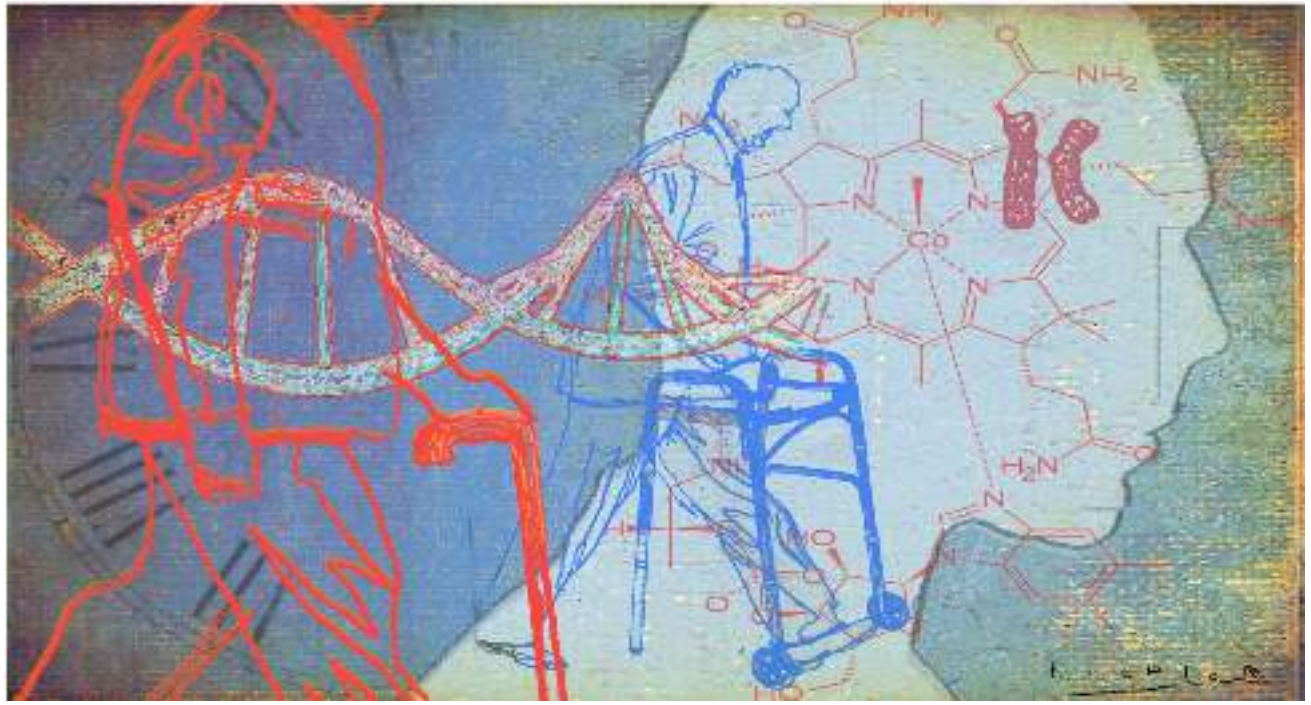


HIV ve Yaşlanma

Dr Özlem Altuntaş Aydın

Başakşehir Çam ve Sakura Şehir SUAM

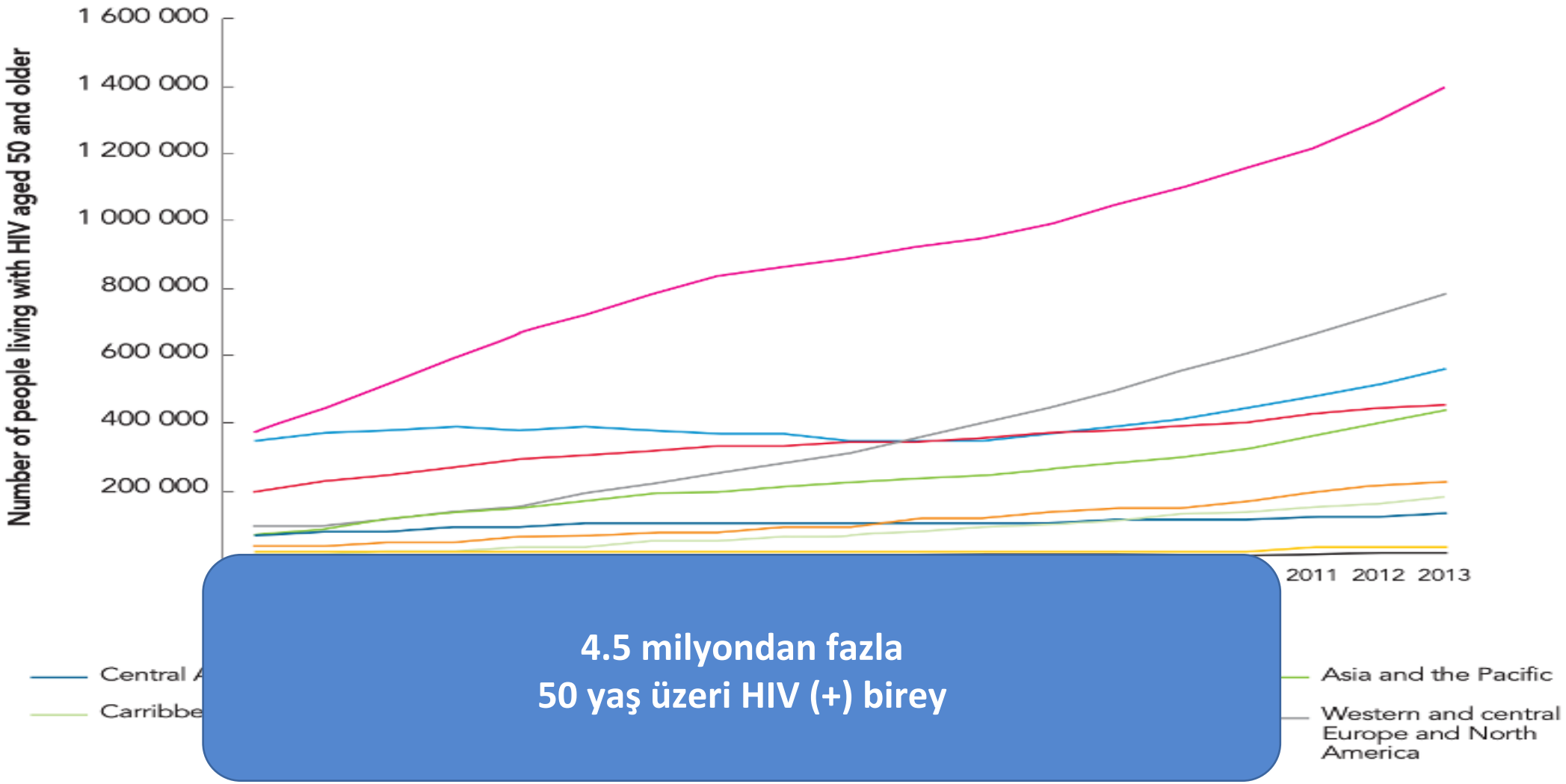
03.09.2021

Yaşlılık

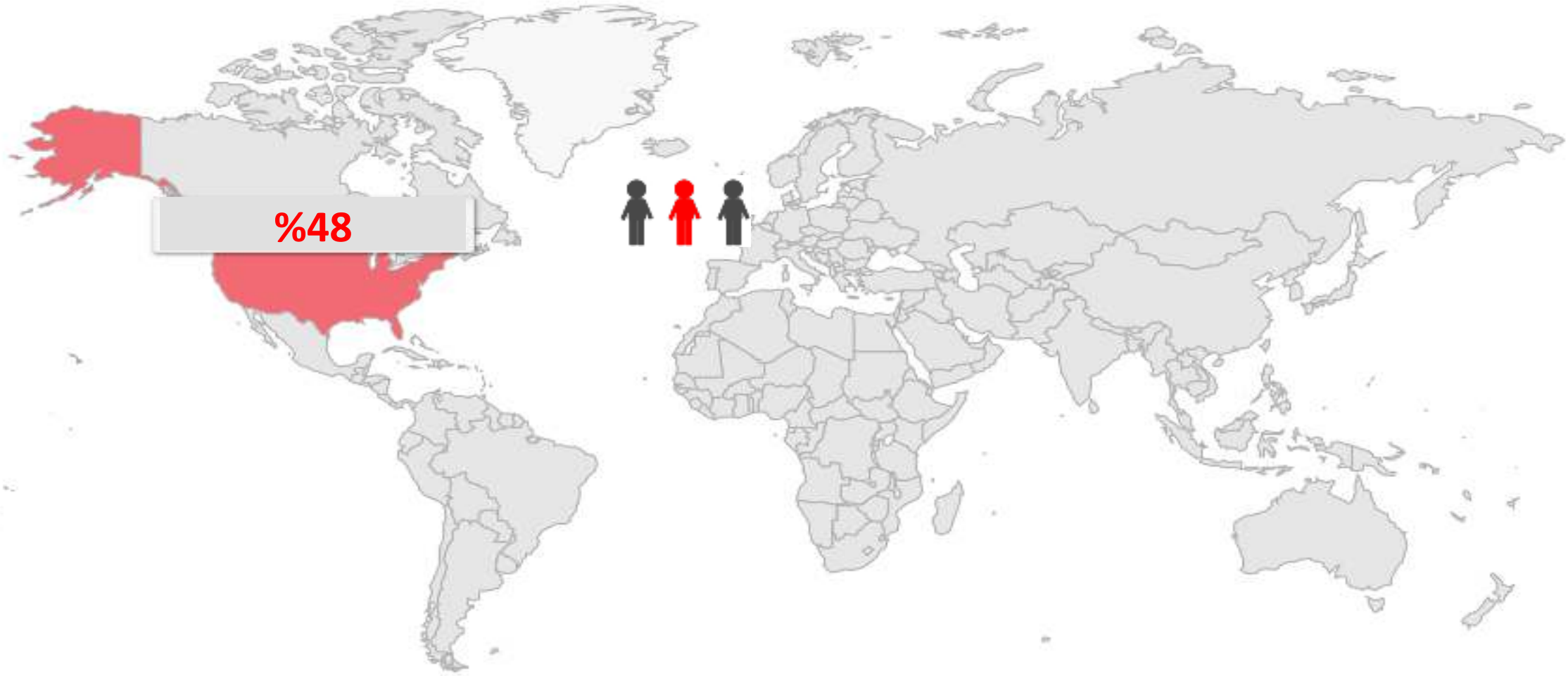
«Düşkünlük» dönemi mi?

Daha uzun yaşam mı?

Estimated number of people living with HIV aged 50 and older by region, 1995–2013

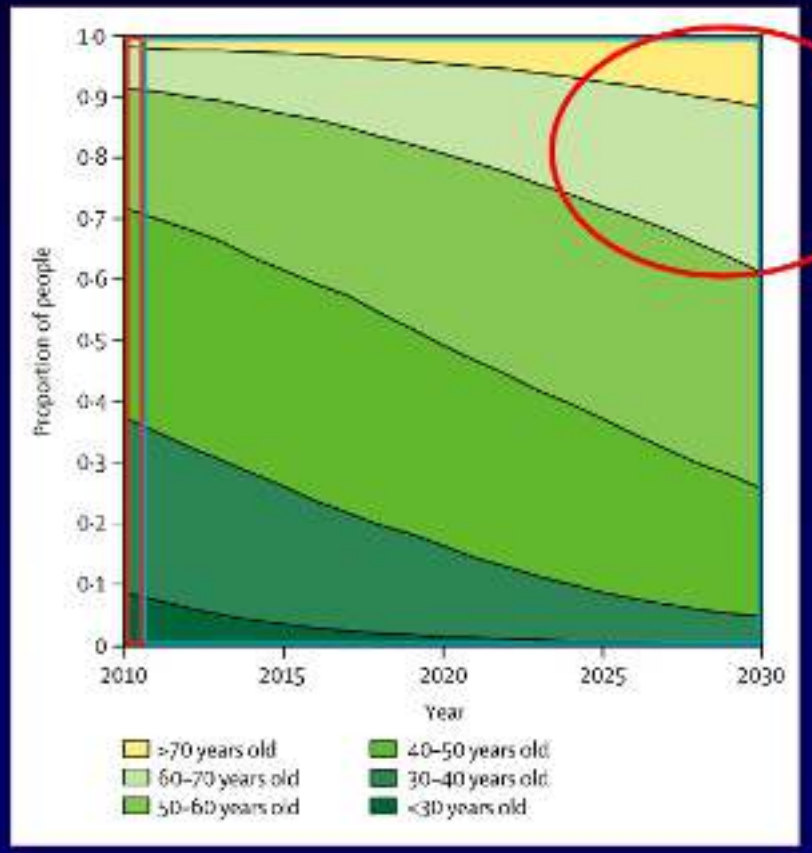


4.5 milyondan fazla
50 yaş üzeri HIV (+) birey



Yeni tanı alan 50 yaş ve üzeri olgular
2006 yılında 1/11
2015 yılında 1/6

Tsunami: projected age distribution of PLWH by 2030



2015

2010- 30% older than 50 and 8% older than 60

2015- 50% older than 50

2030- 75% older than 50 (2.5x increase) and 40% older than 60 (5x increase)

Smit K Lancet Inf Dis

JF

Achieving the fourth 90: healthy aging for people living with HIV

Tiffany G. Harris, Miriam Rabkin and Wafaa M. El-Sadr

AIDS 2018, **32**:1563–1569

Keywords: aging, chronic disease, comorbidity, frailty, HIV, multimorbidity, social support

The availability of potent antiretroviral therapy (ART) has transformed the HIV epidemic, changing HIV disease

HIV among older PLWH and highlight the need for further research to better understand the interaction

HIV ile yaşayan yaşlı birey (PLWH)

- **Hayatının yaşlı döneminde HIV enfeksiyonu tanısı almış kişi**

Hekimlerce risk grubu olarak görülmüyorlar. HIV enfeksiyonu nedenli semptomların (kilo kaybı, halsizlik vb) yaşlanmaya bağlı olduğu düşünülerek test istenmiyor

50 yaş üstü kişilerin %5'den azı kendisi test yaptırıyor, yaş arttıkça test yaptırma oranı azalıyor

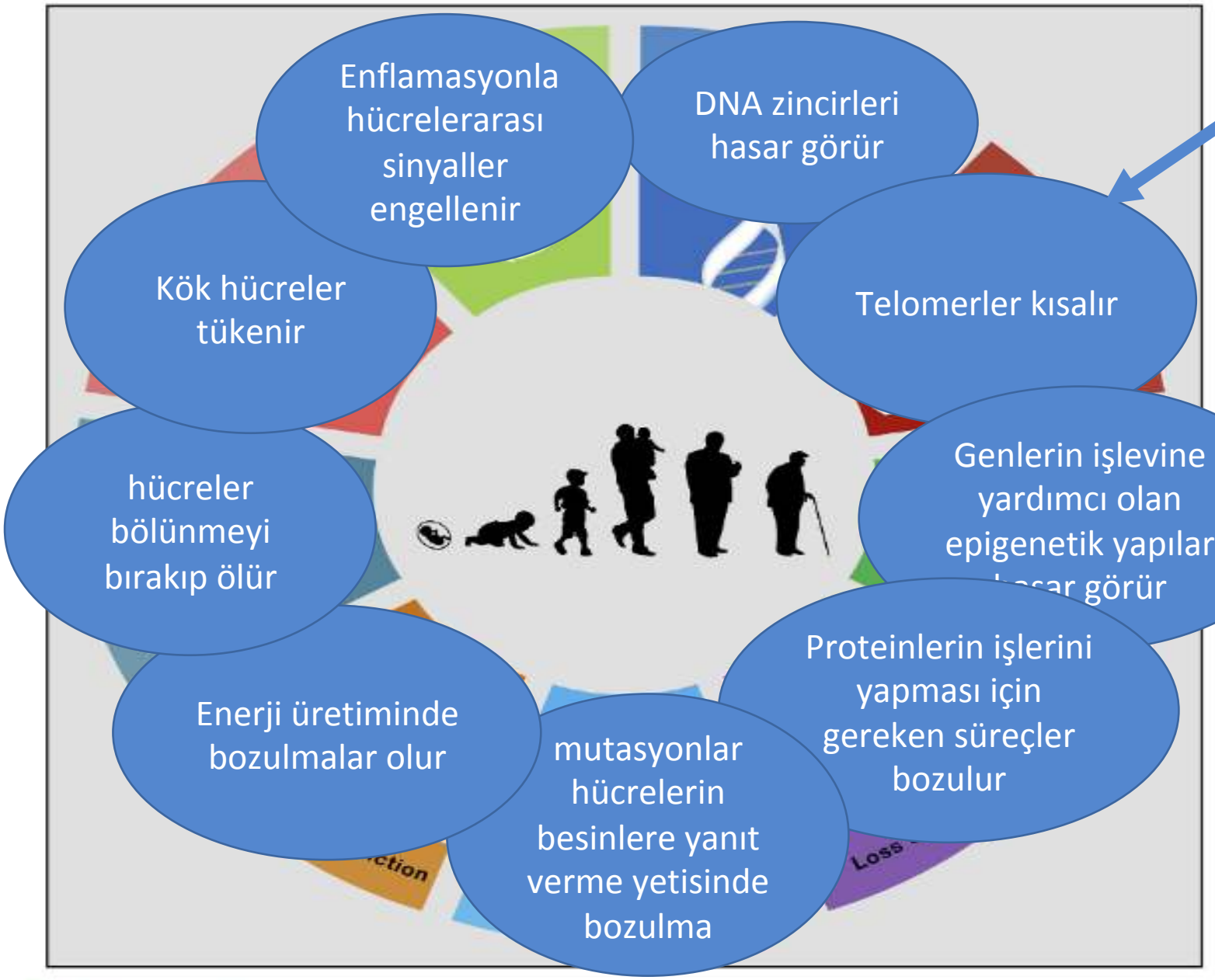
HIV bulaşında gençlerle aynı risklere sahipler. Eş kayıpları fazla, yeni partnerler ediniyorlar

Atrofik vajinit! Gebelik riski yok, erektil disfonk ilaçları, kondom kullanmama

Aileleri, arkadaşları tarafından, işyerinde damgalanma, işlerini kaybetme endişeleri var. HIV ile enfekte olduklarını açıklamaktan ve tedavi almaktan korkuyorlar

Tanı aldıklarında daha geç evrede oluyorlar. ART'ye daha geç başlanıyor

- **HIV enfeksiyonu ile birlikte yaşayıp yaşlanan kişi**



Kromozomların son kısımlarını yıkım ve füzyon gibi olaylardan korur. Hücrenin her bölünmesinde tamir edilmezse kısalır. Belli bir kısalığa ulaşınca hücre çoğalması durur, yaşlanma mekanizmaları tetiklenir. Telomer boyu hücresel yaşlanma indeksi olarak tanımlanır (KVS hast, demans, yaşlanma)

Figure 1. The Hallmarks of Aging
The scheme enumerates the nine hallmarks described in this Review: genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication.

