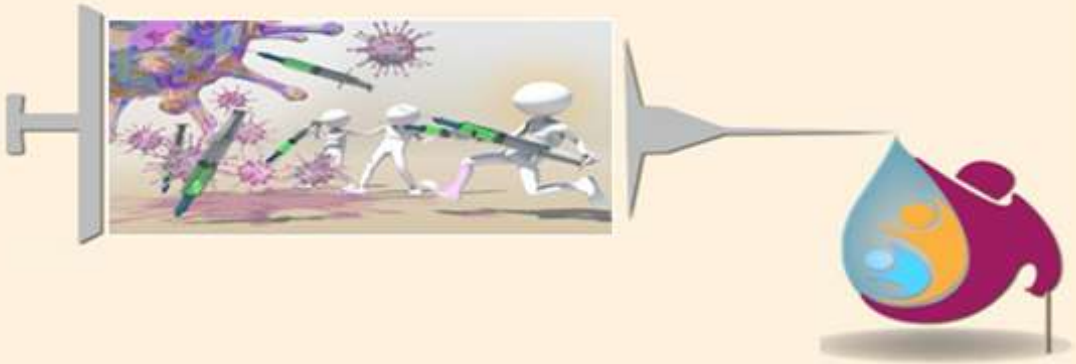
ZONA AŞILAMASI

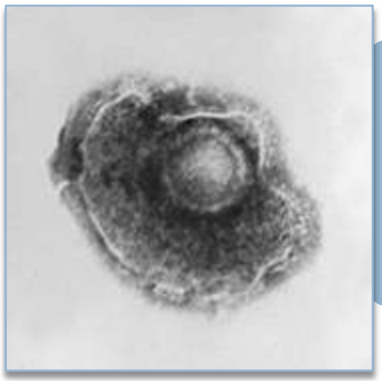
Dr. Emel AZAK
Kocaeli Üniversitesi Tıp Fakültesi
Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD



SUNUM PLANI

- Zona ve ilişkili hastalıklar
- Zona için yüksek riskli gruplar
- Zona immunizasyonu neden yapılmalı
- Zona aşılarının karakteristikleri
- Mevcut immunizasyon pratikleri

ZONA - ETİYOLOJİ



Varisella zoster virus (VZV/HHV3)

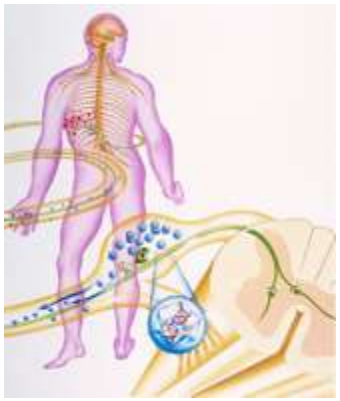
- Su çiçeği
- Zona (Herpes Zoster, Shingles)

Amerika'da yılda 1 milyon vaka
Yaşam boyu zona gelişme riski ~%30

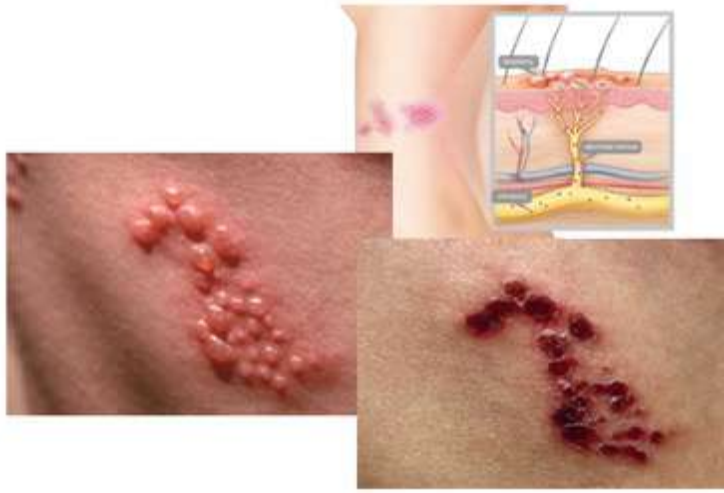
Zerboni L, et al. Nat Rev Microbiol 2014; 12 (3): 197-210
Centers for Disease Control and Prevention

ZONA

- Prodromal dönem
  - Cilt hassasiyeti
  - Baş ağrısı
  - Fotofobi
  - Kırıklık



- Tek taraflı radiküler ağrı
  - Ağrı, acı verici, yakıcı
  - Kaşıntı ve karıncalanma
  - Zoster sine herpete
    - Döküntünün olmadığı sinir ağrısı



- Veziküler döküntü
  - Genellikle yüz ve vücutta
  - 7-10 günde kabuk bağlar
  - 2-4 hafta içinde iyileşir
  - Deri üzerinde pigmentasyon ve skar kalabilir
  - Dermatomal yayılım

Centers for Disease Control and Prevention

Rash and blisters from shingles (herpes zoster) on face The Historical Medical Library of The College of Physicians of Philadelphia

ZONA ENFEKSİYONUNDA AĞRI

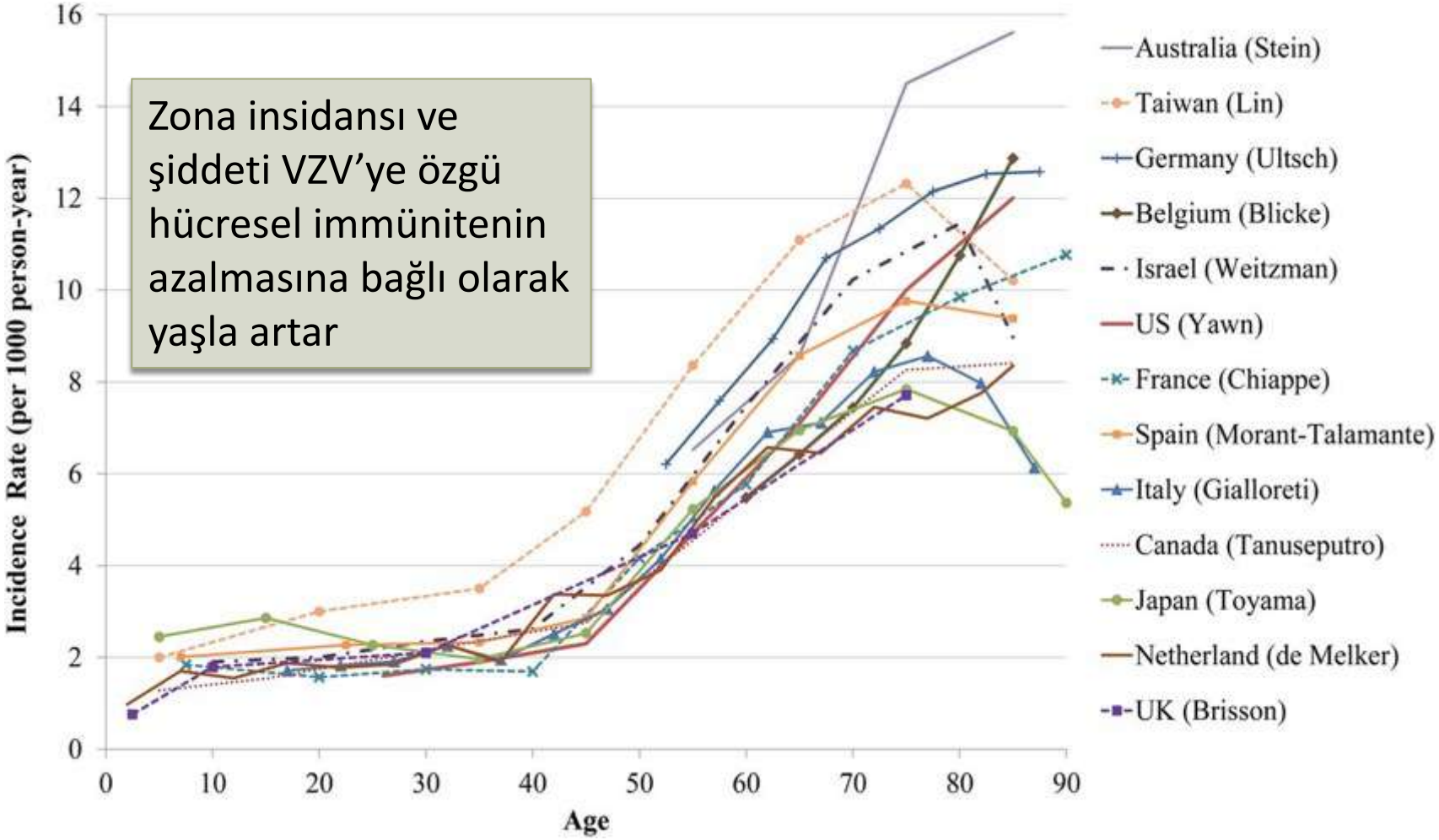
1. Akut ağrı fazı
   - Bir aya kadar

2. Subakut ağrı fazı
   - Döküntü iyileşmesi sonrası 30 - 90 gün

3. Post herpetik nevralji (PHN)
   - Döküntü başlangıcından sonra 90 günden fazla
   - Yıllarca sürebilir
   - Zonanın en sık komplikasyonu

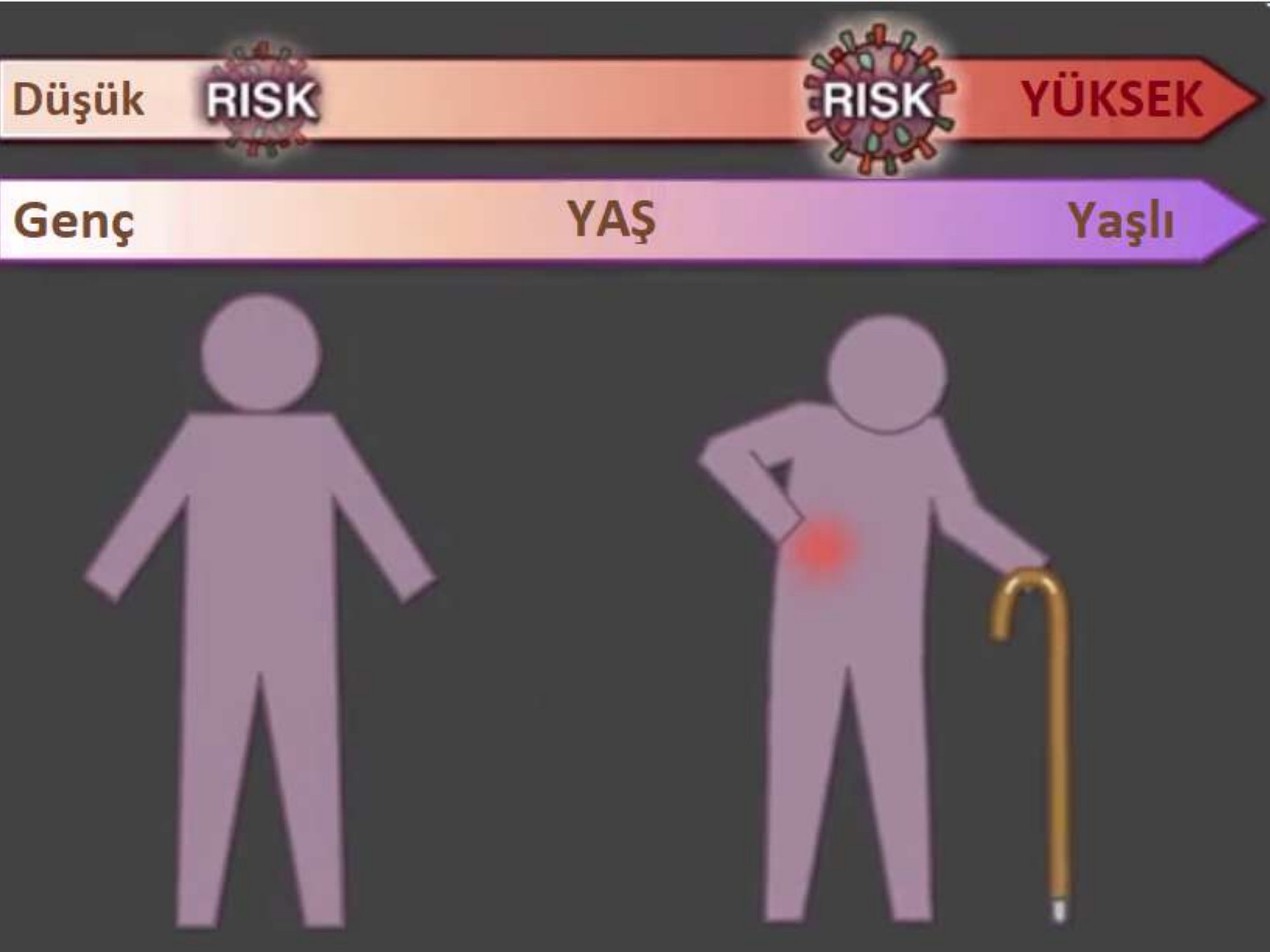
Ther Adv Vaccines. 2015;3(4):109–120

ZONA EPİDEMİYOLOJİ



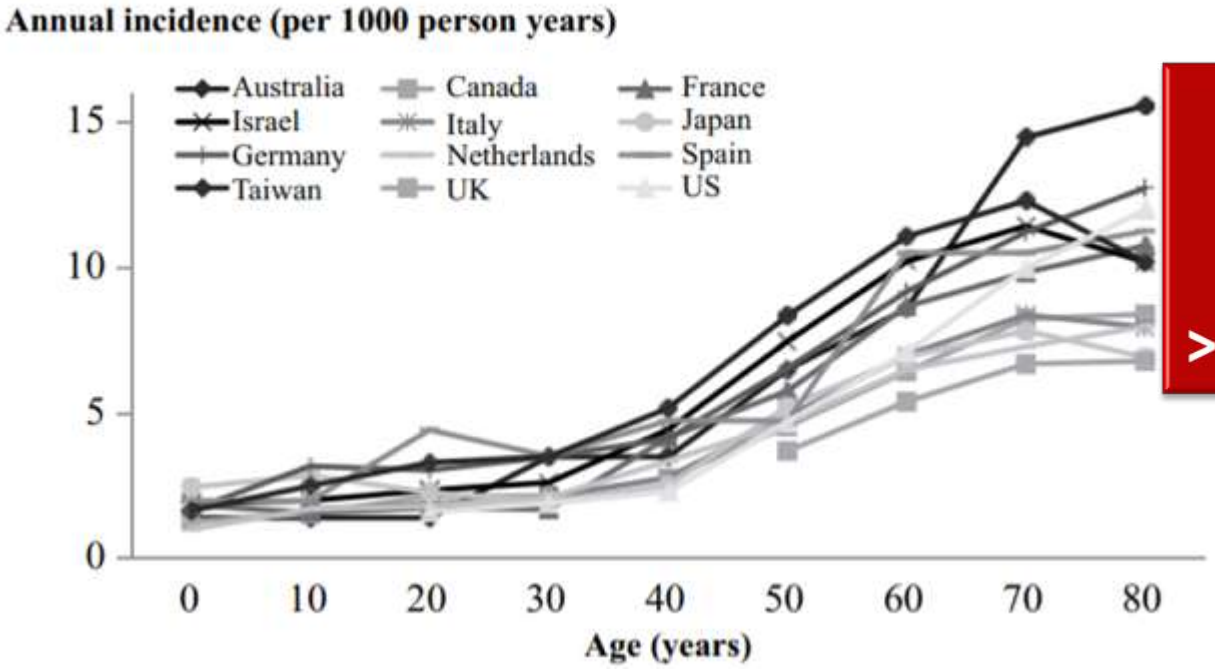
Şekil 1. Kuzey Amerika, Avrupa ve Asya Pasifik'de Zonanın yaş spesifik insidansı

Kosuke Kawai et al. BMJ Open 2014;4:e004833
Bricout H, et al. *BMC Public Health* 2015;15(1):466
Brosio F, et al. Infect Drug Resist. 2018;11:1401–1411


Düşük
RISK
RISK
YÜKSEK
Genç
YAŞ
Yaşlı

Herpes zoster epidemiology, management, and disease and economic burden in Europe: a multidisciplinary perspective

Robert W. Johnson, Marie-José Alvarez-Pasquin, Marc Bijl, Elisabetta Franco, Jacques Gaillat, João G. Clara, Marc Labetoulle, Jean-Pierre Michel, Luigi Naldi, Luis S. Sanmarti and Thomas Weinke



Ortalama insidans
3.4-4.82/1000 kişi yıl

>80 yaş > 11/1000 kişi yıl

Ther Adv Vaccines. 2015;3(4):109–120

Burden of herpes zoster in 16 selected immuncompromised populations in England: a cohort study in the Clinical Practice Research Datalink 2000-2012

Table 2 Incidence rates of HZ per IC status and IC conditions, overall and by age group, HES-CPRD, 2000–2012

	Incidence rate of HZ per 1000 PY (95% CI)						
IC status/condition	**18–49 years**	**50–59 years**	**60–64 years**	**65–69 years**	**70–79 years**	**≥80 years**	**Overall**
IC-free cohort (N=621 588)	2.12 (2.03 to 2.22)	4.90 (4.72 to 5.08)	6.92 (6.64 to 7.20)	8.62 (8.30 to 8.95)	11.04 (10.75 to 11.34)	11.02 (10.64 to 11.41)	6.21 (6.12 to 6.30)
IC cohort (N=621 588)	3.55 (3.[illegible]						7.77 (7.67 to 7.88)
Haematopoietic stem cell transplant (HSCT) (n=1312)	34.14 (26[illegible]						41.70 (35.72 to 48.40)
Solid organ transplantation (SOT) (n=4759)	11.01 (8.[illegible]						12.13 (10.74 to 13.66)
Haematological malignancies (HM) (n=26 959)	8.46 (7.[illegible]						15.19 (14.45 to 15.97)
Solid organ malignancies (SOM) (n=210 259)	4.32 (3.[illegible]						8.81 (8.61 to 9.02)
HIV (n=2522)	11.24 (8.[illegible]						11.78 (9.54 to 14.38)
End-stage renal disease (ESRD) (n=38 134)	8.33 (6.[illegible]						12.25 (11.58 to 12.95)
Polymyalgia rheumatica (PR) (n=26 868)	5.21 (2.[illegible]						12.79 (12.18 to 13.42)
Systemic lupus erythematosus (SLE) (n=5041)	7.91 (6.34 to 9.76)	10.45 (8.16 to 13.18)	12.81 (9.11 to 17.52)	11.06 (7.22 to 16.21)	18.11 (13.72 to 23.46)	17.20 (10.90 to 25.81)	10.95 (9.75 to 12.26)
Rheumatoid arthritis (RA) (n=35 326)	4.74 (4.05 to 5.51)	8.79 (7.86 to 9.81)	11.00 (9.69 to 12.44)	12.61 (11.18 to 14.17)	14.02 (12.83 to 15.29)	14.47 (12.97 to 16.10)	10.58 (10.11 to 11.07)
Inflammatory bowel disease (IBD) (n=31 884)	3.99 (3.56 to 4.46)	6.82 (6.01 to 7.71)	7.98 (6.72 to 9.40)	12.22 (10.46 to 14.20)	11.50 (10.04 to 13.12)	13.86 (11.63 to 16.39)	7.02 (6.63 to 7.42)
Multiple sclerosis (MS) (n=9210)	3.71 (2.96 to 4.61)	5.99 (4.85 to 7.31)	6.94 (5.06 to 9.29)	10.18 (7.43 to 13.63)	7.00 (4.69 to 10.06)	10.17 (5.26 to 17.77)	5.69 (5.07 to 6.36)
Autoimmune thyroiditis (AT) (n=7140)	2.50 (1.82 to 3.35)	6.82 (5.19 to 8.80)	6.49 (4.11 to 9.73)	9.71 (6.22 to 14.45)	10.30 (7.04 to 14.54)	12.52 (7.54 to 19.55)	5.42 (4.70 to 6.22)
Psoriasis (PSOR) (n=117 760)	2.64 (2.47 to 2.82)	5.45 (5.06 to 5.87)	7.43 (6.76 to 8.14)	8.73 (7.93 to 9.60)	10.50 (9.75 to 11.30)	12.24 (11.04 to 13.54)	5.33 (5.15 to 5.51)
Other immunodeficiency conditions (OIC) (n=41 484)	6.16 (5.46 to 6.94)	11.45 (10.23 to 12.78)	13.46 (11.74 to 15.37)	15.00 (13.14 to 17.05)	15.22 (13.81 to 16.72)	16.06 (14.42 to 17.84)	11.83 (11.29 to 12.38)
Corticosteroids exposure (CORTDS) (n=183 646)	3.27 (3.02 to 3.54)	6.99 (6.50 to 7.51)	9.02 (8.30 to 9.78)	9.68 (8.92 to 10.49)	11.47 (10.80 to 12.18)	13.29 (12.22 to 14.43)	7.46 (7.23 to 7.69)
Other immunosuppressive therapies (OIT) (n=12 594)	5.24 (3.76 to 7.11)	7.44 (5.12 to 10.45)	8.46 (5.02 to 13.38)	17.48 (11.88 to 24.81)	14.60 (10.17 to 20.31)	8.09 (3.49 to 15.95)	8.49 (7.25 to 9.89)

CPRD, Clinical Practice Research Datalink; HES, Hospital Episode Statistics; HZ, herpes zoster; IC, immunocompromised; N, total number of individuals; n, Number of individuals with that type of IC; PY, person-years.

