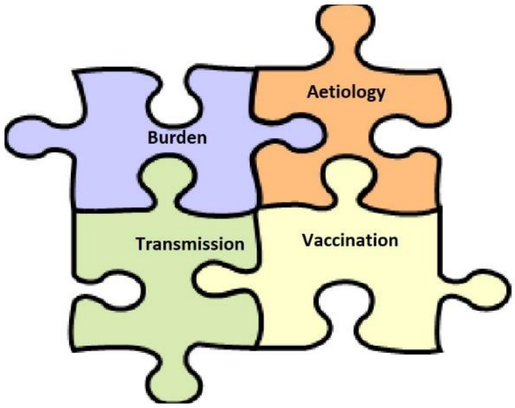
1. AIIMS-CDC Collaboration in understanding influenza epidemiology in India
"Putting the pieces together"

Despite seasonal influenza being identified as a major global public health problem, it was recognized as one in India only after the influenza ('swine-flu') pandemic in 2009-10. This pandemic raised awareness among public health workers, clinicians and public about 'swine-flu'. Since then, both human and avian influenza outbreaks have been detected throughout the country, with increased reporting of hospitalization and deaths associated with influenza. Health care workers, children, and older adults (>=65years) are known to be at increased risk of developing influenza infection.

The public health interventions for prevention and control of influenza are well known. These include:

- Establishing a surveillance system to measure burden and virological parameters
- Vaccination of at-risk population
- Improving access to molecular diagnostics and treatment with anti-viral drugs
- Use of non-pharmaceutical interventions like cough etiquettes, use of masks, closure of shopping centres and other places of mass gathering to slow down the transmission of influenza at individual (high-risk situations) and population level (outbreak situations)

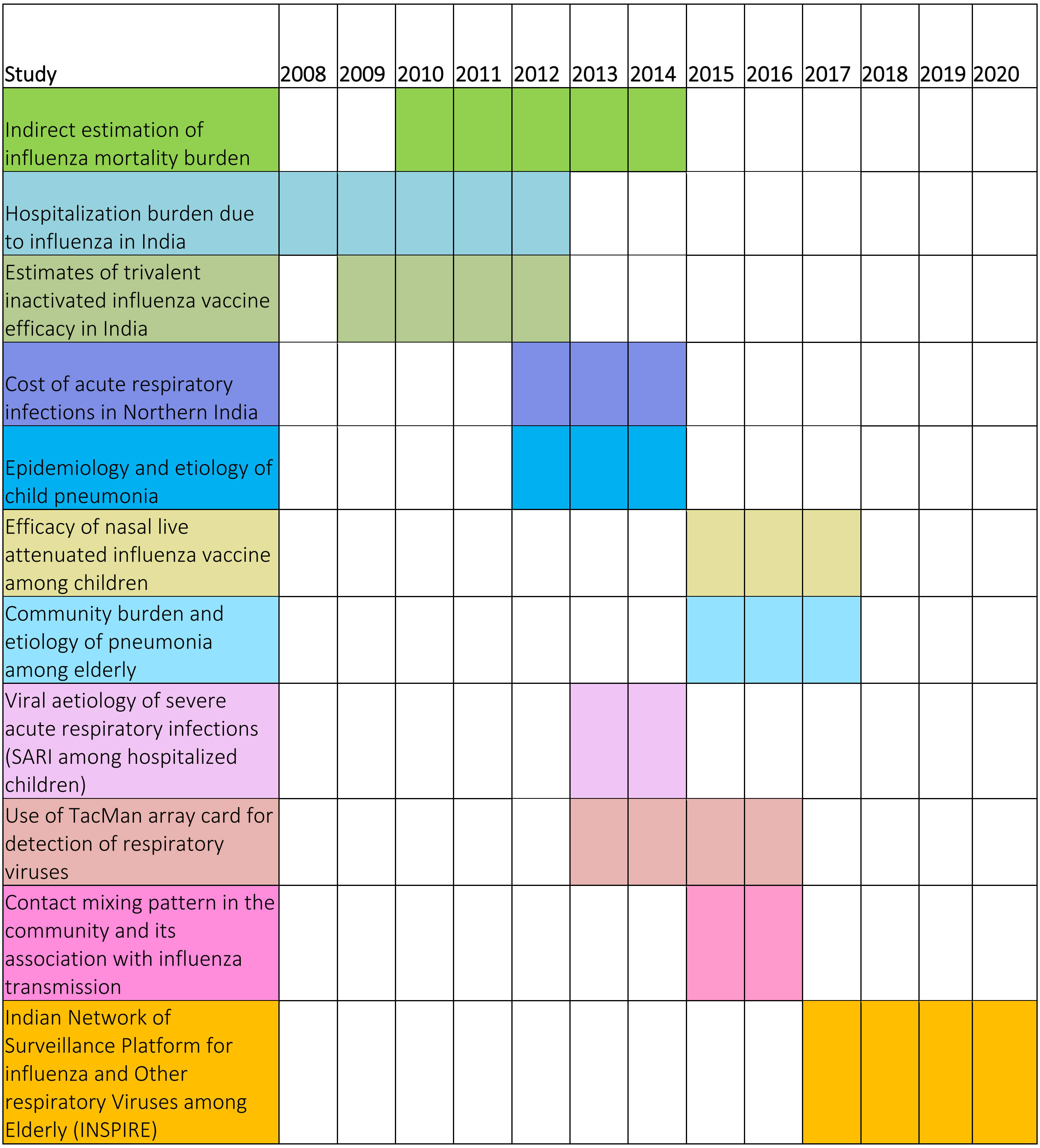
Currently, the guideline on influenza vaccine by the Government of India advises vaccination for health care workers, pregnant women and adults and children with chronic morbidities, but vaccine is not available through any national-level public health program. One of the reasons for this knowledge-action gap is lack of adequate evidence from India on burden of influenza and effectiveness of different interventions to support policy making. Therefore, there is a need to generate local evidence to support advocacy measure.



The *All-India Institute of Medical Sciences* (AIIMS), New Delhi in collaboration with the US Centres for Disease Control and Prevention (CDC) and other academic and research partners has endeavoured to generate evidence to inform public health policy on influenza prevention and control in India. The AIIMS CDC collaborative projects span more than a decade and involve multiple co-operative agreements. They cover different aspects of Influenza epidemiology including community and hospital-based studies of aetiology of acute respiratory infections (ARI), estimation of disease and economic burden of ARIs and influenza in the community among children and elderly, and effectiveness of influenza vaccines. (See figure overleaf). They have also covered other viruses like Respiratory Syncytial Viruses (RSV).

The collaboration has increased over time in both geographical terms (single site at Ballabgarh to multisite studies in India) as well as technical areas like surveillance, burden, aetiology, vaccine effectiveness to population level transmission studies. This exciting body of work showcased in this docket demonstrates as to what can be achieved by a collaborative effort. More such collaborations are needed to make a dent in a large and diverse country like India. Some of the key outcomes of the collaborations include publication of more than 30 papers, three doctoral students as well as inclusion of Indian data in many global estimates.

Timeline of the different studies



2.1 Estimating influenza disease burden in India (IDBI) Platform

There is a need for reliable disease burden estimates especially from low- and middle income countries to provide a better understanding of the impact of influenza in vulnerable communities or subpopulations. Lack of regular testing for influenza among admissions of respiratory infections and lack of population denominators are among the important reasons for lack of information of influenza related hospitalization burden.

WHO approach to influenza burden estimation

To rectify this situation, World Health Organization (WHO) suggests different approaches and sources for estimating influenza disease burden – hospital-based surveillance sites for SARI (Severe Acute Respiratory Infections) or ILI (influenza like illness). These sources provide the numerators for the burden estimates but defining the denominator population is often a challenge. Where such population data is not there, attempts must be made to estimate the catchment population and methods like Health Admission Survey (HAS) and Healthcare Utilization Survey (HUS) are used to correct the estimates. For HAS all health facilities in the catchment area are visited and their hospital discharge registers are used to count number of hospitalised pneumonia patients whereas in HUS house-to-house survey is conducted in a random sample of representative households to know which healthcare facility the families use. The adjoining flow chart summarizes the estimation process using SARI surveillance. We adopted this approach to estimate influenza Hospitalization burden in two health and demographic surveillance system (HDSS) sites of India.

Vadu HDSS, a surveillance system initiated in 2002, is run by Vadu Rural Health Program of the KEM hospital research centre, Pune. (2) Spread over 22 villages of Shirur and Haveli Block of Pune district in Maharashtra, the served population was about 120,000 at the time of the study. The median household size was 3 (IQR 1-5)

KEM Rural Hospital Vadu Budruk

The Ballabgarh HDSS was established in 1,961 to develop a model for rural health-care practice in India. It is spread across 28 villages of Ballabgarh Tehsil of Faridabad District and had a population just under 90,000 during this study. The median household size was 4 (IQR 2-7)

The age and sex compositions of the populations at the two sites were similar, however the population density at Vado was 520 persons per square km as compared to 276 for Ballabgarh

References:

1. World Health Organization. A manual for estimating disease burden associated with seasonal influenza. https://apps.who.int/iris/bitstream/handle/10665/178801/9789241549301_eng.pdf?sequence=1&isAllowed=

2. Patil R, Roy S, Ingole V et.al Profile: Vadu health and demographic surveillance system Pune, India. Journal of Global Health. 2019 Jun;9(1).

3. Kant S, Misra P, Gupta S, et.al. The Ballabgarh health and demographic surveillance system (CRHSP-AIIMS). International Journal of Epidemiology. 2013 Jun 1; 42(3):758-68.

2.1.1 Rates of respiratory virus-associated hospitalization in children aged <5 years in rural northern India

Rationale

This study is the first prospective, population-based study to measure the incidence of respiratory virus-associated hospitalizations among children aged <5 years in rural India.

The epidemiology of respiratory viruses in India were poorly understood because of paucity of laboratory confirmed data using molecular diagnostic assays.

What we did?

During August 2009-July 2011, prospective surveillance of approximately 9,500 children was conducted for hospitalizations of children aged <5 years in villages under CRHSP in Haryana State.

Clinical data and respiratory specimens were collected. Swabs were tested for influenza and parainfluenza viruses, respiratory syncytial virus (RSV), human metapneumovirus, coronaviruses, and adenovirus using real-time polymerase chain reaction rt-PCR.

Average annual hospitalization incidence was calculated using census data and adjusted for hospitalizations reported to occur at non-study hospitals according to a community healthcare utilization survey.

Chi-squared test or Fisher's exact test was used to calculate p-values for categorical variables and the Wilcoxon test was used to compare continuous variables (SAS, version 9.2, SAS Institute Inc., Cary, NC).

What we found?

- During the study period, 245 children aged <5 years were hospitalized with acute medical illness at study hospitals
- Respiratory viruses were detected among 98 (40%) children including 50 (20%) with RSV and 17 (7%) with influenza viruses (9 with influenza A and 8 with influenza B)
- RSV accounted for the highest virus associated hospitalization incidence (34.6/10,000) and 20% of all hospitalizations. There were 11.8/10,000 influenza-associated hospitalizations (7% of hospitalizations).
- The burden was much higher among infants below one year of age.
- RSV and influenza virus detection peaked in winter (November February) and rainy seasons (July), respectively.

Age of children	<5 years		<1 year		1-4 years	
	Hospitalizations	Incidence	Hospitalizations	Incidence	Hospitalizations	Incidence
All-cause hospitalization	245	169.5	138	456.8	107	96.5
Respiratory syncytial virus	50	34.6	30	99.3	20	18.0
Influenza	17	11.8	7	23.2	10	9.0
Adenovirus	13	9.0	6	19.9	7	6.3
Coronavirus 229E	13	9.0	9	29.8	4	3.6
Parainfluenza	10	6.9	5	16.6	5	4.5
Human metapneumovirus	3	2.1	2	6.6	1	0.9

Hospitalizations among children aged <5 years at study hospitals and incidence per 10,000 child-years by respiratory virus, CRHSP, Ballabgarh, India, August 2009-July 2011.

Conclusion

- In our study area, almost 2% children needed hospitalization due to acute medical illness especially infants who had five-fold higher hospitalization rates.

- Two out of five pediatrics admissions were associated with respiratory viruses with RSV alone accounting for almost 50% of respiratory virus associated hospitalizations.

