Economic Evaluation of the Pediatric Immunization Program in Belgium

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BACKGROUND

- Children aged 10 years and younger in Belgium are routinely immunized against 12 pathogens with the following vaccines:
  - Diphtheria, tetanus, acellular pertussis, and inactivate polio (DTaP-IPV)
  - Hexavalent (DTaP–IPV–hepatitis B–Haemophilus influenzae B [DTaP-IPV-HepB-Hib])
  - Measles, mumps, rubella (MMR)
  - Meningococcal C (MenC)
  - Pneumococcal conjugate (PCV13)
  - Rotavirus (RV)
- Prior research has estimated the economic value of pediatric immunization in the United States,[1,2] concluding that immunization yields savings from healthcare payer and societal perspectives, with vaccination costs significantly offset by disease costs averted.
- To our knowledge, no previous research has specifically assessed the broad economic value of pediatric immunization programs (PIP) globally.

OBJECTIVE

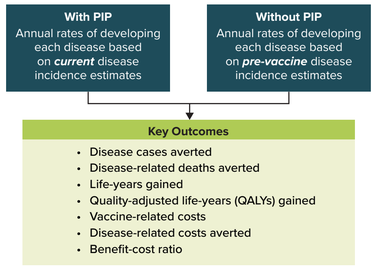
- This study estimates the clinical and economic impact of the PIP in Belgium from both healthcare payer and societal perspectives.

METHODS

Model Overview

- An economic model was developed, with separate decision trees constructed for the 12 vaccine-preventable pathogens covered in Belgium's PIP (i.e., diphtheria, tetanus, pertussis, poliomyelitis [polio], *Haemophilus influenzae B* [Hib], hepatitis B, measles, mumps, rubella, *Streptococcus pneumonia* [*S. pneumoniae*], rotavirus, and meningococcal C).
- The 2018 Belgium birth cohort was modeled for their lifetime, accounting for all-cause mortality and long-term disease complications (where applicable).
- The model considered two perspectives:
  - Healthcare payer perspective, which included the following costs:
    - Vaccination costs (acquisition, administration, and adverse events)
    - Direct medical costs of acute disease cases and long-term complications
  - Societal perspective, which included the following costs (in addition to costs included in the healthcare payer perspective):
    - Patient or caregiver productivity losses associated with acute disease cases and long-term complications
    - Value of time loss associated with disease-related mortality (i.e., patient productivity using the human capital method)
    - Caregiver productivity losses and travel costs for vaccination
- Two analytical scenarios were constructed: one in which routine pediatric immunization occurred according to Belgium's PIP, and one in which no immunization occurred and incidence of modeled diseases were assumed to reflect pre-vaccine levels (Figure 1).

Figure 1. Analytical Scenarios Compared and Key Incremental Outcomes



Model Inputs

- Vaccination occurred according to Belgium's childhood immunization schedule, with coverage values for each dose obtained from regional vaccination coverage studies; these values were weighted to estimate the total coverage for Belgium[3,4] (Table 1).
- Vaccination costs included acquisition (based on public prices), administration, and adverse events. Caregiver productivity losses due to time and travel for vaccination were also incurred.
- Disease incidence estimates were used to calculate the annual number of disease cases (Table 2).
  - **With PIP:** Disease incidence was based on current incidence estimates, which were calculated as average values from the European Centre for Disease Prevention and Control from the 5 most recent years with available data.
  - **Without PIP:** Pre-vaccine disease incidence was estimated before each routine vaccine was recommended, with data from the European Centre for Disease Prevention and Control, Belgium surveillance data, or estimates from the published literature.

