Respiratory Viral Infections in Children

Janet A. Englund, M.D.
Pediatric Infectious Disease,
Seattle Children's Hospital, University of Washington
Fred Hutchinson Cancer Research Ctr

ANMC
Anchorage

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CONFLICT OF INTERESTS

- My children attended daycare.
- Research Support: MedImmune, Novartis, sanofi pasteur
- Government support: VTEU,
- Consultant for FDA, ACIP

COMMON RESPIRATORY VIRUSES: YOU KNOW THESE ALREADY

- Respiratory Syncytial Virus (RSV)
- Influenza A and B
- Parainfluenza viruses 1-3

- THE REST

NEW AND EMERGING RESPIRATORY VIRAL INFECTIONS

- APPRECIATION OF IMPORTANT "OLD" VIRUSES:
  - Adenovirus
  - Rhinovirus
- EPIDEMIOLOGY OF NEW VIRUSES
  - HUMAN METAPNEUMOVIRUS
  - CORONAVIRUS (new types)
  - HUMAN BOCAVIRUS
  - AVIAN INFLUENZA

WHAT IS MOST IMPORTANT FACTOR IN CLINICAL VIROLOGICAL TESTING?

A GOOD SPECIMEN

- Good clinical specimen obtained MOST critical factor in accurate diagnosis.

- Specimen collection should be performed by trained personnel.
- Nasal wash is well tolerated in cooperative adults and does not result in bleeding.
- BAL is specimen of choice in patient with lower respiratory tract disease.
- Nasal swab preferred in uncooperative adults.
- Throat swabs are inferior - why not flip a coin?

RSV: EPIDEMIOLOGY

- Transmission via direct or close contact with secretions, droplets, fomites
- Virus may persist on surfaces for hours
- Annual midwinter epidemics
- Nearly all children infected by 3 years of age
- Shedding in young children up to 1 month
- Even longer shedding in immunocompromised children

THE BEST RSV STUDY EVER: RSV Transmission Study*

	Cuddlers	Touchers	Sitters
No. exposed	7	10	14
No. infected	5	4	0

Cuddlers and Touchers transmit RSV, sitters don't

→ Small particle aerosol not major means of spread

* Hall & Douglas, J Pediatrics 1991

HOW TO PREVENT SPREAD OF RESPIRATORY VIRUSES

- Isolate based on symptoms, not diagnosis
- Hand washing
- Hand washing
- Hand washing

- Consider gown and glove in certain conditions…

RESPIRATORY SYNCTYIAL VIRUS (RSV) CLINICAL DISEASE

- Any age:

  acute respiratory illness, including cold symptoms only, fever, rhinorrhea, sore throat, coryza, cough (in any combination)

- Infants and young children:

  most frequent cause of bronchiolitis, pneumonia, otitis

- Premature infants:

  respiratory signs are minimal but apnea, lethargy, irritability common

- Immunocompromised individuals:

  fever, pneumonia, sinusitis, otitis, ARDS

RSV: Long-Term Sequelae

- Long-term sequelae of RSV infection in children:
  - Some children with severe RSV disease develop long-term abnormalities
  - Genetic predisposition to abnormal airways, small airway size (male gender); also associated with predelection for persistent reactive airway abnormalities*
  - Development of bronchiectasis and persistent pulmonary disease in subpopulations

* Martinez et al, NEJM 1995

Recent Trends in RSV Hospitalizations

- Bronchiolitis hospitalizations increasing
  - 1980-1996: 1.65 million hospitalizations
  - 7 million inpatient days
  - 57% in children <6 months of age
  - 81% in children <1 year of age
  - 239% increase in bronchiolitis hospitalizations in children <6 months old

(Shay DK et al. Bronchiolitis-Associated Hospitalizations Among US Children, 1980-1996. JAMA Vol 282, No 15 1999.)

PREVENTION OF RSV

- At-risk preterm infants or those with chronic lung or heart disease:
  - RSV monoclonal antibody prophylaxis (monthly Synagis)
  - Consider type of childcare
- Healthy term infants: 80% of hospitalized babies with RSV are > 36 weeks gestation
  - Recommend hand washing
  - Deliver your baby in June or July (this might not work in Alaska)
  - ??????????????

AAP Guidelines: RSV Prophylaxis*

- Candidates for Synagis® (palivizumab) prophylaxis:
  - Infants with chronic lung disease <2 years of age at onset of RSV season with medical management of lung disease within 6 M.
  - Infants born at ≤ 28 weeks gestation up to one year of age at the onset of RSV season
  - Infants born at 29-32 weeks gestation up to six months of age at the onset of RSV season
  - Infants born at 32-35 weeks gestation with additional risk factors for severe RSV disease
  - Infants with symptomatic congenital heart disease

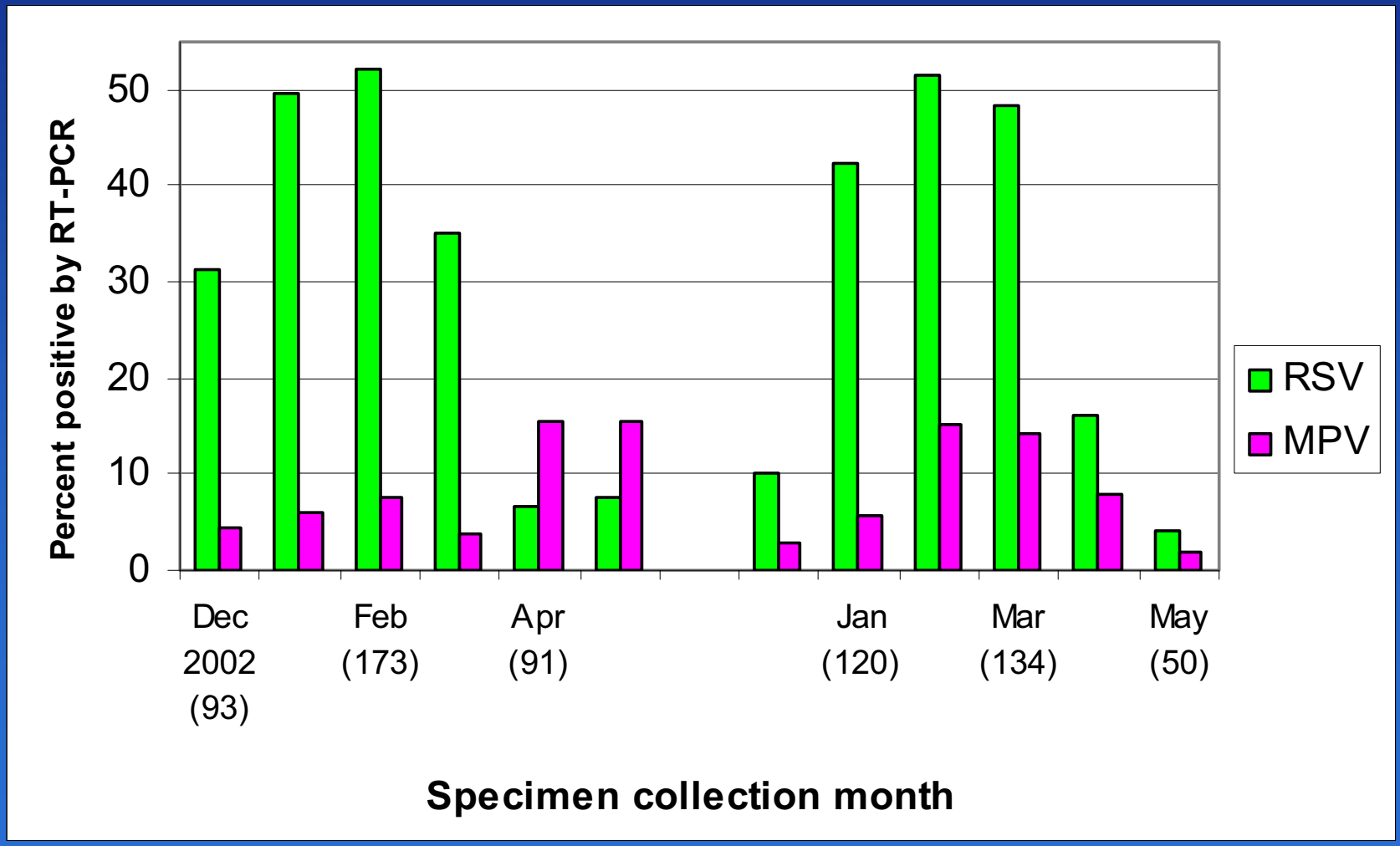
Pediatrics 2003;112:1442-6; 2003 REDBOOK: p525

FORMULATION OF NEW RSV-SPECIFIC MONOCLONAL ANTIBODY

- Multicenter clinical studies ongoing for new version of palivizumab sponsored by MedImmune:
  - 3rd generation, anti-RSV molecule offering significant advantages (higher "potency")
  - 2002: New antibody selected: "Numax"
- 2003: MedImmune submitted IND application to FDA to evaluate Numax.
- 2006: Clinical studies with Numax in children with BPD and cardiac disease completed and submitted to FDA; request for further study in cardiac patients
- 2008: Cardiac study year 2 completed

- ?IS MONTHLY DOSING GOING TO BE NECESSARY??

Human Metapneumovirus Detection at Seattle Children's Hospital



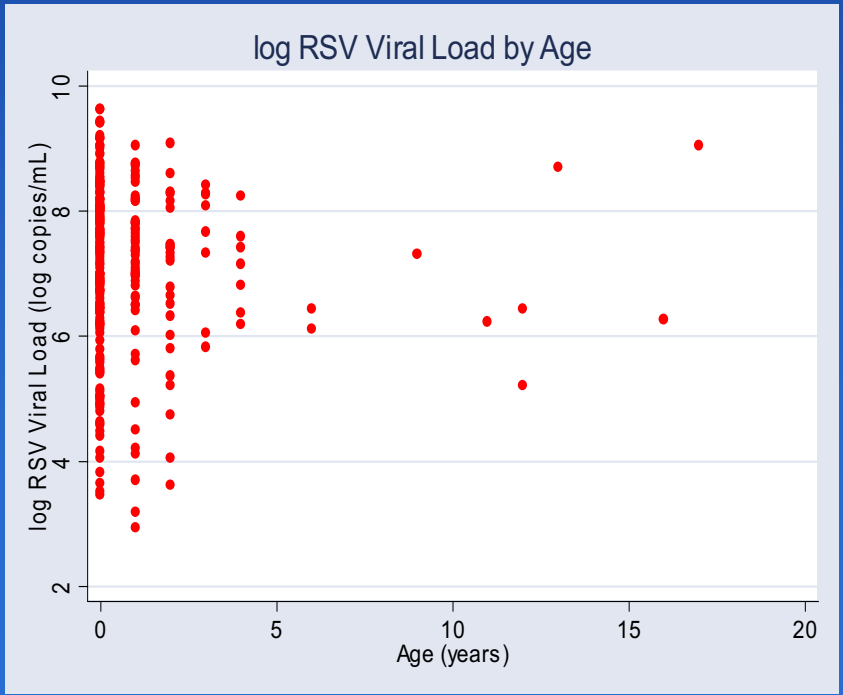
DFA is a great test for RSV Using PCR as the Gold Standard

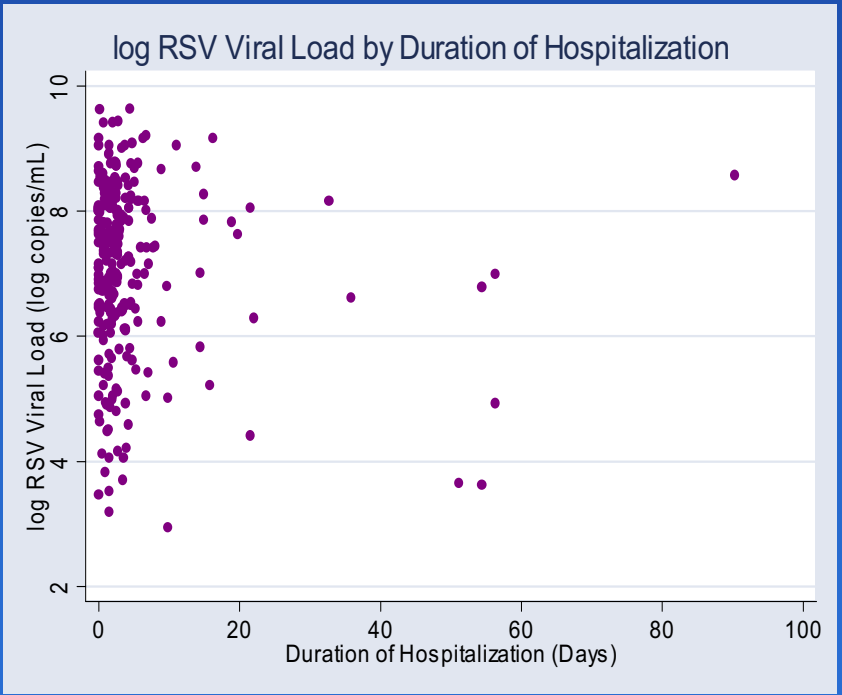
Result		Number (%) of samples (Total = 687)
DFA +	PCR +	257 (37)
DFA +	PCR -	6 (1)
DFA -	PCR +	20 (3)

Sensitivity of DFA = 93% Specificity of DFA = 98%

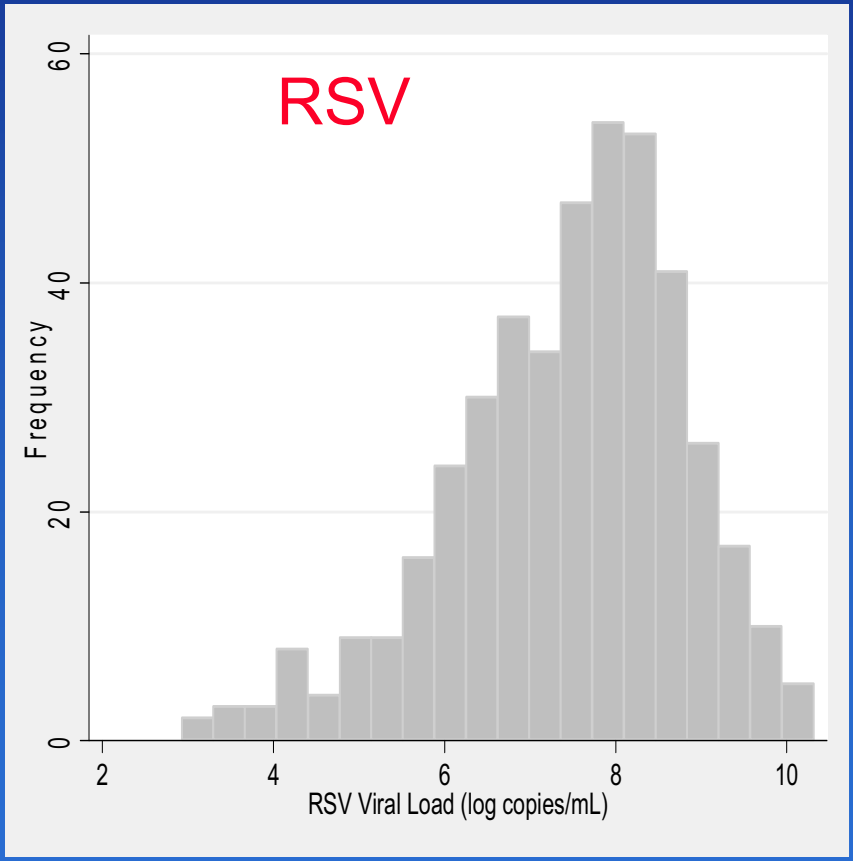
Relationship between RSV Viral Load and Other Covariates

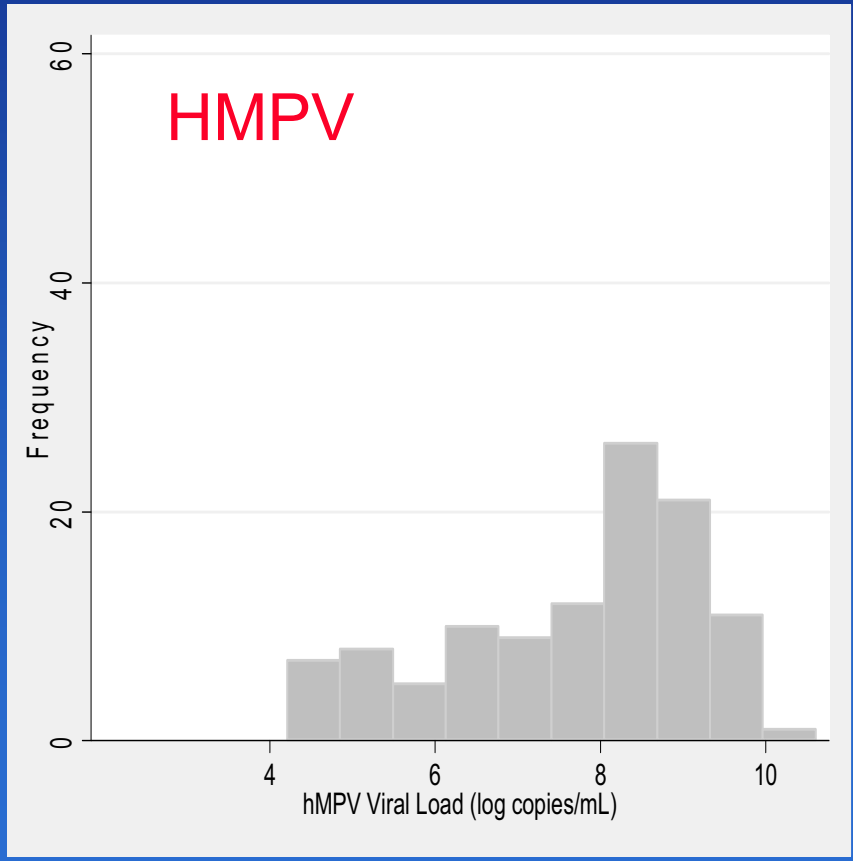
- RSV viral load inversely correlated with age
- No correlation was found between viral load and severity of disease, admission to hospital or admission to ICU.





