

RSV Seasonality and Synagis Recommendations

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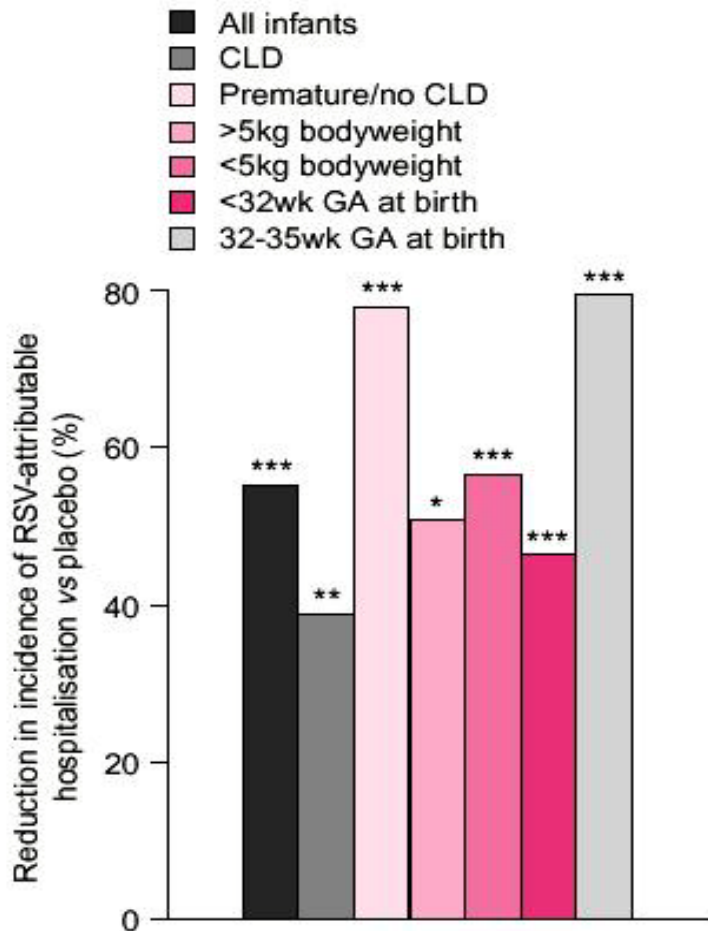
Alaska Division of Public Health



Synagis



- RSV humanized monoclonal antibody
- 55% decrease in RSV-related hospitalizations in high risk infants
- Few side effects
- Cost: \$700-1300 per dose depending on concentration.



Changes to 2009 Redbook RSV Prophylaxis Seasonality

- Five monthly doses in continental US, except:
- “Alaska Native infants in the YK Delta experience not only higher RSV hospitalization rates but also a longer RSV season. Pediatricians from the YK Delta may wish to use CDC-generated RSV hospitalization data from the YK Delta region to assist in determining the onset and offset of RSV season for the appropriate timing of palivizumab administration”

Synagis

Condition	Age	Max doses/season
Chronic Lung Disease	<24 months	6**
Congenital Heart Disease	<24 months	6
<29 wk gestation	<12 months	6
29-<32 wk gestation	<6 months	6
32-<35 wk gestation with sibling<5yr, childcare, crowding, no running water	<3 months	3
*<35 wk with congenital airway/neuromuscular disease	<12 months	6

* AAP committee changed to include full-term infants with congenital airway or neuromuscular disease

** AAP committee – Max. doses per season = 5

Season: November - May 14. 6 doses maximum.

What do the data show?

