for a respiratory pathogen; 21.4% of positive samples collected November-March were positive for influenza. In addition, 14 other respiratory pathogens were detected including subspecies of coronavirus and parainfluenza, respiratory syncytial virus (RSV), adenovirus, human metapneumovirus (hMPV), rhinovirus/ enterovirus (RV/EV), *Chlamydophila pneumoniae* and *Mycoplasma pneumoniae*.

3.2 Impact of Non-Pharmaceutical Interventions on URIs and Influenza in Crowded, Urban Households:[29] 33.3% of deep nasal swabs obtained were positive for influenza of which 43.6% were influenza A and 56.4% were influenza B. Among the 66.7% of swabs that tested negative for influenza, 30.8% were positive for other viruses including RSV, parainfluenza, RV/EV, adenovirus, and hMPV.

3.3 Viral surveillance: As a member of the NewYork-Presbyterian Hospital Department of Infection Prevention and Control and the hospital epidemiologist at Morgan Stanley Children's Hospital, Dr. Saiman has helped to craft interventional strategies to prevent transmission of respiratory pathogens in healthcare settings which include tracking and trending community-onset and healthcare-associated respiratory viral pathogens.

4.**Conduct of Randomized Clinical Trials of ARI/ILI- and Vaccination-Related Behavioral Interventions that were Effective**

4.1 ***Appropriate Care of URIs in Children of Latino Immigrants: The ACURI Project:***[54] ***NCT01916031*** Drs. Stockwell and Larson evaluated the impact of an educational intervention to increase health literacy and decrease pediatric emergency department (PED) visits for ARIs among predominantly Latino Early Head Start families. Intervention families with a young child with an ARI, were less likely to use an inappropriate over-the-counter medication, provide incorrect dosing, and/or bring their child to the pediatric emergency department.

4.2 ***Impact of Non-pharmaceutical Interventions on URIs, Influenza in Crowded, Urban Households:***[29] ***NCT00448981*** Dr. Larson found mask wearing reduced secondary transmission of influenza.

4.3 Text-messaging to Promote Health Literacy and Enhance Vaccine Uptake and Completion: Dr. Stockwell has conducted a number of randomized controlled trails demonstrating the effects of text message vaccination reminders that include educational information to increase administration of influenza and other vaccines.[19-22,41,65] *NCT01146912, NCT01662583, NCT01199666*

5. Collection of Self-Swab Samples: We have piloted the use of self-swabs in preparation for this study. For 30 individuals (15 adults and 15 children) meeting ARI/ILI criteria in our MoSAIC study, the ill adult was asked to obtain a self-swab, or if a child was ill, their parent obtained the swab. The self-swabs were obtained after the staff obtained a swab and left the home. The participants mailed self-swabs to our lab via a pre-stamped mailer. Nearly all (97%) households obtained the self-swab and mailed it back. Overall sensitivity for the self-swab to capture any respiratory pathogen or influenza was 83.3% and 87.5%, respectively. The kappa statistic between research and self-swab was 0.84. Specificity was 100%, and negative and positive predictive values were 78.6% and 100% respectively. Sensitivity for self swabs to detect respiratory pathogens for participants obtaining their own self-swab was 71.4% and for a parent obtaining a swab from their child was 90.9%; sensitivity for influenza was 100% for participants obtaining their own self-swab and 75.0% for a parent obtaining their child's swab. There were no differences in demographic variables, including education level, or days between research staff obtaining the swab and receipt of self-swabs, among participants whose self-swab results correlated with the research swab results versus participants whose self-swabs results did not correlate with research swab results.[47]

We also conducted another pilot self-swab study among the household contacts of symptomatic index cases to assess the proportion of household members with asymptomatic infection with viral respiratory pathogens. We provided 181 households with swabs and instructions for obtaining self-swabs for all individuals (symptomatic and asymptomatic) in the household after a symptomatic family member (index case) was identified for up to seven days. We received 88% of daily swabs from index cases and 81% from non-index household members, which included both related and unrelated household members.

STUDY DESIGN

This is a randomized two arm clinical trial to be conducted over four calendar years with blinded ascertainment of the primary endpoint: PCR assay-based household transmission of influenza infection.

