Estimating Impact of 13-valent Pneumococcal Conjugate Vaccine (PCV13) on Pneumococcal Pneumonia Among U.S. Adults

Ryan Gierke, MPH

Advisory Committee on Immunization Practices

October 24th, 2018

Pneumococcal pneumonia

- *Streptococcus pneumoniae* (pneumococcus) is a common etiology of all-cause pneumonia among adults
- True burden of pneumococcal pneumonia is unknown due to limitations of available diagnostic tests
  - The ratio of bacteremic to non-bacteremic pneumococcal pneumonia estimated to be around 1 to 4 before PCV13 introduction[1]
  - Blood culture: low sensitivity
  - Commercially available urine antigen test (UAT): 75% sensitivity and not routinely used by all providers[2, 3]

[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.

PCV13 Impact on Pneumococcal Pneumonia

- Pneumococcal conjugate vaccine use among children has dramatically reduced invasive pneumococcal disease in adults through indirect effects
- Reductions in pneumonia hospitalizations among children (direct effects) and adults (indirect effects) were documented after introduction of conjugate vaccine in children[1,2]
- PCV13 demonstrated efficacy/effectiveness against PCV13-type pneumococcal pneumonia among older adults[3, 4]

[1]Alicino C., et al (2017). The impact of PCV10 and PCV13 on hospitalization for pneumonia in children... Vaccine 35:5776–5785.
[2]Tsaban G., et al (2017). Indirect (herd) protection, following pneumococcal conjugated vaccines introduction... Vaccine. 35:2882–2891.
[3]Bonten M, et al (2015). Polysaccharide Conjugate Vaccine against Pneumococcal Pneumonia in Adults. N Engl J Med. 372:1114–25.
[4] McLaughlin, J. M., et al (2018). Effectiveness of PCV13 Against Hospitalization for Community-Acquired Pneumonia in Older US Adults: .. Clin Infect Dis.

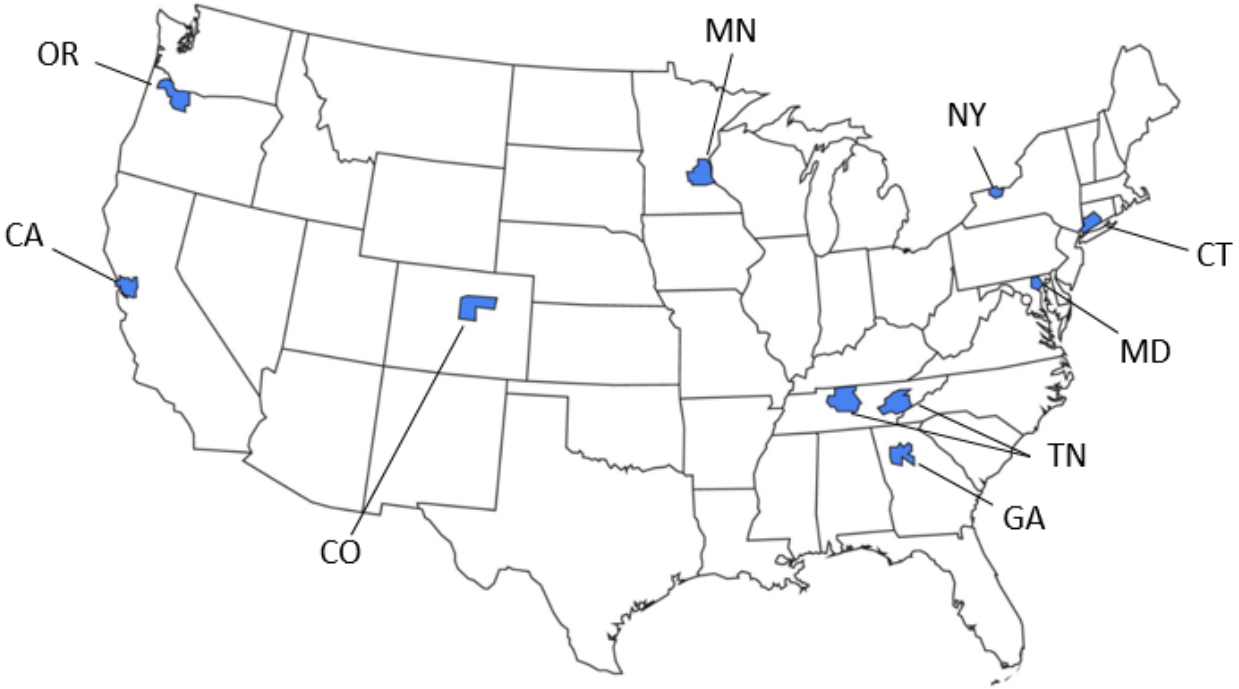
Surveillance for Non-invasive Pneumococcal Pneumonia (SNiPP): Objectives

