

INCREASING ROLE OF SEROTYPE 3 IN INVASIVE PNEUMOCOCCAL DISEASE IN GERMANY, 2000-2016

Stephanie Perniciaro, Matthias Imöhl, and Mark van der Linden
German National Reference Center for Streptococci (GNRCS) and Institute of Medical Microbiology,
University Hospital RWTH-Aachen, Germany

Mark van der Linden
University Hospital RWTH Aachen
Institute of Medical Microbiology
National Reference Center for Streptococci
Pauwelsstrasse 30, 52074 Aachen, Germany
Email: mlinden@ukaachen.de

BACKGROUND AND AIMS

Serotype 3, despite inclusion in the latest pneumococcal conjugate vaccine, persists as a major cause of invasive pneumococcal disease in Germany.

The infant PCV recommendation was given in 2006 (3+1 schedule) and changed in 2015 (to 2+1). Germany lacks a PCV recommendation for older adults. We sought to describe the expansion of serotype 3 as a cause of IPD.

METHODS

3965 serotype 3 isolates were identified by Neufeld-Quellung reaction at the German National Reference Center for Streptococci from July 1, 2000 to June 30, 2017.

RESULTS

In children under 2 and adults over 60, estimated incidence increased from 0.22 to 0.45, and 0.64 to 2.09 cases per 100,000, respectively. Of 55 serotype 3 IPD cases in children born after the release of PCV13 with a known vaccination status, 31 received at least 1 dose of PCV13, but only 5 children had received the appropriate number of doses in the recommended timeframes.

Figure 1. Increasing incidence of Invasive Pneumococcal Disease caused by Serotype 3 in Germany. The incidence of serotype 3 IPD in children under 3 and adults 65 years and older is shown for 2006-2007 and 2016-2017.