J Infect Dis. 2013 Apr;207(7):1157-65. doi: 10.1093/infdis/jit006. Epub 2013 Jan 9.

Inhibition of telomerase activity by human immunodeficiency virus (HIV) nucleos(t)ide reverse transcriptase inhibitors: a potential factor contributing to HIV-associated accelerated aging.

Leeansyah E[1], Cameron PU, Solomon A, Tennakoon S, Velayudham P, Gouillou M, Spelman T, Hearps A, Fairley C, Smit de V, Pierce AB, Armishaw J, Crowe SM, Cooper DA, Koelsch KK, Liu JP, Chuah J, Lewin SR.

Author information

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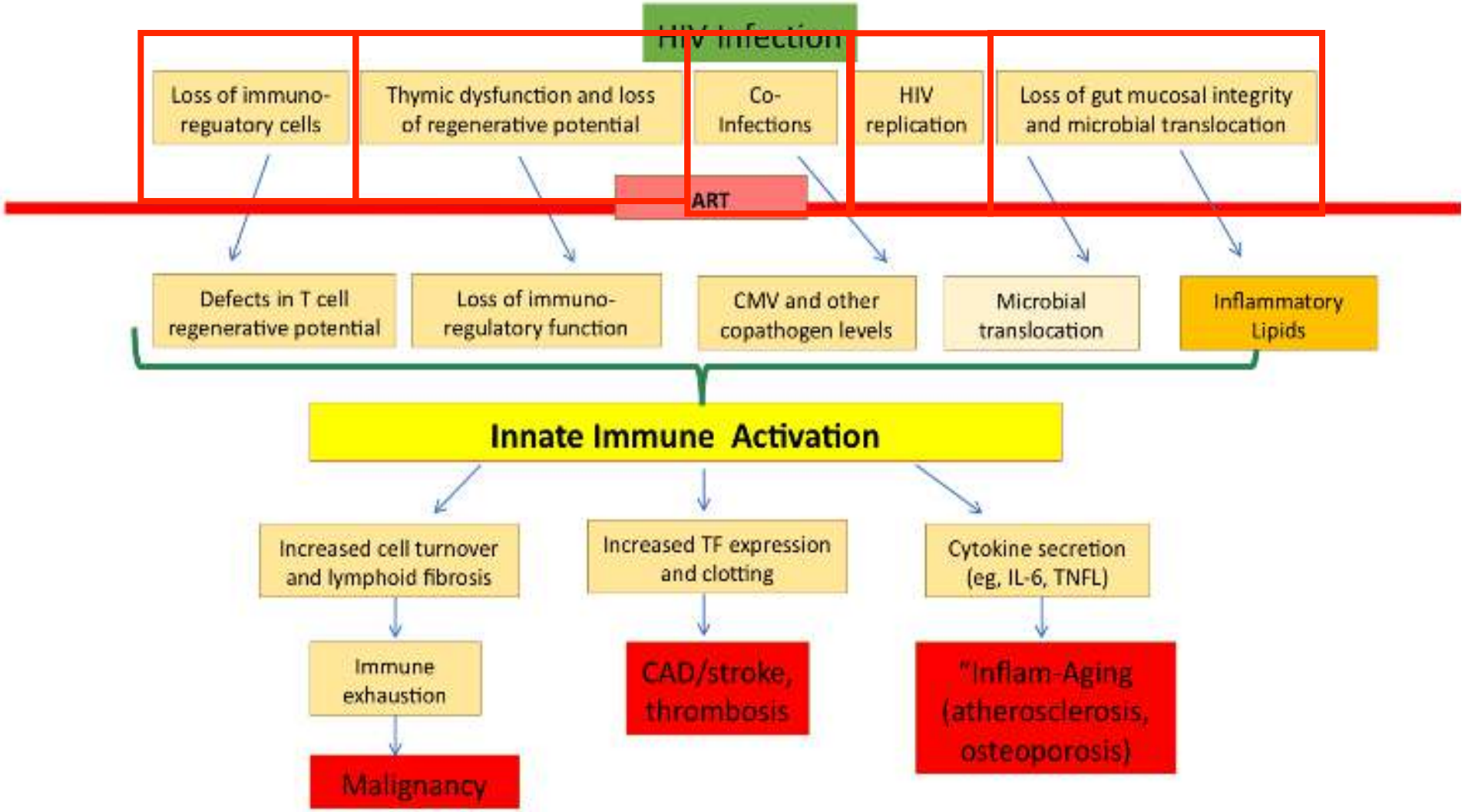
Telomerler telomeraz ile tamir edilir
Telomeraz bir «reverse transcriptase» enzimidir

İnvitro 3TC, ABC, FTC, TDF telomerazı belirgin şekilde inhibe etmekte

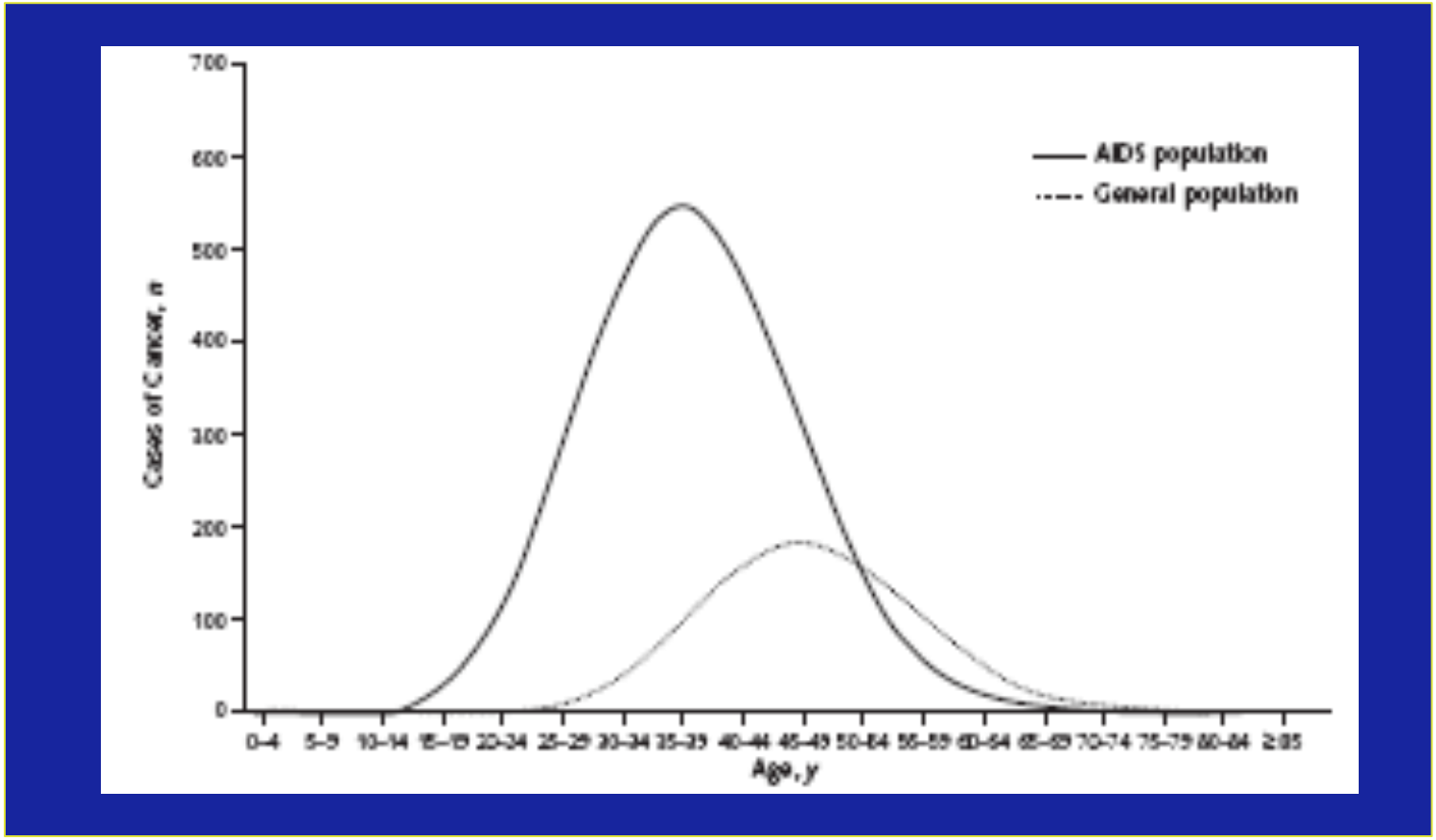
NRTI içeren ART alan HIV pozitif kişilerin telomeraz aktivitesi
- HIV negatif ve
- NRTI içermeyen ART alan HIV pozitif kişilerden önemli ölçüde daha düşük

Bu durum yaşla ve NRTI'nin toplam kullanım süresiyle ilişkili



Deeks SG. 2001. Annu Rev Med, 62:141-55
Appay V, et al. J Pathol. 2008;214:231-241
Lederman ML, et al. Adv Immunol. 2013;119:51-83

Daha sık ve daha erken dönemde



Shiels MS. Ann Intern Med 2010

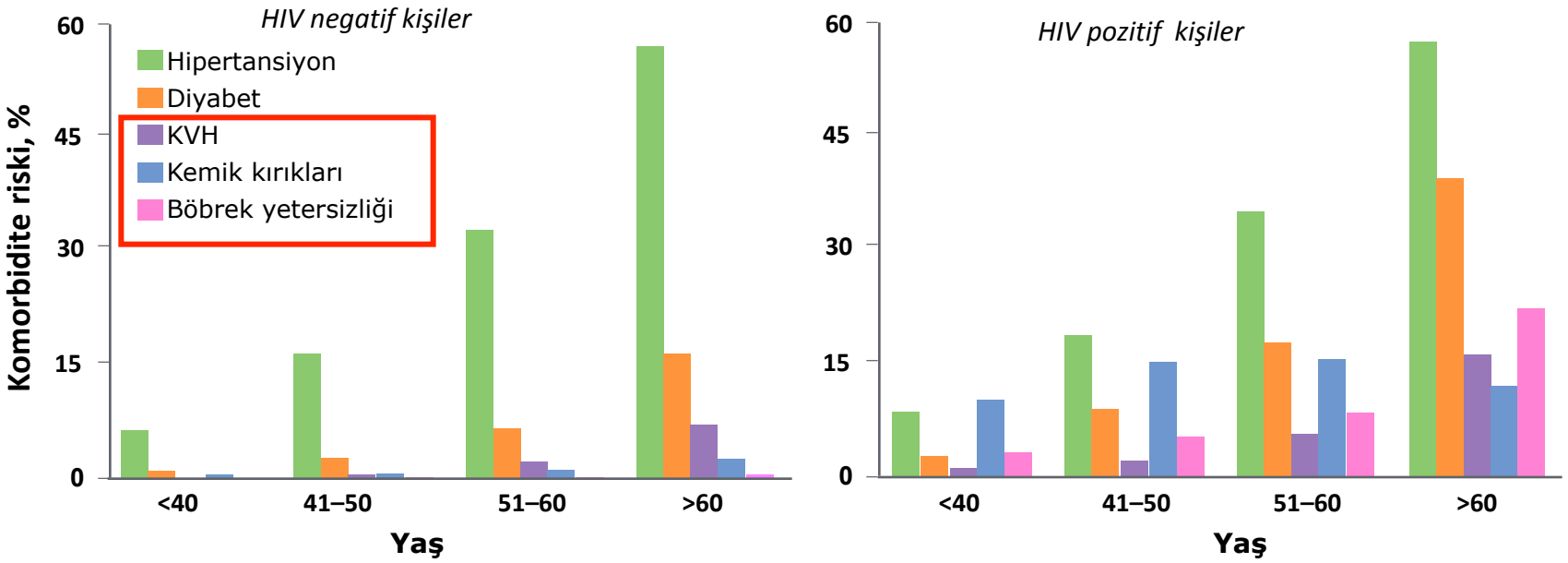
Clin Infect Dis. 2011 Dec;53(11):1120-6. doi: 10.1093/cid/cir627. Epub 2011 Oct 13.

Premature age-related comorbidities among HIV-infected persons compared with the general population.

Guaraldi G[1], Orlando G, Zona S, Menozzi M, Carli F, Garlassi E, Berti A, Rossi E, Roverato A, Palella F.

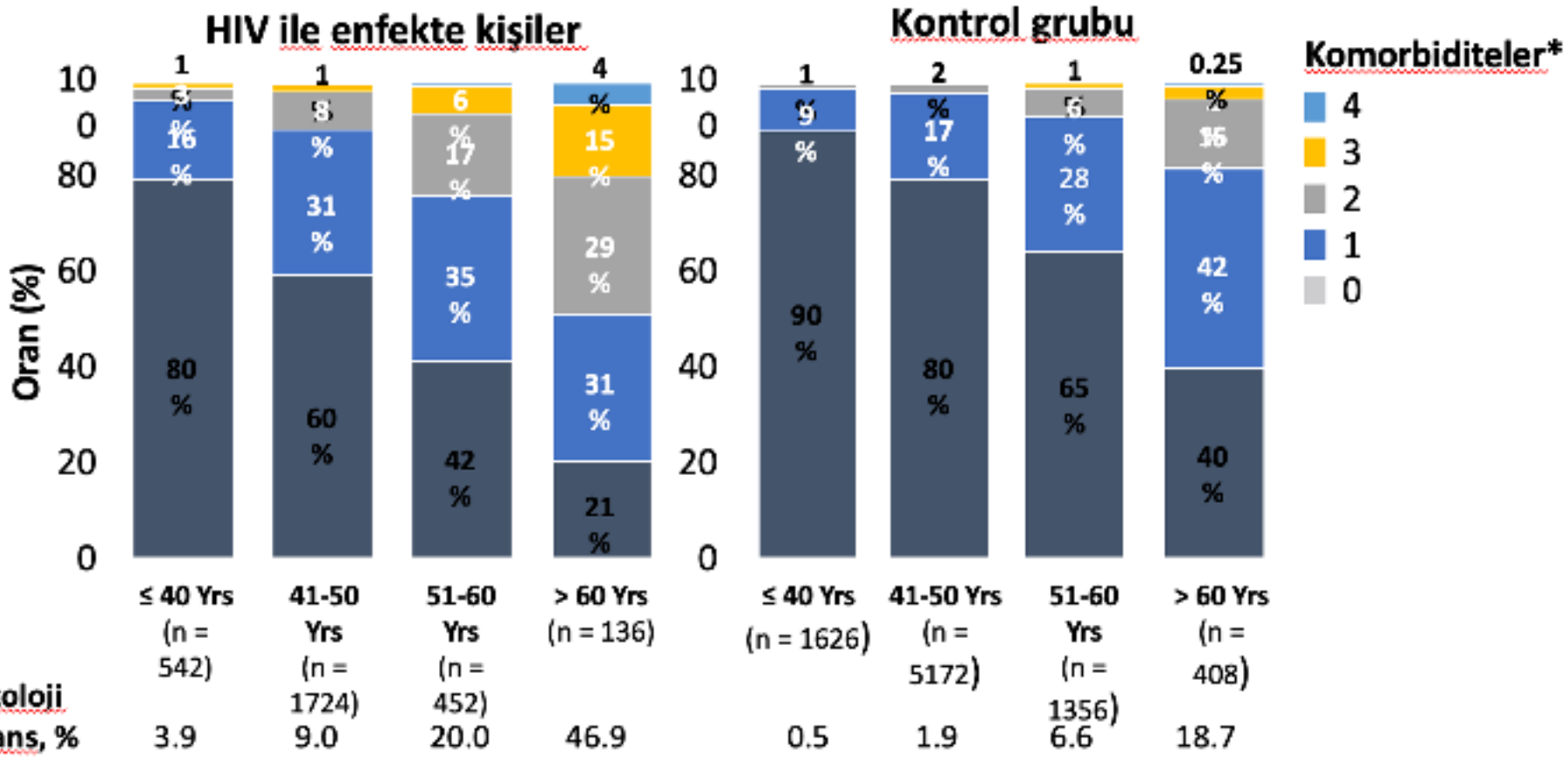
2.854 HIV pozitif - 8.562 HIV negatif kişinin olduğu kohort

HIV serolojisi ve yaşa göre komorbiditelerin prevalansı, 2009



- HIV enfekte bireyler, HIV negatif kişilere kıyasla kardiyovasküler hastalık, kemik kırıkları ve böbrek yetmezliği gelişimine daha duyarlıdır
- Bu komorbiditeler HIV enfekte hastalarda **daha erken** gelişir

Komorbiditeler



*Includes evaluation of HTN, diabetes, hypothyroidism, CVD, and bone fracture.

