HIV ile Yaşayan Bireylerde
Kardivasküler ve Renal Komorbiditeler

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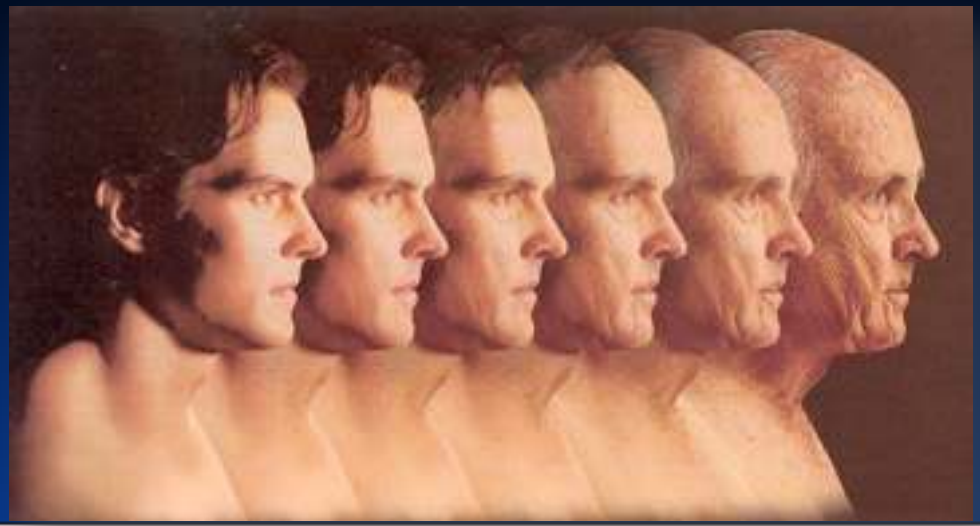
3 Eylül 2021, Türkiye EKMUD HIV Akademisi-Edirne

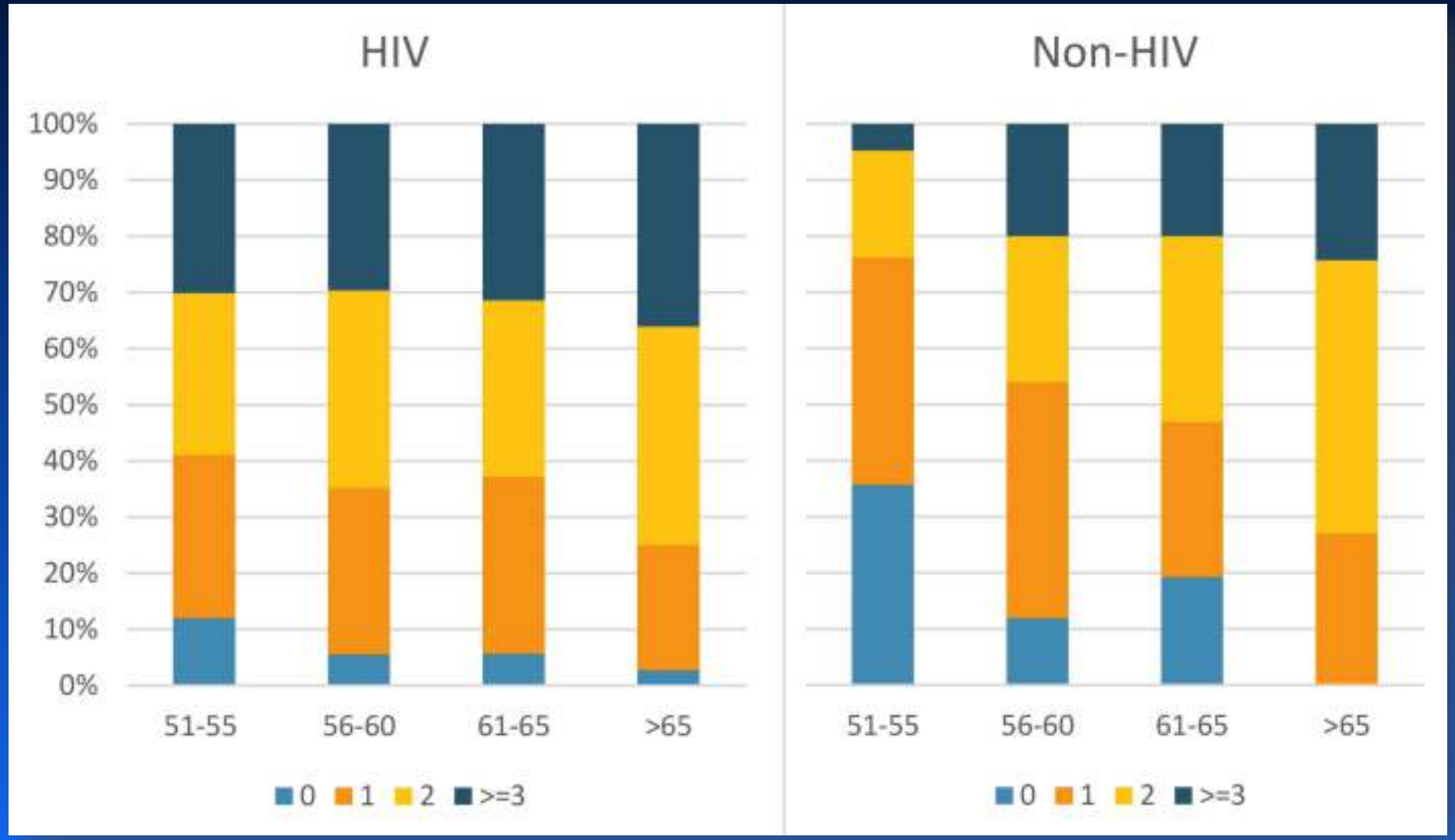
- Epidemiyoloji
- Risk faktörleri
- Göstergeler
- Değerlendirme
- Tedavi ve yönetim



Yaşam süresi

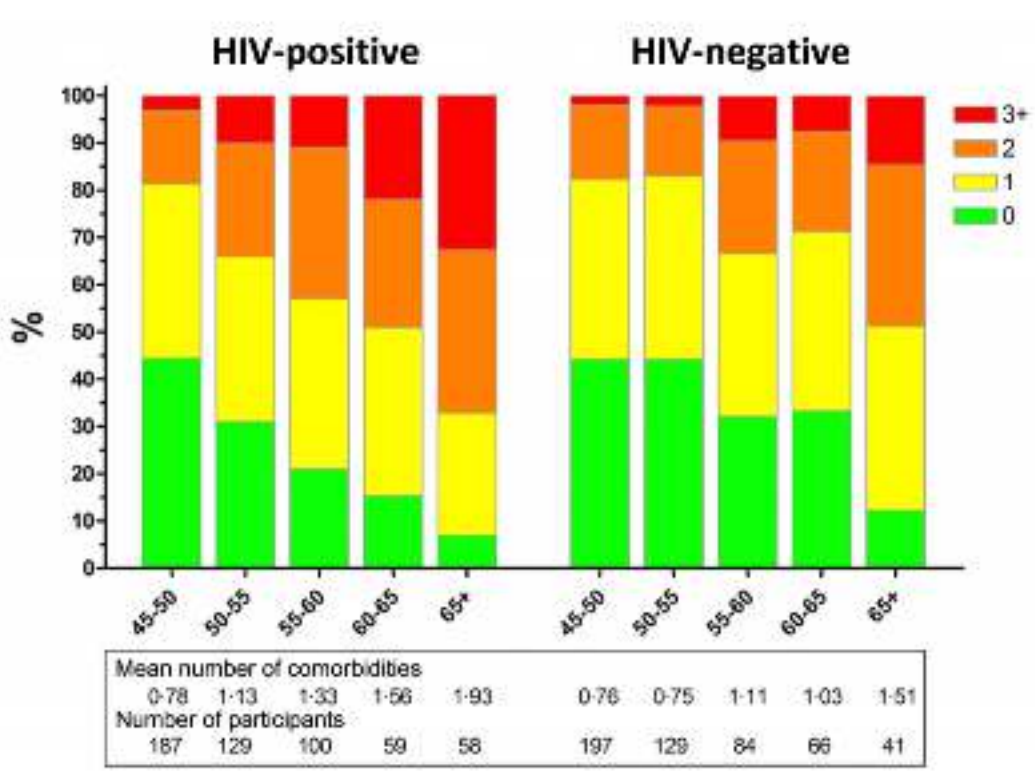
Komorbiditeler

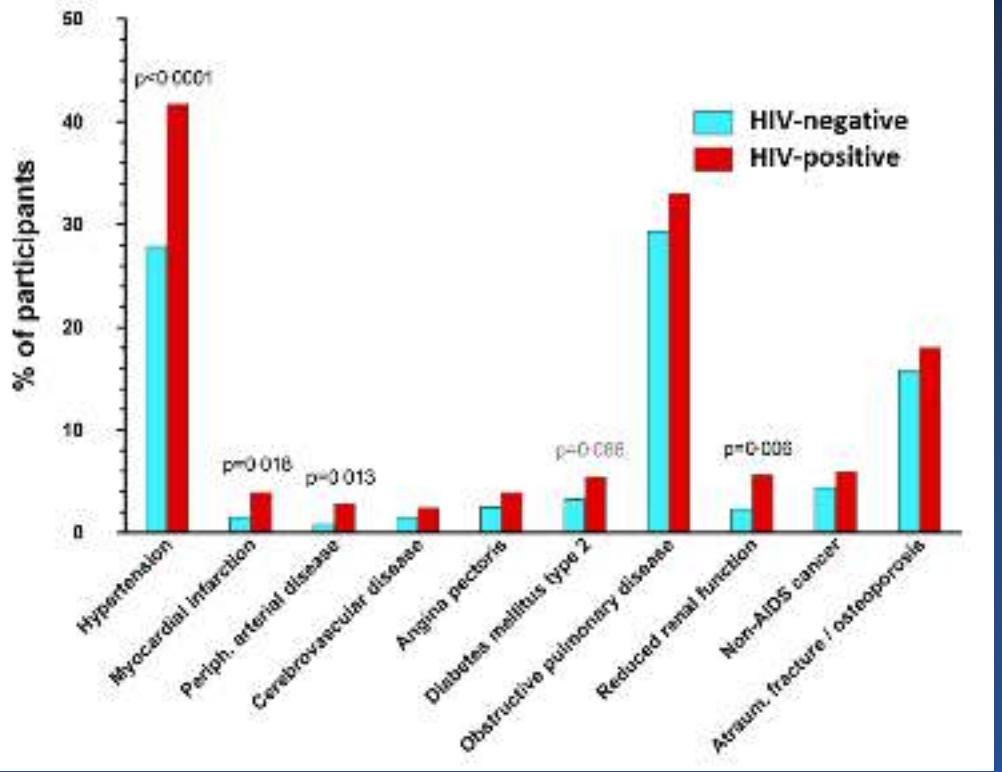
Comorbidity is more common and occurs earlier in persons living with HIV than in HIV-uninfected matched controls, aged 50 years and older: A cross-sectional study



R.A. Maciel et al. / International Journal of Infectious Diseases 70 (2018) 30–35

Cross-sectional Comparison of the Prevalence of Age-Associated Comorbidities and Their Risk Factors Between HIV-Infected and Uninfected Individuals: The AGEhIV Cohort Study





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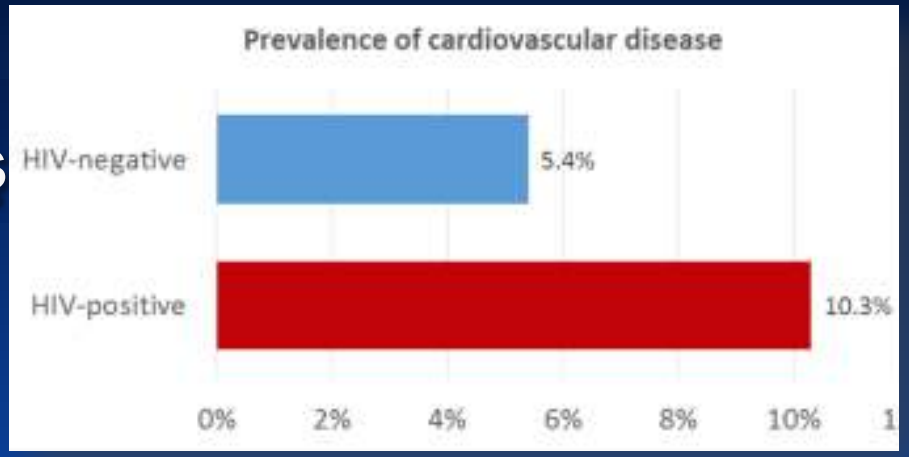
Clinical Infectious Diseases® 2014;59(12):1787–97

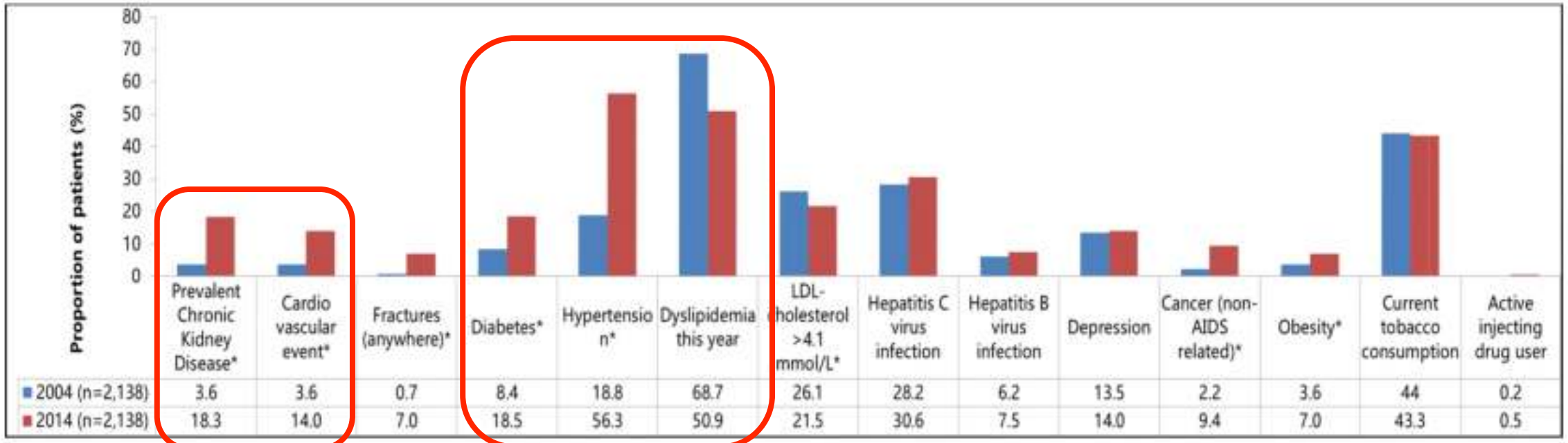
KVH Prevalansı

- Enfekte bireylerde >2 kat yüksek
  - 45 yaş üzerinde daha belirgin artış
- MI riski 2 kat yüksek
- Ani kalp ölümü 4 kat yüksek
- Global HIV ilişkili MI ve stroke yükünde son 2 dekatta 3 kat artış



