Incidence of Invasive Pneumococcal Disease (IPD) by Race, United States, 2008–2016

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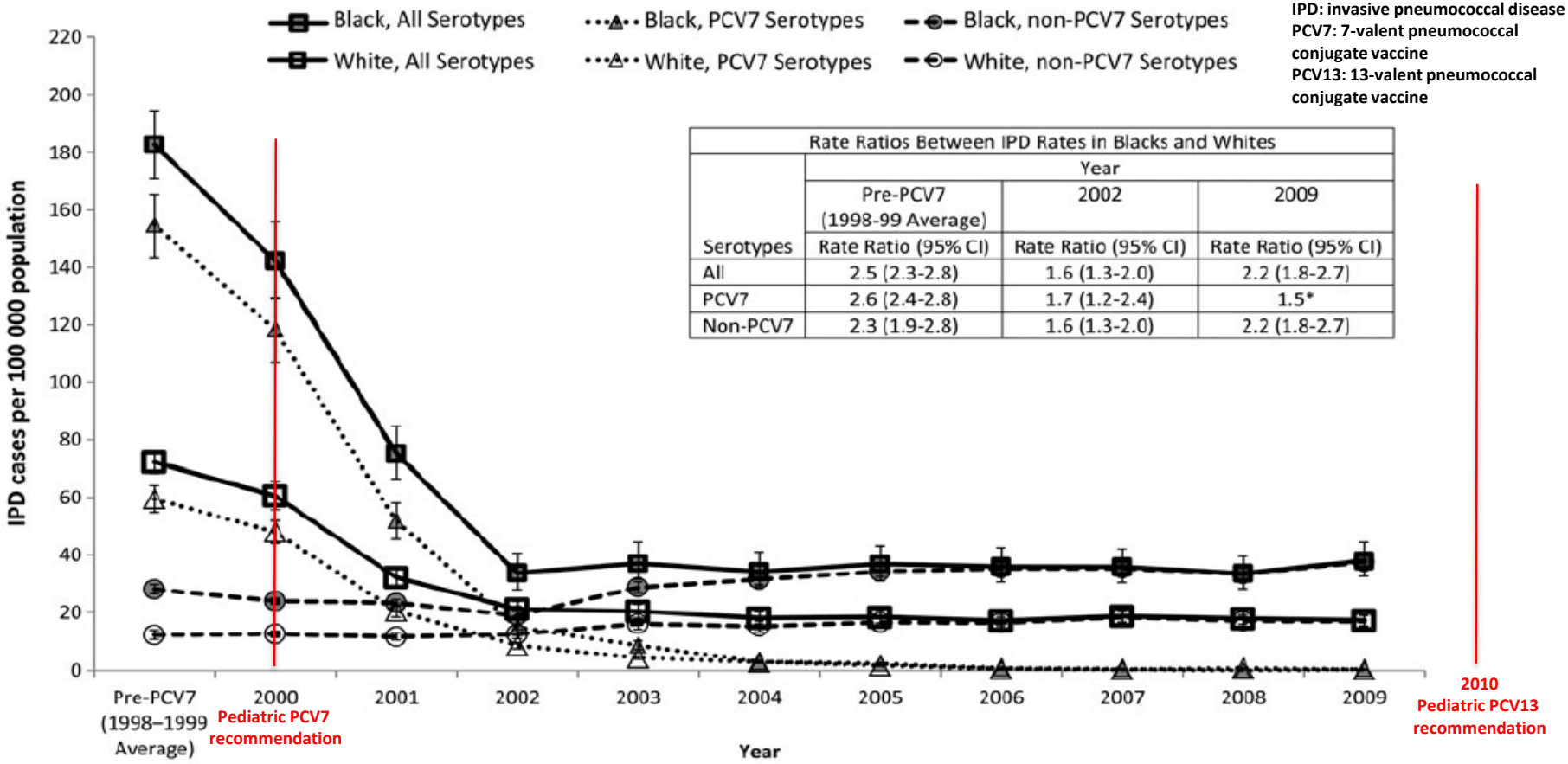
Background

- IPD rates have historically been higher in some racial minorities
- Socioeconomic status (SES) and race are often interdependent, but SES might not account for all differences in IPD incidence between races
- Increased IPD incidence among people of black race might be driven by higher prevalence of certain chronic medical conditions

Observed IPD incidence rates among persons <5 years of age, by race and serotype—Active Bacterial Core surveillance, 1998 –2009 (Wortham, 2014)

CI: confidence interval
IPD: invasive pneumococcal disease
PCV7: 7-valent pneumococcal conjugate vaccine
PCV13: 13-valent pneumococcal conjugate vaccine



