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Serotype distribution of non-invasive *Streptococcus pneumoniae* isolates in Belgium, 2020-2022: a prospective, observational study

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Streptococcus pneumoniae **typically causes either invasive (IPD) or non-invasive disease (NIPD). Although IPD has been generally regarded as more severe, NIPD is by far the more common pneumococcal disease. Contrary to IPD, surveillance of NIPD is largely lacking, making it challenging to assess the full impact of PCV (and PPV) vaccination programs on pneumococcal disease as a whole.**

Methods

- 20-months surveillance study (September 2020-May 2022) with following inclusion and exclusion criteria:
  - **Inclusion criteria**:
    - Patients **living in Belgium** at the time of the study
    - from whom **unduplicated *S. pneumoniae*** samples were isolated
    - from **non-invasive** upper or lower respiratory tract clinical samples
    - diagnosed with pneumonia, sinusitis or otitis
  - **Exclusion criteria**:
    - Patients for whom *S. pneumoniae* was simultaneously isolated from blood or another normally sterile specimen
- **24 participating centres** geographically spread around Belgium
- *S. pneumoniae* isolates were validated using bile solubility assay and optochine resistance and **serotyping** was performed using **FT-IR spectroscopy** (IR Biotyper™) (Passaris *et al*., 2022)
- Testing of antimicrobial resistance (AMR) was performed using the broth microdilution method (Sensititre™) and EUCAST breakpoint tables were used to determine the proportion of AMR in the NIPD population
- Associated **metadata** of all received isolates are summarized in **Table 1**:

	N (%)
Total number of clinical *S. pneumoniae* isolates received	1025
Total number of validated *S. pneumoniae* strains	875
Number of samples with two *S. pneumoniae* strains identified	8
Patient and sample information	
Region	
Wallonia	591 (68.2)
Flanders	263 (30.3)
Brussels	13 (1.5)
Sex	
Male	491 (56.6)
Female	359 (41.4)
Unknown	17 (2.0)
Medical care	
Ambulatory	416 (48.0)
Hospitalised	346 (39.9)
Intensive Care Unit	88 (10.1)
Unknown	17 (2.0)
Comorbidities/Immunocompromised	
Patients with ≥1 comorbidity or immunocompromised	334 (39.0)
Chronic obstructive pulmonary disease	137 (15.7)
Cancer	43 (4.9)
Diabetes	38 (4.3)
Other pathogens	
Specimens with at least one extra pathogen detected	346 (39.9)
Clinical Specimen	
Sputum	367 (42.3)
Endotracheal/Bronchial aspiration	143 (16.5)
Middle ear fluid	79 (9.1)
Nasopharyngeal aspirate/swab	65 (7.5)
Bronchalveolar lavage	61 (7.0)
Sinus	50 (5.8)
Nasal swab	35 (4.0)
Respiratory pus	10 (1.2)
Throat	2 (0.2)
Other	39 (4.5)
Unknown	16 (1.8)
Clinical Diagnosis	
Pneumococcal carriage	154 (17.8)
Unknown	108 (12.5)
Causal pneumococcal infection	605 (69.8)
Lower respiratory tract infections	445 (73.6)
Otitis Media	79 (13.1)
Sinusitis	28 (4.6)
Other	50 (8.3)
Unknown	3 (0.5)
Vaccination status	
Unknown	617 (71.2)
Not vaccinated	120 (13.8)
Vaccinated	123 (14.9)
Prevenar 13	33 (25.4)
Pneumovax 23	9 (7.0)
Synflorix	4 (3.1)
Prevenar 13 and Pneumovax 23	2 (1.5)
Unknown	82 (63.1)

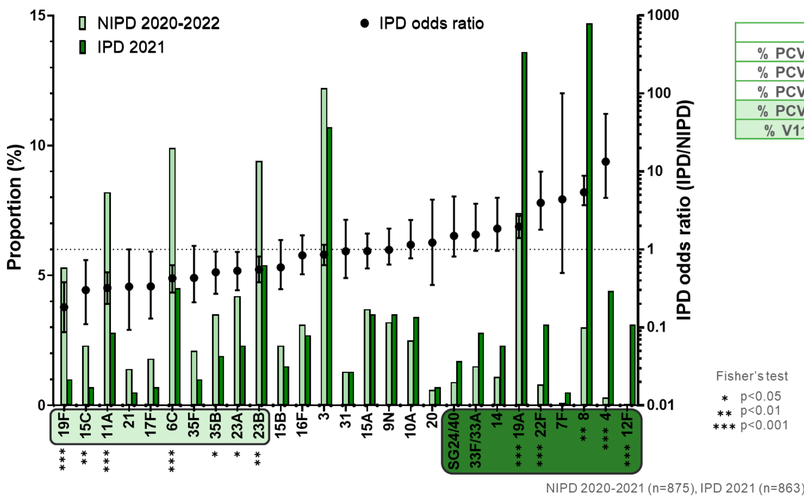
Results

- Serotype distribution for the 875 validated *S. pneumoniae isolates* is shown in **Table 2** (serotypes with prevalence ≥3% listed):