Studies

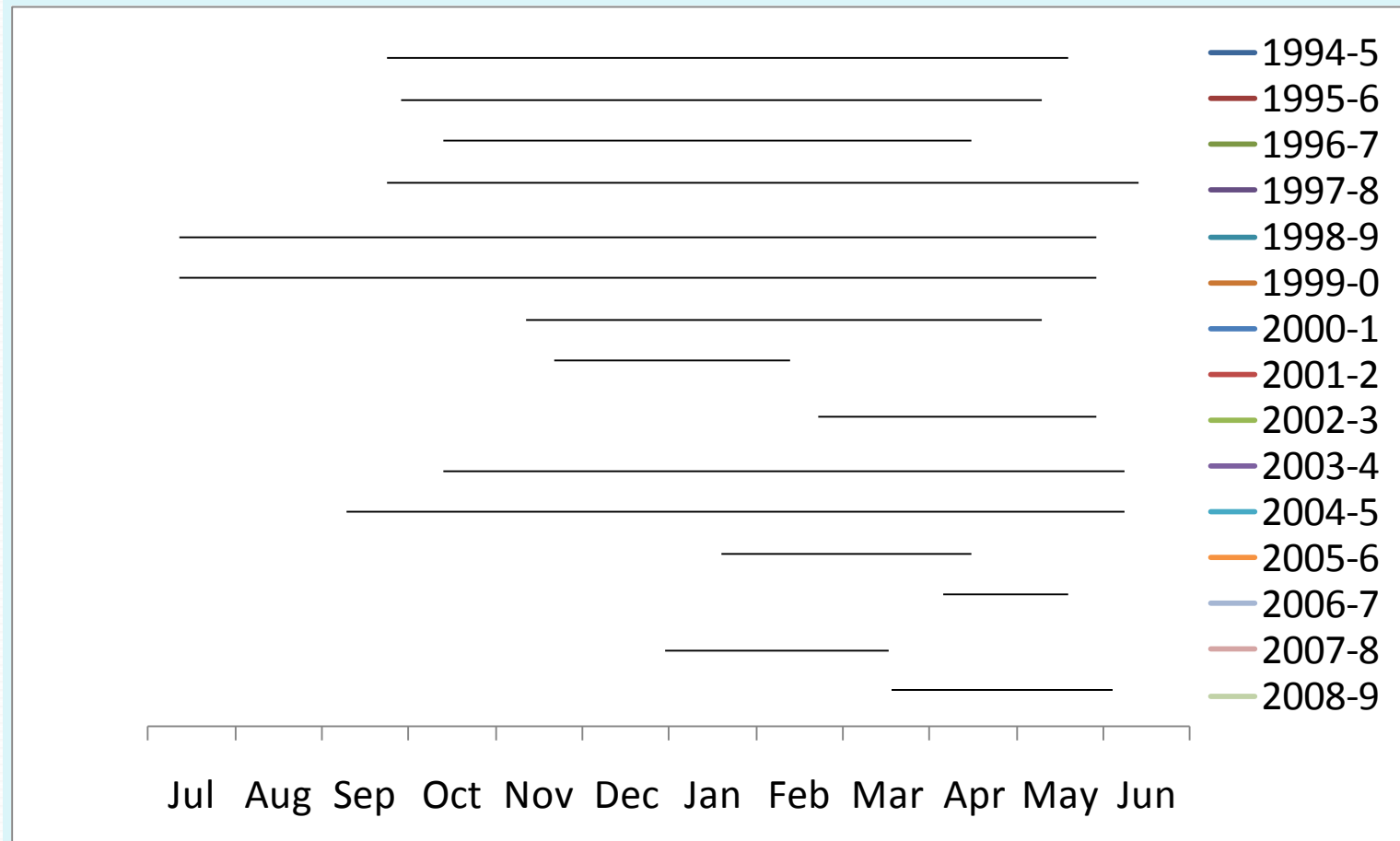
- Extensive studies from Y-K Delta Region
 - Population based
 - Etiologically confirmed cases
 - Prospective
- One statewide study
 - Medicaid, billing data
 - No definitive etiology (based on bronchiolitis or RSV ICD-9 code)
 - Retrospective