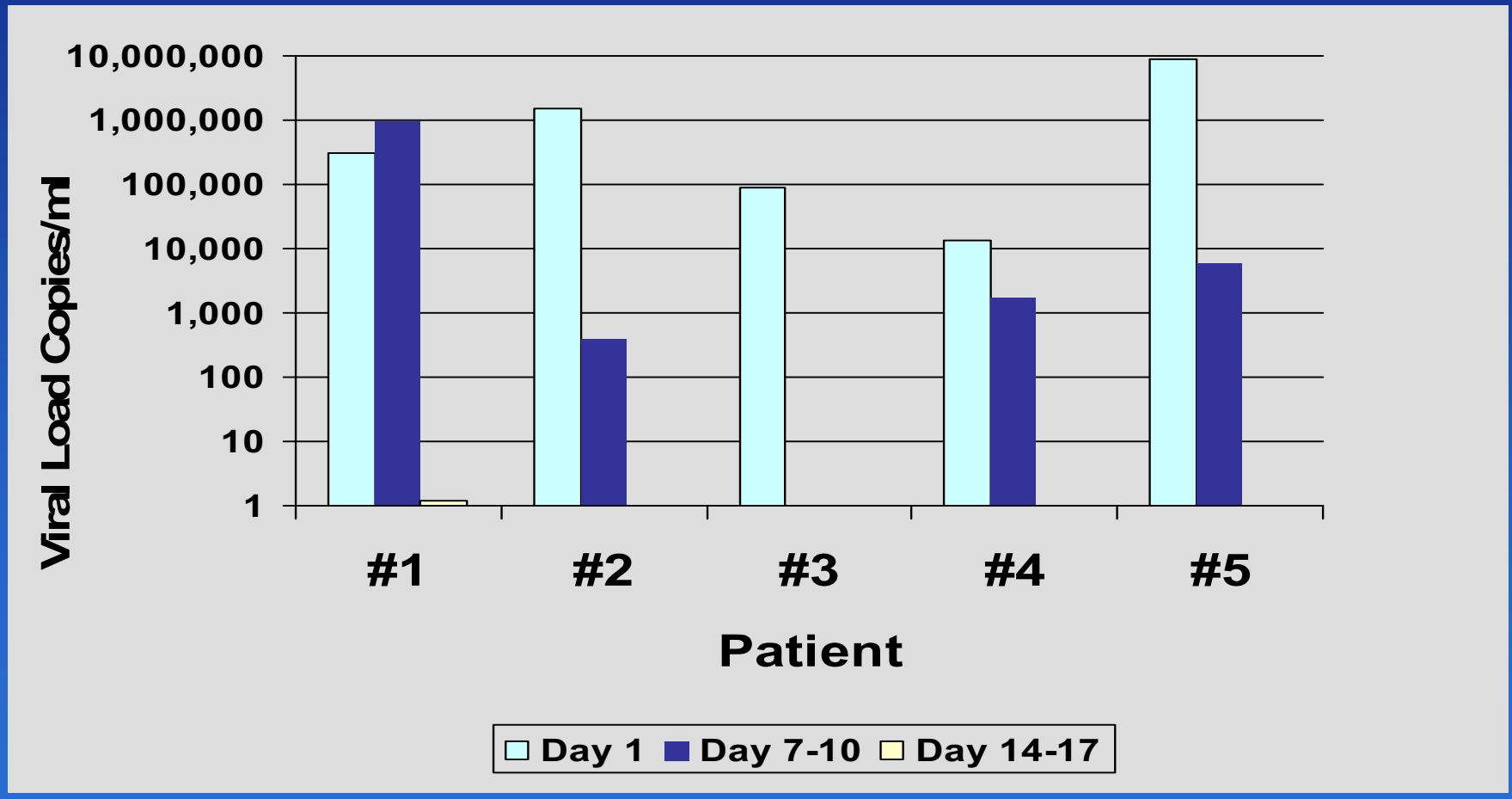
RSV and VIRAL LOAD of RSV (N=418) and HMPV (N=) in Hospitalized Children*





*Martin et al 2008, Diag Micro Infect Dis (in press)

Sequential HMPV Viral Loads Over Time in Outpatient Infants*



*Kunz et al, EJCMID 2008

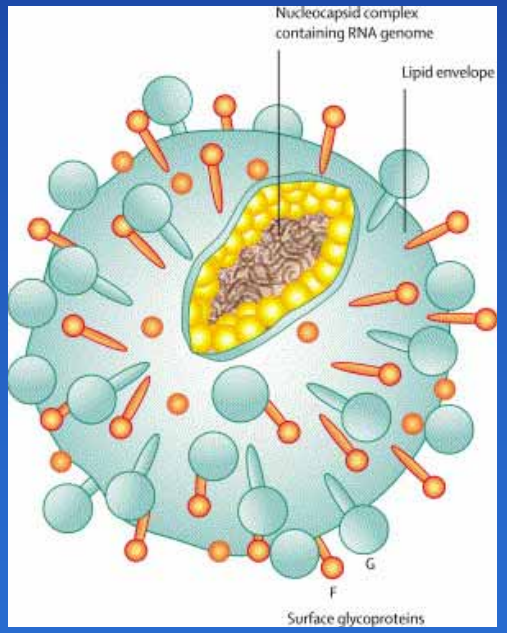
Impact of Bronchiolitis

- Most frequent manifestation of lower respiratory tract infection in young children.
- Results in the hospitalization of 2-3% of children under the age of 1 year[1]; up to 10% in certain high risk populations[2]
- Estimated annual cost of hospitalization for bronchiolitis in children less than 1 year of age is over $700 million[3].

[1]Lancet 2006;368:312, [2] Singleton PIDJ [3]Pediatrics 2006;118:1774

Viral Pathogens of Bronchiolitis

- RSV, the most common virus associated with bronchiolitis, accounts for 40-80% of cases[1].
- Other viral pathogens include:
  - Parainfluenza
  - Adenovirus
  - Influenza
  - Human metapneumovirus



Lancet 2006;368:312

[1]Principles and Practice of Infectious Diseases 2005;6th ed:812

BRONCHIOLITIS: 2006 AAP Guidelines

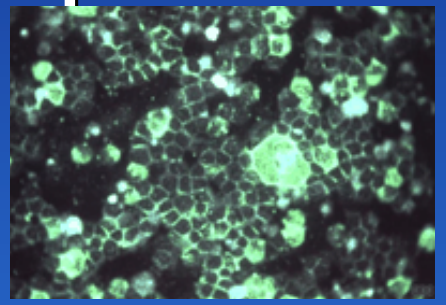
- Diagnose bronchiolitis on basis of history and physical.
- Routine viral testing is not recommended
  - "The knowledge gained from such testing rarely alters management decisions or outcomes for the vast majority of children with clinically diagnosed bronchiolitis."
  - "Virologic testing may be useful when cohorting of patients is feasible."

Pediatrics 2006;118:1774

What are the Viral Pathogens of Bronchiolitis?*

Methods:

- Direct immunofluorescent antibody assay conducted real-time on NW, BAL samples:
  - RSV, parainfluenza (types 1-3)
  - Influenza A and B
  - Adenovirus



- Multiplex Real-Time PCR performed for the above viruses, HMPV, coronavirus
- Limitation: Rhinovirus NOT tested

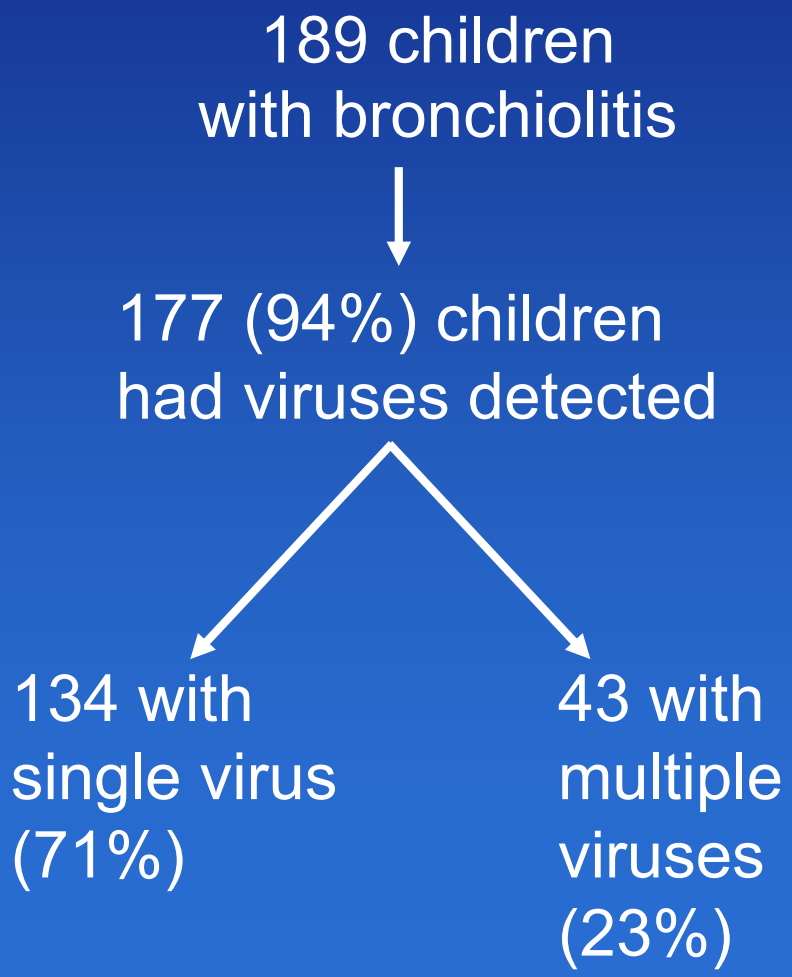
Results*

- 189/831 (23%) of samples collected were from children between 0-36 months evaluated for bronchiolitis.
  - Median age: 6.7 months
  - 54% were male
  - 26% had an underlying disease

- Samples were acquired from:
  - General pediatric ward: 72%
  - Emergency Department: 21%
  - Intensive Care Unit: 7%

*Stempel et al Acta Paediatrica 2008

Results: Viral Pathogens in Children with Clinical Bronchiolitis*



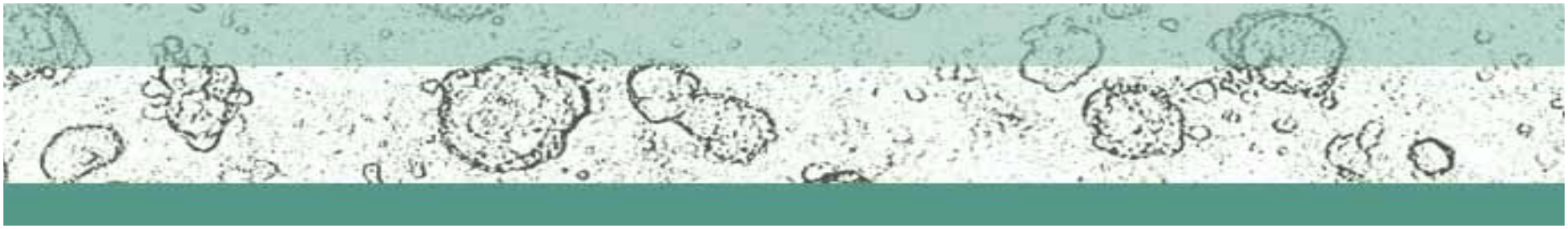
Virus	Number detected (n=220)
RSV	**145**
Adenovirus	**28**
hMPV	**20**
Coronavirus	**14**
Parainfluenza	**12**
Influenza	**1**

*Stempel et al Acta Paediatrica 2008

Respiratory Pathogens in Children with Bronchiolitis, By Age Group

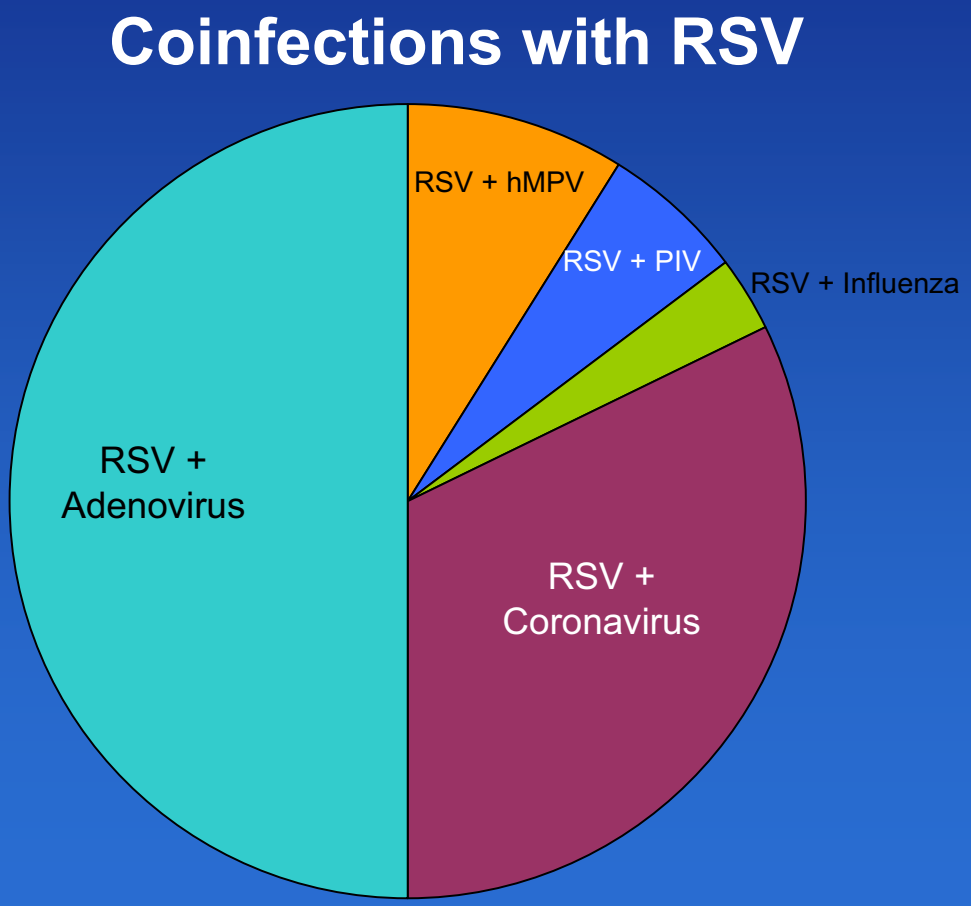
Age	RSV	AdV	hMPV	CoV	PIV	No virus detected
< 6 mo n= 83	84%	5%	10%	6%	2%	5%
6 mo - 1 yr n= 51	73%	22%	14%	6%	12%	6%
1 - 2 yr n= 46	70%	22%	9%	13%	4%	13%
2 - 3 yr n= 9	68%	11%	11%	0	22%	0

TOTAL: 189 Children



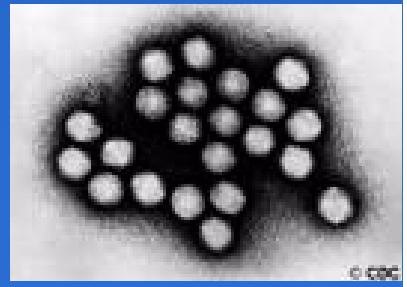
Coinfections

- 43 samples had 2 or more viruses detected, 35 (81%) of these involved RSV
  - 1 sample had a three-way infection: RSV, hMPV, and adenovirus
- 8 other coinfections:
  - hMPV + PIV (n = 4)
  - hMPV + AdV (n=3)
  - PIV + AdV (n=1)



BRONCHIOLITIS: Summary

- High rate of viral detection
  - At least one virus was identified in 94% of children
- RSV is the most predominant pathogen associated with bronchiolitis but 40% of children were infected with other viruses
- 12% of patients had a single infection with a virus other than RSV



Images: AAP Red Book Online

Influenza Makes Headlines…..

Epidemic (annual) influenza outbreaks are a regular and important problem here and worldwide……

Girl, 7, with flu dies; 300 out sick, high school closes

BUT OFFICIALS SAY FLU LEVELS "TYPICAL"

Rare complication kills child in Kent; Blanchet High shuts down until Monday

BY WARREN KING AND BRIAN ALEXANDER
Seattle Times staff reporters

A 7-year-old Kent girl has died of a rare complication of influenza and a private Seattle high school has closed for the rest of the week as the flu season reaches its peak, public-health officials say.

Bishop Blanchet High School in North Seattle announced that it won't reopen until Monday because more than 300 of the Catholic school's 1,080 students have called in sick this week, mostly with flu symptoms.

The Seattle Times

Feb. 2007

Health officials confirm 2nd girl died from flu complications

Marija Alumbaugh, 8, died Wednesday.

BY BRIAN ALEXANDER
Seattle Times staff reporter

The King County Medical Examiner Friday confirmed this season's second pediatric flu death, saying complications from influenza killed 8-year-old Marija Alumbaugh, a second-grader at Laurelhurst Elementary School.

Marija is the second flu death in King County since 1999 — 7-year-old Sarah Horner of Kent died Feb. 5 — but health officials say there doesn't appear to be a connection between the two deaths and that this doesn't appear to be a particularly bad flu season.

"It's understandable that parents would be concerned, and these two cases are unquestionably tragic. What we want to emphasize is that for people who do get ill in the community as a whole, the severity of the illness does not seem to be unusual, any more severe than in recent seasons," said James Apa, spokesman for Public Health — Seattle & King County. "It's important for people to keep in mind, too, that influenza can cause complications — it can be a serious illness."

Both girls died of myocarditis, inflammation of the heart muscle, a rare but serious complication from the flu, according to the medical examiner.

