Invasive Pneumococcal Disease in the U.S.—2008–2016

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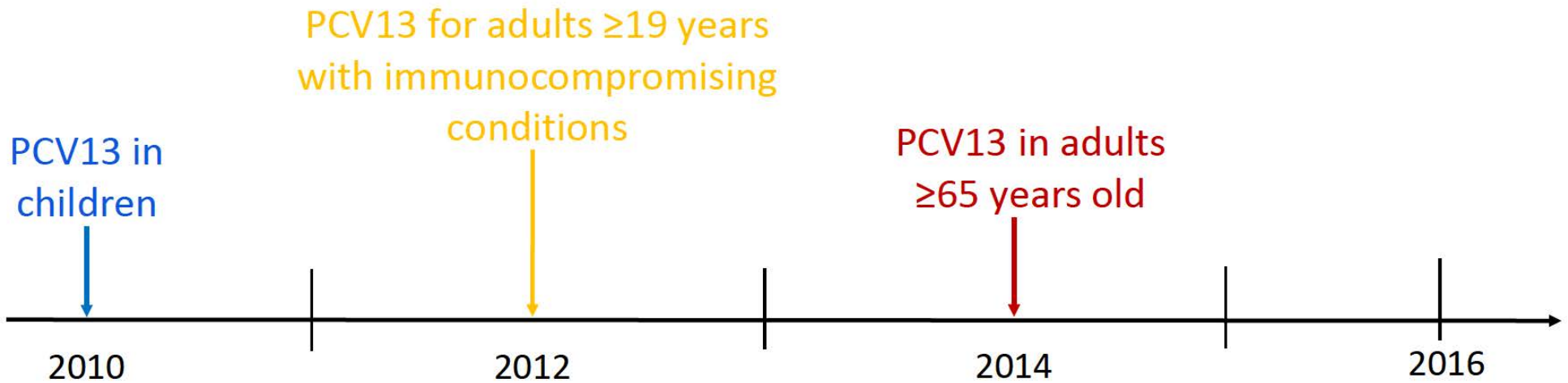
Pogona Ex. 2009
Merck v. Pogona, IPR2026-00374

Background and Aims



- Aim: Evaluate the direct and indirect impact of PCV13 on invasive pneumococcal disease (IPD) in the general population of children and adults and among adults with HIV

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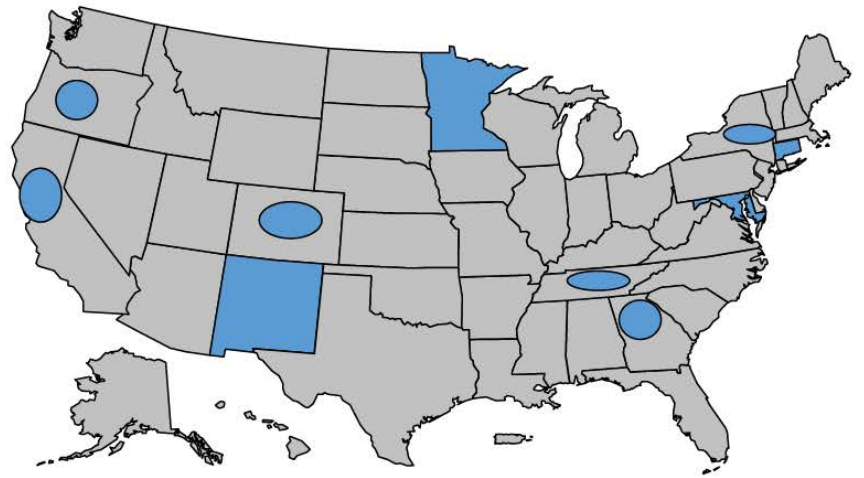
Methods

- **Active Bacterial Core Surveillance (ABCs):**
  - Active laboratory and population-based surveillance, 10 sites
  - Pneumococcus isolated from sterile site



- **US Census Bureau:**
  - Race-bridged post-census population estimates as denominators
- **National HIV surveillance:**
  - People diagnosed with HIV in the ABCs catchment areas
- **Overall and serotype-specific IPD incidence rates (cases per 100,000)**