Guaraldi. Clin Infect Dis. 2011;53:1120.

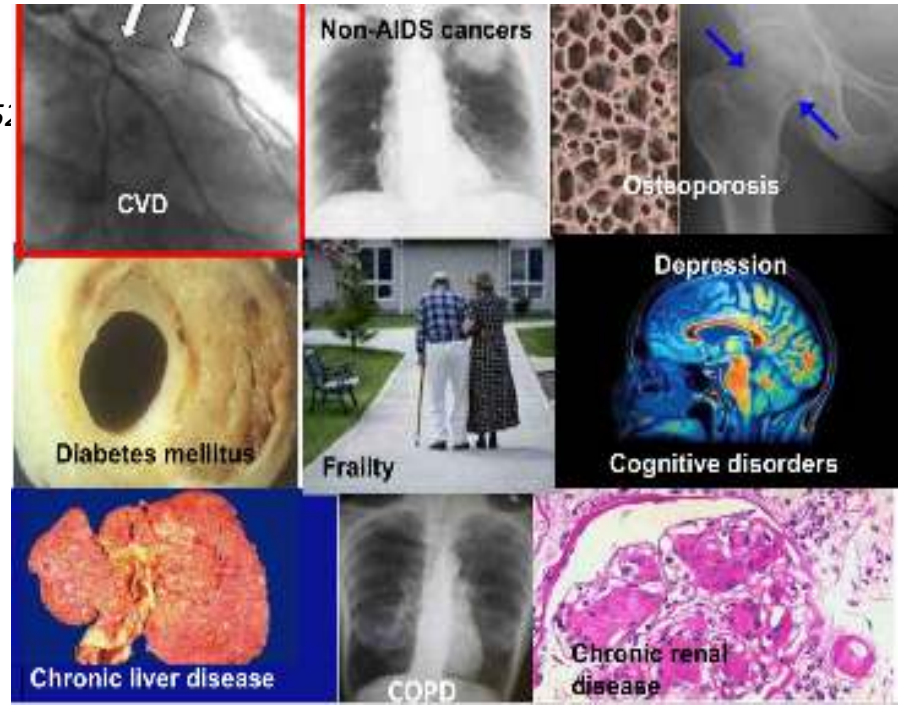
Slide credit: clinicaloptions.com

2003-2013 ABD'de 60 000'den fazla PLWH

1. Hipertansiyon %31-76
2. Hiperlipidemi %22-50
3. Endokrin hastalıklar %22-54

10 yıllık periyotta komorbiditelerde artış !!

Gallant J, et al. J Infect Dis. 2017;216(12):15



HIV enfeksiyonunun uzun dönem sonuçları

- **Erken yaşlanma**
- KVS hastalıklar
- Renal hastalıklar
- AIDS ilişkisiz kanserler
- Osteoporoz
- Kırılganlık
- Nörokognitif fonksiyonlarda azalma

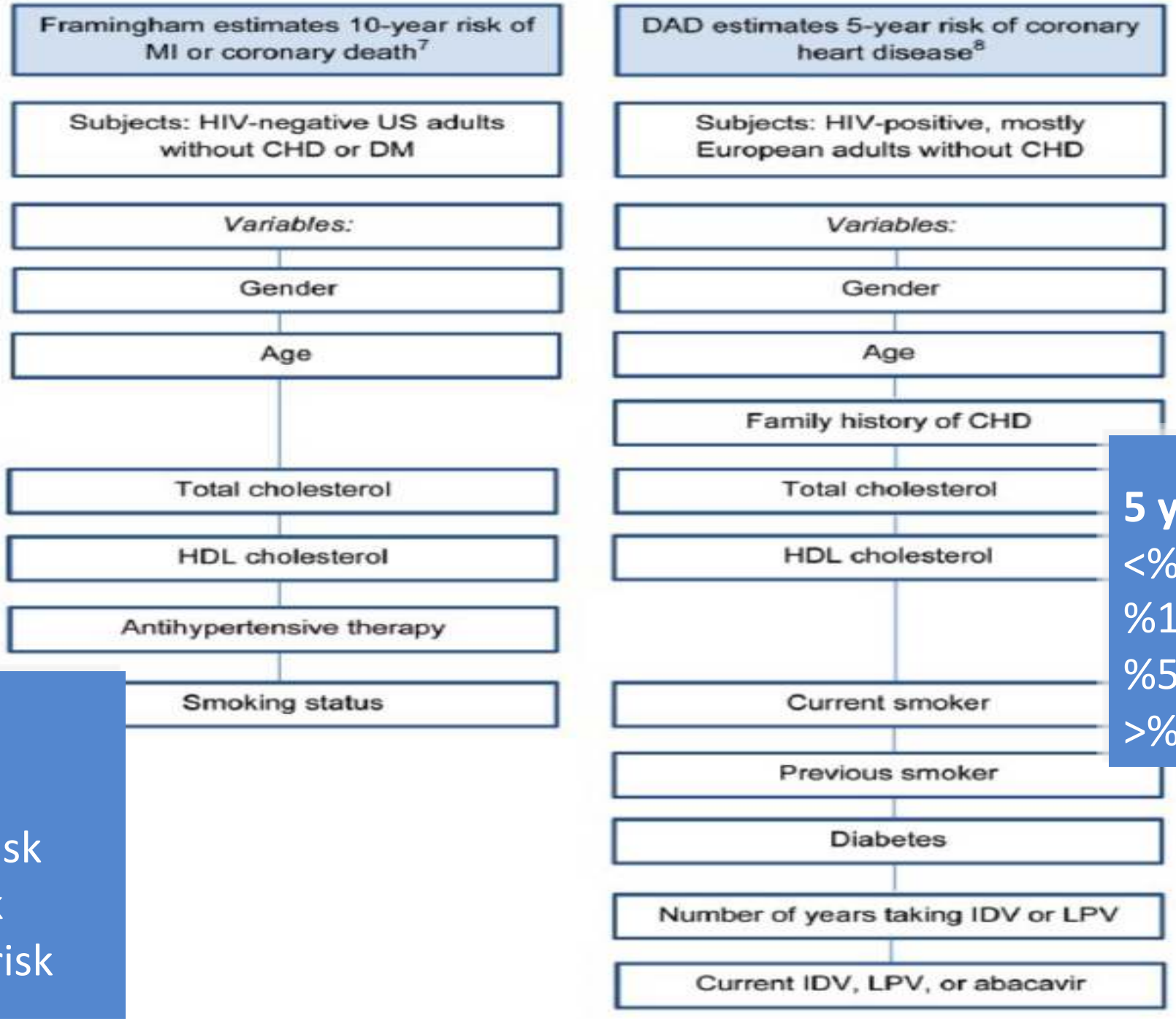
Kardiyovasküler sistem

50 yaş üstü

Glukoz intoleransı
DM
Dislipidemi
Ateroskleroz

Sigara
Alkol
Madde kull
Beslenme bozukluğu
Kilo artışı

Savès M, et al.Clin Infect Dis. 2003;37(2):292
Berry SA, et al. J Acquir Immune Defic Syndr. 2012 Apr;59(4):368-75



10 yılık risk

<%10: Düşük risk
%10-20: Orta risk
>%20: Yüksek risk

5 yıllık risk

<%1: Düşük risk
%1-5: Orta risk
%5-10: Yüksek risk
>%10: Çok yüksek risk

Clin Infect Dis. 2015 Feb 15;60(4):627-38. doi: 10.1093/cid/ciu869. Epub 2014 Oct 30.

Comparison of risk and age at diagnosis of myocardial infarction, end-stage renal disease, and non-AIDS-defining cancer in HIV-infected versus uninfected adults.

Althoff KN[1], McGinnis KA[2], Wyatt CM[3], Freiberg MS[4], Gilbert C[5], Oursler KK[6], Rimland D[7], Rodriguez-Barradas MC[8], Dubrow R[9], Park LS[9], Skanderson M[9], Shiels MS[10], Gange SJ[1], Gebo KA[1], Justice AC[9]; Veterans Aging Cohort Study (VACS).

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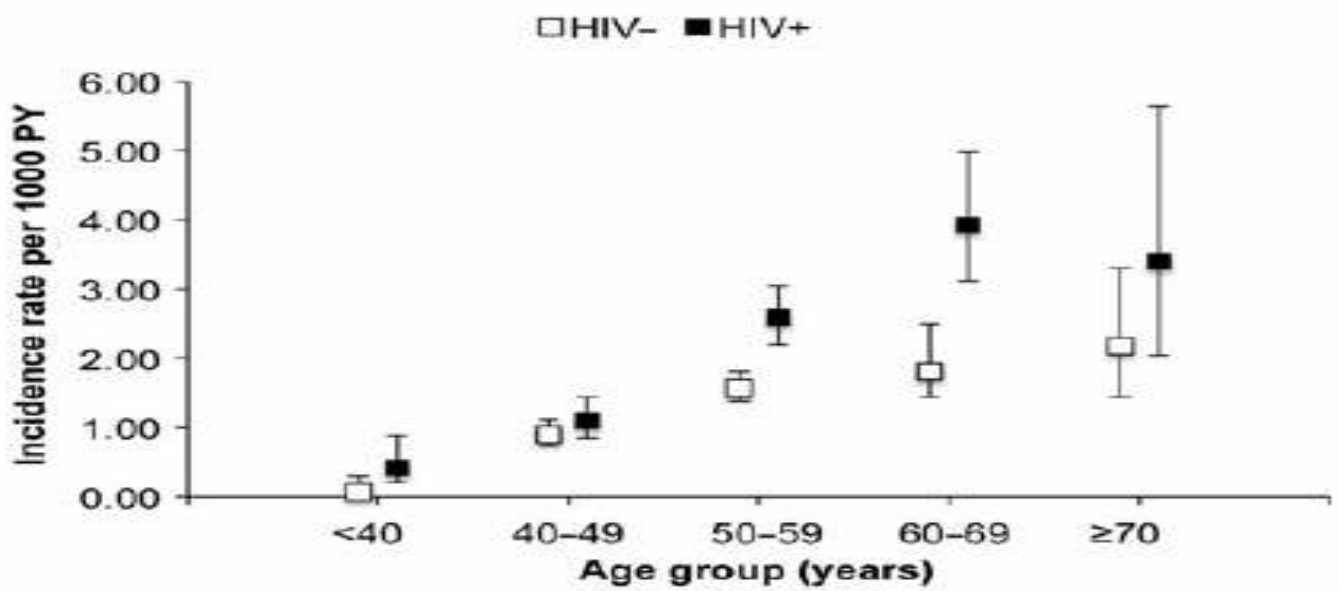
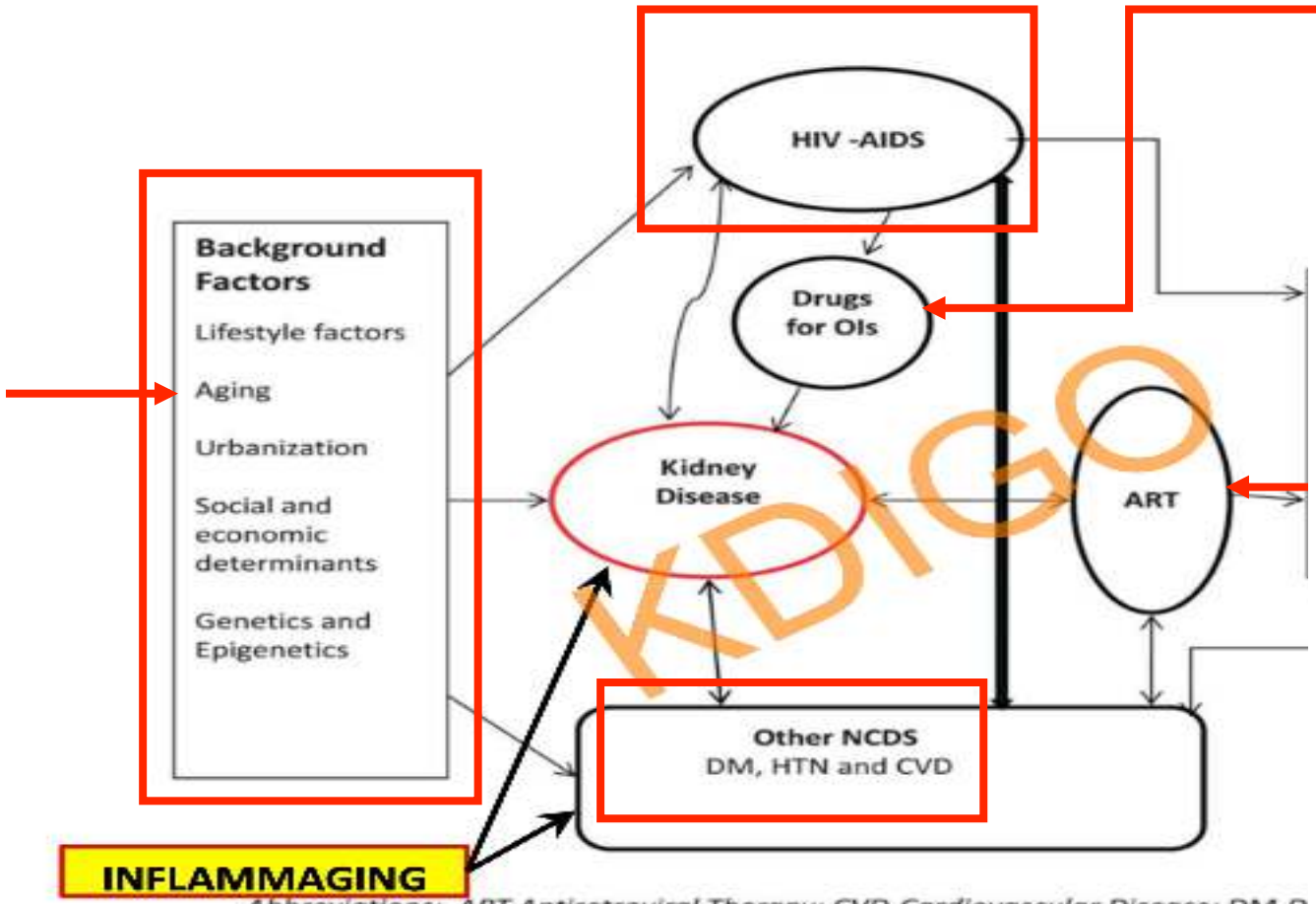
A Myocardial infarction

	# of MI events	PY	IR per 1000 PY	95% CI
HIV–	398	310138	1.28	1.16,1.42
HIV+	291	143844	2.02	1.80,2.27



Renal hastalıklar

Asiklovir
TMP-SMX



Kalyesubula R, Acquir Immune defic Synd. [sup] 2016

Table 1 | HAART-associated kidney disease

Renal syndrome	Medication
Acute kidney injury	
Toxic acute tubular necrosis	Tenofovir, ritonavir, didanosine
Acute interstitial nephritis	Atazanavir, abacavir, indinavir
Crystal nephropathy	Indinavir, atazanavir
Tubulopathies	
Fanconi's syndrome	Tenofovir, didanosine, ritonavir
Renal tubular acidosis	Lamivudine, stavudine
Nephrogenic diabetes insipidus	Tenofovir, didanosine, indinavir
Nephrolithiasis	Indinavir, atazanavir, nelfinavir, amprenavir, saquinavir, efavirenz
Chronic kidney disease	
Chronic interstitial nephritis	Indinavir, tenofovir
Post-AKI kidney disease	Several HAART drugs

Clin Infect Dis. 2015 Feb 15;60(4):627-38. doi: 10.1093/cid/ciu869. Epub 2014 Oct 30.

Comparison of risk and age at diagnosis of myocardial infarction, end-stage renal disease, and non-AIDS-defining cancer in HIV-infected versus uninfected adults.

