

Impact of Real-World Effectiveness vs. Previous Assumptions on Estimates of Economic and Clinical Benefit of 20-Valent Pneumococcal Conjugate Vaccine in Adults Across Countries

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BACKGROUND

- Higher-valent pneumococcal conjugate vaccines (PCVs) for adults were licensed based on immunogenicity and safety as trials against disease endpoints were not feasible
- Consequently, economic evaluations have relied on efficacy estimates from 13-valent pneumococcal conjugate vaccine (PCV13) adjusted for estimated serotype coverage
- However, initial data on real-world effectiveness (RWE) of 20-valent PCV (PCV20) against all-cause pneumonia (ACP) and invasive pneumococcal disease (IPD) among older adults in the United States (US) have recently been presented¹

OBJECTIVE

- To compare health & economic outcomes of PCV20 in adults in various countries when modelled with real-world vaccine effectiveness (VE) estimates vs. earlier assumptions based on PCV13 efficacy and disease surveillance

METHODS

- Previously published cost-effectiveness models evaluating PCV20 in adults were replicated and adapted to incorporate PCV20 RWE²⁻¹²
- All other model inputs were retained from the base case of the original models as described in their respective publications
- Outcomes included cases of pneumococcal disease (hospitalized and non-hospitalized), disease-related deaths, quality-adjusted life-years (QALYs) and direct medical costs
- Non-Euro costs were converted to Euros using current exchange rates
- Outcomes were projected for PCV20 using real-world effectiveness estimates and compared to the results using the original VE assumptions

METHODS (continued)

Table 1. Key Model Characteristics of Included Articles

Country	Population	PCV20 IPD Coverage	Perspective	Time Horizon	Original Currency, Cost Year
Belgium ²	HR Adults, MR ≥50, LR 65-84	75% (18-64), 66.4% (65-99)	Healthcare	Lifetime	EUR 2023
Denmark ³	At-risk 18-64, all adults ≥65	69.2% (18-64), 62.6% (65-99)	Societal	Lifetime	EUR 2022
Germany ⁴	At-risk 18-59, all adults ≥60	68% (18-74), 60% (75-99)	Healthcare	Lifetime	EUR 2022
Greece ⁵	At-risk 18-64, all adults ≥65	65% (18-99)	Healthcare	Lifetime	EUR 2022
Italy ⁶	All adults 65-74	69.6% (18-99)	Healthcare	Lifetime	EUR 2022
Japan ⁷	Adults aged 65, HR 60-64	61% (18-99)	Societal	Lifetime	JPY 2023
Norway ⁸	At-risk 18-64, all adults ≥65	75.4% (18-64), 53.1% (65-99)	Healthcare	Lifetime	EUR 2022
Singapore ⁹	At-risk 18-64, all adults ≥65	63.8% (18-99)	Healthcare	Lifetime	SGD 2023
South Korea ¹⁰	Adults ≥65	59.9% (18-99)	Healthcare	Lifetime	USD 2021
Spain ¹¹	Adults ≥60	62% (18-99)	Healthcare	10 years	EUR 2018
UK ¹²	At-risk 18-64, all adults ≥65	75% (18-64), 64.6% (65-99)	Healthcare	Lifetime	GBP 2020

EUR = Euro, GBP = British Pound, JPY = Japanese Yen, SGD = Singapore Dollar, USD = United States Dollar

PCV20 VE assumptions:

- Original assumption:** Vaccine-type (VT) efficacy vs. IPD & CAP in the original paper, primarily based on the CAPITA PCV13 trial¹³, applied to disease identified as PCV20-VT in surveillance
- Real-world VE:** All-cause effectiveness against IPD & all-cause CAP in Medicare beneficiaries aged ≥65 years (see Table 2)
- Duration:** Typically 100% of initial VE through year 5, 5% annual linear decline from year 6-10, 10% annual decline during year 11-15, no VE thereafter (some variation across models)

Table 2. Vaccine Effectiveness Inputs

	Versus IPD			Versus Inpatient/Outpatient NBP		
	LR	MR	HR	LR	MR	HR
Original VT-VE (CAPITA) [*]	75%	75%	60%	45%	45%	36%
PCV20 real-world all-cause VE	25.6%	25.6%	25.6%	15.2%	15.2%	15.2%

^{*}Original VT-VE for adults aged ≥65 years; values slightly higher in younger adults (up to 81.5% and 55.6% vs VT-IPD and VT-NBP, respectively) for most models; values slightly lower for South Korea; LR = Low Risk, MR = Medium Risk, HR = High Risk, NBP = Non-bacteremic pneumonia