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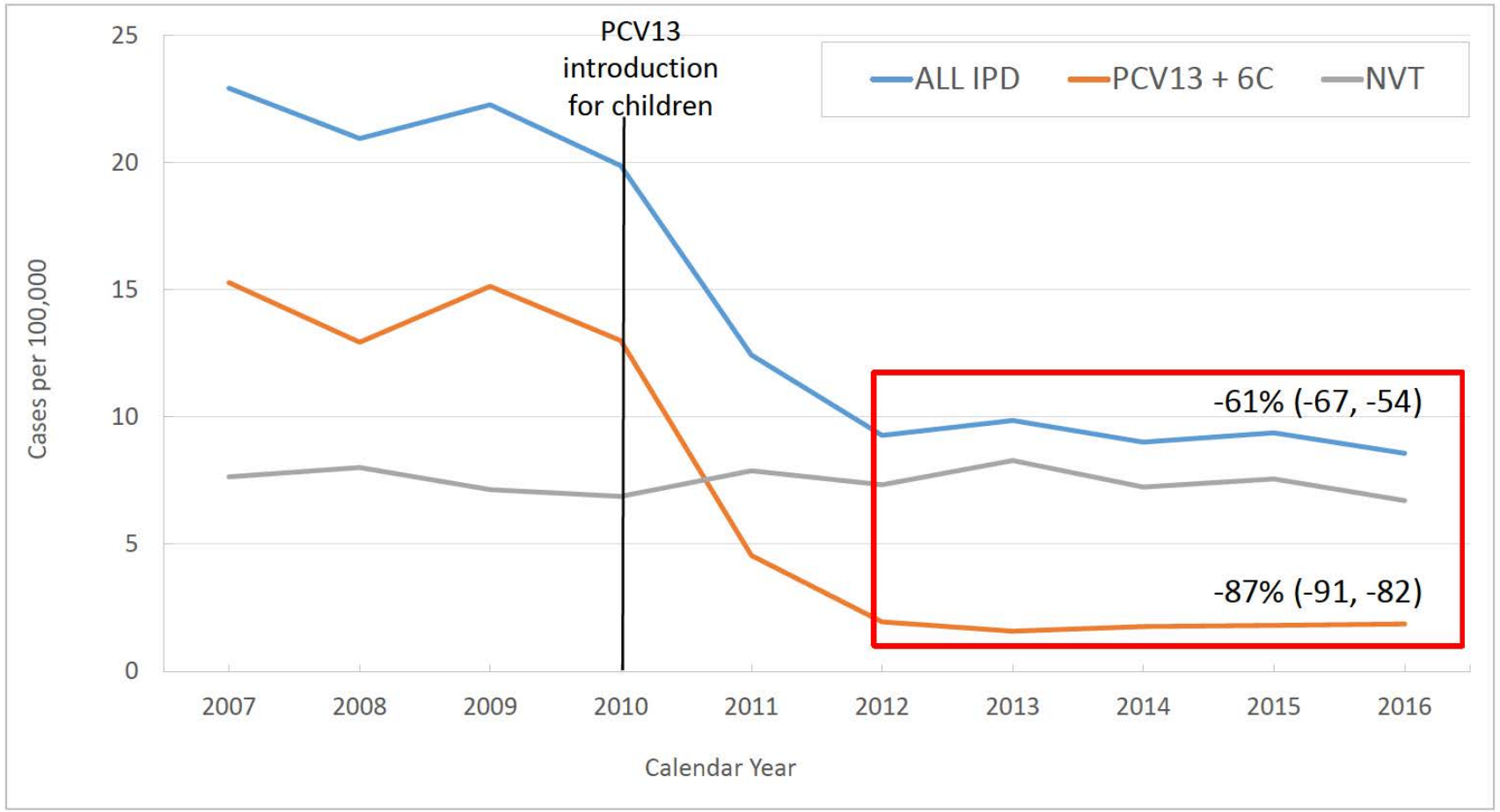
Methods

- Isolates serotyped by Quellung or PCR at reference labs and grouped for analysis:
  - **PCV13 serotypes[1]:** 13 serotypes in PCV13 plus 6C due to cross-protection[2]
  - **PPV11 serotypes[3]:** 11 serotypes unique to PPSV23
  - **Non-vaccine types (NVT):** all other pneumococcal serotypes

