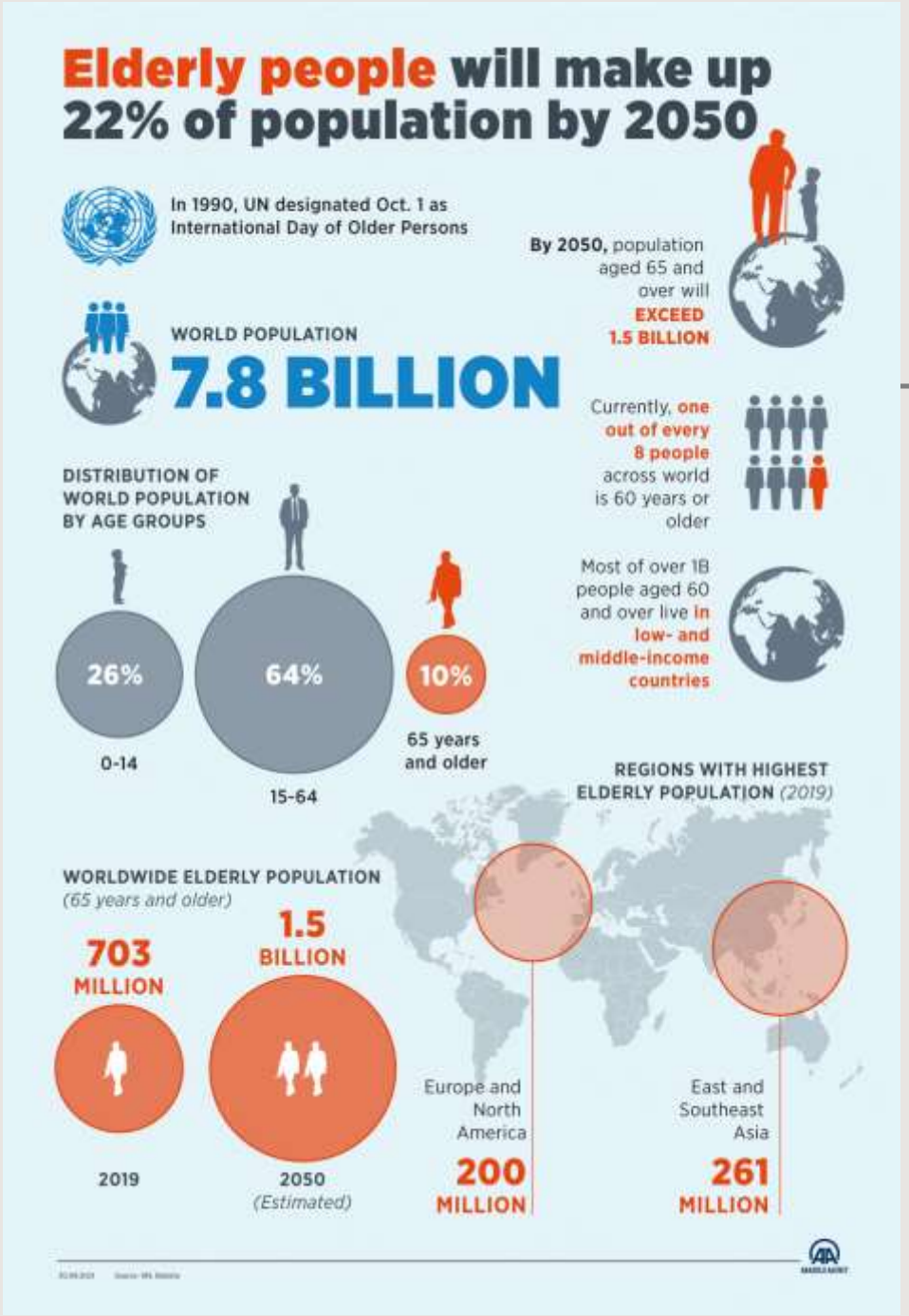
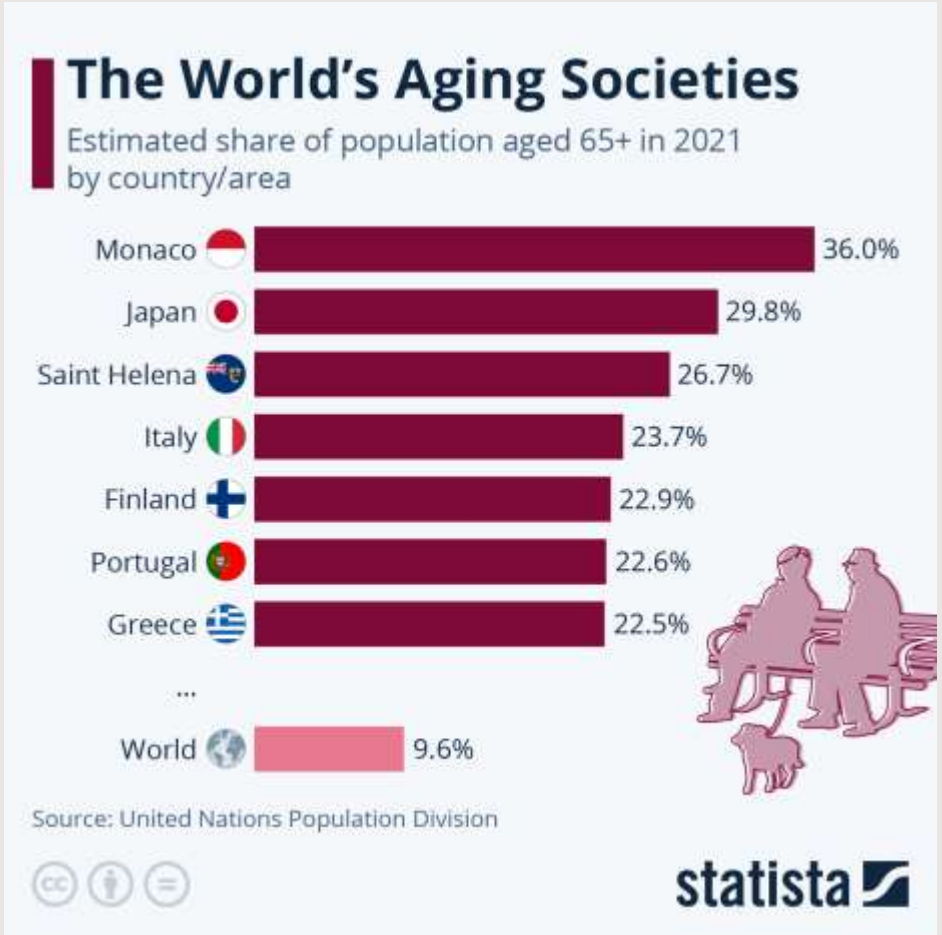

# BAĞIŞIKLAMA PENCERESİNDEN İMMÜN YAŞLANMA

Doç. Dr. Çiğdem EROL

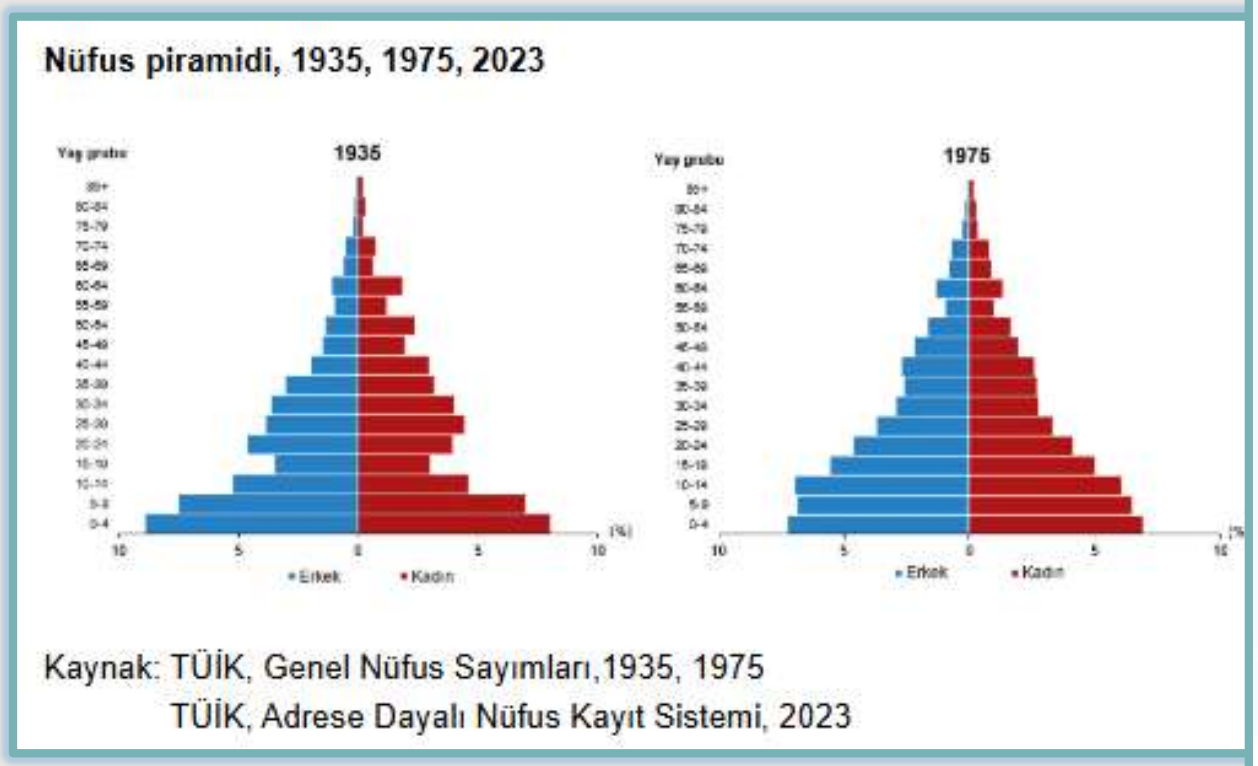


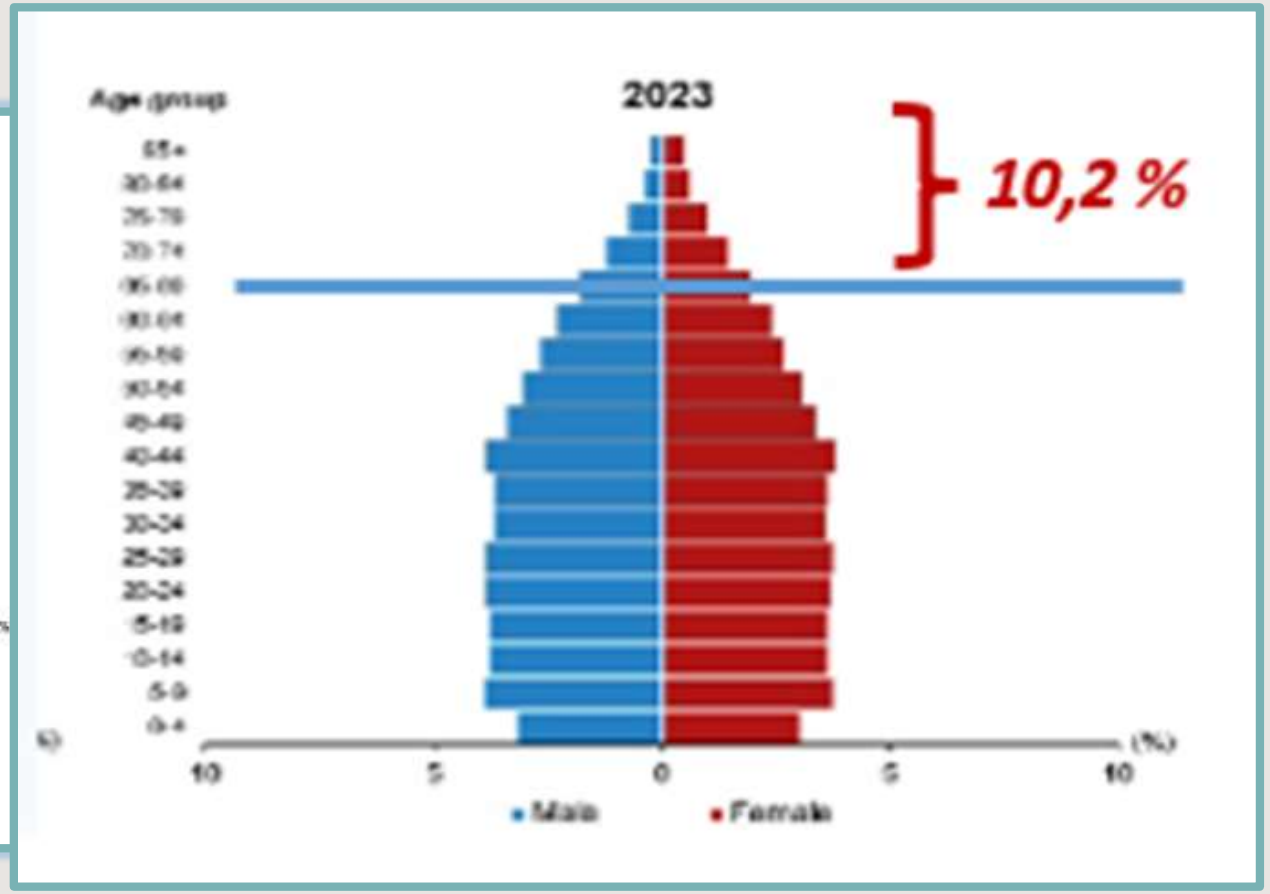

- **2050**…65 yaş ve üzeri nüfus beklentisi ***1.5 milyar (%22)