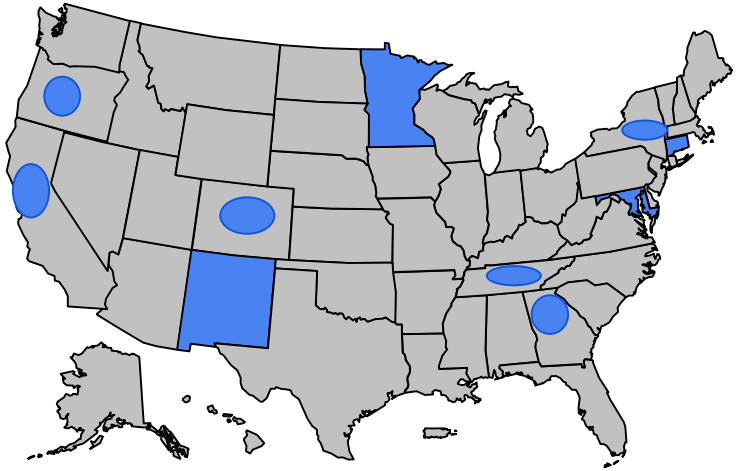
Rate Ratios Between IPD Rates in Blacks and Whites			
	Year		
	Pre-PCV7 (1998-99 Average)	2002	2009
Serotypes	Rate Ratio (95% CI)	Rate Ratio (95% CI)	Rate Ratio (95% CI)
All	2.5 (2.3-2.8)	1.6 (1.3-2.0)	2.2 (1.8-2.7)
PCV7	2.6 (2.4-2.8)	1.7 (1.2-2.4)	1.5*
Non-PCV7	2.3 (1.9-2.8)	1.6 (1.3-2.0)	2.2 (1.8-2.7)

Objective

- Evaluate racial disparities in IPD incidence since PCV13 introduction

Methods

- Active Bacterial Core Surveillance (ABCs):
  - Active laboratory and population-based surveillance
  - Pneumococcus isolated from sterile site
  - Race defined as a single race reported in medical chart
  - Race imputed for the 13% of IPD cases it was missing
- US Census Bureau race-bridged post-census population estimates as denominators



Methods

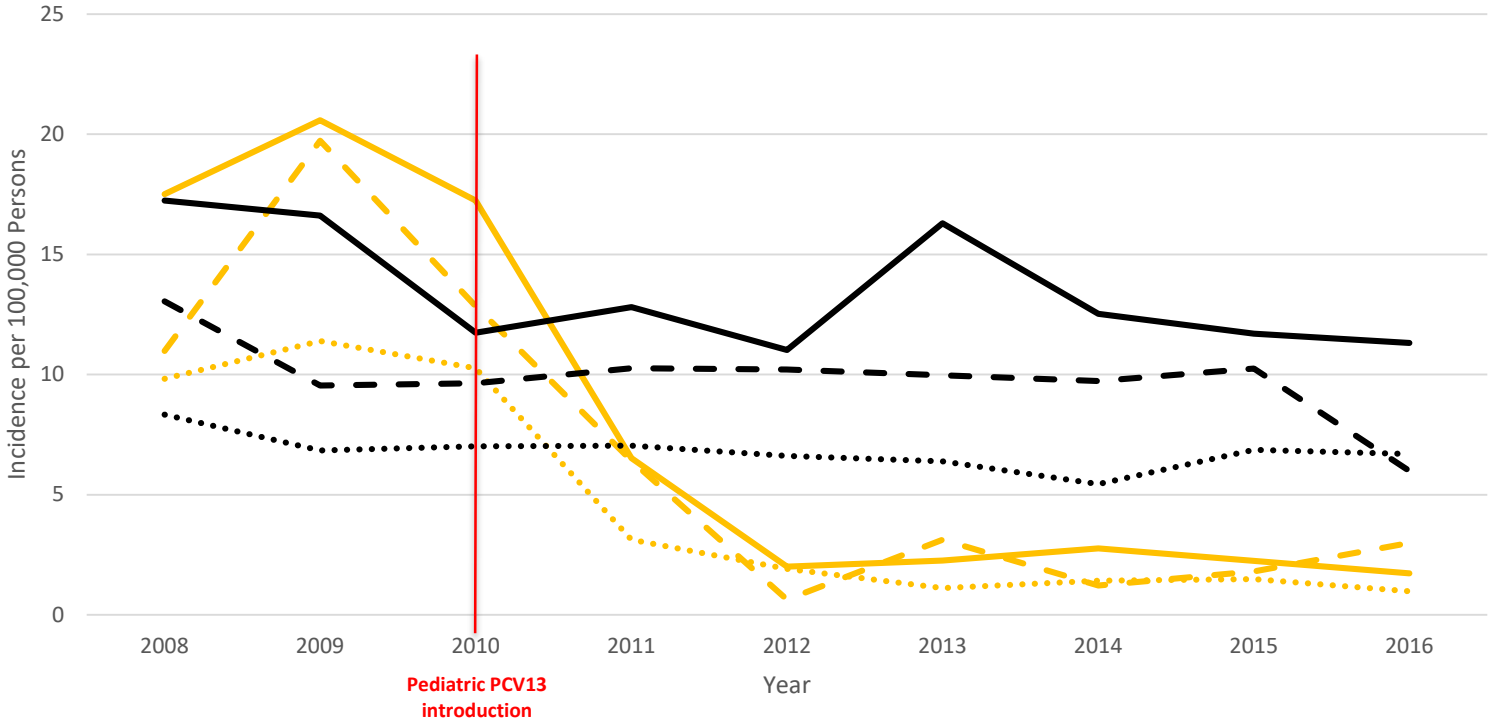
- Isolates serotyped by Quellung or PCR at reference labs and grouped for analysis:
  - For children:
    - PCV13 serotypes[1]: 13 serotypes in PCV13 plus 6C due to cross-protection[2]
    - Non-PCV13 serotypes: all other non-PCV13 or 6C serotypes
  - For adults:
    - PCV13 serotypes as defined in children
    - PPV11 serotypes[3]: 11 serotypes unique to PPSV23
    - Non-vaccine types (NVT): all other non-PCV13, non-PPV11, not 6C pneumococcal serotypes
- Compared overall and serotype-specific IPD incidence (cases/100,000 population) from 2008–2009 (pre-pediatric PCV13 introduction baseline) to 2015–2016

1. Serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F
2. Cooper et al. 2011
3. Serotypes 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F

Race and Syndrome by Age among IPD Cases, 2008–2016

Age in Years:	<5	≥65
Race n (%)		
Black	776 (32%)	1,234 (12%)
White	1,438 (59%)	8,845 (84%)
Other	229 (9%)	434 (4%)
Syndrome n (%)		
Meningitis	224 (9%)	399 (4%)
Bacteremia without Focus	1,074 (44%)	1,618 (15%)
Pneumonia with Bacteremia	813 (33%)	7,998 (76%)

IPD Incidence by Serotype Group among Children <5 Years Old, 2008–2016

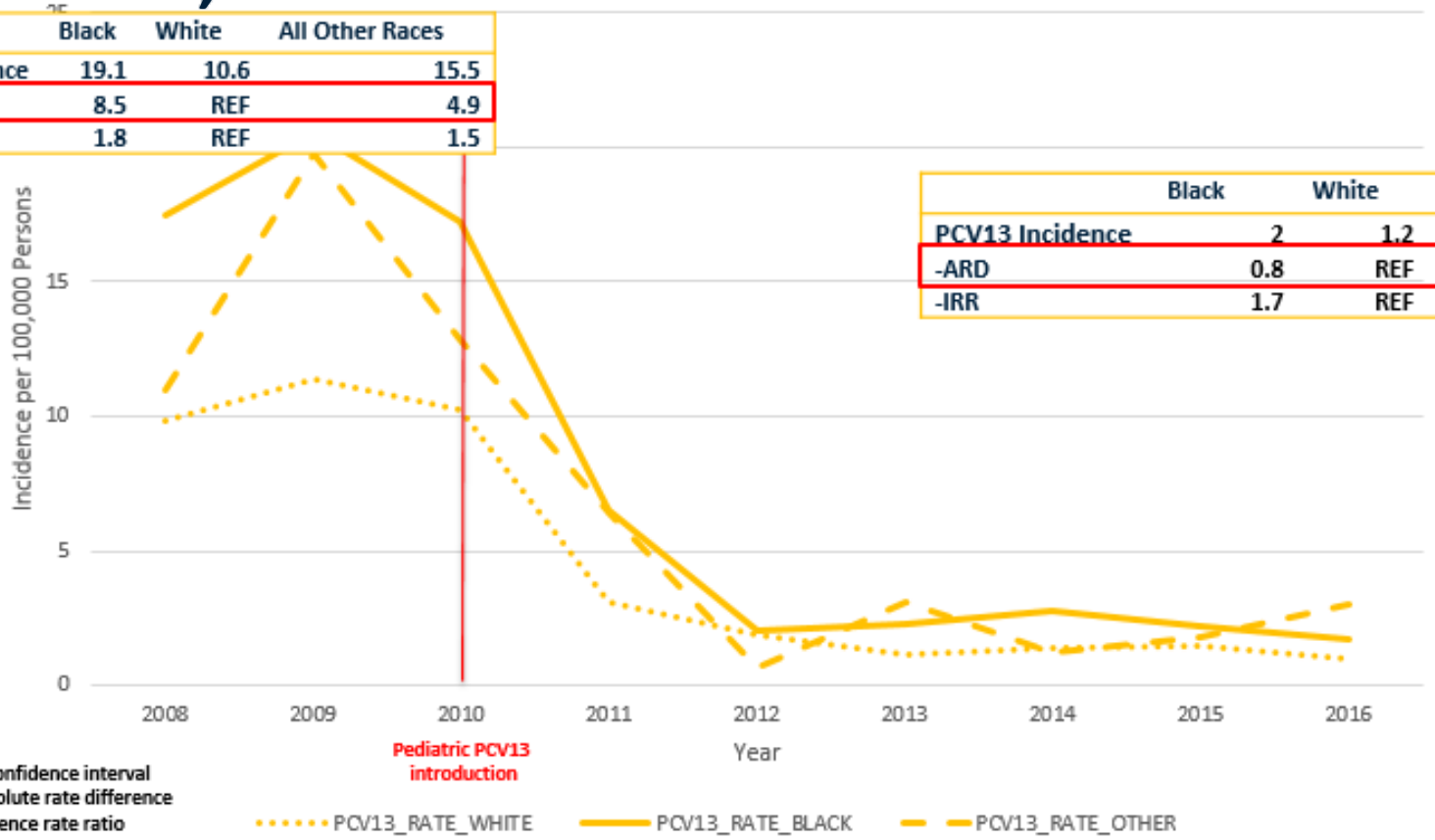


CI: 95% confidence interval
ARD: absolute rate difference
IRR: incidence rate ratio

