Update on Adult Immunization for Pharmacists

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Disclosures

- Research grants: GSK, Merck, Sanofi Pasteur, Pfizer
- Speakers fees and honoraria: GSK, Merck, Pfizer, Sanofi
- Clinical trials: (all) vaccine manufacturers
- Prior member of NACI (Zoster, Rotavirus, Adult immunization and HPV lead), CIC HPV Task Group

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Objectives

- At the end of this session the attendee will:
  - Describe the burden of varicella zoster, rationale for vaccination, and current vaccine recommendations
  - Discuss vaccine options for prevention of influenza in older adults
  - Describe the current guidelines for use of pneumococcal vaccines in adults
  - Review the current recommendations for MMR in HCW

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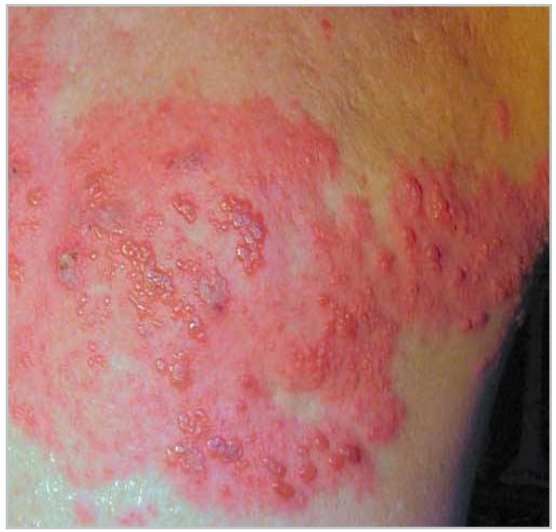
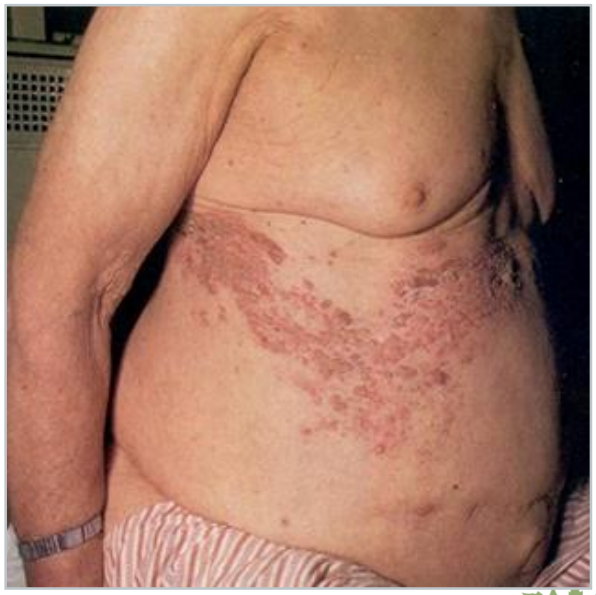
Update on Shingles Vaccines





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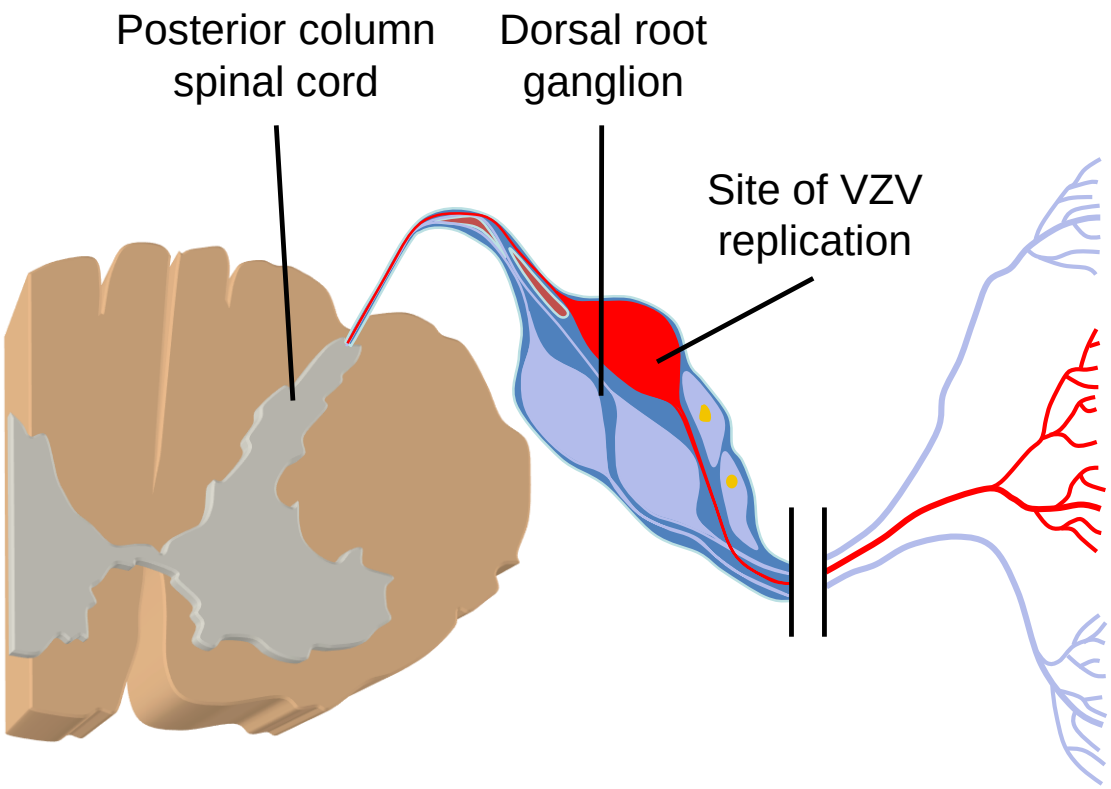
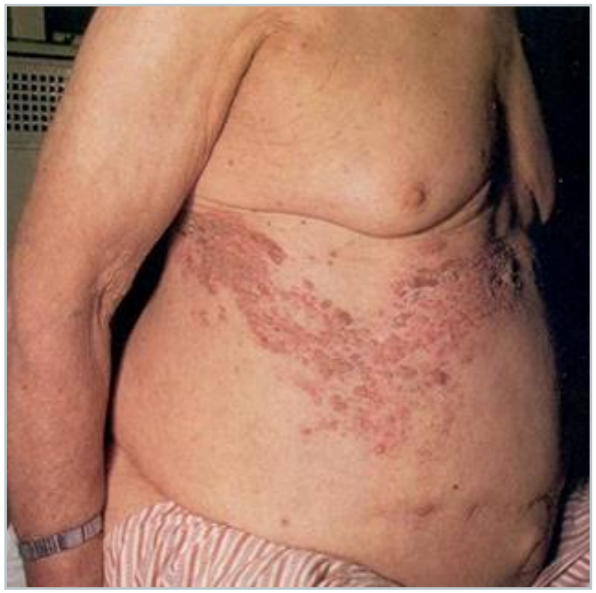
VZV: Pathophysiology of Reactivation





1. Arvin AM. In: Knipe DM et al (eds). *Fields Virology*. Volume 2. Fourth Edition. Lippincott Williams & Wilkins, New York, 2001. pp. 2731-67. 2. Straus SE, et al. In: Freedberg IM, et al (eds). *Fitzpatrick's Dermatology in General Medicine*. Volume 2. Fifth Edition. McGraw-Hill, New York, 1999. pp. 2427-50.

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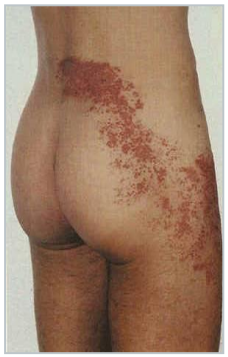
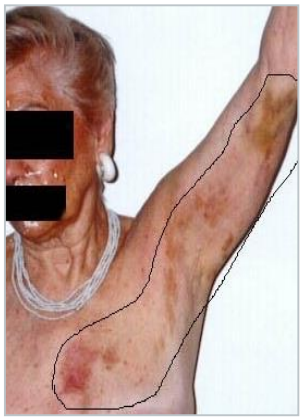
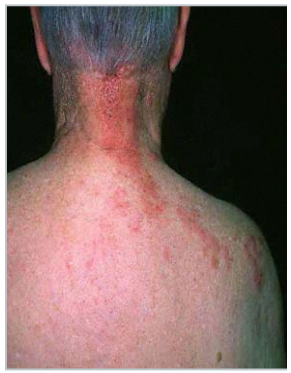
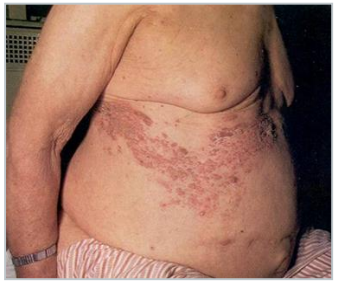
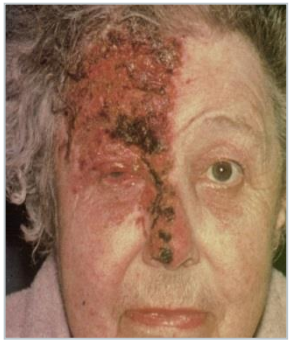
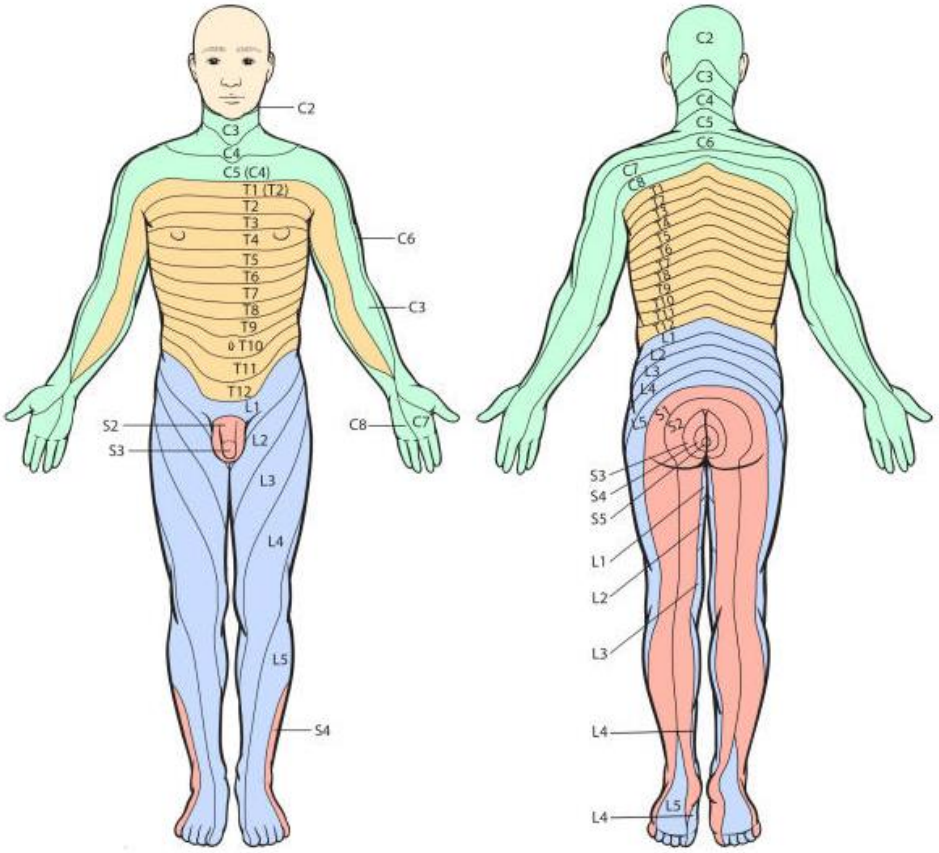
Shingles

- Shingles is a painful vesicular eruption in a dermatomal distribution



Dermatomes are areas on the skin supplied by sensory fibers of the spinal nerves

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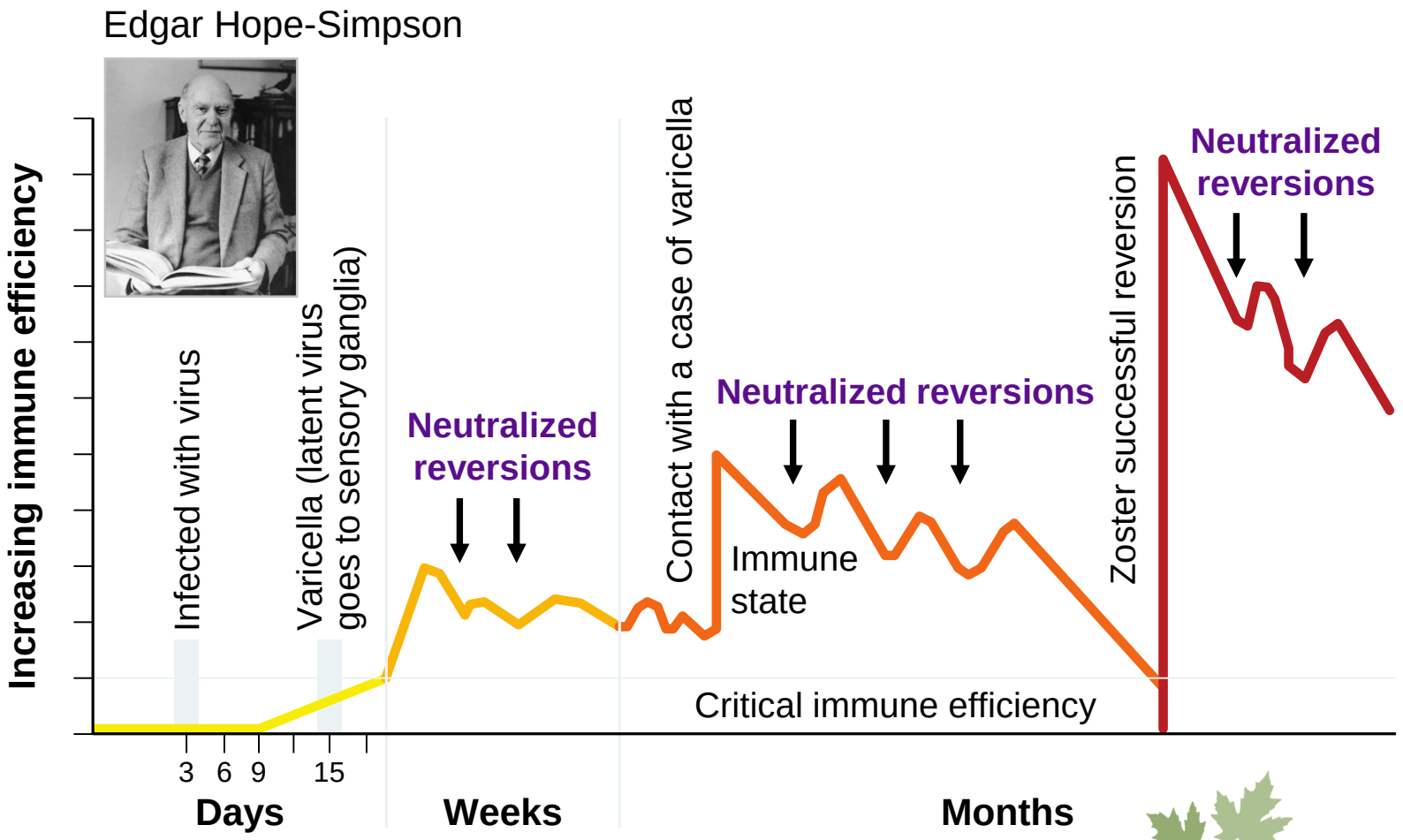
Natural History of VZV



VZV = varicella zoster virus.

Hope-Simpson RE. Proc R Soc Med 1965; 58:9-20.

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HZ Burden and Complications

- 1 out of 3 Canadians will experience an episode of HZ in their lifetime
  - 1 out of 2 for those aged 85 years and older
- Complications can severely affect the patient's quality of life

ACUTE
HZ PAIN
- loss of work
- low quality of life

PHN (10-22%)
Ocular complications
Scarring
Secondary bacterial infections

Stroke

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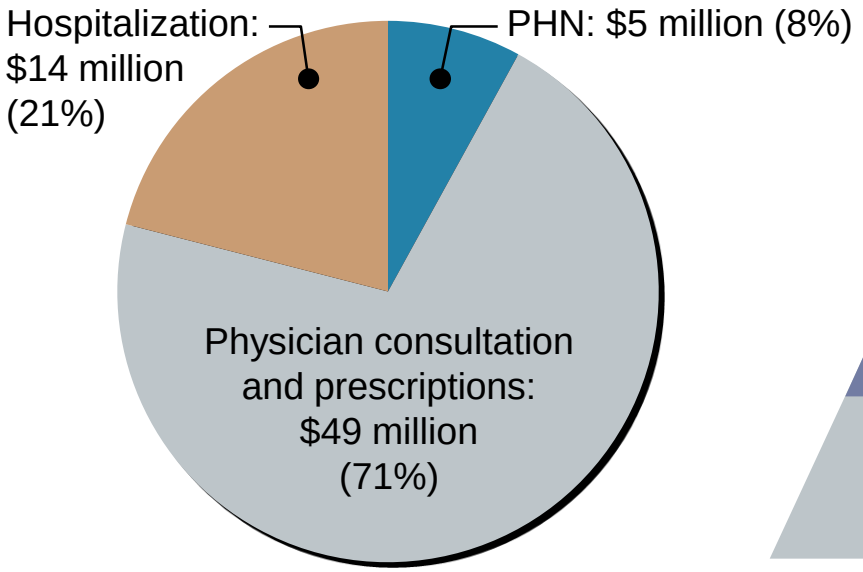
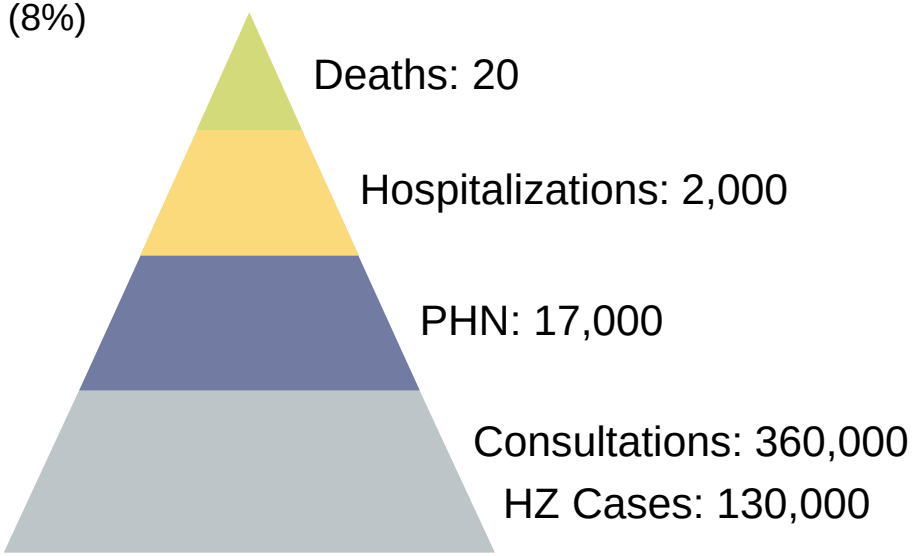
Estimated Annual Burden of HZ in Canada

2005 Healthcare Cost: $69 Million



Number of HZ-related Events in Canada



Conclusion:
Vaccinating 65-year-old adults yields a $33,000 cost per QALY gained (usual threshold is $50,000)

HZ = herpes zoster; PHN = postherpetic neuralgia; QALY = quality-adjusted life year.