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

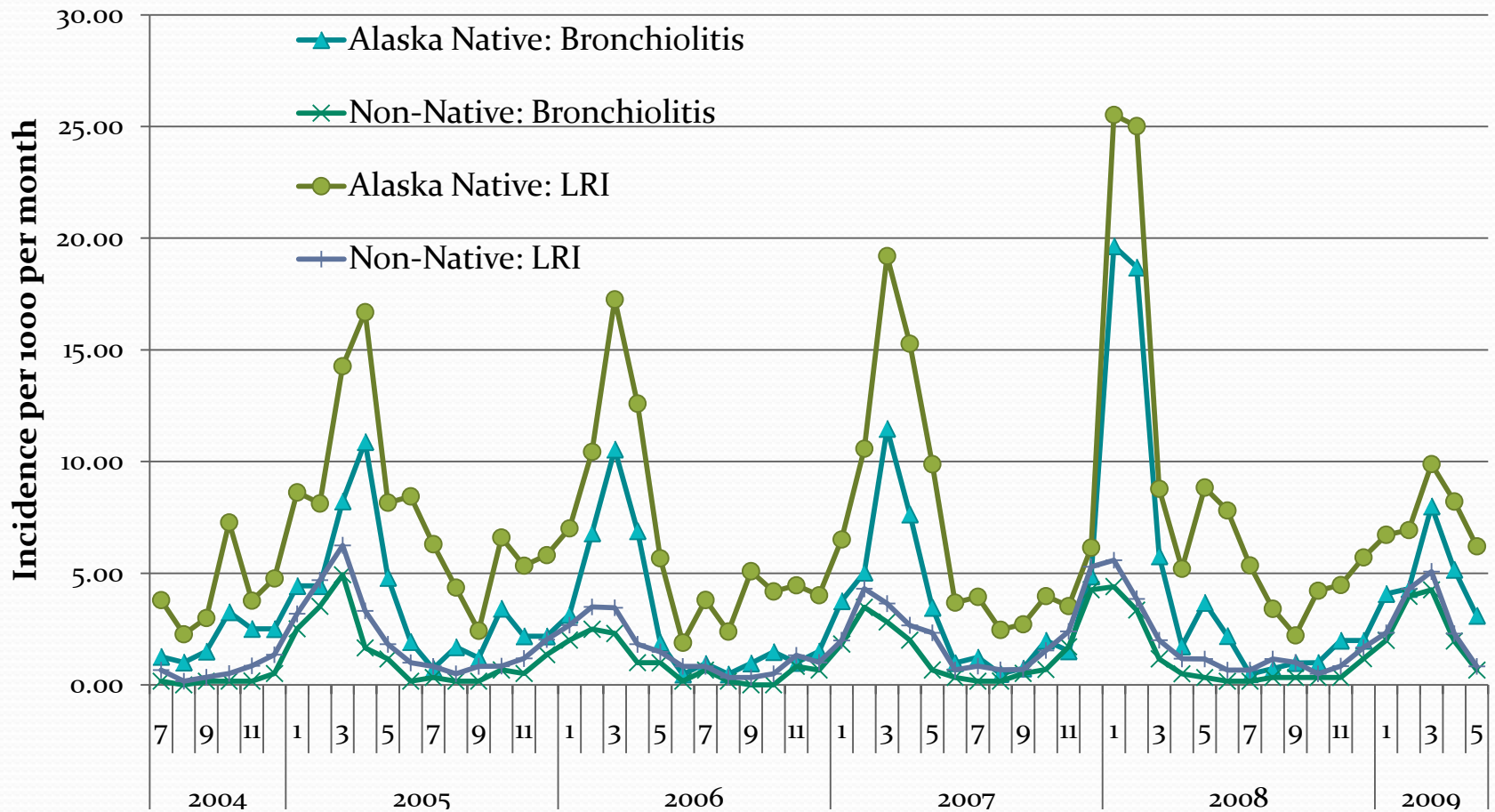
* Mullins JA et al. *Pediatr Infect Dis J*, 2003;22:857-62. Table courtesy of Ros Singleton, MD, US CDC, Arctic Investigations Program