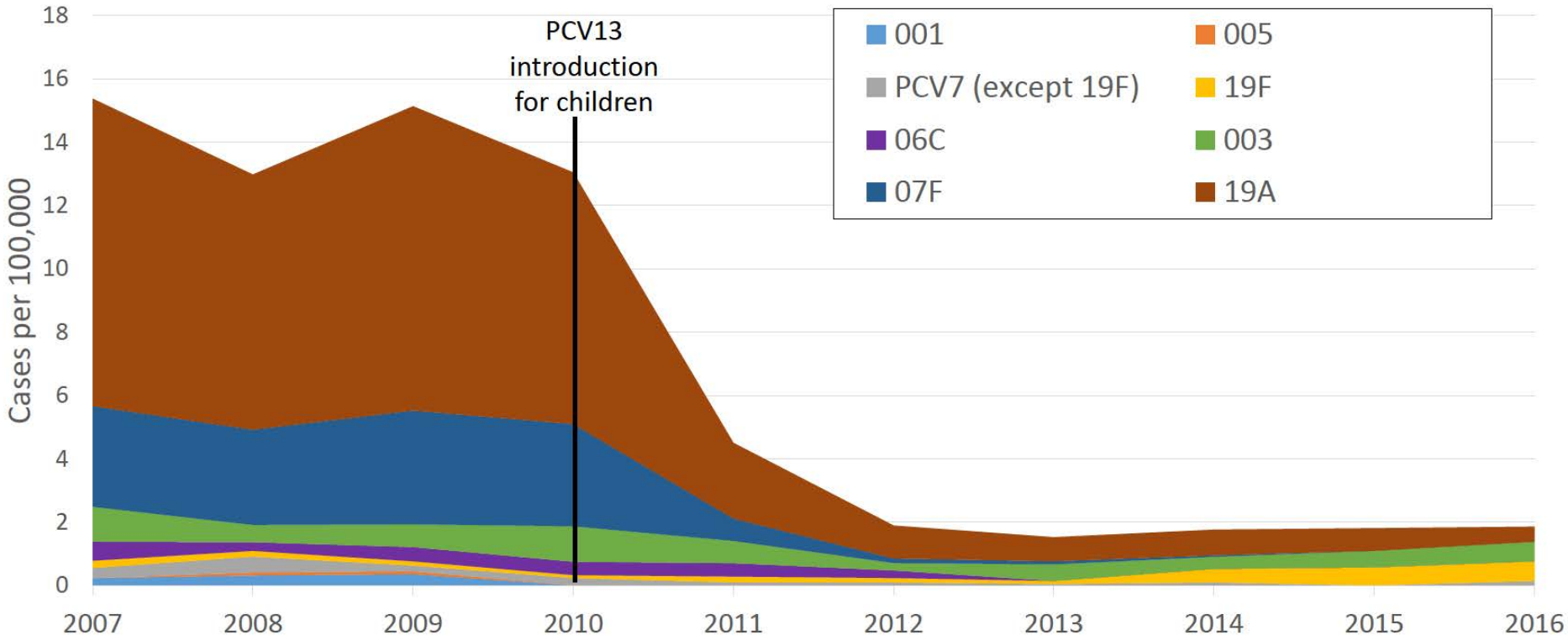
- Compared overall and serotype-specific IPD incidence (cases/100,000 population) pre and post pediatric PCV13 introduction
  - HIV denominator only available 2008–2014
  - Percent reduction in disease incidence (1-RR)