STUDY SETTING AND POPULATION:

This study will be conducted in twelve contiguous, but diverse Neighborhood Tabulation Areas (NTAs) in New York City (Figure 2).[66] Washington Heights/Inwood includes **Marble Hill-Inwood** (MN 1), **Washington Heights North** (MN35), **Washington Heights South** (MN36), extending from West 155th Street to the northern tip of the island. Most (71%) residents are Latino, half are foreign born, and half are English-proficient. Central Harlem consists of **Central Harlem North-Polo Grounds** (MN03) and **Central Harlem South** (MN11), which extends from Central Park North to West 155th Street, and east-west from approximately St Nicholas Avenue to 5th Avenue. Most residents (63%) are Black. East Harlem consists of **East Harlem North** (MN34) and **East Harlem South** (MN33), which extends from approximately E 96th Street to West 145th Street and east-west from 5th Avenue to Harlem River. Most residents are either Hispanic (49%) or Black (31%). The area consisting of West Harlem, Hamilton Heights and Morningside Heights includes **Hamilton Heights** (MN04), **Manhattanville** (MN06), and **Morninside Heights** (MN09), extending from West 106th Street to West 155th Street and east-west from Hudson River to Central Park West/Bradhurst Avenue. The racial/ethnic compositions of this community are more variable. The last area consists of the **Upper West Side** (MN12) and **Lincoln Square** (MN14), extending from West 58th Street to West 106th Street and is bounded on the west by the Hudson River and on the east by Central Park/Central Park West. Most residents (67%) are White. The research team has experience recruiting participants from these communities.[20,21,29,54,55,67]

SAMPLING FRAME, ELIGIBILITY, EXCLUSIONS, SAMPLING, RECRUITMENT, AND RANDOMIZATION

Sampling frame. In order for the study sample to be population-based, we have defined the sampling frame geographically, as just described.

Eligibility and Exclusions. Eligibility and exclusion criteria for households are based on previous studies.[18,29,55] Eligibility will require having at least 3 people per household with one or more <18 years of age, in order to ensure that enough people in the household are at risk (Table 2). Household will be defined as individuals who live in the dwelling including nuclear family members, relatives, friends and boarders.

Sampling. As described below, we will use a roster-based approach and snowball sampling from cooperating organizations in the sampling frame, with random selection from these rosters.

Recruitment. We will recruit potential households from a variety of sources, which we have used previously to recruit study participants, including community social service programs, Head Start programs, community health clinics, and private medical offices. We will recruit with the help of the following organizations:

- Union Settlement Association
- Abyssinian Baptist Church
- Communities of Harlem Health Revival (CHHR)
- Children's Aid Society
- Upper West Side practices affiliated with Columbia University

Table 2: Eligibility and Exclusion Criteria

Eligibility Criteria
- ≥3 persons per household
- At least one person who is less than 18 years old
- English or Spanish speaking
- Household reporter has cell phone with text messaging capabilities
- Household reporter willing to use text messages to report
Exclusion Criteria
- Intention to move away from New York City area in <12 months
- Language other than English or Spanish

Recruitment (continued).

We will also encourage households to notify others in their social networks of the study, thus recruiting via snowball sampling. At each site, we will obtain a roster of patients, enrolled families, or clients (as applicable). From these rosters, the study statistician will identify a random sample to contact. Each family will be contacted in order to assess eligibility and interest in the study. We have had high enrollment rates (>80% of those approached to participate) in our previous studies.[18,29,54] The project coordinator will assess the first eligibility criteria (number of household members, child <18 years-old in household and Spanish/English-speaking. If the household is eligible, the coordinator will ask who is the primary caregiver of the children in the household and then ask if that person has a cellphone with text messaging and if they are willing to be the household reporter, as well as confirm that they and the household are not planning on moving in the next year. If these criteria are met, a home visit for enrollment will be scheduled. The household reporter will provide written consent, which will include being the household reporter and sending and receiving text messages. Other household members will be provided with an information sheet in English or Spanish explaining the study and the request for self-swabs from both ill participants and asymptomatic participants. In our text message surveillance study, these procedures were approved by the Columbia University Medical Center Institutional Review Board. Each study participant will be given a unique study ID coded to their household. Multiple other sources of contact information, if available, will be collected for the household reporter including landline and email address.