Toplam 16 merkez

621 588 hasta

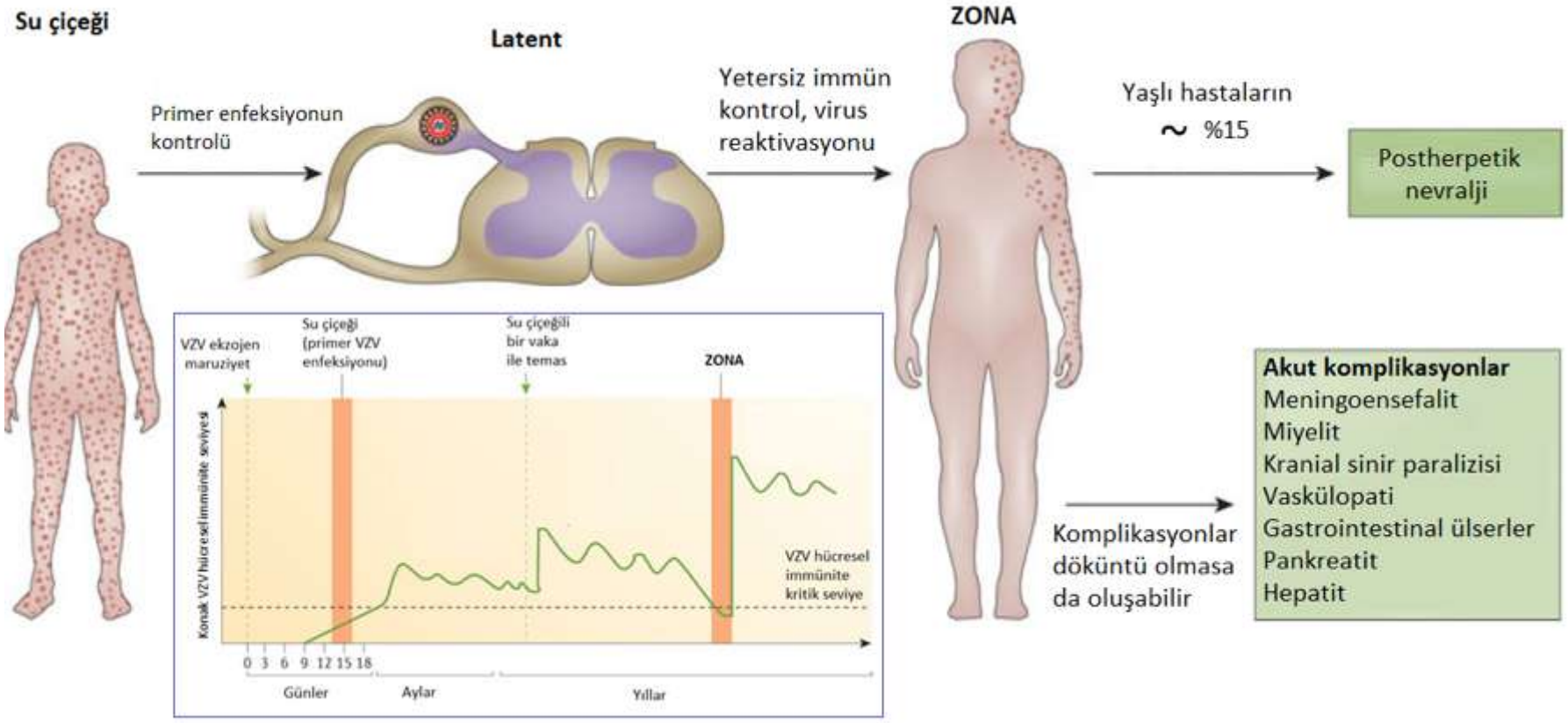
İnsidans:

İmmün kompetan: **6.21/1000 kişi-yıl**

İmmün kompromize: **7.7 / 1000 kişi-yıl**

Yanni EA., et al. BMJ Open 2018;8:e020528

ZONA KOMPLİKASYONLARI



ZONA KOMPLİKASYONLARI

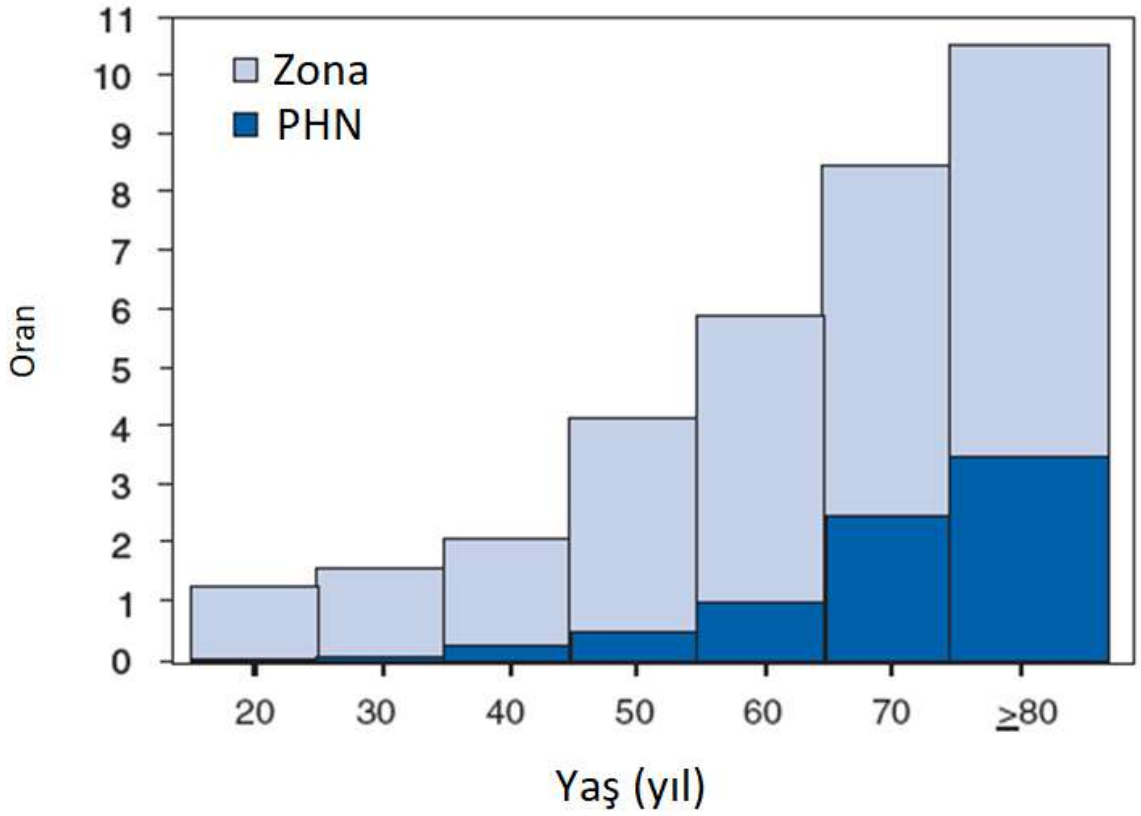
Table 3 Proportion of patients with HZ with PHN, at least one HZ complication other than PHN, or vascular complications as assessed within 90 days of HZ onset, HES-CPRD, 2000–2011

	IC cohort (N=21 146)		IC-free cohort (N=18 583)	
Type of complications	**n (%)**	**95% CI**	**n (%)**	**95% CI**
PHN	2253 (10.65)	10.24 to 11.08	1690 (9.09)	8.68 to 9.52
HZ complications other than PHN (overall)	623 (2.95)	2.72 to 3.18	436 (2.35)	2.13 to 2.57
Ocular	411 (1.94)	1.76 to 2.14	299 (1.61)	1.43 to 1.8
Neurological other than PHN	137 (0.65)	0.54 to 0.77	85 (0.46)	0.37 to 0.57
Disseminated	12 (0.06)	0.03 to 0.1	1 (0.01)	0 to 0.03
Other complications	69 (0.33)	0.25 to 0.41	54 (0.29)	0.22 to 0.38
Vascular complications				
Stroke	88 (0.42)	0.33 to 0.51	105 (0.57)	0.46 to 0.68
Transient ischaemic attack	52 (0.25)	0.18 to 0.32	30 (0.16)	0.11 to 0.23
Optic neuritis, vascular retinitis	9 (0.04)	0.02 to 0.08	5 (0.03)	0.01 to 0.06
Myocardial infarction	36 (0.17)	0.12 to 0.24	23 (0.12)	0.08 to 0.19

CPRD, Clinical Practice Research Datalink; HES, Hospital Episode Statistics; HZ, herpes zoster; IC, immunocompromised; N, Number of patients with HZ; n (%), number (percentage) of the patients with HZ with this complication; PHN, postherpetic neuralgia.

Yanni EA., et al. BMJ Open 2018;8:e020528

Zona ve PHN'nin yaş ile ilişkisi



Şekil. Yaş ile Zona ve PHN oranı (her 1000 hasta yılı için)
Ağrı 30 gün ve daha uzun süreli

İleri yaşta PHN

- Daha olası
- Daha ciddi
- Daha uzun seyirli

http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5705a1.htm

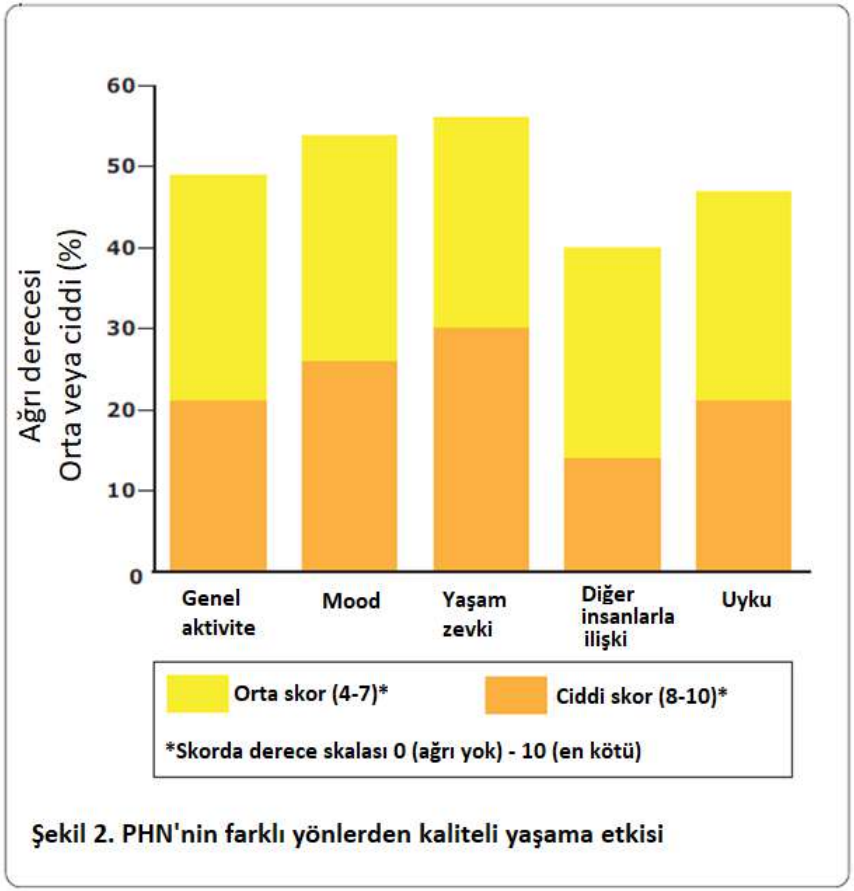
The impact of herpes zoster and post-herpetic neuralgia on quality-of-life

Robert W Johnson*[1], Didier Bouhassira[2], George Kassianos[3], Alain Leplège[4], Kenneth E Schmader[5] and Thomas Weinke[6]

Johnson *et al. BMC Medicine* 2010, **8**:37

Tablo 1. Zona ve PHN'nin kaliteli yaşam üzerine değerlendirilen özellikler

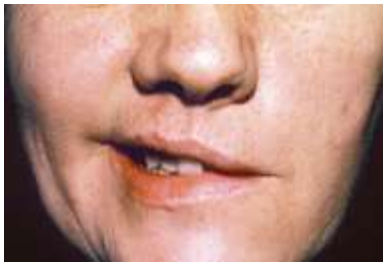
Fiziksel	**Psikolojik**
Yorgunluk İştahsızlık Kilo kaybı Hareketsizlik Uykusuzluk	Depresyon Anksiyete Emosyonel stres Konsantrasyon güçlüğü Endişe
Sosyal	**Fonksiyonel**
Uzaklaşım İzolasyon Daha az sosyal toplantılara katılım Bağımsızlık kaybı Sosyal rolde değişiklik	**Günlük aktivitelerde azalma:** Giyinme, banyo, yemek yeme, hareketlilik, seyahat, yemek pişirme, ev işi, alışveriş

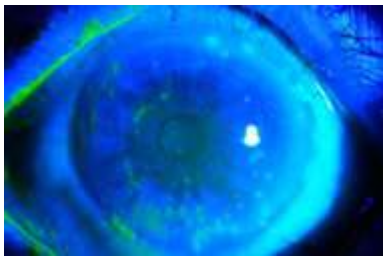


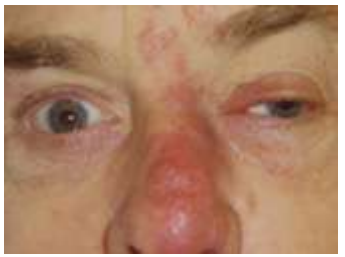
Şekil 2. PHN'nin farklı yönlerden kaliteli yaşama etkisi

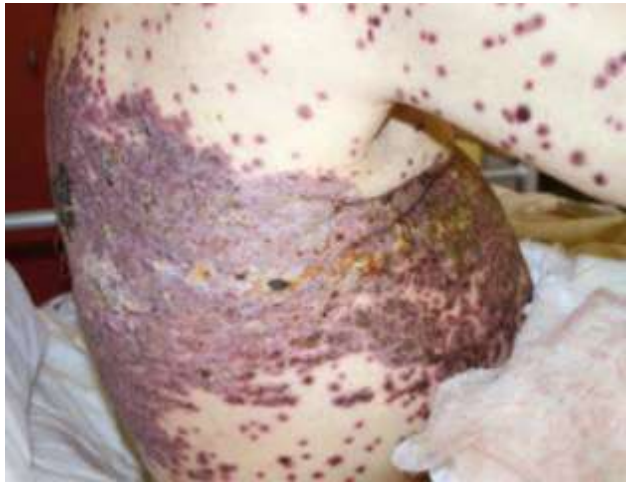
PHN DIŞI ZONA KOMPLİKASYONLARI

Nörolojik	Vertigo Kranial sinir paralizisi (Ör; fasiyal paralizi) İşitme kaybı Ensefalit, Miyelit Motor nöropati Granülomatöz arterit ile sekonder strok
Göz	Pitozis, Sklerit, İridosiklit Sekonder glakom Katarakt, Keratit Körlük, Korioretinit
Dermatolojik	Dissemine zona Postherpetik kaşıntı Sekonder bakteriyel deri enfeksiyonları
Visseral	Pnömoni Peri-Miyokardit Hepatit Ösefajit Miyozit,Artrit









Johnson et al. BMC Medicine 2010, 8:37
Eye & Contact Lens 2019;45: 286–291
Turk J Med Sci 2009; 39 (3): 479-482

The temporal impact of aging on the burden of herpes zoster

Lijoy Varghese[1*], Baudouin Standaert[2], Antonio Olivieri[2,3] and Desmond Curran[2]

Varghese *et al. BMC Geriatrics* (2017) 17:30

Table 2 Population estimates for Australia, Japan and the United States

		United States		Japan		Australia	
	Age group	Population	% of total population	Population	% of total population	Population	% of total population
2001	All	285,796,198		125,974,298		19,308,681	
	>65	35,142,215	12.3	22,301,302	17.7	2,402,399	12.4
	>80	9,411,233	3.3	4,929,411	3.9	567,071	2.9
2015	All	321,773,631		126,573,481		23,968,973	
	>65	47,577,672	14.8	33,342,003	26.3	3,606,102	15.0
	>80	12,100,608	3.8	9,821,543	7.8	930,769	3.9
2030	All	355,764,967		120,127,264		28,481,570	
	>65	73,558,551	20.7	36,551,621	30.4	5,524,027	19.4
	>80	19,378,487	5.4	15,196,468	12.7	1,618,736	5.7

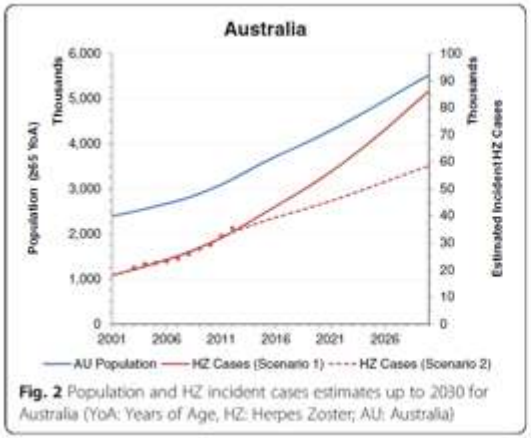


Fig. 2 Population and HZ incident cases estimates up to 2030 for Australia (YoA: Years of Age, HZ: Herpes Zoster; AU: Australia)

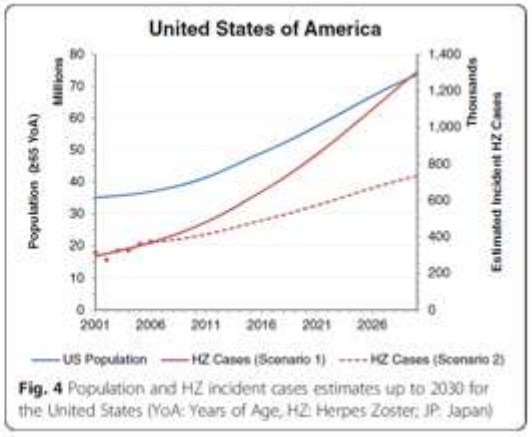


Fig. 4 Population and HZ incident cases estimates up to 2030 for the United States (YoA: Years of Age, HZ: Herpes Zoster; JP: Japan)

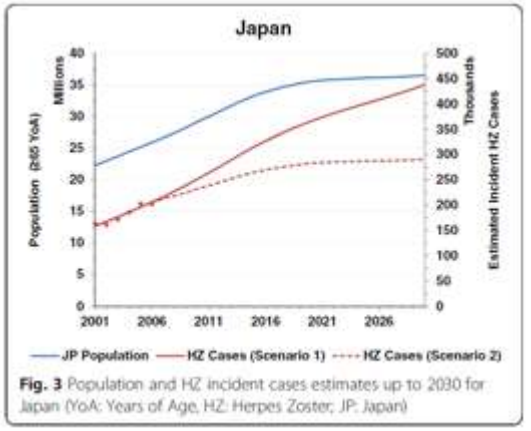


Fig. 3 Population and HZ incident cases estimates up to 2030 for Japan (YoA: Years of Age, HZ: Herpes Zoster; JP: Japan)

The temporal impact of aging on the burden of herpes zoster

Lijoy Varghese[1*], Baudouin Standaert[2], Antonio Olivieri[2,3] and Desmond Curran[2]

Varghese *et al. BMC Geriatrics* (2017) 17:30

Table 4 Estimated HZ-related healthcare cost burden for the ≥65 in the United States in 2030

