Vaccine and Immunization for the Elderly

Pawalee Niamtaworn
BCP, BCPS, FACP

Outlines

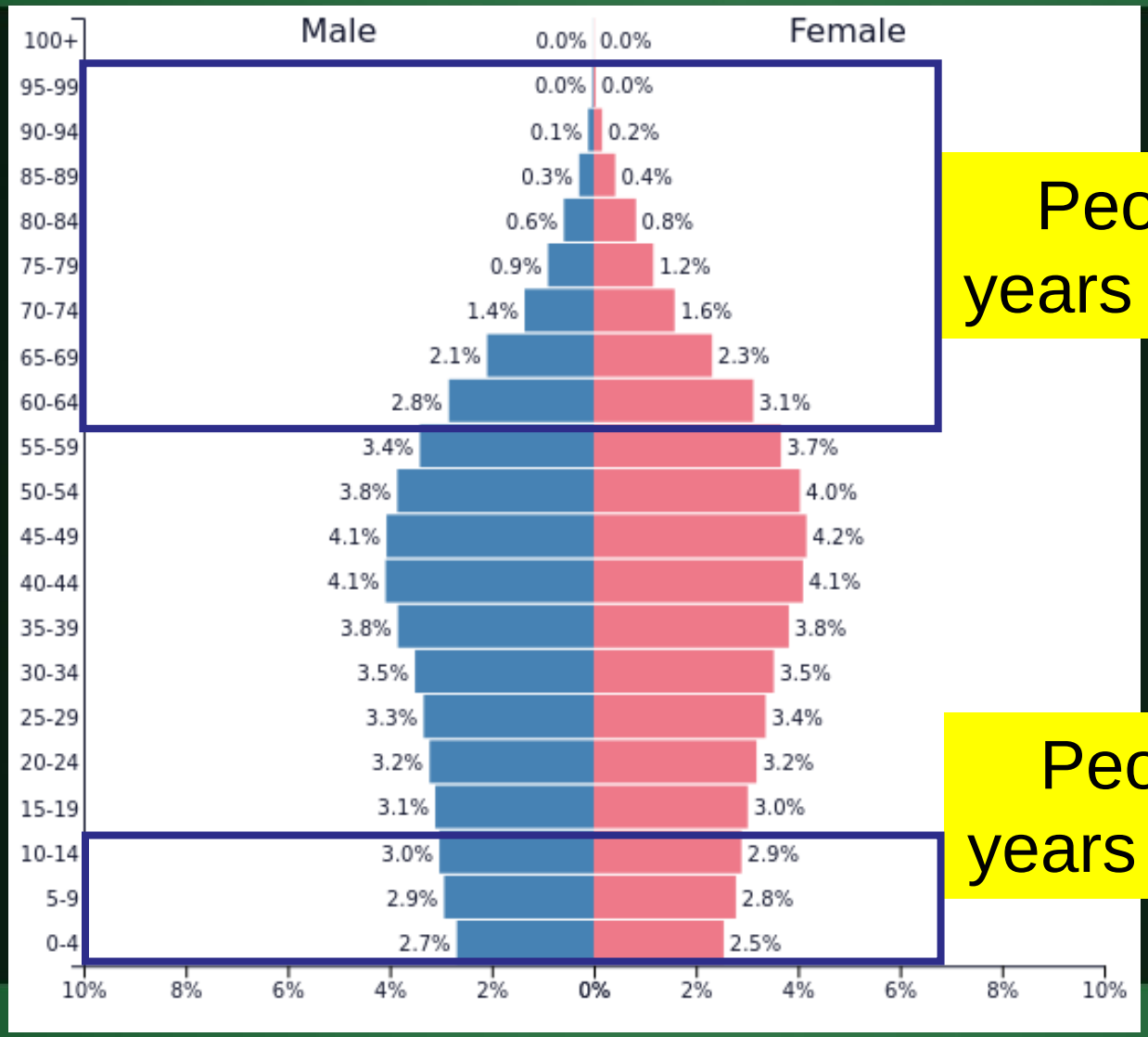
- Overview
- Immunity of older adult
- Vaccine recommendation

Overview

- 2015 – 2050,
  - Population aged > 60 years → from 12% to 22% (900 million to 2 billion)
- At 2020,
  - people aged > 60 years will outnumber children aged < 5 years.
- In 2050,
  - 80% of people aged > 60 yearswill be living in low- and middle-income countries.

Ageing and Health, World Health Organization 2018.

