Solunum Yolu Enfeksiyonları ve Aşıların Başardıkları

İnfluenza Aşılaması

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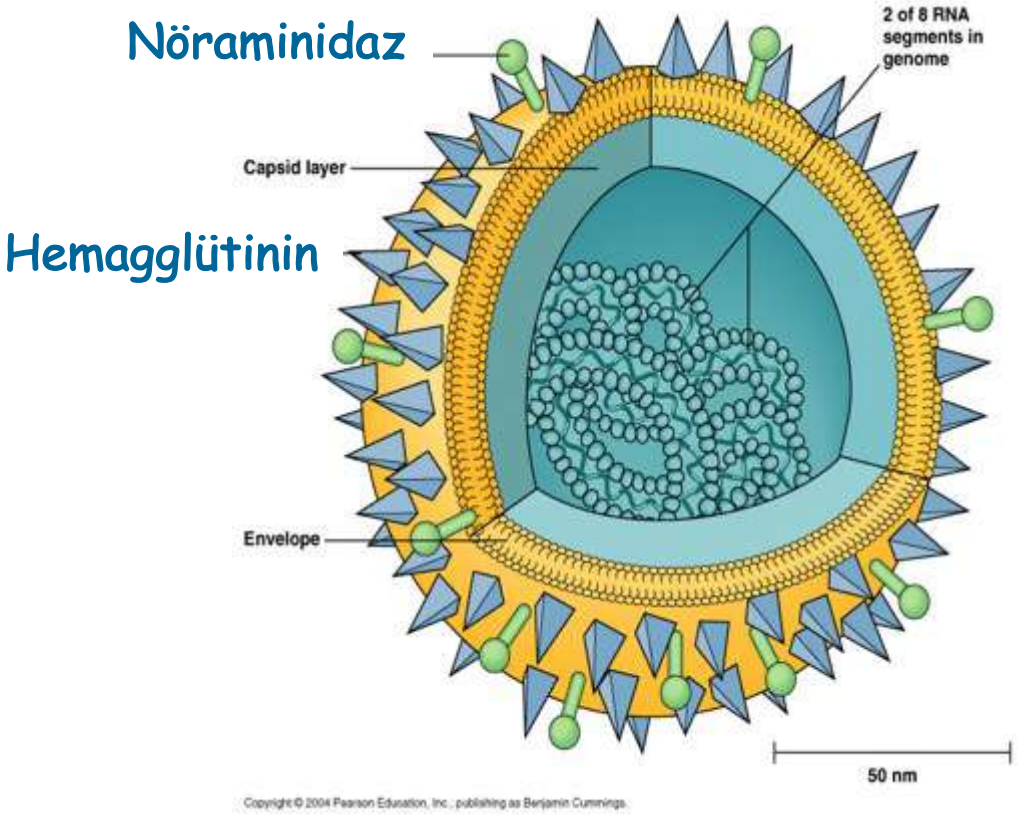
İnfluenza Virüsü

- *Orthomyxoviridae* ailesinden
- Zarflı
- Negatif polariteli
- Tek sarmallı
- RNA virüsü



Virüs Tipleri

Nükleokapsid ve matriks proteinlerine göre üç antijenik tipe ayrılır

- İnfluenza A
- İnfluenza B
- İnfluenza C

	İnfluenza A	Influenza B	Influenza C
Gen segment sayısı	8	8	7
Yapısındaki proteinler	10 M2	11 NB	9 HEF
Konakçı	İnsanlar, domuz, at, kuş, deniz memelileri	Sadece insanlar	İnsanlar, domuzlar
Epidemiyoloji	Antijenik şift ve drift	Sadece antijenik drift	Sadece antijenik drift
Klinik Özellikler	Epidemi-pandemiler Tüm yaş gruplarını etkiler Klinik tablo ağır	Pandemi görülmez Küçük çaplı sporadik salgınlar Genellikle daha hafif klinik tablo Yaşlılar-yüksek riskli kişilerde ağır klinik tablo	Epidemi yapmaz Mevsimsel özelliği olmayan hafif hastalık

Antijenik Değişim

- İnfluenza A virüsünün en önemli özelliklerinden birisi antijenik yapısında oluşan değişimlerdir

Virüsün MİNÖR antijenik değişimleri

↓

ANTİJENİK DRİFT

↓

EPİDEMİ

Virüsün MAJOR antijenik değişimleri

↓

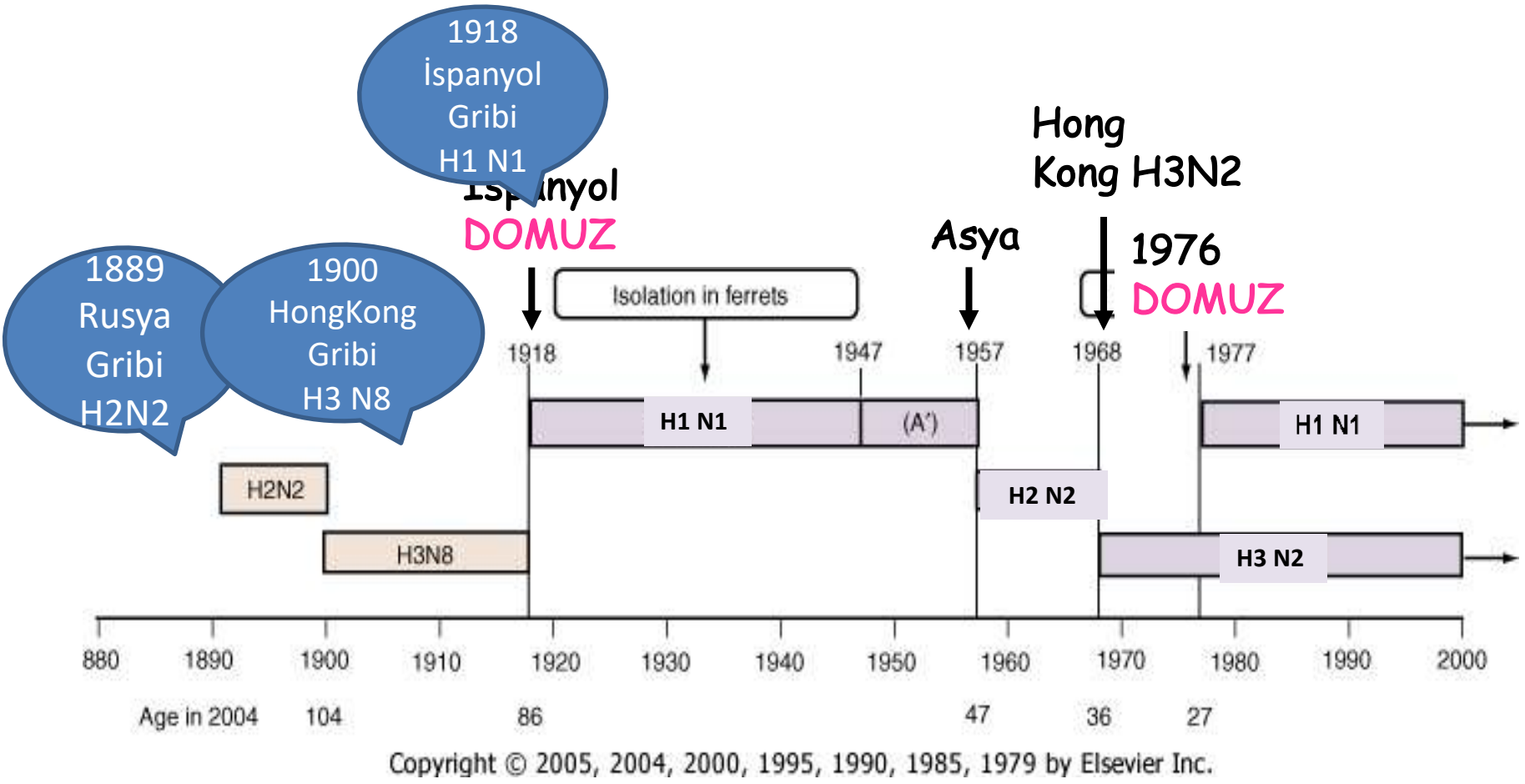
ANTİJENİK ŞİFT

↓

PANDEMİ

İnfluenza pandemisi 500 yıldır bilinmekte

İlk pandemi 16. yüzyılın ilk yarısında, 1510'da



EPIDEMIC INFLUENZA (SPANISH)

This Disease is Highly Communicable.
It May Develop Into a Severe Pneumonia.

There is no medicine which will prevent it.

Keep away from public meetings, theatres and other places where crowds are assembled.

Keep the mouth and nose covered while coughing or sneezing.

When a member of the household becomes ill, place him in a room by himself.

The room should be warm, but well ventilated.

The attendant should put on a mask before entering the room of those ill of the disease.

TO MAKE A MASK

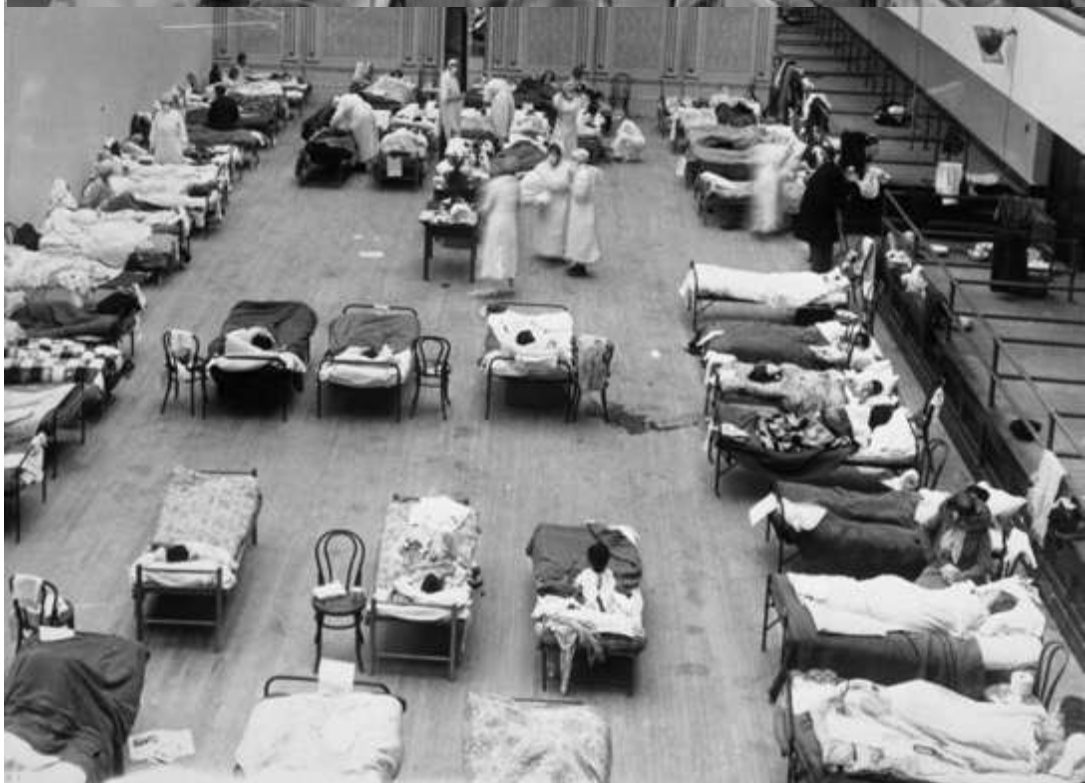
Take a piece of ordinary cheesecloth 6 x 10 inches, fold it to make it 3 x 5 inches. Next fold this to make it 3 x 4 inches. Tie cords about 10 inches long at each corner. Apply over mouth and nose as shown in the picture.

