



Preliminary Evidence to Recommendations for the ongoing review of the PCV13 recommendation for adults ≥ 65 years old

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Current Adult PCV13 Recommendations

- In 2012 ACIP recommended PCV13 in series with PPSV23 for adults ≥ 19 years old with immunocompromising conditions, asplenia, cochlear implants, or cerebrospinal fluid leaks
- In 2014 ACIP added an age based recommendation for PCV13 in series with the previously recommended PPSV23 for all PCV13-naïve adults ≥ 65 years old

Policy Question

- Should PCV13 be administered routinely to all immunocompetent adults aged ≥ 65 years given sustained indirect effects?
 - Population: Immunocompetent adults 65 years and older
 - Intervention: PCV13 at ≥ 65 years old in series with PPSV23 in the context of indirect effects
 - Comparison(s): PPSV23 alone at ≥ 65 years old
 - Outcomes: pneumococcal disease and PCV13 safety

ACIP Evidence to Recommendation (EtR) Framework

- Statement of problem
 - Public health priority
 - Burden of disease
- Benefits and harms
 - Balance of desirable and undesirable effects
 - Certainty in evidence
- Values and preferences of target population
- Acceptability to stakeholders
- Resource use
 - Health economic analyses
- Feasibility
 - Implementation considerations

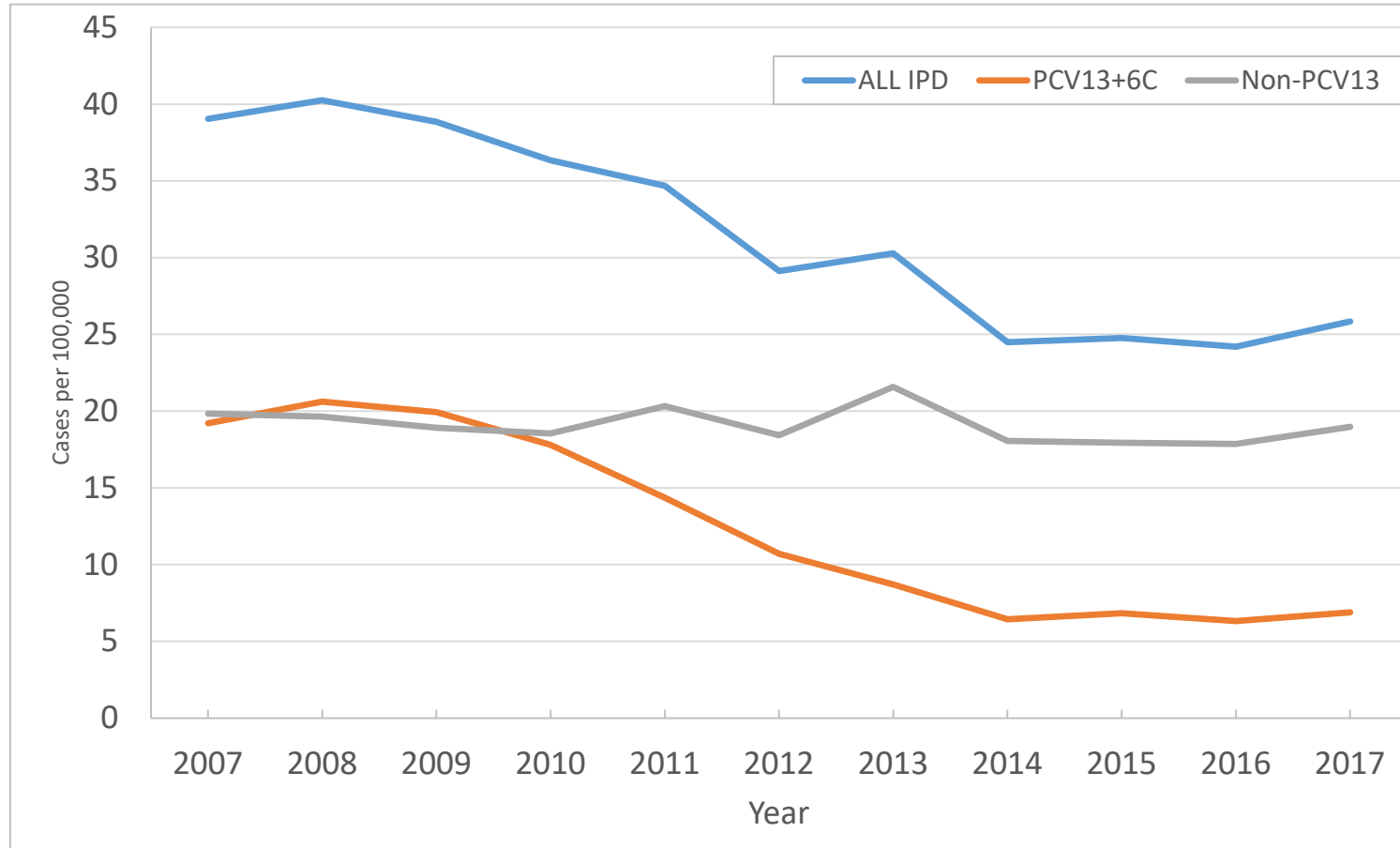
GRADE

- Outcomes
 - Invasive pneumococcal disease (IPD)
 - Non-invasive pneumococcal pneumonia
 - PCV13 safety
- Measures
 - Population trends in disease outcomes
 - Indirect PCV13 effects
 - Direct PCV13 effects

