Review of Health Technology Assessment (HTA) and recommendations for the introduction of higher-valency Pneumococcal Conjugated Vaccine (PCV) in 4 European countries, the United Kingdom (UK), and the United States (US)

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BACKGROUND

- Vaccine recommendations are generally issued at national level by Health Technology Assessment (HTA) agencies and/or National Immunisation Technical Advisory Groups (NITAGs) with different evaluation processes resulting in various conclusions[1]
- Since two decades, pneumococcal conjugated vaccines (PCV) have been largely introduced in National immunisation programmes (NIP) for children but also in elderly and at-risk populations
- With the availability of various PCVs and one pneumococcal polysaccharide vaccine (PPV23), different pneumococcal vaccine recommendations exist across Europe and the US with regards to target population, vaccine used and vaccination schedule[2,3]

OBJECTIVES

- This study aims to understand the process by which NITAGs and HTA agencies have formulated their recommendations for the introduction of PCV10, PCV13, PCV15 or PCV20 after 2009, by

  (i) summarising the evidence considered during assessment

  (ii) identifying key drivers or barriers for new recommendations

METHODS

Search strategy and Data sources

- A narrative review was conducted on NITAGs and HTA agencies websites of France, Germany, Spain, the Netherlands, the UK, and the US
- The search, conducted by 2 reviewers, included pneumococcal vaccines related terms and adapted to each website explored
- Records containing recommendation coupled with evaluation of PCV in children, elderly or risk groups and published between 2009 and 2022 were included
- For the UK and the US, the Joint Committee on Vaccination and Immunisation (JCVI) and the Advisory Committee on Immunisation Practices (ACIP) meeting minutes were consulted but not extracted in full

Data extraction and analysis

- Relevant data pertaining to decision-making of vaccine recommendations was extracted into a pre-specified data extraction grid based on Donadel et al[4] (**Table 1**)

Table 1. Criteria for decision-making framework

1	Burden of disease: IPD, pneumonia, AOM
2	Impact of current vaccination programme: direct impact on targeted population, indirect impact of children vaccination on other population (herd effects)
3	Vaccine safety
4	Vaccine immunogenicity and/or efficacy/effectiveness : against IPD, pneumonia, AOM
5	Public health impact of alternative strategies: direct vaccination impact on targeted population, indirect impact on other age groups (herd effects)
6	Economic evaluations: with IPD, pneumonia, AOM as clinical inputs of models

AOM, acute otitis media; IPD, invasive pneumococcal diseases

RESULTS

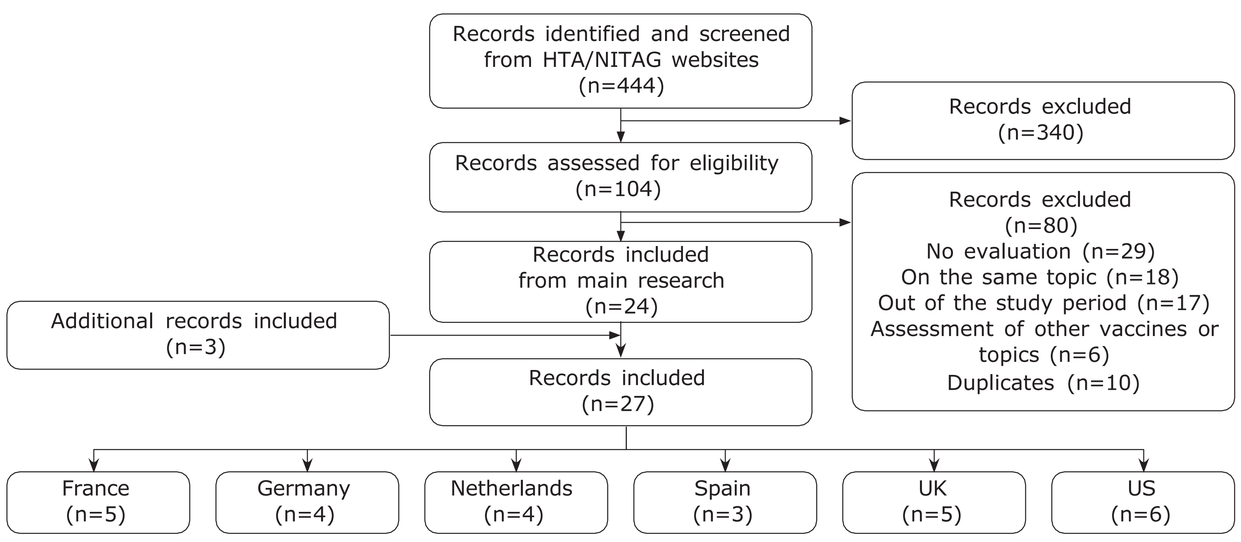
Search results

- Overall, 27 records were identified (**Figure 1**) including 10 assessments of PCV in children, 11 in elderly and 18 in risk groups (defined as individuals with underlying conditions at low risk or high risk for severe pneumococcal disease)
- For children, 8 and 7 records assessed PCV13 and PCV10, respectively. For elderly and risk groups, all records assessed PCV13 except one on PCV15 and PCV20 in both populations and one on PCV10 in at-risk children

Criteria considered in assessements

- The burden of disease and the immunogenicity/efficacy data were the most reported criteria (n=26), followed by the impact of current vaccination programme (n=22), the safety data (n=21), the economic evaluations (n=18), and the public health impact of alternatives (n=12)