PCV13 Serotype IPD Incidence among Children <5 Years Old, 2008–2016

	Black	White	All Other Races
PCV13 Incidence	19.1	10.6	15.5
-ARD	8.5	REF	4.9
-IRR	1.8	REF	1.5

	Black	White	All Other Races
PCV13 Incidence	2	1.2	2.4
-ARD	0.8	REF	1.2
-IRR	1.7	REF	2.0



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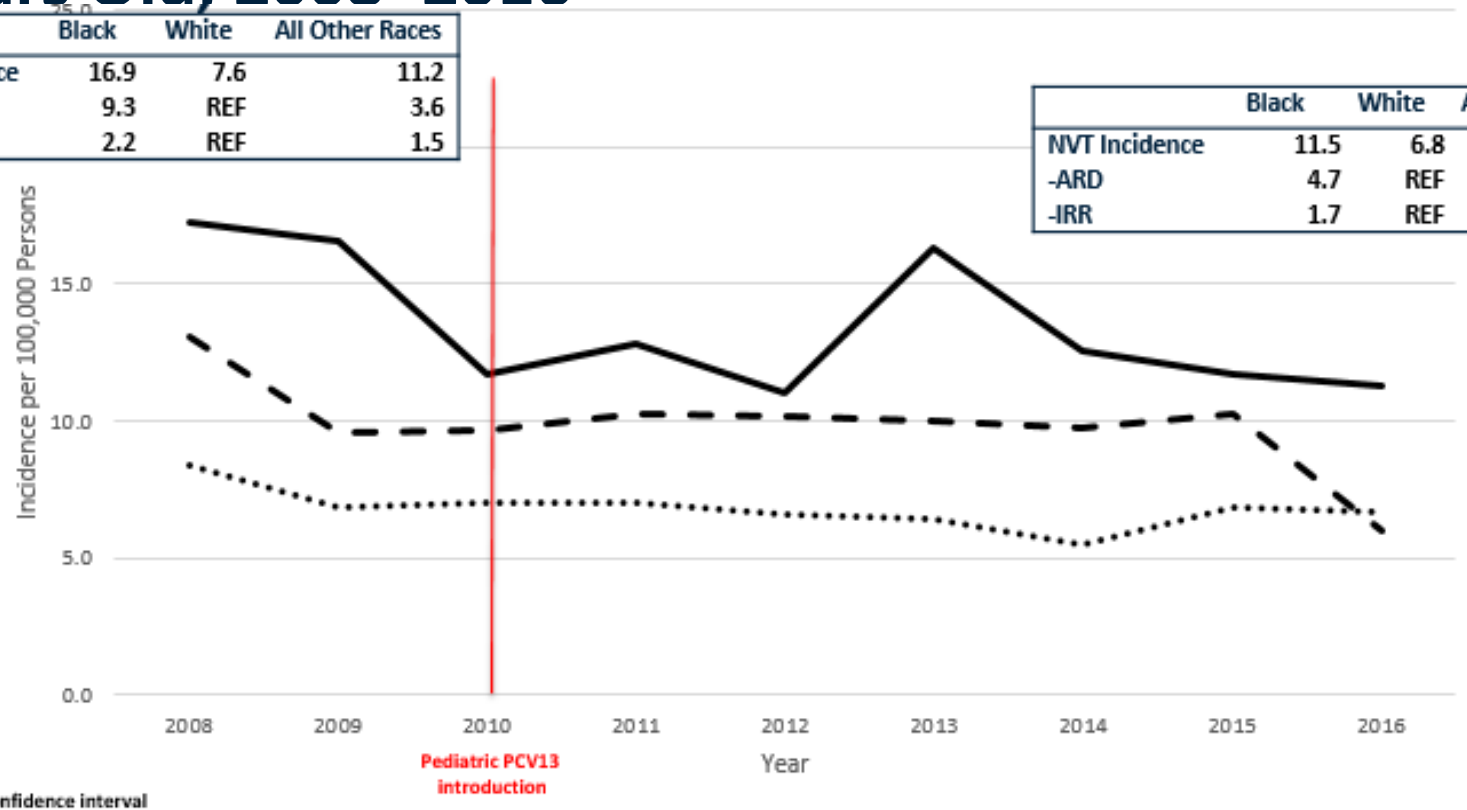
ARD: absolute rate difference
IRR: incidence rate ratio

Non-PCV13 Serotype IPD Incidence among Children <5 Years Old, 2008–2016

	Black	White	All Other Races
NVT Incidence	16.9	7.6	11.2
-ARD	9.3	REF	3.6
-IRR	2.2	REF	1.5

	Black	White	All Other Races
NVT Incidence	11.5	6.8	8.1
-ARD	4.7	REF	1.3
-IRR	1.7	REF	1.2



