

Influenza Incidence Surveillance Project, 2010-2011

A review of previous studies

Heidi Davidson
Influenza Division
Centers for Disease Control and Prevention

2010 – 2011 Study objectives

- Determine the incidence of medically attended ARI and ILI in outpatient settings
- Determine proportion of ARI and ILI that is due to influenza
- Test for other viral etiologies of ARI and ILI

Objective #1:

- Determine the incidence of medically attended ARI and ILI in outpatient settings

Summary of studies evaluating the rates of outpatient visits attributed to ARI or ILI (in children)

Study site	Years	Age range	Case Def	Rate of outpatient visits
Boston	1994-2000	6-23 mos	Both	8.5 / 100 children
TN (Medicaid)	1974-1993	0-5 yrs	Both	6-15 / 100 children
Vanderbilt (TN)	1974-1999	< 1 yrs	Both	93 / 1000 children
		1-2 yrs		110 / 1000 children
NY, OH, TN (NVSN)	2002-2003, 2003-2004	0-5 mos	Both	28-59 / 1000 children
		6-23 mos		52-125 / 1000 children
		24-59 mos		53-88 / 1000 children
		0-59 mos		50-95 / 1000 children

ORIGINAL ARTICLE

The Underrecognized Burden of Influenza in Young Children

Table 4. Outpatient Visits for Acute Respiratory Tract Infection or Fever Associated with Confirmed Influenza.*

Age Group	Visits for Acute Respiratory Tract Infection or Fever Associated with Confirmed Influenza		Mean Rate of Visits for Acute Respiratory Tract Infection or Fever, 1998–2002†	Estimated Rate of Visits Attributable to Influenza‡	
	2002–2003	2003–2004		2002–2003	2003–2004
	% (95% CI)			no./1000 children (95% CI)	
Outpatient clinics					
0–5 mo	4.6 (0.1–15.5)	9.7 (4.0–19.0)	611 (428–794)	28 (7–111)	59 (28–128)
6–23 mo	7.3 (4.0–11.9)	17.5 (12.8–23.1)	711 (555–869)	52 (30–90)	125 (87–179)
24–59 mo	14.9 (10.0–21.1)	24.8 (19.0–31.2)	357 (277–437)	53 (35–81)	88 (64–123)
0–59 mo	10.2 (7.5–13.6)	19.4 (16.0–23.1)	489 (387–591)	50 (35–71)	95 (72–125)
Emergency departments					
0–5 mo	0.0 (0–4.1)	18.2 (11.8–26.2)	127 (95–159)	0	23 (15–36)
6–23 mo	5.5 (2.6–10.2)	26.2 (20.9–32.1)	150 (127–173)	8 (4–16)	39 (30–51)
24–59 mo	11.4 (6.0–19.1)	39.0 (32.0–46.4)	60 (49–71)	7 (4–12)	23 (18–30)
0–59 mo	5.9 (3.7–8.9)	28.8 (25.0–32.7)	94 (78–110)	6 (4–9)	27 (22–33)

* CI denotes confidence interval.

† The mean rate of visits for acute respiratory tract infection or fever per 1000 children was calculated from the National Ambulatory Medical Care Survey/National Hospital Ambulatory Medical Care Survey.¹⁰

‡ Rates were calculated by multiplying the proportions of visits for acute respiratory tract infection or fever associated with confirmed influenza (columns 2 and 3) by the mean rate of visits for acute respiratory tract infection or fever, 1998–2002 (column 4).

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THE EFFECT OF INFLUENZA ON HOSPITALIZATIONS, OUTPATIENT VISITS, AND COURSES OF ANTIBIOTICS IN CHILDREN

KATHLEEN MALETIC NEUZIL, M.D., M.P.H., BEVERLY G. MELLEN, Ph.D., PETER F. WRIGHT, M.D.,
EDWARD F. MITCHEL, JR., M.S., AND MARIE R. GRIFFIN, M.D., M.P.H.

