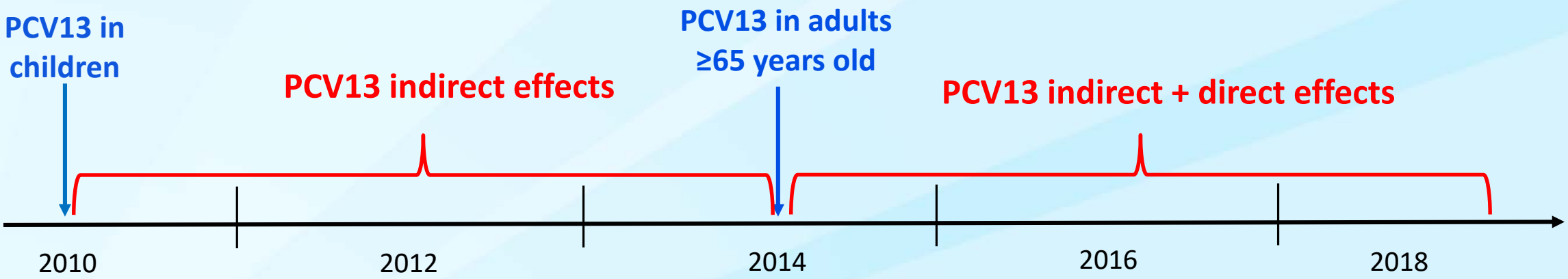
Estimating PCV13 direct and indirect effects on IPD among adults ≥65 years

Tamara Pilishvili, PhD, MPH
Pneumococcal Vaccines Work Group
Respiratory Diseases Branch
National Center for Immunizations and Respiratory Diseases
February 22, 2018

PCV13 recommendations and expected impact on IPD incidence among adults ≥65 years old