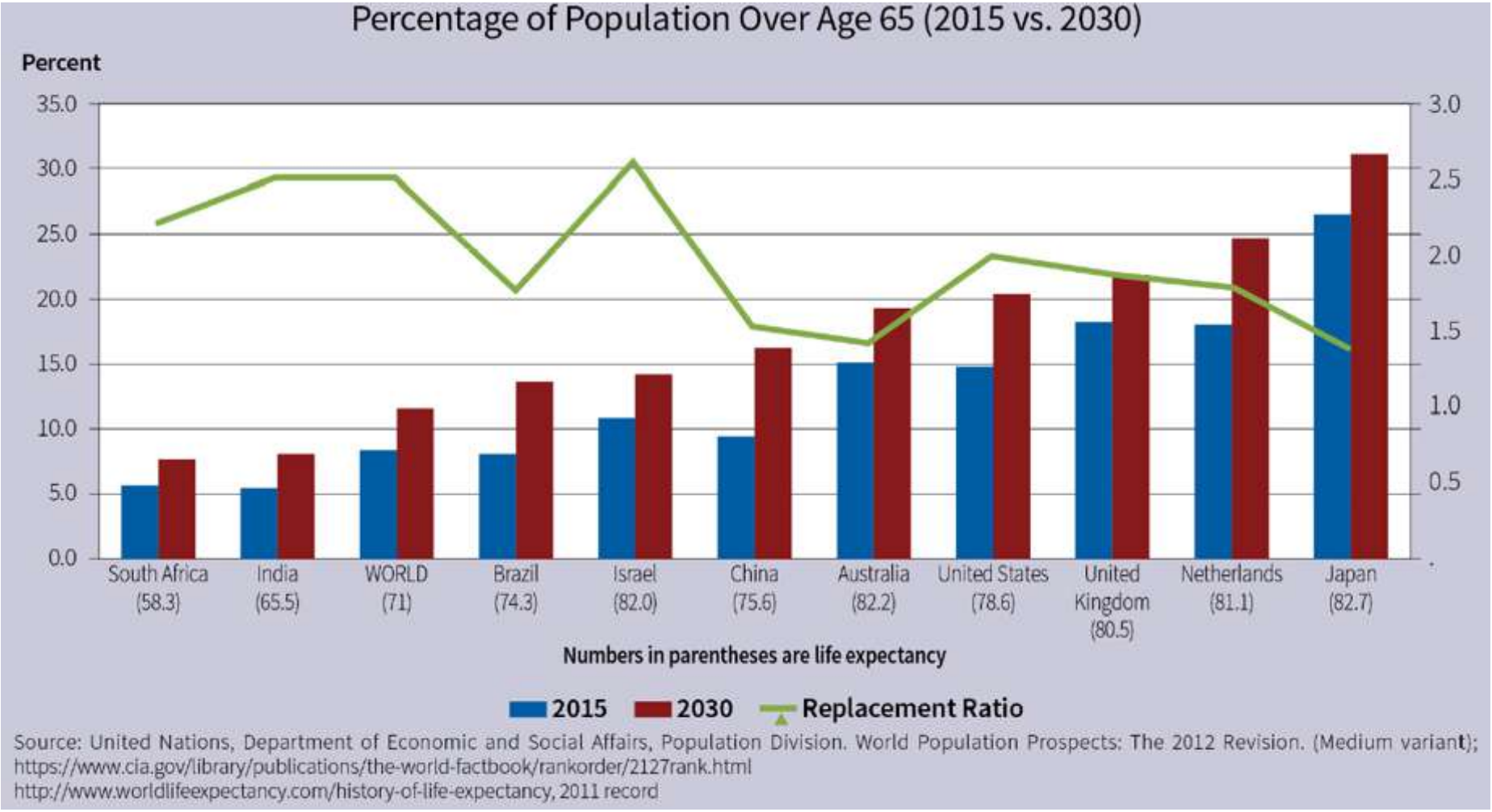
	2005			2030		
	Cost/Case	Cases ('000 s)	Total HZ Costs (US$)	Cost/Case	Cases ('000 s)	Total HZ Costs (US$)
All HZ	$1,851	339	$627,773,213	$3,640	1,303	$4,743,559,326
HZ with PHN or Complications	$4,869	80	$389,153,306	$9,601	306	$2,937,397,732

HZ Herpes Zoster, *PHN* Post-herpetic Neuralgia, *US*\ United States dollar

~ 8 Kat
maliyet artışı

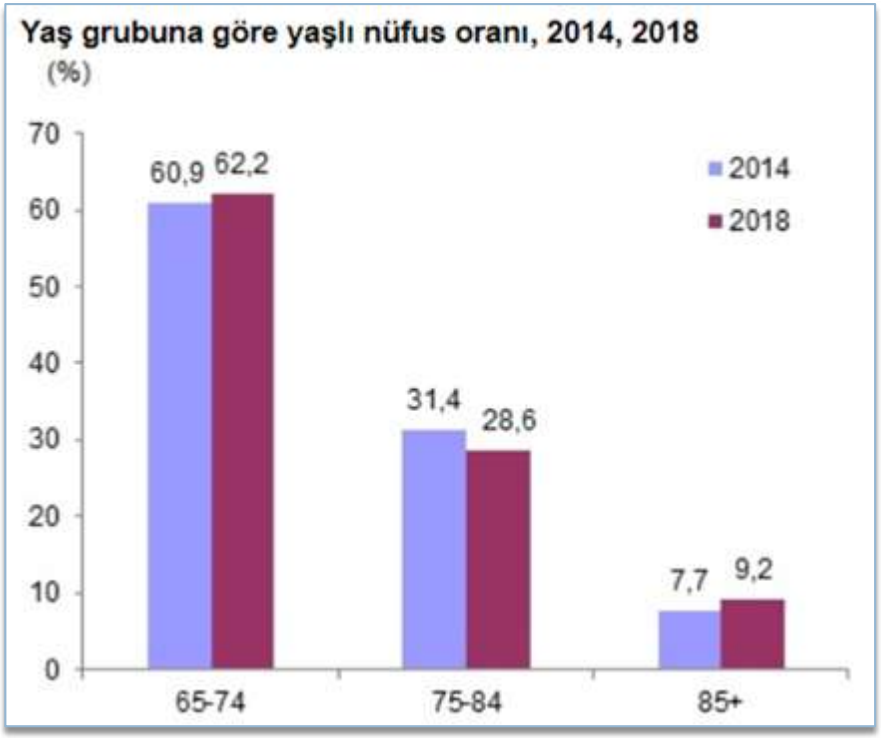
American Academy of Actuaries
Issue Brief DECEMBER 2017

End-of-Life Care in an Aging World: A Global Perspective



Source: United Nations, Department of Economic and Social Affairs, Population Division. World Population Prospects: The 2012 Revision. (Medium variant); https://www.cia.gov/library/publications/the-world-factbook/rankorder/2127rank.html
http://www.worldlifeexpectancy.com/history-of-life-expectancy, 2011 record

ÜLKEMİZDE YAŞLI NÜFUS



≥65 yaş nüfus
2014: 6 192 962
2018: 7 186 204
} 5 yılda %16 artış

Yıl	Yaşlı nüfusun toplam nüfus içindeki oranı, (%)
2014	8
2018	8.8
2023	10.2
2030	12.9
2040	16.3
2060	22.6
2080	25.6

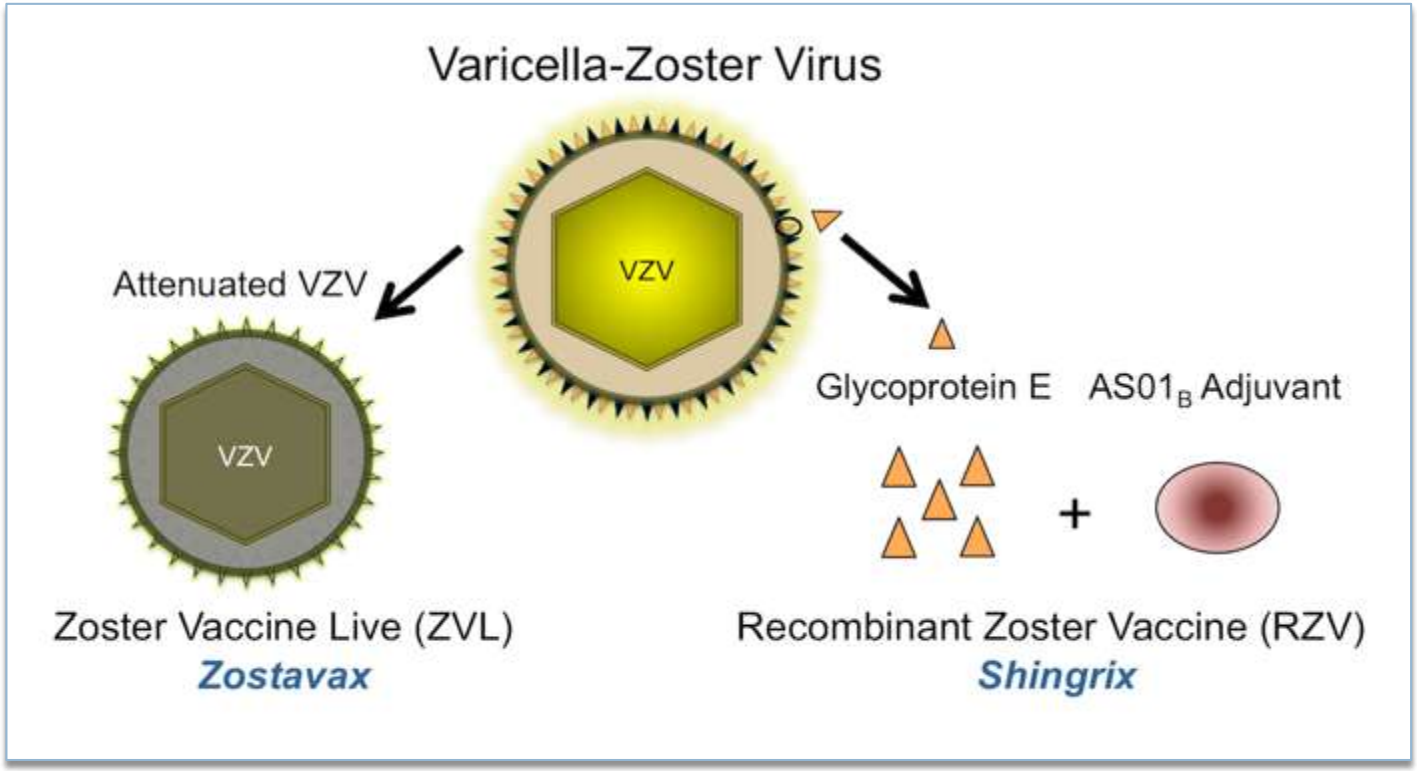
TÜİK, Adrese dayalı nüfuskayıt sistemi, 2014, 2018
Sayı:30699, 18 Mart 2019, tuik.gov.tr

ZONA AŞILAMASINDA AMAÇ

Zonanın

- Epidemiyolojik
- Klinik
- Ekonomik yükünü
- ve
- Yaşam kalitesi üzerindeki olumsuz etkilerini

ZONA AŞILARI



Canlı zona aşısı
CZA

Canlı olmayan, rekombinant aşı
RZA

ZONA AŞILARI

Canlı zona (herpes zoster) aşısı (CZA)

FDA tarafından Mayıs **2006** 'da ≥ 60 yaş
2011'de ≥ 50 yaş için onaylandı
ACIP 2008'den beri ≥ 60 yaş için öneriyor.

Rekombinan zona aşısı (RZA)

FDA tarafından Ekim **2017**'de onaylandı

CZA

- **Varisella aşısı**
  - Canlı, zayıflatılmış VZV Oka suşu (1350 PFU)
- **Canlı Zona Aşısı**
  - Canlı, zayıflatılmış VZV Oka suşu (19400 PFU)

CZA, varisella aşısından
en az 14 kat
daha fazla konsantredir

MMWR Morb Mortal Wkly Rep. 2018;67(3):103–108

CZA - Shingles Prevention Study (SPS)

- Randomize, çift kör, plasebo kontrollü
- Prospektif
- 22 merkezli çalışma
- ≥ 60 yaş
- 38.546 kişi
- 3.12 yıl takip

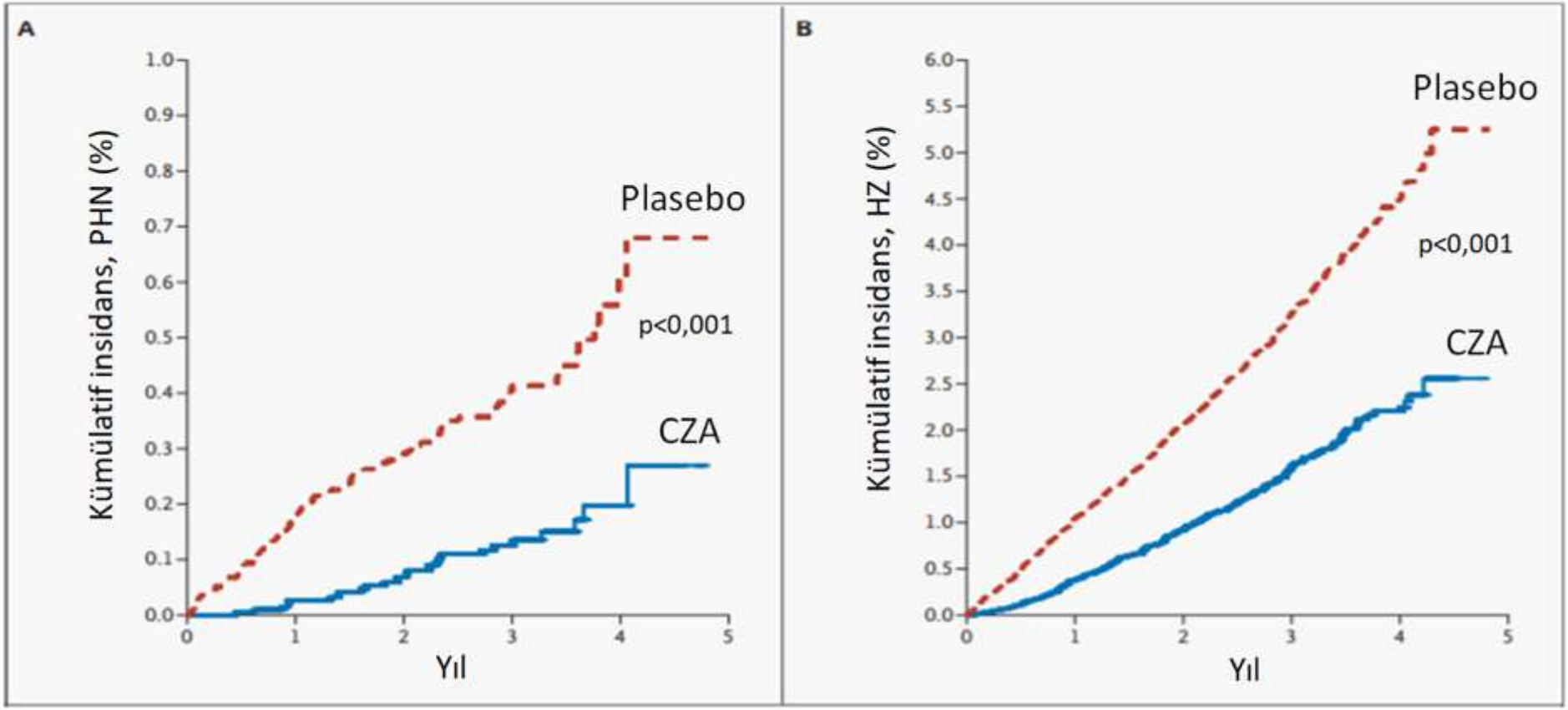
Oxman MN, N Engl J Med 2005; 352 (22):2271-84

CZA - Shingles Prevention Study (SPS)

	Zostavax etkinliği (%95 Güven aralığı)		
	Zona insidansı	PHN insidansı	Hastalık yükü
Tüm sonuçlar	51 (44-58)	67 (48-80)	61 (51-69)
Yaş grubu			
60-69 yaş		66 (20-87)	66 (52-76)
≥ 70 yaş		67 (43-81)	55 (40-67)
Cinsiyet			
Erkek		63 (36-79)	64 (51-73)
Kadın		73 (39-90)	57 (40-70)

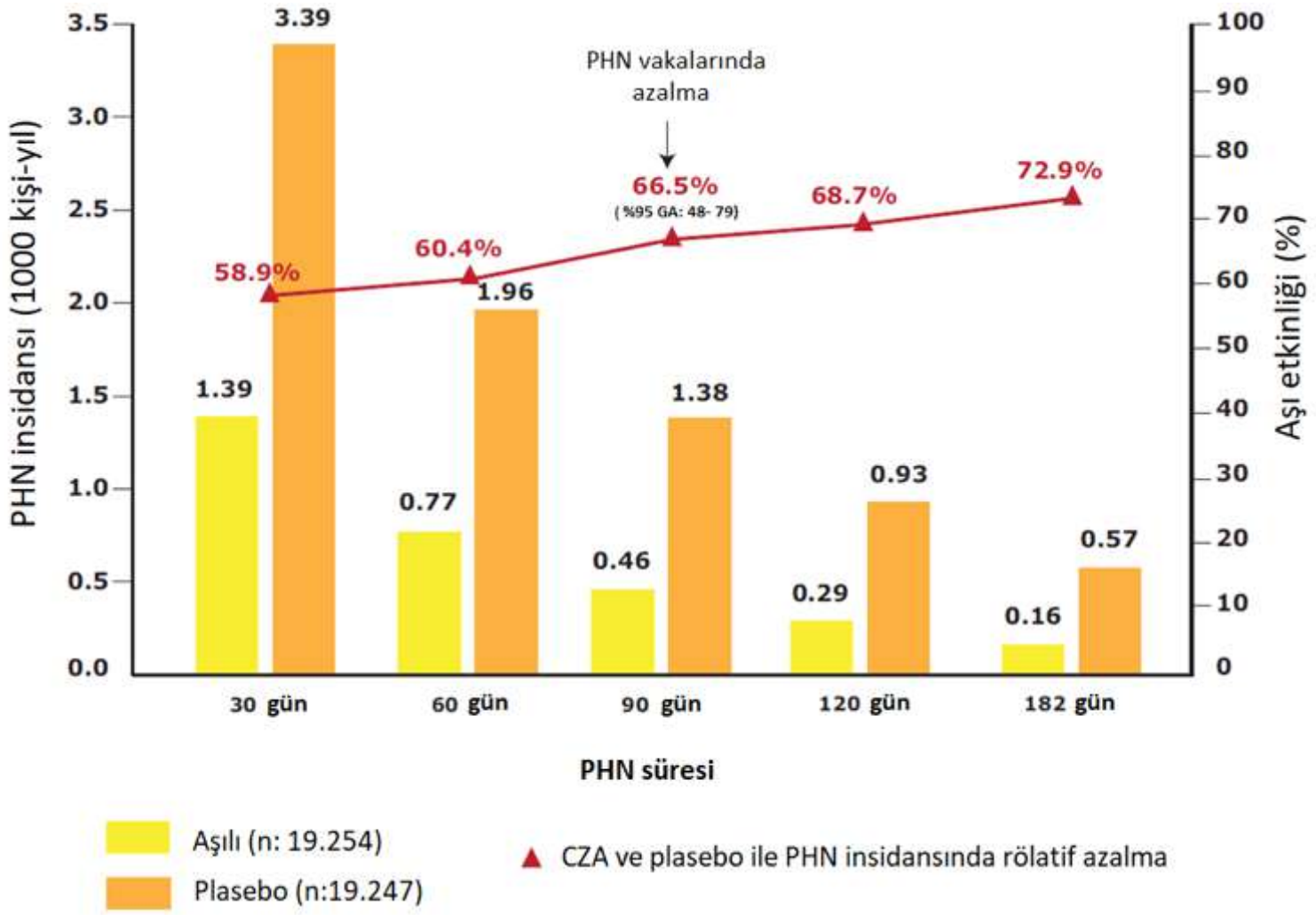
Oxman MN, N Engl J Med 2005; 352 (22):2271-84

CZA - Shingles Prevention Study (SPS)



Oxman MN, N Engl J Med 2005; 352 (22):2271-84

CZA - Shingles Prevention Study (SPS)



Persistence of the Efficacy of Zoster Vaccine in the Shingles Prevention Study and the Short-Term Persistence Substudy

STPS ÇALIŞMASI

K. E. Schmader,[1] M. N. Oxman,[2] M. J. Levin,[3] G. Johnson,[4] J. H. Zhang,[4] R. Betts,[5] V. A. Morrison,[6] L. Gelb,[7] J. C. Guatelli,[2] R. Harbecke,[2] C. Pachucki,[8] S. Keay,[9] B. Menzies,[11] M. R. Griffin,[12] C. Kauffman,[13] A. Marques,[10] J. Toney,[14] P. M. Keller,[15] X. Li,[15] I. S. F. Chan,[15] and P. Annunziato,[15] for the Shingles Prevention Study Group

Table 2. Estimated Efficacy of Zoster Vaccine, by Year After Vaccination, in the Shingles Prevention Study (SPS) Population, the Short-Term Persistence Substudy (STPS) Population, and the Combined SPS and STPS Populations

Time Since Randomization (Years)[a]	Vaccine Efficacy for HZ BOI Point Estimate, % (95% CI)	Vaccine Efficacy for Incidence of PHN Point Estimate, % (95% CI)	Vaccine Efficacy for Incidence of HZ Point Estimate, % (95% CI)
Year 1	79.2 (66.8–86.9)	83.4 (56.7–95.0)	62.0 (49.6–71.6)
Year 2	54.9 (32.0–70.1)	69.8 (27.3–89.1)	48.9 (34.7–60.1)
Year 3	44.4 (17.6–62.5)	38.3 (−44.7 to 75.0)	46.8 (31.1–59.2)
Year 4	66.9 (37.5–82.5)	60.7 (−36.3 to 91.0)	44.6 (20.5–61.8)
Year 5	74.9 (48.6–87.7)	73.8 (−37.8 to 97.3)	43.1 (5.1–66.5)
Year 6	23.6 (−58.1 to 63.1)	32.0 (−100.0 to 87.3)	30.6 (−6.0 to 54.6)
Year 7[b]	72.5 (9.9–91.6)	60.0 (−4.5 to 97.1)	52.8 (−16.5 to 80.5)
SPS			
Years 0.0–4.9	61.1 (51.1–69.1)	66.5 (47.5–79.2)	51.3 (44.2–57.6)
STPS			
Years 3.3–7.8	50.1 (14.1–71.0)	60.1 (−9.8 to 86.7)	39.6 (18.2–55.5)
SPS + STPS			
Years 0.0–7.8	58.6 (48.6–66.6)	64.9 (47.4–77.0)	48.7 (42.0–54.7)

Abbreviations: BOI, burden of illness; CI, confidence interval; HZ, herpes zoster; PHN, postherpetic neuralgia; SPS, Shingles Prevention Study; STPS, Short-Term Persistence Study.

