

Estimating the clinical and economic outcomes of universal varicella and herpes zoster vaccination in Belgium using a dynamic transmission model with dynamic population

Lang JC¹; Nachbar RB²; Xausa I²; Bento-Abreu A³; Merckx B³; Pawaskar M⁴

¹BARDS Health Economic and Decision Sciences, Merck Canada Inc., Kirkland, QC, Canada; ²Wolfram Solutions, Champaign, IL, USA; ³MSD Belgium, Brussels, Belgium; ⁴Merck & Co., Inc., Rahway, NJ, USA

Background

- Varicella (chickenpox) is a highly contagious disease caused by the varicella zoster virus (VZV)¹
- Following primary infection, VZV remains dormant in sensory nerve ganglia and may reactivate later in life, resulting in herpes zoster (HZ; shingles)¹
- Whereas universal varicella vaccination (UVV) programs have been shown to significantly reduce varicella incidence, there is some concern that UVV programs may increase the incidence of HZ in the short term²
 - However, 20 years of UVV program in US showed no increase in HZ incidence¹¹
- MMR vaccination is currently administered at 1 year and 8 years of age; varicella vaccination is not currently included in the national immunization program (NIP) of Belgium³

Objective

- To evaluate the clinical and economic outcomes (for both varicella and HZ) of two-dose UVV in Belgium with and without concurrent HZ vaccination over a 50-year time horizon (2023-2072)

Methods

- A previously published dynamic transmission model with dynamic population age structure was adapted to Belgium⁴
 - Exogenous boosting was modeled using a temporary immunity approach²
 - The model was calibrated to varicella seroprevalence⁵ and herpes zoster incidence^{6,7} from Belgium
- UVV comprised both routine and catch-up vaccination
 - Routine 2-dose varicella vaccination at ages 1 and 8 years with vaccine coverage rates (VCR) of 95% and 90%, respectively
 - Catch-up 1-dose varicella vaccination at age 8 years with a VCR of 70% (1-year program duration)
 - Varicella vaccines were assumed to be quadrivalent measles, mumps, rubella, and varicella (MMRV) vaccines, ie, ProQuad® (Merck & Co., Inc., Rahway, NJ, USA)
 - MMRV vaccination was assumed to replace measles, mumps, and rubella (MMR) vaccination³
- HZ vaccination comprised routine vaccination with Shingrix (GlaxoSmithKline Biologicals, Rixensart, Belgium) at age 60 with 50% VCR
- Four strategies were considered: No vaccination, UVV only, HZ vaccination only, and UVV and HZ vaccination
- Outcomes were estimated over a 50-year time horizon (2023-2072)
- Annual discounting of 3% and 1.5% were applied to costs (reported in 2023 euros) and quality-adjusted life-year (QALY) outcomes, respectively
- Both payer (direct costs only) and societal (direct and indirect costs) perspectives were evaluated
- Selected cost inputs are reported in **Table 1**

Table 1. Selected cost inputs (2023 euros)

Model input	Cost (€)	Reference
Vaccination costs		
Varicella vaccination		
MMR vaccine cost per dose	25.80	8
MMRV vaccine cost per dose	73.69	8
MMRV vaccine marginal cost per dose	47.89	Calculated
MMRV marginal administration cost	0	Assumption
HZ vaccination		
HZ vaccine cost per dose	170.26	8
HZ administration cost	30.00	9,a
Direct treatment costs		
Varicella costs		
Cost per outpatient case	44.25	7
Cost per hospitalization	3,538.29	7
HZ costs		
Cost per outpatient case	<50 years: 67.17 50+ years ^b : 107.57-168.61	Calculated
Cost per hospitalization	<50 years: 5,767 50+ years ^b : 5,890-6,044	Calculated
Indirect treatment costs		
Daily wage (ie, productivity loss)	212.02	10

^aAssumed equal to the cost of a general practitioner consultation.
^bRange of values for age cohorts 50 years and older.

