



Munywoki, PK; Koech, DC; Agoti, CN; Cane, PA; Medley, GF; Nokes, DJ (2018) Continuous invasion by respiratory viruses observed in rural households during a respiratory syncytial virus seasonal outbreak in coastal Kenya. *Clinical infectious diseases*. ISSN 1058-4838  
DOI: <https://doi.org/10.1093/cid/ciy313>

Downloaded from: <http://researchonline.lshtm.ac.uk/4647455/>

DOI: [10.1093/cid/ciy313](https://doi.org/10.1093/cid/ciy313)

#### Usage Guidelines

Please refer to usage guidelines at <http://researchonline.lshtm.ac.uk/policies.html> or alternatively contact [researchonline@lshtm.ac.uk](mailto:researchonline@lshtm.ac.uk).

Available under license: <http://creativecommons.org/licenses/by-nc-nd/2.5/>

## **Continuous invasion by respiratory viruses observed in rural households during a respiratory syncytial virus seasonal outbreak in coastal Kenya**

Patrick K. Munywoki<sup>1,2\*</sup>; Dorothy C. Koech<sup>1</sup>; Charles N. Agoti<sup>1,2</sup>; Patricia A. Cane<sup>3</sup>; Graham F. Medley<sup>4</sup>; D. James Nokes<sup>1,5</sup>

### **Author Affiliations:**

1. Epidemiology and Demography Department, KEMRI-Wellcome Trust Research Programme, Centre for Geographic Medicine Research – Coast, Kilifi, Kenya.
2. Department of Nursing and Public Health, Pwani University, Kilifi, Kenya.
3. High Containment Microbiology, Public Health England, Salisbury, United Kingdom
4. Department of Global Health and Development, London School of Hygiene and Tropical Medicine, University of London, London, United Kingdom.
5. School of Life Sciences and Zeeman Institute: SBIDER, University of Warwick, Coventry, United Kingdom.

**\*Corresponding Author:** Dr. Patrick K. Munywoki, Epidemiology and Demography Department, KEMRI - Wellcome Trust Research Programme, Centre for Geographic Medicine Research – Coast, Hospital Road, P.O. Box 230-80108, Kilifi, Kenya; Tel +254 (0)417 522535; Fax: +254 (0)417 522390; email, [pmunywoki@gmail.com](mailto:pmunywoki@gmail.com).

**Summary points:** This is the first household study using intensive sampling regardless of symptoms together with multiple virus diagnosis in low-income setting. The study reveals a remarkably high frequency of virus illness in households demonstrating the extraordinary opportunity for virus introduction, spread and interaction within households.

**Running title:** Respiratory viruses in Kenyan households

© The Author(s) 2018. Published by Oxford University Press for the Infectious Diseases Society of America.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited.

## Abstract

**Background:** Households are high intensity close-contact environments favorable for transmission of respiratory viruses, yet little is known for low-income settings.

**Methods:** Active surveillance was completed on 47 households in rural coastal Kenya over six months during a respiratory syncytial virus (RSV) season. Nasopharyngeal swabs (NPS) were taken from 483 household members twice-weekly irrespective of symptoms. NPS from 6 households were screened for 15 respiratory viruses by molecular diagnostics and the remainder only for the most frequent viruses observed: rhinovirus (RV), human coronaviruses (hCoV; comprising 229E, OC43 and NL63), adenovirus (AdV) and RSV (A and B).

**Results:** Of 16,928 NPS tested for the common viruses, 4,259 (25.2%) were positive for  $\geq 1$  target; 596 (13.8%) had co-infections. Detection frequencies were 10.5% RV (1780), 7.5% hCoV (1274), 7.3% AdV (1232), and 3.2% RSV (537). On average, each household and individual had six and three different viruses detected over the study period, respectively. RV and hCoV were detected in all the 47 households while AdV and RSV were detected in 45 (95.7%) and 40 (85.1%) households, respectively. The individual risk of infection over the 6-month period were 93.4%, 80.1%, 71.6%, 61.5% and 37.1% for any virus, RV, hCoV, AdV and RSV, respectively. NPS collected during symptomatic days and from younger age groups had higher prevalence of virus detection relative to respective counterparts. RSV was under-represented in households relative to hospital admission data.

**Conclusions:** In this setting respiratory virus infections and associated illness, are ubiquitous in households. Future studies should address the health and economic implications of these observations.

**Key words:** Respiratory viruses; transmission; household; developing countries; Kenya

## Text

### Introduction

The current understanding of respiratory virus epidemiology arises mainly from analysis of specimens collected from individuals seeking care at hospital or health facility, usually focusing on one virus. This approach cannot provide a complete description of viruses in circulation in the community. A proportion of the infections will be asymptomatic or not severe enough to require medical attention, and, respiratory virus infections are typically of short duration. Hence, for a full ecological/epidemiological description requires frequent sampling of individuals in a population regardless of symptoms, which is rarely undertaken. As a result, our understanding of seasonality, persistence patterns and transmission dynamics of most respiratory viruses at the community level remains uncertain. Increased sensitivity and range of pathogens detectable by molecular diagnostics over traditional methods (culture isolation or antigen detection) [1-3] enable enhanced studies of a wide range of respiratory viruses in otherwise healthy populations.

The present study involved respiratory virus screen of over 16,000 respiratory specimens that were collected from members of a rural coastal community in Kenya. The specimens were collected through household-based active surveillance for six months. Deep nasopharyngeal swabs (NPS) were collected from all household members irrespective of symptoms. The intensive surveillance provided detailed infection data that allowed comprehensive investigation of the circulation of the respiratory viruses in the community. Previous reports have described the data on respiratory syncytial virus (RSV) in detail [4-7], and here we present data on a wide range of respiratory viruses.