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Author information

Abstract

BACKGROUND: Altho
associated events, it re
uninfected adults. The
diseases in HIV-infecte

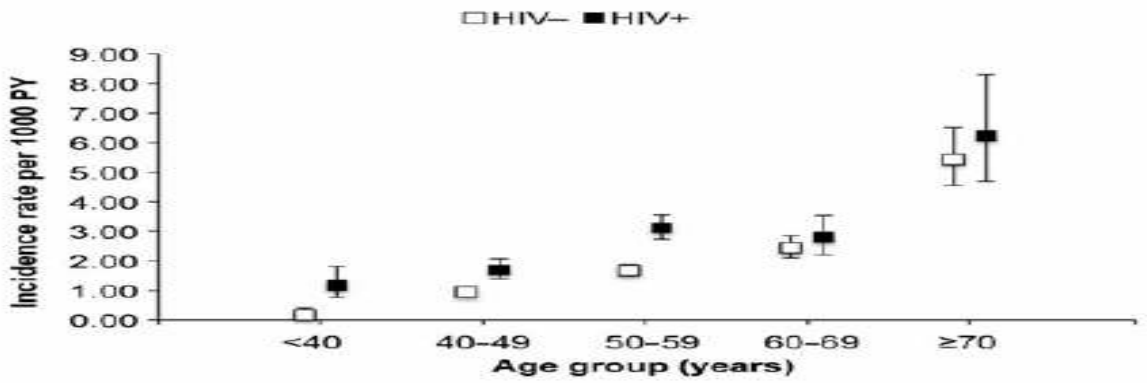
METHODS: The study
uninfected veterans, fr
stage renal disease (E
were estimated using r

RESULTS: A total of 9
and 4179 NADC incide
and NADC (adjusted r
with ESRD at an avera
years). HIV-infected ad
confounders.

CONCLUSIONS: HIV-i
without HIV.

B End-stage renal disease

	# of ESRD events	PY	IR per 1000 PY	95% CI
HIV–	688	408 686	1.68	1.56,1.81
HIV+	447	174 492	2.56	2.33,2.81



t greater risk for aging-
infected compared with
sis of 3 age-associated

d demographically matched
ocardial infarction (MI), end-
, diagnosis by HIV status
ly.

rs and 689 MI, 1135 ESRD,
val [CI], -.59 to .37 years)
cted adults were diagnosed
[95% CI, -.86 to -.07]
ting for important

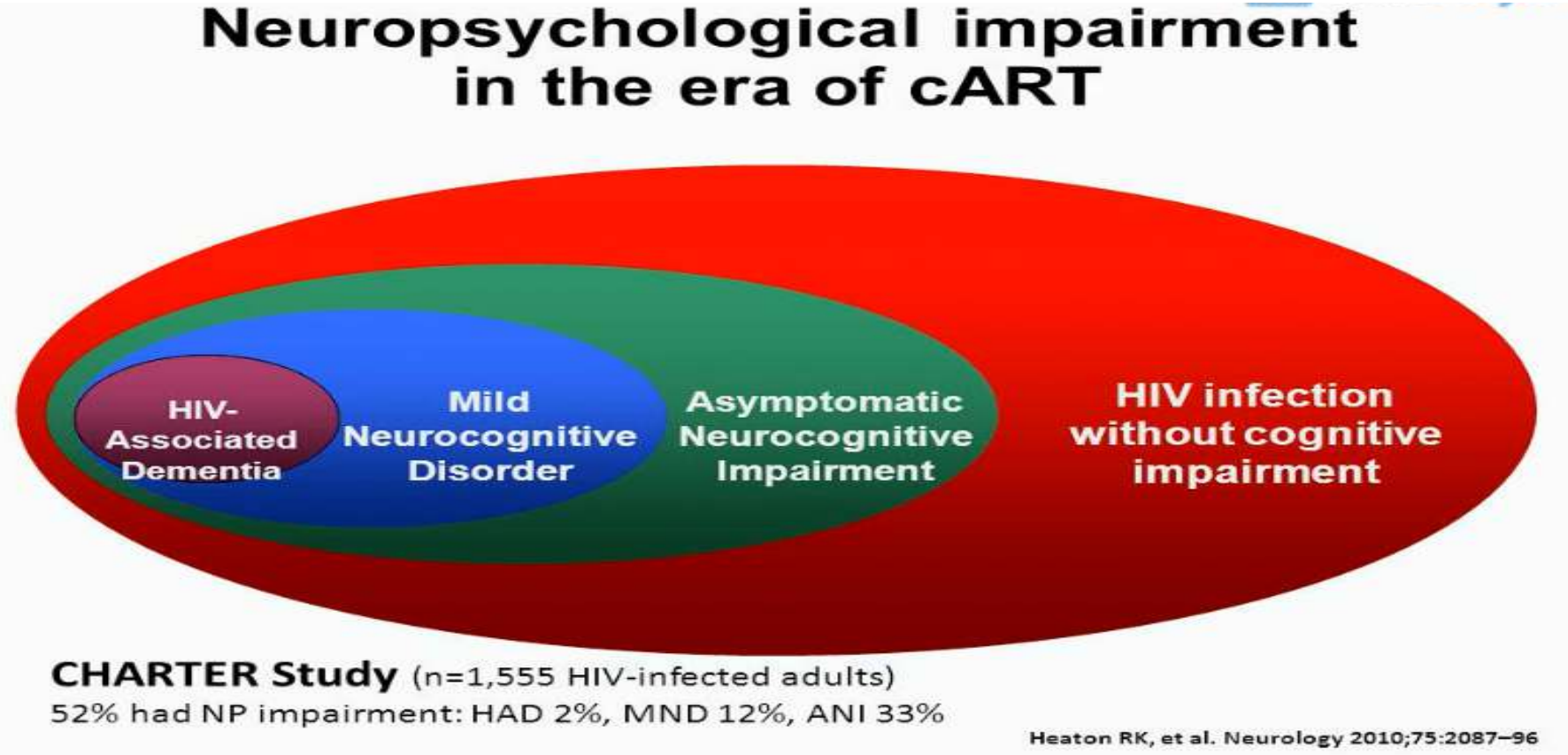
similar ages than those

Yaşlanan HIV ile enfekte bireyler

- ✓ Koenfeksiyonlar (Hepatit B/C)
- ✓ Komorbidite (DM,HT), ART ilişkili böbrek hastalıkları açısından da daha fazla risk altındadır

Kidney International (2018) **93,** 545–559;

Nörolojik durumlar



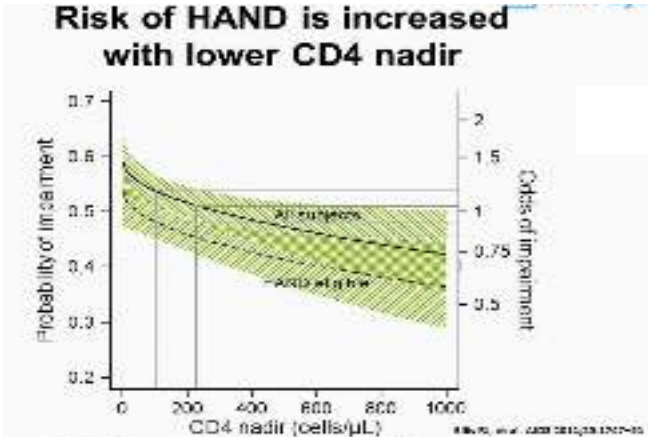
Risk faktörleri

HIV ilişkili durumlar

- Tanıdaki CD4<200/mm^3

(CD4 restorasyonuna rağmen)

- HIV enfeksiyonunun süresi
- AIDS tanımlayıcı durum varlığı
- Kısa ART süresi



Komorbiditeler

- Tanı sırasında ileri yaş
- Yaşlanma (50 yaş üstü)
- Anemi

Neurology. 2004 September 14; 63(5): 822–827.

Higher frequency of dementia in older HIV-1 individuals:

The Hawaii Aging with HIV-1 Cohort

V. Valcour, MD, C. Shikuma, M... MD, P. Poff, PhD, O. Selnes, PhD, P. Holck, PhD, J. Grove,
From the University of Hawaii N... Research Program (Drs. Valcour, Shikuma, Shiramizu, V... A. Burns School of Medicine, Honolulu, HI; and Johns Hopkin... Selnes and Sacktor), Baltimore, MD.

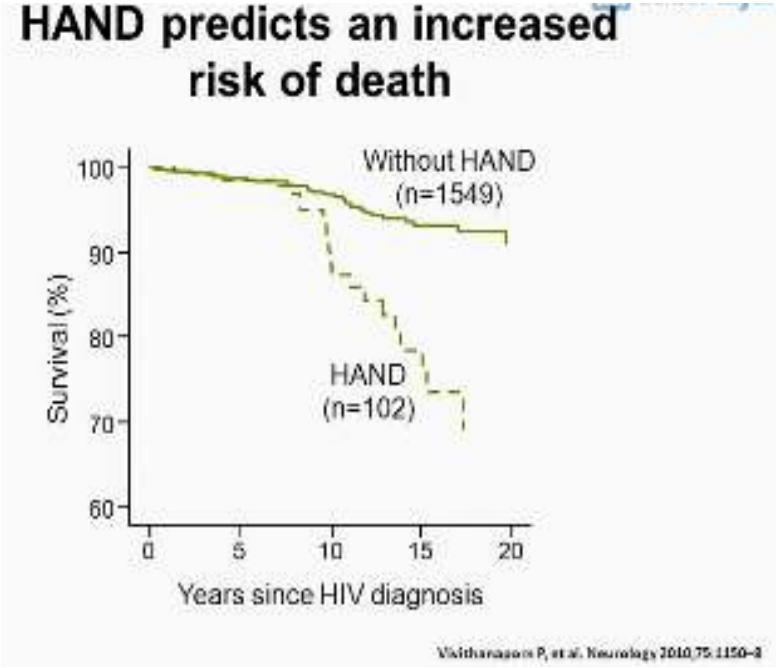
Yaşlı HIV (+) bireylerde X2 fazla

Abstract

Background—Antiretroviral therapy has improved survival for HIV-1-infected individuals. The neuroepidemiologic implications of HIV-1 in an aging population are not well known, particularly the prevalence of HIV-associated dementia (HAD).

HAND’in sonuçları

- Yaşam süresinde azalma
- Kendine bakım ve yaşam kalitesinde azalma
- İş performansında bozulma, yüksek işsizlik oranı
- Araba kullanmada bozukluk, artmış kaza riski
- İlaç uyumunda bozukluk
- Kişisel, ekonomik ve sosyal yaşama yük



Kanserler

PLWH daha erken yaşta kanser tanısı almaktalar

(Sigara, alkol, HBV, HCV, EBV, HPV ve erken yaşlanma)

Ann Intern Med. 2010 Oct 5;153(7):452-60. doi: 10.7326/0003-4819-153-7-201010050-00008.

Age at cancer diagnosis among persons with AIDS in the United States.

Shiels MS[1], Pfeiffer RM, Engels EA.

Author Information

1 National Cancer Institute, National Institutes of Health, Rockville, Maryland 20892, USA. shielsms@mail.nih.gov

Abstract

BACKGROUND: ...at HIV accelerates carcinogenesis...

OBJECTIVE: T... ...ral populations, after adjustment for...

DESIGN: Regi...

SETTING: 15 ...

PARTICIPANT...

MEASUREME... ...al populations, after adjustment for...

RESULTS: The... ...ulation (1.5%) than in the general po... ...ately 20 years younger amon... ...s at diagnosis in the AIDS and gene... ...P > 0.100). In contrast, ages at ... ...antly younger in persons with AIDS than expected in the general population (P < 0.001), and the age at diagnosis of Hodgkin lymphoma was significantly older (median, 42 vs. 40 years; P < 0.001).

LIMITATIONS: Information on other cancer risk factors, including cigarette smoking, was not available. Analysis was restricted to non-Hispanic white and black persons who had AIDS, which could limit the generalizability of the findings to other racial and ethnic groups or to persons with HIV but not AIDS.

CONCLUSION: For most types of cancer, the age at diagnosis is similar in the AIDS and general populations, after adjustment for the ages of the populations at risk. Modest age differences remained for a few types of cancer, which may indicate either acceleration of carcinogenesis by HIV or earlier exposure to cancer risk factors.

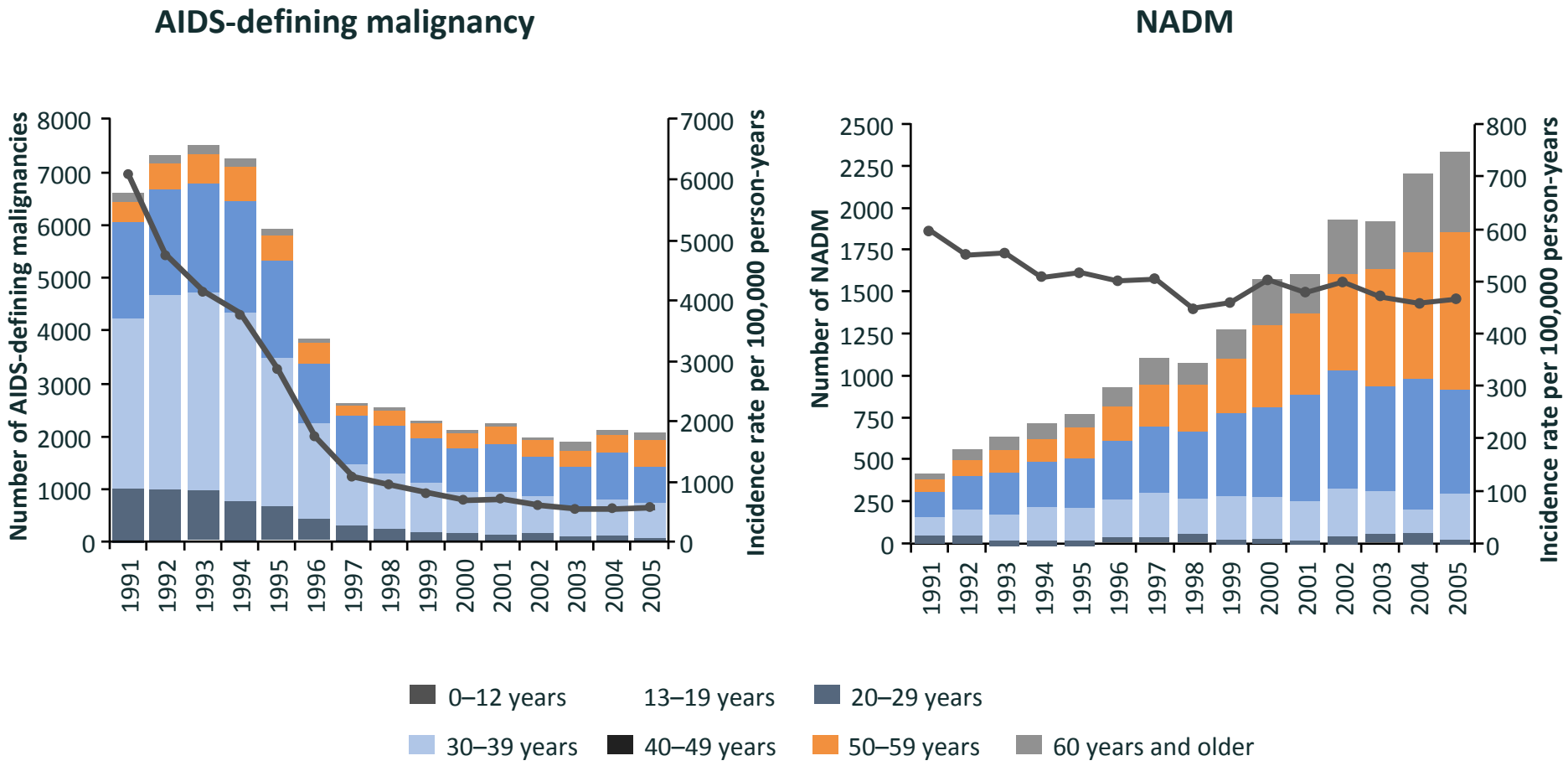
PRIMARY FUNDING SOURCE: National Cancer Institute.

1996-2007

ABD'de 212 055 ileri evre HIV enfekte (AIDS) kişi

Genel popülasyona göre AIDS grubunda çoğu kanserlerin tanı yaşı

20 yıl daha erken



Adapted from Shiels MS et al. J Natl Cancer Inst. 2011;103:753-62

> East Mediterr Health J. 2020 Mar 24;26(3):276–282. doi: 10.26719/emhj.19.030.

Prevalence and mortality of cancer among people living with HIV and AIDS patients: a large cohort study in Turkey

Ozlem Altuntas Aydin [1], Alper Gunduz [2], Fatma Sargin [3], Bilgül Mete [4], Hayat Kumbasar Karaosmanoglu [1], Dilek Yildiz Sevgi [2], Mucahit Yemisen [5], Bulent Durdu [6], Ilyas Dokmetas [2], Fehmi Tabak [4], ACTHIV-IST (Action Against HIV in Istanbul) Study Group

Background: Cancer is responsible for elevated human immunodeficiency virus (HIV)–related mortality but there are insufficient data about cancer in HIV-positive patients in Turkey.

Aims: We aimed to investigate the prevalence and mortality of cancer among people living with HIVand AIDS patients in Istanbul, Turkey.

