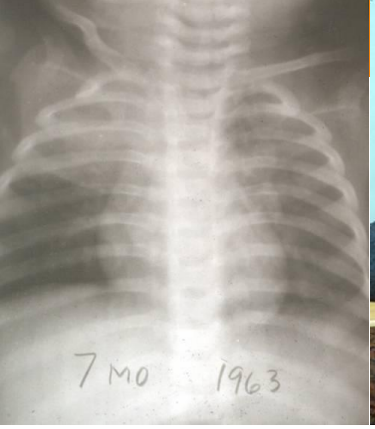
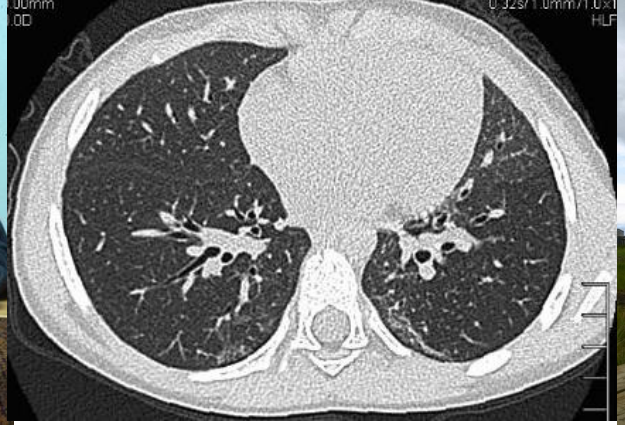


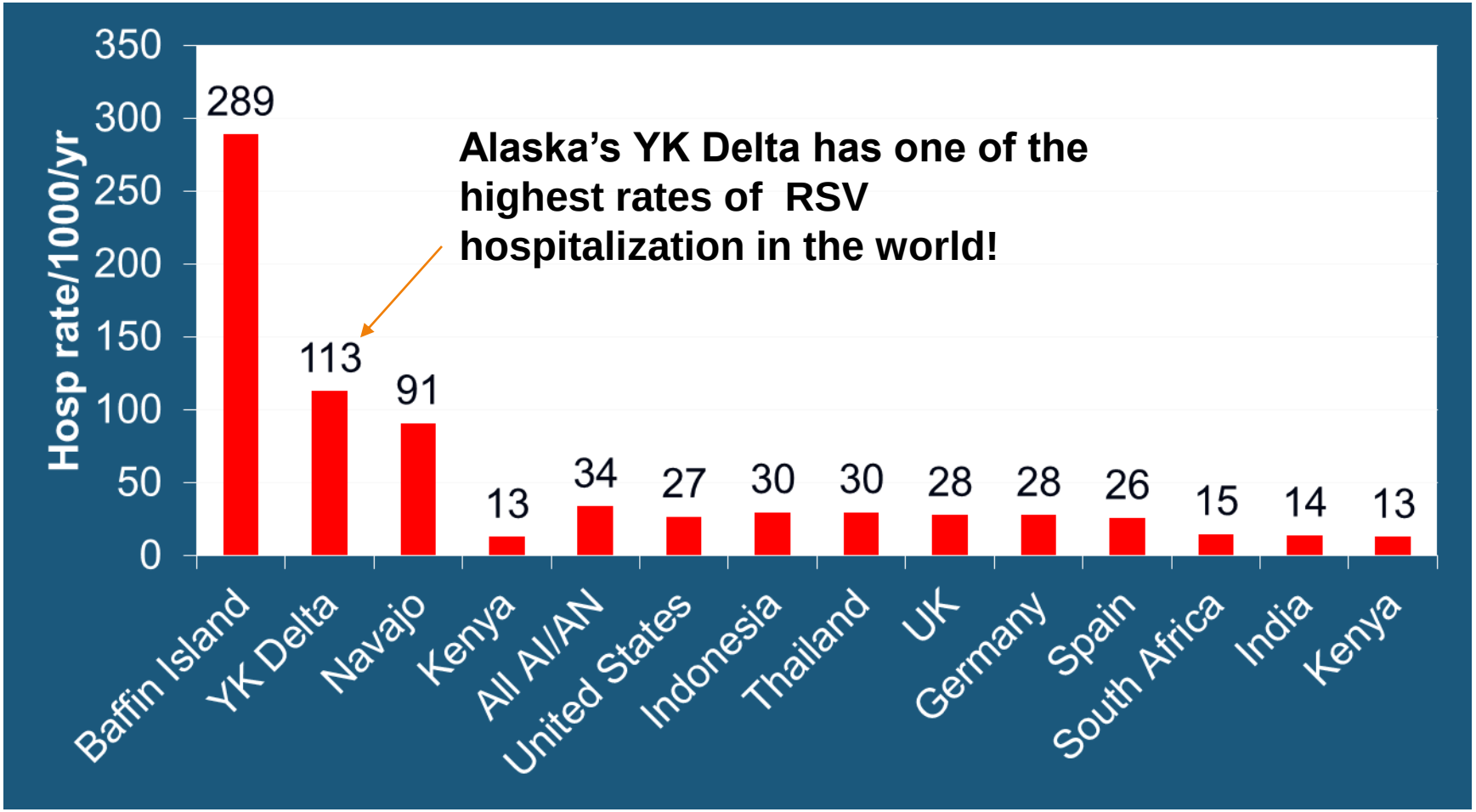
BRONCHIECTASIS: PREVENTION AND MANAGEMENT

YKDRH Medical Staff
March 24, 2016

Rosalyn Singleton MD MPH
Alaska Native Tribal Health Consortium, Clinical & Research Services
Arctic Investigations Program – CDC
ris2@cdc.gov, 907-729-3418