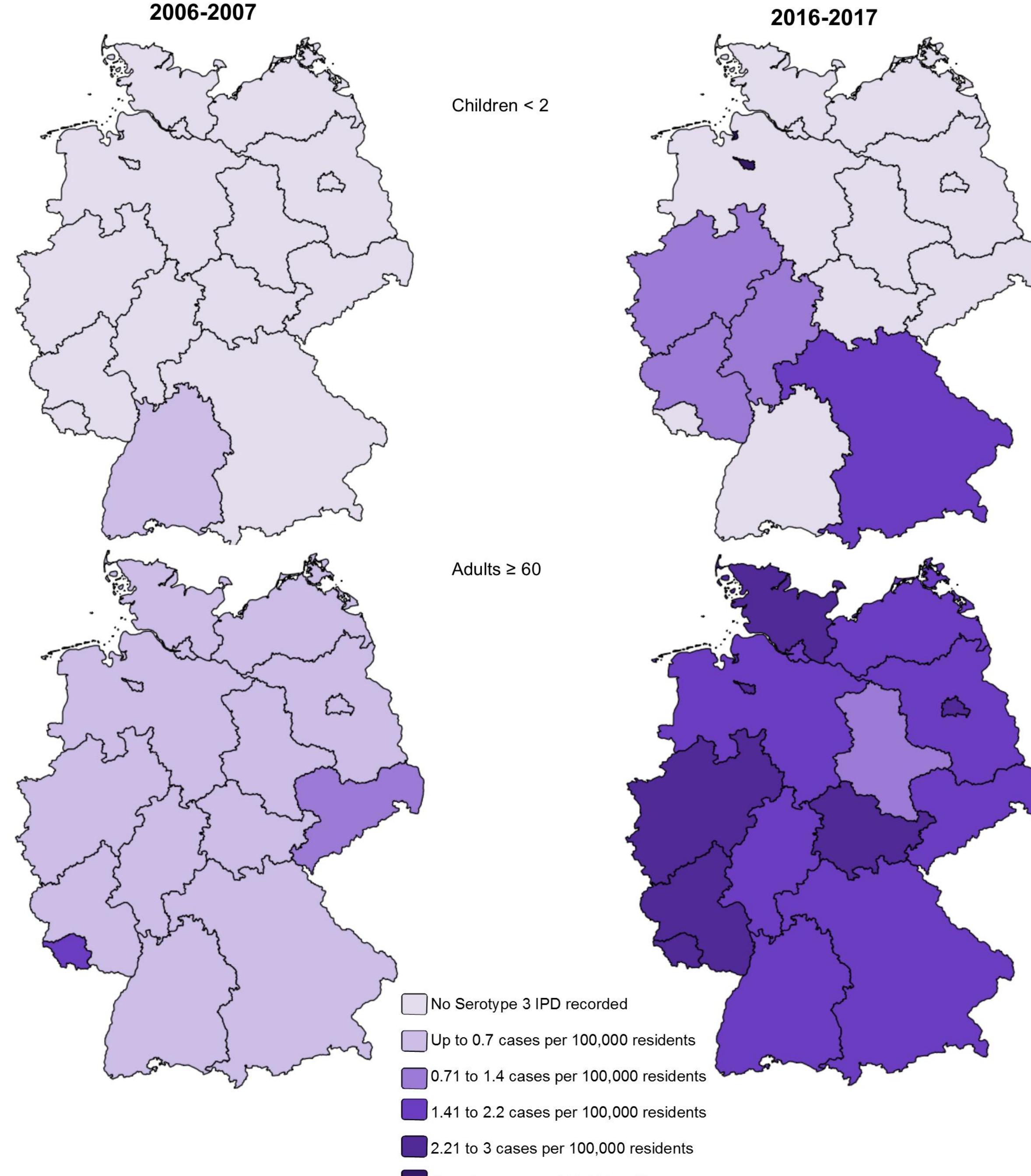


Table 1. Serotype 3 IPD cases in German children by vaccination status. Columns with an asterisk are children correctly vaccinated according to the 3+1 vaccination schedule

| Season | n | Unvaccinated | | Vaccinated At All | | |
|-----------|----|--------------|-------|-------------------|---|----|
| | | PCV7 | PCV10 | PCV13 | * | * |
| 2007-2008 | 3 | 2 | 1 | 0 | 0 | 0 |
| 2008-2009 | 5 | 1 | 4 | 1 | 0 | 0 |
| 2009-2010 | 4 | 2 | 1 | 1 | 1 | 0 |
| 2010-2011 | 6 | 3 | 2 | 0 | 0 | 1 |
| 2011-2012 | 10 | 4 | 2 | 0 | 1 | 3 |
| 2012-2013 | 4 | 0 | 1 | 0 | 0 | 3 |
| 2013-2014 | 7 | 1 | 0 | 0 | 0 | 5 |
| 2014-2015 | 4 | 1 | 1 | 0 | 1 | 2 |
| 2015-2016 | 6 | 1 | 0 | 0 | 1 | 4 |
| 2016-2017 | 13 | 1 | 0 | 0 | 1 | 11 |
| 2017-2018 | 5 | 2 | 0 | 0 | 1 | 2 |

CONCLUSIONS

- Serotype 3 IPD cases are on the rise in Germany.
- It is possible that unvaccinated and under-vaccinated children are acting as a niche for young children
- The lack of a nationwide PCV program could be to blame for the rise in older adults.

Figure 2. Increase of Serotype 3 Invasive Pneumococcal Disease across all age groups in Germany. Serotype 3 IPD isolates are shown as a percentage of all IPD isolates submitted to the German National Reference Center for Streptococci from 2000-2001 to the partial season of 2017-2018.

