Estimating Pneumococcal Pneumonia Burden Among U.S. Adults and Progress on the Research Agenda for Potential Policy Change

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Overview

- Pneumococcal conjugate vaccines have dramatically reduced invasive pneumococcal disease (IPD) in adults through indirect effects
- ACIP recommended routine use of 13-valent pneumococcal conjugate vaccine (PCV13) in series with 23-valent pneumococcal polysaccharide vaccine (PPSV23) for adults aged ≥65 years in 2014
  - PCV13 effective against IPD including pneumonia with bacteremia
  - PCV13 demonstrated efficacy against vaccine-type non-bacteremic pneumococcal pneumonia (NBPP)
- What is the burden of NBPP?
- What is the impact of PCV13 on NBPP for adults ≥65 years old?

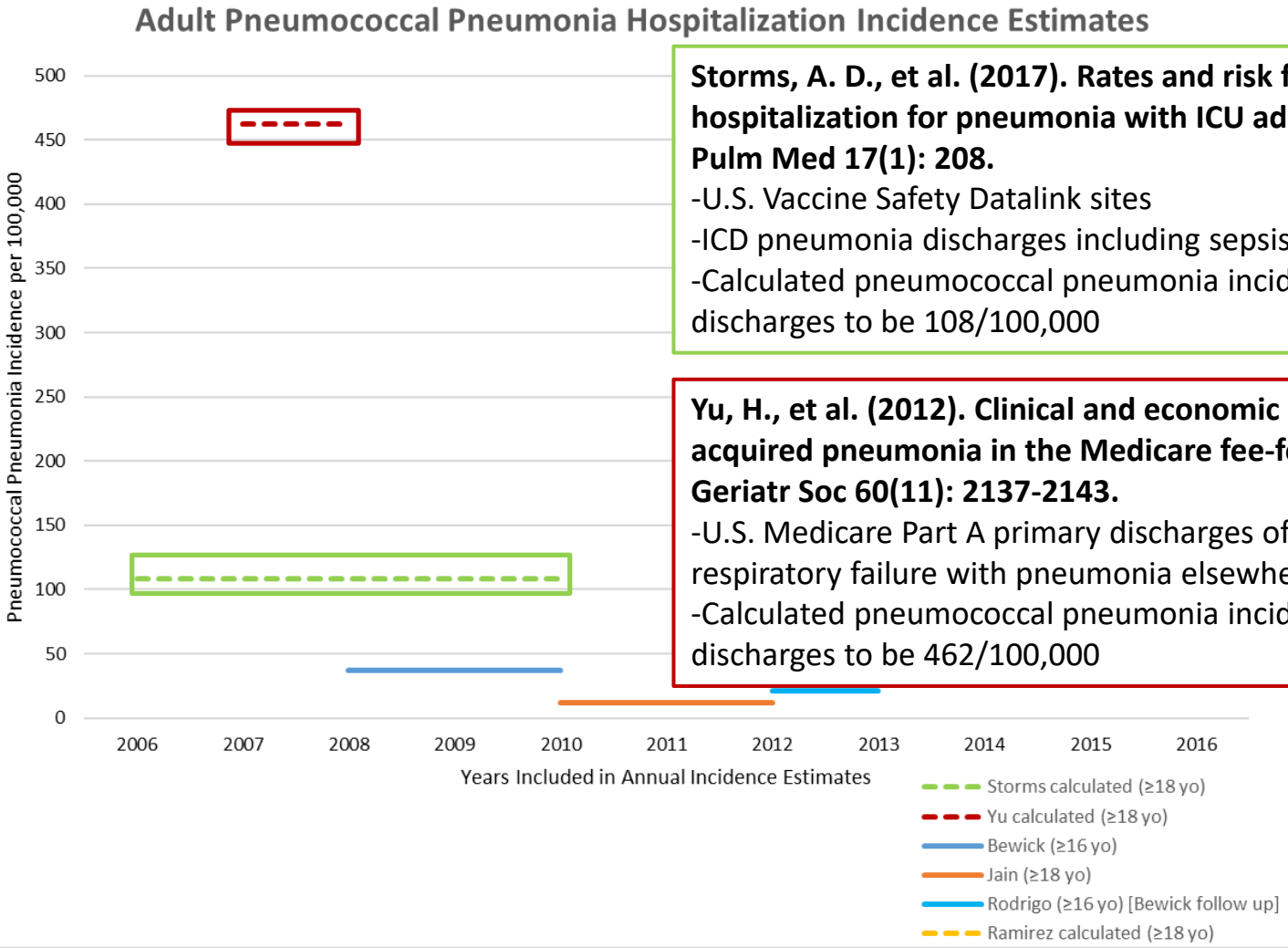
Pneumococcal pneumonia as a cause of community acquired pneumonia (CAP)