Age distribution among Thai population



People aged > 60 years is around 17.8%

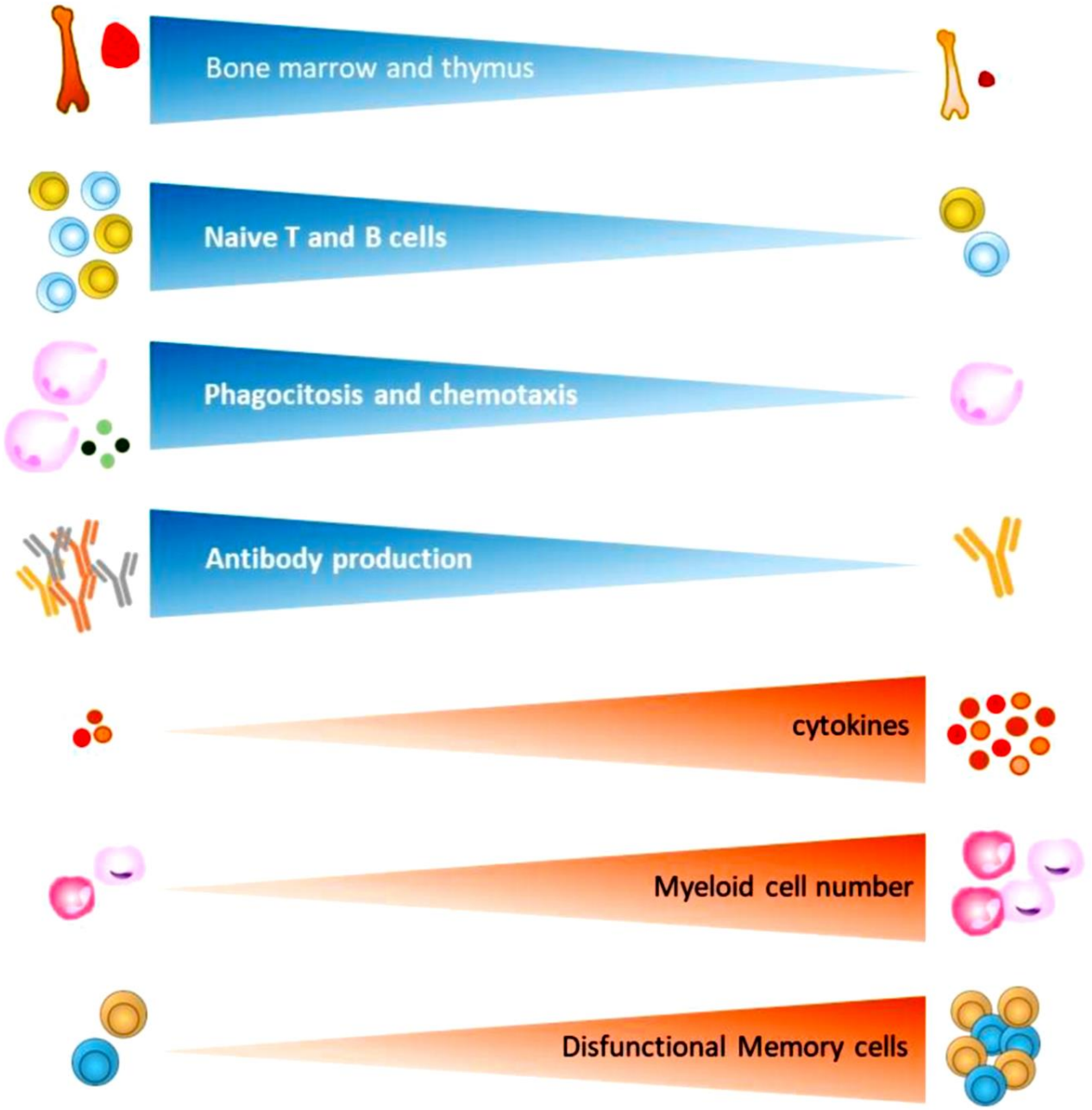
People aged < 15 years is around 16.8%

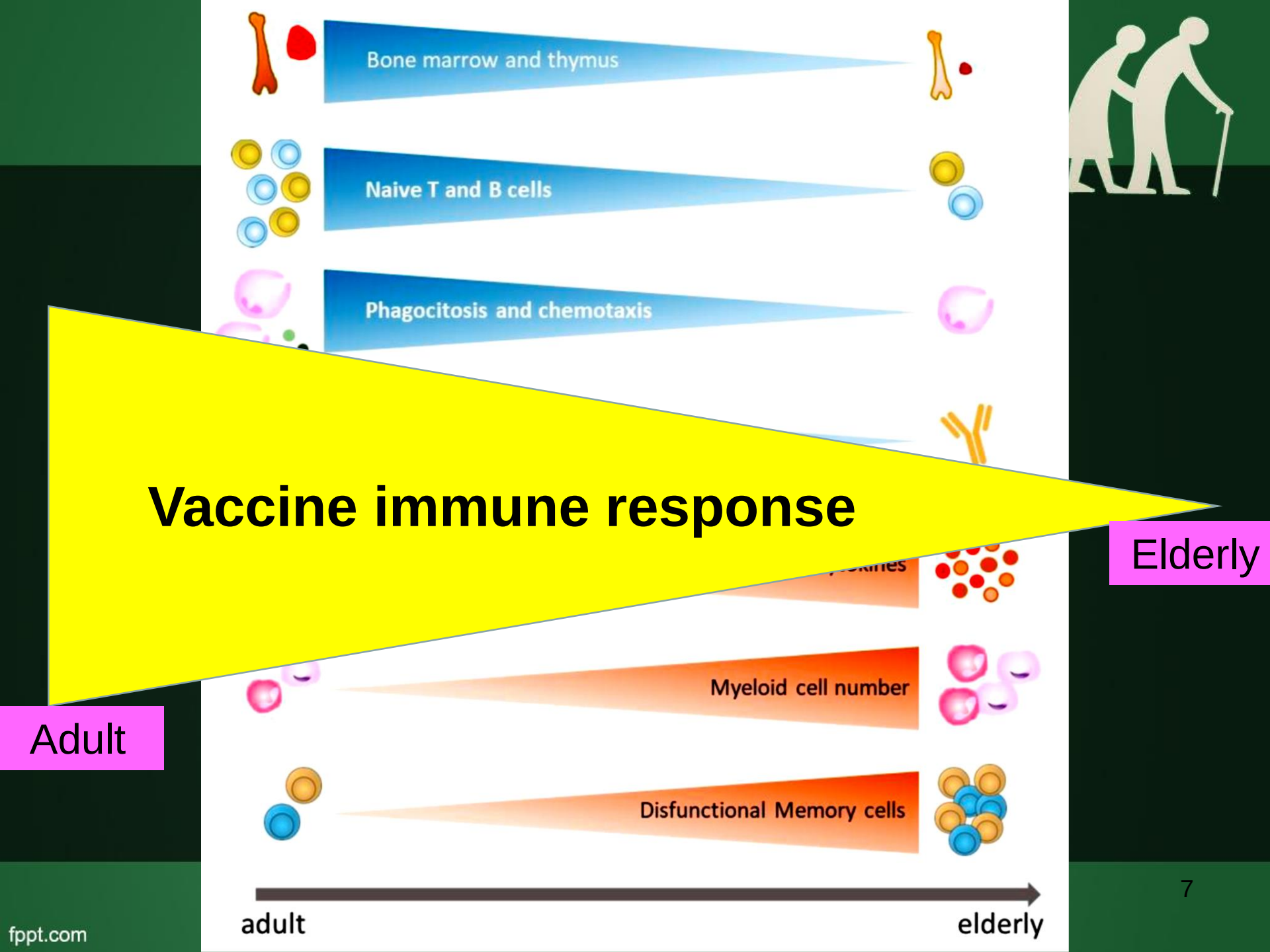
National Statistical Office of Thailand 2018

Ageing and Immunity

- What comes with ageing
  - poorer responses to vaccination
  - lower capacity to mediate anti-cancer responses,
  - more inflammation and tissue damage
  - autoimmunity
  - loss of control of persistent infections

Experimental Gerontology 105 (2018) 4–9


Bone marrow and thymus
Naive T and B cells
Phagocitosis and chemotaxis
Antibody production
cytokines
Myeloid cell number
Disfunctional Memory cells
adult
elderly



Vaccine immune response

Adult

Elderly

Vaccine Recommendation For Elderly

Recommended Adult Immunization Schedule by Age Group, United States, 2019

Vaccine	19–21 years	22–26 years	27–49 years	50–64 years	≥65 years
Influenza inactivated (IIV) or **Influenza recombinant** (RIV)	1 dose annually				
Influenza live attenuated (LAIV)	1 dose annually				
Tetanus, diphtheria, pertussis (Tdap or Td)	1 dose Tdap, then Td booster every 10 yrs				
Measles, mumps, rubella (MMR)	1 or 2 doses depending on indication (if born in 1957 or later)				
Varicella (VAR)	2 doses (if born in 1980 or later)				
Zoster recombinant (RZV) *(preferred)*				2 doses	
Zoster live (ZVL)				1 dose	
Human papillomavirus (HPV) **Female**	2 or 3 doses depending on age at initial vaccination				
Human papillomavirus (HPV) **Male**	2 or 3 doses depending on age at initial vaccination				
Pneumococcal conjugate (PCV13)	1 dose				
Pneumococcal polysaccharide (PPSV23)	1 or 2 doses depending on indication				1 dose
Hepatitis A (HepA)	2 or 3 doses depending on vaccine				
Hepatitis B (HepB)	2 or 3 doses depending on vaccine				
Meningococcal A, C, W, Y (MenACWY)	1 or 2 doses depending on indication, then booster every 5 yrs if risk remains				
Meningococcal B (MenB)	2 or 3 doses depending on vaccine and indication				
***Haemophilus influenzae* type b** (Hib)	1 or 3 doses depending on indication				

Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack evidence of past infection

Recommended vaccination for adults with an additional risk factor or another indication

No recommendation

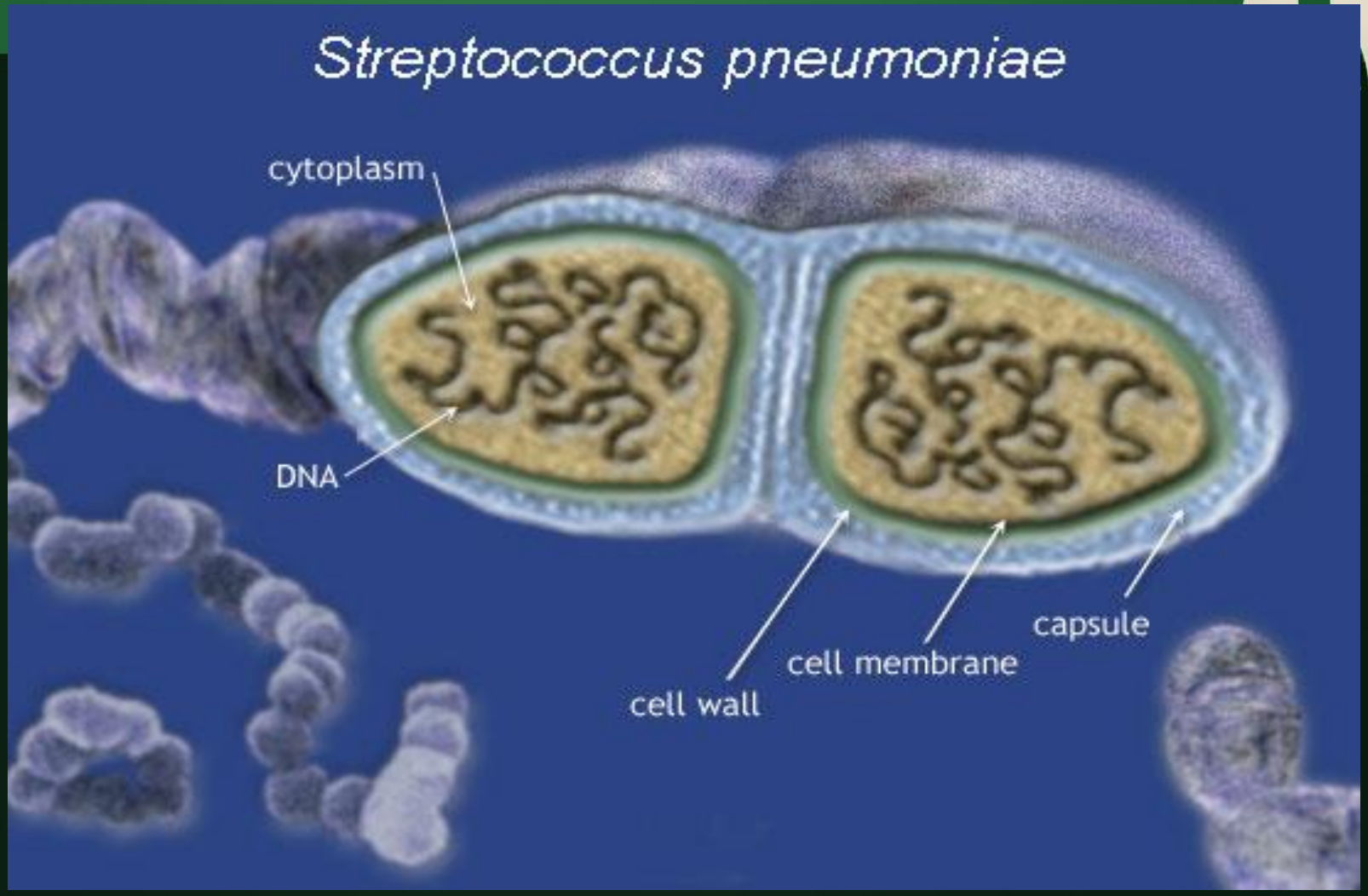
คำแนะนำการให้วัคซีนป้องกันโรคสำหรับผู้ใหญ่และผู้สูงอายุ สมาคมโรคติดเชื้อแห่งประเทศไทย ปี พ.ศ. 2561

Vaccines[1]	Age groups (years)		
	19 – 26 years	27 – 64 years	≥ 65 years
Tetanus, diphtheria, pertussis vaccine (Td or Tdap)[2]	Boost with 1 dose of Td every 10 years (eg. at age 20, 30, 40, 50, 60…..)		
	Substitute one-time of Td with Tdap[3]		
Varicella vaccine[4]	2 doses (consider Anti-VZV IgG test before vaccination)		
Measles, mumps, rubella (MMR) vaccine[5]	2 doses(age ≤ 40 years)		
Human Papillomavirus (HPV) vaccine	3 doses (female)[6]		
	3 doses (male)[7]		
Inactivated influenza vaccine[8]	1 dose annually[9]		
Hepatitis A vaccine[10]	2 doses	2 doses (consider anti HAV IgG test before vaccination)	
Hepatitis B vaccine[11]	3 doses (consider Anti-HBs, Anti-HBc and HBsAg test before vaccination)		
23-valent pneumococcal polysaccharide vaccine (PPV-23)[12]			1 dose
13-valent pneumococcal conjugate vaccine (PCV-13)[13]			1 dose
Dengue vaccine[14]	3 doses (age ≤ 45 years)		
Live-attenuated zoster vaccine[15]			1 dose (age ≥ 60 years)

