



Non-Live Recombinant Herpes Zoster Vaccine (SHINGRIX)

Bottom Line...

- SHINGRIX** is indicated for the **prevention of herpes zoster (HZ or shingles) in adults age ≥ 50**
- SHINGRIX** reduces the risk of **shingles** by 91% (ARR=3.1%, **NNT=32**) & postherpetic neuralgia (PHN) by ~90% (ARR=0.30%, **NNT=333**) in 3 yrs. **NNT: Eg. for every 333 vaccinated with SHINGRIX, 10 shingle cases (age ≥50 years) and 1 PHN cases (age ≥50 years) were prevented over ~ 3 yrs.**
- SHINGRIX** demonstrated efficacy for prevention of shingles effective in all age groups 50-80+. **ZOSTAVAX** less effective with increasing age.
- SHINGRIX** use in patients with a **history of shingles** has been studied {open-label, non-randomized trial (n=93 patients, age 50-89 yr) for 3 months}. ^{ZOSTER-033} Vaccine can be given after shingles symptoms/rash resolved ^{CDN} or ≥1 yr ^{CDN}
- Cost ~ \$ 300 for 2 doses given intramuscularly (IM) 2-6 months apart** (can give up to 12 months apart if needed to increase compliance). (Refrigerate 2 to 8°C; Discard if frozen)
- Canadian NACI'18 recommends SHINGRIX should be offered to individuals >50 yrs without contraindications** including:
 - Individuals previously vaccinated with **ZOSTAVAX**; Re-vaccinate with two doses of RZV at least one year after receiving Zostavax
 - Individuals with a previous episode of herpes zoster disease. Provide two doses of **SHINGRIX** at least one year after herpes zoster episode
 - Immunocompromised individuals, may be considered on a case-by-case assessment of the benefits vs risks**ZOSTAVAX** may be considered for immunocompetent individuals >50 yrs of age without contraindications when **SHINGRIX** is contraindicated, unavailable or inaccessible.
- Advisory Committee on Immunization Practices (ACIP USA) recommends SHINGRIX as the preferred vaccine for preventing shingles and related complications. ACIP also recommends SHINGRIX (give both of the 2 doses) for adults who previously received ZOSTAVAX.**
 - o Administer **SHINGRIX** as early as 8 weeks after **ZOSTAVAX**, but especially after 5 years (as **ZOSTAVAX** efficacy declines over time).
- Outstanding Questions: Is SHINGRIX safe & effective in immunocompromised patients? Is it beneficial for patients with a history of shingles? What is the long-term effectiveness?**

What is SHINGRIX? ^{1,2,3,4,5,6,7,8}

- Herpes Zoster (shingles) vaccine** contains NON-live, recombinant, AS01B adjuvanted herpes zoster vaccine. This vaccine contains antigen glycoprotein E, which is the most abundant antigen in varicella zoster vaccine (VZV) infected cells and the main target for VZV-specific CD4+ T-cell response. This vaccine also includes adjuvant AS01 that helps to elicit an early, high and long-lasting response with less antigen.
- Indicated for prevention of shingles in **patients ≥50yrs. Not** for treating shingles, PHN or preventing primary varicella infection.

Is SHINGRIX effective? Two Studies: Efficacy of the Herpes Zoster Subunit Vaccine: in Adults 70 years of age or older (ZOE-70) ²⁰¹⁶ & in Older Adults (ZOE-50) ²⁰¹⁵

ZOE-70: n = 13,900, mean age ~76 yr, 62-96yr, 22.1% ≥ 80 yr, 0.5% ≥ 90 yr, 45.1% ♂, 19% North American, 51% European, 77% white, ~95% received both doses, 3.7 yr follow-up.
ZOE-50: n=15,411, mean age = 62 yr, 61.2% ♂, 51% European, 19% North American, 72% white, 3.2 yr follow-up
 Both studies: Blinded investigators, participants and those responsible for the evaluation of any study endpoint (study staff who prepared injection were not blinded), RCT, excluded history of shingles, previously vaccinated against varicella or herpes zoster or immunosuppressed, significant underlying illness or other condition that may interfere with study assessments (e.g. cognitive impairment, chronic pain syndrome); no intention to treat analysis was performed.