### Materials and Methods

#### *Data*

The current analysis is of data from a household cohort study undertaken in rural coastal Kenya within the Kilifi Health and Demographic Surveillance System (KHDSS) [8]. The study period spanned from 8<sup>th</sup> December 2009 to 5<sup>th</sup> June 2010. The study design and the details of field operations have been previously described [4-7]. Identifying who infects the infant with RSV in the household was the primary objective of the study [6]. Households were eligible if they had an infant born since the end of the previous RSV epidemic in the study location and at least one older sibling (aged <13 years). The study period spanned one complete RSV season [6]. Deep NPS collections were requested from all household members irrespective of symptoms, once-a-week in the first four weeks and subsequently twice-a-week for the remainder of the study period. Retention of households and individuals in the study was over 80% [6].

#### *Respiratory virus screening using multiplex RT-PCR*

By multiplex real time PCR assay, NPS collections from six households were screened for 15 respiratory virus targets as previously described [6, 9]. These households were selected to represent various household sizes; range 4-37 members. The full assay targets were RSV A and B, rhinovirus (RV), human coronavirus (hCoV-OC43, hCoV-NL63

and hCoV-229E), adenovirus(AdV), parainfluenza virus(PIV types 1-4), influenza(types A, B and C) and human metapneumovirus(hMPV). For the remainder of the NPS collections(from 41 households) screening was limited to the viruses(or virus groups) found most prevalent in the full screen, namely, RV, hCoV(OC43, NL63, 229E), AdV and RSV(A and B). A specimen with a cycle threshold(Ct) value of  $\leq 35.0$  for a specific virus target was considered positive. Targets with a detection rate of  $>5\%$  were considered prevalent and constitute targets take forward for screening of all the NPS collections.

### *Statistical analysis*

Data analyses were undertaken in STATA Version 13.1 (StataCorp, College Station, Texas, USA). Appropriate statistical tests were used that included the Student's t-test, chi-square test and Fisher's exact. Week delimited data on virus detections were plotted to show the temporal distributions and co-circulation at sampling, individual and household level. Overall prevalence of the detected respiratory pathogens in households, individuals and samples are also shown. The crude household and individual attack rates(defined as the household and individual risk of infection over the six months, respectively) were stratified by age, symptom status, household size and gender.

### *Ethical considerations*

An informed written consent was obtained from all the study participants or their parents/guardian. Ethical approval for the study was provided by the KEMRI-Scientific and Ethical Review Committee in Kenya and the University of Warwick Biomedical Research Ethical Committee in the United Kingdom.

## **Results**

### *Baseline characteristics*

The median occupancy in the 47 households was 8 members(range, 4 - 37). The average age of the members in each household at the start of sampling was 15.5(95% CI, 13.2 – 17.9) years. The baseline characteristics of the 6 households that were screened for all the 15 respiratory targets compared to the 41 households whose samples were tested for only the most prevalent respiratory viruses were similar apart from the latter having a higher proportion of school-going children, (25.3% vs. 36.6%, Chi-square p-value=0.049), Table 1. Overall, data from the 47 households with 483 participants is presented. Ten participants who were never sampled were excluded from the subsequent analysis. A total of 16,928 samples collected were tested: 2844 samples from the six households (80 individuals) with full respiratory virus screen and 14,084 samples from the remaining 41 households (403) with select respiratory virus screen.

### *Viruses detected from full respiratory virus screen*

One or more of the 15 respiratory viruses were detected in 864/2844 (30.4%) of the NPS collections, of which 714(82.6%), 126(14.6%), 19(2.2%), 4(0.5%) and 1(0.1%) had one, two, three, four and five viruses (co-)detected. The proportion of samples virus positive was higher for specimens collected while the individual had symptoms, compared to specimens from asymptomatic periods, 52.0%(275/529) vs. 25.4%(589/2315), respectively, chi-square  $p$ -value<0.0001. Those NPS specimens with multiple virus detections had increased frequency of symptoms over single infections, 39.3%(59/150) compared with 30.3%(216/714),  $p$ -value=0.03. The details of the number of samples that were positive for the respective targets are provided in Table 2. Of the 2,844 NPS collections screened, the number positive, by pathogen, was RV 302(10.6%), AdV 270(9.5%), hCoV 217(7.6%), RSV 151(5.3%), PIV 63(2.2%), hMPV 13(0.5%) and influenza 11(0.4%). Of the virus positives, the corresponding number of samples collected from individuals with symptoms, by pathogen, were 103(34.1%), 93 (34.4%), 68(31.3%), 50(33.1%), 18(28.6%), 2 (15.5%), and 6(54.5%).

Over the six-month study period, the number of individuals with at least one infection of any of the target viruses, RV, AdV, hCoV, RSV, PIV, hMPV and influenza were 75(93.8%), 62 (77.5%), 57(71.3%), 58(72.5%), 52(65.0%), 37(46.3%), 11(13.8%) and 8(10.0%), respectively. The corresponding number of symptomatic infections of those ever infected, by pathogen, was 46(61.3%), 33(53.2%), 26(45.6%), 29(50.0%), 25(45.5%), 11(29.7%), 2(18.1%), and 4 (50.0%), respectively. RV, AdV, hCoV and RSV, were the most the prevalent respiratory pathogens. They were each found in all the six households, infecting at least one member and taken forward as the prevalent targets for screening of the NPS collection from the remaining 41 households. The temporal infection profile for the six households(A-F) showing positive samples for each member is shown in Figure 1.

### *Viruses detected from the select respiratory virus screen*

All the 16928 NPS collections from the 47 households had infection data from the seven prevalent respiratory targets(RV, AdV, hCoV(OC43, NL63 and 229E) and RSV(Group A and B)). Of the 16,928 NPS tested, 4259(25.2%) were positive for one or more of the selected respiratory virus targets. Of the virus positives, 3687 (86.6%) were single virus detections, 526 (12.4) dual, 45 (1.1%) were triple, while only 1 (0.02%) had four targets co-detected. Virus positive specimens had a higher probability of being associated with respiratory symptoms compared to virus negative specimens, 34.1%(1450/4259) vs. 16.7%(2114/1266), respectively, chi-square  $p$ <0.0001. The detected viruses in order of frequency were RV(1780, 10.5%), hCoV(1274, 7.5%), AdV(1232, 7.3%) and RSV(537, 3.2%). Of the hCoV detected, 627(49.2%), 399(31.3%) and 212(16.6%) were single infections of OC43, NL63 and 229E respectively and 36(2.8%) had mixed hCoV strains. For the RSV positive specimens, 231(43.0%) and 287(53.4%) had RSV group A and B only, respectively while 19 (3.5%) specimens had both. Of all the virus positive NPS collections, 657(36.9%), 407(33.0%),

410(32.2 %), and 229(42.6%) had symptomatic infections with RV, hCoV, AdV and RSV, respectively.