- Estimate the burden of non-invasive pneumococcal pneumonia
- Evaluate the impact of the 2014 ACIP recommendation for routine PCV13 use among adults 65 years and older

SNiPP Case Ascertainment

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

SNiPP Catchment Area 2013–2016



Average annual population under surveillance = 16 million

Demographics of UAT Positive Case-Patients, 2013–2016

	Pre-PCV13, 2013-2014 (N= 1,856) n (%)	Post-PCV13, 2015-2016 (N= 1,573) n (%)
Age groups, years		
18–49	348 (19)	297 (19)
50–64	554 (30)	537 (34)
≥65	954 (52)	739 (47)
Median age, years (range)	65 (18–102)	63 (18–102)
Male	855 (46)	744 (47)
Hispanic	86 (5)	96 (6)
Race:		
White	1,200 (65)	983 (63)
Black	433 (23)	418 (27)

UAT Positive Case-Patients: Diagnoses and Treatment, 2013–2016

	Pre-PCV13, 2013-2014 (N= 1,856) n (%)	Post-PCV13, 2015-2016 (N= 1,573) n (%)
Community onset[1]	1,602 (86)	1,354 (86)
Radiographically diagnosed pneumonia	1,608 (86)	1,396 (88)
ICU care	655 (35)	494 (32)
Died	119 (7)	88 (6)
Median length of hospitalization, days (range)	5 (0-152)	5 (0-95)
Immunocompromising condition[2]	764 (40)	665 (42)
High risk condition[3]	1,529 (82)	1,297 (83)
Any pneumococcal vaccine receipt (during current hospitalization)	259 (14)	151 (10)
Received PPSV23 0–3 days before UAT	61 (3)	21 (1)

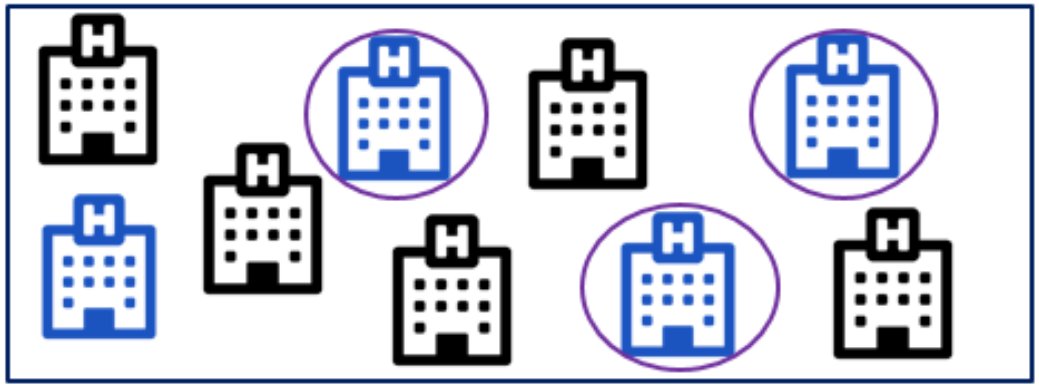
[1]Not having been residing in a hospital setting or admitted at least 72 hours before UAT obtained
[2]Immuncompromising conditions defined as those for which PCV13 and PPSV23 are recommended for adults 19–64 years old
[3]High risk conditions defined as those for which PPSV23 is recommended for adults 19–64 years old

Adjustments to UAT Positive Case Count to Estimate Incidence

- Not all pneumonia cases are tested by UAT
  - Adjust by the proportion of pneumonia discharges[1] tested by pneumococcal UAT
- Not all hospitals use UAT
  - Adjust by the proportion of pneumonia discharges[1] in the catchment area seen at hospitals offering pneumococcal UAT
- UAT not 100% sensitive
  - Adjust to account for pneumococcal UAT sensitivity of 75% [2, 3]

- [1]Pneumonia defined as 1st ICD pneumonia or empyema or 1st ICD sepsis with pneumonia or empyema elsewhere
- [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.