RSV season onset - offset, 1994-2009, YK Delta*

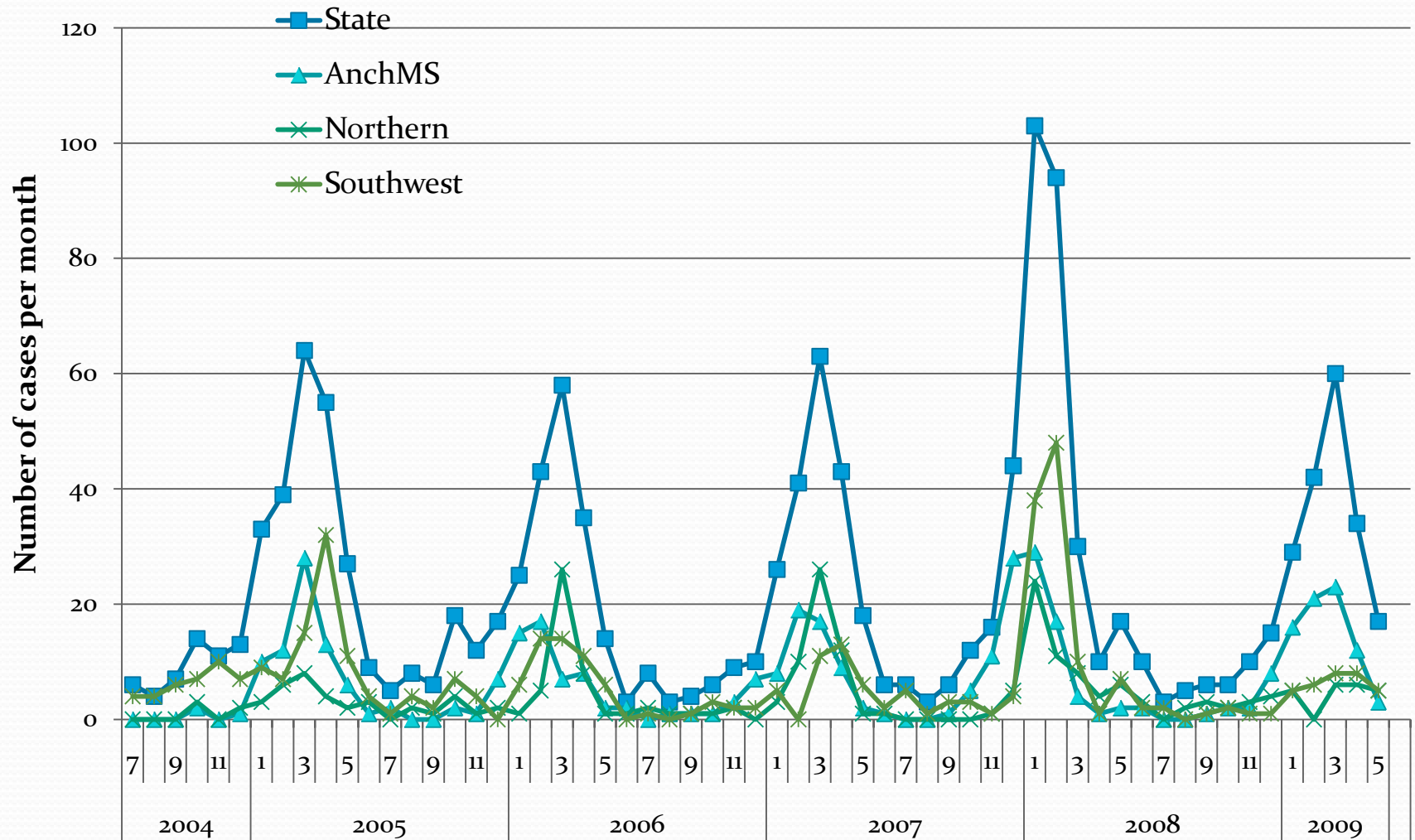


*Courtesy of Ros Singleton, MD, US CDC, Arctic Investigations Program