Statement of the Problem: Invasive Pneumococcal Disease Among Adults ≥ 65

- IPD incidence has dramatically declined since PCV13 introduction in 2010
 - Annual PCV13-type IPD incidence went from 14/100,000 in 2010 to 5/100,000 in 2014
 - Plateaued annual PCV13 IPD incidence since 2014
 - Mortality unchanged at 15%
 - >50% of remaining PCV13 IPD is caused by serotype 3

IPD Incidence Among Adults ≥ 65 Years Old, 2007–2017



Indirect and Direct Model Results for IPD

Table 1. Cumulative estimated number of PCV13-type IPD cases prevented through administration of PCV13 to adults ≥ 65 years (direct effects) 8/2014–5/2017

	Observed, direct+indirect PCV13 effects (A)	Predicted PCV13 indirect effects (B)	ABCs cases prevented through PCV13 direct effects (B)-(A)	Estimated US cases prevented through PCV13 direct effects
PCV13-type (+6C) cases	907	924 (860, 990)	17 (-47, 83)	192 (-472, 868)
PCV13-type (+6C) cases (excluding type 3)	416	472 (427, 520)	56 (12, 104)	579 (123, 1077)

(B)-(A): Total number of PCV13-type IPD cases prevented in adults ≥ 65 years through PCV13 direct effects based on (observed IPD cases) minus (estimated indirect effects)

Vaccine Efficacy/Effectiveness Against PCV13-type IPD

Study	Population	Method	VE	(95%CI)
Bonten 2015 ¹	Dutch adults ≥65 years old (n=84,496)	RCT	75%	(41–91)
Unpublished	US adults ≥65 years old (n=1,530)	Case control	59%*	(11–81)
Unpublished	US Medicare part A and B enrolled adults ≥65 years old (n=10,851)	Case control	47%*	(4–71)

¹Bonten, M. J., et al. (2015). Polysaccharide conjugate vaccine against pneumococcal pneumonia in adults. N Engl J Med 372(12): 1114-1125.

