

Which Serotypes Will Punch Back After Third-Generation Pneumococcal Conjugate Vaccination in Germany?

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INTRODUCTION

Pneumococcal conjugate vaccines (PCVs) were first added to the universal infant vaccine recommendations in Germany in 2006, using a 3+1 schedule, with 3 doses given in the first year of life, and 1 booster dose after the first birthday. The most commonly used product, PCV7, offered protection against 7 serotypes (4, 6B, 9V, 14, 18C, 19F, 23F).

These vaccine-type (VT) serotypes dropped across the board in children under two years of age, while non-vaccine-type (NVT) serotypes rose in their stead. This rebound process became known as serotype replacement.

A second generation of PCVs, the most common one in Germany being PCV13, which protects against 13 serotypes (PCV7 types + 1, 5, 7F, 3, 6A, 19A), was released in 2009, a comparable phenomenon occurred.

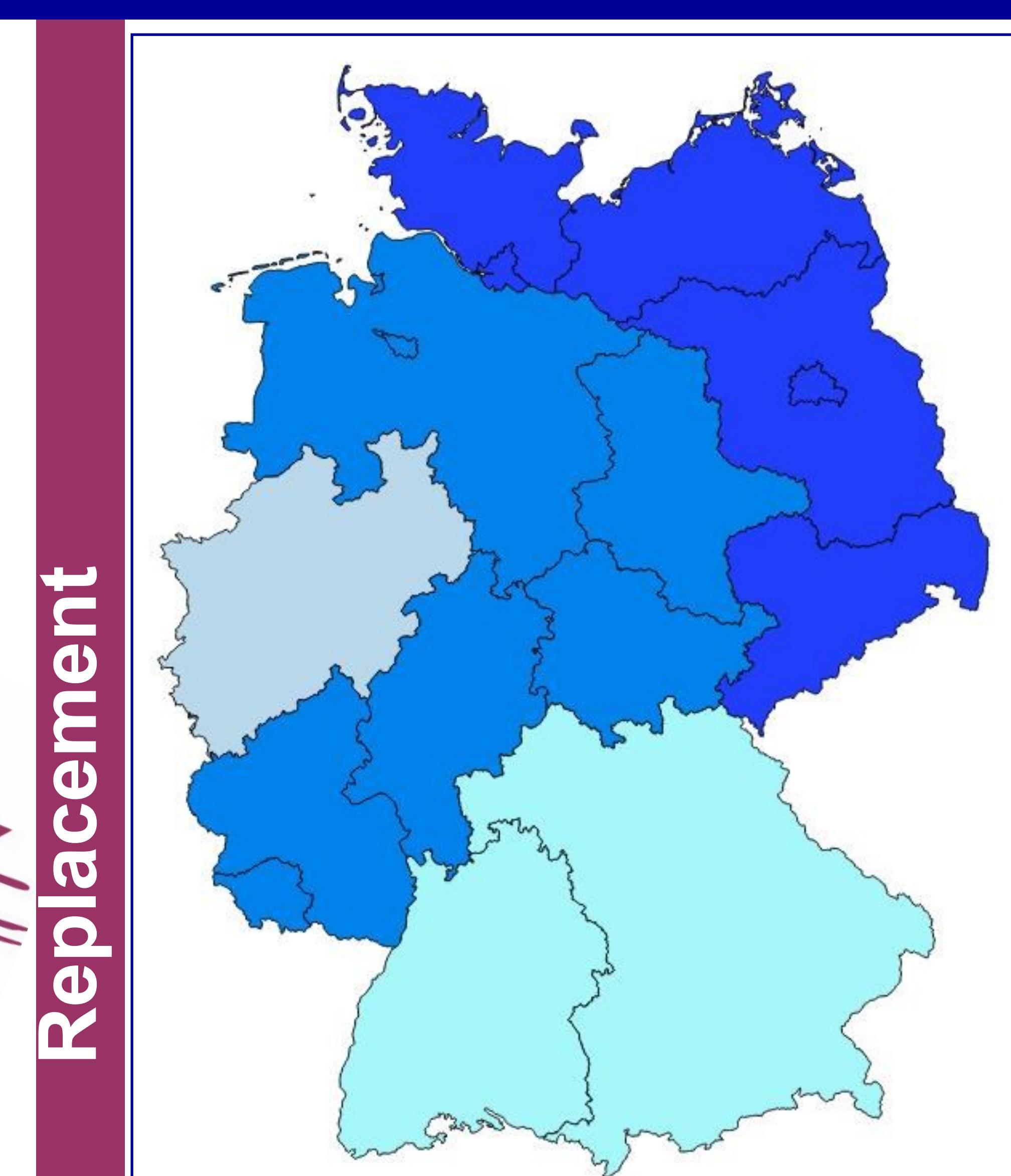
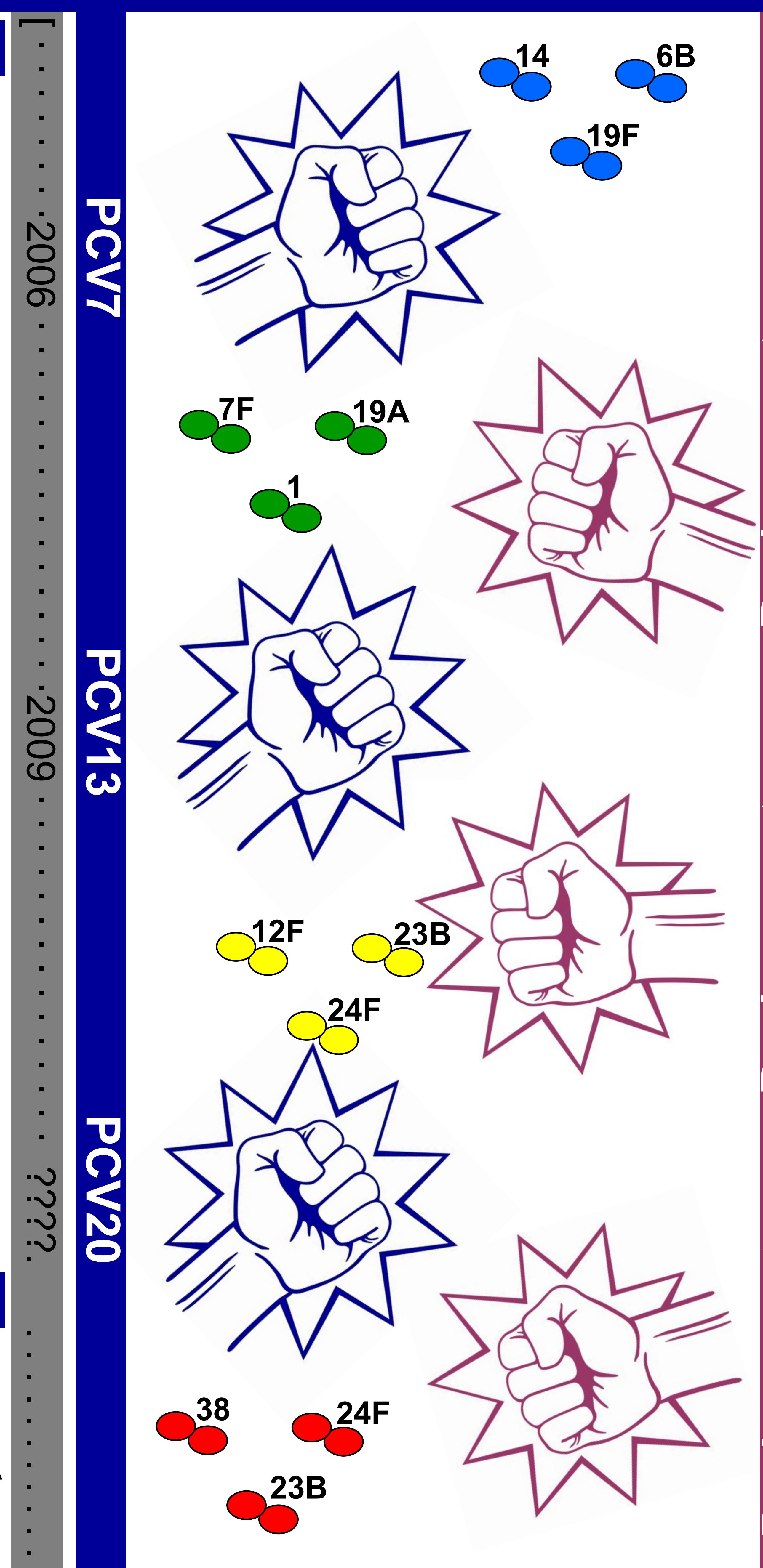
A third generation of PCVs is ready to launch, one of which is PCV20, which will offer protection against 20 serotypes (PCV13 types + 8, 10A, 11A, 12F, 15B, 22F, 33F), but what will happen next?