Randomization Procedures. On study enrollment, we will randomize 400 households (100 from each community) 1:1 to surveillance + education vs. surveillance-only arm, stratified by community and sampling site. Randomization will be conducted by the programmer under the supervision of the study statistician using permuted blocks ensuring balance between the arms. The programmer will enter the study arm the household is randomized to into the text messaging platform database, but arm assignments will not be visible to other research staff. Thus, the statistician and research staff will be blinded to arm.

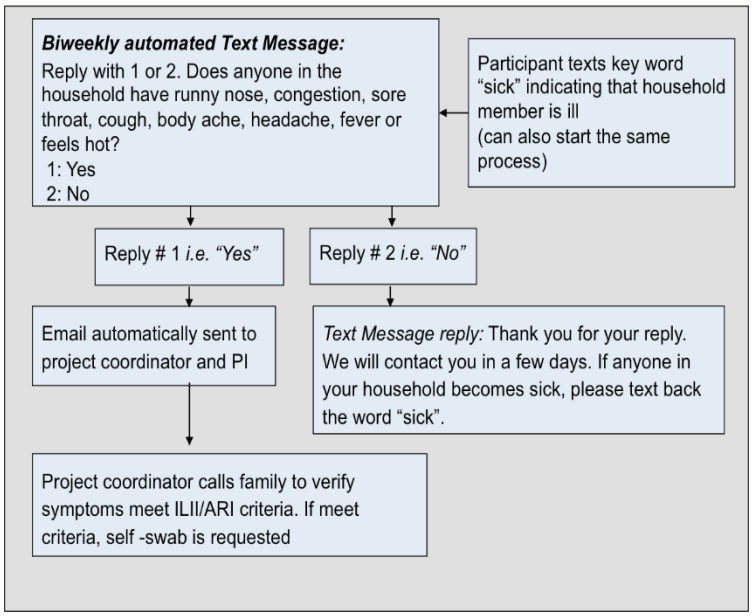
Annual home visits will be made to all enrolled households wanting to continue the next respiratory season to facilitate retention and participation, answer questions, ensure contact information remains correct, update household composition changes, and provide swab kits. Households that continue to meet eligibility criteria (Table 2) may continue into the next respiratory season. Households will receive $50 on enrollment and $25 at this re-enrollment visit; this will aid with enrollment and retention. Participants will also receive compensation for reporting and returning self-swabs as outlined below. If a household no longer meets eligibility criteria during a season or if are lost to follow-up, we will replace households in the same season if there are ≥2 months left in the influenza season or the next year if there are <2months left. Households that leave the study will be replaced using the same procedures as for the baseline sample using 1:1 randomization. Based on previous studies, we expect 10-20% of households to be replaced yearly.[18,29,67]

TEXT MESSAGE SURVEILLANCE FOR ILI/ARI

Both arms (surveillance + education vs. surveillance-only) will receive text messages to perform surveillance of household members for ILI/ARI. The surveillance period will run November through March each year. We have chosen that period since for the past 9 years (with the exception of the 2009 influenza A H1N1 pandemic) the earliest onset of influenza in these communities has been in November and we have seen the vast majority of influenza cases by March.[18,68] If there are unusual influenza patterns, we will be able to start sample collection earlier or end it later. During the surveillance period, each household reporter in all households will automatically receive text messages three-times a week from the text messaging system (a.k.a. *research staff-generated messages*) asking if any household member has symptoms included in the study case definitions for ILI/ARI and asked to respond whether or not anyone is ill (Figure 3). Households will be texted on a Monday, Wednesday and Friday schedule to optimize days between reporting. We have chosen this schedule so that intervention can start within 36 hours of onset. Messages will be sent in English or Spanish based on the

household reporter preference; Dr. Stockwell has extensive experience creating 160-character limited text messages that are linguistically and culturally equivalent in English and Spanish (including messages for ILI/ARI surveillance). In addition to research staff-generated messages, the household reporter will also be able to text the key word, *"sick"* at any time during the surveillance periods to alert staff that someone in the household is ill (a.k.a. *household (HH)-generated messages*), which will lead to a text message cascade (Figure 3). Each household will also receive a refrigerator magnet with study contact information, and the number to text the keyword "*sick*". They will also receive a thermometer and self-swab kits as below. Reporters will use their own cell phone and receive compensation as described below. This strategy for texting and reporting illness has been used successfully in the MoSAIC study.