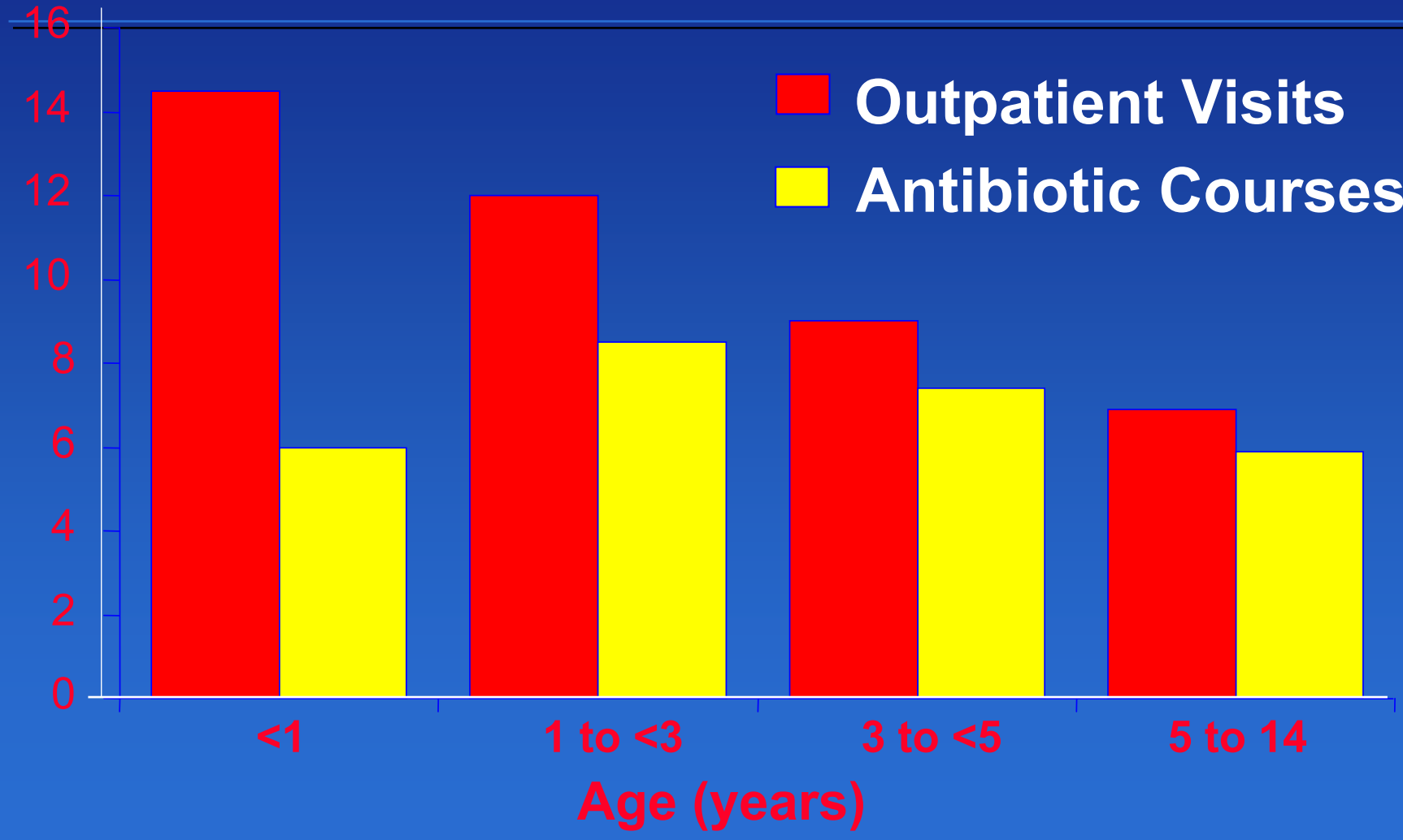
Health officials reminded the public this week that the flu vaccine is

Please see > FLU, B6

"It's important for people to keep in mind, too, that influenza can cause complications – it can be a serious illness."

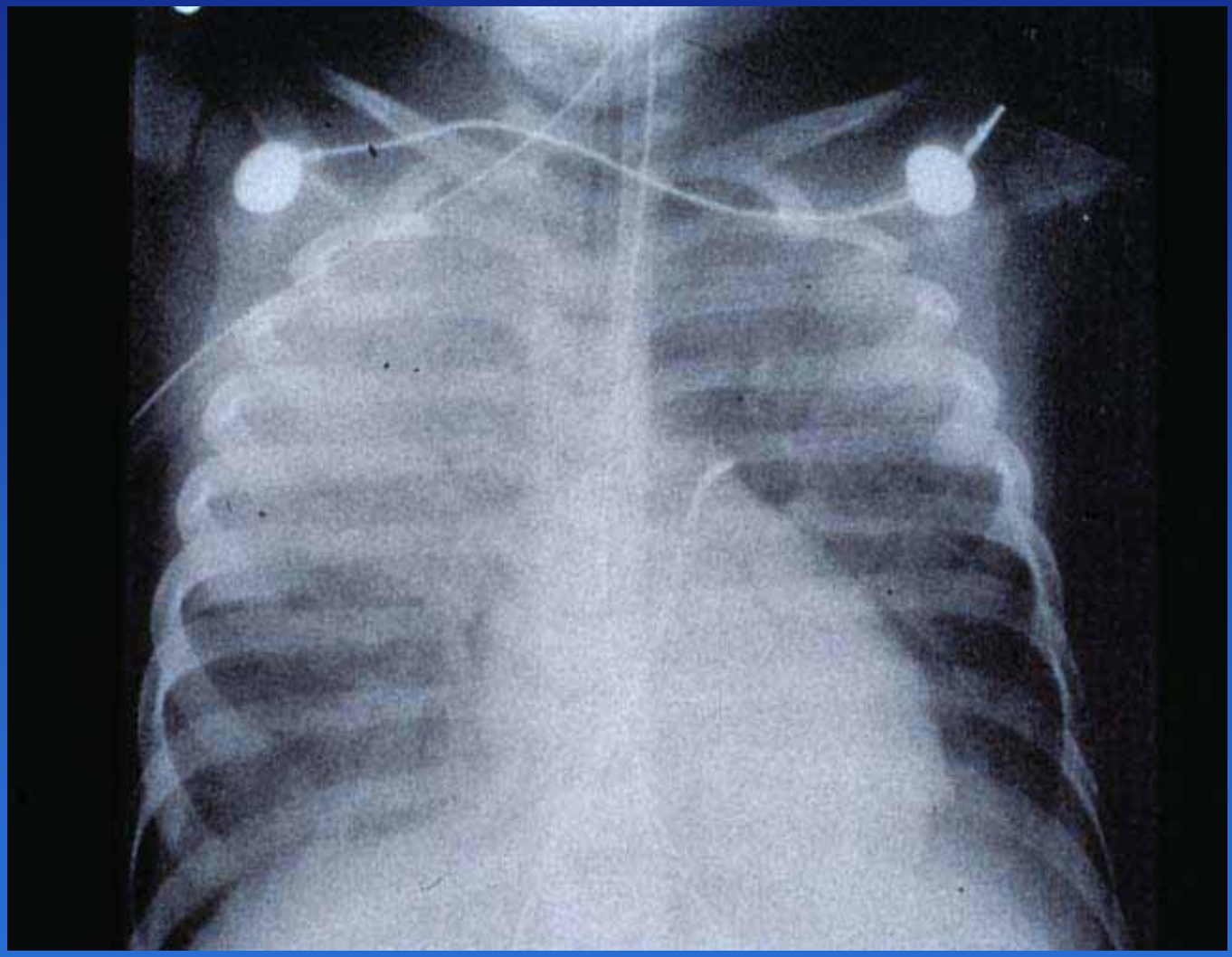
JAMES APA
Public Health – Seattle & King County

Influenza-Attributable Outpatient Events Per 100 Children



Neuzil et al. *NEJM* 2000;342:225-231.

2008: INFLUENZA and MRSA



Fatal influenza pneumonia, 6 year old previously healthy child

US ACIP Influenza Vaccine Recommendations: 2009

- Children >6 months with chronic conditions:
  - Cardiac
  - Renal
  - Metabolic
  - Hematologic
  - Pulmonary
  - Hepatic
  - Neuromuscular disorde
  - Immune compromise
- Children 6-59 months of age
- Healthy household contacts of high-risk groups
- ETC. ETC

- **ALL CHILDREN 6 MONTHS-18 YEARS**

Influenza Vaccine: 2 choices

Trivalent inactivated

- Injection
- Indicated for:
  - >6 months
  - Anyone *
- Need 2 doses first year for children <9 (really!!)

Live attenuated

- Nasal
- Indicated for:
  - 2-49 yrs of age
  - Generally healthy
- Need 2 doses first time for children <9 (maybe)

*except egg allergy, Guillain Barre

Challenges of Influenza Vaccination in Children

- Annual vaccination required
- Logistics (2 doses in short time in fall)
- Vaccine supply
- Costs
- Public perception
- Practical issues (clinic volume, crowded immunization schedule, family inconvenience)

- LOTS OF VACCINE THIS YEAR AND IT'S BEING DELIVERED!

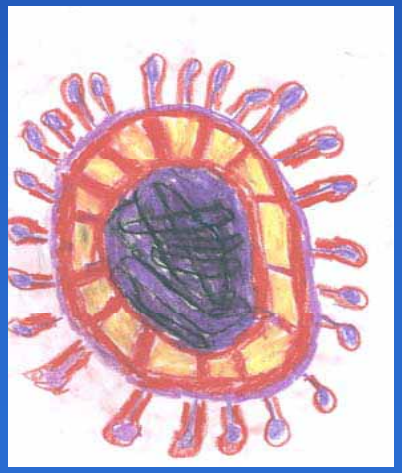
- PREPARE NOW FOR 2009

Diane Kinnunen, RN, with study participants

SARS OUTBREAK 2003:

THE MOST DEADLY CORONAVIRUS

Identified cooperatively using new scientific tools and old fashioned epidemiology…



Artist: Peter Scott, Age 8

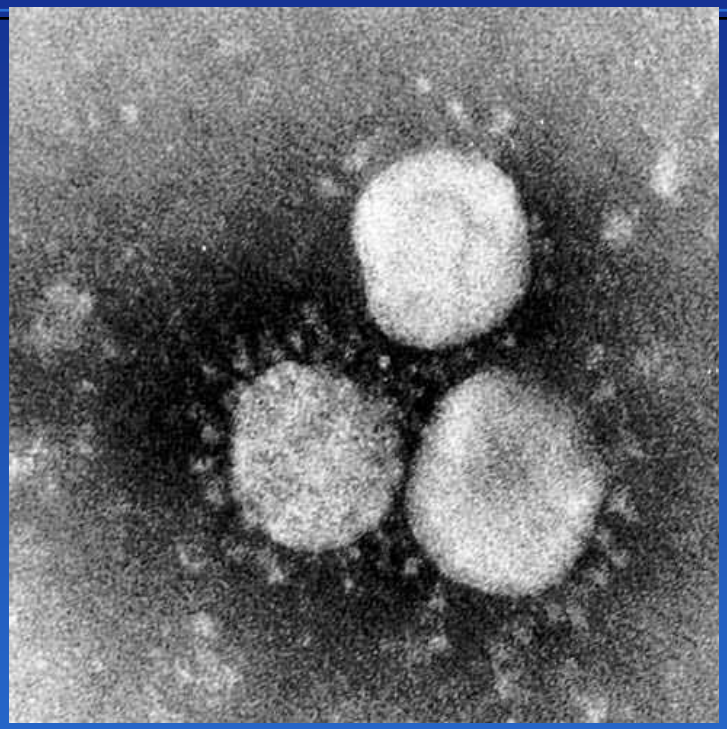
The SARS-Associated Coronavirus

Chinese horseshoe bat reported as reservoir for SARS (*Yuen et al, PNAS 2005)

Tsang et al. NEJM 3/31/03

NEW CORONAVIRUSES

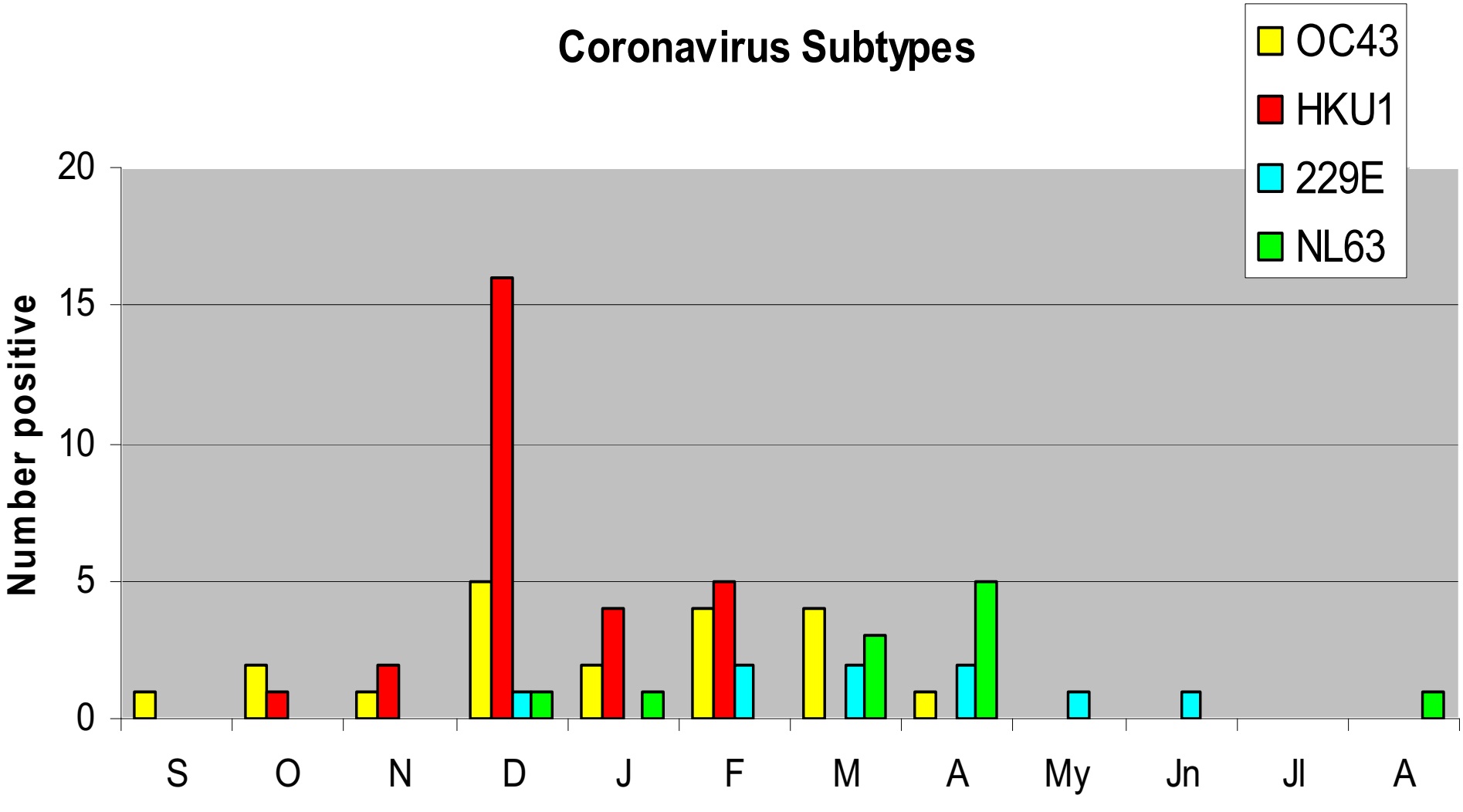
CORONAVIRUS
Group 1:
HCoV-229 E (OLD)
HCoV-NL63
Group 2
HCoV-0C43 (OLD)
CoV-HKU1
Group 3- IBV
SARS-CoV



Crown = spike protein

www.pmarneffei.hku.hk

ALL FOUR CORONAVIRUS SUBTYPES DETECTED IN FALL/WINTER, 2003-4



Kuypers et al Pediatrics 2007;119:e70

CORONAVIRUS-ASSOCIATED PNEUMONIA IN NORMAL CHILDREN*

- Most hospitalized children with coronavirus (14/21, 81%) had underlying diseases
- 4 previously healthy children with CoV as sole respiratory pathogen; 2 had CXR taken
- Radiographically confirmed pneumonia demonstrated in both patients :
  - 14 M girl with RLL consolidation
  - 3 M boy with pleural effusion

14-month girl with “round pneumonia” and coronavirus as sole pathogen

Kuypers et al Pediatrics 2007;119:e70; Heugel et al PIDJ 2007; 26:753

Who's the first researcher to have coronavirus disease in my group? I can't tell due to HIPPA…

BOCAVIRUS

- New virus discovered by investigators at Karolinska Institute, Sweden, using molecular detection methods in respiratory secretions from symptomatic children in whom no other viruses detected
- DNA virus related to BOvine and CAnine parvovirus (BOCA)
- Associated with pneumonia, diarrhea, URI symptoms in multiple published studies, most of which are ER studies or incidence studies in symptomatic hosts.

- IN SEATTLE LONGITUDINAL STUDIES*:
  - Detected in young infants and it never goes away*…
  - Detected in NW of bone marrow transplant patients without any correlation with respiratory symptoms**…
  - Is it a true pathogen?

*Martin et al , abstract IDSA 2008; ** Campbell et al, abstract IDSA 2008

WHAT IS THE IMPORTANCE OF ALL THESE VIRUSES?

- We now have sensitive, reliable methods to detect lots and lots of viruses BUT:
  - Which viruses are most important to children?
  - Which viruses are most important to the medical care system?
  - Which viruses cause absenteeism in children or their parents?
  - What impact does day care have on the spread of respiratory viruses?

Madigan Army Medical Center Day Care Study, 2006-2008*

- **Prospective, longitudinal cohort study of the epidemiology and clinical characteristics of viral respiratory tract infections in children < 3 years of age attending daycare centers at Ft. Lewis, WA.**
- **Active followup facilitated by study nurse on site**
- **Real-time reverse transcription (RT) polymerase chain reaction (PCR) panel utilized to detect 15 respiratory viruses from nasal swabs in symptomatic children**

Toddler room, Ft. Lewis Day Care Center, 2007

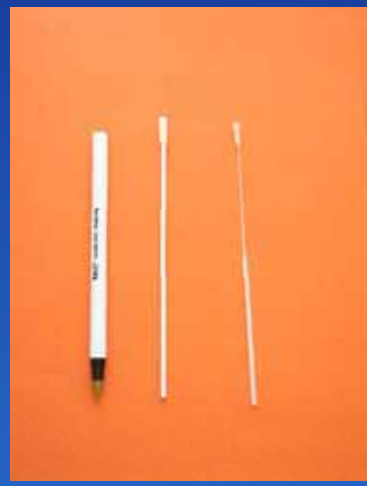
*Fairchok M, et al. IDSA, 2007.