CI: 95% confidence interval
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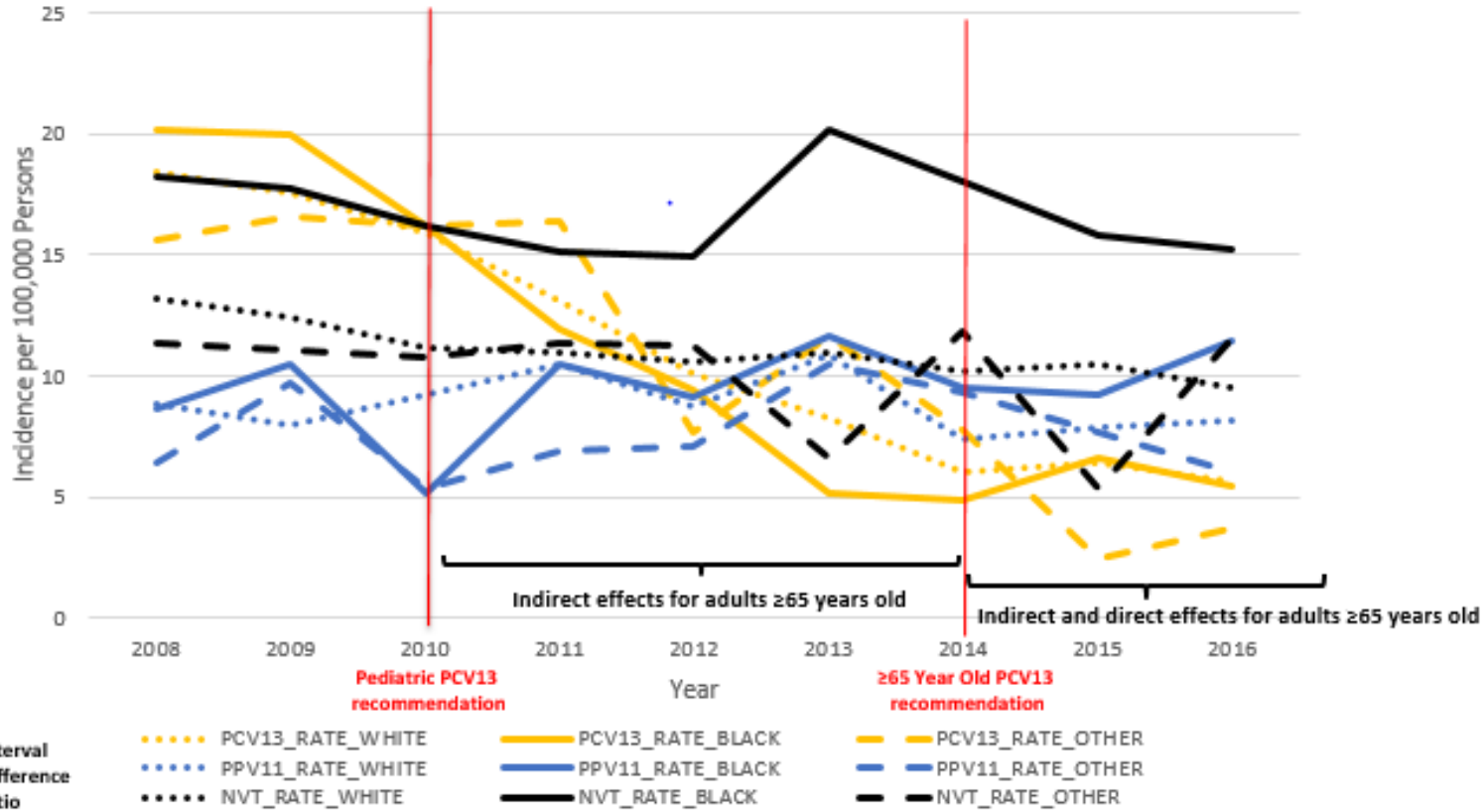
IPD Incidence by Serotype Group among Adults ≥65 Years Old, 2008–2016

