

### **Online Supplementary Material**

The Long-term Clinical and Economic Impact of Universal Varicella Vaccination in Slovenia. *JHEOR*. 2022;9(2):95-102. [doi:10.36469/jheor.2022.37308](https://doi.org/10.36469/jheor.2022.37308)

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This supplementary material has been provided by the authors to give readers additional information about their work.



**Table S1.** Vaccine Characteristics for Modeled Vaccine Formulations

Vaccine/Dose	Failure (%)	Vaccine Take, Range (%)	Duration of Protection, Range (y)	References
First dose				
MSD varicella-containing vaccines	4	100 (93-100)	25 (15-67)	Kuter et al (2004) <sup>1</sup> ; van Hoek et al (2011) <sup>2</sup>
GSK varicella-containing vaccines	5	65.4 (57.2-72.1)	17 (NR)	Holl et al (2016) <sup>3</sup> ; Kuter et al (2004) <sup>1</sup> ; Ouwens et al (2015) <sup>4</sup> ; Prymula et al (2014) <sup>5</sup> ; van Hoek et al (2011) <sup>2</sup>
Second dose				
MSD varicella-containing vaccines	NA	100 (97-100)	77 (38-200)	Kuter et al (2004) <sup>1</sup> ; van Hoek et al (2011) <sup>2</sup>
GSK varicella-containing vaccines	NA	94.9 (92.4-96.6)	77 (NR)	Holl et al (2016) <sup>3</sup> ; Ouwens et al (2015) <sup>4</sup> ; Prymula et al (2014) <sup>5</sup>

Abbreviations: GSK, GlaxoSmithKline Biologicals, Belgium, UK; MSD, Merck & Co, Inc, Rahway, New Jersey; NA, not applicable; NR, not reported.

**Table S2.** Base Model Parameters (Disease-Specific)

Symbol	Description	Value	Source
$1/\omega_m$	Average period of passive immunity	6 months	Gershon et al (1976) <sup>6</sup>
$1/\varepsilon_n, 1/\varepsilon_{vb}$	Average latent period (natural, breakthrough varicella)	14 days	Marin & Bialek (2015) <sup>7</sup> ; Brisson et al (2000) <sup>8</sup>
$1/\gamma_n$	Average infectious period for natural varicella	7 days	Bernstein et al (1993) <sup>9</sup> ; Marin & Bialek (2015) <sup>7</sup>
$1/\gamma_{bv}$	Average infectious period for breakthrough varicella	4.5 days	Izurieta et al (1997) <sup>10</sup>
$\rho_v$	Relative infectivity of breakthrough varicella infection	50%	Seward et al (2004) <sup>11</sup> ; Brisson et al (2000) <sup>8</sup>
$\xi_n, \xi_{pv}, \xi_{vb}$	Rate of endogenous boosting	0	Assumed
$\chi$	Reactivation rate factor on vaccine arms	1/6	Poletti et al (2013) <sup>12</sup>
$\beta$	Transmission matrix		From calibration
$\mu$	Force of mortality		Derived
$d_v$	Case fatality rate for natural varicella (per 100 000)	<1 y: 1.04 1-5 y: 0.26 5-10 y: 0.65 10-15 y: 3.12 15-45 y: 31.22 45-65 y: 322.56 ≥65 y: 1461.06	Wolfson et al (2019) <sup>13</sup>

**Table S3.** Key Model Inputs and Data Source for Varicella Infection in Slovenia

Parameter	Values	Source
<b>Vaccination Costs</b>		
Vaccine <sup>a,b</sup> (€)	Varicella: 31.84 MMRV: 51.52	Centralna baza zdravil <sup>14</sup> ; Österreichischer Apotheker-Verlag <sup>15</sup> ; Uradni List Republike Slovenije, 2020 <sup>16</sup>
Vaccine administration <sup>c</sup> (€)	5.62	Zavod Za Zdravstveno Zavarovanje Slovenije <sup>17</sup>
<b>Direct Costs</b>		
Percentage of cases requiring outpatient visits	0-5 y: 69% 5-9 y: 57% ≥10 y: 100%	Dozsa et al (2017) <sup>18</sup>
Cost per outpatient visit (€)	<15 y: 8.83 ≥15 y: 14.28	Zavod Za Zdravstveno Zavarovanje Slovenije <sup>17</sup>
Percentage of cases requiring hospitalization	<15 y: 0.69 ≥15 y: 1.38	Ahčan et al. 2002 <sup>19</sup> ; Heininger & Seward (2006) <sup>20</sup>
Cost per hospitalization (€)	672.78	Zavod Za Zdravstveno Zavarovanje Slovenije <sup>17</sup>
<b>Indirect Costs</b>		
Days lost from work (outpatient and inpatient)	<18 y: 5.5 18-65 y: 12.3 65+ y: 0	Statistical office of the National Institute of Public Health <sup>21</sup>
Cost per workday lost (€)	64.06	Republika Slovenija Statistični Urad <sup>22</sup>