ISSUED BY THE PROVINCIAL BOARD OF HEALTH

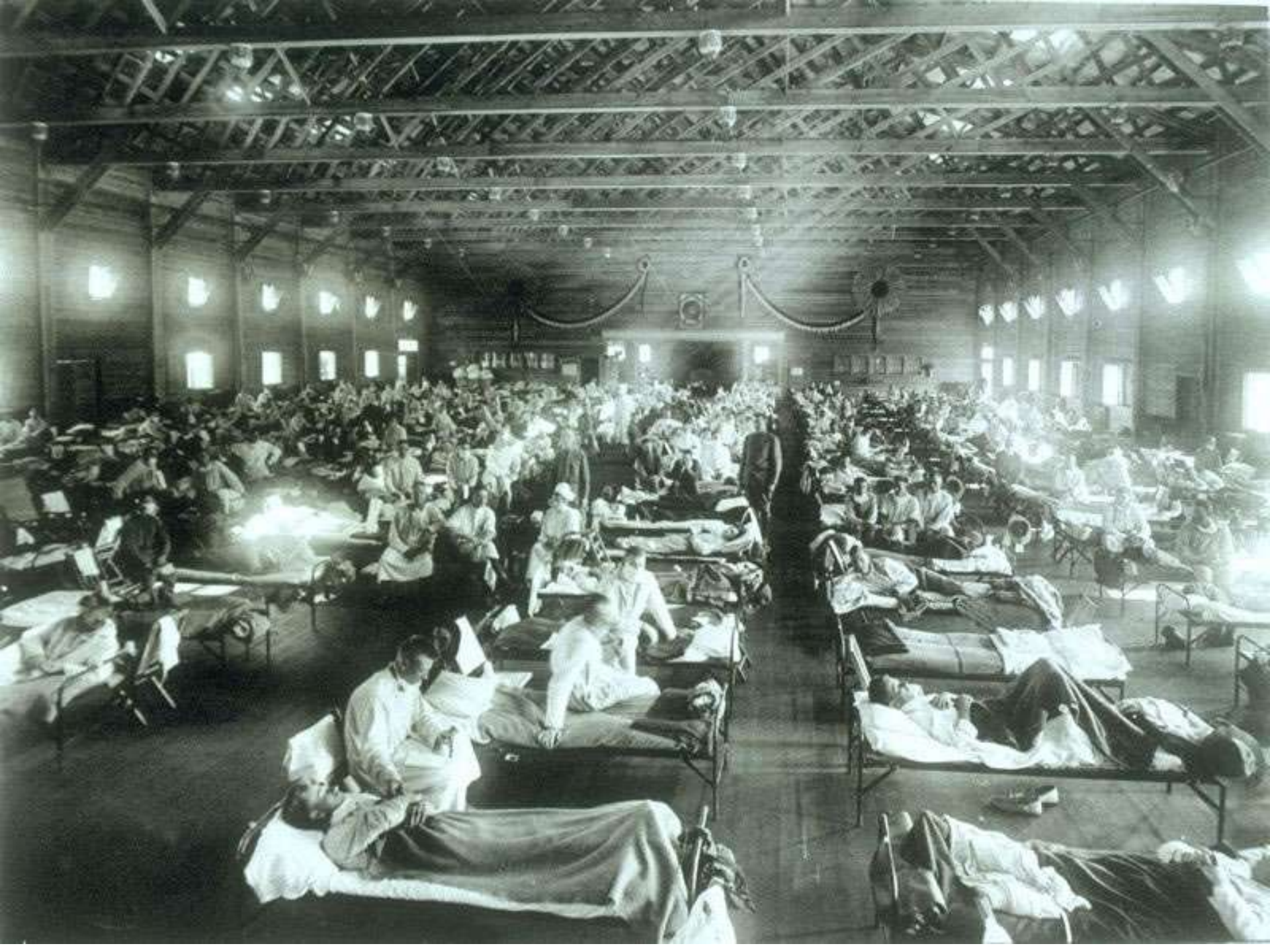
İnfluenza A H1N1 1918-1919

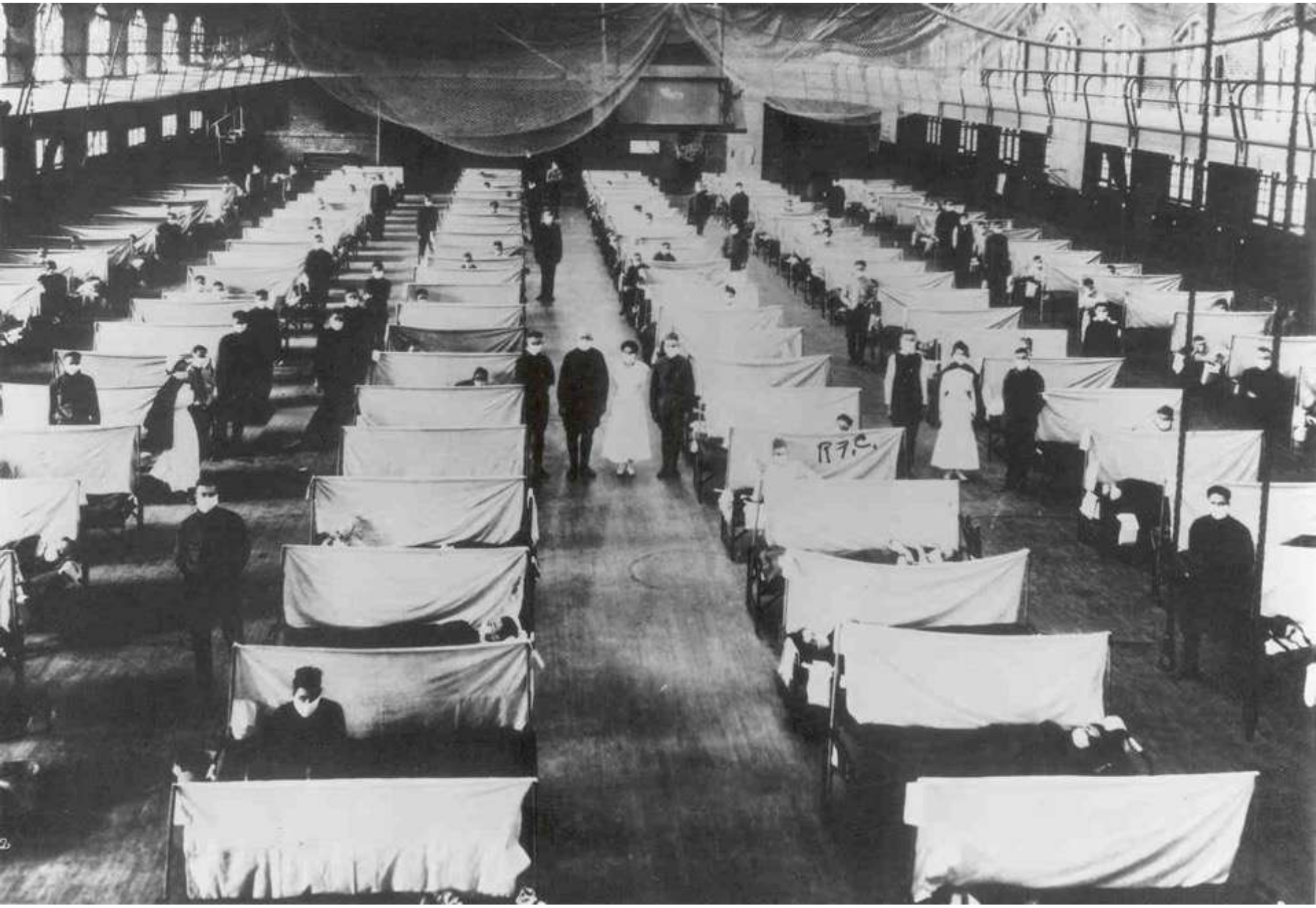
- Dünya nüfusunun 1/3'ü hastalığı klinik geçirmiş
- Vaka-ölüm oranı >%2.5
- Toplam ölüm

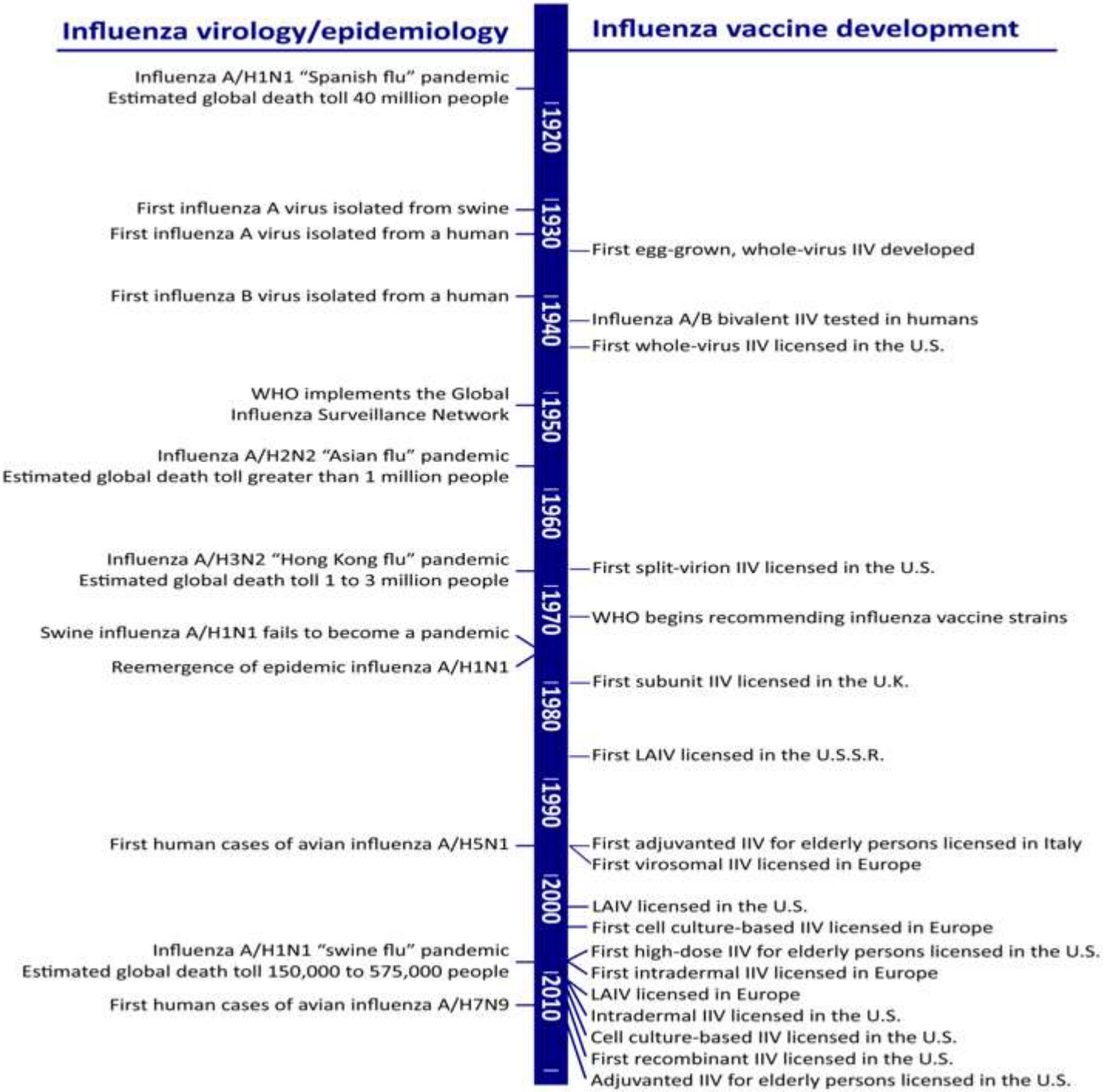
  ~50 milyon




AMERICAN RED CROSS






Influenza virology/epidemiology
Influenza vaccine development
Influenza A/H1N1 "Spanish flu" pandemic
Estimated global death toll 40 million people
1920
First influenza A virus isolated from swine
First influenza A virus isolated from a human
1930
First egg-grown, whole-virus IIV developed
First influenza B virus isolated from a human
1940
Influenza A/B bivalent IIV tested in humans
First whole-virus IIV licensed in the U.S.
WHO implements the Global
Influenza Surveillance Network
1950
Influenza A/H2N2 "Asian flu" pandemic
Estimated global death toll greater than 1 million people
1960
Influenza A/H3N2 "Hong Kong flu" pandemic
Estimated global death toll 1 to 3 million people
First split-virion IIV licensed in the U.S.
1970
WHO begins recommending influenza vaccine strains
Swine influenza A/H1N1 fails to become a pandemic
Reemergence of epidemic influenza A/H1N1
First subunit IIV licensed in the U.K.
1980
First LAIV licensed in the U.S.S.R.
1990
First human cases of avian influenza A/H5N1
First adjuvanted IIV for elderly persons licensed in Italy
First virosomal IIV licensed in Europe
2000
LAIV licensed in the U.S.
First cell culture-based IIV licensed in Europe
Influenza A/H1N1 "swine flu" pandemic
Estimated global death toll 150,000 to 575,000 people
First high-dose IIV for elderly persons licensed in the U.S.
First intradermal IIV licensed in Europe
LAIV licensed in Europe
First human cases of avian influenza A/H7N9
2010
Intradermal IIV licensed in the U.S.
Cell culture-based IIV licensed in the U.S.
First recombinant IIV licensed in the U.S.
Adjuvanted IIV for elderly persons licensed in the U.S.