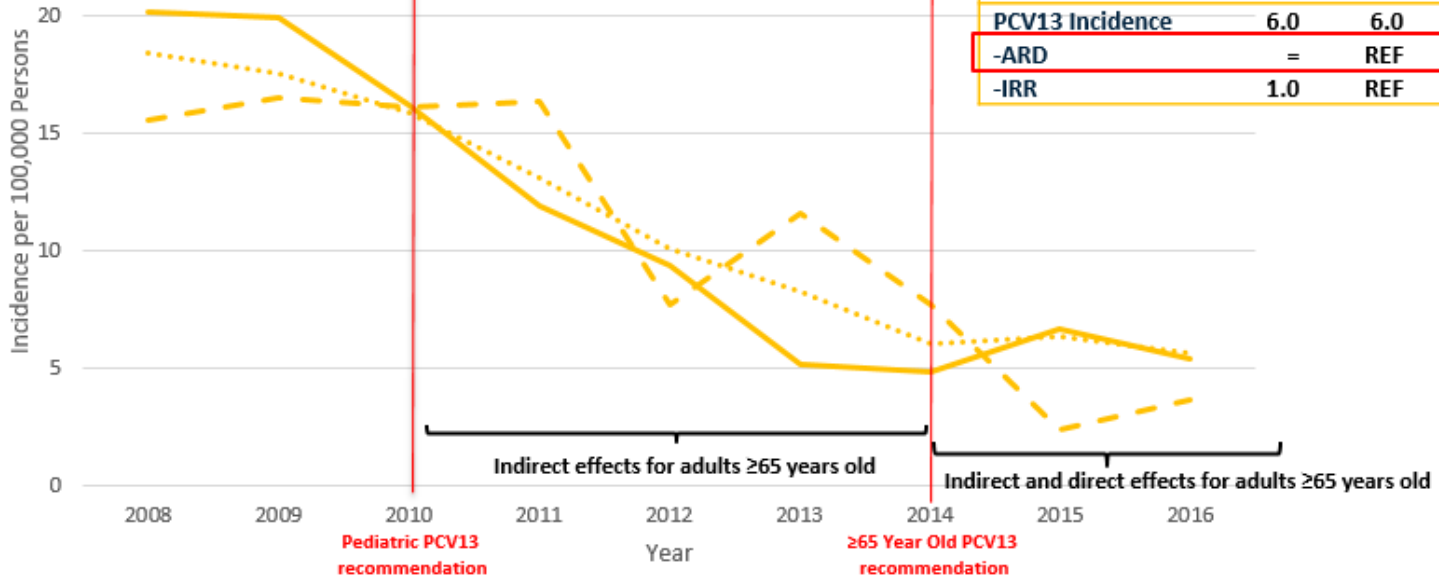


CI: 95% confidence interval
ARD: absolute rate difference
IRR: incidence rate ratio

PCV13 Serotype IPD Incidence among Adults ≥65 Years Old, 2008–2016

	Black	White	All Other Races
PCV13 Incidence	20.1	18.0	16.1
-ARD	2.1	REF	-1.9
-IRR	1.1	REF	0.9

	Black	White	All Other Races
PCV13 Incidence	6.0	6.0	3.1
-ARD	=	REF	-2.9
-IRR	1.0	REF	0.5

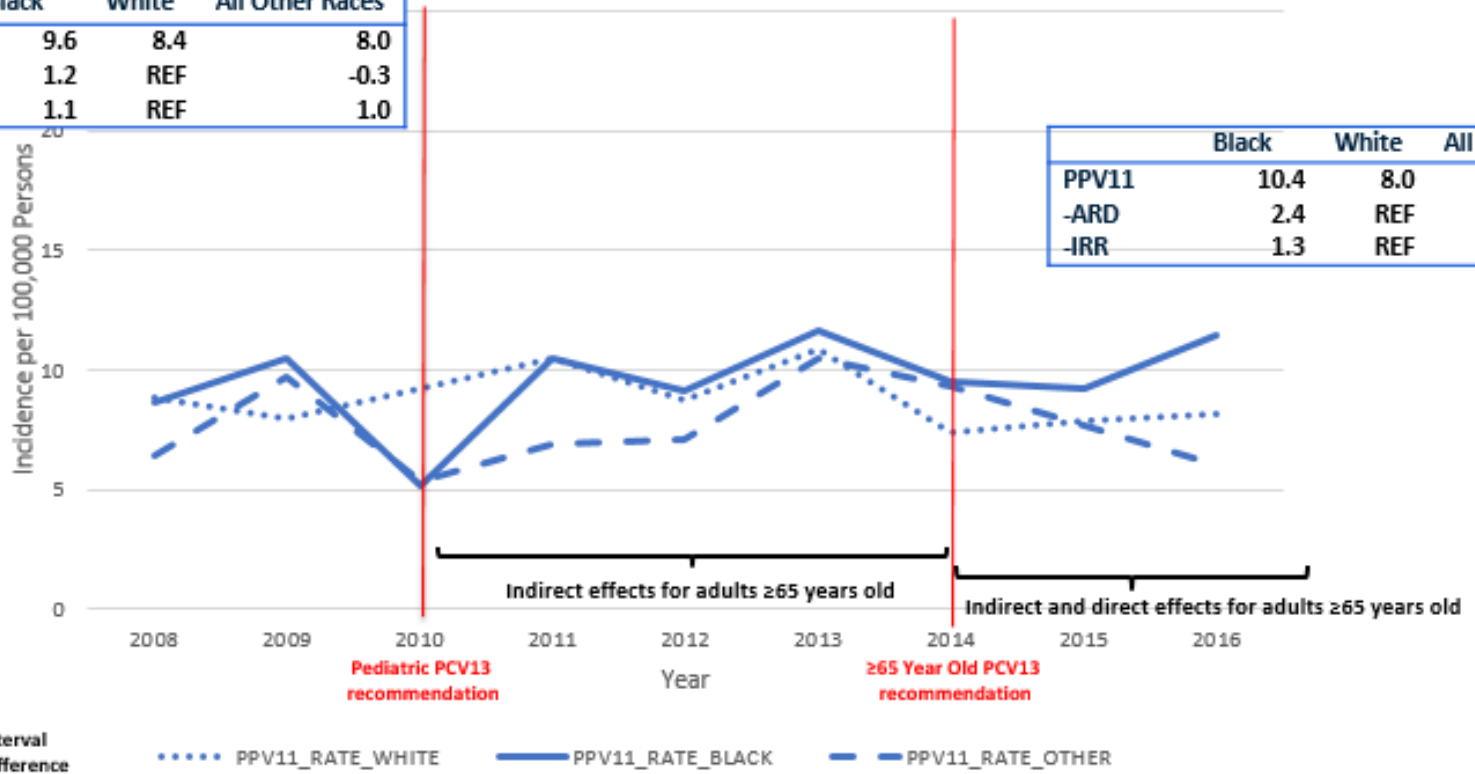


CI: 95% confidence interval
ARD: absolute rate difference
IRR: incidence rate ratio