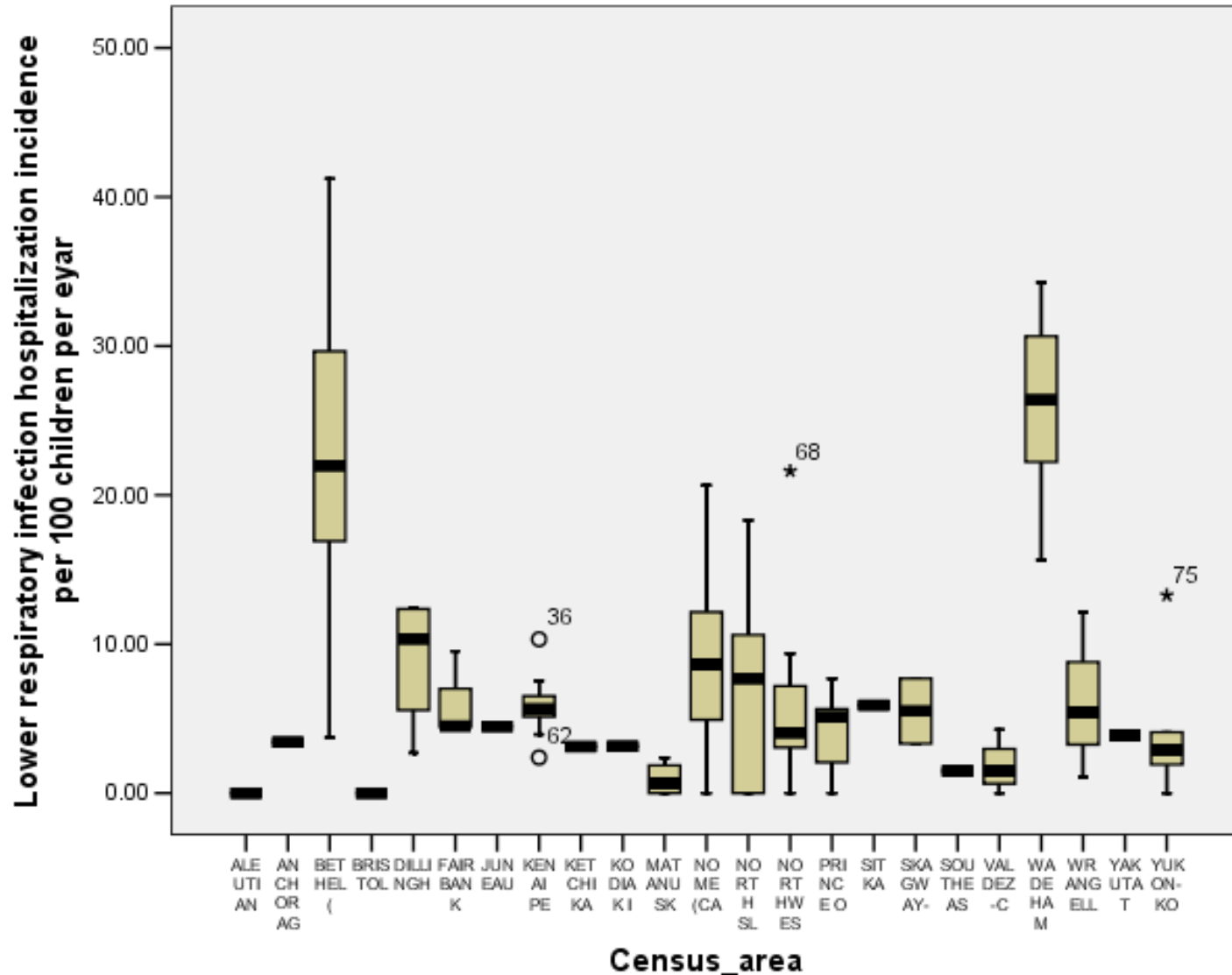
Lower respiratory infection (LRI) and bronchiolitis incidences among children age <2 years by Alaska Native status, Alaska Medicaid