Results

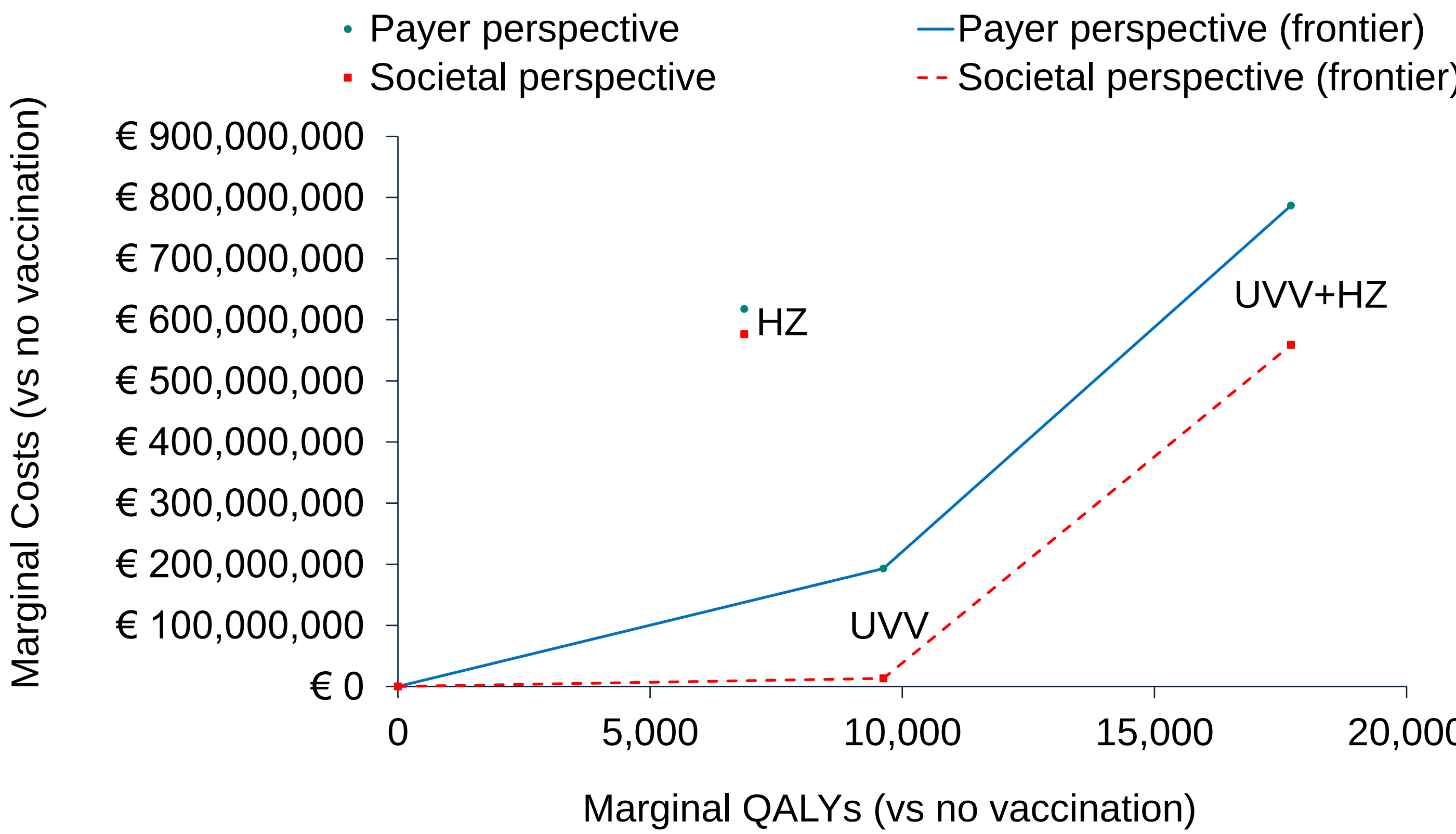
- All strategies resulted in reductions in cumulative varicella and HZ cases over the 50-year time horizon
- Overall, the UVV-only strategy reduced HZ cases by 0.7% relative to no vaccination, however a temporary increase in HZ cases was observed
 - The percent increase in annual HZ cases peaked in 2035 at +3.2%
- Under the HZ vaccination-only and UVV and HZ vaccination strategies, annual HZ cases were lower than under the no vaccination strategy for the entire 50-year time horizon
- The UVV-only strategy resulted in reductions in cumulative varicella cases (90.7%), varicella hospitalizations (89.4%), and varicella mortality (58.2%) (**Table 2**)
- Under both payer and societal perspectives, the cost-effectiveness frontier consisted of the no vaccination, UVV only, and UVV and HZ vaccination strategies; the HZ vaccination-only strategy was dominated (**Figure 1**)
- Under both payer and societal perspectives, the UVV-only strategy was cost effective in Belgium at a willingness to pay (WTP) threshold of 1xGDP (€36,860) (**Table 2, Figure 1**)