- RSV and influenza viruses circulated with clearly defined but different seasonality.

Access the article by scanning the code

Reference:

1. Broor S, Dawood FS, Pandey BG, et.al. Rates of respiratory virus-associated hospitalization in children aged <5 years in rural northern India. JInfect. 2014 Mar;68(3):281-9. doi: 10.1016/j.jinf.2013.11.005. Epub 2013 Nov 21. PMID: 24269675; PMCID: PMC7112698.

2.1.2 Estimation of community-level influenza associate illness in a low resource rural setting in India

Rationale

Most burden studies focus on influenza-associated hospitalization, even though outpatient and non-medically attended influenza infections have been recognized as important considerations when estimating public health impact and cost.

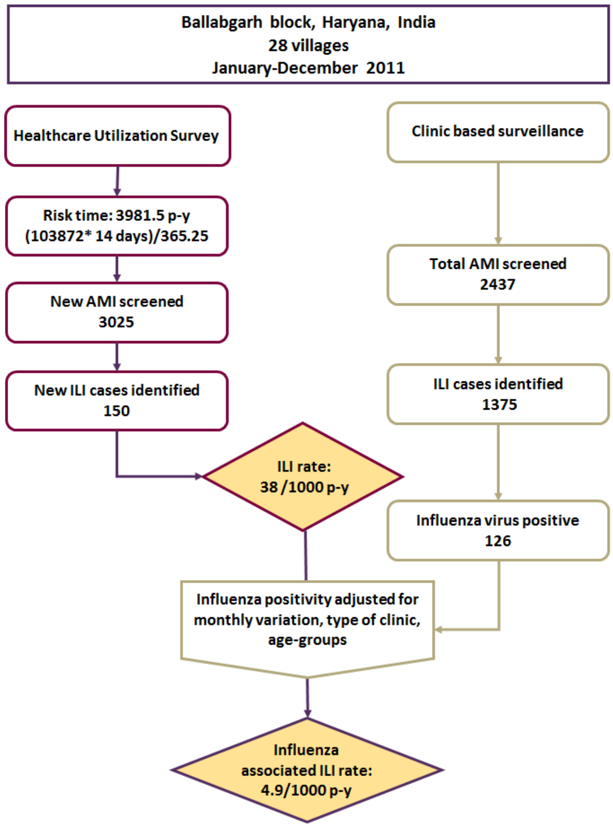
Data on burden estimates and identification of risk groups are crucial for prioritizing influenza prevention and control measures especially in low resource settings of LMICs.

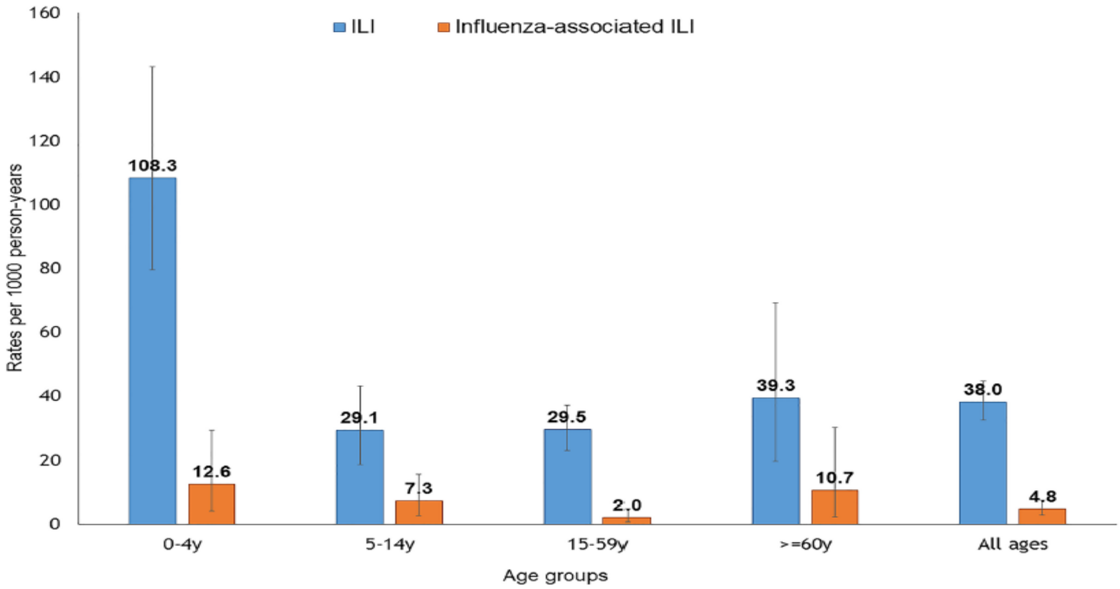
What we did?

- During 2011, we conducted household-based healthcare utilization surveys (HUS) for any acute medical illness (AMI) in preceding 14-days among residents of 28 villages of Ballabgarh, in north India.
- Alongside, we conducted clinic-based surveillance (CBS) at public and private health facilities in the area for AMI clinic type, to estimate the community influenza-associated ILI rates.
- Episodes with illness onset ≤3days and collected nasal and throat swabs for influenza virus testing.
- We applied ILI case definition (measured/reported fever and cough) to HUS and CBS data.
- We attributed 14-days of risk-time per person surveyed in HUS and estimated community ILI rate.
- We used CBS data on influenza positivity and applied it to HUS-based community ILI rates by age, month, and

What we found?

- During the study period, 2,431 AMI (private sector 2,030; public sector 401) cases were screened and 1,372 ILI cases (56.4%) were detected in the CBS
- Among 1,372 ILI cases enrolled from clinics, 126 (9%) had laboratory confirmed influenza (A (H3N2) = 72; B = 54).
- After adjusting for age, month, and clinic type, overall influenza-associated ILI rate was 4.8/1,000 p-y; rates were highest among children <5 years (13) and persons ≥60 years (11)





Rates and 95% confidence intervals per 1,000 person-years of influenza-like illness (ILI) and influenza-associated ILI by age, Ballabgarh, India, 2011.

Conclusion

- We demonstrated the use of an approach similar to the WHO recommended approach for influenza disease burden estimation in a low resource setting.
- The burden of influenza associated ILI is highest among children (<5years) and older adults (≥60 years)
- These findings should be useful for developing influenza vaccination strategies for target age groups especially in low and middle-income countries.

Access the article by scanning the code

Reference:

1. Saha S, Gupta V, Dawood FS, et.al. Estimation of community-level influenza-associated illness in a low resource rural setting in India. PLoS One. 2018 Apr 26; 13(4):e0196495. doi: 10.1371/journal.pone.0196495. PMID: 29698505; PMCID: PMC5919664.

2.1.3 Incidence of influenza-associated hospitalization in rural communities in Western and Northern India

Rationale

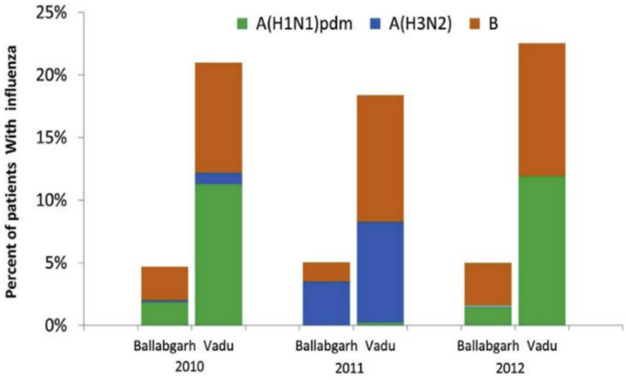
One of the key prerequisites for assessing the public health importance of any health condition is to know its burden, especially serious forms of disease like deaths and hospitalization. However, data on influenza mortality and hospitalization in most developing countries remain sparse because measuring influenza incidence is challenging in these settings due to lack of regular influenza testing, delays in reaching health facilities where influenza testing is available resulting in lower detection rates, and absence of known population denominators.

What we did?

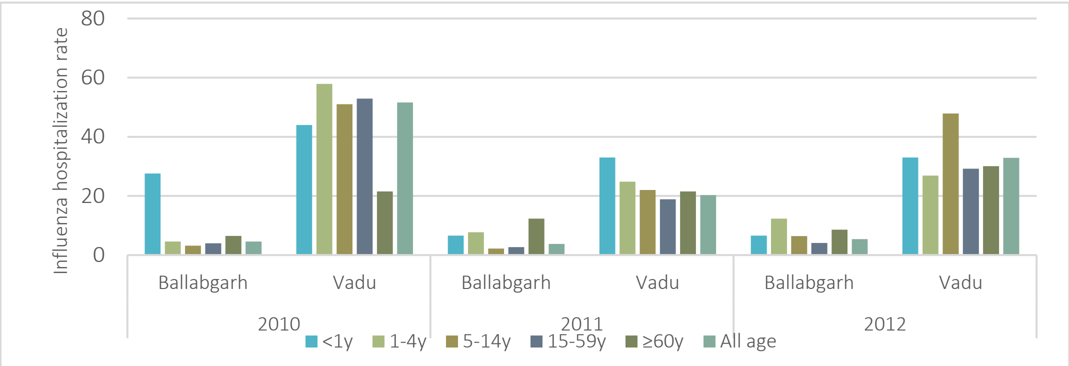
- We conducted a population-based surveillance study in Northern and western India to estimate and compare rates of influenza-associated hospitalization at rural Indian health and demographic surveillance system (HDSS) sites at Ballabgarh and Vadu during 2010-2012.
- The platform and the methods are described in an earlier sheet. We defined the population denominator as people living in the HDSS area.
- Annual healthcare utilization surveys (HUS) were conducted in HDSS households to identify hospitals where the population was most likely to be hospitalized.
- A prospective facility-based surveillance for all hospitalizations (excluding those for trauma, elective surgery and obstetric, ophthalmic, or psychiatric reasons) was conducted at pre-identified large consenting health facilities in and around the HDSS area.
- Newly admitted patients residing in the HDSS area in these hospitals were identified through either a daily telephone call or visit to each participating hospital. Persons hospitalized for elective surgery, trauma, or obstetrics and gynaecologic, orthopaedic, ophthalmologic, or psychiatric conditions were excluded.
- Patients had their clinical details collected, nasopharyngeal swabs taken and tested for influenza viruses.
- The proportion of hospitalizations occurring at non-study facilities was used to adjust for hospitalizations missed through facility-based surveillance.
- Age stratified unadjusted crude annual hospitalization rates were calculated for each calendar year using number of hospitalizations at study facilities and the corresponding mid-year population obtained from HDSS data.

What we found?

- From 2010-2012, 6,004 patients hospitalized with acute medical illness at participating facilities were enrolled (1,717 from Ballabgarh; 4287 from Vadu).
- The proportion of patients in whom influenza was detected was substantially higher at Vadu than Ballabgarh annually (2010: 21% vs. 5%; 2011: 18% vs. 5%; 2012: 23% vs. 5%).
- HUS showed that 69% and 67% of hospitalizations occurred at study facilities at Ballabgarh and Vadu, respectively. Annual influenza-associated hospitalization rates were 5-11 folds higher in Vadu (20.3-51.6 per 10,000) vs. Ballabgarh (3.8-5.4 per 10,000).
- At both sites, influenza A/H1N1pdm09 and B viruses were the predominant viruses detected from hospitalized patients during 2010; A/H3N2 and B during 2011; and A/ H1N1pdm09 and B during 2012 (Demonstrated in the figure)
- During 2010-2012, all-age incidence rates of hospitalization for all acute medical illness were 73-116 per 10,000 in Ballabgarh and 101-225 per 10,000 in Vadu
- Influenza viruses were detected throughout the year, with peaks occurring during July to September in both Vadu and Ballabgarh during all years, coinciding with peaks in rainfall.



Positivity among hospitalized patients by influenza virus subtype in Ballabgarh and Vadu, 2010-2012



Annual cumulative incidence of influenza-associated hospitalizations per 10,000 persons by age and study site.

.

Conclusion

- This study showcases the potential to build on the HDSS sites in India and using the WHO approach for estimation of influenza burden in the Indian context.
- There are widespread differences in the burden of hospitalization due to influenza which needs to be better understood and measured.
- The results of this study can be used for assessment of preventative and treatment interventions for influenza for suitability in the Indian context

Access the article by scanning the code

Reference:

1. Hirve S, Krishnan A, Dawood FS, et.al. Incidence of influenza-associated hospitalization in rural communities in western and northern India, 2010-2012: a multi-site population-based study. J Infect. 2015 Feb;70(2):160-70. doi: 10.1016/j.jinf.2014.08.015.