Bronchiolitis/RSV cases by month and region among children age <2 years, Alaska Medicaid



Lower respiratory infection hospitalization incidence by village, age <2 years, Alaska Medicaid



Season onset and offset for RSV/bronchiolitis, Alaska Medicaid

Year	North	Southwest	Anchorage/Mat-Su
2004-5	Dec-Jun (Feb-Apr)	Sep-Apr (Mar-May)	Jan-May (Jan-Apr)
2005-6	Feb-Apr (Mar-Apr)	Oct-May (Feb-Apr)	Dec-Apr (Dec-Apr)
2006-7	Jan-Apr (Feb-Apr)	Mar-May (Mar-May)	Dec-Apr (Dec-Apr)
2007-8	Dec-Jun (Jan-Mar)	Jan-Mar (Jan-Mar)	Oct-Feb (Nov-Feb)
2008-9 [‡]	Aug-May (Dec-May)	Jan-May (Jan-May)	Dec-Apr (Jan-Apr)
Seasons lasting > 6 months	3 = 60% (0 = 0%)	2 = 40% (0 = 0%)	0 = 0% (0 = 0%)
Seasons with onset before November	1 = 20% (0 = 0%)	1 = 20% (0 = 0%)	1 = 20% (0 = 0%)
Seasons with offset past April	3 = 60% (1 = 20%)	3 = 60% (3 = 60%)	1 = 20% (0 = 0%)

Onset/offset = first /last of any two consecutive months with at least 5 cases or 5% of total yearly cases (10 cases or 10% of total cases)

Summary

- Alaska Native children have high incidences of LRI, bronchiolitis and RSV infection
- Children in Wade Hampton and Bethel census areas particularly at risk
- Season prolonged in most years, for sure in YK Delta, but also likely in other regions