RESULTS

- Compared to original assumptions, use of real-world VE for evaluation of PCV20 across all countries included predicted a total of 679,412 additional hospitalizations prevented (Figure 1), 411,551 additional outpatient cases prevented (Figure 2), and an additional 98,559 prevented deaths (Figure 3), yielding more QALYs (not pictured) and offsetting €2.75 billion more in medical costs over the remaining modelling horizon (Figure 4)
- Magnitude of the difference varied across countries, driven in part by differences in population size, target population for vaccination, uptake, disease attributed to PCV20 types, & time horizon
- On average across all countries, the use of real-world VE for cost-effectiveness analysis of PCV20 resulted in a 3.0% decrease in the total number of hospitalized disease cases, 2.3% decrease in the total number of non-hospitalized cases, 2.4% decrease in the total number of disease deaths and a 3.2% decrease in the total IPD- and all-cause pneumonia-related medical costs relative to the outcomes calculated using original VE assumptions used in the source publications

Figure 1: Incremental Hospitalized Cases Averted During Modeled Time Horizon by PCV20 Using Real-world Effectiveness vs Originally-assumed Effectiveness

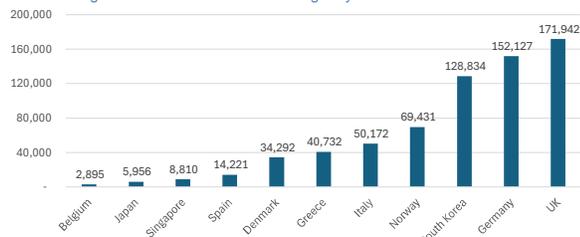
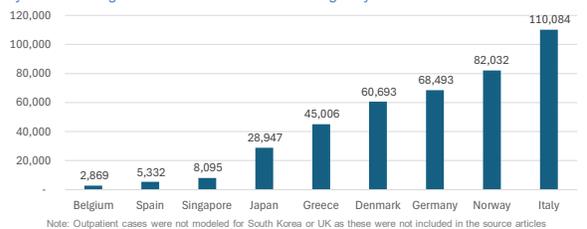


Figure 2: Incremental Non-hospitalized Cases Averted During Modeled Time Horizon by PCV20 Using Real-world Effectiveness vs Originally-assumed Effectiveness



Note: Outpatient cases were not modeled for South Korea or UK as these were not included in the source articles

Figure 3: Incremental Disease-related Deaths Averted by PCV20 During Modeled Time Horizon Using Real-world Effectiveness vs Originally-assumed Effectiveness

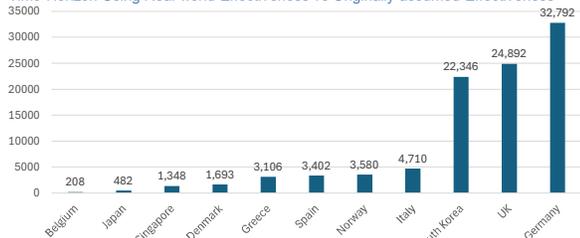
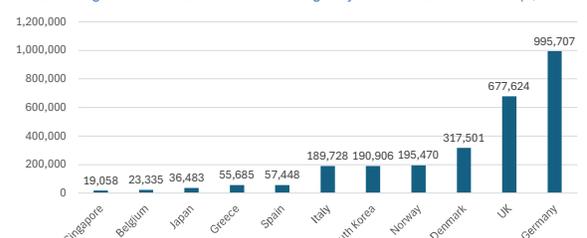


Figure 4: Incremental Direct Medical Costs averted During Modeled Time Horizon by PCV20 Using Real-world Effectiveness vs Originally-assumed Effectiveness (1,000s of Euros)



LIMITATIONS

All-cause VE is expected to vary with local epidemiology, and currently available estimates were measured only in the US. The proportion of pneumonia caused by pneumococcus is generally lower in the US vs. other countries; US-based all-cause VE may underestimate benefits of PCV20 vaccination elsewhere. Outputs should not be compared across countries due to wide variation in model assumptions. Numerous other sources of uncertainty:

- Projections have longer time horizon than measured in studies
- VE observed in Medicare fee-for-service measured among adults aged ≥65 years, may underestimate VE in younger adults
- Inputs beyond VE have a large impact on modelled outcomes and are subject to considerable uncertainty

CONCLUSIONS

- Real-world PCV20 VE data predict markedly greater health & economic benefits than prior VE assumptions employed by cost-effectiveness studies
- This suggests the true impact on public health from adult vaccination with PCV20 may have been underestimated
- Policymakers should consider incorporating emerging real-world PCV20 VE data when considering adult PCV recommendations

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Disclosures

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