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

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

- PCV13 in children
- PCV13 indirect effects
- PCV13 in adults ≥65 years old
- PCV13 indirect + direct effects
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

**Graph:**
- **Y-axis:** Cases per 100,000
- **X-axis:** Year
- **Graph Notes:**
  - Blue line: Observed IPD trend (=direct + indirect effects)
  - Green dashed line: Utilize data available by 2018 review

**Legend:**
- PCV13 introduction for children
- PCV13 introduction for adults

**Text:**
- PCV13 introduction for children
- PCV13 introduction for adults

**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 $\theta$ of the vaccinated are not protected from disease (susceptible), but $(1-\theta)$ are 100% protected.
• Vaccine effectiveness = $1-\theta$
• If $\theta=1$ 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 ($\beta_i$ in the Poisson regression model estimating indirect effect)

• Post-vaccine (post 2014) observed IPD incidence, continued to inform the model
  • Given $\beta_i$, or indirect effects, estimate $\Theta$
  • Given $\Theta$, estimate the new susceptible population, to update estimate the $\beta_i$,

Model:  
\[ NS = NU + \Theta \times NV \]
\[ \log(\text{PCV13type rate } j) = \beta_0 + \beta_i \times X_i j + \log(\text{NS } j) \]
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 (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

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

~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 IPD cases) – (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

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<tr>
<td>Total N of PCV13-type* cases (excluding ST3)</td>
<td>416</td>
<td>472</td>
<td>56(-21, 147)</td>
<td>4305</td>
<td>4883</td>
<td>579(-219, 1523)</td>
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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 expected through indirect effects 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

Observed PCV13-type IPD trends in Adults 50–64 years

Predicted PCV13-type IPD trends in Adults ≥65 Years (indirect effects only)
Method 2: Estimate Expected Indirect Effects in Adults ≥65 Years Based on Observed IPD Incidence among Adults 50–64 years

Observed PCV13-type IPD trends in Adults ≥65 Years

Observed PCV13-type IPD trends in Adults 50–64 years

Predicted PCV13-type IPD trends in Adults ≥65 Years
(indirect effects only)

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

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<td>Observed Cases (A)</td>
<td>Predicted indirect (B) (95% CI)</td>
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<td>907</td>
<td>914 (812, 1027)</td>
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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

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<td>Total N of PCV13-type* cases (excluding ST3)</td>
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<td>489 (410, 576)</td>
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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