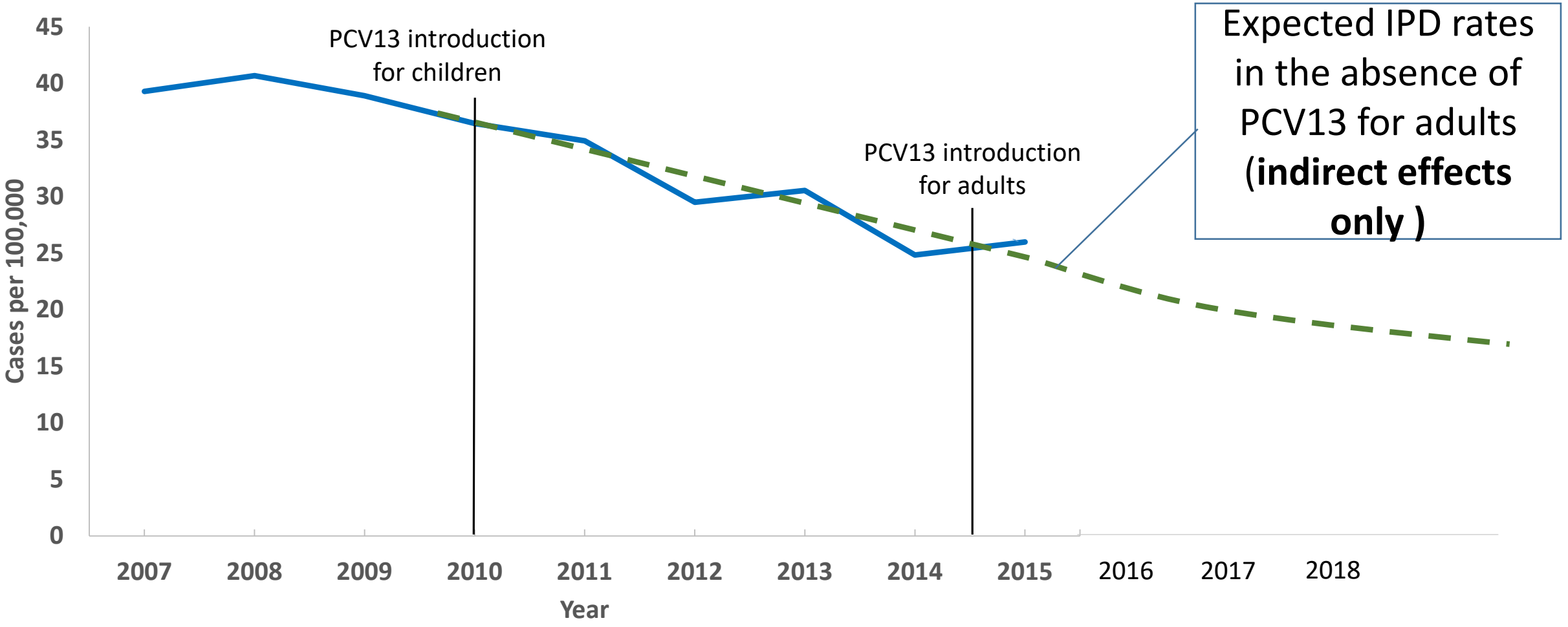


Objectives

- **Estimating PCV13 indirect and direct effects in adults ≥ 65 years**

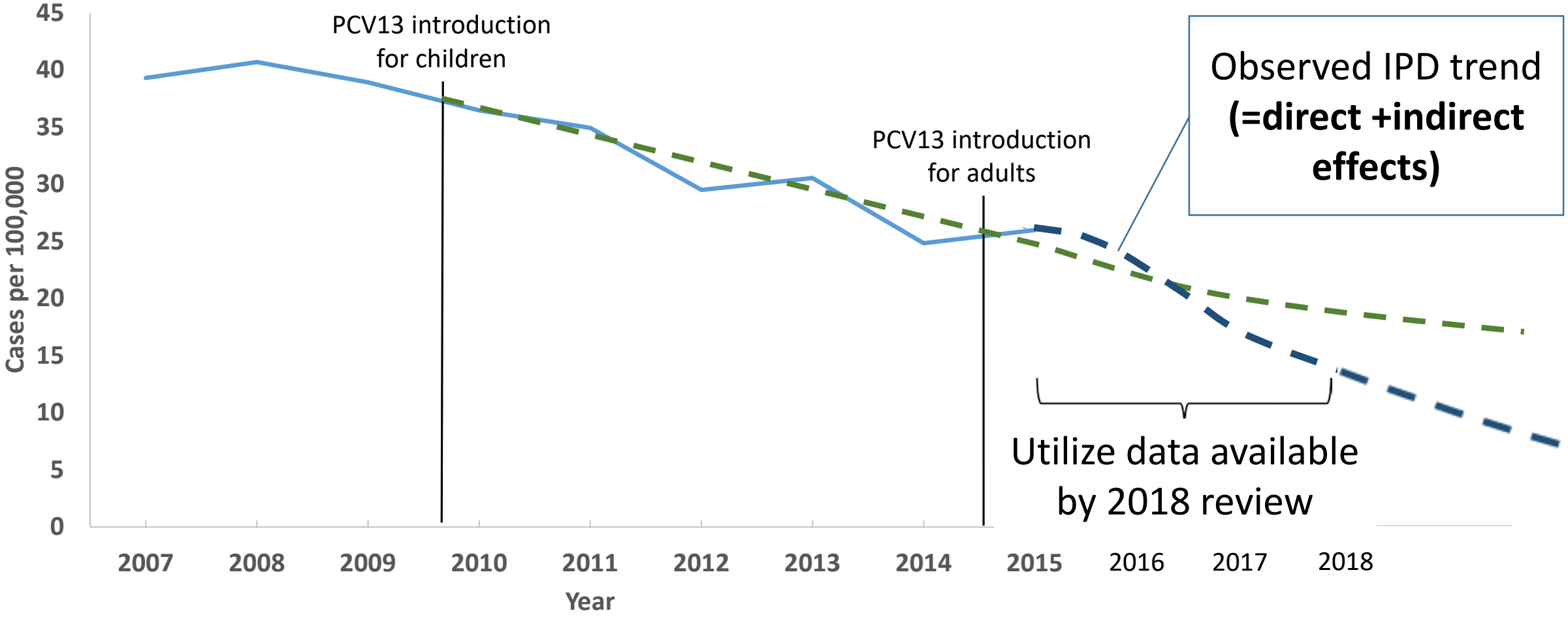
1. Estimate IPD incidence expected through indirect effects only (i.e. in the absence of PCV13 recommendation for ≥65 year old adults in 2014)
2. Estimate the contribution of direct PCV13 effects from the observed (total effects) vs expected (indirect effects only) IPD incidence

1. Estimate expected IPD incidence due to indirect PCV13 effects only



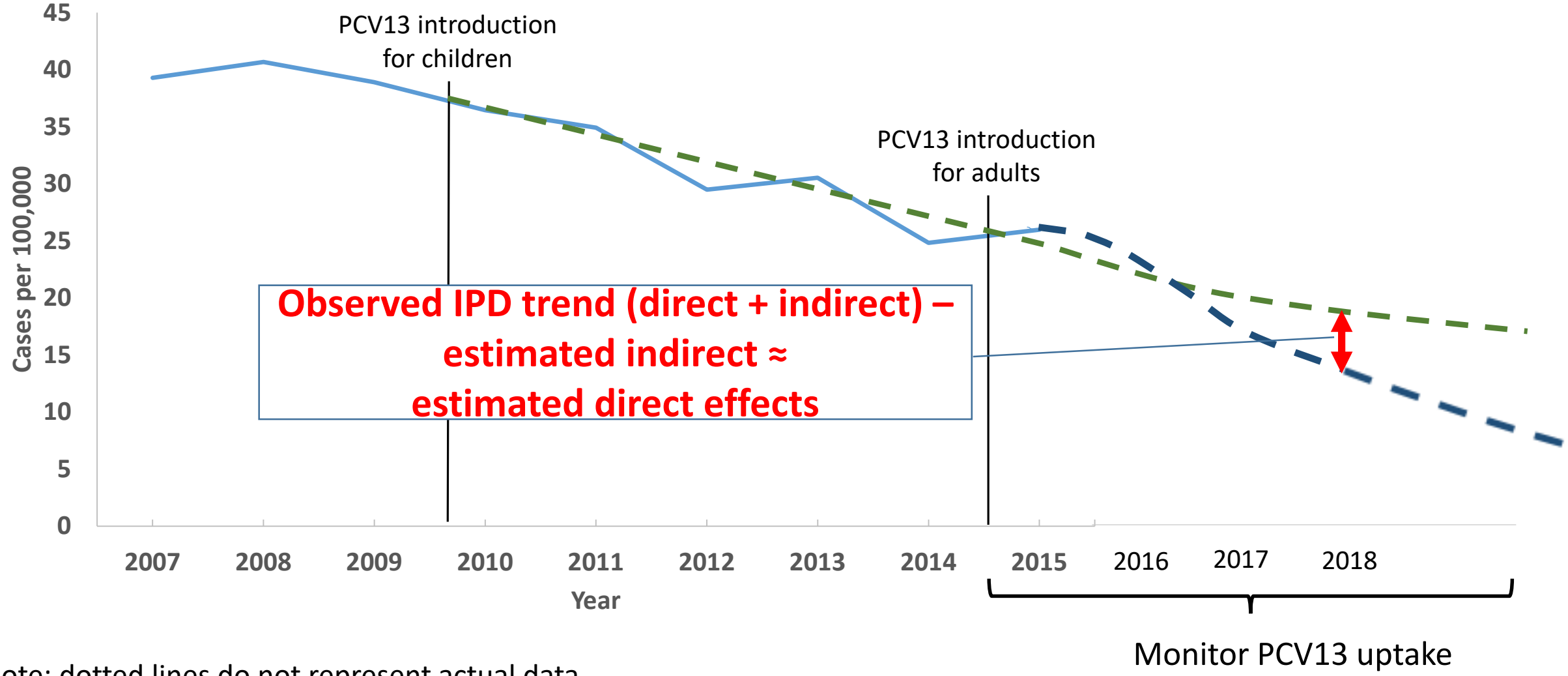
Note: dotted lines do not represent actual data