Figure 3: Flow diagram of influenza-like illness (ILI) and acute respiratory infection (ARI) surveillance protocol



If the household reporter misses a week of reporting, they will be contacted by the research team using their contact information, and if needed via a home visit, to confirm their cell number, to identify reasons for not reporting, and to update contact information including any new number to be used. Based on our previous work, we expect to contact less than 20 (5%) households monthly. Similar to our previous studies, a payment of $15/month will be provided to household reporters who respond to ≥75% of the text messages during the previous month (i.e., at least 9 text messages/month) to defray the costs of the required text messages The payment will be made remotely via a refillable cash card.

Confirmation of ARI/ILI Symptoms via Phone Calls. Any *research staff or HH -generated message* indicating illness in a household member will trigger an automatic email notifying research staff. Staff will immediately contact (within 2-4 hours) the household reporter to confirm ARI/ILI symptoms. The use of text messaging to perform the first level of surveillance allows staff to focus on households with ill participants, which we expect to be about 5-15 households at any given reporting day. In the MoSAIC study, we successfully contacted all families within 12 hours of reporting via text message, 7 days a week. Symptoms will be confirmed over the phone using the Symptoms Reporting Form used in previous studies[18,29,54,69] (Appendix).[18,29] Anyone meeting case definition for ARI or ILI will be swabbed. The CDC-provided case definition for ARI is presence of at least two of the following: (1) rhinorrhea/nasal congestion; (2) sore throat; (3) cough; (4) fever/feverishness; (5) myalgia. The ILI definition is at least two of the following signs and symptoms: fever, cough, headache, sore throat, or myalgia.[16] In addition, for those <1 years-old, a swab will be collected even if rhinorrhea is the only symptom; young children have viral illnesses that manifest differently than in adults.[70] We are using ARI and ILI criteria to collect swabs, since a poor correlation between CDC ILI definitions and influenza has been noted by ourselves and others.[71]

Obtaining of Self-Swab Nasal Samples. At enrollment, we will provide households with our pilot tested self-swab kits. The research staff will demonstrate to the household reporter how to obtain the swab, including an observation of the reporter taking a self-swab. Ill participants can self-swab or the household reporter can obtain the swab or a parent can obtain their child's swab. Households will also be given a simple written instruction sheet (Appendix) and a link to a brief YouTube video that we will create to demonstrate how to take the swab; both will be in English and Spanish. We will offer support for the self-swabbing, if needed, in a step-wise fashion.[49] We will first provide further instruction and support over the telephone, then, if needed, the research staff will visit the home to supervise collection, and if that fails, the staff will collect the specimen. In our pilot studies of self-swabbing of ill participants and of asymptomatic household members, all households reported that the process for taking the swabs went well without any issues.

Samples will be collected from the anterior nares using flocked swabs,[72] which have a sensitivity of 91-98.5% and specificity of 100% compared with nasopharyngeal aspirate.[73,74] Each household will be provided with a kit that includes multiple nasal swabs, labeled containers with universal transport media, plastic

specimen bags, and pre-addressed/pre-stamped waterproof mailers with absorbent paper inside in case of spill. Households will be instructed on the importance of making sure the container is closed, how to put the container in the specimen bag, and how to place the bag in the mailer and seal the mailer. We will ask that the households keep their unused kits in their refrigerator so they will be highly likely to recall the kits' location. Each household's kit will contain a list of stickers with unique ID numbers for each household member matched to the person's name. Families will be asked to put the relevant sticker and date of collection on the specimen.