iNFLUENZA

- Her yıl 1 milyar yeni vaka
- 3-5 milyon ağır vaka
- 290 000-650 000 influenza ilişkili ölüm

- Mevsimsel influenzanın önlenmesi
- Hayvanlardan insanlara influenza bulaşının önlenmesi
- Bir sonraki pandemiye hazırlık

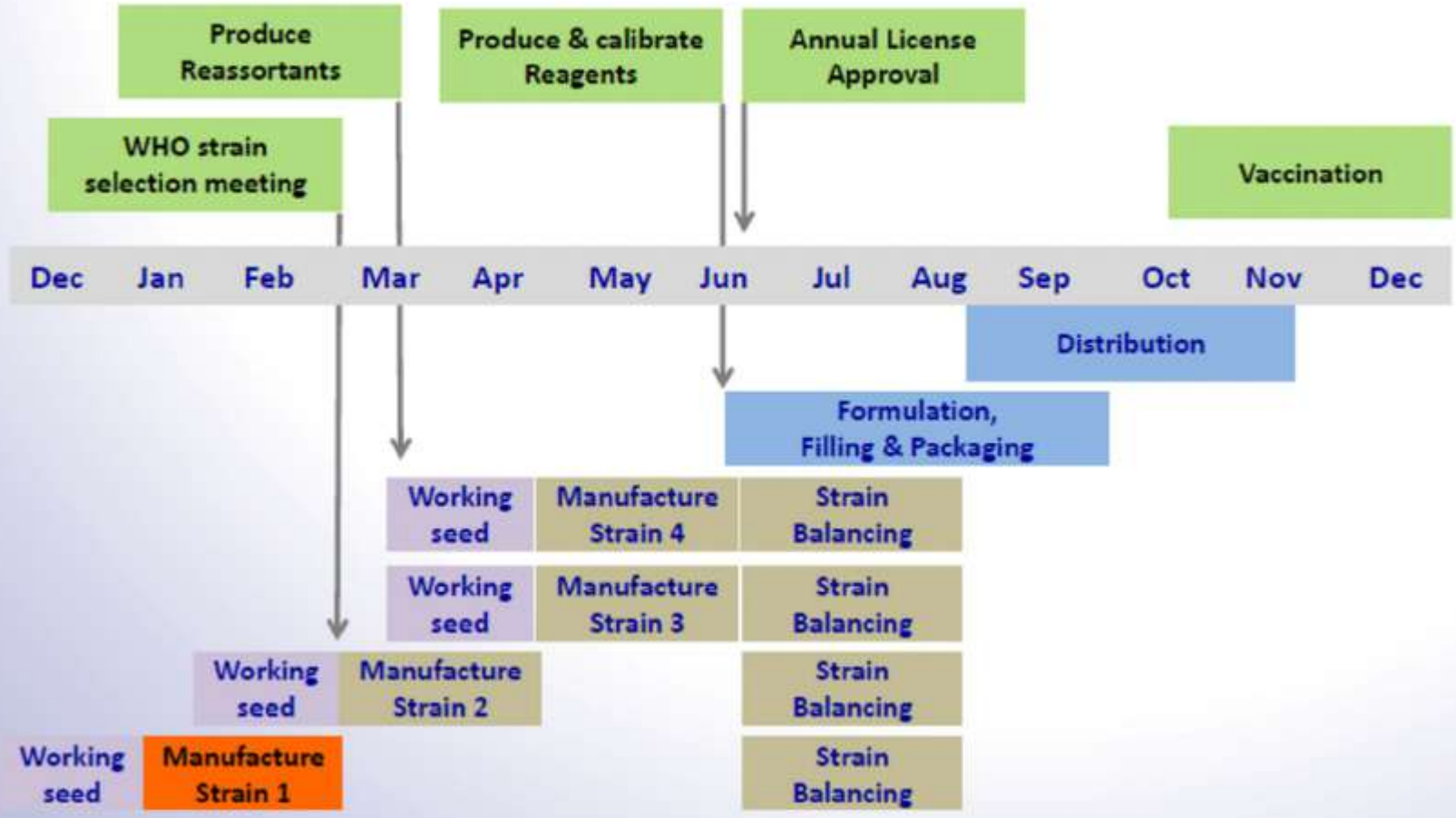
İnfluenza Aşısı

- 1977 yılından günümüze, influenza aşıları, A/H3N2, A/H1N1 ve B virüslerinin en güncel antijenik varyantlarını içerir
- Aşının antijenik içeriği her yıl yenilenir

WHO Global Influenza Surveillance and Response System

- Şubat sonu Mart Başı Kuzey yarıküre aşı içeriğinin belirlenmesi → Dağıtım Eylül ayı başında
- Eylül ayı Güney yarıküre aşı içeriğinin belirlenmesi → Dağıtım Mart ayı

Influenza Manufacturing Cycle



Aşı içeriği

Kuzey yarıküre 2019-2020 sezonu için aşı içeriği; **21 Şubat 2019 (*21 Mart 2019'da güncellendi*)**

- A/Brisbane/02/2018 (H1N1) pdm09-like virus;
- A/Kansas/14/2017 (H3N2)-like virus;
- B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage)
- B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage);

Güney yarıküre 2019 sezonu (Nisan-Eylül) için aşı içeriği;

- A/Michigan/45/2015 (H1N1) pdm09-like virus
- A/Switzerland/8060/2017 (H3N2)-like virus;
- B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage)
- B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage);

İnfluenza Aşısı

- Trivalan influenza aşısı: İnfluenza A (H1N1), influenza A (H3N2), influenza B
- Kuadrivalan influenza aşısı: 2 İnfluenza A ve 2 İnfluenza B
- İnaktif influenza aşısı (Tüm virüs aşısı, split virüs aşısı: tüm virüs bir deterjan ile muamele edilir), subunit aşılar (HA ve NA komponentleri diğer virüs antijenlerinden ayrılır)
- İnaktif aşılar:
  - Yüksek doz formulasyonu
  - Adjuvan formulasyonu
- Canlı attenüe aşı
- Her aşı tipi için üretici firma kendi güvenlik profilini ve yaş gurubu endikasyonlarını belirler.

Kuadrivalan influenza aşısı:

- DSÖ 2013-2014 sezonunda dördüncü suşun aşıya eklenmesini önerdi
- Aynı sezonda, dolaşımda farklı iki influenza B virüsü : Yamagata ve Victoria.
- **İkisi arasında çapraz koruma sınırlı**
- ABD'de 2001-2011 sezonlarının %50'sinde Avrupa'da 2003-2011 sezonlarının %50'sinde

→ Dolaşımdaki influenza B virüsleri aşı suşundan farklı

Hum Vaccin Immunother 2016;12:993-1002 J Prev Med Hyg 2016; 57: E28-E33

TABLE 1. Influenza vaccines — United States, 2019–20 influenza season*

Trade name (Manufacturer)	Presentation	Age indication	HA (IIVs and RIV4) or virus count (LAIV4) for each vaccine virus (per dose)	Route	Mercury (from thimerosal) (μg/0.5mL)
IIV4—Standard Dose—Egg based†					
Afluria Quadrivalent (Seqirus)	0.25-mL PFS§	6 through 35 mos	7.5 μg/0.25 mL§	IM¶	—
	0.5-mL PFS§	≥3 yrs	15 μg/0.5 mL§		—
	5.0-mL MDV§	≥6 mos (needle/syringe) 18 through 64 yrs (jet injector)			24.5
Fluarix Quadrivalent (GlaxoSmithKline)	0.5-mL PFS	≥6 mos	15 μg/0.5 mL	IM¶	—
FluLaval Quadrivalent (GlaxoSmithKline)	0.5-mL PFS	≥6 mos	15 μg/0.5 mL	IM¶	—
	5.0-mL MDV	≥6 mos			<25
Fluzone Quadrivalent (Sanofi Pasteur)	0.25-mL PFS**	6 through 35 mos	7.5 μg/0.25 mL**	IM¶	—
	0.5-mL PFS**	≥6 mos	15 μg/0.5 mL**		—
	0.5-mL SDV**	≥6 mos			—
	5.0-mL MDV**	≥6 mos			25
IIV4—Standard Dose—Cell culture based (ccIIV4)					
Flucelvax Quadrivalent (Seqirus)	0.5-mL PFS	≥4 yrs	15 μg/0.5 mL	IM¶	—
	5.0-mL MDV	≥4 yrs			25
IIV3—High Dose—Egg based† (HD-IIV3)					
Fluzone High-Dose (Sanofi Pasteur)	0.5-mL PFS	≥65 yrs	60 μg/0.5 mL	IM¶	—
IIV3—Standard Dose—Egg based† with MF59 adjuvant (aIIV3)					
Fluad (Seqirus)	0.5-mL PFS	≥65 yrs	15 μg/0.5 mL	IM¶	—
RIV4—Recombinant HA					
Flublok Quadrivalent (Sanofi Pasteur)	0.5-mL PFS	≥18 yrs	45 μg/0.5 mL	IM¶	—
LAIV4—Egg based†					
FluMist Quadrivalent (AstraZeneca)	0.2-mL prefilled single-use intranasal sprayer	2 through 49 yrs	$10^{6.5–7.5}$ fluorescent focus units/0.2 mL	NAS	—

Abbreviations: ACIP = Advisory Committee on Immunization Practices; FDA = Food and Drug Administration; HA = hemagglutinin; IIV3 = inactivated influenza vaccine

VAXIGRIP TETRA, 0,5 mL IM/SC Enjeksiyon İçin Süspansiyon İçeren Kullanıma Hazır Enjektör Kuadrivalan Grip Aşısı (Split Virion, İnaktif)

2019/2020 SUŞLARI

Kas içine veya deri altına uygulanır.

Steril

Etkin maddeler:

Aşağıdaki suşları* içeren (inaktif, split) influenza virüsüdür:

A/Brisbane/02/2018 (H1N1)pdm09 - (A/Brisbane/02/2018, IVR-190) benzeri suş. . . . . 15 mikrogram HA**

A/Kansas/14/2017 (H3N2) - (A/Kansas/14/2017, NYMC X-327) benzeri suş. . . . . 15 mikrogram HA**

B/Colorado/06/2017 - (B/Maryland/15/2016, NYMC BX-69A) benzeri suş . . . . . 15 mikrogram HA**

B/Phuket/3073/2013 - (B/Phuket/3073/2013, yabanıl tip) benzeri suş. . . . . 15 mikrogram HA**

0,5 ml doz başına

* sağlıklı tavuk sürülerinden elde edilen fertilize tavuk yumurtalarında üretilmiştir

** hemaglutinin

Bu aşı, 2019/2020 sezonuna ilişkin Avrupa Birliği (AB) kararına ve DSÖ (Dünya Sağlık Örgütü) önerilerine (Kuzey Yarımküre) uygundur.