DAYCARE STUDY: Methods

- Respiratory tract infection defined as the presence of 2 of 5 symptoms (cough, rhinorhea, wheezing, fever, or nasal congestion).
- Posterior nasal swab obtained at enrollment, and weekly during each respiratory illness until symptoms resolved.
- Daily symptom diary completed by child's caretaker until illness resolved.
- Standardized form completed by MD at clinic visit

Laboratory Methods

- Nylon flocked swab (Copan Diagnostics, Corona, CA) applied in the posterior nasopharynx, rinsed vigorously in 0.5 ml of lysis buffer, and discarded

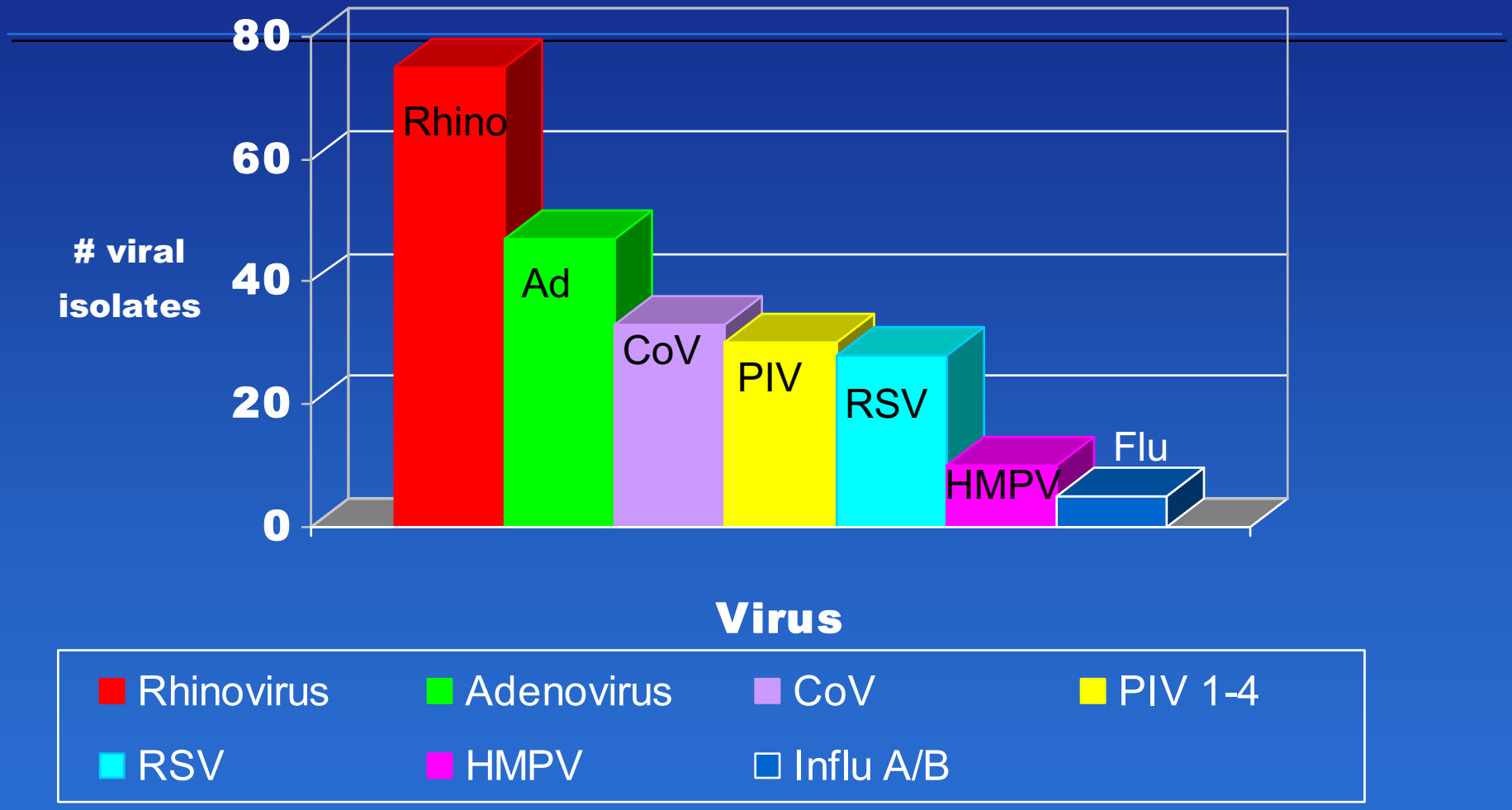


- Total nucleic acid was extracted from the buffer using previously described techniques (Kuypers et al, J Clin Micro 2007)
- RT-PCR detected:
  - RSV A/B
  - Human metapneumovirus (HMPV),
  - PIV 1-4
  - Influenza A/B
  - Rhinovirus (RhV)
  - Human coronaviruses (4 types)
  - Adenoviruses (AdV); Bocavirus

Burden of Respiratory Illness in Daycare Attendees < 30 M

	Mean (Range)
Symptomatic episodes per child per year	6.2 (0-9)
Symptomatic episodes per 100 child-weeks	12.1
% days with respiratory symptoms	20% (0-89%)
Duration of symptoms	7.4 days (1-64)

Results: Virus Identification



≥ one virus detected in 149/242 (61.5%) respiratory infections

Impact of Viral Infection

	Medical Care Visits N (%)	Mean Days of Day Care Missed	Mean Parental Days of Work Missed
All Illness Episodes (242)	123 (51)	1.4	1.3
RSV (28)	23 (82)	1.7	1.8 (p=.02)
RhV (75)	40 (53)	1.1	1.1
AdV (47)	25 (53)	1.4	1.1
CoV (33)	19 (58)	1.7	1.3
PIV (30)	19 (63)	.9	.9
HMPV (10)	6 (60)	1.6	1.1

Spread of RSV in Day Care Modules

- At least one RSV infection was observed in children attending 7/13 separate classroom modules
- Subsequent RSV cases documented in 4/7 of these rooms, occurring from 1 to 10 days later.
- In rooms with 5-15 children enrolled, the rate of RSV infection rapidly increases:
  - After first case: 31%-57% of study children in the same room are symptomatically infected with RSV within one month

DAYCARE STUDY: Conclusions

- Similar frequency of symptomatic respiratory tract infections in daycare attendees now compared with 30 years ago
- Multiple respiratory viruses, including RSV, parainfluenza, and other viruses not previously detectable (rhino, HMPV) were responsible for substantial disease.
- RSV had the greatest clinical impact of all viruses, as measured by febrile episodes, medical visits, missed days of day care and parental absenteeism from work.
- Symptomatic RSV disease within individual rooms increased rapidly with infection rates within individual rooms of 31% to 57% one month later

Future Questions

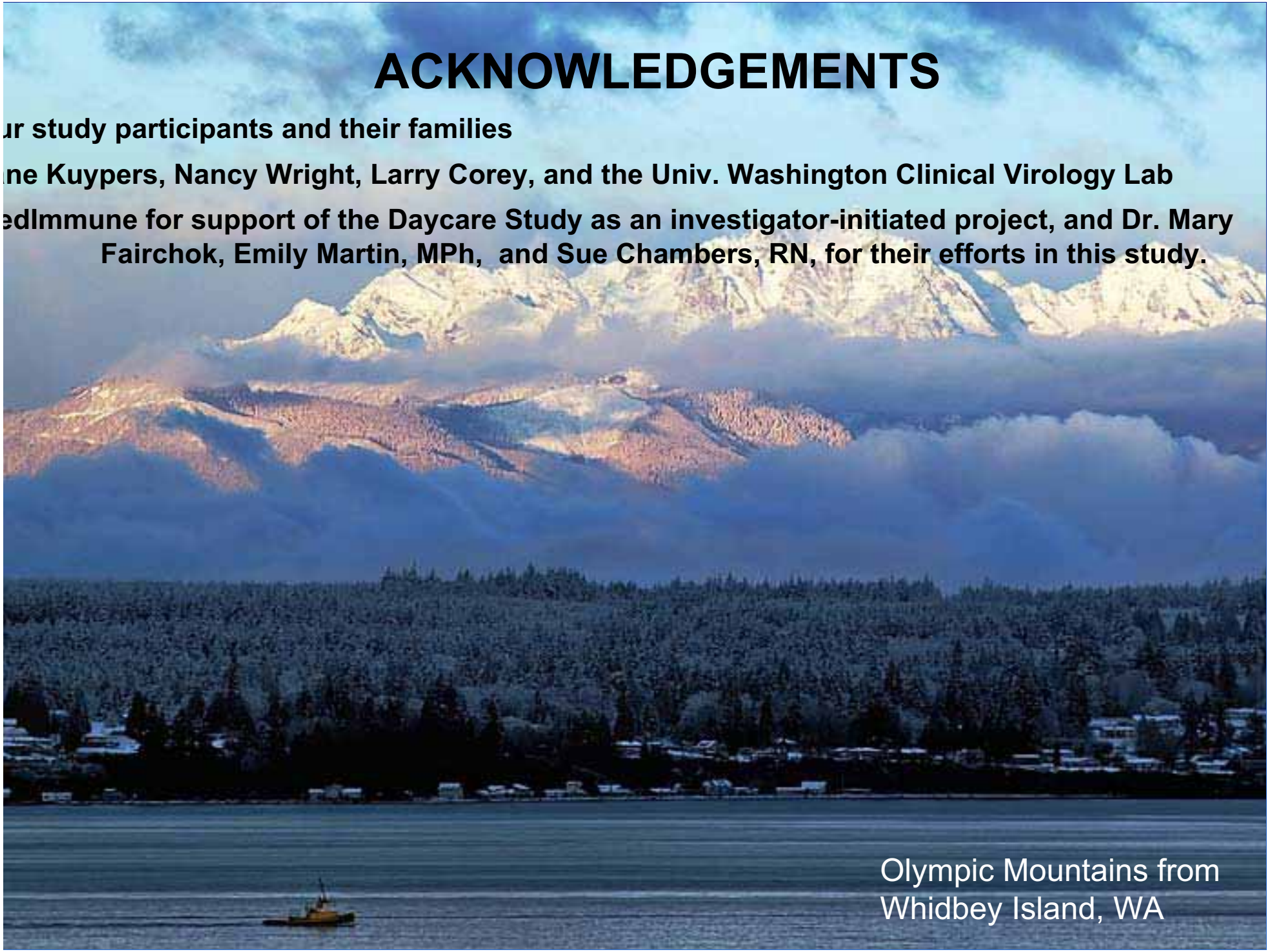
- What is the role of specific pathogens in viral respiratory disease progression and severity?
- How do viral coinfections impact disease course?
- What is the utility of viral diagnosis for cohorting and management?

ACKNOWLEDGEMENTS

ur study participants and their families

ne Kuypers, Nancy Wright, Larry Corey, and the Univ. Washington Clinical Virology Lab

edImmune for support of the Daycare Study as an investigator-initiated project, and Dr. Mary Fairchok, Emily Martin, MPh, and Sue Chambers, RN, for their efforts in this study.

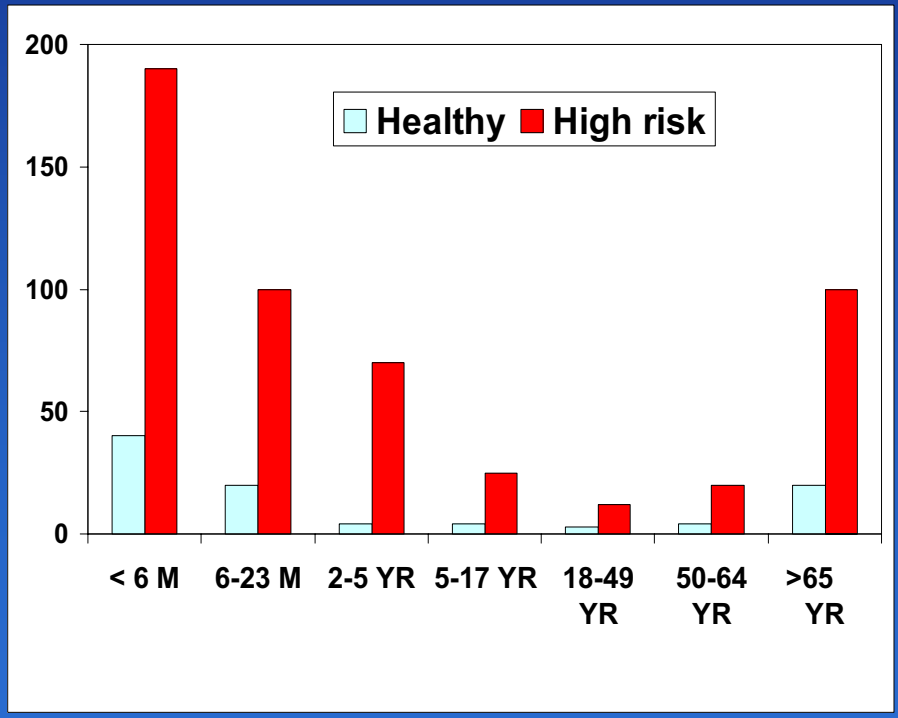


Olympic Mountains from Whidbey Island, WA

INFLUENZA: AGE-RELATED DISEASE

- Young children are at high risk for influenza-related disease and complications.
- Children < 6 months of age have the highest rates of hospitalization and medically-attended illnesses of any age group, but no licensed influenza vaccine for this age group.
- No licensed effective antiviral available for this population.

Influenza-associated Hospitalizations per 10,000 Healthy and High Risk Persons by Age Group*

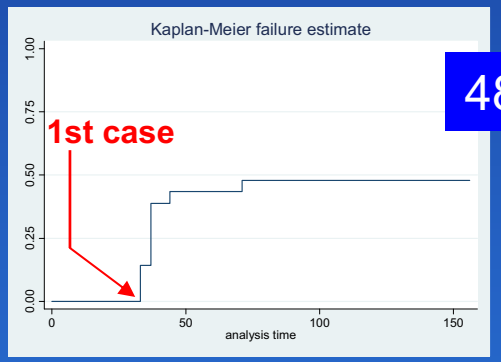


* Glezen et al. Am Rev Respir Dis 1987;155:1119-26;
Neuzil et al. NEJM 2000;342:225-231;
Neuzil et al. J Pediatr 2000;137:856-864.

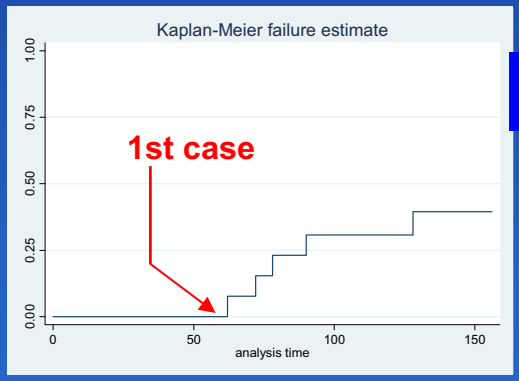
RSV Acquisition in Day Care Settings

Rates of children becoming infected with RSV in individual classrooms over time, based on Kaplan-Meier Failure estimates

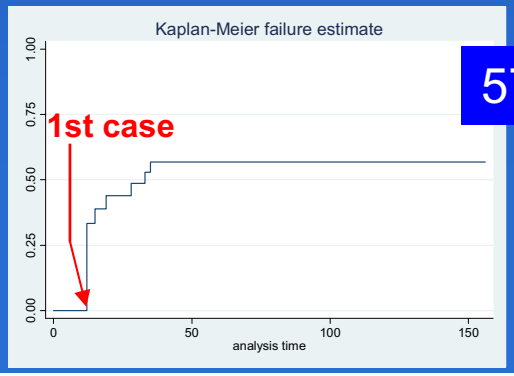
(Note: failure = infection)