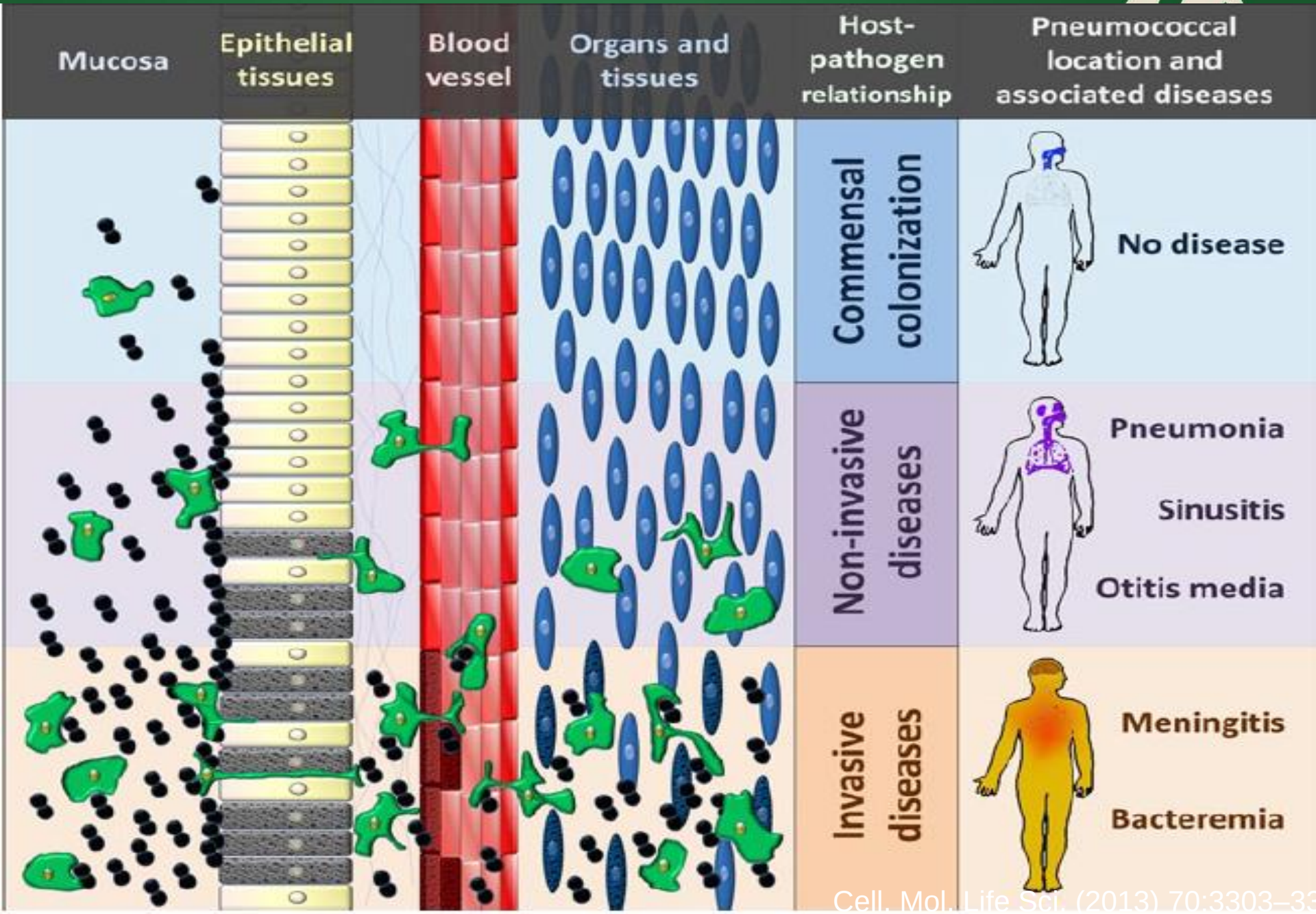
Recommended vaccine	Optional vaccine (considered in specific conditions: ตารางที่ 2)	Not recommended	Contraindication

Pneumococcal Disease

- Streptococcus pneumoniae
- Gram-positive diplococci
- Encapsulated bacterium
- More than 90 serotypes have been identified.
- Reservoir → human nasopharnx
- Mode of transmission
  - Contact with respiratory droplets

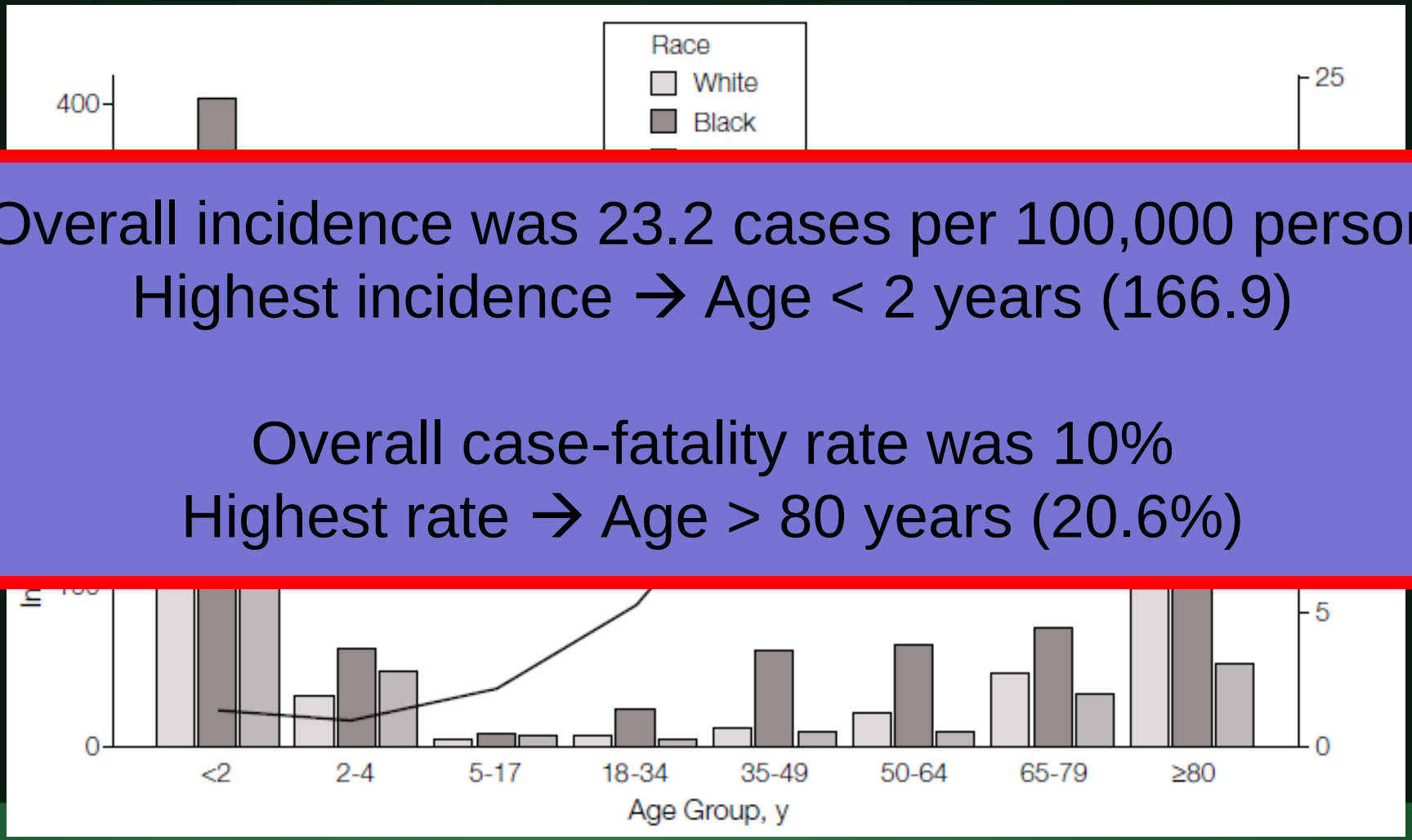

Streptococcus pneumoniae
cytoplasm
DNA
cell wall
cell membrane
capsule

Pneumococcal disease



Cell. Mol. Life Sci. (2013) 70:3303–33

Incidence and case-fatality rate of invasive pneumococcal disease by race and age group, US 1998



Overall incidence was 23.2 cases per 100,000 person
Highest incidence → Age < 2 years (166.9)

Overall case-fatality rate was 10%
Highest rate → Age > 80 years (20.6%)

JAMA 2001; 285: 1729-1735.