- *S. pneumoniae* is a common cause of CAP
  - Estimated to cause 27% of CAP pre-PCV13[1]
- CAP incidence attributable to *S. pneumoniae* is difficult to estimate
  - Blood culture has low sensitivity
    - Detects 25% of pneumococcal pneumonia cases
  - Pneumococcal urinary antigen test (UAT)
    - Pooled sensitivity 74–75% and specificity 95–97%[2, 3]
    - Not universally available or routinely used by all providers

[1]Said M.A., et al (2013). Estimating the burden of pneumococcal pneumonia among adults... PloS one. 8(4):e60273. Epub 2013 Apr 2

[2]Horita, N., et al (2013). Sensitivity and specificity of the Streptococcus pneumoniae urinary antigen test… Respirology 18(8): 1177-83.

[3]Sinclair, A., et al (2013). Systematic review and meta-analysis of a urine-based pneumococcal antigen test… J Clin Microbiol 51(7): 2303-2310.



Storms, A. D., et al. (2017). Rates and risk factors associated with hospitalization for pneumonia with ICU admission among adults. BMC Pulm Med 17(1): 208.

-U.S. Vaccine Safety Datalink sites

-ICD pneumonia discharges including sepsis and respiratory failure

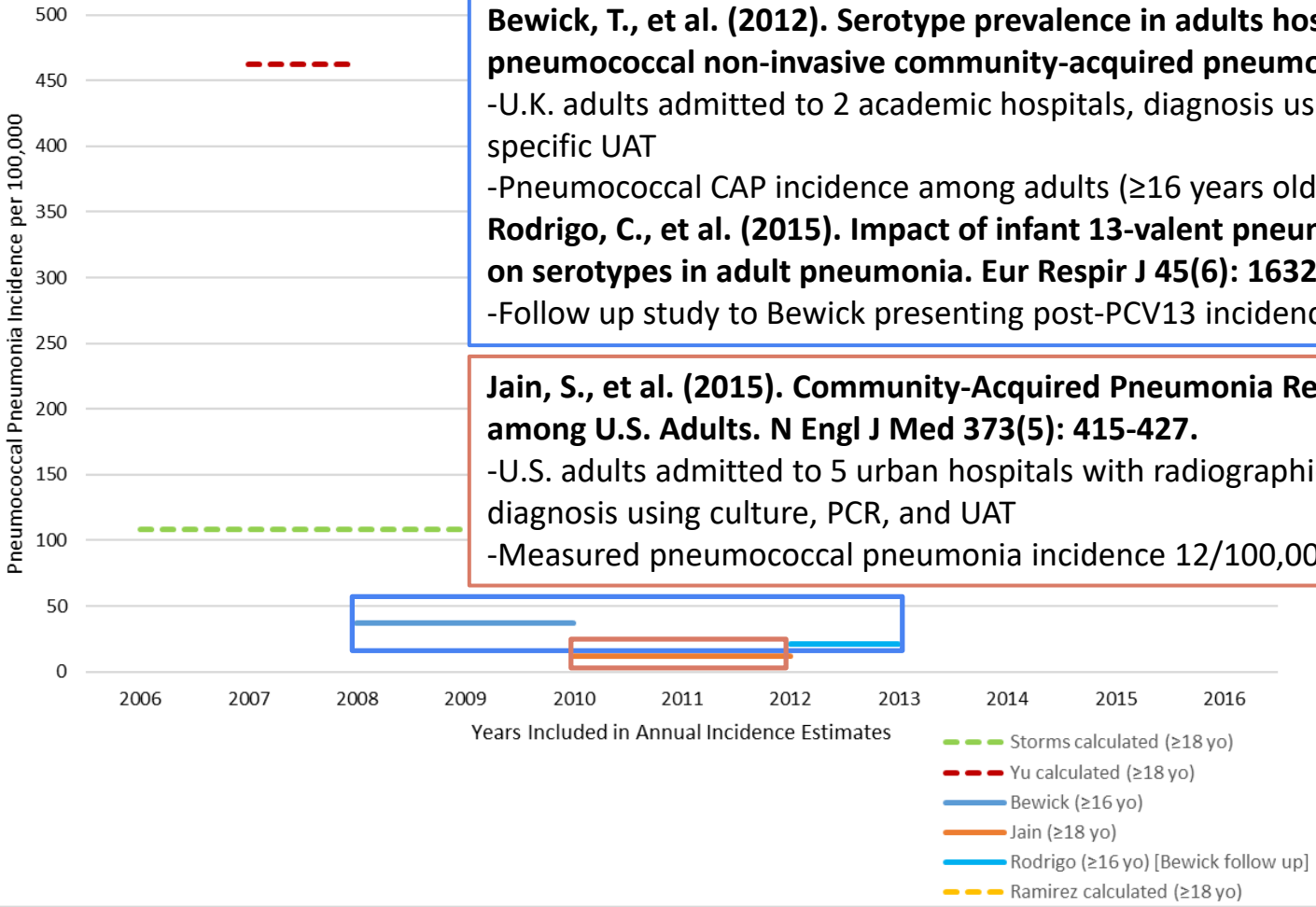
-Calculated pneumococcal pneumonia incidence as 27% of pneumonia discharges to be 108/100,000