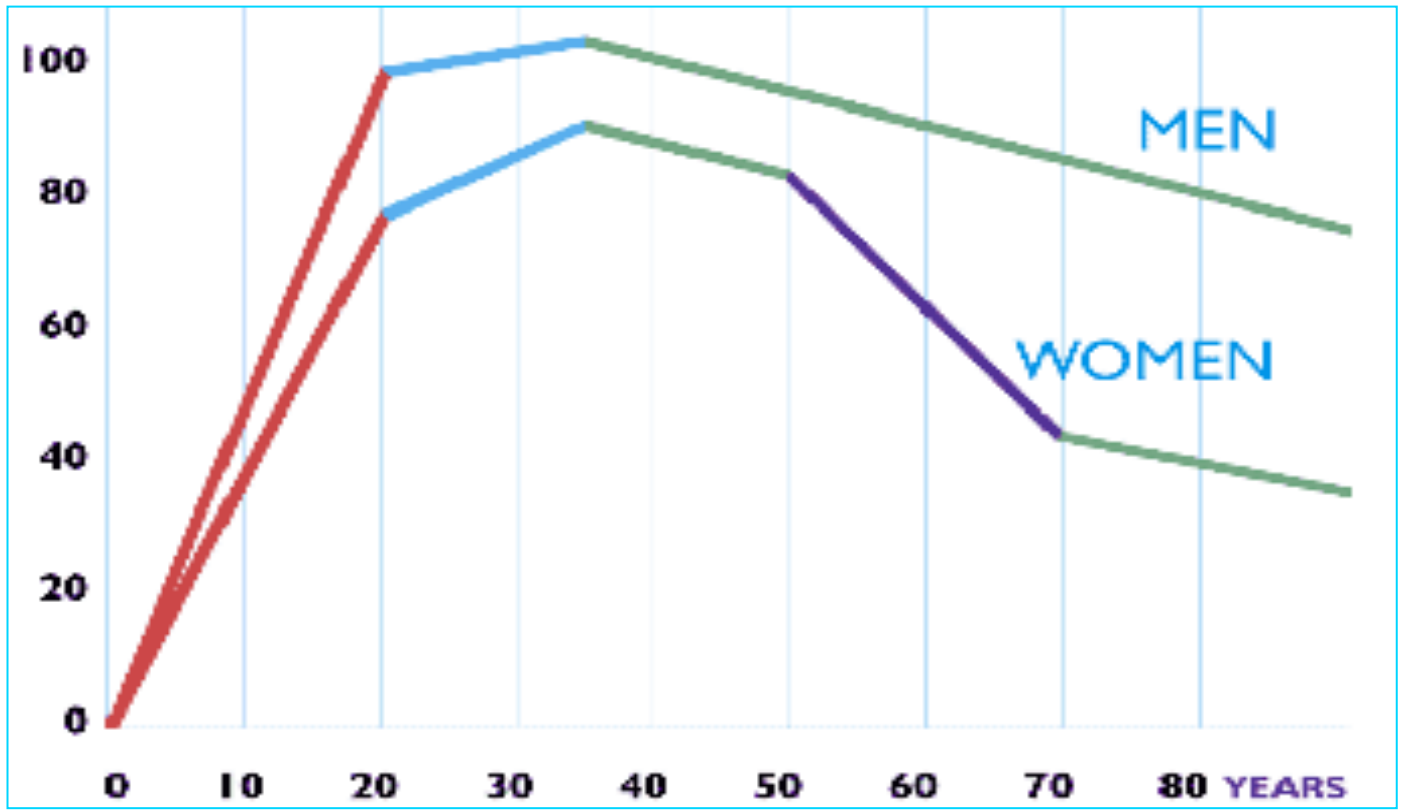
Methods: Between January 1998 and December 2016, people living with HIVand AIDS patients were enrolled in this study by the ACTHIV-IST Study Group, which consists of 5 centres to follow-up HIV-positive patients in Istanbul. The cancer diagnoses included AIDS-defining cancers (ADCs) and non AIDS-defining cancers (NADCs).

Results: Among 1872 patients, 37 (1.9%) were diagnosed with concurrent cancer. Eleven patients were diagnosed during follow-up; the prevalence of cancer among people living with HIVand AIDS patients was 2.6%. Among 48 cancer patients, 35 patients had ADCs, and 32 of them were diagnosed at their first hospital admission. There were 1007 late presenters and 39 of them had cancer (29 were ADCs). The most prevalent NADCs were gastrointestinal, genitourinary, and pulmonary cancers. NADCs were mostly diagnosed during follow-up of patients. The mortality of this group was significantly higher than that of patients with ADCs (53.9% vs 22.9%).

Conclusions: These results indicate the importance of cancer screening at diagnosis and during follow-up of HIV infection. A detailed physical examination contributes to diagnosis of the most prevalent ADCs (Kaposi's sarcoma and non-Hodgkin's lymphoma), especially in late presenters. For NADCs, individual risk factors should be considered.

Keywords: AIDS; cancer; human immunodeficiency virus; mortality; prevalence.

Kemik Sağlığı



Düşük VKİ

Azalmış fiziksel aktivite

Sigara kullanımı

Alkol kullanımı

IVDU

Hipogonadizm

D vit eksikliği

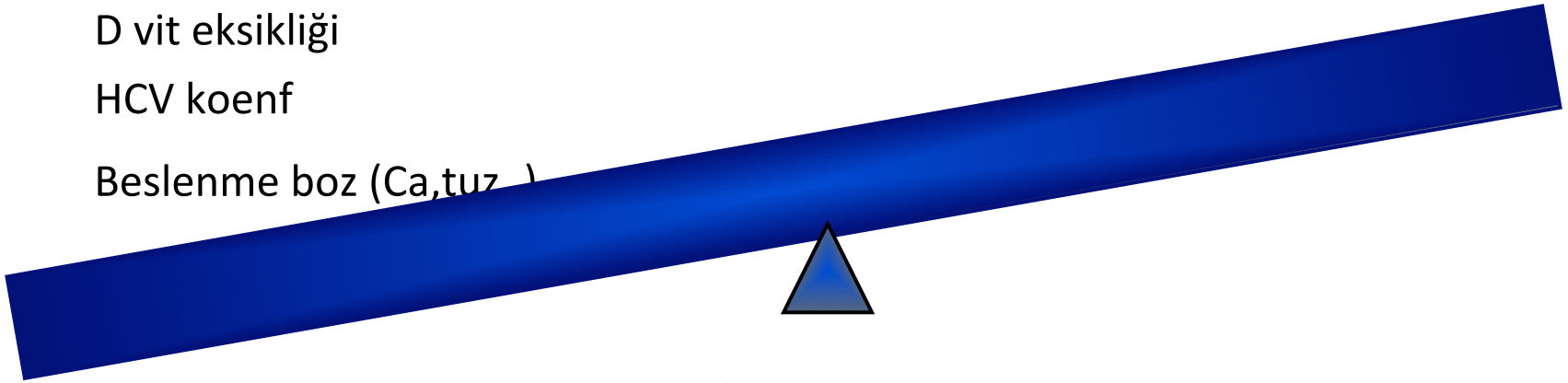
HCV koenf

Beslenme boz (Ca,tuz..)

- Östrojen metabolizmasını ⇧

- Kadmiyumun kemik met. etkisi

- Osteoprogenitör hücrelerin osteoblastik farklılaşmasını bozar



Yıkım

Kemik dengesi

Yapım

Vpr, gp 120 osteoklastik aktiviteyi stimule

p55-gag osteoblastik aktiviteyi suprese ve

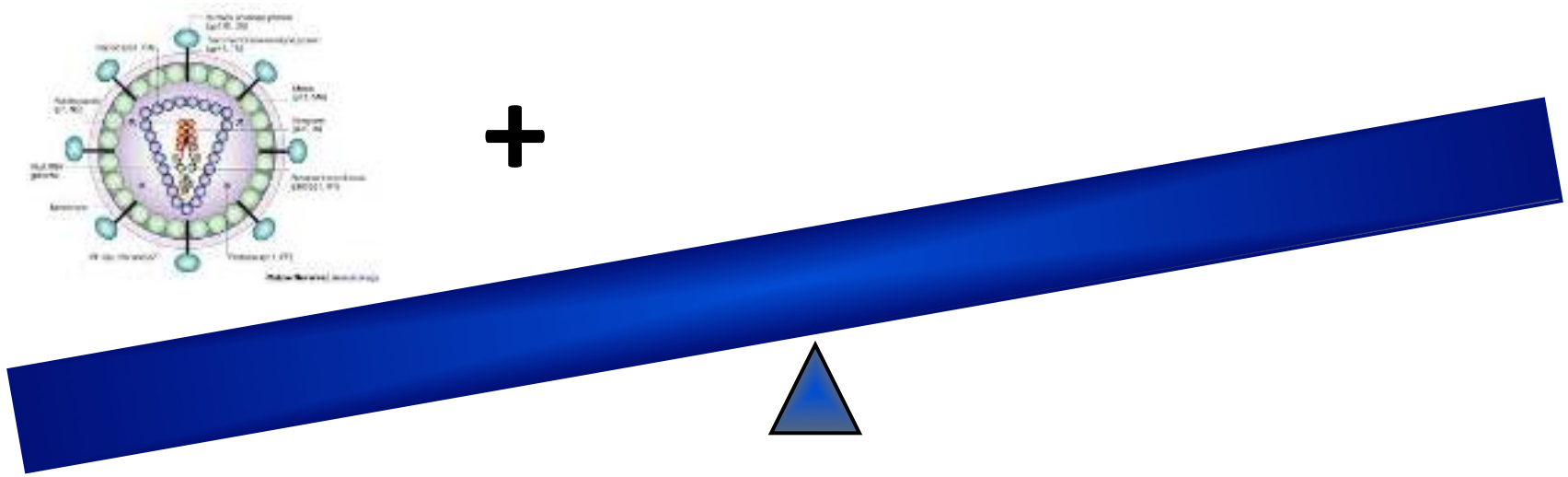
osteoblastik apopitozu arttırır

TNFα, IL-6 kemik rezobsiyonunu arttırır

Aktive T-hücrelerinden Receptor-Activator NFκB

(RANKL) salımı artar– (potent osteoklast aktivator)

HIV osteoproteregin (RANKL'a karşıt etki) üretiminde azalma



Kemik dengesi

Harris VW, JID 2012:205:391-398

PIs osteoklast/blast farklılaşmasını inhibe eder

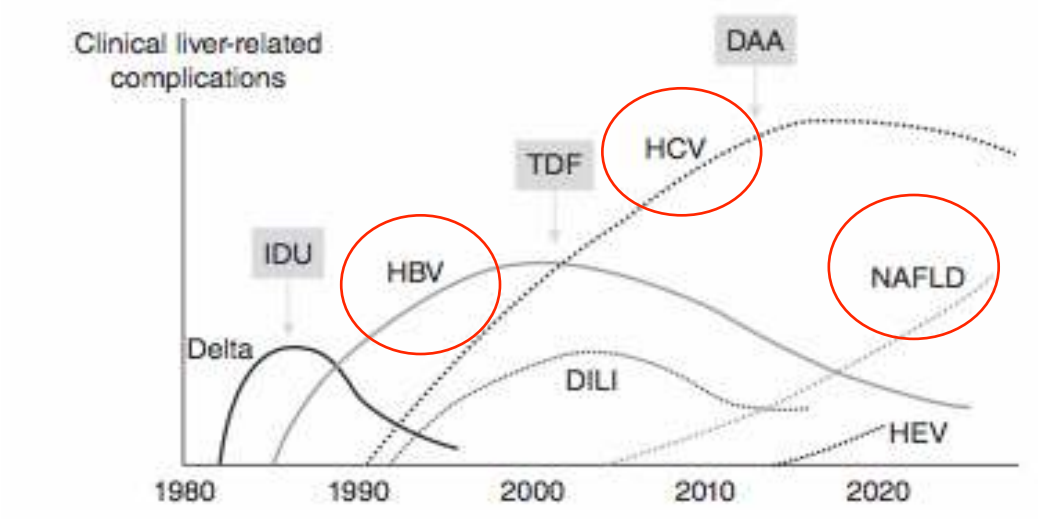
1-α-hidroksilaz activitesini inhibe ederek D vit sentezini azaltır

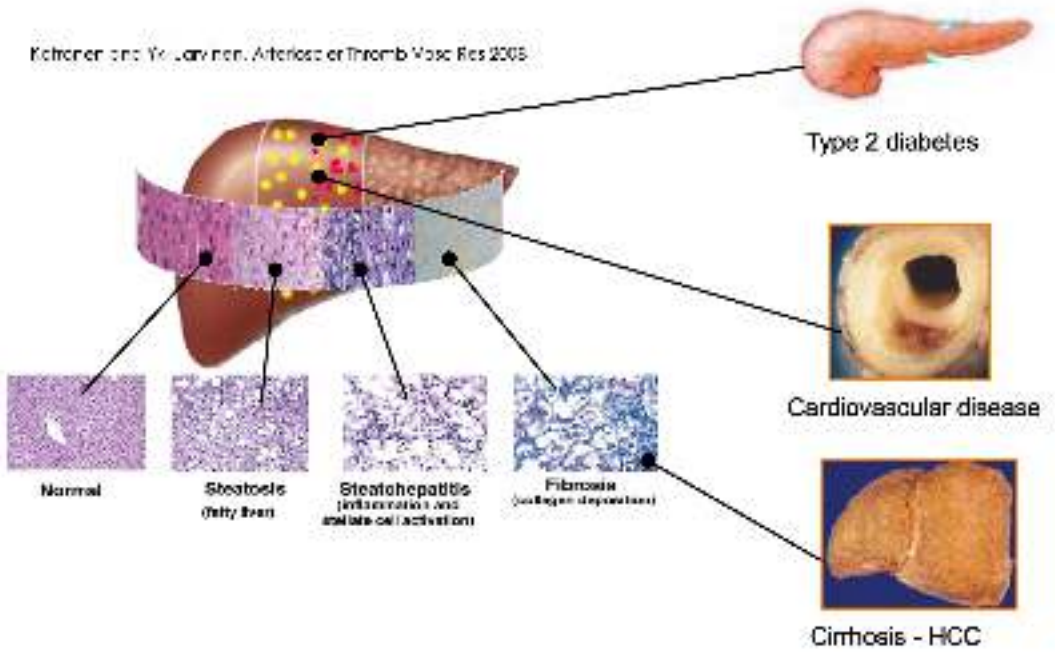
Efavirenz Dvit metabolizmasını hızlandırır

TDF (Tenofovir Disoproxil Fumarate) renal proksimal tubal toksisite sonucu fosfat düşüklüğü ve artmış kemik döngüsü ile indirekt etki

Kemik dengesi

Karaciğer Hastalığı



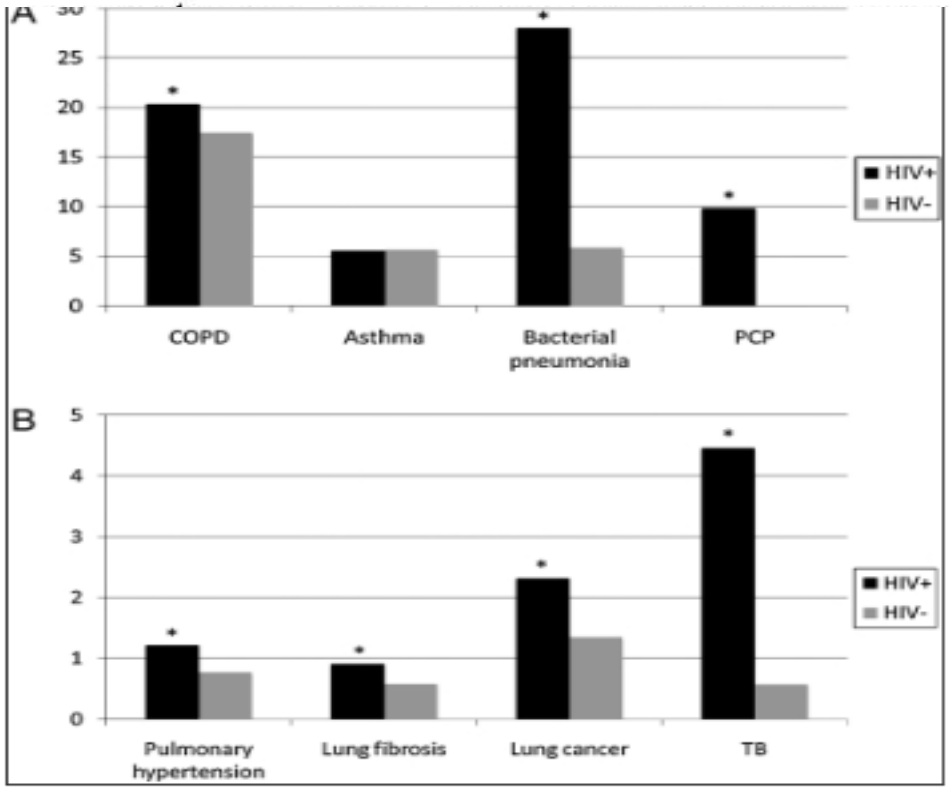


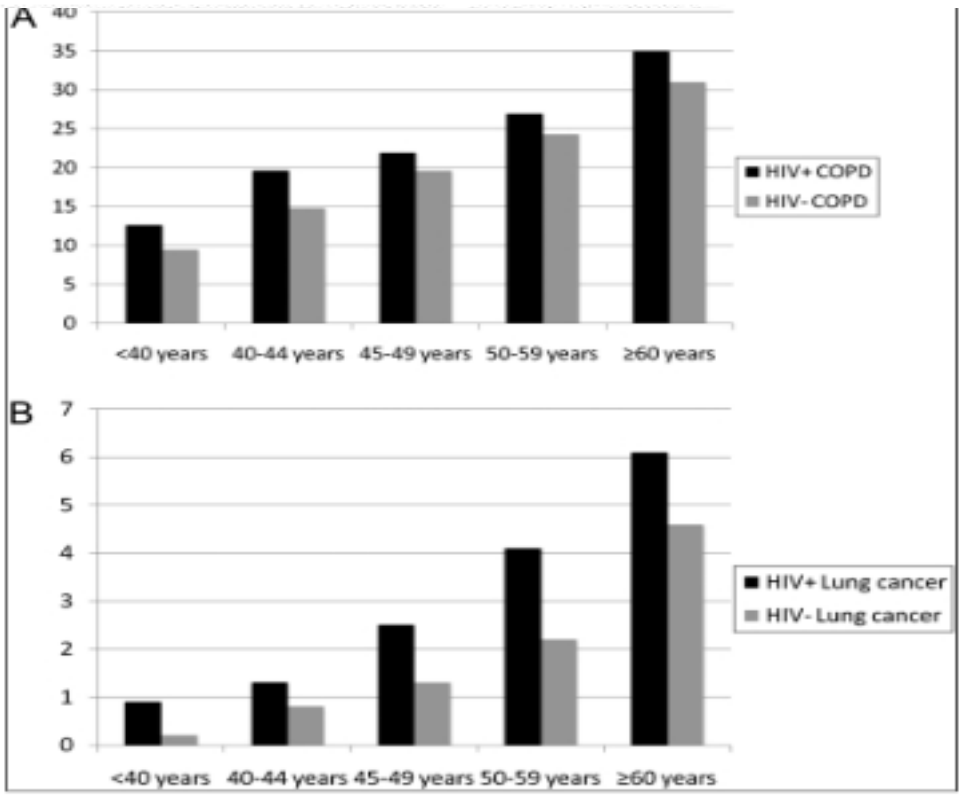
DAA, direct-acting antivirals; TDF, tenofovir; IDU, intravenous drug users; NAFLD, non-alcoholic fatty liver disease; DILI, drug-induced liver injury; HEV, hepatitis E virus

Akciğer hastalığı

Am J Respir Crit Care Med. 2011 Feb 1;183(3):388-95. doi: 10.1164/rccm.201006-0836OC. Epub 2010 Sep 17.