Circulation 2018;138:1100-1112

Evolution of comorbidities in people living with HIV between 2004 and 2014: cross- sectional analyses from ANRS CO3 Aquitaine cohort



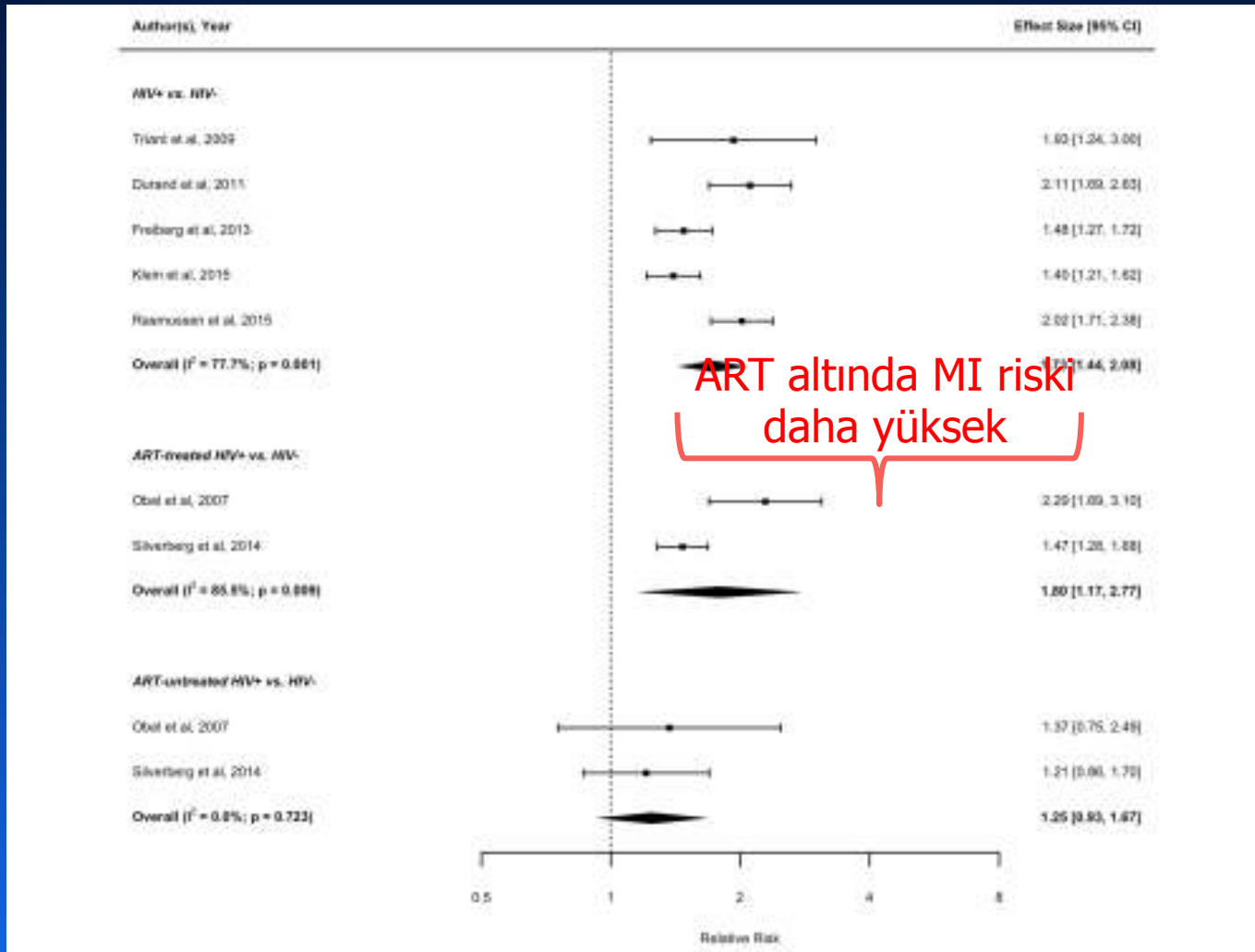
	Prevalent Chronic Kidney Disease*	Cardio vascular event*	Fractures (anywhere)*	Diabetes*	Hypertension*	Dyslipidemia this year	LDL-cholesterol >4.1 mmol/L*	Hepatitis C virus infection	Hepatitis B virus infection	Depression	Cancer (non-AIDS related)*	Obesity*	Current tobacco consumption	Active injecting drug user
2004 (n=2,138)	3.6	3.6	0.7	8.4	18.8	68.7	26.1	28.2	6.2	13.5	2.2	3.6	44	0.2
2014 (n=2,138)	18.3	14.0	7.0	18.5	56.3	50.9	21.5	30.6	7.5	14.0	9.4	7.0	43.3	0.5

*p<0.01 for comparison between 2004 and 2014

Chronic Comorbidities in 2004 and 2014, ANRS CO3 Aquitaine Cohort

Bonnet et al. BMC Infectious Diseases (2020) 20:850

Risk of myocardial infarction among people living with HIV: an updated systematic review and meta-analysis



Forest plot of the meta-analysis of the risk of MI associated with HIV infection. ART, antiretroviral therapy.

Eyawo O, et al. BMJ Open 2019;9:e025874.

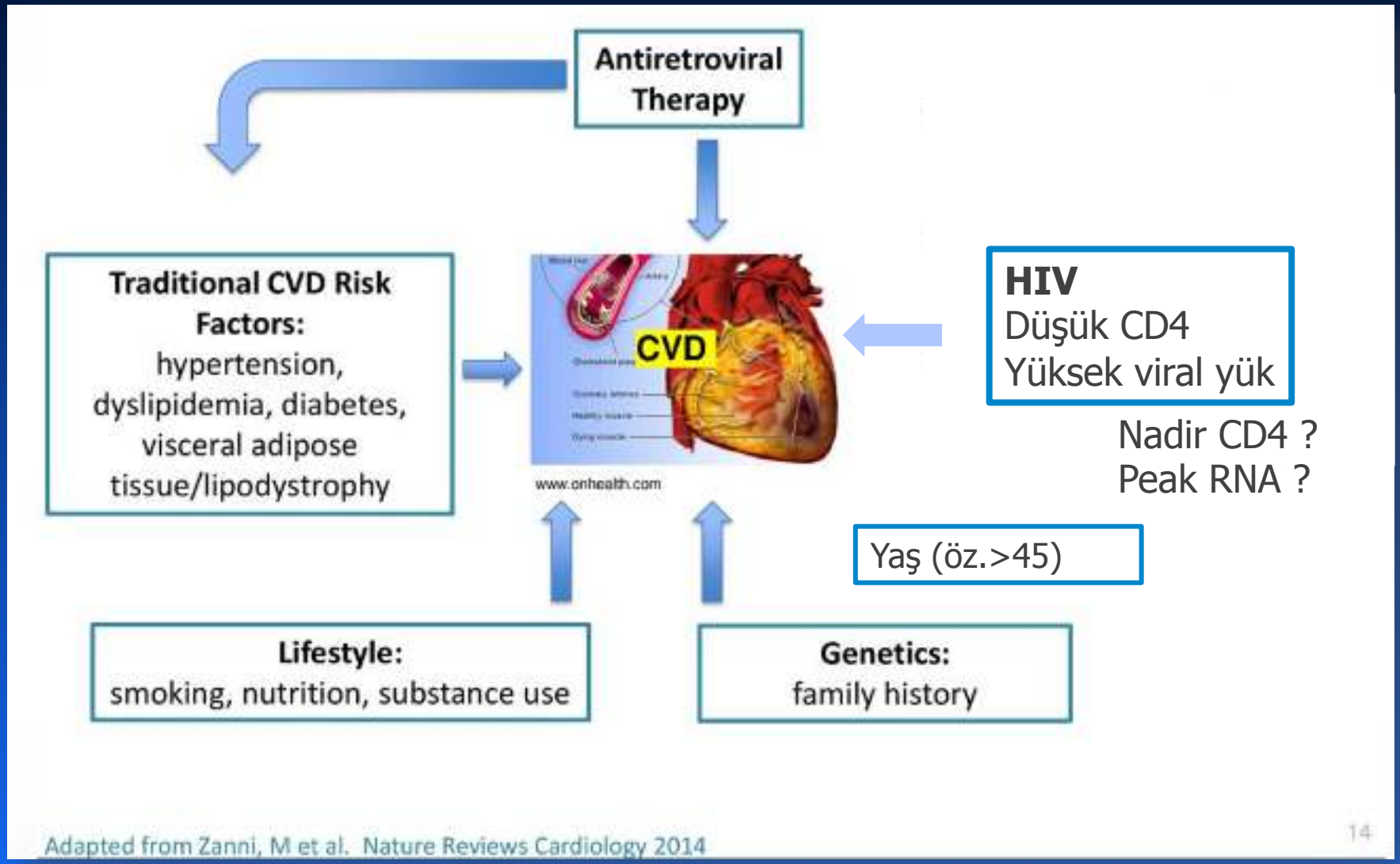
Poster Presentation

PE11/19 - Prevalence of Age-associated Non-infectious Comorbidities among HIV-infected Patients in Turkey

V. Korten[1], T. Yıldırmak[2], D. Gökengin[3], S. Gencer[4], M. Fincanci[5], A. Çağatay[6], N. Ceran[7], A. Inan[7], G. Mermut[3], D. Yagci Çağlayik[1], G. Eren[5], F. Şimşek[2], HIV-TR Cohort

- 2015-2017
- N=262, >40 yaş
- Hiperlipidemi %22.4
- HT %16.5
- DM %9.1

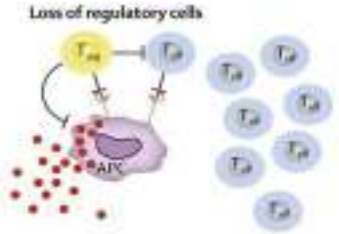
Risk faktörleri



- ART ile birlikte
  - ilaç toksisitesi,
  - düşük HDL-K, yüksek TG
  - vücut yağ dağılımda bozukluk,
  - metabolik sorunlar (dislipidemi, DM, ve KVH) artıyor
- ART kesilmesi ile de KVH riski artıyor
  - Kardioprotektif etki ortadan kalkıyor, tekrar proinflamatuvar sitokinler artıyor, HDL-K azalıyor.

- **Proteaz inhibitörleri**
  - **Dislipidemi, hiperkolesterolemi, hipertrigliseridemi**
  - **Ritonavir**
    - Atazanavir-r < Darunavir-r < Iopinavir-r
- **NNRTIs**
  - **Tot.kolesterol ve LDL-kolesterolde artış**
  - **Rilpivirine < efavirenz**
- **NRTIs**
  - **TAF < TDF < abacavir-lamivudin**
- **INTIs**

Loss of regulatory cells

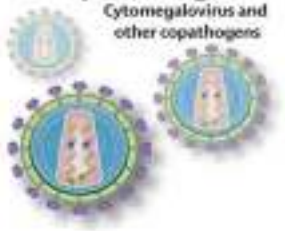


ART toxicity

ART toxicity, lipodystrophy, and traditional risk factors

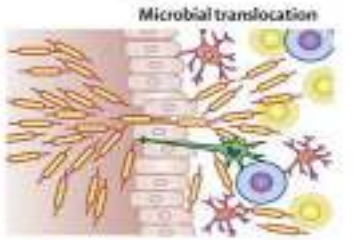
CMV & other pathogens

Cytomegalovirus and other copathogens



HIV Infection

Microbial translocation



Inflammation

- Monocyte activation
- T-cell activation
- Endothelium adhesion
- Dyslipidemia
- Hypercoagulation

Unknown factors

Traditional risk factors

HIV Atherosclerosis

1

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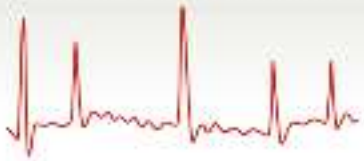
Canadian Journal of Cardiology 35 (2019) 238-248

KV Hastalıklar

	Pre-ART	First-generation ART regimens	Contemporary ART regimens	Future: Optimized ART regimens	Future: Curative therapies
HIV treatment	No HIV-specific therapy	• PI • NRTI • NNRTI	• PI • NRTI • NNRTI • CCR5 antagonist • Integrase inhibitor	• Early ART initiation • Two-drug regimens • Injectable medications • New therapeutic targets	• Stem-cell-based therapies • Strategies to eliminate latency • Genome editing • Broadly neutralizing antibodies
Inflammatory and immunological status	• AIDS • Inflammation	• Immunodeficiency • Chronic inflammation	• Immunodeficiency • Chronic inflammation	Chronic inflammation	Eradication of HIV infection
Cardiovascular complications	• Pericardial effusion • Dilated cardiomyopathy	• Atherosclerosis • Myocardial infarction • Dilated cardiomyopathy • Stroke • Peripheral artery disease	• Heart failure • Atrial fibrillation • Sudden cardiac death • Coronary heart disease	• Increased risk of cardiovascular diseases	