For the index case, we will ask that samples be obtained the same day as the report of illness to facilitate the yield of respiratory pathogens. We will then ask that everyone else in the household is swabbed 3 and 5 days after the onset of symptoms in the index case. We have chosen this timing, to maximize yield for influenza, since it has been estimated that the time between influenza infection in an index case and infection of secondary household contacts is 3.4 days [3.1, 3.7].[7,10,13,24] It was also found that a single sample on day 4 or day 5 since the symptoms onset of the index case would have the most "detectable" infections circulating in households.[24] Households will be texted reminders on day 3 and 5 requesting that these samples be taken, and will be asked to text back confirmation. Households that do not text back confirmation will be called. We will ask that swabs be kept in their refrigerator, until mailing, as in our pilot study.

Once all samples are collected they will be placed in a pre-addressed, pre-stamped mailer and dropped into the regular mail, as in our pilot. They will be texted a final time on day 7 asking if swabs were sent back, and will be called if do not respond. An episode of ILI/ARI within a household will be considered completed when the last person within a household is symptom-free for 5 consecutive days; after that, new symptoms within a household would trigger consideration of a new ILI/ARI episode. As additional compensation for their time, households will receive $5.00 when the swabs are received. We will track kits that are used, and a new kit will be mailed overnight when a household as used up all kits.

Laboratory Confirmation of Respiratory Pathogens. When a mailed swab sample is received, it will be logged into a database and placed in a designated refrigerator (2-8^{o}C) prior to processing. Samples that cannot be fully processed within 48 hours will be aliquoted frozen at minus 80^{0}C. Samples will be analyzed using the FilmArray instrument Respiratory Panel developed by BioFire Diagnostics,[75-77] which has FDA 510(k) clearance as an *in vitro* diagnostic device for nasal swab specimens, and is the testing system we use in our current MoSAIC study. The Respiratory Panel applies multiplex reverse-transcriptase polymerase chain reaction (RT-PCR) to identify 20 respiratory pathogens using a variety of gene targets for specific pathogens[75](Appendix). Detected pathogens include Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza A subtype H1 2009, Influenza B, adenovirus, 4 subtypes of coronavirus and 4 subtypes of parainfluenza, human metapneumovirus, respiratory syncytial virus, rhinovirus/enterovirus, *Mycoplasma pneumoniae, Chlamydophilia pneumoniae* and *Bortadella pertussis*. The sensitivity of FilmArray Respiratory Panel ranges from 87-100% and specificity from 89-100%. Previous studies have shown that the rates of detection of respiratory viruses by RT-PCR can be up to 2-fold higher than by conventional viral culture.[78] Testing will be performed within a research laboratory at Columbia University Medical Center and the technologist, Ms. Wang, is the chief technologist on our MoSAIC study which also uses the FilmArray system. She will be supervised by Dr. Saiman. Dr. LaRussa will provide expertise in viral diagnostic testing. Quality control will be performed for all new lots and shipments using validation panels as per the manufacturer's recommendations for research studies. The technical failure rate has been estimated to be 2-4%;[76,77] but in our current study, the failure rate has been only 1.3%. In the event of technical failure, there is adequate residual viral transport media volume to perform a second test. For households with an influenza positive index case, if both d3 and d5 samples in a household member are negative, the d5 sample will be re-tested. The residual viral culture media containing the sample and swab will be stored in a minus 80^{0}C freezer. Results will not be shared with participants and Ms. Wang and project coordinator will be blinded to study arm. However, if a household's index case has a negative result two episodes in a row, the study team may further assess the episodes and review with the household how to take the swab as well as the importance that symptoms be met.

Blinding. Participants cannot be blinded as to which group they are randomized. Laboratory technicians ascertaining the primary endpoint will be blinded as to arm assignment, and the research staff will also be blinded as above. The data analysis will be blinded as to group assignment by using a dummy variable for intervention vs. comparison until the analyses are completed.

TEXT MESSAGE-BASED INTERVENTION

While ***all*** households will receive the surveillance text messages, we will randomize households within each surveillance community to ***additionally*** receive educational text message about ways to decrease household

transmission (surveillance + education arm) vs. standard care (surveillance-only arm). We will then assess the impact of the educational text messages primarily on secondary attack rates of influenza within households.

The comparison arm will not receive any educational text messages, only the surveillance ones as above.