2. Estimate direct effects of PCV13 from the observed (total) and expected (indirect) IPD incidence



Note: dotted lines do not represent actual data

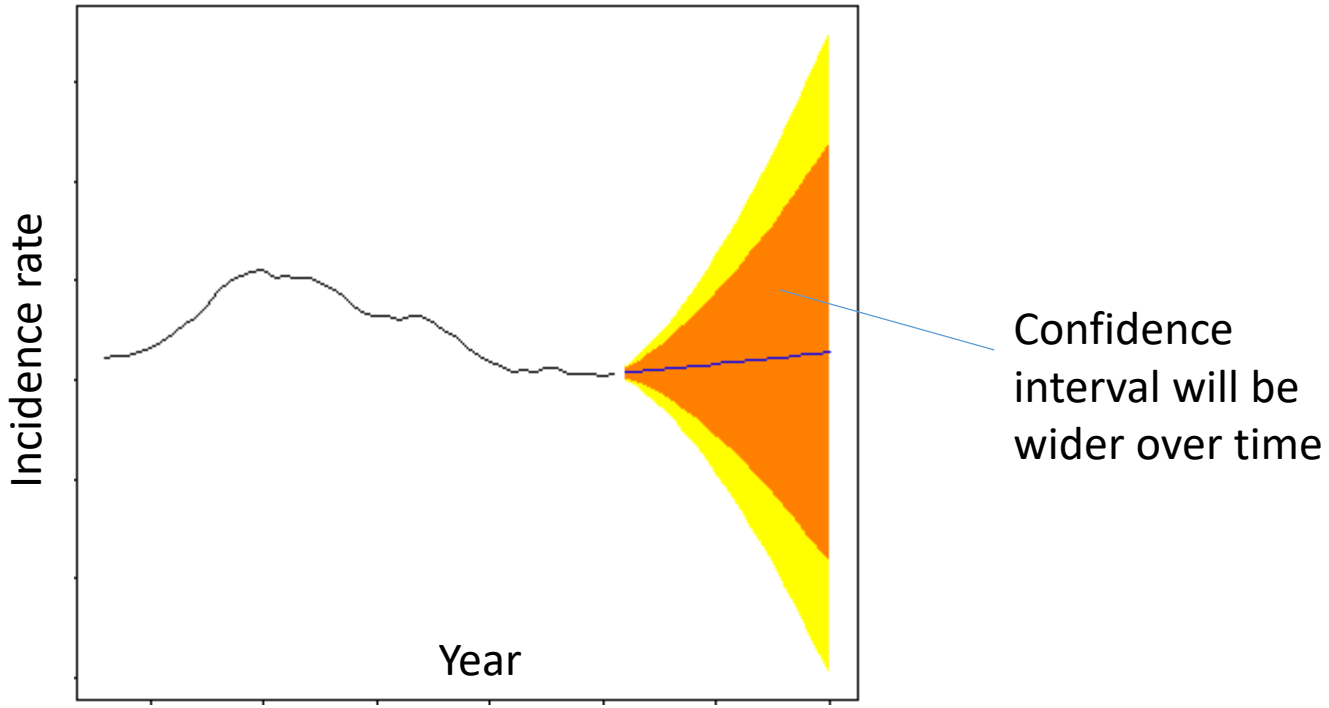
2. Estimate direct effects of PCV13 based the observed and expected IPD trend



Note: dotted lines do not represent actual data

Limitations of this approach

- Assuming that linear trends for indirect effects will continue to be observed
- Prediction for PCV13 indirect effects are made based on ~4 years of data (2010-2014) and will be less accurate over time



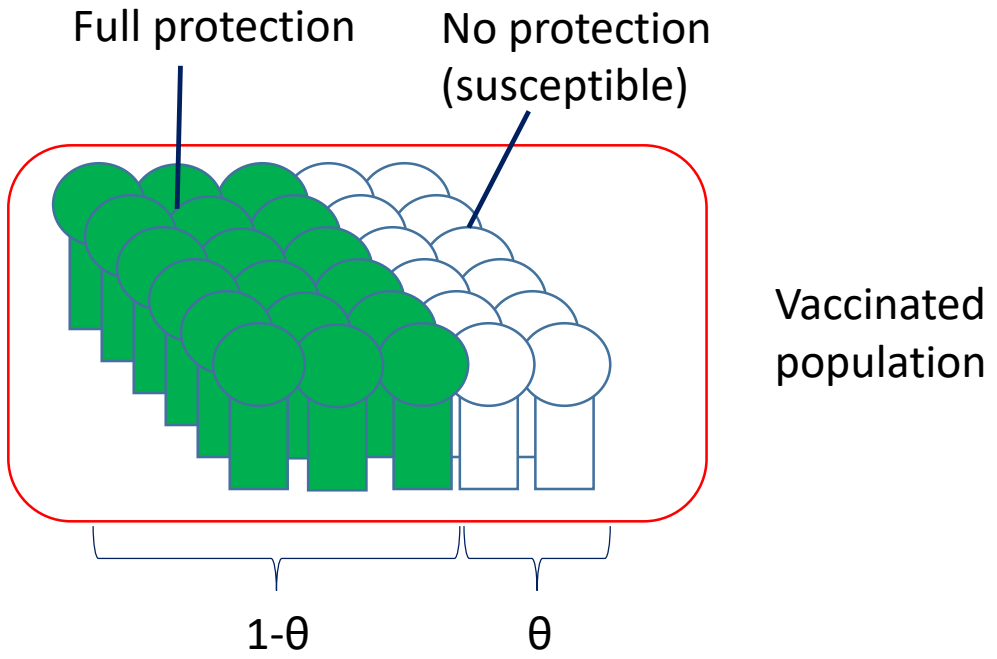
Methods

Two different mathematical models evaluated

1. Estimating contribution of direct and indirect effects on disease trends among adults ≥ 65 years utilizing data on IPD incidence among adults ≥ 65 years, adults 50-64 years old, and PCV13 uptake, controlling for seasonality
2. Predicting indirect effects in adults ≥65 years ONLY using the relationship between disease rates in adults 50–64 years (no PCV13 use) and adults ≥65 years pre-PCV13 (pre-2014 recommendation)