*includes PCV13 and serotype 6C

Statement of the Problem: Non-Invasive Pneumococcal Pneumonia Among Adults ≥ 65

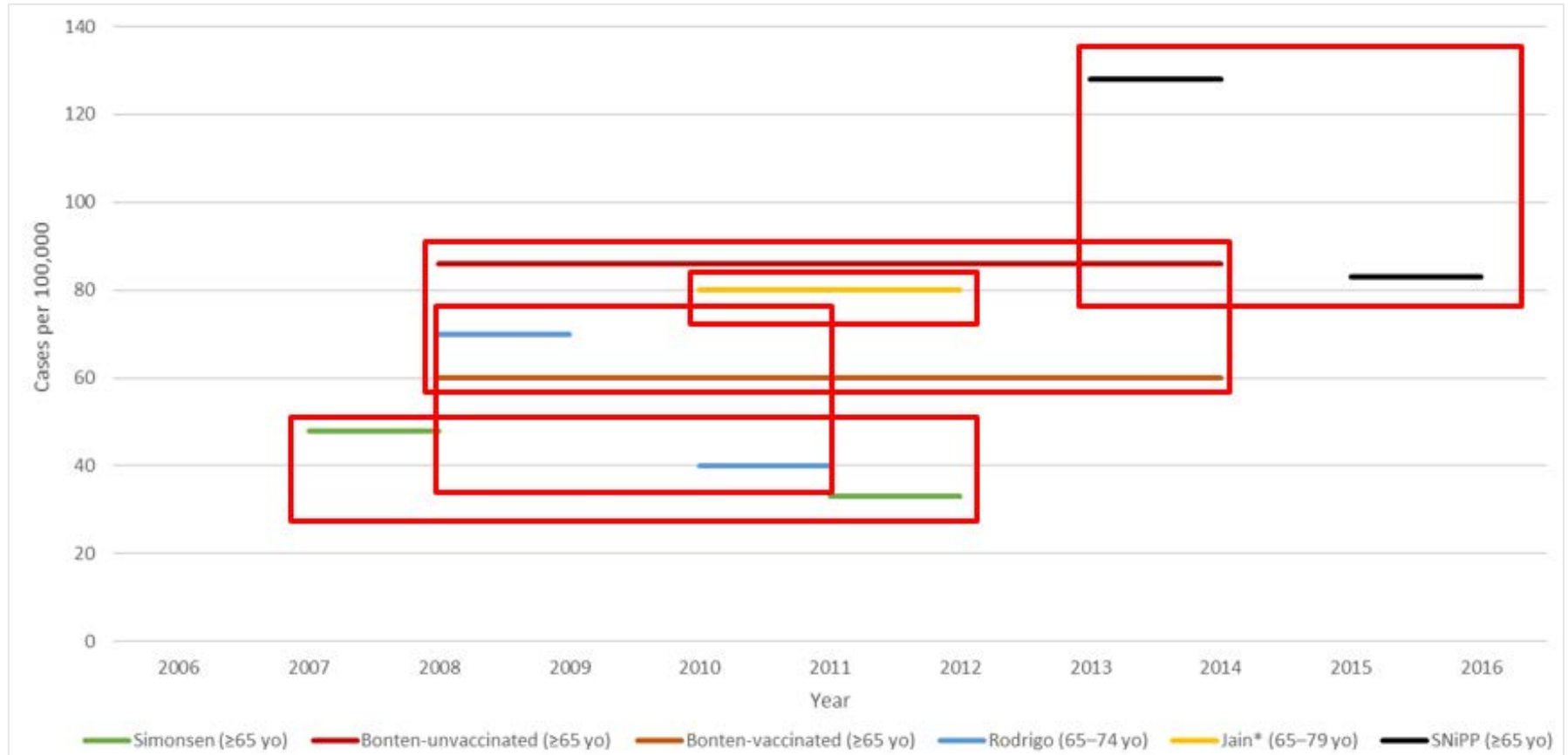
- Majority of the disease burden in older adults
- Incidence more difficult to measure than IPD
 - All cause pneumonia 630–2,300/100,000¹
 - Approximately 5% pneumonia in adults ≥ 65 years olds caused by PCV13 serotypes²
 - In hospital case fatality 4–9%²

¹ Jain et. al. lowest, Ramirez et. al. highest, also includes Griffin et. al., Hayes et. al., and Simonsen et. al.

² McLaughlin et. al. and Hammitt et al June 2018 ACIP pneumococcal session presentation.

³ Huang reanalysis (unpublished) lowest, Griffin et. al. highest, also includes Huang et. al., Rodrigo et. al., Ramirez et. al., and Hayes et. al.