<sup>a</sup>Varilrix<sup>®</sup> is not currently available in Slovenia, therefore, price parity with Varivax<sup>®</sup> was assumed.

<sup>b</sup>MMRV prices have been adjusted to reflect the V-component of the vaccine only.

<sup>c</sup>Vaccine administration costs include immunization, exam, organization, vaccination schedule, vaccine purchase, editing records, and reports. No additional administration costs are assumed for MMRV at the second dose.

**Table S4.** Health State Utility Values Used in the Model

Health State	Utility by Age (y)							
	<18	18-25	25-35	35-45	45-55	55-65	65-75	75+
Healthy ( $q_h$ ) <sup>23</sup>	0.869	0.869	0.841	0.794	0.712	0.619	0.554	0.498
	Utility by Age (y)							
	<15	15-40	40-60	60-70	70-80	80+		
Natural varicella ( $q_n$ ) <sup>24</sup>	0.79	0.74	0.74	0.74	0.74	0.74		
Breakthrough varicella ( $q_v$ ) <sup>24</sup>	0.92	0.92	0.92	0.92	0.92	0.92		

Figure S1. Model Calibration to Observed Prevaccination Varicella Seroprevalence by Age in Slovenia

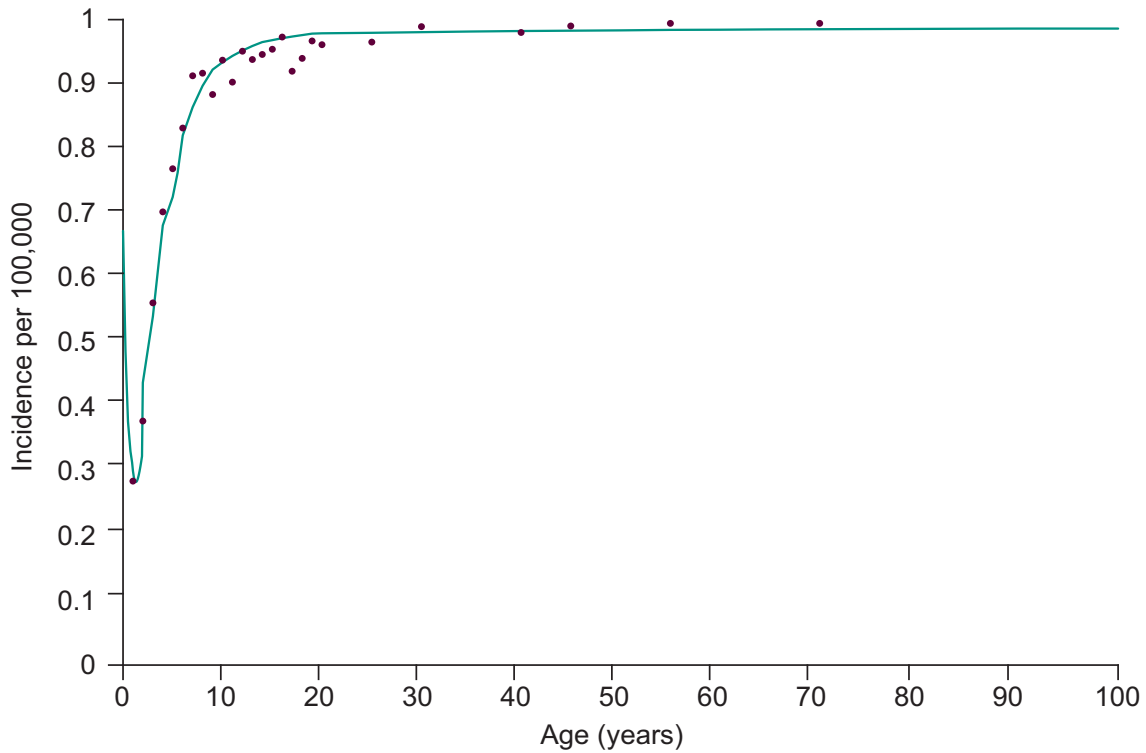
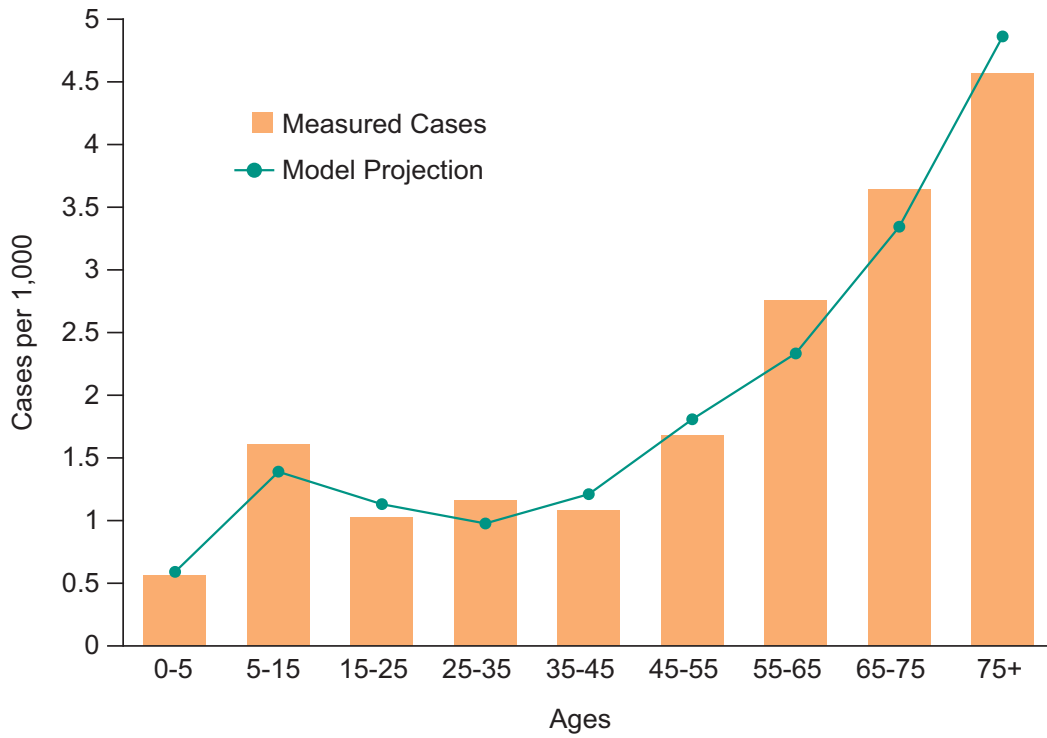
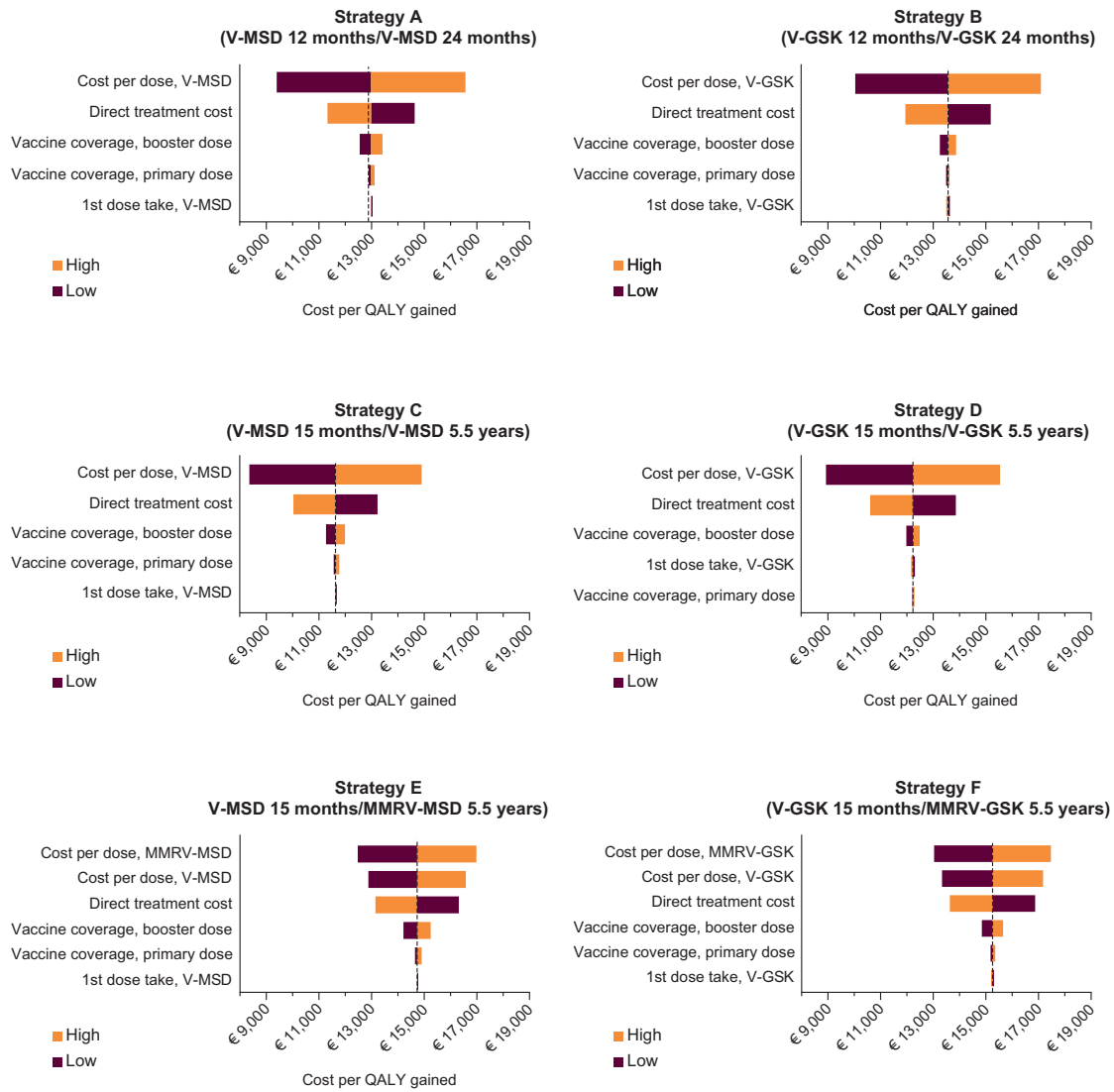