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

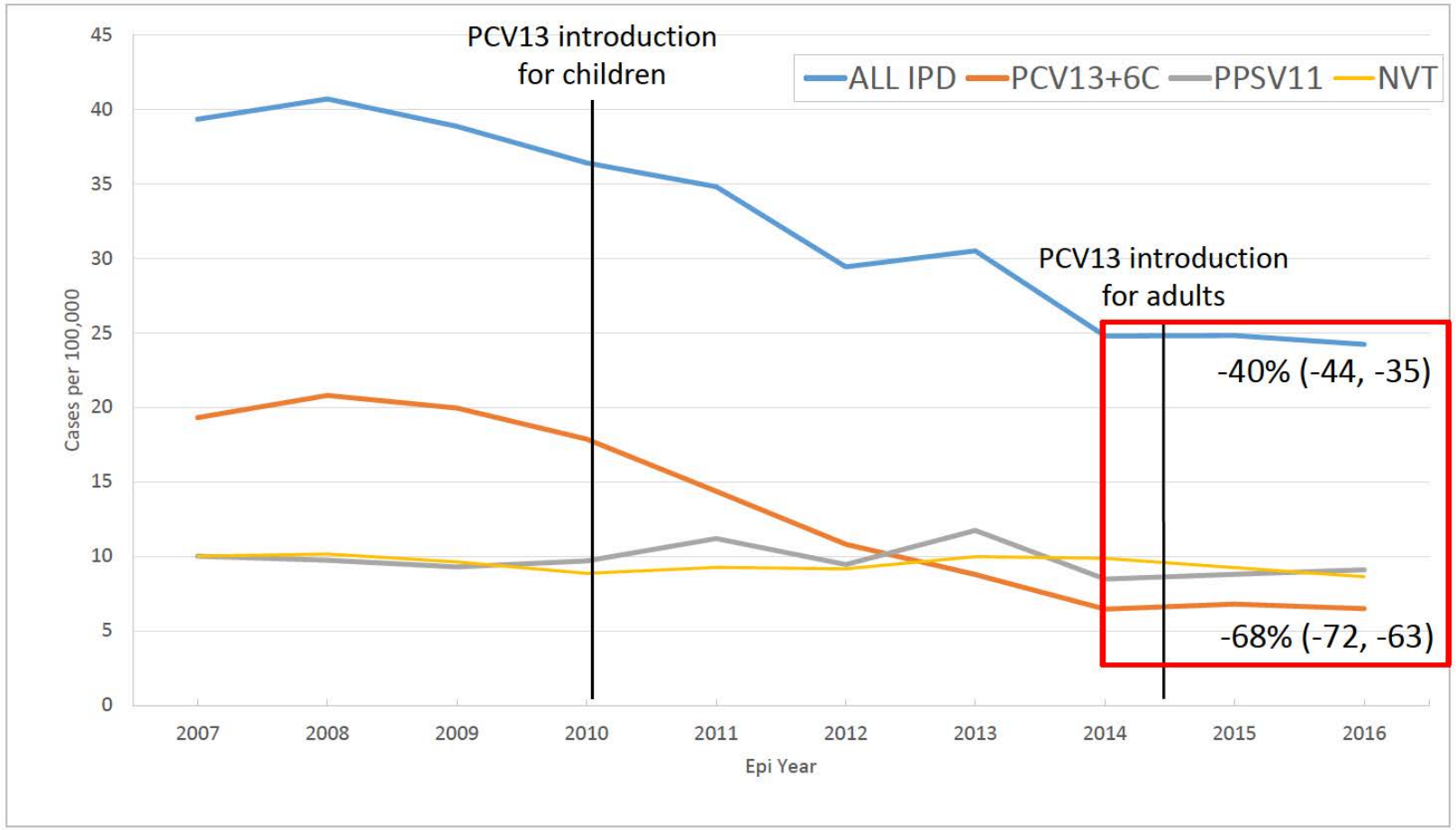
IPD rates among children < 5 years old, 2007–2016