Brisson M, et al. Hum Vaccin 2008; 4(3):238-45.

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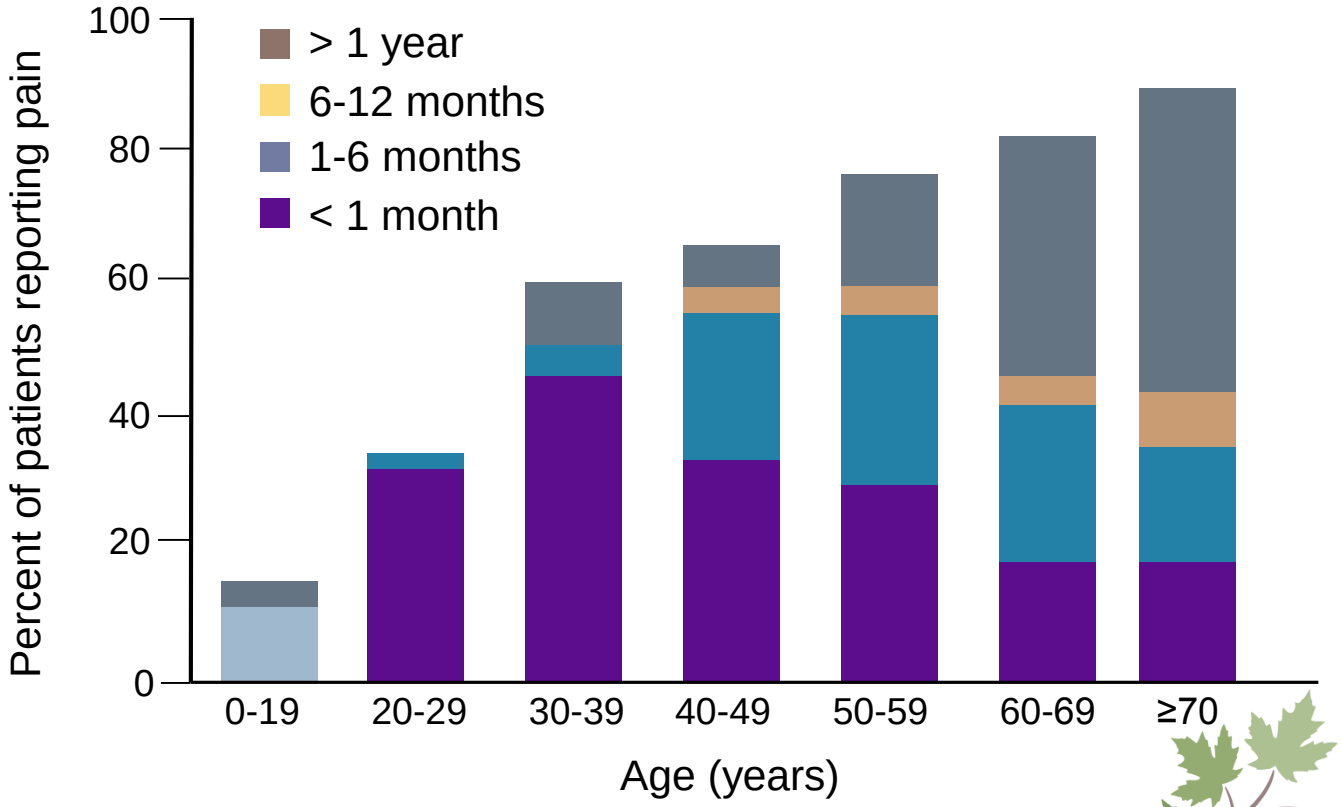
Prevalence and Duration of PHN (PHN: Pain for > 30 Days After Rash Onset)

Prevalence and duration of acute pain and PHN increase with age



de Moragas JM, et al. AMA Arch Derm 1957; 75(2):193-6.
Kost RG, et al. N Engl J Med 1996; 335(1):32-42.

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The Shingles Prevention Study (SPS)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 2, 2005 VOL. 352 NO. 22

A Vaccine to Prevent Herpes Zoster and Postherpetic Neuralgia in Older Adults

Oxman MN, et al. N Engl J Med 2005; 352:2271-84.

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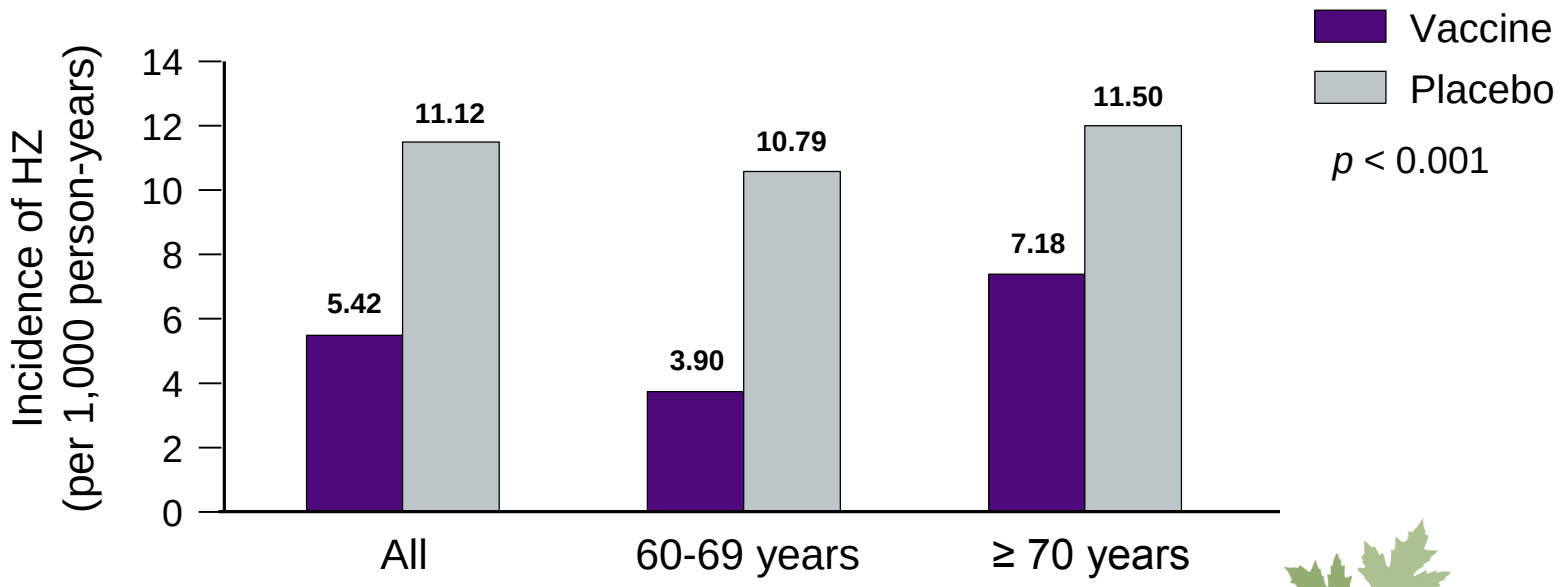
SPS Results:
Vaccine Efficacy – HZ Incidence by Age

Efficacy:	**51.3%**	**63.9%**	**37.6%**
(95% CI):	(44.2-57.6)	(55.5-79.9)	(25.0-48.1)



Oxman MN, et al. N Engl J Med 2005; 352:2271-84.

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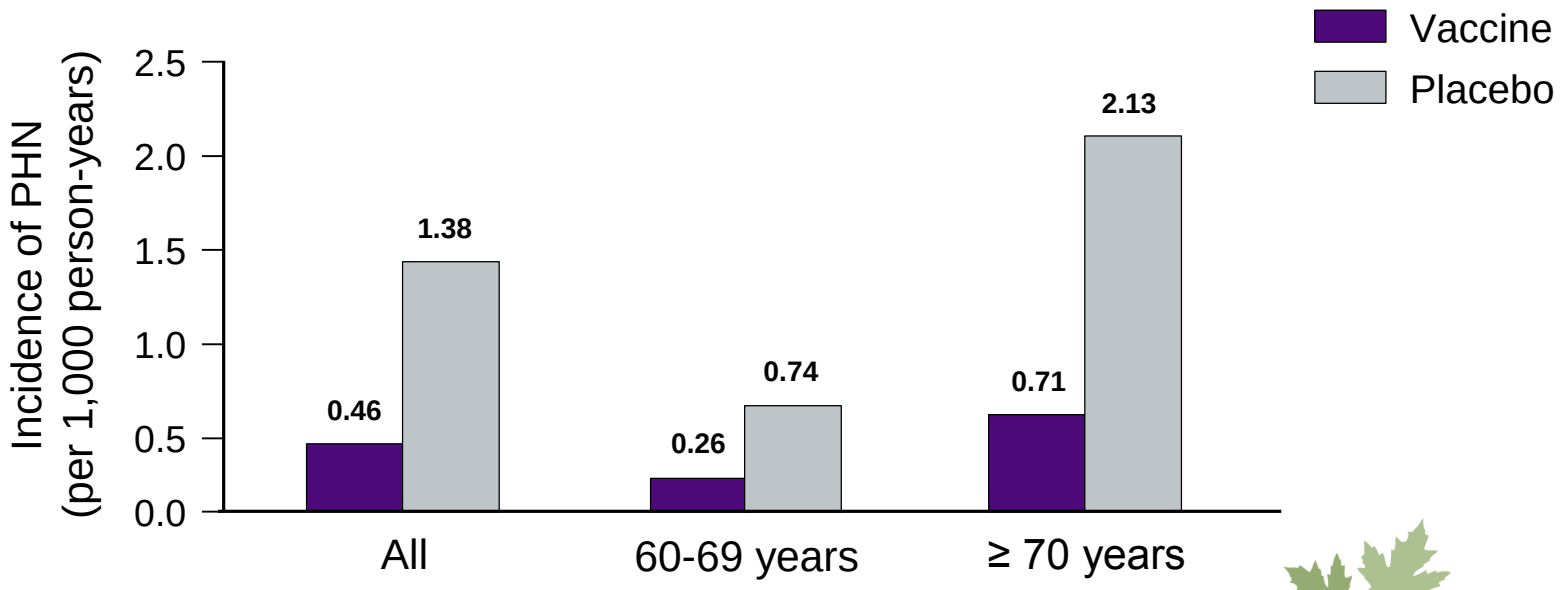
SPS Results:
Vaccine Efficacy – PHN Incidence by Age

	All	60-69 years	≥ 70 years
Efficacy (95% CI)	**66.5%** (47.5-79.2)	**65.7%** (20.4-86.7)	**66.8%** (43.3-81.3)



Oxman MN, et al. N Engl J Med 2005; 352:2271-84.

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Summary of post-marketing (Real-world) Effectiveness: immunocompetent subjects

Table 1 Summary of the characteristics and results from three retrospective cohort (nested case–control) studies assessing the effectiveness of the live-attenuated herpes zoster vaccine, Zostavax, in immunocompetent subjects

Characteristics					Vaccine effectiveness, % (95% CI)			
Study ID	**Study setting/ period**	**Median follow-up, years**	**Population**	**Total/vaccinated subjects**	**Herpes zoster**	**Post-herpetic neuralgia**	**Ophthalmic zoster**	**Hospitalization for herpes zoster**
Tseng et al. [35]	KPSC/ 2007–2009	1.6	Immunocompetent subjects aged ≥60 years	303,044/75,761	55 (52; 58)	NA	63 (39; 77)	65 (49; 76)
Langan et al. [36]	Medicare/ 2007–2009	1.6	Immunocompetent and immunocompromised subjects aged ≥65 years	766,330/29,785[a] 625,409/24,392[b]	48 (39; 56)[a] 51 (41; 59)[b]	62 (37; 77)[c] 59 (21; 79)[d]	NA	NA
Tseng et al. [37]	KPSC/ 2007–2014	Not reported	Immunocompetent subjects aged ≥60 years	704,312/176,078	51 (50; 53)	NA	NA	NA

KPSC Kaiser Permanente Southern California, *CI* confidence interval, *NA* not assessed

[a] Overall study population (immunocompetent and immunocompromised subjects)

[b] Only immunocompetent subjects

[c] Postherpetic neuralgia at 30 days

[d] Postherpetic neuralgia at 90 days

Ansaldi et al., Adv Ther (2016) 33:1094–1104

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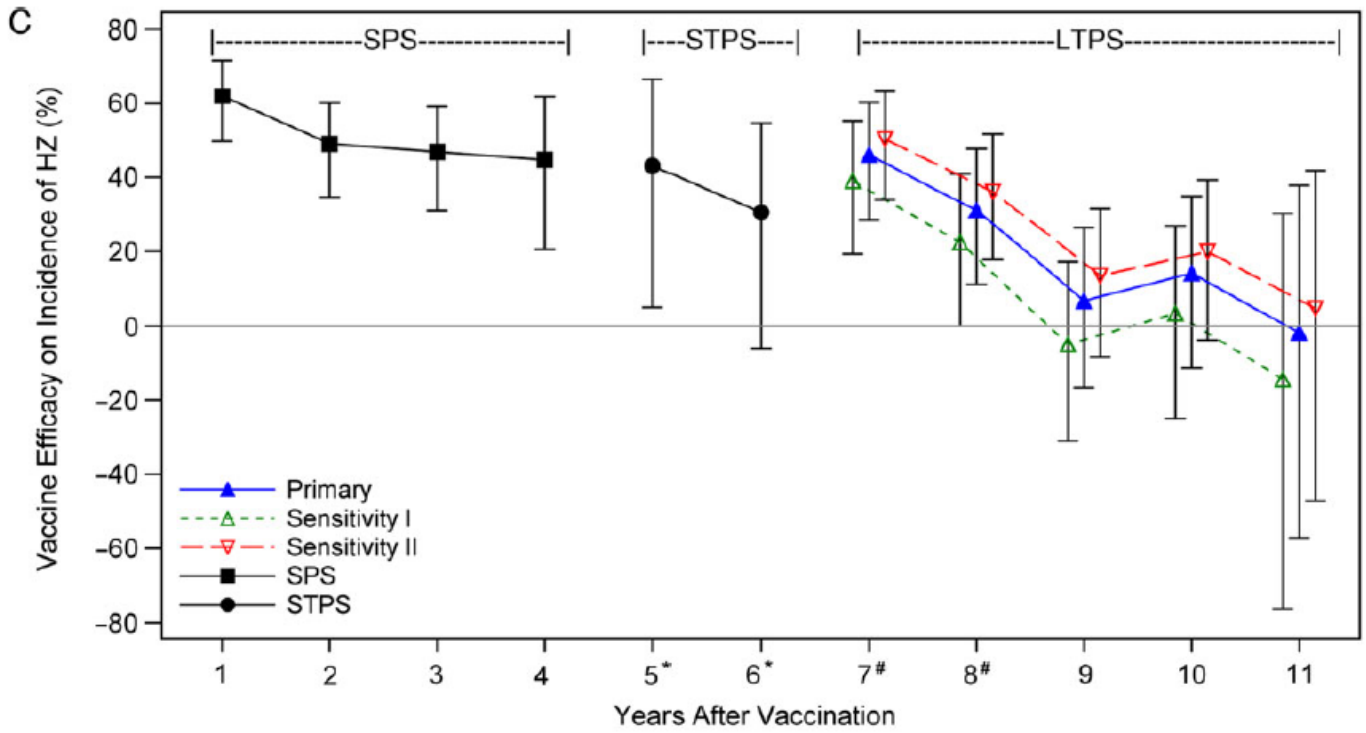
HZ Vaccine Duration of Protection



Primary						46.0	31.1	6.8	14.1	-1.7
Sensitivity I						39.1	22.4	-4.9	3.4	-14.2
Sensitivity II						50.2	36.2	13.4	19.9	4.8
SPS	62.0	48.9	46.8	44.6						
STPS					43.1	30.6				