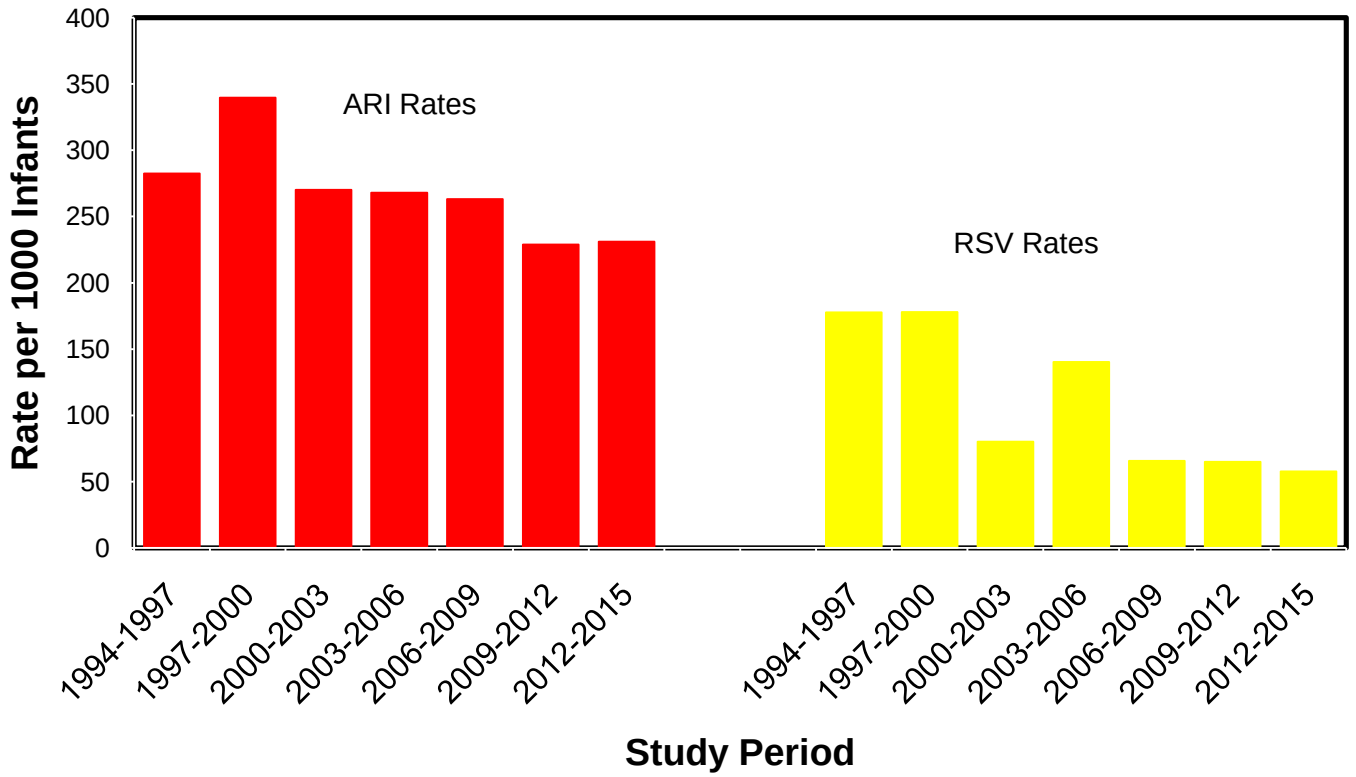
Problem: High rates of Lung Disease

Global RSV Estimates: Rate of Severe or Hospitalized RSV/1000 infants/year



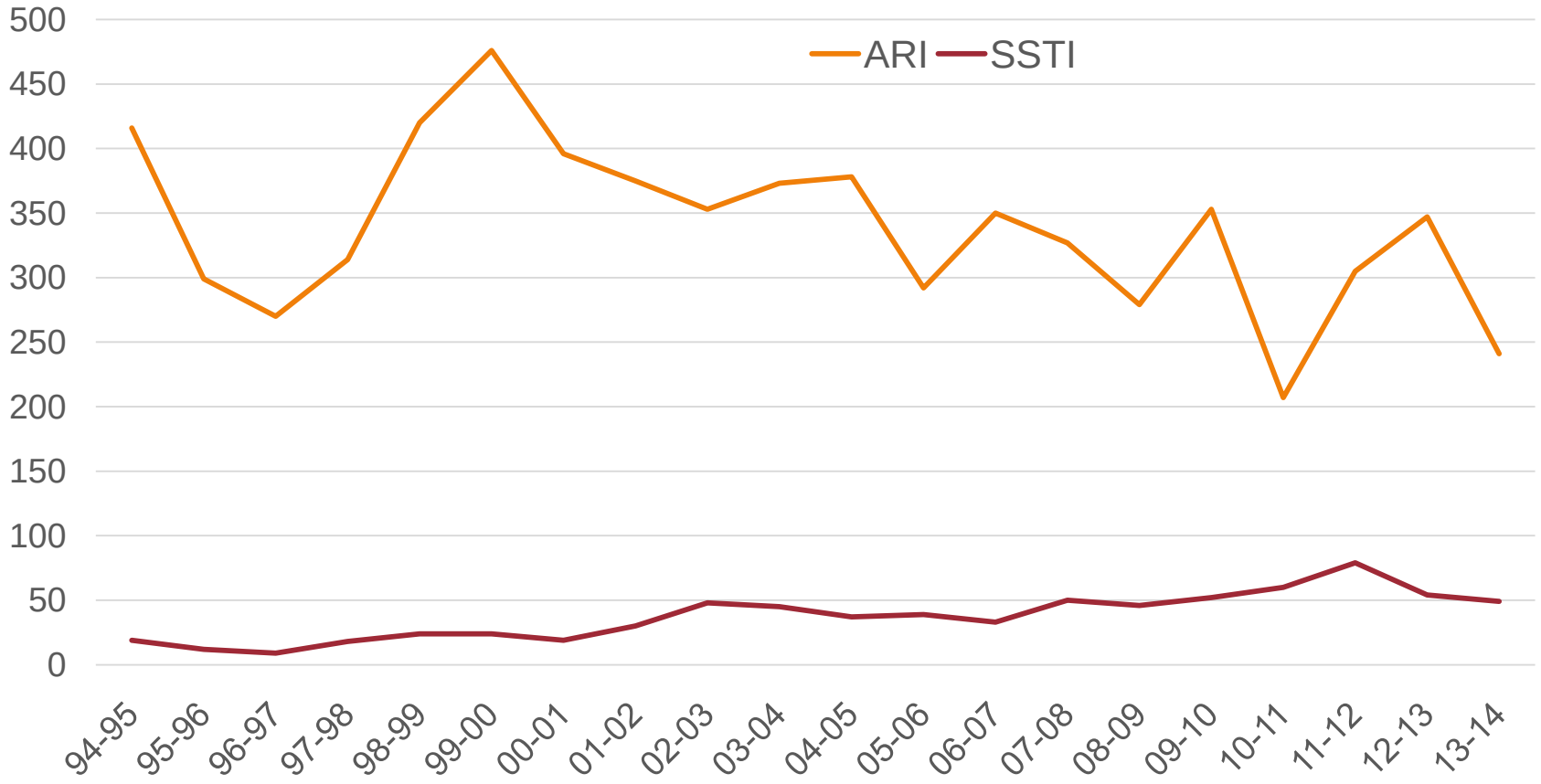
Nair H et al. Global burden of RSV…Lancet 2010;375:1545-55; Banerji. PIDJ 2009.

RSV Hospitalization Rates in the YK Delta, Alaska



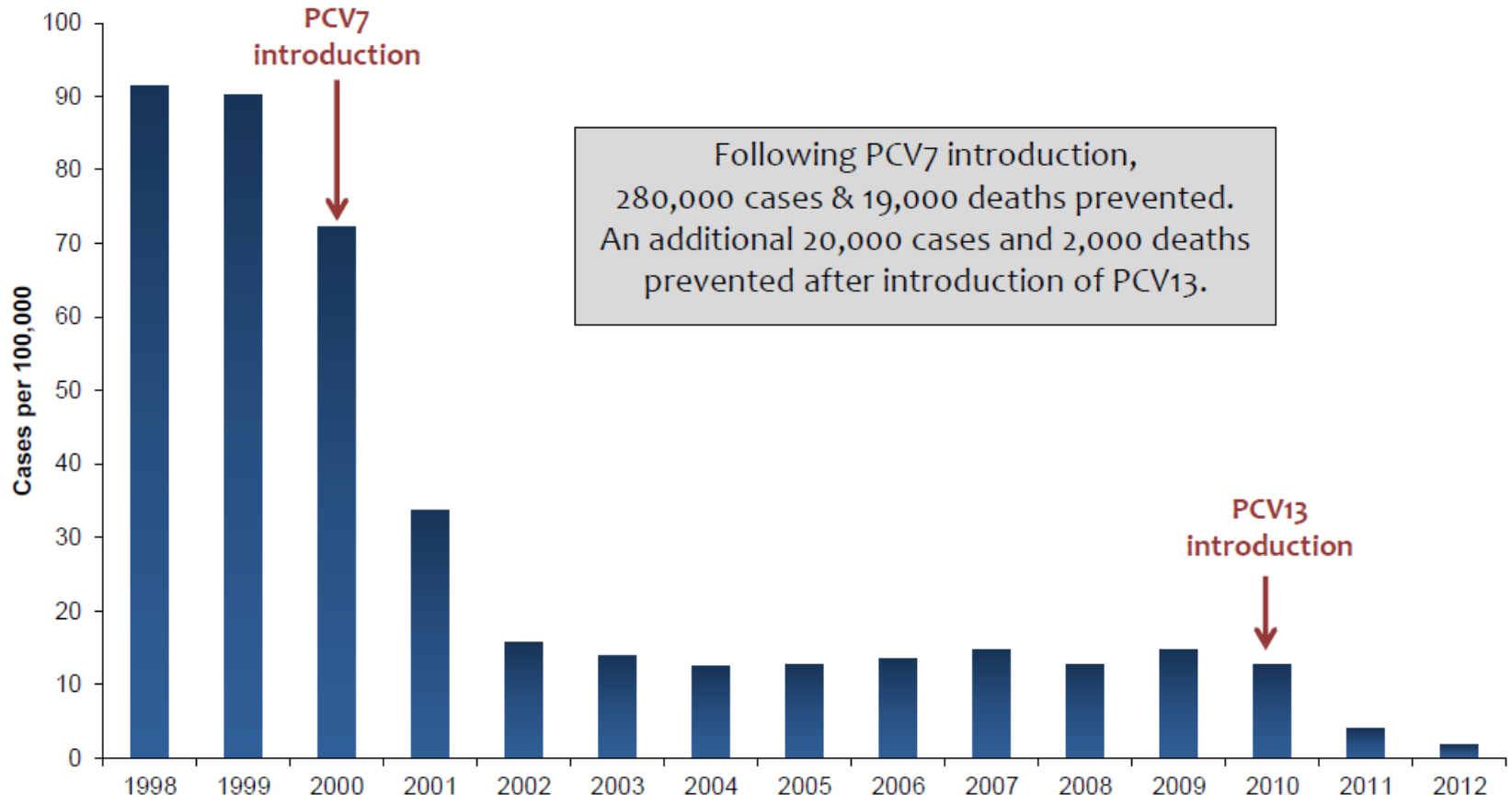
AIP-CDC unpublished

ARI and SSTI Hospitalizations, YK children < 3 yrs, 1994-2014



ARI= Acute Respiratory Infection. SSTI = Skin and Soft Tissue Infection

Impact of PCV, Invasive pneumococcal disease, children <5 yr, 1998-2012



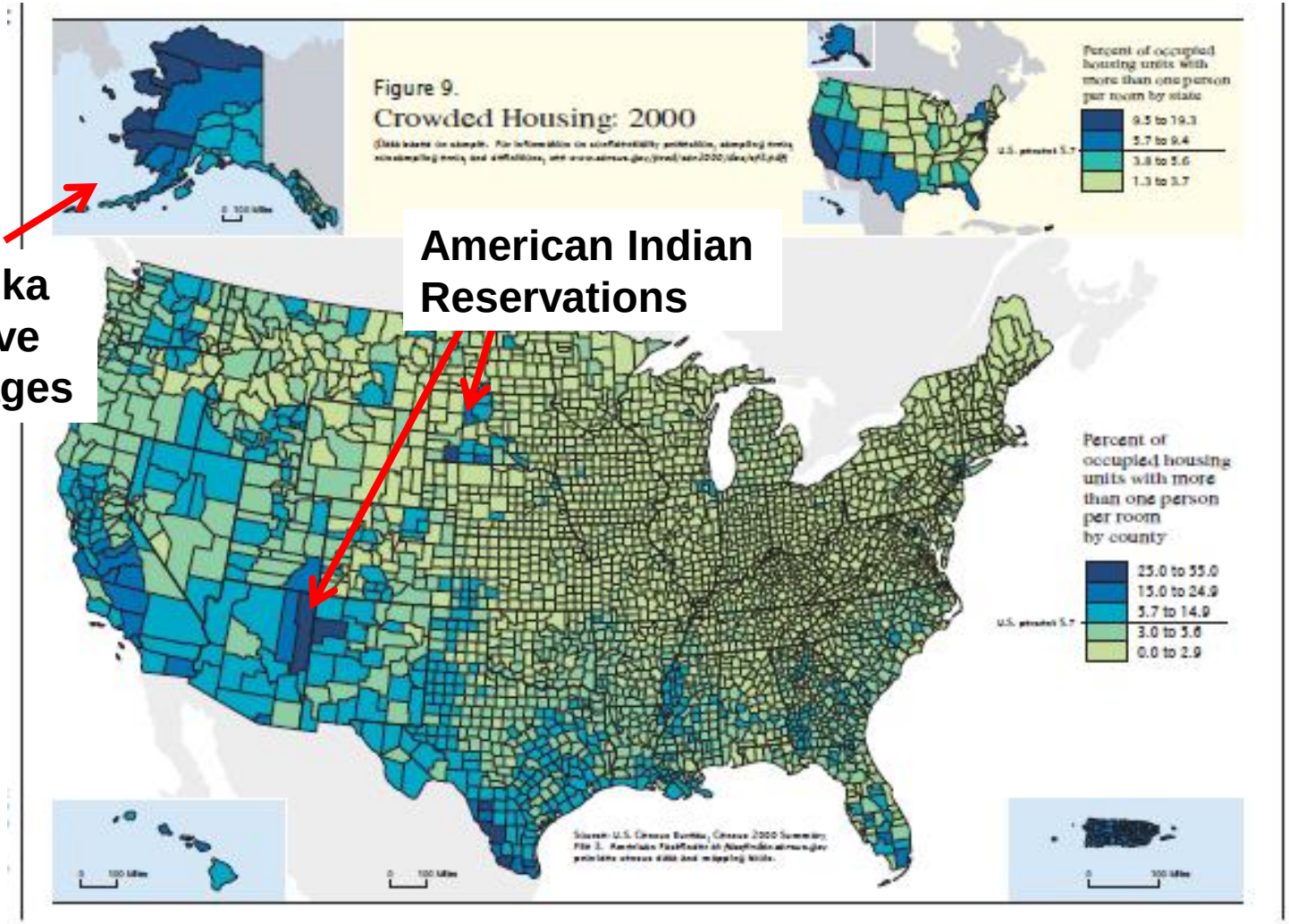
CDC, unpublished

Risk Factors for LRTI and RSV Hospitalizations, Alaska Native children

- Medically high-risk (premie, congenital heart disease, or chronic lung disease)
- Absence of breastfeeding
- Household crowding
- <2 rooms with sinks
- No piped water
- Woodstove in the house
- Vomiting after feeding
- Low income