Yu, H., et al. (2012). Clinical and economic burden of community-acquired pneumonia in the Medicare fee-for-service population. J Am Geriatr Soc 60(11): 2137-2143.

-U.S. Medicare Part A primary discharges of pneumonia or sepsis or respiratory failure with pneumonia elsewhere

-Calculated pneumococcal pneumonia incidence as 27% of pneumonia discharges to be 462/100,000

Adult Pneumococcal Pneumonia Hospitalization Incidence Estimates



Bewick, T., et al. (2012). Serotype prevalence in adults hospitalised with pneumococcal non-invasive community-acquired pneumonia. Thorax 67(6): 540-545.

-U.K. adults admitted to 2 academic hospitals, diagnosis using culture and serotype specific UAT

-Pneumococcal CAP incidence among adults (≥16 years old) 37/100,000

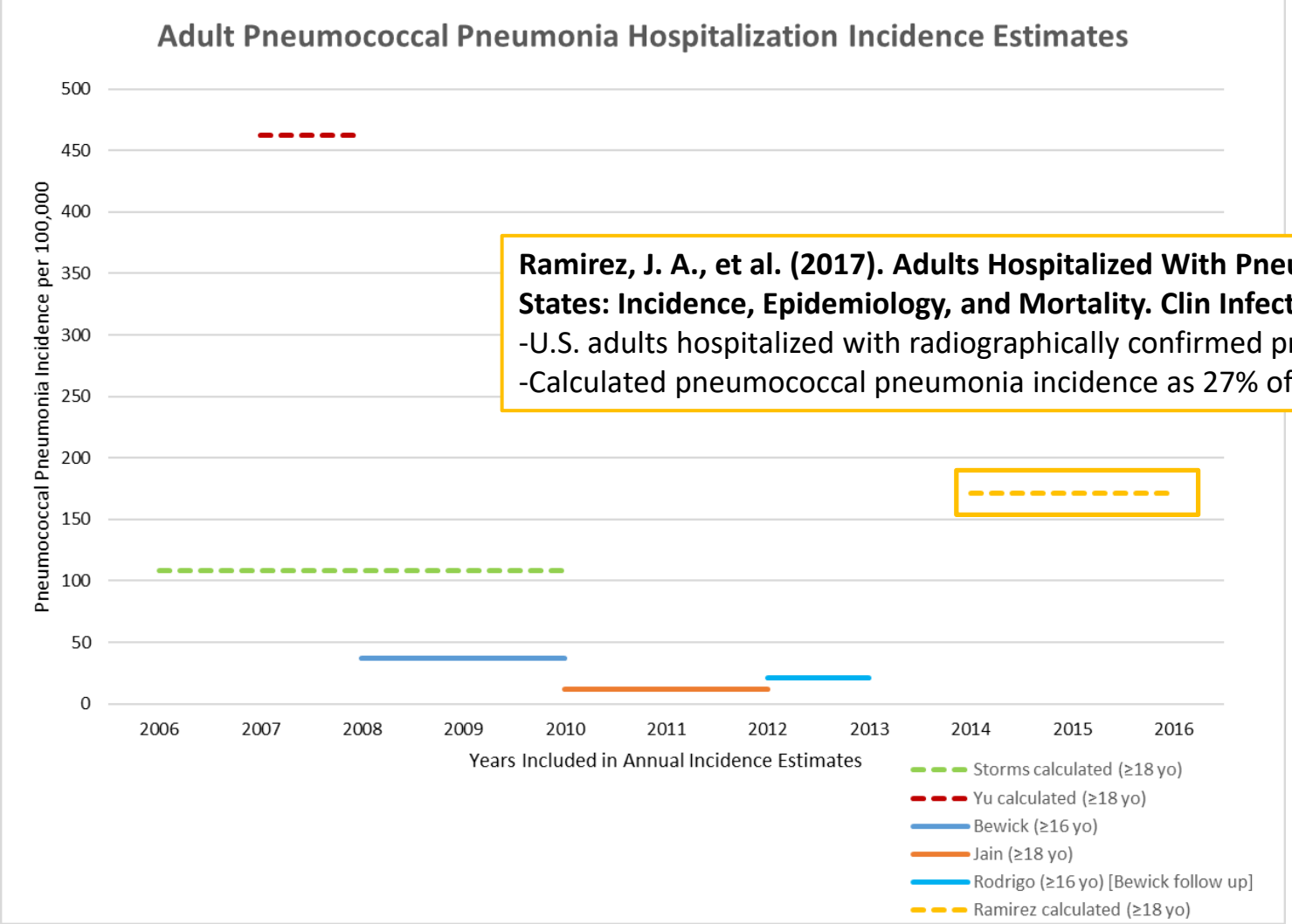
Rodrigo, C., et al. (2015). Impact of infant 13-valent pneumococcal conjugate vaccine on serotypes in adult pneumonia. Eur Respir J 45(6): 1632-1641.

-Follow up study to Bewick presenting post-PCV13 incidence 21/100,000

Jain, S., et al. (2015). Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults. N Engl J Med 373(5): 415-427.

-U.S. adults admitted to 5 urban hospitals with radiographically confirmed pneumonia, diagnosis using culture, PCR, and UAT

-Measured pneumococcal pneumonia incidence 12/100,000, which was 5% of CAP