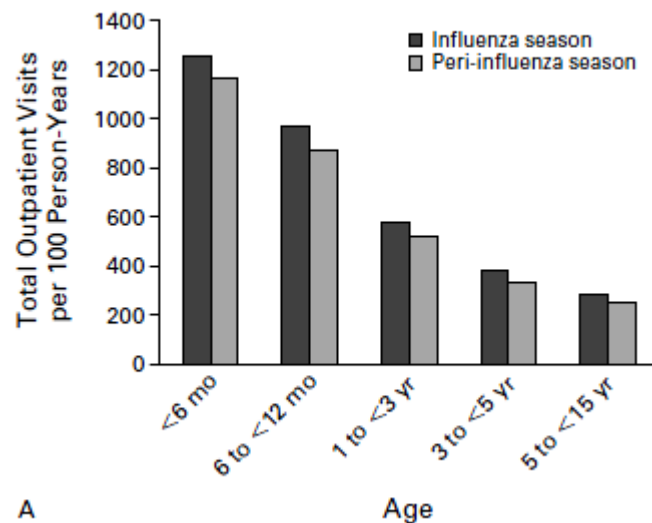


Figure 1. Rates of Outpatient Visits and Courses of Antibiotics Attributable to the Treatment of Influenza, According to Age, during the Influenza and Peri-Influenza Seasons.

Panel A shows the average total age-specific numbers of outpatient visits per 100 person-years. Panel B shows the average total age-specific numbers of courses of antibiotics prescribed per 100 person-years. Panel C shows the average excess age-specific numbers of outpatient visits and courses of antibiotics per 100 children per year.

Notes

- In the NVSN study, only 17.2 % of children seen in outpatient settings with lab-confirmed influenza were actually given a diagnosis of influenza by their providers
 - Surveillance that relies on data from physician-directed testing alone substantially underestimates the burden
- Average annual rates of outpatient visits due to flu were between 10 and 250 times as high as hospitalization rates for children 0-5 years
- For every 100 children aged < 2 yrs, 5-6 cases of acute otitis media that could be attributed to flu occurred annually

Infection with influenza A/Victoria virus in Houston families, 1976

By L. H. TABER,* A. PAREDES, W. P. GLEZEN
AND R. B. COUCH

*Influenza Research Center, Departments of Paediatrics,
Microbiology and Immunology, Baylor College of Medicine,
1200 Moursund Avenue, Houston, Texas 77030*

Table 2. *Clinical manifestations of influenza A/Victoria/75 infection by age*

Age group (years)	Number infected	Number with indicated illness					% ARI	% ILI
		N	None	Afebrile URI*	Febrile URI	Lower respiratory disease		
0-1	14	37	2	2	7†	3‡	5.4	18.9
1-4	7	21	5	1	1	—	4.8	4.8
5-19	10	30	7	—	3§	—	--	10
20-29	8	47	5	1	2	—	2.1	4.3
30-47	4	20	2	—	—	2	--	--

* Upper respiratory illness.

† One hospitalized with unexplained fever, later developed URI.

‡ One hospitalized with pneumonia.

§ One hospitalized with associated encephalitis.

37 families, 155 study participants
for 1 influenza season

Notes

- Not much data available on incidence of medically attended ARI vs. ILI (*and* covering all age groups)
- The rates calculated in these studies could be an overestimation or underestimation of the true burden of influenza
 - Due to factors such as:
 - Co-circulation of other respiratory viruses such as RSV (overestimation)
 - Selective testing by physicians only during periods of known influenza activity (underestimation)

UK Studies



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Influenza diagnosis and treatment: a view from clinical practice

Douglas Munro Fleming

*Birmingham Research Unit of The Royal College of General Practitioners, Lordswood House,
54 Lordswood Road, Harborne, Birmingham B17 9DB, UK (dfleming@rcgp-bru.demon.co.uk)*