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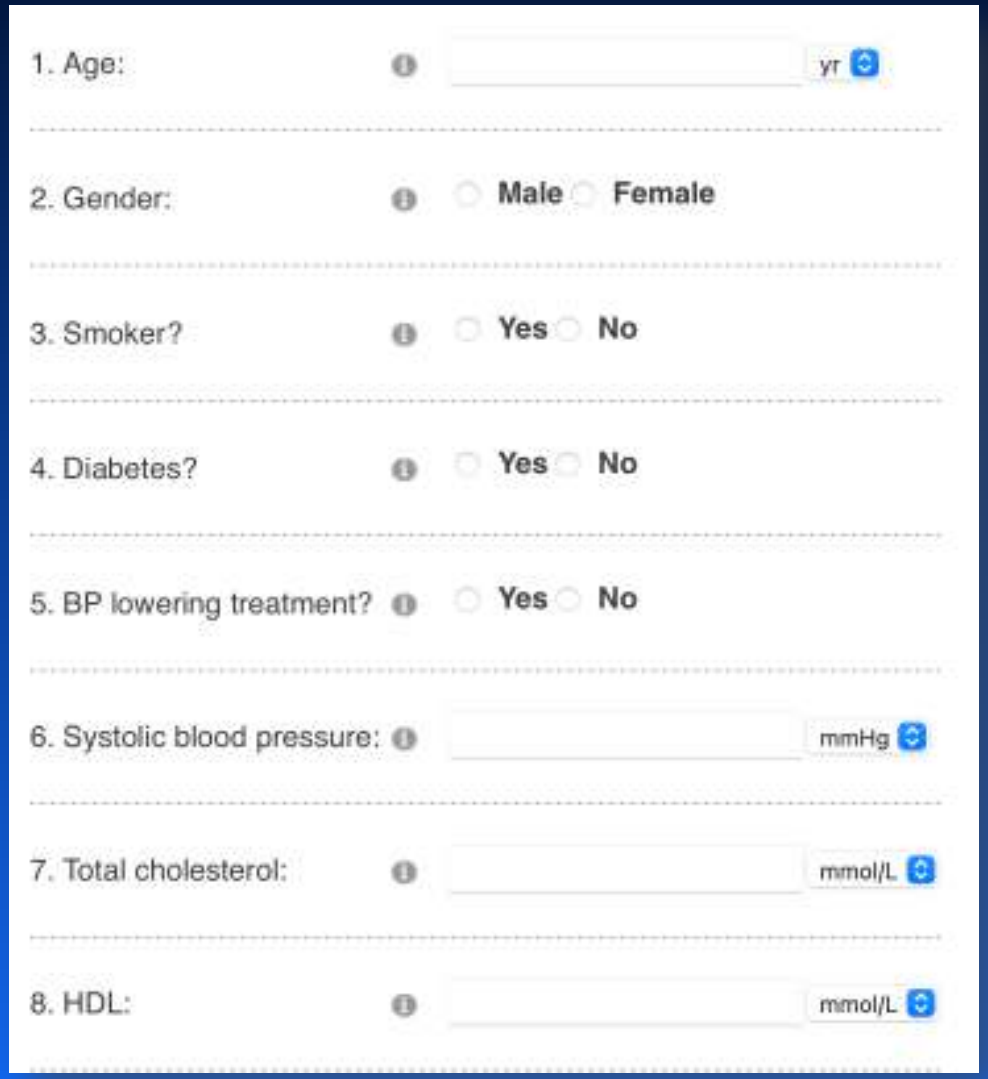
Hsue, P.Y., Waters, D.D. *Nat Rev Cardiol* **16,** 745–759 (2019)

İlk değerlendirmede…

Risk faktörlerinin araştırılması:

- **Sigara alışkanlığı**
- **Diyet**
- **Egzersiz**
- **Ailede KAH, HT, DM**
- **FM.de KB, bel çevresi, VKİ**
- **Lab: Açlık lipid seviyeleri, AKŞ, HbA1c**

Framingham hesaplaması



https://www.chip.dk/Resources/Clinical-risk-scores

Risk hesaplaması

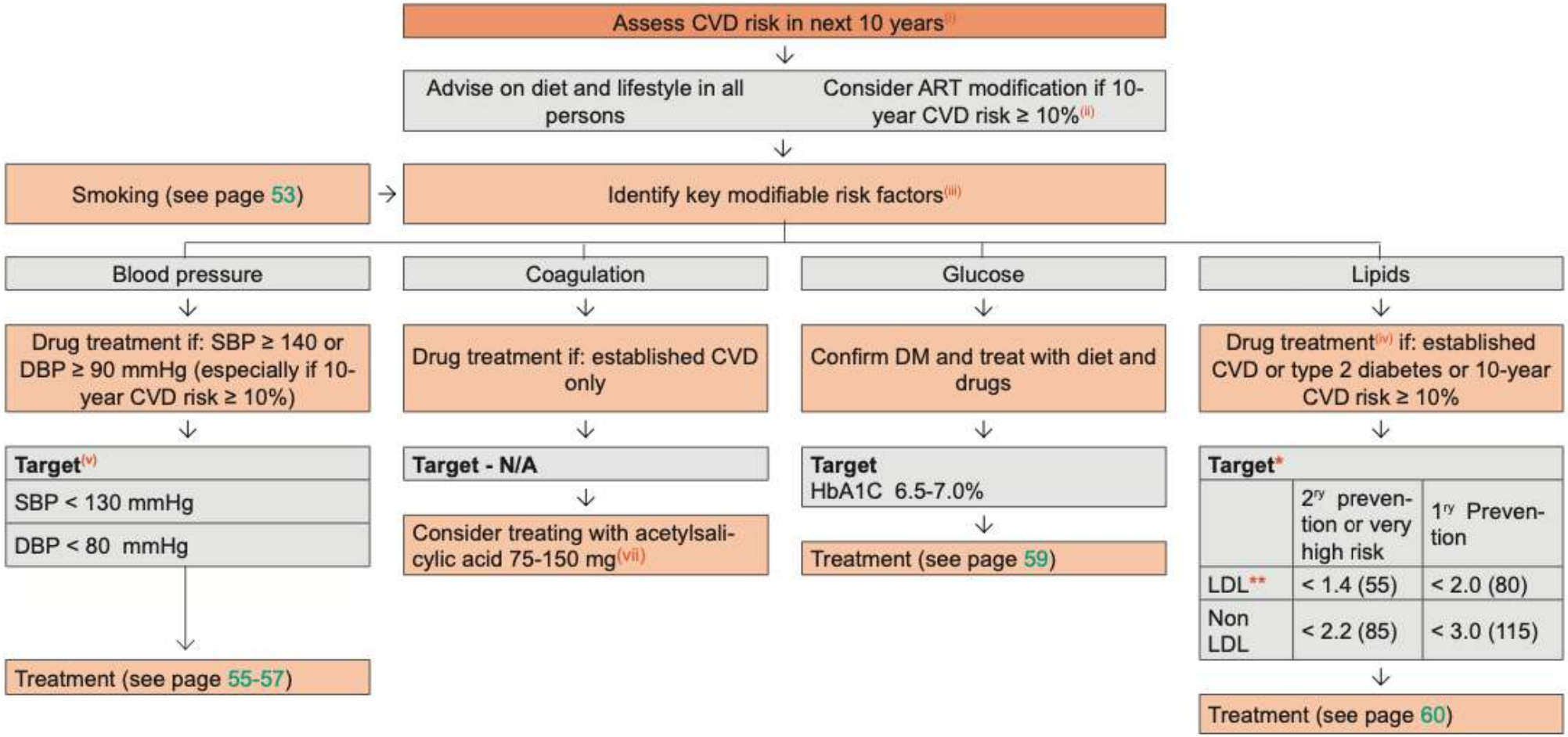
Risk Score	Population	Target Cardiovascular Events	Variables Included
FRS- CHD (Framingham)	30 – 74 years	Angina, MI, CHD death, coronary insufficiency	Age, Total Cholesterol, HDL-C, BP, Diabetes status, Smoking, Gender
ATP3-FRS-CHD (ATP3)	>20 years	MI, CHD death	Age, Total Cholesterol, HDL-C, BP, Smoking, Gender, Antihypertension Medication use
DAD (DAD)	HIV, European	MI	Age, Total Cholesterol, HDL-C, BP, Diabetes status, Smoking, Gender, Abacavir use, Duration of indinavir use, Duration of lopinavir use
2013 ACC/AHA ASCVD Pooled Cohort Equations (ASCVD)	40 – 79 years	MI, CHD death, stroke	Age, Total Cholesterol, HDL-C, BP, Diabetes status, Smoking, Gender, White or African American Ethnicity, Antihypertension Medication use

Riski azaltmak

- Yaşam stilinin değişmesi (sigara, alkol, diyet, fiziksel aktivite,…)
- Gereğinde statin tedavisi
- KB kontrolü
- DM tedavisi

Prevention of Cardiovascular Disease (CVD)

Principles: The intensity of efforts to prevent CVD depends on the underlying risk of CVD, which can be estimated(i). The preventive efforts are diverse in nature and require involvement of a relevant specialist, in particular if the risk of CVD is high and always in persons with a history of CVD

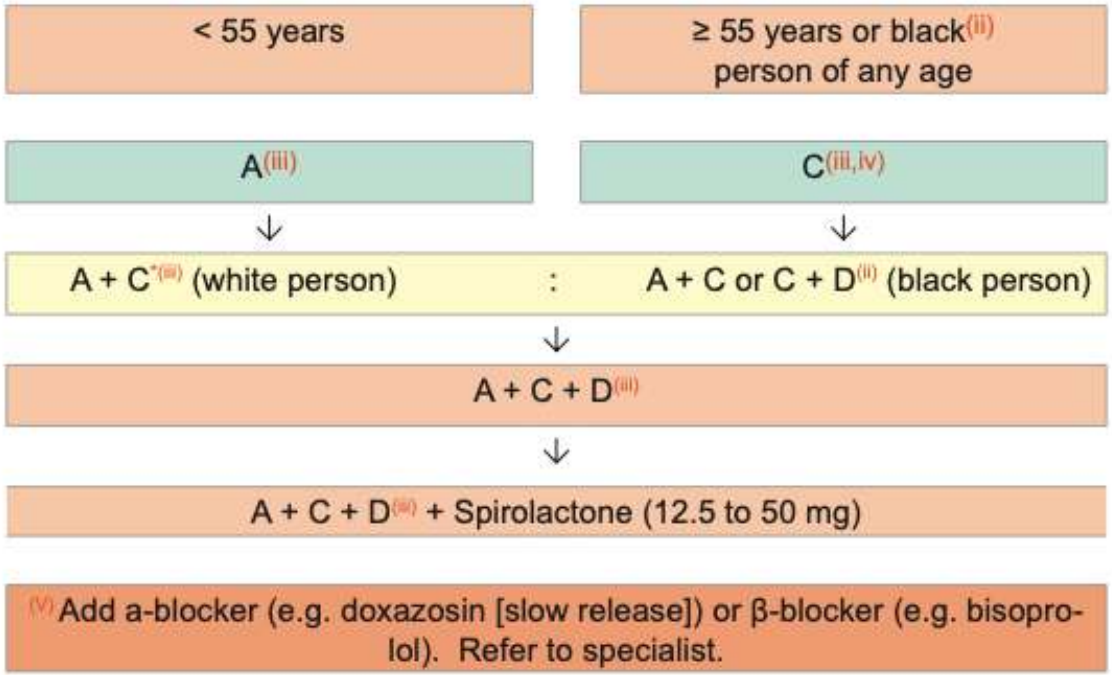


Hypertension: Diagnosis, Grading and Management

Other risk factors, asymptomatic organ damage or disease	Blood pressure (mmHg)	Blood pressure (mmHg)	Blood pressure (mmHg)	Blood pressure (mmHg)
	High normal SBP 130-139 or DBP 85-89	Grade 1 hypertension SBP 140-159 or DBP 90-99	Grade 2 hypertension SBP 160-179 or DBP 100-109	Grade 3 hypertension SBP ≥ 180 or DBP ≥ 110
No other risk factors	• Lifestyle changes[i] • No BP drug intervention	• Lifestyle changes[i] for several months • Then add BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] for several weeks • Then add BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] • Immediate BP drugs targeting < 130/80[ii]
1-2 risk factors	• Lifestyle changes[i] • No BP drug intervention	• Lifestyle changes[i] for several weeks • Then add BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] for several weeks • Then add BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] • Immediate BP drugs targeting < 130/80[ii]
≥ 3 risk factors	• Lifestyle changes[i] • i.e. no BP drug intervention	• Lifestyle changes[i] for several weeks • Then add BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] • BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] • Immediate BP drugs targeting < 130/80[ii]
Organ damage, CKD stage 3 or diabetes	• Lifestyle changes[i] • Consider blood pressure drugs targeting < 130/80[ii]	• Lifestyle changes[i] • BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] • BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] • Immediate BP drugs targeting < 130/80[ii]
Symptomatic CVD, CKD stage ≥ 4 or diabetes with organ damage/risk factors	• Lifestyle changes[i] • Consider blood pressure drugs targeting < 130/80[ii]	• Lifestyle changes[i] • BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] • BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] • Immediate BP drugs targeting < 130/80[ii]

Hypertension: Drug Sequencing Management

Choosing drugs[i] for persons newly diagnosed with hypertension



A ACE inhibitor (e.g. perindopril, lisinopril or ramipril) or angiotensin receptor blockers (ARB) (e.g. losartan, candesartan)

C Dihydropyridine calcium-channel blocker (e.g. amlodipine). If not tolerated or if deemed at high risk of heart failure, 'D' drugs can be used instead. Where a C drug is preferred but not tolerated, verapamil or diltiazem may be used (note: dose with caution with PIs as these may increase plasma concentrations of these calcium-channel blockers, potentially leading to toxic reactions)

D Thiazide-type diuretic. e.g. indapamide or chlorthalidone as a first choice. This excludes thiazides (e.g. hydrochlorothiazide (HCTZ), bendroflumethiazide etc.). However, if thiazide-type diuretics are not available low-dose thiazides may be used as a treatment alternative

i Two antihypertensive drugs (ideally administered as single tablet combinations, where available) are increasingly recommended both as first-line therapy (A + C or A + D) and second-line therapy particularly if the initial pre-treatment SBP is ≥ 160 mmHg

ii Black persons are those of African or Caribbean descent, and not mixed race, Asian or Chinese persons. Either A+C or C+D can be used for this

iii Wait 4-6 weeks to assess whether target, see page xx, is achieved; if not, go to next step

iv Some calcium-channel blockers interact marginally with the pharmacokinetics of ARVs, see Drug-drug Interactions between Antihypertensives and ARVs

v Requirement of 4-5 drugs to manage hypertension needs specialist advice

* Use A+D if C not tolerated

Type 2 Diabetes: Diagnosis

Diagnostic criteria[i]