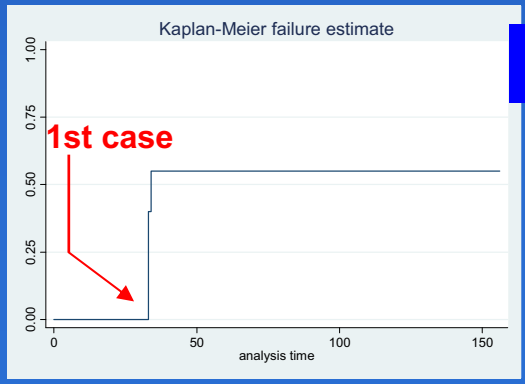
48%



31%



57%



55%

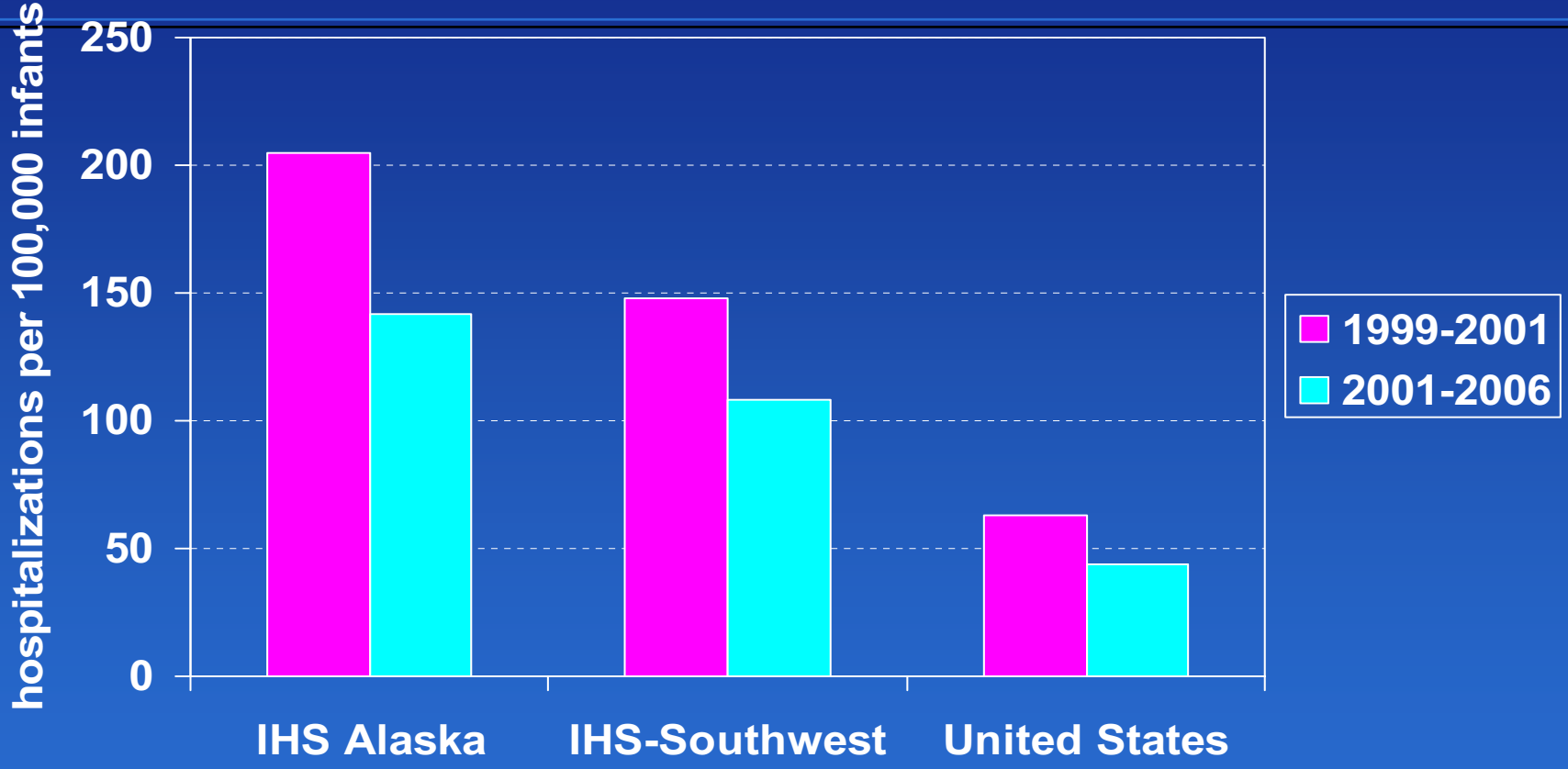
Unique Features of Respiratory Infections and RSV in Alaska:

Rosalyn Singleton MD,
ANTHC
AIP-CDC
Anchorage, Alaska
729-3418
ris2@cdc.gov

Outline

- RSV Background
  - Active surveillance (1993-1996)
  - Case-control Study
  - RSV Follow-up Study
- RSV – Impact of Synagis
- RSV Disease and Seasonality - Alaska
- Effect of water service on LRTIs and RSV
- Viral etiology of Respiratory Infections
- Synagis recommendations in Alaska

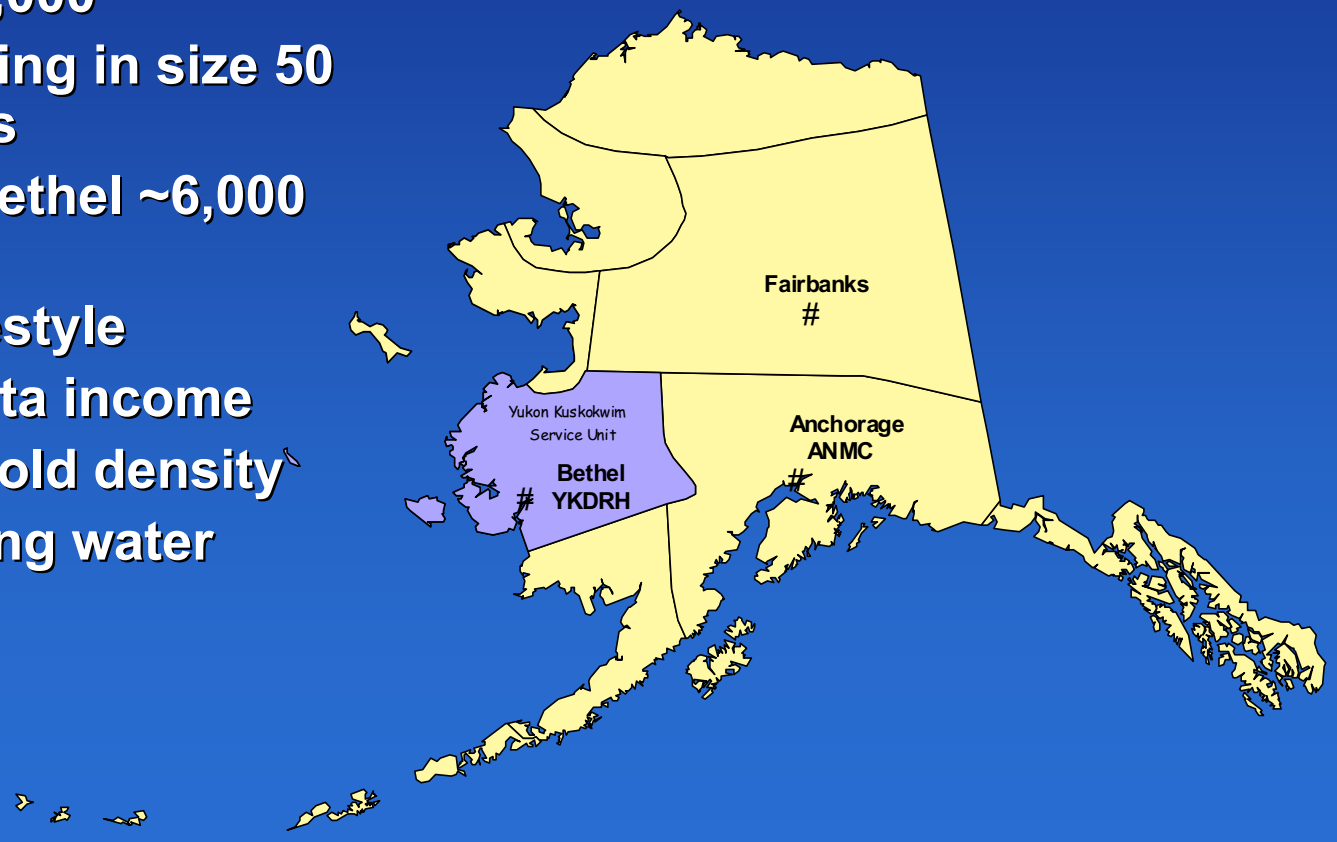
Trends in Respiratory hospitalizations among AI/AN & US infants



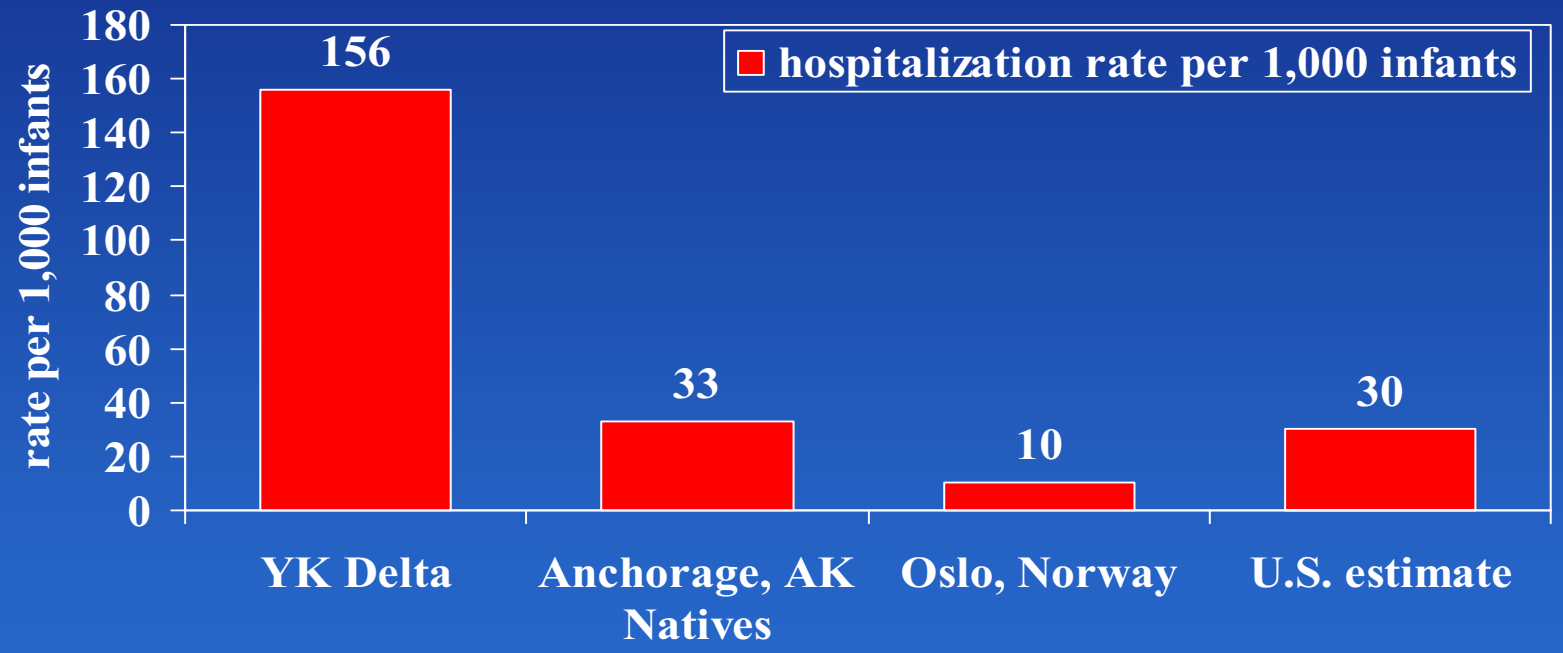
- LRTI hospitalizations decreased for AI/AN infants in Alaska and Southwest, and the general US population of infants.
- However, the LRTI hospitalization rate for Alaska Native infants is still three-fold higher than the rate for US infants.

Background: YK Delta

- 195,000 square km
- Population – 25,000
- 52 villages ranging in size 50 to 1,000 persons
- Regional Hub-Bethel ~6,000 persons
- Subsistence lifestyle
- Lowest per capita income
- Highest household density
- Lowest % running water



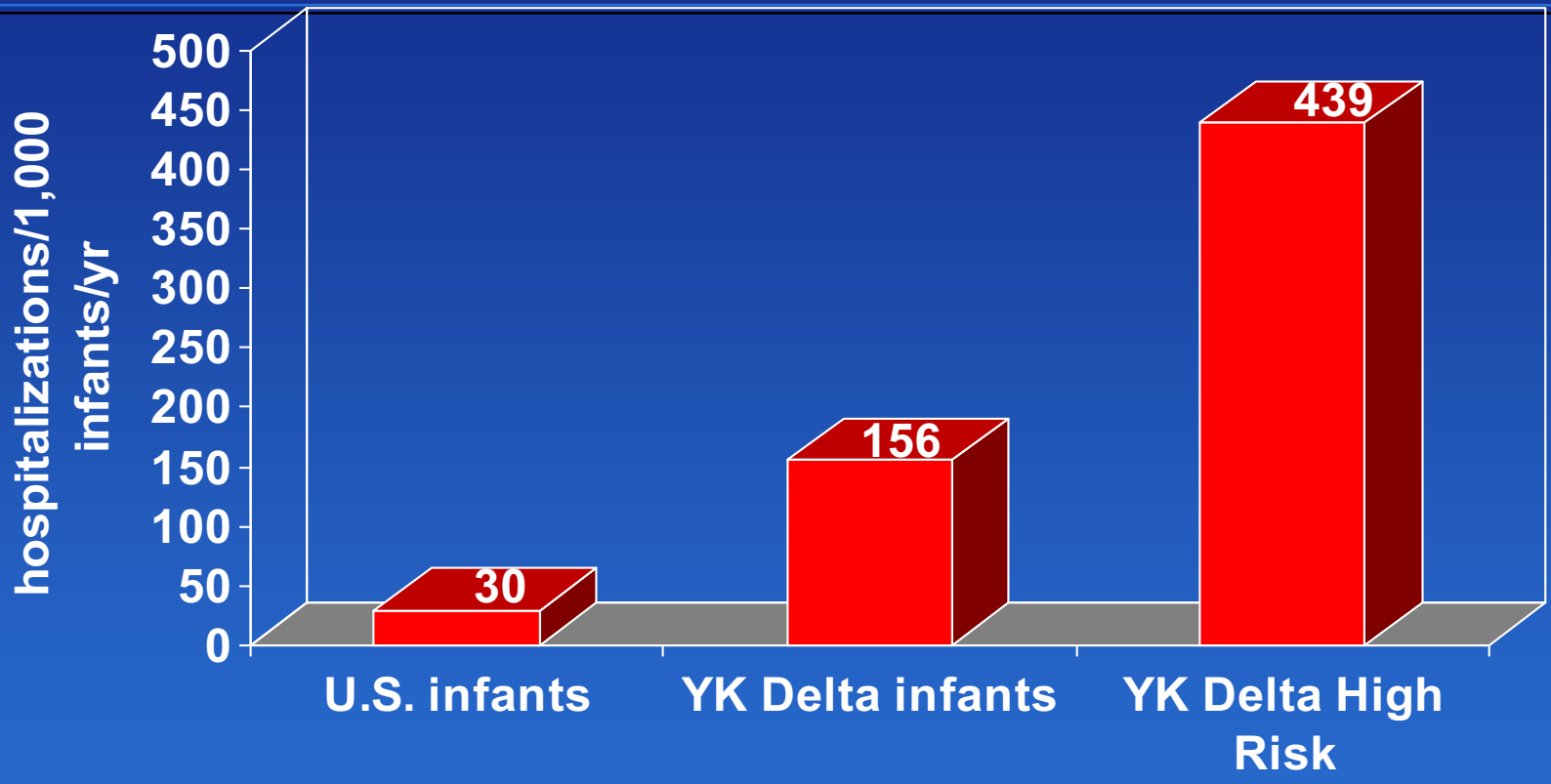
RSV Surveillance Study 1993-1996:
YK Delta RSV hospitalization rate



YK Delta RSV hospitalization rate was the highest reported in the literature.

Karron RA. J Infect Dis 1999;180:41-49.

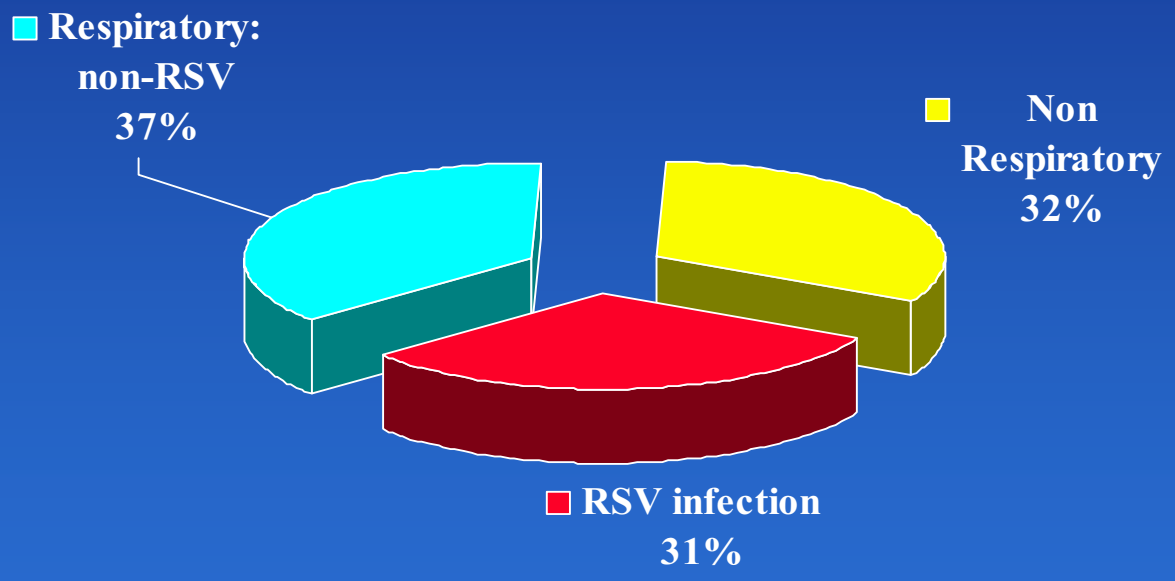
RSV Hospitalizations: YK 1993-96



Over 15% of all YK Delta infants and over 40% of high risk YK Delta infants (premature, CLD, CHD) were hospitalized yearly with RSV.