CID 2012; 55(10):1320-28

Long-term Persistence of Zoster Vaccine Efficacy

LTPS ÇALIŞMASI

Vicki A. Morrison,[1] Gary R. Johnson,[2] Kenneth E. Schmader,[3] Myron J. Levin,[4] Jane H. Zhang,[2] David J. Looney,[5] Robert Betts,[6] Larry Gelb,[7] John C. Guatelli,[5] Ruth Harbecke,[5] Connie Pachucki,[8] Susan Keay,[9] Barbara Menzies,[10] Marie R. Griffin,[11] Carol A. Kauffman,[12] Adriana Marques,[13] John Toney,[14] Kathy Boardman,[15] Shu-Chih Su,[16] Xiaoming Li,[16] Ivan S. F. Chan,[16] Janie Parrino,[16] Paula Annunziato,[16] and Michael N. Oxman[5]; for the Shingles Prevention Study Group[a]

(4.7-11.6 yıl)

Table 3. Vaccine Efficacy of Zoster Vaccine Estimated for Years Postvaccination in the Shingles Prevention Study, the Short-Term Persistence Substudy, and the Long-Term Persistence Substudy

Time Period Since Randomization[a], y	No. of PY	Burden of Illness (Zoster Vaccine Group)	Vaccine Efficacy for HZ BOI Point Estimate (95% CI)	Incidence of PHN (Zoster Vaccine Group)	Vaccine Efficacy for Incidence of PHN Point Estimate (95% CI)	Incidence of HZ (Zoster Vaccine Group)	Vaccine Efficacy for Incidence of HZ Point Estimate (95% CI)
SPS + STPS[b]							
Year 1	17 584	0.43	79.2 (66.8–86.9)	0.28	83.4 (56.7–95.0)	3.9	62.0 (49.6–71.6)
Year 2	18 869	0.78	54.9 (32.0–70.1)	0.37	69.8 (27.3–89.1)	5.4	48.9 (34.7–60.1)
Year 3	15 181	0.98	44.4 (17.6–62.5)	0.66	38.3 (−44.7 to 75.0)	6.1	46.8 (31.1–59.2)
Year 4[a]	6264	0.76	66.9 (37.5–82.5)	0.64	60.7 (−36.3 to 91.0)	7.8	44.6 (20.5–61.8)
Year 5[a]	3180	0.68	74.9 (48.6–87.7)	0.63	73.8 (−37.8 to 97.3)	8.2	43.1 (5.1–66.5)
Year 6[a]	4850	1.81	23.6 (−58.1 to 63.1)	0.83	32.0 (−100.0 to 87.3)	9.9	30.6 (−6.0 to 54.6)
LTPS							
Year 7[c]	6865	1.37	47.7 (20.9–65.5)	1.31	26.3 (−40.0 to 66.3)	7.0	46.0 (28.4–60.2)
Year 8[c]	6564	1.46	46.2 (25.8–61.0)	1.37	27.5 (−37.5 to 66.9)	9.0	31.1 (11.2–47.6)
Year 9	6280	2.04	27.6 (4.5–45.1)	0.80	60.5 (7.7–87.2)	12.3	6.8 (−16.5 to 26.4)
Year 10	5005	1.95	33.3 (1.5–54.8)	1.20	44.2 (−21.5 to 79.5)	11.4	14.1 (−11.3 to 34.9)
Year 11	1470	2.80	7.9 (−48.6 to 42.9)	2.04	11.5 (−100.0 to 81.7)	13.6	−1.7 (−57.1 to 37.9)
SPS (years 0.0–4.9)[b]	58 203	0.73	61.1 (51.1–69.1)	0.46	66.5 (47.5–79.2)	5.4	51.3 (44.2–57.6)
STPS (years 3.3–7.8)[b]	9967	1.42	50.1 (14.1–71.0)	0.70	60.1 (−8.8 to 86.7)	8.4	39.6 (18.2–55.5)
LTPS (years 4.7–11.6)	25 250	1.74	37.3 (26.7–46.4)	1.27	35.4 (8.8–55.8)	10.3	21.1 (10.9–30.4)

Results of the primary vaccine efficacy analysis by year postvaccination are reported here for the SPS + STPS (years 1–6), and for the LTPS (years 7–11).

Abbreviations: BOI, burden of illness; CI, confidence interval; HZ, herpes zoster; LTPS, Long-Term Persistence Substudy; PHN, postherpetic neuralgia; PY, person-years; SPS, Shingles Prevention Study (primary efficacy study for the zoster vaccine); STPS, Short-Term Persistence Substudy.

Clin Infect Dis. 2012 Apr 1; 54(7): 922–928.

ZEST ÇALIŞMASI

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

Kenneth E. Schmader,[1,2] Myron J. Levin,[3] John W. Gnann, Jr,[4,5] Shelly A. McNeil,[6] Timo Vesikari,[7] Robert F. Betts,[8] Susan Keay,[9] Jon E. Stek,[10] Nickoya D. Bundick,[10] Shu-Chih Su,[10] Yanli Zhao,[10] Xiaoming Li,[10] Ivan S. F. Chan,[10] Paula W. Annunziato,[10] and Janie Parrino[10]

Table 2. Incidence of Confirmed Herpes Zoster Cases

	Zoster Vaccine (N = 11 211)				Placebo (N = 11 228)				
Population	HZ Cases	No.	Total Follow-up[a]	Estimated Incidence[b]	HZ Cases	No.	Total Follow-up[a]	Estimated Incidence[b]	Vaccine Efficacy (95% CI)
ITT (entire study duration)	30	11 211	15 042.85	1.99	99	11 228	15 009.62	6.60	69.8% (54.1–80.6)
ITT 0.0–0.5 years	9	11 186	5536.77	1.62	39	11 210	5541.08	7.04	76.9% (51.5–90.2)
ITT >0.5–1.0 years	13	10 954	5420.64	2.40	36	10 953	5407.72	6.66	64.0% (30.4–82.5)
ITT >1.0–1.5 years	7	10 747	3513.60	2.00	20	10 712	3496.06	5.72	65.2% (14.3–87.6)
ITT >1.5 years	1	3743	571.84	1.75	4	3728	564.76	7.08	75.3% (−149.5–99.5)
MITT	26	11 165	14 124.16	1.84	94	11 189	14 091.27	6.67	72.4% (57.0–82.9)

Abrreviations: CI, confidence interval; HZ, herpes zoster; ITT, intent-to-treat population; MITT, modified intent-to-treat population.

[a] Total follow-up calculated as person-years.

[b] Estimated incidence calculated as per 1000 person-years.

CZA (ZOSTAVAX®) ETKİNLİĞİ

	Zostavax etkinliği (%95 Güven aralığı)		
	Herpes zoster	**PHN**	**Hastalık yükü**
Yaş grubu (yıl)			
50 - 59	70% (54 - 81)	Veri yok	73% (53 - 85)
60 - 69	64% (56 - 71)	66% (20 - 87)	66% (52 - 76)
70 - 79	41% (28 - 52)	Veri yok	Veri yok
≥ 70	38% (28 - 52)	67% (43 - 81)	55% (40 - 67)
≥ 80	18% (–29 - 48)	Veri yok	Veri yok
Aşılama sonrası izlem			
0.0 - 3.1 yıl	51% (44 - 58)	67% (48 - 79)	61% (51 - 69)
3.3 - 7.8 yıl	40% (18 - 56)	60% (–10 - 87)	50% (14 - 71)
4.7 - 11.6 yıl	21% (11 - 30)	35% (9 - 56)	37% (27 - 46)

Human Vaccines & Immunotherapeutics 11:5, 1157–1164; May 2015; © 2015 Taylor & Francis Group, LLC

Herpes zoster vaccine effectiveness and manifestations of herpes zoster and associated pain by vaccination status

Mona Marin[1,*], Barbara P Yawn[2], Craig M Hales[1], Peter C Wollan[2], Stephanie R Bialek[1], John Zhang[1], Marge J Kurland[2], and Rafael Harpaz[1]

[1]National Center for Immunization and Respiratory Diseases; Centers for Disease Control and Prevention; Atlanta, GA USA; [2]Department of Research; Olmsted Medical Center; Rochester, MN USA

Tablo 2. Zona ve zona ilişkili durumlarda aşının etkinliği

	Aşı etkinliği (%95 GA)
Zona tüm katılımcılar	54 (32 - 69)
Zana yaş gruplarına göre	
Aşılı 60-69 yaş	67 (43 - 81)
Aşılı ≥ 70 yaş	38 (0- 64)
Zona prodrom	58 (31- 75)
Zona klinik	70 (33 - 87)
PHN	
Ağrı 30 gün	61 (22 -80)
Ağrı 60 gün	69 (0 – 91)
Ağrı 90 gün	55 (0 – 92)

Lisans sonrası ilk toplum bazlı çalışma
≥ 60 yaş

SPS Çalışmasının İstenmeyen Olaylar Takibi
(aşılamadan 0- 42 gün sonra)

İstenmeyen olay	CZA (n: 3345) %	Plasebo (n:3271) %
Enjeksiyon bölgesi		
Eritem	36	7
Ağrı/hassasiyet	35	9
Şişlik	26	5
Hematom	2	1
Kaşıntı	7	1
Sıcaklık	2	0.3
Döküntü	0.3	0.1
Ateş (≥38°C)	0.8	0.9
Sistemik	6	5

Oxman MN, N Engl J Med 2005; 352 (22):2271-84

Annals of Internal Medicine

Ann Intern Med. 2010;152:545-554.

ARTICLE

Safety of Herpes Zoster Vaccine in the Shingles Prevention Study

A Randomized Trial

Michael S. Simberkoff, MD; Robert D. Arbeit, MD; Gary R. Johnson, MS; Michael N. Oxman, MD; Kathy D. Boardman, RPh; Heather M. Williams, RN; Myron J. Levin, MD; Kenneth E. Schmader, MD; Lawrence D. Gelb, MD; Susan Keay, MD, PhD; Kathleen Neuzil, MD; Richard N. Greenberg, MD; Marie R. Griffin, MD; Larry E. Davis, MD; Vicki A. Morrison, MD; and Paula W. Annunziato, MD, for the Shingles Prevention Study Group

38 546 katılımcı

Aşı sonrası 42 gün izlem

Veri 37 388 (%97) katılımcıdan elde edildi

Alt çalışma grubu 6616 katılımcıdan

6575 (%99) katılımcıdan güvenlik verisi elde edildi.

Ortalama takip süresi 3.39 yıl (1gün-5.4 yıl) (1998-2004)

HZ aşı 24600PFU

SPS Çalışmasının İstenmeyen Olaylar Takibi (aşılamadan 0- 42 gün sonra)

İstenmeyen olay	60-69 yaş		≥70 yaş	
	CZA %	Plasebo %	CZA %	Plasebo %
Enjeksiyon bölgesi ≥ 1	**57**	**19**	**39**	**14**
Eritem	42	8	29	6
Ağrı/hassasiyet	43	10	25	7
Şişlik	32	5	20	4
Hematom	1	2	2	1
Kaşıntı	10	1	5	1
Sıcaklık	2	0.4	1	0.3
Döküntü	0.7	0.1	0.5	0.3
Ciddi	**1**	**1**	**2**	**2**

Ann Intern Med 2010; 152: 545-554

CZA'nın ruhsatlandırılması sonrası 10 yıllık güvenlik değerlendirilmesi

İstenmeyen olay	Toplam (n: 45.898), n(%)	Ciddi (n: 4.607), n(%)
Enjeksiyon bölgesi reaksiyonları	9396 (20.5)	192 (4.2)
Zona	3943 (8.6)	373 (8.1)
Döküntü	1922 (4.2)	163 (3.5)
Eritem (enjeksiyon yeri dışı)	628 (1.4)	48 (1.0)
Ağrı	614 (1.3)	85 (1.8)
Kaşıntı	536 (1.2)	40 (0.9)
Baş ağrısı	471 (1)	64 (1.4)
Ateş	454 (0.99)	69 (1.4)
Ekstremitede ağrı	439 (0.96)	59 (0.97)
Periferal ödem	308 (0.67)	24 (0.52)
Blister	291 (0.63)	39 (0.85)
Parestezi	238 (0.52)	43 (0,93)
Halsizlik	229 (0.5)	38 (0.82)
Bulantı	222 (0.48)	51 (1.1)
Selülit	218 (0.47)	33 (0.72)
Su çiçeği	217 (0.47)	28 (0.61)
Artralji	215 (0.47)	44 (0.96)
Ürtiker	213 (0.46)	23 (0.50)
Oftalmik zona	143 (0.31)	32 (0.69)
Dissemine zona	15 (<0.1)	10 (0.22)
Nekrotizan retinit	4 (<0.1)	4 (<0.1)
ADEM (Akut dissemine ensefalomiyelit	3 (<0.1)	3 (<0.1)

Willis ED, et al. Vaccine. 2017;35(52):7231–7239

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2018, VOL. 14, NO. 8, 1963–1969
https://doi.org/10.1080/21645515.2018.1456598

RESEARCH PAPER

Post-licensure safety surveillance of zoster vaccine live (Zostavax®) in the United States, Vaccine Adverse Event Reporting System (VAERS), 2006–2015

Elaine R. Miller[a], Paige Lewis[a], Tom T. Shimabukuro[a], John Su[a], Pedro Moro[a], Emily Jane Woo[b], Christopher Jankosky[b], and Maria Cano[a]

Table 2. Most commonly reported adverse events among persons aged ≥50 years following zoster vaccine live (ZVL) in VAERS, May 2006–January 2015[1], based on automated analysis.

Non-serious reports

MedDRA Preferred Term[2]	Total[3] N = 17,089	ZVL alone N = 15,397
	n (%)	n (%)
Injection site erythema	4,661 (27)	4,193 (27)
Injection site swelling	2,854 (17)	2,555 (17)
Herpes zoster	2,781 (16)	2,644 (17)
Rash	2,283 (13)	2,094 (14)
Erythema	2,215 (13)	1,943 (13)
Injection site pain	1,993 (12)	1,743 (11)
Pruritus	1,947 (11)	1,768 (11)
Pain	1,811 (11)	1,605 (10)
Injection site warmth	1,791 (10)	1,625 (11)
Injection site pruritus	1,714 (10)	1,575 (10)

Table 2. Most commonly reported adverse events among persons aged ≥50 years following zoster vaccine live (ZVL) in VAERS, May 2006–January 2015[1], based on automated analysis.

Serious reports[1]

MedDRA Preferred Term[2]	Total[3] N = 851	ZVL alone N = 753
	n (%)	n (%)
Herpes zoster	228 (27)	221 (29)
Pain	154 (18)	133 (18)
Rash	131 (15)	123 (16)
Pyrexia	118 (14)	90 (12)
Dyspnea	114 (13)	94 (12)
Asthenia	104 (12)	78 (10)
Headache	97 (11)	81 (11)
White blood cell count increased	96 (11)	75 (10)
Nausea	91 (11)	75 (10)
Dizziness	81 (10)	63 (8)

Genel olarak, CZA
- İyi tolere edilir
- Sistemik YE az
- Hafif-orta derecede enjeksiyon bölgesi YE

Vaccine 32 (2014) 1645–1653

Review

Cost-effectiveness of vaccination against herpes zoster and postherpetic neuralgia: a critical review

Kosuke Kawai [a,*], Emmanuelle Preaud [b], Florence Baron-Papillon [b], Nathalie Largeron [b], Camilo J. Acosta [a]

[a] Global Health Outcomes, Merck & Co., Inc., West Point, PA, USA
[b] Department of Market Access and Economics, Sanofi Pasteur MSD, France

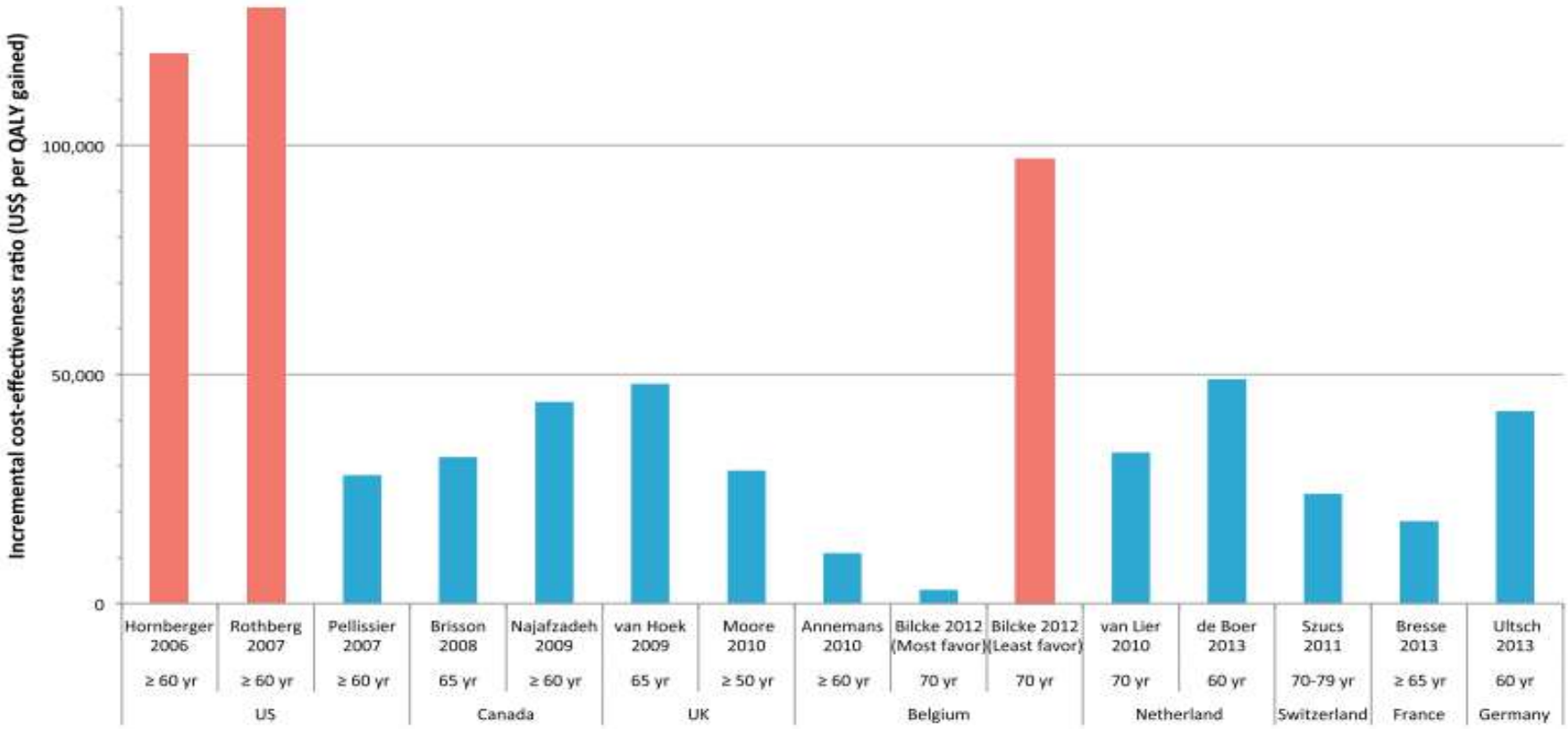


Figure 1. Cost-effectiveness of vaccination against herpes zoster in North America and Europe.
Blue bar indicates studies showing that vaccination is likely to be cost-effective. Red bar indicates studies showing that vaccination is not cost-effective. Bilcke et al. conducted analyses for the most in favor of vaccination and the least in favor of vaccination. Bilcke et al. had difficulty in making conclusions regarding cost-effectiveness because of uncertainty in key parameters. van Lier et al. and Ultsch et al. could not determine cost-effectiveness.