	Fasting plasma glucose mmol/L (mg/dL)[ii]	Oral glucose tolerance test (OGTT) 2-h value mmol/L (mg/dL)[iii]	HbA1c[iv] (mmol/mol)
Diabetes	≥ 7.0 (126) OR→	≥ 11.1 (200)	≥ 6.5% (≥ 48)
Impaired glucose tolerance (IGT)	< 7.0 (126) AND→	7.8 – 11.0 (140-199)	Prediabetes 5.7-6.4% (39-47)
Impaired fasting glucose (IFG)	5.7– 6.9 AND (100-125)	< 7.8 (140)	

Type 2 Diabetes[i]: Management

If modification of lifestyle measures is insufficient

↓

Metformin(ii) start dose (500-850 mg qd), increase to maximum tolerated dose of 2(-3) g/day over 4-6 weeks[ii]

↓

HbA1c > 6.5-7% (> 48-53 mmol/mol)

↓

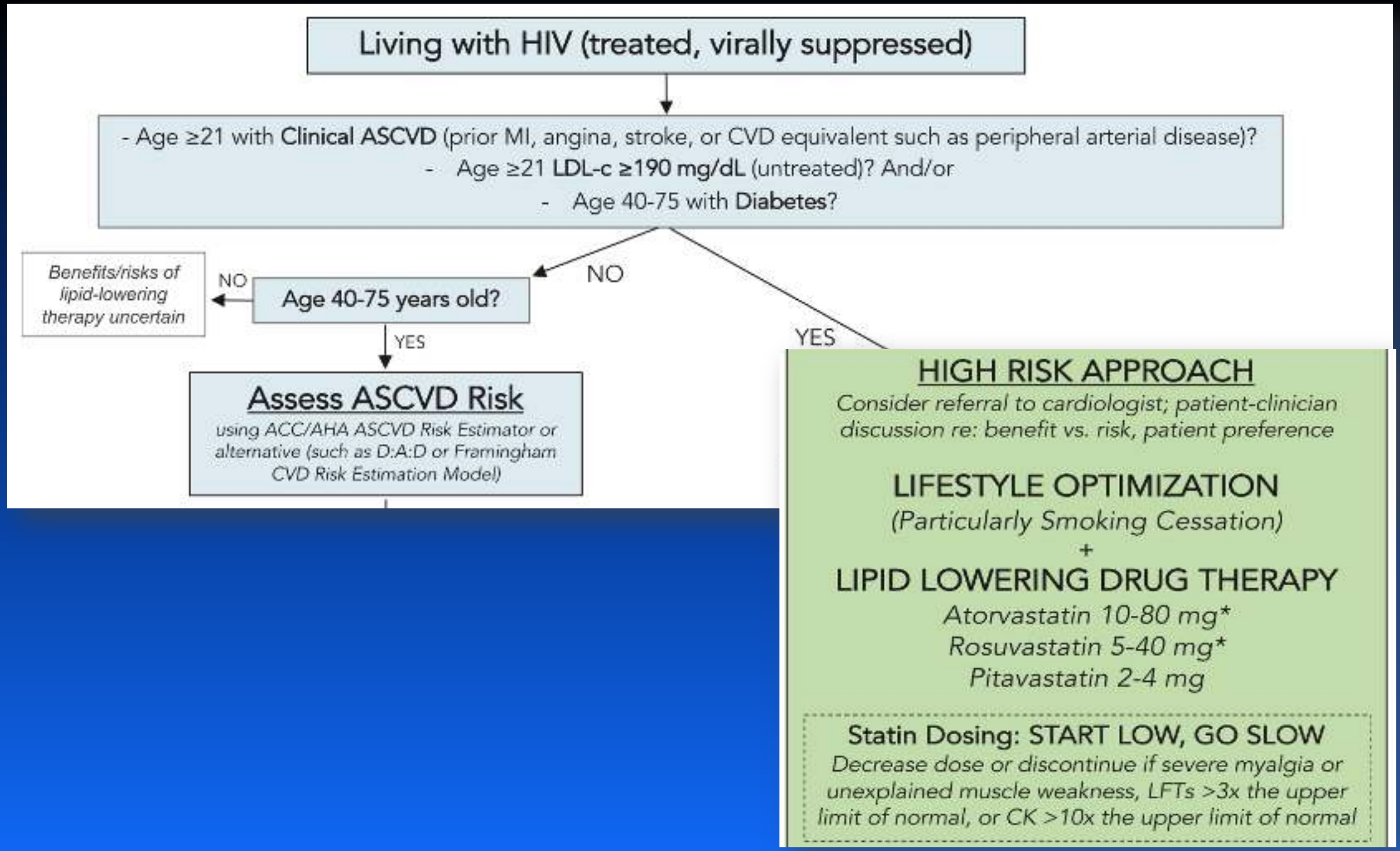
Metformin[i] + sulfonylureas or thiazolidinedione or DPP-4 inhibitor or SGLT-2 inhibitor or GLP-1 agonist or insulin

↓

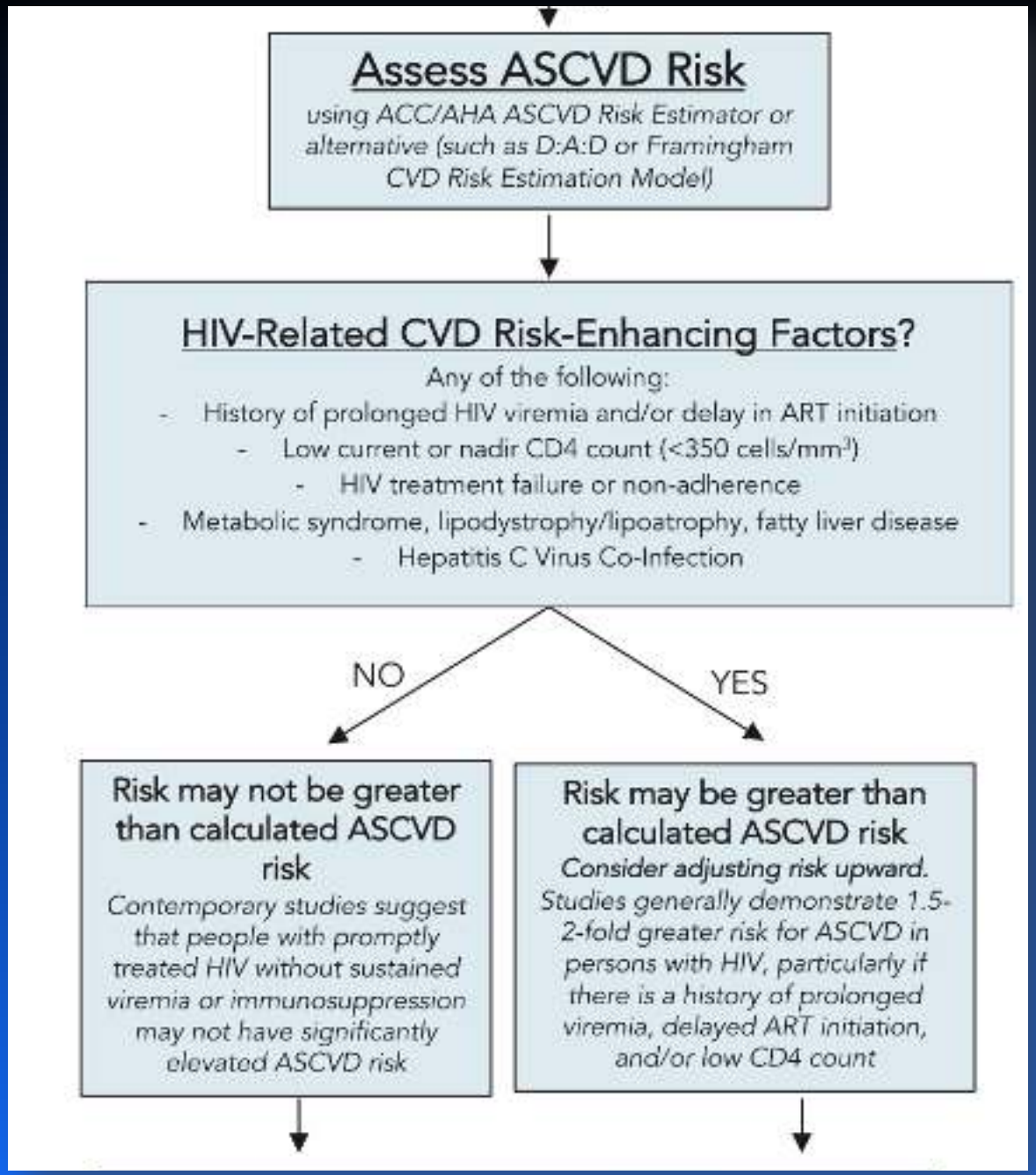
HbA1c > 6.5-7% (> 48-53 mmol/mol)

↓

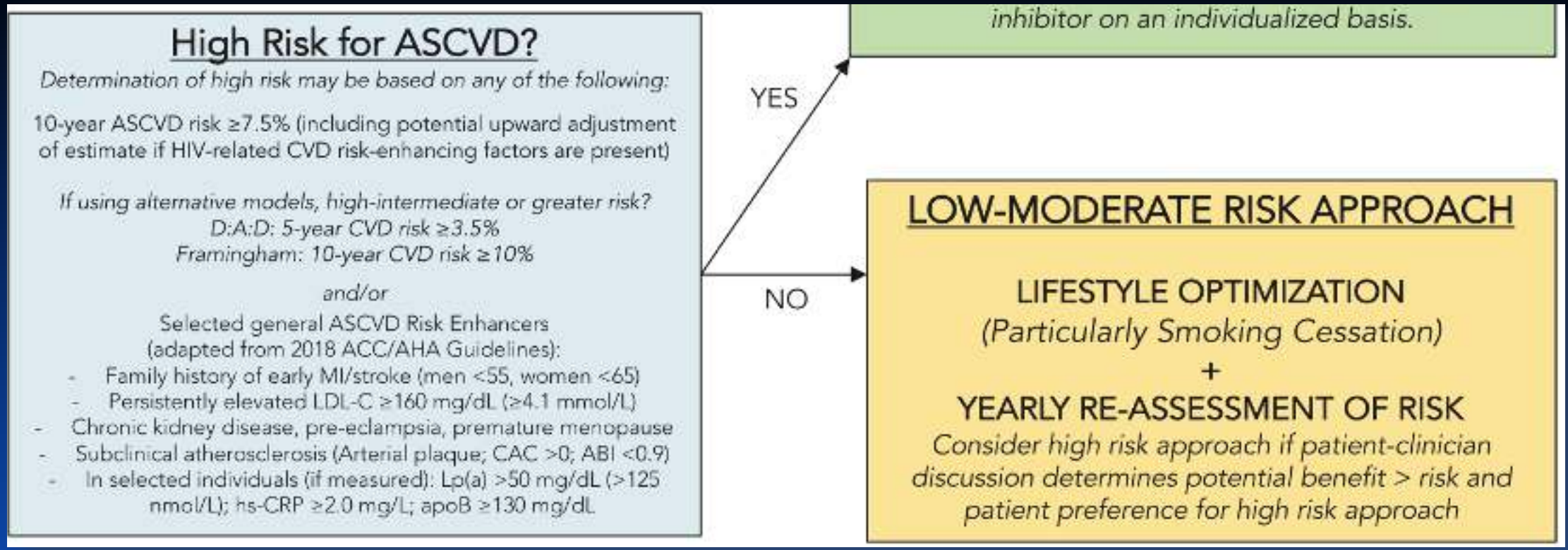
Refer to specialist for triple therapy – use insulin



AHA. Circulation. 2019;140:e98–e124.



AHA. Circulation. 2019;140:e98–e124.



AHA. Circulation. 2019;140:e98–e124.

HIGH RISK APPROACH

Consider referral to cardiologist; patient-clinician discussion re: benefit vs. risk, patient preference

LIFESTYLE OPTIMIZATION

(Particularly Smoking Cessation)

+

LIPID LOWERING DRUG THERAPY

*Atorvastatin 10-80 mg**

*Rosuvastatin 5-40 mg**

Pitavastatin 2-4 mg

Statin Dosing: START LOW, GO SLOW

Decrease dose or discontinue if severe myalgia or unexplained muscle weakness, LFTs >3x the upper limit of normal, or CK >10x the upper limit of normal

**Exercise caution due to drug interactions at high end of dose range; consider if very high risk and/or known CAD. If familial hypercholesterolemia, severe statin intolerance, or insufficient response to statin as determined by clinician: consider ezetimibe +/- PCSK9 inhibitor on an individualized basis.*

AHA. Circulation. 2019;140:e98–e124.

Lipid düşürücü tedavi

- KVH, Tip-2 DM, Yüksek KVH riski varsa

→statinler kullanılmalı !!!

  - Statin tedavisi KVH riskini %20-30 azaltır.
  - İlaç etkileşimlerine dikkat!!!

- Ciddi TG yüksekliği varsa

→fibrat başlanır.