The frequency distribution of the viruses circulating in the community during the study period are shown for the 6 households with full respiratory virus screen versus the 47 households with select respiratory screen in Figures 2a and b, respectively. For comparison, Figure 2c illustrates the frequency distribution of virus infections in paediatric(<5 years old) pneumonia admissions to Kilifi County Hospital over the same period [6], showing a markedly higher frequency of RV, RSV, hMPV and PIV3 detections than in the households.

#### *Number of different respiratory infections over the study period*

Of the seven selected virus targets, each household had a median of six (range of 3 – 7) detected over the 6-month study period, Figure 3(a). A higher median number (9 (range 8 – 15)) of targets were detected for the 6 households with full(15) respiratory virus screen (Figure 3(d)). At the individual level, a median of three different viruses (range of 0 – 6) were detected per person over the study period, Figure 3(b). The corresponding median was four (range of 0 – 9) for the individuals with complete virus screening, Figure 3 (e). Of the virus positive samples, 13.4%(572/4,259) and 17.4%(150/864) had two or more viruses detected based on the screening of the select and full respiratory virus screen, respectively(Figure 3(c) and Figure 3(f)).

#### *Seasonality of the respiratory viruses*

RSV infections were first detected in the area from the hospital surveillance at the end of November 2009(Figure S1) but began circulating in the community study cohort early January 2010(Figure 4), peaking in March and fading out by end of May 2010; the outbreak comprised of RSV A and RSV B at similar frequency, 43.0% vs 53.4%. HCoV had two major peaks, one in February and one in May, and a minor peak in early April 2010. The major peaks were mainly linked with increased detection of both hCoV-OC43 and NL63 while the minor peak was composed only of hCoV-OC43. Throughout the study, adenoviruses had a consistently high prevalence with no apparent peak times. The prevalence of RV was at its peak in January, gradually declined over the study period and was at its lowest at the end of May 2010. The observed seasonal patterns were evident even after aggregating the data to assess the weekly detection rates of the viruses at sample, individual or household level(Figure 4). From the six households with full respiratory virus screen, similar seasonal patterns were observed albeit with greater variability(Figure S2). The PIVs, influenza viruses, and hMPV were rarely detected throughout the six-month study period (Figure S2) – and this was also observed from the hospital virus surveillance(Figure S1).

### *Household and individual risk of infection over the six-month period*

RV and hCoV were detected in all the 47 households while AdV and RSV were detected in 45(95.7%) and 40(85.1%) households, respectively, Table 2. All the households had at least one member with a symptomatic infection and by pathogen, symptomatic infections were detected in 46(97.9%) for RV, 45(95.7%) for hCoV, 42(89.4%) for AdV and 34(72.3%) for RSV of the households. The individual risk of infection (numbers) were 93.4%(451), 80.1%(387), 71.6%(346), 61.5%(297) and 37.1%(179) for any virus, RV, hCoV, AdV and RSV, respectively, Table 2. The corresponding individual risk (numbers) for symptomatic infections were 61.7%(298), 49.5%(239), 34.0%(164), 27.3%(132) and 22.0%(106), respectively.

### *Individual risk of infection by symptom status*

Age-specific attack rates for the prevalent viruses significantly decreased with age, Table 3 and Figure 5. This age association was enhanced for the symptomatic infections. Unlike other targets whose the highest attack rates were among young children aged <1 year, AdV had highest attack rates among the older children aged 1-4 years. The groupings based on age were closely related to those based on the relationship to the study infant hence the pattern of attack rates according to relationships were similar to that of the age groups(Table 3 and Table S1). Notably, the attack rates regardless of symptoms in mothers were higher than in fathers for all the studied viruses and this was significant statistically( $p$ -value=0.04). There were no statistically significant differences in the attack rates regardless of symptoms by sex and school going status, Table 3. However, for the symptomatic infections the attack rates for RSV were significantly higher in males than in females(26.6% vs.18.2%,  $p$ -value=0.026). The attack rates by household sizes varied by pathogen and illness status. Households with fewer household members(4-7) had higher attack rates than larger households that was statistically significant for RV, hCoV and RSV irrespective of symptoms. For symptomatic infections, only RSV showed a significant association by household size, Table S1.

## **Discussion**

This is the first study to provide detailed infection patterns of respiratory viruses derived from a household-based active surveillance applying molecular techniques in low income settings. Applying intensive sampling regardless of symptoms together with multiple virus diagnostics, our household study reveals a remarkably high prevalence of respiratory viruses in the rural setting of coastal Kenya. This demonstrates the extraordinarily enabling environment for virus spread coherent with earlier reports for RSV infections[5-7]. Although interpretation of virus presence by molecular diagnostics should be undertaken with care, it seems very plausible that households with young infants provide a reservoir of respiratory pathogens that are disseminated into the community.



Even though the study was designed to coincide with the local RSV season, a diverse range of respiratory viruses were shown to co-circulate. AdV, hCoV, and RV were the most prevalent during the RSV epidemic. These respiratory viruses were detected in a quarter of the tested samples. Similar circulation of respiratory viruses was observed from virus watch family studies (1960s-1970s) in Michigan and Seattle, US despite using less sensitive diagnostic techniques (culture and serology) [10-14]. In the US families, RV predominated after school opening, partly explaining the concordance findings since our surveillance covered school periods [10, 14, 15]. The Tecumseh family study identified OC43 as the most common hCoV strain as observed in the current study [14]. A recent US family study using molecular techniques identified NL63 as the most prevalent [16].

Some of the pathogens were uncommon, and it is likely that a seasonal peak of some viruses fell outside the study period. In this location, peak occurrence of influenza (A or B) is in the second half of each year based on inpatient pediatric surveillance [17, 18]. HMPV circulated prior to the start of RSV season as shown in supplementary data from corresponding hospital data (Figure S1) unlike previous studies reporting co-circulation with RSV [19].