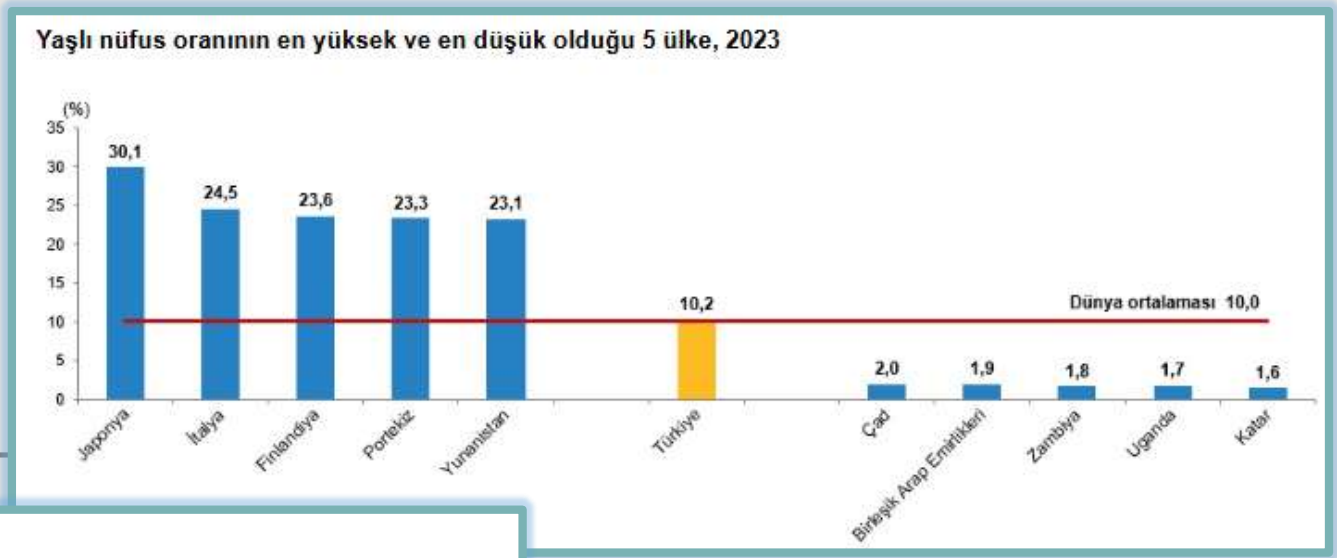


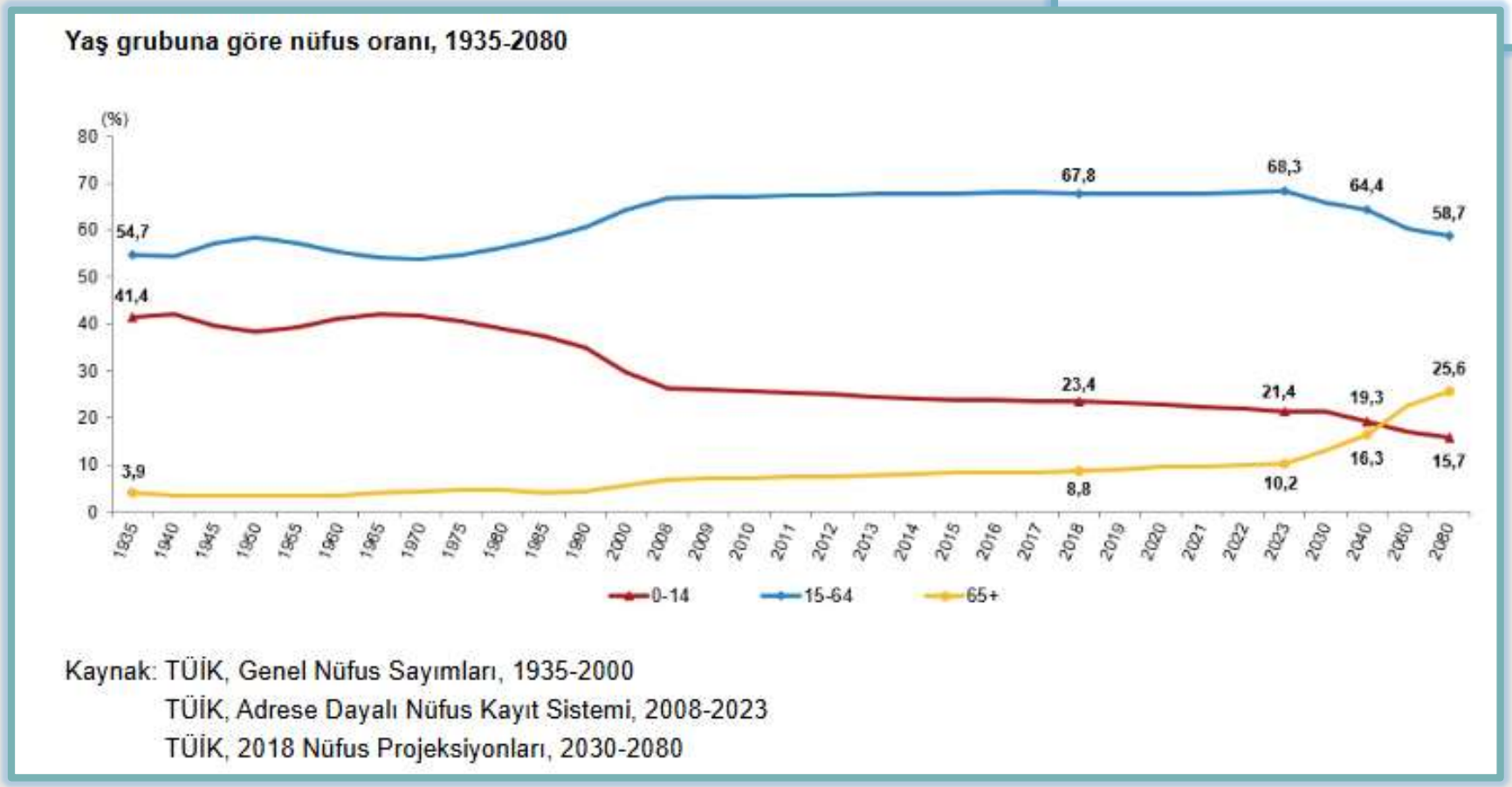

**Türkiye'de**

**Ortanca yaş kadınlarda 34,7'ye, erkeklerde 33,2'ye yükseldi.***




**65 yaş üzeri kişi sayısı:**

**2018**: 7.186.204
**2023:** 8.722.806 (%21,4 ARTIŞ)

**65 yaş üzeri kişi oranı:**

**2018**: %8,8
**2023:** %10,2

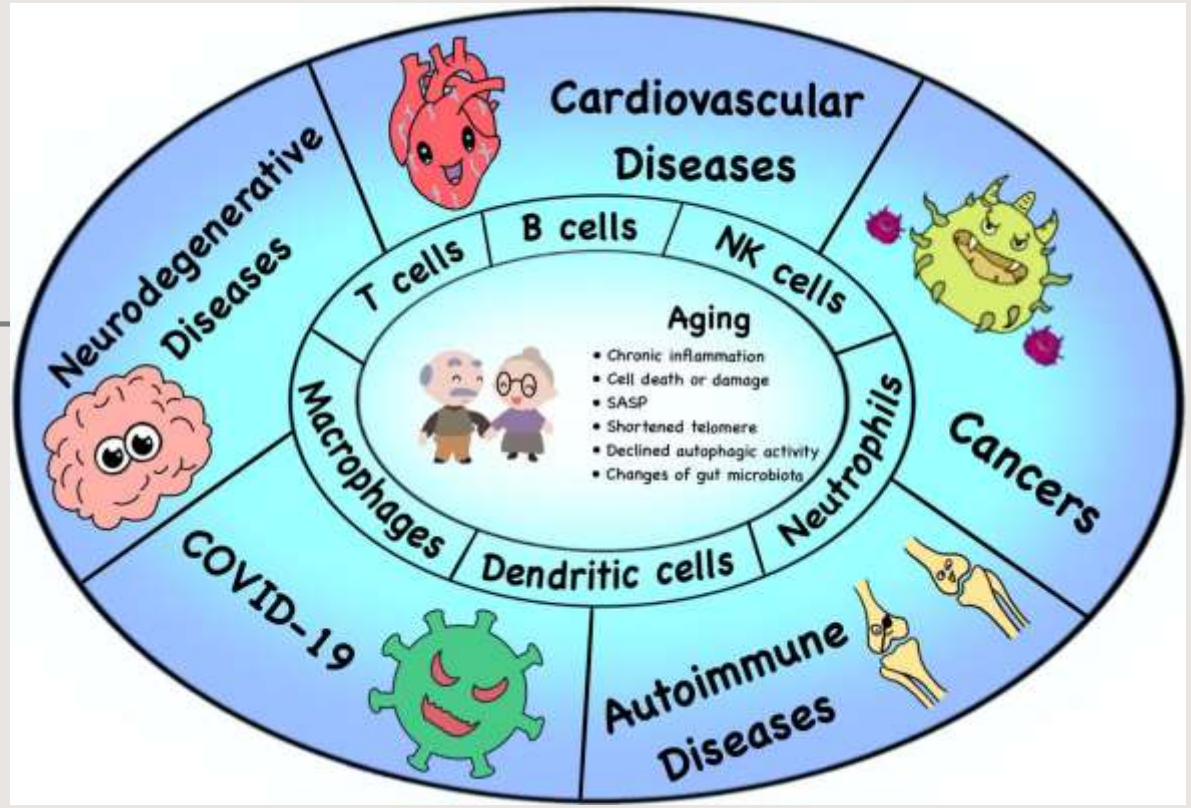
**Nüfus projeksiyonu ile**

**2030: %12,9**
**2040: %16,3**
**2060: %22,6**
**2080: %25,6**


Yaşam süresindeki bu dikkat çekici artış ile sağlık süresi (kronik hastalıklardan ve sakatlıklardan arınmış yaşam süresi) ~~orantılı değil~~

Aslında yaşlanma, yaşlanmanın ana risk faktörü olduğu 'yaşlanmanın kronik hastalıkları' olarak adlandırılan bir dizi kronik durumun artan prevalansı ile ilişkili

- ateroskleroz (inme ve miyokard enfarktüsüne yol açan),
- nörodejeneratif hastalıklar (Parkinson ve Alzheimer),
- tip 2 diyabet,
- osteoartrit,
- makula dejenerasyonu ve glokom,
- işitme kaybı ve
- Bir çok kanser türü...




Asıl sorun:

İMMÜN YAŞLANMA **=IMMUNOSENESCENCE**


# İnfeksiyon Hastalıkları

# ve

# Bağışıklama Penceresinden

- Yaşlı bireyler viral ve bakteriyel infeksiyonlara daha duyarlı..
- İnfeksiyonlar daha sık ve daha ağır seyirli...