Am. J. Trop. Med. Hyg., 93(6), 2015, pp. 1140–1147
doi:10.4269/ajtmh.15-0429

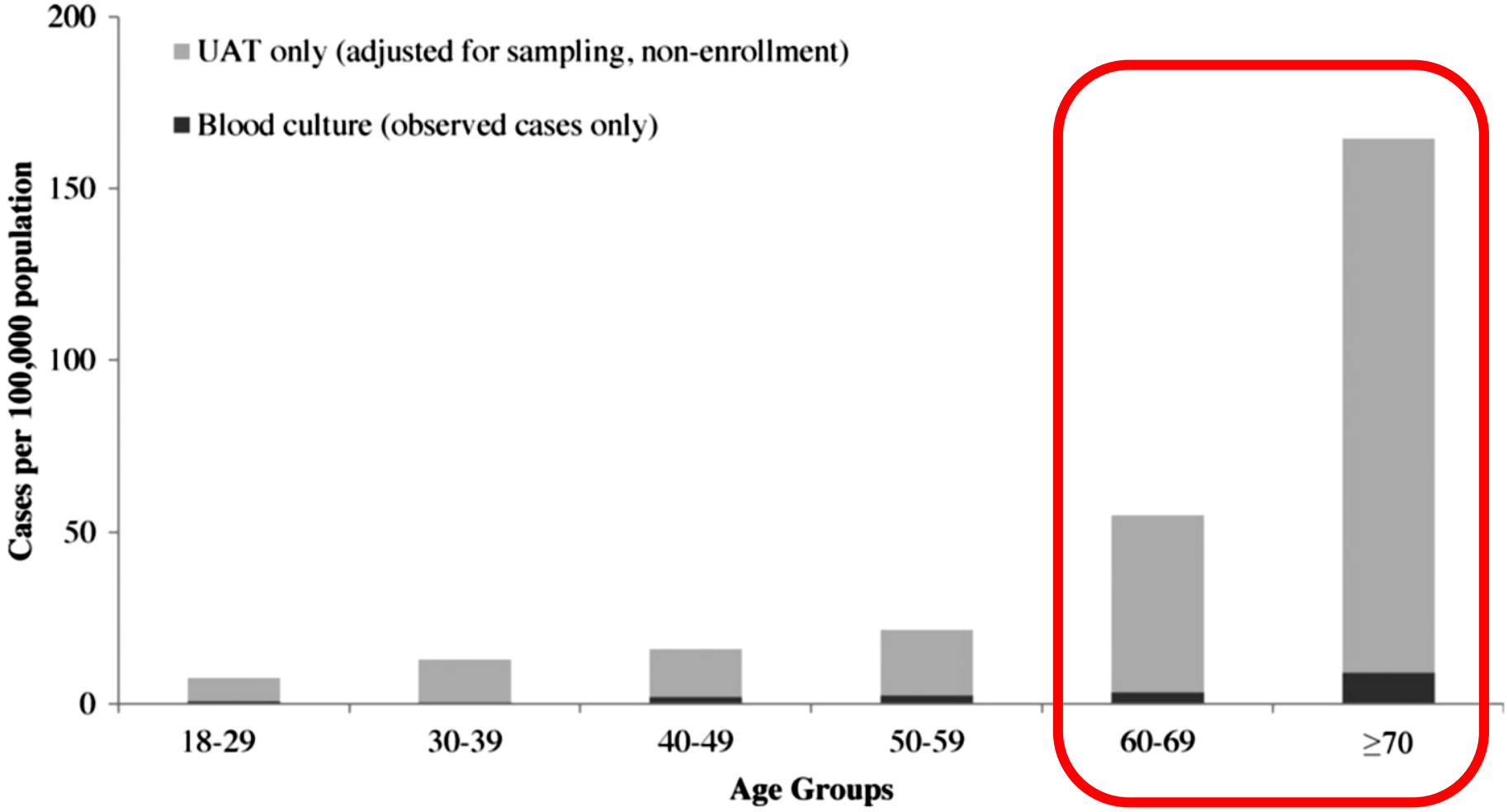
Incidence of Pneumococcal Pneumonia among Adults in Rural Thailand, 2006–2011: Implications for Pneumococcal Vaccine Considerations

Barameht Piralam,* Sara M. Tomczyk, Julia C. Rhodes, Somsak Thamthitiwat, Christopher J. Gregory, Sonja J. Olsen, Prabda Praphasiri, Pongpun Sawatwong, Sathapana Naorat, Somrak Chantra, Peera Areerat, Cameron P. Hurst, Matthew R. Moore, Charung Muangchana, and Henry C. Baggett

Nakhon Phanom Provincial Health Office, Nakhon Phanom Province, Thailand; Faculty of Public Health, Khon Kaen University, Khon Kaen Province, Thailand; Epidemic Intelligence Service, Division of Scientific Education and Professional Development, Centers for Disease Control and Prevention, Atlanta, Georgia; National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; International Emerging Infections Program, Global Disease Detection Center, Thailand Ministry of Public Health–United States Centers for Disease Control and Prevention Collaboration, Nonthaburi, Thailand; Division of Global Health Protection, Centers for Disease Control and Prevention, Atlanta, Georgia; Influenza Division, Centers for Disease Control and Prevention, Atlanta, Georgia; Influenza Program, Thailand Ministry of Public Health–United States Centers for Disease Control and Prevention Collaboration, Nonthaburi, Thailand; Sa Kaeo Provincial Health Office, Sa Kaeo Province, Thailand; National Vaccine Institute, Nonthaburi, Thailand; Faculty of Medicine, Khon Kaen University, Khon Kaen Province, Thailand

- An active, population-based surveillance study
- 20 acute care hospitals in Sa Kaeo Province and Nakhon Phanom Province
- Study period: 2002 – 2014

Incidence of pneumococcal pneumonia hospitalizations by age group among adults in rural Thailand, 2006–2011.



PNEUMOCOCCAL MENINGITIS AT A THAI HOSPITAL OVER A 10-YEAR PERIOD: CLINICAL OUTCOMES, SEROTYPES, AND ANTIMICROBIAL SUSCEPTIBILITY PATTERNS

Juthathip Suphanklang[1,2], Wichai Santimaleeworagun[1,3], Sudaluck Thunyaharn[4] and Jantima Traipattanakul[5]

[1]Department of Pharmacy, Faculty of Pharmacy, Silpakorn University, Nakhon Pathom; [2]College of Pharmacotherapy Thailand, Pharmacy Council, Nonthaburi; [3]Antibiotic Renaissance Project and Antibiotic Optimization and Patient Care Project by Pharmaceutical Initiative for Resistant Bacteria and Infectious Diseases Working Group (PIRBIG); [4]Faculty of Medical Technology, Nakhonratchasima College, Nakhon Ratchasima; [5]Division of Infectious Disease, Department of Medicine, Phramongkutklao Hospital, Bangkok, Thailand

Mortality rate for pneumococcal meningitis was 37.5%!!!
(6 out of 16 had died.)

Southeast Asian J Trop Med Public Health 2017; 48(6): 1281-1289.

Pneumococcal vaccine milestone

Year	Vaccines
1940s	4-valent PPSV (military recruits and elderly in the US)
1970s	6 – 14-valent PPSV (mineworker in South Africa and Papua New Guinea)
1977	14-valent PPSV was licensed
1983	23-valent PPSV was licensed
2000	First PCV vaccine – PCV-7
2009	PCV-10 was licensed in Canada and Europe
2010	PCV-13 was approved

Polysaccharide vs. Conjugated

Characteristic	Pure Polysaccharide	Protein-conjugated Polysaccharide
T-cell	Independent	Dependent
Immunogenicity	Low	High
Nasopharynx carriage	Not prevent	Prevent

Available Vaccines

PCV 7	4	6B	9V	14	18 C	19 F	23 F

Conjugated to non-toxic diphtheria toxin (CRM197) (Prevnar7)

PCV 10	4	6B	9V	14	18 C	19 F	23 F	1	5	7F

Mix carriers; protein D of H. influenzae, diphtheria (18C), andtetanus toxoids (19F) (Synflorix)

PCV 13	4	6B	9V	14	18 C	19 F	23 F	1	5	7F	6A	3	19 A

Conjugated to non-toxic diphtheria toxin (CRM197) (Prevnar13)

PPSV 23	4	6B	9V	14	18 C	19 F	23 F	1	5	7F	3	19 A	2	8	9N	10 A	11 A	12 F	15 B	17 F	20	22 F	33 F

Purified capsular polysaccharide antigens (Pneumovax23)

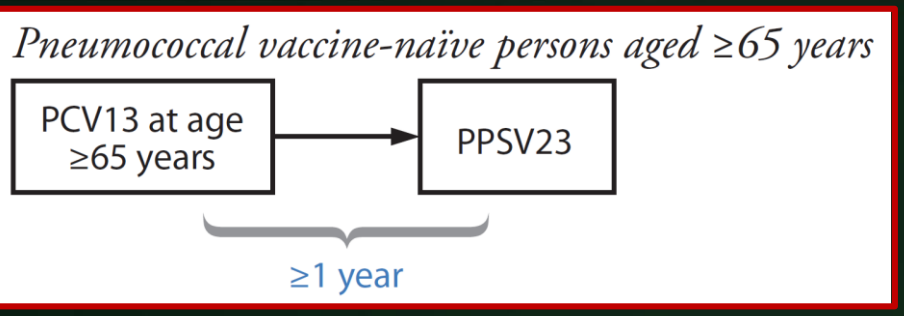
Dose and Administration

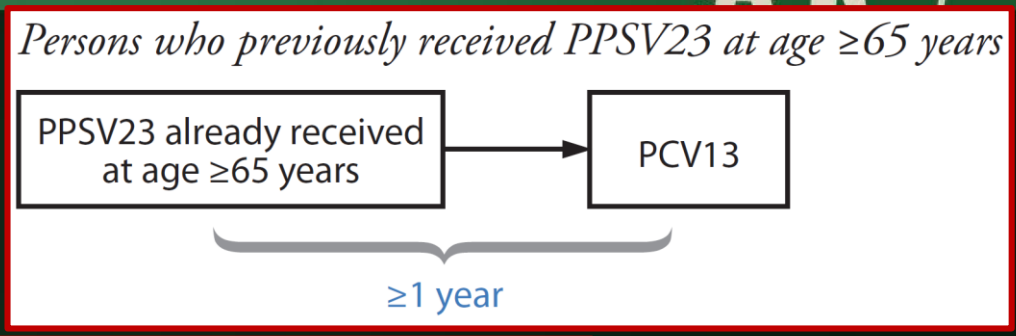
PPSV23 (Pneumovax®23)	PCV13 (Prevnar13®)
Manufacturer: *Merck* *www.merckvaccines.com/Products/Pneumovax/Pages/home*	***Manufacturer:*** *Pfizer* *http://www.pfizerpro.com/hcp/prevnar13*
How Supplied: 0.5mL Single Dose Vial Multi-Dose (5 dose Vial)	***How Supplied:*** Prefilled Syringe (10 per Package)
Storage and Handling: Refrigerate on Arrival Store at 2°C to 8°C DO NOT FREEZE Discard after the expiration date	***Storage and Handling:*** Refrigerate on Arrival Store at 2°C to 8°C DO NOT FREEZE Discard after the expiration date
Special instructions: None	***Special instructions:*** Shake well to obtain a homogeneous white suspension
Route of Administration: 0.5mL IM or SQ	***Route of Administration:*** 0.5mL IM ONLY