HIV infection and risk for incident pulmonary diseases in the combination antiretroviral therapy era.





Kırılgan yaşlı

- İstemsiz kilo kaybı
- Bitkinlik – tükenmişlik
- Kas güçsüzlüğü
- Yavaş yürüme
- Fiziksel aktivitede ↓

  (3'ünün varlığı)

Frailty in the Context of Ageing

Frailty defines age-related exhaustion of homeostatic reserves. An individual with frailty is exposed to enhanced vulnerability to stressors, and associated risk of negative health-related outcomes. This geriatric syndrome, comprising biological, psychological and social issues is more prevalent than expected in PLWH compared to HIV-negative matched controls [21].The most common instruments to measure frailty include the Frailty Phenotype [22] and Frailty Index [23]

Feature	Frailty Phenotype	Frailty Index
Clinical definition	Based on presence of signs, symptoms (pre-disability syndrome)	Based on presence of diseases, disabilities (accumulation of deficits)
How to assess	Assessed by five specific features [22]: 1. self-reported weight loss (a) 2. self-reported exhaustion (b) 3. low levels of physical activity as measured by Minnesota Leisure physical activity questionnaire (c) 4. measured 4 m walk speed time (d) 5. measured grip strength (e)	A frailty index is calculated based on the number of health deficits out of > 30 assessed health deficits [23] Health variables, including signs and symptoms of disease, laboratory measures, and self-reported data Data routinely collected in medical records can be included if they characterise age-related, acquired health deficits which cover a range of physiologic systems
How to interpret	Categorical variables Total score of 5 items: 0 deficits = fit 1-2 deficits = pre-frail 3 + deficits = frail	Continuous variables Index ranges from 0 to 1: < 0.25 = fit 0.25 - 0.4 = frail > 0.4 = most frail
How to address frailty [24]	Promote Comprehensive Geriatric Assessment (CGA), aimed at personalising interventions according to benefits/priorities for a given person through a multidisciplinary diagnostic and treatment process, that identifies medical, psychosocial, and functional limitations aimed at maximising overall health with ageing and the improvement of quality of life	
Recommendations [25], [26]	In PLWH who are frail: 1. Sustain and recover physical function impairment and sarcopenia prescribing physical activity with a resistance training component 2. Address polypharmacy by reducing or deprescribing any inappropriate/superfluous medications, see Prescribing in Elderly PLWH 3. Screen for, and address modifiable causes of fatigue 4. For PLWH exhibiting unintentional weight loss, screen for reversible causes and consider food fortification and protein/caloric supplementation 5. Prescribe vitamin D for individuals deficient in vitamin D, see page 62	

(a) Self-reported unintentional weight loss was considered present if exceeding 4.5 kg in the last year or 2.3 kg in the last 6 months

(b) Exhaustion is present if the participant answers "occasionally" or "most of the time" to either one of the following statements: During the last week, how often have you felt that (i) everything you did was an effort, or (ii) you could not 'get going'

(c) Low physical activity was considered present if participant answered 'yes, limited a lot' when asked whether their health limits vigorous activities such as running, lifting heavy objects, participating in strenuous sports

(d) Walk speed time, is measured by a 4-meter walking test in usual pace, one trial) A deficit is assigned according to the following gender-specific criteria
- Men: height ≤ 173 cm and speed ≤ 0.6531 m/s; height > 173 cm and speed ≤ 0.762 m/s
- Women: height ≤ 159 cm and speed ≤ 0.6531 m/s; height > 159 cm and speed ≤ 0.762 m/s

(e) Maximum grip strength can be assessed using a handheld dynamometer the mean value of three consecutive measurements of the dominant hand (adjusted by sex and BMI quartile based on CHS population [23]):
- Men: BMI ≤ 24 kg and strength < 29 kg; BMI 24.1–26 and strength < 30 kg; BMI 26.1–28 and strength < 30 kg; BMI > 28 and strength < 32 kg
- Women: BMI ≤ 23 and strength < 17 kg; BMI 23.1–26 and strength < 17.3 kg; BMI 26.1–29 and strength < 18 kg; BMI > 29 and strength < 21 kg

HIV infection is independently associated with frailty in middle-aged HIV type 1-infected individuals compared with similar but uninfected controls

Katherine W. Kooij[a], Ferdinand W.N.M. Wit[a,b], Judith Schouten[a,c], Marc van der Valk[b], Mieke H. Godfried[b], Ineke G. Stolte[b,d], Maria Prins[b,d], Julian Falutz[e], Peter Reiss[a,b,f], on behalf of the AGE$_h$IV Cohort Study Group

Background: Frailty is an age-related syndrome of decreased physiological reserve and resistance to stressors, associated with increased morbidity and mortality in the general elderly population. An increased prevalence of frailty has been reported amongst HIV-infected individuals.

Methods: Fried frailty phenotype was systematically assessed in predominantly virologically suppressed HIV type 1 (HIV-1)-infected and otherwise comparable HIV-uninfected participants aged at least 45 at enrollment into the AGE$_h$IV Cohort Study. Multivariable ordinal logistic regression was used to investigate associations between HIV- and antiretroviral therapy-related covariates, markers of inflammation and body composition and prefrailty/frailty.

Results: Data were available for 521 HIV-infected and 513 HIV-uninfected individuals. Prevalence of frailty (10.6 versus 2.7%) and prefrailty (50.7 versus 36.3%) were significantly higher in HIV-infected individuals ($P_{trend} < 0.001$). HIV infection remained statistically significantly associated with prefrailty/frailty after adjustment for age, sex, race/ethnicity, smoking, hepatitis C infection, comorbidities and depression [adjusted odds ratio (OR_{adj}) 2.16, $P < 0.001$]. A higher waist-to-hip ratio attenuated the coefficient of HIV-infected status (OR_{adj} 1.93, $P < 0.001$), but not waist- or hip-circumference individually or markers of inflammation. Within the HIV-infected group, parameters related to body composition were most strongly and independently associated with prefrailty/frailty: current BMI less than 20 kg/m^2 (OR 2.83, $P < 0.001$), nadir BMI less than 20 kg/m^2 (OR 2.51, $P < 0.001$) and waist-to-hip ratio (OR 1.79 per 0.1 higher, $P < 0.001$).

Conclusion: HIV infection was independently associated with prefrailty/frailty in middle-aged HIV-infected patients compared with HIV-uninfected controls. This partly may be mediated by the higher waist- and lower hip-circumference in the HIV-infected individuals, potentially partially caused by lipodystrophy, and in part be a consequence of historic weight loss associated with advanced HIV-disease.

AIDS 2016, **30**:241–250

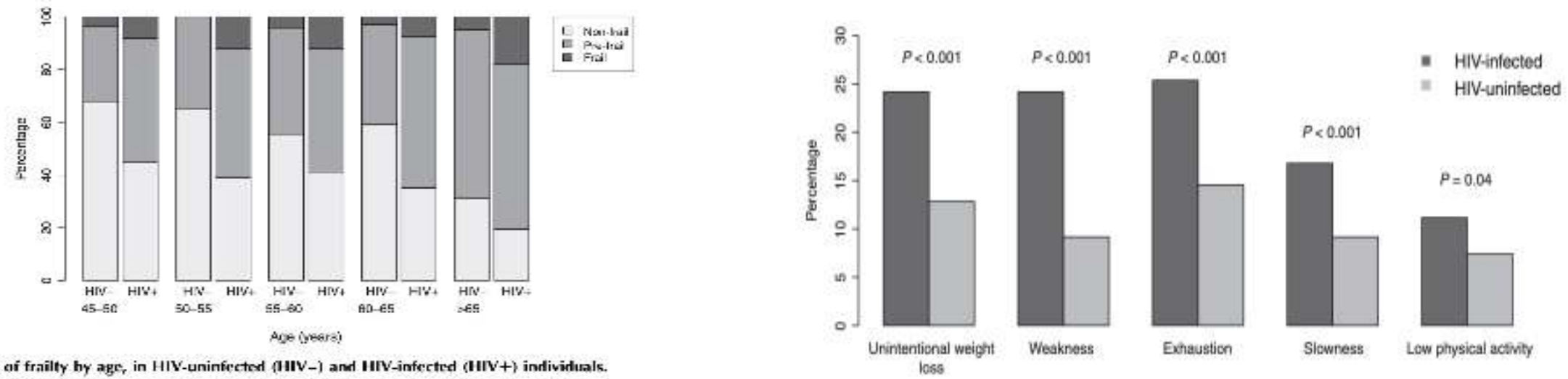


Fig. 1. Prevalence of frailty by age, in HIV-uninfected (HIV−) and HIV-infected (HIV+) individuals.

- HIV ile enfekte bireyler **yaşlandıkça**, aynı bireyde sıklıkla **birden fazla komorbidite** ortaya çıkmakta, **daha kırılgan ve engelli** hale gelmektedir

- HIV enfekte kişileri takip eden hekimler komorbideteler konusunda uzman değil
- Komorbiditeler nedeniyle kişilerin başvurduğu diğer branş hekimleri de HIV enfeksiyonu ve ART kullanımına aşina değiller

Part IV Prevention and Management of Co-morbidities in PLWH

Successful management of PLWH goes beyond provision of effective ART, with increasing focus attributed to the appropriate management of co-morbidities in order to ensure the best outcomes for PLWH. Recognised co-morbidities that disproportionately affect PLWH include cardiovascular, pulmonary, hepatic, metabolic, neoplastic, renal, bone, central nervous system disorders as well as sexual dysfunction. Many of these conditions significantly impact populations as they grow older. Recognising that older persons comprise a significant proportion of many populations living with HIV, the current version of the Guidelines suggests HIV-specific age cut-offs for screening for many of these co-morbidities as well as the introduction of a new section offering guidance on screening for frailty in older PLWH.

Potential contributors to co-morbidity pathogenesis include a higher prevalence of recognised risk factors, potential toxicities from ART-exposure, and HIV infection (or co-infections with CMV and HCV) contributing to immune dysfunction/dysregulation, chronic immune activation and inflammation. Taking this into consideration, particular focus should be paid to cessation of smoking, which contributes to many of the co-morbidities described.

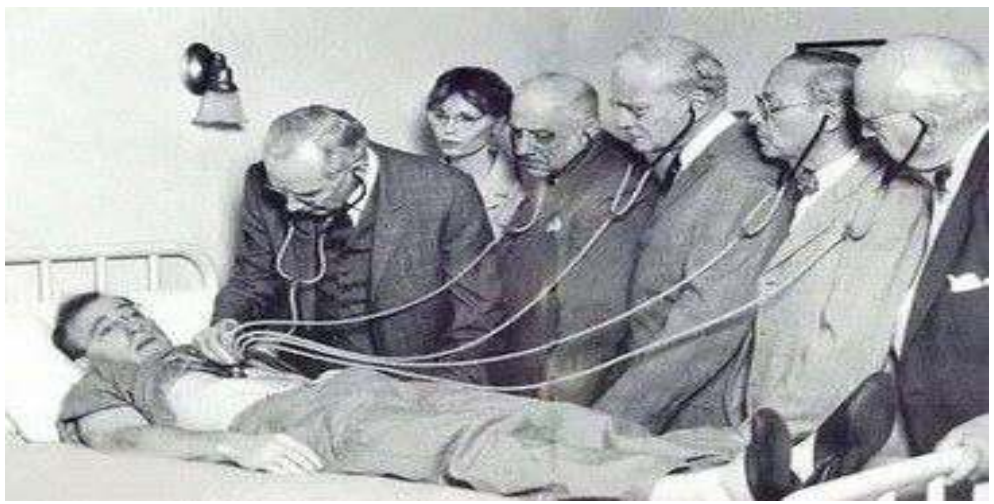
Health care professionals other than HIV specialists, who are involved in the care of PLWH and who are not familiar with the use of ART, should consult their HIV specialist colleagues before introducing or modifying any treatments for co-morbidities. As intervals between visits to HIV clinics are increasingly extended, PLWH may need more frequent review by their primary care doctor and we would encourage establishment of formal shared-care arrangements to optimise management of co-morbidities and prevent unwanted drug-drug interactions.

Conversely, many HIV doctors are not specialists in managing co-morbidities and should seek expert advice where appropriate in the prevention and management of such conditions. Situations where consultation is generally recommended are indicated elsewhere in this document.

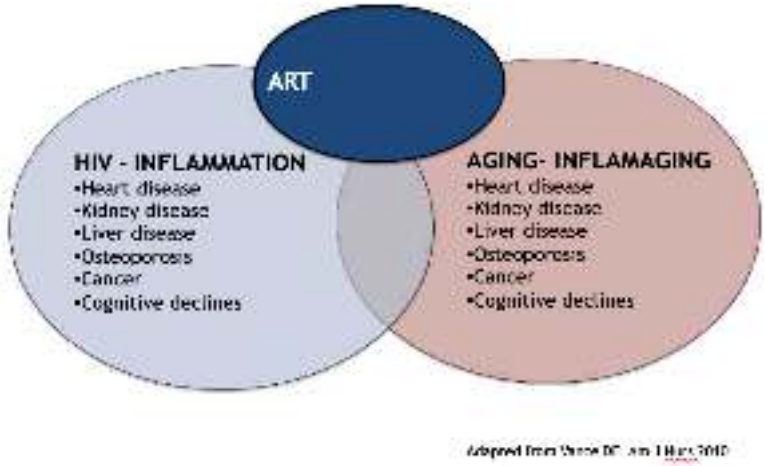
In particular, as individuals with treated HIV age, some individuals may experience multiple co-morbidities, which may contribute to frailty and disability. Such circumstances may require a comprehensive "geriatric-type" multidimensional, multidisciplinary assessment aimed at appropriately capturing the composite of medical, psychosocial and functional capabilities and limitations of elderly PLWH. Suggesting for this approach are included in this version of the Guidelines. One area that requires further exploration is how co-morbidities impact on overall quality of life and an appropriate approach to mitigate this. This issue will be a focus of the Guidelines panel going forward.

Depending on future clinical research findings, these recommendations will be regularly updated as required. The online versions at http://www.eacsociety.org and the EACS Guidelines App contain more detailed information and links to other relevant websites; these will be regularly updated.

The current recommendations highlight co-morbidities that are seen frequently in the routine care of PLWH and those for which specific issues should be considered.



Yaşlılarda ART



- ART ile CD4 artışı yetersiz (timus yetersizliği)
- Sigara, madde kullanımı vb. davranışsal risklerin de kombinasyonu ile komorbiditeler (renal, kardiyovasküler, hepatik, kemik metabolizması, endokrinolojik)
- Polifarmasi (≥5 ilaç yaşlılarda sık)
- İlaç-ilaç etkileşimleri
- Advers etkiler (renal, karaciğer, KVS, kemik sağlığı)
  - **Uzun süreli ART'ye maruziyet**
  - ART değiştirilme ihtiyacı !!!
- Nörokognitif yetersizlikler nedeniyle ART uyumunda bozukluk

AIDS. 2010 Oct 23;24(16):2469-78. doi: 10.1097/QAD.0b013e32833ed774

Virologic and immunologic response to HAART, by age and regimen class.

