

GRADE Table 2. Effectiveness of one dose varicella vaccination in immunocompetent children (9 months to 12 years of age) in preventing severe varicella (evidence available for within the first 10 years after vaccination)

Population: Immunocompetent children (9 month to 12 years of age)

Intervention: One dose varicella vaccination

Comparison: Placebo/ no vaccination

Outcome: Severe varicella (mostly defined as >500 lesions, complication requiring physician visit, hospitalization, death); two studies defined severe disease as >250 and >200 lesions and two defined severity in accordance with a modified disease severity score from clinical trials

<i>What is the scientific evidence of the effectiveness of one dose of varicella vaccination (versus placebo/no vaccination) in preventing severe varicella disease (≥500 lesions) in immunocompetent children (9 month to 12 years of age)?</i>				
			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating		29/ Observational ¹	2
	Factors decreasing confidence	Limitation in study design	None serious	0
		Inconsistency	None serious	0
		Indirectness	None serious	0
		Imprecision	None serious	0
		Publication bias	None serious	0
	Factors increasing confidence	Large effect	Applicable ²	+2
		Dose-response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			4
Summary of Findings	Statement on quality of evidence			We are very confident that the true effect lies close to that of the estimate of effect on health outcome
	Conclusion			A single dose of varicella vaccination is highly effective to protect children of 9 months to 12 years against severe varicella disease, with vaccine effectiveness (VE) of 95% for preventing moderate-severe disease and VE of 99% for preventing severe disease only.

¹ Two systematic reviews (Seward et al. 2008; Bayer et al. 2007) and a [systematic review](#) conducted by WHO on the current literature (through October 2013) identified 25 relevant observational studies. Included studies provided vaccine effectiveness data on the predefined outcome of severe varicella or on moderate-severe varicella. Studies that did not specifically report a VE value reported that no cases of hospitalization or severe complications were observed. Single dose varicella VE against moderate and severe disease ranged from 78 – 100%, with an approximate mean VE of 95%, irrespective of vaccine type. Of the sixteen studies reporting a VE value against severe varicella, fifteen reported a VE of 100% and only one study (Huang, 2011) reported a VE of 85%.

² Upgraded by two levels as strong evidence from observational studies of a vaccine effectiveness of 80% or higher with no major residual confounders. Vaccine effectiveness against severe varicella was 100% in 15/16 studies. In addition to effectiveness on an individual level, decline in incidence in all age groups over time, not only age-group targeted by vaccination program, suggests induction of community protection (Marin et al 2008, Marin et al 2011, Lopez et al 2011, Guris et al 2008).

Reference List

1. Seward JF, Marin M, Vazquez M. Varicella vaccine effectiveness in the US vaccination program: a review. *J Infect Dis* 2008;197 Suppl 2:S82-S89.
2. Outbreak of varicella among vaccinated children--Michigan, 2003 27. *MMWR Morb Mortal Wkly Rep* 2004;53(18):389-392.
3. Varicella outbreak among vaccinated children--Nebraska, 2004 22. *MMWR Morb Mortal Wkly Rep* 2006;55(27):749-752.
4. Arnedo-Pena A, Puig-Barbera J, Aznar-Orenga MA et al. Varicella vaccine effectiveness during an outbreak in a partially vaccinated population in Spain 4. *Pediatr Infect Dis J* 2006;25(9):774-778.
5. Buchholz U, Moolenaar R, Peterson C, Mascola L. Varicella outbreaks after vaccine licensure: should they make you chicken? 1. *Pediatrics* 1999;104(3 Pt 1):561-563.
6. Cenoz MG, Martinez-Artola V, Guevara M, Ezpeleta C, Barricarte A, Castilla J. Effectiveness of one and two doses of varicella vaccine in preventing laboratory-confirmed cases in children in Navarre, Spain 1. *Hum Vaccin Immunother* 2013;9(5).
7. Clements DA, Moreira SP, Coplan PM, Bland CL, Walter EB. Postlicensure study of varicella vaccine effectiveness in a day-care setting. *Pediatr Infect Dis J* 1999;18(12):1047-1050.
8. Galil K, Lee B, Strine T et al. Outbreak of varicella at a day-care center despite vaccination. *N Engl J Med* 2002;347(24):1909-1915.
9. Galil K, Fair E, Mountcastle N, Britz P, Seward J. Younger age at vaccination may increase risk of varicella vaccine failure 8. *J Infect Dis* 2002;186(1):102-105.
10. Gould PL, Leung J, Scott C et al. An outbreak of varicella in elementary school children with two-dose varicella vaccine recipients--Arkansas, 2006. *Pediatr Infect Dis J* 2009;28(8):678-681.
11. Haddad MB, Hill MB, Pavia AT et al. Vaccine effectiveness during a varicella outbreak among schoolchildren: Utah, 2002-2003 1. *Pediatrics* 2005;115(6):1488-1493.
12. Huang WC, Huang LM, Chang IS, Tsai FY, Chang LY. Varicella breakthrough infection and vaccine effectiveness in Taiwan 4. *Vaccine* 2011;29(15):2756-2760.
13. Izurieta HS, Strebel PM, Blake PA. Postlicensure effectiveness of varicella vaccine during an outbreak in a child care center 5. *JAMA* 1997;278(18):1495-1499.
14. Kilic A, Unuvar E, Yilmaz C, Yildiz I, Oguz F, Sidal M. The effectiveness of varicella vaccination during an outbreak in a children's day-care center 2. *Vaccine* 2008;26(27-28):3371-3372.
15. Lai CC, Chen SC, Jiang DD. An outbreak of varicella among schoolchildren in Taipei. *BMC Public Health* 2011;11:226.