- İnfeksiyonlardan korunmada aşılama en mantıklı çözüm ?!
- 65 yaş üzeri bireylerde primer aşı yanıtları oldukça düşük !!☹
- Bu yetersiz yanıtta hem innate hem de adaptif immün sistemde yaşlanmaya bağlı ortaya çıkan değişiklikler etkili

Vaccine 38 (2020) 8264–8272


## Cardinal features of immune system aging

**Weakened antimicrobial immunity**

- Susceptibility to respiratory infections
- Reactivation of chronic viral infections (e.g.,

**Impaired antivaccine responses**

**Insufficient protection against malignancies**

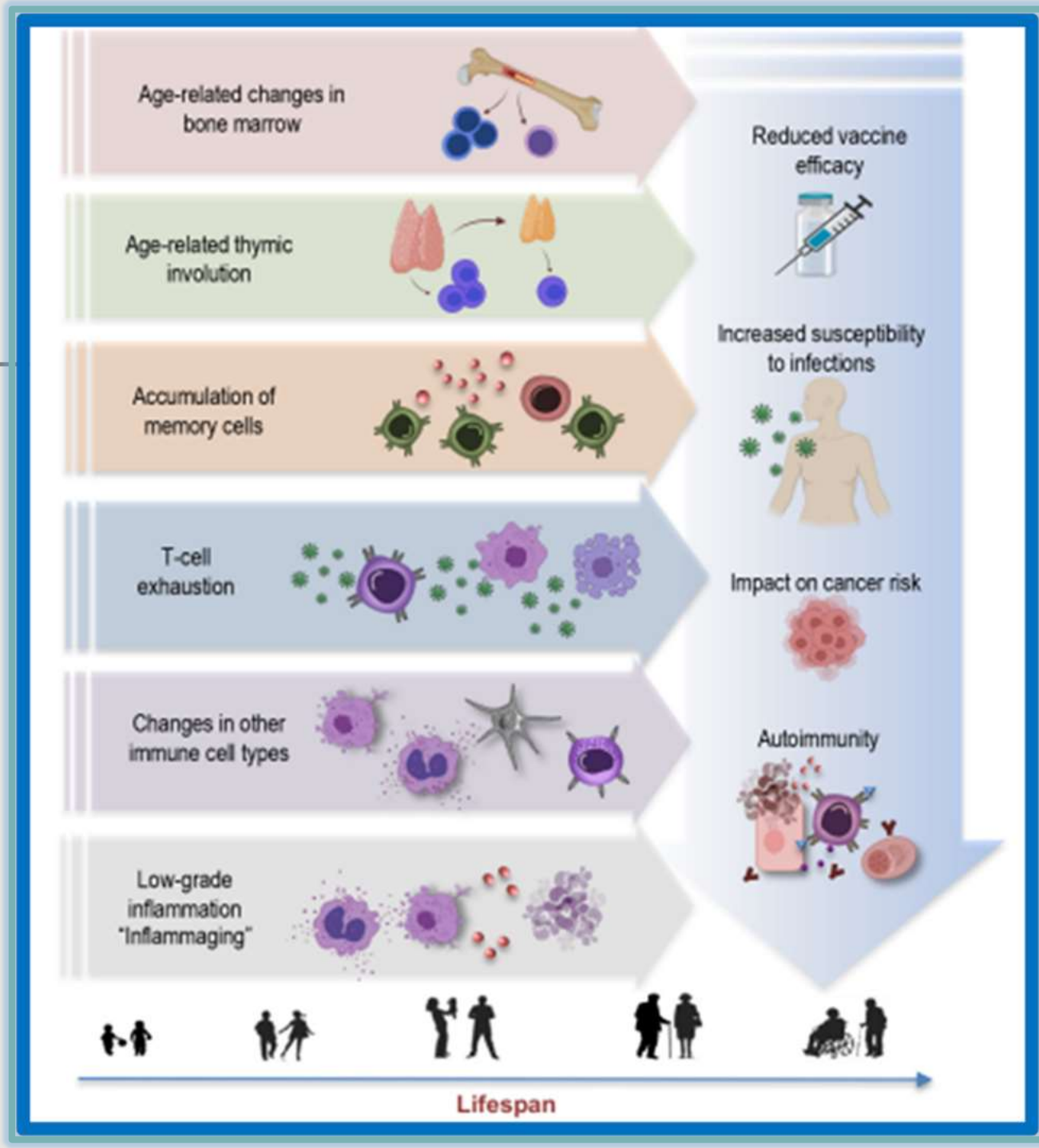
**Predisposition for unopposed tissue inflammation**

- Atherosclerotic disease
- Osteoarthritis
- Neurodegenerative disease

**Failing wound repair mechanisms**

- İnfluenza
- RSV
- HSv- zona
- Pnömokok inf.


- **Kemik iliğinde değişiklikler**
- **Timik involusyon**
- **Hafıza hücrelerinin birikmesi**
- **Diğer immün hücrelerde değişiklikler**
- **Düşük düzeyli- kronik inflamasyon (inflammaging)*****




# Immunosenescence…
# İmmün yaşlanma***

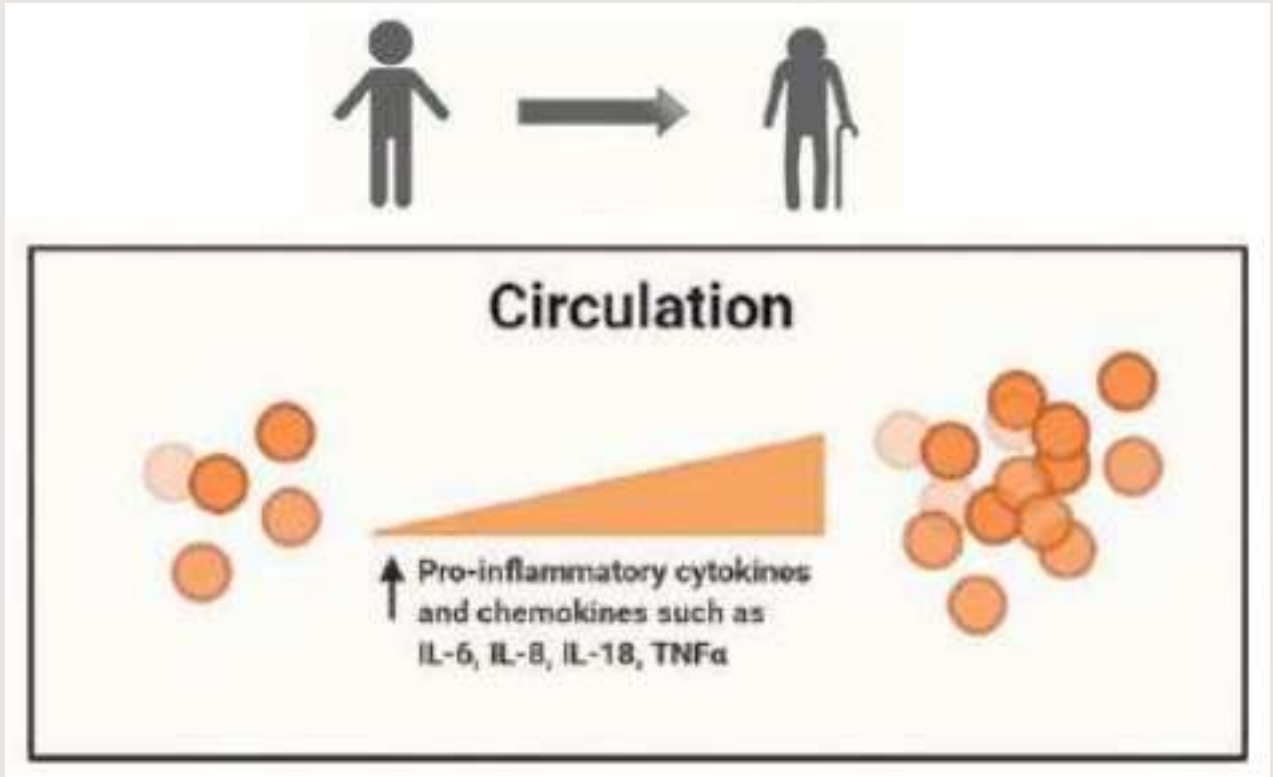
İmmün sistemin ana bölüml

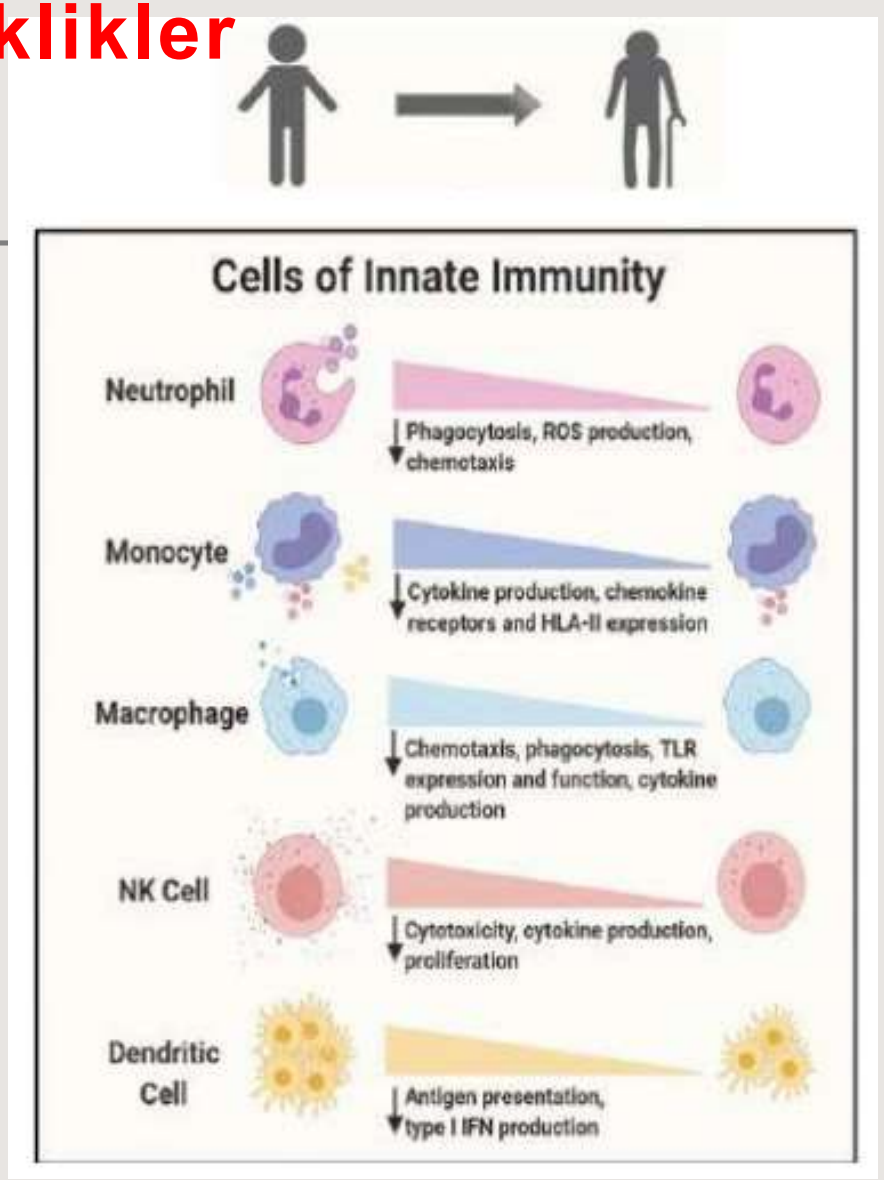
- Fizyolojik bariyerler,
- İnnate immünite
- Adaptif immunite

| | CELL TYPE | CHARACTERISTICS |
|---|---|---|
| Innate Immunity | Neutrophils | ↓ Phagocytic chemotaxis capability<br>↓ Superoxide anion production<br>↓ Ability to respond to soluble factors (GM-CSF) and bacteria (LPS, fMLP)<br>↓ Molecule recruitment into lipid raft, apoptosis and signal transduction |
| | Dendritic cells | |
| | Macrophages | |
| | NK cells | |
| Adaptive Immunity | Cellular Response | Thymus | Involution from age of 9 months, thymic remnant after 50 years |
| | | T Cells | Variable number (↓ proliferation to PHA, varying age and health status) - HLA B8/DR3 associated with high proliferative responses<br>↑ Proportion of memory cells (CD45RO⁺), especially CD8⁺<br>↓ Proportion of naïve cells (CD45RA⁺)<br>↓ Proliferative capacity<br>↓ Synthesis of IL-2 receptor and IL-2 in memory cells<br>↓ CD28⁻<br>↑ CD28⁻T cells mainly CD8⁺ CD28⁻ (characterized by oligoclonal expansion, shortening of telomeres, potential decreased proliferation, resistance to apoptosis, and increased production of TNF-α and IL-6)<br>↓ CD4 T lymphocytes<br>Change from Th1 response to Th2 response with ↓cell-mediated responses directed against intracellular bacteria (Th1 function) and relative preservation of humoral (Th2 function)<br>↓ Treg population (CD4⁺ CD25⁺) that plays a role in the manifestations of autoimmunity<br>Impaired immunological synapse formation and signaling pathways (calcium response, phosphorylations)<br>↓ CD4/CD8 rate |

| | | CELL TYPE | CHARACTERISTICS |
|---|---|---|---|
| Adaptive Immunity | Humoral Response | B Cells | ↓ pre-B lymphocytes with peripheral B lymphocyte count unchanged<br>↑ CD5⁺ B cells (CD19⁺ CD5⁺ clones B) that produce low affinity antibodies without cooperation of T cell ↓ naïve B cells<br>Accumulation of memory B cells with ↓ diversity and affinity of antibodies<br>Reach primary humoral response (dependent T cell cooperation).<br>Conserved secondary humoral response |
| | | Immunoglobulins | ↑ serum levels of IgA and IgG (IgG1, IgG2 and IgG4). Monoclonal immunoglobulin production by CD19⁺ CD5⁺ clones<br>Secretion self-Ab non organ-specific (rheumatoid factor, antinuclear antibodies, antiphospholipid antithyroglobulines and parietal cells) |
| | | Interleukins | ↓ IL-2 production because ↓ cooperation of T cells with antibody producer B cells<br>↑ Production of IL-4, IL-6, IL-8, IL-10 and TNF-α<br>↓ Production of IL-1 and IFN-γ |