1. Morrisor. [illegible]
2. National Advisory Committee on Immunization (NACI) 2014. PHAC Publication 130536.

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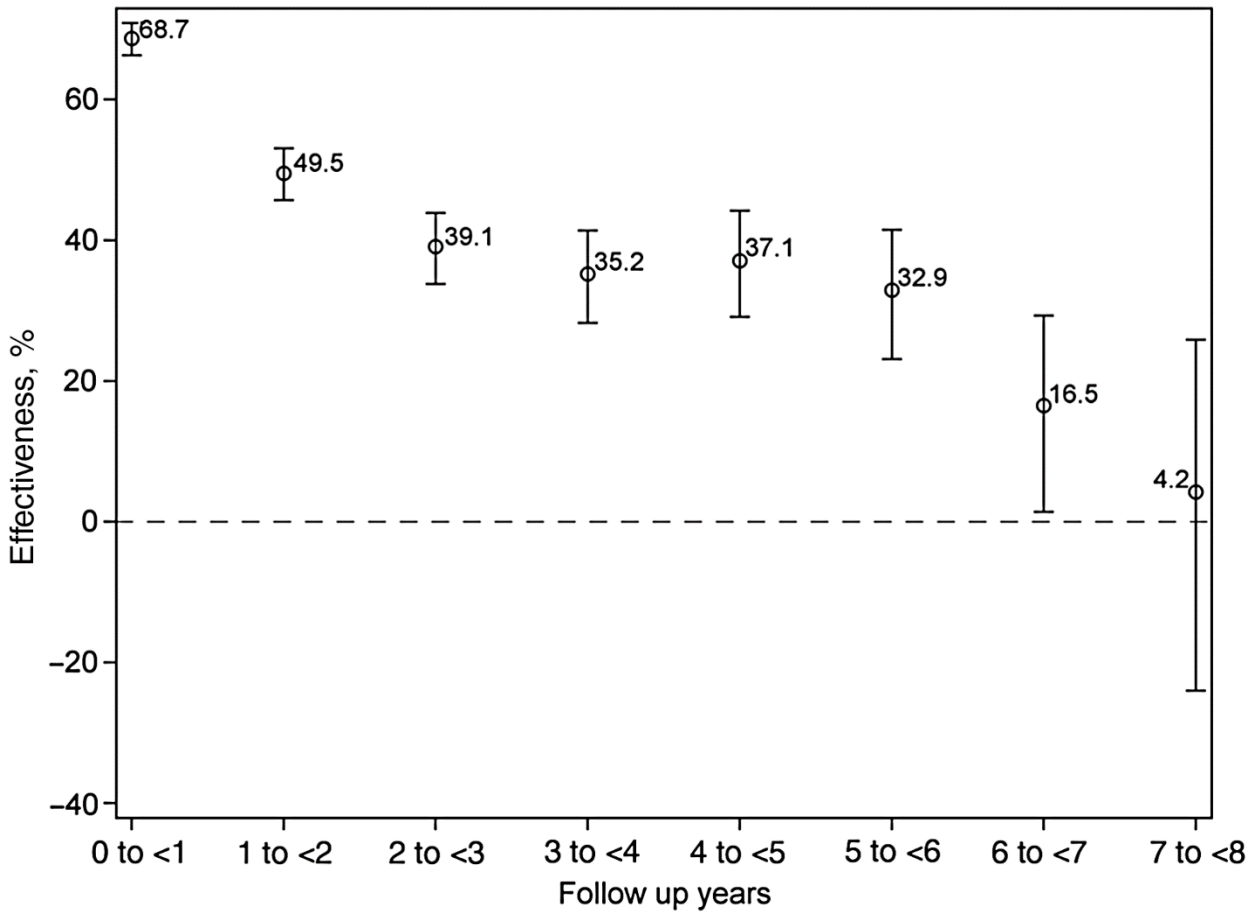
HZ Vaccine Duration of Protection



From: Declining Effectiveness of Herpes Zoster Vaccine in Adults Aged ≥60 Years

J Infect Dis. 2016;213(12):1872-1875. doi:10.1093/infdis/jiw047

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Duration of protection against PHN

Table 5. Effectiveness of ZOSTAVAX in reducing the risk of PHN by age at vaccination and time since vaccination

	Age at Vaccination								All Ages Combined
	50-59 Years		60-69 Years		70-79 Years		80+ Years		
	PHN Cases	VE % (95% CI)	PHN Cases	VE % (95% CI)	PHN Cases	VE % (95% CI)	PHN Cases	VE % (95% CI)	VE % (95% CI)
Overall VE	5	63% (11, 85)	119	71% (65, 76)	134	70% (63, 75)	64	62% (50, 71)	**69% (65, 72)**
Time since vaccination (years)									
30 days to <1 year	4	31% (-85, 75)	15	85% (75, 91)	15	86% (76, 92)	13	77% (61, 87)	82% (76, 87)
1 to <2 years	1	81% (-39, 97)	27	67% (51, 77)	30	66% (50, 76)	13	65% (40, 80)	66% (57, 73)
2 to <3 years	0		21	67% (49, 79)	28	60% (42, 73)	15	38% (-3, 63)	60% (49, 69)
3 to <4 years	0		16	71% (53, 83)	17	70% (52, 82)	8	53% (5, 77)	68% (57, 77)
4 to <5 years			17	64% (41, 78)	22	55% (31, 71)	5	62% (9, 85)	60% (45, 70)
5 to <6 years			14	61% (33, 77)	12	69% (44, 82)	6	34% (-49, 71)	61% (45, 73)
6 to <7 years			5	78% (47, 91)	9	62% (26, 81)	4	22% (-114,71)	65% (44, 79)
7 to <8 years			4	47% (-44, 81)	1	87% (8, 98)	0	~	70% (28, 88)

VE was calculated as (1-hazard ratio)*100.
Cox models adjusted for calendar time, age, sex, race/ethnic group, healthcare resource utilization (flu vaccination, # of weeks of outpatient visits per year), comorbid conditions (DxCG score, HCUP risk score), immunocompromised status during follow-up.
Abbreviations: VE denotes vaccine effectiveness; CI confidence interval; DxCG diagnostic cost group; HCUP healthcare cost and utilization project.

Marks M, Barlett J, Fireman B et al. Poster presented at: Canadian Pain Society Annual Scientific Meeting 2017 May 23-26; Halifax CA

Vaccine effectiveness in immunocompromised adults

Characteristics						Results		
Study ID	Study setting/ period	Median follow-up, days	Population	Total/vaccinated subjects	VCR, %	HZ incidence per 1000 person-years (95% CI)		VE against HZ, % (95% CI)
						Vaccinated	Unvaccinated	
Zhang et al. [49]	Medicare/ 2006–2009	730	Individuals diagnosed with rheumatoid arthritis, psoriatic arthritis, psoriasis, ankylosing spondylitis or inflammatory bowel disease (Crohn's disease or ulcerative colitis) aged ≥60 years	463,541/18,683	4.0	6.7 (5.7; 7.9)	11.6 (11.4; 11.9)	39 (29;48)
Langan et al. [36]	Medicare/ 2007–2009	584	Individuals with rheumatoid arthritis, inflammatory bowel disease aged ≥65 years (34% aged ≥80 years)	140,925/5531	2.3	5.4 (4.6; 6.4)	10.0 (9.8; 10.2)	37 (6; 58)[b]
Tseng et al. [50]	KPSC/ 2007–2012	730	Individuals who had received chemotherapy with myelosuppressive agents aged ≥60 years	21,476/4710	21.9	12.9 (10.5; 15.8)	22.1 (20.3; 23.9)	42 (27; 54)[a]

KPSC Kaiser Permanente Southern California, *CI* confidence interval, *VCR* vaccine coverage rate, *VE* vaccine effectiveness

[a] Adjusted VE against HZ

[b] VE in immunosuppressed individuals

KPSC Kaiser Permanente Southern California, CI confidence interval, VCR vaccine coverage rate, VE vaccine effectiveness

a Adjusted VE against HZ

b VE in immunosuppressed individuals

Ansaldi et al., Adv Ther (2016) 33:1094–1104

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SPS Adverse Events

	Vaccine n = 19,270	Placebo n = 19,276
Vaccine-related systemic events	6.3%	4.95%
Injection site reactions Erythema Pain or tenderness Swelling	48.3% 35.8% 34.5% 26.2%	16.6% 7.0% 8.5% 4.5%
All were different with $p < 0.05$		

Oxman MN, et al. N Engl J Med 2005; 352:2271-84.

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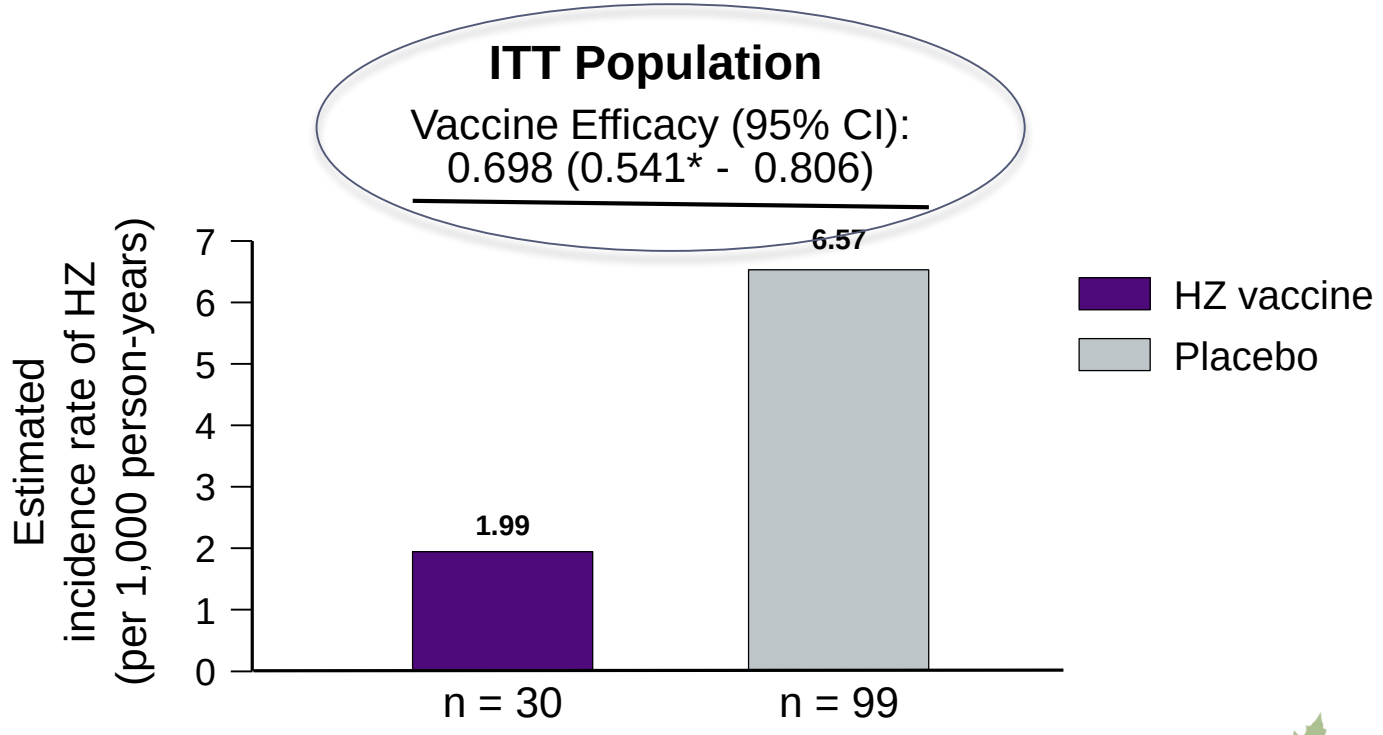
Efficacy, Safety, and Tolerability of HZ Vaccine in Persons Aged 50–59 Years



*A lower bound of > 25% indicates that the success criterion was met

Schmader K, et al. Clin Infect Dis 2012; 54(7):922-8.

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NACI Recommendations

Immunization with HZ vaccine for **immunocompetent** adults:

- Vaccine is recommended for adults ≥ 60 years of age
- Vaccine may be used in adults 50-59 years of age
- Vaccine may be administered to individuals ≥ 50 years old with a prior history of HZ. Based on expert opinion, it is recommended that the vaccine be given at least one year following the last episode of HZ
  - Annual recurrence rate in immunocompetent adults has varied across studies/methods:
    - Yawn et al 2011: 5.7% recurrence rate over 8 years (and 12% in immunocompromised adults)

See supplementary slides for more detailed NACI recommendations.

National Advisory Committee on Immunization (NACI) 2014. PHAC Publication 130536.

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NACI Recommendations (cont'd)

Immunization with HZ vaccine for **immunosuppressed** adults:

- Individuals on low-dose immunosuppressive therapy
  - It is reasonable to consider HZ vaccine in patients on lower doses of immunosuppressive agents: prednisone < 20 mg/day; methotrexate ≤ 0.4 mg/kg/week, azathioprine ≤ 3.0 mg/kg/day; 6-mercaptopurine ≤ 1.5 mg/kg/day
- Individuals on anti-TNF biologics
  - HZ vaccine may be used; on a case-by-case basis after review with an expert in immunodeficiency

See supplementary slides for more detailed NACI recommendations.

National Advisory Committee on Immunization (NACI) 2014. PHAC Publication 130536.

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FAQs

- Use in people who have had shingles? YES; wait 1 yr
- Can I give with flu and pneumococcal vaccines? YES
- Can I give to people under 50? YES (off label)- special attention to those with anticipated immunosuppression
- What should I do with IC patients requesting vaccination? Give HZ/su vaccine

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy of an Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults

Himal Lal, M.D., Anthony L. Cunningham, M.B., B.S., M.D., Olivier Godeaux, M.D., Roman Chlibek, M.D., Ph.D., Javier Diez-Domingo, M.D., Ph.D., Shinn-Jang Hwang, M.D., Myron J. Levin, M.D., Janet E. McElhaney, M.D., Airi Poder, M.D., Joan Puig-Barberà, M.D., M.P.H., Ph.D., Timo Vesikari, M.D., Ph.D., Daisuke Watanabe, M.D., Ph.D., Lily Weckx, M.D., Ph.D., Toufik Zahaf, Ph.D., and Thomas C. Heineman, M.D., Ph.D., for the ZOE-50 Study Group*

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Recombinant adjuvanted subunit vaccine

- Glycoprotein E
- $ASO1_B$- MPL + QS21 – novel adjuvant which stimulates strong $CD4$ T cells and humoral responses
- RDBPC trial- n= ~7700/arm, healthy adults 50+y
- Vaccine vs placebo IM at 0, 2 mos

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Vaccine Efficacy

Table 2. Vaccine Efficacy against the First or Only Episode of Herpes Zoster Infection.*

Cohort and Age Group	HZ/su Group				Placebo Group				Vaccine Efficacy†
	No. of Participants	No. of Confirmed Cases	Cumulative Follow-up Period ‡	Rate of Herpes Zoster	No. of Participants	No. of Confirmed Cases	Cumulative Follow-up Period‡	Rate of Herpes Zoster	
			person-yr	*no./1000 person-yr*			*person-yr*	*no./1000 person-yr*	*% (95% CI)*
Modified vaccinated cohort									
All participants in cohort	7344	6	23,297.0	0.3	7415	210	23,170.5	9.1	97.2 (93.7–99.0)
50–59 yr	3492	3	11,161.3	0.3	3525	87	11,134.7	7.8	96.6 (89.6–99.3)
60–69 yr	2141	2	7,007.9	0.3	2166	75	6,952.7	10.8	97.4 (90.1–99.7)
70 yr or older	1711	1	5,127.9	0.2	1724	48	5,083.0	9.4	97.9 (87.9–100.0)
Total vaccinated cohort									
All participants in cohort	7698	9	25,584.5	0.4	7713	235	25,359.9	9.3	96.2 (92.7–98.3)
50–59 yr	3645	3	12,244.9	0.2	3644	95	12,162.5	7.8	96.9 (90.6–99.4)
60–69 yr	2244	5	7,674.1	0.7	2246	83	7,581.8	10.9	94.1 (85.6–98.1)
70 yr or older	1809	1	5,665.5	0.2	1823	57	5,615.6	10.2	98.3 (89.9–100.0)

Table 3. Adverse Events and Reactogenicity.*

Variable	HZ/su Group		Placebo Group	
	no. of participants/total no.	*% (95% CI)*	*no. of participants/total no.*	*% (95% CI)*
Reactogenicity subgroup	4460		4466	
Within 30 days after vaccination				
Unsolicited report of adverse event	1308	29.3 (28.0–30.7)	1226	27.5 (26.1–28.8)
Grade 3 unsolicited report of adverse event†	208	4.7 (4.1–5.3)	151	3.4 (2.9–4.0)
Within 7 days after vaccination				
Solicited or unsolicited report of adverse event	3765	84.4 (83.3–85.5)	1689	37.8 (36.4–39.3)
Grade 3 solicited or unsolicited report of adverse event†	760	17.0 (15.9–18.2)	145	3.2 (2.7–3.8)
Grade 3 solicited or unsolicited report of adverse event related to vaccination	694	15.6 (14.5–16.7)	83	1.9 (1.5–2.3)
Solicited report of injection-site reaction	3571/4382	81.5 (80.3–82.6)	522/4377	11.9 (11.0–12.9)
Pain	3464/4382	79.1 (77.8–80.2)	490/4377	11.2 (10.3–12.2)
Redness	1664/4382	38.0 (36.5–39.4)	59/4377	1.3 (1.0–1.7)
Swelling	1153/4382	26.3 (25.0–27.6)	46/4377	1.1 (0.8–1.4)
Grade 3 solicited report of injection-site reaction†	417/4382	9.5 (8.7–10.4)	16/4377	0.4 (0.2–0.6)
Solicited report of systemic reaction	2894/4375	66.1 (64.7–67.6)	1293/4378	29.5 (28.2–30.9)
Myalgia	2025/4375	46.3 (44.8–47.8)	530/4378	12.1 (11.2–13.1)
Fatigue	2008/4375	45.9 (44.4–47.4)	728/4378	16.6 (15.5–17.8)
Headache	1716/4375	39.2 (37.8–40.7)	700/4378	16.0 (14.9–17.1)
Shivering	1232/4375	28.2 (26.8–29.5)	259/4378	5.9 (5.2–6.7)
Fever	939/4375	21.5 (20.3–22.7)	132/4378	3.0 (2.5–3.6)
Gastrointestinal symptoms	788/4375	18.0 (16.9–19.2)	387/4378	8.8 (8.0–9.7)
Grade 3 solicited report of systemic reaction†	498/4375	11.4 (10.5–12.4)	106/4378	2.4 (2.0–2.9)

Conclusions

- Adjuvanted subunit vaccine demonstrates excellent efficacy in healthy adults of all ages
- Excellent immunogenicity in HIV/HSCT
- Efficacy in immunocompromised patients being evaluated
- May fill important gap for prevention of HZ in IC hosts
- Adverse event profile and 2 dose schedule may pose challenges for optimal uptake

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Current Status

- Authorized for use in Canada Oct 2017; avail now
- No NACI statement yet- Spring 2018 (?)
- US ACIP- preferential recommendation for recombinant vaccine in immunocompetent persons aged 50+; revaccinate those prev vaccinated with live attenuated vaccine (≥ 8 weeks later)
- ACIP and NACI recommendation regarding use in IC patients pending; Note no contraindication/precaution in PM

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Update on influenza vaccines for older adults

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The Effect of Immunosenescence

Incidence of serious outcomes of influenza ↑

While **adults over 65** represent just **15% of the Canadian population…**

...they experience:

- **70% of influenza-related hospitalizations AND**
- **>90% of influenza-related deaths**

Statistics Canada Population projections: Canada, the provinces and territories, 2013 to 2063. Available at: http://www.statcan.gc.ca/dailyquotidien/140917/dq140917aeng.htm. Accessed on October 8, 2015.
Public Health Agency of Canada (PHAC). FluWatch. May 3 to May 9, 2015.