2.1.4 Direct and indirect protection due to inactivated trivalent influenza vaccine in rural India

Rationale

Vaccines protect against infection by providing direct protection (to those immunized) as well as indirect protection (to those not immunized by breaking the chain of transmission). Presence of indirect protection provide additional justification for the introduction of a vaccine for population level prevention. This was the first randomised control trial designed to investigate whether influenza vaccination of children would protect them and their household members in rural India from laboratory confirmed influenza infection.

What we did?

- From Nov 2009 to May 2012, we did a randomised, double blinded, controlled study in three villages in north India. Children aged 6 months to 10 years were eligible for vaccination as and when they became age-eligible throughout the study.
- Households were randomly assigned (1:1) by a computer-based system to intramuscular trivalent inactivated influenza vaccine (IIV3) or a control of inactivated poliovirus vaccine (IPV) in the beginning of the study; vaccination occurred once a year for 3 years.
- The primary efficacy outcome was laboratory-confirmed influenza in a vaccinated child with febrile acute respiratory illness, analysed in the modified intention-to treat population (i.e., children one dose of vaccine, were under surveillance, and had not an influenza infection within 15 days of last vaccine dose)
- The secondary outcome for indirect effectiveness was febrile acute respiratory illness in an unvaccinated household members of vaccine study participants. Data from each year were analysed separately.
- Vaccine efficacy was estimated for each year separately using a Cox proportional hazards model accounting for random-effect clustering by household (frailty model).
- This trial is registered with ClinicalTrials.gov, number NCT00934245.

What have we found?

- We enrolled 3,208 households, of which 1,959 had vaccine-eligible children. 1,010 households were assigned to IIV3 and 949 households were assigned to IPV.
- We annually vaccinated 4,345 children (2,132 with IIV3 and 2,213 with IPV) from 1868 households (968 with IIV3 and 900 with IPV)
- We followed these vaccinated children and 10,813 un-vaccinated household contacts from Nov 2009 to May 2012
- In year 1, IIV3 vaccine efficacy was 25·6% [95% CI 6·8–40·6]; in year 2, it was 41·0% [24·1–54·1]; p<0·0001) which increased to 74·2% [57·8–84·3] in Year 3.

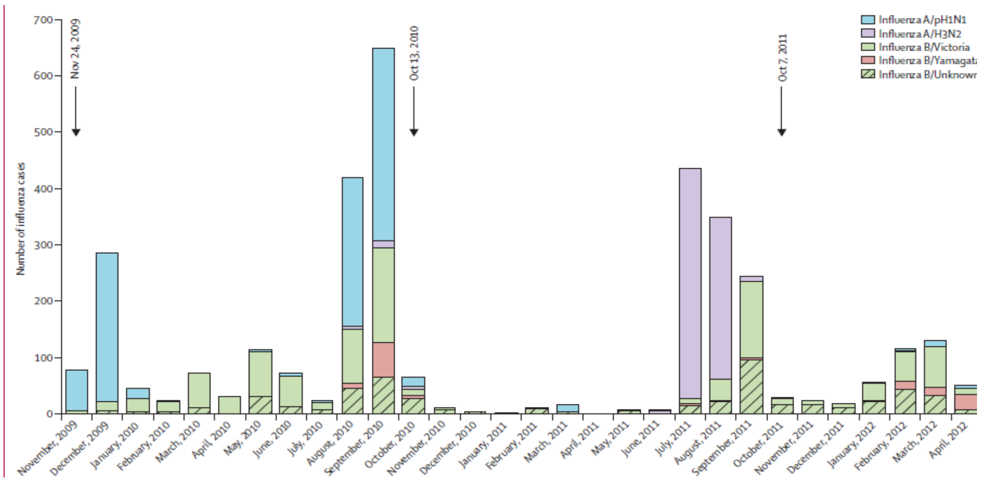


Fig: Number of laboratory-confirmed influenza cases by month and year, from November 2009, to April, 2012, among vaccinated children and unvaccinated individuals

- Indirect vaccine effectiveness was statistically significant only in year 3 (38·1%) when influenza was detected in 39 (0.9%) of 4,323 IIV3-allocated and 60 (1.5%) of 4121 IPV-allocated household unvaccinated individuals.
- The most common adverse events reported in both groups were fever and tenderness at site. No vaccine-related deaths or serious adverse events occurred in either group.

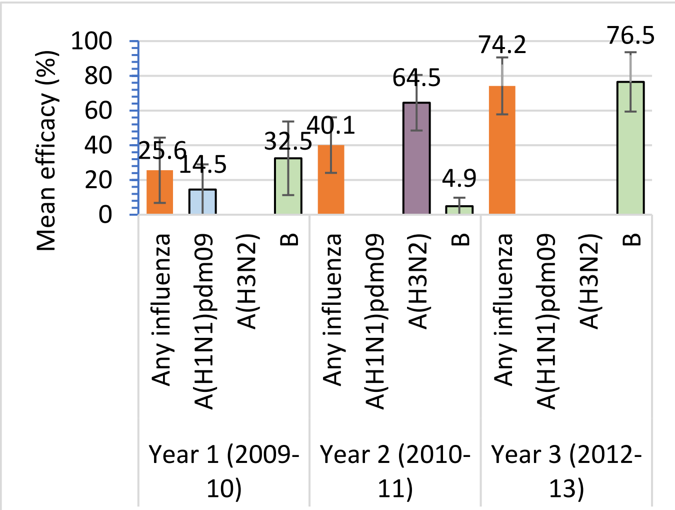


Figure 1 Total efficacy of any vaccination with trivalent inactivated influenza vaccine for the prevention of laboratory confirmed influenza

Conclusion

- Inactivated influenza vaccine provides modest protection among children and increases with repeated annual immunizations. The evidence of indirect protection among household members of the vaccinated children was inconclusive
- Vaccine efficacy data together with cost-effectiveness and burden estimates of influenza can inform policy in India, especially regarding the WHO recommendations for influenza vaccination of young children

Access the article by scanning the code

Reference:

1. Sullender WM, Fowler KB, Gupta V, et.al. Efficacy of inactivated trivalent influenza vaccine in rural India: a 3-year cluster-randomised controlled trial. Lancet Glob Health. 2019 Jul;7(7):e940-e950. doi: 10.1016/S2214-109X(19)30079-8. PMID: 31200893; PMCID: PMC7347003.

2.1.5 Validity of clinical case definitions for influenza surveillance among hospitalized patients

Rationale

An increasing number of countries are conducting surveillance for influenza to better understand circulating viral types and subtypes, detect influenza outbreaks, and estimate influenza disease burden.

However, clinical case definitions used for the detection of influenza vary substantially, depending in part on surveillance objectives, and few have been systematically evaluated for their sensitivity and specificity.
Systematic evaluation of clinical case definitions is critical for influenza disease burden estimates as inappropriate case definition can miss out influenza cases or affect efficiency of the system.

What we did?

- During July 2009–August 2011, we collected clinical data and specimens (nasal and throat swabs) from rural patients hospitalized for acute medical illnesses at CRHSP, Ballabgarh India.
- Specimens were then tested for influenza viruses.
- "Reported fever'' and additional sign–symptom combinations were also evaluated.

- Case definitions evaluated the following:
  - ✓ Influenza-like illness (ILI) Sudden onset of a fever over 38°C, and either cough or sore throat in the absence of other diagnoses.
  - ✓ Severe Acute Respiratory Illness (SARI) in ≥5 year age: Sudden onset of Fever over 38°C and either cough or sore throat, shortness of breath or difficulty breathing, and requiring hospital admission
  - ✓ Severe Acute Respiratory Illness (SARI) in <5 year age: Any child <5 years old clinically suspected of having Pneumonia or severe/very severe pneumonia, and requiring hospital admission
  - ✓ Acute Respiratory Infection (ARI): ≥1 of the following: cough (new or worsened), sore throat, difficulty breathing or nasal discharge
  - ✓ Febrile Acute Respiratory Illness: Sudden onset of fever and one or more of cough, sore throat, difficulty breathing, runny nose, or ear ache

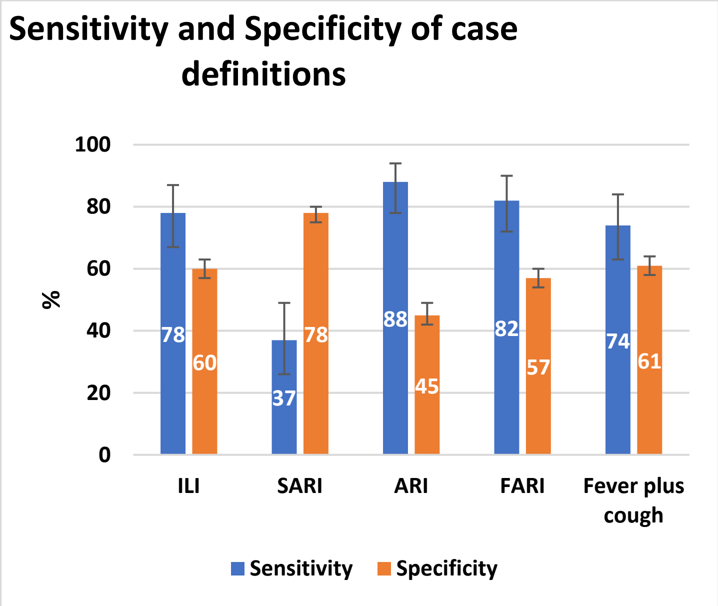
What we found?

- We enrolled 1043 hospitalized patients, including 257 children <5 years of age.

- Seventy-four patients tested influenza virus positive (including 28 A (H1N1) pdm09).Among the 257 inpatients <5 years of age, 18 (7%) had specimens positive for influenza viruses.

- Sensitivity (95 % CI) and specificity (95% CI) for influenza infection were 78% (67-87) and 60% (57-63) for ILI (measured ⁄ reported fever); 37% (26-49) and 78% (75-80) for SARI (measured ⁄ reported fever); 82% (72-90) and 57% (54-60) for FARI (measured ⁄ reported fever); 88% (78-94) and 45% (42-49) for ARI; and 74% (63-84) and 61% (58-64) for measured ⁄ reported fever plus cough.

- Case definitions that included measured fever had lower sensitivity.



Conclusion

- Modified ILI and FARI with measured / reported fever provided good balance between sensitivity and specificity among hospitalized patients.
- Our findings support the WHO review of case definitions used for influenza surveillance and contribute evidence to inform these discussions

Access the article by scanning the code

Reference:

1. Gupta V, Dawood FS, Rai SK, et.al Validity of clinical case definitions for influenza surveillance among hospitalized patients: results from a rural community in North India. Influenza Other Respir Viruses. 2013 May;7(3):321-9. doi: 10.1111/j.1750-2659.2012.00401.x. Epub 2012 Jul 16. PMID: 22804843; PMCID: PMC5779832

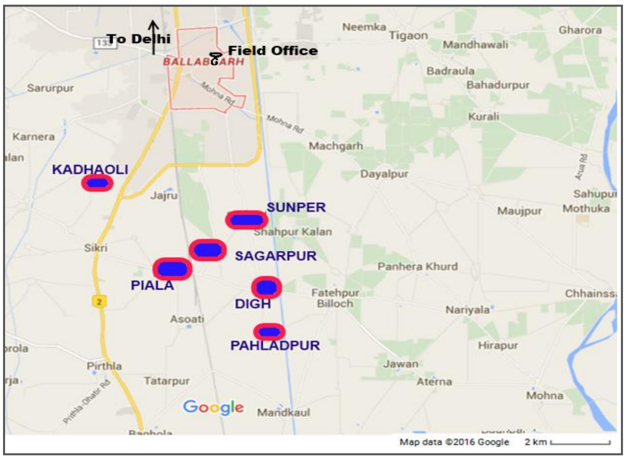
2.2 Ballabgarh Platform

AIIMS-CDC Surveillance platform at Ballabgarh for study on acute respiratory tract infections was established in the year 2012 with an initial focus on children aged less than 10 years and later expanded to older adults i.e., persons aged 60 years or, more.