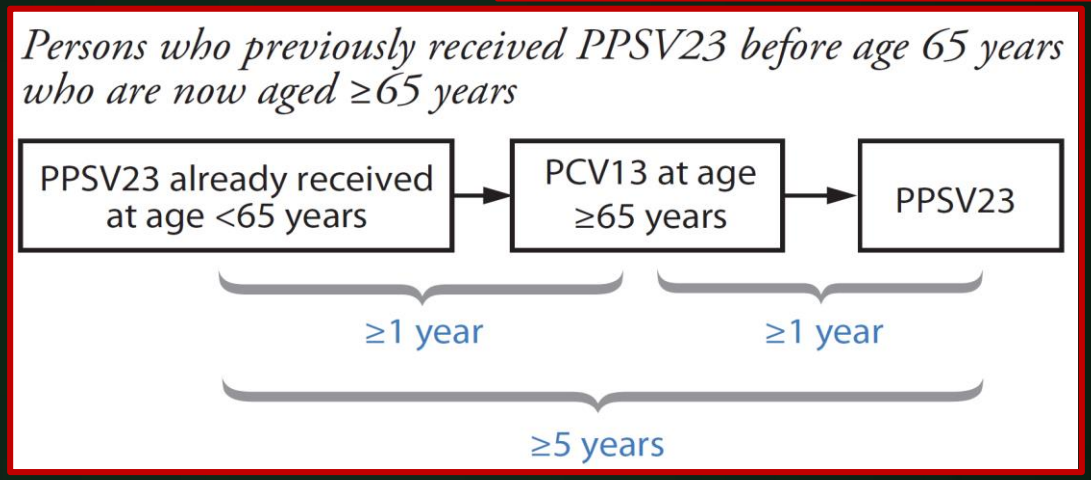
Recommendation for adult

Medical indication	Underlying medical condition	PCV13 for ≥ 19 years	PPSV23* for 19 through 64 years		PCV13 at ≥ 65 years	PPSV23 at ≥ 65 years
		Recommended	Recommended	Revaccination	Recommended	Recommended
None	None of the below				✓	✓ ≥ 1 year after PCV13
Immunocompetent persons	Alcoholism		✓		✓	✓ ≥ 1 year after PCV13 ≥ 5 years after any PPSV23 at < 65 years
	Chronic heart disease†					
	Chronic liver disease					
	Chronic lung disease§					
	Cigarette smoking					
	Diabetes mellitus					
	Cochlear implants	✓	✓ ≥ 8 weeks after PCV13		✓ If no previous PCV13 vaccination	✓ ≥ 8 weeks after PCV13 ≥ 5 years after any PPSV23 at < 65 years
	CSF leaks					
Persons with functional or anatomic asplenia	Congenital or acquired asplenia	✓	✓ ≥ 8 weeks after PCV13	✓ ≥ 5 years after first dose PPSV23	✓ If no previous PCV13 vaccination	✓ ≥ 8 weeks after PCV13 ≥ 5 years after any PPSV23 at < 65 years
	Sickle cell disease/other hemoglobinopathies					
Immunocompromised persons	Chronic renal failure	✓	✓ ≥ 8 weeks after PCV13	✓ ≥ 5 years after first dose PPSV23	✓ If no previous PCV13 vaccination	✓ ≥ 8 weeks after PCV13 ≥ 5 years after any PPSV23 at < 65 years
	Congenital or acquired immunodeficiencies¶					
	Generalized malignancy					
	HIV infection					
	Hodgkin disease					
	Iatrogenic immunosuppression‡					
	Leukemia					
	Lymphoma					
	Multiple myeloma					
	Nephrotic syndrome					
	Solid organ transplant					

Interval between PCV13 and PPSV23







For immunocompetent adults who previously received PPSV23 when aged <65 years and for whom an additional dose of PPSV23 is indicated when aged ≥65 years, this subsequent PPSV23 dose should be given ≥1 year after PCV13 and ≥5 years after the most recent dose of PPSV23.

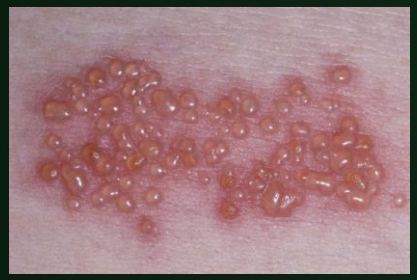
For adults aged ≥65 years with immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leaks, or cochlear implants, the recommended interval between PCV13 followed by PPSV23 is ≥8 weeks.

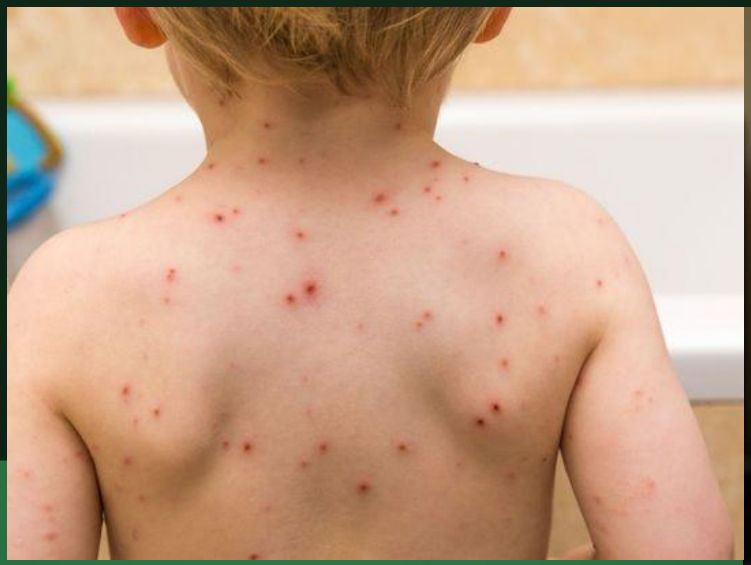
MMWR 2014. (Errantumin 2015)