IPD rates among children < 5 years old by PCV13 plus 6C serotypes, 2007–2016



IPD rates among adults ≥ 65 years, 2007–2016



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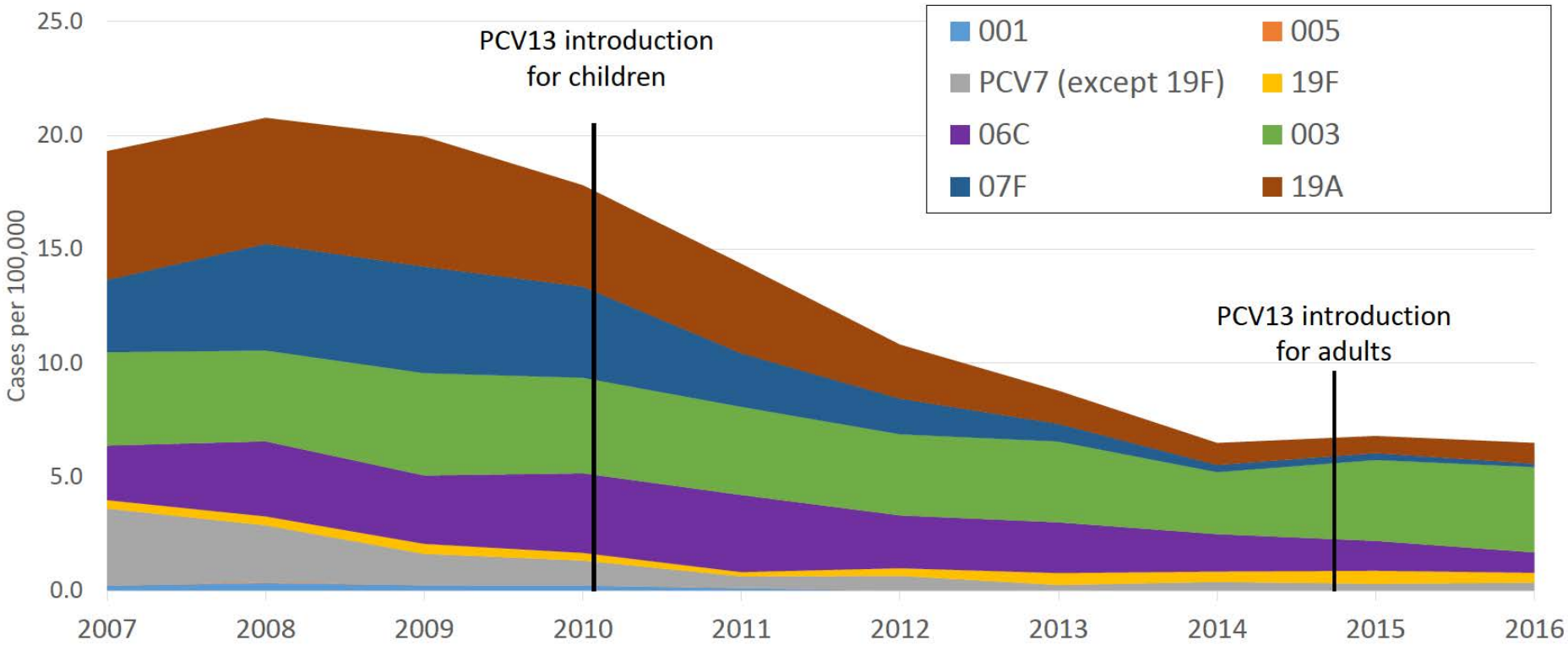


Rank order of non-PCV13 serotypes causing IPD, 2015-2016

Children < 5 years

TYPE	Cases/100,000
23B	0.62
22F	0.62
33F	0.57
15C	0.52
15A	0.48
35B	0.43
10A	0.33
12F	0.29
15B	0.29
38	0.19
other	1.67

Adults ≥ 65 years

TYPE	Cases/100,000
22F	2.57
23A	1.33
35B	1.31
15A	1.16
33F	0.97
16F	0.88
11A	0.82
9N	0.72
23B	0.67
12F	0.61
other	4.66

Green denotes serotypes common to both age groups

Changes in pneumococcal meningitis incidence by age and serotype group, 2007-2008 vs. 2016

Age (years)	Serotype group	2016 % change (95%CI)
<5	PCV13+6C	-81.9 (-93.7, -47.7)*
	Non-PCV13	27.1 (-31.8, 137)
	ALL IPD	-34 (-59.6, 7.8)
≥65	PCV13+6C	-76.1 (-90.6, -39.5)*
	PPSV11	-5.3 (-57.9, 113.2)
	NVT	-32.4 (-66.9, 38.3)
	ALL IPD	-43.6 (-64, -11.7)*

