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Cost-effectiveness of V114 (PCV15) in active immunization of the pediatric population for the prevention of pneumococcal disease in France

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Background

- *Streptococcus pneumoniae* (*Sp*) is responsible for pneumococcal disease (PD), which includes:
  - Invasive pneumococcal disease (IPD): meningitis, septicemia or pneumococcal bacteremia,
  - Non-invasive pneumococcal disease (nIPD): acute otitis media (AOM) of the infants and children and non-bacteremic pneumococcal pneumonia (NBPP)
- PD prevention relies on vaccination, which is mandatory from the age of 2 months in all infants born since January 1st, 2018.
- In children, PREVENAR13® (PCV13) is recommended since 2009 (2+1 schedule at 2, 4 and 11 months), and contains 13 serotypes of *Sp*.
- VAXNEUVANCE® (PCV15 or V114) is a new pneumococcal polysaccharide conjugate vaccine, which contains 15 *Sp* serotypes (*i.e.,* two additional serotypes compared to PCV13: 22F and 33F).
- On October 21, 2022, V114 obtained a Marketing Authorization in the pediatric population and was recommended by the French NiTAG in 2023.

Objective

- To evaluate the cost-effectiveness of V114 compared to PCV13 in active immunization for the prevention of IPD, NBPP and AOM caused by *Streptococcus pneumoniae* in infants, children and adolescents.

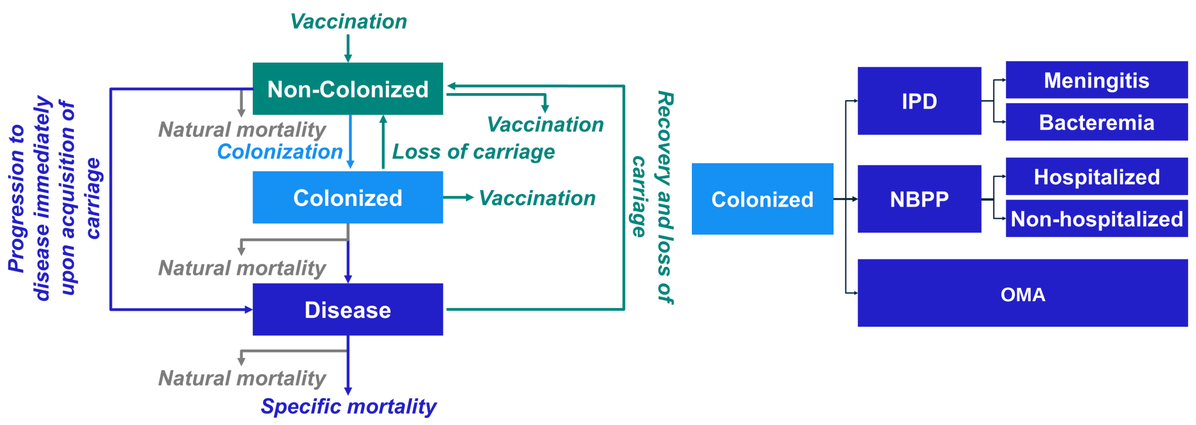
Method

Economic model

- A dynamic transmission model (DTM) was developed, with three components:
  - **Demographic component** (reproduces and simulates the demographic characteristics of the French population by age group).
  - **Epidemiological component** (simulates the transmission of Sp, the epidemiology of PD, and the consequences of vaccination on them).
  - **Cost-effectiveness component** (epidemiological results are associated with cost and quality of life data).
- The entire French population is simulated to account for all individuals whose health is affected by V114:
  - **<u>Directly</u>** in the pediatric population
  - **<u>Indirectly</u>** in the adult population, through the indirect effect of V114 on the reduction of the transmission of Sp.

Figure 1. Structure of the DTM

A. Epidemiological component ***B. PD clinical manifestations***



Clinical parameters – efficacy and utility scores

- V114 vaccine effectiveness (VE)[1,2,3] against IPD in infants was calculated using the correlates of protection method validated by WHO,[4,5] for common serotypes (ST) with PCV13. For the two additional STs (22F and 33F), V114 VE was estimated from the study by Siber et al.[6] (average VE of 93% as antibody titers by opsonophagocytic activity (OPA) >0.35 µg/mL).
- V114 and PCV13 VE against nIPD were determined based on data from the international literature.[7,8,9]
- Annual disutility was applied for individuals with IPD or NBPP cases to baseline utilities from the general French adult population. For patients with post-meningitis sequalae, a disutility was applied the 1st year, and from the following year, an average utility of 0.693 was applied until death or the end of the simulation.