Dual or multiple infections were common (range, 13.4 – 17.4%). A prospective cohort study in a daycare centre in the USA using comparable molecular techniques reported a co-infection rate of 27% among the symptomatic young children [20], indicating that this high burden of viral coinfection, especially among children, is global. Detection of coinfection was higher among the symptomatic cases as has been reported in hospital based surveillance studies [21-23].

At least one virus was detected in 93.4% of the study participants over the six-month study, and on average, each individual had evidence of three different viral infections. Given the close contacts of individuals in the households, the participants' exposure to the investigated respiratory viruses was high - over 95% of the households had one or more members detected with RV, hCoV and AdV. The individual attack rates declined with increasing age for most of the target pathogens, most likely due to acquisition of immunity following previous infections. School-going children are usually respiratory virus introducers to households [6, 24] but did not seem to have higher individual attack rates compared to non-school goers for the studied viruses. Fathers had consistently and significantly lower attack rates compared to mothers. In this community fathers are likely to have fewer interactions with the young infants and children relative to mothers which could partly explain the disparity in attack rates. Empirical data on contact patterns within households might help elucidate this observation. Individuals in larger households (> 7 members) had lower attack rates than in smaller households and this pattern was significant for RV, AdV and RSV. This may be related to the structure of households which comprise of one or more buildings units and larger occupancy would tend to have more building units, between which there may be less interaction than in a single building unit household.

The frequency distribution of viruses in the community does not reflect that in the hospital which provides a reminder that hospital data do not describe well infection transmission in the community, but the disease that arises, and this is clearly virus specific, i.e. very much higher prevalence of RSV, hMPV, PIV3 and, interestingly, rhinoviruses amongst hospital cases than in the community.

The study has some limitations. First, the study was designed with a focus on RSV, and that here we are presenting an observational data set from essentially a “convenience” sample for a small number of viruses for a short period. A surveillance over a longer period and investigating a wider range of respiratory viruses would provide more comprehensive data on viruses circulation. Multiple years of study would compensate for year-to-year variation. Second, our sample was households with infants, so it might possible households without infants would have a lower prevalence. Thirdly, only a small number of households had their samples subjected to full respiratory screen. Given the clustering of respiratory infections by households, it is possible a different set of households might have resulted in an additional choice of targets for screening. However, the similarities in circulation of the respiratory viruses in the community study and the hospital surveillance do not support this view. Lastly, virus infection was deduced from molecular diagnostics, which do not necessarily equate with the presence of potentially infectious virus – leading to over-estimation of infectiousness. Each multiplex in the molecular screen may have reduced sensitivity for detecting co-infections as compared to single target assays.

In conclusion, respiratory virus infections and associated illness in this setting, are ubiquitous in households. The molecular screen of these specimens revealed continuous and considerable respiratory virus circulation and infection frequency in this population that varied with virus species, and subject age. The study here unveils previously unknown patterns of respiratory pathogen circulation in a rural low-income population. The remarkable frequency of virus infections of multiple species and strains lends itself to an ecological analysis of interactions that may be influential in virus ecology. The aetiology of respiratory disease and immunological burden of respiratory viruses in children is worthy of further study. In addition, investigation on the human virome in the nasopharynx would provide insight on these viruses and how they affect human health and disease. Future studies should address the health and economic implications of these observations.

### **Acknowledgements**

We acknowledge the Viral Epidemiology and Control group at KEMRI-Wellcome Trust Research Programme in Kilifi, Kenya for their critique of an earlier version of the manuscript. Special appreciation goes to the study field workers and laboratory technicians for their commitment in the sample collection and testing, respectively. The article is published with the permission of the Director of the Kenya Medical Research Institute.

*Funding*

This work was supported by the Wellcome Trust, United Kingdom [grant numbers 102975, 090853, 084633, and 206748].

*Conflict of interest*

All the authors declare no conflict of interest.

## References

1. Munywoki PK, Hamid F, Mutunga M, Welch S, Cane P, Nokes DJ. Improved detection of respiratory viruses in pediatric outpatients with acute respiratory illness by real-time PCR using nasopharyngeal flocked swabs. *Journal of clinical microbiology* **2011**; 49(9): 3365-7.
2. Falsey AR, Formica MA, Treanor JJ, Walsh EE. Comparison of quantitative reverse transcription-PCR to viral culture for assessment of respiratory syncytial virus shedding. *Journal of clinical microbiology* **2003**; 41(9): 4160-5.
3. Liao RS, Tomalty LL, Majury A, Zoutman DE. Comparison of viral isolation and multiplex real-time reverse transcription-PCR for confirmation of respiratory syncytial virus and influenza virus detection by antigen immunoassays. *Journal of clinical microbiology* **2009**; 47(3): 527-32.
4. Munywoki PK, Koech DC, Agoti CN, et al. Frequent Asymptomatic Respiratory Syncytial Virus Infections During an Epidemic in a Rural Kenyan Household Cohort. *The Journal of infectious diseases* **2015**; 212(11): 1711-8.
5. Munywoki PK, Koech DC, Agoti CN, et al. Influence of age, severity of infection, and co-infection on the duration of respiratory syncytial virus (RSV) shedding. *Epidemiol Infect* **2015**; 143(4): 804-12.
6. Munywoki PK, Koech DC, Agoti CN, et al. The source of respiratory syncytial virus infection in infants: a household cohort study in rural Kenya. *The Journal of infectious diseases* **2014**; 209(11): 1685-92.
7. Wathuo M, Medley GF, Nokes DJ, Munywoki PK. Quantification and determinants of the amount of respiratory syncytial virus (RSV) shed using real time PCR data from a longitudinal household study. *Wellcome open research* **2016**; 1(27): 27.
8. Scott JA, Bauni E, Moisi JC, et al. Profile: The Kilifi Health and Demographic Surveillance System (KHDSS). *International Journal of Epidemiology* **2012**; 41(3): 650-7.
9. Gunson RN, Collins TC, Carman WF. Real-time RT-PCR detection of 12 respiratory viral infections in four triplex reactions. *J Clin Virol* **2005**; 33(4): 341-4.
10. Monto AS, Bryan ER, Ohmit S. Rhinovirus infections in Tecumseh, Michigan: frequency of illness and number of serotypes. *The Journal of infectious diseases* **1987**; 156(1): 43-9.
11. Monto AS, Napier JA, Metzner HL. The Tecumseh study of respiratory illness. I. Plan of study and observations on syndromes of acute respiratory disease. *Am J Epidemiol* **1971**; 94(3): 269-79.
12. Monto AS, Koopman JS, Bryan ER. The Tecumseh Study of Illness. XIV. Occurrence of respiratory viruses, 1976-1981. *Am J Epidemiol* **1986**; 124(3): 359-67.
13. Cooney MK, Hall CE, Fox JP. The Seattle virus watch. 3. Evaluation of isolation methods and summary of infections detected by virus isolations. *Am J Epidemiol* **1972**; 96(4): 286-305.

