Pneumococcal serotype replacement in England: the bias of increased reporting

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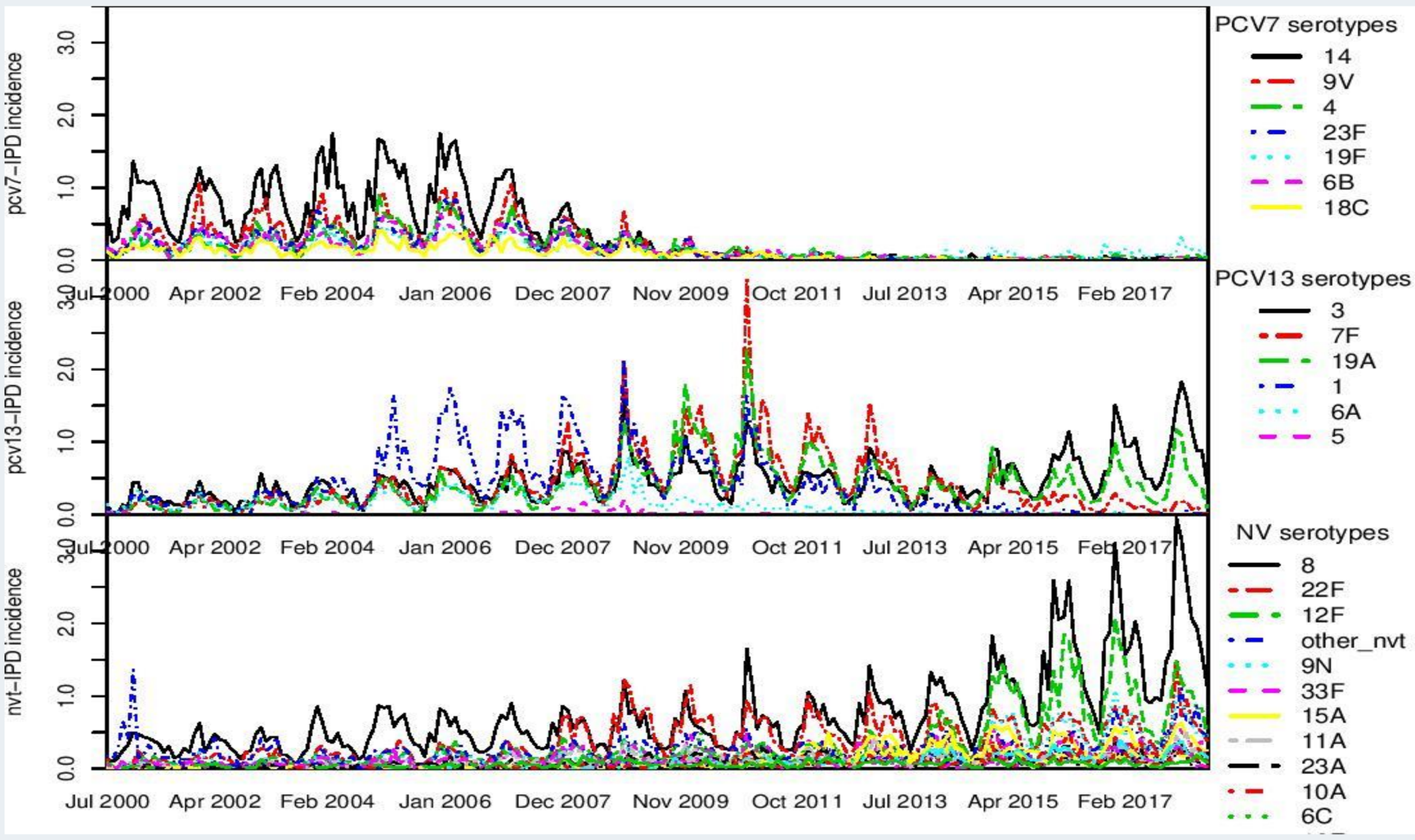
Introduction

- **Prevention** of pneumococcal disease is a priority due to
  - high burden of disease
  - increasing resistance of *S. Pneumoniae* to multiple classes of antibiotics.
- **Infant routine immunisation** programs have been implemented to prevent infections due to the most clinically relevant serotypes.
- Protection against serotypes included in the vaccine opened an ecological niche that altered serotype epidemiology, a phenomenon known as serotype replacement



Challenges

- A moderate to small decline in pneumococcal disease burden has been observed following vaccine introduction, in terms of pneumonia, otitis media and invasive pneumococcal disease
- It is unclear to which extent the benefit of the vaccine is eroded by serotype replacement
- Serotype-specific information on invasive pneumococcal disease, routinely collected through surveillance systems, can assist in disentangling these two quantities
- However, the observed temporal trends may be confounded by changes in testing and reporting