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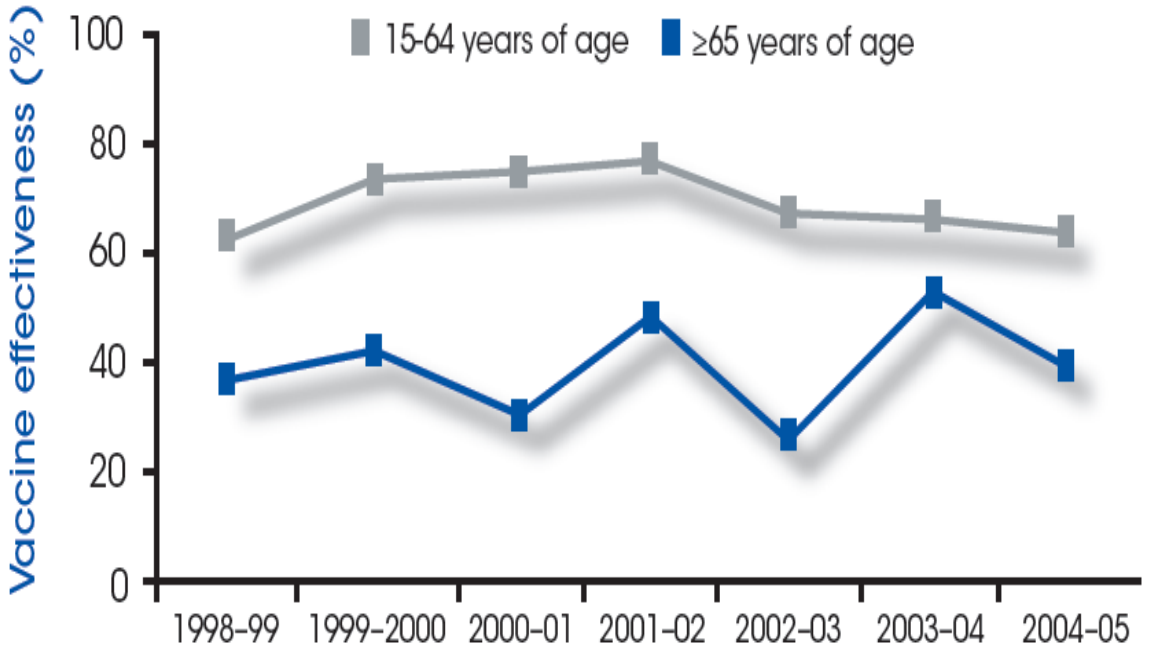
The Effect of Immunosenescence

Response to vaccination ↓



Adapted from Monto, 2009.

Monto AS, Ansaldi F, Aspinall R, et al. Vaccine. 2009;27:5043-5053.

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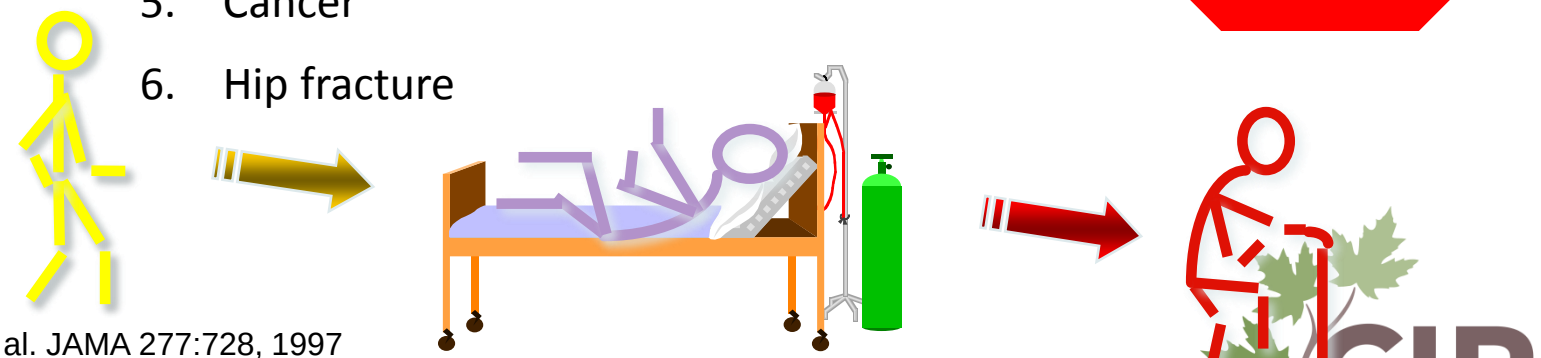
Vaccine Preventable Disability

Catastrophic disability

- Defined as a loss of independence in ≥ 3 activities of daily living
- 72% who experience catastrophic disability have been hospitalized
- Leading causes of catastrophic disability

1. Strokes
2. CHF
3. **Pneumonia and influenza**
4. Ischemic heart disease
5. Cancer
6. Hip fracture

15% of 65+ hospitalized with influenza



Ferrucci et al. JAMA 277:728, 1997
Barker et al. Arch Int Med 158:645, 1998
Falsey et al. *N Engl J Med*. 2005;352:1749
Andrew et al, IDWeek 2016

Figure credit Dr. Janet McElhaney

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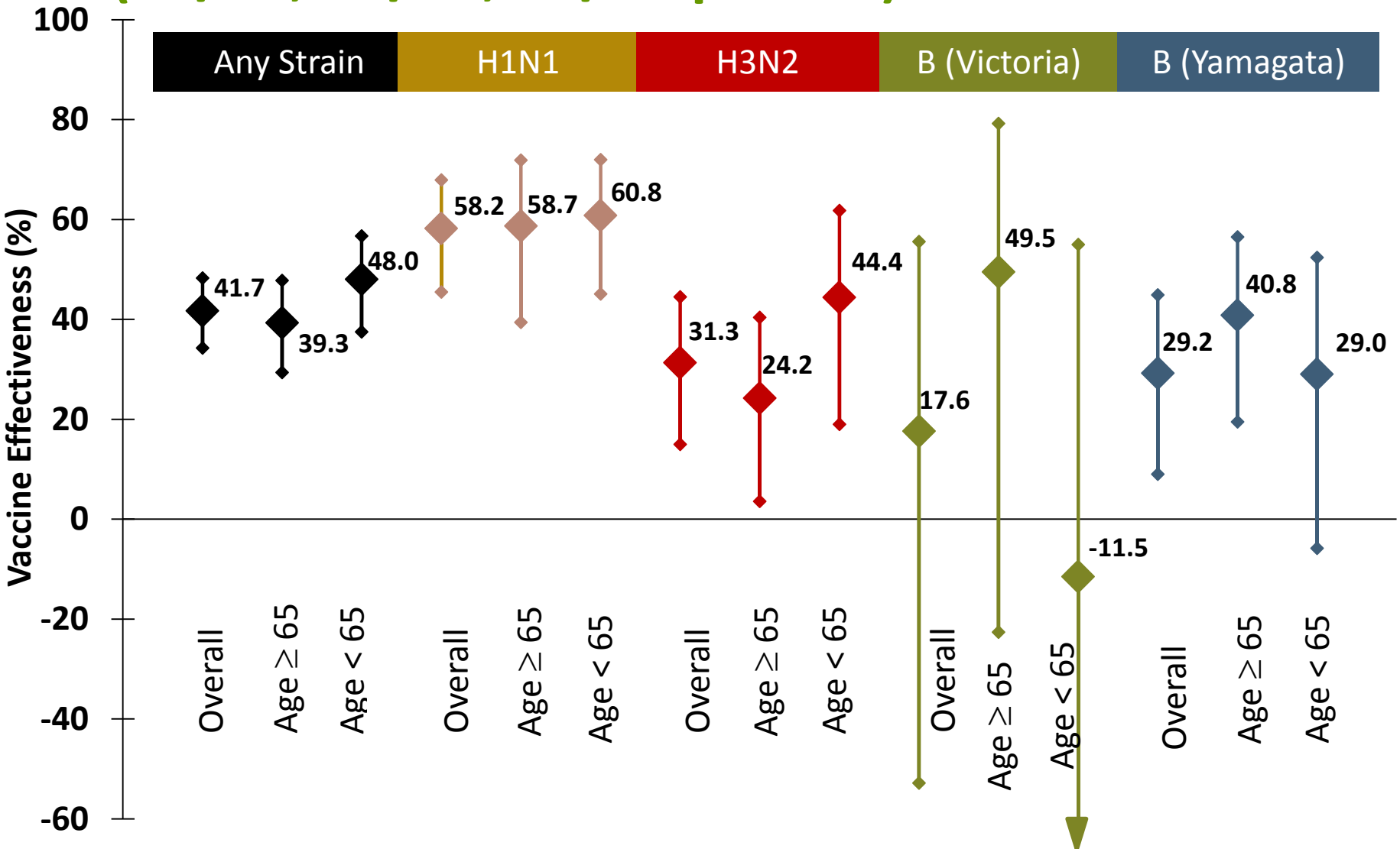
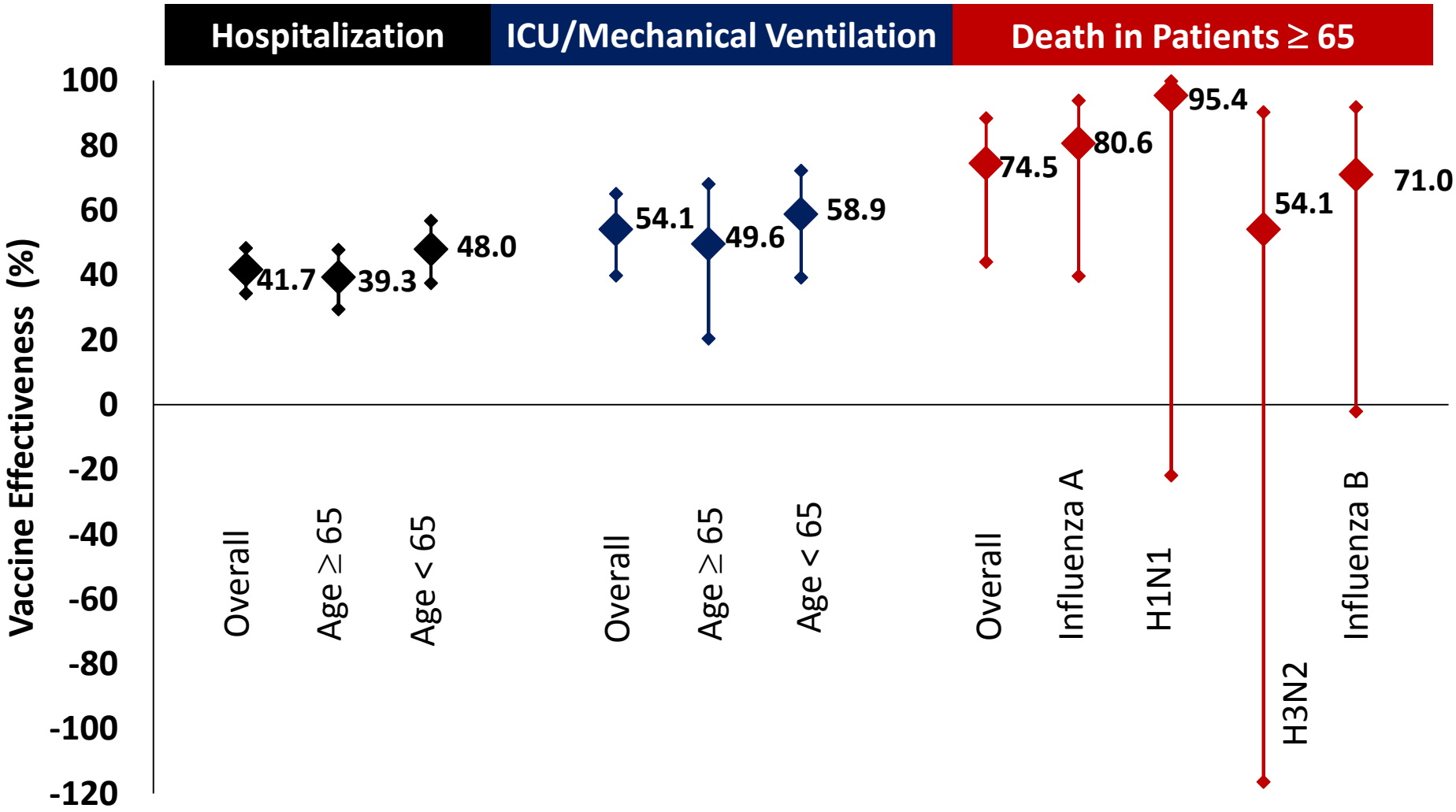
Adjusted VE estimate by influenza subtype (11/12, 12/13, 13/14 pooled)



Adjusted VE estimate by severity (11/12, 12/13, 13/14 pooled)



Not all older adults are alike!

	Non-frail N=92	Pre-frail N=229	Frail N=165	Most frail N=19	p-value
Mean age (SD), years	76.0 (7.9)	79.0 (7.7)	81.9 (8.1)	84.5 (7.7)	<0.001
Influenza vaccination, n (%)	54 (58.7)	156 (68.1)	126 (76.4)	15 (78.9)	0.663
Influenza case, n (%)	35 (38.0)	64 (27.9)	67 (40.6)	10 (52.6)	0.018
Admitted from a LTCF, n (%)	0 (0.0)	3 (1.3)	16 (9.7)	12 (63.2)	<0.001
Admitted to ICU, n (%)	15 (16.3)	25 (10.9)	19 (11.5)	1 (5.3)	0.36
Died, n (%)	5 (5.4)	9 (3.9)	25 (15.2)	5 (26.3)	0.023
VE against influenza-hospitalization, % (95% CI)	**77.6%** (39.3, 91.7)	**51.0%** (5.2, 74.7)	**59.6%** (8.0, 82.3)	**−24.8%** (-1040.4, 86.3)	

Andrew et. al, IDWeek 2016, Oct. 26-30, 2016, New Orleans, LO (Abstract p710)

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- Overall matched, adjusted effectiveness to prevent **hospitalization** in adults ≥ 65y over 3 seasons (2011/12- 2013/14) was

42% (34-48%)

- Effectiveness for the prevention of **death** was

75% (44-88%)

Vaccination remains the best way to protect against influenza but improved vaccines for this vulnerable population urgently needed.

McNeil et al. IDWeek 2016, Oct. 26-30, 2016, New Orleans, LO, Abstract O910

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“Enhanced” Influenza Vaccines for Older Adults: Can we do better?