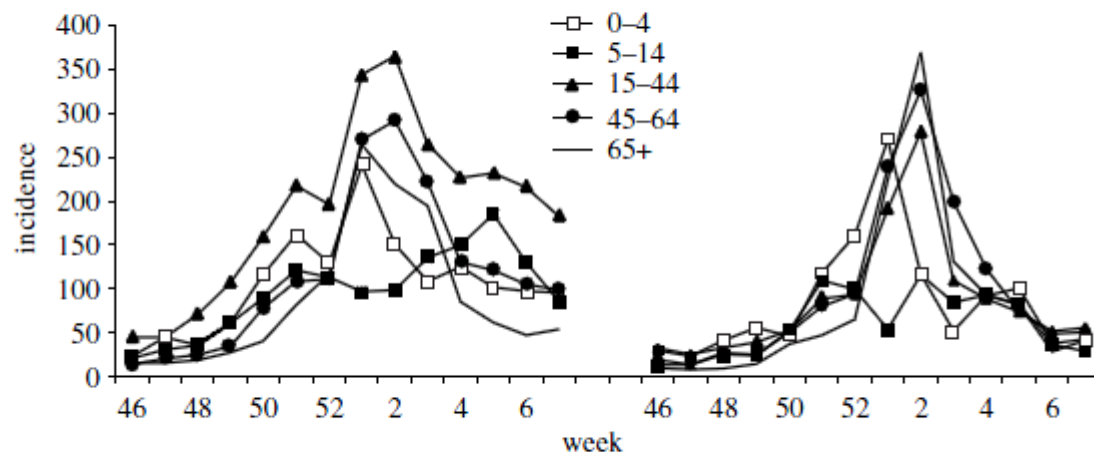


Figure 6. Incidence of ILI (per 100 000) by age group in 1996–1997 (left) and 1998–1999 (right).

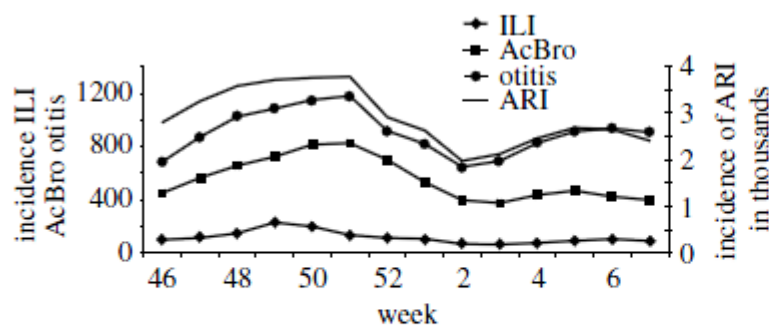


Figure 7. Incidence of respiratory illnesses by week averaged over 10 winters from 1989–1990 to 1998–1999 in children of 0–4 years (per 100 000).

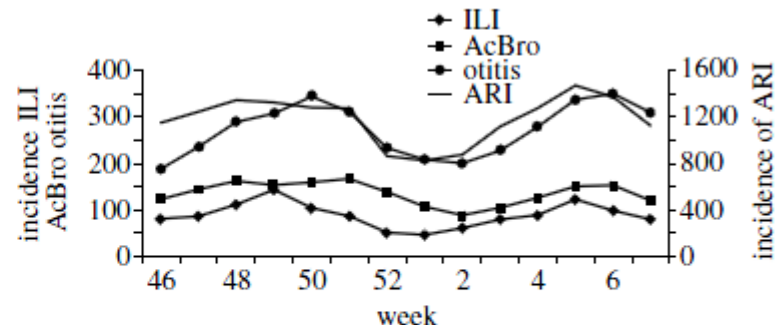


Figure 8. Incidence of respiratory illnesses by week averaged over 10 winters from 1989 to 1998 in children of the 5–14 years age group (per 100 000).