Althoff KN[1], Justice AC, Gange SJ, Deeks SG, Saag MS, Silverberg MJ, Gill MJ, Lau B, Napravnik S, Jedlicki L, Klein MB, Gebo KA; North American AIDS Cohort Collaboration on Research Design (NA-ACCORD).

Collaborators (55)

Author Information

1 Johns Hopkins University, Baltimore, Maryland 21287, USA.

Erratum in
AIDS.2011 Jan 28;25(3):397.

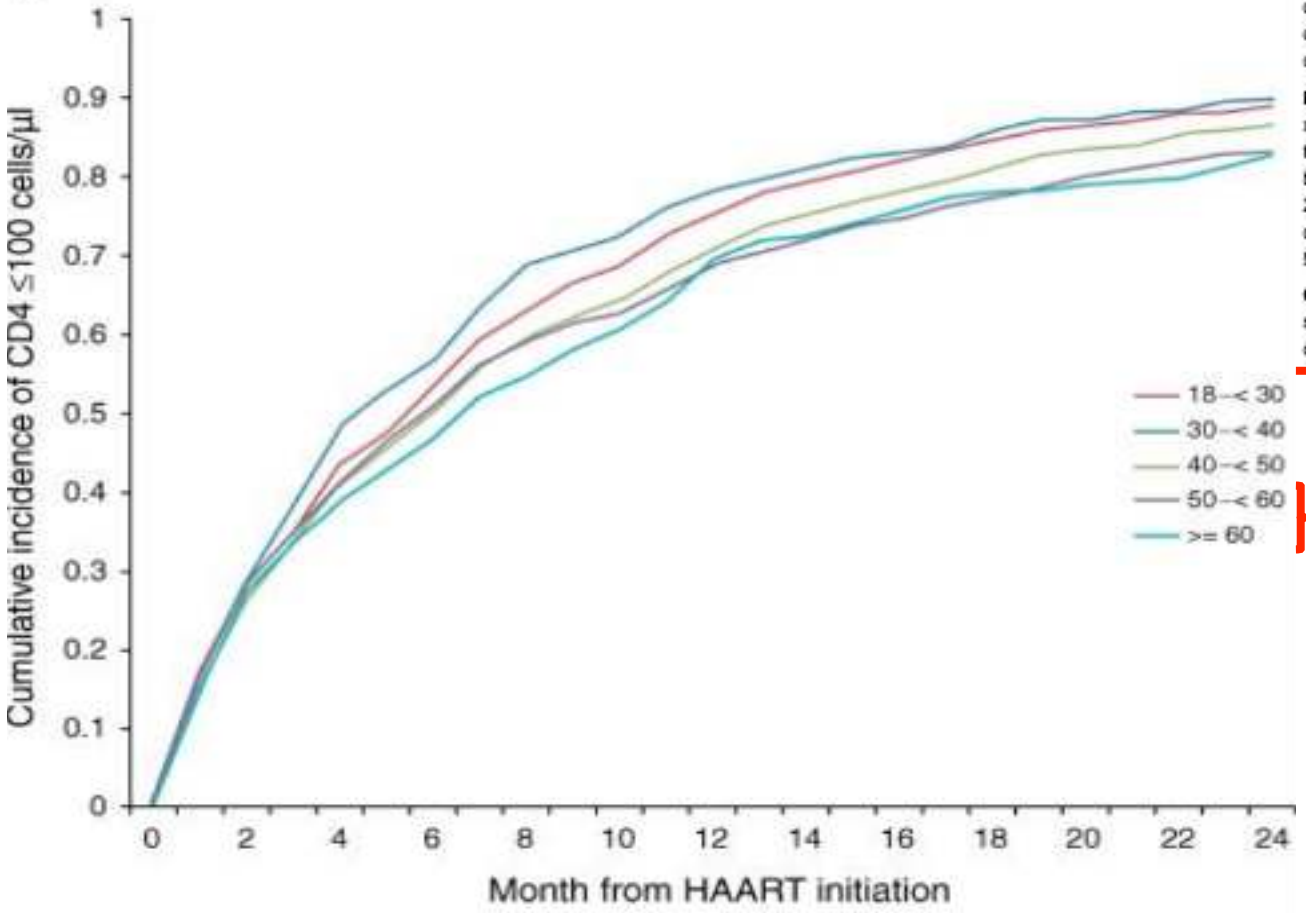
Abstract

OBJECTIVE: To determine the impact of age and initial HAART regimen class on virologic and immunologic response within 24 m initiation.

DESIGN: Pooled analysis of data from 19 prospective cohort studies in the North American AIDS Cohort Collaboration on Researc Design (NA-ACCORD).

METHODS: Twelve thousand, one hundred and ninety-six antiretroviral-naive adults who initiated HAART between 1998 and 200 boosted protease inhibitor-based regimen or a nonnucleoside reverse transcriptase inhibitor (NNRTI)-based regimen were include study. Discrete time-to-event models estimated adjusted hazard odds ratios (aHOR) and 95% confidence intervals (CIs) for suppr load (≤500 copies/ml) and, separately, at least 100 cells/μl increase in CD4 cell count. Truncated, stabilized inverse probability we accounted for selection biases from discontinuation of initial regimen class.

RESULTS: Among 12 196 eligible participants (mean age = 42 years), 50% changed regimen classes after initiation (57 and 48%



AIDS. 2004 Oct 21;18(15):2029-38.

Immunologic and clinical responses to highly active antiretroviral therapy over 50 years of age. Results from the French Hospital Database on HIV.

Grabar S[1], Kousignian I, Sobel A, Le Bras P, Gasnault J, Enel P, Juno C, Maherzat A, Lang JM, Costagliola D.

Author Information

1 Department of Biostatistics, Cochin Hospital, University Paris V, Paris, France. grabar@cochin.univ-paris5.fr

Abstract

OBJECTIVE: To study immunologic and clinical responses to HAART in patients over 50 years old.

DESIGN AND METHODS: A prospective cohort study which included 68 hospitals in France. A total of 3015 antiretroviral-naive patients, 401 of whom were aged 50 years or over, were enrolled following initiation of HAART. The influence of age on the mean CD4 cell count increase on HAART was studied by using a two-slope mixed model. Progression, defined by the occurrence of a new AIDS-defining event (ADE) or death, was studied by Cox multivariate analyses.

RESULTS: Among patients with baseline HIV RNA above 5 log copies/ml, CD4 mean increase during the first 6 months on HAART was +42.9 x 10(6) cells/l per month in patients under 50 years and +36.9 x 10(6) cells/l per month in patients over 50 years ($P < 0.0001$); subsequently, the respective monthly changes were +17.9 and +15.6 x 10(6) cells/l per month ($P < 0.0001$). Similar trends were observed in patients with baseline HIV RNA below 5 log copies/ml, and also after stratification for the baseline CD4 cell count. After a median follow-up of 31.5 months, 263 patients had a new ADE and 44 patients died. After adjustment for baseline characteristics, older patients had a significantly higher risk of clinical progression (hazard ratio (HR) = 1.52 [95% confidence interval (CI), 1.15-2.00]) and were more likely to achieve a viral load below 500 copies/ml [HR = 1.23, (95% CI, 1.11-1.38)].

CONCLUSION: Patients over 50 years of age have an immunologic response to HAART. However, their CD4 cell reconstitution is significantly slower than in younger patients, despite a better virologic response. This impaired immunologic response may explain their higher risk of clinical progression.

İlaç uyumu iyi

Arch Intern Med. 2007 Apr 9;167(7):684-91.

Older age and the response to and tolerability of antiretroviral therapy.

Silverberg MJ[1], Leyden W, Horberg MA, DeLorenze GN, Klein D, Quesenberry CP Jr.

Author Information

1 Division of Research, Kaiser Permanente Northern California, 2000 Broadway, Oakland, CA 94612, USA. Michael.J.Silverberg@kp.org

Abstract

BACKGROUND: The unique h
study, especially in terms of the

METHODS: Changes in HIV cli
group), 1834 patients aged 40

RESULTS: Patients 50 years o
initiation (hazard ratio [HR], 1.1
RNA level rebound (to > or =10
after adjustment for adherence
121.3, and 111.8 CD4 T cells/m
through 6, older patients had la
39, 40-49, and > or =50 years,
remained in year 1 (P =.02) bu
Metabolic (glucose and lipids),
among older patients.

CONCLUSION: Despite a highe
improved virological outcomes

Drugs Aging. 2013 Oct;30(10):809-19. doi: 10.1007/s40266-013-0107-7.

Aging, antiretrovirals, and adherence: a meta analysis of adherence among er HIV-infecte individuals.

Ghidei L, Simone MJ, Salow MJ, Zimmerman KM, Paquin AM, Skarf LM, Kostas TR, Rudolph JL.

Abstract

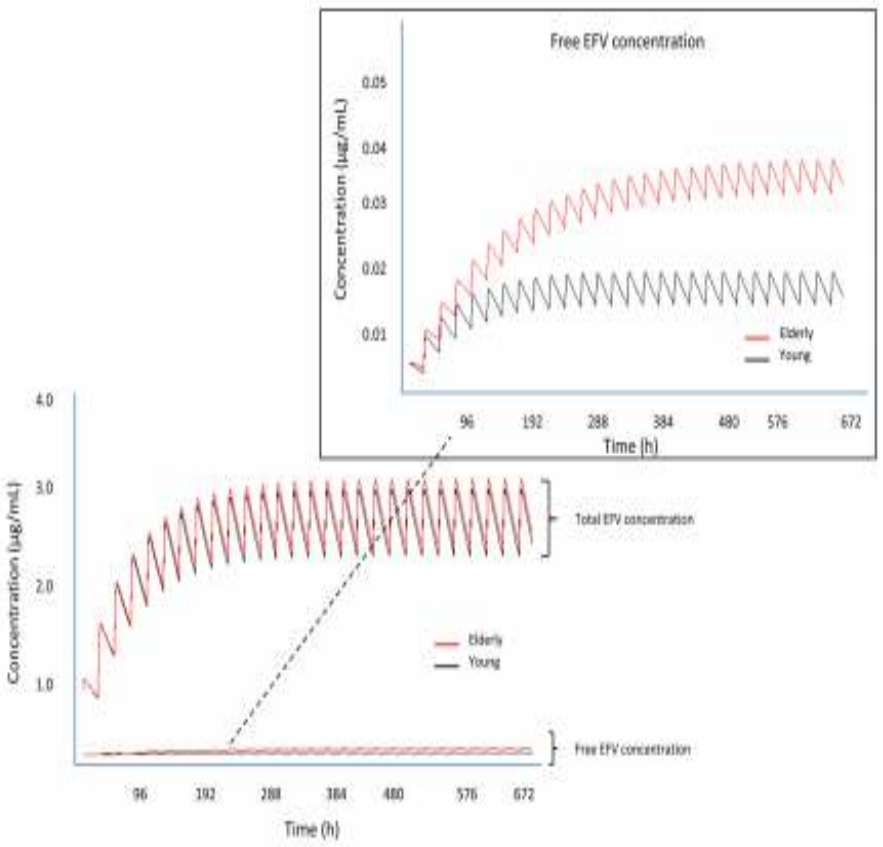
INTRODUCTION: Older adults are generally considered to be at greater risk for medication non-adherence due to factors such as medication complexity, side effects, cost, and cognitive decline. However, this generalization may not apply to older adults with human immunodeficiency virus (HIV). Regardless of age, suboptimal adherence to antiretroviral therapy (ART) can lead to increased viral load, immunosuppression, drug-resistant viral strains, co-morbidities, and opportunistic infections. Understanding trends of adherence to ART among older adults is critical, especially as the population of people living with HIV grows older.

OBJECTIVES: The purpose of this systematic review and meta-analysis is to determine if older individuals with HIV are less likely to be non-adherent to antiretroviral therapy than younger individuals with HIV.

DESIGN: A systematic search in PubMed, Embase, and PsycINFO was conducted to identify peer-reviewed articles evaluating adherence to ART in older adults. Two independent reviewers screened abstracts, applied inclusion criteria, and appraised study quality. The bibliographies of qualifying studies were searched. Data were abstracted from studies by two independent authors. Meta-analyses were conducted, and adherence levels were reported as the relative risk of non-adherence in older individuals compared to younger individuals.

RESULTS: The systematic search yielded 1,848 abstracts. Twelve studies met full inclusion criteria. The overall meta-analysis found that older age reduced risk for nonadherence by 27 % (relative risk (RR) 0.72, 95 % confidence interval (CI) 0.64–0.82). Studies assessing both short-term and long-term adherence demonstrated a significant reduction in non-adherence among older patients (RR 0.75, 95 % CI 0.64–0.87 and RR 0.65, 95 % CI 0.50–0.85, respectively).

CONCLUSIONS: Older adults with HIV have a reduced risk for non-adherence to ART than their younger counterparts. Future studies should seek to elucidate contributing factors of adherence among older individuals with HIV.



Schoen JC, et al. Expert Opin Drug Metab Toxicol. 2013, 9(5):573-88.

Yaşlılarda fizyolojik olarak

- ✓ Yağ dokusunda artış
- ✓ Gastrik pH artışı
- ✓ Azalmış albümin düzeyi
- ✓ Sitokrom p450 enzim sisteminde değişim PK'i değiştirebilir

Ayrıca

- ✓ Kalp yetmezliği
- ✓ Siroz
- ✓ Kardiyak output ve hepatik kan akımını azaltan durumlar

- ART altında renal, hepatik fonksiyonlar yakından takip edilmeli, gereğinde modifikasyon
- Toksisite nedeniyle ART değişim oranı yaştaki her 10 yıllık artış için %1.28

Polifarmasi

J Antimicrob Chemother 2011; **66**: 2107–2111
doi:10.1093/jac/dkr248 Advance Access publication 16 June 2011

Journal of Antimicrobial Chemotherapy

Ageing with HIV: medication use and risk for potential drug–drug interactions

Catia Marzolini[1]*, David Back[2], Rainer Weber[3], Hansjakob Furrer[4], Matthias Cavassini[5], Alexandra Calmy[6], Pietro Vernazza[7], Enos Bernasconi[8], Saye Khoo[2], Manuel Battegay[1] and Luigia Elzi[1] on behalf of the Swiss HIV Cohort Study†