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Adjuvanted TIV

- Standard dose TIV adjuvanted with MF-59 (no adjuvanted QIV)
- Squalene oil-in-water adjuvant; mechanism of action not fully known
  - Licensed in >20 countries; >85 mil doses distributed
  - enhance antigen persistence at the injection site and increase recruitment and activation of antigen presenting cells
  - Improved immunogenicity and cross protection in children and older adults

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Effectiveness of Adjuvanted TIV

- Single RCT vs non-adjuvanted TIV against ILI showed similar effectiveness (Frey et al, Vaccine 2014)
- (Most) observational studies suggest improved VE vs non-adj TIV in prevention of lab-confirmed influenza; methodologic limitations with most

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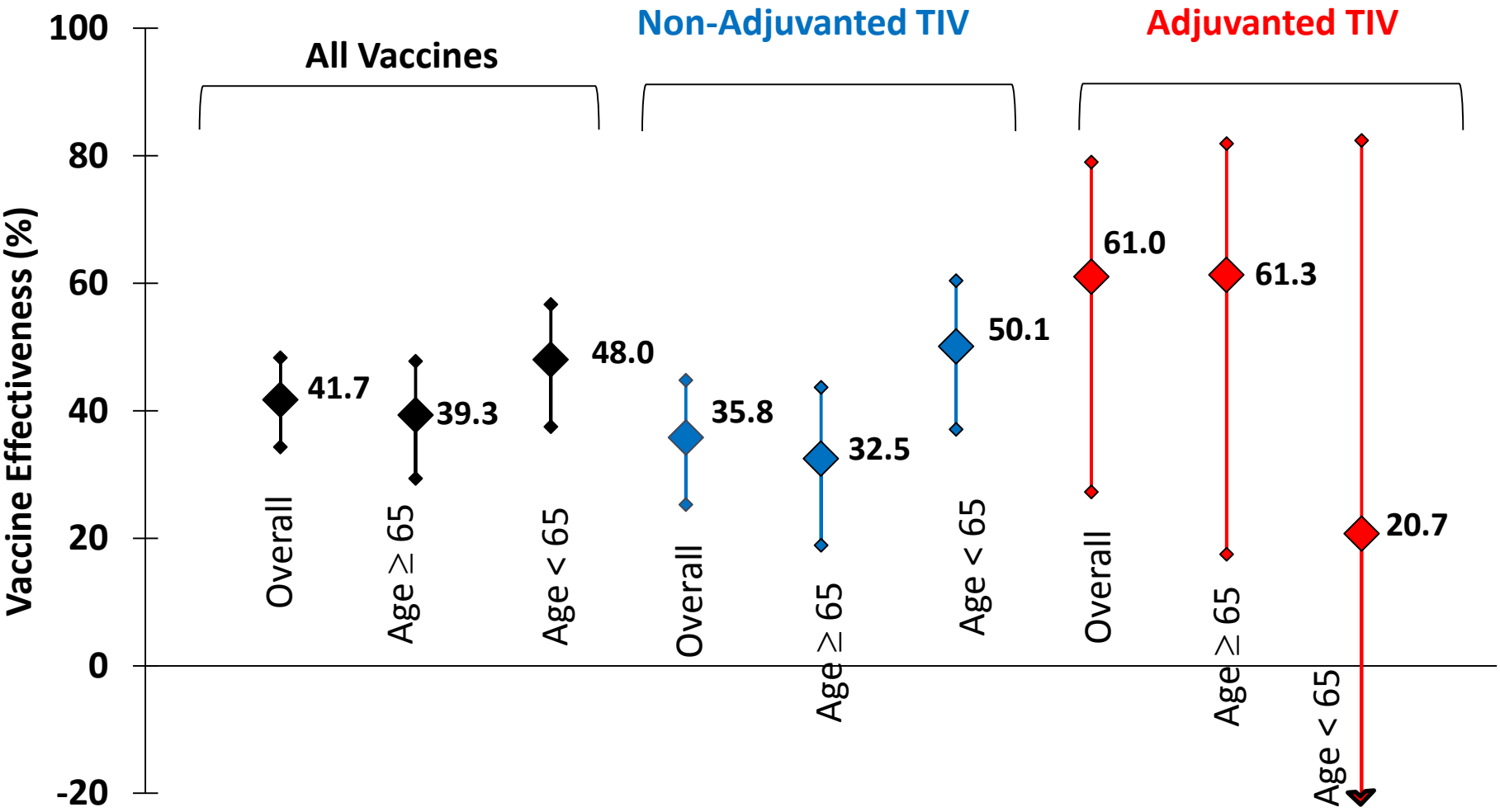
Adjusted VE estimate by vaccine type (11/12, 12/13, 13/14 pooled)

McNeil et al, IDWeek 2016



High-Dose TIV

- 60 mcg hemagglutinin (HA) of each influenza strain per 0.5 mL dose (4 times that of standard-dose influenza vaccines)
- Trivalent, inactivated, split-virus influenza vaccine
- No adjuvant, antibiotic, gelatin, or preservative
- Authorized for use in ≥65y in Canada Sept. 2015; Available in Canada as of 2016/17.
- Not publicly funded in NS. Cost: $88.79 (Shopper's); ~$65 (Costco)

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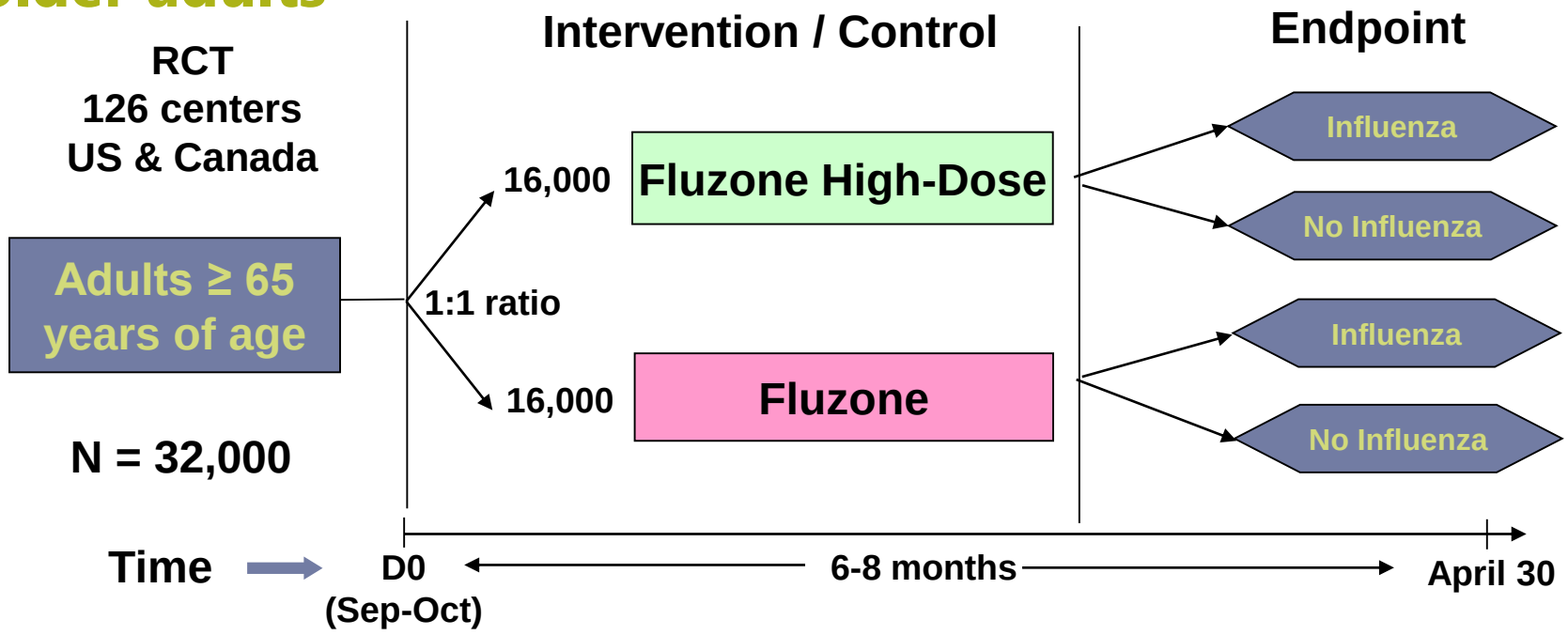
High-Dose vs standard dose vaccine RCT in low-risk older adults



- Study conducted over two influenza seasons (11/12, 12/13)
- Primary endpoint based on influenza caused by any influenza strain associated with a protocol-defined ILI

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Relative Vaccine Efficacy of High-Dose Vaccine

Benefit demonstrated across age groups, influenza types, comorbidities, and frailty-associated conditions

PRIMARY ENDPOINT

24.2%

more efficacious*

(95% CI: 9.7; 36.5)

Demonstrated SUPERIOR EFFICACY against lab-confirmed ILI compared to standard dose Vaccine[3]

65-74 Years of Age	75+ Years of Age
19.7%	32.4%
(95% CI: 0.4; 35.4)	*(95% CI: 12.5; 52.5)*
≥1 High-Risk Comorbidity	**1 Frailty-Associated Condition**
22.1%	27.5%
(95% CI: 3.9; 37.0)	*(95% CI: 0.4; 47.2)*
Similar to Vaccine Strains	**Culture-confirmed Influenza**
35.3%	23.1%
(95% CI: 12.5; 52.5)	*(95% CI: 7.5; 36.2)*

**against laboratory-confirmed influenza illness caused by any virus type or subtype in adults 65 years of age and older*

DiazGranados et al, N Engl J Med 2014;371:635-645
DiazGranados et al, Vaccine 2015; 33:4565–4571
FLUZONE® High-Dose vaccine. Product Monograph. Sanofi Pasteur Inc.; September 2015.

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Baseline Comorbid Conditions in Study Participants

- **2/3 of participants had 1 or more chronic condition**
- **1/3 of participants had 2 or more chronic conditions**
- **The most common comorbid conditions included:**
  - **Diabetes mellitus (22%-23% of each group)**
  - **Coronary artery disease (17.1% of each group)**
  - **Chronic obstructive lung disease (9.4% of each group)**
  - **Asthma (8.8% of each group)**
  - **Atrial fibrillation (~7% of each group)**
  - **Valvular heart disease (4.6% of each group)**
  - **Congestive heart failure (2.8% of each group)**
- **~74% of both groups received influenza vaccine the previous season**

Reference: DiazGranados CA, et al. *N Engl J Med.* 2014;371(7):635-645.

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Real World Effectiveness of High-Dose vaccine

- Izurieta *et al* – joint study by the **US CDC**, **FDA**, and the **Centers for Medicare and Medicaid Services (CMS)**
    - analysis of CMS data from the 2012-2013 influenza season among the **~2.5 million Medicare beneficiaries** comparing High-Dose vaccine to standard-dose influenza vaccines
    - High dose vaccine:
        - **22%** (95% CI: 15-29%) more effective in prevention of lab-confirmed ILI
        - **22%** (95% CI: 16-27) more effective in preventing influenza related ED visits and hospitalization
        - 36% (95%CI: 13-54) more effective in people 85y+

Izurieta HS et al. Lancet Infect Dis 2015;15:293-300

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Safety and tolerability

Adverse	High-dose vaccine (%)	Standard-dose vaccine (%)
Injection site reactions		
Pain	35.6	24.3
Erythema	14.9	10.8
Swelling	8.9	5.8
Systemic adverse events		
Myalgia	21.4	18.3
Malaise	18	14
Headache	16.8	14.4
Fever	8.9	5.8

FLUZONE® High-Dose Influenza Virus Vaccine Product Monograph. Date of Approval: September 2015
Falsey A, et al. *J Infect Dis.* 2009;200(2):172-180.

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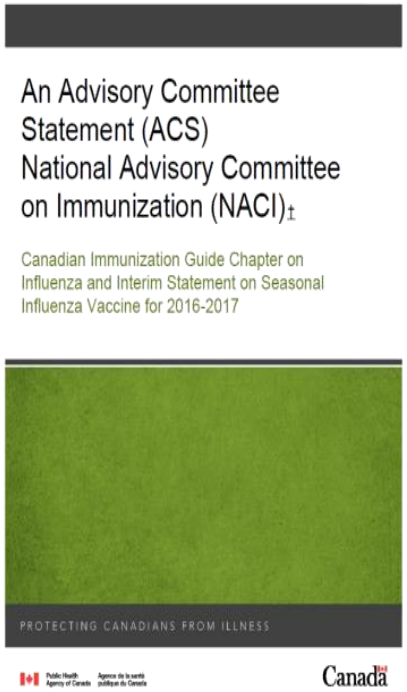
Key changes to NACI recommendations for 2016/17



- LAIV no longer recommended <u>preferentially</u> for children; quadrivalent <u>preferred</u> (can use live-attenuated or inactivated)
- Q-LAIV may be used without special precautions in persons with egg allergy (irrespective of severity)
- Adults with neurologic or neurodevelopmental conditions added to high-risk group

An Advisory Committee Statement (ACS)/National Advisory Committee on Immunization (NACI): Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2016–2017.

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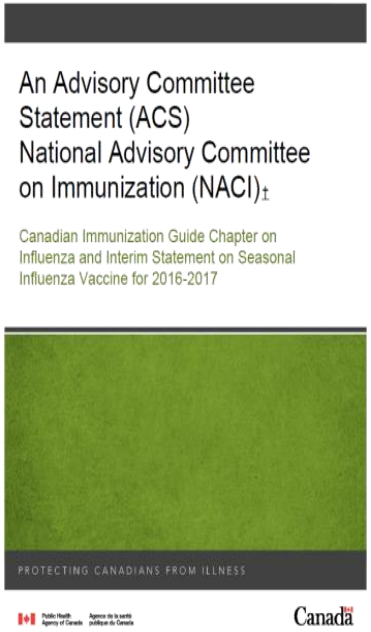
Key changes to NACI recommendations for 2016/17 (cont.)



"Based on the available evidence, NACI concludes that there is evidence that high dose TIV should provide **superior protection** compared with standard dose TIV for adults ≥65 years of age. This superior relative protection compared to standard dose TIV appears to increase with increasing age over 65 years. A similar conclusion has not been reached for adjuvanted TIV."

"Considering the burden of disease associated with influenza A(H3N2) and the evidence of superior efficacy of high dose TIV compared to standard dose TIV, it appears that **high dose TIV would provide the greatest benefit to the ≥65 years age group**."

An Advisory Committee Statement (ACS)/National Advisory Committee on Immunization (NACI): Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2016–2017.

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Conclusions

- Standard TIV provides moderate protection against hospitalization in older adults
- VE is similar in non-frail adults and younger adults
- VE increases as severity of the outcome assessed increases (death> ICU/ventilation> hospitalization)
- Both adjuvanted TIV and high-dose TIV offer improved effectiveness in older adults
- Based on RCT data, NACI concluded that high-dose TIV offers superior protection and greatest benefit in older adults
- Improved relative efficacy of high-dose vaccine in elderly and frail coupled with evidence of conserved VE in non-frail adults may allow prioritization of enhanced vaccines

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Update on Pneumococcal Disease and Prevention

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Risk Factors for Pneumococcal Disease

- **Age specific**
  - <2 years (immature immune system)
  - ≥65 years (immunosenescence)
- **Lifestyle related**
  - Alcoholism
  - Smoking
  - **Homelessness**
  - **Illicit drug use**
- Organ related
  - Functional or anatomic asplenia
  - Chronic diseases of the heart, lung, liver, or kidneys (**including asthma**)
  - Cerebrospinal fluid leakage
  - Organ transplantation
- **Immunosuppressive conditions**
  - Diabetes mellitus
  - Congenital or acquired immunodeficiency (including HIV)
  - Hematological or generalized malignancies
  - Hematopoietic cell transplantation
  - Immunosuppressive therapy (including systemic corticosteroids)
- **Other**
  - Cochlear implants

1. WHO. *Wkly Epidemiol Rec*. 2008;83(42):373-384.
2. CDC. *MMWR Morb Mortal Wkly Rep*. 2009;57(53):Q1-Q4.
3. Weiskopf D et al. *Transpl Int*. 2009;22(11):1041-1050.
4. Weinberger B et al. *Clin Infect Dis*. 2008;46(7):1078-1084.

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ORIGINAL ARTICLE

Asthma as a Risk Factor for Invasive Pneumococcal Disease

Thomas R. Talbot, M.D., M.P.H., Tina V. Hartert, M.D., M.P.H., Ed Mitchel, M.S., Natasha B. Halasa, M.D., M.P.H., Patrick G. Arbogast, Ph.D., Katherine A. Poehling, M.D., M.P.H., William Schaffner, M.D., Allen S. Craig, M.D., and Marie R. Griffin, M.D., M.P.H.

N Engl J Med 2005;35:2082-2090.

RESULTS:

- 18% of cases and 8.1% of controls had asthma
- Annual incidence rates of IPD:
  - 1.2/10,000 healthy persons
  - 2.3/10,000 persons with low-risk asthma
  - 4.2/10,000 persons with high-risk asthma

Adjusted OR = 2.4 (95% CI 1.8-3.3)
NNV= 306 (PCV-13); 533 (PPV23)
vs 225 (PPV23 in 65+)

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Indications for Immunization

- Asplenia/hyposplenism (Remember IBD)
- Chronic cardiorespiratory disease
- Cirrhosis
- Alcoholism
- Chronic renal disease/nephrotic syndrome
- Diabetes
- CSF leak/cochlear implant
- Multiple myeloma
- Smokers
- Illicit drug use
- Homeless
- Asthma requiring care in the preceeding 12 months

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PPV: Uptake

- Despite publicly funded programs in all P/Ts, coverage rates consistently low
- In Ontario:
  - 14% in <65yo with comorbidity
  - 33% in ≥65yo healthy
  - 55% in ≥ 65yo with comorbidity

Al-Sukhni W et al Vaccine 2008; 26:1432-1437

- Edmonton: 22% of adults admitted with CAP

Johnstone 2007; 167: 1938-1943

- Canada (PCIRN SOS Network)- 53% of adults admitted with CAP *McNeil et al; IDSA 2016*