Message Generation. When an ILI/ARI is reported, research staff will log it into the text message application. If the household is in the surveillance + education arm, the system will automatically send one educational message to the household reporter a day for three days; if it is surveillance-only the system will not send a message. This allows research staff to remain blinded. Messages will be based on whether it is an adult or child who is the index case (Appendix). We have chosen three messages since after that most within-household transmission will have occurred. The household reporter will be instructed on enrollment that they are to read the text message to the household members. We have designed 4 sets of message to be used in order per household i.e. each household will start with set one (see Appendix for adult and child-specific sets of messages). The message will be targeted to be from the recruitment site (e.g. doctor's office, Head Start). We will track reports of undelivered messages; these are visible in the text message application.

Intervention Message Design Including Cultural Sensitivity. We have designed sample sets of messages (see Appendix) based on the Health Belief Model that includes the CDC recommended information to decrease influenza and other respiratory pathogen transmission, the relevant literature, and the team's expertise in text messaging, influenza, disease transmission, health literacy and the community. As mentioned above, our team includes Dr. Dodi Meyer, an expert in cultural competency, who runs a health literacy program that has been federally funded, *Health Education and Adult Literacy*. Messages will include information that an ill individual can pass the respiratory illness to their household members, that transmission can harmful to household members, suggestions for behavior change, and the effectiveness of behavior change (Figure 4). Some of the messages will be interactive since in our previous vaccination-related intervention, we found that including one interactive message increased the intervention effect.[20,41] While keeping within the 160-character count, we designed messages to be no more than a 5th grade reading level according to the Flesch–Kincaid readability test,[79] and in accordance with national guidelines.[80] The messages will have the same content for English and Spanish-speaking families, ensuring proper linguistic and cultural equivalency. In our previous text messaging studies, we used equivalent English and Spanish content and found no interaction between intervention effects and language of message.[19] Using the same content in English and Spanish allows comparisons across the study population. Our team has expertise in completing such translations in 11 text messaging studies.[18-22,41,62-65,81] We will follow the best practices for translation[82] which include preparing a preliminary version in Spanish, back-translation by a second person unfamiliar with the original English messages, and examination of the original English, preliminary Spanish and back-translated English versions. We then will show the final draft versions to five other bilingual staff members in our Division of Child and Adolescent Health who represent different Spanish-speaking countries to ensure the messages are linguistically and culturally congruent. The next step will include pretesting messages, as delineated below. We will then adjust messages and repeat the above steps accordingly. Team members will meet a last time to assess content validity and equivalency of final messages.

Figure 4: Examples of Potential Set Text Messages for a Sick Adult

Text Message Examples	Health Belief Model Factor
Audubon Clinic: People with flu and other viruses could get others sick up to 5-7 days after they themselves get sick. It could be much worse than a bad cold!	Perceived susceptibility of contracting the disease Perceived severity of the disease.
Audubon Clinic: Avoid others getting sick in your house. Wash hands often with soap and water or use an alcohol-based hand sanitizer.	Perceived barriers to adoption of the behavior
Audubon Clinic: Have a household talk about how to prevent spreading the flu and other viruses. It has been shown to work!	Perceived effectiveness of the behavior

Pretesting. We will pre-test the educational messages in person with households in all 4 communities following our previous field-testing protocol. For the Washington Heights community, we will sample families from the MoSAIC study. For the West Harlem, Hamilton Heights and Morningside Heights area, we will recruit households from two of the health centers associated with NewYork-Presbyterian Hospital serving those neighborhoods, and for the Upper Westside area we will recruit from two general pediatric practices affiliated with CUMC. For the Harlem area, we will recruit through the Communities of Harlem Health Revival (letter of support). Households with whom we pretest messages must meet the same eligibility criteria as those for the study and will not be eligible to be randomized. After obtaining informed consent, the project coordinator will text the proposed messages and ask the respondent to feedback in their own words what the message meant

to them. The coordinator will also ask about any problems or suggested changes. This process will be iterative until no new message changes are made. The translation process will repeated with the final messages. We anticipate needing 40 households, 10 from each community, to pretest the messages. Households will receive a round-trip New York City subway Metrocard worth $5.00 for participating in the pre-test.