Located in Faridabad District of the north Indian state of Haryana, the area is situated approximately 40 km south of New Delhi and falls within the National Capital Region of Delhi.

It consists of six villages of Sunper, Sagarpur, Digh, Pahladpur, Piala and Kadhaoli. The area has a borderline hot semi-arid climate just short of a dry-winter humid subtropical climate. Three seasons are recorded: winter (October to February), summer (March to June) and monsoon (July to September), with an average annual precipitation of 752 mm.

The communities are typically agrarian with creeping urbanization from the nearby Ballabgarh town. Healthcare in the study villages is through three public health sub-centres where auxiliary nurse-midwives provide primary health care services and supplemented by unqualified private health practitioners. Nearby Ballabgarh town has a secondary level government health facility as well as a multitude of private health facilities. Several big tertiary care private hospitals exist in the nearby Faridabad town.



An annual census carried out in these villages since 2012 update demographic details of this population. Table summarises household characteristics in the study area.

Household characteristics (N= 2292)	Value
Percentage of houses with	
Land ownership	42.2
Head of household with agriculture related occupation	18.1
Ground water as main source of drinking water	61.8
Piped water in own house	26.2
Access to water seal latrine	74.7
Wood/cow dung as main Fuel used for cooking	69.1
Tobacco smoker in the HH	60.5
Mean (±Standard Deviation) number of:	
Persons per household	5.97 (±2.61)
Children≤10 years per household	1.75 (±1.54)
Sleeping rooms per household	1.89 (±0.98)

Domiciliary Surveillance for Acute Respiratory infections

2.2.1 Epidemiology & Etiology of Pneumonia in Children

Rationale

Pneumonia is a leading cause of hospitalization and death among children worldwide. In India, around one-fifths of all deaths in children below five years are estimated to be due to pneumonia. Specific evidence-based public health measures for prevention and treatment of pneumonia requires better understanding of their aetiology. This information is currently available only from few hospital-based studies with little or no information being available from community-based studies in India.

What we did?

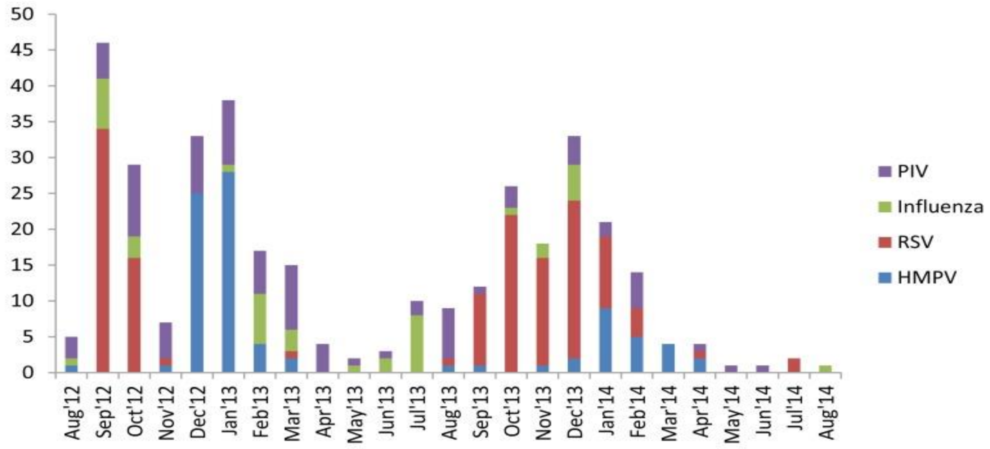
- We conducted a two-year cohort study in the AIIMS-CDC Ballabgarh platform described earlier to estimate agent-specific burden of pneumonia in children.
- We followed 3,765 under-ten children weekly at home from August 2012-August 2014, and looked for acute respiratory infections (ARI) - cough, sore throat, rhinorrhoea, ear discharge, and shortness of breath.
- Symptomatic children were assessed for pneumonia, severe pneumonia and very severe pneumonia using WHO Integrated Management of Childhood Illnesses (IMCI) for children <5 years old and Integrated Management of Adolescent and Adult (IMAI) Illness for children 5 to 10 years of age.
- Nasal and throat swabs were obtained from all pneumonia cases and asymptomatic controls and tested using reverse transcriptase and polymerase chain reaction (RT-PCR) for Respiratory syncytial virus (RSV), Human metapneumovirus (hMPV), Parainfluenza Virus (PIV), Influenza virus (IV) and processed as per CDC protocols.
- Andersen-Gill method of Cox-regression model was used to measure person-time for estimating ARI episodes and person time contribution to allow for recurrent events.
- We calculated agent-specific etiologic fraction to estimate agent-specific incidence rates.

What we found?

- Incidence of pneumonia in the under-five children was 0.36 per child-year. RSV (16%) was most often detected followed by PIV and hMPV (10% each) and influenza viruses (4.8%).
- Agent specific pneumonia incidences in the under-five age group were RSV (0.06), hMPV (0.03), PIV (0.03), and IV (0.01) episode per child-year.
- Both ARI and pneumonia incidence peaked in winters (November-January).
- hMPV demonstrated a clear winter peak (December-January) and RSV usually peaked in the months of September-October.
- PIV was present throughout the year whereas influenza virus demonstrated varied seasonality during the two years (See figure below)

Incidence (per child-year) of all-cause and agent specific pneumonia in children

Age group (Years)	All cause pneumonia	RSV	IV	hMPV	PIV
< 1	0.96	0.14	0.02	0.08	0.08
1-2	0.52	0.09	0.02	0.05	0.05
2-5	0.16	0.02	0.01	0.01	0.01
<5	0.36	0.06	0.01	0.03	0.03
5 or more	0.03	None of the viruses detected			



Seasonality of respiratory infections among children in Ballabgarh, northern India, 2012-14

Conclusion

- These results from rural north India demonstrate the high burden of pneumonia among children especially in the first year. Respiratory viruses have an important role in pneumonia aetiology
- The results of this study confirm the need for population-level access to treatment and preventive measures for respiratory infections in children

.

Access the article by scanning the code

Reference:

1. Krishnan A, Kumar R, Broor S, et al. Epidemiology of viral acute lower respiratory infections in a community-based cohort of rural north Indian children. *J Glob Health*. 2019;9(1):010433. doi:10.7189/jogh.09.010433

2.2.2 Efficacy of live attenuated and inactivated influenza vaccines among children in rural India: A 2-year, randomized, triple-blind, placebo-controlled trial

Rationale

Influenza vaccine use in India is limited. This is due to many reasons including poor delineation of its burden and lack of data on efficacy of vaccines from India. We assessed efficacy of nasally administered live attenuated influenza vaccine (LAIV) and injectable inactivated influenza vaccine (IIV) among children aged 2-10 years in rural India through a randomized triple (participant-observer-analyst) blind, placebo-controlled trial over 2 years.

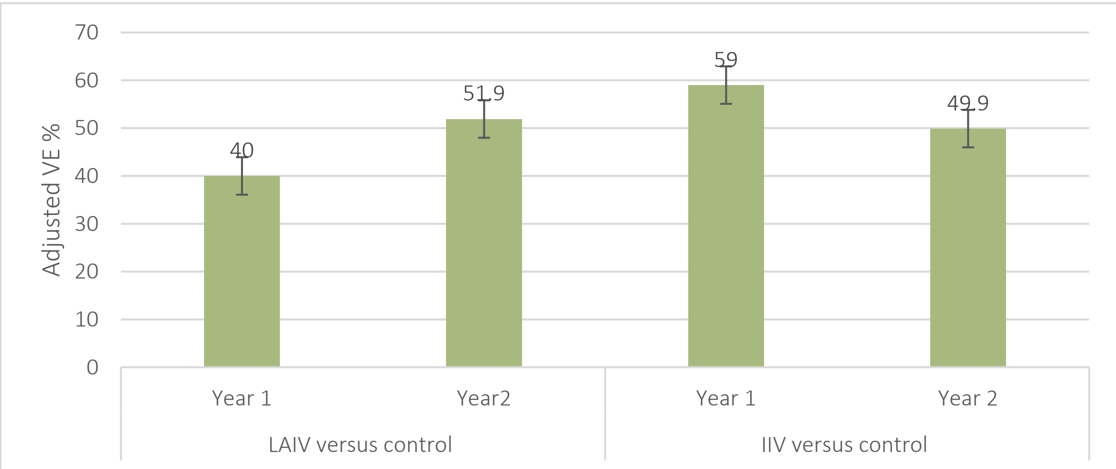
What we did?

- The study was conducted from June 2015 to July 2017 with immunizations in June-July 2015 and 2016 among children in 6 villages which were part of the AIIMS-CDC Surveillance platform at the Ballabgarh block of Faridabad district in Haryana, India.
- Children aged 2-10 years were randomly allocated to intranasal LAIV, injectable IIV, intranasal placebo, or injectable inactivated polio vaccine (IPV) in a 2:2:1:1 ratio.
- In June 2016, vaccination was repeated per original allocation.
- Overall, 3,041 children received LAIV (n = 1,015), IIV (n = 1,010), nasal placebo (n = 507), or IPV (n = 509).
- Through weekly home visits, nasal and throat swabs were collected from children with febrile acute

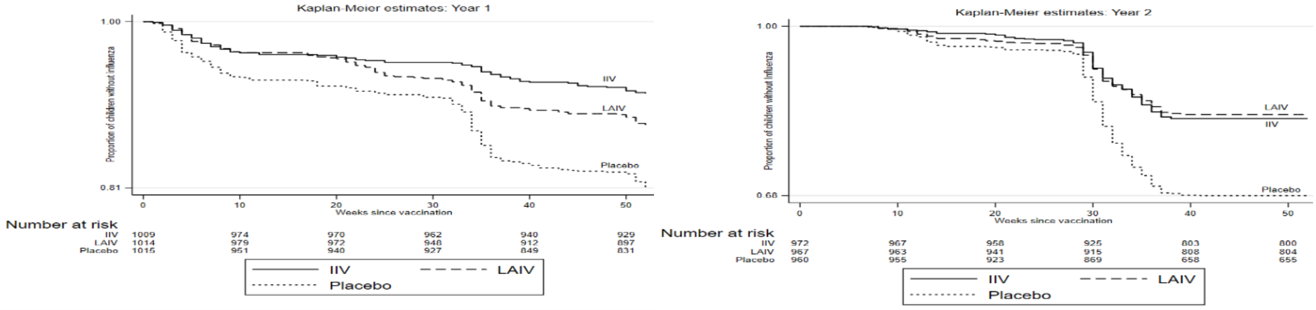
respiratory infection (FARI) and tested for influenza virus.
- The primary outcome was laboratory-confirmed influenza-associated FARI;
- Vaccine efficacy (VE) was calculated for each year using modified intention-to-treat (mITT) analysis by cox-proportional hazard model.
- The trial was registered in the Clinical Trials Registry of India CTRI/2015/06/005902.

What we found?

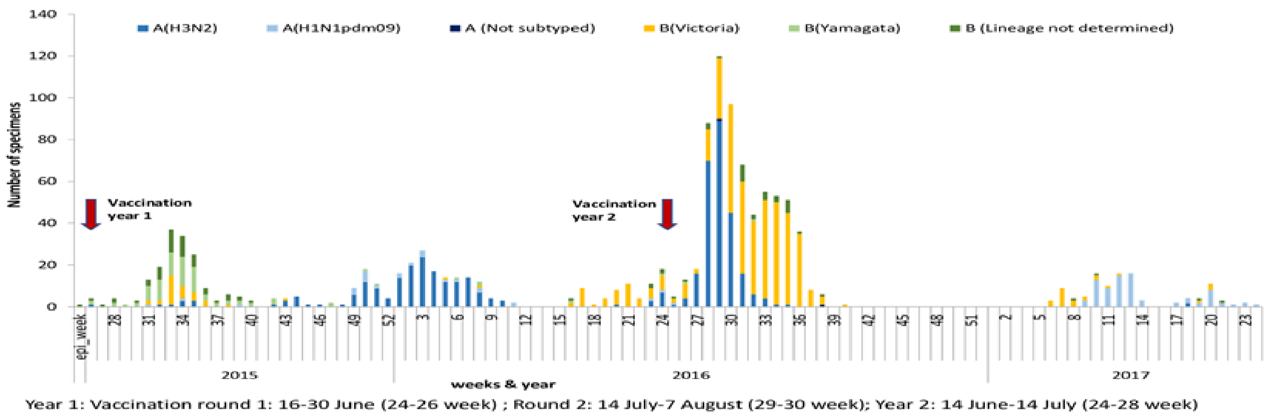
- Mean age of children was 6.5 years with 20% aged 9 to 10 years.
- In Year 1, VE was 40.0% (95% CI: 25.2 to 51.9) for LAIV which increased to 51.9% (95% CI: 42.0 to 60.1) in the second year.
- For IIV, VE was 59.0% (95% CI: 47.8 to 67.9) in Year 1 and 49.9% (95% CI: 39.2 to 58.7) in year 2.
- No Serious adverse events attributable to vaccine were reported



Vaccine efficacy of live attenuated and inactivated influenza vaccines in preventing laboratory-confirmed influenza illness, by study year.