Table 1 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				
or					
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	
or				or	
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

Table 2 Recommended Adult Immunization Schedule by Medical Condition and Other Indications United States, 2019

Vaccine	Pregnancy	Immuno-compromised (excluding HIV infection)	HIV infection CD4 count <200	HIV infection CD4 count ≥200	Asplenia, complement deficiencies	End-stage renal disease, on hemodialysis	Heart or lung disease, alcoholism[1]	Chronic liver disease	Diabetes	Health care personnel[2]	Men who have sex with men
IIV or RIV	1 dose annually										
or										or	
LAIV	CONTRAINDICATED						PRECAUTION			1 dose annually	
Tdap or Td	1 dose Tdap each pregnancy	1 dose Tdap, then Td booster every 10 yrs									
MMR	CONTRAINDICATED	1 or 2 doses depending on indication									
VAR	CONTRAINDICATED	2 doses									
RZV *(preferred)*	DELAY				2 doses at age ≥50 yrs						
or					or						
ZVL	CONTRAINDICATED				1 dose at age ≥60 yrs						
HPV Female	DELAY	3 doses through age 26 yrs			2 or 3 doses through age 26 yrs						
HPV Male		3 doses through age 26 yrs			2 or 3 doses through age 21 yrs						2 or 3 doses through age 26 yrs
PCV13		1 dose									
PPSV23		1, 2, or 3 doses depending on age and indication									
HepA		2 or 3 doses depending on vaccine									
HepB		2 or 3 doses depending on vaccine									
MenACWY		1 or 2 doses depending on indication, then booster every 5 yrs if risk remains									
MenB	PRECAUTION	2 or 3 doses depending on vaccine and indication									
Hib		3 doses HSCT[3] recipients only			1 dose						

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

Precaution—vaccine might be indicated if benefit of protection outweighs risk of adverse reaction

Delay vaccination until after pregnancy if vaccine is indicated

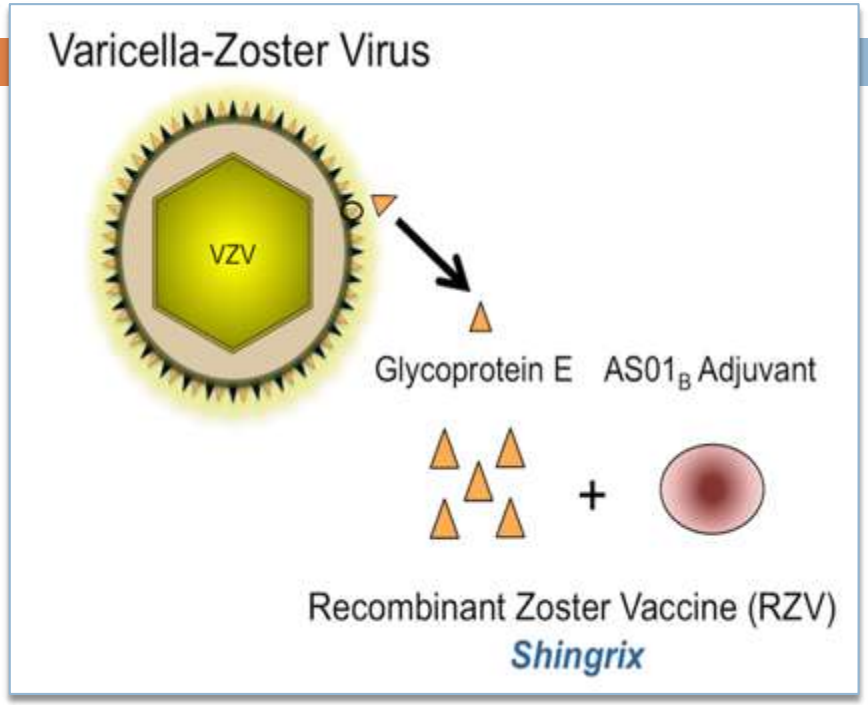
Contraindicated—vaccine should not be administered because of risk for serious adverse reaction

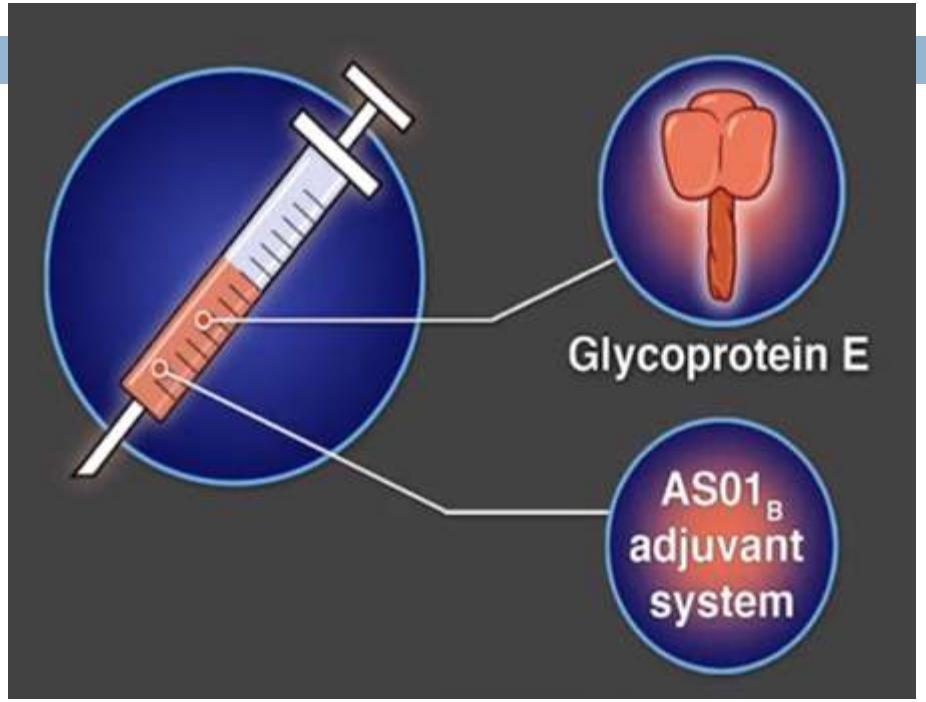
No recommendation

1. Precaution for LAIV does not apply to alcoholism.

Juliette Borda

Rekombinant Zona Aşısı (RZA)





2017'de FDA ve 2018'de Avrupa Komisyonu tarafından onaylandı
RZV, VZV'nin glikoprotein E'sini (gE) içerir
AS01B adjuvanı ile adjuvanlanmış aşı

J Infect Dis. 2018;217(11):1750–1760
N Engl J Med. 2016;375(11):1019–1032
MMWR Morb Mortal Wkly Rep. 2018;67(3):103–108
https://ec.europa.eu/health/documents/community register/2018/20180321140171/dec_140171_en.pdf

RZA

- 25 Ekim 2017'de ACIP (Advisory Committee on Immunization Practices) (ACIP) ≥50 yaş immunkompetan erişkinler için önerildi
- Zona ve ilişkili komplikasyonları önlemek için önceden CZA uygulanan immunkompetan erişkinler için önerdi.
- RZV zona ve ilişkili komplikasyonları önlemek için CZA'ya tercih edilir.

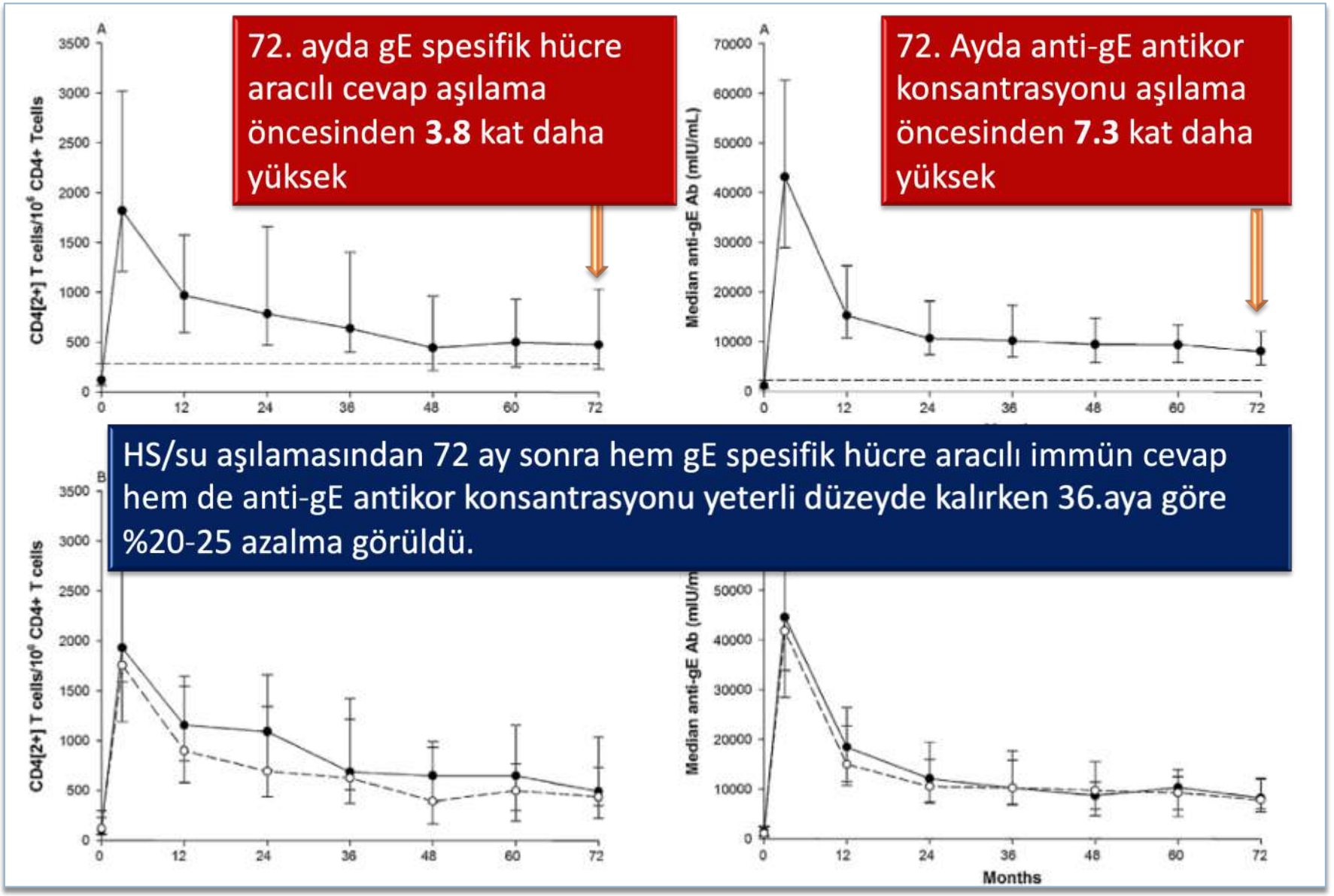
MMWR Morb Mortal Wkly Rep. 2018;67(3):103–108

Vaccine 34 (2016) 863–868

Long-term immunogenicity and safety of an investigational herpes zoster subunit vaccine in older adults

Roman Chlibek[a], Karlis Pauksens[b], Lars Rombo[c,d], Gini van Rijckevorsel[e], Jan H. Richardus[f], Georg Plassmann[g], Tino F. Schwarz[h], Grégory Catteau[i], Himal Lal[j,*], Thomas C. Heineman[j]

- Faz II, açık etiketli, çok merkezli çalışma
- 50µg gE/ASO1B formulasyonu
- 2 doz HZ/su aşı, IM, O.5ml, deltoid kasa
- Aşı sonrası altı yıl immün cevap değerlendirilmiş
  - gE spesifik hücre aracılı immün cevap
  - anti-gE antikor konsantrasyonu



A. Tüm populasyonda ≥60 yaş
B. Siyah noktalı düz çizgi 60-69 yaş, beyaz noktalı kesikli çizgi ≥70y

Chlibek R,et al. Vaccine 2016; 34: 863-8

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2018, VOL. 14, NO. 6, 1370–1377
https://doi.org/10.1080/21645515.2018.1442162

RESEARCH PAPER

Persistence of immune response to an adjuvanted varicella-zoster virus subunit vaccine for up to year nine in older adults

Tino F. Schwarz[a], Stephanie Volpe[b], Gregory Catteau[c], Roman Chlibek[d], Marie Pierre David[e], Jan Hendrik Richardus[f], Himal Lal[g], Lidia Oostvogels[b], Karlis Pauksens[h], Stephanie Ravault[i], Lars Rombo[j], Gerard Sonder[k], Jan Smetana[d], Thomas Heineman[l], and Adriana Bastidas[b]

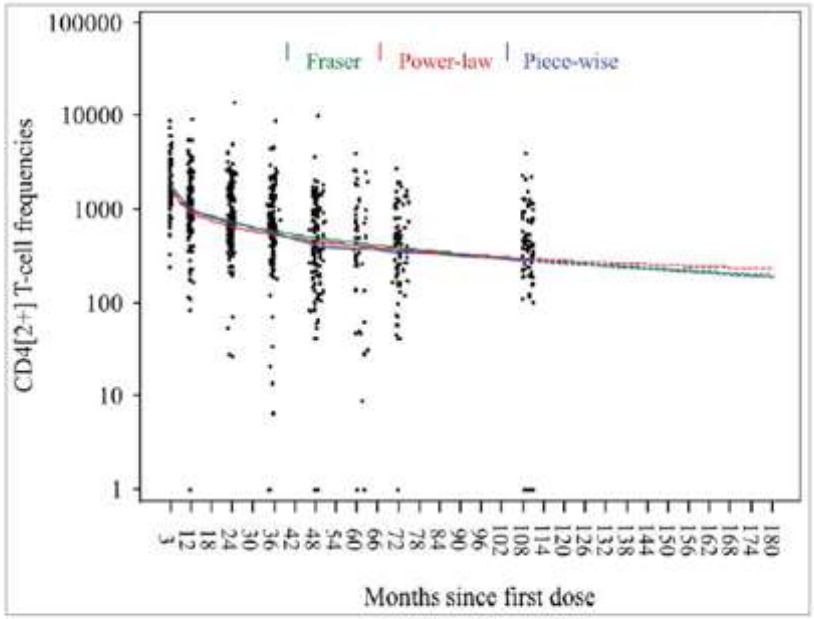


Figure 3. Predicted geometric means of frequencies of gE-specific CD4[2+] T cells based on three statistical prediction models (piece-wise linear, power-law, Fraser).

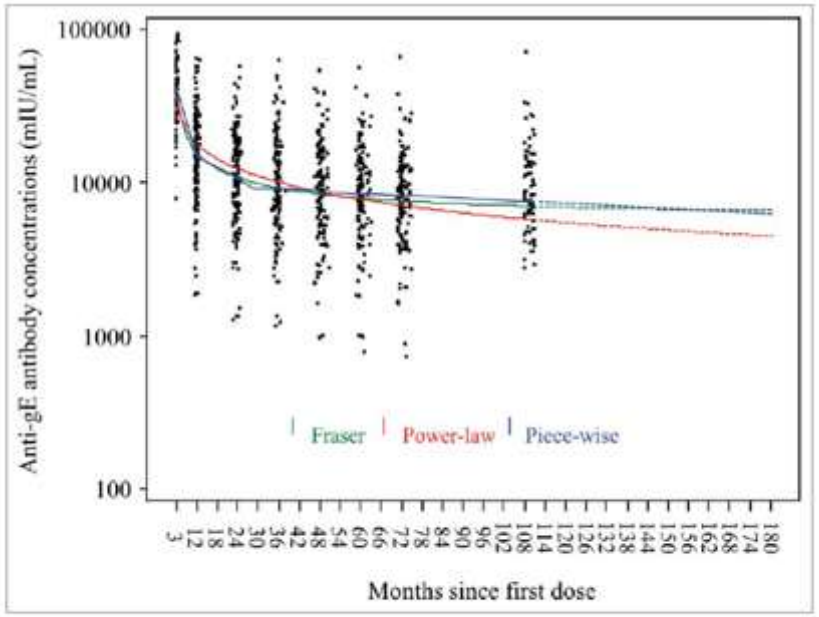


Figure 4. Predictions of anti-gE antibody geometric mean concentrations based on three statistical prediction models (piece-wise linear, power-law, Fraser).

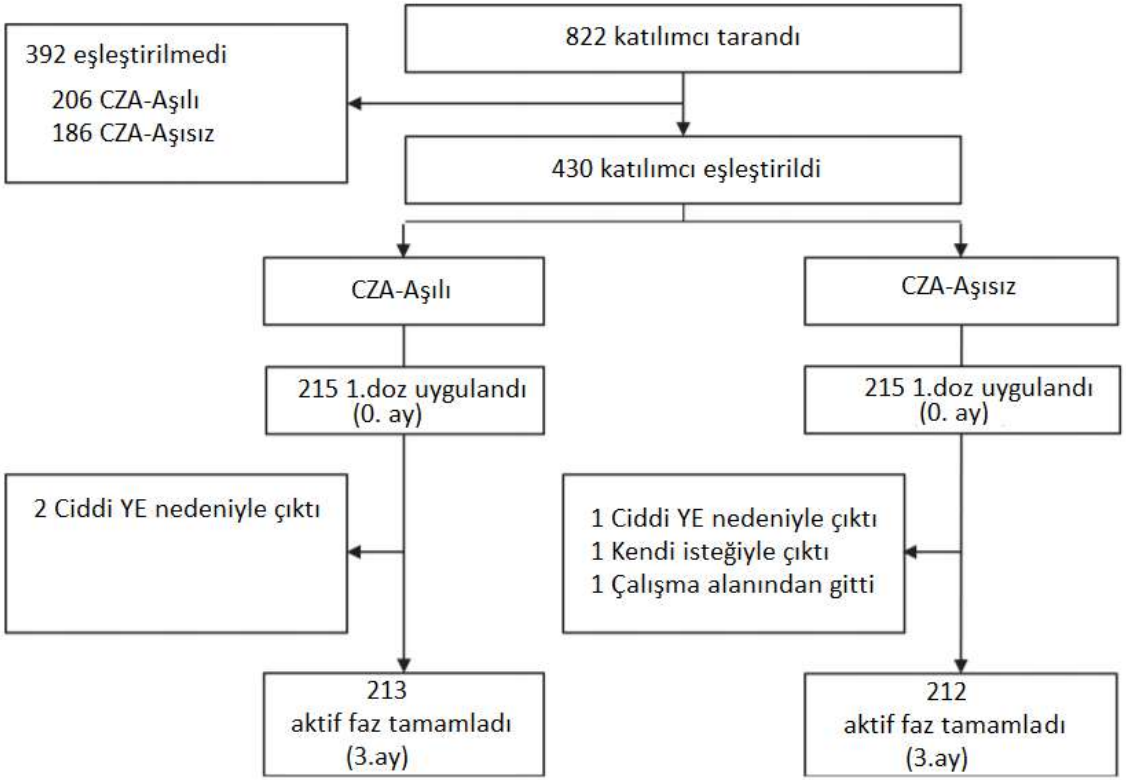
HZ/su aşılama sonrası **9 yıl** hem hücresel hem humoral immünite aşılama öncesi üzerinde.
İmmün cevabın **15 yıl** bazal değerin üzerinde devam edeceği tahmin edilmiştir.