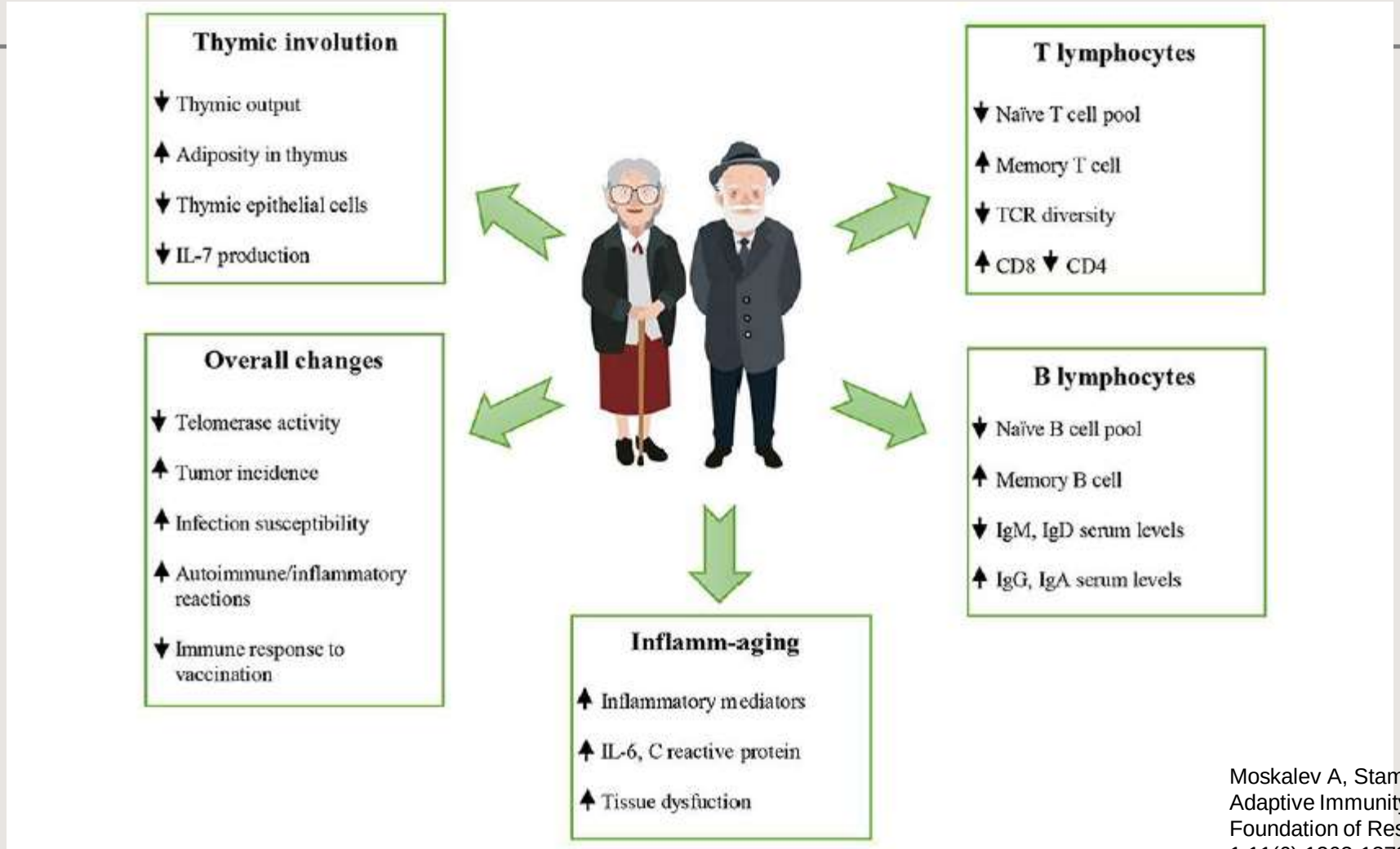

# İnnate immünitede değişiklikler



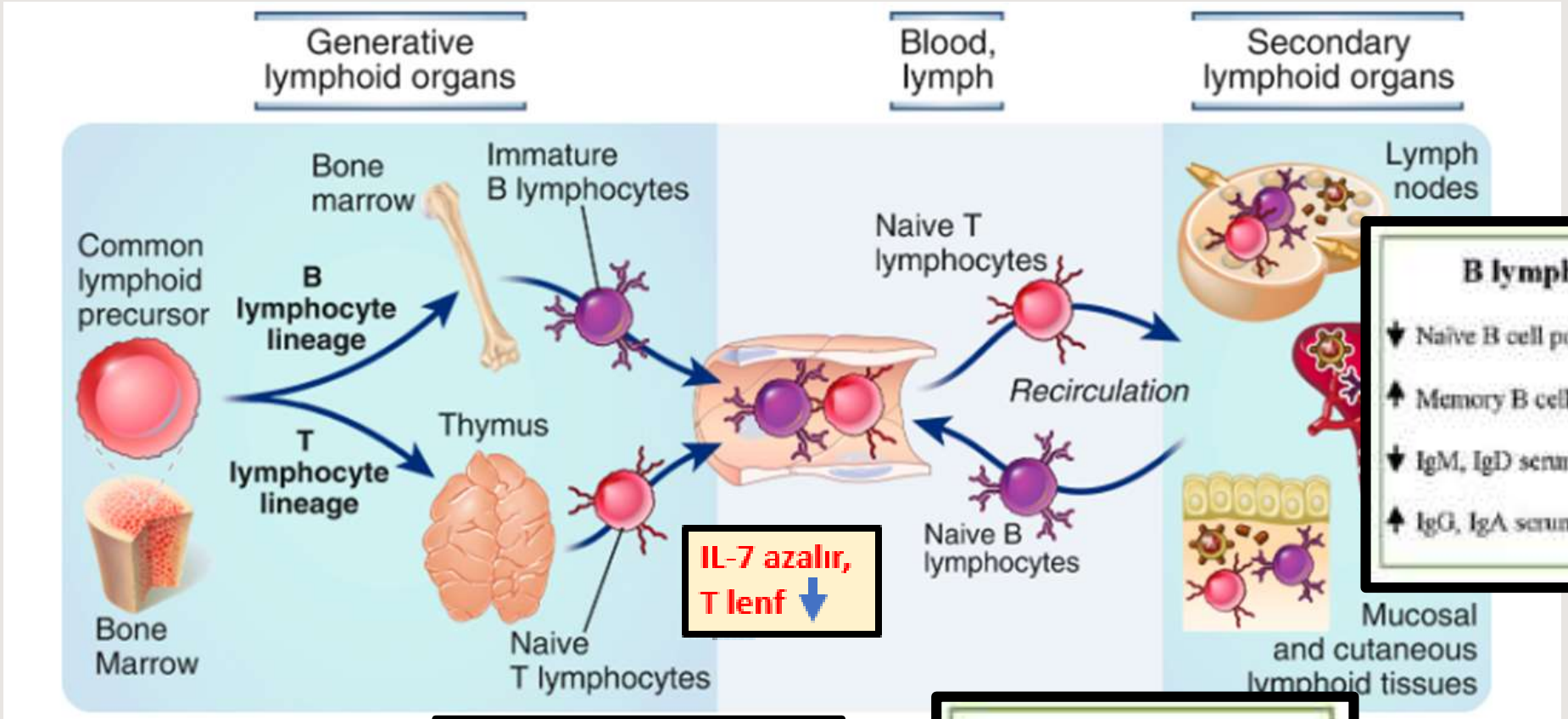




Bulut Ö. et al. Intern Immunol, 2022

# Edinsel immünitede değişiklikler




Moskalev A, Stambler I, Caruso C. Innate and Adaptive Immunity in Aging and Longevity: The Foundation of Resilience. Aging Dis. 2020 Dec




**Kemik iliği değişiklikleri**

- ??????

**Timus:**

- Yağlanma artar
- Timik epitel h. Azalır
- IL-7 üretimi azalır

HHS Public Access
Author manuscript
*Curr Stem Cell Rep*. Author manuscript; available in PMC 2019 August 26.

Published in final edited form as:
*Curr Stem Cell Rep*. 2018 June ; 4(2): 166–181. doi:10.1007/s40778-018-0128-6.

# Signaling Pathways Regulating Hematopoietic Stem Cell and Progenitor Aging

**Abhishek K. Singh**[1,2,4], **Mark J. Althoff**[1,2,3,4], **Jose A. Cancelas**[1,2,3]

[1]Division of Experimental Hematology and Cancer Biology, Cincinnati Children's Hospital Medical Center

[2]Hoxworth Blood Center, University of Cincinnati College of Medicine

[3]Cancer & Cell Biology Program, University of Cincinnati College of Medicine

- Kemik iliği kök hücresi yaşlanması;
  - niş ve intrinsik faktörlerden,
  - hücre dışı matris dayanıklılığından,
  - sistemik inflamasyondan
  - diğer sistemik faktörlerden  etkilenir.
- Yaşla birlikte,
  - HSC'ler hedef bulma ve rejeneratif kapasiteyi azaltır
  - Proinflamatuar miyeloid yönlü farklılaşmayı artırır