14. Monto AS, Lim SK. The Tecumseh study of respiratory illness. VI. Frequency of and relationship between outbreaks of coronavirus infection. *The Journal of infectious diseases* **1974**; 129(3): 271-6.
15. Gwaltney JM, Jr., Hendley JO, Simon G, Jordan WS, Jr. Rhinovirus infections in an industrial population. I. The occurrence of illness. *The New England journal of medicine* **1966**; 275(23): 1261-8.
16. Monto AS, Malosh RE, Petrie JG, Thompson MG, Ohmit SE. Frequency of Acute Respiratory Illnesses and Circulation of Respiratory Viruses in Households with Children over Three Surveillance Seasons. *The Journal of infectious diseases* **2014**.
17. Emukule GO, Mott JA, Spreuwenberg P, et al. Influenza activity in Kenya, 2007-2013: timing, association with climatic factors, and implications for vaccination campaigns. *Influenza and other respiratory viruses* **2016**; 10(5): 375-85.
18. Onyango CO, Njeru R, Kazungu S, et al. Influenza surveillance among children with pneumonia admitted to a district hospital in coastal Kenya, 2007-2010. *The Journal of infectious diseases* **2012**; 206 Suppl 1: S61-7.
19. Semple MG, Cowell A, Dove W, et al. Dual infection of infants by human metapneumovirus and human respiratory syncytial virus is strongly associated with severe bronchiolitis. *The Journal of infectious diseases* **2005**; 191(3): 382-6.
20. Fairchok MP, Martin ET, Chambers S, et al. Epidemiology of viral respiratory tract infections in a prospective cohort of infants and toddlers attending daycare. *J Clin Virol* **2010**; 49(1): 16-20.
21. Marccone DN, Ellis A, Videla C, et al. Viral etiology of acute respiratory infections in hospitalized and outpatient children in Buenos Aires, Argentina. *The Pediatric infectious disease journal* **2013**; 32(3): e105-10.
22. Bonzel L, Tenenbaum T, Schrotten H, Schildgen O, Schweitzer-Krantz S, Adams O. Frequent detection of viral coinfection in children hospitalized with acute respiratory tract infection using a real-time polymerase chain reaction. *The Pediatric infectious disease journal* **2008**; 27(7): 589-94.
23. Fowlkes A, Giorgi A, Erdman D, et al. Viruses associated with acute respiratory infections and influenza-like illness among outpatients from the Influenza Incidence Surveillance Project, 2010-2011. *The Journal of infectious diseases* **2014**; 209(11): 1715-25.
24. Hall CB, Geiman JM, Biggar R, Kotok DI, Hogan PM, Douglas GR, Jr. Respiratory syncytial virus infections within families. *New England Journal Medicine* **1976**; 294(8): 414-9.

## Tables

Table 1: Baseline characteristics of the households and individuals with select and full respiratory virus screening

Characteristic	Full Screen (HHs=6; participants=83)	Select screen (HHs=41; participants=410)	P – value
Household sizes, Median (IQR)	10.5 (5 – 15)	8 (7 – 11)	0.8602
No. (%) of school-going children	21 (25.3)	150 (36.6)	0.049
Number (%) of male individuals	31 (37.4)	190 (46.3)	0.133
Number (%) of specimens per person			
0	7 (1.7)	3 (3.6)	
1-9	34 (8.3)	5 (6.0)	0.437
10-19	18 (4.4)	5(6.0)	
20-29	38 (9.3)	8 (9.6)	
30-39	100 (24.4)	14(16.9)	
40-44	140 (34.2)	36(43.4)	
45-50	73 (17.8)	12(14.5)	
Age groups, in years <sup>1</sup>			
<1y	10 (12.1)	45 (11.0)	0.467
1– 4y	16 (19.3)	66 (16.1)	
5– 14y	24 (28.9)	141 (34.4)	
15– 39y	22 (26.5)	125 (30.5)	
>=40y	11 (13.3)	33 (8.1)	

Key: IQR, interquartile range; 1, age at start of sampling

Table 2: Respiratory virus detections in households, participants and NPS collections by screening strategy

Description	Full respiratory virus screen						Select respiratory virus screen					
	Household (n=6)		Participants <sup>1</sup> (n=80)		Samples (n=2844)		Household (n=47)		Participants <sup>1</sup> (n=483)		Samples (n=16918)	
	n	%	n	%	n	%	n	%	n	%	n	%
Any virus detected (all)	6	100.0	75	93.8	864	30.4	-	-	-	-	-	-
Any virus detected (select)	6	100.0	75	93.8	803	28.2	47	100.0	451	93.4	4259	25.2
Rhinoviruses (RV)	6	100.0	62	77.5	302	10.6	47	100.0	387	80.1	1780	10.5
Adenoviruses (AdV)	6	100.0	57	71.3	270	9.5	45	95.7	297	61.5	1232	7.3
Human coronaviruses (hCoV)	6	100.0	58	72.5	217	7.6	47	100.0	346	71.6	1274	7.5
OC43	5	83.3	45	56.3	116	4.1	44	93.6	215	44.5	651	3.8
NL63	4	66.7	35	43.8	95	3.3	33	70.2	163	33.7	418	2.5
229E	3	50.0	7	8.8	8	0.3	30	63.8	119	24.6	241	1.4
RSV	6	100.0	52	65.0	151	5.3	40	85.1	179	37.1	537	3.2
Group A	5	83.3	33	41.3	86	3.0	25	53.2	88	18.2	250	1.5
Group B	5	83.3	21	26.3	66	2.3	34	72.3	113	23.4	306	1.8
PIV	6	100.0	37	46.3	63	2.2	-	-	-	-	-	-
Type 1	4	66.7	6	7.5	6	0.2	-	-	-	-	-	-
Type 2	3	50.0	14	17.5	16	0.6	-	-	-	-	-	-