Estimating Incidence from Catchment Area Hospitals



Hospitals not offering UAT in catchment

Hospitals that offer UAT and report cases

Hospitals reporting the proportion of pneumonia tested by UAT

- Sites obtain total number of all-cause pneumonia discharges within the catchment area
- Defined all-cause pneumonia as 1st ICD code pneumonia or empyema, or 1st ICD code sepsis with pneumonia or empyema listed elsewhere
- Select hospitals obtain a random sample of pneumonia discharges to determine the proportion tested by UAT

Model: Percent Pneumonia Tested by UAT

- Regular fixed effects logistic regression
  - Inputs: sampled number of pneumonia cases and number of pneumonia tested within the sample
    - Predictors: year, age group, hospital characteristics[1], site
  - Interactions: site*year, site*age group, year*age group
- Output: annual % pneumonia tested by UAT for hospitals with at least one pneumonia patient tested by UAT
  - By year, age group, and hospital

[1]Hospital characteristics including size, case mix index, payment scheme, teaching and university affiliation assessed

Model: Percent Pneumonia Positive by UAT

- Generalized linear mixed effects
  - Inputs: UAT positive cases, % pneumonia tested estimated from logistic regression model
    - Predictors: year and age group (fixed effects)
      hospital and site (random effects)
  - Interactions: none significant
- Output: annual % of pneumonia positive by UAT
  - Aggregated for all hospitals and sites included in the model
  - By age group and year

Model Assumptions

- UAT testing among pneumonia cases is random, after stratifying by hospitals, age group, and year
- Hospital characteristic effects are assumed to be random (different, but following a common normal distribution)
- Testing practices from hospitals reporting UAT cases and those not reporting follow a similar distribution