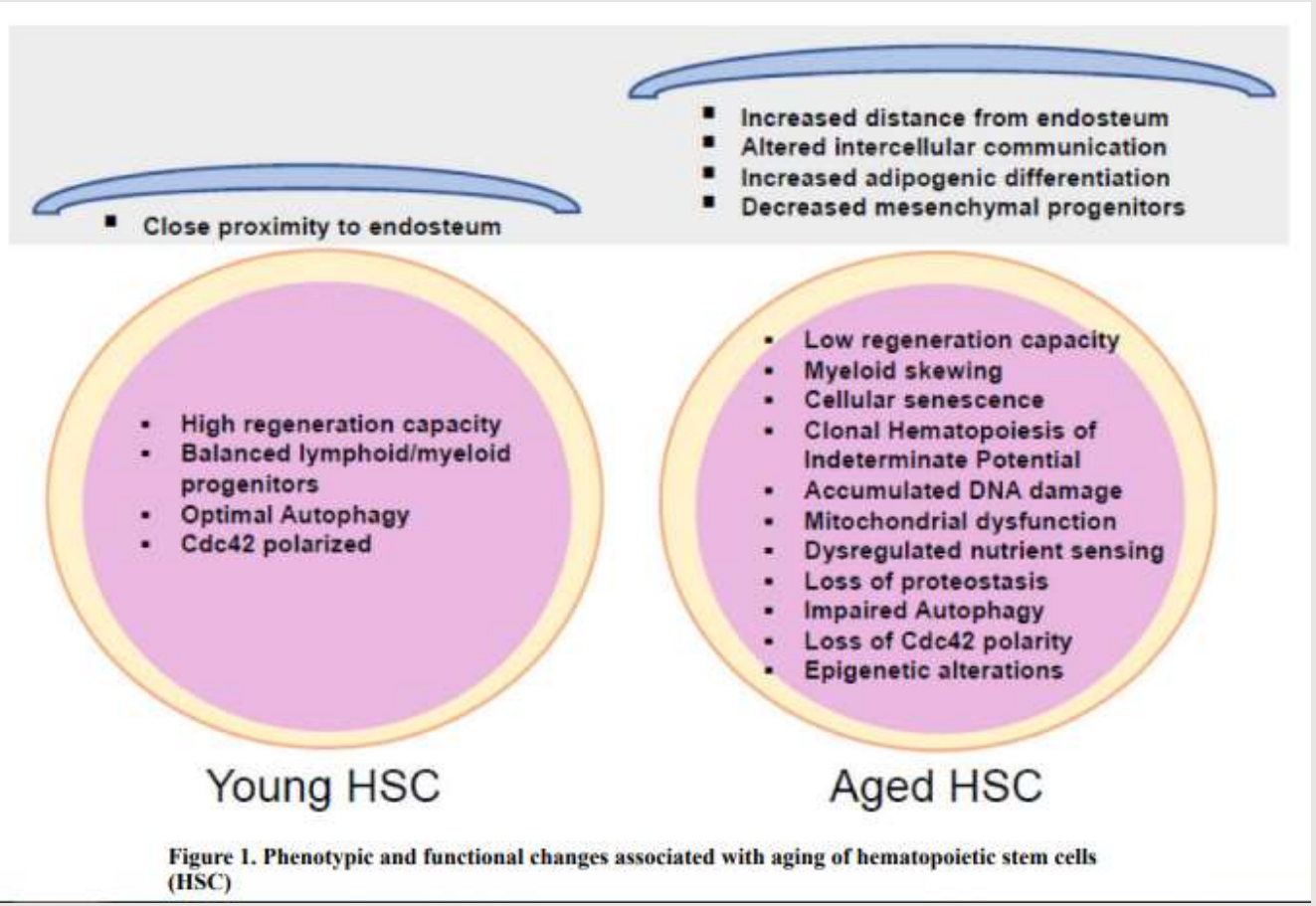



**Figure 1. Phenotypic and functional changes associated with aging of hematopoietic stem cells (HSC)**


Vaccine 38 (2020) 8264–8272

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Review

# Understanding immunosenescence and its impact on vaccination of older adults

Jessica C. Allen, Franklin R. Toapanta, Wilbur Chen, Sharon M. Tennant *

*Center for Vaccine Development and Global Health, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD, USA*


Bozulmuş antijen sunumu

T lenfosit üretiminin azalması

Uygunsuz sitokin salınımı

Efektör T hücre fonksiyonlarında azalma

- Hafıza T hücre fonksiyonlarında körelme

- Lenfoid doku bozulması
- Thf fonks. defekti
- Yeni antijenlere yanıt geliştirememe

- Naif T lenf popülasyonunun azalması
- Proliferasyon azalması
- TCR çeşitliliğinin azalması

Antikor defektleri
- Yetersiz izotip dönüşümü ve somatik hipermutasyon
- Azalmış titre ve efektör fonk.



mune deficits in older adults. Abbreviations: DC, dendritic cell; MΦ, macrophage; $T_{FH}$, T follicular helper; TCR, T cell receptor.


# İleri Yaş ve İmmün Yaşlanmaya Bağlı Görülme Sıklığı ve Şiddeti Artan/ Aşı ile Korunulabilen Enfeksiyonlar

. COVID-19

. İnfluenza

. Pnömokokkal infeksiyonlar

. RSV infeksiyonu

. Zona (Shingles)

...


Ageing Research Reviews 65 (2021) 101205

Contents lists available at ScienceDirect

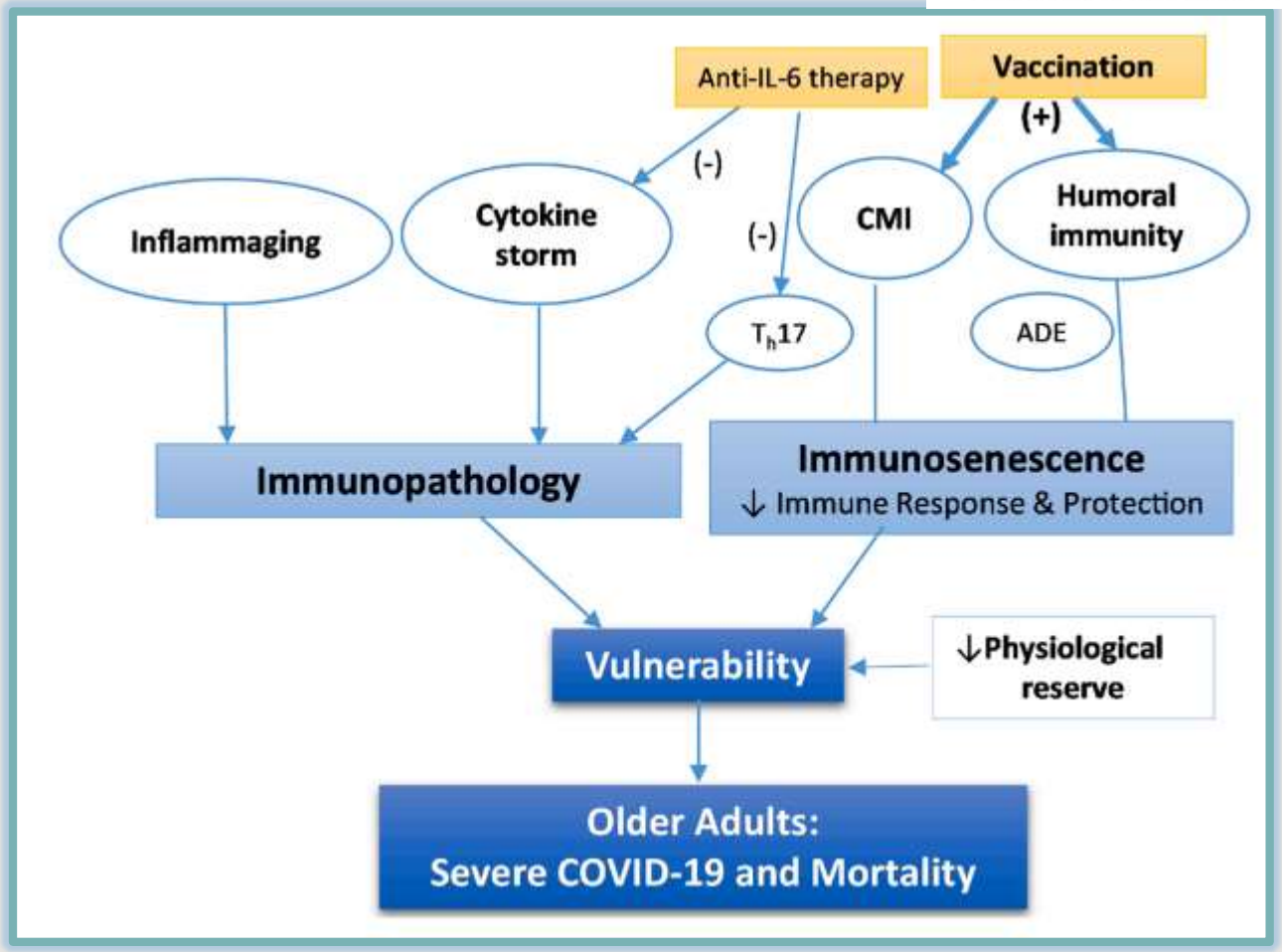
Ageing Research Reviews

journal homepage: www.elsevier.com/locate/arr

Review

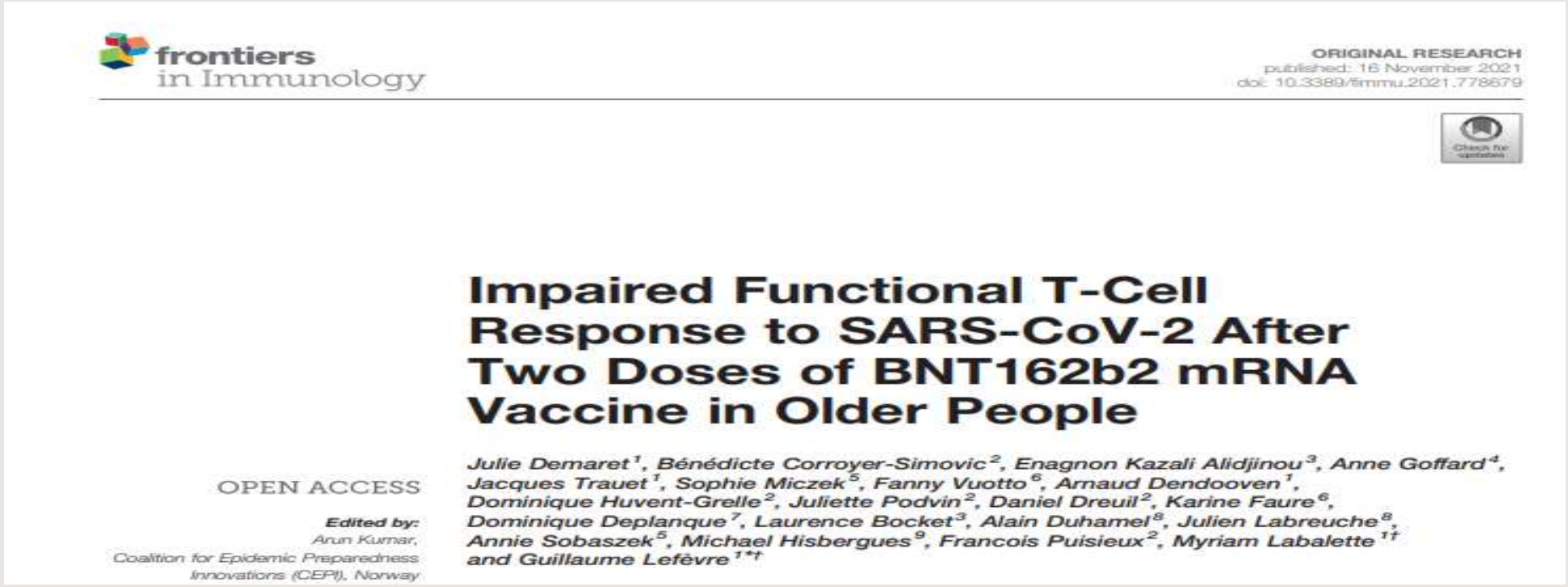
## Aging in COVID-19: Vulnerability, immunity and intervention

Yiyin Chen [a], Sabra L. Klein [b], Brian T. Garibaldi [c], Huifen Li [d], Cunjin Wu [d,e], Nicole M. Osevala [f], Taisheng Li [g], Joseph B. Margolick [b], Graham Pawelec [h,i], Sean X. Leng [b,d,*]




# COVID-19 Aşılaması

- Pandemi sürecinde hastalık ağırlığını ve mortaliteyi belirleyen en önemli risk faktörlerinden biri İLERİ YAŞ**
- Sorunlar;
  - Hangi aşı ? (aşı türü)
  - Yeni varyantlar !
  - Hastalığı geçirmiş olanlar ?
  - Ek hastalık varlığı !?



frontiers in Immunology

ORIGINAL RESEARCH
published: 16 November 2021
doi: 10.3389/fimmu.2021.778679

# Impaired Functional T-Cell Response to SARS-CoV-2 After Two Doses of BNT162b2 mRNA Vaccine in Older People

*Julie Demaret[1], Bénédicte Corroyer-Simovic[2], Enagnon Kazali Alidjinou[3], Anne Goffard[4], Jacques Trauet[1], Sophie Miczek[5], Fanny Vuotto[6], Arnaud Dendooven[1], Dominique Huvent-Grelle[2], Juliette Podvin[2], Daniel Dreuil[2], Karine Faure[6], Dominique Deplanque[7], Laurence Bocket[3], Alain Duhamel[8], Julien Labreuche[8], Annie Sobaszek[5], Michael Hisbergues[9], Francois Puisieux[2], Myriam Labalette[1†] and Guillaume Lefèvre[1*†]*

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**Edited by:**
*Arun Kumar,*
*Coalition for Epidemic Preparedness Innovations (CEPI), Norway*

*** “inflammageing” ve yüksek plazma TNFalfa düzeyleri zayıf antikor yanıtları ile ilişkili bulunmuş

* COVID-19 naif yaşlı hastalarda CD4+ ve CD8+ hücre sayıları düşük, fonksiyonları zayıf ve antikor yanıtı düşük

* Daha önce COVID-19 geçirmiş ve iyileşmiş kişilerde aşı etkinliği çok yüksek


vaccines

MDPI

Review

# Impact of Immunosenescence on Vaccine Immune Responses and Countermeasures

Li Chen [1,2], Chengwei Shao [1,2], Jingxin Li [1,2,*] and Fengcai Zhu [1,2,*]

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## ***Yaşlı bireylerde aşı yanıtları daha zayıf

- İmmün sistem hücrelerinde gen ekspresyonunda zayıflama
- Çeşitliliğin (diversity) azalması
- İmmün reseptör repertuvarının daralması
- Antijen spesifik klonal ekspansiyon kapasitesinin azalması
- Naif B lenfosit sayısında ve sekresyon kapasitesinde azalma ( aşılama sonrası daha düşük antikor düzeyleri !!!)
- T lenfositlerde de TCR repertuarında azalma, antijen tanıma kapasitesinde azalma
- T lenfositlerde de klonal ekspansiyonda azalma...