Type 3	5	83.3	19	23.8	30	1.1	-	-	-	-	-	-
Type 4	5	83.3	14	17.5	21	0.7	-	-	-	-	-	-
Human metapneumovirus (hMPV)	4	66.7	11	13.8	13	0.5	-	-	-	-	-	-
Influenza viruses (Flu)	4	66.7	8	10.0	11	0.4	-	-	-	-	-	-
Type A	3	50.0	5	6.3	7	0.2	-	-	-	-	-	-
Type B	1	16.7	2	2.5	2	0.1	-	-	-	-	-	-
Type C	2	33.3	5	6.3	6	0.2	-	-	-	-	-	-
URTI	6	100.0	63	78.8	529	18.6						

---

Key: 1, Excludes 3 and 10 participants from full and select pathogen screening, respectively, who were never sampled



**Table 3: Crude individual attack rates of the common respiratory viral infections detected regardless of symptoms stratified by various characteristics**

Characteristics	Categories	N	Any virus		Rhinovirus		Adenovirus		Coronavirus		RSV	
			n	%	n	%	n	%	n	%	n	%
Age in years	<1	55	53	<b>96.4</b>	52	<b>94.5</b>	28	<b>50.9</b>	42	<b>76.4</b>	31	<b>56.4</b>
	1-4	82	80	<b>97.6</b>	79	<b>96.3</b>	64	<b>78.0</b>	64	<b>78.0</b>	41	<b>50.0</b>
	5-14	163	157	<b>96.3</b>	144	<b>88.3</b>	118	<b>72.4</b>	125	<b>76.7</b>	66	<b>40.5</b>
	15-39	141	125	<b>88.7</b>	89	<b>63.1</b>	66	<b>46.8</b>	93	<b>66.0</b>	33	<b>23.4</b>
	≥40	42	36	<b>85.7</b>	23	<b>54.8</b>	21	<b>50.0</b>	22	<b>52.4</b>	8	<b>19.0</b>
Relation to the infant	The infant	47	46	<b>97.9</b>	45	<b>95.7</b>	26	<b>55.3</b>	37	78.7	27	<b>57.4</b>
	Sibling	162	157	<b>96.9</b>	154	<b>95.1</b>	124	<b>76.5</b>	124	76.5	87	<b>53.7</b>
	Cousin	124	116	<b>93.5</b>	100	<b>80.6</b>	76	<b>61.3</b>	91	73.4	56	<b>45.2</b>
	Mother	46	45	<b>97.8</b>	35	<b>76.1</b>	29	<b>63.0</b>	27	58.7	16	<b>34.8</b>
	Father	30	25	<b>83.3</b>	16	<b>53.3</b>	15	<b>50.0</b>	17	56.7	7	<b>23.3</b>
	Other HH members	74	62	<b>83.9</b>	37	<b>50.0</b>	27	<b>36.5</b>	50	67.6	22	<b>29.7</b>
Sex	Female	269	252	93.7	215	79.9	169	62.8	186	69.1	96	35.7
	Male	214	199	93.0	172	80.4	128	59.8	160	74.8	83	38.8

School going	No	313	289	92.3	246	78.6	184	58.8	217	69.3	119	38.0
	Yes	170	162	95.3	141	82.9	113	66.5	129	75.9	60	35.3
Number of individuals per HH (household sizes)	4 to 7	95	93	97.9	84	<b>88.4</b>	66	<b>69.5</b>	75	<b>78.9</b>	48	<b>50.5</b>
	8 to10	120	109	90.8	100	<b>83.3</b>	87	<b>72.5</b>	77	<b>64.2</b>	26	<b>21.7</b>
	11 to 16	144	135	93.8	110	<b>76.4</b>	77	<b>53.5</b>	97	<b>67.4</b>	49	<b>34.0</b>
	17 to 37	124	114	91.9	93	<b>75.0</b>	67	<b>54.0</b>	97	<b>78.2</b>	56	<b>45.2</b>

---

*Key: The bold values indicate statistically significant based on Chi-square tests, p-value<0.05.*

