Re-emergence of serotype 4 in invasive pneumococcal disease (IPD) among adults in Germany

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BACKGROUND

Invasive pneumococcal disease (IPD) in Germany has been monitored by the RLS since 1992. After the introduction of childhood PCV vaccination in 2006, the prevalence of serotype 4 IPD among adults was reduced to 0.6% in 2014/15, due to herd protection. Since then, a steep increase in the proportion of serotype 4 has been observed, particularly among 18-49-year-olds.

METHODS

The RLS has monitored the epidemiology of invasive pneumococcal disease (IPD) in Germany since 1992. All isolates were serotyped using the Neufeld-Quellung-reaction. Pneumococcal seasons are from July in one year to June in the next year, except for 2025/26: July 2025 – March 2026. IPD surveillance in Germany was, in part, sponsored by Pfizer and Merck.

RESULTS

As a result of the childhood vaccination program, serotype 4 prevalence among children <18 years has reduced to 0.3% (1/312) in 2024/25 and 0% (0/148) in 2025/26 (**Fig1**).

Among adults ≥18 years, serotype 4 IPD showed a similar decrease, reaching minimum levels in 2014/15. Since the season 2015/16, however, the prevalence of serotype 4 has continuously increased in adults ≥18 years of age, from 0,6% (15/2501) in 2014/15 to 5.0% (351/7052) in 2024/25 and 7.0% (263/3731) in 2025/26. The increase was most prominent among 18–49-year-olds; 2014/15: 1.5% (5/341), 2024/25: 13.9% (124/889), 2025/26: 20.4% (95/465), whereas among adults aged 50-59 years serotype 4 prevalence increased from 0.6% (2/347) in 2014/15 to 12.2% (53/433) in 2025/26, among 60-75-year-olds from 0,5% (5/924) to 6.3% (90/1435) and among adults >75 years from 0.3% (3/889) to 1.8% (35/1398; **Fig 2**).

From 2015/16 to 2025/26, among 18-49-year-olds, the majority of serotype 4 IPD cases occurred in males (77.0%, 395/513), with a median age of 40 years (50-59-year-olds: 73.2%, 60-75y: 67,8%, >75y: 53.7%; **Fig 3**). For adults with non-serotype 4 IPD, percentages of male patients were: 60.3, 59.2, 57.0 and 48.5 for the respective age groups.

Among 513 serotype 4 IPD cases in adults 18-49 years old submitted between 2015/16 and 2025/26, a residence was known for 470 (91.6%). Half of these patients were living in 13 larger cities (50.0%, 235/470), with 95 (20.2%) from Berlin (**Fig 4**). Only 23.5% of non-serotype 4 IPD cases were reported from these 13 cities. For only 20 patients (4.3%, 20/470, all male) homelessness was reported, and only one patient was reported with drug use. In older age groups, drug use was not reported, and homelessness for only 2.1%, 1,6% and 1,5% for the respective age groups.

The expansion of serotype 4 in the age group 18-49 years of age, has reduced the serotype coverage of PCV21 from 83.8% in 2015/16 to 67.7% in 2025/26, whereas the serotype coverage of PCV20 increased from 66.5% to 75.5% over the same period (**Fig 5**).