The Journal of Infectious Diseases
The Journal of Infectious Diseases® 2017;216:1343–51

Immunogenicity and Safety of the HZ/su Adjuvanted Herpes Zoster Subunit Vaccine in Adults Previously Vaccinated With a Live Attenuated Herpes Zoster Vaccine

Katrijn Grupping,[1] Laura Campora,[1] Martine Douha,[1] Thomas C. Heineman,[2] Nicola P. Klein,[3] Himal Lal,[4] James Peterson,[5] Ilse Vastiau,[1] and Lidia Oostvogels[1]

- Faz III
- Çok merkezli
- ≥ 65 yaş
- CZA aşılamasından ≥ 5 yıl geçmiş
- HZ/su iki ay arayla iki doz
- İmmün cevap değerlendirilmiş



The Journal of Infectious Diseases
The Journal of Infectious Diseases® 2017;216:1343–51

Immunogenicity and Safety of the HZ/su Adjuvanted Herpes Zoster Subunit Vaccine in Adults Previously Vaccinated With a Live Attenuated Herpes Zoster Vaccine

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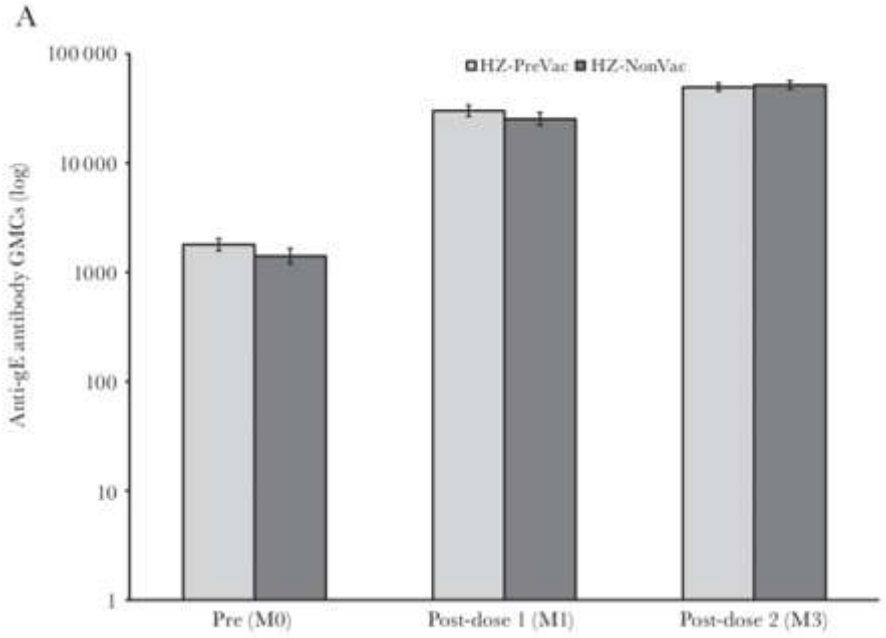
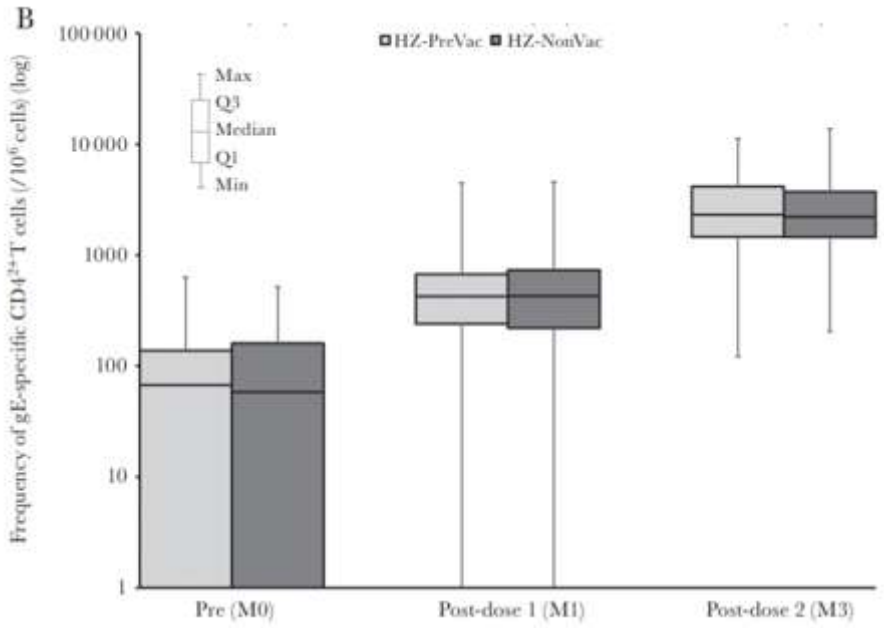




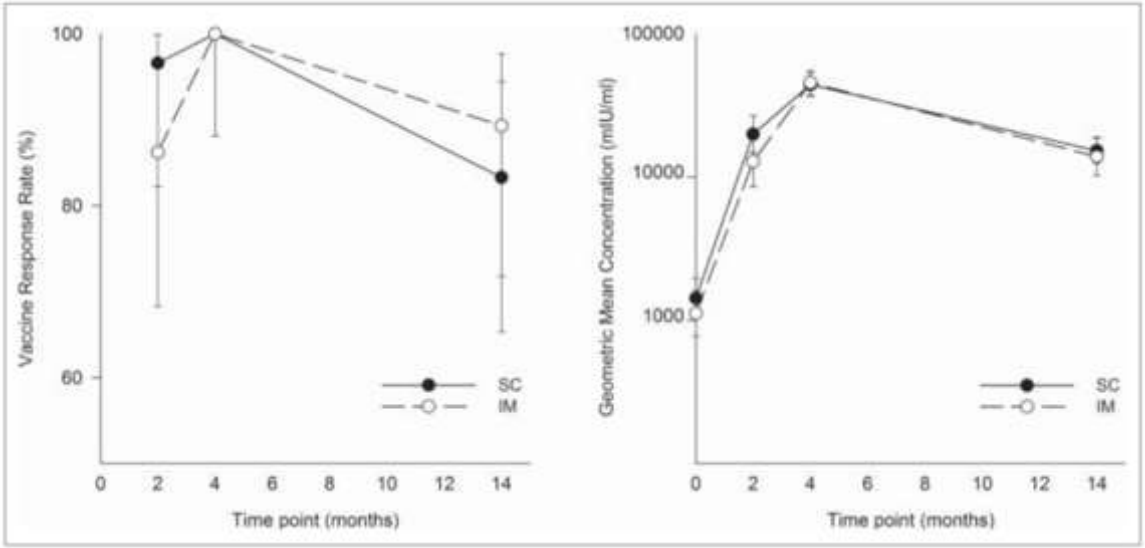
Önceden CZA olanlarda RZA ile tekrar aşılama immun cevabı güçlendiriyor

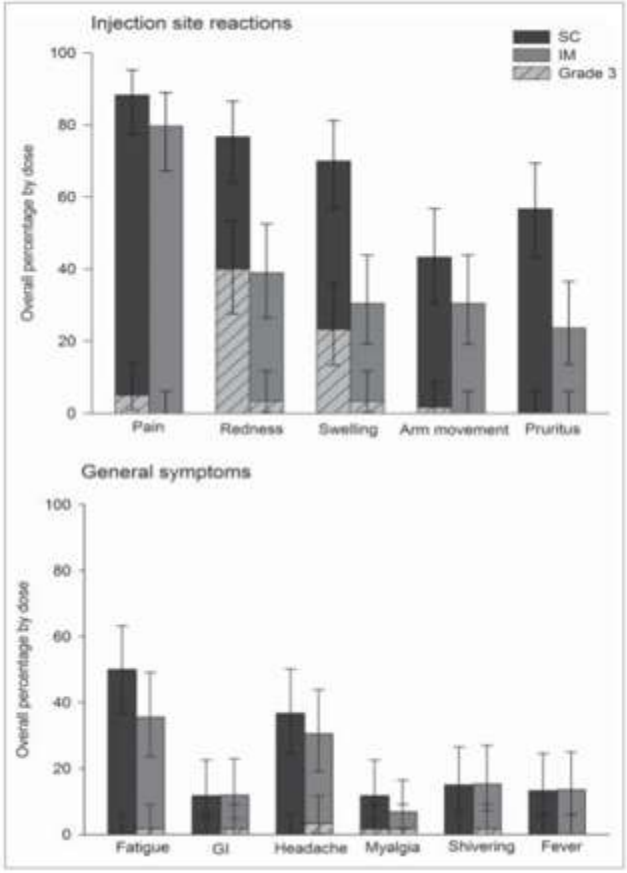
HUMAN VACCINES & IMMUNOTHERAPEUTICS
2017, VOL. 13, NO. 3, 574–578
http://dx.doi.org/10.1080/21645515.2016.1232787

RESEARCH PAPER

Safety and immunogenicity of a Herpes Zoster subunit vaccine in Japanese population aged ≥50 years when administered subcutaneously vs. intramuscularly

Peter Vink[a], Masanari Shiramoto[b], Masayuki Ogawa[c], Masahiro Eda[c], Martine Douha[d], Thomas Heineman[a,†], and Himal Lal[a,††]





Hem SC hem de IM uygulamada
benzer immun yanıt
SC yolda daha fazla YE

RZA'nın etkinliğini değerlendiren preklinik çalışmalar

ZOE-50	2015 FazIII Çok merkezli (18 ülke) Randomize, vaka-kontrol çalışması ≥50 yaş HZ/su aşı etkinliği ve güvenliği değerlendirme
ZOE-70	2016 FazIII Çok merkezli (18 ülke) ≥70 yaş HZ/su aşı etkinliği ve güvenliği değerlendirme

Lal H, et al. N Engl J Med. 2015;372(22):2087–2096
Cunningham AL, et al. N Engl J Med. 2016;375(11):1019–1032

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 28, 2015 VOL. 372 NO. 22

Efficacy of an Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults

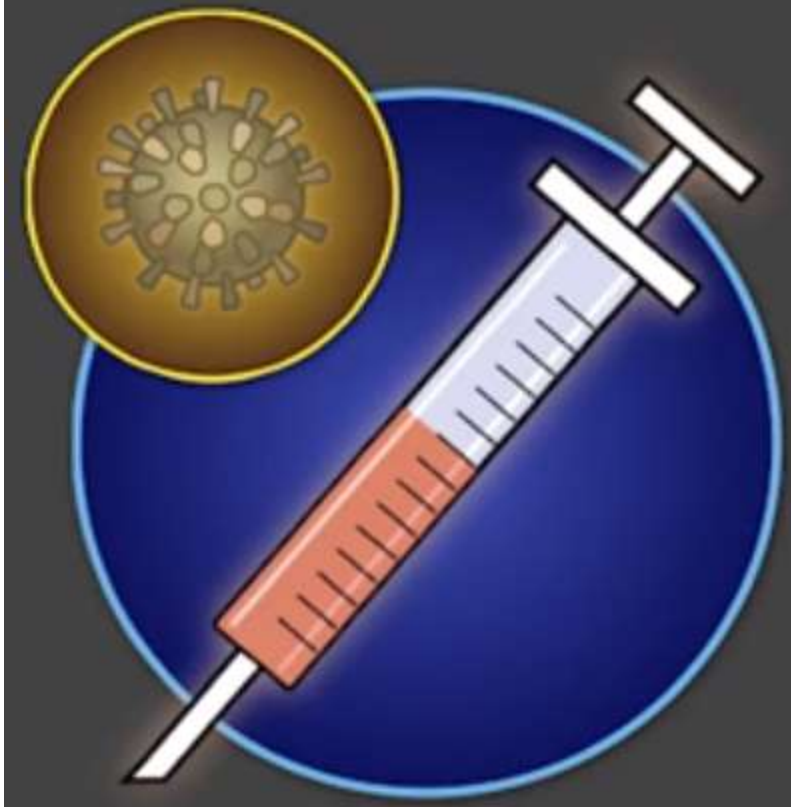
Himal Lal, M.D., Anthony L. Cunningham, M.B., B.S., M.D., Olivier Godeaux, M.D., Roman Chlibek, M.D., Ph.D., Javier Diez-Domingo, M.D., Ph.D., Shinn-Jang Hwang, M.D., Myron J. Levin, M. Airi Poder, M.D., Joan Puig-Barberà, M.D., M.P.H., Ph.D., Timo Vesikari, M.D., Ph.D., Lily Weckx, M.D., Ph.D., Toufik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

ZOE-50 ÇALIŞMASI

Tablo 1. ZOE-50: HZ/su Zona İnsidansına Etkinliği

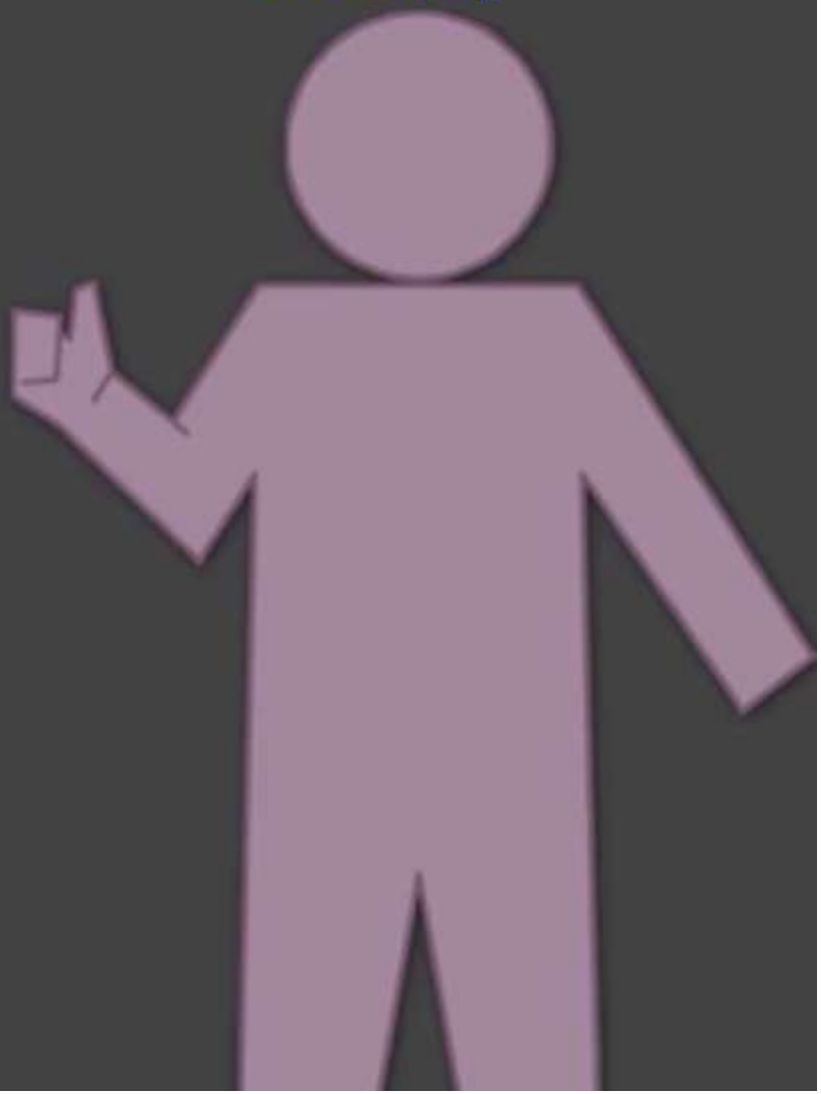
Yaş grubu (Yıl)	HZ/su			Plasebo			% etkinlik (%95 GA)
	N	n	Zona insidansı 1000 kişi-yıl	N	n	Zona insidansı 1000 kişi-yıl	
Toplam (≥ 50)	7344	6	0.3	7415	210	9.1	97.2 (93.7-99)
50-59	3492	3	0.3	3525	87	7.8	96,9 (89.6-99.3)
60-69	2141	2	0.3	2166	75	10.8	97.4 (90.1-99.7)
≥ 70	1711	1	0.2	1724	48	9.4	97.9 (87.9-100)

Faz III klinik çalışma



Azalmış Risk

≥ 50 yaş




≥ 70 yaş
Etkinlik ve
Güvenlik ?

14.816 katılımcı

≥ 70 yaş

Dışlama kriterleri

- Önceden aşılı (Suçiçeği veya zona)
- Zona öyküsü olanlar
- İmmunkompromize kişiler

13.900 katılımcı

- Ort. Yaş 75.6 yıl
- >80 yaş %22.1
- Yaklaşık %95 2 doza aşı

Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older

Anthony L. Cunningham, M.B., B.S., M.D., Himal Lal, M.D., Martina Kovac, M.D., Roman Chlibek, M.D., Ph.D., Shinn-Jang Hwang, M.D., Javier Díez-Domingo, M.D., Ph.D., Olivier Godeaux, M.D., Myron J. Levin, M.D., Janet E. McElhaney, M.D., Joan Puig-Barberà, M.D., M.P.H., Ph.D., Carline Vanden Abeele, M.Sc., Timo Vesikari, M.D., Ph.D., et al., for the ZOE-70 Study Group*

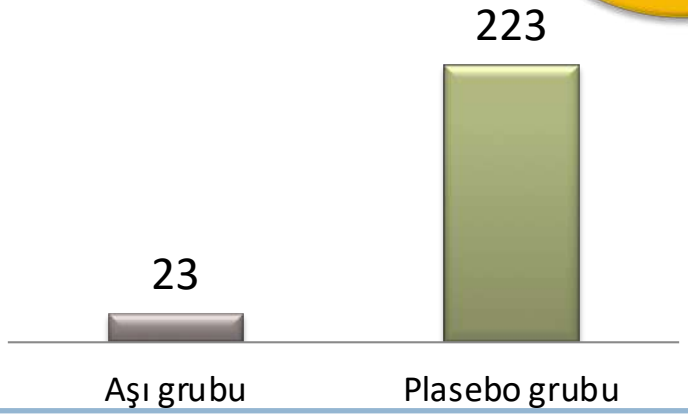
N Engl J Med 2016; 375:1019-1032

Tablo 1. ZOE-70: HZ/su Zona İnsidansına Etkinliği

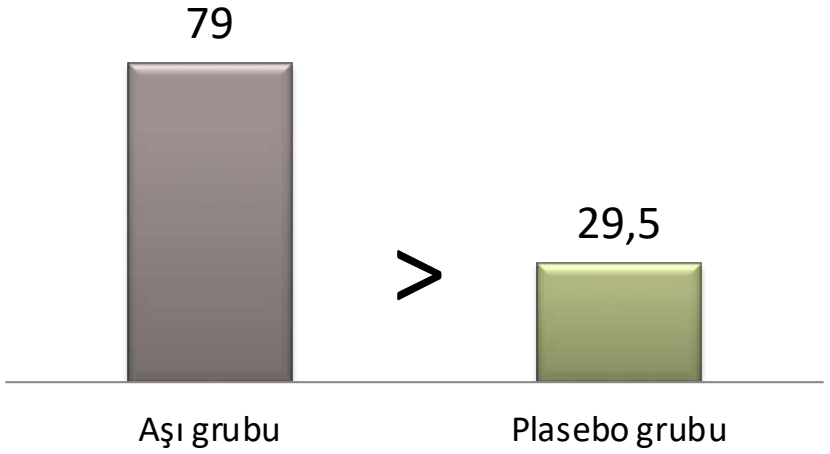
Yaş grubu (Yıl)	HZ/su			Plasebo			% Etkinlik (%95 GA)
	N	n	Zona insidansı 1000 kişi-yıl	N	n	Zona insidansı 1000 kişi-yıl	
Toplam (≥ 70)	6541	23	0.9	6622	223	9.2	**89.8** (84.3-93.7)
70-79	5144	17	0.9	5189	169	8.8	**90.0** (83.5-94.3)
≥ 80	1427	6	1.2	1433	54	11.0	**89.1** (74.7-96.2)