Statistical model

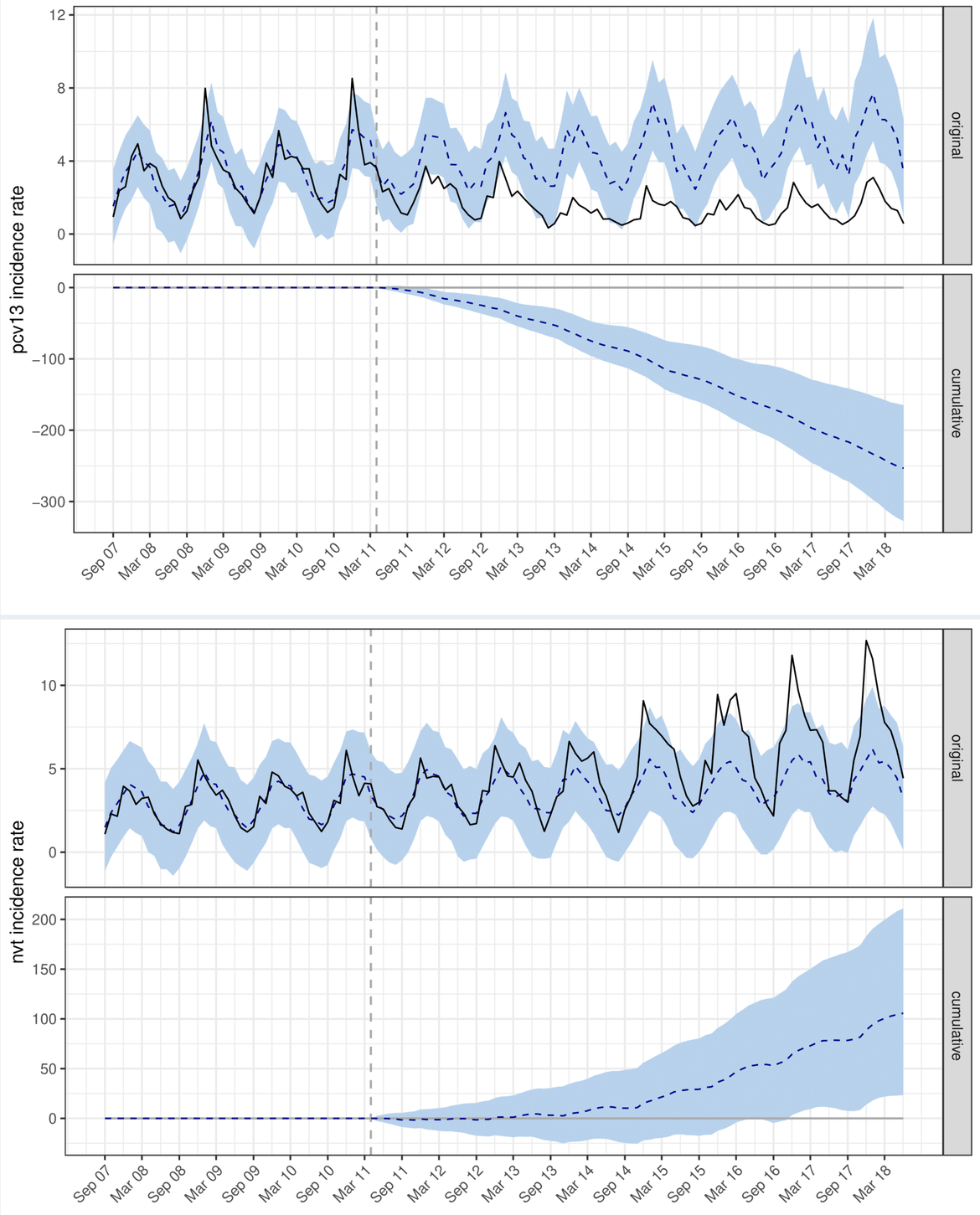
- Monthly serotype-specific IPD incidence from 2000 to 2018, covering PCV7 and PCV13 introductions in 2006 and 2010
- We estimate the counterfactual of what IPD incidence would have been observed had PCVs not been introduced, by age and PCV group
- We follow the Causal Impact method, including control time series of pathogens unaffected by PCVs to adjust for time-dependent confounding

Impact on PCV-IPD

PCV7	% change	% lb	% ub
all_age	-63.90	-81.00	-47.60
0-4	-63.50	-72.00	-53.30
5-14	-32.50	-66.50	-3.10
15-44	-29.90	-42.40	-17.70
45-64	-15.90	-28.90	-8.80
65+	-9.00	-15.20	-2.30
non-PCV7	% change	% lb	% ub
all_age	-65.60	-85.60	-42.20
0-4	-49.80	-63.80	-32.20
5-14	-46.90	-66.10	-29.10
15-44	-36.50	-57.40	-12.70
45-64	-19.30	-52.80	4.70
65+	-27.60	-46.20	-8.10

Impact on NVT-IPD

PCV13	% change	% lb	% ub
all_age	36.90	15.40	66.20
0-4	-22.20	-39.40	-3.90
5-14	-6.30	-26.00	13.90
15-44	-14.80	-34.90	10.10
45-64	-18.10	-55.50	14.40
65+	4.00	-33.90	36.50
non-PCV13	% change	% lb	% ub
all_age	31.80	6.70	63.50
0-4	58.80	24.40	105.00
5-14	16.90	-19.70	49.10
15-44	6.10	-17.40	21.00
45-64	25.20	-12.40	49.50
65+	-12.10	-31.50	2.30



Discussion

- Our model disentangles the impact of PCVs and improved surveillance on the changes in IPD incidence
- After adjusting for confounding, we identify serotype replacement when looking at the population overall
- We fail to identify such an effect after stratifying by age, except for the significative +58.8% of NVT in children <5, however these estimates are affected by large uncertainty due to small sample sizes.