Ramirez, J. A., et al. (2017). Adults Hospitalized With Pneumonia in the United States: Incidence, Epidemiology, and Mortality. Clin Infect Dis 65(11): 1806-1812.
-U.S. adults hospitalized with radiographically confirmed pneumonia in Louisville, KY
-Calculated pneumococcal pneumonia incidence as 27% of CAP 171/100,000

Surveillance for Non-invasive Pneumococcal Pneumonia (SNiPP): Objectives

- Describe noninvasive pneumococcal pneumonia among adults
- Estimate the disease burden of noninvasive pneumococcal pneumonia
- Examine the potential impact of the 2014 ACIP recommendation for routine PCV13 among adults 65 years and older

SNiPP: Methods

- Built into Active Bacterial Core surveillance (ABCs)
- Cases defined as adults (≥18 years) hospitalized with clinically or radiographically confirmed pneumonia and a positive pneumococcal urinary antigen test (UAT)
  - Cases excluded if invasive pneumococcal disease (IPD) or another positive UAT within 30 days
- Prospective since 2015 with retrospective data collection to 2013
  - Pre-PCV13 period (≥65 year old PCV13 recommendation) 2013–2014
  - Post-PCV13 period 2015–2016

Characteristics of SNiPP Cases, 2013–2014

Characteristics	All cases (N=1,213)	
Median age (range)	64 years	(18–102)
≥65 years old (%)	605	(50%)
Median from admission to diagnosis	1 day	(-2–30)
Median hospitalization length in days (range)	5 days	(1–152)
Radiographically confirmed pneumonia (%)	1,208	(99%)
ICU admissions (%)	402	(33%)
Died (%)	75	(6%)