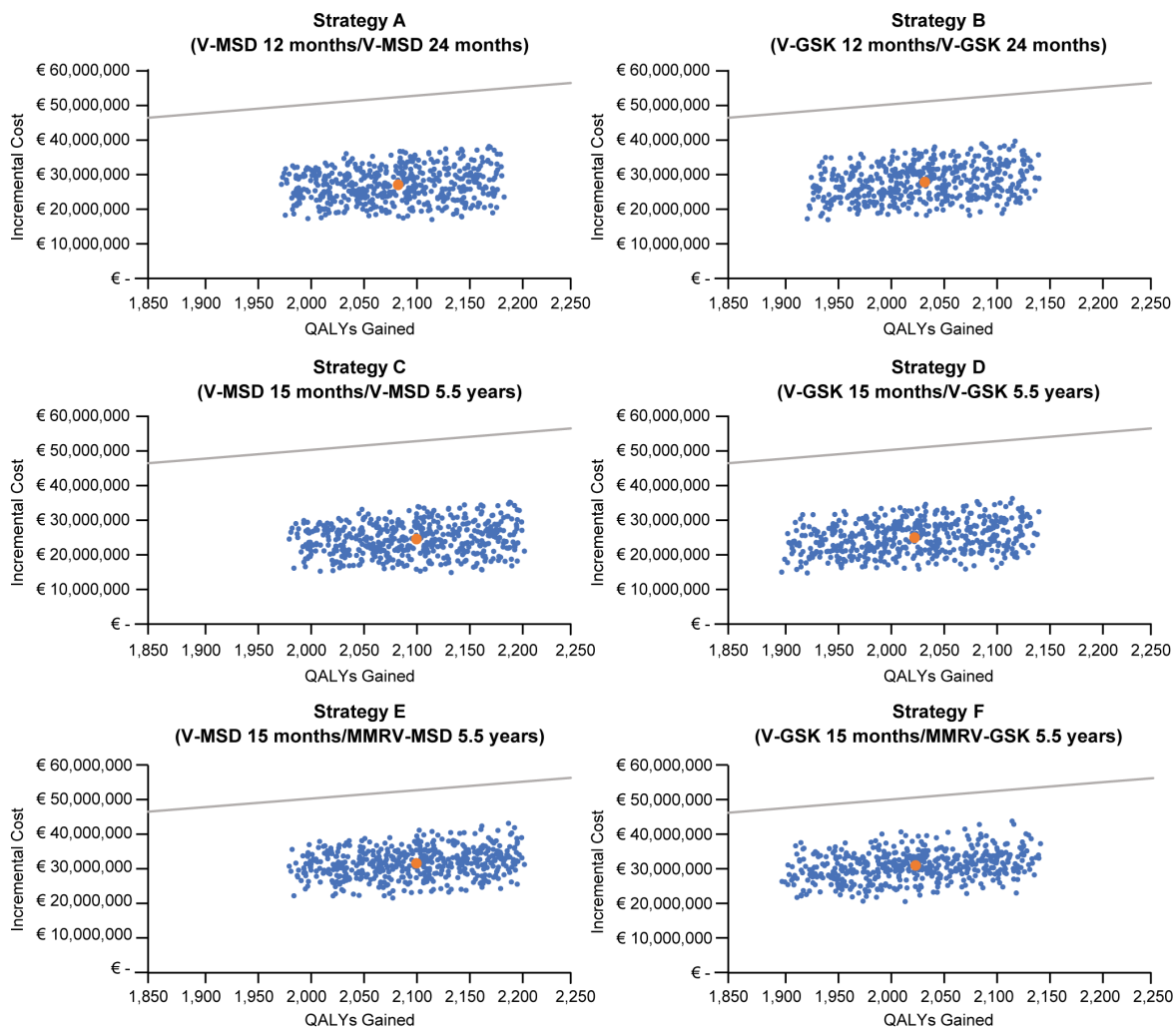
Figure S2. Model Calibration to Observed Prevaccination Herpes Zoster Incidence by Age in Slovenia