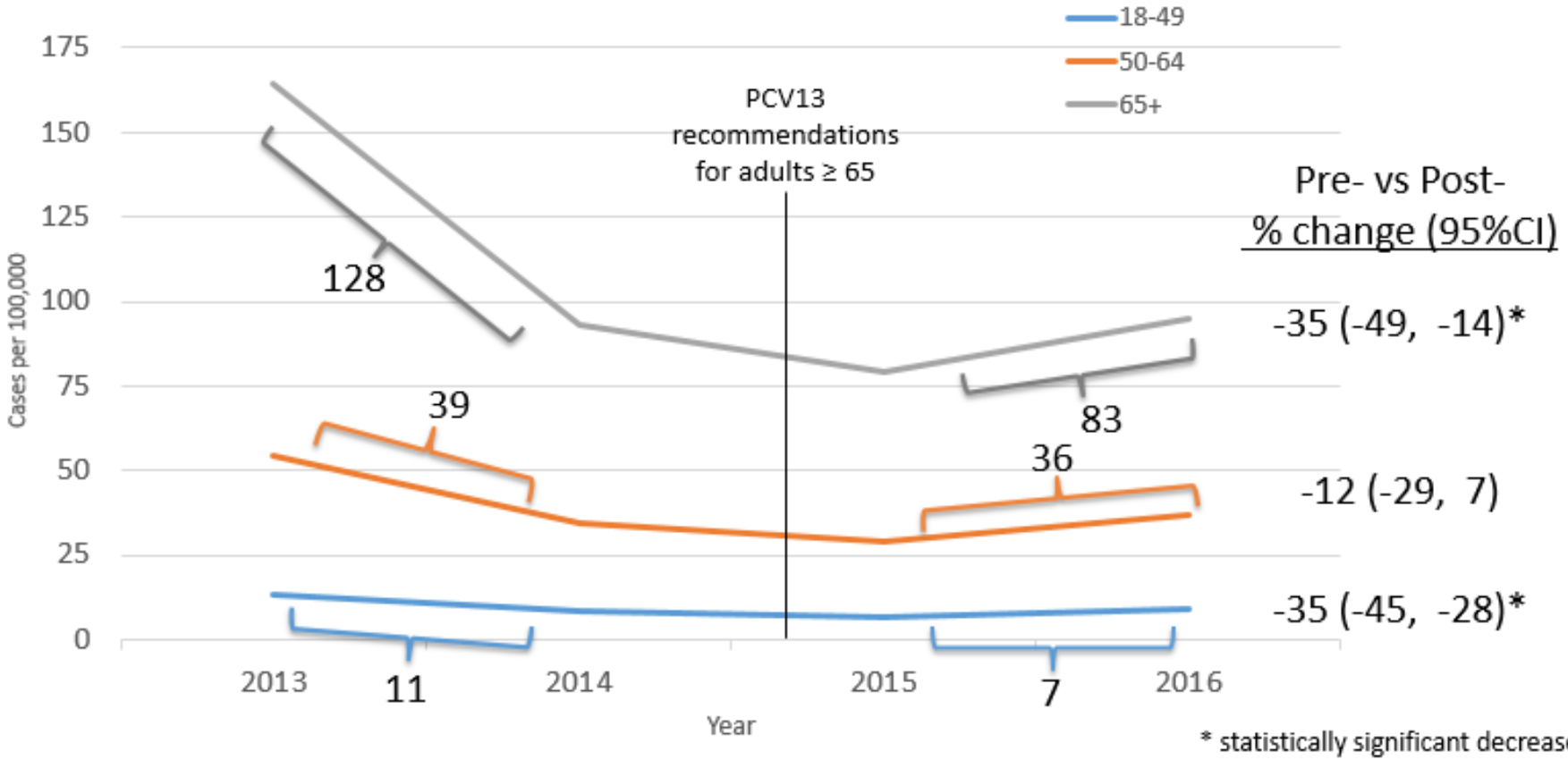
Final Adjustments

- Estimate number of non-invasive pneumococcal pneumonia cases by
  - Multiplying percent UAT positive (obtained from the generalized mixed linear model) by the total number of pneumonia cases within the catchment area
  - Inflating the case count to account for UAT sensitivity (75%)

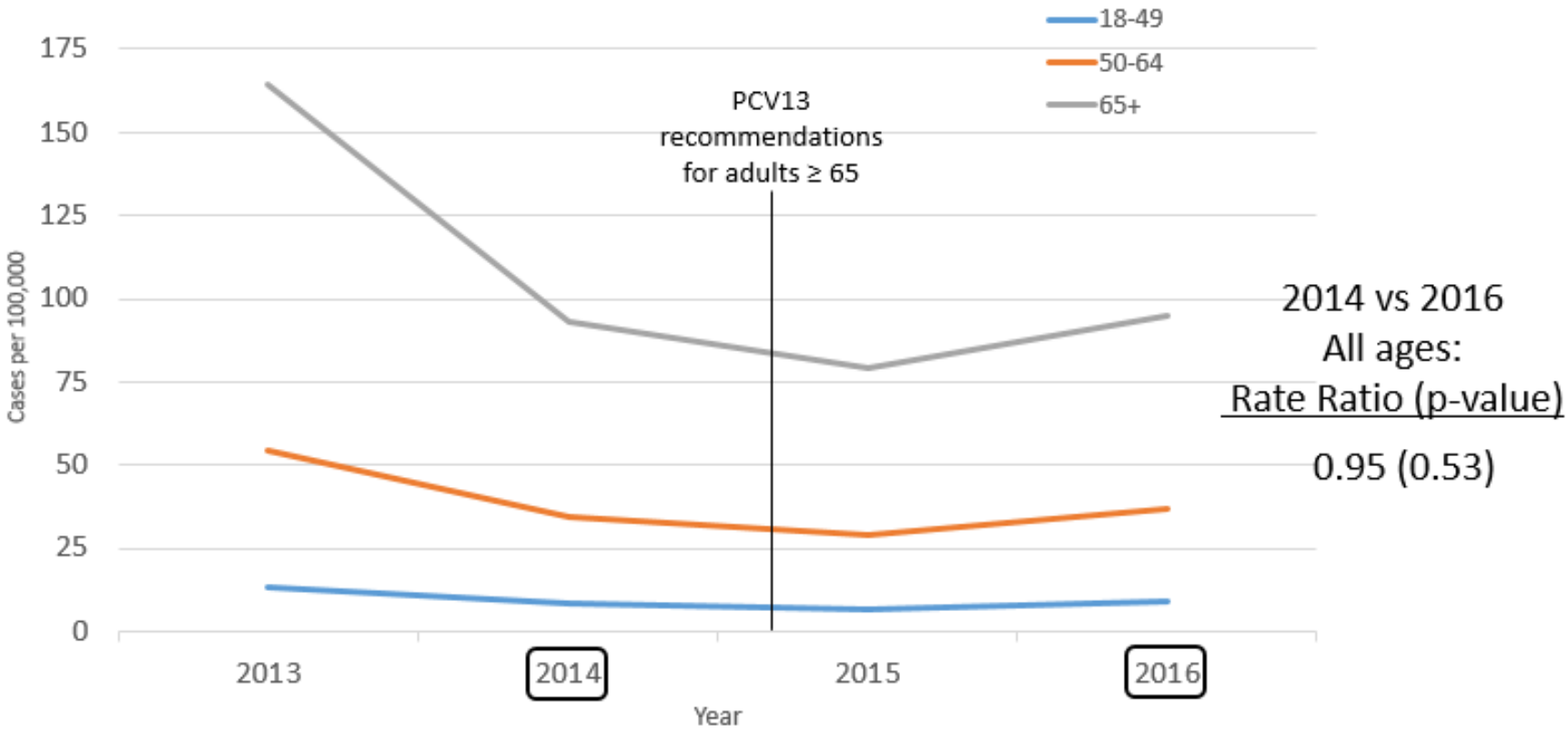
Estimated Non-Invasive Pneumococcal Pneumonia Incidence Pre vs. Post PCV13 Recommendation for Adults ≥ 65 Years Old