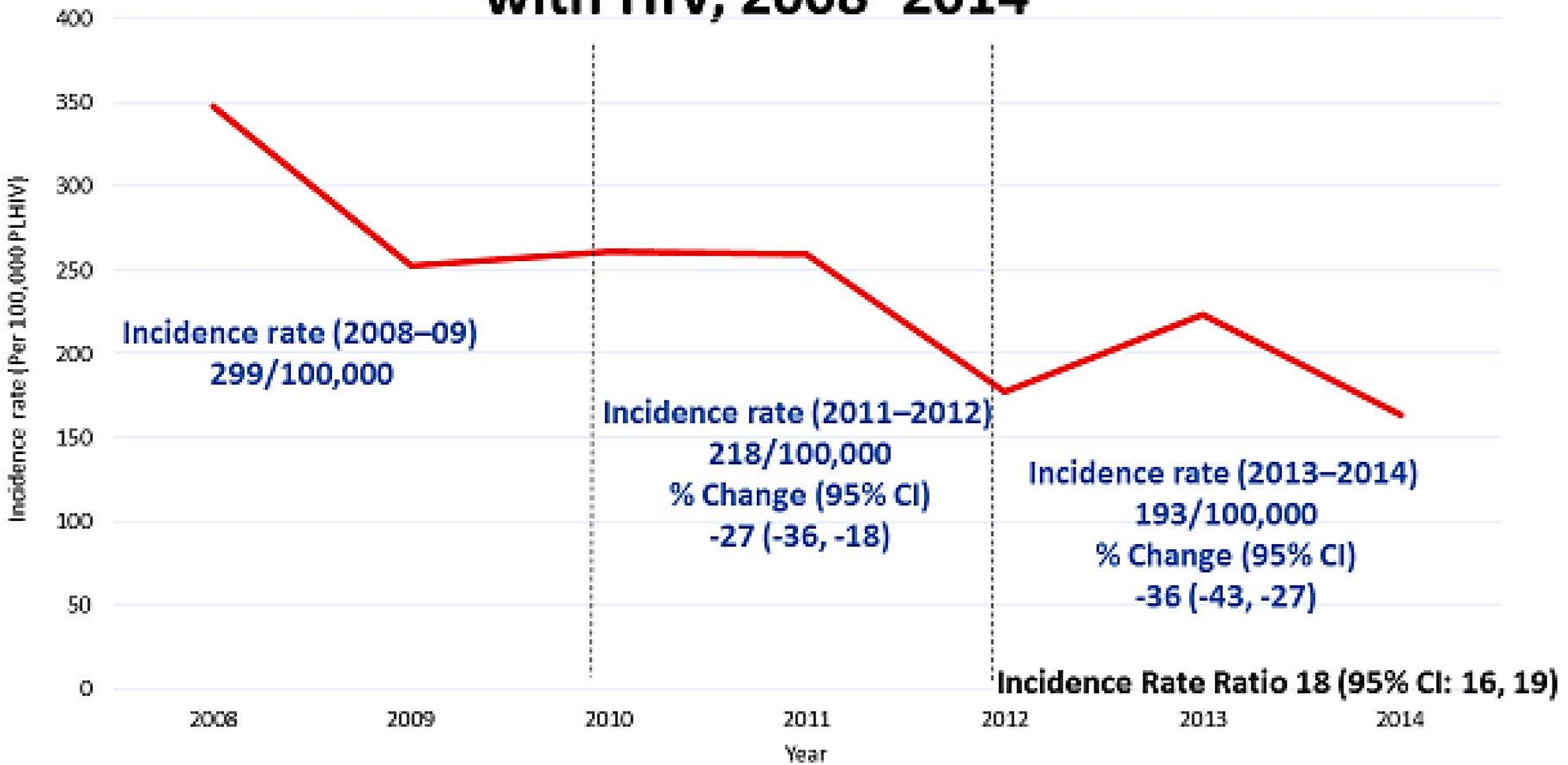
* statistically significant decrease

Characteristics of IPD cases among adults ≥19 years with and without HIV, 2008–2014