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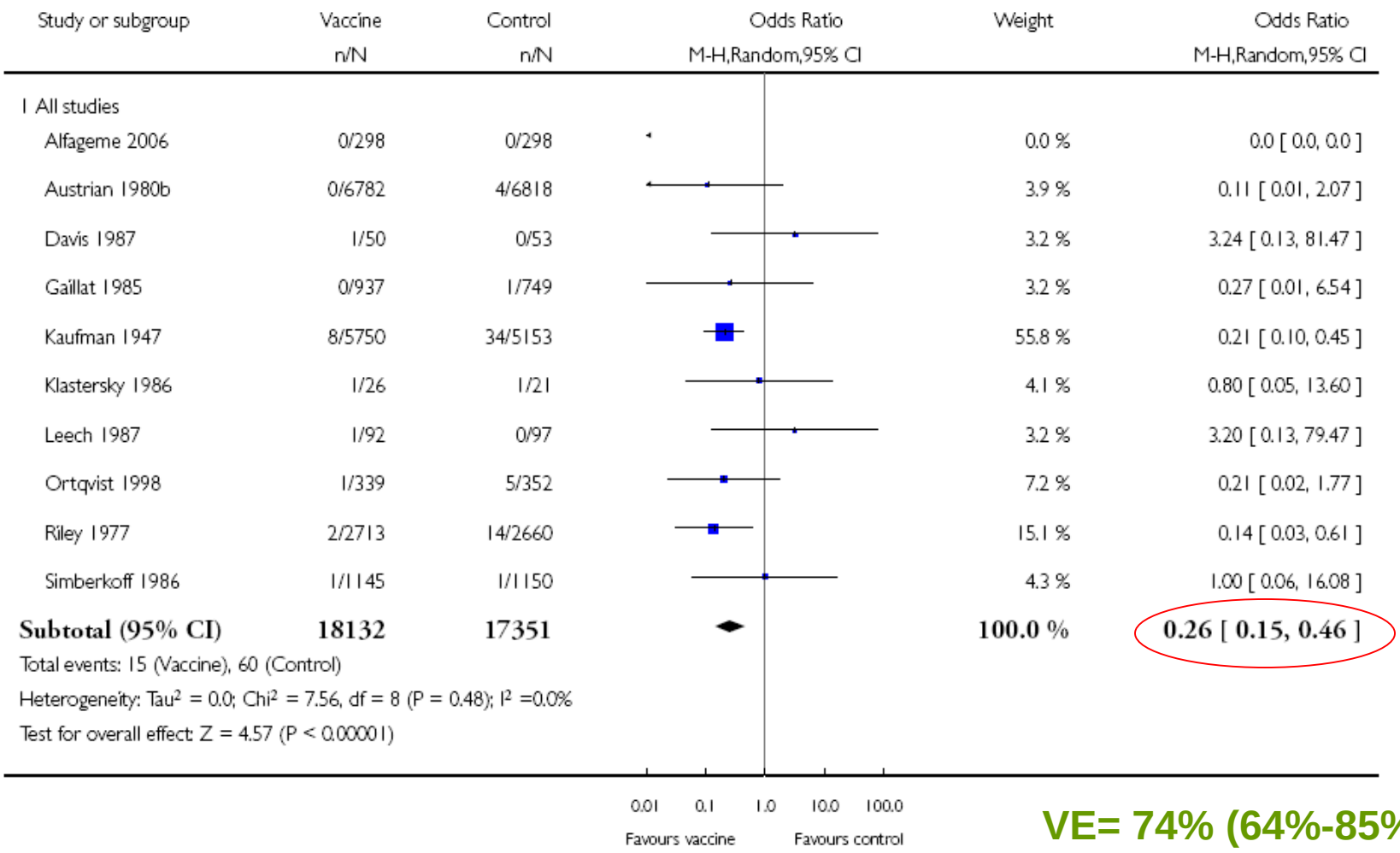
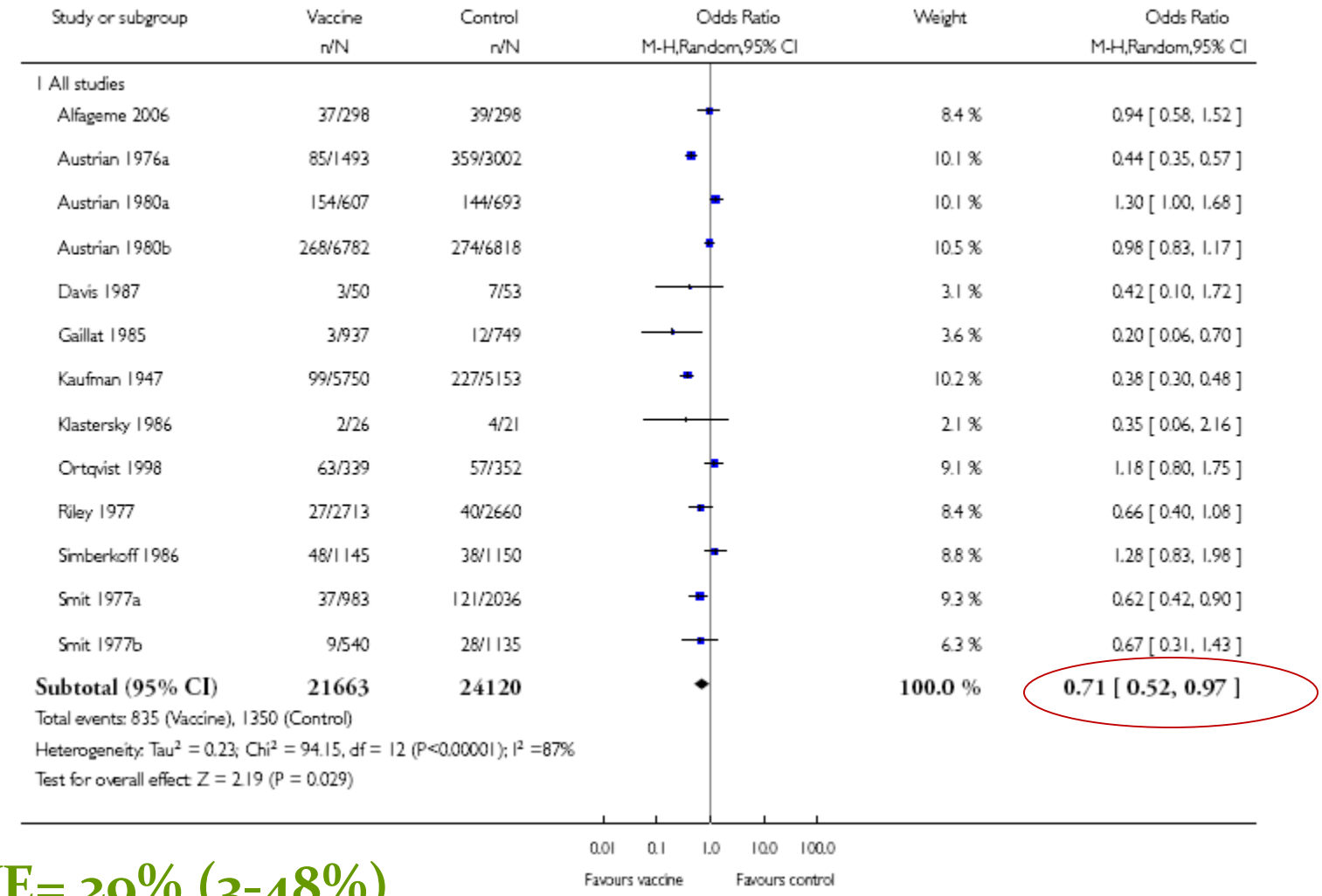
Risk of IPD: PPV vs. Placebo



VE= 74% (64%-85%)

All Cause Pneumonia: PPV vs. Placebo



Study or subgroup	Vaccine n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 All studies					
Alfageme 2006	37/298	39/298		8.4 %	0.94 [0.58, 1.52]
Austrian 1976a	85/1493	359/3002		10.1 %	0.44 [0.35, 0.57]
Austrian 1980a	154/607	144/693		10.1 %	1.30 [1.00, 1.68]
Austrian 1980b	268/6782	274/6818		10.5 %	0.98 [0.83, 1.17]
Davis 1987	3/50	7/53		3.1 %	0.42 [0.10, 1.72]
Gaillat 1985	3/937	12/749		3.6 %	0.20 [0.06, 0.70]
Kaufman 1947	99/5750	227/5153		10.2 %	0.38 [0.30, 0.48]
Klastersky 1986	2/26	4/21		2.1 %	0.35 [0.06, 2.16]
Ortqvist 1998	63/339	57/352		9.1 %	1.18 [0.80, 1.75]
Riley 1977	27/2713	40/2660		8.4 %	0.66 [0.40, 1.08]
Simberkoff 1986	48/1145	38/1150		8.8 %	1.28 [0.83, 1.98]
Smit 1977a	37/983	121/2036		9.3 %	0.62 [0.42, 0.90]
Smit 1977b	9/540	28/1135		6.3 %	0.67 [0.31, 1.43]
Subtotal (95% CI)	**21663**	**24120**		**100.0 %**	**0.71 [0.52, 0.97]**

Total events: 835 (Vaccine), 1350 (Control)

Heterogeneity: $Tau^2 = 0.23$; $Chi^2 = 94.15$, df = 12 ($P<0.00001$); $I^2 = 87\%$

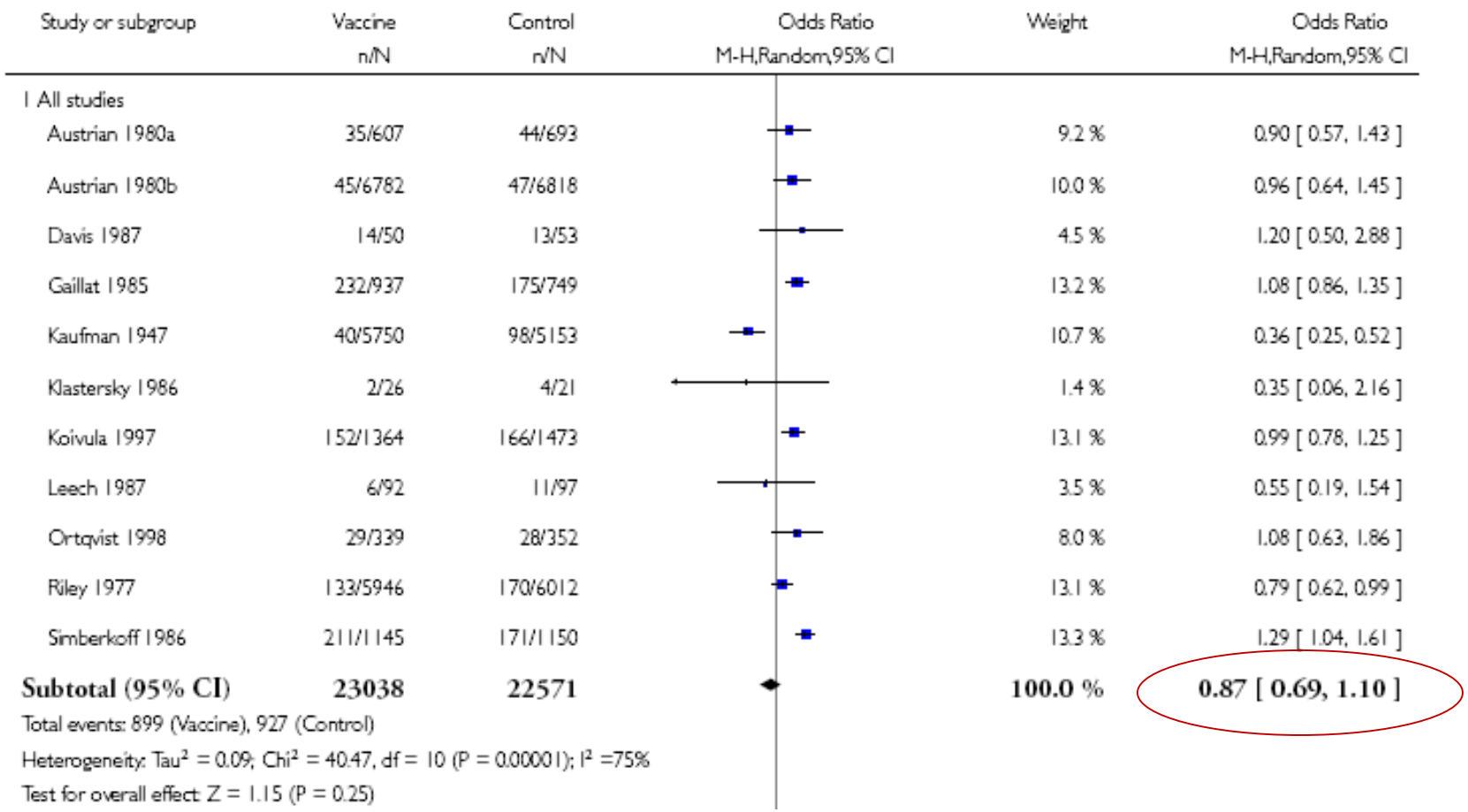
Test for overall effect: Z = 2.19 (P = 0.029)

0.01 0.1 1.0 10.0 100.0

Favours vaccine Favours control

VE= 29% (3-48%)

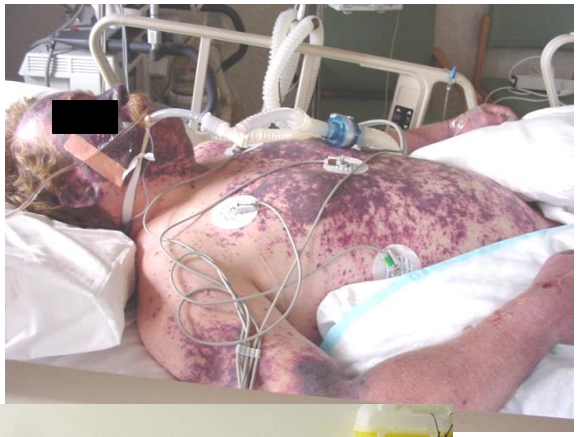
All Cause Mortality: PPV vs. Placebo

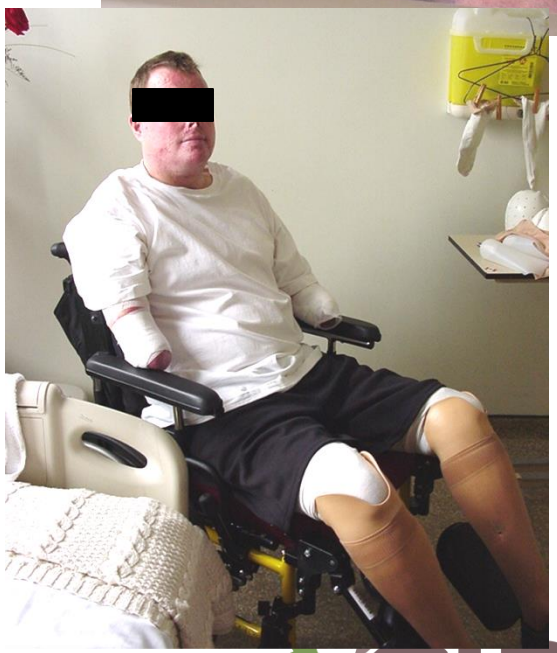


Study or subgroup	Vaccine n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 All studies					
Austrian 1980a	35/607	44/693		9.2 %	0.90 [0.57, 1.43]
Austrian 1980b	45/6782	47/6818		10.0 %	0.96 [0.64, 1.45]
Davis 1987	14/50	13/53		4.5 %	1.20 [0.50, 2.88]
Gaillat 1985	232/937	175/749		13.2 %	1.08 [0.86, 1.35]
Kaufman 1947	40/5750	98/5153		10.7 %	0.36 [0.25, 0.52]
Klastersky 1986	2/26	4/21		1.4 %	0.35 [0.06, 2.16]
Koivula 1997	152/1364	166/1473		13.1 %	0.99 [0.78, 1.25]
Leech 1987	6/92	11/97		3.5 %	0.55 [0.19, 1.54]
Ortqvist 1998	29/339	28/352		8.0 %	1.08 [0.63, 1.86]
Riley 1977	133/5946	170/6012		13.1 %	0.79 [0.62, 0.99]
Simberkoff 1986	211/1145	171/1150		13.3 %	1.29 [1.04, 1.61]
Subtotal (95% CI)	**23038**	**22571**		**100.0 %**	**0.87 [0.69, 1.10]**
Total events: 899 (Vaccine), 927 (Control)					
Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 40.47$, df = 10 (P = 0.00001); $I^2 = 75\%$					
Test for overall effect: Z = 1.15 (P = 0.25)					

Cochrane: Conclusions

- Results of meta-analysis supports the use of PPV to prevent IPD
- Minimal benefit for all-cause pneumonia
- Does not support the routine use of PPV to prevent all-cause pneumonia or mortality





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Two types of pneumococcal vaccines available

Type	Description	Options	Serotypes
Pneumococcal polysaccharide vaccines **(PPSV)**	Polysaccharide antigens	**PPSV23** Pneumovax® 23	Antigens of 23 pneumococcal serotypes: **1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F**, 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F
Pneumococcal conjugate vaccine **(PCV)**	Polysaccharide antigens joined to a protein (conjugated)	**PCV13*** Prevnar 13®	Antigens of 13 pneumococcal serotypes: **1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F**, 6A**

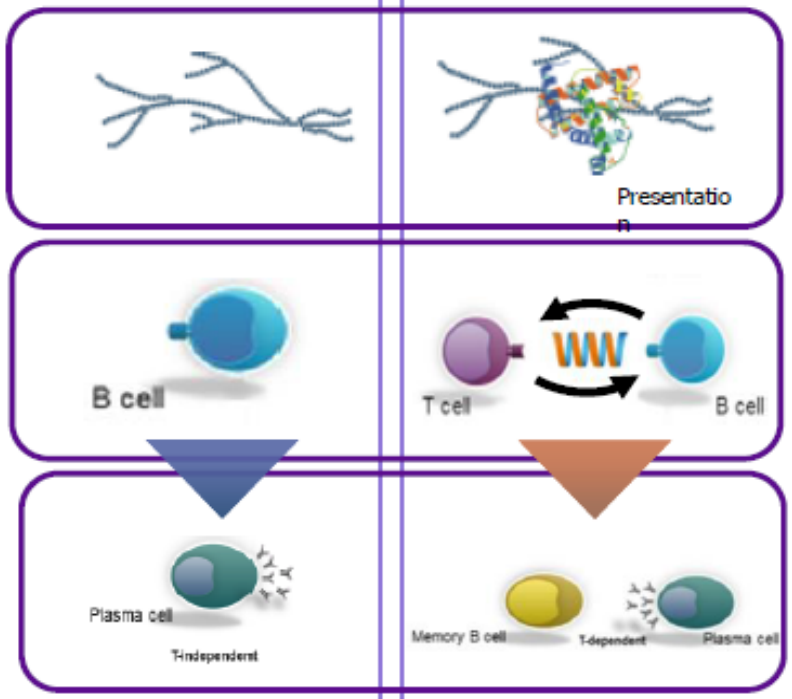
*PCV13 replaced the previous version of PCV, known as PCV7, which included 7 pneumococcal serotypes.
**6A is unique to PCV13

15 Serotypes Cause the Majority of Disease.[2]

1. PHAC. National Advisory Committee on Immunization (NACI). Statement on the Use of Conjugate Pneumococcal Vaccine – 13 valent in Adults (Pneu-C-13). Available at: http://www.phac-aspc.gc.ca/publicat/codr-rmtc/13vol39/acs-doc-5/index-eng.php
2. PHAC. Invasive Pneumococcal Disease for Heath Professionals. Available at: http://www.phac-aspc.gc.ca/im/vpd-mev/pneumococcal-pneumococcie/professionals-professionnels-eng.php

Rationale for conjugation

Polysaccharide Vaccine[1-3]	Conjugate Vaccine[1-4]
• Contain polysaccharide antigens	• Contain polysaccharide antigens covalently linked to a carrier protein
• Stimulate B cells to produce antibodies	• Stimulate T cells to help B cells produce antibodies and generate immune memory
• T cell-*independent* immune response	• T cell-*dependent* immune response



1. Siegrist CA. In: Plotkin et al, eds. *Vaccines*. 5th ed. Philadelphia, PA: Saunders Elsevier; 2008:17-36. **2.** de Roux A, et al. *Clin Infect Dis*. 2008;46:1015-1023. **3.** Clutterbuck EA, et al. *Immunology*. 2006;119:328-337. **4.** Pollard AJ, et al. *Nat Rev Immunol*. 2009;9:213-220.