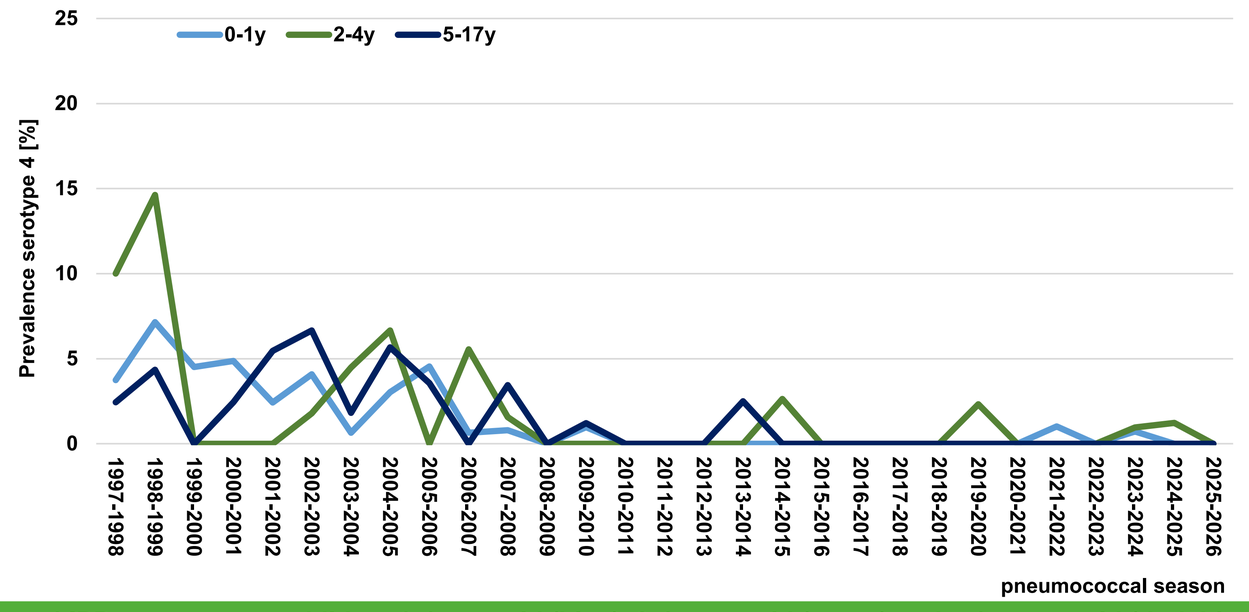

Figure 1: Prevalence of serotype 4 IPD cases among children 0-1 year old (blue), 2-4 years old (green) and 5-17 years old (dark blue), in Germany.

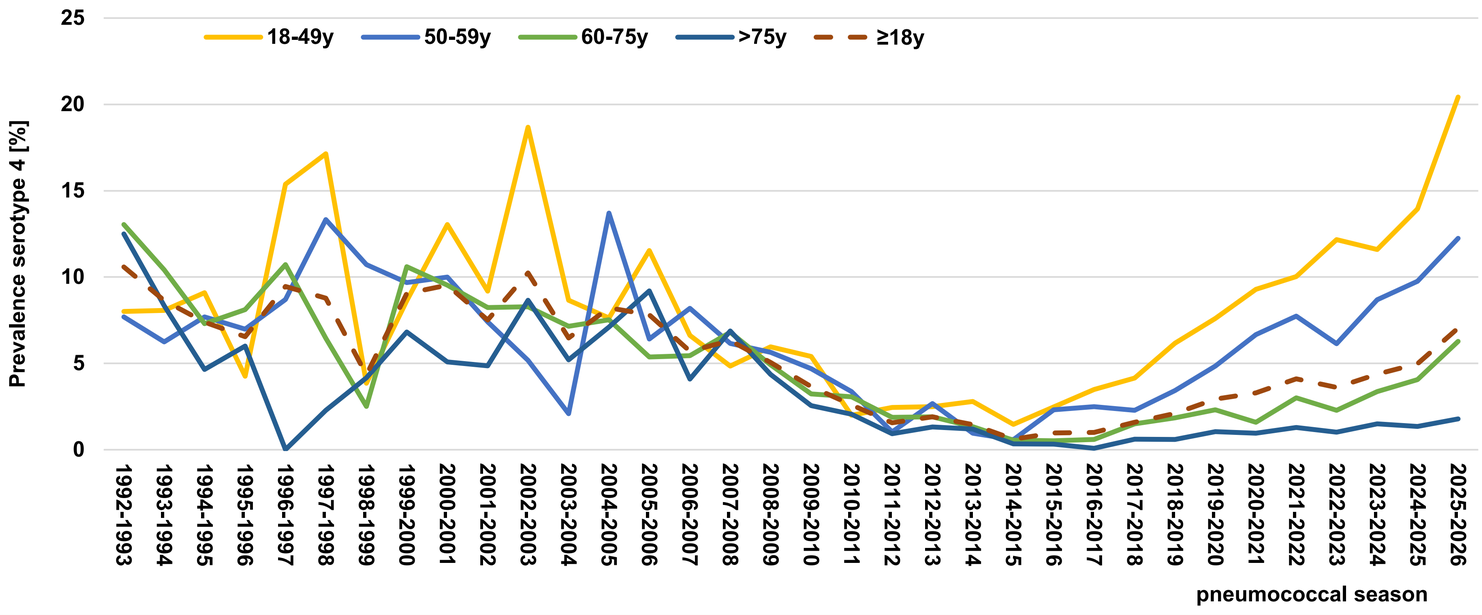

Figure 2: Prevalence of serotype 4 IPD cases among adults 18-49 years old (yellow), 50-59 years old (blue), 60-75 years old (green), >75 years old (dark blue) and ≥ 18 years old (brown, dashed), in Germany.