- ***Yardımcı maddeler***: sodyum klorür, potasyum klorür, disodyum fosfat dihidrat,

* yumurta (ovalbumin, tavuk p
gibi çok küçük miktarlarda
varsa,
- Sizde ya da çocuğunuzda yük
bir hastalık varsa, siz ya da
ertelenmelidir.

VAXIGRIP TETRA'yı aşağıdaki
Eğer sizde veya çocuğunuzda aş
bilgilendiriniz:
- Zayıf bağışıklık yanıtı (bağ
etkileyen ilaçların kullanımı),
- Kanama sorunu ya da kolayc

VAXIGRIP TETRA kullanmadan önc
Doktorunuz, size veya çocuğu
gerektiğine karar verecektir.
İğnenin kullanıldığı herhangi b
bayılma meydana gelebilir (ço
sizde ya da çocuğunuzda dah
ortaya çıkmış olması halinde,
Tüm aşılarda olduğu gibi, VAXI
Eğer grip aşısının uygulam
herhangi bir nedenden dol
Çünkü kısa süre önce aşı
sonuçları gözlenmiştir.

VAXIGRIP TETRA'nın yiye
Yiyecek ve içeceklerle etkile

Yan Etki

- İntramusküler Enjeksiyon (TIV):
  - Lokal reaksiyonlar:
    - ağrı %20-50
    - kızarıklık %10-13
    - şişlik %6-8
  - Miyalji: %18-30
  - Başağrısı: %14-30
  - Kırgınlık: %14-22
  - Ateş: %2-3
  - Alerjik reaksiyonlar:milyonda<1
  - Guillain Barre Sendromu: milyonda 1

MMWR 2010; 59(RR-8)

- İntradermal (ID)
  - Lokal reaksiyonlar:
    - kızarıklık %76
    - şişlik %57
    - ağrı %51
    - kaşıntı %47
  - Sistemik yan etkiler TIV'e benzer
- Nazal Sprey (LAIV)
    - öksürük %14
    - Burun akıntısı %45
    - Boğaz ağrısı %28
    - Titreme %9

Belshe RB et al. Clin Infect Dis 2004;39:920--7.

İnfluenza Aşı Kontrendikasyonları

Aşı	Kontrendikasyon	Dikkat edilmesi gereken durumlar
Inaktive İnfluenza aşısı (IIV)	Aşı komponentlerinden birine karşı ciddi allerjik reaksiyon öyküsü veya daha önce influenza aşılaması sırasında ciddi allerjik reaksiyon gelişimi	Orta derece/ şiddetli akut hastalığı olanlara yapılması ertelenmeli İnfluenza aşısından sonra 6 hafta içerisinde Guillain-Barré sendromu gelişimi
Rekombinant influenza aşısı	Aşı komponentlerinden birine karşı ciddi allerjik reaksiyon öyküsü	
Canlı attenüe influenza aşısı (LAIV)	Aşı komponentlerinden birine karşı ciddi allerjik reaksiyon öyküsü , Astım (2-4 yaş), İmmün yetmezlik, Aspirin veya salisilat tedavisi alan çocuk ve adolesanlar Gebeler	Orta derece/ şiddetli akut hastalığı olanlara yapılması ertelenmeli İnfluenza aşısından sonra 6 hafta içerisinde Guillain-Barré sendromu gelişimi Kronik Kalp Hastalığı, Diyabet, Hemoglobinopatiler, >5 yaş astım,

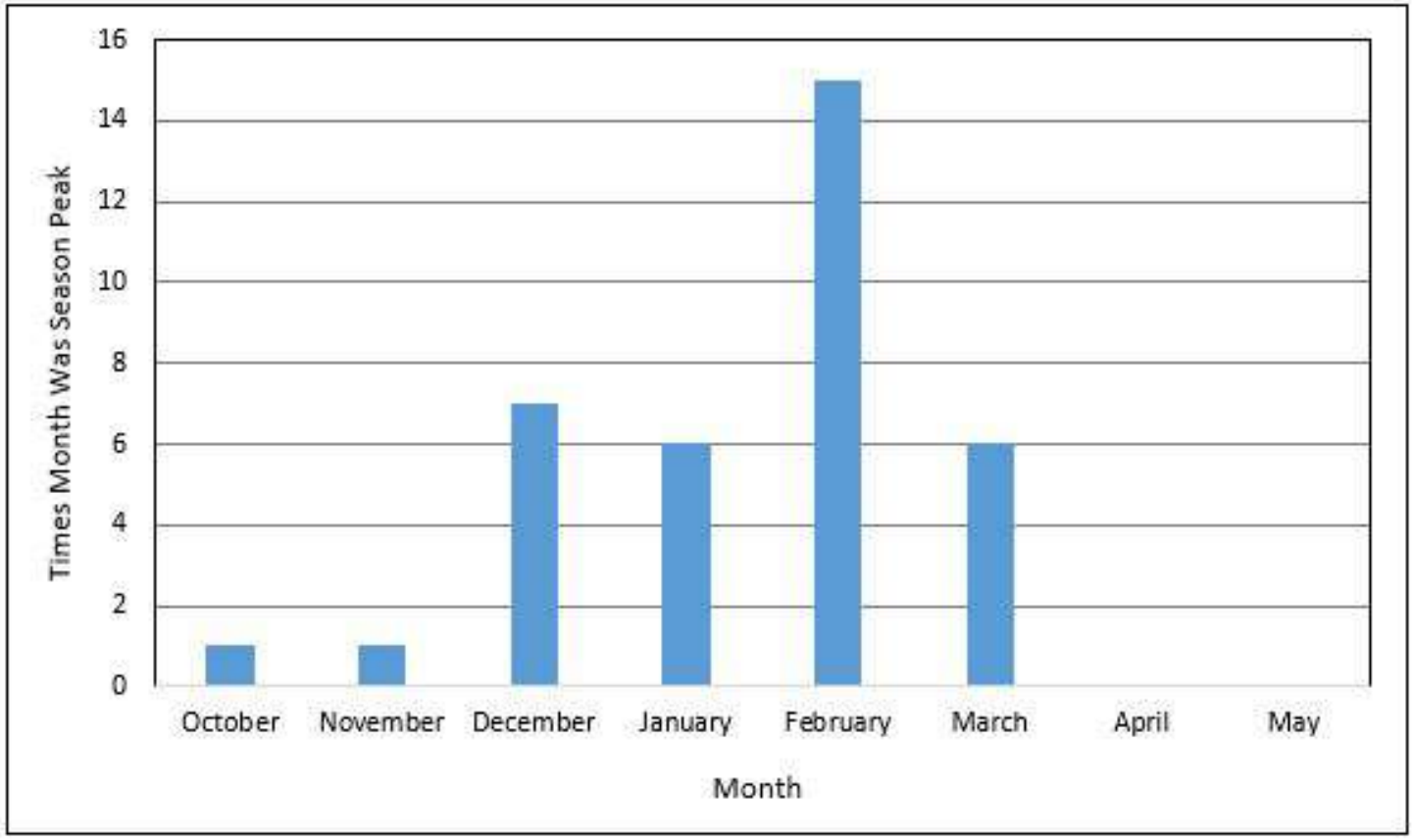
Aşılama Zamanı

- İnfluenza aktivitesi başlamadan önce
- Tercihen Ekim sonuna kadar yapılmalı
- İnfluenza aktivitesine bağlı olarak virüs dolaştığı sürece aşılamaya devam edilebilir
- Erişkinde koruyucu antikor yanıtı aşılamadan iki hafta sonra ortaya çıkmakta