Is PCV13 better than PPV23 in adults? Immunogenicity

- Mixed results when immunogenicity of PCV-7 compared to PPV-23:
  - Liver transplant: Not more immunogenic *Kumar CID 2008;47(7)*
  - Renal transplant: Better response to 2/7 serotypes but no difference at 3y *Kumar JID 2003;187(10)*
  - HSCT: Better response at 12mos (90.8% vs 55.6%; p=0.02) *Kumar CID 2007;45(12)*
  - Elderly: Better early response but no diff by 1y *Jackson Vaccine 2007;25(20)*

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Effectiveness?

- Only effectiveness data avail for PCV in immunocompromised adults is in pts with HIV

Vaccine	End Point	Vaccine Efficacy (95% CI)
HIV-Infected Adults in Uganda: PPSV23 vs Placebo[1] October 1995 – June 1998		
PPSV23 (n = 1392)*	Vaccine serotype IPD	–100% (–100%, 14%)
	All-cause pneumonia	–89% (–100%, –12%)
HIV-Infected Adults in Malawi: PCV7 vs Placebo[2] February 2003 – October 2007		
PCV7 (n = 496)†	Vaccine serotype IPD	74% (30%, 90%)
	All-cause pneumonia	25% (–19%, 53%)

1. French N et al. *Lancet*. 2000;355:2106-2111.
2. French N et al. *N Engl J Med*. 2010;362:812-822.

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Polysaccharide Conjugate Vaccine against Pneumococcal Pneumonia in Adults

N ENGL J MED 372;12 NEJM.ORG MARCH 19, 2015

CAPiTA

- Randomized, double-blind, placebo-controlled trial (Sept. 2008- Aug. 2013)
- N= ~42,000 per arm
- CAP confirmed by CXR and etiology assessed using novel type-specific urinary antigen
- Mean duration of follow-up = 4y

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CAPiTA- Results

- First episode vaccine-type CAP- 49 cases vs 90 cases: VE 45.6% (95%CI: 21.8-62.5%)
  - **NNV= 1110 (760-3500)**
- First episode vaccine-type non-invasive, non-bacteremic CAP- 33 vs 60: VE 45.0% (95%CI: 14.2-65.3%)
  - **NNV= 1620 (1110-5130)**
- First episode vaccine-type IPD- 7 vs 28: VE 75.0% (41.4-90.8%)
  - **NNV= 2128**
- All-cause CAP – 747 vs 787: VE 5.1% (-5.1-14.2%)

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Policy considerations for use of PCV13 in older adults

- Burden/incidence of pneumococcal disease in adults- IPD and CAP
- Serotype distribution of *S. pneumoniae* causing CAP in adults given routine PCV13 use in infants since 2011 (residual disease burden)
- Feasibility/acceptability of use of 2 pneumococcal vaccines in older adults
- Cost effectiveness/budget impact

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Proportion of vaccine-preventable-type SpnCAP over time based on UAD_{PCV13} (2011-2015)

Age	Serotypes / serotypable (%) *				
	2011	2012	2013	2014	2015
<65y	22/125 (**17.6**)	34/219 (**15.5**)	47/425 (**11.1**)	31/395 (**7.9**)	33/251 (**13.2**)
≥50y	30/263 (**11.4**)	54/474 (**11.4**)	67/883 (**7.6**)	35/806 (**4.3**)	42/574 (**7.3**)
≥65y	17/191 (**8.9**)	34/330 (**10.3**)	39/611 (**6.4**)	19/549 (**3.5**)	22/415 (**5.3**)
Total	39/316 (**12.3**)	68/549 (**12.4**)	86/1036 (**8.3**)	50/944 (**5.3**)	55/666 (**8.3**)

Immunocompetent Adults

- Indications: Age ≥65y, underlying comorbidities (including asthma), smoking, illicit drug use, homeless
- Single dose of PPSV23
- **NEW:** all patients aged ≥ 65 should receive 1 dose IRRESPECTIVE of a dose given <65y; interval = 5y
- PCV13: Good evidence to recommend PCV13 followed by PPV23 in immunocompetent adults 65+ not previously immunized against pneumococcal disease for prevention of CAP and IPD (NACI)

http://publications.gc.ca/collections/collection_2015/aspc-phac/HP40-135-2015-eng.pdf

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Immunocompromised Adults

- Functional or anatomical asplenia (remember IBD)
- Sickle cell disease
- Hepatic cirrhosis
- Chronic renal failure or nephrotic syndrome
- HIV
- Other immunocompromising conditions/meds

- **PCV13** X 1 lifetime dose
- PLUS **TWO** doses **PPSV 23** (5y apart); one additional dose at age 65y if both doses provided <65y

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NACI recommendation for pneumococcal vaccination for high-risk groups — at-a-glance

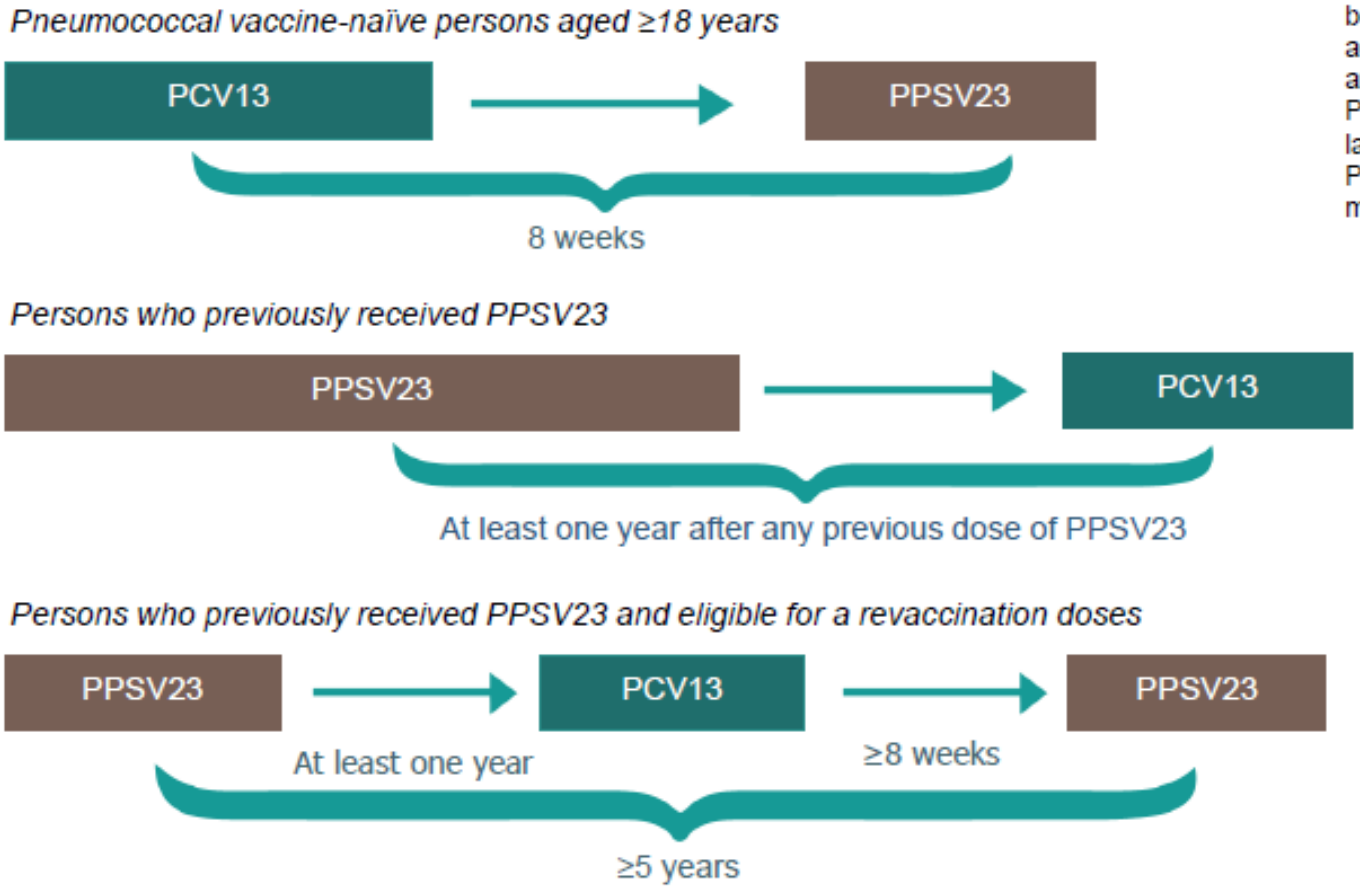
Risk Group	PCV13 Recommended	PPSV23 Recommended	PPSV23 Revaccination at 5 yrs
Adults with hematopoietic stem cell transplants (HSCT)	✔	✔	✔
Adults with HIV	✔	✔	✔
Adults with Asthma		✔	
Adults with immunosuppressive conditions including:			
Asplenia (anatomical or functional)	✔	✔	✔
Sickle cell disease or other hemoglobinopathies	✔	✔	✔
Congenital immunodeficiencies*	✔	✔	✔
Immunosuppressive therapy†	✔	✔	✔
Malignant neoplasms including leukemia and lymphoma	✔	✔	✔
Solid organ or islet cell transplant (candidate or recipient)	✔	✔	✔

* Involving any part of the immune system, including B-lymphocyte (humoral) immunity, T-lymphocyte (cell) mediated immunity, complement system (properdin, or factor D deficiencies), or phagocytic functions.

† Including use of long-term corticosteroids, chemotherapy, radiation therapy, post-organ-transplant therapy, and certain disease modifying antirheumatic drugs.

PHAC. National Advisory Committee on Immunization (NACI). Statement on the Use of Conjugate Pneumococcal Vaccine – 13-valent in Adults (Pneu-C-13)

Pneumococcal conjugate vaccine (PCV13) dose sequence — NACI recommendations



Minimum interval between sequential administration of PCV13 and PPSV23 is 8 weeks; PPSV23 can be given later than 8 weeks after PCV13 if this window is missed.

PHAC. National Advisory Committee on Immunization (NACI). Statement on the Use of Conjugate Pneumococcal Vaccine – 13 valent in Adults (Pneu-C-13). Available at: http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/13vol39/acs-dcc-5/index-eng.php

Conclusions

- Pneumococcal CAP and IPD are associated with considerable morbidity and mortality in Canadian adults
- Most pneumococcal disease is potentially vaccine preventable
- PPSV23 uptake suboptimal
- Vaccine recommendations complex
- Understanding the residual disease burden in adults due to PCV13 serotypes is critical to inform vaccine recommendations in this population

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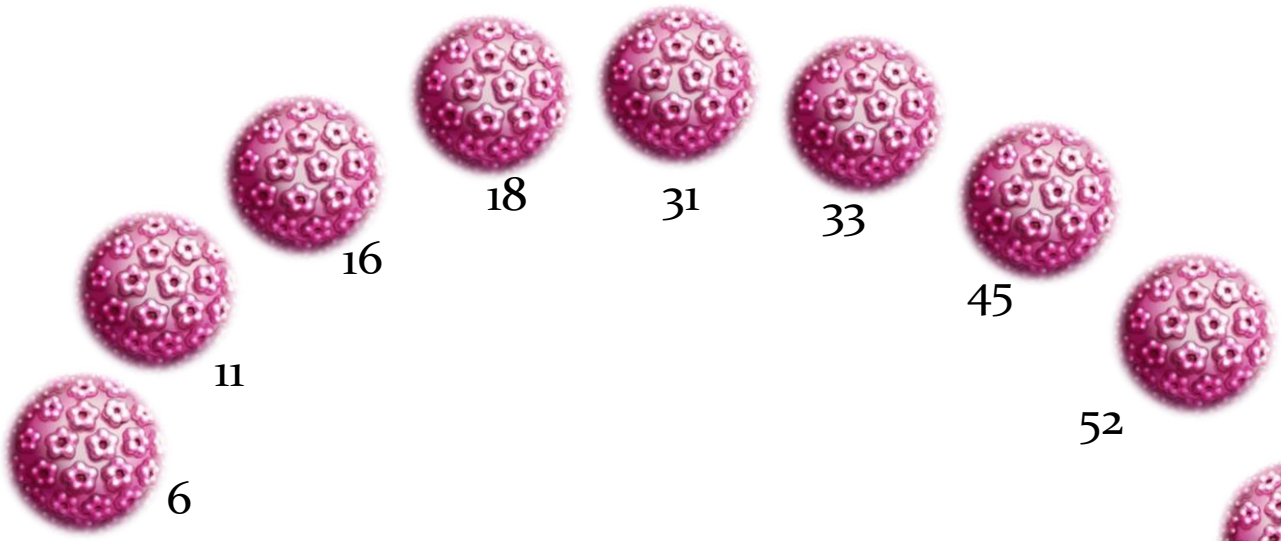
New Generation HPV vaccine: Gardasil9



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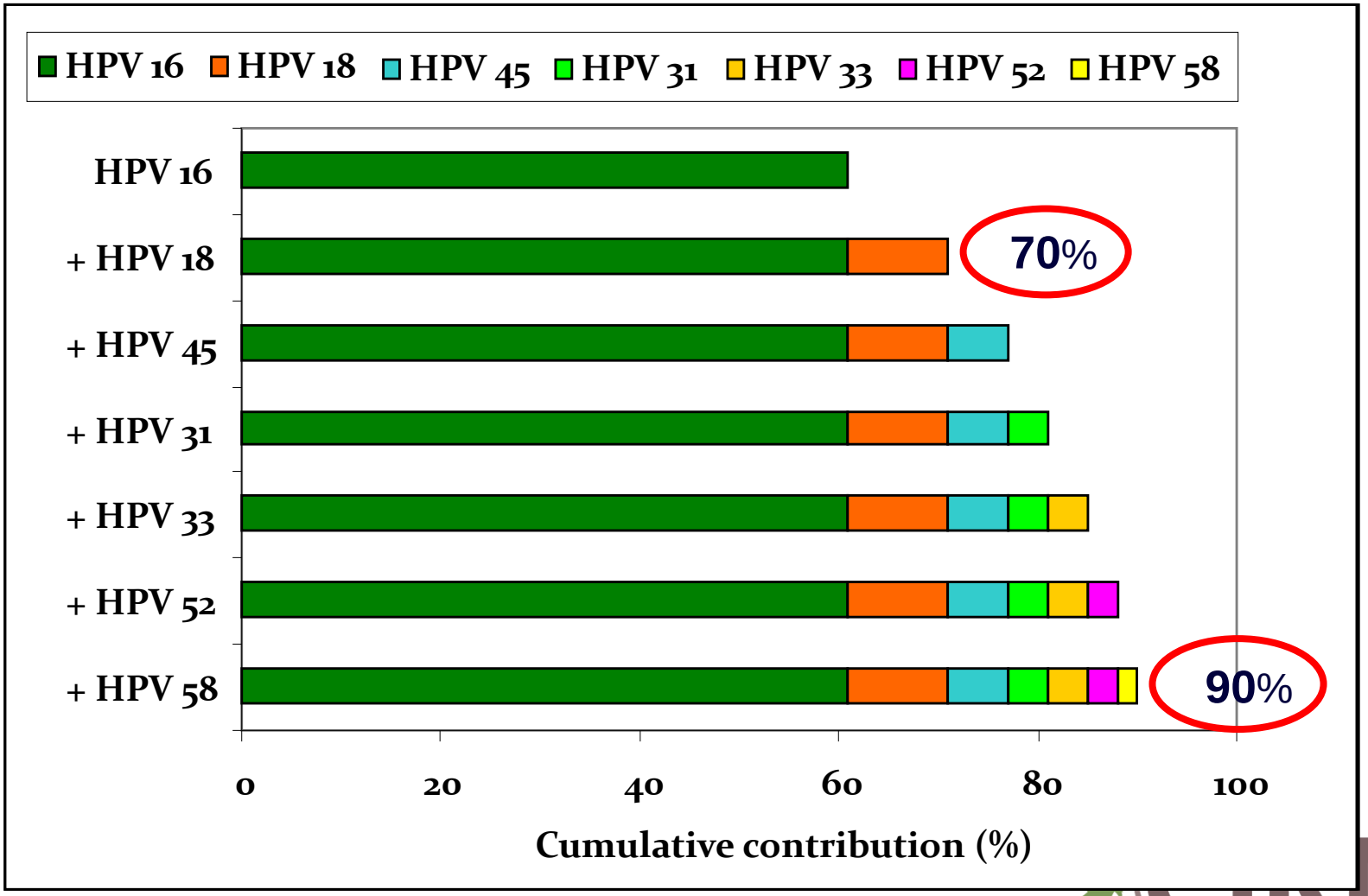
Most frequent HPV genotypes in invasive cervical cancers 1990-2010, by region

Region	No. of Cases	HPV genotypes (in order of prevalence)
World	30 848	16, 18, 58, 33, 45, 31, 52, 35
Africa	2011	16, 18, 45, 33, 35, 52, 51, 58
Eastern Asia	11 651	16, 18, 58, 52, 33, 31, 45, 59
Western/Central Asia	2051	16, 18, 45, 33, 31, 35, 58, 52
Europe	9015	16, 18, 31, 33, 45, 35, 58, 52
North America	2485	16, 18, 45, 31, 33, 52, 35, 39, 59, 58
South/Central America	3010	16, 18, 31, 45, 33, 58, 52, 35
Oceania	625	16, 18, 45, 73, 39, 35, 31, 53, 33, 52

Li N. International Journal of Cancer. 2011;128:927-935

Relative contribution of HPV types to cervical cancers, worldwide



de Sanjose et al. Lancet Oncol. 11:1048-56 (2010)

Efficacy of a novel 9-valent HPV vaccine in 16-26 year old women

Endpoint	9vHPV vaccine No cases/n	qHPV Vaccine No of cases/n	Efficacy (95%CI)
High grade HPV31/33/45/52/58 cervical/vulvar/vaginal disease	1/6016	30/6017	96.7 % (80.9-99.8)
Any grade HPV31/33/45/52/58 cervical/vulvar/vaginal disease	3/6016	103/6017	97.1 % (91.8-99.2)
HPV31/33/45/52/58 6 months related persistent infection	35/5939	810/5953	96.0 % (94.4-97.2)

Joura E. Abstract SS 8-4 Eurogin Florence Nov 3-6, 2013

Immunogenicity of HPV9 in boys and girls 9-15 years old; comparison to women 16-26 years old

- At 4 weeks post-dose 3, over 99% of girls, boys, and young women in the primary analysis population seroconverted for all 9 HPV types
- Non-inferiority of the Ab responses for all 9 HPV types in both girls and boys, 9 to 15 years of age relative to Ab responses in young women, was established.
- Therefore HPV9 vaccine efficacy findings in young women 16 to 26 years of age can be bridged to adolescent girls and boys 9 to 15 years of age.