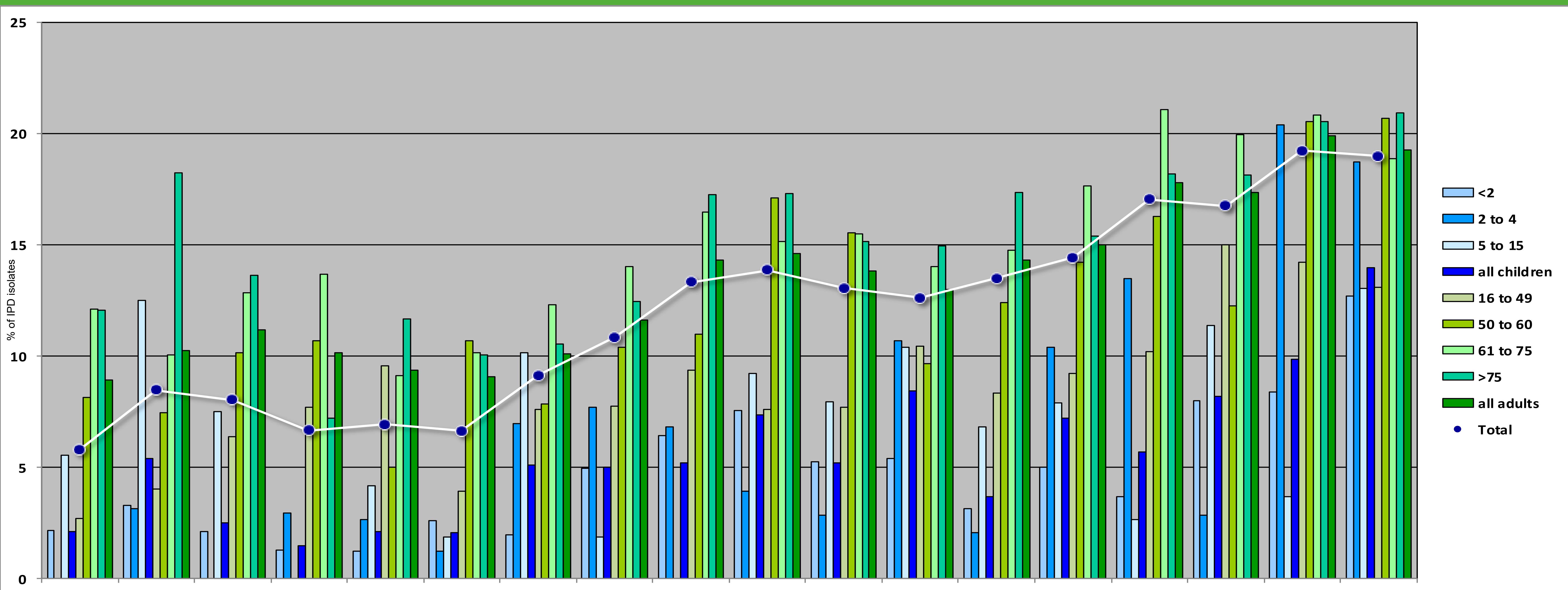
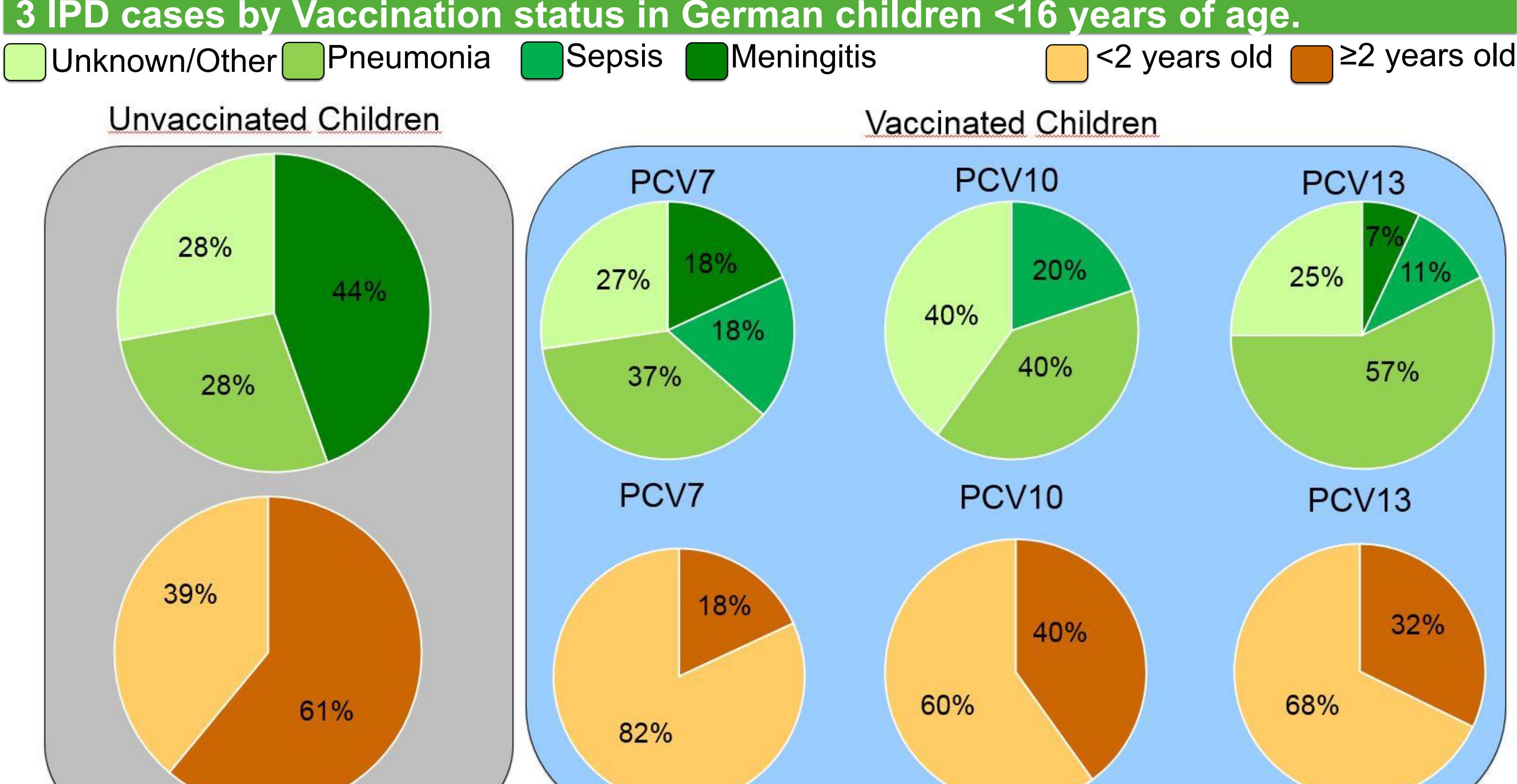