Cause of Hospitalization

YK Delta children < 3 years old, 1993-96



RSV Case Control Study 1993-96

	OR	P value
Breastfed >half feeds	0.38	0.001
Breastfed within 8 wks	0.44	0.004
Any Breastfeeding (age ≥6 mo.)	0.25	<0.001
≥4 children in home	2.13	0.011
≥2 persons/room	1.72	0.024
Shares bed (age ≥6 months)	2.20	0.036
High Risk infant (premature, CLD, CHD)	6.63	<0.001

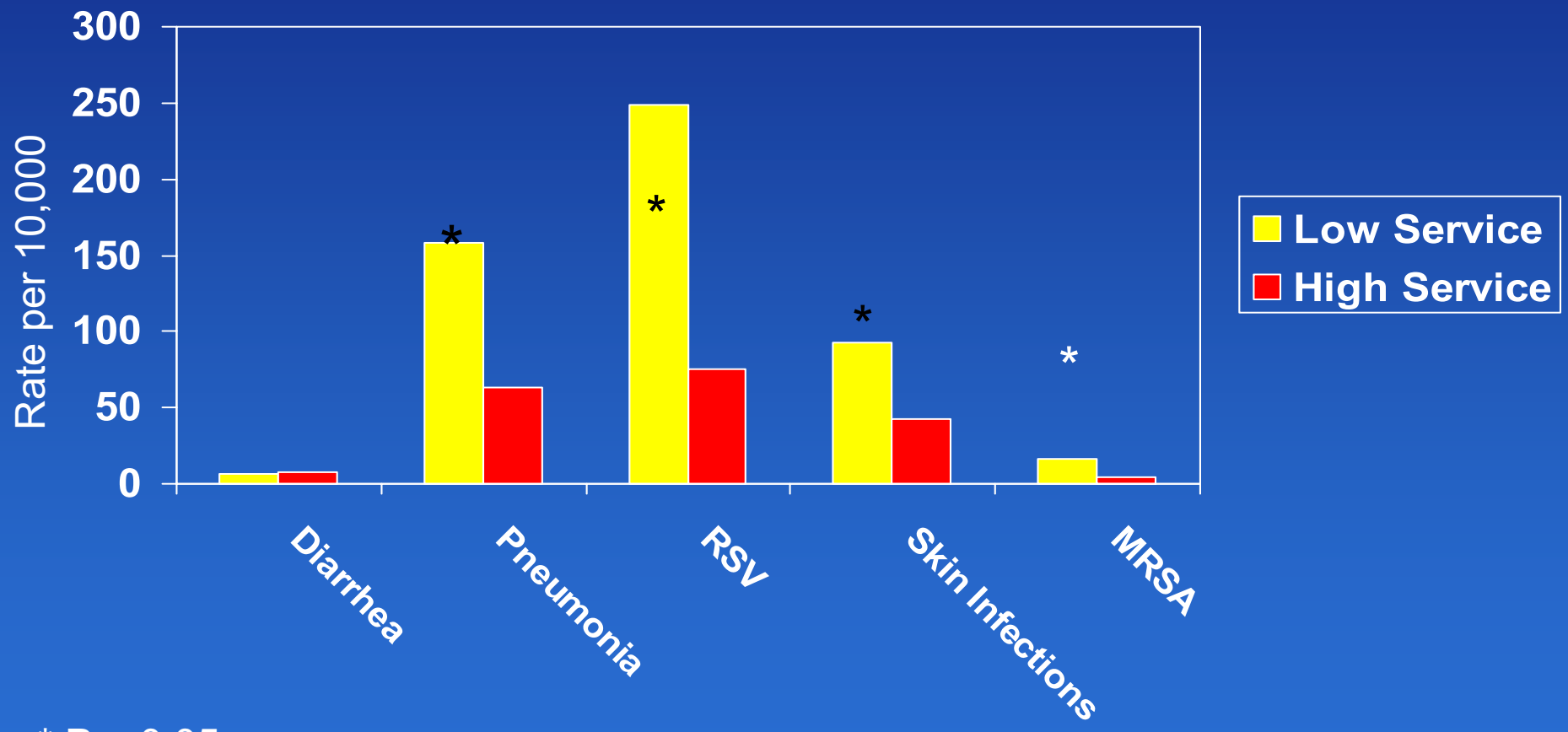
Bulkow L, Singleton R, Karron R, Harrison L. *Pediatrics* 2002;109:210-216.

Why is RSV hospitalization higher in YK Delta?

Transmission, Transmission, Transmission!

Service Unit	H20 Service Level	Socio-economic Factors [a]	
		HH Size	Per Capita Income
Anchorage (municipality)	Assume 100%	3.2	20.0
Anchorage (rural)	99%	3.3	17.8
Barrow	100%	3.9	17.4
Bristol Bay	90%	3.4	17.0
Interior	95%	3.1	14.9
Kotzebue	88%	4.4	14.7
Norton Sound	75%	3.8	9.8
Southeast	98%	3.1	19.8
YK Delta	61%	4.7	6.5

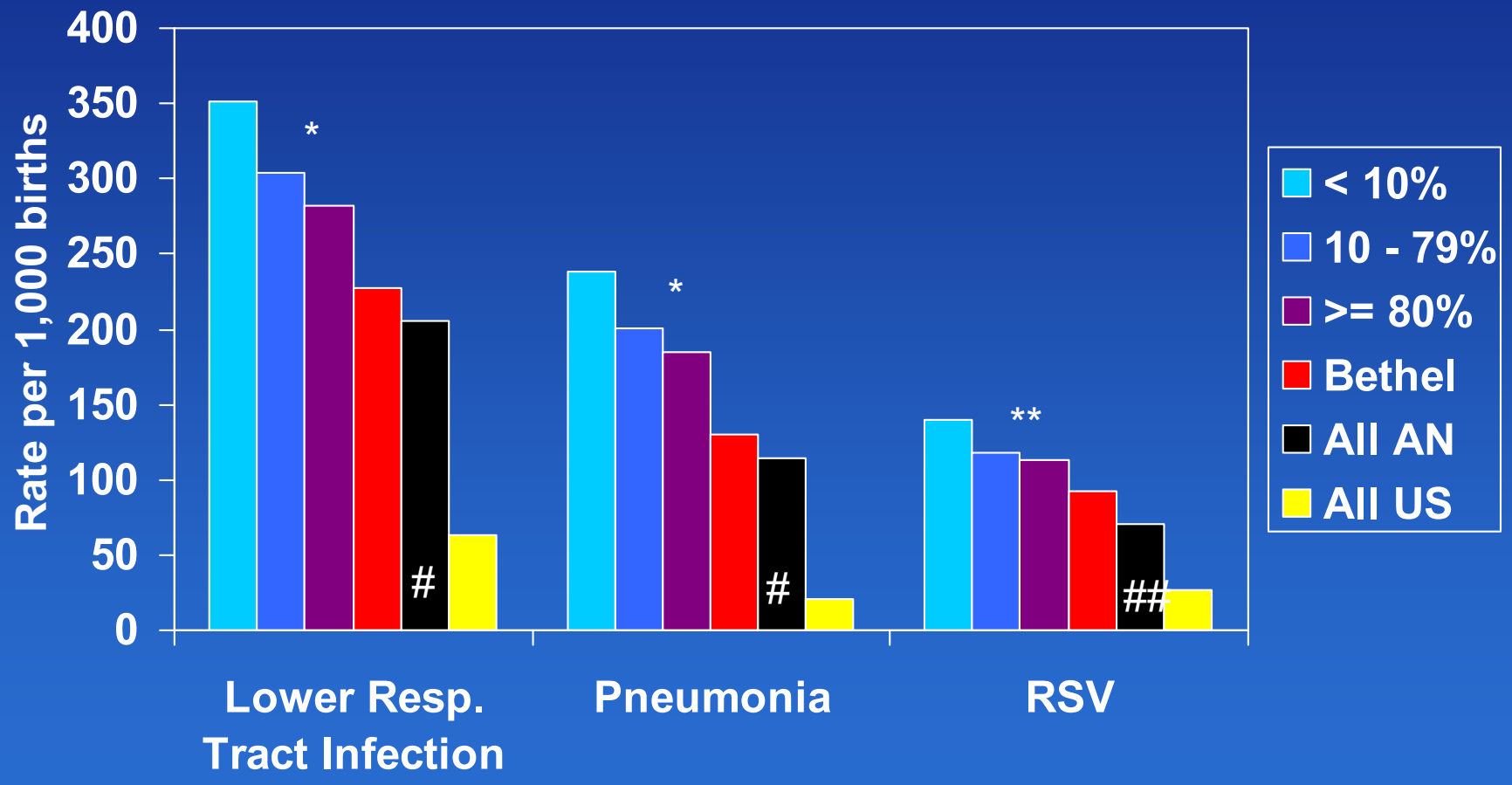
Hospitalization Rates for "High" and "Low" Water Service Regions, Alaska, 2000-2004



* P < 0.05

Hennessy et al, AJPH, 2008, 98, 1-7

Hospitalization rates for infants by village water service, 1999-2004, YK region, all Alaska Native and U.S. infants, 2000-2001.



* P < 0.05 for trend, YK Region

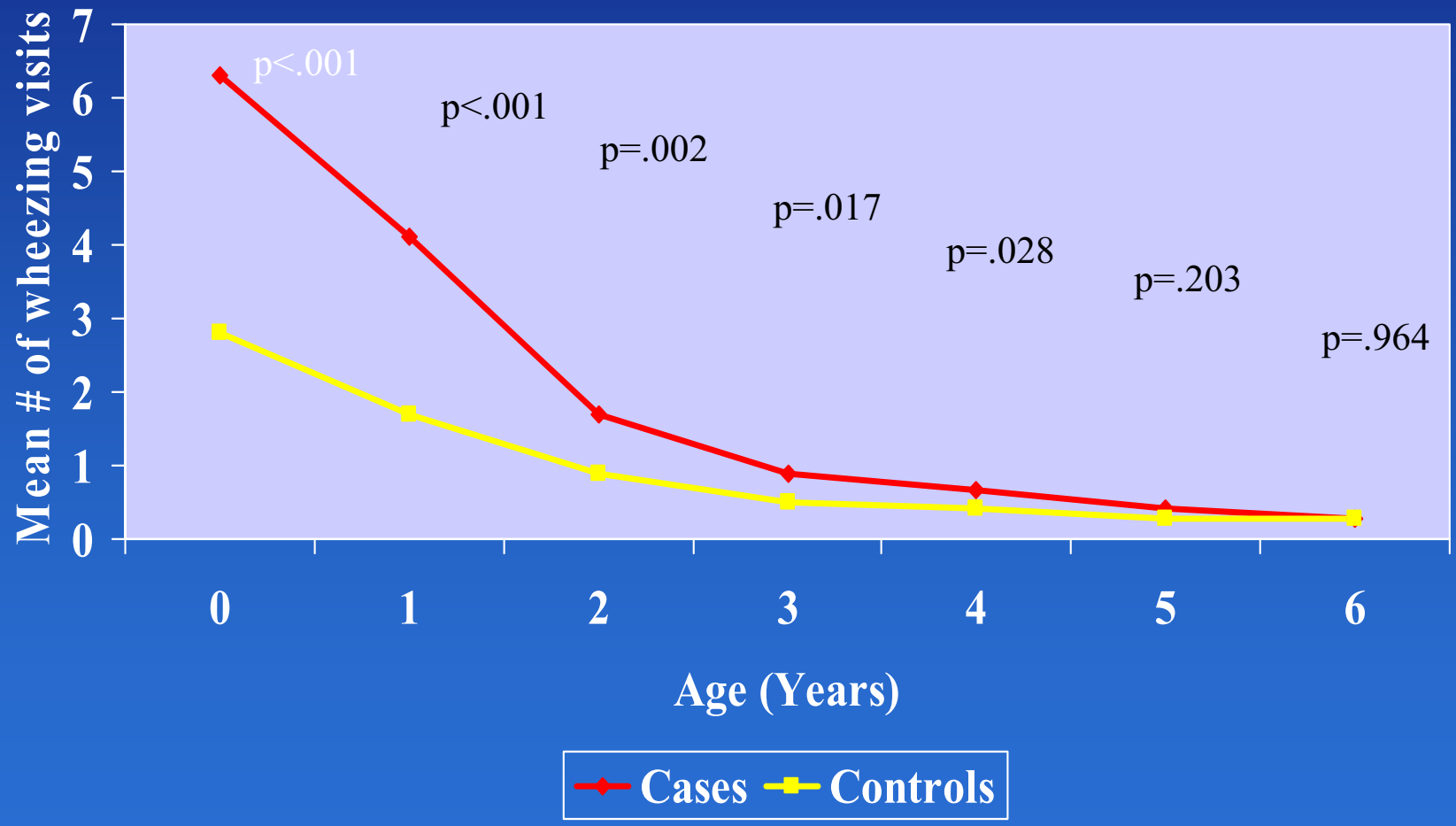
** P= 0.08 for trend, YK Region

\# *Ped Infect Dis J*, April 2005

\## *Pediatrics*, Oct 2004

Hennessy et al, AJPH, 2008, 98, 1-7

Mean number of visits with wheezing per child by year

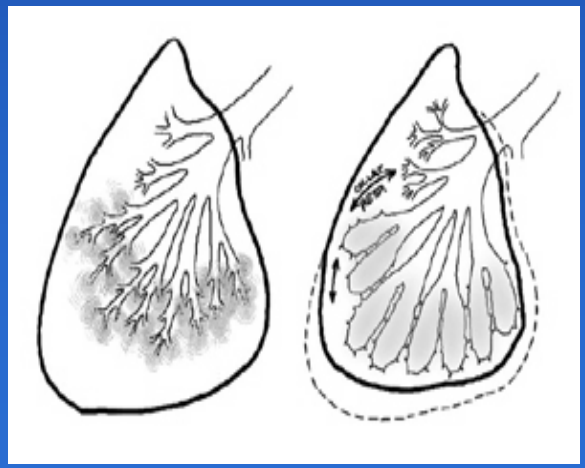


Singleton RJ et al. PEDIATRICS 2003;112:285-90.

RSV Follow-up Study:
Chest x-ray findings:

- 58% had at least one pneumonia before 2 yrs.
- 11% had x-ray findings of bronchiectasis after 2 years.
- Children with pneumonias were more likely to develop bronchiectasis.
- RSV cases were not more likely to develop bronchiectasis

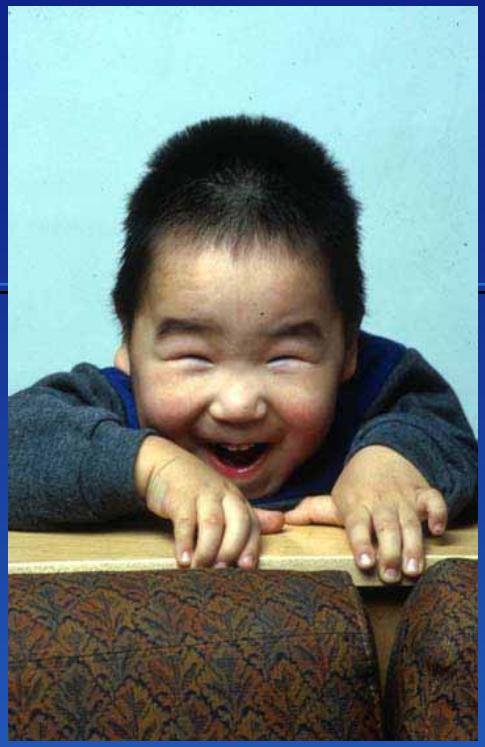
pneumonia



Normal lung bronchiectasis

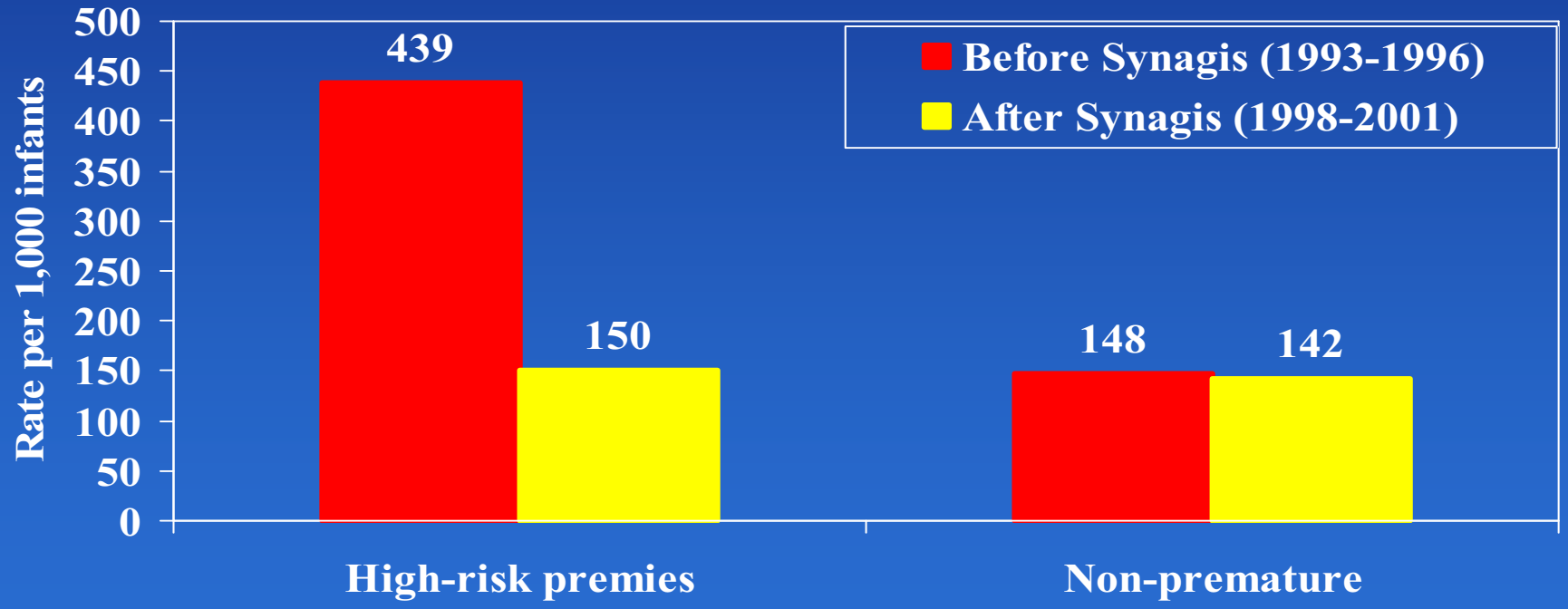
Non-CF Bronchiectasis in Indigenous Children

Alaska Natives (YK)	11-20 per 1,000 births
Australian Aborigines	14.7 per 1,000 children
New Zealand Maori/Pacific Islanders	50 per 100,000 children
Finland	0.4 per 100,000 children



- Indigenous children from developed countries have disproportionate rates of bronchiectasis
- The main common risk factor is early and recurrent pneumonias
- International collaboration to study bronchiectasis prevention and treatment

AK Native Synagis Study:
RSV Hospitalization Rate, YK infants, before and after Synagis



After Synagis, the rate in premies decreased 3-fold, while the rate in non-premies was stable.