Kalpan Meir curves of time to influenza infection by vaccine/Placebo group and study



Influenza circulation in the study area during June 2015 June 2017

- During both years, LAIV and IIV were protective against influenza A (H3N2) viruses. However, LAIV had limited efficacy against influenza A (H1N1) pdm09 for both years

- During year1, influenza virus circulation peaked twice, in August 2015 with predominantly influenza B (Yamagata)) and from December 2015 to February 2016 with predominantly influenza A (H3N2) strains.

Conclusion

- Both live attenuated and inactivated influenza vaccines had similar and moderate level of effectiveness in preventing influenza infection among children.
- Their usefulness for introduction of IIV or LAIV into national immunization platforms needs to be evaluate based on these results and other considerations including cost and operational aspects

Reference:

1. Krishnan A, Dar L, Saha S, et.al Efficacy of live attenuated and inactivated influenza vaccines among children in rural India: A 2-year, randomized, triple-blind, placebo-controlled trial. PLoS Med. 2021 Apr 29;18(4):e1003609. doi: 10.1371/journal.pmed.1003609. PMID: 33914729; PMCID: PMC8118535

2.2.3 Incidence, risk factors, and viral aetiology of community-acquired acute lower respiratory tract infection among older adults in rural north India

Rationale

Acute lower respiratory tract infection (LRTI) is an important cause of morbidity and mortality among older adults globally. LRTI has been associated with high rates of hospitalization among older adults. As the proportion of older adults increase with increasing life-expectancy in India, LRTI among older adults is likely to become a significant public health problem. We established a dynamic cohort of community-dwelling older adults (≥60 years of age) in rural north India to generate evidence on incidence and viral aetiology of LRTI.

What we did?

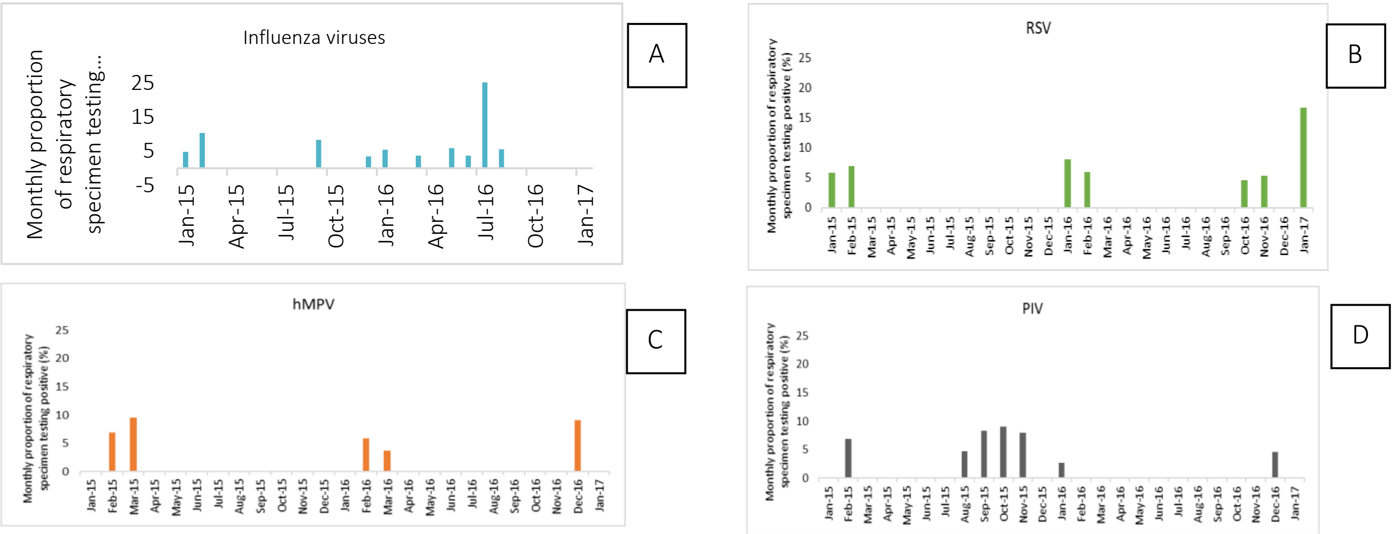
- A dynamic cohort of 1,403 older adults from 979 households was established during January 2015 to January 2017 in five villages in the Ballabgarh block in the Faridabad district of Haryana.
- All participants were followed-up through weekly surveillance for acute respiratory infections (ARI) at home by trained nurses. ARI was identified based on new onset of either cough, nasal discharge, sore throat, or difficulty in breathing; or worsening of any pre-existing respiratory symptoms (cough, difficulty in breathing, increase in sputum production). In those with chronic bronchitis, definition was modified to include new onset of fever in past 7 days.
- ARI cases were classified as either LRTI, or in those without symptoms and signs suggestive of LRTI as acute upper respiratory tract infection (URTI). LRTI was defined as ARI with respiratory rate ≥ 20 and presence of one or more of lower respiratory symptoms of productive cough, chest pain on breathing or wheezing.
- Nurses recruited asymptomatic controls without symptoms of ARI in the previous 7 days in the ratio of 1:1 for every case of LRTI. Controls were matched for age, sex and neighbourhood.
- Mid-turbinate nasal and throat specimens were obtained from all LRTI cases and asymptomatic controls. Real-time reverse transcription polymerase chain reaction (rRT-PCR) was performed for detection of influenza viruses, respiratory syncytial virus (RSV), human metapneumovirus (hMPV), and parainfluenza viruses 1-3 (PIV).

- Adjusted incidence rate ratios (aIRR) were calculated for these risk factors through multi-level Poisson regression modelling, adjusting for above-listed risk factors at the individual level, as well as clustering at the household level. Prevalence of each pathogen was calculated as the proportion of LRTI episodes associated with the specific pathogen out of all LRTI episodes detected among the participants.
- Agent-specific crude LRTI incidence rates were calculated after estimation of its etiologic fraction.

What we found?

- The incidence of LRTI per 1000 person-years was 248.3 (95% CI = 229.3-268.8); 291.9 (95% CI = 262-325.3) among men and 211.0 (95% CI = 187.6-237.3) among women. Incidence of LRTI increased with age among both men and women.
- The LRTI hospitalization rate per 1000 person-years was 12.7 (95% CI = 8.9-18.1): 16.9 (95% CI = 10.8-26.6) among men and 9.1 (95% CI = 5.2-16.1) among women.
- Persons with pre-existing chronic bronchitis as compared to those without (IRR = 4.7, 95% CI = 3.9-5.6); aged 65-74 years (IRR = 1.6, 95% CI = 1.3-2.0) and ≥75 years (IRR = 1.8, 95% CI = 1.4-2.4) as compared to 60-64 years; and persons in poorest wealth quintile (IRR = 1.4, 95% CI = 1.1-1.8); as compared to wealthiest quintile were at higher risk for LRT.
- Viral pathogens were detected in 10.1% of the LRTI cases. The viruses detected among LRTI cases were influenza (3.8%), RSV (3.0%), hMPV (1.5%), and PIV (1.9%). The agent-specific incidence per 1000 person-years varied from 2.2 (hMPV) to 7.9 (influenza viruses).

Age and sex-specific incidence of LRTI and viral agent specific LRTI among older adults in rural Ballabgarh, India					
Age group, years	Incidence of LRTI (per 1000 person-years)	Incidence of viral agent specific LRTI (per 1000 person-years)			
		Influenza viruses	Respiratory syncytial virus	Human metapneumovirus	Parainfluenza viruses
60–64	144.7 (122.5- 171.0)	5.3 (1.6-13.2)	2.6 (0.5-8.1)	0.6 (0–6.5)	4.9 (0.9-12.9)
65–74	283.9 (252.5-319.2)	8.4 (3.1-17.7)	7.6(2.4-14.7)	2.5 (0–9.4)	3.1 (0.5-10.0)
≥75	375.1 (325.2-432.8)	11.7 (3.8-27.5)	10.1 (2.7-22.3)	4.8 (0–18.6)	3.1 (0.3-14.8)
Total	248.3 (229.3-268.8)	7.9 (3.6-13.3)	6.2 (2.3-9.8)	2.2 (0–6.2)	1.8 (0.9-8.0)



Monthly detection of respiratory viruses among adult's age ≥60 years with acute lower respiratory tract infections (LRTI) in rural Ballabgarh, India, January 2015–January 2017.
A. Influenza viruses; B. Respiratory syncytial virus; C. Human meta-pneumovirus; D. Parainfluenza viruses

Conclusion

- The high burden of LRTI in this population and associated mortality point out the need for multi-modal interventions including vaccination against involved pathogens; support for smoking cessation for management of chronic bronchitis; and appropriate management of co-existing morbidities.
- In India, currently there is no public health vaccination program for older adults, and only limited influenza or pneumococcal vaccination use in the private sector for older adults. India's National Programme for the Healthcare of Elderly provides an ideal platform for introduction of these interventions in the country.

Access the article by scanning the code

Reference:

1. Kumar R, Dar L, Amarchand R, et al. Incidence, risk factors, and viral etiology of community-acquired acute lower respiratory tract infection among older adults in rural north India. *J Glob Health*. 2021; 11:04027. Published 2021 Apr 3. doi:10.7189/jogh.11.04027

2.2.4 Epidemiology of influenza and other respiratory pathogens among hospitalized children <5 years in Delhi, India using a multi-pathogen molecular diagnostic testing

Rationale

Pediatric acute respiratory infections (ARI) are a major cause of hospitalization and deaths, but data on respiratory pathogens responsible for ARI are limited in India.

We studied the prevalence of respiratory viruses among children aged <5 years hospitalized with severe acute respiratory infections (SARI) in Delhi, India

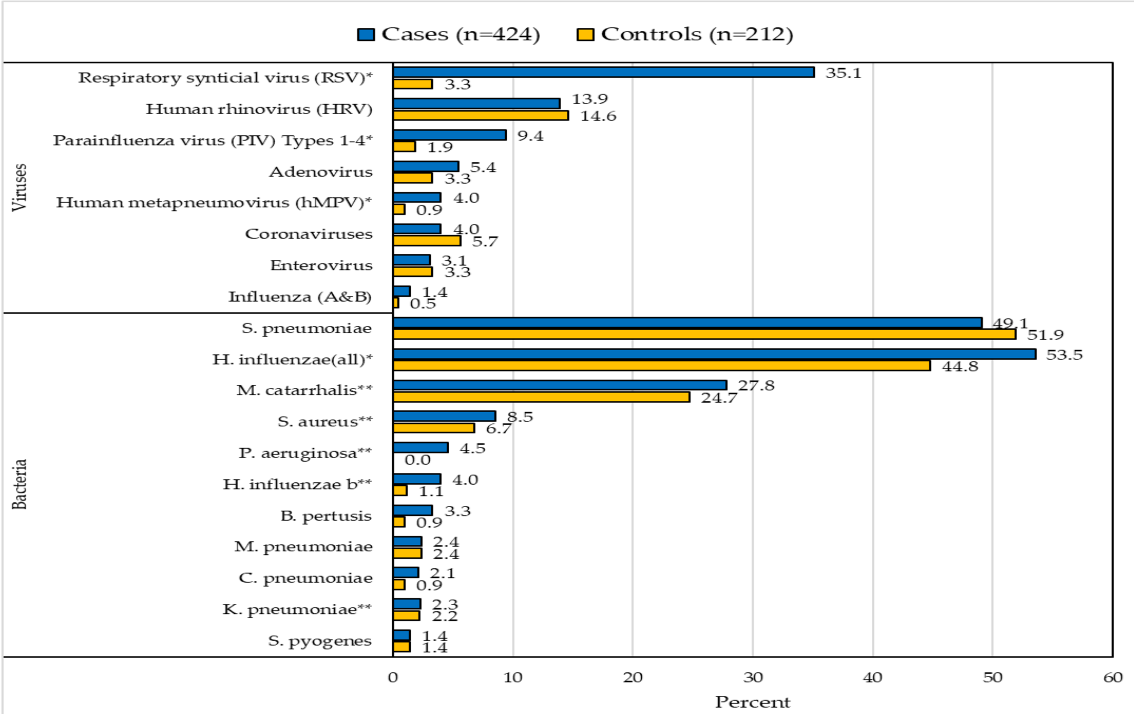
What we did?