Table 1. Persons presenting with ARI per 100 000 population of England and Wales: average percentage of ARI attributable to influenza during the winters of 1989–1999.

age group	cumulative incidence			persons in England and Wales	
	ARI	attributable to influenza	% attributable to influenza	ARI	influenza
0–4 years	78 939	4069	5.2	25.64	1.32
5–14 years	32 468	3492	10.8	22.06	2.37
15–44 years	20 714	1696	8.2	45.56	3.73
45–64 years	18 493	1603	8.7	22.38	1.94
65+ years	21 346	1622	7.6	17.69	1.34
all ages	25 493	2205	8.6	133.65	11.56

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all ages	25 493	2205	8.6	133.65	11.56

Relative proportion of ARI that is attributable to influenza is lower in preschool age children than in other age groups

Why?

- Adults less likely to consult with minor resp illnesses
- Young children develop sharper febrile response to resp infections, increased pressure to consult MD
- Young children more susceptible to more resp infections (particularly RSV)
- Doctors may be more resistant to diagnosing influenza in young children, compared to other resp etiologies

Objective #2:

- Determine proportion of ARI and ILI that is due to influenza

% positive for influenza among ARI and ILI

Study site	Years	Age range	Case def?	# positive/total tests	Test type	% pos
NY, OH, TN (NVSN)	2003-2004, 2004-2005	0-5 yrs	ARI (ILI)	76 / 362(03-04) 108 / 752 (04-05)	rtPCR	21 14.4
MI (Tecumseh)	1971-1976	All ages	ARI	200 / 2,227	Cx	9
MI (Ford Co.)	1997-1998	18-64 yrs	ILI	20 / 87	Cx	23
Houston, TX	1974-1976	All ages	ILI	1,819 / 10,146	Sero	17.9
UK	1995-1996	All ages	ILI	218 / 619	rtPCR	35.2
	1996-1997	All ages	ILI	331/ 808	rtPCR	41
	1997-1998	All ages	ILI	160 / 799	rtPCR	20
Paris	1994-1995	>1 yr	ILI	35 / 130	IF	26.9
Bangladesh	May 2007 – Dec 2008	All ages	ILI	375/ 3621	rtPCR	10
Finland	1994-1995	Young adults	ARI	12 / 200	rtPCR	6
Brazil	2001-2003	≥ 18 yrs	ARI/ILI	89 / 420	rtPCR	21.2
Worldwide (Glaxo)	1994-1998	Adolescents and adults	ILI	2470 / 3744	Cx + Sero	66

Factors affecting test outcome

- % positive will vary by time of year (when during influenza season, what other viruses circulating)
- Affected by predominant influenza virus circulating that year, vaccine match to circulating strains
- Case definition that is capturing patients for testing
- Age of the patient
- Test type used for diagnosis
- Selective testing practices
- ARI/ILI often used interchangeably in these studies

Objective #3:

- Test for other viral etiologies of ARI and ILI

Acute respiratory illness in the community. Frequency of illness and the agents involved

A. S. MONTO* AND K. M. SULLIVAN†

*Department of Epidemiology, School of Public Health,
University of Michigan, Ann Arbor*

Table 7. *Estimated percentage of all respiratory illnesses caused by specific etiologic agents. Percentage of such illnesses with physician consultation and annual numbers of each in the population (10 000) of Tecumseh Michigan, USA*

Etiologic agent	Percent of all illnesses caused by each agent	Number of illnesses caused by each agent per 10 000 population	Percent illnesses with consultation	Number illnesses with consultation per 10 000 population
Rhinoviruses	34	8325	17.6	1465
Coronaviruses	14	3428	17.6	603
Influenza	9	2204	37.9	835
Bacterial	8	1959	48.6	952
Parainfluenza viruses	4	979	26.2	257
Respiratory syncytial viruses	4	979	55.6	544
Adenoviruses	2	490	43.2	212
Other viruses	2	490	27.8	136
Unknown and/or non-infectious	23	5630	21.5	1211
Total	100	24484	25.4	6215

Acute Respiratory Infection and Influenza-Like Illness Viral Etiologies in Brazilian Adults