Case Count Adjustments for Incidence Estimates

- **Not all suspected pneumococcal pneumonia cases are tested by UAT**
  - Adjust the UAT case count by the proportion of pneumonia tested by UAT at that hospital (Adjustment A)
    - Obtained from hospital discharge records and clinical labs
- **Not all hospitals use UAT**
  - Adjust the UAT case count by the proportion of pneumonia in the catchment area that was seen at hospitals offering UAT (Adjustment B)
    - Obtained from hospital discharge records and county level discharge data

Adjustment Methods

- Pneumonia discharges* tested by pneumococcal UAT (Adjustment A)
  - Sample of hospital within the catchment area (n 22)
    - Randomly select sample 20 pneumonia discharges/age group/month
    - Match randomly selected sample with laboratory pneumococcal UAT (positive and negative)
- Pneumonia discharges* in the catchment area seen at hospitals offering pneumococcal UAT (Adjustment B)
  - 37 hospitals in 7 urban areas (CO, CT, GA, MD, NY, and 2 TN)
  - 70% have 200–500 beds/hospital

*Pneumonia defined as 1st ICD pneumonia or empyema or 1st ICD sepsis with pneumonia or empyema elsewhere

Hospital Characteristics Across Catchment Areas Included in Adjustments

Location	Reported UAT Positive Cases	Hospitals with UAT Positive Cases		Average 2013–2014 Population (Total 10,000,148)
		% Pneumonia Tested by UAT (n 22 hospitals)	% Catchment Area Pneumonia (n 37 hospitals)	
CO	121	32%	11%	1,984,144
CT	282	47%	63%	1,421,074
GA	42	13%	17%	2,908,215
MD	551	72%	83%	1,137,326
NY	131	60%	42%	588,107
TN_1	9	2%	34%	1,220,755
TN_2	29	14%	36%	740,530
Average	**166**	**32%**	**41%**	

Preliminary Annual Incidence Estimates, 2013–2014

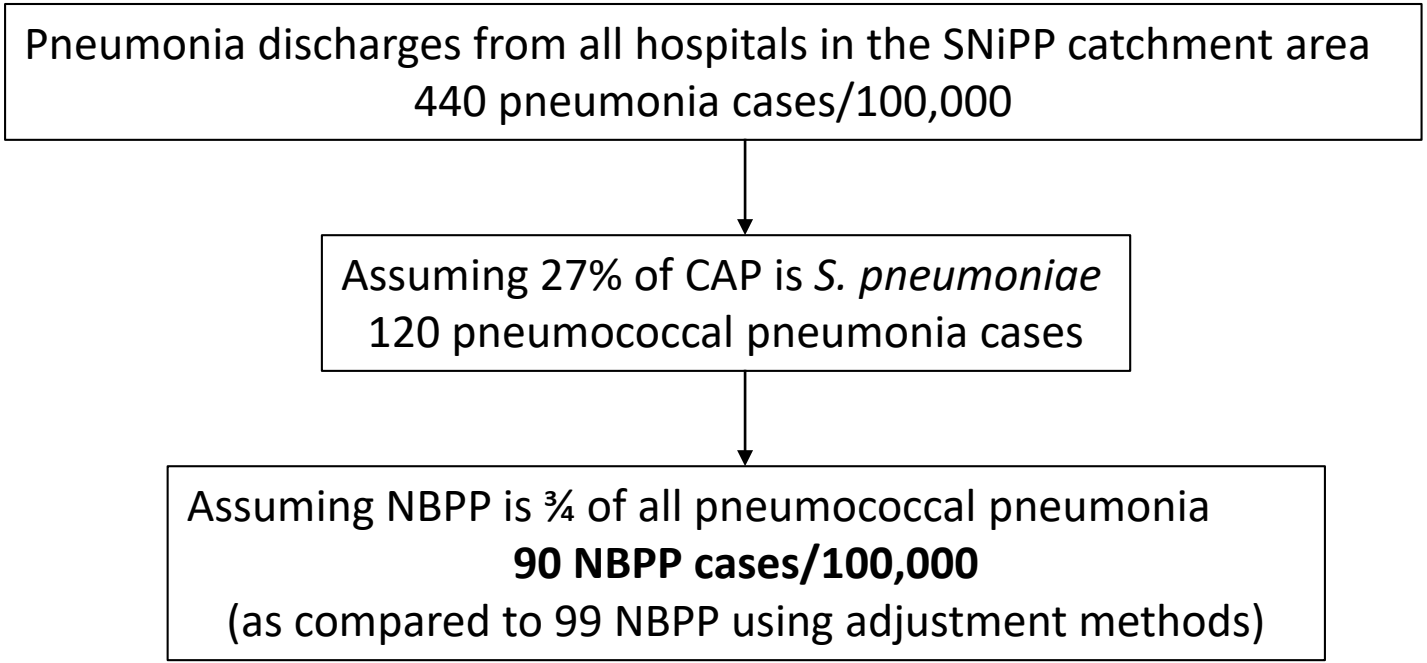
- Crude incidence based on reported UAT positive NBPP cases only
  - 6 cases/100,000
- Adjusted annual incidence area hospitals (n 22)
  - **99 cases/100,000**
  - Examined incidence by percent of pneumonia tested by UAT