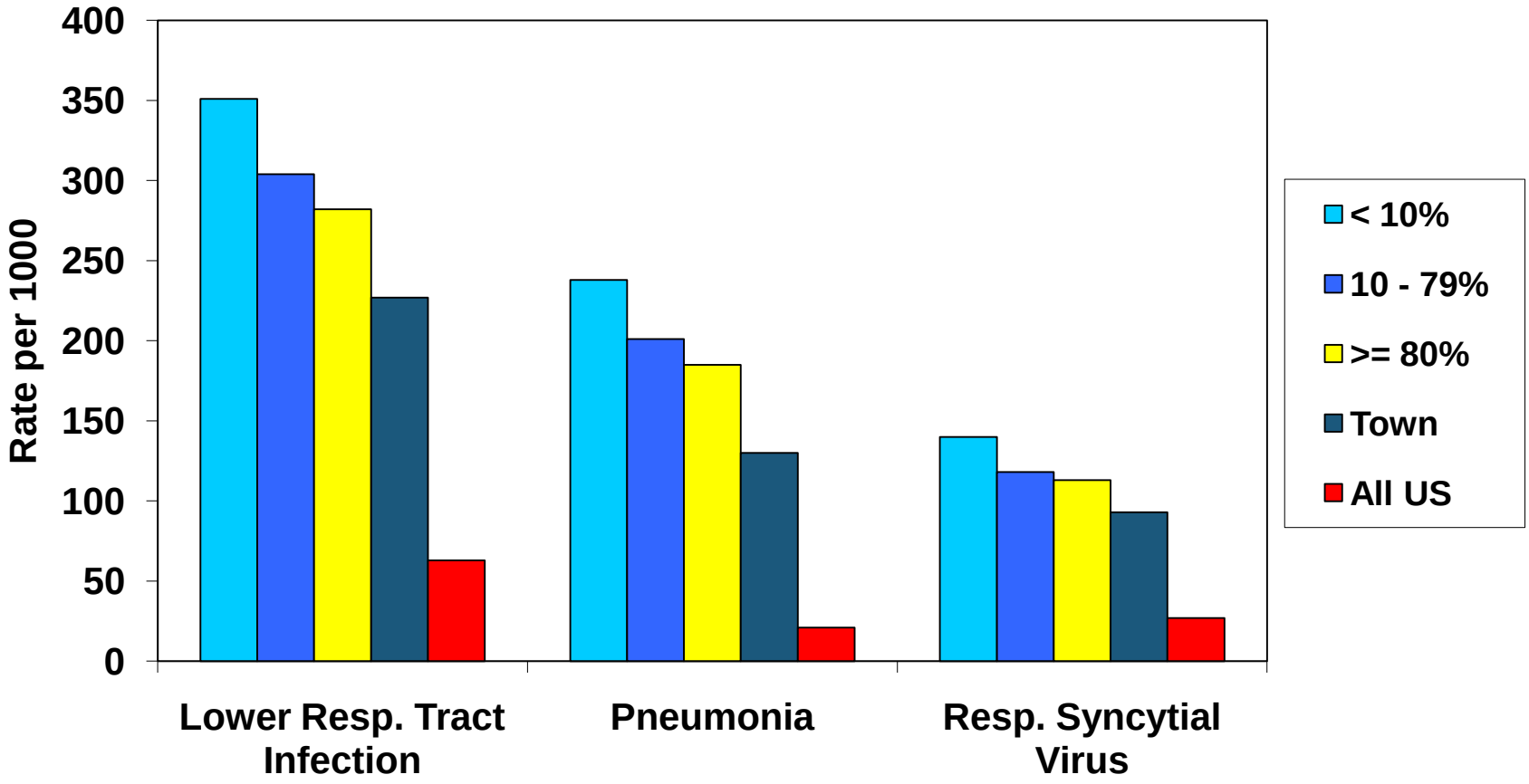
Bulkow LR et al. Risk Factors for Hospitalization With LRTIs in Children in Rural Alaska. Pediatrics 2012
Bulkow LR et al. Risk factors for severe RSV infection among Alaska native children. Pediatrics 2002
Bruden et al, 18 years of RSV Surveillance. Ped Infect Dis J, 2015, In press.

Household Crowding in the U.S. 2000 Census Data



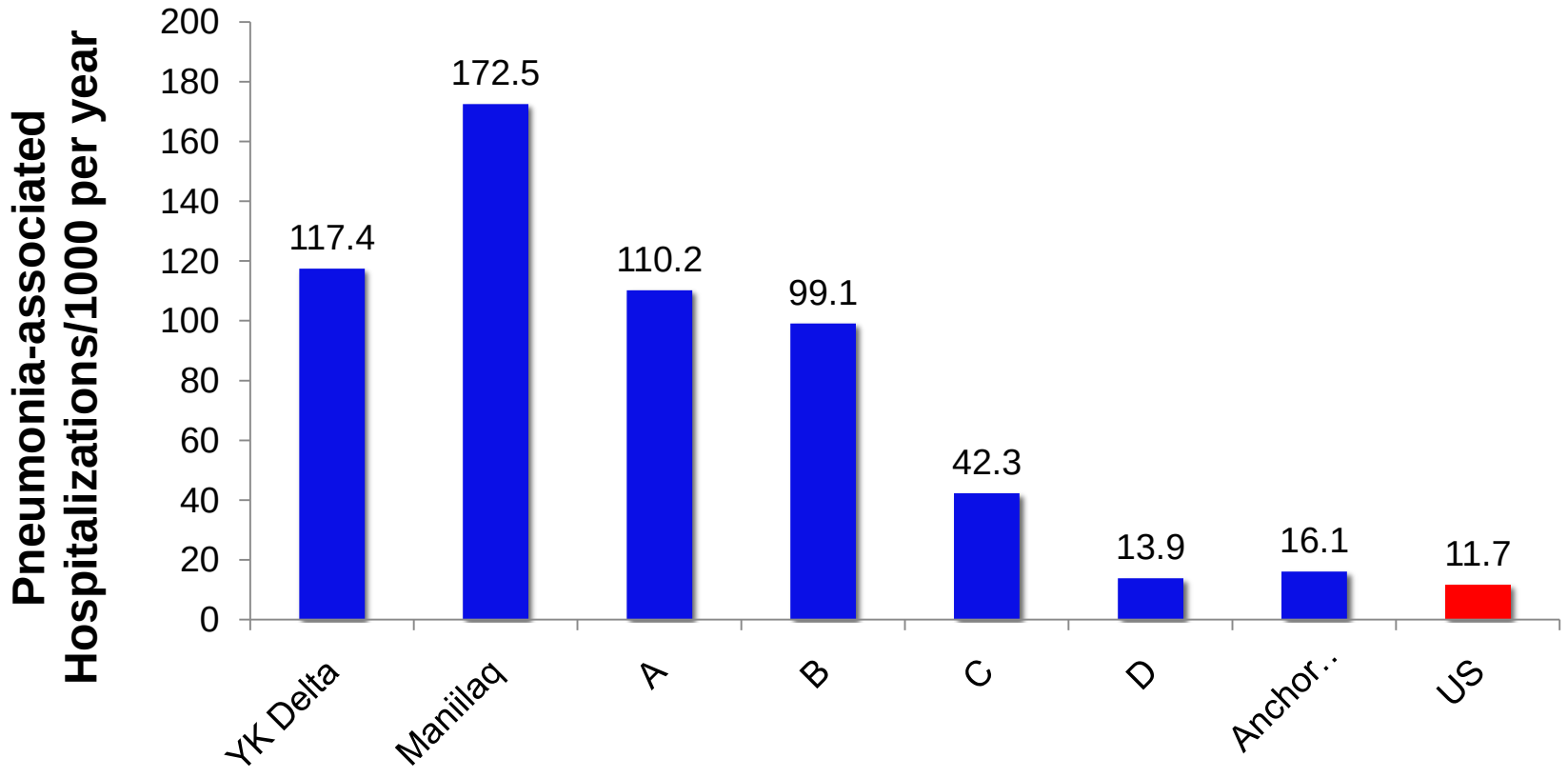
Structural and Occupancy Characteristics of Housing: 2000. Census 2000 brief. US Census Bureau,

Hospitalization rate among infants by percentage of rural Alaska village homes with water service, 1999–2004



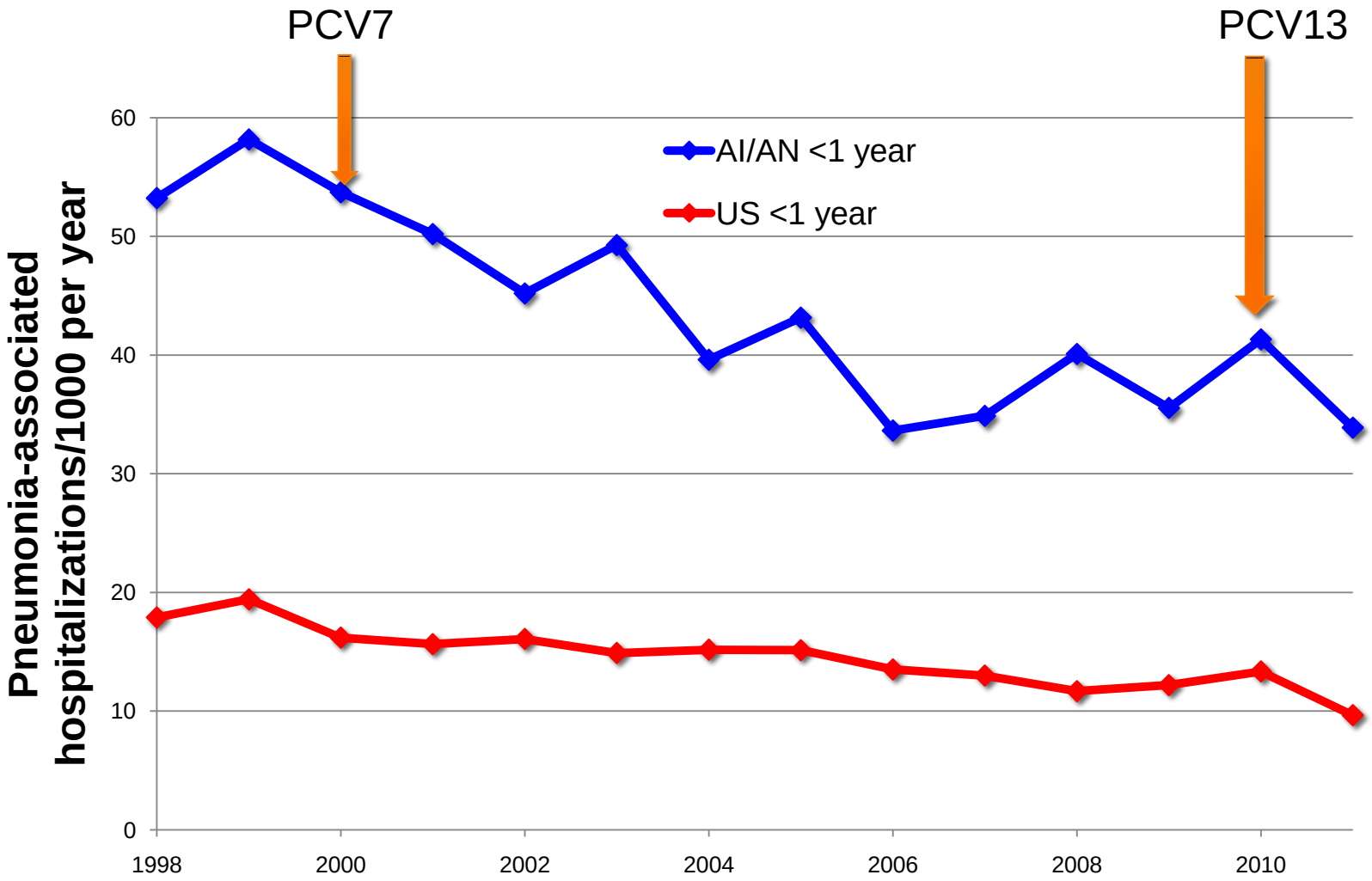
Hennessy TW et al. In-home water service and the risk of respiratory tract,. AJPH 2008.