Clinical Outcomes (Pooled ZOE-70 & ZOE-50)*	Vaccine %, n = 8250		Placebo %, n = 8346		RRR		ARR		NNT over ~3yrs NNH within 7 days		Efficacy:
	ZOE-50 N=4382	ZOE-70 N=505	ZOE-50 N=4382	ZOE-70 N=505	ZOE-50	ZOE-70	ZOE-50	ZOE-70	ZOE-50 NNH	ZOE-70 NNH	
Incidence of shingles (overall)	0.30%, n=25		3.40%, n=284		91.3%		3.10%		NNT = 32		<input type="checkbox"/> Efficacy for prevention of shingles decreases over time (97.6% → 87.9% over 4 years) <input type="checkbox"/> Optimal age for benefit in incidence of PHN: Age > 69 SHINGRIX vs ZOSTAVAX studies: <input type="checkbox"/> ZOSTAVAX - higher incidence of <u>Shingles</u> in 3.1year study (n=38,546): ⁹ <ul style="list-style-type: none"> o Overall Age ≥ 60 yrs: 1.64% vs 3.33% placebo o Age 60-69yrs: 1.18% vs 3.22% placebo o Age >70yrs: 2.17% vs. 3.46% placebo <input type="checkbox"/> ZOSTAVAX - higher incidence of <u>PHN</u> in 3.1year study: <ul style="list-style-type: none"> o Overall Age ≥ 60 yrs: 0.14% vs 0.42% placebo o Age 60-69yrs: 0.08% vs 0.22% placebo o Age >70yrs: 0.21% vs. 0.64% placebo <input type="checkbox"/> ZOSTAVAX - More frail, more active surveillance, and/or the use of a more sensitive case definition?
Age 70-79 yr	0.29% (n=19/6468)		3.30% (n=284/8346)		91.3%		3.01%		33 / 3 yrs		
Age ≥ 80 yr	0.34% (n=6/1782)		3.79% (n=68/1792)		91.4%		3.45%		29 / 3 yrs		
Year 1	0.02% (n=2/8250)		0.99% (n=83/8346)		97.6%		0.97%		103@1yr		
Year 2	0.09% (n=7/8039)		1.08% (n=87/8024)		92.0%		0.99%		156@2yr		
Year 3	0.12% (n=9/7736)		0.76% (n=58/7661)		84.7%		0.64%		172@3yr		
Year 4	0.09% (n=7/7426)		0.77% (n=56/7267)		87.9%		0.68%		147@4yr		
Incidence of PHN ≥ 70 yr	0.05%, (n=4/8250)		0.43% (n=36/8346)		88.8%		0.38%		NNT over 3.8y		
≥ 50 yr	0.03% (n=4/13881)		0.33% (n=46/14035)		91.2%		0.30%		263		
Age 50-59 yr	0.00% (n=0/3491)		0.23% (n=8/3523)		100.0%		0.23%		435		
Age 60-69 yr	0.00% (n=0/2140)		0.09% (n=2/2166)		100.0%		0.09%		1111		
Age 70-79 yr	0.03% (n=2/6468)		0.44% (n=29/6554)		93.0%		0.41%		244		
Age ≥ 80 yr	0.11% (n=2/1782)		0.39% (n=7/1792)		71.2%		0.28%		357		
Injection-site Reaction ≤ 7 days	ZOE-50 N=4382	ZOE-70 N=505	ZOE-50 N=4382	ZOE-70 N=505	ZOE-50	ZOE-70	ZOE-50	ZOE-70	ZOE-50 NNH	ZOE-70 NNH	<input type="checkbox"/> Adverse reactions: <input type="checkbox"/> More pain, redness & swelling x 2-3days <input type="checkbox"/> More Grade 3 injection site reaction = redness & swelling > 100mm (NNH=11-12 in 7 days) <input type="checkbox"/> More systemic reactions x 1-2 days <input type="checkbox"/> Grade 3 solicited systemic reactions (prevents normal activity) were more frequent after 2 nd dose (8.5%, 95% CI, 7.7 to 9.4) than after 1 st dose (5.9%, 95% CI, 5.2 to 6.6) ^{ZOE-50}
Pain	79.1%	68.7%	11.2%	8.5%	85.8%	87.6%	67.9%	60.2%	1	2	
Redness	38.0%	39.2%	1.3%	1.0%	96.6%	97.4%	36.7%	38.2%	3	3	
Swelling	26.3%	22.6%	1.1%	0.4%	95.8%	98.2%	25.2%	22.2%	4	5	
Grade 3 reaction#	9.5%	8.5%	0.4%	0.2%	95.8%	97.6%	9.1%	8.3%	11	12	
Systemic Reaction within 7 days	ZOE-50 N=4375	ZOE-70 N=504	ZOE-50 N=4378	ZOE-70 N=505	ZOE-50	ZOE-70	ZOE-50	ZOE-70	ZOE-50 NNH	ZOE-70 NNH	
Fatigue	45.9%	32.9%	16.6%	15.2%	63.8%	53.8%	29.3%	17.7%	3	6	
Myalgia	46.3%	31.2%	12.1%	8.1%	73.9%	74.0%	34.2%	23.1%	3	4	
Headache	39.2%	24.6%	16.0	10.9%	59.2%	55.7%	23.2%	13.7%	4	7	
Shivering	28.2%	14.9%	5.9%	4.4%	79.1%	70.5% ⁷⁷	22.3%	10.5%	4	10	
Fever	21.5%	12.3%	3.0%	2.6%	86.0%	8.9%	18.5%	9.7%	5	10	
GI symptoms	18.0%	10.9%	8.8%	7.9%	51.1%	27.5%	9.2%	3.0%	11	33	
Grade 3 reaction^	11.4%	6.0%	2.4%	2.0%	78.9%	66.7%	9.0%	4.0%	11	25	