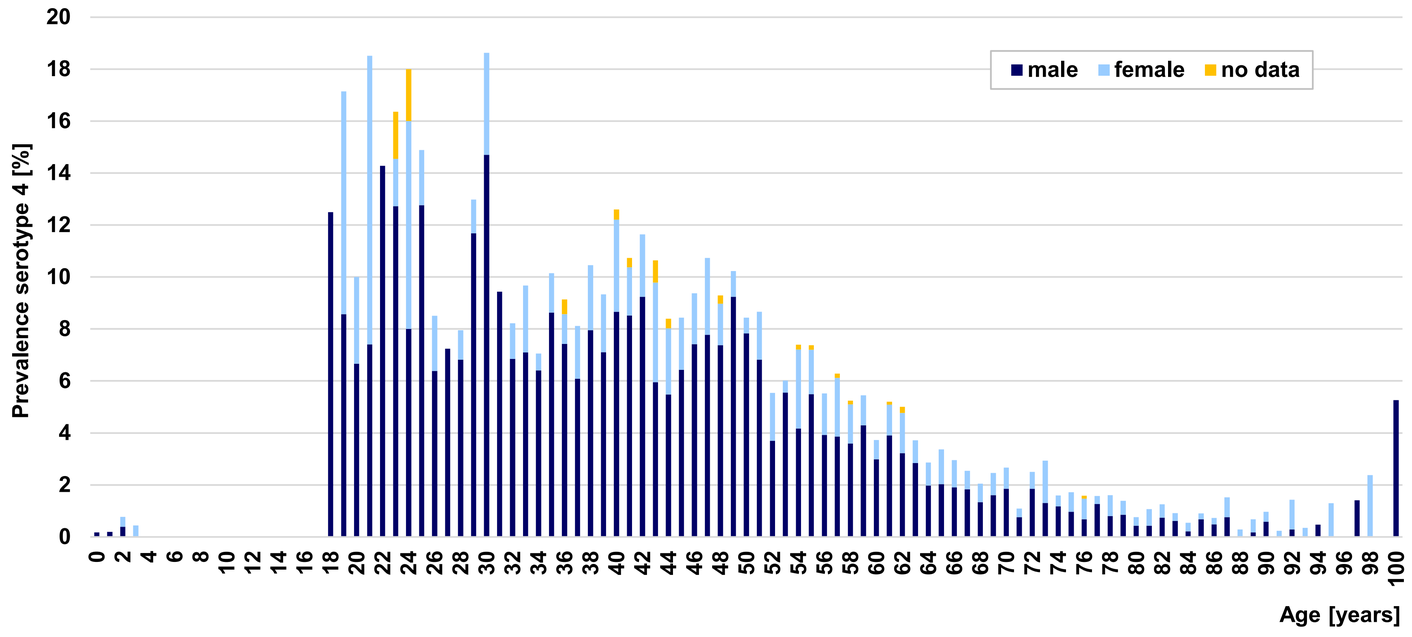

Figure 3: Prevalence of serotype 4 IPD cases per age (in years) in Germany for the seasons 2015/16 to 2025/26.

CONCLUSIONS

Serotype 4 IPD has almost completely disappeared among children <18 years since the introduction of childhood PCV vaccination in Germany.

After an initial decrease, an increase in serotype 4 IPD among adults ≥18 years has been observed since 2015/16.

The increase is strongest among 18-49-year-olds, mostly affecting male patients, living in larger cities.

A direct correlation to housing situation and substance use could not be ascertained due to missing information.

The expansion of serotype 4 beyond certain risk groups and despite eradication among children is worrisome and indicates circulation among adults.