Table 1. Childhood Immunization Schedule, Coverage Estimates, and Vaccine Acquisition Costs

Vaccine	Age at vaccination	Coverage[a]	Acquisition cost per dose[b]
DTaP-IPV	5 years	84.5%	€30.08
Hexavalent (DTaP-IPV-HepB-Hib)	2, 3, 4, 15 months	92.6%	€53.66
Meningitis C	15 months	92.6%	€35.63
MMR	12 months, 10 years	87.7%	€25.19
PCV13	2, 4, 12 months	94.1%	€74.55
Rotavirus	2 doses: 2, 3 months	88.6%	€68.80[c]
	3 doses: 2, 3, 4 months		

[a] Vaccine coverage values are a weighted average of the vaccine coverage rates[3,4] and population proportion for Flanders and Wallonia.

[b] Values for vaccine list price per dose are from RIZIV/INAMI[5] and CBIP.[6]

[c] The cost shown is a weighted average between the 2-dose vaccine cost (€71.48) and 3-dose vaccine cost (€51.82). 76.5% of the 88.6% vaccinated for rotavirus received the 2-dose vaccine; the remaining 12.1% received the 3-dose vaccine.

Table 2. Pre-Vaccine and Vaccine Era Disease Incidence Estimates

Disease	Disease incidence per 100,000	
	Without PIP (pre-vaccine)[a]	With PIP (vaccine era)[a]
Diphtheria[7,8]	8	< 1
Hepatitis B[9]	< 1-36[b]	< 1-36
Hib[10,11]	6-69[c]	< 1
Measles[12,13]	15-9,451	1-21
Meningitis C[14-16]	< 1-16	0 to < 1
Mumps[12,17]	77-5,430	1-6
Pertussis[18,19]	10-1,041	5-58
S. pneumoniae		
Invasive pneumococcal disease[20-24]	5-156	2-51
Sp hospitalizations[24-26]	12-716	11-652
Sp outpatient visits[21,24,26]	43-961	42-945
Sp acute otitis media[24,27]	525-5,968[d]	148-1,604[d]
Polio[29,30]	5	0
Rotavirus[31-35]		
Hospitalizations	755-2,372	143-300
Outpatient visits	3,964	798
Rubella[36,37]	0-897	< 1
Tetanus[38,39]	< 1-2	0

Note: Population sizes for Belgium from Statbel were used to calculate incidence rates from reported cases (when applicable).

[a] A range indicates that incidence varies by age group within the presented range.

[b] Reporting of hepatitis B incidence improved after the introduction of a hepatitis B vaccination, so pre-vaccine incidence is likely significantly underreported. Therefore, pre-vaccine incidence was assumed to be the same as vaccine era incidence.

[c] Incidence range is among ages 0-4 years. Incidence was not modeled for ages 5+ years.

[d] Incidence range is among ages 0-17 years. Incidence was not modeled for ages 18+ years.

- Disease severity and cost data were obtained from previous studies. Costs were presented in 2020 Euros.
  - Disease cases in both scenarios were assumed to be treated with the current-day standard of care in Belgium to account for improvements in medical care over time.
- The impact of the Belgium PIP on quality of life was measured through inclusion of the following (with estimates obtained from the published literature):
  - QALYs lost due to vaccine-related adverse events
  - QALYs lost due to acute disease cases and long-term complication
  - QALYs lost due to disease-related mortality
- Analyses
  - Health outcomes and costs were discounted at annual rates of 1.5% and 3.0%, respectively.[40]
  - A benefit-cost ratio (BCR) was calculated for the Belgium PIP by dividing the costs of disease cases averted by the net vaccination costs.
  - Additional scenarios were conducted to consider the following:
    - Hypothetical inclusion of routine varicella immunization
    - Hypothetical inclusion of routine meningococcal B immunization

RESULTS

Table 3. Incremental Health Outcomes by Disease

Disease	Cases averted	Premature deaths averted	LYs gained	QALYs gained
Diphtheria	460	46	1,532	1,348
Hib	116	4	207	306
Measles	84,725	68	3,071	3,425
Meningitis C	67	9	387	414
Mumps	59,938	0	0	261
Pertussis	7,089	3	134	225
Polio	294	6	196	250
Rotavirus[a]	23,822	1	46	133
Rubella	7,989	< 1	4	34
S. pneumoniae[b]	41,768	68	1,221	1,357
Tetanus	56	8	264	234
Total	**226,324**	**214**	**7,062**	**7,988**

Note: Health outcomes are not shown for hepatitis B as cases averted are 0.