Age group (years old)	Number of cases		Adjusted incidence per 100,000 n (95%CI)
	Reported	Adjusted	
Pre PCV13 Recommendation for ≥65 Year Olds (2013–2014)			
18–49	249	524	11 (8, 16)
50–64	391	790	39 (27, 53)
≥65	625	1725	128 (92, 174)
Post PCV13 Recommendation for ≥65 Year Olds (2015–2016)			
18–49	203	357	7 (5, 11)
50–64	364	758	36 (26, 49)
≥65	457	1196	83 (60, 113)

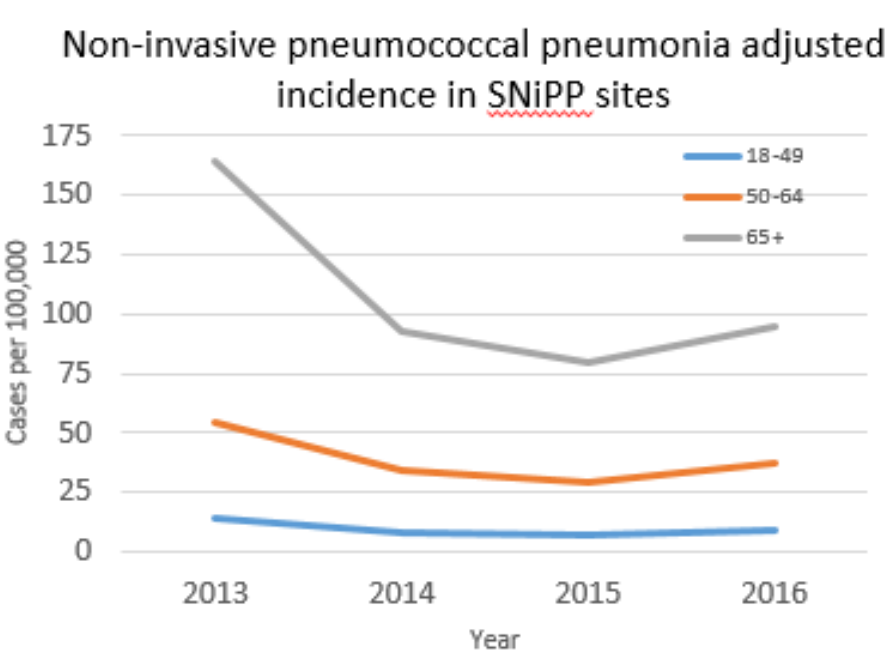
Annual Non-Invasive Pneumococcal Pneumonia Incidence by Age Group, 2013-2016