Method 1: All-or-Nothing Model

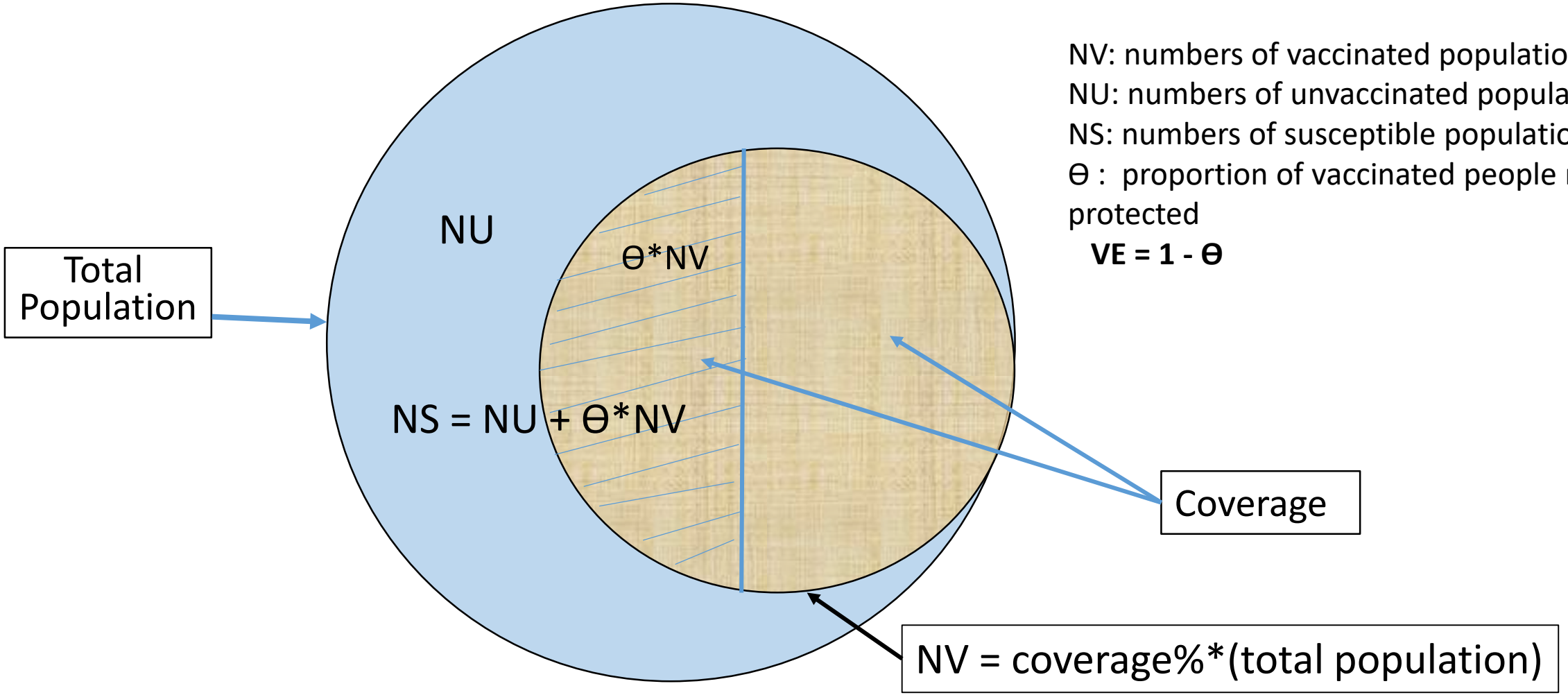
- Assumes that proportion θ of the vaccinated are not protected from disease (susceptible), but (1-θ) are 100% protected.
- Vaccine effectiveness= **1-θ**
- **If θ=1** there is no protection from the vaccine (indirect effects only)
- Unvaccinated population continues to experience indirect effects only



Slide courtesy M. Kobayashi

Method 1: All-or-Nothing Model

Susceptible population=unvaccinated + θ*vaccinated



NV: numbers of vaccinated population
NU: numbers of unvaccinated population
NS: numbers of susceptible population
Θ : proportion of vaccinated people not protected