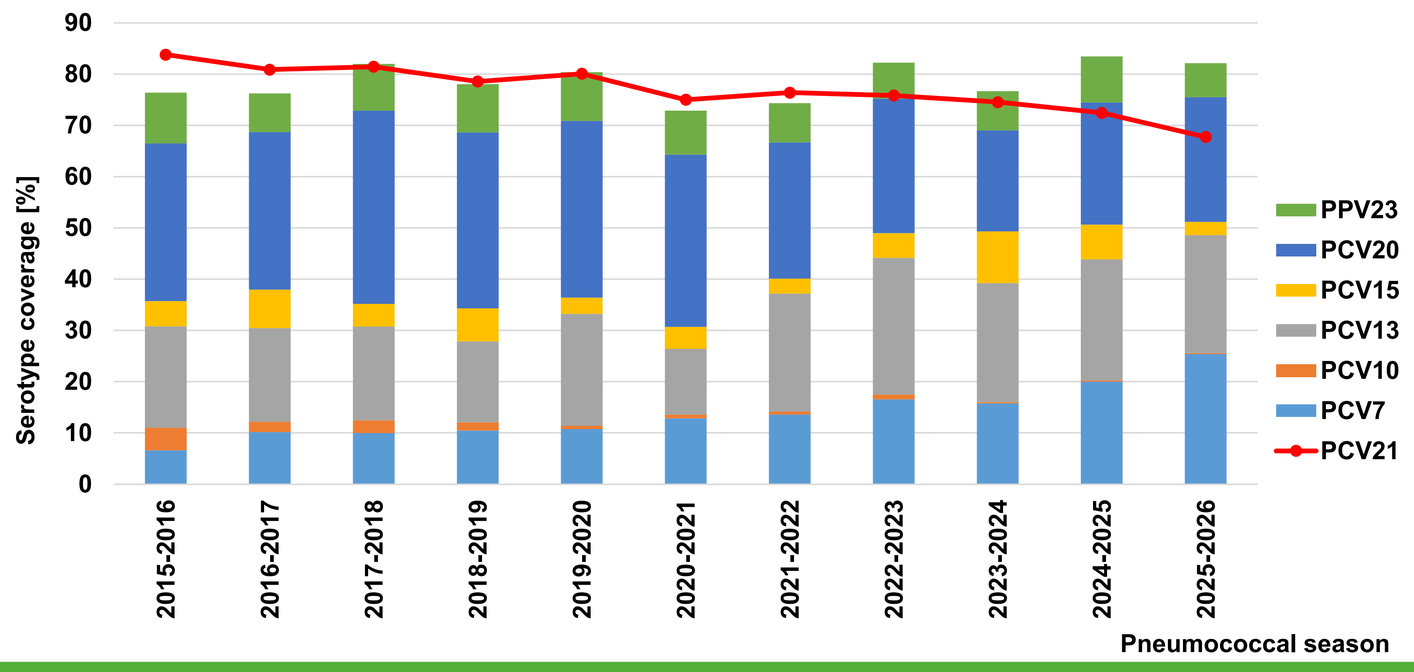

Figure 5: Serotype coverage of different vaccine formulations among IPD in adults 18-49 years of age in Germany, 2015/16 to 2025/26.

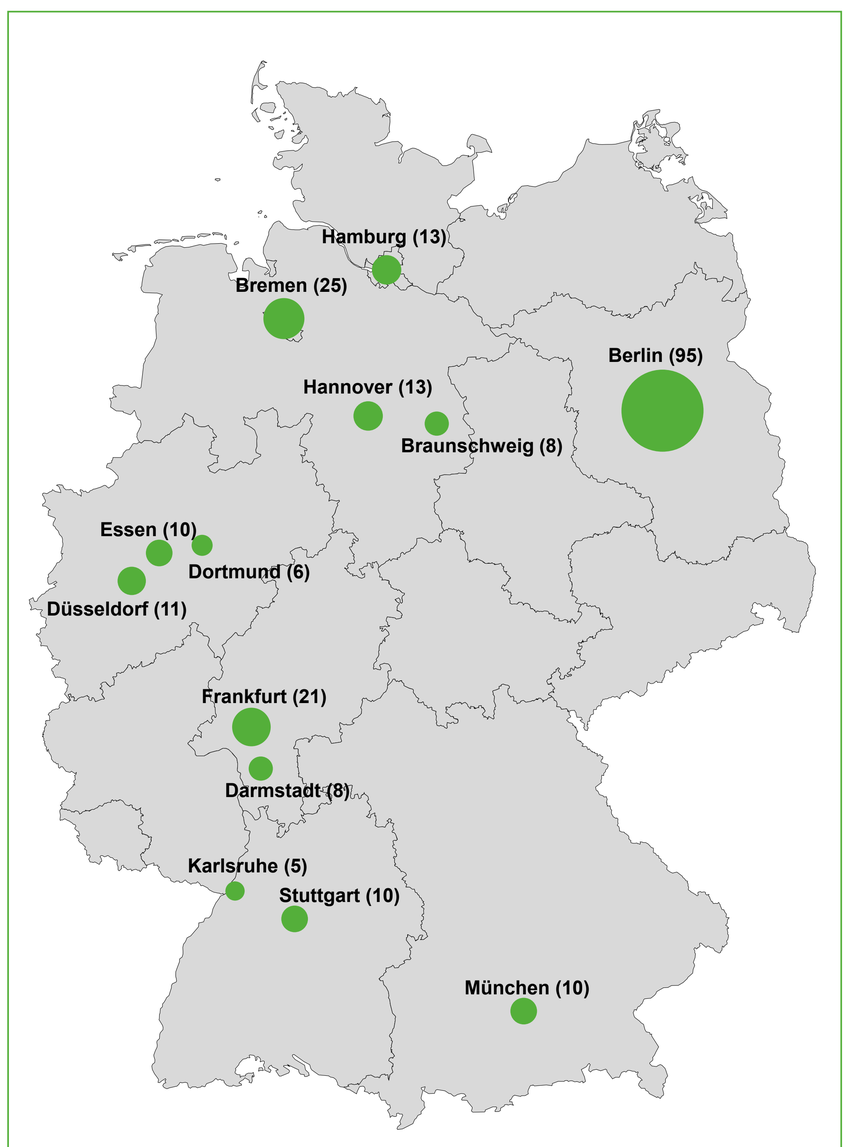

Figure 4: IPD cases with serotype 4 in the age group 18-49 years, reported in ten larger cities, between 2015/16 and 2025/26.