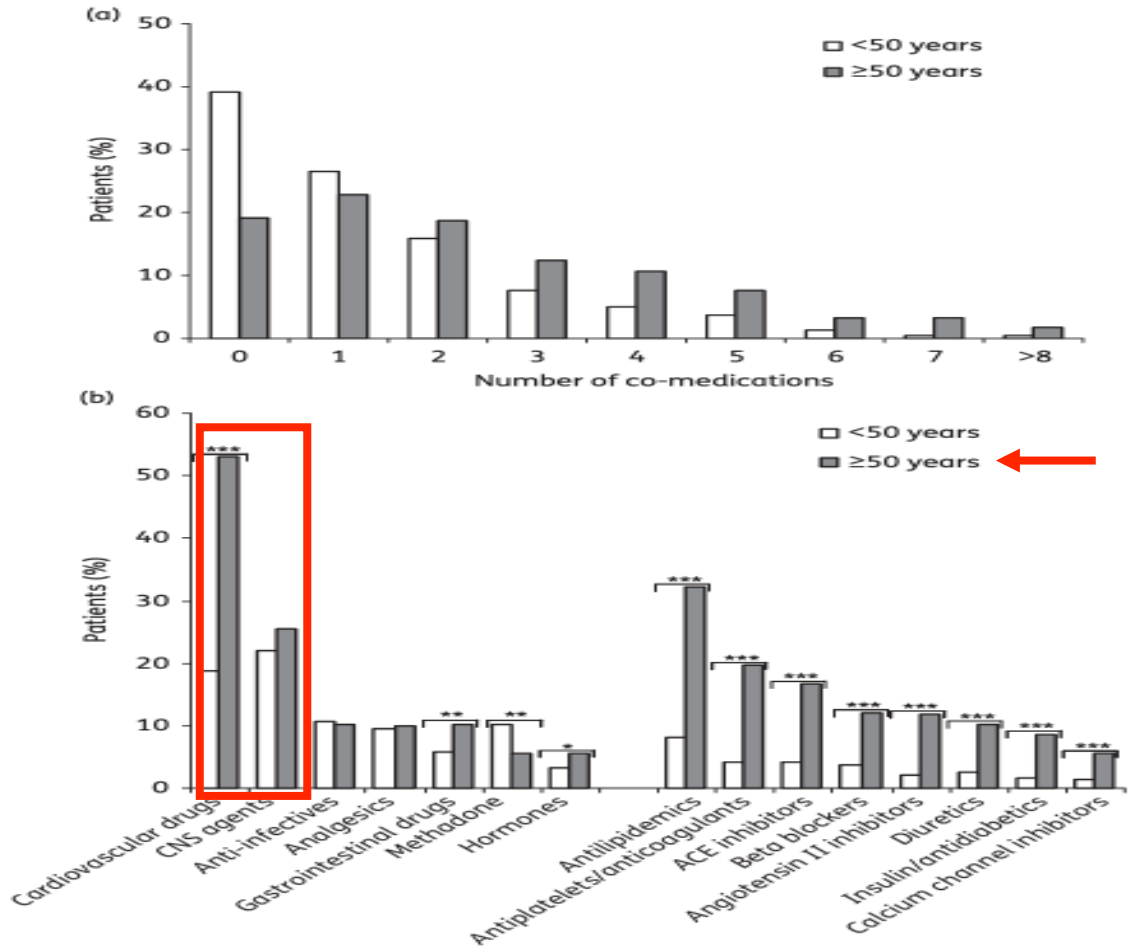


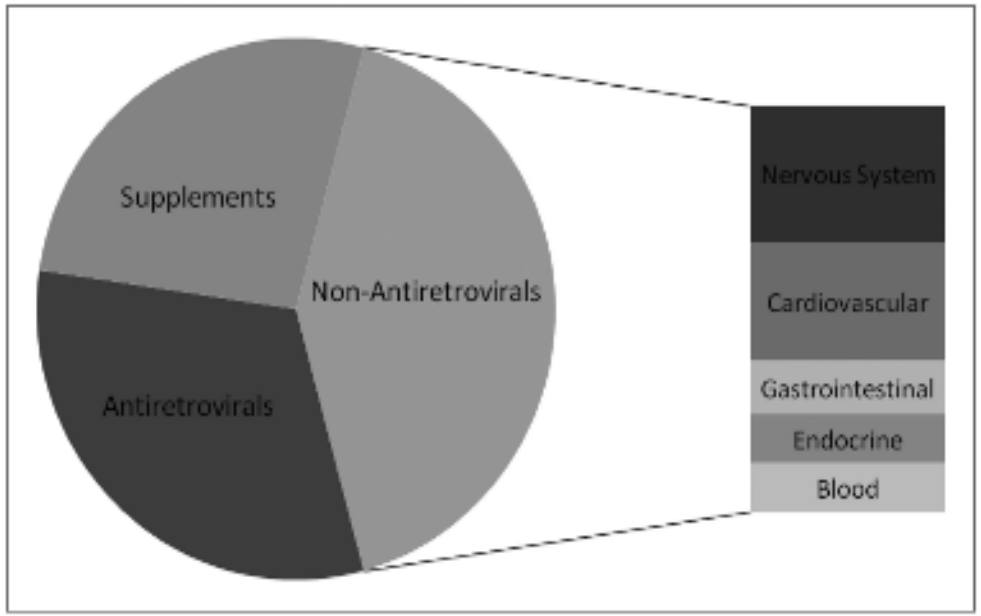
Figure 1. Number of co-medications (a) and therapeutic drug classes (b) used in patients age <50 years or ≥50 years. (b) Each bar represents the percentage of patients using one or more drugs of the corresponding therapeutic class. Detailed use of cardiovascular drugs is presented in the right-hand half of the figure. CNS agents included anxiolytics/sedatives, antidepressants, antipsychotics and anticonvulsants. Anti-infectives included antibacterials, antivirals, antifungals and antimycobacterials. Analgesics included anti-inflammatory drugs, paracetamol and narcotic analgesics. Gastrointestinal drugs included proton pump inhibitors, antidiarrhoea drugs and H_2 blockers. *$P<0.05$, **$P<0.01$, ***$P<0.001$.

Published in final edited form as:
J Am Geriatr Soc. 2014 March ; 62(3): 447–453. doi:10.1111/jgs.12695.

Polypharmacy, Drug-Drug Interactions, and Potentially Inappropriate Medications in Older HIV-Infected Adults

Meredith Greene, MD[1,2], Michael A. Steinman, MD[1,2], Ian R. McNicholl, PharmD[3,4], and Victor Valcour, MD, PhD[1,5]

[1]Division of Geriatrics, Department of Medicine, University of California San Francisco, San Francisco, CA



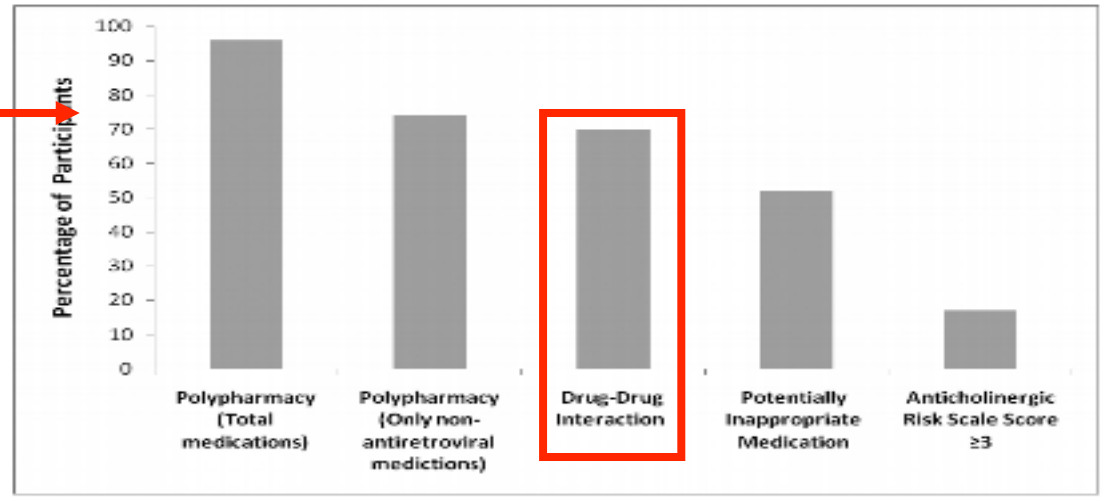


Figure 2.
Percentage of HIV-Infected Participants with Medication-Related Problems. Each bar represents the percentage of participants with each listed medication-related problem. In this figure, polypharmacy is defined as ≥5 medications.

Yaşlılara İlaç Yazmak

EACS European AIDS Clinical Society

[10], [11], [12] numaralı kaynaklardan uyarlanmıştır

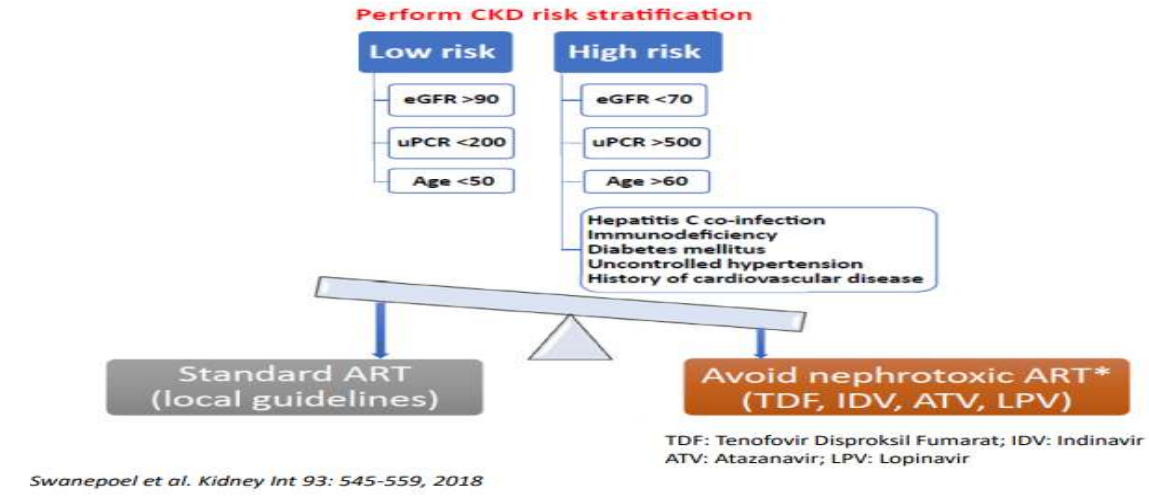
i-iii Beers ve STOPP kriterleri, geriatrik farmakoterapi uzmanlarının yaşlıların uygun olmayan reçeteli ilaç yükünü tespit etmek ve azaltmak için geliştirdikleri araçlardır. Uygun olmayan ilaçlara örnek olarak: bazı hastalıkları olan yaşlı bireylerde ilaç-hastalık etkileşimine sebep olabilecek, yaşlılarda advers ilaç reaksiyonları riskini artırmakla ilişkilendirilmiş, yaşlılarda düşme riskini artırdığı öngörülen veya organ fonksiyon bozukluklarında kaçınılması gereken ilaçlar verilebilir. START kriterleri, spesifik bir sağlık durumu olan yaşlı bireylerde olası eksik ilaç yazımına ilişkin kanıta dayalı göstergelerden oluşmaktadır.

BHIVA guidelines for the routine investigation and monitoring of adult HIV-1-positive individuals (2019 interim update)

3.9 Monitoring of older patients

History	Investigations
• All medications (prescribed and non-prescribed) are reviewed and documented at every clinic visit	• Fragility fracture risk assessment in all patients over 50 years every 3 years • Screening for colorectal and breast cancers should be offered in accordance with national guidelines • Do an annual cardiovascular risk assessment in all patients over 40

- Rehberlerde kişisel ihtiyaca göre 2-4 kez/yıl değerlendirme önerilmektedir
- Komorbiditelerin öngörülmesi (Framingham, DAD, Frax)

KVS risk azaltma	Sigara bırakma Diyet Egzersiz Statin kullanımını değerlendirme ART seçimi – Kardiyak ve lipid parametrelere uygun
Osteoporoz	DXA Beslenme, D vitamini Bifosfonatlar Egzersiz ART seçimi – ABC veya TAF
Renal takip	

Diagnosis of kidney disease

		eGFR[i]			
		> 60 mL/min	> 60 mL/min, but accelerated decline of eGFR*	> 30 - ≤ 60 mL/min	≤ 30 mL/min
Proteinuria (mg/mmol)[iii]	UA/C[iii] < 3	Düzenli takip			
	UA/C[iii] 3-30	**KBH için risk faktörlerini ve ART dahil nefrotoksik ilaçları kontrol edin. Gerekli olduğunda ilaçları kesin veya doz ayarlaması yapın. Renal ultrason yapın. Herhangi bir düzeyde proteinüriyle birlikte hematüri varsa nefroloğa sevk edin. Yeni KBH gelişimi veya eGFR'da progresif düşüş olursa nefroloğa sevk edin.**			**KBH için risk faktörlerini ve ART dahil nefrotoksik ilaçları kontrol edin Gerekli olduğunda ilaçları kesilip, doz ayarlaması yapın Renal ultrason çekin Acilen nefroloğa sevk edin**
	UA/C[iii] > 30				

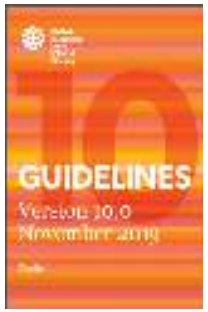
* Defined as decrease in e

ii. İdrar tahlili: Proteinüri/hematüri taramak için idrar daldırma çubuğu testi kullanın.

Proteinüri ≥ 1+ ise glomeruler hastalık için idrarda albumin/kreatinin (UA/C) bakın veya hem glomeruler hem de tubuler hastalık için idrarda protein/kreatinin (UP/C) bakın.

Proteinüri, >2-3 hafta ara ile ≥ 2 sefer doğrulanmışsa persistan kabul edilir.

iii. KDIGO screening values for UA/C are: < 3, 3-30 and > 30 mg/mmoL ve UP/C: < 15, 15-50, > 50 mg/mmol



Kanser: Tarama Yöntemleri (I)

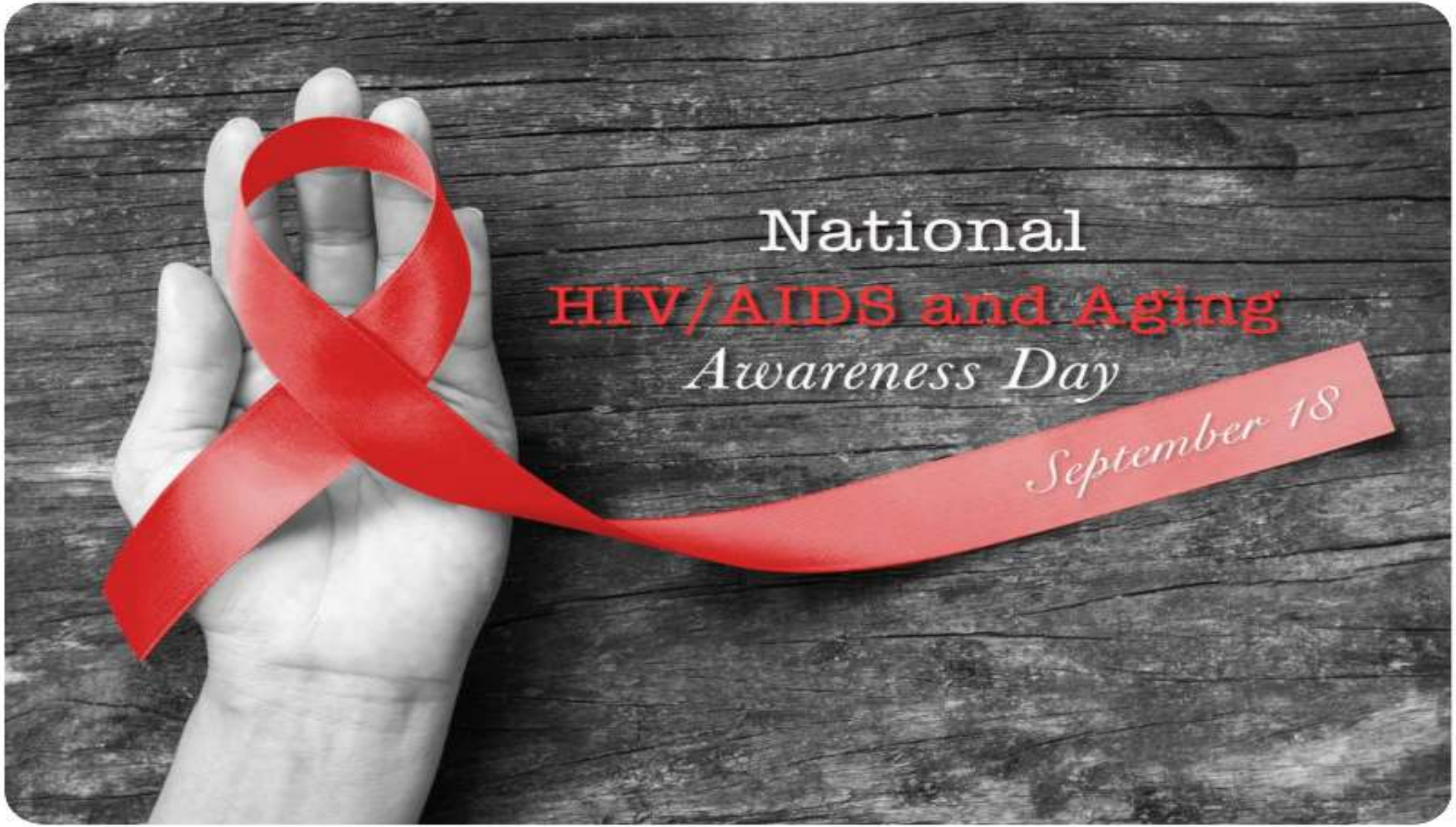
Sorun	Bireyler	İşlem	Yarara ilişkin kanıt	Tarama sıklığı	Ek yorumlar
Anal kanser	MSM ve HPV ilişkili displazisi olan bireyler (II)	Dijital rektal muayene ± anal sitoloji	Bilinmiyor, bazı uzmanlar savunuyor	1-3 yılda bir	Anal sitoloji anormalse, anoskopi
Meme kanseri		Mamografi	↓ Meme kanseri mortalitesi	1-3 yılda bir	
Servikal kanser	HIV pozitif kadınlar 21 yaşın üzerinde veya cinsel hayatın başlamasını takip eden 1 yıl içinde	Sıvı bazlı servikal sitoloji testi	↓ Cervical cancer mortality	1-3 yılda bir	HPV testi taramaya yardımcı olabilir
Kolorektal kanser	Beklenen yaşam süresi >10 yıl olan 50-80 yaş arası bireyler	Yılda bir kez dışkıda gizli kan testi veya 5 yılda bir sigmoidoskopi veya 10 yılda bir kolonoskopi	↓ Kolorektal kanser mortalite	1-3 yılda bir	
Hepatoselüler Karsinom (HSK)	Sirozlu bireyler, HBV koenfeksiyonu olup HSK riski yüksek olanlar veya kronik hepatit öyküsü olanlar (III)	Ultrason (ve alfa-fetoprotein)	Cerrahi eradikasyon olanağını artıran erken tanı	6 ayda bir	Bkz. sayfa 58 ve 81
Prostat kanseri	Beklenen yaşam süresi >10 yıl olan 50 yaş üzeri erkekler	PSA (IV)	PSA kullanımı tartışmalıdır	2-4 yılda bir	Avantaj: ↑ erken tanı prostat kanseri spesifik mortalitede az oranda ↓ Dezavantaj: gereksiz tedavi, tedavinin yaşam kalitesi üzerinde istenmeyen etkileri

- Depresyon tarama soruları
- Nörokognitif bozukluk (MoCA testi)

Sonuç olarak HIV ile yaşlanan bireyler

- Daha hızlı yaşlanıyorlar
- Komorbiteler (kvs, renal, nörolojik,kemik, metabolik, kanserler) daha sık ve daha erken
- Polifarmasi, ilaç etkileşimleri, PK
- Komorbiditelere göre ART seçimi

- ART'ye uyum iyi ama immünolojik yanıt az
- Advers etkiler
- **Uzun süreli ART kullanımının kümülatif etkisi**


National
HIV/AIDS and Aging
Awareness Day
September 18