Doğrulanmış vakalar ~3.7 yıl takip

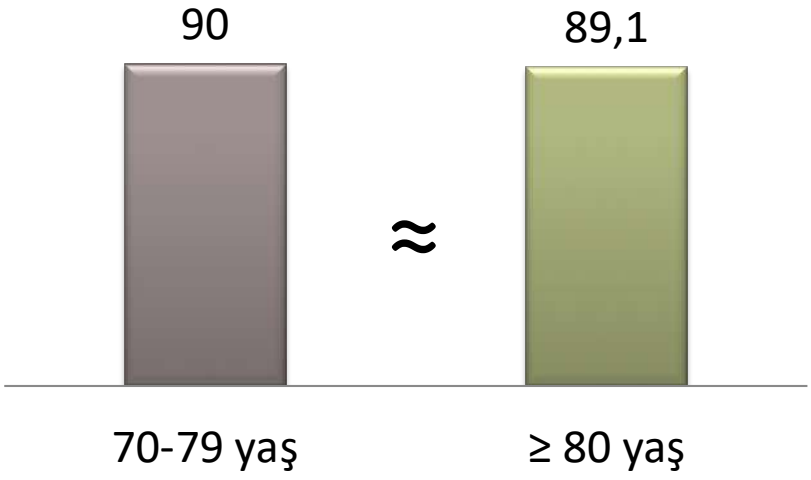
Toplam etkinlik ~%90



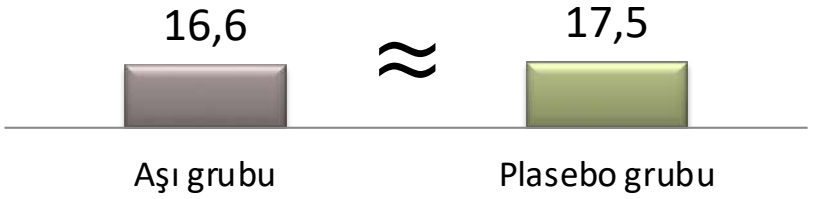
Enjeksiyon yeri ve sistemik reaksiyonlar, %

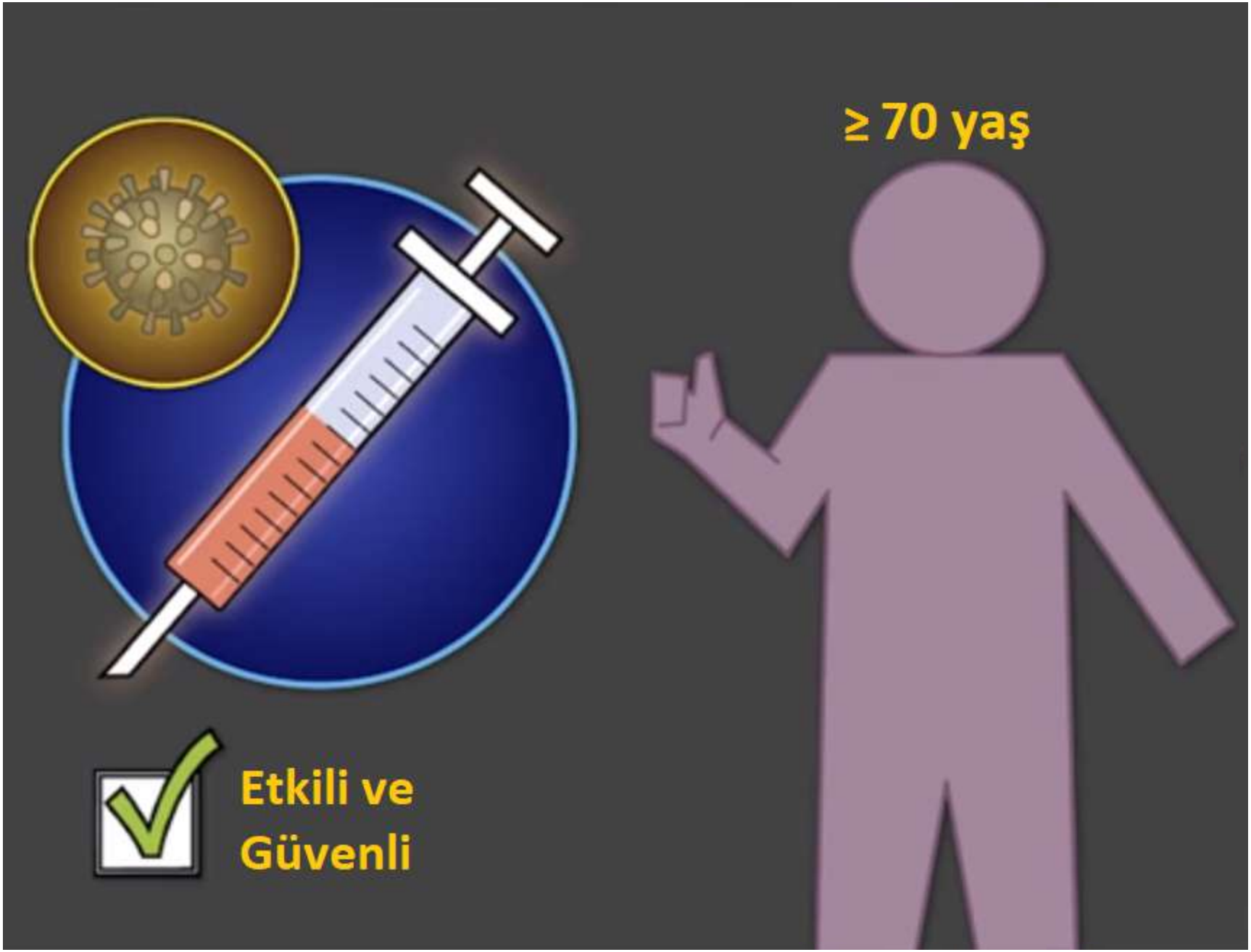


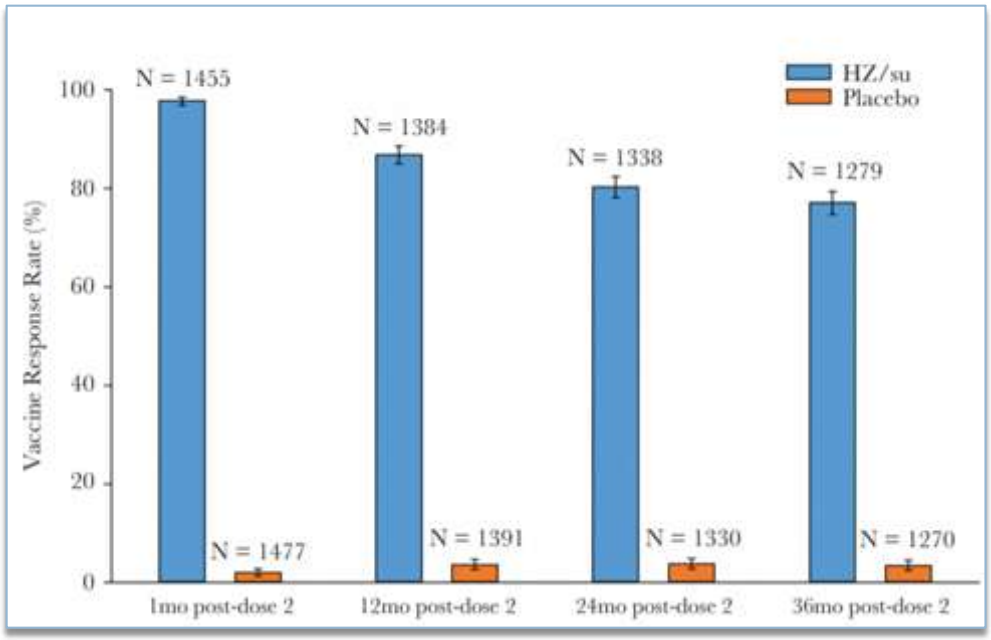
Aşı etkinliği, %

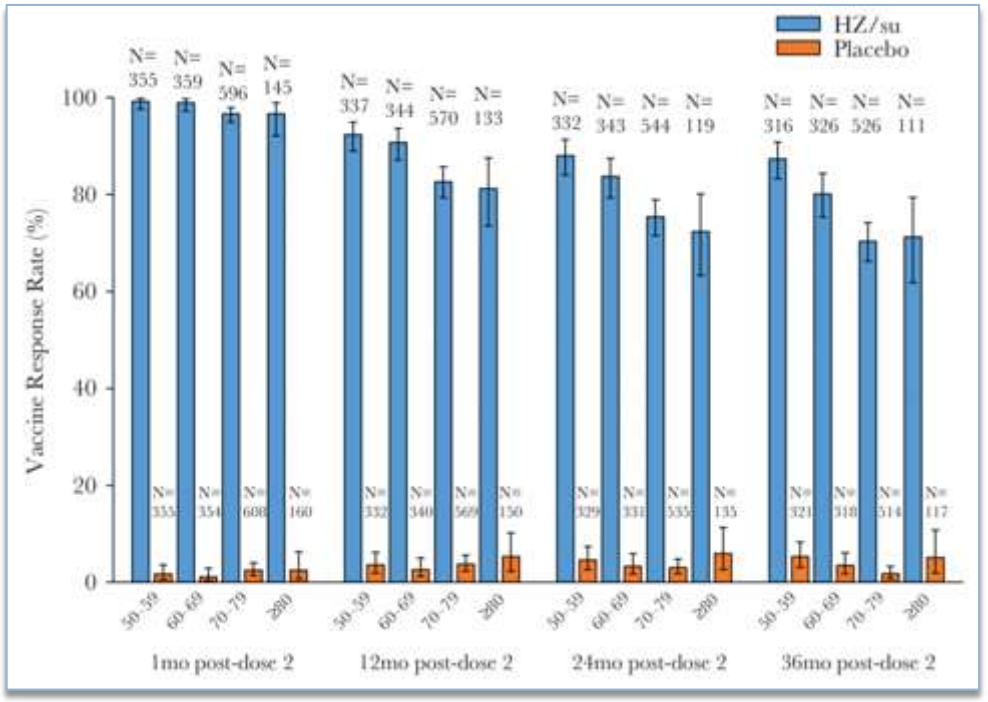


Ciddi yan etkilerin oranı, %




≥ 70 yaş
Etkili ve
Güvenli





ZOE-50: ≥50 ve ZOE-70: ≥70 çalışmasına katılan deneklerde aşılamadan **<u>üç yıl sonra</u>**, immün yanıtın kalıcı olduğu görülmüştür.

Cunningham AL, Heineman TC, Lal H, et al. Immune responses to a recombinant glycoprotein E Herpes Zoster vaccine in adults aged 50 years or older. J Infect Dis 2018;217(11):1750–1760

Vaccine 36 (2018) 1537–1541

Short communication

Complications of herpes zoster in immunocompetent older adults: Incidence in vaccine and placebo groups in two large phase 3 trials

Martina Kovac [a], Himal Lal [b,1], Anthony L. Cunningham [c,d], Myron J. Levin [e], Robert W. Johnson [f], Laura Campora [g], Antonio Volpi [h], Thomas C. Heineman [b,2,*], for the ZOE-50/70 Study Group [3]

HZ-related complications (other than PHN) in participants with a confirmed HZ episode in the ZOE-50/ZOE-70 pooled population (modified vaccinated cohort)*

Complications	HZ/su (N = 13,881)			Placebo (N = 14,035)		
	Number of participants with a confirmed HZ episode	Participants with at least one specified HZ-related complication#		Number of participants with a confirmed HZ episode	Participants with at least one specified HZ-related complication#	
		n	%		n	%
Ophthalmic disease						
50–59 years	4	0	0.0	103	0	0.0
60–69 years	3	0	0.0	90	1	1.1
70–79 years	19	1	5.3	216	4	1.9
≥80 years	6	0				
Overall	32	1				
Disseminated disease						
50–59 years	4	0				
60–69 years	3	0				
70–79 years	19	0				
≥80 years	6	0				
Overall	32	0				
Neurologic disease						
50–59 years	4	0				
60–69 years	3	0				
70–79 years	19	0				
≥80 years	6	0				
Overall	32	0				
HZ vasculitis						
50–59 years	4	0	0.0	103	0	0.0
60–69 years	3	0	0.0	90	1	1.1
70–79 years	19	0	0.0	216	0	0.0
≥80 years	6	0	0.0	68	0	0.0
Overall	32	0	0.0	477	1	0.2
Subjects with at least one HZ-related complication						
50–59 years	4	0 (0)	0.0	103	1 (1)	1.0
60–69 years	3	0 (0)	0.0	90	3 (3)	3.3
70–79 years	19	1 (1)	5.3	216	8 (9)	3.7
≥80 years	6	0 (0)	0.0	68	4 (4)	5.9
Overall	32	1 (1)	3.1	477	16 (17)	3.4

HZ, herpes zoster; HZ/su, herpes zoster subunit vaccine; PHN, postherpetic neuralgia.
No cases of visceral disease or stroke were diagnosed in participants with a confirmed HZ episode. Therefore, these categories are not shown in this table.
* The modified vaccinated cohort excluded participants who did not receive the second dose of the herpes zoster subunit vaccine (HZ/su) or placebo or who had a confirmed episode of herpes zoster within 1 month (30 days) after the second dose.
# All confirmed HZ episodes considered. Numbers in parentheses represent the number of HZ-related complications.

Benzer şekilde, kayıtlı kişilerin izlem değerlendirmesinde, PHN dışı komplikasyonlar ve HZ ile ilişkili hastaneye yatışlar plasebo grubundan daha düşük

Kovac M, et al. Vaccine. 2018;36(12):1537–1541

Lancet 2018; 391: 2116–27

Inactivated varicella zoster vaccine in autologous haemopoietic stem-cell transplant recipients: an international, multicentre, randomised, double-blind, placebo-controlled trial

*Drew J Winston, Kathleen M Mullane, Oliver A Cornely, Michael J Boeckh, Janice Wes Brown, Steven A Pergam, Igoris Trociukas, Pavel Žák, Michael D Craig, Genovefa A Papanicolaou, Juan D Velez, Jens Panse, Kimberly Hurtado, Doreen A Fernsler, Jon E Stek, Lei Pang, Shu-Chih Su, Yanli Zhao, Ivan S F Chan, Susan S Kaplan, Janie Parrino, Ingi Lee, Zoran Popmihajlov, Paula W Annunziato, Ann Arvin, on behalf of the V212 Protocol 001 Trial Team**

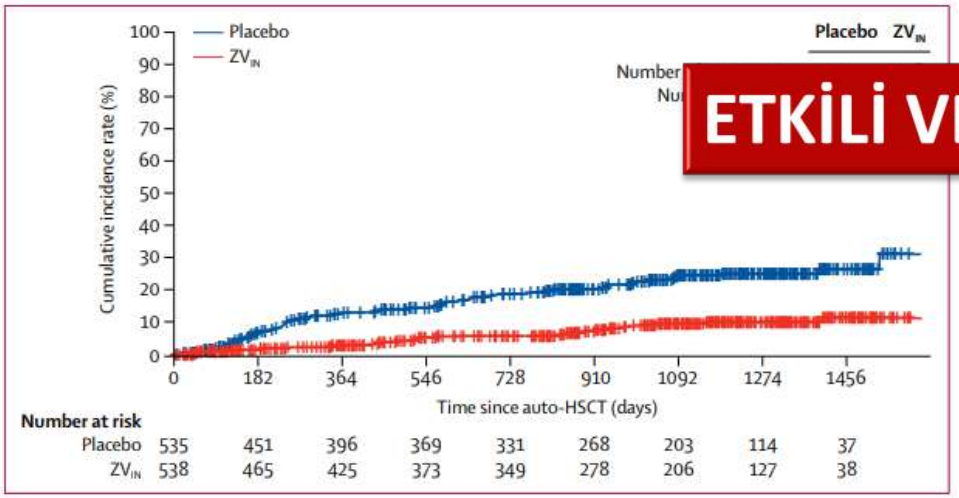


Figure 2: **Cumulative incidence of confirmed herpes zoster cases, per treatment group in the mITT population**
Estimate of the cumulative incidence of confirmed herpes zoster in the inactivated varicella zoster virus vaccine (ZV$_{IN}$) consistency lot group versus the placebo group in the mITT population. auto-HSCT=autologous haemopoietic stem-cell transplantation. mITT=modified intention to treat.

ETKİLİ VE GÜVENLİ

	Inactivated varicella zoster virus vaccine*	Placebo (n=554)	Risk difference (95% CI)	p value
	[illegible]%)	537 (97%)	1·1% (–0·7 to 3·0)	0·249
Vaccine-related adverse event†	214 (33%)	70 (13%)	20·0% (15·5 to 24·5)	<0·0001
Vaccine-related injection site adverse event‡	191 (29%)	36 (7%)	22·6% (18·5 to 26·6)	<0·0001
Vaccine-related non-injection site adverse event	42 (6%)	38 (7%)	–0·4% (–3·3 to 2·4)	0·804
Serious adverse event	216 (33%)	181 (33%)	0·2% (–5·1 to 5·5)	0·942
Serious vaccine-related adverse event	5 (1%)	5 (1%)	–0·1% (–1·4 to 1·1)	0·834
Discontinued because of adverse event	20 (3%)	17 (3%)	0·0% (–2·1 to 2·0)	0·994
Death	41 (6%)	35 (6%)	–0·1% (–2·9 to 2·7)	0·965

Data are n (%) unless otherwise specified. All adverse events observed from the time of first dose of vaccine through to 28 days after the fourth dose were recorded. *All participants who were in the consistency lot group and the high-antigen lot group. †Determined by an investigator to be related to the vaccine. ‡Pain, erythema, swelling, or induration at injection site.

Table 4: **Summary of adverse events**

Winston DJ, et al. Lancet. 2018;391(10135):2116–2127

Clinical Infectious Diseases CID 2019

INVITED ARTICLE

VACCINES: Stanley Plotkin, Section Editor

Adjuvanted Recombinant Glycoprotein E Herpes Zoster Vaccine

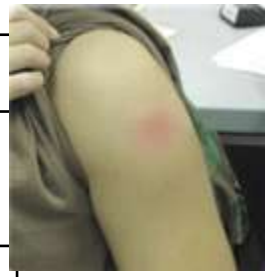
Myron J. Levin[1,2] and Adriana Weinberg[1,2,3]

İmmunkompremize Kişilerde RZA'ya İmmun Yanıt ve Güvenlik

Hastalık	Zamanlama	Antikor		Hücresel immun yanıt		Açıklama
		Cevap	RZA/ Plasebo	Cevap	RZA/ Plasebo	
Solid malignite (n: 141 kemoterapi öncesi; n:40 kemoterapide)	Kemoterapi öncesi 8-30 gün	**%94** (KT öncesi)	23.2	**%50** (KT öncesi)	9.9	1-2 ay içinde 2 doz; kemoterapi ile uygulandığı zaman zayıf cevap
	Kemoterapide	**%64** (KT ile)	Veri yok	Veri yok	Veri yok	
Böbrek nakli (n:121)	Nakil sonrası ≥ 4 ay stabil	**%80**	12.9	**%71**	15.5	Rejeksiyonda artış yok
HIV (n:120)	CD4 >200; ART stabil	**%92-98**	~%50	**>%85**	~16	3 doz: 0,2,6.ay; 3.doz gerekli değil; viral yük ve CD4+ etkisi yok

AŞI YAN ETKİ

	ZOE-50		ZOE-70	
	HZ/su %	Plasebo %	HZ/su %	Plasebo %
Enjeksiyon yeri reaksiyonları	81.5	11.9	74.1	9.9
Ağrı	79.1	11.2	68.7	8.5
Kızarıklık	38	1.3	39.2	1.0
Şişlik	26.3	1.1	22.6	0.4
Grade 3 enjeksiyon yeri reaksiyonu	9.5	0.4	8.5	0.2
Sistemik reaksiyon	66.1	29.5	53.0	25.1
Miyalji	46.3	12.1	32.9	15.2
Yorgunluk	45.9	16.6	31.2	8.1
Başağrısı	39.2	16.0	24.6	10.9
Titreme	28.2	5.9	14.9	4.4
Ateş	21.5	3.0	12.3	2.6
Gastrointestinal semptomlar	18.0	8.8	10.9	7.9
Grade 3 sistemik reaksiyon	11.4	2.4	6.0	2.0



6773 denekten % 85'inde lokal veya sistemik reaksiyonlar

MMWR 2019; 68(4): 91-94
Centers for Disease Control and Prevention
Maltz F, DRUG FORECAST, 2019; 4 (7): 406-10

YANETKİ

TABLE 1. Characteristics of recombinant zoster vaccine (RZV) reports submitted to VAERS — United States, October 2017–June 2018

Report characteristic	No. (%)
Total reports	4,381 (100)
Sex	
Women	2,870 (65.5)
Men	1,265 (28.9)
Not reported or unknown	246 (5.6)
Seriousness*	
Nonserious	4,251 (97.0)
Serious†	130 (3.0)
Type of reporter	
Health care professional	1,661 (37.9)
Manufacturer	1,661 (37.9)
Patient	801 (18.3)
Other	236 (5.4)
Parent/Guardian/Caretaker	22 (0.5)
Age group (yrs)	
<50§	27 (0.6)
50–59	956 (21.8)
60–69	1,467 (33.5)
70–79	988 (22.6)
≥80	251 (5.7)
Not reported or unknown	692 (15.8)
RZV given alone¶	4,167 (95.1)

Abbreviation: VAERS = Vaccine Adverse Event Reporting System.