**Tüm aşı türlerinde yaşlılarda gençlere göre yanıt düşük !**

**Table 1.** Age-Related Immunological Response Characteristics Among Different COVID-19 Vaccine Platforms.

| Vaccine Type | Specific Product | Age-Related Immunological Response Characteristics | References |
|---|---|---|---|
| Inactivated Vaccines | CoronaVac | Inflammatory markers (IL-6, TNF-α/β, MIP-β, and IFN-γ) negatively correlate across the aging spectrum. Older individuals show delayed antibody responses, lower antibody titers, and faster decline compared to younger adults. | [25] |
| | BBIBP-CorV | Lower antibody titers were observed in individuals > 60 years. Advanced age correlates with slower antibody production rates. | [26] |
| | CoviVac | No significant age-related differences were observed; seroconversion rates > 85% in both 18–60 and >60 age groups. | [27] |
| mRNA Vaccines | BNT162b2 | Negative correlation between age and spike protein-binding antibodies and neutralizing antibodies. Older group (86 years) showed a 10-fold decrease in neutralizing antibody titers. IFN-γ and IL-2 negatively correlated with age ($r = -0.49$). | [30–33] |
| | SYS6006 | Significantly lower GMTs in the older group compared to adults: younger group: 232.1 (20 µg), 130.6 (30 µg); older group: 48.7 (20 µg), 66.7 (30 µg). | [34] |
| Viral Vector Vaccines | Ad5-vectored vaccine | Subjects ≥ 55 years showed significantly lower responses compared to younger subjects: RBD-specific ELISA antibodies ($p = 0.0018$), live virus-neutralizing antibodies ($p < 0.0001$), pseudovirus-neutralizing antibodies ($p = 0.046$). | [37] |
| | Ad26.COV2.S | Subjects ≥ 65 years demonstrated slower initial antibody production; after a booster dose at 3 months, they achieved comparable levels to younger adults. | [38] |




# Comparative effectiveness of 3 or 4 doses of mRNA and inactivated whole-virus vaccines against COVID-19 infection, hospitalization and severe outcomes among elderly in Singapore

Celine Y. Tan,[a,*] Calvin J. Chiew,[a,b] Vernon J. Lee,[a,c] Benjamin Ong,[a,d] David Chien Lye,[b,d,e,f] and Kelvin Bryan Tan[a,c]

[a]Ministry of Health, Singapore
[b]National Centre for Infectious Diseases, Singapore
[c]Saw Swee Hock School of Public Health, National University of Singapore, Singapore
[d]Yong Loo Lin School of Medicine, National University of Singapore, Singapore
[e]Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore
[f]Department of Infectious Diseases, Tan Tock Seng Hospital, Singapore

- **>60 yaş 3 ya da 4 doz mRNA ve inaktif aşı etkinlik karşılaştırması**
- **Şubat-Eylül 2022 arası**
- **Semptomatik hastalık, Ağır COVID-19, hastane yatışı Individuals who had previous documented SARS-CoV-2 infection were excluded**
- **Ağır COVID….. O2 ihtiyacı, YBÜ gereksinimi, ölüm**

| Number of doses and type of vaccine | Person-days at risk | Events | | | Incidence per million person-days | | | Adjusted incidence rate ratios (95% CI)[a] | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Infection | Hospitalization | Severe | Infection | Hospitalization | Severe | Infection | Hospitalization | Severe |
| 3 doses, mRNA[b] | 124,822,336 | 197,657 | 9453 | 1439 | 1584 | 76 | 12 | 1 [Ref] | 1 [Ref] | 1 [Ref] |
| 3 doses, inactivated whole-virus[c] | 2,635,200 | 4136 | 291 | 57 | 1570 | 110 | 22 | 1.13 (1.09–1.16) | 1.52 (1.36–1.71) | 1.90 (1.45–2.47) |
| 3 doses, combination[d] | 667,710 | 1250 | 45 | 6 | 1872 | 67 | 9 | 1.31 (1.24–1.38) | 1.08 (0.81–1.45) | NA[e] |
| 4 doses, mRNA[b] | 18,785,302 | 17,513 | 1045 | 138 | 932 | 56 | 7 | 0.81 (0.80–0.83) | 0.49 (0.46–0.52) | 0.39 (0.32–0.47) |
| 4 doses, inactivated whole-virus[c] | 115,562 | 130 | 10 | 1 | 1125 | 87 | 9 | 1.05 (0.88–1.24) | 1.02 (0.55–1.90) | NA[e] |
| 4 doses, combination[d] | 168,876 | 256 | 16 | 2 | 1516 | 95 | 12 | 1.24 (1.10–1.41) | 1.26 (0.77–2.06) | NA[e] |

CI, confidence interval. [a]Adjusted for age, sex, ethnicity, housing type, date of reporting (to control for daily infection rate) and date of last vaccine dose using Poisson regression. [b]BNT-162b2 or mRNA-1273. [c]CoronaVac or BBIBP-CorV. [d]Combination of mRNA vaccine and inactivated whole-virus vaccine. [e]Due to the small number of individuals who received a combination of vaccine types or four doses of inactivated whole-virus vaccine, the sample sizes are too small for meaningful analyses.

*Table 1:* **Incidence and rate ratios of symptomatic SARS CoV-2 infection, COVID-19 related hospitalization and severe COVID-19 by number of doses and type of vaccine.**

- **803,911 hasta**
- **3 doz İnaktif Aşı olanlar 3 doz mRNA aşısı olanlara göre daha fazla ;**

  ***semptomatik hastalık, (IRR 1.13; 95% CI 1.09–1.16),**

  ***COVID-19 ilişkili hastane yatışı (IRR 1.52; 95% CI 1.36–1.71)**

  ***Ağır COVID-19 (IRR 1.90; 95% CI 1.45–2.47)**

- **4. doz mRNA aşısı olanlar da korunma daha fazla *****
- **4. doz inaktif aşı ya da kombine aşılamada aynı etki gösterilmemiş.**
- **infection (IRR 0.81; 95% CI 0.80–0.83),**
- **hospitalization (IRR 0.49; 95% CI 0.46 –0.52) and**
- **severe COVID-19 (IRR 0.39; 95% CI 0.32 –0.47).**

Current Microbiology (2023) 80:206
https://doi.org/10.1007/s00284-023-03322-z

SHORT COMMUNICATION

# Effectiveness of Inactivated and mRNA COVID-19 Vaccines Against SARS-CoV-2 Infection, Severe Disease and Mortality in the Geriatric Population

Yasemin Genç Bahçe[1] · Ömer Acer[2] · Osman Özüdoğru[3]

## Aşı tiplerine göre bağışıklık yanıtları

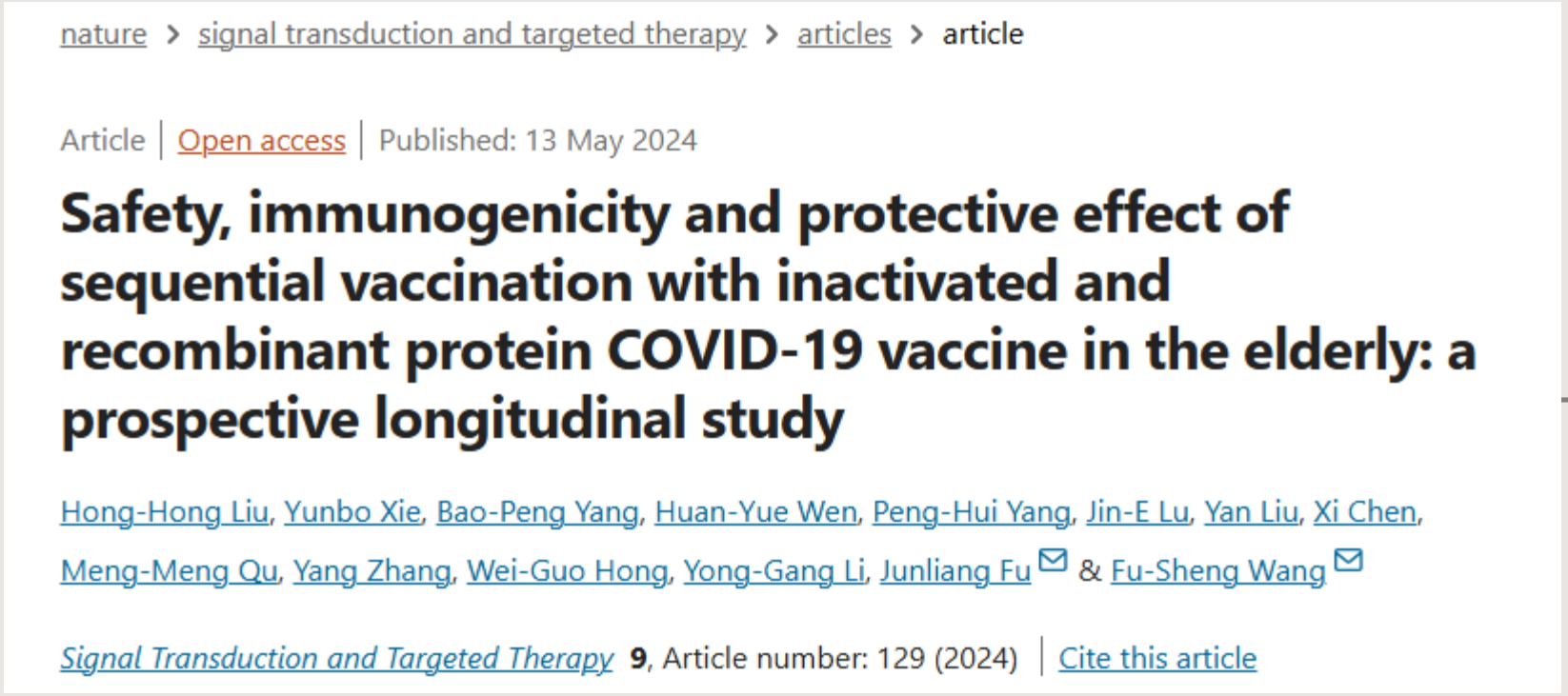
- Pfizer–BioNTech vs CoronaVac
- >65 yaş…6168 hasta…Ağır enfeksiyon- Mortalite

*2 doz CoronaVac

- Hastane yatışını önleme %50
- YBÜ ihtiyacını önleme %53
- Mortalite önleme %56

*2 doz BioNTech

- Hastane yatışını önleme %89
- YBÜ ihtiyacını önleme %79
- Mortalite önleme %79



nature > signal transduction and targeted therapy > articles > article

Article | Open access | Published: 13 May 2024

# Safety, immunogenicity and protective effect of sequential vaccination with inactivated and recombinant protein COVID-19 vaccine in the elderly: a prospective longitudinal study

Hong-Hong Liu, Yunbo Xie, Bao-Peng Yang, Huan-Yue Wen, Peng-Hui Yang, Jin-E Lu, Yan Liu, Xi Chen, Meng-Meng Qu, Yang Zhang, Wei-Guo Hong, Yong-Gang Li, Junliang Fu & Fu-Sheng Wang

*Signal Transduction and Targeted Therapy* **9**, Article number: 129 (2024) | Cite this article

- Başlangıçta inaktif aşı ile aşılananlarda, booster protein aşı ile yapıldığında yanıt belirgin artıyor
- Yine de gençlerden düşük
- İlk doz sonrası ....Nötralizan antikor gelişimi 1.dozda %12,7 vs %38,4,

- Ek hastalık, ilaç kullanımları !!