[a] Rotavirus total "cases" are reported as a sum of rotavirus-related hospitalizations, emergency department visits, outpatient visits, and nonmedically attended cases. The "cases" sum may be an overestimate of total rotavirus cases in the population, as some events may have multiple rotavirus-related visits.

[b] Total S. pneumoniae "cases" are reported as a sum of cases of invasive pneumococcal disease, pneumococcal pneumonia, and acute otitis media.

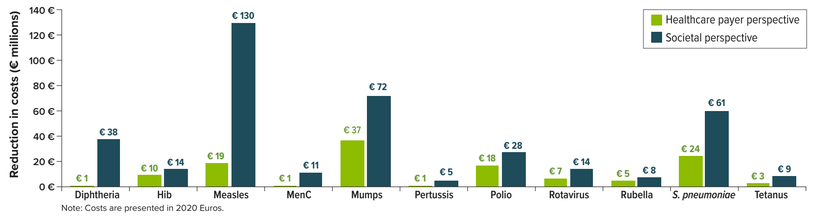
Table 4. Incremental Costs and Benefit-Cost Ratio for the Belgium PIP by Perspective

Incremental outcome	Healthcare payer perspective (€ millions)	Societal perspective (€ millions)
Vaccination costs		
Acquisition	€79	€79
Administration	€11	€11
Adverse events	€1	€1
Time and travel for vaccination	–	€31
Disease-related costs		
Disease treatment	−€126	−€126
Productivity loss due to disease	–	−€110
Productivity loss due to disease-related mortality	–	−€155
Total incremental costs	**−€34**	**−€267**
Benefit-cost ratio	**1.37**	**3.18**
Value of QALYs saved[a]	**–**	**€296**

Note: Costs are presented in 2020 Euros.

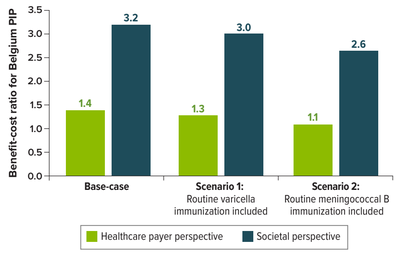
[a] The value of QALYs saved is calculated by multiplying the total QALYs saved with the PIP by a willingness-to-pay threshold of €37,000, which is roughly the GDP per capita in Belgium.

Figure 2. Societal Disease-Related Cost Savings by Disease



Note: Costs are presented in 2020 Euros.

Figure 3. Scenario Analysis Results



Note: A benefit-cost ratio greater than 1 indicates that each Euro invested in the PIP results in more than 1 Euro of disease-related cost savings.

LIMITATIONS

- Underreporting was not considered in disease incidence estimates with and without the PIP.
- Vaccine acquisition costs were obtained from public prices, which do not reflect tender prices and thus likely significantly overestimate vaccine acquisition costs.
- Reporting of HepB incidence improved after the introduction of HepB vaccination, which may result in an underestimate of incidence reductions due to vaccination.
- A static modeling approach was applied for each disease, and as such, important externalities (e.g., herd protection) were not included.
- Limited data were available in the literature for some model inputs defining disease incidence costs, particularly for diseases that are no longer prevalent in Belgium.

CONCLUSIONS

- This analysis estimated that, for one birth cohort of children born in 2018, more than 200,000 disease cases and 200 premature disease-related deaths were prevented due to Belgium's PIP.
- Each Euro invested in childhood immunization resulted in approximately €3 in societal disease-related cost savings for Belgium's PIP.
- Belgium's PIP, which has not previously been systematically assessed, brings large-scale prevention of disease-related morbidity, premature mortality, and associated costs. This highlights the value of continued investment in the PIP.

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