Pneumonia hospitalizations, Alaska Native infants, by region, 2009-2011



Pneumonia hospitalization rate in Alaska Native infants in rural western Alaska is >10 times the rate in the U.S. and one of the highest rates reported worldwide.

Pneumonia-associated hospitalizations, AI/AN and US infants, 1998-2011



Foote E, et al. J Circumpolar Health. 2015 Nov 5;74:2925

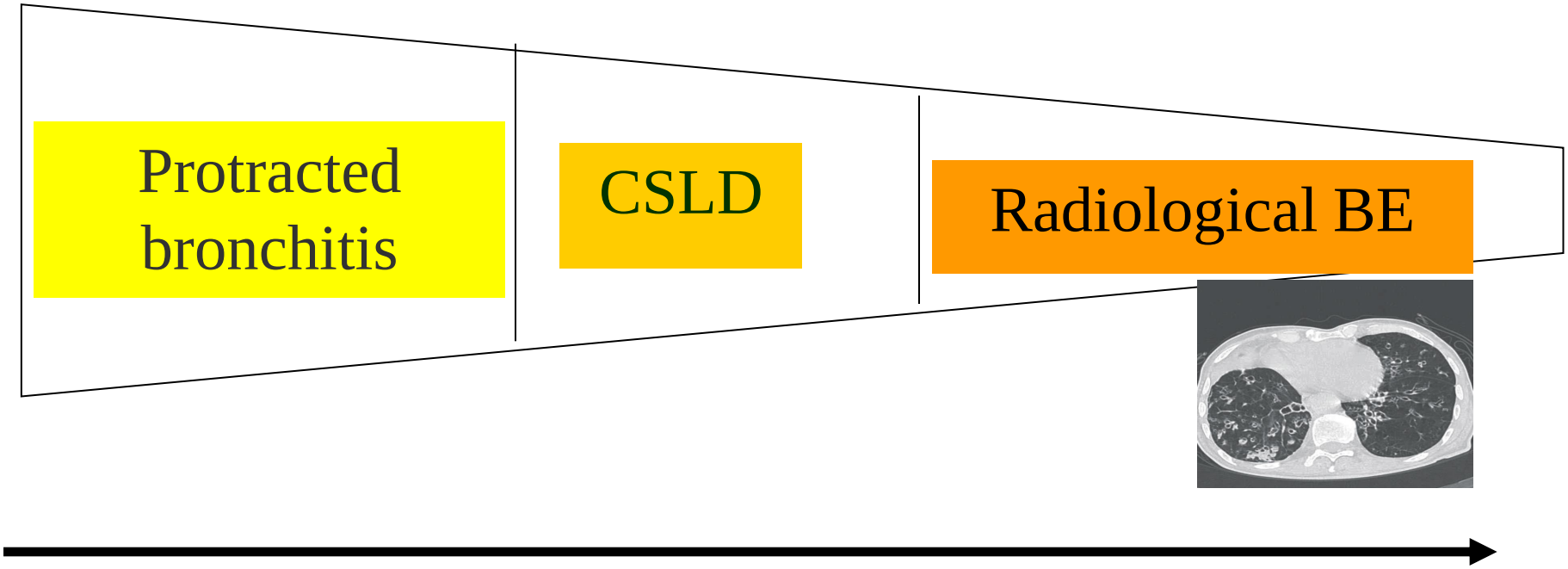
Long-term effects of Pneumonia

- **Decreased lung function in Adulthood**
  - Adults with childhood pneumonia had lower FEV1 than others

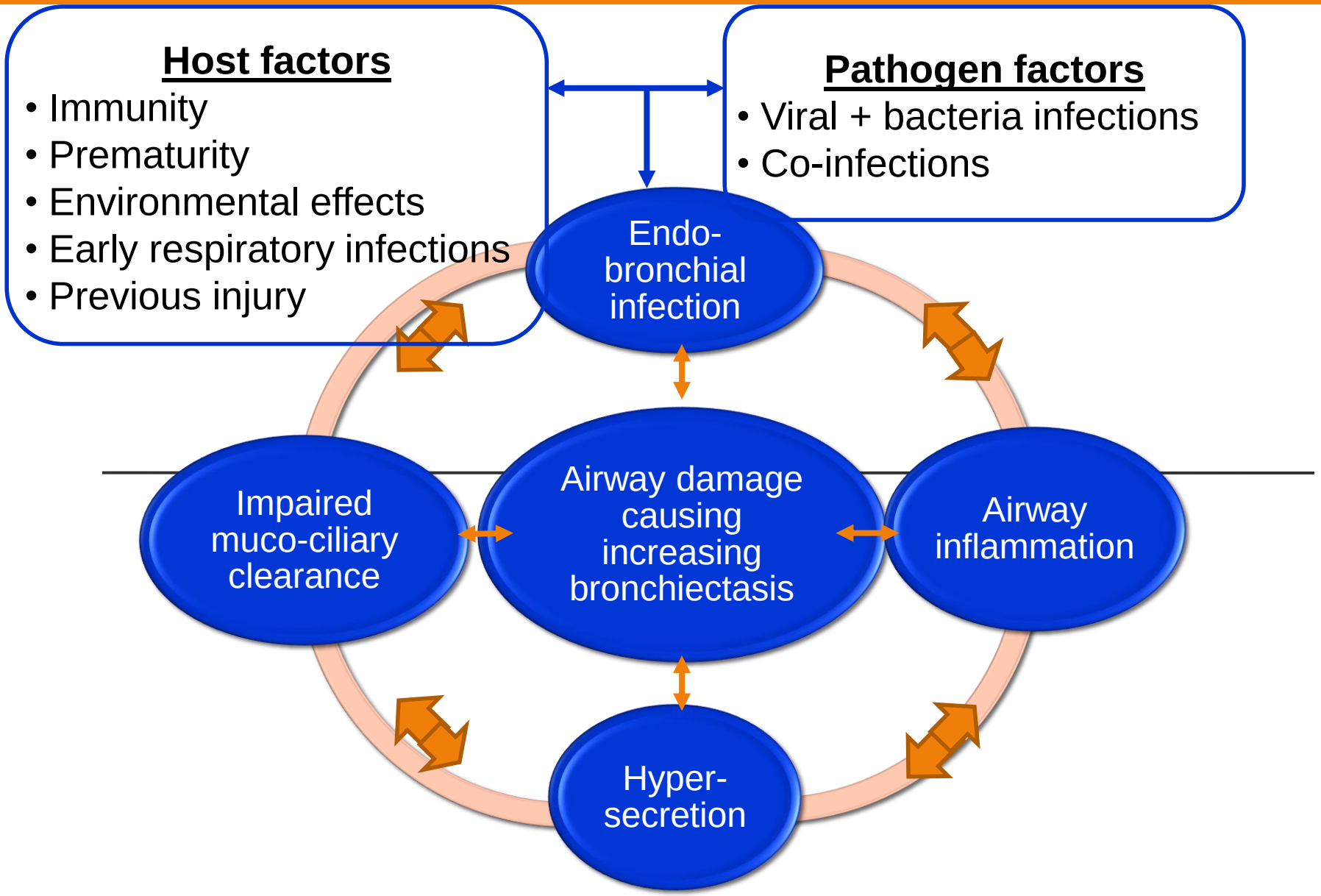
- **Chronic Suppurative Lung Disease/Bronchiectasis**
  - Airway damage leads to “ectasia” and loss of elasticity of bronchi
  - Loss of muco-ciliary function leads to difficulty clearing secretions
  - Classic symptom is **“Chronic Wet Cough”**
  - Progression of disease from protracted bronchitis to chronic suppurative lung disease (3 episodes at least 3 months each) and CT scan confirmed Bronchiectasis

Spectrum: Chronic Suppurative Lung Disease

Progression of disease process



Pediatric Pulmonol 2008;43:519-31

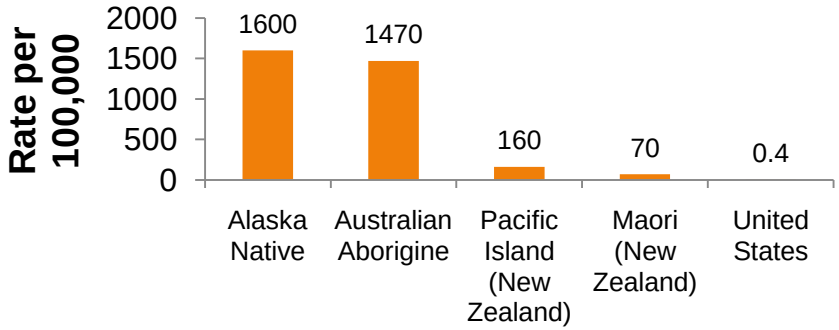


The Vicious Cycle of Bronchiectasis/Chronic Suppurative Lung Disease

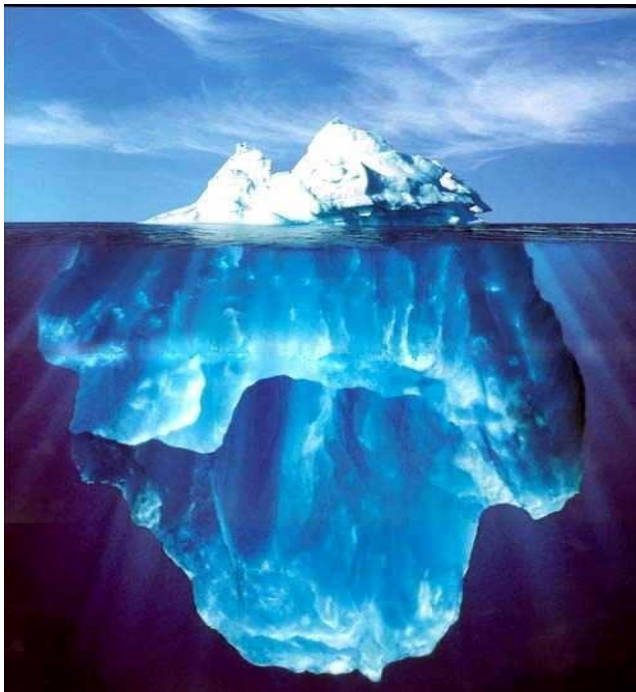
Worldwide Prevalence

What we know!