Serotype	Number of strains (%)
3	107 (12.2)
6C	87 (9.9)
23B	82 (9.4)
11A	72 (8.2)
19A	65 (7.4)
19F	46 (5.3)
23A	37 (4.2)
15A	32 (3.7)
UNKNOWN	32 (3.7)
35B	31 (3.5)
9N	28 (3.2)
16F	27 (3.1)
8	26 (3.0)

PCV7 ST
PCV13-non-PCV7 ST
PCV20-non-PCV13 ST
PPV23 unique ST

- Comparison of the serotype distribution of the IPD population compared to the NIPD population shows marked differences (**Figure 1**)



	NIPD (2020-2022)	IPD (2021)
% PCV13 serotypes	27.0	32.5
% PCV15 serotypes	29.3	38.4
% PCV20 serotypes	45.3	65.9
% PCV24 serotypes	50.9	71.0
% V116 serotypes	68.9	77.8

Figure 1*: Comparison of the serotype distribution and coverage of different vaccines between the IPD and NIPD population. The IPD odds ratio shows how likely it is to find a serotype in the IPD/NIPD population. PCV24 and V116 vaccines are shaded green as they have not been approved yet.*

- Comparison of AMR of NIPD isolates vs. IPD isolates shows elevated levels of resistance for NIPD isolates (**Figure 2A**) and AMR has increased over time for β –lactams (**Figure 2B**)

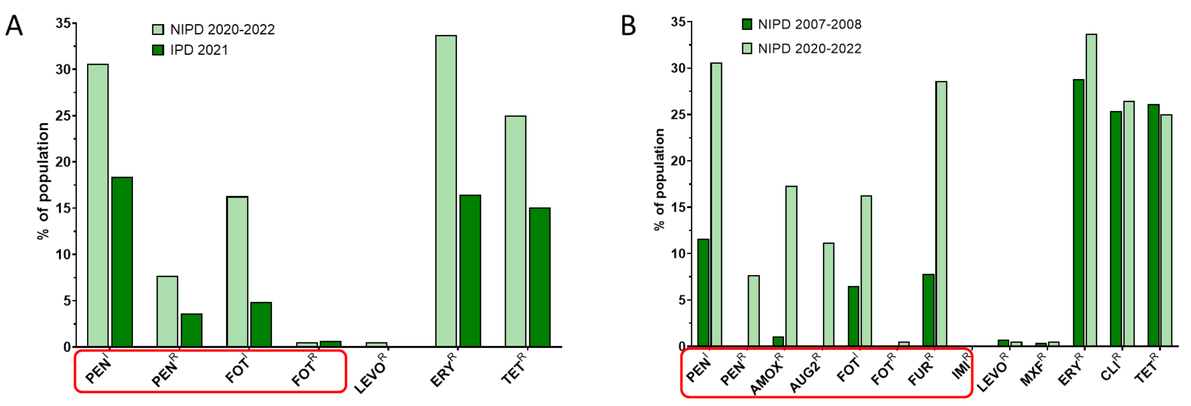


Figure 2*: A) Comparison of AMR levels for different antibiotics between the IPD and NIPD population. B) Comparison of AMR levels for different antibiotics for the NIPD population at different time periods. β-lactam antibiotics are highlighted by a red rectangle. PEN, penicillin; FOT, cefotaxime; LEVO, levofloxacin; ERY, ertythromycin; TET, tetracycline; AMOX, amoxicillin; AUG2, Amoxicillin-clavulanic acid; FUR, cefuroxime; IMI, imipenem; MXF, moxifloxacin; CLI, clindamycin.*

Conclusion

The results of this 20-months surveillance study show the persistent circulation of ST3 and ST19A (included in PCV13) and ST19F (included in PCV7 and PCV13), in the NIPD population in Belgium. Moreover, serotypes that are not included in any currently licensed PCV vaccine make up >50% of the NIPD population. The data presented in this study support the need for surveillance of NIPD along with IPD, to fully understand the contribution of each serotype to pneumococcal disease and to inform future vaccination programs.

REFERENCES

- Passaris I. *et al*., *J Clin Microbiol* 2022

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