VE = 1 - Θ

Slide courtesy M. Kobayashi

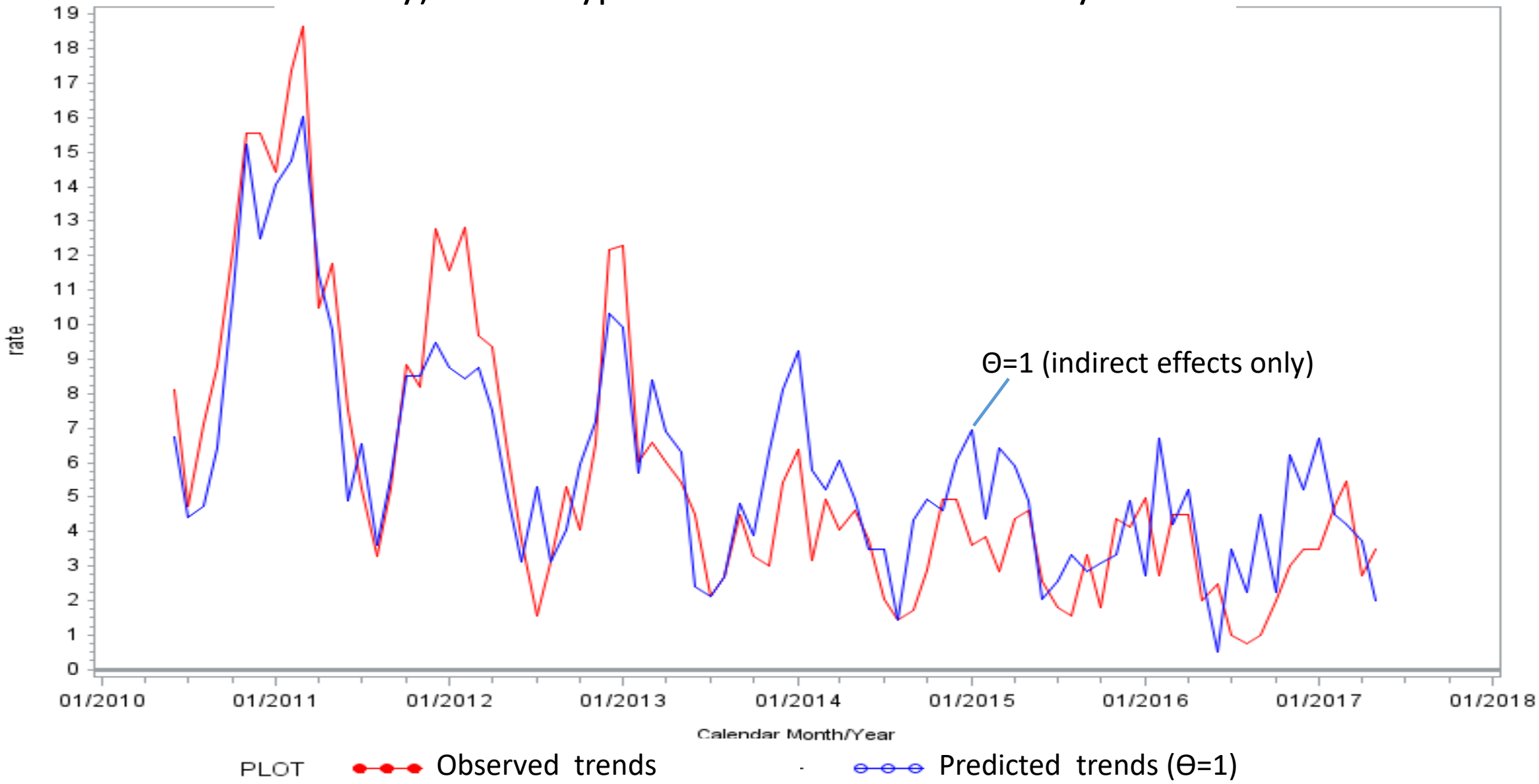
Method 1: All-or-Nothing Model

- Pre-vaccine IPD incidence will inform the model on the changes post-vaccine among the **susceptible** population
- Use Poisson regression to model IPD rates among susceptible population representing indirect effects (β_i in the Poisson regression model estimating indirect effect)
- Post-vaccine (post 2014) observed IPD incidence, continued to inform the model
  - Given β_i, or indirect effects, estimate Θ
  - Given Θ, estimate the new susceptible population, to update estimate the β_i,

Model: $NS = NU + \Theta * NV$

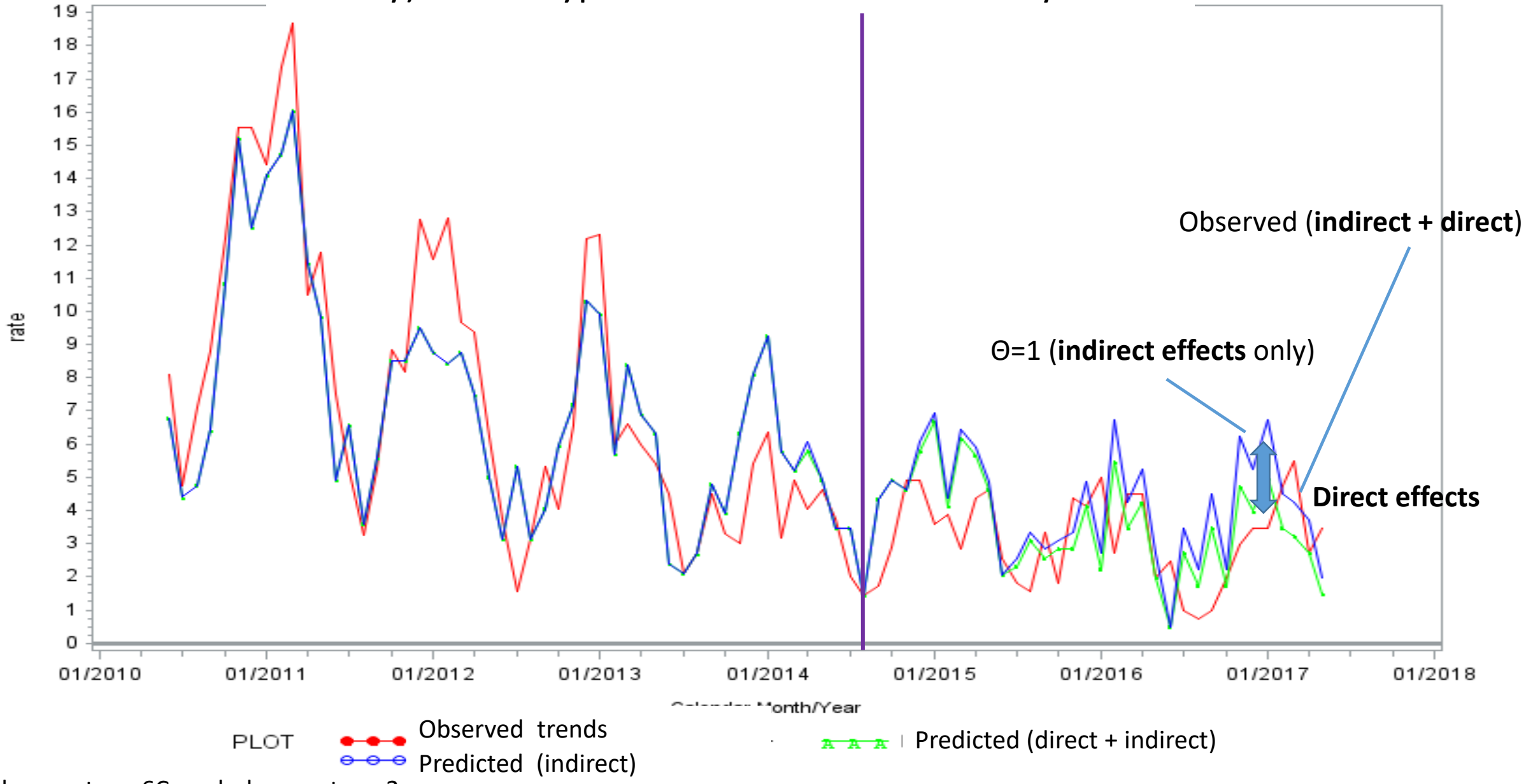
$\log(\text{PCV13type rate } j) = \beta_0 + \beta_i * \mathbf{X_i\, j} + \log(NS\ j)$