- Alaska YK Delta: 1 in 63 children
- Central Australia: 1 in 68
- NZ Maori/Pacific: 1 in 2000
- U.S.: 1 in 250,000



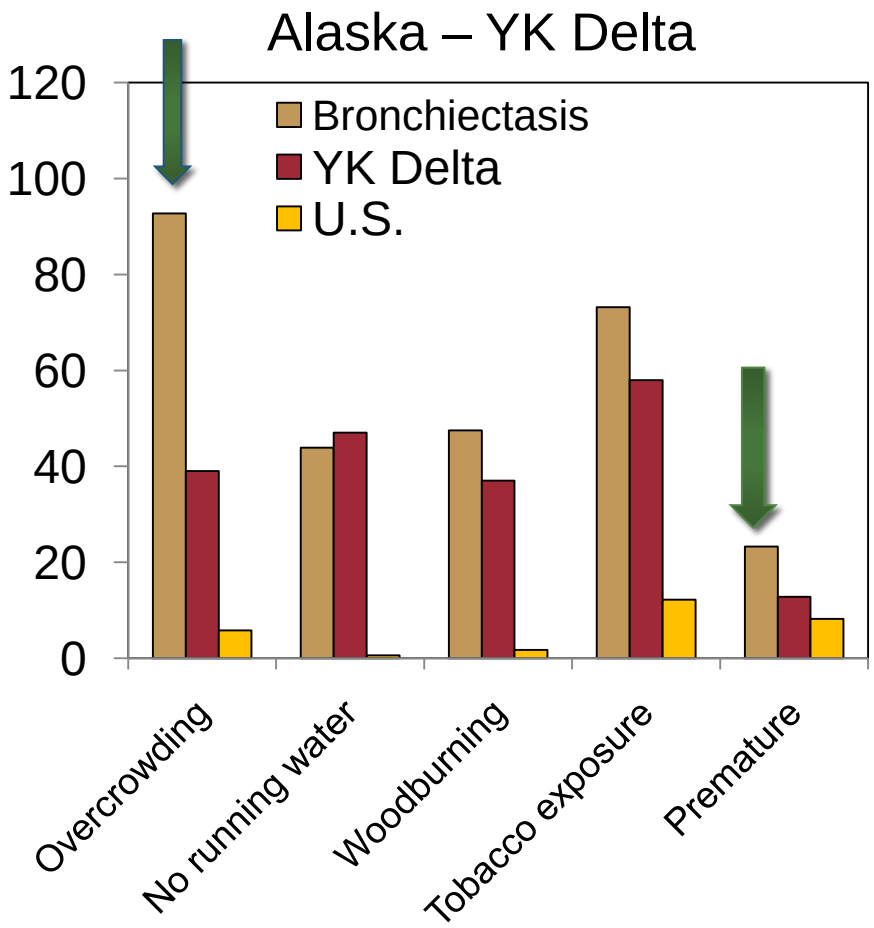
In contrast,
Cystic Fibrosis in Australia = 1 in 30,000 but gets lots of $$$ for research and treatment

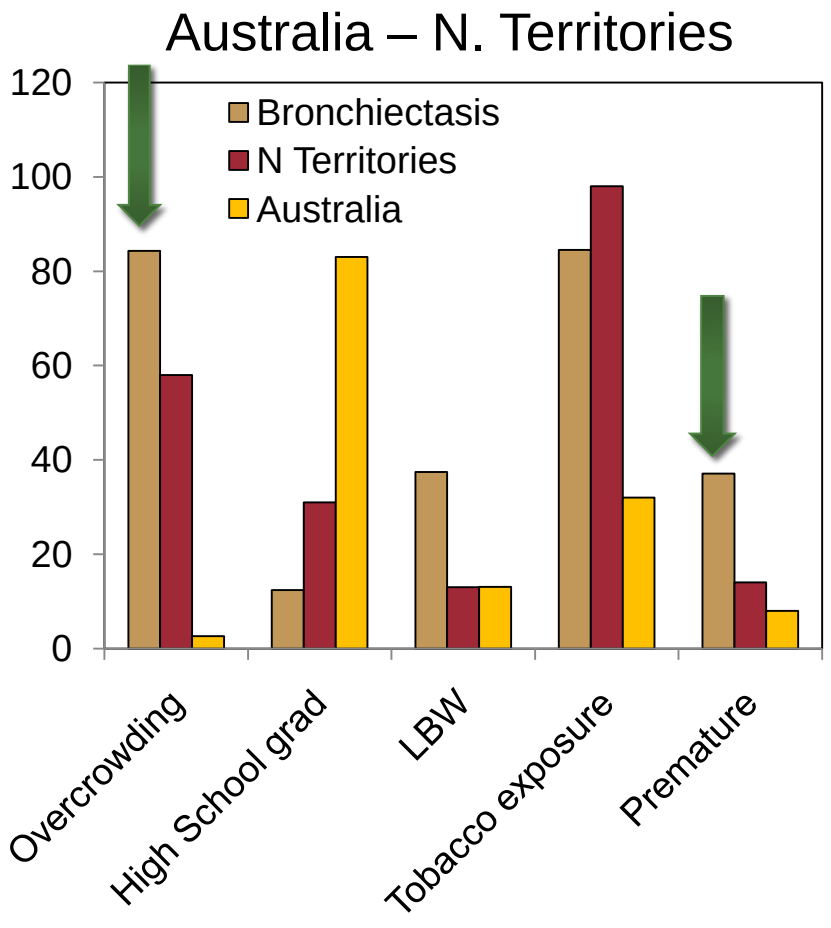


This is just the tip of the iceberg!

CSLD/Bronchiectasis probably occurs at the same high rates in countries with high rates of pneumonia

Children with bronchiectasis compared with local and national population: YK/Australia

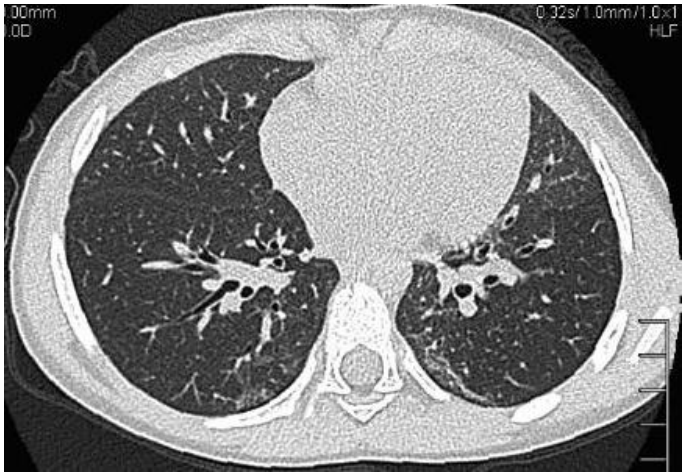


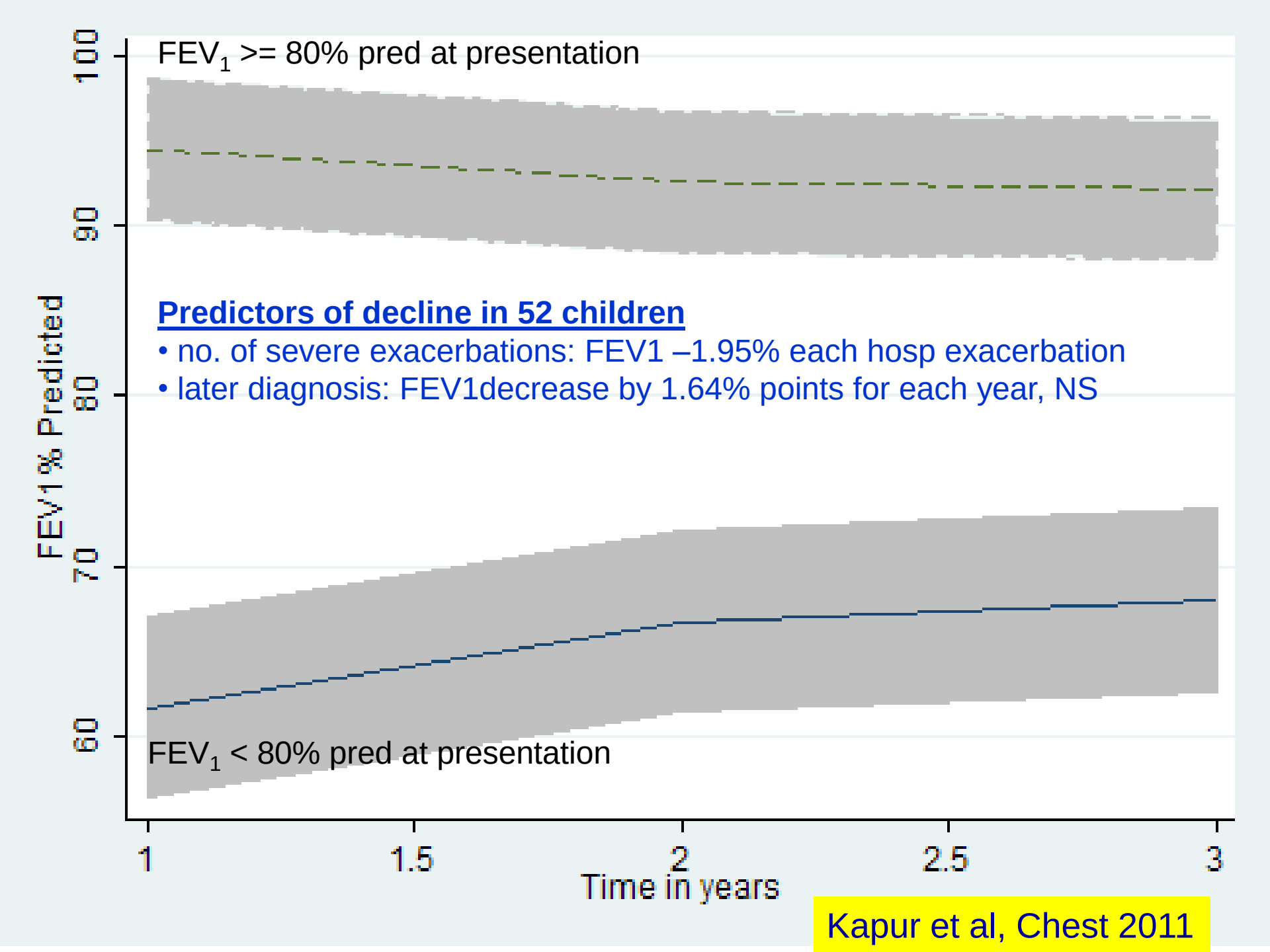


Singleton RJ et al. Indigenous children from three countries with non-cystic fibrosis chronic suppurative lung disease/bronchiectasis. Pediatr Pulmonol 2014

Why CSLD-bronchiectasis is important

- High Prevalence; Increasingly recognized
- Burden of disease high, affects Quality of Life, lung function.
- Leads to early COPD and death.
- Early diagnosis and treatment can prevent decline in lung function (FEV1)