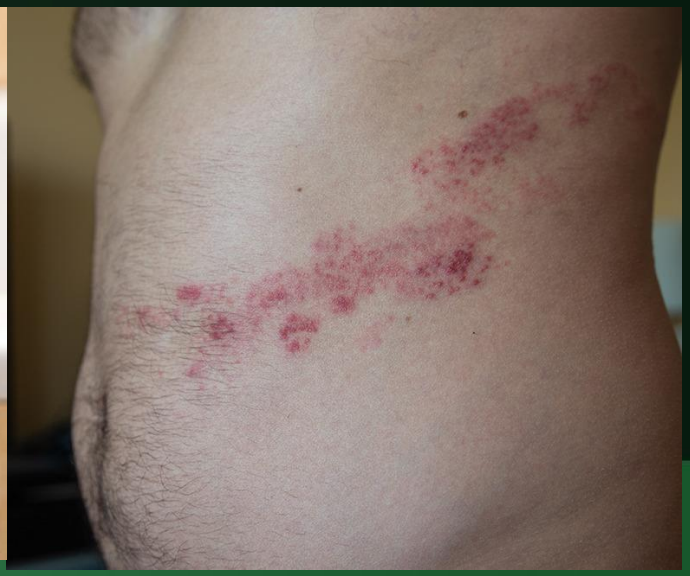
Herpes Zoster Vaccine

Overview

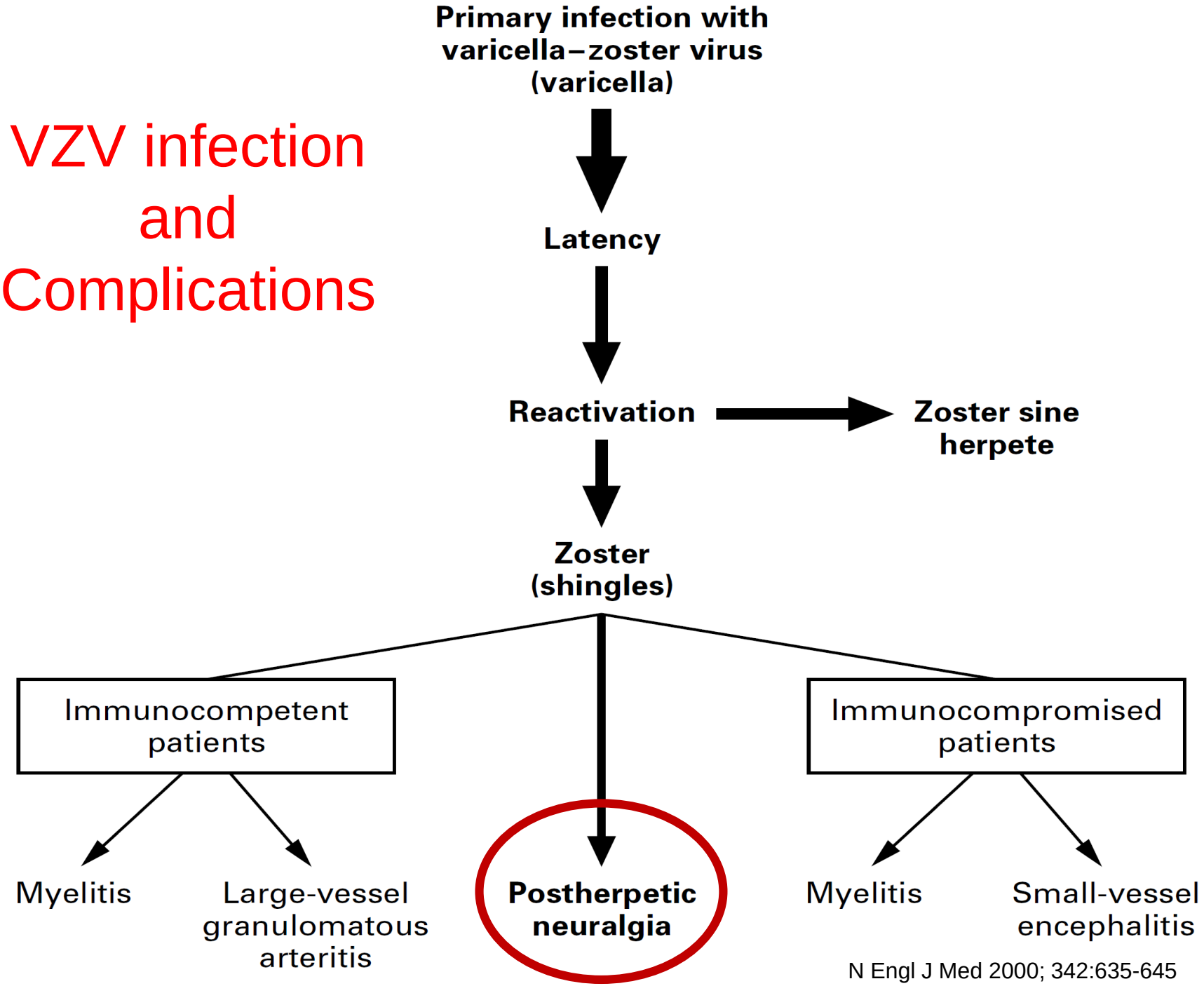
- Varicella zoster virus (VZV)
- Human herpes virus 3
- Transmitted by the respiratory route (droplets) or direct contact
- Clinical manifestation: pus-filled vesicles
- Virus may remain latent in dorsal root ganglia





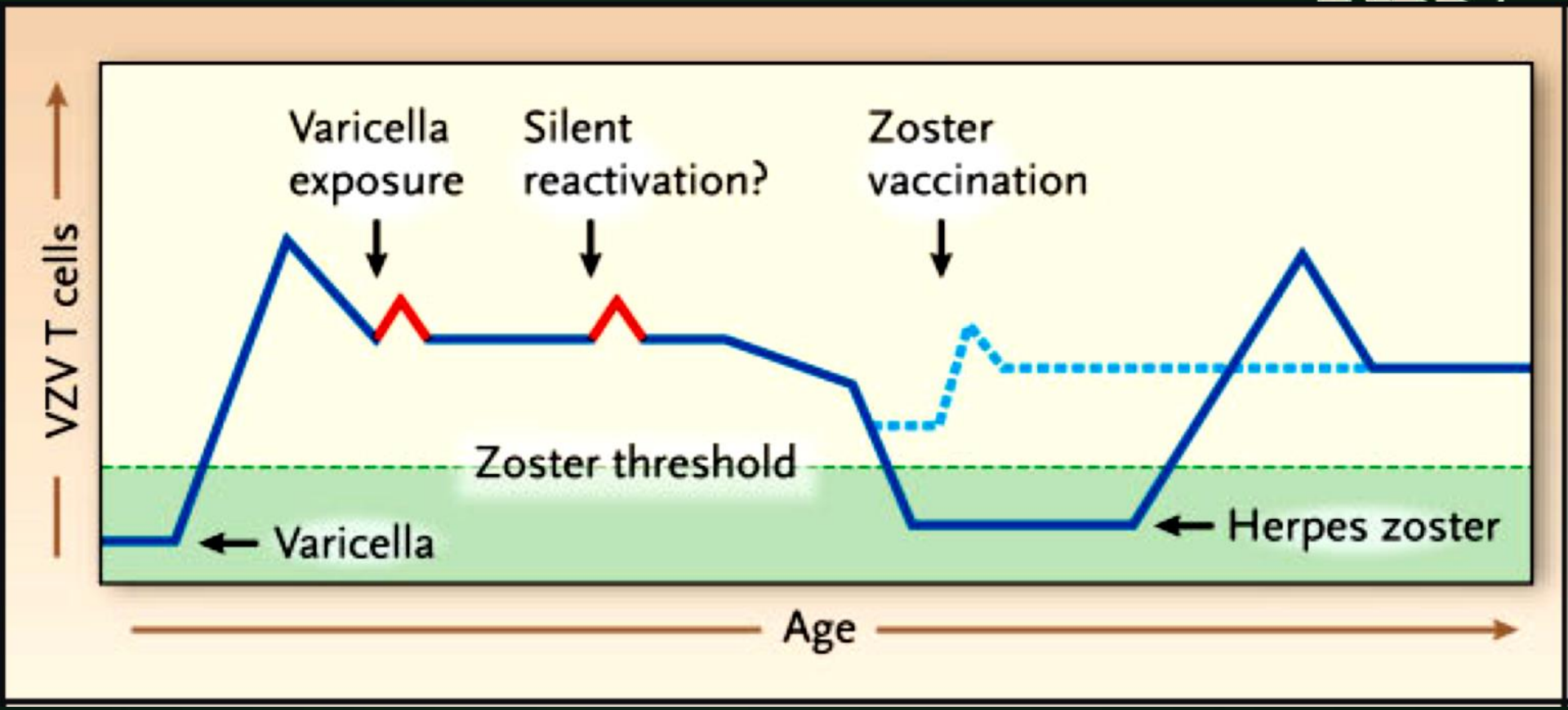


VZV infection and Complications



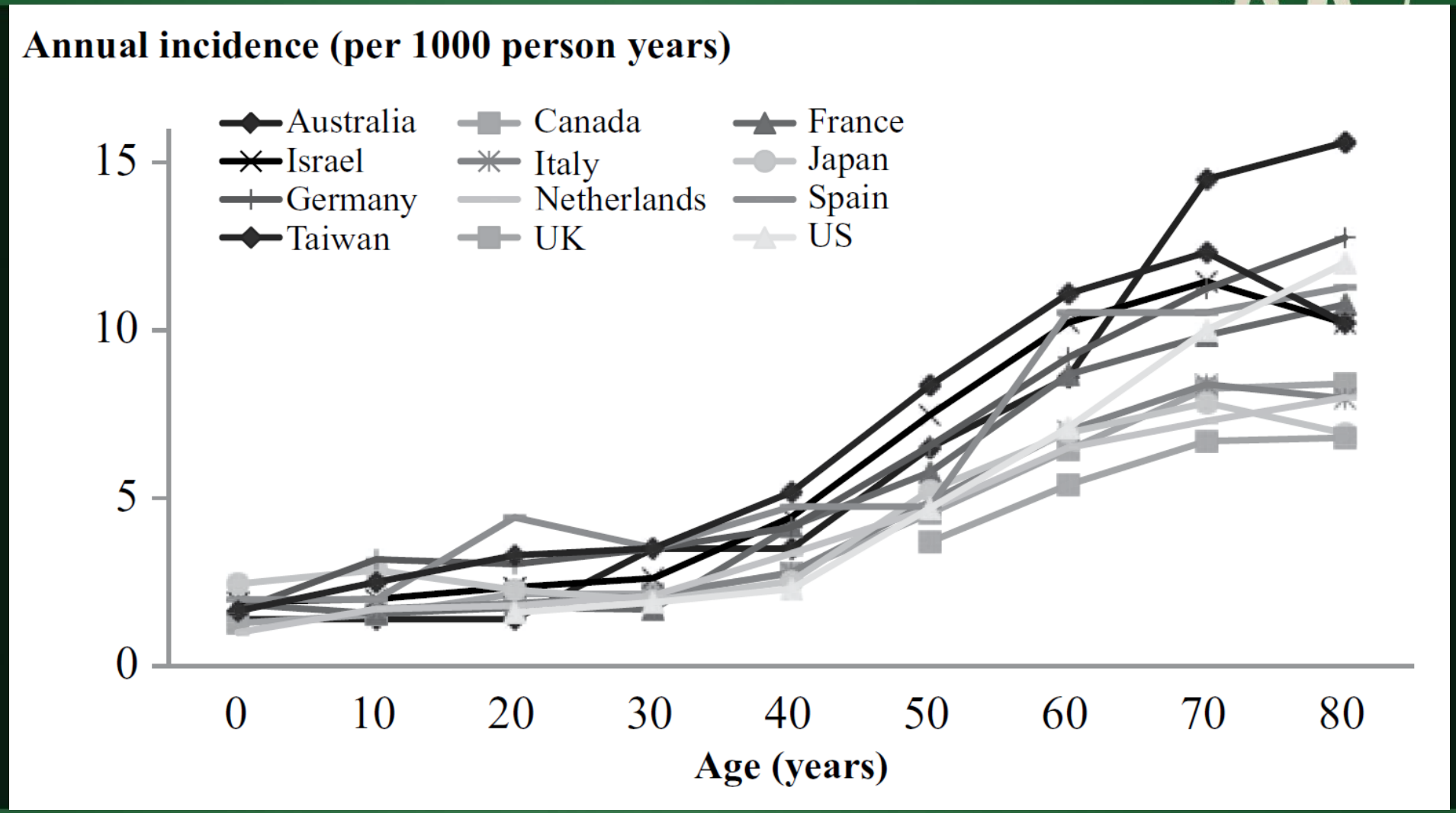
N Engl J Med 2000; 342:635-645

Host and VZV infection



N Engl J Med 2005; 352:2266-2267

Incidence of Herpes Zoster Infection



Ther Adv Vaccines. 2015;3(4):109–120.