- Study design: Prospective observational study
- Sites: Kalawati Saran Children's Hospital, Delhi, in northern India
- Period: August 2013–June 2014
- Study participants: Children <5 years of age fulfilling the case-definition of SARI
- Enrollment:
    - Hospitalized children were screened within 24 hours of admission for eligibility and two SARI cases were systematically enrolled per day
    - An age matched control without any acute illness was enrolled from the outpatient clinic within 24 hours of the case's enrolment
- Data & specimens: Clinical data and nasopharyngeal swabs were collected from enrolled participants parainfluenza viruses (PIV) 1, 2, 3 and 4 using TaqMan ViiA7™ real-time PCR machine on TaqMan Array Card designed to detect common viral and bacterial respiratory pathogens
- Laboratory confirmation: Samples were tested for respiratory syncytial virus (RSV) A and B, influenza viruses, rhinoviruses (HRV)/enteroviruses, adenovirus (ADV), bocavirus (BoV), human metapneumovirus (hMPV) A and B, coronaviruses (OC43, NL65,C229E)
- Data entry was done in tool developed in Epi Info 7 and analysed using STATA 12/SE

Prevalence of each pathogen among cases and controls were compared using chi-square or Fisher's exact test ($p<0.05$)

What we found?

- During the study period, 2,130 children aged <5years who had SARI were screened.
- 425 (20%) cases and 212 age-matched outpatient controls were enrolled.
- The median age was 6.3 months.
- Viral detections were more common in cases than controls (68% v/s 29%), while bacterial detections among were comparable (cases: 69%; controls: 66%).
- RSV (35%) was the most common virus detected among cases.
- Influenza viruses were detected among 6 (2.4%) cases.
- H. influenzae (all serotypes) (54% cases, 45% controls) was the most commonly detected bacteria and significantly more common in cases than controls ($p<0.05$).



Distribution of viruses and bacteria detected in children aged <5years hospitalized with severe acute respiratory illness (SARI) by age group in Delhi, India (2013-14)
** Pathogens significantly more common in cases than controls (p-value<0.05)*
*** These pathogens were tested only among 176 cases and 89 controls*

Conclusion:

- Respiratory viruses, especially RSV, was an important contributor to SARI hospitalizations among those <5 years in north India.
- Understanding the interactions between viruses and bacteria detected in the naso/oropharynx and their relationship to disease in the lung may lead to methods for reducing respiratory illness in children.

Reference:

1. Siddhartha Saha, Varinder Singh, Satinder Aneja, et al. Epidemiology of influenza and other respiratory pathogens among hospitalized children (ABSTRACT# P-82) Poster session presented at: 1OPTIONS for Influenza -IX; 2016 Aug 24-28; Chicago.

2.2.5 Cost of acute respiratory infections in Northern India

Rationale

Acute respiratory infections (ARI), in addition to causing substantial morbidity and mortality, also result in economic losses through increased use of healthcare resources and loss in productivity.

There is limited information on costs of ARIs in low-or-middle-income countries where disease severity may be worse because of delayed healthcare seeking and where out-of-pocket costs may have an even higher impact on already impoverished populations.

What we did?

- A cost-of-illness study was conducted in three communities in India to document the economic impact of ARI-related hospitalizations and outpatient visits in public and private facilities, and patient costs for non-medically attended ARI.
- Between September 2012 to March 2013, twenty-four health facilities covering all three levels of medical care participated in the study, including 4 tertiary, 9 secondary and 11 primary care facilities of New Delhi, Faridabad (Haryana) and Srinagar (Jammu & Kashmir) of India.
- Hospitalized patients were eligible for enrolment if they were hospitalized at least overnight, and ARI was the primary diagnosis for the admission.
- Non-medically attended participants were recruited from community.
- All information was self-reported by patients during in-person or telephone follow-up interview

Analysis:

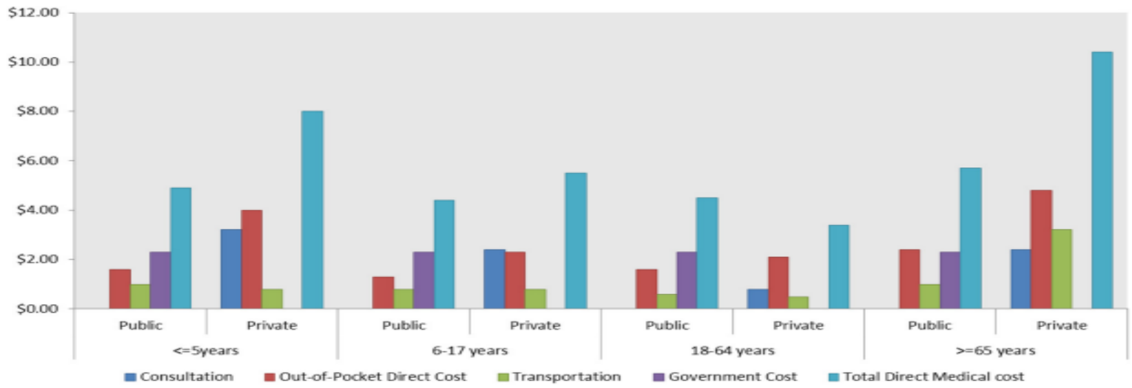
- Primary outcome variable was median cost of an episode inclusive of all health care received.
- WHO-CHOICE estimates were used for the cost of consultation/bed in public facilities
- For estimation of indirect cost median per capita income of US$1,104 per year was used.

What we found?

- A total 1,766 patients with ARI were enrolled, including 452 hospitalized patients, 1,056 outpatients, and 259 non-medically attended patients.
- The total direct cost of an ARI episode requiring outpatient care was US$4- $6 for public and $3-$10 for private institutions based on age groups. (See figure below)
- The total direct cost of an ARI episode requiring hospitalized care was $54-$120 in public and $135-$355 in private institutions.
- The cost of ARI among those hospitalized was highest among persons aged > = 65 years and lowest among children aged < 5 years.

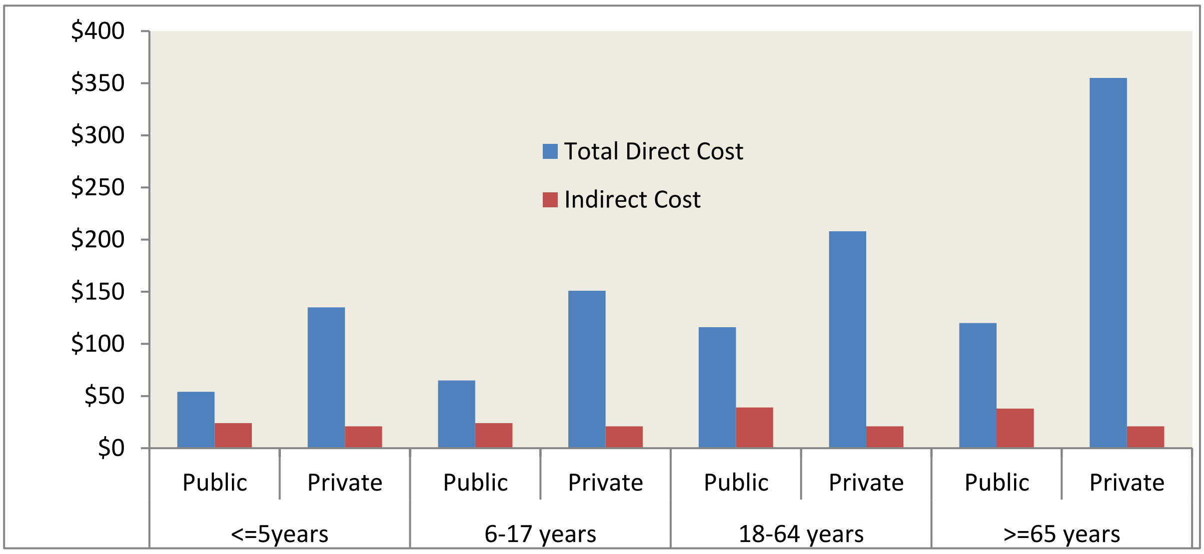
Definitions used in the study

- ARI - as per the European Centre for Disease Prevention and Control case definition or a clinician's diagnosis of one.
- Level of Health Facilities
  - Primary - facilities providing outpatient and emergency care only.
  - Secondary - facilities providing both outpatient/inpatient care but not intensive care.
  - Tertiary - facilities capable of providing intensive care.
- Valuation of costs:
  - Direct Medical cost included cost of admission, consultation, medications, or diagnostics such as radiologic and laboratory studies
  - Direct non-medical cost included transportation, and lodging fees.
  - Indirect cost was monetary value of lost earnings of adult patients and caregivers due to illness.



Median Costs (US$) of Inpatient-ARI in Northern India by Age and Health factor

- Among all inpatients, 14% (62/451) reported that they missed work due to their hospitalization and 61% (274/451) reported that a caregiver missed work.
- Indirect costs due to missed workdays were 16-25% of total costs. The direct out-of-pocket cost of hospitalized ARI was 34% of annual per capita income.



Median Costs (US$) of Inpatient-ARI in Northern India by Age and Type of Facility

Conclusion

- The cost of hospitalized ARI episodes in India is high relative to median per capita income.
- The cost estimates can inform cost effectiveness evaluations of proven ARI prevention strategies including vaccination

Access the article by scanning the

Reference:

1. Peasah SK, Purakayastha DR, Koul PA, et.al The cost of acute respiratory infections in Northern India: a multi-site study. BMC Public Health. 2015 Apr 7; 15:330.

2.3 INSPIRE Multisite Platform

A multicentric community-based surveillance network that was established to estimate incidence, study risk factors, healthcare utilisation and economic burden associated with influenza and respiratory syncytial virus (RSV) in India. The initial focus of this platform has been the older adults i.e., persons aged 60 years or, more.

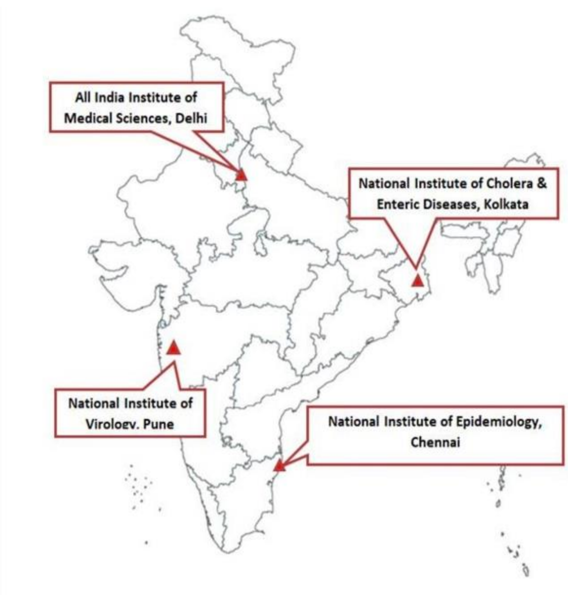
Four publicly funded national institutions—the National Institute of Virology in Pune (west), National Institute of Epidemiology in Chennai (south), National Institute of Cholera and Enteric Diseases in Kolkata (east) and All India Institute of Medical Science (AIIMS) in Delhi (north) are participating, these are shown in the adjoining map.