FEV1 >= 80% pred at presentation
Predictors of decline in 52 children
• no. of severe exacerbations: FEV1 –1.95% each hosp exacerbation
• later diagnosis: FEV1decrease by 1.64% points for each year, NS
FEV1 < 80% pred at presentation
FEV1% Predicted
100
90
80
70
60
1
1.5
2
2.5
3
Time in years
Kapur et al, Chest 2011

Treatment principles

Diagnose early and look for treatable etiologies

- Reduce infection-inflammation
  - Treat early and exacerbations ‘aggressively’
  - Airway hygiene clearance
  - Vaccinations
- Improve other factors contributing
  - Attention to nutrition
  - Detect complications, pollutants
- Systematic care
  - Regular review, multi-disciplinary care
  - Education, enhance self care and management

Reduce infection-inflammation

The principles

- Infection leads to increased inflammation
- Clinically:
  - Most kids look well
  - Generally only wet (productive) cough
  - In exacerbations: fever very rare
  - When first diagnosed it is possible to get kids cough free

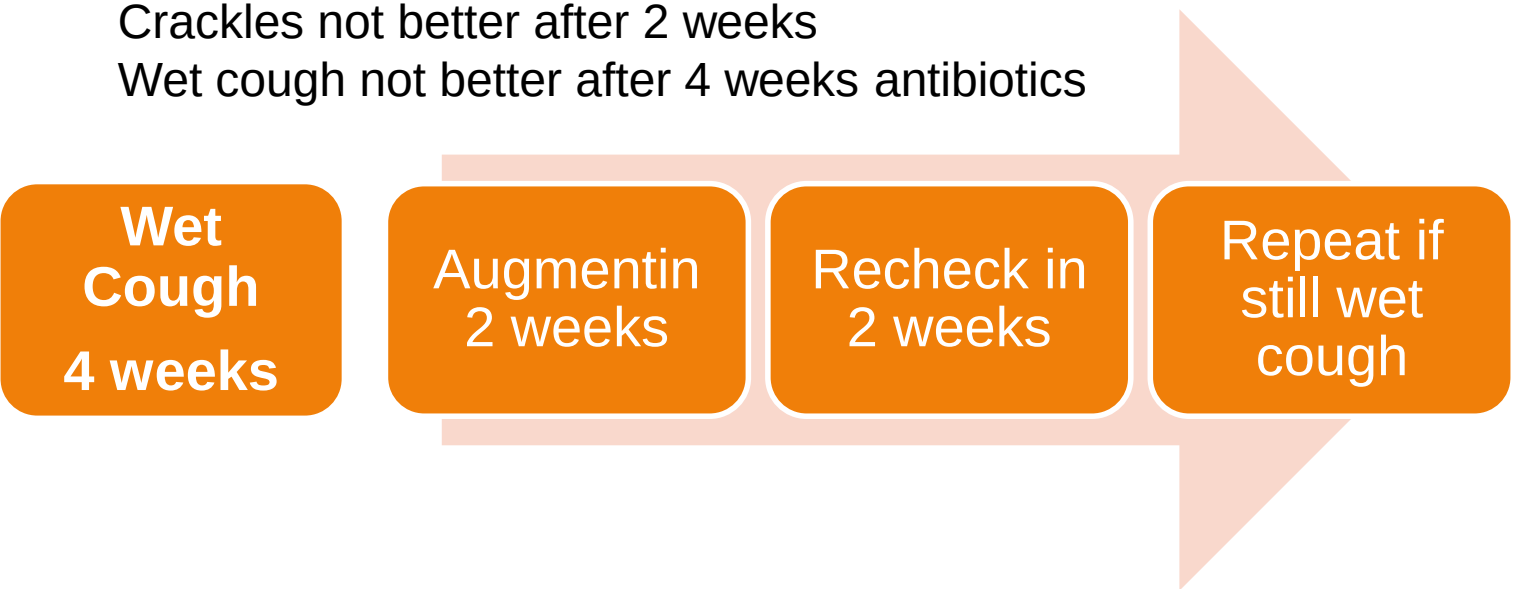
Child with Wet Cough ≥ 4 weeks

Chang A et al. A cough algorithm for chronic cough. Pediatrics 2013;131:e1576-e1583

Assessment: Look for underlying diagnosis:Chest x-ray. Consider Spirometry if >5 years. Consider TB/pertussis testing. Address tobacco smoke, other pollutants. Rhinosinusitis/Upper Airway symptoms - treat for rhinosinusitis

Wheeze/dyspnea – treat if asthma
Feeding/neuro-dev issues – treat aspiration/GERD
Recurrent bronchitis/pneumonia
FTT
Crackles not better after 2 weeks
Wet cough not better after 4 weeks antibiotics

→ Consult with Pulmonologist

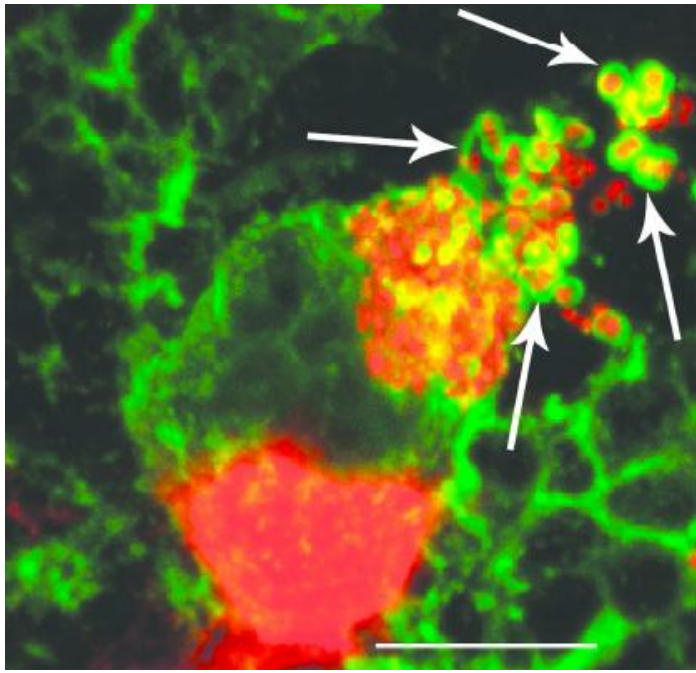


Consult with Pulmonologist

Antibiotics

Antibiotics breaks infection/inflammation cycle

- Protracted Bronchitis" Children with wet cough > 1 month.
  - May need 2 weeks of Augmentin; likely biofilm related
- CSLD: Aim for cough free as baseline
- Bronchiectasis
  - Intermittent:
    - Treat exacerbations
      - Augmentin - outpatient
      - Ceftriaxone - inpatient
    - 1 month of antibiotics as a trial to dry cough
  - Maintenance
    - ≥2 exacerbations per year
    - Not responsive to intermittent
    - Azithromycin 30 mg/kg once weekly



Marsh et al, 2014

Pulmonary Exacerbations: Bronchiectasis

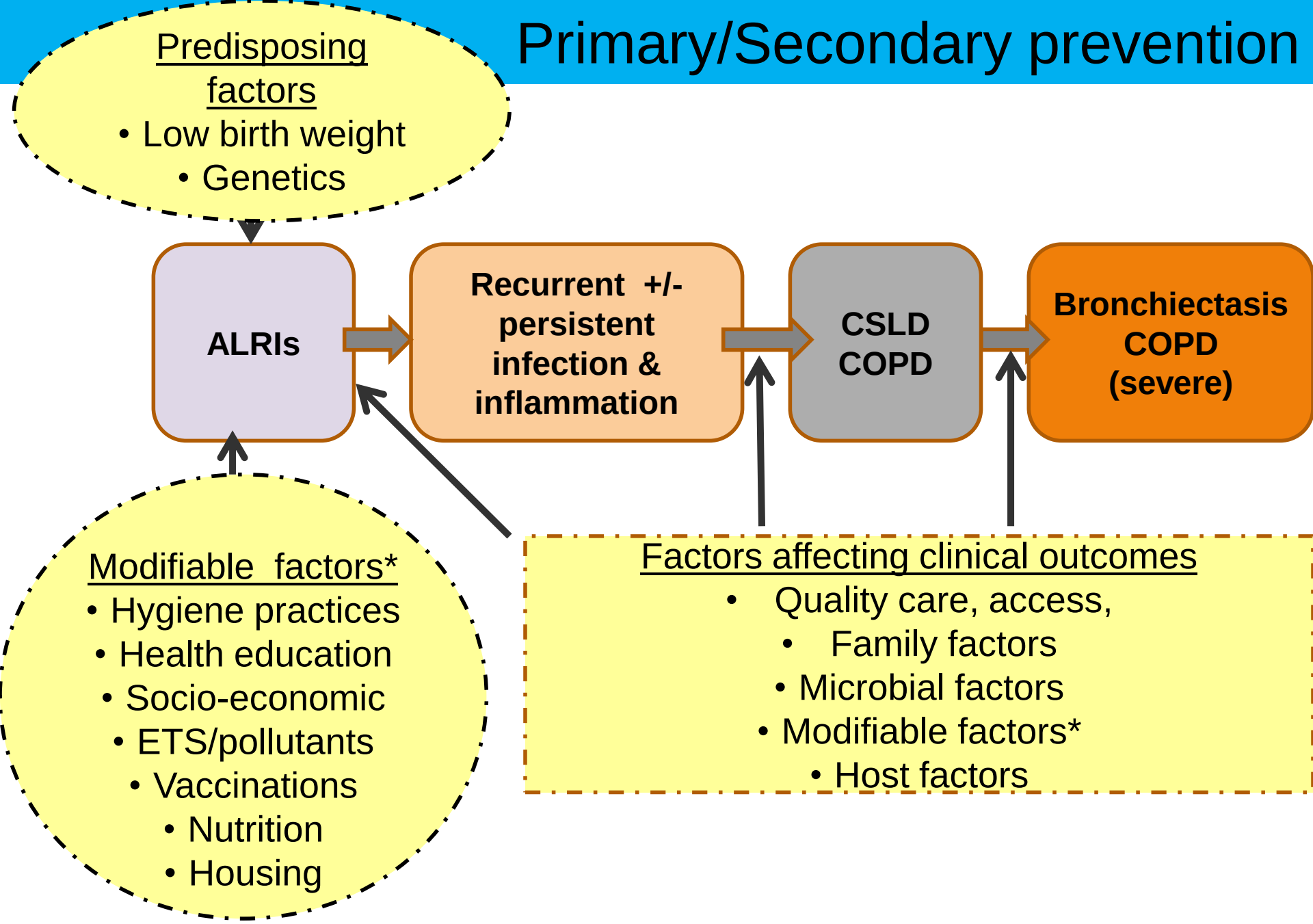
- **Definition**: Increased cough or sputum volume, fatigue, dyspnea, hemoptysis, reduced FEV1, new chest findings, new chest radiograph density AND new antibiotic treatment

- **Risk Factors:** young age, severe LRIs/pneumonia in first year of life, recent LRI/pneumonia, recurrent Exacerbations

- **Why Important:** Severe exacerbations associated with decrease in FEV1

Redding et al, CHEST 2014:146;762-4

Primary/Secondary prevention



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urce - for people working, studying, or interested in addressing
lander peoples. We aim to provide quality information and
digenous peoples.