Observed (indirect + direct) and Predicted (indirect only) PCV13-type IPD Trends in Adults ≥65 years



*includes serotype 6C, excludes serotype 3

Observed (indirect + direct) and Predicted (indirect only) PCV13-type IPD Trends in Adults ≥65 years



*includes serotype 6C, excludes serotype 3

Method 1. Estimated Number of PCV13-type IPD Cases Prevented Through Direct Effects in Adults ≥65 years during 8/2014–5/2017

	Observed cases, direct+indirect (A)	Predicted indirect (B)	ABCs cases prevented through PCV13 direct effects (B)-(A)	Estimated US cases, direct+indirect (A)	Predicted indirect (B)	US cases prevented through PCV13 direct effects (B)-(A)
Total N of PCV13-type cases	907	924 (817, 1037)	17(-89, 130)	9355	9551 (8446, 10712)	192 (-911, 1356)

~100 cases prevented annually

Pre-PCV13 period used: 2/2013–7/2014

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

*includes serotype 6C

Method 1. Estimated Number of PCV13-type IPD Cases Prevented Through Direct Effects in Adults ≥65 years during 8/2014–5/2017

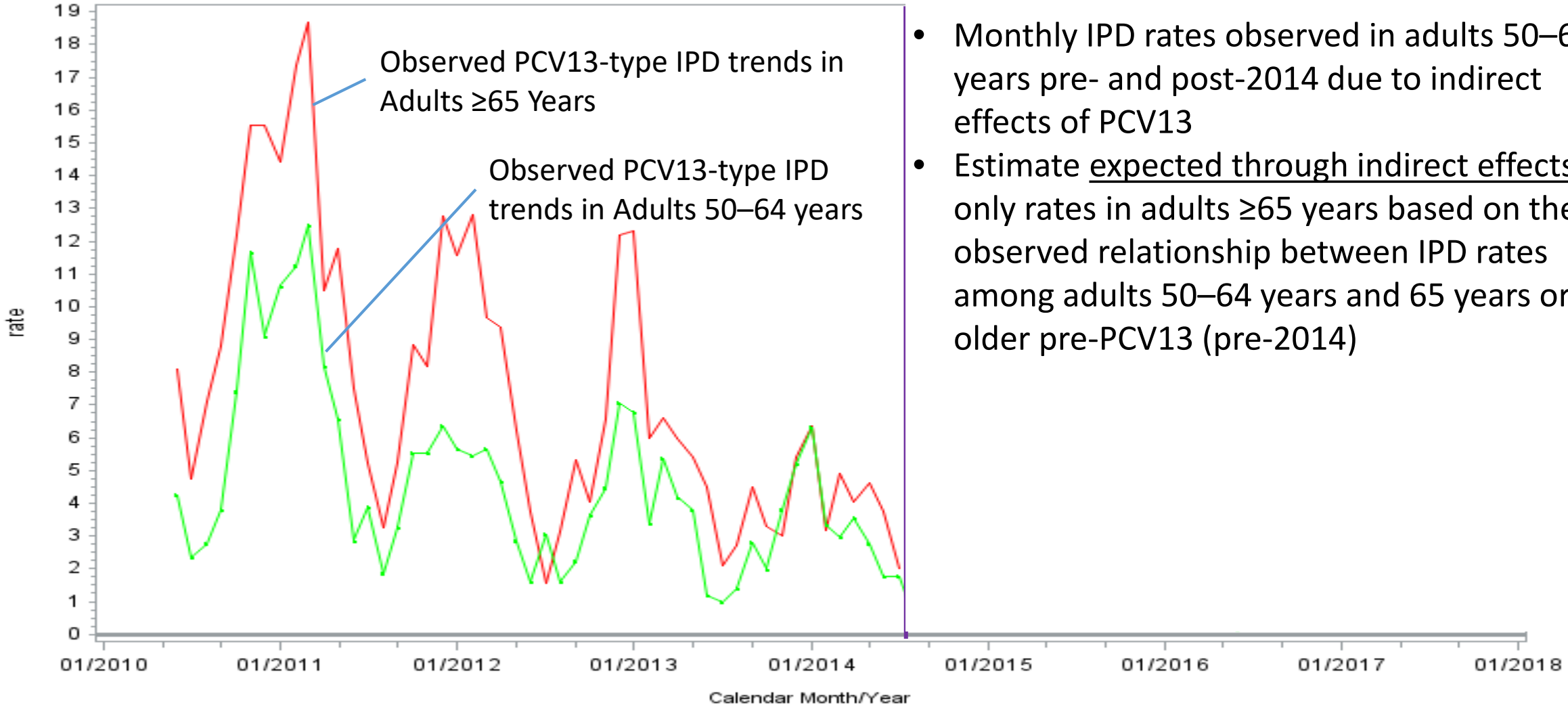
	Observed cases, direct+indirect (A)	Predicted indirect (B)	ABCs cases prevented through PCV13 direct effects (B)-(A)	Estimated US cases, direct+indirect (A)	Predicted indirect (B)	US cases prevented through PCV13 direct effects (B)-(A)
Total N of PCV13-type* cases	907	924 (817, 1037)	17(-89, 130)	9355	9551 (8446, 10712)	192 (-911, 1356)
Total N of PCV13-type* cases **(excluding ST3)**	416	472 (395, 563)	56(-21, 147)	4305	4883 (4085, 5825)	579 (-219, 1523)