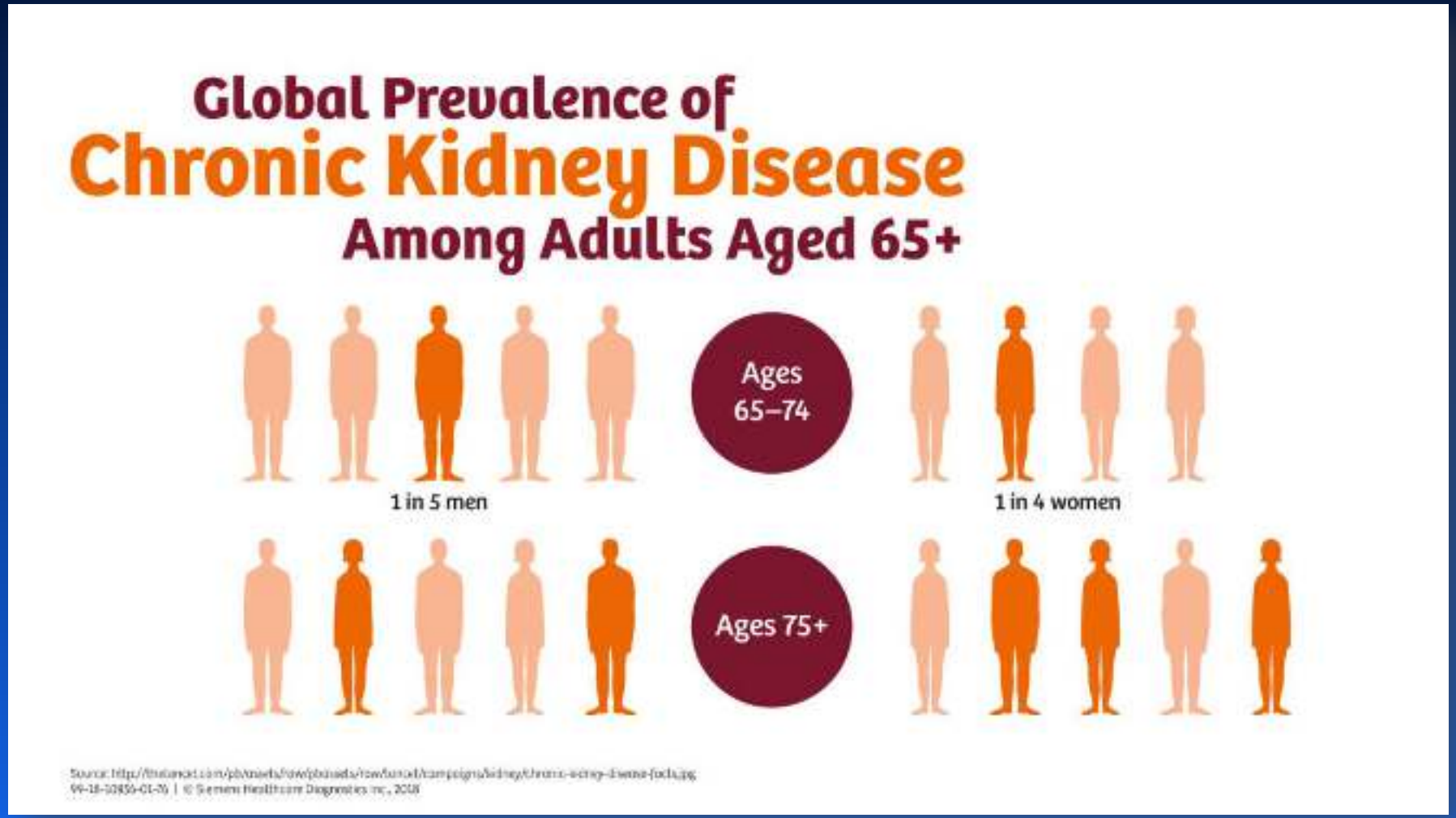
Drugs used to lower LDL-c

Drug class	Drug	Dose	Side effects	Advise on use of statin together with ART	
				use with PI/r	use with NNRTIs
Statin[i,ix]	atorvastatin[ii]	10-80 mg qd	Gastrointestinal symptoms, headache, insomnia, rhabdomyolysis (rare) and toxic hepatitis	Start with low dose[v] (max: 40 mg)	Consider higher dose[v]
	fluvastatin[iii]	20-80 mg qd		Consider higher dose[vi]	Consider higher dose[vi]
	pravastatin[iii]	20-80 mg qd		Consider higher dose[vi,vii]	Consider higher dose[vi]
	rosuvastatin[ii]	5-40 mg qd		Start with low dose[v] (max: 20 mg)	Start with low dose[v]
	simvastatin[ii]	10-40 mg qd		Contraindicated	
Intestinal cholesterol absorption inhibitor↓[i,viii]	ezetimibe[iv]	10 mg qd	Gastrointestinal symptoms	No known drug-drug interactions with ART	
PCSK9-inhibitor[x]	evolocumab	140 mg 2 weekly or 420 mg monthly	Nil	No drug-drug interactions anticipated	

- Düşük dozda statin başlanıp toksisiteden kaçarak LDL-kol düşüşünü arttırmaya çalışılır.
- CPK ve KCFT izlenir

ART seçimi

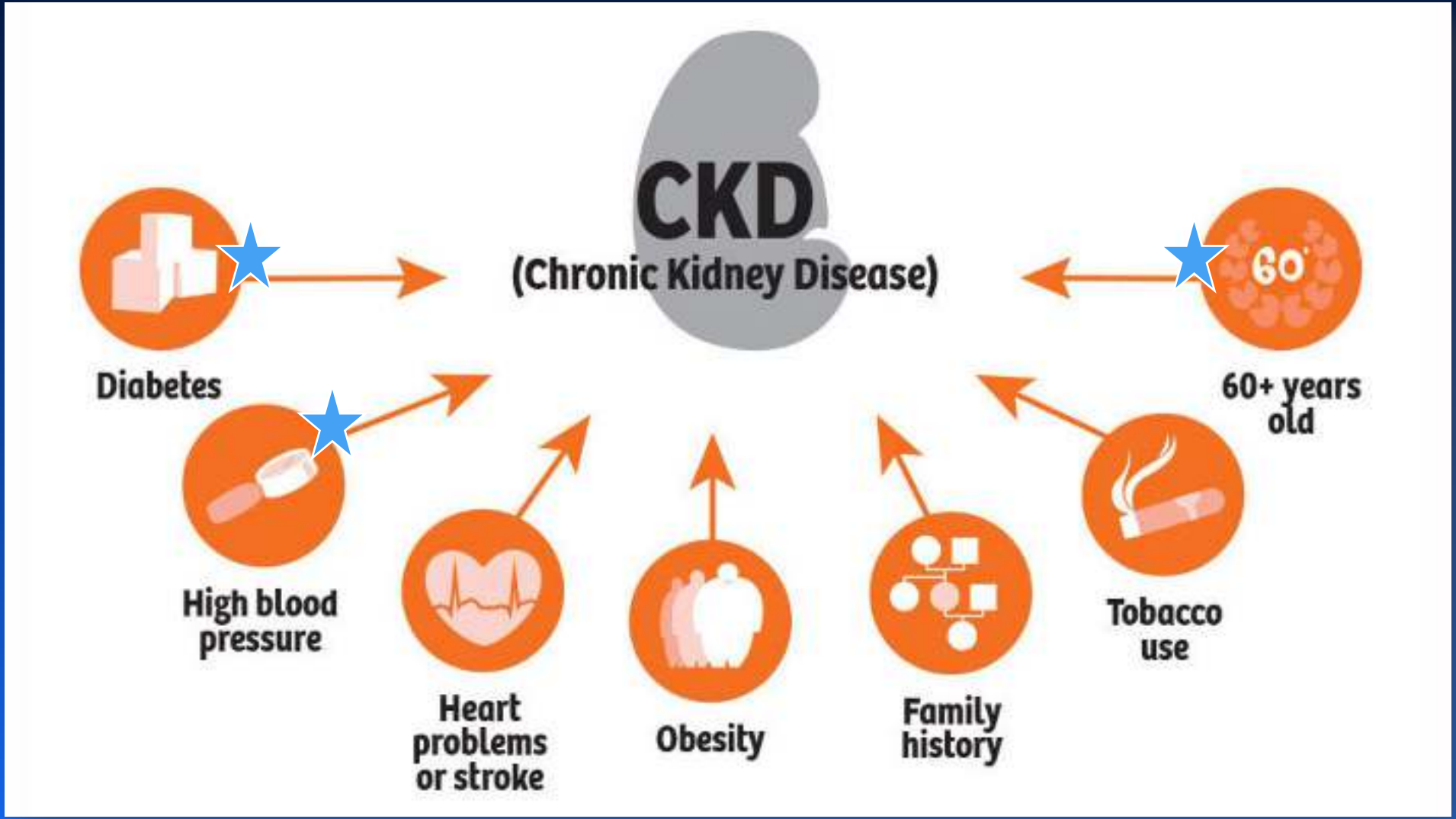
- Naif hastada ilk seçenekler uygun
- Deneyimli, ART altında ve lipid profili bozuk hastada rejimi değiştirmenin kısıtlı faydası olabilir…??
- Dislipidemik, viral supresyon sağlanmış hastada lopinavir/r veya diğer PIs > INSTIs
- PIs >NNRTI (rilpivirin, darunavir)

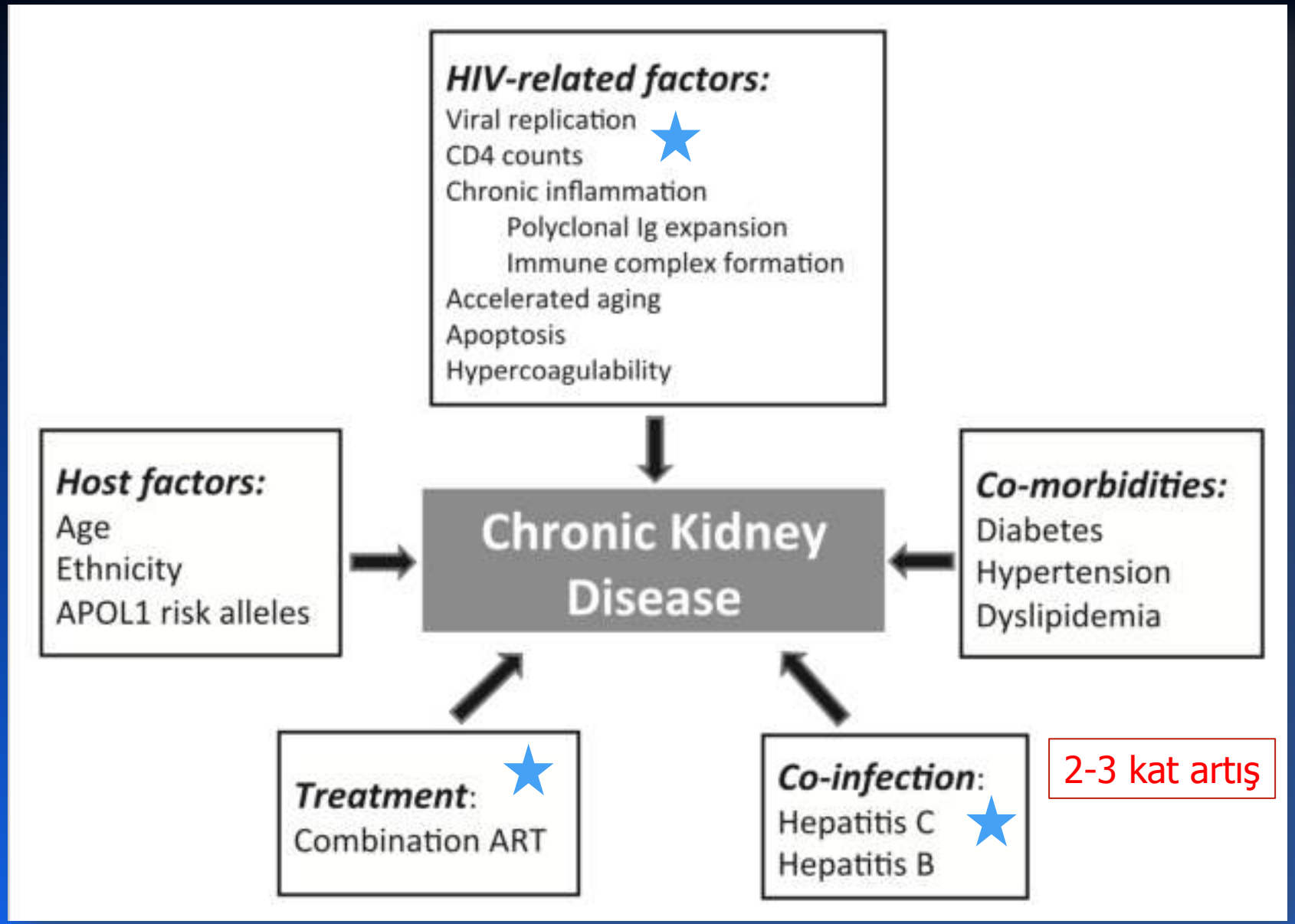

Global Prevalence of
Chronic Kidney Disease
Among Adults Aged 65+
Ages 65–74
1 in 5 men
1 in 4 women
Ages 75+

KBH Prevalansı

- Avrupa'da %2.5, Kuzey Amerika'da %7.4
- İnfekte olmayan bireylerle karşılaştırıldığında;
  - 2-5 kat yüksek
  - SDBH gelişme sıklığı 2-20 kat yüksek
- Proteinüri varlığı da kriter alındığında %33