METHODS

We assessed the IPD serotype distribution patterns and proportions in children under two, from July 1, 2000 through June 30, 2018. A comparable vaccine effectiveness for the third-generation VT serotypes to that established for PCV13 was assumed. in children under two years of age.

Analyses were conducted for Germany as a whole and separately for four distinct, population-normalized, geographic regions in Germany, due to previously established regional variations in NVT serotype prominence.

Changes in serotype proportions following onset of first and second generation PCVs were assessed with Fisher's exact test; a Dunn-Šidák correction was applied for multiple comparison, yielding a significance threshold of $P < 0.00093$.



Geographic Group	Top Serotypes After 2nd Generation PCV	Top Serotypes After 3rd Generation PCV
Group 1 North Rhine-Westphalia	19A, 10A, 38	38, 24F, 23B
Group 2 Bremen, Hesse, Lower Saxony, Rhineland-Palatinate, Saarland, Saxony-Anhalt, Thuringia	10A, 24F, 22F	24F, 38, 15C
Group 3 Berlin, Brandenburg, Hamburg, Mecklenburg-Western Pomerania, Saxony, Schleswig-Holstein	10A, 15C, 24F	15C, 24F, 23B
Group 4 Baden-Württemberg, Bavaria	10A, 24F, 3	24F, 38, 23B

RESULTS

Despite a significant overall decline in reported invasive pneumococcal disease (IPD) in children under two after the onset of the universal PCV recommendation, a substantial burden of disease persists.

Following first generation (PCV7) implementation, VT serotypes decreased, while individual serotypes 19A ($P = 8.05 \times 10^{-7}$), 7F ($P = 3.55 \times 10^{-7}$), and 1 ($P = 2.54 \times 10^{-4}$) increased the most.

Following second generation (PCV10 and PCV13) implementation, VT serotypes collectively decreased, while individual serotypes 23B ($P = 7.97 \times 10^{-8}$), 24F ($P = 9.50 \times 10^{-6}$), and 12F ($P = 7.33 \times 10^{-5}$) increased most.

Following third generation (PCV15 and PCV20) implementation, we anticipate that the new VT serotypes will collectively decrease in IPD in children under two, and that individual serotypes 23B, 24F, and 38 will increase the most in IPD in children under two in Germany.

CONCLUSIONS

- PCVs are effective
- Serotype replacement is a concern
- After arrival of 3rd generation PCVs, we predict that serotypes **38, 24F, and 23B** will increase in IPD cases in children under two in Germany