16. Lee BR, Feaver SL, Miller CA, Hedberg CW, Ehresmann KR. An elementary school outbreak of varicella attributed to vaccine failure: policy implications 9. *J Infect Dis* 2004;190(3):477-483.
17. Liese JG, Cohen C, Rack A et al. The effectiveness of varicella vaccination in children in Germany: a case-control study 2. *Pediatr Infect Dis J* 2013;32(9):998-1004.
18. Lopez AS, Guris D, Zimmerman L et al. One dose of varicella vaccine does not prevent school outbreaks: is it time for a second dose? 5. *Pediatrics* 2006;117(6):e1070-e1077.
19. Lu L, Suo L, Li J et al. A varicella outbreak in a school with high one-dose vaccination coverage, Beijing, China. *Vaccine* 2012;30(34):5094-5098.
20. Marin M, Nguyen HQ, Keen J et al. Importance of catch-up vaccination: experience from a varicella outbreak, Maine, 2002-2003 8. *Pediatrics* 2005;115(4):900-905.
21. Miron D, Lavi I, Kitov R, Hendler A. Vaccine effectiveness and severity of varicella among previously vaccinated children during outbreaks in day-care centers with low vaccination coverage. *Pediatr Infect Dis J* 2005;24(3):233-236.
22. Parker AA, Reynolds MA, Leung J et al. Challenges to implementing second-dose varicella vaccination during an outbreak in the absence of a routine 2-dose vaccination requirement--Maine, 2006 2. *J Infect Dis* 2008;197 Suppl 2:S101-S107.
23. 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.
24. Sheffer R, Segal D, Rahamani S et al. Effectiveness of the Oka/GSK attenuated varicella vaccine for the prevention of chickenpox in clinical practice in Israel 1. *Pediatr Infect Dis J* 2005;24(5):434-437.
25. Spackova M, Wiese-Posselt M, Dehnert M, Matysiak-Klose D, Heininger U, Siedler A. Comparative varicella vaccine effectiveness during outbreaks in day-care centres 2. *Vaccine* 2010;28(3):686-691.
26. Tafuri S, Martinelli D, Prato R, Germinario C. Vaccine effectiveness evaluation during a varicella outbreak among children of primary schools and day-care centers in a region which adopted UMV 1. *Hum Vaccin Immunother* 2013;9(1):184-188.
27. Tugwell BD, Lee LE, Gillette H, Lorber EM, Hedberg K, Cieslak PR. Chickenpox outbreak in a highly vaccinated school population 1. *Pediatrics* 2004;113(3 Pt 1):455-459.
28. Vally H, Dowse GK, Eastwood K, Cameron S. An outbreak of chickenpox at a child care centre in Western Australia. Costs to the community and implications for vaccination policy 2. *Aust N Z J Public Health* 2007;31(2):113-119.
29. Vazquez M, LaRussa PS, Gershon AA, Steinberg SP, Freudigman K, Shapiro ED. The effectiveness of the varicella vaccine in clinical practice. *N Engl J Med* 2001;344(13):955-960.
30. Vazquez M, LaRussa PS, Gershon AA et al. Effectiveness over time of varicella vaccine 2. *JAMA* 2004;291(7):851-855.

31. Bayer O, Heininger U, Heiligensetzer C, Von KR. Metaanalysis of vaccine effectiveness in varicella outbreaks 1. *Vaccine* 2007;25(37-38):6655-6660.
32. Marin M, Meissner HC, Seward JF. Varicella prevention in the United States: a review of successes and challenges 3. *Pediatrics* 2008;122(3):e744-e751.
33. Marin M, Zhang JX, Seward JF. Near elimination of varicella deaths in the US after implementation of the vaccination program 1. *Pediatrics* 2011;128(2):214-220.
34. Lopez AS, Zhang J, Brown C, Bialek S. Varicella-related hospitalizations in the United States, 2000-2006: the 1-dose varicella vaccination era 5. *Pediatrics* 2011;127(2):238-245.
35. Guris D, Jumaan AO, Mascola L et al. Changing varicella epidemiology in active surveillance sites--United States, 1995-2005 1. *J Infect Dis* 2008;197 Suppl 2:S71-S75.