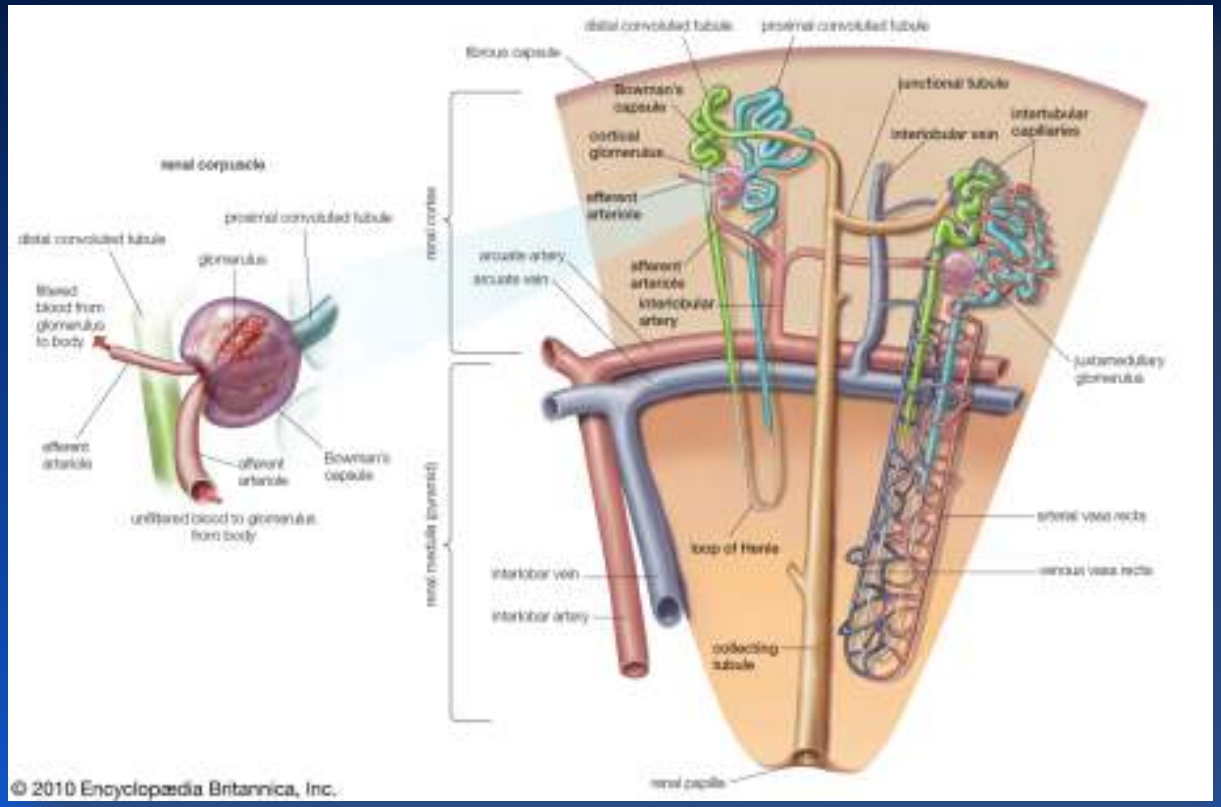
Klasik risk faktörleri



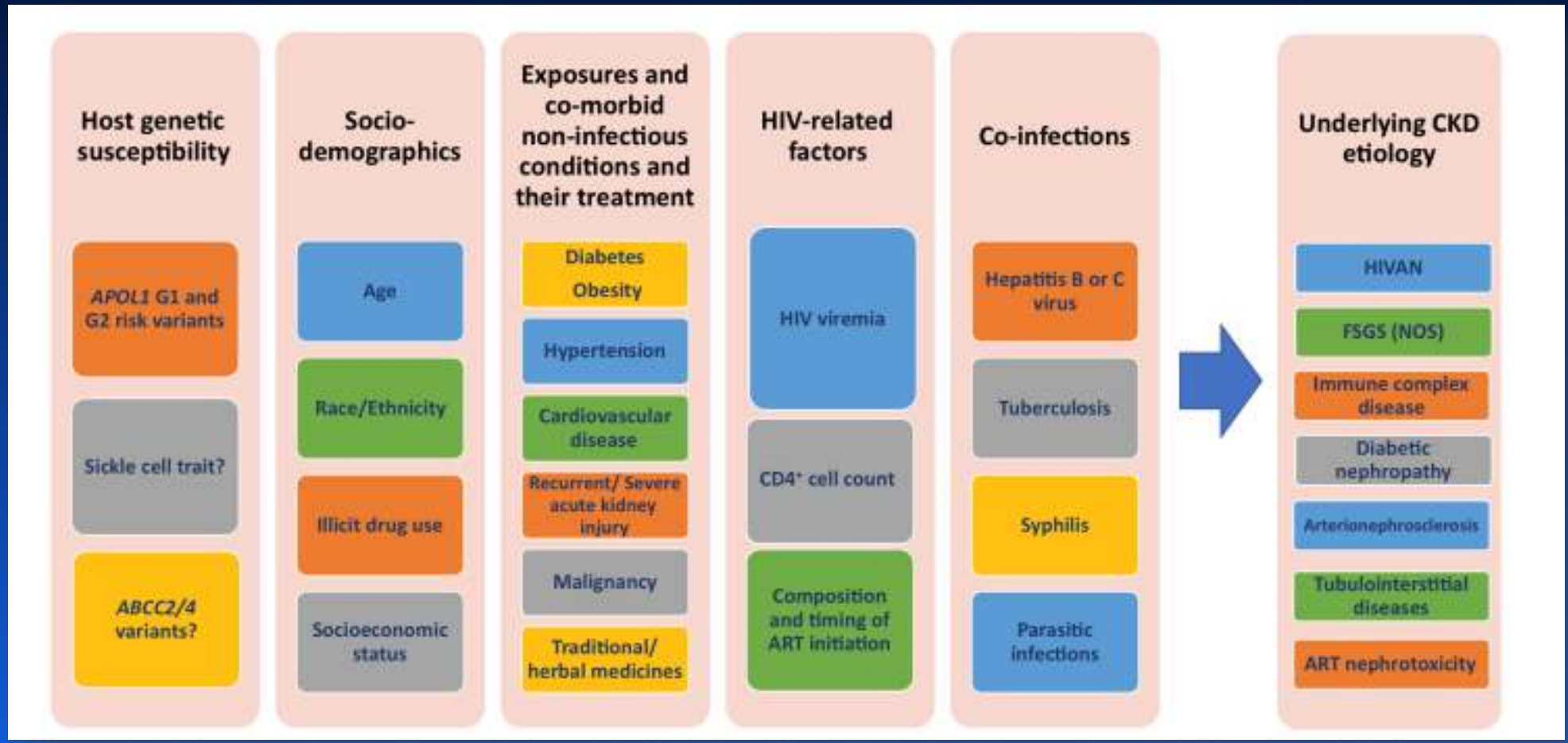

HIV-related factors:
Viral replication
CD4 counts
Chronic inflammation
Polyclonal Ig expansion
Immune complex formation
Accelerated aging
Apoptosis
Hypercoagulability
Host factors:
Age
Ethnicity
APOL1 risk alleles
Chronic Kidney Disease
Co-morbidities:
Diabetes
Hypertension
Dyslipidemia
Treatment:
Combination ART
Co-infection:
Hepatitis C
Hepatitis B
2-3 kat artış

Böbrek tutulum mekanizmaları

- Renal parenkimal hücreler üzerinde virüsün sitopatik etkisi (direkt etki)
- İndirekt etkileri
  - HIV antijenlerine hiperimmun reaksiyon
  - Böbrekte depolanan immun komplekslerin oluşması
  - Nefrotoksik ilaçlar
  - Diğer koenfeksiyonlar



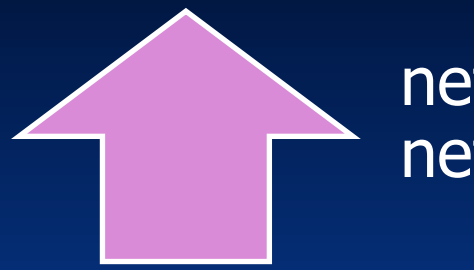
HIV ilişkili KBH



SG-2021/09

CR Swanepoel et al. Kidney disease and HIV: a KDIGO conference report

- Son 35 yıl içersinde böbrek hastalığının etyolojisi değişti:



nefrotoksisite, DM ve nefroanjiosklerozda artma

glomerular hastalıkta azalma

- Son yıllarda hipertansif ve diabetik nefropati, BH nedenlerinin %50'sinden fazlasından sorumlu

Campos P, et al. Clinical Kidney Journal, 2016, vol. 9, no. 6, 772–781

ART ilişkili nefrotoksisite

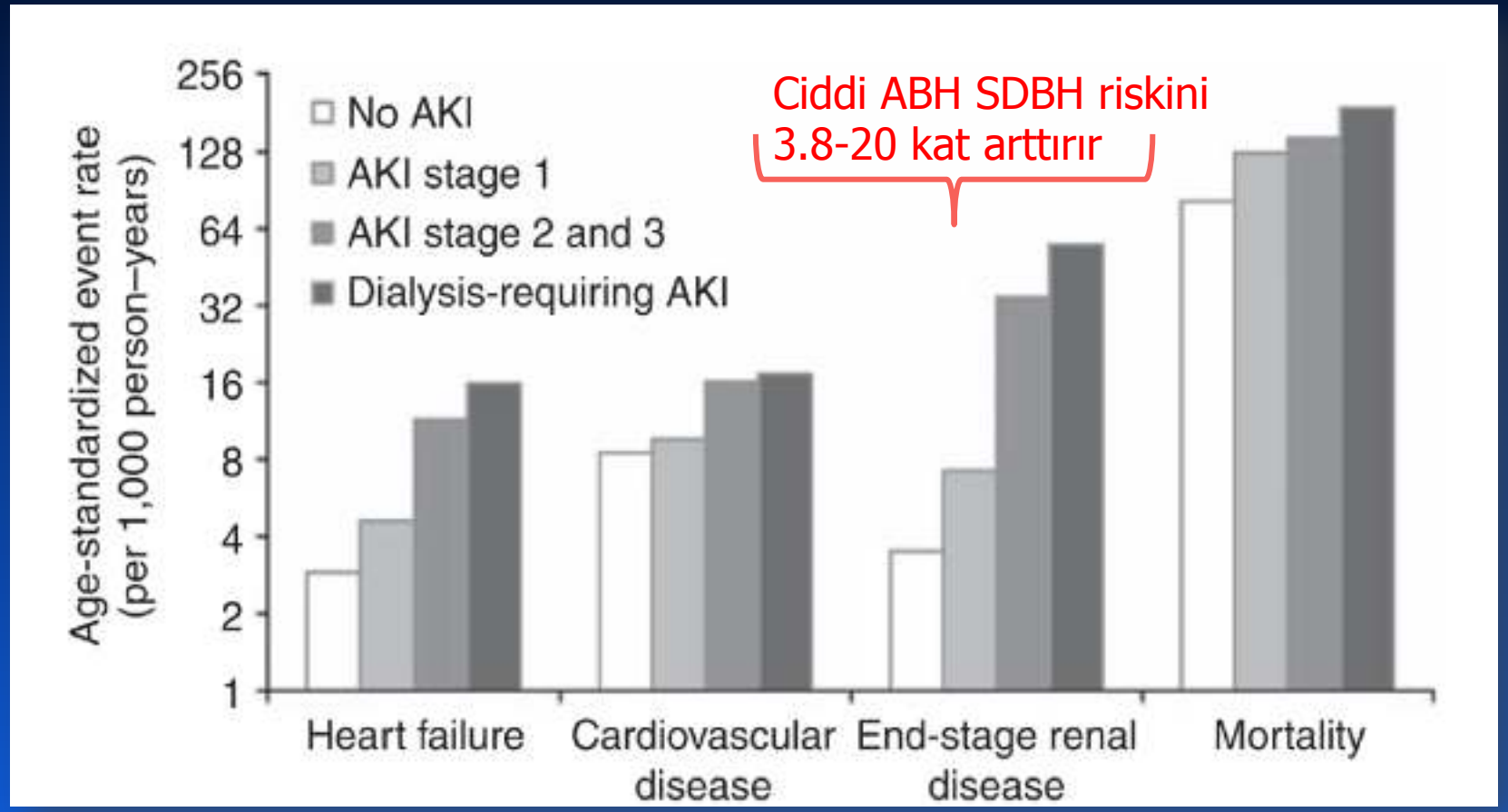
- ART ilişkili ABH tedavinin ilk yılında, özellikle ilk 3 ayda daha sık (10 kat)
- İleri evre ve ciddi KBH nadir
  - Tedavi alan hastalar yakından takip ediliyor ve erken müdahele ediliyor
- Sıklıkla KBH ile ilişkili olanlar; indinavir, atazanavir, tenofovir disoproxil fumarate (TDF), lopinavir/ritonavir

Campos P, et al. Clinical Kidney Journal, 2016, vol. 9, no. 6, 772–781

BH neden önemli?

- Mortalite yüksek
  - Azalmış GFR ve albuminuri mortalite ile ilişkili
    - ABH 5 kat (%27)
    - Dializ gerektiren ABH'de 3 kat
- Diğer olumsuz sonuçlar yüksek
  - KVH riski 6 kat yüksek

Choi AI, et al. Circulation 2010; 121:651–8.
Wyatt CM, et al. Immune Defic Syndr 2010; 55:73–7.



Jhoi AI, et al. *Kidney Int*. 2010 September ; 78(5): 478–485.

Böbrek hasarı göstergeleri

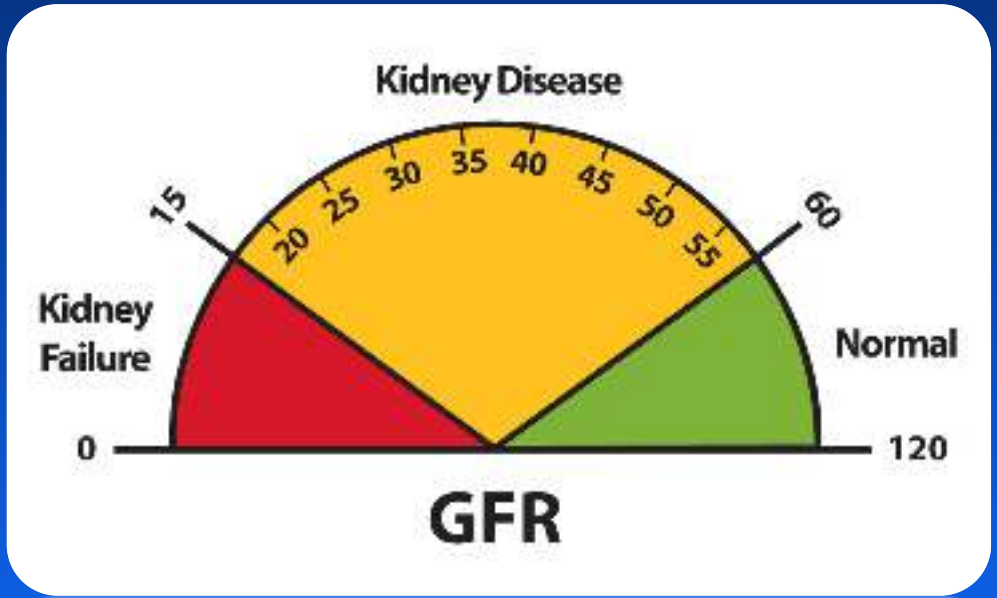
- Albuminuri veya proteinuri
- Tübüler hastalığa bağlı elektrolit ve diğer anormallikler
- Histolojik olarak belirlenmiş anormallikler
- Görüntüleme ile belirlenmiş yapısal anormallikler
- Böbrek transplantasyon öyküsü