International Journal of
*Molecular Sciences*

MDPI

*Article*

# Humoral and Cellular Immune Response Elicited by the BNT162b2 COVID-19 Vaccine Booster in Elderly

Daniela Dalla Gasperina [1], Giovanni Veronesi [2], Carlo M. Castelletti [3], Stefania Varchetta [4], Sabrina Ottolini [5], Dalila Mele [6], Giuseppe Ferrari [3], Amruth K. B. Shaik [7], Fabrizio Celesti [8], Francesco Dentali [9], Roberto S. Accolla [7] and Greta Forlani [7,*]

- Booster dozlar önemli
- Doğal enfeksiyon + aşı… daha uzun süreli hücresel ve humoral yanıt (kurtulabilenlerde ?!)

www.nature.com/scientificreports

**scientific** reports

Check for updates

OPEN

# Antibody response in elderly vaccinated four times with an mRNA anti-COVID-19 vaccine

Alexander Rouvinski[1,8], Ahuva Friedman[1,8], Saveliy Kirillov[1,2,8], Jordan Hannink Attal[3,4], Sujata Kumari[1,5], Jamal Fahoum[5], Reuven Wiener[5], Sophie Magen[6], Yevgeni Plotkin[7], Daniel Chemtob[3,4] & Herve Bercovier[1]


*** FDA… 22 Ağustos 2024…2024–2025 COVID-19 aşısı Moderna ve Pfizer-BioNTech (KP. 2 temelli ) …≥12 yaş

# COVID-19 Aşılaması ACIP Önerisi

**Table 1** Recommended Adult Immunization Schedule by Age Group, United States, 2025

| Vaccine | 19–26 years | 27–49 years | 50–64 years | ≥65 years |
|---|---|---|---|---|
| COVID-19 | 1 or more doses of 2024–2025 vaccine (See Notes) | | | 2 or more doses 2024-2025(See Notes) |
| Influenza live, attenuated (LAIV3) | 1 dose annually | | | |
| Respiratory Syncytial Virus (RSV) | Seasonal administration during pregnancy (See Notes) | | 60 through 74 years (See Notes) | ≥75 years |
| Tetanus, diphtheria, pertussis (Tdap or Td) | 1 dose Tdap each pregnancy; 1 dose Td/Tdap for wound management (See Notes) | | | |
| | 1 dose Tdap, then Td or Tdap booster every 10 years | | | |
| Measles, mumps, rubella (MMR) | 1 or 2 doses depending on indication (if born in 1957 or later) | | For healthcare personnel (See Notes) | |
| Varicella (VAR) | 2 doses (if born in 1980 or later) | 2 doses | | |
| Zoster recombinant (RZV) | 2 doses for immunocompromising conditions (See Notes) | 2 doses | | |
| Human papillomavirus (HPV) | 2 or 3 doses depending on age at initial vaccination or condition | 27 through 45 years | | |
| Pneumococcal (PCV15, PCV20, PCV21, PPSV23) | | See Notes | See Notes | |
| Hepatitis A (HepA) | 2, 3, or 4 doses depending on vaccine | | | |
| Hepatitis B (HepB) | 2, 3, or 4 doses depending on vaccine or condition | | | |
| Meningococcal A, C, W, Y (MenACWY) | 1 or 2 doses depending on indication (See Notes for booster recommendations) | | | |
| Meningococcal B (MenB) | 19 through 23 years | 2 or 3 doses depending on vaccine and indication (See Notes for booster recommendations) | | |
| *Haemophilus influenzae* type b (Hib) | 1 or 3 doses depending on indication | | | |
| Mpox | 2 doses | | | |
| Inactivated poliovirus (IPV) | Complete 3-dose series if incompletely vaccinated. Self-report of previous doses acceptable (See Notes) | | | |

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

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

Recommended vaccination based on shared clinical decision-making

No Guidance/ Not Applicable

DRAFT NOT APPROVED FOR PUBLIC DISTRIBUTION

- **Age 65 years or older:** administer an additional dose (dose 2) 6 months after dose 1 (minimum interval 2 months). If unvaccinated and receiving Novavax, administer 2-dose series as initial vaccination series, then dose 3 at least 6 months (minimum interval 2 months) after dose 2 using any 2024–25 COVID–19 vaccine (Moderna or Novavax or Pfizer–BioNTech).

*** Daha önceki aşılama durumuna göre 2 ya da daha fazla doz 2024-2025 aşısı (Moderna-Biontech-Novavax)**


# İnfluenza Bağışıklaması

- Yıllık İnfluenza bağışıklaması;

  Ağır hastalığın önlenmesi (hastane yatışı- mortalite)

  Uzun dönem etkilerin önlenmesi (MI, inme,...)

  Viral yayılımın önlenmesi

- Mevcut aşılar;

  inaktif / rekombinant/ Canlı atenüe (Inf A H1N1, H3N2 ve 2 ayrı influenza B suşu)

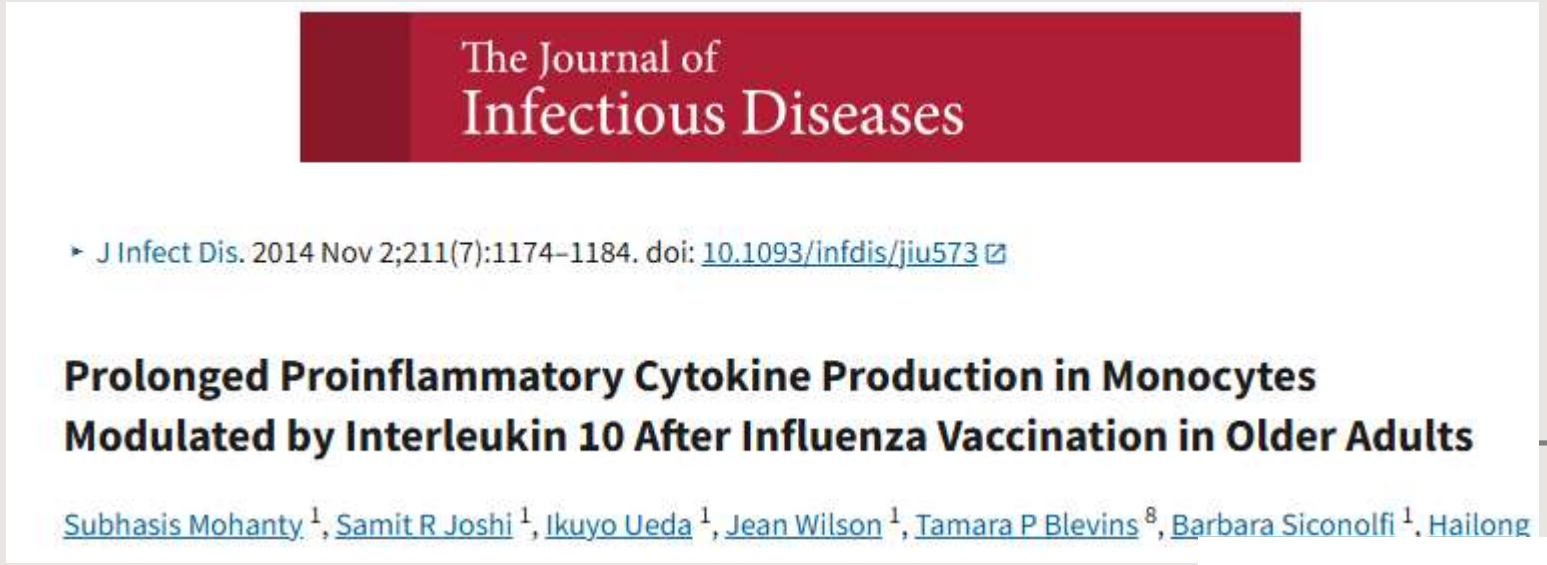
** HA ve NA antjenlerindeki çeşitliliğe bağlı aşı etkililiği değişken


- Genel olarak etkinlik antijenik çeşitliliğe bağlı olarak yaklaşık %60

  Gençlerde %70-90

  >65 yaş %30-50

- Hem inaktif hem de rekombinant aşılar için benzer!
- Canlı aşıların da ileri yaşta (immünokompromize?) güvenliliği tartışmalı



The Journal of Infectious Diseases

J Infect Dis. 2014 Nov 2;211(7):1174–1184. doi: 10.1093/infdis/jiu573

**Prolonged Proinflammatory Cytokine Production in Monocytes Modulated by Interleukin 10 After Influenza Vaccination in Older Adults**

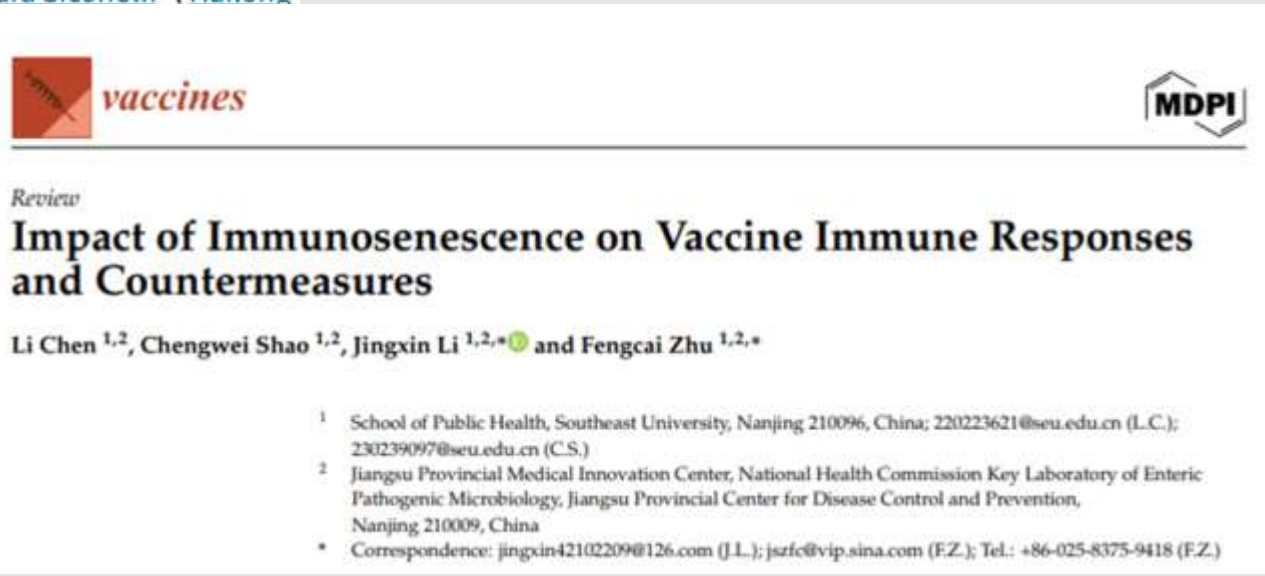
Subhasis Mohanty [1], Samit R Joshi [1], Ikuyo Ueda [1], Jean Wilson [1], Tamara P Blevins [8], Barbara Siconolfi [1], Hailong

** Aşı sonrası IL-6 ve TNF alfa aktivitesi yaşlılarda sınırlı (artmış IL-10???)

** Dörtlü aşı daha iyi yanıt ?!

(daha fazla antijen daha iyi yanıt)

** ETKİNLİĞİ ARTTIRMA STRATEJİLERİ



vaccines

MDPI

*Review*

**Impact of Immunosenescence on Vaccine Immune Responses and Countermeasures**

Li Chen [1,2], Chengwei Shao [1,2], Jingxin Li [1,2,*] and Fengcai Zhu [1,2,*]

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Agarwal *et al. Immunity & Ageing* (2018) 15:19
https://doi.org/10.1186/s12979-018-0124-9

Immunity & Ageing

RESEARCH Open Access

# Immune response to influenza vaccination in the elderly is altered by chronic medication use

Divyansh Agarwal[1], Kenneth E. Schmader[2], Andrew V. Kossenkov[3], Susan Doyle[2], Raj Kurupati[3] and Hildegund C. J. Ertl[3*]

- Kronik hastalıkların getirdiği yanıt azlığı
- Kronik ilaç kullanımı ???
- Uzun süreli metformin kullanımı ?  NSAID ? Statins?
- Ab üretiminde azalma, B-hücrelerde fenotipik değişiklikler, hücre dağılımlarında değişiklikler….