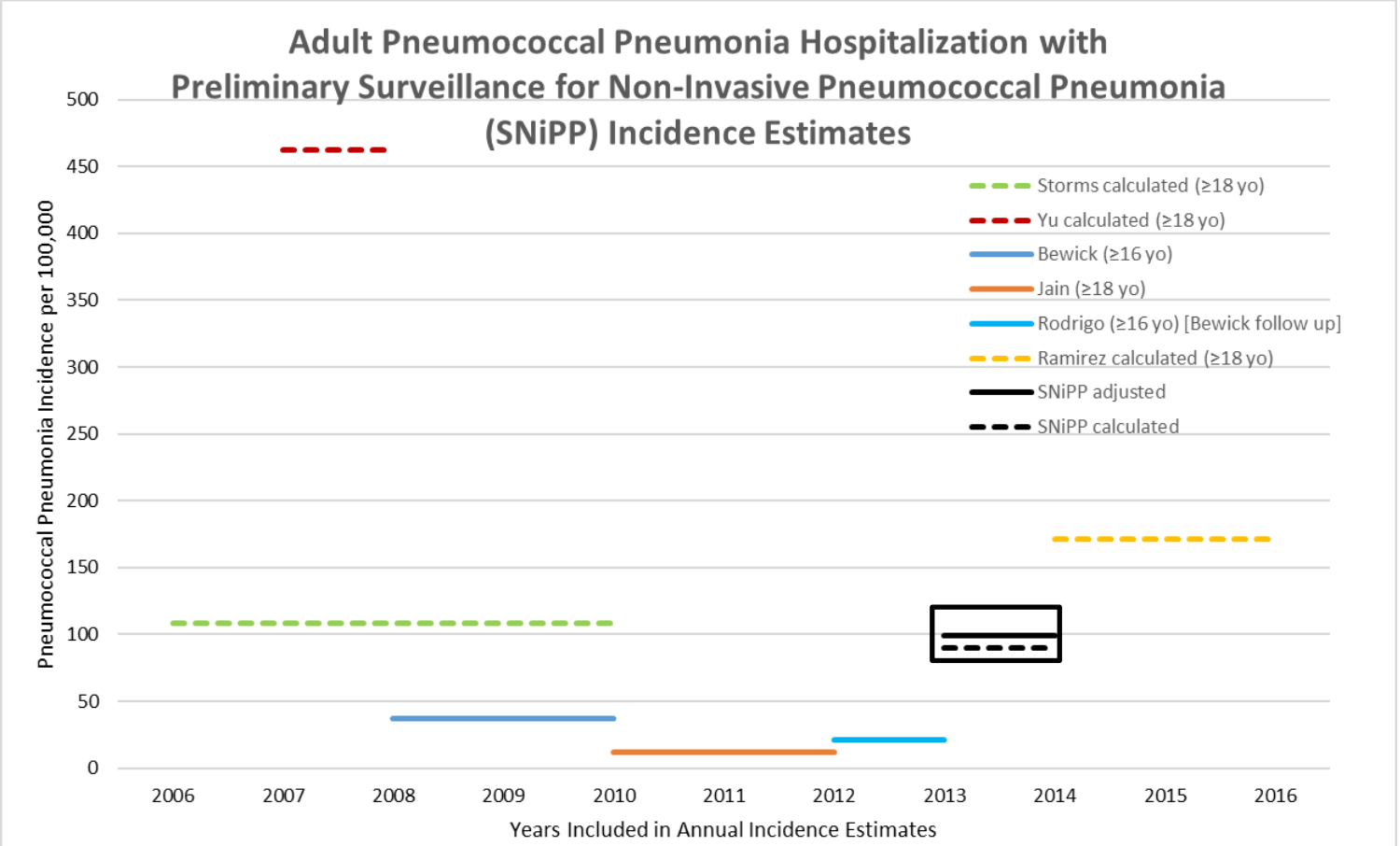
% pneumonia tested by UAT	Number of hospitals	Incidence per 100,000	(Range by hospital)
10%	16	82	(13–173)
30%	11	79	(13–173)
50%	6	97	(49–173)