**Figure S3.** Change in ICER vs No Vaccination After Varying Economic Parameters and Vaccine Properties, From the Payer Perspective

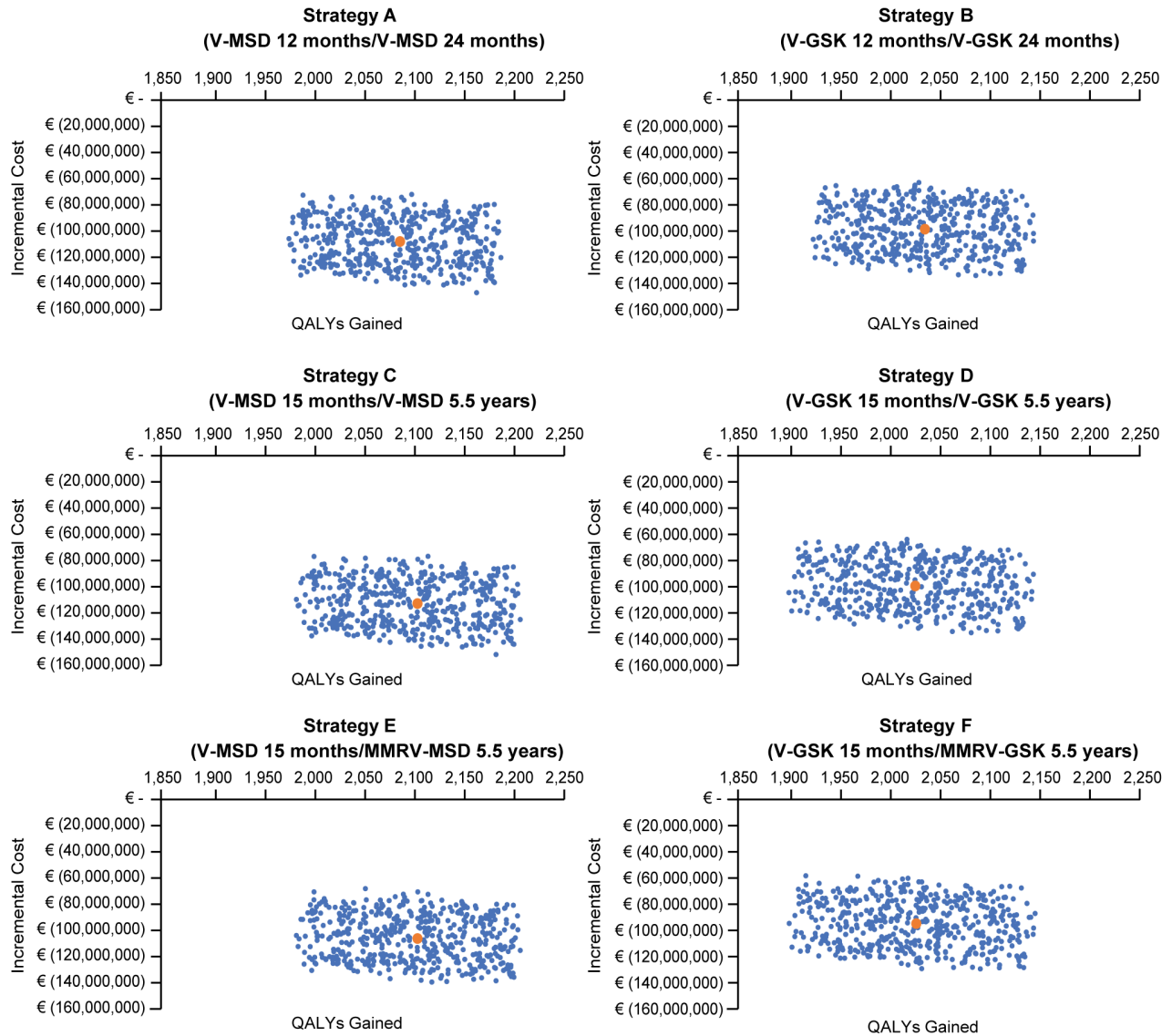


Abbreviations: GSK, GlaxoSmithKline Biologicals, Belgium, UK; MMRV, measles, mumps, rubella, and varicella vaccine; MSD, Merck & Co, Inc, Rahway, New Jersey; QALY, quality-adjusted life-year; V, varicella vaccine.

**Figure S4.** Results of Probabilistic Sensitivity Analysis Varying Economic Parameters and Vaccine Properties, From the Payer Perspective

Solid gray line represents the cost-effectiveness threshold of €25 000 per QALY gained for Slovenia.

Abbreviations: GSK, GlaxoSmithKline Biologicals, Belgium, UK; MMRV, measles, mumps, rubella, and varicella vaccine; MSD, Merck & Co, Inc, Rahway, New Jersey; QALYs, quality-adjusted life-years; V, varicella vaccine.

**Figure S5.** Results of Probabilistic Sensitivity Analysis Varying Economic Parameters and Vaccine Properties, From the Societal Perspective

Abbreviations: GSK, GlaxoSmithKline Biologicals, Belgium, UK; MMRV, measles, mumps, rubella, and varicella vaccine; MSD, Merck & Co, Inc, Rahway, New Jersey; QALYs, quality-adjusted life-years; V, varicella vaccine.