*Modified Vaccinated Cohort = excluded participants who did not receive the second dose of the herpes zoster subunit vaccine or placebo or who had a confirmed episode of herpes zoster within 1 month after the second dose. #Grade 3 injection site reaction = redness & swelling in the affected area > 100mm [^]Grade 3 systemic reaction = prevents normal activity

What are potential adverse events and drug interactions with SHINGRIX? 1-3,5,10,11,12,13

- Common adverse events include** (compared to placebo):
 - Reactions were transient, with median durations of 2 to 3 days for injection-site reactions, 1 to 2 days for systemic reactions, and 1 to 2 days for grade 3 reactions. Most reactions were considered mild to moderate in intensity.
 - More redness and swelling > 100mm to affected area lasting 1-2 days (NNH=11-12 in 7 days).
 - More systemic reactions that prevented normal activity for 1-2 days (NNH=11 to 25 in 7 days).
 - **Injection site reactions:** pain, redness, swelling; and **systemic reactions:** myalgia, fatigue, headache, shivering, fever, GI symptoms.
 - For age > 70, the overall frequency and severity of the reactions did not increase significantly after 2nd dose^{ZOE-70}.
 - For ages 50-70, systemic reactions that prevented normal activity were more frequent after 2nd dose (8.5%) than after the first dose (5.9%)^{ZOE-50}.
- Interactions:** Can be administered with other live vaccines & inactivated vaccines.
 - Can be given concomitantly with unadjuvanted seasonal influenza vaccine at different injection sites.¹⁴
 - Must **not** be mixed with any other products in the same syringe.

What are other potential cautions regarding the use of SHINGRIX? 1-3,5

- SHINGRIX is contraindicated if:** *Consider deferring in acute illness/fever!*
 - Patients have a known hypersensitivity to the active substances or to any component of the vaccine.
- Can SHINGRIX be used in immunocompromised patients?**
 - Yes, limited data in patients with autologous Haematopoietic Cell Transplant (HCT) & HIV indicate no safety concerns 1-yr post-vaccination.
- Pregnancy or Breastfeeding is not a contraindication.

Is administration of SHINGRIX cost effective?¹⁵

- SHINGRIX** costs ~ \$300 for 2 doses.
- SHINGRIX** was more effective and less expensive than the live attenuated herpes zoster vaccine at all ages and had an incremental cost-effectiveness ratio from \$20,038 to \$30,084 per quality-adjusted life year compared to no vaccination (US study, non-pharmaceutical funding).

What are the Current Vaccination Recommendations for Herpes Zoster Vaccine (SHINGRIX)?^{16,17,18,19} NACI & ACIP = national advisory committees

- NACI 2018** : Canadian NACI recommends **SHINGRIX** should be offered to individuals ≥50 yrs without contraindications.
- USA – ACIP 2017**: preferred vaccine for preventing shingles & related complications for all ≥50 yrs, including those who previously received **ZOSTAVAX**.
- History of chicken pox:** HZV can be administered (not studied).