Groshskopf LA. MMWR Recomm Rep 2016; 65:1

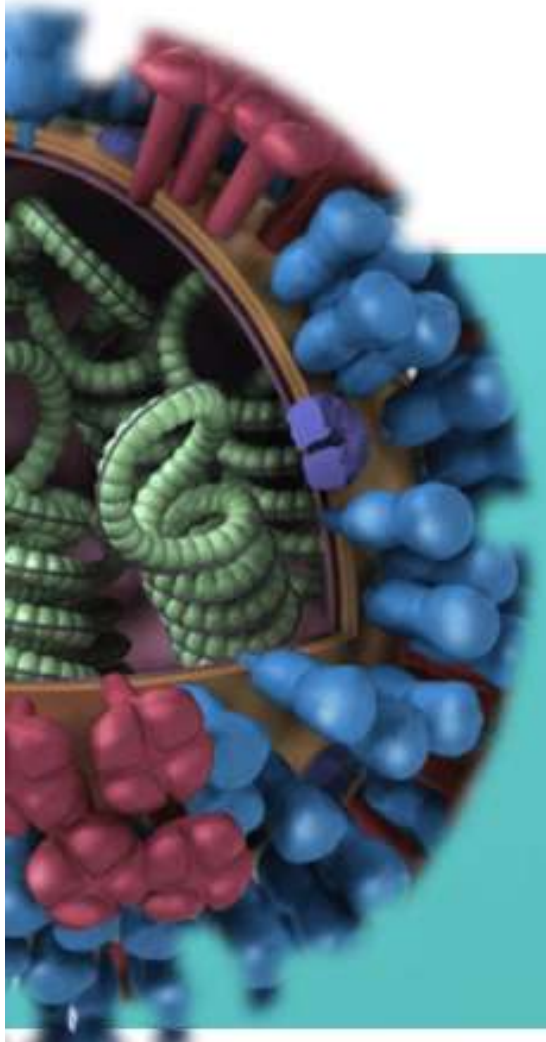
Aylara göre influenza aktivitesi

1982-1983 ile 2017-2018 arası



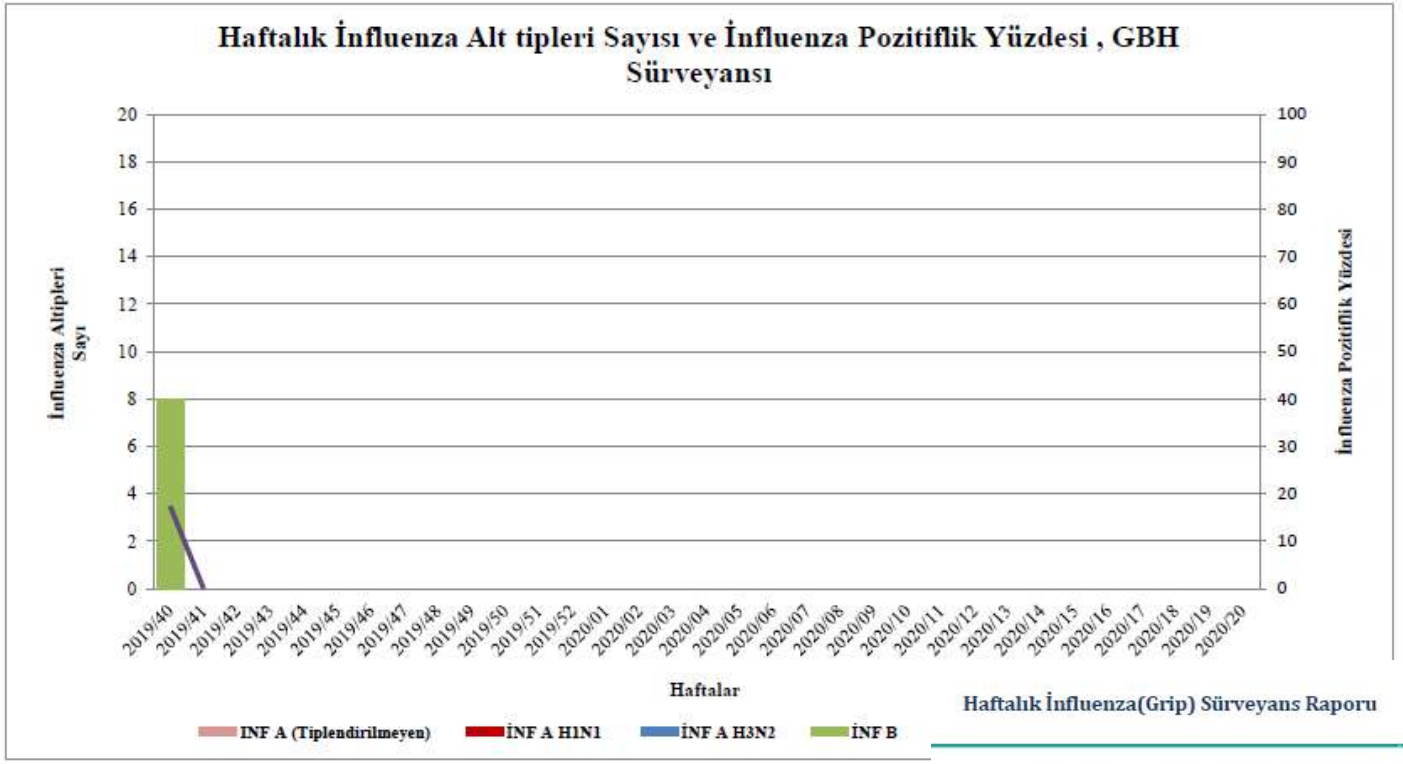
T.C.
SAĞLIK BAKANLIĞI
Halk Sağlığı Genel Müdürlüğü
Bulaşıcı Hastalıklar Dairesi Başkanlığı

Halk Sağlığı Genel
Müdürlüğü



Haftalık İnfluenza (Grip) Sürveyans Raporu

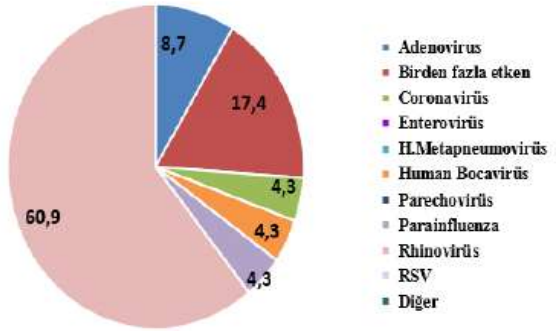
2019/41. Hafta (7– 13 Ekim 2019)



Grafik-2: Ülkemizde Sentinel Grip Benzeri Hastalık Sürveyansı kapsamında haftalık tespit edilen İ yüzdesi.

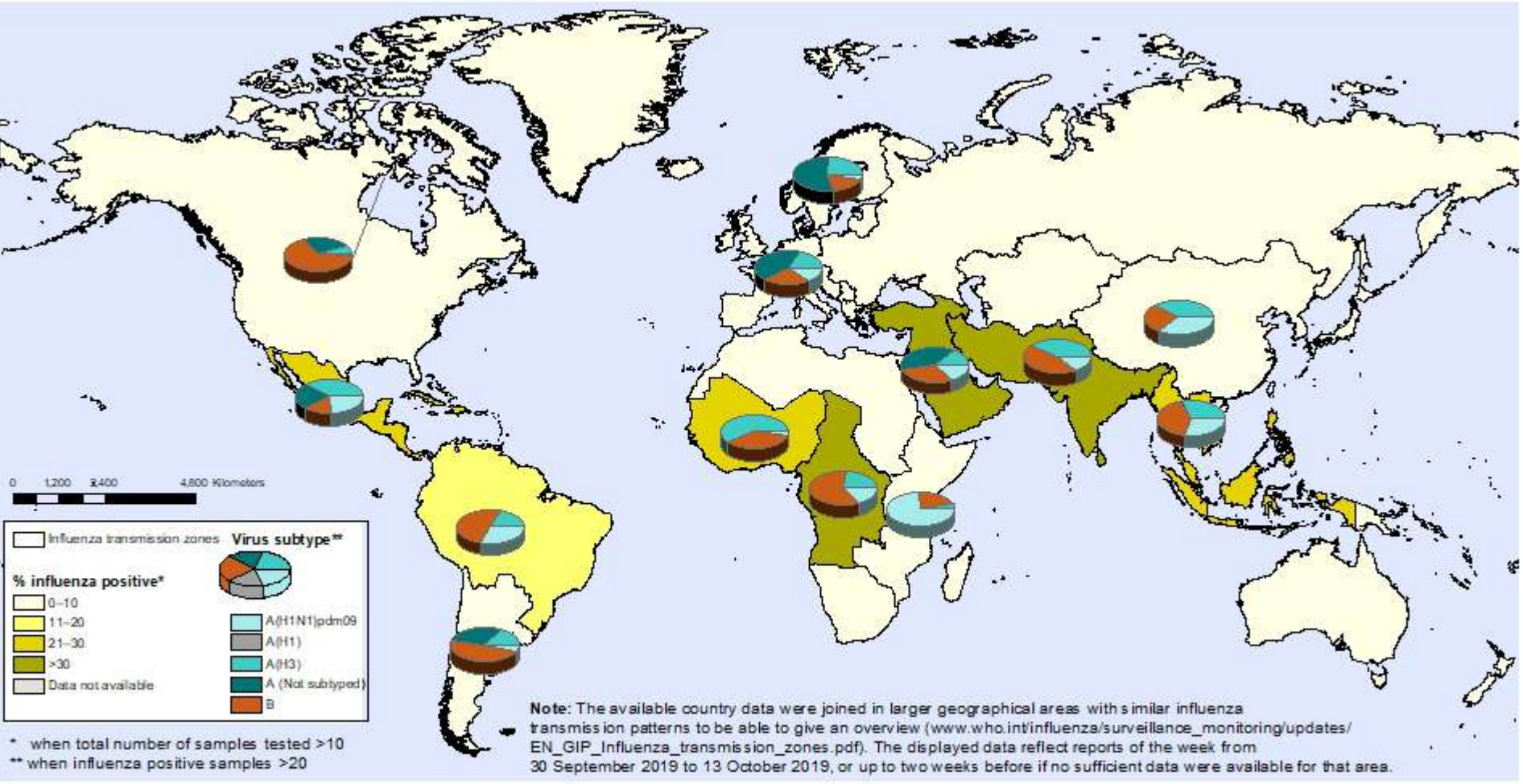
Haftalık İnfluenza(Grip) Sürveyans Raporu
41. Hafta (7– 13 Ekim 2019)

Diğer Solunum Yolu Virüsleri (DSYV) Pozitif SARI Numunelerinin DSYV'ü Alt Tipi Yüzde Dağılımı, 2019-2020 İnfluenza Sezonu.



Percentage of respiratory specimens that tested positive for influenza
By influenza transmission zone

Status as of 25 October 2019



Note: The available country data were joined in larger geographical areas with similar influenza transmission patterns to be able to give an overview (www.who.int/influenza/surveillance_monitoring/updates/EN_GIP_Influenza_transmission_zones.pdf). The displayed data reflect reports of the week from 30 September 2019 to 13 October 2019, or up to two weeks before if no sufficient data were available for that area.

* when total number of samples tested >10
** when influenza positive samples >20

Data Source:
Global Influenza Surveillance and Response System (GISRS),
FluNet (www.who.int/flunet)

World Health Organization

Ciddi İnfluenza İnfeksiyonu

- **Kimler risk altında?**
- Gebeler
- Çocuklar <5 yaş
- >65 yaş
- Kronik hastalığı olanlar (HIV/AIDS, astım, kalp hastalıkları, akciğer hastalıkları, diabet)
- Maruziyet artışı (sağlık çalışanları)

İnfluenza Aşıs

- **Yüksek derecede ö**
  - **Gebeler**
- Öncelik:
  - 6-5
  - >
  - Kron pireyler
  - Sağlık ç

6 Aydan Büyük Herkese

Gebeler

- İmmün yanıtta değişiklik
- Kardiyovasküler, pulmoner fonksiyonlarda değişiklik
- Ciddi influenza
- Komplikasyon sık
- Spontan fetüs kaybı
- Preterm doğum
- İnaktive aşı önerilir

- Maternal antikorlar transplasental geçer, doğum sonrası bebeği birkaç ay korur
- Yeni doğanın henüz aşılanamadığı dönemde korunmasını sağlar
- Gebelerin aşılanması;
  - Yeni doğanda laboratuvar ile doğrulanmış influenza riskini azaltır.
- Yan etki insidansında artış yok

Loubet P. Expert Rev Vaccines. 2016 ;15:1507-1518.
Groshskopf LA. MMWR Recomm Rep 2016; 65:1

Effectiveness of Seasonal Trivalent Influenza Vaccine for Preventing Influenza Virus Illness Among Pregnant Women: A Population-Based Case-Control Study During the 2010–2011 and 2011–2012 Influenza Seasons

**Mark G. Thompson,[1] De-Kun Li,[2,3] Pat Shifflett,[4] Leslie Z. Sokolow,[1,5] Jea
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Sarah Ball,[4] Jennifer L. Williams,[7] Stephanie A. Irving,[6] Davi
Influenza Project Workgroup**

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Oakland, California; [3]Department of Health Research
Massachusetts; [5]Battelle Memorial Institute
[7]National Center on Birth Defects and D

Background. Alt ended for all pregnant wom assessed laboratory-confirme

M -2011 and 2011–2012) among d and Oregon. We compared the pro- nscription polymerase chain reaction) with ory illness (ARI) who tested negative for influen- d trimester).

ated during the study season compared to 58% and 63% vacci- atched ARI-negative controls, respectively. The adjusted VE of the A and B was 44% (95% confidence interval [CI], 5%–67%) using the (95% CI, 24%–72%) using the ARI-negative controls. Receipt of the prior s an effect similar to receipt of the current season's vaccine. As such, vaccination in eit had statistically similar adjusted VE using influenza-negative controls (VE point estimates rang and ARI-negative controls (48%–76%).

Con ns. Influenza vaccination reduced the risk of ARI associated with laboratory-confirmed influenza among pregnant women by about one-half, similar to VE observed among all adults during these seasons.

Keywords. influenza; influenza vaccines; vaccine effectiveness; pregnancy; acute respiratory illness.

Received 30 August 2013; accepted 4 November 2013; electronically published 26 November 2013.

Correspondence: Mark G. Thompson, PhD, Influenza Division, Centers for Disease Control and Prevention, 1600 Clifton Rd NE, MS A-32, Atlanta, GA 30333 (isq8@cdc.gov).

Clinical Infectious Diseases 2014;58(4):449–57

DOI: 10.1093/cid/cit750

Because pregnant women appear to be vulnerable to severe disease and secondary complications from influenza [1], vaccination with trivalent inactivated influenza vaccine (TIV) is recommended for all pregnant women in the United States [2]. TIV coverage in this population has risen to about 50% in the United States [3], but no vaccine effectiveness (VE) studies of TIV among pregnant women have assessed laboratory-confirmed

İnfluenza aşısı gebelerde grip ilişkili akut solunum sistemi infeksiyonunu %50 azaltmakta

Clinical Infectious Diseases

MAJOR ARTICLE

Influenza Vaccine Effectiveness in Preventing Influenza-associated Hospitalizations During Pregnancy: A Multi-country Retrospective Test Negative Design Study, 2010–2016

Mark G. Thompson,[1] Jeffrey C. Kwong,[2,3,4,5,6] Annette K. Regan,[7,8] Mark A. Katz,[9,10,11] Steven J. Drews,[12,13] Eduardo Azziz-Baumgartner,[1] Nicola P. Klein,[14] Hannah Chung,[7] Paul V. Effler,[15] Becca S. Feldman,[9] Kimberley Simmonds,[16,17] Brandy E. Wyant,[18] Fatimah S. Dawood,[1] Michael L. Jackson,[19] Deshayne B. Fell,[2,20,21] Avram Levy,[22] Noam Barda,[9] Lawrence W. Svenson,[17,23,24,25] Rebecca V. Fink,[18] Sarah W. Ball,[18] and Allison Naleway[26]; for the PREVENT Workgroup[a]

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İnfluenza aşısı gebelerde influenzaya bağlı hastaneye yatışı %40 azaltmakta

Background. To date, no study has examined influenza vaccine effectiveness (IVE) against laboratory-confirmed influenza-associated hospitalizations during pregnancy.