DATA COLLECTION AND MANAGEMENT FOR BOTH ARMS

Survey Tools. Household and individual data will be gathered from the household reporter using two methods: a Demographic Survey adapted from previous studies[18,29] and a Household Intake Form (Appendix). Surveys will be verbally administered by research staff at the baseline (enrollment) home visit in the reporter's preferred language, English or Spanish. We will obtain the following data at enrollment and update it annually:

- *Individual characteristics* (age, sex, race/ ethnicity, place of birth, length of time in U.S., preferred language, education, insurance, employment status, school/daycare, hours outside the home, general health status, presence of chronic respiratory disease or other illness, smoking/exposure to second-hand smoke).
- *Household characteristics* (composition, household density [ratio of people to bedrooms]).

Symptom Reports. We will call on day 10 after symptom onset of index case to assess ILI/ARI symptoms in household members, care sought, if anti-viral medication taken, and current influenza vaccination status (including type of vaccine) using the Follow-up form (Appendix).

Data Management. All data collection and storage will be HIPAA compliant as outlined in the Human Subjects Protection. Dr. Stockwell will supervise file cleaning and perform quality checks at least monthly. All study related documents and swab samples will contain a unique identifier for each participant.

STATISTICAL PLAN: Data analysis will be performed using SAS (Cary, NC).

AIM: To assess the impact of an educational intervention delivered by text messaging on transmission of influenza within households

All analyses will be based on randomized arm assignment (intention-to-treat). An ill person will be considered an ILI/ARI index case for a household if, at the onset of illness, no one else in the household had been symptomatic within the previous 5 days.[29] Non-index household members will be defined as secondary cases if they are confirmed by RT-PCR as influenza-positive on day 3 or day 5 swab (symptomatic or asymptomatic).[16] Five days was selected based on our previous studies and the influenza incubation period.[29] The secondary attack rate will be defined as the number of secondary cases of laboratory-confirmed influenza (both symptomatic and asymptomatic) divided by the number of household members minus one (the index case). Secondary attack rates will be compared between the arms - surveillance plus education vs. surveillance-only - using chi square tests and a generalized linear mixed model (logistic regression for binary response, mixed model for clustering within a household). We will assess other co-variates in the models including for the index patient and household contacts: age, sex, vaccination status including vaccine type, antiviral use (treatment or prophylaxis), previous illness episodes reported for the household, influenza season and years in study.

Secondarily, we will assess the intervention's impact on additional outcomes using the same analyses as above: defining secondary cases based on (1) ILI-criteria (fever, cough, headache, sore throat, or myalgia) within 5 days of illness of index case; (2) ARI criteria (≥2 of a) rhinorrhea/nasal congestion; b) sore throat; c) cough; d) fever/feverishness; e) myalgia); (3) any laboratory-confirmed pathogen that is the same as the index case including non-influenza pathogens. An additional set of secondary outcome measures will be to assess the secondary attack rate at the household (cluster) level defined as the percentage of households with at least one secondary case as defined in the analyses above.

We will minimize the amount of missing household-time due to attrition by replacing households who are lost to follow up that year if there are ≥2 months left in the influenza season or the next year if there are <2 months left. We recognize that reasons for dropping out may be correlated with the outcome; this cannot be tested directly in the data. We will therefore add an indicator in the models for replacement households and test for association. Also, we will perform sensitivity analyses analyzing only the originally randomized study sample (exclude replacement households). Weak or no association for the indicator variable and consistency in the association between random arm assignment and outcome between the whole sample and the sample excluding replacement households will be interpreted as evidence supporting use of the entire sample. We will also conduct sensitivity analyses in which we assign the outcome of secondary transmission in the replacement sample to infection to make it a worse case scenario, with the caveat that this will only be possible if the dropout rate is low. If dropout rate is high, the range of possible estimation is too large.