Older Adult Pneumococcal Pneumonia Hospitalization Incidence by Study



*Doubled reported pneumococcal pneumonia incidence in Jain et al based on reanalysis of specimens in Wunderink et al using Pfizer serotype specific pneumococcal UAT

Indirect Effects Measured in Pneumonia

- Most studies show modest declines in all cause pneumonia after pediatric PCV introduction, but before 2014 recommendation¹
 - Large effect seen with more specific codes such as lobar pneumonia²
 - Less consistent effect in older ages³
- Non-invasive pneumococcal pneumonia among ≥ 65 year olds decreased (Jan 2013 to Dec 2016)
 - 35% relative reduction (95%CI: 14, 49), driven by 2013 to 2014 declines⁴

¹ Tsaban et. al.

² Simonsen et. al., Lessa et. al. October 2018 ACIP

³ Lessa et. al. presented Oct 2018 ACIP

⁴ Gierke et. al. presented Oct 2018 ACIP

Combined Direct and Indirect Effects in Pneumonia Since PCV13 Recommended for Adults ≥ 65 Years Old

- PCV13-type pneumonia among ≥ 65 years olds decreased (Jun 2014 to May 2016)
 - 31% relative reduction (95%CI: 8.3, 43.9)¹
- Non-invasive pneumococcal pneumonia among ≥ 65 year olds decreased
 - No statistically significant decrease in incidence between 2014 and 2016²

¹ Swirdlow et. al. Jun 2018 ACIP

² Gierke et. al. presented Oct 2018 ACIP

Vaccine Efficacy/Effectiveness Against PCV13-type Pneumonia

Study	Population	Method	VE	(95%CI)
Bonten 2015 ¹	Dutch adults ≥65 years old (n=84,496)	RCT	45%	(14–65)
McLaughlin ²	U.S. adults ≥65 years old (n=2,034)	Cohort using a test negative design	73%	(13–92)

¹Bonten, M. J., et al. (2015). Polysaccharide conjugate vaccine against pneumococcal pneumonia in adults. N Engl J Med 372(12): 1114-1125.

²McLaughlin, J. M., et al. (2018). Effectiveness of 13-Valent Pneumococcal Conjugate Vaccine Against Hospitalization for Community-Acquired Pneumonia in Older US Adults: A Test-Negative Design. Clin Infect Dis. doi 10.1093/cid/ciy312.

PCV13 Safety Outcomes

- Harms of PCV13 in Adults ≥65 Years Old

Study	No. of subjects	Serious Adverse Events Incidence in Controls	Serious Adverse Events in Vaccinated	Death in Controls	Death in Vaccinated
FDA 2011 ¹	6,000 (6 RCTs)	—	0.2-1.1% ^a	—	0.3% (16/6000) ^{a, b}
Haber 2016 ²	US population	—	152	—	14
Tseng 2018 ³	545,272	<0.1% (PPSV)	<0.1% ^c	—	—

¹US Food and Drug Administration. *Vaccines and Related Biological Products Advisory Committee (VRBPAC) adult indication briefing document: Prevnar 13*. Silver Spring, MD2011. a. No difference between the treatment groups as measured by risk difference per 1000 (95% CI), b. No deaths were considered vaccine related

² Haber, P., et al. (2016). Post-licensure surveillance of 13-valent pneumococcal conjugate vaccine (PCV13) in adults aged 19years old in the United States, Vaccine Adverse Event Reporting System (VAERS), June 1, 2012-December 31, 2015. *Vaccine* 34(50): 6330-6334.

³Tseng, H. F., et al. (2018). Pneumococcal Conjugate Vaccine Safety in Elderly Adults. *Open Forum Infect Dis* 5(6): ofy100. c. anaphylaxis relative risk 1.32, but not statistically significant (95%CI 0.2-5.8). All others <1.

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Tentative Timeline

- Upcoming ACIP meeting (February 2019)
 - Results of outstanding pneumonia studies
 - Completed Evidence to Recommendation Framework with GRADE
- Anticipated schedule for vote either February or June 2019

Upcoming ACIP Meetings

- Policy question under consideration:
 - Should PCV13 be administered routinely to all immunocompetent adults aged ≥ 65 years in a setting of sustained PCV13 indirect effects?
- Which domains of the EtR framework warrant additional exploration regarding continued use of PCV13 in immunocompetent adults ≥ 65 years?
 - Benefit, risks
 - Values
 - Acceptability
 - Resource use
 - Feasibility

Thank you!

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.