Each institution has identified a nearby site where they were already engaged with the community. Though influenza detection is seen throughout the year in all sites, the peak influenza activity varies between sites. Table below summarizes site characteristics

In addition to establishing study communities, this platform has also strengthened laboratory services and established data management system at all sites. The ongoing research studies to generate evidence base for burden and risk factors of influenza and other respiratory viruses among elderly in India will inform policy makers for appropriate prevention and control strategies for them. This platform was also leveraged for studying Covid epidemiology and a household transmission study is underway.

	Ballabgarh	Chennai	Kolkata	Pune
Setting	Rural	Peri-urban	Urban slum	Urban slum
Influenza peak activity	Jan-Feb, Jul-Sep	Nov-Dec	Jun-Jul	Jul-Aug
Annual range of temperature	8-39 ºC	21-37 ºC	14-38 ºC	11-38 ºC
Annual Rainfall	752 mm	1383 mm	1837 mm	803 mm

Environmental characteristics of project sites



Bird's eye view of Kolkata study site

Access the article by scanning the code

Reference:

1. Krishnan A, Dar L, Amarchand R, et al. Cohort profile: Indian Network of Population-Based Surveillance Platforms for influenza and Other Respiratory Viruses among the Elderly (INSPIRE). BMJ Open. 2021; 11(10):e052473. Published 2021 Oct 7. Doi: 10.1136/bmjopen-2021-052473

2.3.1 Incidence of influenza-associated acute respiratory infection among adults aged ≥60 years in a multi-site community cohort in India

Rationale:

Acute respiratory infections are one of leading contributors of mortality among older adults globally; influenza virus is one of the common viral pathogens. An estimated 2.9% of deaths in people aged >70 years in India are caused by respiratory infections, and 11.6% are attributable to chronic respiratory conditions. As per the 2011 census, older adults (aged ≥60 years) account for 8% (104 million) of the total population of India; this proportion is projected to reach 19% by the year 2050.

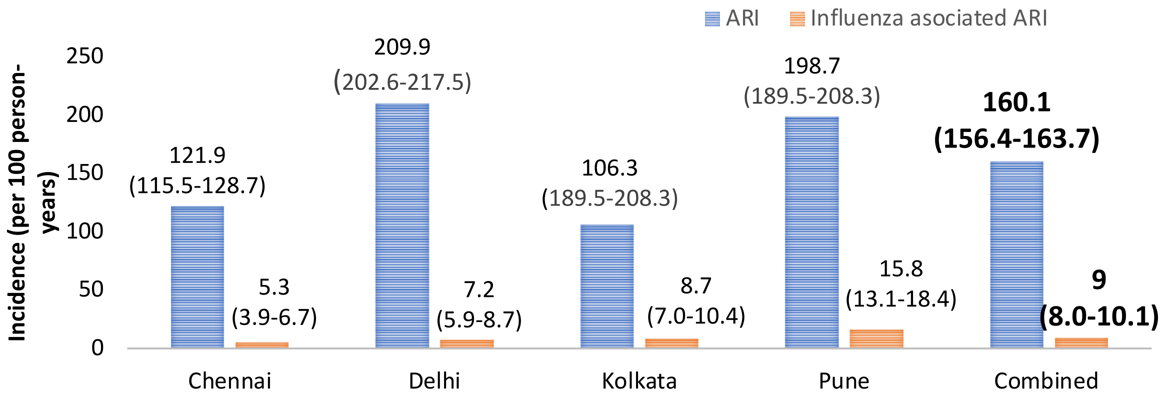
We initiated a multicentric community-dwelling cohort of older adults or elderly (aged ≥60 years) named 'Indian Network of Population-Based Surveillance Platforms for influenza and Other Respiratory Viruses among the Elderly (INSPIRE)' to estimate the incidence of influenza-associated acute respiratory infection (ARI).

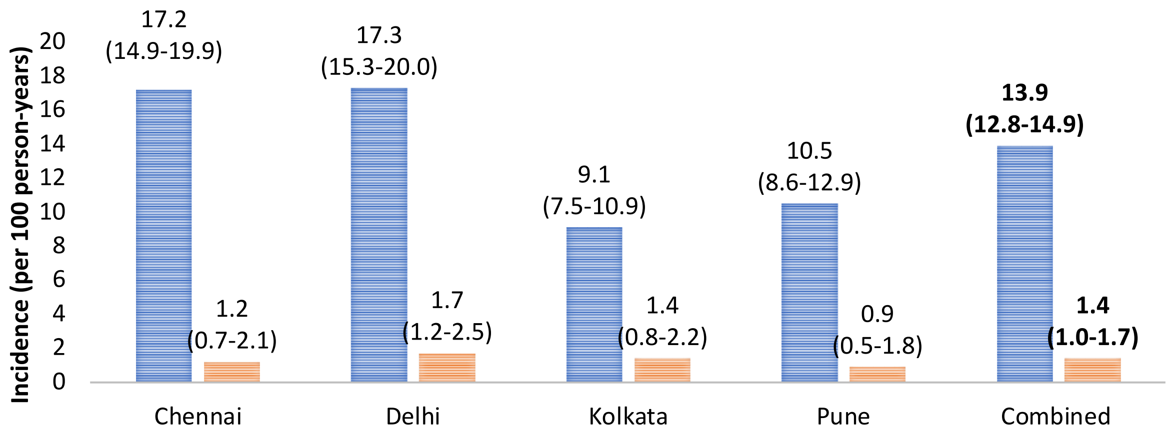
What we did?

- The four-site INSPIRE Network at Pune (west), Chennai (south), and Kolkata (east) and in Ballabgarh (north) has been described previously.
- We established dynamic cohort of 5,336 community-dwelling older adults aged ≥60 years starting in May 2018 and began surveillance for symptomatic respiratory infections on 2 July 2018.
- Trained nurses conducted weekly household surveillance for ARI. We defined ARI as new onset/ worsening of cough or difficulty in breathing in the last seven days and ALRI as ARI plus dyspnea or chest pain, a respiratory rate of >20 breaths/minute, and either measured fever or a reported symptom complex of fever, sweating, headache and myalgia.
- Nurses collected nasal and oropharyngeal swabs from all ALRI cases and 20% of randomly selected ARI cases not meeting ALRI criteria for influenza testing by RT-PCR.
- We extrapolated the monthly influenza positivity rate among tested non-ALRI cases to the monthly non-ALRI incidence in the cohort and then calculated ARI incidence as the sum of non-ALRI and ALRI incidence.
- We estimated the incidence of influenza associated ARI and ALRI per 1000 person-years(py) with 95% confidence interval using normal approximation method. Here we are reporting the incidence in the first year of surveillance

What we found?

- Mean age of cohort was 66.8 years (SD-6.5 years). 42.5% of the participants were females and 70.8% had any self-reported morbidity. Only 0.2% had received influenza vaccine in last one year.
- Incidence of acute respiratory infection was 160.1 episodes/100 person-years while the incidence of influenza-associated ARI was 9.1 episodes/100 person-years. Incidence of ARI varied across sites; it was 209.9 episodes/100 person-years at Delhi and 106.3 episodes/100 person-years at Kolkata. Incidence of influenza-associated ARI was maximum at Pune (15.8 episodes/100 person-years) and least at Chennai (5.3 episodes/100 person-years).
- Incidence of ALRI was 13.9 episodes/100 person-years and influenza-associated ALRI was 1.4 episodes/100 person-years. Incidence of ALRI was maximum in Delhi (17.3 episodes/100 person-years) and Chennai (17.2 episodes/100 person-years) and least in Kolkata (9.1 episodes/100 person-years). Incidence of influenza-associated ALRI varied from 1.7 episodes/100 person-years at Delhi to 0.9 episodes/100 person-years at Delhi.
- At all sites, influenza transmission had two peaks; a bigger peak during monsoon and smaller one during winter season.





Conclusion

- On an average, 9% of older adults had an episode of influenza-associated ARI and 1-2 % of older adults had an episode of influenza-associated ALRI annually. 10% of ALRI episodes could be due to influenza. Hence, prevention of influenza through measures like vaccination can help reduce the burden of morbidity and mortality in this age group.

3. Burden of Influenza-associated respiratory and circulatory mortality in India, 2010-13

Rationale

Currently, no national estimates of influenza-associated deaths are available for India. Estimates of influenza mortality for India could guide policy for prevention and control measures, by identifying the burden among populations at risk of influenza-associated death. As that influenza is often not listed as an underlying cause during medical certification of deaths, influenza-associated mortality estimation is often conducted using indirect estimation methods with statistical modeling procedures which use virological surveillance and cause of death data at population level.

What we did?

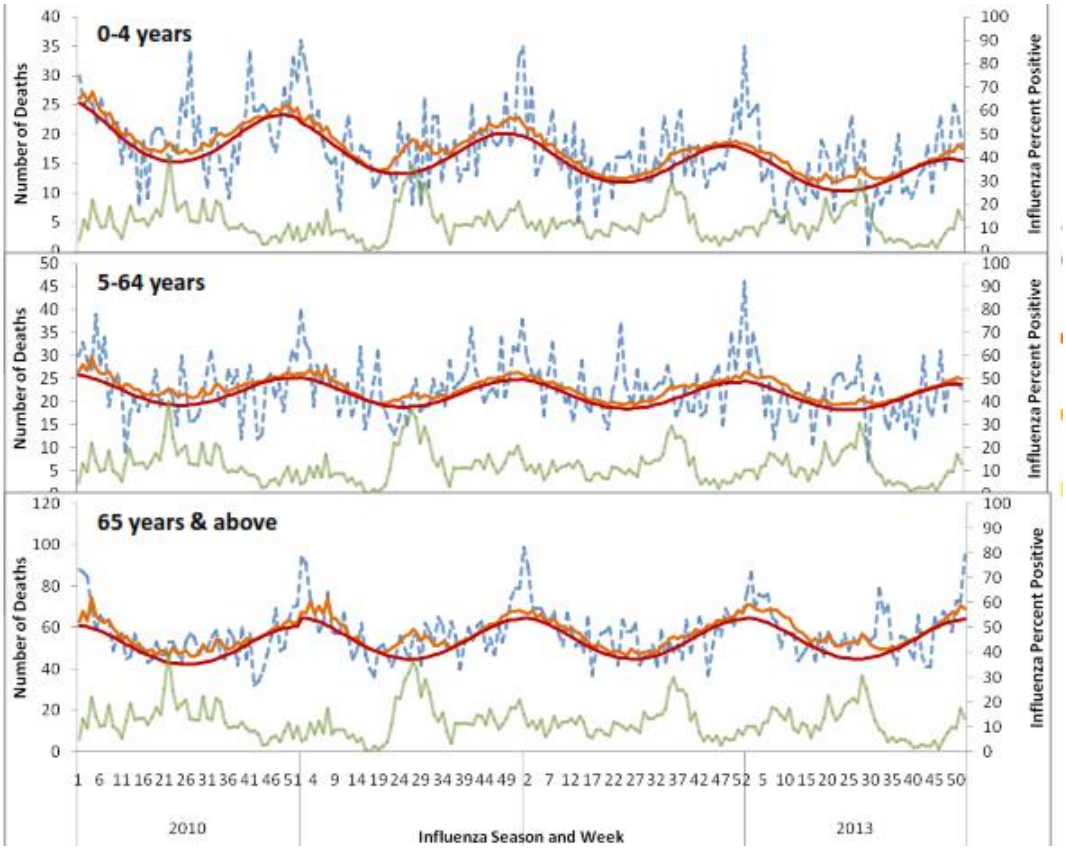
- We obtained weekly death data for 2010 through 2013 collected through the Sample Registration System (SRS), the only nationally representative mortality data available for India. We obtained weekly counts of respiratory and circulatory deaths for 2010-2013 by three age groups (<5, 5-64, ≥65 years).
- Viral surveillance data was obtained from the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV) lab network which were located across ten cities in eight states providing geographic and climatic representation of India. Patients with influenza-like illness (ILI) and severe acute respiratory infection (SARI) were randomly selected and enrolled into the surveillance system.
- Specimens were tested for influenza viruses using reverse-transcription polymerase chain reaction (RT-PCR) from 2010 to 2013 year-round. We obtained weekly numbers of specimens positive for influenza viruses by type (A or B) and influenza A subtype (H1N1pdm09 or H3N2)
- Generalized linear regression with negative binomial distribution was used to model weekly respiratory and circulatory deaths by age group and proportion of specimens positive for influenza by subtype; excess deaths above the seasonal baseline were taken as an estimate of influenza-associated mortality counts and rates.