Methods. The Pregnancy Influenza Vaccine Effectiveness Network (PREVENT) consisted of public health or healthcare systems with integrated laboratory, medical, and vaccination records in Australia, Canada (Alberta and Ontario), Israel, and the United States (California, Oregon, and Washington). Sites identified pregnant women aged 18 through 50 years whose pregnancies overlapped with local influenza seasons from 2010 through 2016. Administrative data were used to identify hospitalizations with acute respiratory or febrile illness (ARFI) and clinician-ordered real-time reverse transcription polymerase chain reaction (rRT-PCR) testing for influenza viruses. Overall IVE was estimated using the test-negative design and adjusting for site, season, season timing, and high-risk medical conditions.

Results. Among 19450 hospitalizations with an ARFI discharge diagnosis (across 25 site-specific study seasons), only 1030 (6%) of the pregnant women were tested for influenza viruses by rRT-PCR. Approximately half of these women had pneumonia or influenza discharge diagnoses (54%). Influenza A or B virus infections were detected in 598/1030 (58%) of the ARFI hospitalizations with influenza testing. Across sites and seasons, 13% of rRT-PCR-confirmed influenza-positive pregnant women were vaccinated compared with 22% of influenza-negative pregnant women; the adjusted overall IVE was 40% (95% confidence interval = 12%–59%) against influenza-associated hospitalization during pregnancy.

Conclusion. Between 2010 and 2016, influenza vaccines offered moderate protection against laboratory-confirmed influenza-associated hospitalizations during pregnancy, which may further inform the benefits of maternal influenza vaccination programs.

Keywords. pregnant women; pregnancy; influenza; vaccine effectiveness; hospitalization.

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REVIEW

Effectiveness of influenza vaccines in preventing severe influenza illness among adults: A systematic review and meta-analysis of test-negative design case-control studies

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[c] *Université Libre de Bruxelles, School of Public Health, Brussels, Belgium*
[d] *US Centers for Disease Control and Prevention (CDC), Influenza Division, Atlanta, USA*
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KEYWORDS
Influenza;
Vaccine effectiveness;
Hospitalization;
Adults;
Systematic review;
Meta-analysis

Summary *Objectives:* Summary evidence of influenza vaccine effectiveness (IVE) against hospitalized influenza is lacking. We conducted a meta-analysis of studies reporting IVE against laboratory-confirmed hospitalized influenza among adults.
Methods: We searched Pubmed (January 2009 to November 2016) for studies that used test-negative design (TND) to enrol patients hospitalized with influenza-associated conditions. Two independent authors selected relevant articles. We calculated pooled IVE against any and (sub)type specific influenza among all adults, and stratified by age group (18–64 and 65 years and above) using random-effects models.
Results: We identified 3411 publications and 30 met our inclusion criteria. Between 2010–11 and 2014–15, the pooled seasonal IVE was 41% (95%CI:34;48) for any influenza (51% (95%CI:44;58) among people aged 18–64y and 37% (95%CI:30;44) among ≥65 years). IVE was 48% (95%CI:37;59),

- **İnfluenza aşısı çocuklarda, erişkinlerde ve yaşlılarda influenza ile ilişkili hastaneye yatışı azaltmaktadır.**
- **İnfluenza aşısı erişkinlerde influenza ile ilişkili hastaneye yatışı %40 azaltmaktadır.**
- **2016-2017 sezonunda aşılama ile yaklaşık 85000 influenza ilişkili hastaneye yatış önlenmiştir.**

- 2017-18 influenza sezonunda influenza A(H3N2) ağırlıkla görülmüş
- Aşı 7.1 milyon hastalığı, 3.7 milyon poliklinik başvurusunu
- 109000 hastaneye yatışı
- 8000 ölümü engellemiştir.
- Aşılama influenza ilişkili hastalığın ağırlığını azaltmakta.

Doyle JD, et al. MMWR Morb Mortal Wkly Rep. 2019 Feb 15; 68(6): 135–139.

Clinical Infectious Diseases

MAJOR ARTICLE

Influenza Vaccination Modifies Disease Severity Among Community-dwelling Adults Hospitalized With Influenza

Carmen Arriola,[1] Shikha Garg,[1] Evan J Anderson,[2,3] Patrician A Ryan,[4] Andrea George,[5] Shelley M Zansky,[6] Nancy Bennett,[7] Arthur Reingold,[8] Marisa Bargsten,[9] Lisa Miller,[10] Kimberly Yousey-Hindes,[11] Lilith Tatham,[12] Susan R Bohm,[13] Ruth Lynfield,[14] Ann Thomas,[15]

İnfluenza aşısı, aşı olup hastalananlarda hastalığın daha hafif geçirilmesini sağlamakta
İnfluenzaya bağlı ölüm, yoğun bakım ihtiyacı daha az,
Yoğun bakımda kalış süresi, hastanede kalış süresi daha kısa

Methods. We analyzed data from the 2013–14 influenza season and used propensity score matching to account for the probability of vaccination within age strata (18–49, 50–64, and ≥65 years). Death, intensive care unit (ICU) admission, and hospital and ICU lengths of stay (LOS) were outcome measures for severity. Multivariable logistic regression and competing risk models were used to compare disease severity between vaccinated and unvaccinated patients, adjusting for timing of antiviral treatment and time from illness onset to hospitalization.

Results. Influenza vaccination was associated with a reduction in the odds of in-hospital death among patients aged 18–49 years (adjusted odds ratios [aOR] = 0.21; 95% confidence interval [CI], 0.05 to 0.97), 50–64 years (aOR = 0.48; 95% CI, 0.24 to 0.97), and ≥65 years (aOR = 0.39; 95% CI, 0.17 to 0.66). Vaccination also reduced ICU admission among patients aged 18–49 years (aOR = 0.63; 95% CI, 0.42 to 0.93) and ≥65 years (aOR = 0.63; 95% CI, 0.48 to 0.81), and shortened ICU LOS among those 50–64 years (adjusted relative hazards [aRH] = 1.36; 95% CI, 1.06 to 1.74) and ≥65 years (aRH = 1.34; 95% CI, 1.06 to 1.73), and hospital LOS among 50–64 years (aRH = 1.13; 95% CI, 1.02 to 1.26) and ≥65 years (aRH = 1.24; 95% CI, 1.13 to 1.37).

Conclusions. Influenza vaccination during 2013–14 influenza season attenuated adv… pitalized with laboratory-confirmed influenza.

Keywords. Influenza vaccination; adults; disease severity

original report

Influenza Vaccine Effectiveness Among Patients With Cancer: A Population-Based Study Using Health Administrative and Laboratory Testing Data From Ontario, Canada

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Kanserli hastalarda influenza aşısı hastaneye yatışı %20 azaltmış

abstract

PURPOSE Seasonal influenza vaccination is recommended for patients with cancer despite concerns of disease or treatment-associated immunosuppression. The objective of this study was to evaluate vaccine effectiveness (VE) against laboratory-confirmed influenza for patients with cancer.

PATIENTS AND METHODS We conducted an observational test-negative design study of previously diagnosed patients with cancer 18 years of age and older who underwent influenza testing during the 2010-2011 to 2015-2016 influenza seasons in Ontario, Canada. We linked individual-level cancer registry, respiratory virus testing, and health administrative data to identify the study population and outcomes. Vaccination status was determined from physician and pharmacist billing claims. We used multivariable logistic regression to estimate VE, adjusting for age, sex, rurality, income quintile, cancer characteristics, chemotherapy exposure, comorbidities, previous health care use, influenza season, and calendar time.

RESULTS We identified 26,463 patients with cancer who underwent influenza testing, with 4,320 test-positive cases (16%) and 11,783 (45%) vaccinated. Mean age was 70 years, 52% were male, mean time since diagnosis was 6 years, 69% had solid tumor malignancies, and 23% received active chemotherapy. VE against laboratory-confirmed influenza was 21% (95% CI, 15% to 26%), and VE against laboratory-confirmed influenza hospitalization was 20% (95% CI, 13% to 26%). For patients with solid tumor malignancies, VE was 25% (95% CI, 18% to 31%), compared with 8% (95% CI, −5% to 19%) for patients with hematologic malignancies ($P = .015$). Active chemotherapy usage did not significantly affect VE, especially among patients with solid tumor cancer.

CONCLUSION Our results support recommendations for influenza vaccination for patients with cancer. VE was decreased for patients with hematologic malignancies, and there was no significant difference in VE among patients with solid tumor cancer receiving active chemotherapy. Strategies to optimize influenza prevention among patients with cancer are warranted.

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Influenza vaccine effectiveness in preventing influenza-associated intensive care admissions and attenuating severe disease among adults in New Zealand 2012–2015

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2012-2015 yılları arasında influenza aşısı sayesinde influenza ile ilişkili yoğun bakım ihtiyacı %59 azalmıştır.

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Influenza vaccine
Vaccine effectiveness
Intensive care unit
Test negative design
Hospital

Background: Little is known about inactivated influenza vaccine effectiveness (IVE) in preventing very severe disease, including influenza-associated intensive care unit (ICU) admissions.
Methods: The Southern Hemisphere Influenza and Vaccine Effectiveness Research and Surveillance (SHIVERS) project enrolled adults (aged ≥ 18 years) with acute respiratory illness (ARI) in general ward (GW) hospital settings (n = 3034) and ICUs (n = 101) during 2012–2015. IVE was assessed using a test-negative design comparing the odds of influenza vaccination among influenza positives vs. negatives (confirmed by real-time reverse transcription polymerase chain reaction). All models were adjusted for season, weeks from season peak, and a vaccination propensity score.
Results: Influenza virus infection was confirmed in 28% of GW hospital and 41% of ICU patients; influenza vaccination was documented for 56% and 41%, respectively. Across seasons, IVE was 37% (95% confidence intervals [CI] = 23–48%) among GW patients and 82% (95% CI = 45–94%) among ICU patients. IVE point estimates were > 70% against ICU influenza and consistently higher than IVE against GW influenza when stratified by season, by virus (sub)types, and for adults with or without chronic medical conditions and for both adults aged <65 and ≥65 years old. Among hospitalized influenza positives, influenza vaccination was associated with a 59% reduction in the odds of ICU admission (aOR = 0.41, 95% CI = 0.18–0.96) and with shorter ICU lengths of stay (LOS), but not with radiograph-confirmed pneumonia or GW hospital LOS.
Conclusion: Inactivated influenza vaccines prevented influenza-associated ICU admissions, may have higher effectiveness in ICU than GW hospital settings, and appeared to reduce the risk of severe disease among those who are infected despite vaccination.

1. Introduction

Although the preventive benefit of inactivated influenza vaccines (IIVs) has been studied extensively [1,2], the extent to which IIVs avert the most severe manifestations of influenza disease and possibly attenuate disease severity among adults infected despite vaccination remains unclear. To date, there are no statistically significant estimates of influenza vaccine effectiveness (IVE) against influenza-associated intensive care unit (ICU) admissions

Effectiveness of Influenza Vaccination on Hospitalizations and Risk Factors for Severe Outcomes in Hospitalized Patients With COPD

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BACKGROUND: The effectiveness of influenza vaccination in reducing influenza-related hospitalizations among patients with COPD is not well described, and influenza vaccination uptake remains suboptimal.