Pre-PCV13 period used: 2/2013–7/2014

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

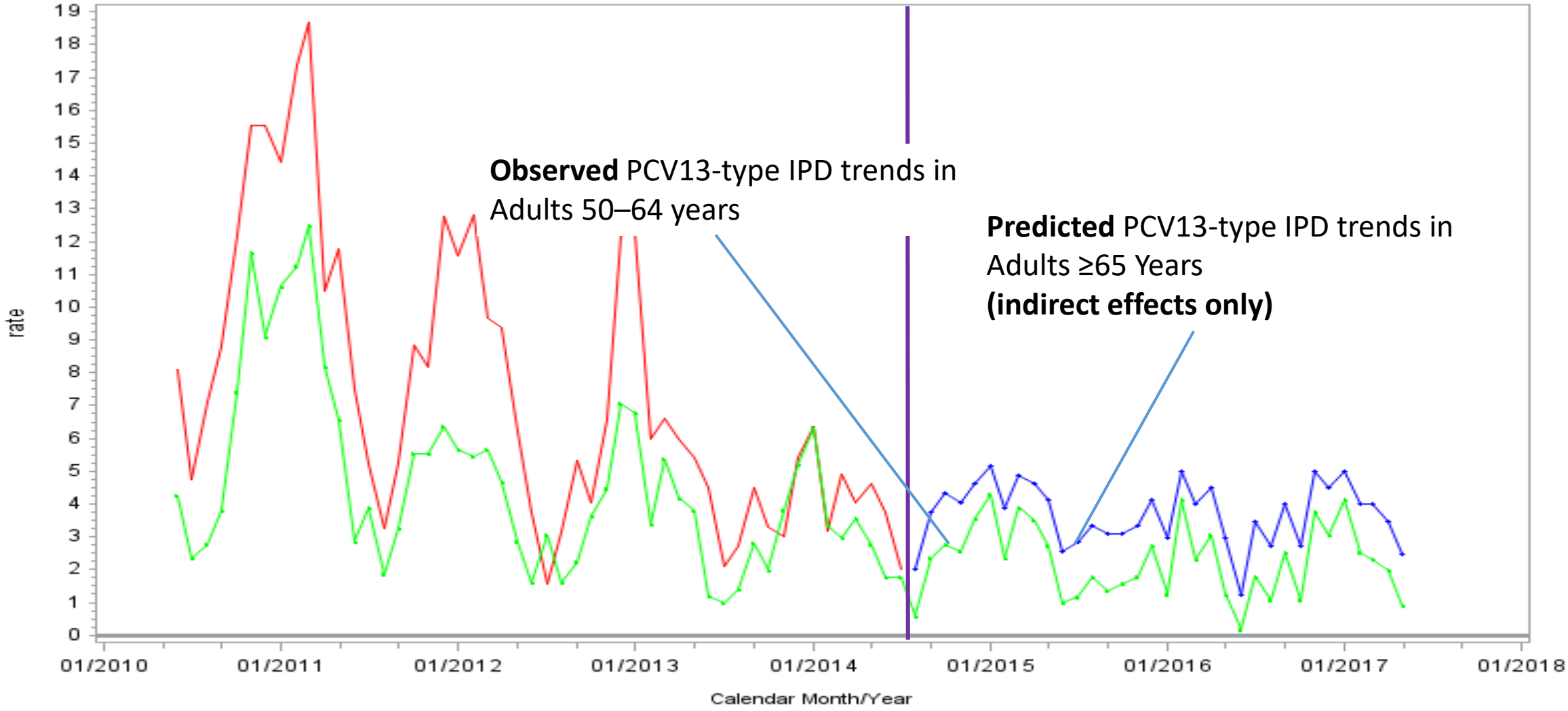
*includes serotype 6C

Method 2: Estimate Expected Indirect Effects in Adults ≥65 Years Based on Observed IPD Incidence among Adults 50–64 years