# İnfluenza Bağışıklaması

**Notes** Recommended Adult Immunization Schedule for Ages 19 Years or Older, United States, 2025

**Influenza vaccination**

- **Age 65 years or older:** Any one of high-dose inactivated influenza vaccine (HD-IIV3), recombinan influenza vaccine (RIV3), or adjuvanted inactivated influenza vaccine (aIIV3) is preferred. If none of these three vaccines is available, then any other age-appropriate influenza vaccine should be used.

65 yaş ve üzeri;

- Yüksek doz inaktif aşı
- Adjuvanlı inaktif aşı
- Rekombinant aşı

- Bunlar yoksa ulaşılabilen aşı yapılmalı !!!


# Pnömokok Aşılaması

- 50 yaş üzeri mortalite pnömokokkal enfeksiyonlarda yüksek ****
- Genellikle 65 yaş üzeri, kronik hastalık da olanlarda ağır hastalık riski ***
- Başlangıçta önerilen dual aşılama (konjuge + PSV)

EUROPEAN CLINICAL RESPIRATORY JOURNAL
2023, VOL. 10, 2168354
https://doi.org/10.1080/20018525.2023.2168354

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REVIEW ARTICLE

OPEN ACCESS

# Vaccine effectiveness of the pneumococcal polysaccharide and conjugated vaccines in elderly and high-risk populations in preventing invasive pneumococcal disease: a systematic search and meta-analysis

Melina Gade Sikjær[a,b*], Andreas Arnholdt Pedersen[a,b*], Mari Stenvold Wik[b], Synne Smith Stensholt[b], Ole Hilberg[a,b] and Anders Løkke[a,b]

[a]Department of Medicine, Lillebaelt Hospital, Vejle, Denmark; [b]Department of Regional Health Research, University of Southern Denmark, Odense, Vejle

- IPH önlemede her iki aşı da aşılanmayanlara göre etkili
- Tek başına PSV23 etkisi ?
- Konjuge aşı…. T-lenfosit yanıtları ve T h bağımlı B h yanıtları**
- PCV21 yanıtları????


CDC

Advisory Committee on Immunization Practices (ACIP)

EXPLORE TOPICS

SEARCH

SEPTEMBER 9, 2024

# GRADE: 20-valent pneumococcal conjugate vaccine (PCV20) for adults aged ≥65 years

The evidence type for use of PCV20 in adults aged ≥65 years was determined to be 2 (moderate certainty of evidence). The ACIP reviewed the results of both GRADE analysis and the Evidence to Recommendations (EtR) framework in June 2021. An updated EtR table was shared with the ACIP in September 2021. In October 2021, the ACIP recommended use of PCV20 for all adults aged ≥65 years who have not previously received a pneumococcal conjugate vaccine or whose previous vaccination history is unknown.

**Ekim 2021 itibariyle 65 yaş üzeri öneri *****


# Pnömokok Aşılaması

**Notes** Recommended Adult Immunization Schedule for Ages 19 Years or Older, United States, 2025

**Pneumococcal vaccination**

**Routine vaccination**

- **Age 50 years or older who have:**
  - **Not previously received a dose of PCV13, PCV15, PCV20, or PCV21 or whose previous vaccination history is unknown:** 1 dose PCV15 or 1 dose PCV20 or 1 dose PCV21.
    - If PCV15 is used, administer 1 dose PPSV23 at least 1 year after the PCV15 dose (may use minimum interval of 8 weeks for adults with an immunocompromising condition,* cochlear implant, or cerebrospinal fluid leak).

- **Previously received only PCV13:** 1 dose PCV20 or 1 dose PCV21at least 1 year after the last PCV13 dose.
- **Previously received only PPSV23:** 1 dose PCV15 or 1 dose PCV20 or 1 dose PCV21. Administer either PCV15 or PCV20 or PCV21 at least 1 year after the last PPSV23 dose.

- **Previously received both PCV13 and PPSV23, AND PPSV23 was received at age 65 years or older:** Based on shared clinical decision-making, 1 dose of PCV20 or 1 dose of PCV21 at least 5 years after the last pneumococcal vaccine dose.


# Zoster Aşısı ( Zona aşılaması)

## Yaşlanan bağışıklık sistemi latent VZV'nin reaktivasyonuna neden olur

- İmmün yaşlanma, hümoral ve hücre aracılı bağışıklığın azalmasına neden olur
- İmmün yaşlanmanın özellikleri:
  - Düzensiz sitokin üretimi
  - Birikmiş lenf nodu fibrozisi
  - Lenfosit disfonksiyonu

- İmmün yaşlanma viral ve bakteriyel infeksiyonların artan şiddeti/sekeli ile ilişkili
  - Yaşa bağlı komorbiditeler zona komplikasyon riskini artırır
- Hücre aracılı bağışıklığı azaltan durumlar (lenfoproliferatif hastalık, HIV infeksiyonu vb), aynı yaştaki kişilere göre 20-100 kat daha fazla risk artırır.

Crooke SN, et al. Immun Aging. 2019;16:25.
Saguil A, et al. Am Fam Physician. 2017;96:656-63


# Zoster Aşısı ( Zona aşılaması)

**2 farklı aşı;

1. Canlı atenüe zoster aşısı (ZVL)

Etkinliği yaş ileledikçe daha düşük

50–60 yaş arası 69.8%; > 60 yaş 65.5%; > 70 yaş 55.4%

2. Rekombinant zoster aşısı (RZV, Shingrix)

**Akut zona ataklarının önlenmesinde ve post herpetik nevraljide etkinliği 80 yaş grubunda dahi 90%

**Uzun dönem etki (8 yıl) %83


# Zoster Aşısı ( Zona aşılaması)

- T hücre aracılı ve humoral yanıt **(50–59, 60–69, ve ≥70 yaş),
- 2 doz sonrası uzun süreli yanıt
- Ancak ilk aşılanma yaşı önemli** Ne kadar erken o kadar iyi yanıt*
- 70 yaş üzerinde antikor üretimi ve t hücre yanıtları daha düşük


*vaccines*

MDPI

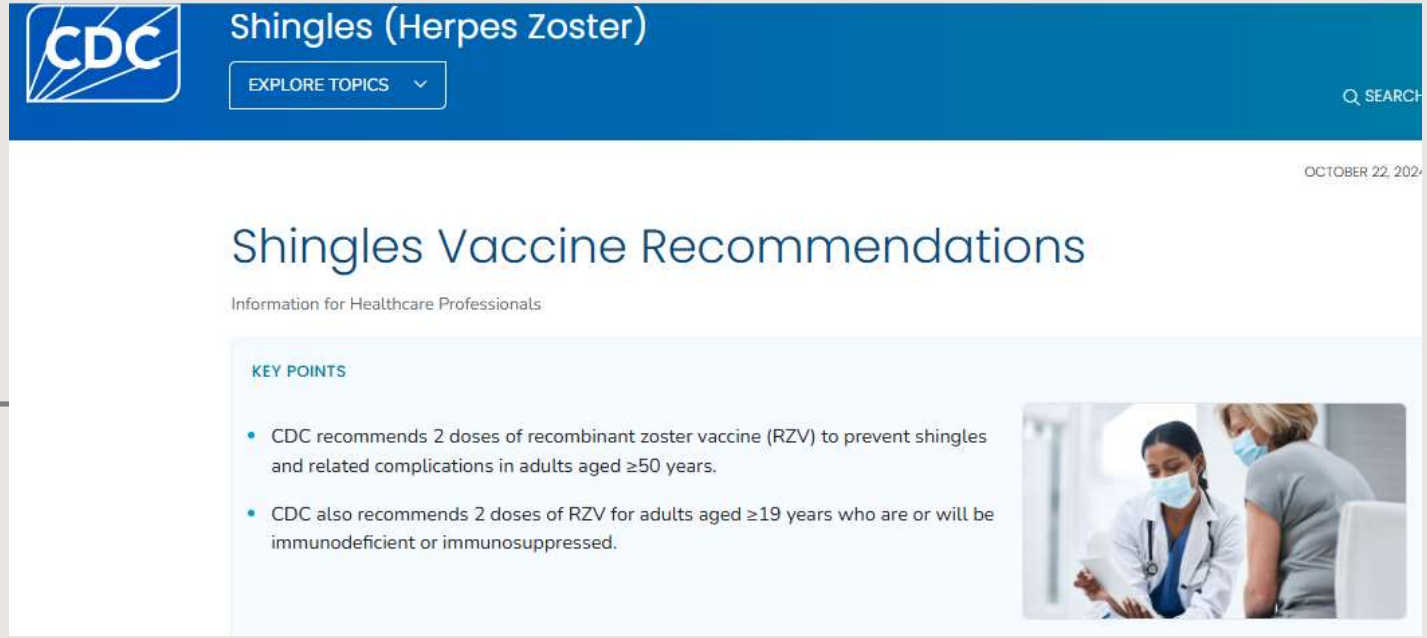
*Review*

# Impact of Immunosenescence on Vaccine Immune Responses and Countermeasures

Li Chen [1,2], Chengwei Shao [1,2], Jingxin Li [1,2,*] and Fengcai Zhu [1,2,*]

**Table 2.** Comparative Analysis of Two Herpes Zoster Prophylactic Modalities: Live Attenuated (ZVL) versus Subunit Vaccine (RZV).

| Characteristics | ZVL | RZV |
|---|---|---|
| Vaccine Efficacy % (95% CI) | | |
| 50–59 years | 69.8 (54.1–80.6) [67] | 96.6 (89.6–99.3) [72] |
| 60–69 years | 65.5 (51.5–75.5) [66] | 97.4 (90.1–99.7) [72] |
| ≥70 years | 55.4 (39.9–66.9) [66] | 97.9 (87.9–100.0) [72] |
| Long-term Efficacy% (95% CI) | | |
| Year 1 | 68.7 (66.3–70.9) [68] or 67.5 (65.4–69.5) [69] | 97.7 (93.1–99.5) [73] |
| Year 2 | 47.2 (44.1–50.1) [69] | 92.7 (86.2–96.6) [73] |
| Year 3 | 39.1 (33.8–43.9) [68] | 92.4 (85.0–96.6) [73] |
| Year 6 | 32.9 (23.1–41.5) [68] | 84.9 (70.4–93.1) [73] |
| Year 7 | 16.5 (1.4–29.3) [68] | 85.3 (71.3–93.3) [73] |
| Year 8 | 4.2 (−24.0 to 25.9) [68] or 31.8 (15.1–45.2) [69] | 84.1 (64.4–94.0) [73] |


>50 yaş, 2-6 ay ara ile 2 doz rekombinant aşı**

•Daha önce Zona öyküsü olsun olmasın !!!

•Daha önce Zostavax öyküsü olsa da yapılması öneriliyor

•Varicella serolojisi bakılması önerilmiyor


# RSV Aşılaması

## June 2024 ACIP Recommendations for RSV Vaccination in Older Adults:

**ACIP recommends all adults aged ≥75 years and adults aged 60–74 years who are at increased risk of severe RSV disease receive a single dose of RSV vaccine.[1,2]**

1. Recommendation is for any Food and Drug Administration–approved RSV vaccine (Arexvy [GSK]; Abrysvo [Pfizer]; or mResvia [Moderna]). There is no product preference.
2. Eligible adults are currently recommended to receive a single dose of RSV vaccine; adu already received RSV vaccination should not receive another dose.

://www.cdc.gov/mmwr/volumes/73/wr/mm7332e1.htm?s_cid=mm7332e1_w

## Current FDA-approved RSV vaccines

- **Protein subunit (based on RSV F protein in prefusion conformation)**
  - GSK Arexvy[1]: monovalent RSV-A, $AS01_E$ adjuvant
  - Pfizer Abrysvo[2]: bivalent RSV-A/RSV-B, no adjuvant
- **Messenger RNA (mRNA, encoding RSV F protein in prefusion conformation)**
  - Moderna mResvia[3]: monovalent RSV-A, no adjuvant


# RSV Aşılaması

vaccines

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Review

## Impact of Immunosenescence on Vaccine Immune Responses and Countermeasures

Li Chen [1,2], Chengwei Shao [1,2], Jingxin Li [1,2,*] and Fengcai Zhu [1,2,*]

- Gençler ile belirgin aşı yanıtı farkı yok
- Hümoral yanıt (nötralizan antikor yanıtı) bir miktar azalmış,
- Ancak T hücre yanıtları 70 yaş üzerinde de benzer....


# Teşekkürler...