Rapid increase of vaccine serotype 4 (GPSC162) invasive pneumococcal disease in young adults since 2020 in Belgium

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BACKGROUND

- **Following introduction of pneumococcal vaccination for children in Belgium in 2007**: vaccine preventable **serotype 4 IPD almost disappeared** (<0.5% of all IPD cases)

- **Since 2020, resurgence of serotype 4**
  - 2022: 6.9% of all IPD cases
  - 2023: 9.6% of all IPD cases

METHODS

- **Stable laboratory-based surveillance for IPD in Belgium**: +/- 100 laboratories, spread even across the country, send isolates to the National Reference Center
- **Capsular typing** (Quellung reaction) **for all IPD cases from 2007 to 2023**
- **Serotype 4 strains from 2022 (n=102) were characterized by whole-genome sequencing**:
  - DNA extraction with DSP DNA Mini Kit QIAsymphony SP (Qiagen)
  - Library preparation with Illumina DNA Prep Kit at the Nucleomics Core facility, KU Leuven
  - Short-read sequencing with NextSeq2000 platform (PE250 600 cycli, Illumina)
  - Downstream bioinformatics by Pathogenwatch to **determine multi-locus sequence type** (**MLST**) and **Global Pneumococcal Sequence Cluster** (**GPSC**)

RESULTS

Increasing number of serotype 4 cases since 2020

- Despite overall low numbers of IPD cases during the COVID-19 pandemic: important **increase of serotype 4 infections since early 2020** (Figure 1)
- Proportion of serotype 4 in time:
  - PCV7 period: decrease from 55 cases in 2007 to 17 cases in 2011
  - PCV13 period 1: further decrease to 7 cases in 2015
  - PCV10 period: stable period ranging between 6 and 9 infections per year
  - PCV13 period 2: increase from 6 to 167 cases, starting from 2020 on
  - **2023: overall ranked third (9.6%)**