Australian Collaborations with Menzies in Darwin

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Follow-up of the International Bronchiectasis Observational Study

- **Objective:**
  Follow-up the 2005 YK Delta and Australian International Bronchiectasis Observational cohort study children to evaluate their current lung and factors affecting progression or recession of bronchiectasis.

Method:

- One-time clinical evaluation of participants by pulmonologist with chest x-ray, pulmonary function tests and microbiology of nasal samples.

Investigators

- Rosalyn Singleton MD - ANTHC, CDC
- Greg Redding MD - U Washington (pediatric pulmonologist)
- Joe Klejka MD, Lori Chikoyak, Leslie Hermann, Mien Chyi – YKHC
- Gabrielle McCallum – Darwin, Australia

Status:

- Data collection in progress.
- Some children have resolved their lung condition.
- Some children have respiratory symptoms and are losing lung function.

Preventing and improving the management of chronic suppurative lung disease in Indigenous children of Australia, USA, and Malaysia.

Year: Australian funding proposal for 2017-2021

Organization: Menzies School of Health Research

Goal: (pending funding) Prevent development and worsening of chronic suppurative lung disease (CSLD) and bronchiectasis in Indigenous children.

Methods: Develop model to follow children at CSLD risk. Adapt evidence-based CSLD guidelines for Alaska Natives. Workshops to train health providers to recognize and manage children with CSLD.

Proposed workshop locations: ANMC, YKHC, ?Norton Sound

Investigators:

- Anne Chang– Menzies School of Health Research, Darwin, Australia
- Rosalyn Singleton, Connie Jesson – ANTHC, Clinical Research Services
- Greg Redding – U Washington (pediatric pulmonologist)

Status: ANTHC pre-approval obtained. Awaiting notice of funding in late 2016.

Partnering with:
ANTHC Div. Environmental Health &Engineering
ANTHC Community Health and Environment

Improving the Respiratory Health of Alaska Native People through Home-based Interventions: The Healthy Homes Study

Background and Methods:

- Alaska Native children have high rates of pneumonia and bronchiolitis hospitalizations and chronic lung disease:
  - Evaluate the impact of simple home renovations and education on improving respiratory symptoms
  - Measure indoor air quality, respiratory visits, and respiratory symptoms before and after interventions

Institutions:

- ANTHC DEHE
- AIP- CDC
- YKHC
- BBAHC

Investigators:

- AJ Salkoski
- Troy Ritter REHS, MPH
- Rosalyn Singleton MD
- Thomas Hennessy MD
- Jennifer Dobson REHS, MS
- Leif Albertson REHS, MS
- Joseph Klejka MD
- Lisa Bulkow MS
- Jennifer Skarada
- George Goodwin

Status: In 4th and final year of the study. Writing up baseline data.

Methods

- Choose YKHC and BBAHC communities
- Choose eligible homes with child who has chronic lung problems
- ANTHC, Regional Health Corporation Staff, & Housing Authority Staff assess home:
  - Inadequate ventilation, leaky woodstove, moisture problems
  - Identify contaminants
  - Identify risky behaviors
- The resident, housing and environmental health personnel decide scope of work
- ANTHC Environmental Health does air sampling and household education
- Housing Personnel complete modifications

New and/or Improved Vents

Ventilation intake plugged with a rag

New ventilation intake

Woodstove Replacement

Old woodstove

New EPA-certified, low-emission woodstove

How do study houses compare with other U.S. homes?

Housing	Study houses	US houses
Mean # occupants	7.3	2.6
Median sq. feet	920	2,465
% >1 person/room	73%	3%
% with woodstove primary heat	16%	2%
% w/ smokers	49%	26%
% no running water	60%	0.5%

U.S. data from 2008-2012 Census, American Community Survey

Smaller, crowded, more smokers & woodstove use, less running water

Healthy Homes Study: Baseline findings

- **Indoor Air Quality**
  - High Volatile Organic Compounds (VOCs) and Particulates (PM2.5)

- **Respiratory symptoms in study household children**
  - Case children and other household children had high rates of cough between colds, hospitalization for lung infections, history of pneumonia, and wheezing.
- **Household factors and child symptoms**
  - VOCs
  - Primary wood heat
  - PM2.5

- Cough between colds

  - VOCs

- Wheeze between colds
- Asthma diagnosis

Environmental Health Hospital Consultation Study

Year: 2016-2019

Organizations: ANTHC, SCF, YKHC, other THOs

Objectives: Pilot project to determine the feasibility of a hospital-based environmental consultation program at ANMC.

Methods: Environmental Health staff provide consult to caregivers, equip them with techniques/ tools to improve indoor air quality, make referrals to village housing if needed.

Evaluate: Changes in behaviors, child resp. visits and hospitalizations.

Investigators:

- Korie Hickel, AJ Salkoski, Joy Britt – ANTHC, Community Environment and Health
- Rosalyn Singleton, Gretchen Day– ANTHC, Clinical Research Services
- Christine Tan, Whitney Elliott, Matt Hirschfeld – ANMC Pediatric Hospitalists

Environmental Health Hospital Consultation Study

Status:

- IRB and YKHC approval for Year 1
- Seeking other tribal organization approvals for Year 2-3

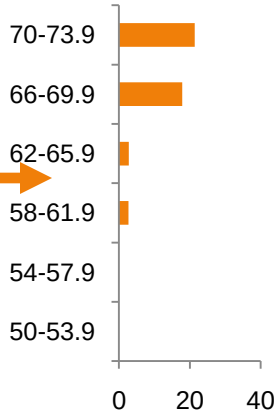
Norton Sound: We presented the study to the Committee to invite Norton Sound to participate in Year 2.

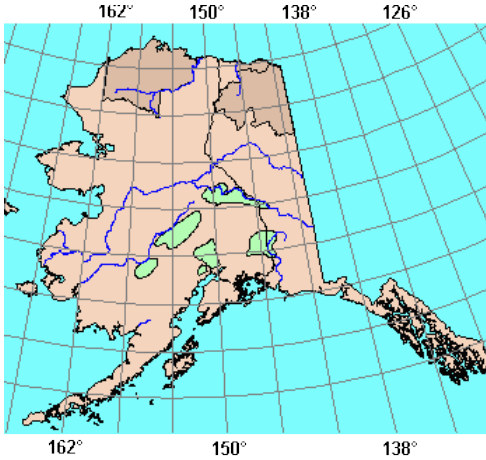
What does participation involve?

Eligible children from Norton Sound hospitalized at ANMC would be invited to participate in: environmental health consultation and possible referral to village housing.

Study Results: Rickets and Vitamin D Deficiency in Alaska Native children

- Rickets visits and diagnoses more common in Alaska Native children than in the US or other IHS Areas
- Rickets diagnosis increased with:
  - Increasing latitude
  - Diagnosis of malnutrition





- Rickets and vitamin D deficiency occurred in both breastfed and formula fed infants
- Rickets and vitamin D deficiency were more common in infants who did not receive vitamin D supplementation.

Confirms importance of AAP recommended vitamin D supplementation of infants to prevent vitamin D deficiency

Serologic Survey of Biomarkers for Traditional Marine Diet and Vitamin D Levels in YK Delta Childbearing-aged Women

Objective: Explore how intake of traditional marine foods and serum Vitamin D levels have changed in YK women from 1960's through the present

Method: Test Specimen Bank serum samples of YK Delta women 20-29 years old at points from 1960s to 1990s, for biomarkers of traditional marine diet ($\delta^{15}N$) and 25-OH vitamin D levels

Investigators

- Diane O'Brien PhD, Center for AK Native Health Research (CANHR)
- Rosalyn Singleton MD, ANTHC
- Ken Thummel PhD, U Wash, Pharmacy, CANHR
- Bert Boyer PhD, U of Fairbanks, CANHR
- Lisa Bulkow MS, AIP-CDC
- Joseph Klejka MD, YKHC

Results: Vitamin D levels and intake of traditional marine foods were highly correlated and decreased in YK child-bearing aged women during 1960-1990s.
Status: data analysis completed, submitted manuscript.

Serum Vitamin D and $\delta^{15}N$ values, YK Delta women, 20-29 yrs, 1960s-2010s

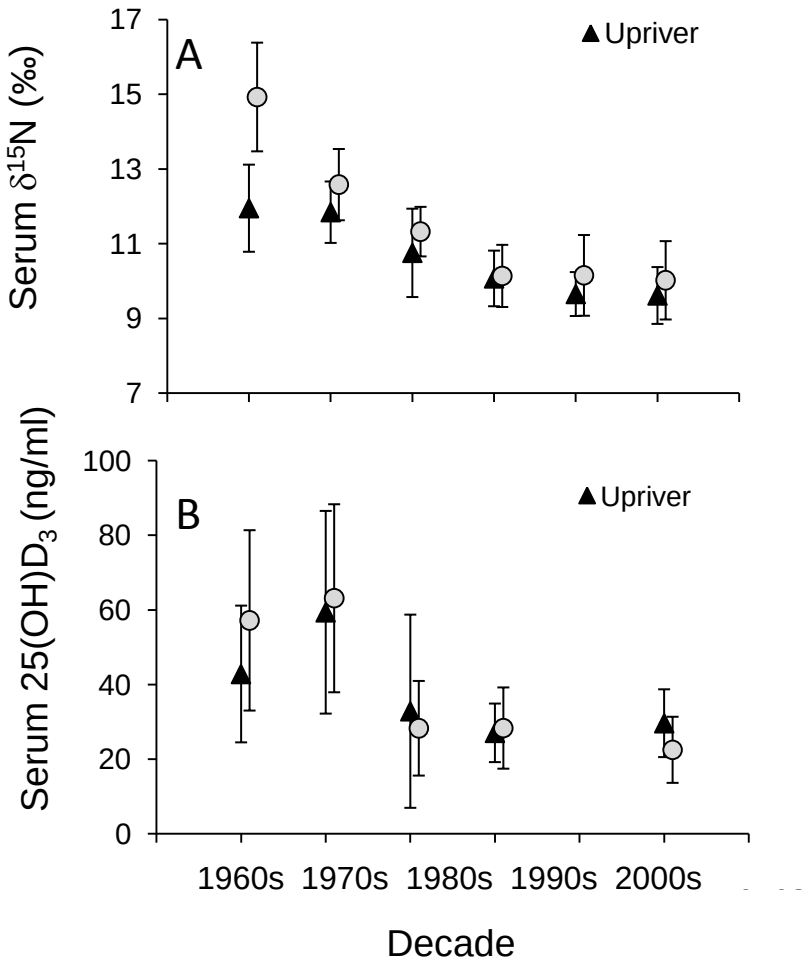


Fig 2

Vit D and Delta 15N (log scale) highly correlated - Pearson correlation ($p<0.001$)

Investigate Association of Prenatal Vitamin D Deficiency with Early Childhood Caries in a Pediatric Alaska Native Population

Year: 2016

Background: Alaska Native children have one of the highest rates of early childhood caries.