## Figure legends

**Figure 1:** The temporal infection profile for the six households showing positive samples for each member.

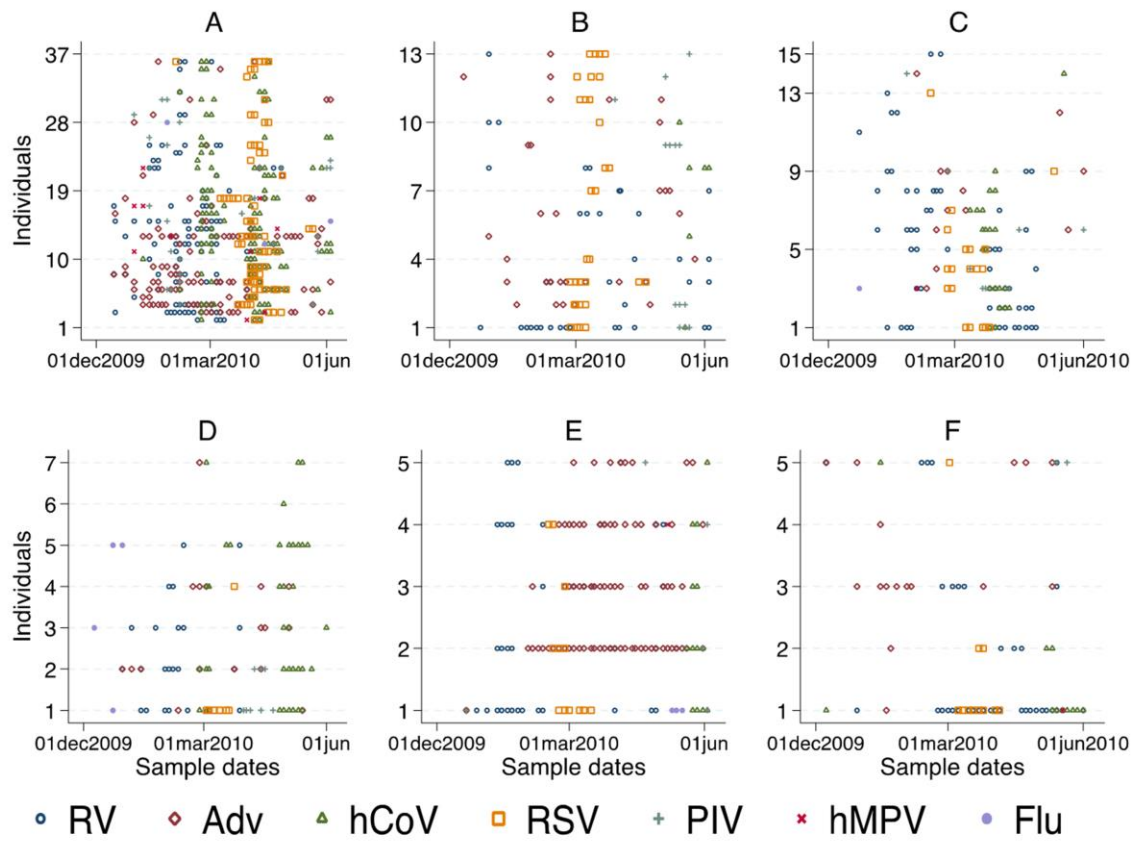
**Figure 2:** Frequency distribution of the number of different viruses detected per (a & d) household, (b & e) person and (c & f) per sample over the study period. Panels a –c represent the screening for common respiratory pathogens in all the 47 households while panels d-f show full screening in the six households. The vertical lines represent the respective mean values.

**Figure 3:** Frequency distribution of the detected respiratory viruses in NPS collections from the (a) six households with full respiratory screen and (b) the 47 households for the common targets screen and (c) inpatient samples collected over the same study period, December 2009-June 2010. RV, rhinoviruses; Adv, adenoviruses; hCoV-OC43, hCoV-NL63 and hCoV-229E are strains of human coronaviruses; RSV A and B, respiratory syncytial virus group A and B; PIV 1, 2, 3 and 4, parainfluenza type 1, 2, 3, and 4; HMPV, human metapneumoviruses; Flu A, B and C, influenza type A, B and C

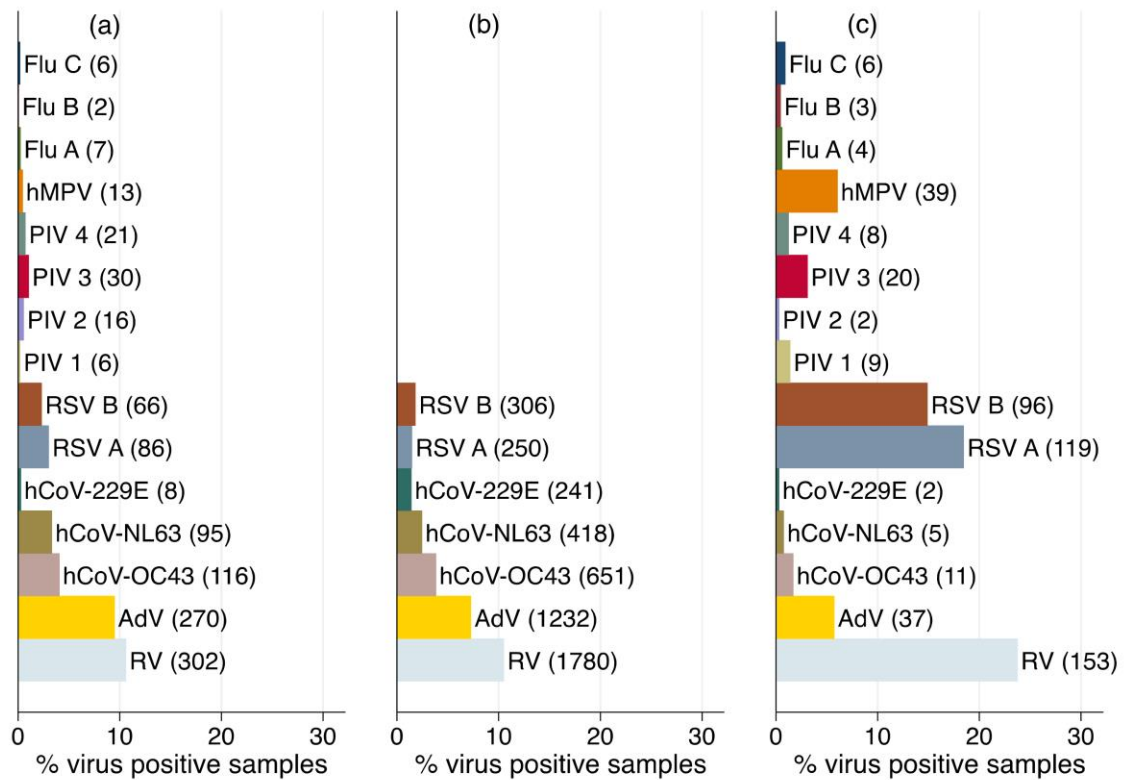
**Figure 4:** Number of nasopharyngeal swabs (NPS) tested from the 47 households and viruses detected in (a) Households (HHs), (b) Persons and (c) Samples per week over the study period. The vertical dashed line denotes the start of the main study period, 10th Jan 2010. Rhino, rhinoviruses; Adeno, adenoviruses; corona, coronaviruses; RSV, respiratory syncytial virus group A and/or B

**Figure 5:** Age-specific attack rates for the (a) common respiratory viruses, (b) RSV groups and (c) hCoV strains among the 483 individuals sampled over the six-month period.