PPSV23 Unique Serotype IPD Incidence among Adults ≥65 Years Old, 2008–2016

	Black	White	All Other Races
PPV11	9.6	8.4	8.0
-ARD	1.2	REF	-0.3
-IRR	1.1	REF	1.0

	Black	White	All Other Races
PPV11	10.4	8.0	6.8
-ARD	2.4	REF	-1.2
-IRR	1.3	REF	0.9

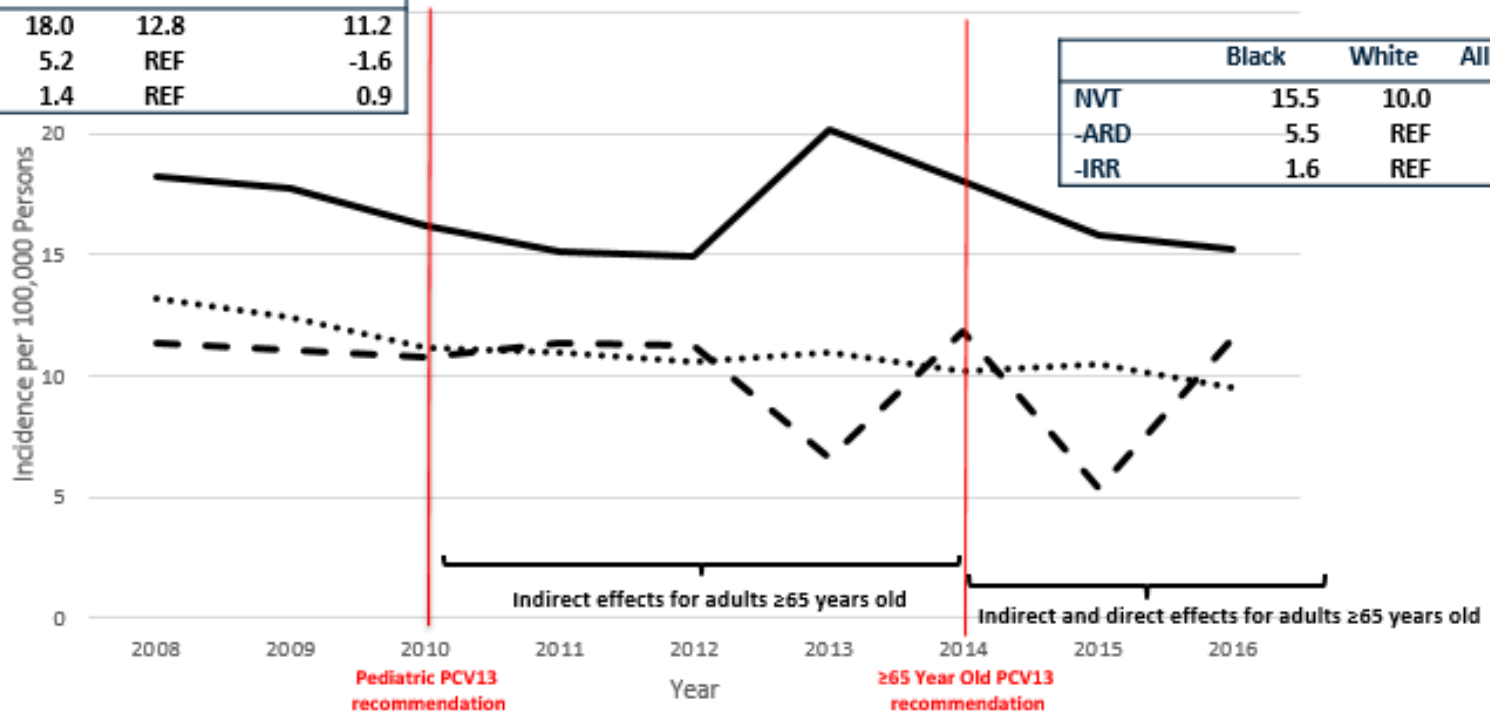


CI: 95% confidence interval
ARD: absolute rate difference
IRR: incidence rate ratio

Non-Vaccine Serotype IPD Incidence among Adults ≥65 Years Old, 2008–2016

	Black	White	All Other Races
NVT	18.0	12.8	11.2
-ARD	5.2	REF	-1.6
-IRR	1.4	REF	0.9

	Black	White	All Other Races
NVT	15.5	10.0	8.5
-ARD	5.5	REF	-1.5
-IRR	1.6	REF	0.9



CI: 95% confidence interval
ARD: absolute rate difference
IRR: incidence rate ratio

Incidence Comparisons Before and After PCV13 Introduction

	2008–2009		2015–2016	
	Black*	All Other Races*	Black*	All Other Races*
Children <5 Years Old				
PCV13 IPD Absolute Rate Difference (ARD)	8.5	4.9	0.8	1.2
PCV13 IPD Incidence Rate Ratio (IRR)	1.8	1.5	1.7	2.0
Total IPD ARD	17.8	8.6	5.5	2.5
Total IPD IRR	2.0	1.5	1.7	1.3
Adults ≥65 Years Old				
PCV13 IPD ARD	2.1	-1.9	=	-2.9
PCV13 IPD IRR	1.1	0.9	1.0	0.5
Total IPD ARD	8.5	-3.8	7.9	-5.6
Total IPD IRR	1.2	0.9	1.3	0.8

*Incidence among persons of white race used as reference group

Preliminary Conclusions

- IPD incidence has dramatically decreased for all racial groups driven by reduction in PCV13-type IPD
- PCVs have nearly eliminated the absolute difference in PCV13-type IPD incidence between people of black and white races
- Disparities in IPD remain due to non-vaccine type IPD
- Further analysis is planned to look at the contribution of SES and underlying medical conditions by race

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Thank you!