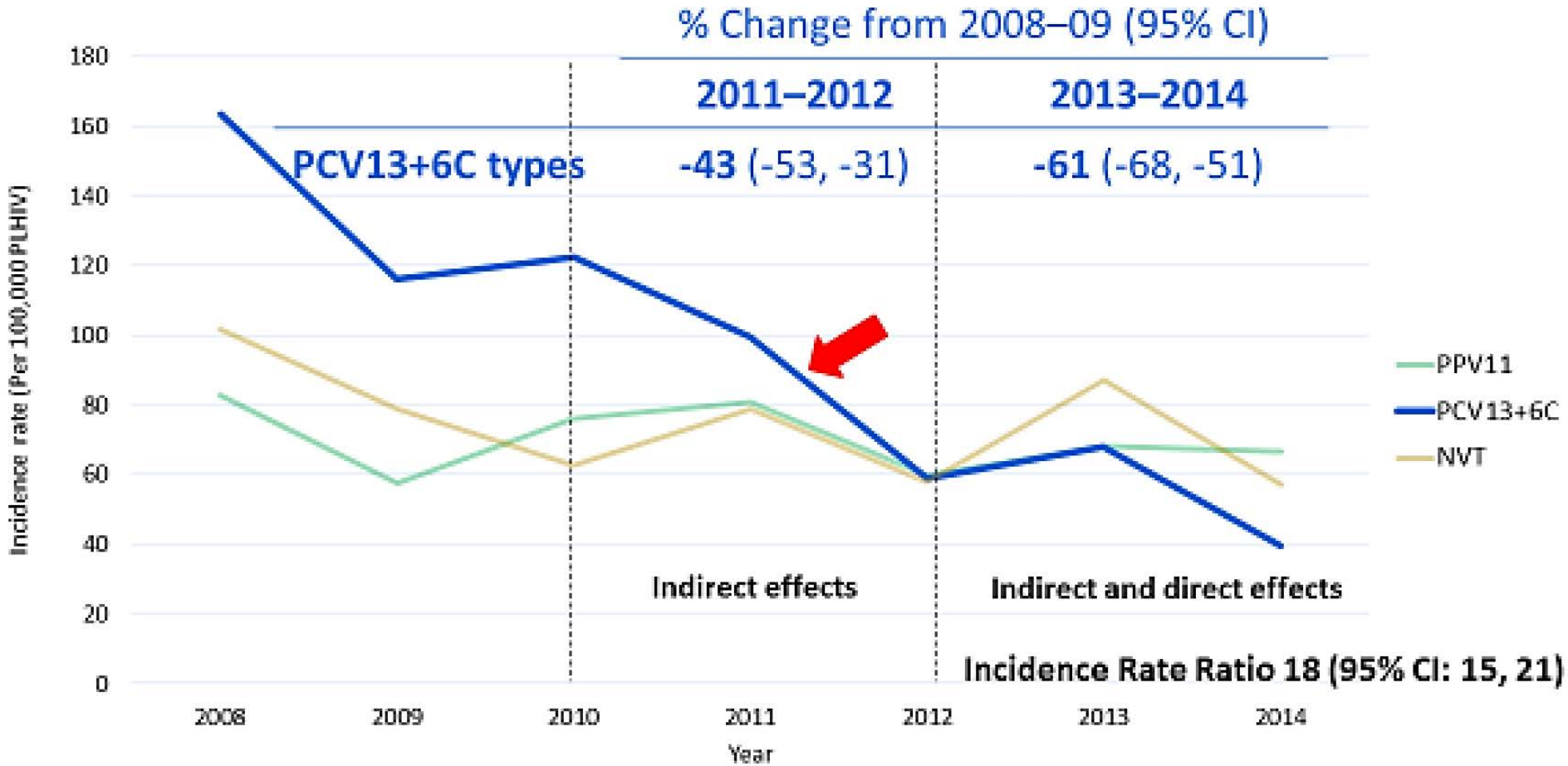
- IPD cases with HIV more likely to be:
  - **Younger** (median age: 47yrs [19–88] vs. 61yrs [19–104])
  - **Male** (60.8% vs 50.9%)
  - **Black race** (69.6% vs 16.9%)

	Case fatality (%)	
Age groups	**PLHIV (n=1,662)**	**Non-PLHIV (n=18,071)**
19–34 years	3.7	4.5
35–49 years	5.7	8.4
50–64 years	9.2	10.7
≥65 years	17.0	15.3

Changes in IPD incidence rate in adults ≥19 years living with HIV, 2008–2014



Changes in IPD incidence rate by serotype group in adults ≥19 years living with HIV, 2008–2014