METHODS: Data were analyzed from a national, prospective, multicenter cohort study including patients with COPD, hospitalized with any acute respiratory illness or exacerbation between 2011 and 2015. All patients underwent nasopharyngeal swab screening with polymerase chain reaction (PCR) testing for influenza. The primary outcome was an influenza-related hospitalization. We identified influenza-positive cases and negative control subjects and used multivariable logistic regression with a standard test-negative design to estimate the vaccine effectiveness for preventing influenza-related hospitalizations.

RESULTS: Among 4,755 hospitalized patients with COPD, 4,198 (88.3%) patients with known vaccination status were analyzed. The adjusted analysis showed a 38% reduction in influenza-related hospitalizations in vaccinated vs unvaccinated individuals. Influenza-positive patients (n = 1,833 [38.5%]) experienced higher crude mortality (9.7% vs 7.9%; $P = .047$) and critical illness (17.2% vs 12.1%; $P < .001$) compared with influenza-negative patients. Risk factors for mortality in influenza-positive patients included age > 75 years (OR, 3.7 [95% CI, 0.4-30.3]), cardiac comorbidity (OR, 2.0 [95% CI, 1.3-3.2]), residence in long-term care (OR, 2.6 [95% CI, 1.5-4.5]), and home oxygen use (OR, 2.9 [95% CI, 1.6-5.1]).

CONCLUSIONS: Influenza vaccination significantly reduced influenza-related hospitalization among patients with COPD. Initiatives to increase vaccination uptake and early use of antiviral agents among patients with COPD could reduce influenza-related hospitalization and critical illness and improve health-care costs in this vulnerable population.

TRIAL REGISTRY: ClinicalTrials.govNo.:NCT01517191; URL www.clinicaltrials.gov

CHEST 2019; 155(1):69-78

KOAH'lı hastalarda influenza ilişkili hastaneye yatışı %38 azaltmakta,

Original Investigation

Association Between Influenza Vaccination and Cardiovascular Outcomes in High-Risk Patients

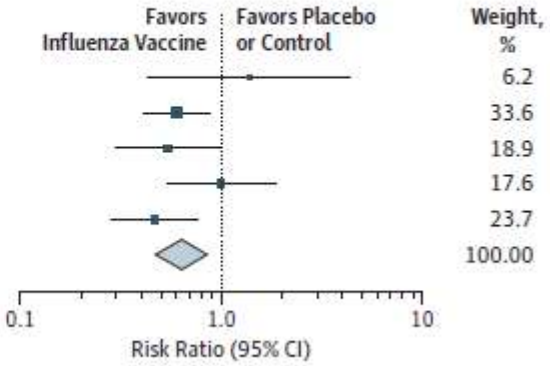
A Meta-analysis

- **İnfluenza aşısı olanlarda major kardiovasküler olaylar daha az görülmüş**
- **En yüksek etki yüksek riskli koroner arter hastalığı olanlarda**

Figure 2. Major Adverse Cardiovascular Events Comparing Influenza Vaccine vs Control

Study	Influenza Vaccine: No. of Events	Influenza Vaccine: Total Participants	Placebo or Control: No. of Events	Placebo or Control: Total Participants	Risk Ratio (95% CI)
Govaert et al,[41] 1994	7	927	5	911	1.38 (0.44-4.32)
FLUVACS,[20,21] 2004	32	145	54	147	0.60 (0.41-0.87)
FLUCAD,[22,23] 2008	16	325	30	333	0.55 (0.30-0.98)
De Villiers et al,[42] 2009	20	1620	20	1622	1.00 (0.54-1.85)
Phrommintikul et al,[24] 2011	20	221	42	218	0.47 (0.29-0.77)
Total (95% CI)	95	3238	151	3231	0.64 (0.48-0.86)

Heterogeneity: $\tau^2 = 0.03$; $\chi^2_4 = 5.59$, ($P = .23$); $I^2 = 28\%$
Test for overall effect: $Z = 2.93$ ($P = .003$)



Udel JA. JAMA. 2013 Oct 23;310(16):1711-20

İnfluenza aşısı

- Diabet ve Kronik Akciğer Hastalığı olanlarda hastaneye yatış ihtiyacını,
- KOAH alevlenmesini azaltmakta

Colquhoun AJ. Epidemiol Infect.1997 Dec; 119(3): 335–341.
Nichol KL. Ann Intern Med. 1999;130:397–403.
https://apps.who.int/iris/handle/10665/255203.

Effectiveness of Influenza Vaccine Against Life-threatening RT-PCR-confirmed Influenza Illness in US Children, 2010–2012

Jill M. Ferdinands,[1,2] Lauren E. W. Olsho,[3] Anna A. Agan,[4] Niranjan Bhat,[5] Ryan M. Sullivan,[4] Mark Hall,[6] Peter M. Mourani,[7] Mark Thompson,[1] and Adrienne G. Randolph[4] on behalf of the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network

[1]Influenza Division, US Centers for Disease Control and Prevention, and [2]Battelle Memorial Institute, Atlanta, Georgia; [3]Abt Associates, Inc., Cambridge, and [4]Department of Anesthesia, Perioperative and Pain Medicine (Critical Care), Boston Children's Hospital, Massachusetts; [5]Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland; [6]Division of Critical Care Medicine, Nationwide Children's Hospital, Columbus, Ohio and [7]Section of Critical Care Medicine, Department of Pediatrics, University of Colorado School of Medicine and Children's Hospital Colorado, Aurora

(See the editorial commentary by Peters and Poehling on pages 671–3.)

Background. No studies have examined the effectiveness of influenza vaccine against intensive care unit (ICU) admission associated with influenza virus infection among children.

Methods. In 2010–2011 and 2011–2012, children aged 6 months to 17 years admitted to 21 US pediatric intensive care units (PICUs) with acute severe respiratory illness and testing positive for influenza were enrolled as cases; children who tested negative were PICU controls. Community controls were children without an influenza-related hospitalization, matched to cases by comorbidities and geographic region. Vaccine effectiveness was estimated with logistic regression models.

Results. We analyzed data from 44 cases, 172 PICU controls, and 93 community controls. Eighteen percent of cases, 31% of PICU controls, and 51% of community controls were fully vaccinated. Compared to unvaccinated

- **2010-2011 ve 2011-2012 influenza sezonlarında aşılama ile çocuklarda influenza ilişkili yoğun bakım ihtiyacı %74,**
- **Hayatı tehdit eden influenza riski 1/3 azalmıştır.**

Vaccine xxx (xxxx) xxx

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Effectiveness of influenza vaccine in children in preventing influenza associated hospitalisation, 2018/19, England

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İnfluenza aşısı 2-17 yaş arası çocuklarda hastaneye yatışı azaltmış

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Hospitalisation

ABSTRACT

2013/14 saw the start of the introduction of a new live attenuated influenza vaccine (LAIV) programme for children in England. 2018/19 saw co-circulation of both A(H1N1)pdm09 and A(H3N2), when LAIV was offered to all healthy children 2–9 years of age. LAIV effectiveness against influenza hospitalisation is not well described. This paper presents the 2018/19 end-of-season adjusted vaccine effectiveness (aVE) against laboratory confirmed influenza related hospitalisation in children aged 2–17. The test negative case control approach was used to estimate aVE by influenza A subtype and vaccine type. Cases and controls were selected from a sentinel laboratory surveillance system which collates details of individuals tested for influenza with reverse-transcription polymerase chain reaction (RT-PCR) on respiratory samples. Vaccine and clinical history was obtained from general practitioners of study participants. There were 307 hospitalised cases and 679 hospitalised controls. End-of-season influenza aVE was 53.0% (95% CI: 33.3, 66.8) against influenza confirmed hospitalisation; 63.5% (95% CI: 34.4, 79.7) against influenza A(H1N1)pdm09 hospitalisation and 31.1% (95% CI: −53.9, 69.2) against influenza A(H3N2). LAIV aVE was 49.1% (95% CI: 25.9, 65.0) for any influenza and 70.7% (95% CI: 41.8, 85.3) for A(H1N1)pdm09, whereas for those receiving quadrivalent inactivated influenza vaccine (QIV), aVE was 64.4% (95% CI: 29.4, 82.0) and 44.4% (95% CI: −51.9, 79.6) respectively. We provide evidence of overall significant VE for both LAIV and QIV against influenza associated hospitalisation in children 2–17 years of age, most notably against influenza A(H1N1)pdm09, with non-significant protection against A(H3N2).

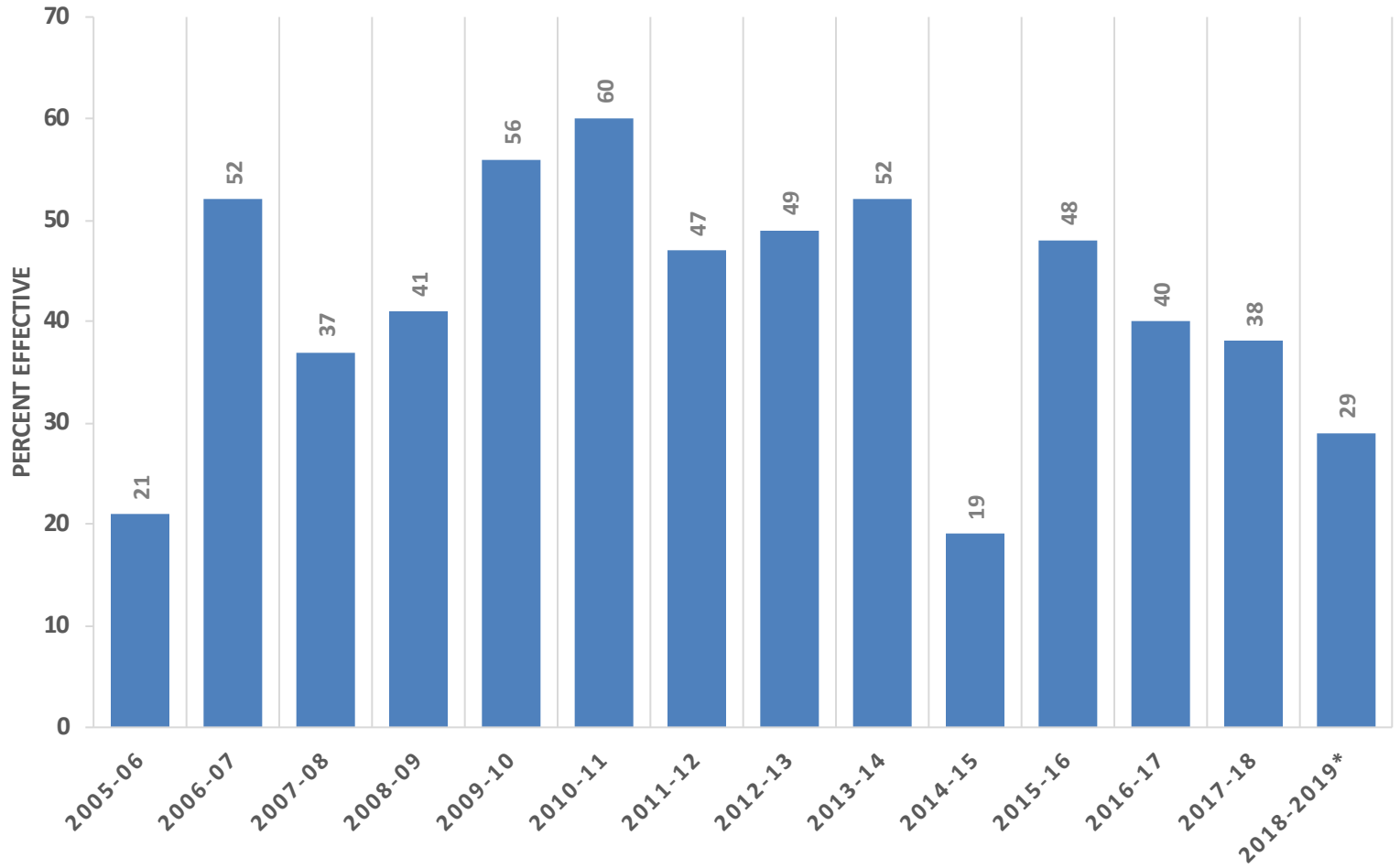
Aşı Etkinliği

- Aşılanan kişinin sağlık durumu ve yaşı
- Aşı içeriği ve dolaşımdaki virüslerin eşleşmesi

İnfluenza aşısı etkinliği

- İnfluenza aşısı etkinliği %40-60
- İnfluenza aşısı toplumda influenza hastalığı riskini aşı içeriğindeki virüsler ile sirkülasyondaki virüsler eşleştiğinde %40 ile %60 oranında azaltır.
- 2018-2019sezonu aşısı influenza B ve influenza A(H1N1) viruslerine karşı yüksek, influenza A(H3N2) virusüne karşı düşük düzeyde koruma sağlamış.