What we found?

- Across all age groups, a mean of 1, 27,092 (95% CI=64,046-1, 90,139) annual influenza-associated respiratory and circulatory deaths may occur in India.
- Estimated annual influenza-associated respiratory mortality rates were highest for those ≥65 years followed by those <5 years. Influenza-associated circulatory death rates were also higher among those ≥65 years as compared to those aged <65 years.
- The peaks in influenza-associated mortality are depicted in figure and their timings vary from year to year. Most influenza-associated deaths occurred within the typical influenza season in India, which generally occurs from April to September each year.
- Among person's ≥65 years, highest rates of influenza-associated respiratory mortality were observed for influenza A viruses, notably the influenza A (H1N1pdm09) virus with limited mortality associated with influenza B viruses.

Respiratory deaths (95% CI)			Circulatory deaths (95% CI)		Respiratory & Circulatory deaths (95% CI)
<5 years	5 to 64 years	≥65 years	<65 years	≥65 years	All age
11,203 (0-24,998)	11,025 (0-24,500)	34,275 (6,178-62,371)	22,395 (0-53,576)	48,194 (5,283-91,105)	1,27,092 (64,046-1,90,139)

Estimated influenza-associated annual respiratory and circulatory deaths by age group, India, 2010–2013 (average)



Observed respiratory deaths and predicted influenza-associated respiratory deaths and proportion positive for influenza viruses by age group, week, and year. The dotted blue line represents respiratory deaths, the green line represents influenza percent positive, the dark red line represents expected baseline mortality, and the wavy orange line represents predicted mortality. The number of excess influenza-associated deaths are the difference between the orange and red lines

Conclusion

- We observed a high burden of influenza-associated mortality among adults ≥65 years and children <5 years.
- These estimates may be useful for advocacy for prevention and control for influenza, including the consideration of older adults and under-5 children as a high burden group for vaccination.
- Improvements to influenza virus surveillance and vital registration systems in India would increase the robustness of future estimates of influenza-associated disease burden.

Access the article by scanning the code

Reference:

1. Narayan VV, Iuliano AD, Roguski K, et al. Burden of influenza-associated respiratory and circulatory mortality in India, 2010-2013. *J Glob Health*. 2020; 10(1):010402. doi:10.7189/jogh.10.010402

4. Respiratory syncytial virus among children hospitalized with acute lower respiratory infection in Kashmir, a temperate region in northern India

Rationale

Acute lower respiratory infections (ALRI) are a leading cause of hospitalizations in children especially due to viral pathogens

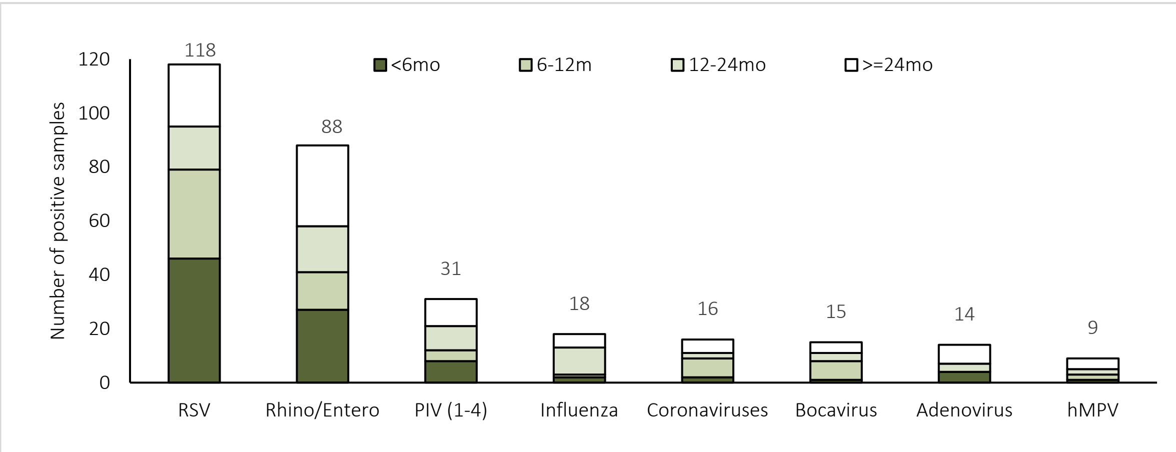
Studies in the last decade have reported prevalence of respiratory viruses among children hospitalized with ALRI from different parts of India with tropical climate, but none are reported from Kashmir, a temperate region of north India

What we did?

- Study design: Prospective observational study
- Sites: Two tertiary care hospitals of Srinagar, in northern India
- Period: October 2013–September 2014
- Study participants: Children <5 years of age fulfilling the case-definition of SARI

Case definition:
Children 3-59 months of age with history of or measured fever (≥38°C) with cough and onset in the last 7 days requiring hospitalization.
Children less than 3 months of age a physician diagnosed acute lower respiratory infection

- Enrollment: Hospitalized children were screened within 24 hours of admission for eligibility and two SARI cases were systematically enrolled per day
- Data: Demographic and clinical data were collected and entered in Epi-Info7 and analysed using STATA-14.
- Laboratory confirmation: Nasopharyngeal swabs were tested for respiratory syncytial virus (RSV) A and B, influenza viruses, rhinoviruses (HRV)/enteroviruses, adenovirus (ADV), bocavirus (BoV), human metapneumovirus (hMPV) A and B, coronaviruses (OC43, NL65,C229E), and parainfluenza viruses (PIV) 1, 2, 3 and 4 using standardized duplex real-time polymerase chain reaction
- Sequencing: RSV were characterized for G genes for phylogenetic study



Distribution of viruses detected in children aged <5years hospitalized with severe acute respiratory illness (SARI) by age group in Srinagar, India (2013-14)

What we found?

- Among 4,548 respiratory illness admissions screened, 1,026 met the SARI case definition, and 412 were enrolled (aged 15 days to 58 months, median 12 months)
- Among the enrolled participants, 257 (62%) had any virus detected; RSV was most commonly detected (n=118; 28%)
- Of the RSV viruses sub-typed (n=116), the majority were type B (94, 80%)
- Phylogenetic analysis of G gene of RSV showed circulation of the BA9 genotype with 60 base-pair nucleotide duplication
- Antibiotics were used in 60.5% (95% CI: 55.6–65.3) of all enrolled SARI cases.

Conclusion

- Our study showed that over half of the SARI admissions among <5 years were due to respiratory viruses.
- RSV was the most common virus detected among the children with SARI especially among infants
- Such data on viral detection helps guide clinicians for appropriate treatment strategies for hospitalized SARI cases especially in India.

5. Dynamic Patterns of Circulating Seasonal and Pandemic A (H1N1) pdm09 Influenza Viruses From2007–2010 in and around Delhi, India

Rationale:

Influenza is a widespread viral infection and a major cause of morbidity and mortality. Improved understanding of the temporal and geographic circulation of influenza viruses and the impact of influenza among populations living in tropical and subtropical regions is essential for the development of influenza prevention and control strategies in those areas.

What we did?

- Study type: Influenza surveillance study
- Study site/Participants:
    - A subset of patients with influenza-like illness (ILI) presented at an Employee Health Clinic (EHS) at All India Institute of Medical Sciences (AIIMS), New Delhi (urban)
    - Pediatric outpatient department of a civil hospital at Ballabgarh (peri-urban), under the Comprehensive Rural Health Services Project (CRHSP) of AIIMS, in Delhi region
- Study period: January 2007- December 2010.
- 3264 nasopharyngeal samples from years 2007 (n=510), 2008 (n =822), 2009 (n=1071), and 2010 (n=661) were tested for influenza either by virus isolation or by real-time RT-PCR (since April 2009)

What we found?

- 541/3264 (17%) were positive for influenza viruses.
- Influenza positivity was lower in 2007 (55/710; 8%) and 2008 (55/822; 7%) followed by a marked increase in influenza positivity in 2009 (315/1071; 29%), primarily due to the emergence of Influenza A(H1N1) pdm09 in August of 2009
- Influenza A (H1N1) pdm09 accounted for > 50% of infections in both 2009 and 2010, whereas A (H3N2) accounted for >44% infections in 2010
- Further analysis from July 2009 (at the time of emergence of pandemic influenza in Delhi) to December 2010, the percentage positivity for influenza A(H1N1) pdm09 was higher (19.8%–29.3%) in all age groups except >35 years age group than seasonal influenza positivity (8.6%–11.8%)
- The highest influenza positivity was observed in the >5–18 years old age group (112/ 266; 42%), followed by the 18–25 years old group (42/108; 39%).
- More importantly Influenza A(H1N1)pdm09 positivity was 29% and 27.8% respectively among children between >5–18 (78/ 112) and >18–25 years of age (30/42) when compared to >35 years age group
- Further, the percentage positivity for Influenza A(H1N1)pdm09 was higher (19.8%–29.3%) in all age group except >35 years age group than seasonal influenza positivity (8.6%–11.8%)

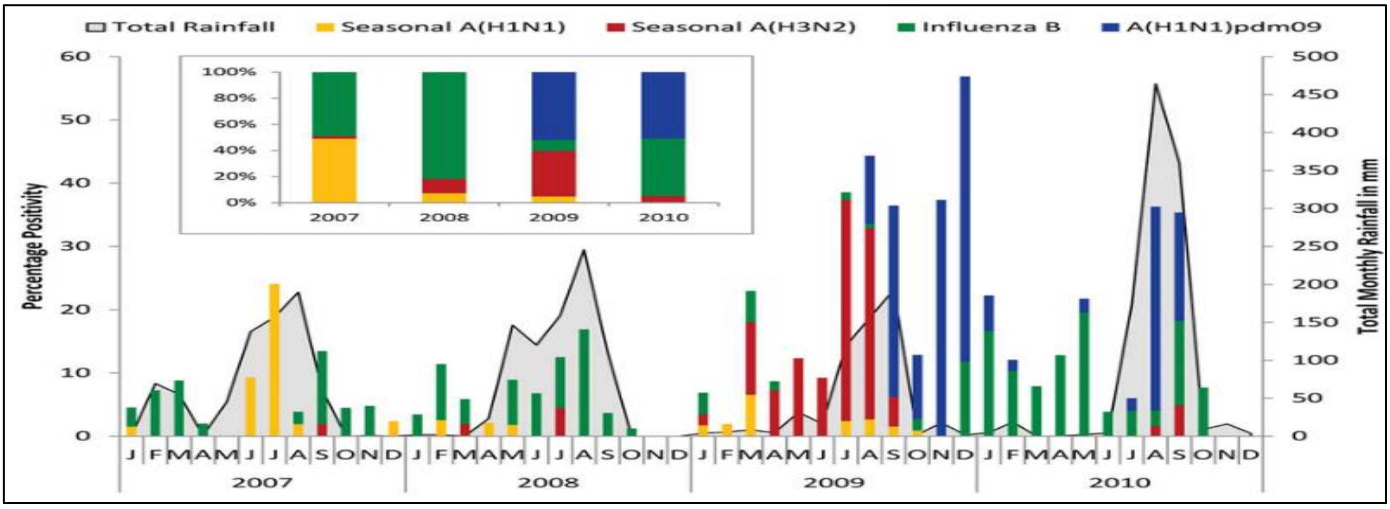


Figure 1 Monthly trends and seasonality of influenza viruses in Delhi. The left axis shows the percent monthly distribution of seasonal influenza (Yellow bar A(H1N1); red bar A(H3N2); and green bar representing Influenza B) and pandemic A(H1N1) pdm09 (Blueline) with total monthly rainfall (grey shade) is shown on right axis for each year. The inset shows overall distribution of influenza types and subtypes for years 2007- 2010.

Conclusion:

Sentinel surveillance indicated that the influenza viruses circulate year-round in the Delhi (north India) area and contributes significantly to the number of ILI patients seeking care in government facilities in urban and peri-urban areas of Delhi, especially during the rainy and winter seasons.

Access the article by the code

Reference:

Broor S, Krishnan A, Roy D, Dhakad S, Kaushik S, Mir M et al. Dynamic Patterns of Circulating Seasonal and Pandemic A(H1N1)pdm09 Influenza Viruses From 2007–2010 in and around Delhi, India. PLoS ONE. 2012;7(1):e29129.