Limitations

- Missing data from hospitals and laboratories
- Reliant on administrative codes (ICD) for adjustments
- Sampling methods used to estimate percent of pneumonia tested by UAT
  - Not all hospitals offering UAT sampled
  - Variability in the percent of pneumonia tested by UAT

Alternative Methods for Estimating NBPP Incidence: SNiPP Pneumonia Discharges, 2013-2014




Adult Pneumococcal Pneumonia Hospitalization with Preliminary Surveillance for Non-Invasive Pneumococcal Pneumonia (SNiPP) Incidence Estimates
Pneumococcal Pneumonia Incidence per 100,000
500
450
400
350
300
250
200
150
100
50
0
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
Years Included in Annual Incidence Estimates
Storms calculated (≥18 yo)
Yu calculated (≥18 yo)
Bewick (≥16 yo)
Jain (≥18 yo)
Rodrigo (≥16 yo) [Bewick follow up]
Ramirez calculated (≥18 yo)
SNiPP adjusted
SNiPP calculated

SNiPP: Next Steps

- Complete data collection and cleaning
- Model the proportion of patients with pneumonia discharge diagnoses tested by UAT (Adjustment A) for hospitals not sampled
- Examine age adjusted annual incidence
- Compare incidence in 2013–2014 to 2015–2016 to look at PCV13 impact

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Progress on the Research Agenda for Potential Policy Change

Key Questions

- In light of indirect effects observed, what is the impact of direct effects of PCV13 on pneumococcal disease among adults ≥65 years old?

- What benefits would we expect from continued PCV13 use among adults ≥65 years old?

Evidence Presented to Date

- Pneumococcal carriage among adults ≥65 years old
  - Very low pneumococcal carriage (1.8%)
  - PCV13-type carriage 0.2% in 2015-2016
- PCV13 coverage among adults ≥65 years old around 40%
  - Lower among 19–64 year olds, but varies by indication

Evidence Presented to Date

- Invasive pneumococcal disease (IPD)
  - PCV13-type IPD declined among all age groups
  - IPD incidence in adults ≥65 years old plateaued in 2014-2016
  - Modeled direct and indirect PCV13 effects on IPD in adults ≥65 years old project relatively few cases prevented
  - Serotype 3 IPD does not follow the same pattern as other PCV13-types

Evidence Presented to Date

Vaccine effectiveness (VE) against PCV13-type* IPD

Study	Population	VE	(95% Confidence Interval)
CAPiTA	Randomized control trial Dutch adults ≥65 years old	75%	(41–91)
CDC Traditional Methods	IPD cases identified through ABCs matched with population-based controls	65%	(19–85)
CDC CMS	Medicare part B IPD cases matched with controls	47%	(4–71)

* CDC Traditional Methods and CDC CMS VE includes serotype 6C

VE against PCV13-type pneumococcal pneumonia

Study	Population	VE	(95% Confidence Interval)
CAPiTA	Randomized control trial Dutch adults ≥65 years old	45%	(14–65)
Louisville Pneumonia Study	Test negative design in a cohort U.S. adults ≥65 years old	73%	(13–92)

Upcoming ACIP Meetings

- Continued updates about PCV13 impact on pneumonia
- Model estimating public health impact and cost-effectiveness of different policy options including:
  - No PCV13 for adults ≥65 years old
  - Expanding indications for adults <65 years old

Discussion

- What additional information will the committee need to help determine whether continued PCV13 use in adults ≥65 years old is warranted?

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.