Effectiveness of Seasonal Flu Vaccines from the 2005 – 2019 Flu Seasons



*Vaccine effectiveness estimates for 2018-2019 were presented to ACIP on June 27, 2019.

Source: https://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm

Adjusted Vaccine Effectiveness Estimates For Influenza Seasons from 2005 – 2019

Influenza Season	Reference	Study Site(s)	No. of Patients	Adjusted Overall VE (%)	95% CI
2005-06	Belongia 2009	WI	346	21	-52, 59
2006-07	Belongia 2009	WI	871	52	22 ,70
2007-08	Belongia 2011	WI	1914	37	22, 49
2008-09	Unpublished	WI, MI, NY, TN	6713	41	30, 50
2009-10	Griffin 2011	WI, MI, NY, TN	6757	56	23, 75
2010-11	Treanor 2011	WI, MI, NY, TN	4757	60	53, 66
2011-12	Ohmit 2014	WI, MI, PA, TX, WA	4771	47	36, 56
2012-13	McLean 2014	WI, MI, PA, TX, WA	6452	49	43, 55
2013-14	Gaglani 2016	WI, MI, PA, TX, WA	5999	52	44, 59
2014-15	Zimmerman 2016	WI, MI, PA, TX, WA	9311	19	10, 27
2015-16	Jackson 2017	WI, MI, PA, TX, WA	6879	48	41, 55
2016-17	Flannery 2018	WI, MI, PA, TX, WA	7410	40	32, 46
2017-18	Rolfes 2019	WI, MI, PA, TX, WA	8,436	38	31, 43
2018-19*	Unpublished Final Estimates*	WI, MI, PA, TX, WA	10,041	29*	21, 35

*Vaccine effectiveness estimates for 2018-2019 were presented to ACIP on June 27, 2019.

Source: https://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm

Interim Estimates of 2018–19 Seasonal Influenza Vaccine Effectiveness — United States, February 2019

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Aşı Etkinliği %47
6 ay-17 yaş arasında %61

In the United States, ann… ARI with cough with influenza is recommended … reated with influenza (https://www.cdc.gov/flu/…) during this illness. Effectiveness of seasonal inf… patients or their guardians, participants or their proxies were interviewed to collect demographic data, information on general and current health status and symptoms, and 2018–19 influenza vaccination status. Nasal and oropharyngeal swabs (or nasal swabs alone for children aged <2 years) were collected to obtain respiratory specimens. Nasal and oropharyngeal swabs were placed together in a single tube of viral transport medium and tested at U.S. Flu VE Network laboratories using CDC's real-time reverse transcription–polymerase chain reaction (real-time RT-PCR) protocol for detection and identification of influenza viruses. Participants (including children aged <9 years, who require 2 vaccine doses during their first vaccination season) were considered vaccinated if they received ≥1 dose of any seasonal influenza vaccine ≥14 days before illness onset, according to medical records and registries (at the Wisconsin site); medical records and self-report (at the Pennsylvania, Texas, and Washington sites); or self-report only (at the Michigan site). Vaccine effectiveness against all influenza virus types combined and against viruses by type/subtype was estimated as 100% x

During each influenza season since 2004–05, CDC has estimated the effectiveness of seasonal influenza vaccine to prevent laboratory-confirmed influenza associated with medically attended acute respiratory illness (ARI). This interim report uses data from 3,254 children and adults enrolled in the U.S. Influenza Vaccine Effectiveness Network (U.S. Flu VE Network) during November 23, 2018–February 2, 2019. During this period, overall adjusted vaccine effectiveness against all influenza virus infection associated with medically attended ARI was 47% (95% confidence interval [CI] = 34%–57%). For children aged 6 months–17 years, overall vaccine effectiveness was 61% (44%–73%). Seventy-four percent of influenza A infections for which subtype information was available were caused by A(H1N1)pdm09 viruses. Vaccine effectiveness was estimated to be 46% (30%–58%) against illness caused by influenza A(H1N1)pdm09 viruses. CDC recommends that health care providers continue to administer influenza vaccine because influenza activity is ongoing and the vaccine can still prevent illness, hospitalization, and death associated with cur-

Spread of antigenically drifted influenza A(H3N2) viruses and vaccine effectiveness in the United States during the 2018-2019 season

- 2018-2019 influenza sezonu dolaşımdaki virüsler:
  - (%48) A(H1N1)pdm09
  - (%49) A(H3N2); (clade 3C.3a %93)
- Antijenik drift ile ortaya çıkan A(H3N2) clade 3C.3a virüsünün 2018-2019 yılının son dönemlerinde baskın olması aşı etkinliğinin azalmasına yol açmıştır.

Flannery B, J Infect Dis. 2019 Oct 30.

- İnfluenza A(H1N1)pdm09'a karşı orta dereceli,
- A(H3N2)'e karşı düşük dereceli etkinlik
- A(H1N1)pdm09'a karşı yüksek etkinlik sadece çocuk/ adolesanlarda ve Vaxigrip-tetra® ile A(H3N2)'a karşı orta dereceli etkinlik Fluad® ile

Moderate influenza vaccine effectiveness against A(H1N1)pdm09 virus, and low effectiveness against A(H3N2) subtype, 2018/19 season in Italy

Stefania Bellino, Antonino Bella, Simona Puzelli, Angela Di Martino, Marzia Facchini, Ornella Punzo, Patrizio Pezzotti & Maria Rita Castruccithe InfluNet Study Group

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Clinical Infectious Diseases

INVITED ARTICLE

VACCINES: Stanley Plotkin, Section Editor

Influenza Vaccine Effectiveness: Defining the H3N2 Problem

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Observational studies have consistently shown that influenza vaccine effectiveness (VE) is lower for H3N2 relative to H1N1pdm09 and type B, and this is not entirely explained by antigenic match. The triad of virus, vaccine, and host immunity provides a framework to examine contributing factors. Antigenic evolution facilitates H3N2 immune escape, and increasing glycosylation of the hemagglutinin shields antigenic sites from antibody binding. Egg passage adaptation of vaccine viruses generates mutations that alter glycosylation, impair the neutralizing antibody response, and reduce VE. Complex host immune factors may also influence H3N2 VE, including early childhood imprinting and repeated vaccination, but their role is uncertain. Of the triad of contributing factors, only changes to the vaccine are readily achievable. However, it is unclear whether current licensed non–egg-based vaccines generate superior protection against H3N2. The optimal strategy remains to be defined, but newer vaccine technology platforms offer great potential.

Keywords. influenza; H3N2; vaccine effectiveness.

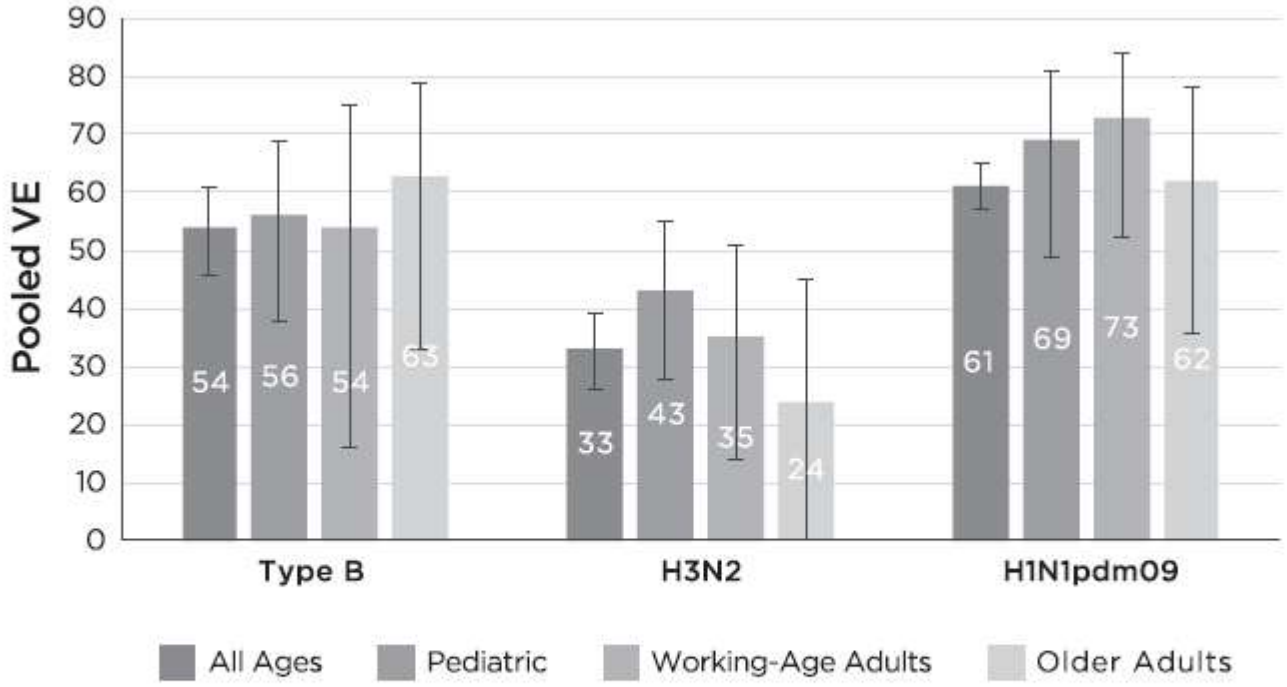

Figure 1. Results of meta-analysis showing pooled influenza vaccine effectiveness by age group and subtype [11]. Pediatric age groups included any age range <20 years; working-age adults included any age range within 20–64 years; older adults included any age range >60 years. The latter 2 groups were mutually exclusive despite the age range overlap. Vertical bars show 95% confidence intervals. Abbreviation: VE, vaccine effectiveness.

Influenza Aşı Etkinliği: H3N2 Problemi

- H3N2 etkinliği H1N1pdm09 ve influenza B serotiplerine göre daha az
- Antijenik eşleşme ile açıklanamıyor
- Hemagglutinin bölgesinde artmış glikozilasyon → H3N2'nin immun kaçışı
- Aşı viruslerinin yumurtadaki pasajı → glikozilasyonu değiştiren mutasyonlar → nötralizan antikor cevabının bozulması → Aşı etkinliğinde azalma

- Kompleks konak immun cevabı ile ilişkili faktörler?
- Yumurtada üretilmeyen aşılarda H3N2 bağışıklığı daha iyi olabilir mi?
- Strateji?

Edward A Belongia, Huong Q McLean, Influenza Vaccine Effectiveness: Defining the H3N2 Problem, *Clinical Infectious Diseases*, 69(10); 15 November 2019: 1817–1823


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