Singleton et al. Pediatr Inf Dis J. 2003;22:540-6

Community Health Aide Synagis® Project

- **Problem:** Poor compliance in Synagis® recipients
  - protected 67% of the RSV season
  - received 74% of projected doses
- **Reason:**
  - Community Health Aides Infants uncomfortable giving Synagis®
  - Infants flown to Bethel for doses
- **Synagis® Project:**
  1. Train CHAs to mix and administer Synagis® in village
  2. Set up database and reminders for Synagis® infants
  3. Evaluate compliance before and after project

YK Delta Synagis Compliance:

"BEFORE" AND "AFTER" Health Aide project

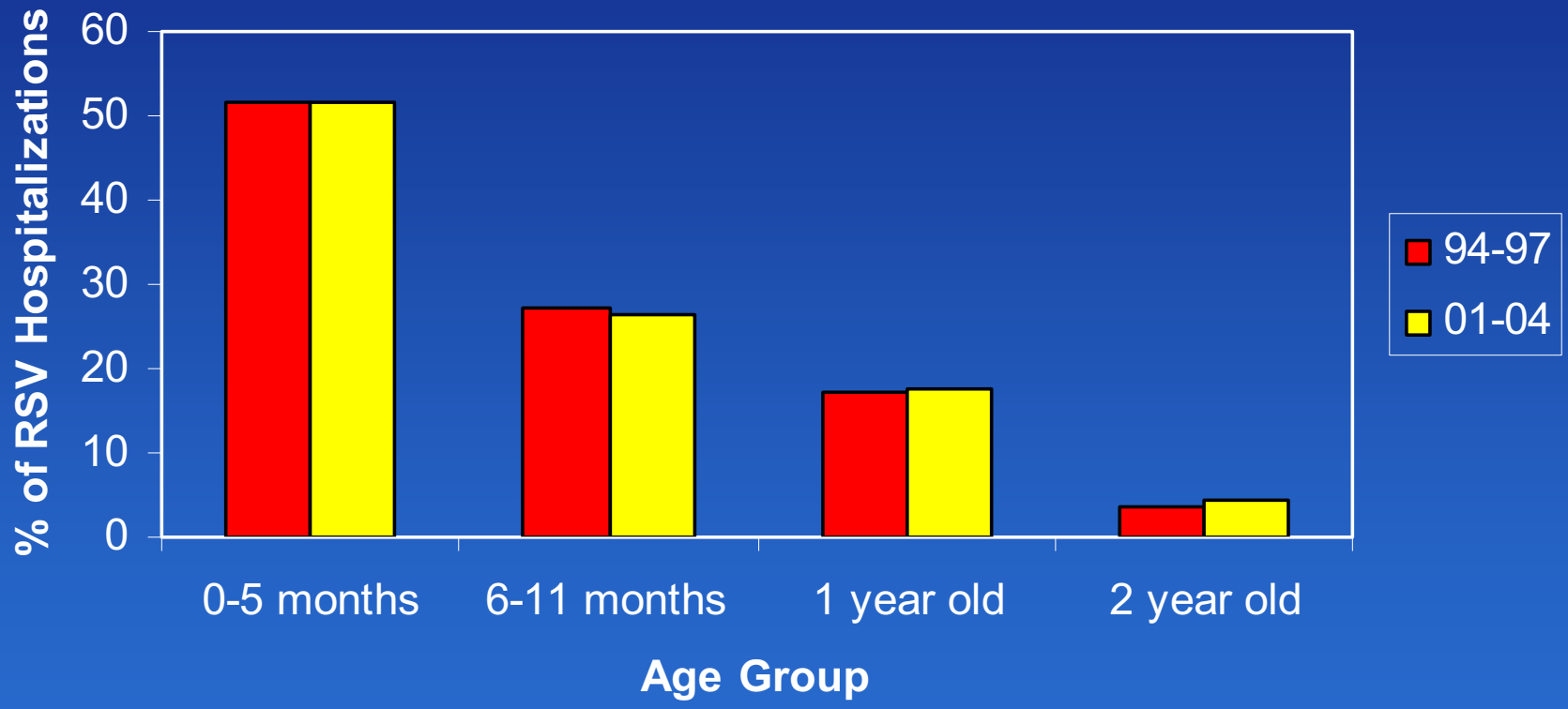
	% of days protected
1998 –2001 "BEFORE Project"	69.7%
2003 –2004 "AFTER Project"	*83.2%

* Protected days are < 32 days of Synagis between Oct 1 and May 31.

87.8% of all projected Synagis doses were given in the 2003-4 vs.74% in 1998-2001

Singleton et al. Int J Circumpolar Health 2006:65:4-7

Age Distribution of RSV Hospitalizations, YKD



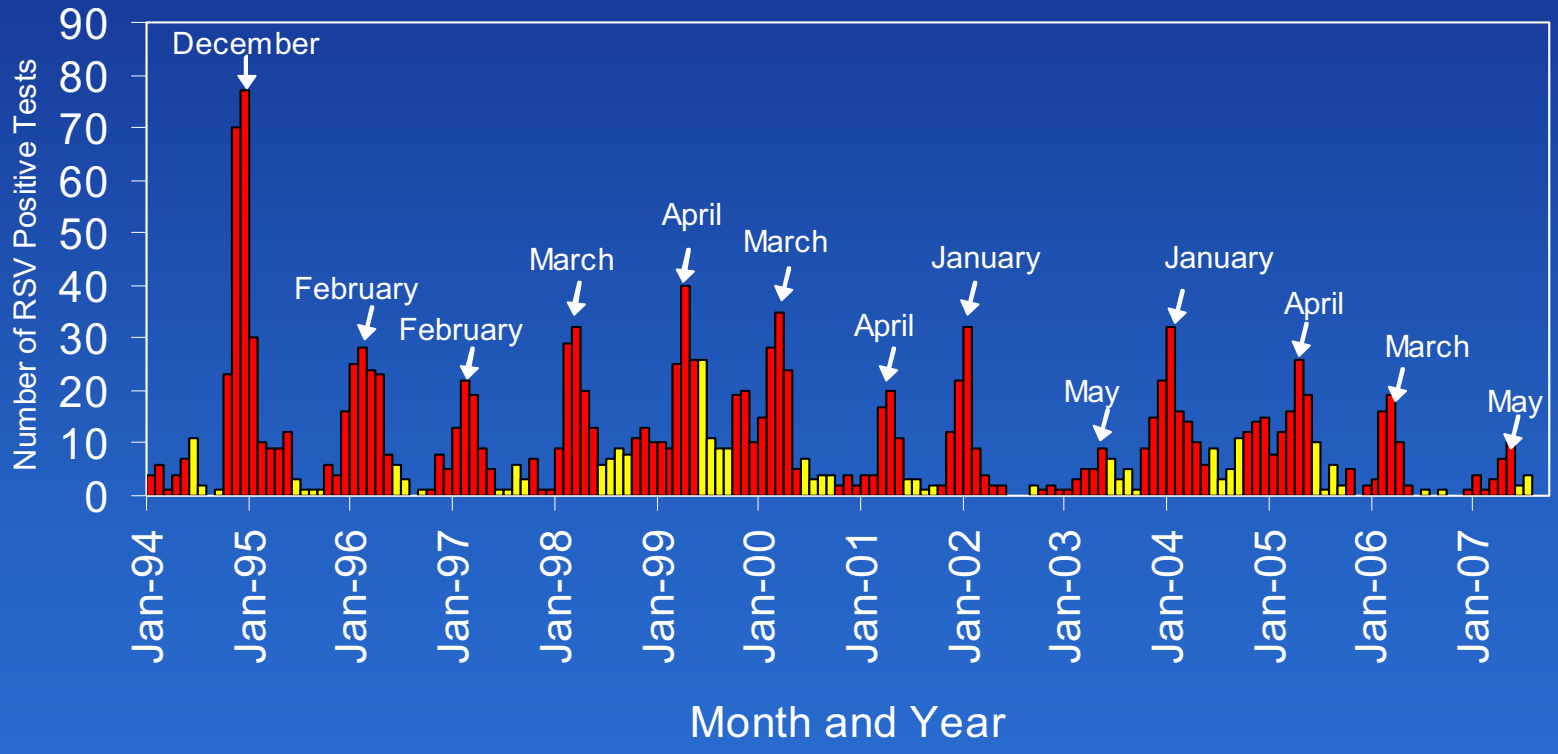
1994-2004:

10% of RSV hospitalizations in children <1 month.
50% of RSV hospitalizations in children <6 months.
79% of RSV hospitalizations in children < 12 months.
97% of RSV hospitalizations in children < 24 months

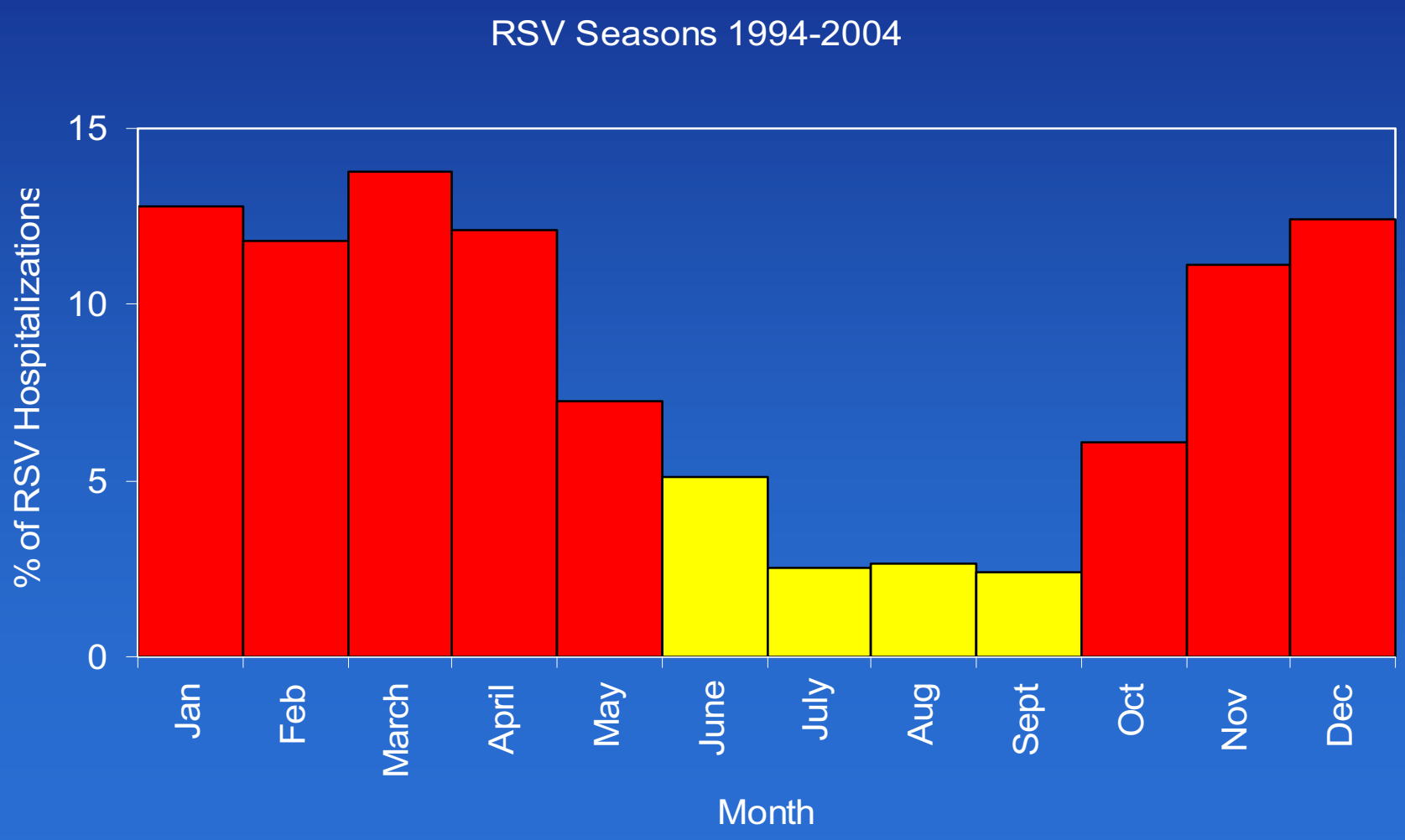
RSV Seasonality

- RSV season varies widely by year
- There are consistently 4 low RSV months (June-September)
- We calculated RSV seasonality using the analysis published by Mullins. YK Delta median RSV season was 31 weeks compared with 15 weeks for the U.S.

RSV Hospitalizations, YK Delta by month, 1994-2007



Percent of RSV hospitalizations by month, 1994-2004

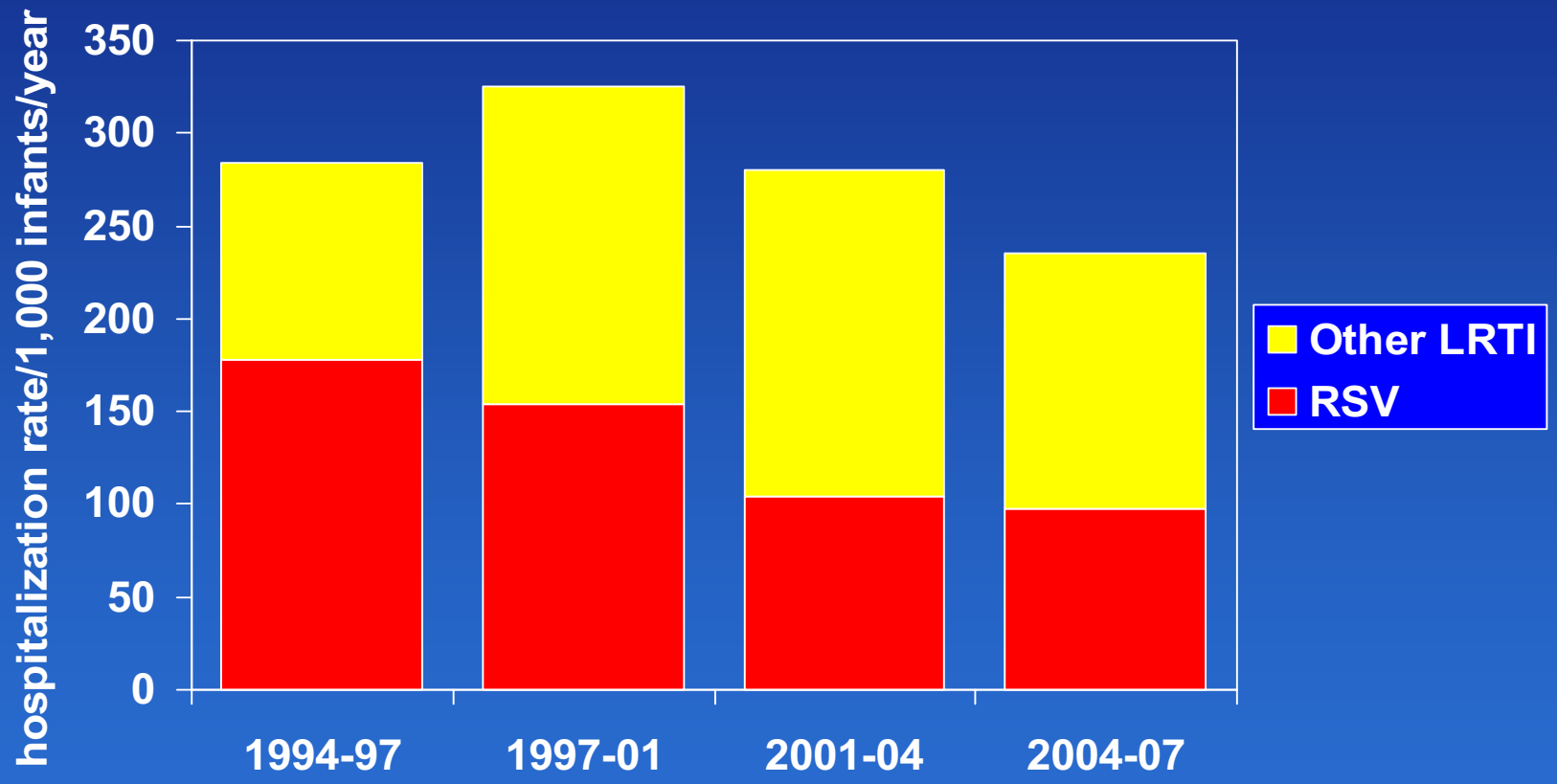


RSV SEASONALITY:
YK Delta vs. Lower 48

Location	Onset (median)	Peak (median)	Offset (median)	Duration (wk)
***Nation**	**late Dec**	**early Feb**	**end Mar**	**15**
***West**	**End Dec**	**Mid-Feb**	**End Mar**	**14**
***South**	**Late Nov**	**Early Jan**	**Mid Mar**	**16**
YK Delta	Oct 14-20	Feb 20-26	May 19-25	31

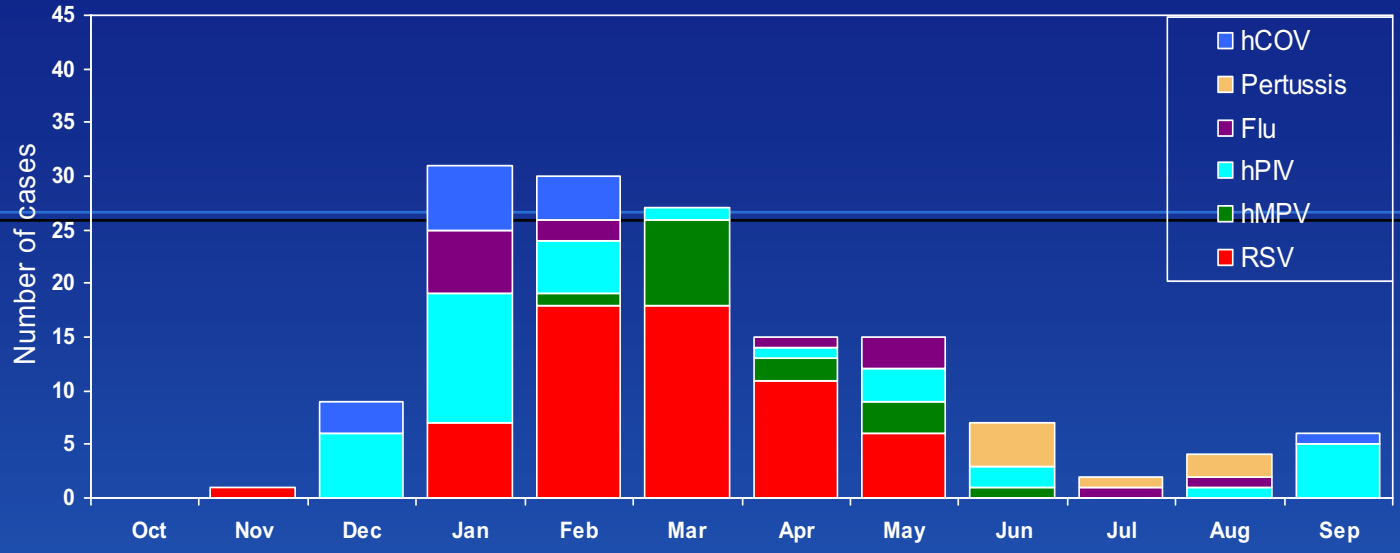
* Mullins JA et al. Pediatr Infect Dis J, 2003;22:857-62