How long after a shingles episode can the Herpes Zoster Vaccine be given?

- No official or specific recommendation for **SHINGRIX**.
- Canada:** It is recommended that at least 1 year elapse between the last shingles episode and zoster vaccination. Herpes ophthalmicus has recurred following **ZOSTAVAX II** but causality was not established.
- CDC:** Vaccine can be administered after the acute stage and symptoms/rash have subsided, no specific time frame.
- History of HZ:** patients can be vaccinated. In theory, prior episodes of HZ ↑ immunity & ↓ likelihood of recurrences, but observational evidence is contradictory.^{20,21} A recent study reports the risk of recurrence is ↓ for 12 to 18 months after having HZ so vaccination could be delayed by ≥1 year to take advantage of this natural immunity.²⁰

How is SHINGRIX supplied? What is the dosage and how is it administered? 1-3,5

- Supplied as 2 vials: (1) single dose lyophilized gE powder and (2) adjuvant suspension vials both refrigerated (2-8°C) and protected from light.
- Reconstitute prior to administration: **Administer vaccine promptly**. If this is not possible, store in refrigerator (2-8°C) and use within 6 hours. Discard if not used within 6 hours. The reconstituted vaccine is an opalescent, colourless to pale brownish liquid. Discard if frozen.
- Before administration: withdraw the reconstituted vaccine into a sterile syringe and attach a new needle to use for the injection.
- 2 doses of 0.5mL each; an initial dose at Month 0 followed by a second dose administered between 2 and 6 month later.
- Intramuscular (IM) injection only**, preferably in the deltoid muscle.

Uncertainties

- Persons with a history of herpes zoster or had herpes zoster vaccination were excluded from ZOE-50 and ZOE-70 trials.
- Can the non-live herpes zoster vaccine be effective and safe in frail elderly or immunocompromised patients over the long term?
- Of those in the vaccinated group who do get shingles, are severity and complications reduced? Is efficacy retained over longer term?
- As more severe PHN is likely the most important issue, to what extent were the more severe/persistent PHN cases prevented?

What are the advantages and disadvantages of SHINGRIX vs. ZOSTAVAX?

Advantages of SHINGRIX	Disadvantages of SHINGRIX
<ul style="list-style-type: none"> <input type="checkbox"/> Non-live vaccine – option for immunocompromised persons? <input type="checkbox"/> Higher efficacy rate (91% vs. 51%), although different patient population studied <input type="checkbox"/> Easier storage requirements (refrigerate, can last up to 6 hours in refrigerator after reconstituted). If inadvertently left out of fridge & then put back in fridge, it is stable at room temperature for up to 72hr. <input type="checkbox"/> More cost-effective <input type="checkbox"/> ZOSTAVAX contains gelatin & neomycin, which may induce reaction 	<ul style="list-style-type: none"> <input type="checkbox"/> Higher reactogenicity, more injection site reactions (pain, redness, swelling), systemic reactions (fatigue, myalgia, headache, shivering, fever, GI symptoms) <input type="checkbox"/> More local redness and swelling (>100mm) & Grade 3 systemic reactions (prevents normal activity) that last for an average median of 1-2 days. <input type="checkbox"/> 2-dose schedule
<input type="checkbox"/> ZOSTAVAX is administered SC, SHINGRIX is administered IM – this could be an advantage or disadvantage, depending on personal preference	

Shingles Extras ^{27,22}:

- Antivirals (e.g. valacyclovir 1g TID or acyclovir 800mg 5x/day) x 7 days \$70; effective in shingles treatment for age >50 if used within 24-72hrs of rash onset.
- See RxFiles **ZOSTAVAX** Q&A.
- See RxFiles Chronic Non-Cancer Pain chart for PHN pain treatment (11th Ed, pg 99) → e.g. nortriptyline, gabapentin, opioid, capsaicin.
- See RxFiles Adult Vaccines Chart (11th ed, pg 77).