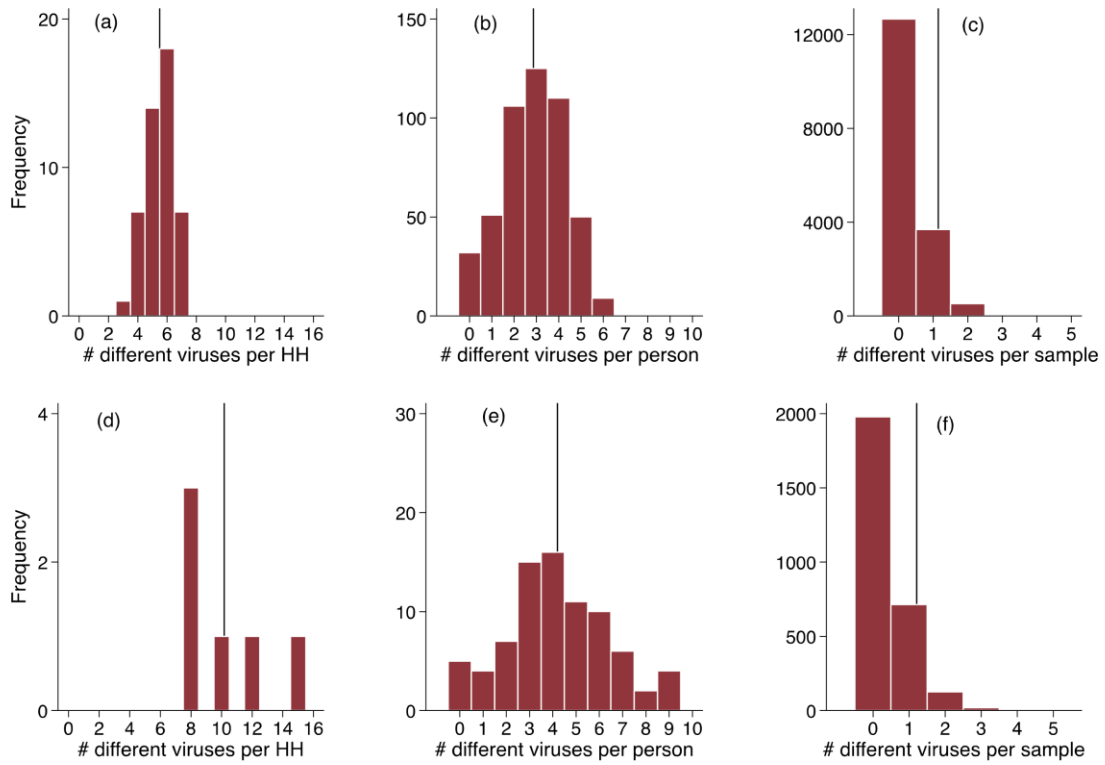
**Figure 1**



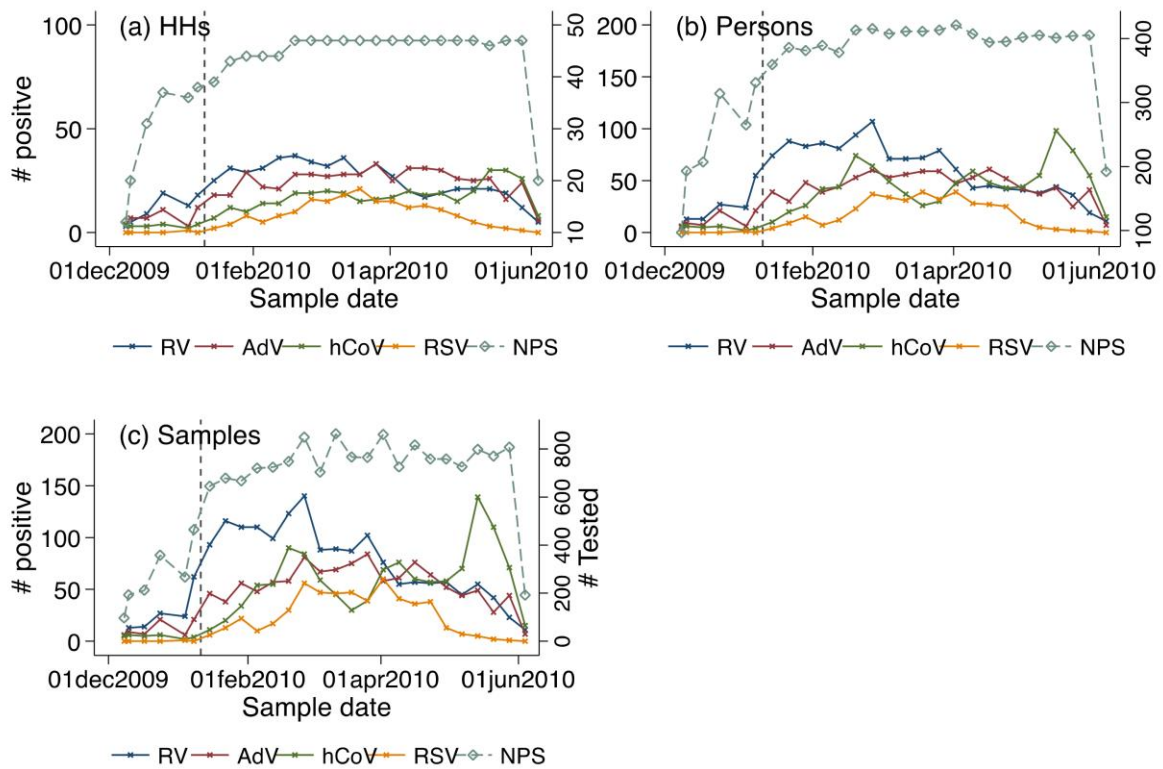
**Figure 2**



**Figure 3**



**Figure 4**



**Figure 5**