Nancy Bellei,^{1*} Emerson Carraro,¹ Ana Perosa,¹ Aripuana Watanabe,¹ Eurico Arruda,² and Celso Granato¹

¹Clinical Virology Laboratory, Infectious Diseases Unit, Medicine Department, Sao Paulo Federal University, Sao Paulo, SP, Brazil

²Ribeirão Preto Medicine School, São Paulo State University, Sao Paulo, SP, Brazil

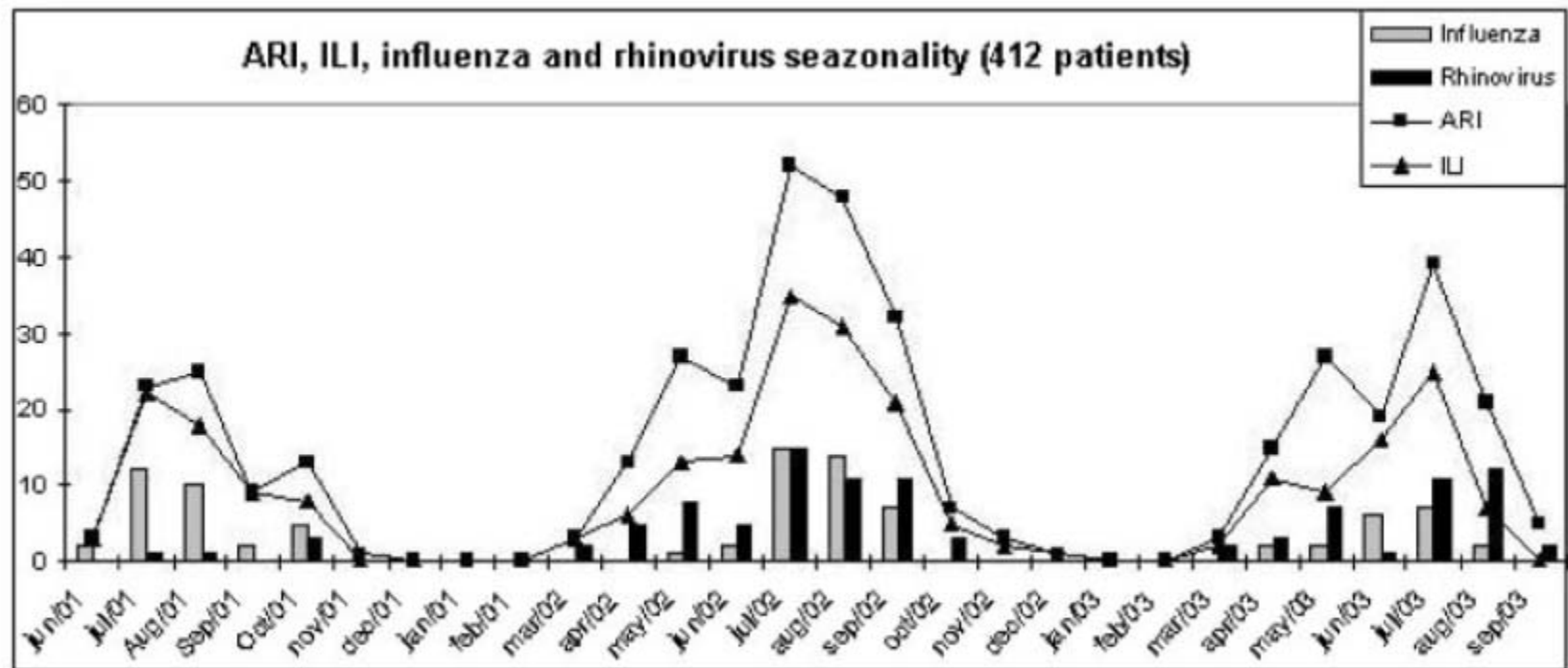


Fig. 1. Adult ARI and ILI case distribution and viral etiologies (influenza and rhinovirus) in Sao Paulo, Brazil (2001–2003).