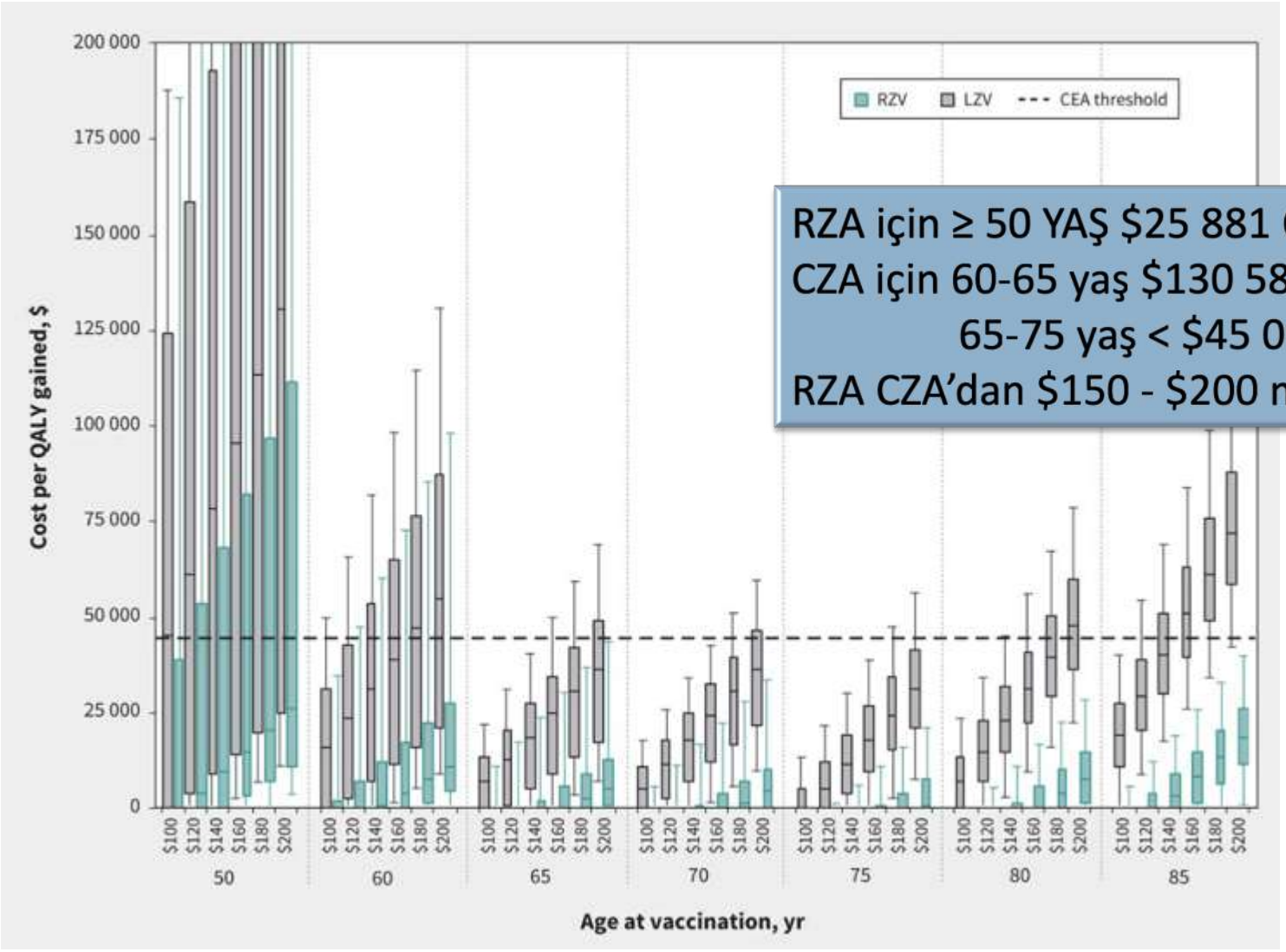
En sık bildirilen YE	
YE	**%**
Ateş	23.6
Enjeksiyon yerinde ağrı	22.5
Enjeksiyon yerinde eritem	20.1
Ağrı	19.5
Titreme	19.3
Baş ağrısı	16.7
Yorgunluk	16.0
Ekstremitede ağrı	15.8
Enjeksiyon yerinde şişlik	13.4
Miyalji	12.1

MMWR 2019; 68(4): 91-94

Effectiveness and cost-effectiveness of vaccination against herpes zoster in Canada: a modelling study

Mélanie Drolet, Zhou Zhou, Chantal Sauvageau, Philippe DeWals, Vladimir Gilca, Rachid Amini, Élodie Bénard and Marc Brisson

CMAJ August 26, 2019 191 (34) E932-E939; DOI: https://doi.org/10.1503/cmaj.190274



RZA için ≥ 50 YAŞ $25 881 QALY
CZA için 60-65 yaş $130 587 QALY
65-75 yaş < $45 000 QALY
RZA CZA'dan $150 - $200 maliyet etkin

Table 1 Recommended Adult Immunization Schedule by Age Group United States, 2019

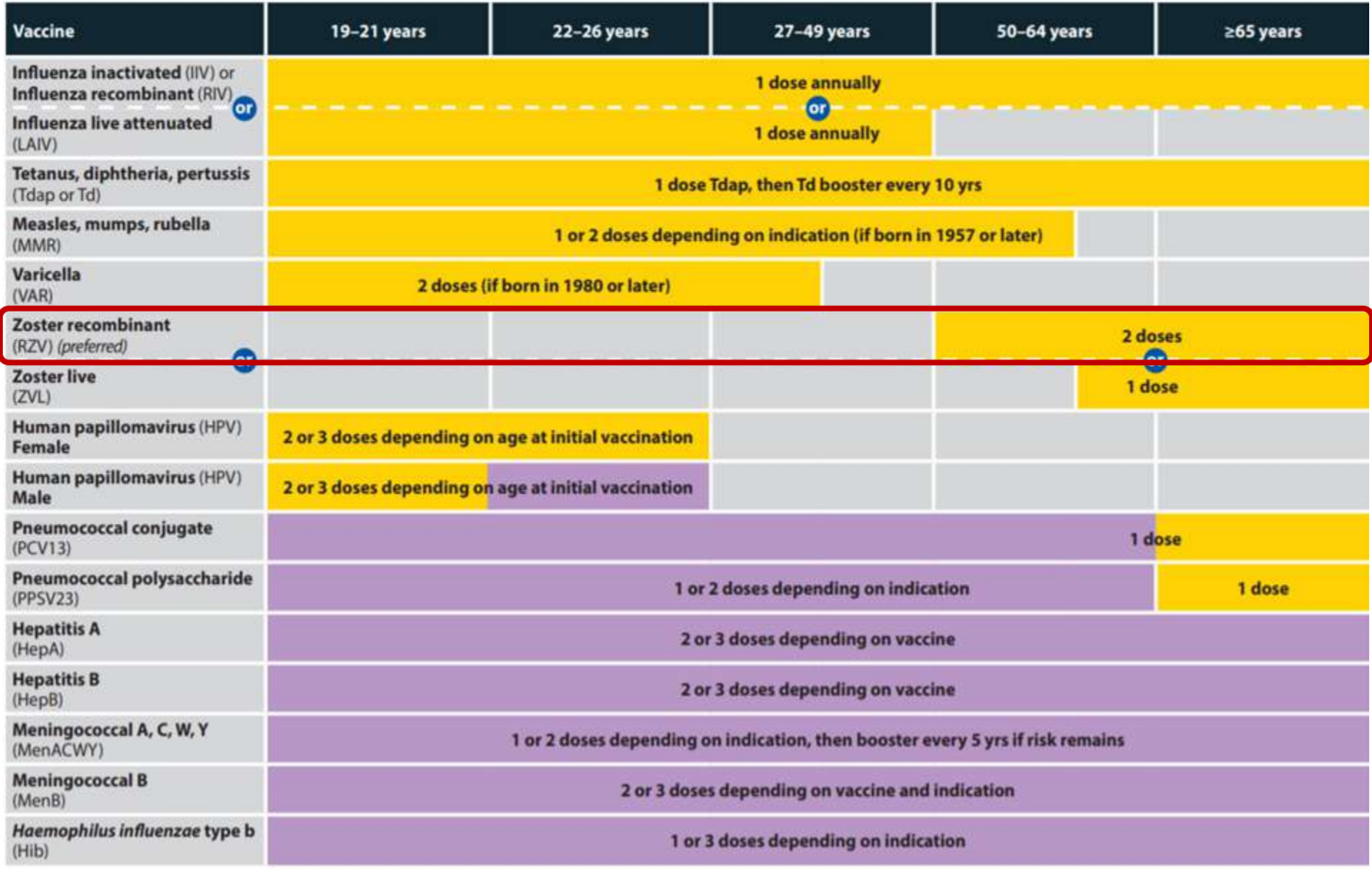


Table 2 Recommended Adult Immunization Schedule by Medical Condition and Other Indications United States, 2019

Vaccine	Pregnancy	Immuno-compromised (excluding HIV infection)	HIV infection CD4 count <200	HIV infection CD4 count ≥200	Asplenia, complement deficiencies	End-stage renal disease, on hemodialysis	Heart or lung disease, alcoholism[1]	Chronic liver disease	Diabetes	Health care personnel[2]	Men who have sex with men
IIV or RIV	1 dose annually										
or										or	
LAIV	CONTRAINDICATED						PRECAUTION			1 dose annually	
Tdap or Td	1 dose Tdap each pregnancy	1 dose Tdap, then Td booster every 10 yrs									
MMR	CONTRAINDICATED	1 or 2 doses depending on indication									
VAR	CONTRAINDICATED	2 doses									
RZV *(preferred)*	DELAY	2 doses at age ≥50 yrs									
or											
ZVL	CONTRAINDICATED	1 dose at age ≥60 yrs									
HPV Female	DELAY	3 doses through age 26 yrs			2 or 3 doses through age 26 yrs						
HPV Male		3 doses through age 26 yrs			2 or 3 doses through age 21 yrs						2 or 3 doses through age 26 yrs
PCV13		1 dose									
PPSV23		1, 2, or 3 doses depending on age and indication									
HepA		2 or 3 doses depending on vaccine									
HepB		2 or 3 doses depending on vaccine									
MenACWY		1 or 2 doses depending on indication, then booster every 5 yrs if risk remains									
MenB	PRECAUTION	2 or 3 doses depending on vaccine and indication									
Hib		3 doses HSCT[3] recipients only			1 dose						

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

Precaution—vaccine might be indicated if benefit of protection outweighs risk of adverse reaction

Delay vaccination until after pregnancy if vaccine is indicated

Contraindicated—vaccine should not be administered because of risk for serious adverse reaction

No recommendation

1. Precaution for LAIV does not apply to alcoholism.


DEPOLAMA
ve
UYGULAMA

ZONA AŞILARI

Canlı zona (herpes zoster) aşısı (CZA)

Bir flakon liyofilize toz
Bir flakon steril çözücü/çözücü içeren kullanıma hazır enjektör

Rekombinan zona aşısı (RZA)

Bir flakon liyofilize glikoprotein E antijeni
Bir flakon adjuvan süspansiyon

ZONA AŞILARINDA UYGULAMA VE DEPOLAMA

Aşı tipi	CZA (canlı atenüe virus)	RZA (rekombinant adjuvanlı, inaktif)
Depolama	**Flakonlar karıştırılmadan önce:** Liyofilize aşı orijinal kutusunda dondurucuda -50°C ve -15°C. Çözücü ayrı olarak buzdolabında 2-8°C veya oda ısısında 20-25°C arasında saklanmalı	**Flakonları(antijen ve adjuvan) karıştırılmadan önce**: 2-8°C 'de buzdolabında saklanmalı
Uygulama	**Flakonlar karıştırıldıktan sonra:** CZA hemen uygulanmalı. Dondurulmamalı veya karıştırılan aşı donma ısısısına maruz bırakılmamalı. **30 dakika** içinde uygulanmayan aşı atılmalı	**Flakonlar karıştırıldıktan sonra:** Hemen uygulanmalı veya **altı saat** içinde kullanılmak şartıyla buzdolabında 2-8°C'de saklanabilir. Altı saat içinde kullanılmazsa atılmalı
Uygulama yolu	SC enjeksiyon, üst kol posterior triseps	IM enjeksiyon, deltoid kas
Doz	Tek doz	2 doz, 2-6 ay arayla
Yaş	≥ 60 yaş	≥ 50 yaş
Kontrendikasyon	Aşıya, jelatin, neomisine hipersensitivite, immünosüpresyon, gebelik	Aşıya hipersensitivite
Maliyet	**268$**, bir doz için	**346$**, iki doz için

Shingrix prescribing information. Rixensart, Belgium: GlaxoSmithKline Biologicals; 2018
Zostavax prescribing information. Whitehouse Station, NJ: Merck & Co., Inc; 2006-2018
CDC, Vaccine Storage and Handling, 2018
Maltz F, DRUG FORECAST, 2019; 4 (7): 406-10

ZONA AŞILARI DEPOLAMA

Canlı zona (herpes zoster) aşısı (CZA)

Rekombinan zona aşısı (RZA)

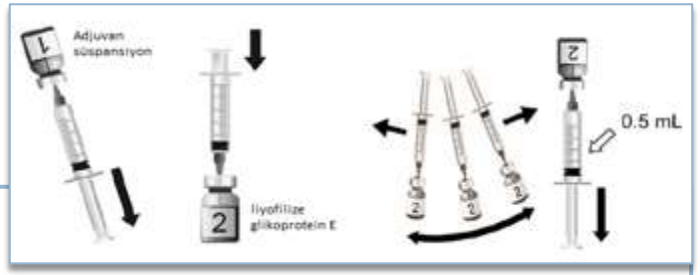
Liyofilize toz

çözücü

AŞI KARIŞIMININ HAZIRLANMASI

CZA:

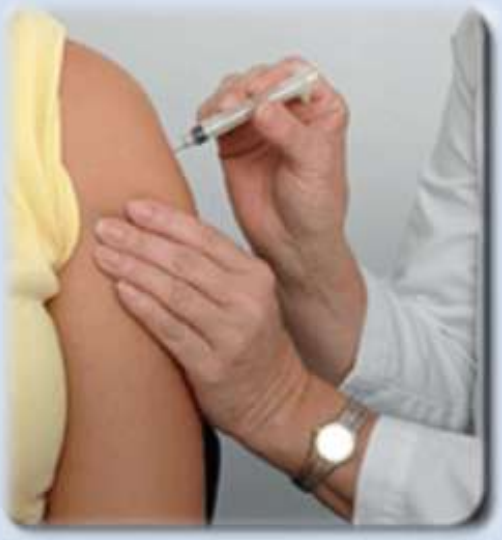
- Kullanım öncesi, çözücü yavaşça liyofilize aşı içeren flakona enjekte edilir.
- Yavaşça sallanır
- Partikül ve/veya renk değişikliği olup olmadığı gözlemlenir. Şayet böyle bir durum mevcutsa aşı atılmalıdır
- Karışım CZA yarı bulanık yarı saydam arası beyaza yakın renkten açık sarıya kadar değişen bir sıvıdır.
- Karışım sonrası aşı **0.65 ml**'dir.



RZA:

- Adjuvan suspansiyon yavaşça liyofilize glikoprotein E antijeni içeren flakona enjekte edilir.
- Nazikçe flakon karıştırılır.
- Partikül ve/veya renk değişikliği olup olmadığı gözlemlenir. Şayet böyle bir durum mevcutsa aşı atılmalıdır.
- Karıştırılmış RZA'nın opak, renksiz soluk kahverenkli olması gereklidir.
- Karışım sonrası aşı **0.5 ml**'dir.

UYGULAMA

RZA	CZA
 İntramüsküler	 Subkutan

UYGULAMADA DİKKAT

- Zona aşısı çocuklarda ve suçiçeği aşısı yerine kullanılmamalıdır.
- Suçiçeği aşısı yanlışlıkla zona yerine 50 yaş ve üstü erişkinlere uygulanırsa, ACIP özel güvenlik endişesine gerek olmadığını belirtiyor, fakat kişi zona aşısı olmuş düşünülmez.
- Ya RZA veya CZA (tercihen RZA) yanlışlıkla yapılan suçiçeği aşı dozundan **en az sekiz hafta sonra** uygulanması gerekir.
- Eğer RZA suçiçeği aşısının yapılmasından sonraki sekiz haftadan önce yapılmışsa tekrar edilmesi gerekmez.

UYGULAMADA DİKKAT

- Herhangi tip zona aşısı diğer endike olan aşılarla aynı zamanda uygulanabilir.
- Her endike aşı ayrı enjektörle ve farklı anatomik bölgeden uygulanması gerekir.
- ACIP önerisi: CZA sonrası uygulanacak bir canlı aşı en az 28 gün sonra veya aynı anda uygulanmalı.

UYGULAMADA DİKKAT

- CZA PPD'ye pozitif cevabı süprese edebilir.
  - Bu süpresyon tüberkülozla enfekte bir kişide yanlış negatif sonuca neden olabilir.
  - TB testine ve CZA'ya gereksinim varsa:
    - PPD ve CZA aynı anda uygulanabilir (tercih edilen)
    - İlk önce PPD verip test sonucu için kişi geldiğinde CZA'nın yapılması
    - Yakında CZA uygulanmışsa, PPD aşıdan **en az dört hafta sonraya** ertelenmelidir.
- RZV ve PPD herhangi bir zamanda verilebilirler.

Küresel Aşılama Stratejileri

Ülke	Öneri yaşı	Önerilen aşı	Ulusal sağlık sistemi tarafından ödeme
Avustralya	70-79 yaş	CZA	Evet
Avusturya	≥ 50 yaş	RZA	Hayır
Kanada	≥ 50 yaş	RZA	Sadece Ontorio eyaleti
Çek Cumhuriyeti	≥ 50 yaş ve spesifik gruplar	CZA	Hayır
Fransa	65-74 yaş, yakalama 75-79	CZA	Evet
Almanya	≥ 60 yaş	RZA	Evet
Yunanistan	≥ 60 yaş	CZA	Evet
İtalya	≥ 65 yaş ve spesifik gruplar	CZA	Evet
Japonya	≥ 50 yaş	VVL[a]	Hayır
Yeni Zelenda	65 yaş, yakalama 66-80 yaş	CZA	Evet
Birleşik Krallık	70-78 yaş	CZA	Evet
Amerika Birleşik Devletleri	≥ 50 yaş	RZA[b]	Hayır

VVL[a] : Canlı suçiçeği aşısı HZ önlemesi için CZA'na benzer (42000-67000 PFU/doz), RZV tercihen ≥ 50 yaş immunkompetan erişkin için öneriliyor; CZA ≥ 60 yaş sağlıklı erişkinde hala kullanılmaktadır

SONUÇ

- Zona erişkin yaş grubunda önemli bir morbidite nedeni ve kaliteli yaşam üzerinde birçok olumsuz etkiye neden olmaktadır.
- Zona aşılaması zona görülme sıklığı ve zona ilişkili komplikasyonları önlemek için bir önceliktir.
- Şu anda iki zona aşısı mevcuttur.
  - CZA 2006 yılında, RZA 2017 yılında FDA tarafından onaylanmıştır.
- Aşılama uygulamalarında ACIP tercihen RZA'yı önermektedir.
- CZA etkinliğinin zamanla azalmasına rağmen, ≥60 yaş immünokompetan yetişkinlerde zonanın önlenmesi için bir seçenek olmaya devam etmektedir.

Gerçek Sevgi Korumaktır

Aşıyla Hem Çocuklar

Hem Erişkinler

Hastalıklardan

Korunabilir!

Teşekkürlerimle...