RSV and LRTI Hospitalization Rates YK Delta; 1994 to present

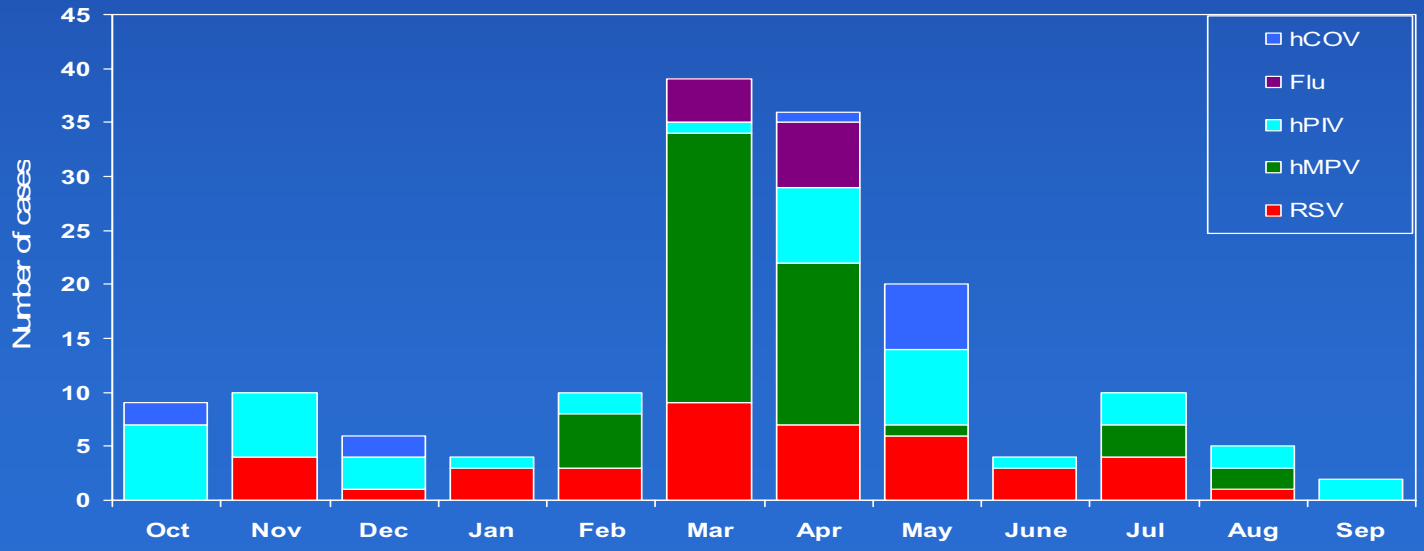


LRTI and RSV hospitalization rates appear lower in 2004-7.

Hospitalized Cases, Oct 2005-Sep 2006

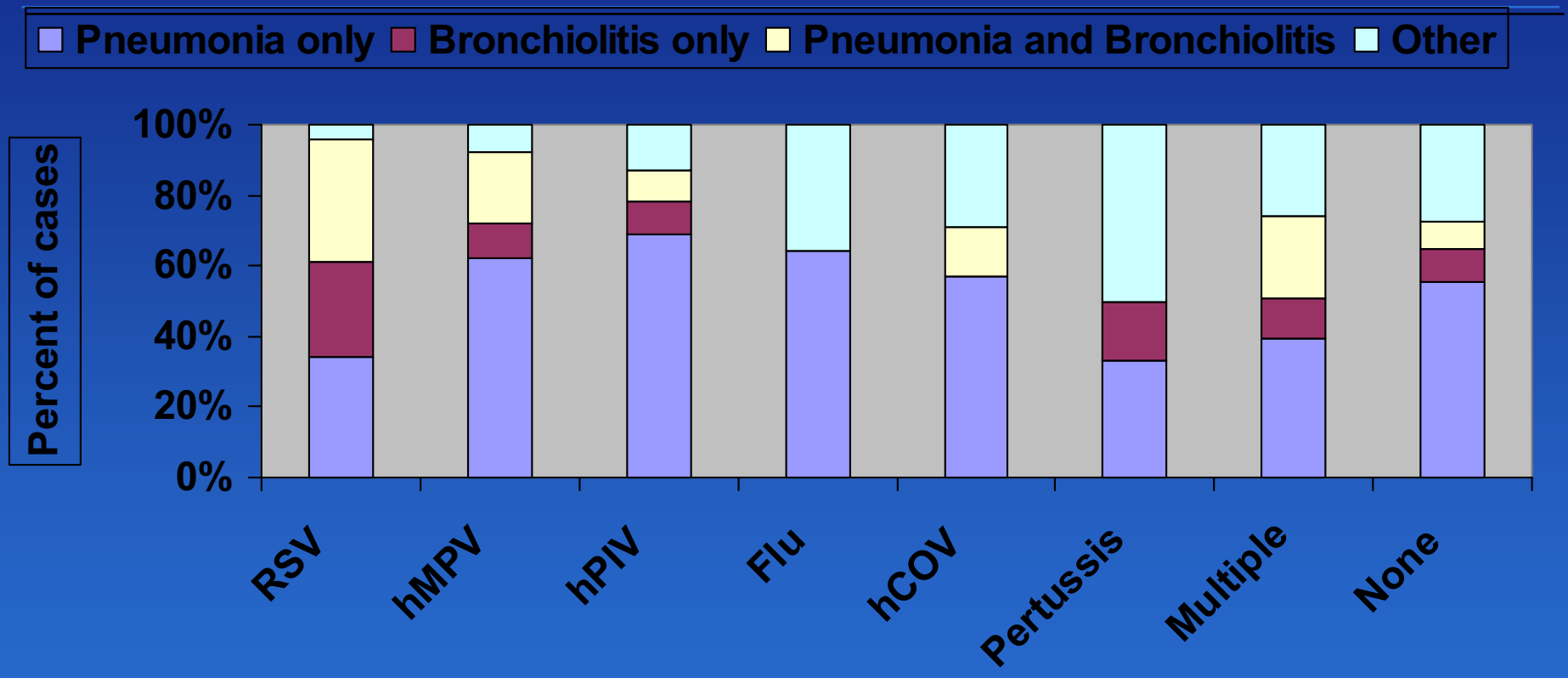


Hospitalized Cases, Oct 2006-Sep 2007



Rhinovirus results not included.

Clinical Presentation by Virus



RSV:

Comparison RSV Binax with Study PCR
Respiratory Virus Study

	PCR +	PCR -*
Binax +	**47**	**5**
Binax -	**22**	**188**

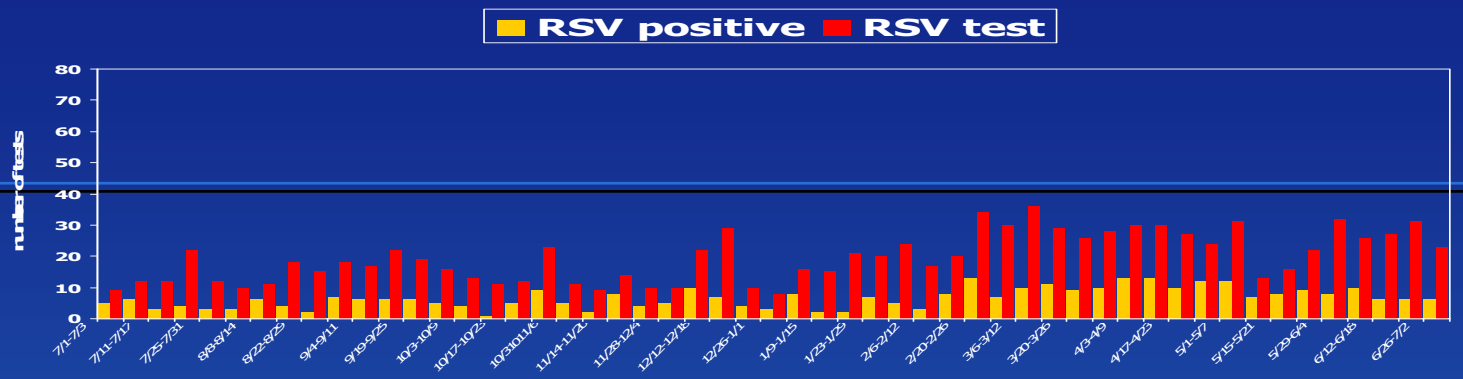
Rapid test EIA compared with PCR:

- Sensitivity : 68%
- Specificity: 97%

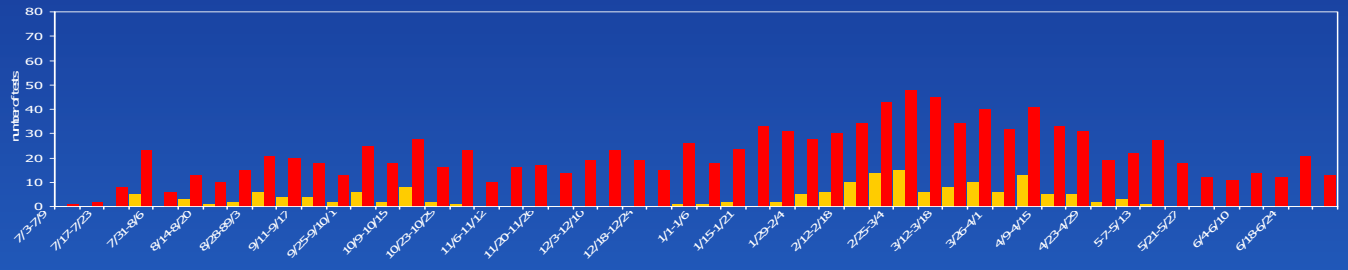
* NP Wash closest to Swab.

RSV Test Results, YKDRH: 7/2004-6/2008 by year

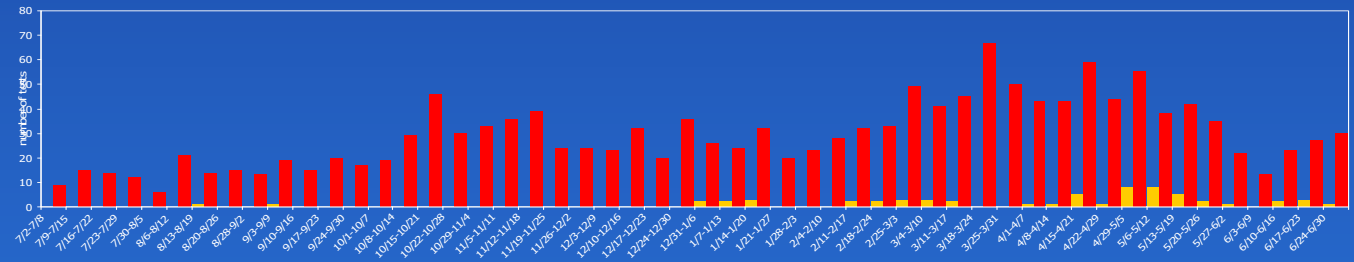
2004-5



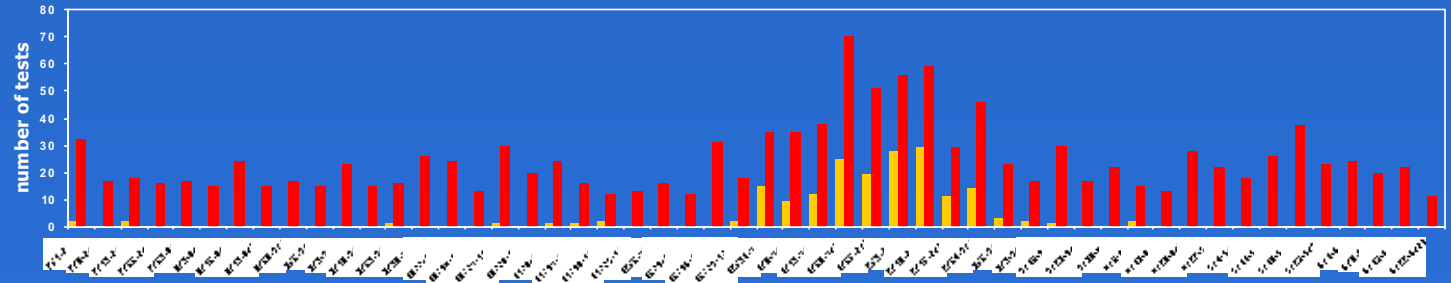
2005-6



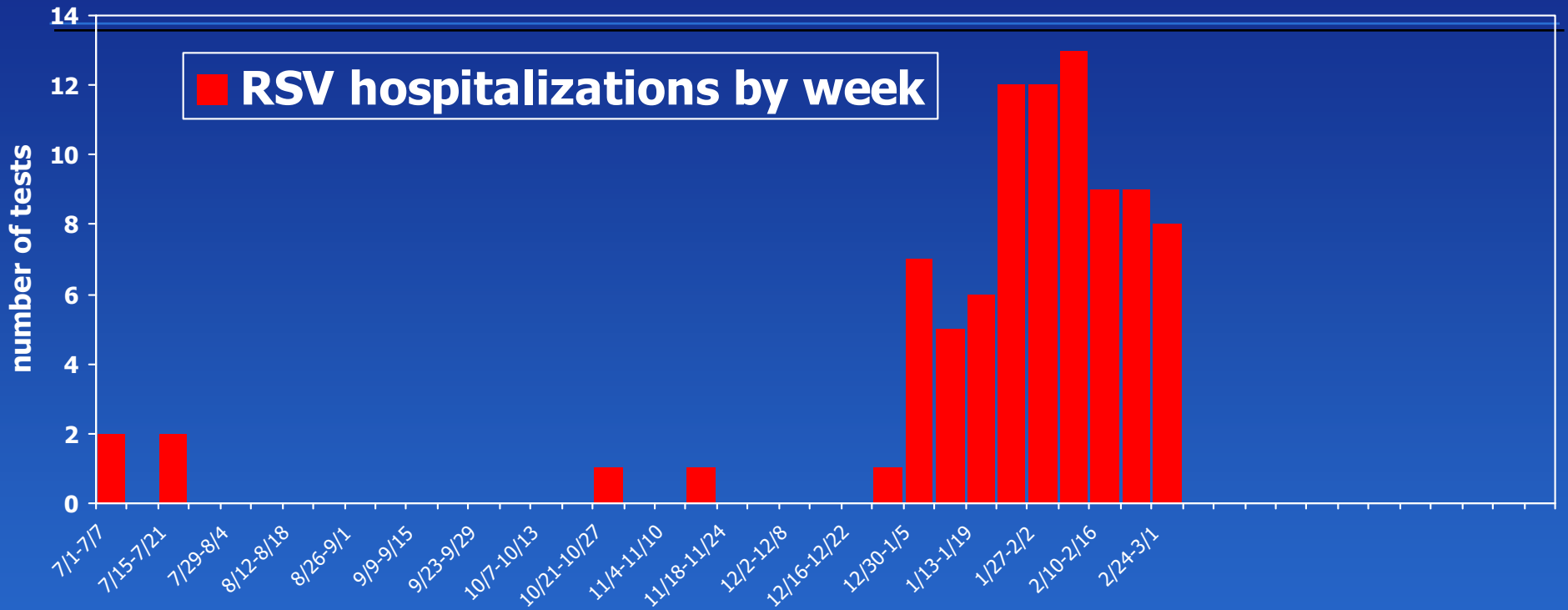
2006-7



2007-8



RSV outbreak, YKD 1/1/08 – 3/8/08



- Over 80 YK infants were hospitalized with RSV during Jan-March 2008
- The State activated the Emergency Operations Center
- YK personnel participated in teleconferences and communication with the State and other hospitals
- Hospitals filled up, but no babies were transferred out of the State

RSV and PH Preparedness

- Increase in rural disease filled Anchorage pediatric beds to capacity (2007)
- Partnership with AAPP to improve ability to care for children: supplies, equipment, and staff (2008)
- Working with rural and Anchorage hospitals to improving tracking of RSV; assist rural & Anchorage hospitals

State of Alaska Epidemiology

Bulletin

Bulletin No. 15 07/27/2006

Respiratory Syncytial Virus Seasonality in Alaska: Implications for Palivizumab Administration

Recommendations for Alaska:

2. Health-care providers should administer palivizumab monthly between October 1 and May 31 to high-risk infants and children who meet the American Academy of Pediatrics criteria.

Synagis Recommendations for Alaska

- Administer palivizumab monthly between October 1 and May 31 to high-risk infants and children who meet criteria.
- Prophylaxis should be considered for infants 32-35 weeks of gestation born after April 1, 2008 if 2 or more risk factors are present.

AAP Criteria	Other recognized risk factors
■School aged siblings ■Daycare attendance (>= 2 unrelated kids, >=4 hours/week) ■Congenital airway abnormalities ■Neuromuscular disease ■Exposure to tobacco smoke/ environmental air pollutants	■ Multiple births ■ Crowded living environment >= 3 people per child's bedroom, >= 7 people per household) ■ Birth weight < 2500 grams ■ Lack of running water