Cost parameters

- Direct medical costs (in €2022) were assessed, from a health system perspective, considering all French health system stakeholders.
- The following costs were considered: treatment acquisition and administration, inpatient management of IPD and nIPD, and outpatient management of nIPD.

Assessment of the model by the authorities

- The methodology of V114 cost-effectiveness analysis was assessed by the HAS and deemed “acceptable”.

Results

Base case analysis

- Over a 65-year time-horizon and in the overall population, the introduction of V114 at the claimed price in the pediatric population would allow to avert vs. PCV13:
  - **60,443 IPD cases** (reduction of 11.9 % vs. PCV13), including **1,197 post-meningitis sequelae** (reduction of 11.4%)
  - **428,078 NBPP cases** (reduction of 2.5%)
  - **9,453 AOM cases** (reduction of 0.11%)
  - **11,492 deaths linked to PD**, including 11% of them in the population of active individuals aged 15-65 (n=1,258) and 87% among people aged ≥65 years (n=9,962).
- Introduction of V114 in the pediatric population would lead to **cost savings of more than 300 millions € compared to PCV13** over 65 years**.**
- **Thus, V114 is a dominant strategy in children vs. PCV13.**

Table 1. Public health results – base-case analysis (Time horizon : 65 years)

Health outcomes	PCV13	V114	Increment (V114 - PCV13)
IPD	508,828	448,385	-60,443 (-11.9%)
Bacteremia	463,740	408,433	-55,307 (-11.9%)
Meningitis	45,087	39,951	-5,136 (-11.4%)
Post-meningitis sequelae	10,505	9,309	-1,197 (-11.4%)
NBPP	16,908,309	16,480,231	-428,078 (-2.5%)
Hospitalized NBPP	1,295,385	1,262,860	-32,525 (-2.5%)
Non-hospitalized NBPP	15,612,924	15,217,371	-395,553 (-2.5%)
AOM	72,315,372	72,235,919	-79,453 (-0.11%)
Death (total)	247,272	235,780	-11,492 (-4.6%)
IPD	53,758	47,048	-6,710 (-12.5%)
Hospitalized NBPP	110,452	107,729	-2,723 (-2.5%)
Non-hospitalized NBPP	83,062	81,003	-2,059 (-2.5%)

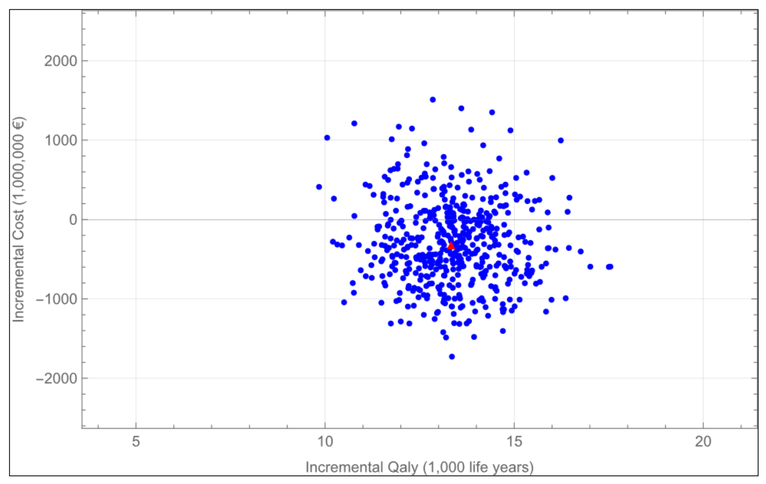
Table 2. Cost-effectiveness results – base-case analysis (Time horizon : 65 years)

Vaccine strategy	Costs	LYs	QALYs	ICER (€/LY)	ICER (€/QALY)
PCV13	€ 16.1 billion	2.2 billion	2.0 billion	-	-
V114	€ 15.8 billion	2.2 billion	2.0 billion	**Dominant**	**Dominant**
Increment	**€ -309 million (-1,9%)**	**5 494**	**13 330**	NA	NA

Sensitivity analyses

- V114 remains the dominant strategy in all scenarios and deterministic sensitivity analyses
- According to the probabilistic sensitivity analysis, the dispersion of results leads to 71.5% of iterations with incremental costs lower than zero (i.e., dominance).

Figure 2. Results for 500 PSA iterations



Conclusion

- Vaccination of the pediatric population with V114 at the claimed price appears to be the dominant strategy compared to PCV13 over a 65 years time-horizon (lower costs, better health outcomes).
- These results are due to V114-induced robust immune response against all serotypes included in the historical PCVs and two additional serotypes, protecting infants from the primary vaccination series.

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