Additional articles:

- Breuer J, Pacou M, Gauthier A, et al. Herpes zoster as a risk factor for stroke and TIA: A retrospective cohort study in the UK. *Neurology*. 2014 Jan 21;82(3):206-12
- Cohen JI. Clinical practice: Herpes zoster. *N Engl J Med*. 2013 Jul 18;369(3):255-63.
- Forbes HJ, Bhaskaran K, Thomas S, et al. Quantification of risk factors for herpes zoster: population based case-control study. *BMJ: British Medical Journal* 348 (2014).
- Irwin MR, Levin MJ, Laudenslager ML, et al. Varicella Zoster Virus-Specific Immune Responses to a Herpes Zoster Vaccine in Elderly Recipients With Major Depression and the Impact of Antidepressant Medications. *Clin Infect Dis*. 2013 Feb 13.
- Keating GM. Shingles (herpes zoster) vaccine (zostavax®): a review of its use in the prevention of herpes zoster and postherpetic neuralgia in adults aged ≥50 years. *Drugs*. 2013 Jul;73(11):1227-44.
- Kim MC, Yun SC, Lee HB, et al. Herpes Zoster Increases the Risk of Stroke and Myocardial Infarction. *J Am Coll Cardiol*. 2017 Jul 11;70(2):295-296.
- Kolber MR, Korownyk C, Nickonchuk T. Zoster vaccine. *Can Fam Physician*. 2013 Feb;59(2):157.
- Izurieta HS, Wernecke M, Kelman J, et al. Effectiveness and Duration of Protection Provided by the Live-attenuated **Herpes Zoster Vaccine** in the Medicare Population Ages 65 Years and Older. *Clin Infect Dis*. 2017 Mar 15;64(6):785-793.
- Langan SM, Smeeth L, Margolis DJ, Thomas SL. Herpes zoster vaccine effectiveness against incident herpes zoster and post-herpetic neuralgia in an older US population: a cohort study. *PLoS Med* 2013;10:e1001420.
- Langan SM, Minassian C, Smeeth L, Thomas SL. Risk of Stroke Following Herpes Zoster: A Self-Controlled Case-Series Study. *Clin Infect Dis*. 2014 Apr 2.
- Minassian C, Thomas SL, Smeeth L, et al. **Acute Cardiovascular Events after Herpes Zoster**: A Self-Controlled Case Series Analysis in Vaccinated and Unvaccinated Older Residents of the United States. *PLoS Med*. 2015 Dec 15;12(12):e1001919.
- Nilsson J, Cassel T, Lindquist L. **Burden of herpes zoster and post-herpetic neuralgia** in Sweden. *BMC Infect Dis*. 2015 May 22;15:215.
- Schmader KE, Oxman MN, Levin MJ, et al. Shingles Prevention Study Group. Persistence of the efficacy of zoster vaccine in the shingles prevention study and the short-term persistence substudy. *Clin Infect Dis*. 2012 Nov 15;55(10):1320-8.
- Tseng HF, Smith N, Sy LS, Jacobsen SJ. Evaluation of the incidence of herpes zoster after concomitant administration of zoster vaccine and polysaccharide pneumococcal vaccine. *Vaccine*. 2011 May 9;29(20):3628-32
- Tseng HF, Lewin B, Hales CM, et al. Zoster Vaccine and the Risk of Postherpetic Neuralgia in Patients Who Developed Herpes Zoster Despite Having Received the Zoster Vaccine. *J Infect Dis*. 2015 Jun 1.
- Tricco AC, et al. Efficacy, effectiveness, and safety of **herpes zoster vaccines** in adults aged 50 and older: systematic review and network meta-analysis. *BMJ* 2018;636:k4029.
- Yawn BP, Gilden D. The global epidemiology of herpes zoster. *Neurology*. 2013 Sep 3;81(10):928-30.
- ZOSTER-033. Immunogenicity and safety of GSK Biologicals' Herpes Zoster vaccine GSK1437173A in adults with a prior episode of herpes zoster. <https://www.gsk-clinicalstudyregister.com/files2/116796-Clinical-Study-Result-Summary.pdf>

References: Inactivated Herpes Zoster Vaccine (SHINGRIX)