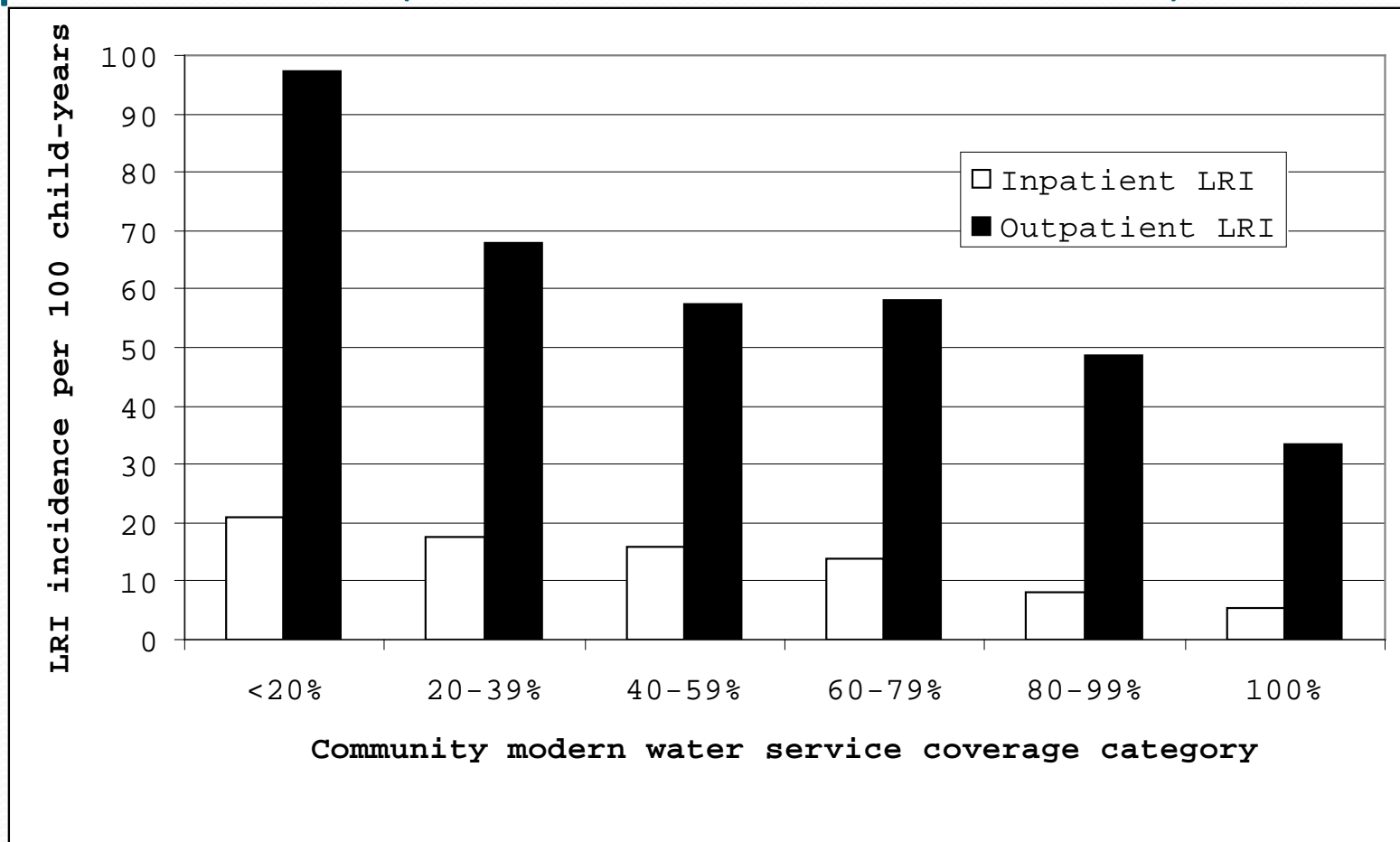
Potential Strategies*

- **A. Old Alaska:**
 - AAP risk groups, no limit on doses (except age boundaries)
- **B. Current US:**
 - AAP risk groups, max 5 doses
- **C. Current Alaska:**
 - AAP risk groups, max 6 doses
- **D. Full Year:**
 - AAP risk group, full first year of life
- **E. Expanded chronic lung disease:**
 - AAP risk groups, max 6 doses
 - all babies under 35 weeks GA
 - expanded definition of chronic lung disease (includes asthma)
- **F. Plus 1:**
 - AAP risk groups, max 6 doses
 - Every baby born during RSV season receives one dose before leaving the hospital
- **G. Plus 3:**
 - AAP risk groups, max 6 doses
 - All other babies receive a maximum of 3 doses during the RSV season if they are less than 3 months old

*Courtesy of Ros Singleton, MD, US CDC, Arctic Investigations Program

Why do Alaska Native children in Western and Northern regions have such high rates of disease?

Hypothesis 1: Lack of in-home water and modern septic services (Gessner, J Pediatr 2008;152:666-70).