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

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

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

Formulating a Question to Re-Evaluate the Adult Age Based PCV13 Recommendation

- 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, mortality, and vaccine safety

Grading of Recommendations Assessment, Development and Evaluation (GRADE) Process

- Choosing Outcomes
  - PCV13-type IPD
  - Non-bacteremic pneumococcal pneumonia (NBPP) as measured by all-cause pneumonia, NBPP, and PCV13-type pneumonia
  - Mortality due to IPD and NBPP
  - Serious or systemic events associated with PCV13

Evidence Added Today--Safety

- No new safety signals or unexpected patters observed in VAERS surveillance
- No increase in adverse events observed VSD cohort study
- Will continue to monitor and provide updates as needed

Results: RRs for medically attended AE for PCV13 v. PPSV23

Adverse Event (risk window)	PPV23 AE counts (N = 232591)	PCV13 AE counts (N = 313136)	Unadjusted RR	95% Wald Confidence Limits		IPTW Adjusted RR	95% Wald Confidence Limits	
G1. Cardiovascular events (1-42)								
Acute myocardial infarction	375	534	1.05	0.92	1.19	0.73	0.61	0.88
Acute pericarditis	8	6	0.55	0.19	1.59	0.90	0.27	2.94
Atrial fibrillation	430	702	1.20	1.06	1.35	0.67	0.57	0.80
Cardiomyopathy &heart failure	566	838	1.09	0.98	1.21	0.62	0.54	0.72
G2. Bell's Palsy (1-42)	57	69	0.89	0.63	1.26	0.69	0.41	1.15
G3. Guillain-Barre Syndrome (1-42)	8	4	0.37	0.11	1.22	0.21	0.05	0.78
G4. Syncope (day 0)	75	22	0.22	0.14	0.35	0.13	0.07	0.25
G5. Erythema multiforme (1-42)	2	2	0.73	0.10	5.22	0.94	0.13	6.71
G6. Thrombocytopenia (1-28)								
Thrombocytopenia I	21	17	0.60	0.31	1.13	0.66	0.25	1.76
Thrombocytopenia II	100	96	0.71	0.53	0.94	0.44	0.31	0.61
G7. Cellulitis and infection (1-7)	1393	1915	1.02	0.95	1.09	0.89	0.81	0.98
G8. Allergic reaction (1-7)	70	49	0.52	0.36	0.75	0.47	0.30	0.73
G9. Anaphylaxis (0-1)	4	5	0.93	0.25	3.46	1.32	0.30	5.79

All anaphylaxis diagnoses at 0-1 days following vaccination were chart reviewed and one patient receiving 5 vaccines concomitantly, including PCV13, was confirmed as anaphylaxis

Evidence Added Today--Pneumonia

- Pneumococcal pneumonia causing a high burden of disease
  - From Jun 2014 to May 2016, PCV13-type pneumonia among ≥65 years olds decreased (31% relative reduction [95% CI: 8.3, 43.9])
    - Limited ability to observe trends in 2 years
    - Combined direct and indirect effects
  - 4–6% pneumonia in adults ≥65 years olds caused by PCV13 serotypes
  - 66% of pneumonia incidence in adults ≥65 years olds was in patients with immunocompromising conditions or HCAP
- Population characteristics and case definitions contribute to variation in pneumonia incidence
- Studies estimating all-cause and pneumococcal pneumonia incidence and vaccine impact are anticipated in October

Evidence Added Today—Evaluation of Racial Disparities in Pneumococcal Disease

- Pediatric PCV introduction has reduced racial disparities in IPD
  - IPD incidence has dramatically decreased for all racial groups driven by reduction in PCV13-type IPD, nearly eliminating the absolute difference in PCV13-type IPD incidence between people of different races
- Carriage of PCV13 serotypes in American Indian children and adults similar overall carriage in the U.S.
- Among American Indians in the southwestern US, 26% of chest x-ray confirmed pneumonia was caused by pneumococcus, but PCV13-types did not predominate

Tentative Timeline

- Data to be shared with ACIP at the upcoming meeting (October 2018)
  - PCV13 impact on all-cause pneumonia and NBPP from studies examining administrative and clinical surveillance data
  - Potential public health impact and cost-effectiveness of changing the PCV13 policy for adults ≥65 years old
- EtR with GRADE finalized by the following meeting (February 2019)
- Potential vote (February or if additional time needed 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?
- What additional evidence should be included in future presentations to ACIP and GRADE review to help the committee with decision making?

Thank you!

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