Acute Respiratory Infection and Influenza-Like Illness Viral Etiologies in Brazilian Adults

Nancy Bellei,^{1*} Emerson Carraro,¹ Ana Perosa,¹ Aripuana Watanabe,¹ Eurico Arruda,² and Celso Granato¹

¹*Clinical Virology Laboratory, Infectious Diseases Unit, Medicine Department, Sao Paulo Federal University, Sao Paulo, SP, Brazil*

²*Ribeirão Preto Medicine School, São Paulo State University, Sao Paulo, SP, Brazil*

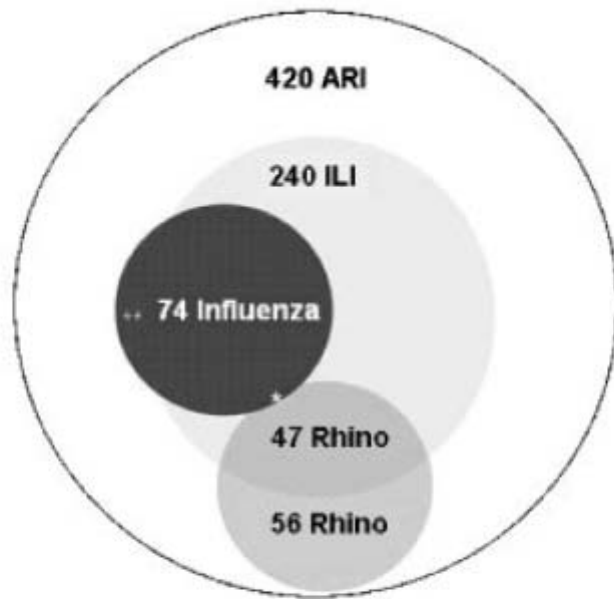
TABLE I. Viral Etiology-Related Distribution of Ages (Median, Years) and Symptom Frequency (%) in Adults With ARI

	Influenza (89) ^a	Rhinovirus (103)	hMPV (24)	Adenovirus (17)	RSV (10)	Coronavirus (18)	Enterovirus (9)
Age	27	31	39	34	39	40	29
Fever	91.0	50.5	54.2	58.8	60.0	55.6	55.6
Cough	85.4	80.6	79.2	88.2	80.0	72.2	77.8
Coryza	76.4	91.3	87.5	82.3	100	88.9	100
Sore throat	51.7	60.2	58.3	76.5	80.0	44.4	22.2
Headache	85.4	75.7	75.0	70.6	60.0	88.9	66.7
Myalgia	78.6	59.2	70.8	52.9	50.0	61.1	55.6
Chills	66.3	44.7	45.8	70.6	40.0	50.0	55.6

^aNumber of samples.

- 420 specimens collected, 260 positive (including 14 coinfections)
- Coinfections included combinations of all viruses tested except RSV

Flu = ILI ? Colds = ARI?



*Influenza and rhinovirus co-infection detected in one patient.

** Laboratory confirmed influenza in 15 patients presenting ARI without ILI.

Fig. 2. Diagram of ARI and ILI cases, and those caused by influenza and rhinovirus.

A diagnosis of ILI was made in 240 (57.1%) of 420 patients with ARI. Influenza was detected in 30.9%, rhinovirus in 19.6%, and other respiratory viruses in 13.7% of the ILI cases. The majority of influenza-positive cases (86.9%) presented with ILI symptoms, in contrast to 46.9% for those cases positive for rhinovirus.

Summary

- What contributions is this study providing to the existing knowledge base of ARI and ILI burden?
 - Rare opportunity to conduct population-based surveillance in an outpatient setting, update etiology studies, improve data used for the assessment of the impact of influenza vaccination (most only use ILI, hosp and death)
 - Comparison of ARI and ILI with respect to burden, etiologies, symptoms
 - Evaluation of symptoms common for different pathogens