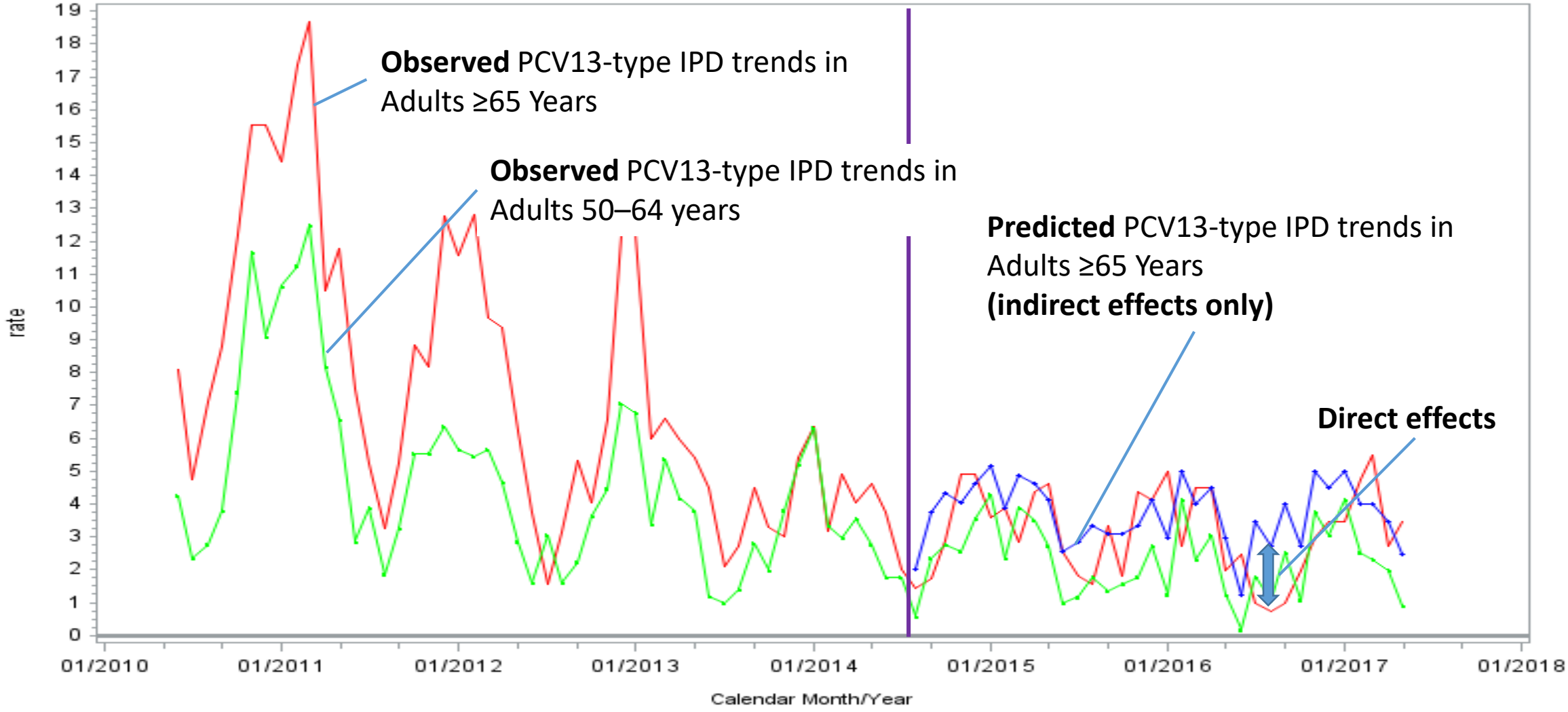


- Monthly IPD rates observed in adults 50–64 years pre- and post-2014 due to indirect effects of PCV13
- Estimate <u>expected through indirect effects</u> only rates in adults ≥65 years based on the observed relationship between IPD rates among adults 50–64 years and 65 years or older pre-PCV13 (pre-2014)

Method 2: Estimate Expected Indirect Effects in Adults ≥65 Years Based on Observed IPD Incidence among Adults 50–64 years



Method 2: Estimate Expected Indirect Effects in Adults ≥65 Years Based on Observed IPD Incidence among Adults 50–64 years



Method 2. Estimated Number of PCV13-type IPD Cases Prevented Through Direct Effects in Adults ≥65 years during 8/2014–5/2017

	ABCs population			US population		
	Observed Cases (A)	Predicted indirect (B) (95% CI)	(B)-(A) (95% CI)	Estimated US cases (A)	Predicted indirect (B)	(B)-(A)
Total N of PCV13-type* cases	907	914 (812, 1027)	7 (-96, 120)	9355	9438 (8383, 10608)	83 (-974, 1252)

Pre-PCV13 period used to predict post-PCV13 trends: 2/2013–7/2014

(B)-(A): Total number of PCV13-type* IPD cases prevented in adults ≥65 years through direct effects based on (Observed IPD cases) – (Predicted indirect effects)

*includes serotype 6C

Method 2. Estimated Number of PCV13-type IPD Cases Prevented Through Direct Effects in Adults ≥65 years during 8/2014–5/2017

	ABCs population			US population		
	Observed Cases (A)	Predicted indirect (B) (95% CI)	(B)-(A) (95% CI)	Estimated US cases (A)	Predicted indirect (B)	(B)-(A)
Total N of PCV13-type* cases	907	914 (812, 1027)	7 (-96, 120)	9355	9438 (8383, 10608)	83 (-974, 1252)
Total N of PCV13-type* cases **(excluding ST3)**	416	489 (410, 576)	73 (-7, 160)	4353	5055 (4237, 5957)	757 (-67, 1651)

Pre-PCV13 period used to predict post-PCV13 trends: 2/2013–7/2014

(B)-(A): Total number of PCV13-type* IPD cases prevented in adults ≥65 years through direct effects based on (Observed IPD cases) – (Predicted indirect effects)

*includes serotype 6C

Conclusions

- No additional indirect effects predicted using both models in the absence of PCV13 adult recommendation
  - Limited indirect effects estimated for IPD caused by PCV13 serotypes, excluding type 3
- Limited direct effects observed in a setting of ~40% PCV13 uptake
  - Confidence limits include null value
  - Predictions based on small numbers of PCV13 type cases remaining following observed PCV13 indirect effects
- Similar analyses ongoing to estimate PCV13 direct vs. indirect effects on all-cause pneumonia

Thank you

- Wei Xing
- Miwako Kobayashi
- Nong Shang