Van Damme, P. Abstract SS 8-5 EUROGIN, Florence Nov 3-6, 2013

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Conclusion

- HPV9 is non-inferior to HPV4 for HPV 6,11,16,18
- HPV9 induces strong Ab response and excellent efficacy against HPV31,33,45,52,58 (97% against CIN2+)
- Responses to HPV9 are similar in males and females
- HPV9 is safe and well tolerated in women previously vaccinated with HPV4 (data not shown)
- Replacing HPV4 with HPV9 will be a challenge as no efficacy data in males, no data on 2 doses, etc---- unlikely to get similar indications=== big dilemma for policy makers!

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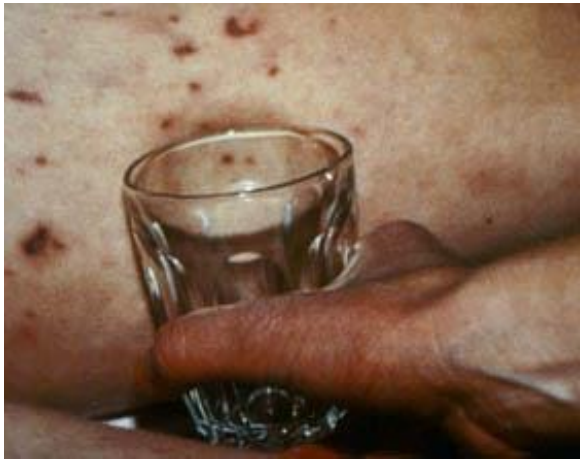
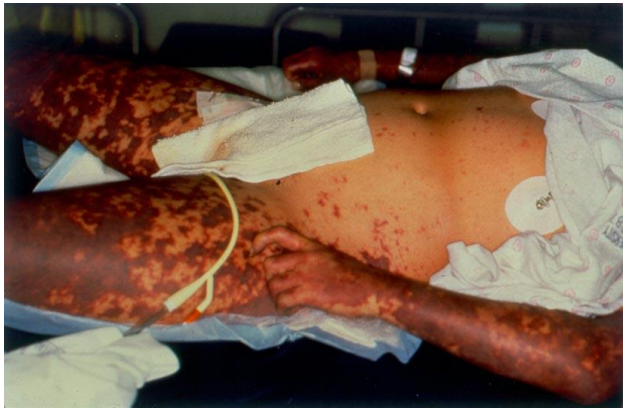
Meningitis vaccines





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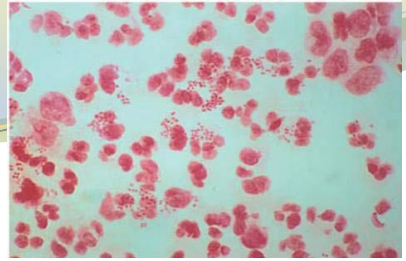

Neisseria meningitidis

- Encapsulated Gram negative diplococci
- Serotype based on polysaccharide capsule
- Serotypes A, B, C, Y, W-135 cause human disease
- Colonizes the oropharynx of up to 10%
- Transmitted by respiratory droplets and direct contact
- Risk of transmission low- 2-4 cases per 1000 household contacts (500-800x risk in general population)

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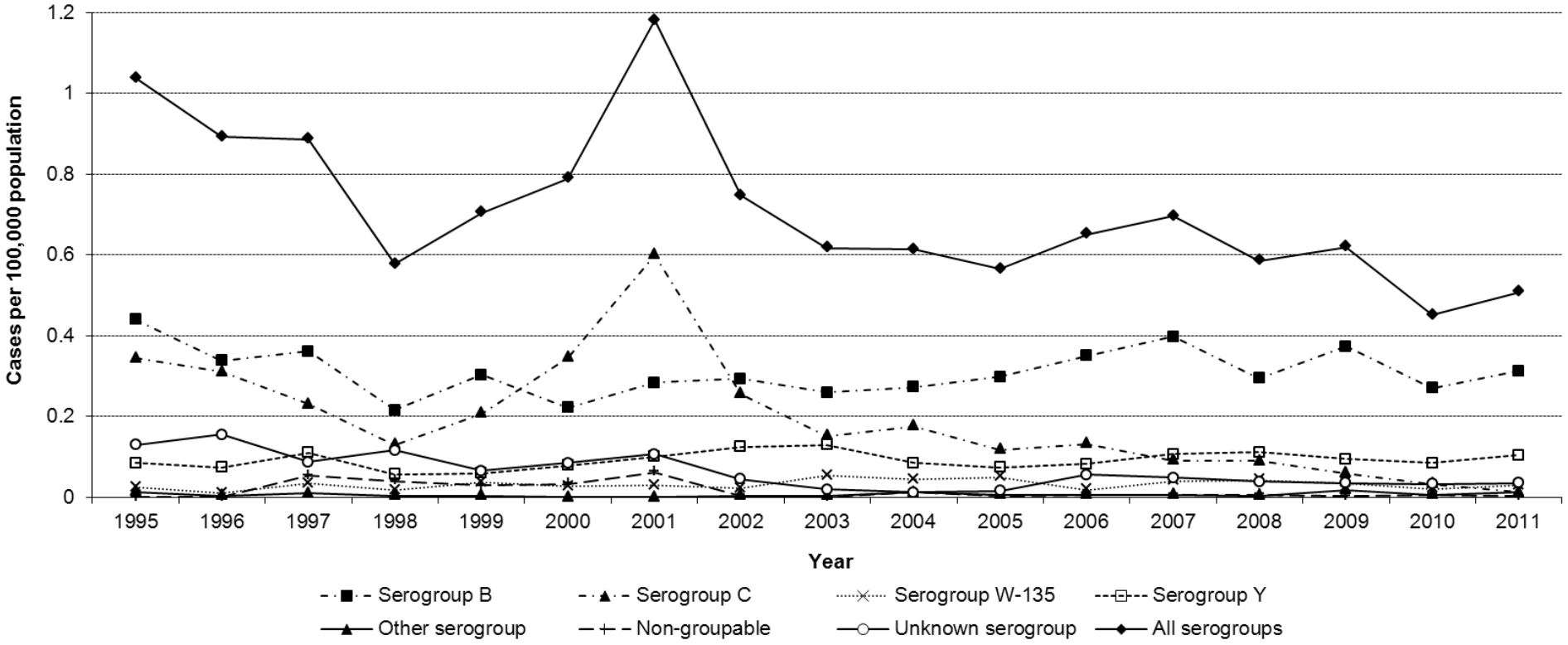
IMD in Canada: 1995-2011



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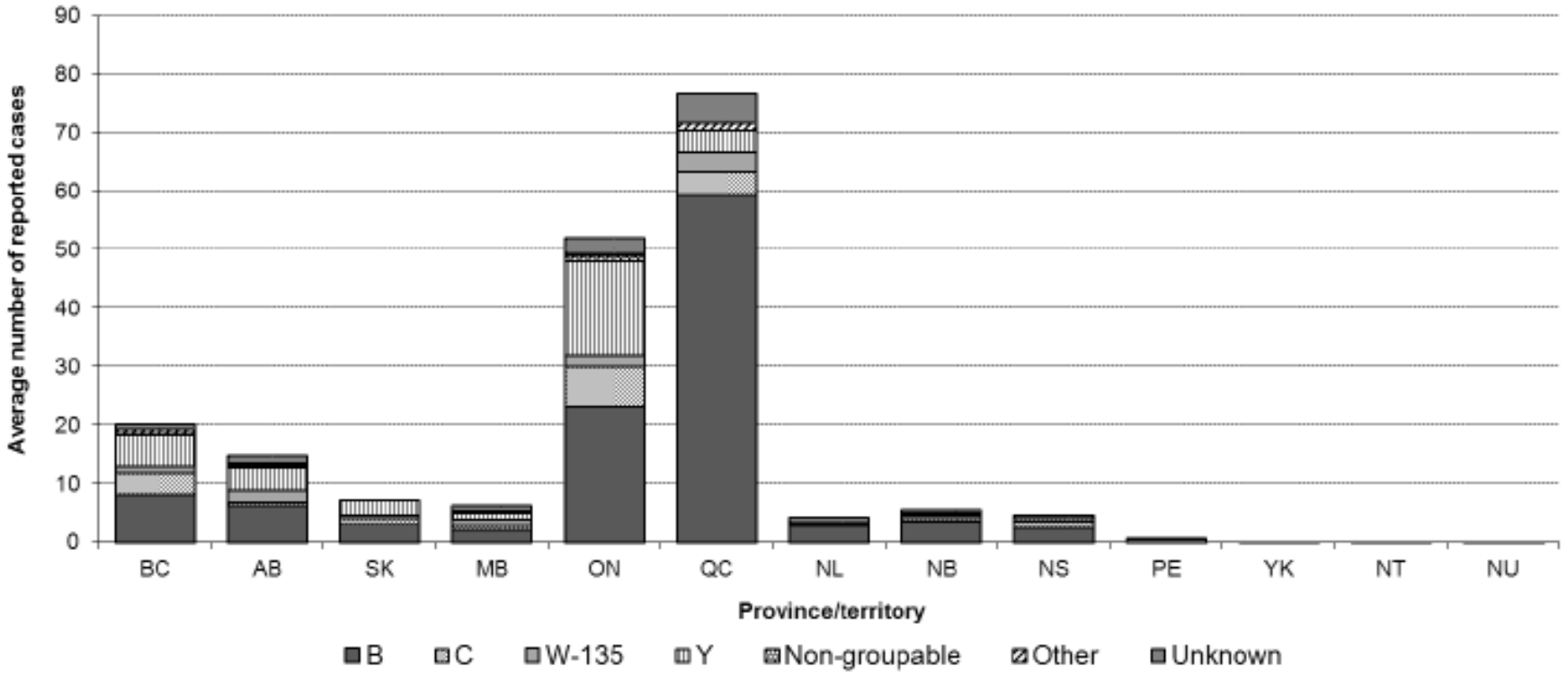
Summary of IMD in Canada by serotype (2007-2011)

Serogroup	2011		2007 to 2011			
	Number of cases	Incidence (cases per 100,000 population)	Average annual number of cases (range)	Average annual incidence (cases per 100,000 population)	Median age (years)	Case fatality ratio
A	0	0	0.2 (0 to 1)	0	16	0.0%
B	108	0.31	111 (92 to 131)	0.33	16	6.0%
C	4	0.01	19 (4 to 30)	0.06	44.5	15.3%
W-135	10	0.03	11.2 (7 to 14)	0.03	38	8.5%
Y	36	0.10	33.8 (29 to 37)	0.10	47	12.1%
Other	4	0.01	3 (1 to 6)	0.01	34	0%
Non-groupable	1	0	1.6 (1 to 2)	0	28	10.0%
Unknown	12	0.04	12.8 (11 to 16)	0.04	16.5	8.2%
All serogroups	175	0.51	192.4 (154 to 229)	0.57	20	8.2%

Summary of IMD in Canada by P/T



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Available meningococcal vaccines

	Age indication	Schedule	Manufacturer
Monovalent Men C-C			
Meningitec Menjugate NeisVac-C			Pfizer Novartis Baxter
Quadrivalent Men-C			
Menactra Menveo Nimenrix	9mos-55y 2mos-55y 12mos-55y		Sanofi Novartis GSK
4CMenB (Bexsero)	2-17y	1-10y – 2 doses, 2m apart ≥11y- 2d, 1 mos apart	

NACI- who should get Quadrivalent Conj Men A,C, Y, W-135 vaccine?

- Persons 2-(55)y (either vaccine):
  - functional/anatomic asplenia*
  - complement deficiency and other specified immunodeficiency (congenital)*
  - HSCT*
  - SOT, HIV
  - travelers
  - lab personnel
  - military recruits
  - close contacts of non C disease*

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FAQ's

- Does it matter which quad vaccine? NO
- Do I have to wait a certain amount of time if they have received Men-C-C in school? NO
- If receiving quad Men vaccine before grade 7, should they still get the grade 7 dose? YES
- Can I give Quad men and Men B at the same time? YES
- How much does it cost? ~$150/dose

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N. menigitidis Type B- Bexsero

- Bexsero- 4 component protein vaccine
- Surveillance suggests will cover ~2/3 of Canadian Men B strains
- 3 dose series in infants; 2 doses in adolescents (up to 10y give 2 months apart; ≥11y give 1 month apart)

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NACI recommendations

- Individuals >2 mos who are:
  - At high risk of meningococcal disease
  - Have been in close contact with a case of serogroup B IMD
  - Who may be at risk due to an outbreak
  - **Who are without contraindications and who wish to be immunized**

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Why didn't NACI recommend a universal infant program?

- Rare disease
- Vaccine only covers about 2/3 of strains
- No efficacy or duration of protection data (only immunogenicity)
- No data on impact on colonization
- Temp≥38 C observed in 61% of infants when given with other routine vaccines (vs 38% when given alone)

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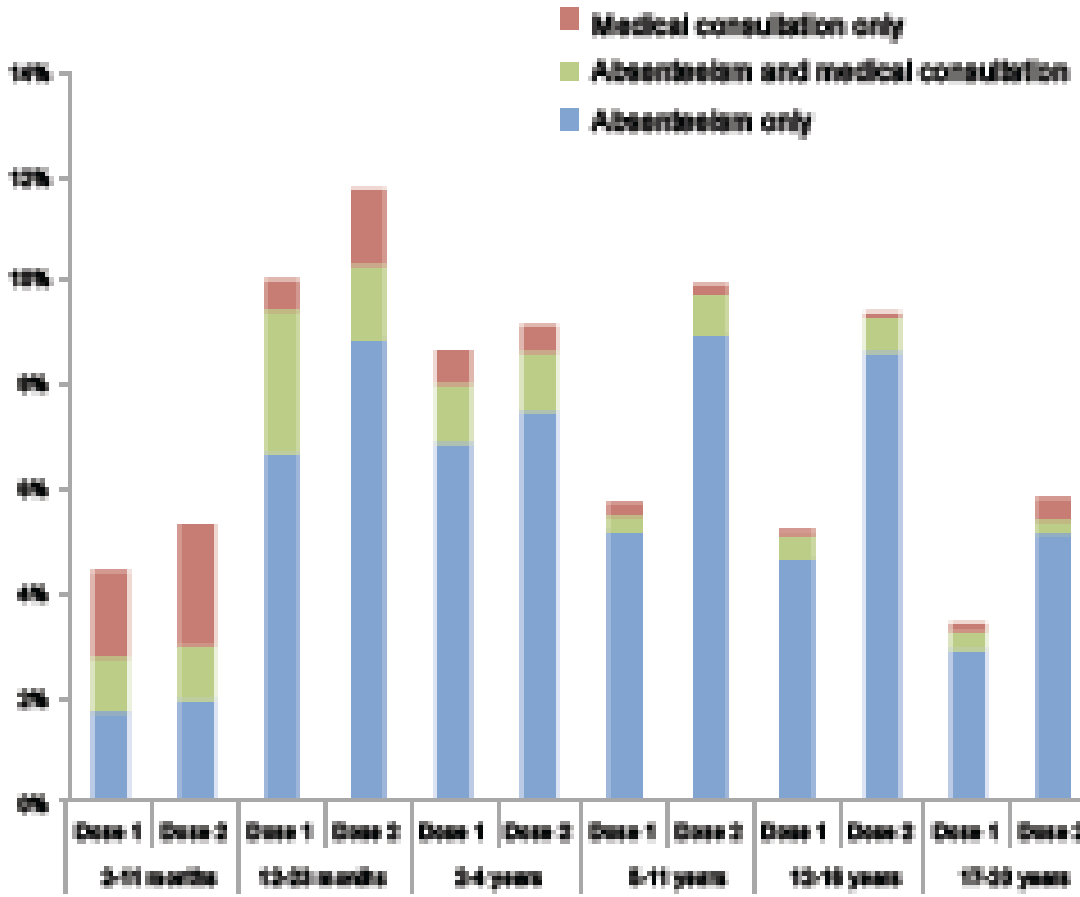
Absenteeism/medical visit



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Summary of AE's

- Fever on day 1 or 2 expected in 10-20% and is reduced by prophylactic acetaminophen
- 5-10% will miss school or work for 1-2d for general malaise or sore arm occurring within 48h
- No serious adverse events observed in 46,000 kids <20y in Quebec in 2014

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FAQs

- Can I give Bexsero and quadrivalent vaccine at the same time? YES
- Is it OK to give to adults? YES
- How much does it cost? ~$140/dose

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MMR boosters in adults**

- Non-immune
  - adults born in or after 1970*- 1 dose
  - Students born in or after 1970- 2 doses
  - **HCW-** irrespective of year of birth- 2 doses
  - Military personnel- irrespective of year of birth- 2 doses
  - Travellers: Born after 1970- 2 doses; before 1970- 1 dose

*proof of immunity= documentation of 2 doses of MMR after first Bday, OR history of lab-confirmed infection OR Lab evidence of immunity

Persons born **before 1970 considered immune unless in a high-risk group

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QUESTIONS & DISCUSSION