Missing Data. We will document missing data and classify by variable and arm. We will then assess any relationships between missingness and covariates such as demographics or arm. Missing data due to attrition was discussed above. Missing data due to other reasons will also need to be taken into account. The main concern related to the primary outcome will be household contacts who do not obtain swabs. We will impute these data using multiple imputation following the methodology of Rubin.[83] A more conservative approach would be to consider all household members missing swab data to be failures[8] (to have been infected with influenza), but this is highly unlikely to be an accurate reflection of the true case, unduly weights drop-outs in the analysis, and is not the currently preferred approach to missing data.[84,85] Covariate data may also be missing. We will also impute these variables using multiple imputation following the methodology of Rubin.[83]

Exploratory Aim: To compare the yield of text message ILI/ARI surveillance among subgroups in a diverse, community sample

We will use Pearson chi square to assess relationship between text message response rates and community, reporter's race/ethnicity, insurance and education. This will be defined as number of responses received per message sent. If more than one variable is significantly related to reporting rates ($p<0.1$), we will develop multivariable logistic models to assess this relationship. We will also assess response rates by arm.

SAMPLE SIZE AND POWER

We have based our sample size on the primary outcome. With 200 households per arm and an average of 3.8 persons/household, we will have 88% power to detect a decrease in secondary attack rates of laboratory-confirmed influenza from 12% (surveillance-only) to 5% (surveillance + education), based on type I error of 5% and an intracluster correlation coefficient of 0.29. The intracluster correlation, expected transmission rates for the surveillance-only arm, and effect size are derived from the paper by Cowling *et al.,* reporting a reduction from 12% to 5% between the hand hygiene and usual care arms in SAR when a non-text message based behavioral intervention was started at ≤36 hours of illness onset in the index case using laboratory-confirmed influenza as an outcome.[16] In the MoSAIC study, secondary attack rates for laboratory-confirmed influenza have been 16.6% therefore an expected rate of 12% in the surveillance-only arm is conservative. We will also be powered for our secondary outcome; we will have 91% power to detect a decrease in symptomatic ILI/ARI from 23% to 11%.[16] If we lose 80 households (20%) per season, we will still have at least 80% power to detect the decreases in both the primary and secondary outcome as above, even without household replacement.

POTENTIAL CHALLENGES AND SOLUTIONS Table 3

Challenge	Solution
1. Recruitment and retention	In our previous community studies retention was excellent. In our MoSAIC study, 75.9% of households recruited in year 1 were still in the study in year 3.
2. Non-representative sample	Since eligibility criteria include ≥3 members and ≥1 child, the sample will not be fully representative of the communities. However, the benefits of these inclusion criteria include higher likelihood of infection and transmission.
3. Reporting bias	3x/a week texting will decrease recall bias. We have shown under- and over-reporting to be low and confirmed the validity of household symptom self-reports.
4. Cell phone numbers change/disconnected	We will have multiple ways to contact household reporters and will contact those who have not reported for one month.
5. Effect on participants seeking care	Staff will not provide medical advice, and will refer participants to their own health provider, as was the process in our previous studies, without event.
6. Missed samples	We will offer support for the self-swabbing as needed in a step-wise fashion.[49]
7. Self swabs being obtained days 3 and 5	We have chosen these days in order to maximize yield for influenza while keeping testing feasible. We may miss some non-influenza viruses with longer incubation periods
8. Using U.S Postal Service	This allows best access for individuals who may not live near a FedEx or UPS drop box.
9. Reporting November through March	We have based surveillance on usual influenza patterns; if there are unusual influenza patterns, we will be able to start sample collection early or end it later.

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PUBLIC HEALTH IMPLICATIONS AND DISSEMINATION

We propose to assess the impact of a text message-based educational intervention on household transmission primarily of influenza and secondarily of ILI and other respiratory viruses. If successful, information gathered could provide new insights in decreasing influenza both during seasonal outbreaks and pandemics. It may also, in a future pandemic, be useful to help identify those in need of antiviral treatment and prophylaxis.

TIMELINE Table 4

	Pre-start	mths 1-6	mths 7-12	mths 13-41	mths 14-48
IRB submission	X				
Hire/train staff, Pretest messages, Set up intervention		X			
Household recruitment, Randomization			X		
Surveillance; Intervention				X	
Lab and Data Analysis, Manuscript Preparation				X	X

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