Table 2. Cumulative outcomes and frontier analysis

Strategy	Varicella cases n (% averted)	HZ cases n (% averted)	QALYs lost	Costs (€; in thousands)		Incremental ICER ^a	
				Payer perspective	Societal perspective	Payer perspective	Societal perspective
No vaccination	6,527,751	3,437,667	66,414	€635,748	€1,523,656	N/A	
UVV only	605,864 (90.7%)	3,412,142 (0.7%)	56,787	€828,753	€1,536,953	€20,048	€1,381
HZ vaccination only	6,525,904 (0%)	3,044,798 (11.4%)	59,545	€1,253,339	€2,099,961	Dominated	
UVV and HZ vaccination	585,523 (91.0%)	2,944,787 (14.3%)	48,706	€1,442,637	€2,082,437	€73,494	€67,505

^aIncremental cost-effectiveness ratio.

Figure 1. Cost-effectiveness frontier



Limitations

- Exogenous boosting was modeled using a temporary immunity approach. Research on alternative approaches to modeling exogenous boosting, eg, the progressive immunity approach, is ongoing
- We assumed that there was no productivity loss for individuals who contracted HZ after retirement (ie, ages 65 and older); therefore, the incremental ICER for the UVV and HZ vaccination strategy under the societal perspective can be considered a conservative estimate
- Sensitivity analysis was not conducted as part of this study and is left as future work

Conclusions

Two-dose UVV significantly reduced the burden of varicella with marginal impact on HZ incidence and was cost effective in Belgium compared to no vaccination

Disclosures

- This study was funded by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.
- JCL is an employee of Merck Canada Inc., a subsidiary of Merck & Co., Inc., Rahway, NJ, USA. MP is an employee of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA. ABA and BM are employees of MSD subsidiaries of Merck & Co., Inc., Rahway, NJ, USA. RBN and IX are employees of Wolfram Research Inc. under contract to Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA. JCL, MP, ABA, BM, and RBN may hold stock or stock options in Merck & Co., Inc., Rahway, NJ, USA.

Acknowledgments

We would like to acknowledge Jessica Vandenhaute and Margot Van Elsen (Medical Affairs, MSD Belgium, Brussels, Belgium) for their contributions in developing the vaccination strategies considered in this analysis.

References

- Heininger U, Seward JF. *Lancet*. 2006;368(9544):1365-1476.
- Talbird SE, et al. *Expert Rev Vaccines*. 2018;17(11):1021-1035.
- Health Belgium. Calendrier vaccinal de base recommandé par le Conseil Supérieur de la Santé – Juin 2021. 2021. <https://www.health.belgium.be/fr/avis-9606-calendrier-vaccinal-de-base>. Accessed March 7, 2024.
- Sharomi O, et al. *Vaccines (Basel)*. 2022;10(9):1416.
- Mossong J, et al. *Epidemiol Infect*. 2008;136(8):1059-1068.
- Truyers C, et al. *BMC Med Inform Decis Mak*. 2014;14:48.
- Bilcke J, et al. *Epidemiol Infect*. 2012;140(11):2096-2109.
- Belgian Center for Pharmacotherapeutic Information. Vaccin tegen zona. 2023. <https://www.bcfi.be/nl/chapters/13?frag=20636>. Accessed March 21, 2023.
- The General Practitioner. General practitioners: consultation rates 2024. 2024. <https://www.cm.be/en/services-and-benefits/general-practitioner-rates-consultation>. Accessed April 15, 2024.
- StatBel. An overview of Belgian wages and salaries, 2022. <https://statbel.fgov.be/en/themes/work-training/wages-and-labourcost/overview-belgian-wages-and-salaries>. Accessed May 11, 2023.
- Leung, J et al. *The Journal of Infectious Diseases*. 2022: 226(Suppl. 4): S470-S477.