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Herpes zoster and postherpetic neuralgia: incidence and risk indicators using a general practice research database

Wim Opstelten, Jan W Mauritz, Niek J de Wit, Albert JM van Wijck[a], Wim AB Stalman[b] and Gerrit A van Essen

Opstelten W, Mauritz JW, de Wit NJ, van Wijck AJM, Stalman WAB and van Essen GA. Herpes zoster and postherpetic neuralgia: incidence and risk indicators using a general practice research database. *Family Practice* 2002; **19:** 471–475.

- A retrospective study using General Practice Research database in The Netherlands during 1994 – 1999.
- 837 cases with diagnosis of HZ infection

Risk of Postherpetic Neuralgia

Age group (no. of HZ patients)	After 1 month			After 3 months		
	n	%	(95% CI)	*n*	%	(95% CI)
⩽44 years ($n = 317$)	3	0.9	(0.2–2.7)	1	0.3	(0.01–1.7)
45–54 years ($n = 127$)	5	3.9	(1.3–9.0)	1	0.8	(0.02–4.3)
55–64 years ($n = 139$)	9	6.5	(3.0–11.9)	4	2.9	(0.8–7.2)
65–74 years ($n = 121$)	13	10.7	(5.2–16.3)	4	3.3	(0.9–8.3)
⩾75 years ($n = 133$)	24	18.0	(11.5–24.6)	12	9.0	(4.8–15.2)

Herpes Zoster Vaccine (Zostavax)

- Licensed in 2006
- Live, attenuated VZV
- Oka/Merck strain
  - Same strain used in the varicella vaccine, but more potent

Herpes Zoster Vaccine (Zostavax™)

- Licensed in 2006 (MSD)
- Live, attenuated VZV
- Oka/Merck strain
  - Same strain used in the varicella vaccine, but more potent

The NEW ENGLAND JOURNAL of MEDICINE

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

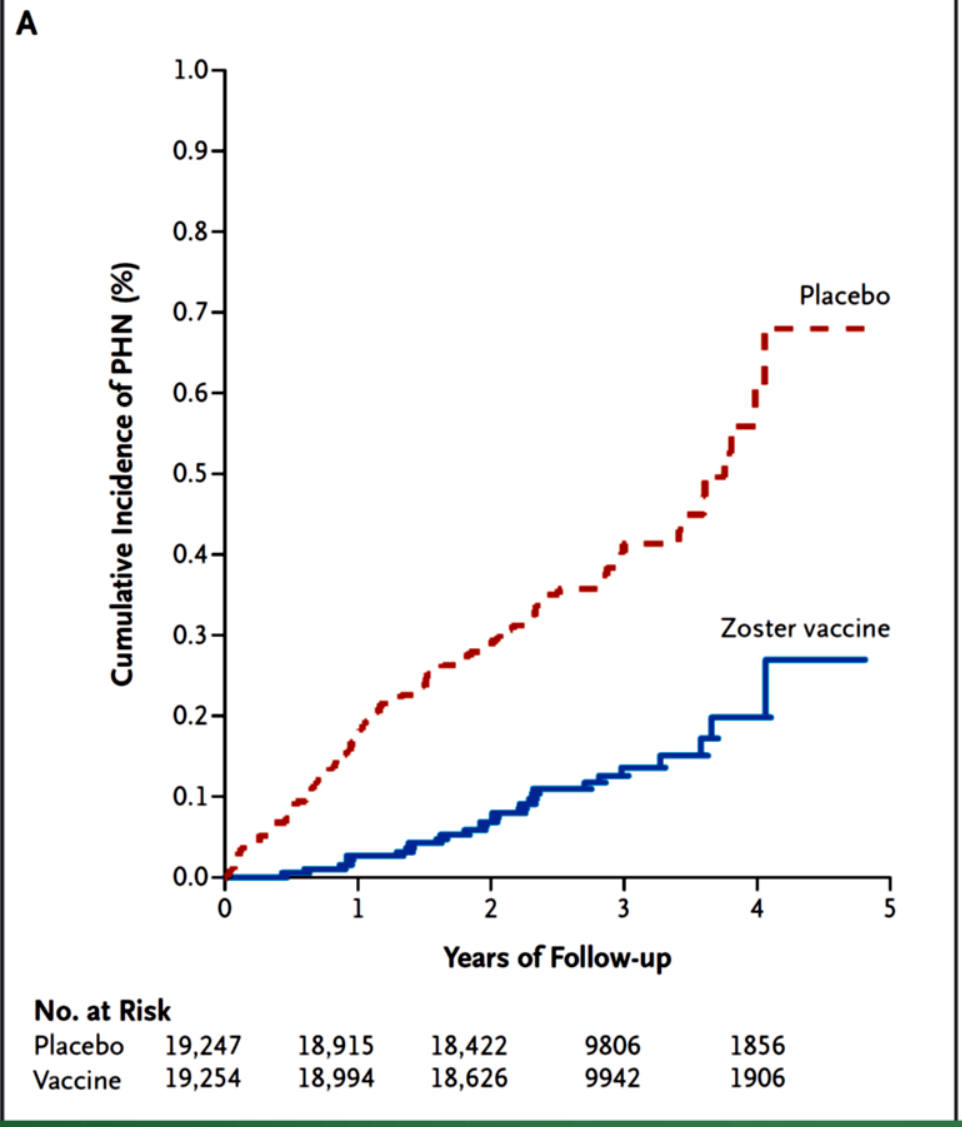
A Vaccine to Prevent Herpes Zoster and Postherpetic Neuralgia in Older Adults

M.N. Oxman, M.D., M.J. Levin, M.D., G.R. Johnson, M.S., K.E. Schmader, M.D., S.E. Straus, M.D., L.D. Gelb, M.D., R.D. Arbeit, M.D., M.S. Simberkoff, M.D., A.A. Gershon, M.D., L.E. Davis, M.D., A. Weinberg, M.D., K.D. Boardman, R.Ph., H.M. Williams, R.N., M.S.N., J. Hongyuan Zhang, Ph.D., P.N. Peduzzi, Ph.D., C.E. Beisel, Ph.D., V.A. Morrison, M.D., J.C. Guatelli, M.D., P.A. Brooks, M.D., C.A. Kauffman, M.D., C.T. Pachucki, M.D., K.M. Neuzil, M.D., M.P.H., R.F. Betts, M.D., P.F. Wright, M.D., M.R. Griffin, M.D., M.P.H., P. Brunell, M.D., N.E. Soto, M.D., A.R. Marques, M.D., S.K. Keay, M.D., Ph.D., R.P. Goodman, M.D., D.J. Cotton, M.D., M.P.H., J.W. Gnann, Jr., M.D., J. Loutit, M.D., M. Holodniy, M.D., W.A. Keitel, M.D., G.E. Crawford, M.D., S.-S. Yeh, M.D., Ph.D., Z. Lobo, M.D., J.F. Toney, M.D., R.N. Greenberg, M.D., P.M. Keller, Ph.D., R. Harbecke, Ph.D., A.R. Hayward, M.D., Ph.D., M.R. Irwin, M.D., T.C. Kyriakides, Ph.D., C.Y. Chan, M.D., I.S.F. Chan, Ph.D., W.W.B. Wang, Ph.D., P.W. Annunziato, M.D., and J.L. Silber, M.D., for the Shingles Prevention Study Group*

Table 1. Baseline Characteristics of the Study Participants.*

Characteristic	Vaccine Group (N=19,270)	Placebo Group (N=19,276)
Demographic		
Age — no. (%)		
60–69 yr	10,378 (53.9)	10,369 (53.8)†
≥70 yr	8,892 (46.1)	8,907 (46.2)
Sex — no. (%)		
Male	11,403 (59.2)	11,357 (58.9)
Female	7,867 (40.8)	7,919 (41.1)
Race — no. (%)‡		
White	18,393 (95.4)	18,381 (95.4)
Black	395 (2.0)	420 (2.2)
Hispanic	265 (1.4)	248 (1.3)
Other or unknown	217 (1.1)	227 (1.2)