CID 2014;59:e96-138

KBH Tanımı

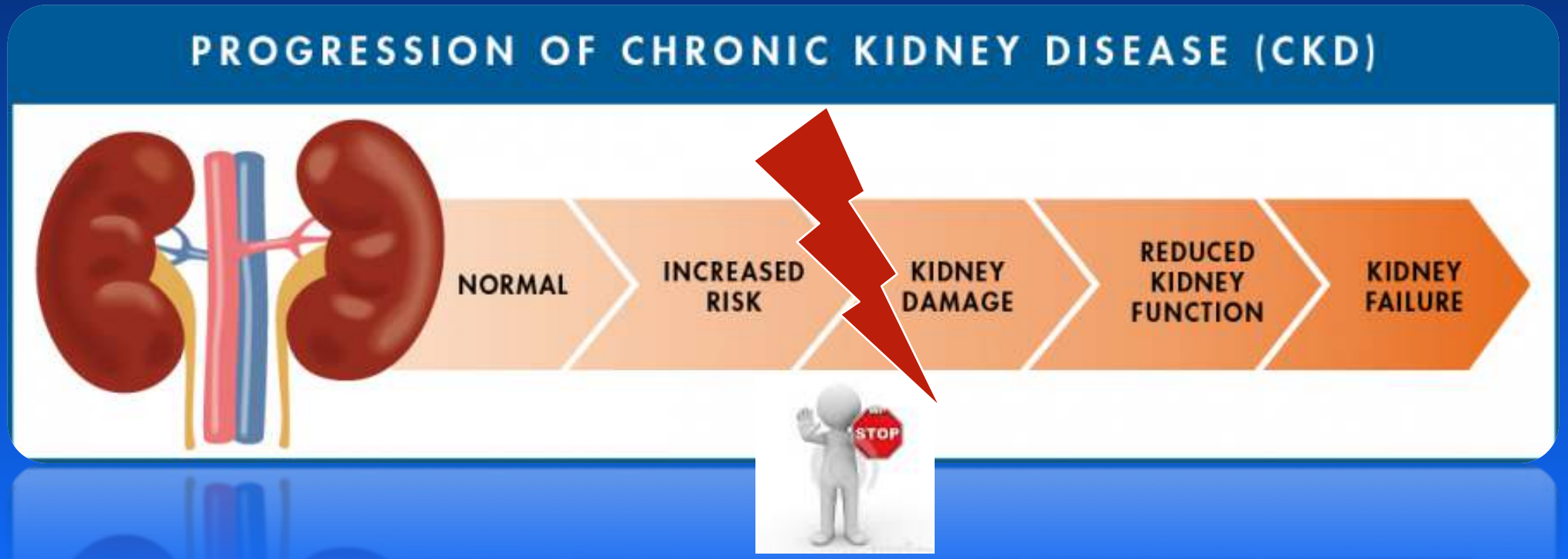
Böbrek hasar göstergeleri olmasa bile,

3 aydan uzun süre GFR <60 mL/dk/1.73 m^2



ABH ve KBH riskini ortadan kaldırmak için en iyi strateji

- Immuno-virolojik kontrol için erken ART başlamak
- Renal disfonksiyonu erken tanımak ve önlem almak



İlk değerlendirme

Amaç:

- Risk faktörlerini tanımlamak
- Gizli KBH varsa tanımlamak
  - Etyolojisini aydınlatmak
  - Progresyonunu önlemek
- Değiştirilebilir faktörlerin üzerine gitmek

Jose L. Gorriz, et al. Nefrologia 2014;34(Suppl.2):1-81

Demographic factors

- Advanced age
- Black race
- Low body weight

Factors associated with VIH infection

- Viral replication
- CD4+ lymphocyte nadir <200 cells/µl
- Previous diagnosis of AIDS due to category C clinical events

Concomitant diseases

- High blood pressure
- Diabetes mellitus
- Chronic hepatitis due to HCV or HBV

Use of potentially nephrotoxic drugs

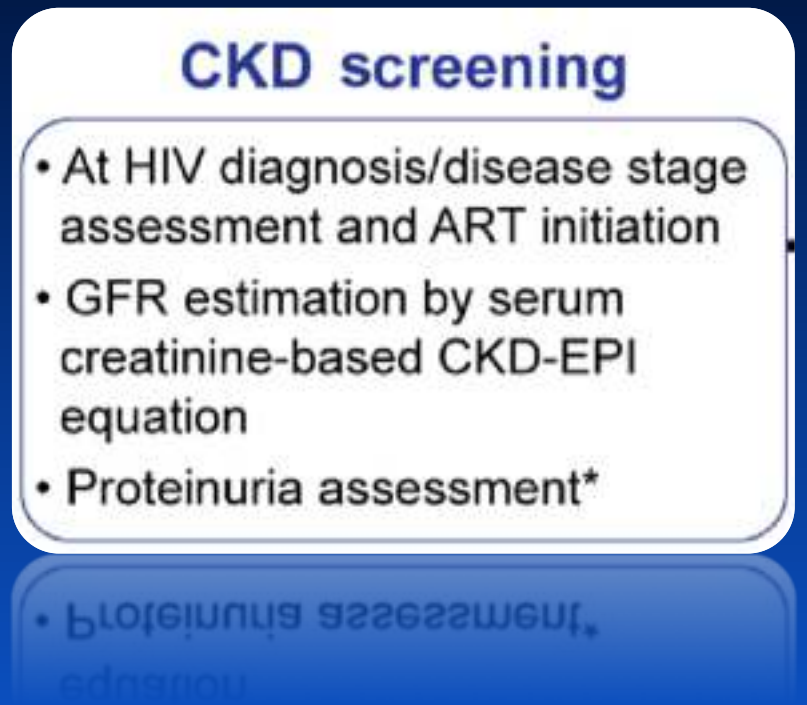
- Antiretroviral drugs: tenofovir, indinavir
- Others: non-steroidal anti-inflammatory drugs, aminoglycosides, amphotericin B, cidofovir, co-trimoxazole sulfadiazine, acyclovir, foscarnet

Comorbidities that may favour CKD progression:

- Smoking habit
- Obesity
- High blood pressure
- Low blood pressure (systolic BP <100mmHg)
- Episodes of volume depletion (vomiting-diarrhoea, diuretics),
- Heart failure – low output
- Infections (sepsis)
- Urinary tract obstruction
- Acute pyelonephritis
- Atherosclerosis (ischemic nephropathy)
- Chronic Hepatitis C

Jose L. Gorriz, et al. Nefrologia 2014;34(Suppl.2):1-81

- Anamnezde mevcut hastalıklar, aile öyküsü, ilaçlar
- FM'de KB ve vücut ağırlığı
- Temel lab testleri:
  - Serumda kreatinin, fosfat
  - eGFR (CKD-EPI)
  - Tam idrar analizi
    - Glukosüri (strip)
    - İdrar sedimenti
    - Proteinüri veya albuminüri
  - Spot idrarda protein/kreatinin oranı (UP/C) ve albümin/kreatinin oranı (UA/C)



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Kidney Int. 2018;93(3):545–559

eGFR hesaplaması

- Serum kreatinin tercih edilir
  - Serum cystatin C;
    - tübüler kreatinin sekresyonunu engelleyen ilaçları alan hastalarda düşünülebilir.
    - Uzun süreli mortaliteyi daha iyi öngörebilir fakat inflamasyon durumunda yanıltıcı olabilir
- CKD Epidemiology Collaboration (CKD-EPI) formülü
  - Dolutegravir, rilpivirine, ritonavir veya cobistat CrCl'nde 5-20 ml/dk daha düşük hesaplamaya yol açabilir !!!
- Cockcroft–Gault
  - Daha az doğru
  - fakat daha pratik ve doz ayarlaması için önerilir

24 saatlik idrarda CrCl??

- eGFR'ye üstünlüğü yok
- Ancak, belirli durumlarda yapılabilir
  - Uç kilolar (VKİ <19 kg/m2 veya >35kg/m2)
  - Ciddi kas anormallikleri
  - Ciddi KC hastalığı

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İdrar analizi

- Proteinüri
- Hematüri varlığını ortaya koymak

- Glukozüri (TDF alan hastalarda görülebilir)

Albuminuri veya proteinuri

- Böbrek hasarını en iyi gösteren parametreler
  - KBH tanı ve sınıflamasında en sık kullanılan kriterler
- Son evre böbrek hastalığına progresyon için GFR'ye kıyasla daha iyi, daha erken bir gösterge

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- Proteinuri
  - Albuminuri
    - glomeruler hastalığı gösterir
  - Düşük-molekül-ağırlıklı proteinlerin (β-2 microglobulin, immunoglobulin light chains, retinol binding protein) artışı
    - proximal tubular hasarı

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- İdrar test stripi
  - Semikantitatif
  - Esas olarak albuminüriyi belirler (düşük-molekül-ağırlıklı proteinleri belirlemez)
  - Üriner enfeksiyonu belirlemede (esteraz ve nitrit), tübüler anormallikler (non-hiperglisemik glukozüri) veya üriner sediment anormallikleri (hematüri) için yararlı olabilir

- İdrarda albümin veya protein konsantrasyonlarının (mg) kreatinin konsantrasyonuna (g) oranı (uACR, uPCR)
  - Klinik olarak en yararlı ölçüm
  - Random idrar örneği (tercihen sabah ilk idrar örneği) 24 saatliğe yakın sonuç verir.
  - Nefrotik sınırda proteinüri (>3g/gün) varsa 24 saatlik idrar örneği önerilir.