Table 2. Resistance to ≥3 classes of antibiotics and Penicillin Nonsusceptibility in Serotype 3 IPD cases in Germany, 2000-2001 to the partial season of 2017-2018.

The 2015 CLSI breakpoints were applied. Penicillin Non-Susceptibility (PenNS) was determined using the oral penicillin breakpoints.

| Season | Serotype 3 IPD | MDR | Pen NS | Most Common Resistance Profile (number of isolates) |
|-----------|----------------|-----|--------|---|
| 2000-2001 | 30 | 0 | 1 | -- |
| 2001-2002 | 56 | 0 | 0 | -- |
| 2002-2003 | 53 | 1 | 1 | lincosamide, macrolide, tetracycline (1) |
| 2003-2004 | 45 | 0 | 0 | -- |
| 2004-2005 | 59 | 1 | 0 | phenicol, lincosamide, macrolide, tetracycline, glycopeptide, (1) |
| 2005-2006 | 56 | 0 | 0 | -- |
| 2006-2007 | 139 | 1 | 0 | phenicol, lincosamide, tetracycline (1) |
| 2007-2008 | 218 | 0 | 1 | -- |
| 2008-2009 | 300 | 8 | 0 | lincosamide, macrolide, tetracycline (6) |
| 2009-2010 | 309 | 6 | 1 | phenicol, lincosamide, macrolide, tetracycline (2) AND lincosamide, macrolide, tetracycline (2) |
| 2010-2011 | 331 | 9 | 0 | lincosamide, macrolide, tetracycline (8) |
| 2011-2012 | 283 | 7 | 0 | lincosamide, macrolide, tetracycline (5) |
| 2012-2013 | 324 | 5 | 0 | lincosamide, macrolide, tetracycline (3) |
| 2013-2014 | 322 | 12 | 0 | phenicol, lincosamide, macrolide, tetracycline (8) |
| 2014-2015 | 454 | 12 | 0 | lincosamide, macrolide, tetracycline (9) |
| 2015-2016 | 478 | 11 | 0 | phenicol, lincosamide, macrolide, tetracycline (5) AND lincosamide, macrolide, tetracycline (5) |
| 2016-2017 | 624 | 12 | 3 | phenicol, lincosamide, macrolide, tetracycline (7) |
| 2017-2018 | 321 | 6 | 2 | phenicol, lincosamide, macrolide, tetracycline (3) |

Figure 3A and 3B. Distribution of Clinical Diagnoses (3A) and Age (3B) of Serotype 3 IPD cases by Vaccination status in German children <16 years of age.



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