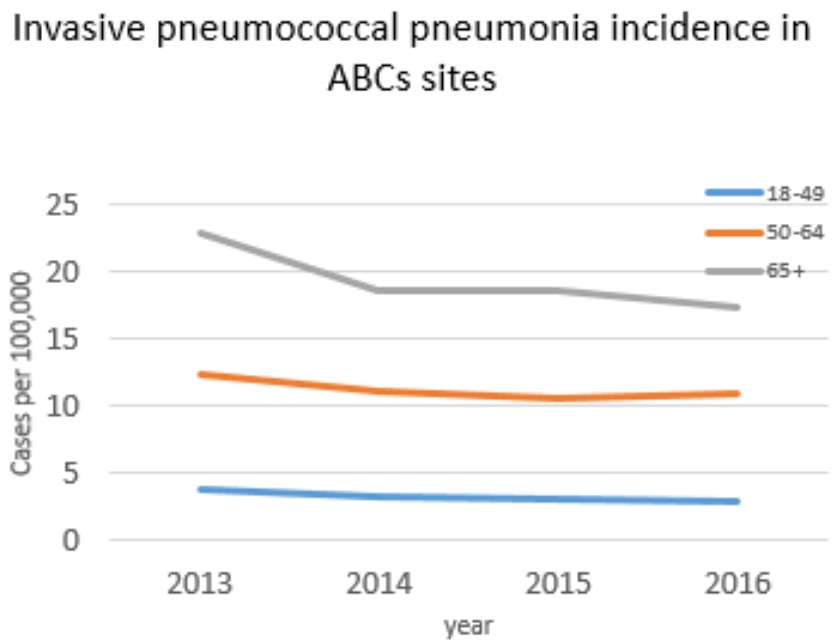


Annual Non-Invasive Pneumococcal Pneumonia Incidence by Age Group, 2013-2016



Comparing Non-Invasive to Invasive Pneumonia





Key points:

- Non-invasive pneumonia incidence 3-7 times higher than invasive pneumococcal pneumonia
- Changes in the incidence of non-invasive pneumonia and invasive pneumococcal pneumonia similar
- Post 2014 recommendation, no additional reductions observed

Limitations

- UAT testing practices are likely not at random
- Adjusted incidence based on ICD codes for pneumonia: coding practices may change over time and by hospital/site
- Relatively short time periods for both pre- and post-PCV13 data
- Serotype distribution unknown
  - Unable to determine burden of vaccine-type pneumonia
  - Unable to determine if increases in non-vaccine type pneumonia minimize overall reductions
- Direct effects cannot be estimated without pneumococcal vaccination status of cases

Conclusions

- Pneumococcal pneumonia continues to contribute to a high burden of disease among adults
- Decreases most dramatic before 2014 (indirect PCV13 effects)
- No additional reductions apparent after 2014
- Changes in incidence of pneumococcal pneumonia similar to those observed in invasive pneumococcal pneumonia during 2013-2016

Acknowledgements

California

- Art Reingold
- Gretchen Rothrock
- Mirasol Apostol
- Tara Scheuer
- Alison Ryan

Colorado

- Karen Edge
- Nisha Alden
- Samantha Hoss

Connecticut

- Susan Petit
- Summer Shore
- Matthew Cartter
- Therese Rabatsky-Erh

Georgia

- Monica Farley
- Amelia Blumberg
- Amy Tunali
- Stepy Thomas

Maryland

- Lee Harrison
- Kathleen Shutt
- Vijitha Lahanda Wadu
- Rosemary Hollick
- Rachel Park
- Joanne Benton

Minnesota

- Ruth Lynfield
- Kathy Como-Sabetti
- Katherine Schleiss

New York

- Nancy Bennett
- Alison Muse
- Suzanne McGuire
- Kari Burzlaff
- Rachel Wester
- Debra Blog

Oregon

- Ann Thomas
- Tasha Poissant
- Heather Jamieson

Tennessee

- William Schaffner
- Tiffanie Markus
- Brenda Barnes

CDC ABCs Team

- Melissa Arvay
- Huong Pham
- Tamar Pilishvili
- Cyndy Whitney
- Ryan Gierke
- Olivia Almendares
- Stephanie Schrag
- Tracy Pondo
- Nong Shang
- Trey Spiller
- Fernanda Lessa
- Gayle Langley

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