Kidney Int. 2018;93(3):545–559

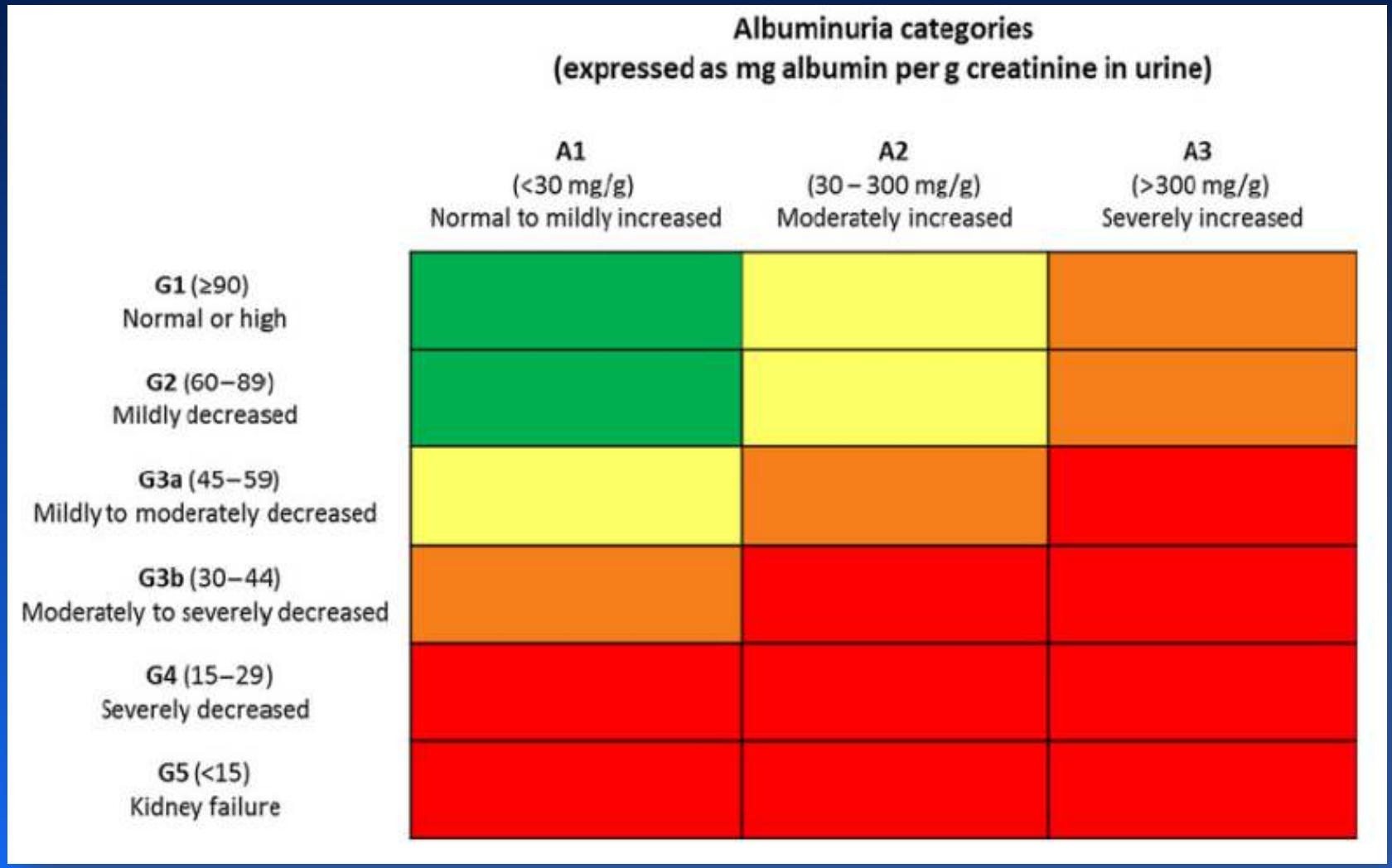
Albuminüri ve Proteinüri Sınıflaması

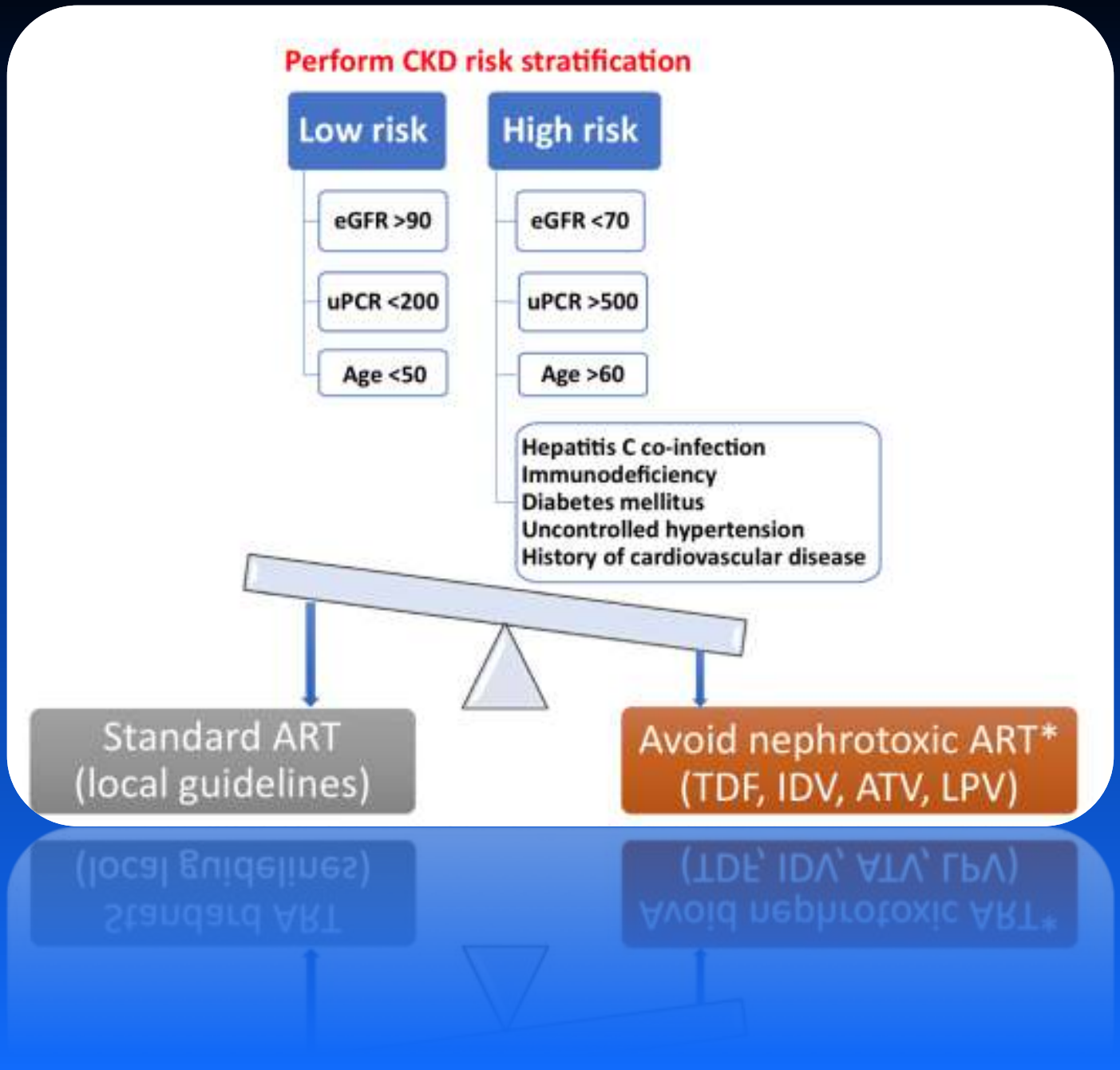
Measurement	Normal to Mildly Increased (A1)	Moderately Increased (A2)	Severely Increased (A3)
AER, mg/24 h	<30	30–300	>300
PER, mg/24 h	<150	150–500	>500
ACR			
mg/mmol	<3	3–30	>30
mg/g	<30	30–300	>300
PCR			
mg/mmol	<15	15–50	>50
mg/g	<150	150–500	>500
Protein reagent strip	Negative or trace	Trace to 1+	1+ or greater

KBH Prognoz Sınıflaması

(KDIGO-Kidney Disease Improving Global Outcomes)

Tüm sebeplere bağlı mortalite, KVH mortalitesi, son dönem renal yetmezlik, akut renal yetmezlik riski

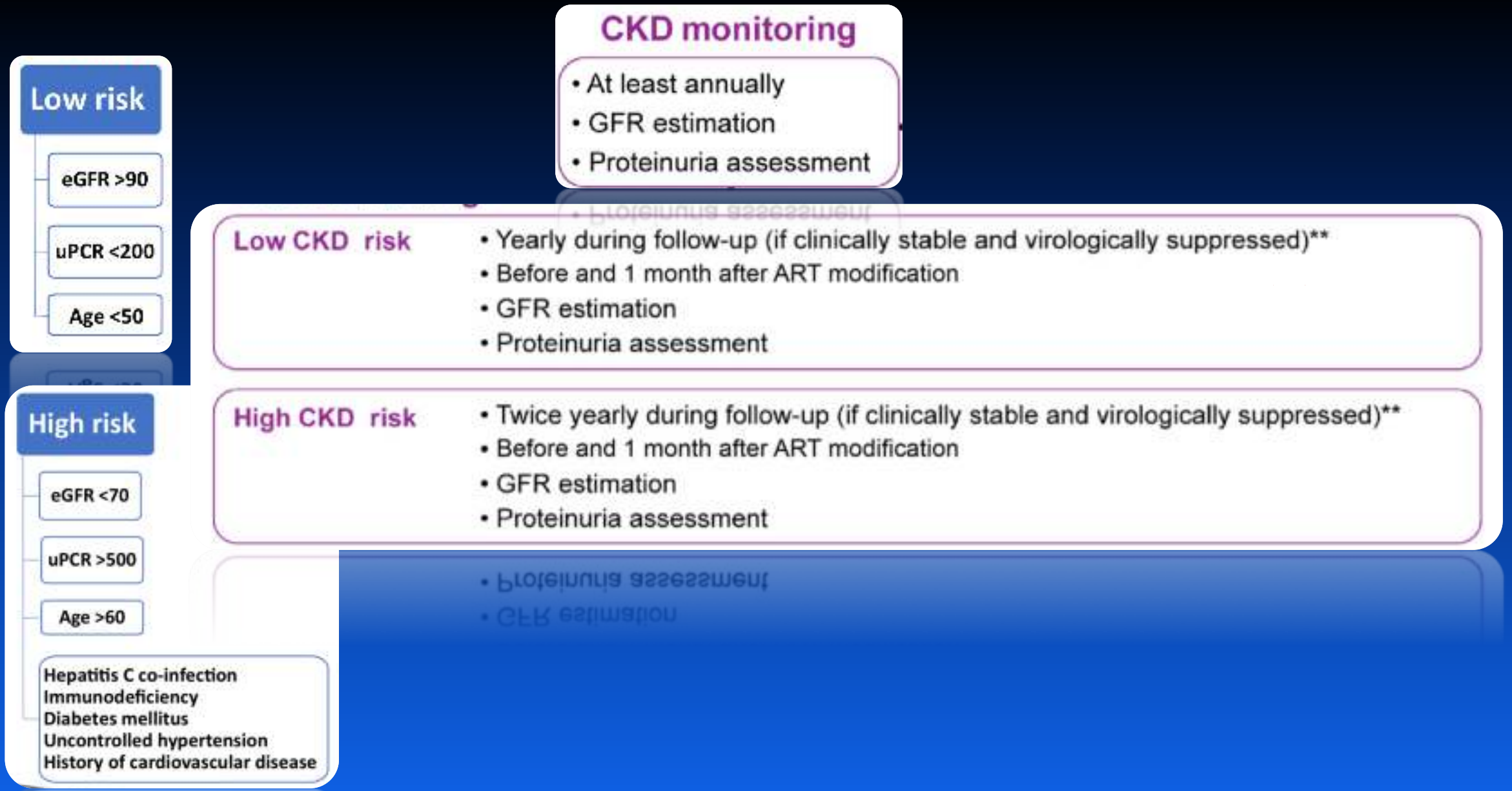



Perform CKD risk stratification
Low risk
High risk
eGFR >90
uPCR <200
Age <50
eGFR <70
uPCR >500
Age >60
Hepatitis C co-infection
Immunodeficiency
Diabetes mellitus
Uncontrolled hypertension
History of cardiovascular disease
Standard ART
(local guidelines)
Avoid nephrotoxic ART*
(TDF, IDV, ATV, LPV)

İzlem

- Genelde renal fonksiyonlar yavaşça azalır, klinik olarak belirsizdir.
- Kristalüri varlığı potansiyel nefrotoksisiteye işaret eder.

Campos P, et al. Clinical Kidney Journal, 2016, vol. 9, no. 6, 772–781



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On TDF plus ritonavir or cobicistat	• Twice yearly during follow-up (if clinically stable; more frequently if eGFR decline or marked hypophosphatemia is present) • GFR estimation • Proteinuria assessment • Serum phosphorus • Urinalysis • Fractional excretion of phosphate and urinary low-molecular weight protein in those suspected to have developed proximal tubulopathy

Kidney Int. 2018;93(3):545–559

eGFR ↓

UP/C ↑

Hipofosfatemi

Normoglisemik glukozüri

Tübüler hasar şüphesi

SG-2021/09

Jose L. Gorriz, et al. Nefrologia 2014;34(Suppl.2):1-81

Proksimal Tübüler Disfonksiyon Göstergeleri

- Hipokalemi
- Hipofosfatemi
- Glikozüri
- Serum bikorbonat seviyesinde azalma
- Fraksiyonel fosfat atılımı >%20 (n<%10)
- Fraksiyonel ürik asit atılımı >%20 (n<%15)
- İdrarda albümin/protein oranı <0.4 (>0.4 ise glomerular hastalığı gösterir)

- Normal fosfat ve ürik asit atılımı (<20%) tübülün hasarlı olmadığını gösterir
- Yüksek FEP (>20%) çok spesifik değildir, primer veya sekonder hiperparatiroidizmden ve 25(OH) vit.D seviyelerinden etkilenebilir.

Jose L. Gorriz, et al. Nefrologia 2014;34(Suppl.2):1-81

- İdrarda Albumin/Protein oranı (UA/P)
  - >0.4 ise glomerüler proteinüri (GN, HT, DM)
  - <0.4 ise tübüler proteinüri
    - tübüler reabsorbsiyon bozukluğuna bağlı düşük moleküler ağırlıklı proteinlerin artışı (β2 mikroglobulin dahil)
    - Ürik asit ve fosfor atılım fraksiyonlarının artmasıyla veya β2 mikroglobulin/kreatinin oranı ile doğrulanır
  - Sensitivite 88%, spesifisite 99%.

Jose L. Gorriz, et al. Nefrologia 2014;34(Suppl.2):1-81

Kidney Disease: Definition, Diagnosis and Management

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)[ii]	UA/C[ii] < 3	Regular follow-up			• Check risk factors for CKD and nephrotoxic medicines including ART[iv] • Discontinue or adjust drug dosages where appropriate[v] • Perform renal ultrasound • Urgent referral to nephrologist
	UA/C[ii] 3-30	• Check risk factors for CKD[x] and nephrotoxic medicines including ART[iv, x] • Discontinue or adjust drug dosages where appropriate[v] • Perform renal ultrasound • If haematuria present with any level of proteinuria refer to nephrologist • Refer to nephrologist if new CKD or progressive decline in eGFR			
	UA/C[ii] > 30				

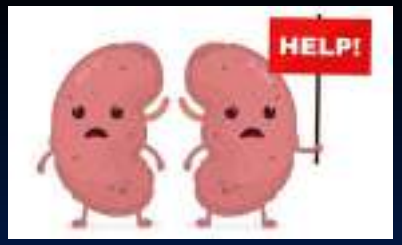
* Defined as decrease in eGFR of 5 mL/min per year for ≥3 consecutive years or confirmed 25% eGFR decline from baseline

KBH – ART Yönetimi

- NRTIs
  - Doz ayarlaması (ABC hariç)
  - Birleşik ilaç kombinasyonlarından kaçınılmalı
  - TDF ve diğer nefrotoksik ilaçlardan kaçınılmalı
  - TDF alan hastada GFR azalması >25% ve <60 mL/dk ise (öz.prox.tub.dysfxn. kanıtı varsa) alternatif ART
- NNRTIs, PIs, INSTIs – doz ayarlaması gerekli değil.

CID 2014;59:e96-138

Nefroloğa danış!!!



- GFR'de ciddi (>%25) azalma ve GFR <60 mL/dk (nefrotoksik ilacın uzaklaştırılmasına rağmen)
- Albuminüri/proteinüri veya yüksek KB ile beraber hematüri
- Albuminüri >300 mg/gün
- İleri KBH (GFR <30mL/dk)

Nephrology referral

Among patients with the following:

- Unexplained AKI or CKD
- Rapid kidney function decline
- New onset or worsening proteinuria
- CKD Stage G3b/G4 for kidney replacement therapy preparation and kidney transplant evaluation

CID 2014;59:e96-138

Tedavi

- Nefrotoksik ajan ortadan kaldırılmalı
- KB ve DM kontrol altında olmalı
- KVH risk faktörleri ve dislipidemi kontrolü
- HT ve/veya Proteinuri ciddiyse, ACE inh. veya ARBs

Campos P, et al. Clinical Kidney Journal, 2016, vol. 9, no. 6, 772–781

KBH – Diğer tedaviler

- ACE inhibitörleri veya angiotensin II receptor blokerleri (ARB),
  - doğrulanmış veya klinik şüpheli HIVAN
  - Klinik olarak ciddi albuminüri (diyabetik hastada >30 mg/gün; nondiyabetik hastalarda >300 mg/gün)
- Statinler
  - KVH'ı önlemek için
    - KVH riski en yüksek olan hastalarda (>7.5% 10-year risk of cardiovascular disease) uygun görüldüğü gibi
- Aspirin (75–100 mg/day) KVH'ı önlemek için düşünülebilir
- Kortikosteroidler ART, ACE inh veya ARBs'lerine yardımcı olarak biyopsi ile doğrulanmış HIVAN için düşünülebilir

CID 2014;59:e96-138

Table 5 | Selection criteria for potential HIV-positive kidney transplant recipients

- Meets standard criteria for kidney transplant recipients, *plus* the following:
- Effective HIV suppression for ≥6 months prior to transplantation
  - Undetectable plasma HIV-1 RNA
  - CD4+ cell count > 200 cells/mm^3
- No active opportunistic infections
- No history of:
  - Progressive multifocal leukoencephalopathy
  - Primary central nervous system lymphoma
  - Pulmonary aspergillosis
  - Visceral Kaposi's sarcoma
  - Coccidiomycosis
  - Chronic intestinal cryptosporidiosis >1 month
- Hepatology evaluation for patients co-infected with hepatitis B or hepatitis C virus

Criteria adapted from Stock *et al.* and Muller E *et al.*[132,137]

Kidney Int. 2018;93(3):545–559

Son söz…

Teşekkür Ederiz..