- 1 Gagliardi A, Andriolo B, Torloni M, Soares B. Vaccines for preventing herpes zoster in older adults (Review). *Cochrane Database of Systematic Reviews*. 2016;3:CD008858. DOI: 10.1001/14651858.CD008858.pub3.
- 2 Shingrix Monograph, RxTx, accessed December 28, 2017
- 3 ZOE-50 Study Group. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. *N Engl J Med*. 2015;372:2087-96
- 4 ZOE-70 Study Group. Efficacy of the herpes zoster subunit vaccine in adults 70 years of age or older. *N Engl J Med* 2016;375:1019-32.
- 5 Centers for Disease Control and Prevention. Shingles (Herpes Zoster). <https://www.cdc.gov/shingles/vaccination.html>, accessed December 28, 2017.
- 6 Liesegang TJ. Varicella zoster virus vaccines: effective, but concerns linger. *Can J Ophthalmol*. 2009 Aug;44(4):379-84
- 7 Bajwa ZH, Warfield CA, Crovo DG. Postherpetic neuralgia. In: UpToDate Online. UpToDate Waltham, MA. Available from: www.uptodate.com (accessed September 2009).
- 8 Jung, Beth F., Johnson, Robert W., Griffin, David R.J., Dworkin, Robert H. Risk factors for postherpetic neuralgia in patients with herpes zoster *Neurology* 2004 62: 1545-1551.
- 9 Oxman M, Levin M, Johnson G, Schmader K, Straus S, Gelb L, et al. A Vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. *N Engl J Med* 2005;352:2271-84.
- 10 Tseng HF, Smith N, Sy LS, Jacobsen SJ. Evaluation of the incidence of herpes zoster after concomitant administration of zoster vaccine and polysaccharide pneumococcal vaccine. *Vaccine* 2011;29:3628-32.
- 11 Shapiro M, Kvern B, Watson P et al. Update on herpes zoster vaccination. *CFP* 2011;57:1127-31.
- 12 CDC. Herpes zoster vaccination for health care professional. June 28, 2012. Available at <http://www.cdc.gov/vaccines/vpd-vac/shingles/hcp-vaccination.htm>. Accessed October 2012.
- 13 National Advisory Committee on Immunization (NACI). Canadian immunization guide. 7th ed. Ottawa, ON: Public Health Agency of Canada; 2006. Available from: <http://origin.phac-aspc.gc.ca/publicat/cig-gci/index-eng.php>. Accessed September 2012.
- 14 Schwarz T, Aggarwal N, Moeckesch B, Schenkenberger I, Claeys C, Douha M, et al. Immunogenicity and safety of an adjuvanted herpes zoster subunit vaccine coadministered with seasonal influenza vaccine in adults aged 50 years or older. *The Journal of Infectious Diseases*. 2017;216(11):1352-1361.
- 15 Le P, Rothberg M. Cost-effectiveness of the adjuvanted herpes zoster subunit vaccine in older adults. *JAMA Intern Med*. Published online January 2, 2018. Doi:10.1001/jamainternmed.2017.7431
- 16 National Advisory Committee on Immunization (NACI). Advisory. Statement on the recommended use of herpes zoster vaccine. *Can Commun Dis Rep* 2010;36(ACS-1):1-19. Available at <http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10pdf/36-ac-1.pdf>. Accessed September 2012.
- 17 Centers for Disease Control and Prevention. Shingles (Herpes Zoster) Vaccination Information for Healthcare Providers. Advisory Committee on Immunization Practices (ACIP) 2017 Prevention of Herpes Zoster. <https://www.cdc.gov/vaccines/vpd/shingles/hcp/index.html>, accessed December 30, 2017
- 18 Harpaz R, et al. Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2008 Jun 6;57(RR-5):1-30.
- 19 Update on Herpes Zoster Vaccine: Licensure for Persons Aged 50 Through 59 Years. *Morbidity and Mortality Weekly Report (MMWR)* November 11, 2011 / 60(44):1528-1528 <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6044a5.htm>.
- 20 Yawn BP, Wollan PC, Kurland MJ, St Sauver JL, Saddier P. Herpes zoster recurrences more frequent than previously reported. *Mayo Clin Proc*. 2011 Feb;86(2):88-93. (Shingles ~6% at 8yrs)
- 21 Tseng HF, Chi M, Smith N, et al. Herpes Zoster Vaccine and the Incidence of Recurrent Herpes Zoster in an Immunocompetent Elderly Population. *J Infect Dis*. 2012 Jun 4.
- 22 Fashner J, Bell AL. Herpes Zoster and Postherpetic Neuralgia: Prevention and Management. *Am Fam Physician*. 2011 Jun 15;83(12):1432-1437.