Objective: Evaluate the influence of maternal prenatal vitamin D levels on development of early childhood caries.

Method: Retrospective analysis of relationship between vitamin D deficient levels from Maternal Organic Monitoring study and early childhood caries in their infants.

Investigators

- Kendra Sticka MD, Med, RDN – UAA
- Timothy Thomas MD, Rosalyn Singleton MD, Gretchen Day MS, Jonathan Newman MS - ANTHC
- Joseph Klejka MD, Dane Lenaker DDS - YKHC

Status: submitting for CTR-IN grant funding with UAA

NIH Grant offering:

IDeA Pediatric Clinical Trials Network

Due Date: April 15 2016

Background: Research has had dramatic effect on Alaska health: INH prophylaxis trials, Hib vaccine trial were important landmarks. However, ANTHC/tribal has had little success in competing for NIH funding. This RFA is a Pediatric Clinical Trials Network among IDeA states who represent rural and unrepresented populations.

Objective: Develop research expertise and conduct pediatric clinical trials – focused on environmental impacts on health (respiratory infections, birth outcomes, obesity, neurodevelopment)

Method: ANTHC/SCF collaborate to participate in Network clinical trials and build research infrastructure and expertise.

Proposed Investigators

- Investigators: Rosalyn Singleton, Matt Hirschfeld, Melissa Howell, Theresa Dulski
- ANTHC C&RS Timothy Thomas MD, Gretchen Day, Jonathan Newman

Status: writing application.

Next Steps:

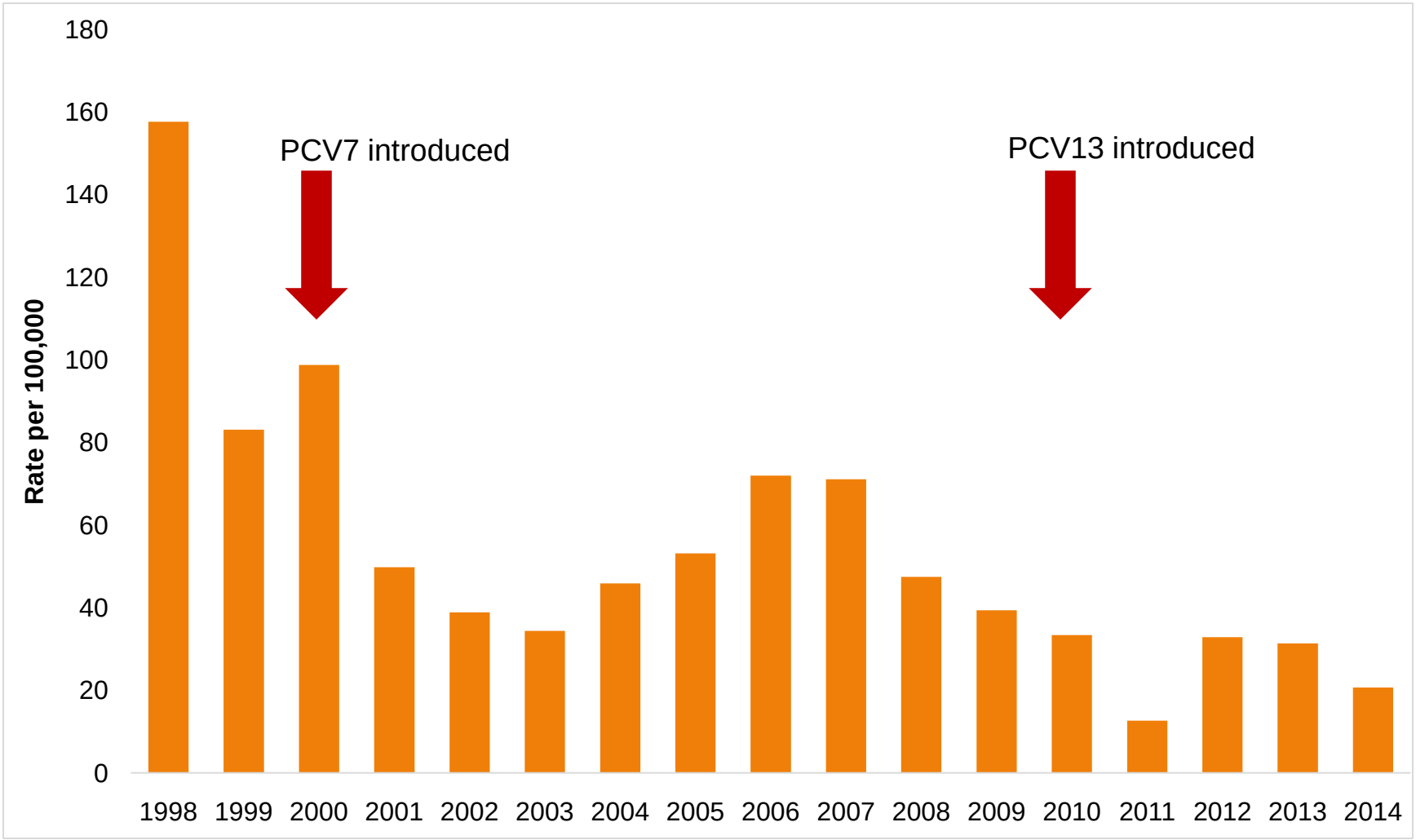
Work with Tribal Organizations to:

- Provide optimal vitamin D supplementation for infants
  - Breastfeeding infants and infants taking <1 liter formula
- Provide optimal vitamin D supplementation for pregnant women
  - 400IU/day in prenatal vitamins. May need more – like 2000 IU/day
- Increase fish consumption in all.

Hep A Vaccine – Longlasting!

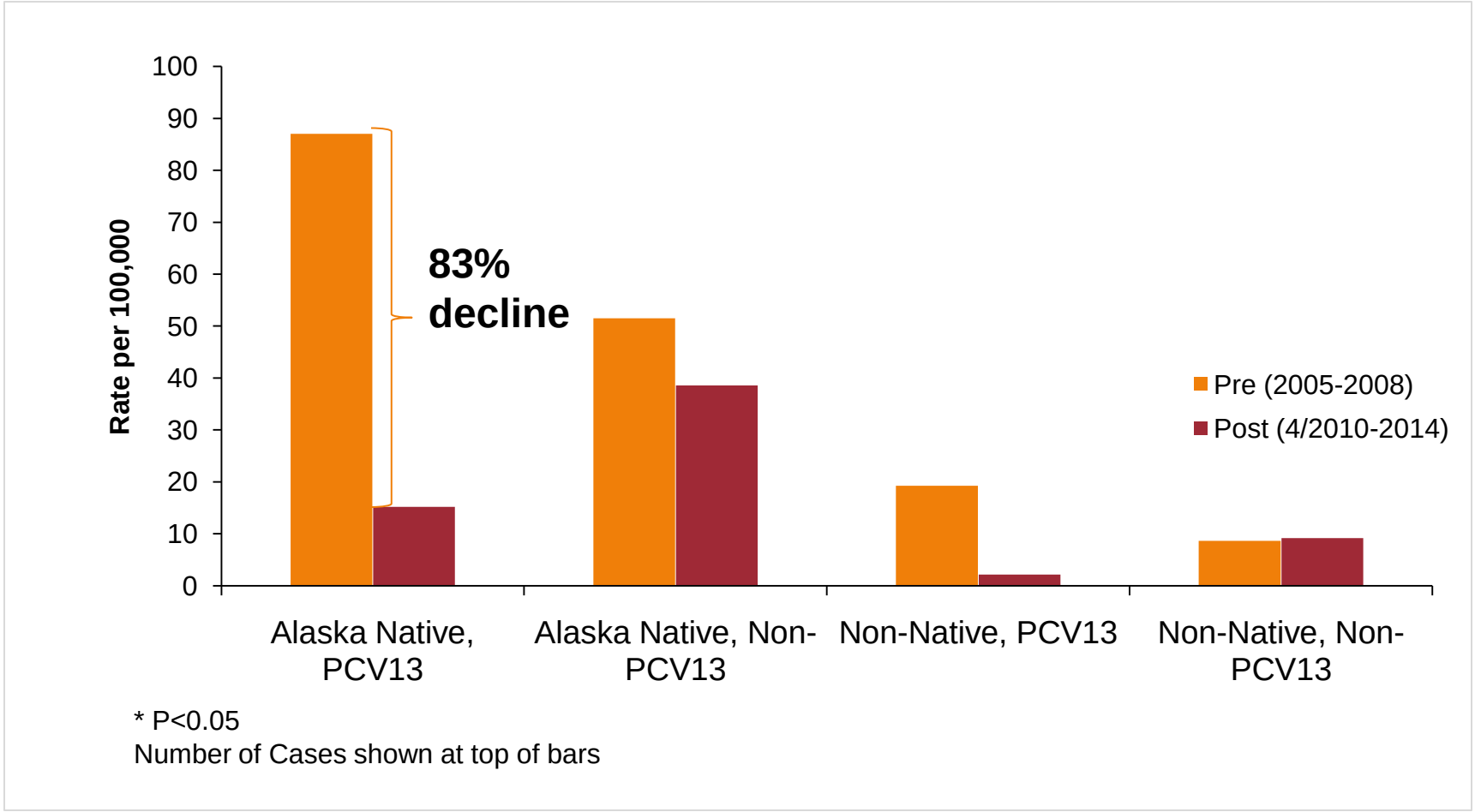
- How long do patients vaccinated against hepatitis A virus (HAV) as babies remain seropositive?
- Spradling et al. looked at anti-HAV 6 years postvaccination in a cohort of 183 Native Alaskans. Seropositivity (anti-HAV ≥20 mIU/mL) was observed in 100% of those with a seronegative mother who were vaccinated at 12 months.
- Modeling shows – 84% of those seropositive will stay seropositive after 30 years.
- No booster needed.
- (Hepatology 2016;63:703-711)

Invasive Pneumococcal Disease, Alaska, Children <5 years old.



Arctic Investigations Program – CDC, unpublished

Invasive Pneumococcal Disease in Alaska Children <5 years: Post PCV13



Bruce M, Vaccine 2015;33:4813-4819

Update: No cases in Alaska children < 5 y during last half of 2015!

In Summary:

- We discussed inequities and progress in Alaska Native health issues:
  - respiratory infections,
  - Bronchiectasis
  - Indoor air quality
  - vitamin D deficiency/rickets, and
  - vaccine-preventable disease.

Next Steps:

- work with environmental health partners to improve housing factors and decreased water access associated with child respiratory infections
- work with tribal health providers to increase early recognition of children with at risk for bronchiectasis and provide optimal treatment.
- work with researchers and tribal health providers to provide optimal vitamin D supplementation for children and prenatal women and increase fish consumption

Thank You!