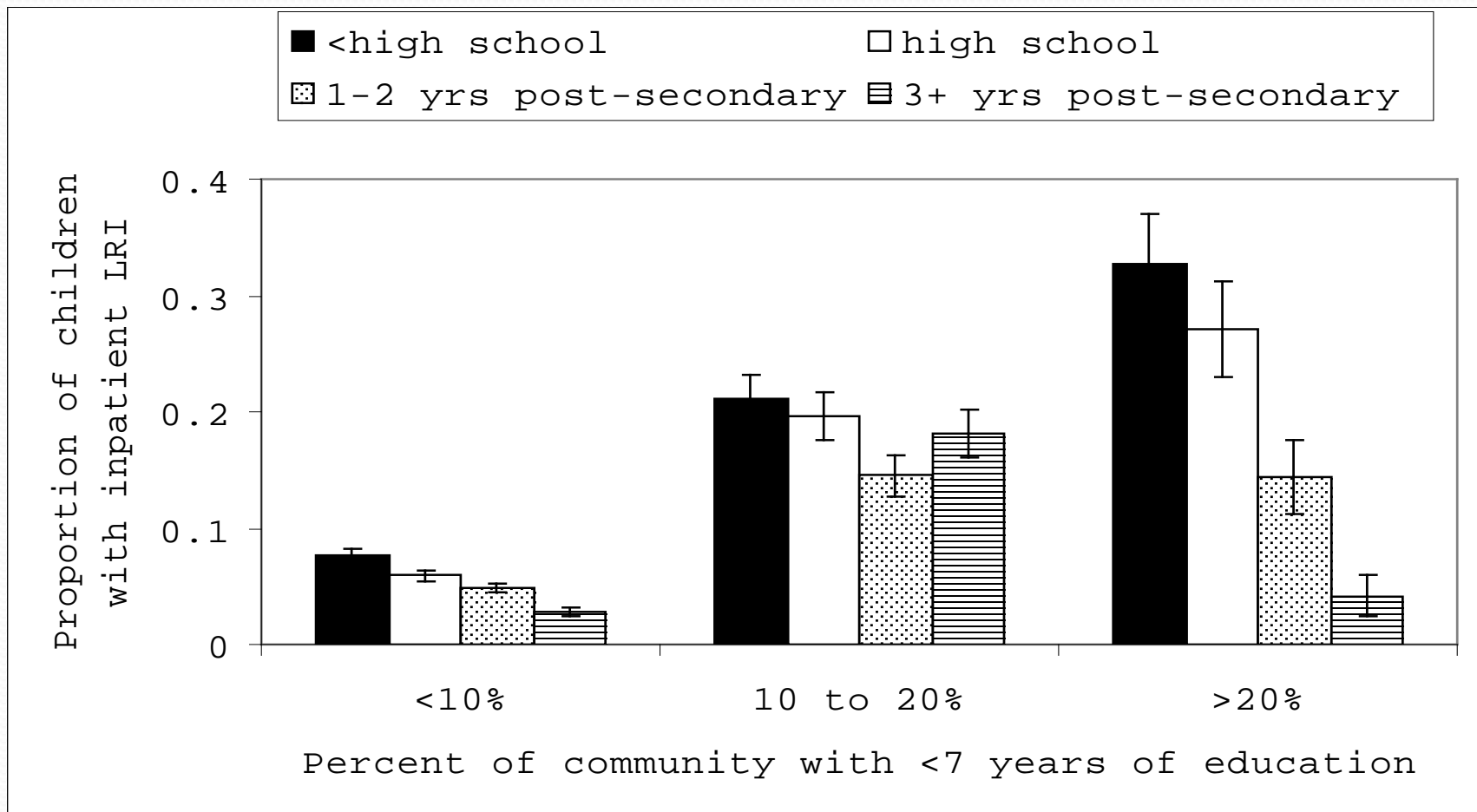


Shows mean LRI incidence in a community by percentage of homes in community with modern water/septic services, Alaska Medicaid..

BUT: No correlation between improvement in water services and decline in LRI incidence

Hypothesis 2: Community and maternal education

(Gessner et al, J Epidemiol Community Health 2010;64:130-5)



Shows the mean percent of Medicaid enrolled children that had inpatient LRI by category of maternal education and community education. Effect independent of various confounders including water service.

BUT: How does this work?

Hypothesis 3: CPT1A deficiency

(Gessner et al, Pediatrics, in press)

- Highly prevalent gene variant, exclusively among children with Alaska Native parents, particularly Inuit populations
- Associated with infant mortality among Alaska Native infants on preliminary investigation
- May interact with other disease to promote severity
- May help explain presentation with severe symptoms/hospitalizations
- BUT: does not explain overall increase in incidence

Other hypotheses

- Household crowding: some studies have found an effect, others have not
- Socio-economic status: most studies have not found an effect
- Genetic susceptibility to infectious diseases: no evidence for this