## REFERENCES

1. Kuter B, Matthews H, Shinefield H, et al. Ten year follow-up of healthy children who received one or two injections of varicella vaccine. *Pediatr Infect Dis J.* 2004;23(2):132-137.
2. Van Hoek AJ, Melegaro A, Zagheni E, Edmunds WJ, Gay N. Modelling the impact of a combined varicella and zoster vaccination programme on the epidemiology of varicella zoster virus in England. *Vaccine.* 2011;29(13):2411-2420.
3. Holl K, Sauboin C, Amodio E, Bonanni P, Gabutti G. Coverage, efficacy or dosing interval: which factor predominantly influences the impact of routine childhood vaccination for the prevention of varicella? A model-based study for Italy. *BMC Public Health.* 2016;16(1):1-11.
4. Ouwens MJ, Littlewood KJ, Sauboin C, et al. The impact of 2-dose routine measles, mumps, rubella, and varicella vaccination in France on the epidemiology of varicella and zoster using a dynamic model with an empirical contact matrix. *Clin Ther.* 2015;37(4):816-829. e810.
5. Prymula R, Bergsaker MR, Esposito S, et al. Protection against varicella with two doses of combined measles-mumps-rubella-varicella vaccine versus one dose of monovalent varicella vaccine: a multicentre, observer-blind, randomised, controlled trial. *Lancet.* 2014;383(9925):1313-1324.
6. Gershon AA, Raker R, Steinberg S, Topf-Olstein B, Drusin LM. Antibody to varicella-zoster virus in parturient women and their offspring during the first year of life. *Pediatrics.* 1976;58(5):692-696.
7. Marin M, Bialek SR. Varicella/Herpes Zoster. In: *Control of Communicable Diseases Manual.* 16th ed. Washington, DC: American Public Health Association; 2015.
8. Brisson M, Edmunds W, Gay N, Law B, De Serres G. Modelling the impact of immunization on the epidemiology of varicella zoster virus. *Epidemiol Infect.* 2000;125(3):651-669.
9. Bernstein HH, Rothstein EP, Watson BM, et al. Clinical survey of natural varicella compared with breakthrough varicella after immunization with live attenuated Oka/Merck varicella vaccine. *Pediatrics.* 1993;92(6):833-837.
10. Izurieta HS, Strebel PM, Blake PA. Postlicensure effectiveness of varicella vaccine during an outbreak in a child care center. *JAMA.* 1997;278(18):1495-1499.
11. Seward JF, Zhang JX, Maupin TJ, Mascola L, Jumaan AO. Contagiousness of varicella in vaccinated cases: a household contact study. *JAMA.* 2004;292(6):704-708.
12. Poletti P, Melegaro A, Ajelli M, et al. Perspectives on the impact of varicella immunization on herpes zoster. A model-based evaluation from three European countries. *PLoS One.* 2013;8(4):e60732.
13. Wolfson LJ, Daniels VJ, Pillsbury M, et al. Cost-effectiveness analysis of universal varicella vaccination in Turkey using a dynamic transmission model. *PLoS One.* 2019;14(8):e0220921.
14. Centralna baza zdravil. Podrobni podatki o zdravilu - Varivax; Nacionalna šifra zdravila: 041599. 2019. Accessed November 2021. <http://www.cbz.si/cbz/bazazdr2.nsf/o/94A96582A326CDEBC12579C2003F64AC?opendocument>
15. Österreichischer Apotheker-Verlag. Waren Verzeichnis. Accessed November 2021. <https://warenverzeichnis.apoverlag.at/>
16. Uradni List Republike Slovenije. Državni Zbor 16 March 2020. Accessed November 2021. <https://www.uradni-list.si/pdf/2020/Uru2020026.pdf>
17. Zavod Za Zdravstveno Zavarovanje Slovenije. Akontativne cene 2020. Published 2020 (SD 2018). Accessed December 2019. <http://www.zzs.si>
18. Dozsa C, Mezner, Z., Patri, L., Benedek, A., Kalmar, J., Weiss, T.J., et al. The costs and benefits of varicella vaccination in Hungary. Paper presented at: World Congress of the Society for Pediatric Infectious Disease (WSPID): 10th conference. December 2-5, 2017; Shenzhen, China.
19. Ahčan J, Cizman M, Pleterski-Rigler D, Rakar R. Value of universal childhood varicella vaccination in Slovenia. *Zdr Vestn.* 2002;71(11):667-672.
20. Heininger U, Seward JF. Varicella. *Lancet.* 2006;368(9544):1365-1376.
21. Statistical office of the National Institute of Public Health. Data for 2014–2018. Email communication; April 2020.
22. Republika Slovenija Statistični Urad. Plače in stroški dela. Accessed November 2021. <https://www.stat.si/StatWeb/Field/Index/15>
23. Szende A, Janssen B, Cabases J. Self-Reported Population Health: An International Perspective based on EQ-5D. Dordrecht (NL): Springer; 2014.
24. Brisson M, Edmunds WJ. Varicella vaccination in England and Wales: cost-utility analysis. *Arch Dis Child.* 2003;88(10):862-869.