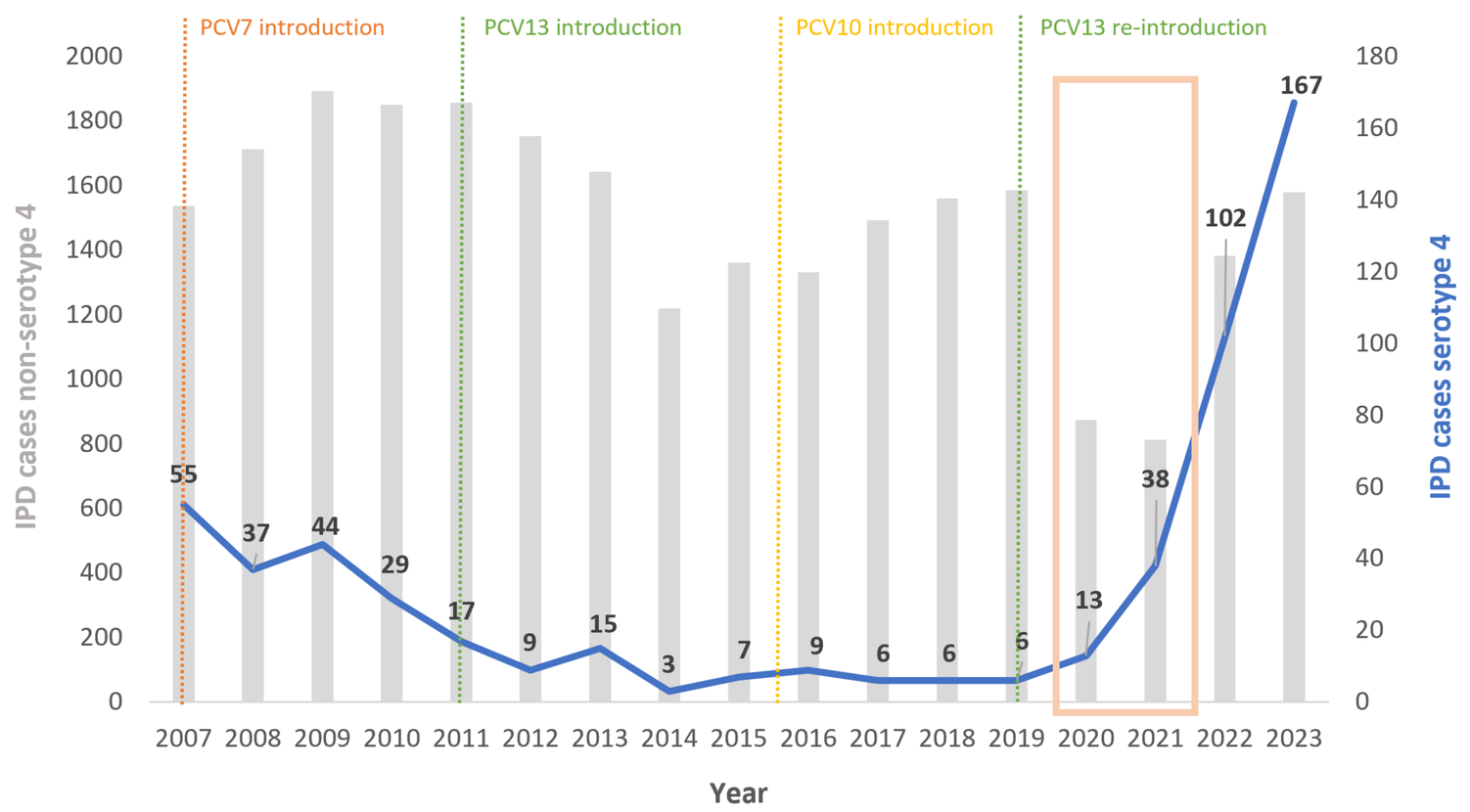

Figure 1: Number of IPD isolates between 2007 and 2023: serotype 4 (blue line) and non-serotype 4 infections (grey bars). The period of the COVID-19 pandemic is indicated by an orange bar. The number of IPD cases of serotype 4 is indicated for each year.

Serotype 4 mainly in young male adults

- The **increase of serotype 4 (2020-2023)**:
  - Mainly pronounced in **males**: 78.8% vs 55.5% for non-serotypes 4
  - Majority of infections in **age category 18-64 years**: 75.6% (18-49y: 46.6% and 50-64y: 29.1%)
  - Geography different compared to non-serotype 4 infections:
    - **More frequent in Brussels-Capital region** (32.2% vs 9.9%)
    - **Less frequent in Flanders** (northern part) (28.1% vs 60.2%)
    - Enriched in large cities (not shown in Figure 2)

Dominance of sequence types 801 and 15063 (93.2%)

- Sequencing of 102 serotype 4 strains (2022) identified **six ST types**:
  - **ST801: 71.6%** (GPSC162)
  - **ST15063: 21.6%** (GPSC162)
  - Rare STs: 205 (3.9%) - 1022, 5838 and 13753 (each <1.0%)
  - Geographical differences for the major STs (Figure 2)

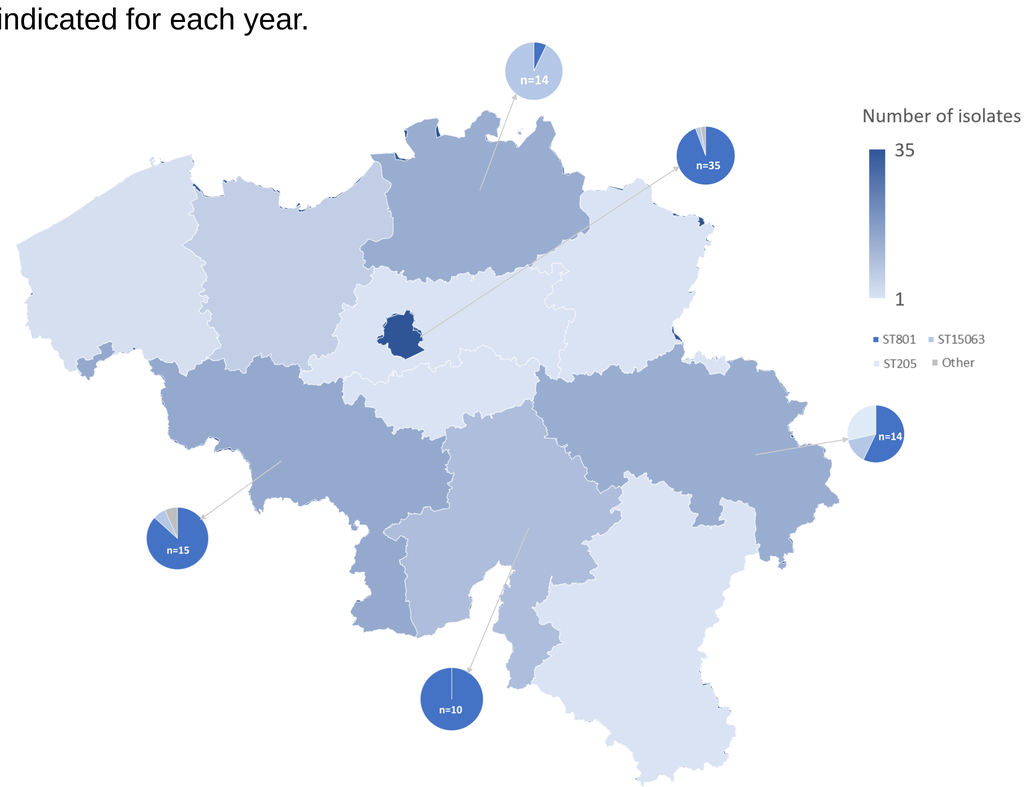

Figure 2: Number of IPD serotype 4 isolates mapped per Belgian province for the year 2022 (n=102). Sequence types are visualized for the provinces with 10 or more isolates.

CONCLUSION

The **continued increase of serotype 4 IPD since early 2020** is due to an increase in infections in **younger adults (18-49 years), mainly males and living in specific regions in the country**. **Two clones (ST801 and 15063**: 93.2%) are responsible for this **worrisome increase of a vaccine serotype in an age group currently not targeted for vaccination**, accounting for 1 in 4 infections for the young adults in 2023. Further characterization of the serotype 4 cases and genomic comparisons are ongoing to better understand this evolution.

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