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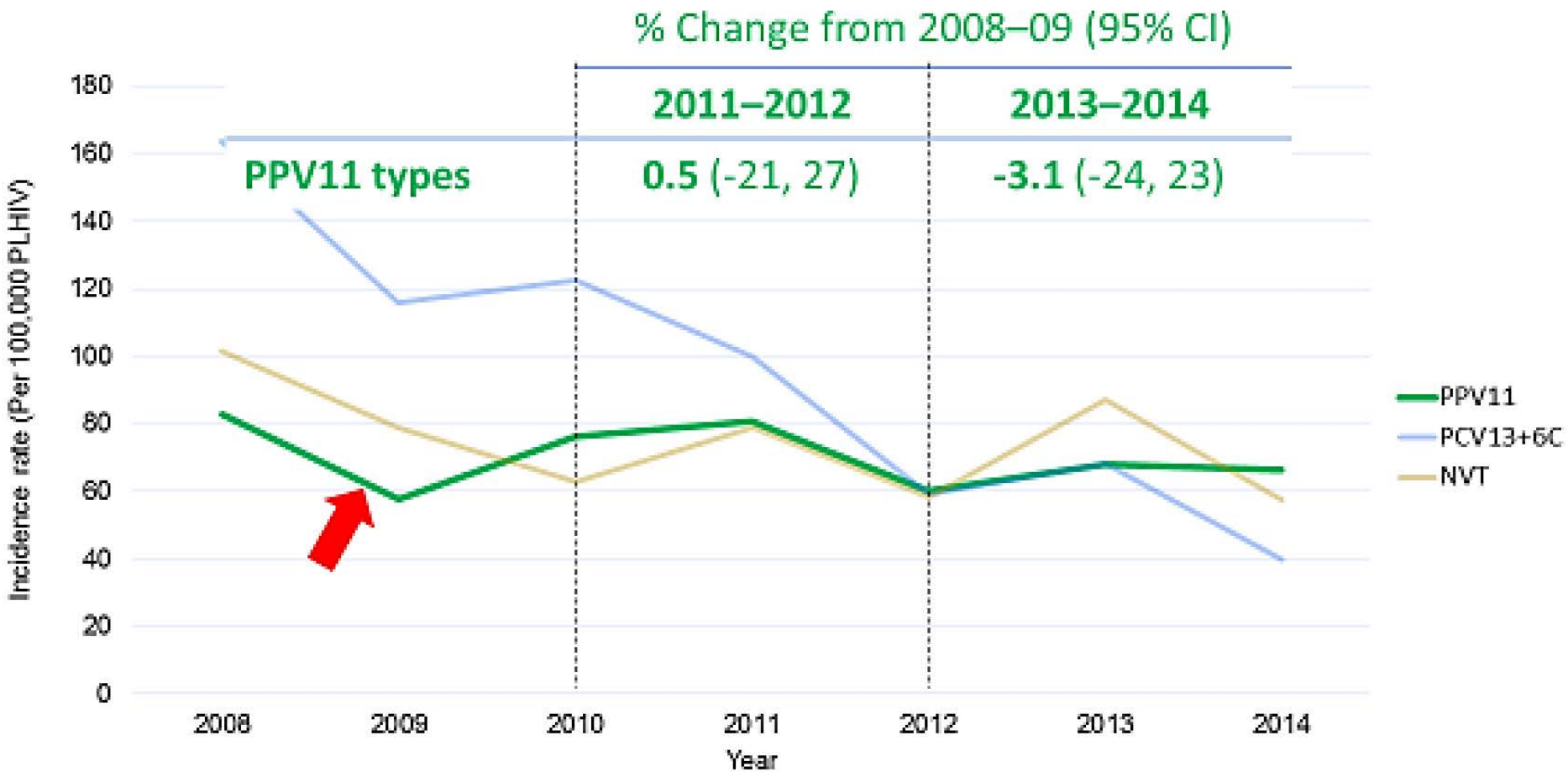

Summary

- Significant reductions in overall and PCV13 serotype IPD among children and adults since PCV13 introduction
  - Reductions driven by types 19A and 7F
  - Rates plateaued in 2014–2016
  - No further reductions in PCV13 serotype IPD among adults ≥65 years since 2014 adult PCV13 recommendations
  - Despite reductions, IPD rates including PCV13 serotypes, remained high in adults with HIV compared to those without HIV
- No large increases in any non-PCV13 serotype among children or adults, including those living with HIV
- Similar trends observed for pneumococcal meningitis

Conclusions

- In the 6 years post-PCV13 introduction, sustained benefits in overall IPD and IPD caused by the PCV13 serotypes in children and adults

- No evidence of serotype replacement in children or general population of adults

- Continue monitoring changes in disease and serotype distribution to inform new vaccine policy

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Thank you

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