Cumulative Incidence of Postherpetic Neuralgia and Herpes Zoster



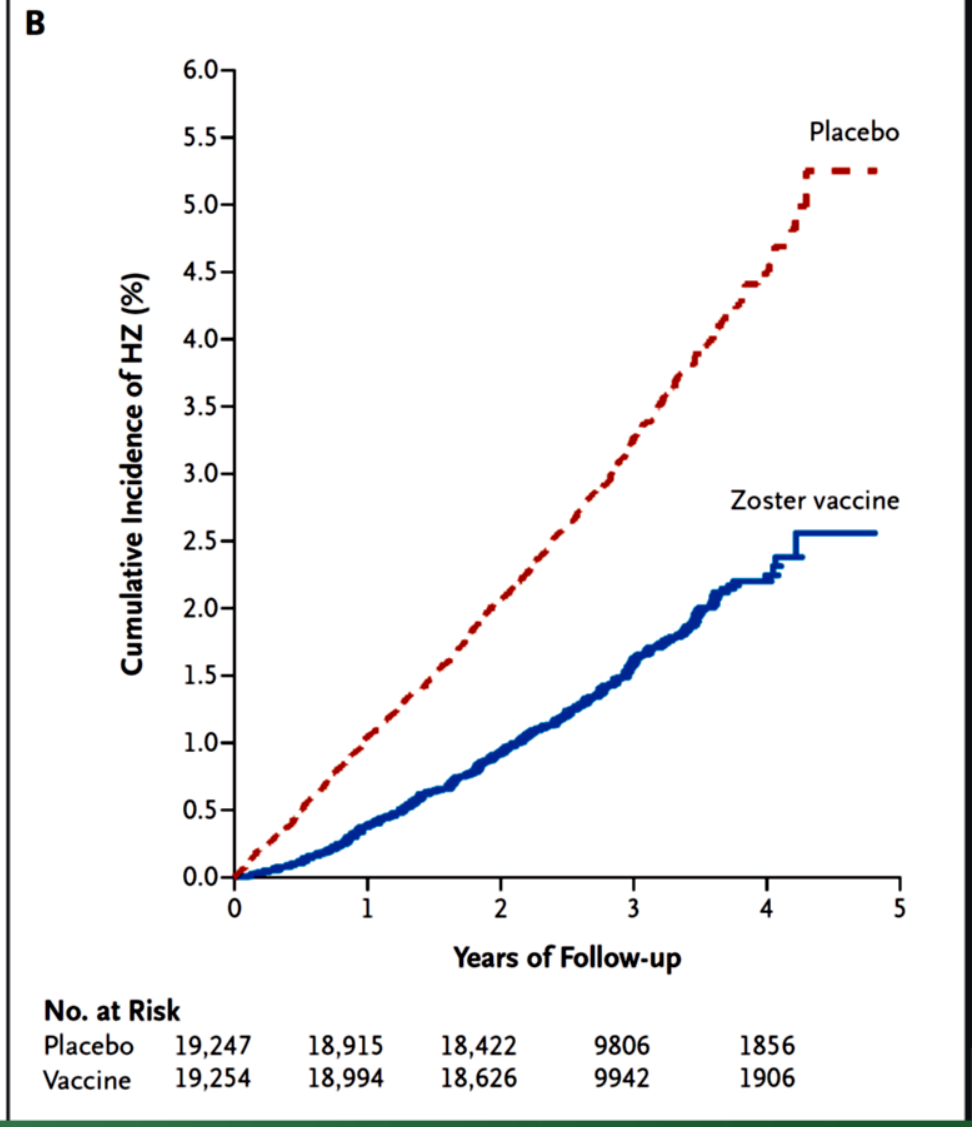
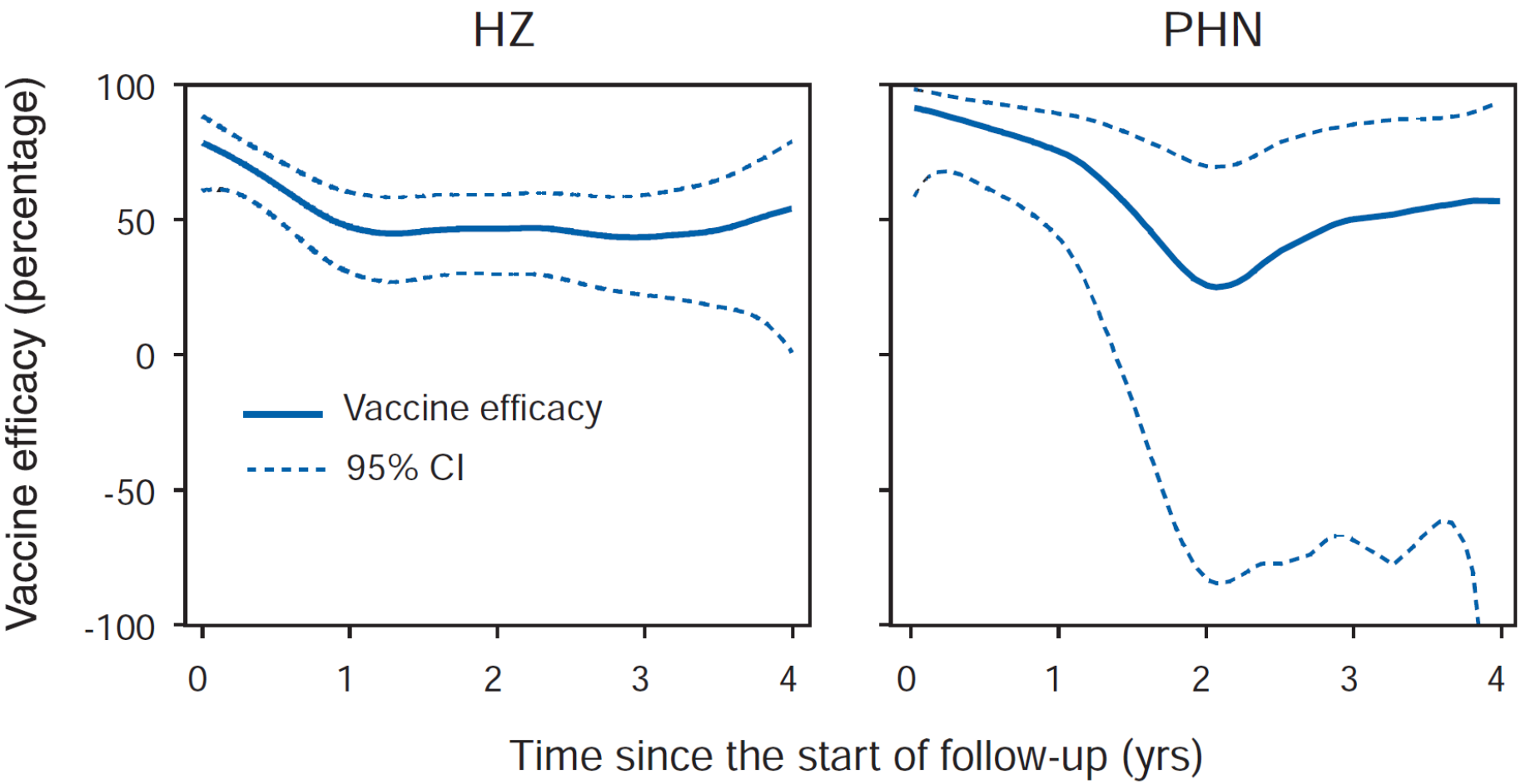


FIGURE 4. Duration of zoster vaccine efficacy for preventing zoster and postherpetic neuralgia (PHN)



Prevention of Herpes Zoster, MMWR 2008.

Recommendation

- In October 2008, the Advisory Committee on Immunization Practices (ACIP) recommended a dose of the herpes zoster vaccine (HZV) for all adults ≥60 years of age unless they have contraindications.

- Administered as a single 0.65-mL dose subcutaneously in the deltoid region of the upper arm.

- Most common adverse events were injection site-related events (e.g., erythema, pain, swelling, warmth, and pruritis)

Contraindications for Zostavax™

- Immunosuppression (high-dose steroids, biological response modifiers, chemotherapy, AIDS) is a contraindication for HZV

- HZV is not recommended for persons aged ≥60 years who have received the varicella vaccine.

Shingrix™- Herpes Zoster subunit vaccine (HZ/su)

- FDA approved on Oct 20, 2017 (GSK)
- An adjuvanted recombinant protein subunit vaccine
  - 2 components; Adjuvant ASO1B and Glycoprotein E
- Dosing recommendation
  - 2 doses, IM at 0, 2 months (max interval=6 months)

Efficacy of Shingrix™

Table 2 Protective efficacy of recombinant zoster vaccine (RZV) against herpes zoster and postherpetic neuralgia in adults

Study	Age (years)	RZV			Placebo			Vaccine efficacy
		No. of sub	No. of cases	IR/1000 PY	No. of sub	No. of cases	IR/1000 PY	[95% CI]
Herpes zoster								
ZOE-50	≥50	7344	6	0.3	7415	210	9.1	97.2 [93.7–99.0][a]
	50–59	3492	3	0.3	3525	87	7.8	96.6 [89.6–99.3]
	60–69	2141	2	0.3	2166	75	10.8	97.4 [90.1–99.7]
	≥70	1711	1	0.2	1724	48	9.4	97.9 [87.9–100.0]
ZOE-70	≥70	6541	23	0.9	6622	223	9.2	89.8 [84.2–93.7][a]
	70–79	5114	17	0.9	5189	169	8.8	90.0 [83.5–94.4]
	≥80	1427	6	1.2	1433	54	11.0	89.1 [74.6–96.2]
Pooled analysis	≥70	8250	25	0.8	8346	284	9.3	91.3 [86.8–94.5][a]
	70–79	6468	19	0.8	6554	216	8.9	91.3 [86.0–94.9]
	≥80	1782	6	1.0	1792	68	11.1	91.4 [80.2–97.0]
Postherpetic neuralgia								
Pooled analysis	≥70	8250	4	0.1	8346	36	1.2	88.8 (68.7–97.1)[a]
	≥50	13,881	4	0.1	14,035	46	0.9	91.2 (75.9–97.7)
	50–59	3491	0	0.0	3523	8	0.6	100.0 (40.8–100.0
	60–69	2140	0	0.0	2166	2	0.2	100.0 (−442.9 to 100.0)
	70–79	6468	2	0.1	6554	29	1.2	93.0 (72.4–99.2)
	≥80	1782	2	0.3	1792	7	1.1	71.2 (−51.6 to 97.1)

Results from the ZOE-50 [30] and ZOE-70 [31] trials, and a pooled analysis [31] of these trials (modified vaccinated cohort)

IR incidence rate, *PY* person-year, *sub* subjects

[a]Primary objective

Drugs Aging. 2018 Dec;35(12):1031-1040

Safety of Shingrix™

- Grade 1-3 injection site reactions (pain, redness, and swelling) were higher in vaccine-group compared to placebo (9.4% vs 0.3%).
- Grade 1-3 systemic reactions (myalgia, fatigue, headache, shivering, fever, and GI symptoms) were higher than placebo group (10.8% vs 2.4%).
- Serious adverse events were similar in both groups.

Conclusions

- Immunization in elderly is very important in terms of disease prevention and decrease burden of diseases.

- As a pharmacist, we should educate, screen and motivate people to keep their immunization uptodate.