Figure 1. Inclusion/exclusion flowchart



Evolution, drivers or barriers for new recommendations

- France, Spain, the Netherlands, the UK, and the US issued positive recommendations for replacing PCV7 by higher-valency PCVs in childhood NIPs. The Netherlands recommended the use of both PCV10 and PCV13, and the other countries recommended PCV13 only. Even if Germany recommended PCV10 and PCV13 no evaluation report was identified during the search
- For the elderly, the US recommended first the routine use of PCV13 in series with PPV23 and later the use of PCV15 in series with PPV23 or PCV20 alone. Contrastingly, the 5 other countries advised against the use of PCV13 in this population (PCV15 and PCV20 not being evaluated yet by European HTA bodies and NITAGs)
- All countries introduced PCV13 in risk groups vaccination programmes. Germany, Spain, the Netherlands, and the UK limited the use of PCV13 to high risk groups only whereas France and the US recommended its use in all risk groups
- Main drivers or barriers for PCV recommendations are detailed in **Table 2**

Table 2. Key drivers and barriers for PCV recommendation by population

Population	Vaccine	Recommendation	Country	Main Drivers or barriers
Children	PCV13	Positive	FR ES NL UK US	✓**Burden of disease:** higher serotype coverage and potential benefits in terms of IPD prevented ✓**Vaccination impact (direct, indirect):** important herd effect from childhood vaccination in other age-groups ✓**Immunogenicity/safety:** vaccine profile comparable to PCV7 one ✓**Economic evaluations:** most likely favorable cost-effectiveness results compared to PCV7 or PCV10
	PCV10	Negative	FR ES UK	✓**Burden of disease:** lower serotype coverage than PCV13 and important burden due to the 3 additional serotypes
		Positive	NL	✓**Immunogenicity/safety:** vaccine profile comparable to PCV7 one
Elderly	PCV13	Negative	FR DE ES NL UK	✓**Burden of disease:** lower serotype coverage than PPV23 ✓**Vaccination impact (indirect):** decreasing trend of IPD attributable to PCV13-serotypes in elderly ✓**Economic evaluations:** unfavorable cost-effectiveness results compared to PPV23 alone
		Positive	US	✓**Burden of disease:** remaining burden due to PCV13-serotypes in elderly ✓**Immunogenicity/efficacy:** positive efficacy data of PCV13 against IPD and pneumonia in elderly ✓**Economic evaluations:** PCV13 in series with PPV23 is the most likely favorable scenario
	PCV15/ PCV20	Positive	US	✓**Burden of disease:** remaining burden due to PCV15 and PCV20-serotypes ✓**Immunogenicity/safety:** PCV15 and PCV20 vaccine profiles comparable to PCV13 one ✓**Economic evaluations:** the use of PCV15 in series with PPV23 or PCV20 alone was cost-saving
Risk groups	PCV13	Positive (high risk groups)	DE ES NL	✓**Burden of disease:** high incidence of IPD in these populations ✓**Immunogenicity/efficacy:** stronger and longer immune response of PCV13 compared to PPV23 ✓**Economic evaluations:** in favor of PCV13 use (when conducted)
		Positive (all risk groups)	FR US*	✓**Burden of disease:** important pneumonia and IPD burden observed in adults with comorbidities ✓**Economic evaluations:** cost-effective strategy compared to elderly vaccination (France) or PPV23 alone (the US)
		Negative (all risk groups)	UK	✓**Vaccination impact (indirect):** decreasing trend of IPD cases attributable to PCV13-serotypes
	PCV15/ PCV20	Positive	US	✓**Burden of disease:** remaining burden due to PCV15 and PCV20-serotypes ✓**Economic evaluations:** cost estimates with PCV15 and PCV20 were considered acceptable

IPD, invasive pneumococcal disease; PCV, pneumococcal conjugated vaccine; PPV, pneumococcal polysaccharide vaccine

*In the US, PCV13 was first introduced on all risk groups (2014) but later limited to a shared clinical decision-making due to low impact of the vaccination programme and less favorable economic evalutions

DISCUSSION AND CONCLUSION

- The burden of disease and the immunogenicity or efficacy data were almost always reported and were main drivers of recommendations for PCVs. Even if generally less reported then other criteria, the economic evaluations played a major role in final decisions
- Higher-valency PCVs has been widely introduced in childhood NIPs but their recommendation has been more limited in risk groups and even more in elderly, given the importance of herd effect from childhood vaccination resulting in a decreasing vaccine serotype incidence and unfavorable economic evaluations
- This study provides an overview of data used in decision-making for higher-valency PCV recommendations and will be of interest to anticipate the evolution of recommendations with next generation of PCVs

LIMITATIONS

- The restricted number of countries selected did not provide an exhaustive overview of the global landscape of pneumococcal vaccination strategies but reflected general trends[5,6]
- The data extraction was based on a pre-specified list and therefore did not cover all criteria potentially evaluated. However, this list was based on the most common criteria for decision-making when adopting new vaccines[4,7]

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CONFLICT OF INTEREST

R. N. K. is currently an intern at Sanofi. K. L. and P. F. are employees of Certara. E. L. is an employee of Sanofi and may hold company shares/stocks. No other disclosures were reported

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