



# HIV ile Yaşayan Bireylerde Kardiyovasküler Hastalıklar

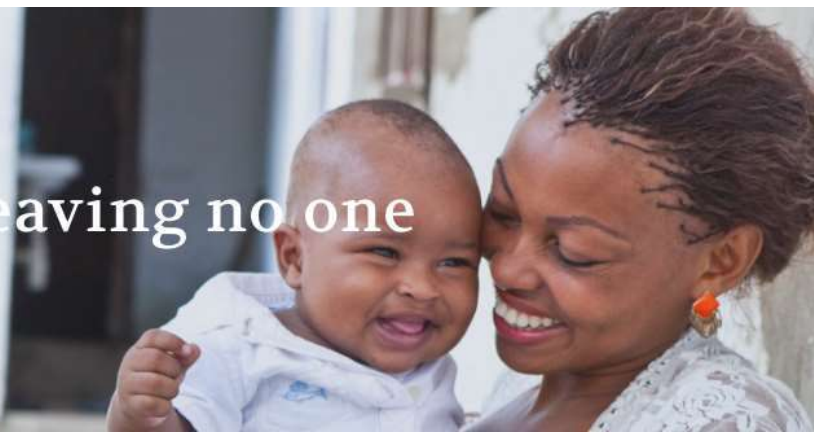
**Prof. Dr. Elif Tükenmez Tigen**

*Marmara Üniversitesi Pendik Eğitim  
ve Araştırma Hastanesi*



ABOUT

Saving lives, leaving no one behind



**1.3**  
**MILLION**

people were newly infected with HIV in  
2023

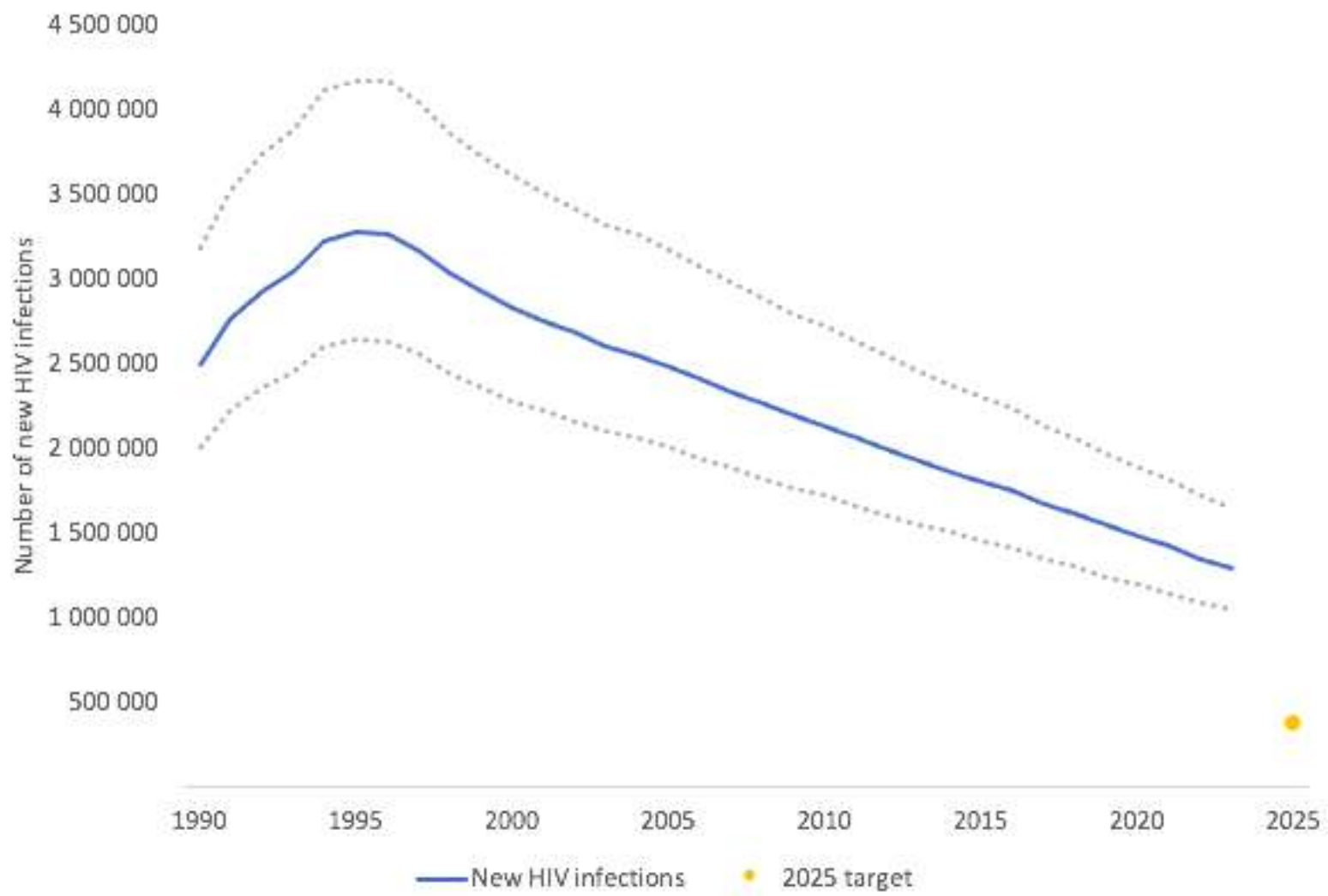
**39.9**  
**MILLION**

people were living with HIV in 2023

**630**  
**THOUSAND**

people died of AIDS-related illnesses in  
2023

### Number of new HIV infections, global, 1990–2023, and 2025 target



Source: UNAIDS 2024 epidemiological estimates



## HIV / AIDS TOPLAM VAKA VE ÖLÜM SAYILARININ SON 5 YIL DAĞILIMI

YILLAR	HIV	AIDS	TOPLAM	ÖLÜM
2019	4159	139	4298	40
2020	3128	75	3203	47
2021	4182	103	4285	52
2022	5591	119	5710	67
2023	1677	51	1728	17

\*08 Kasım 2023 tarihi itibari ile doğrulama testi pozitif tespit edilerek bildirim yapılan vakalar



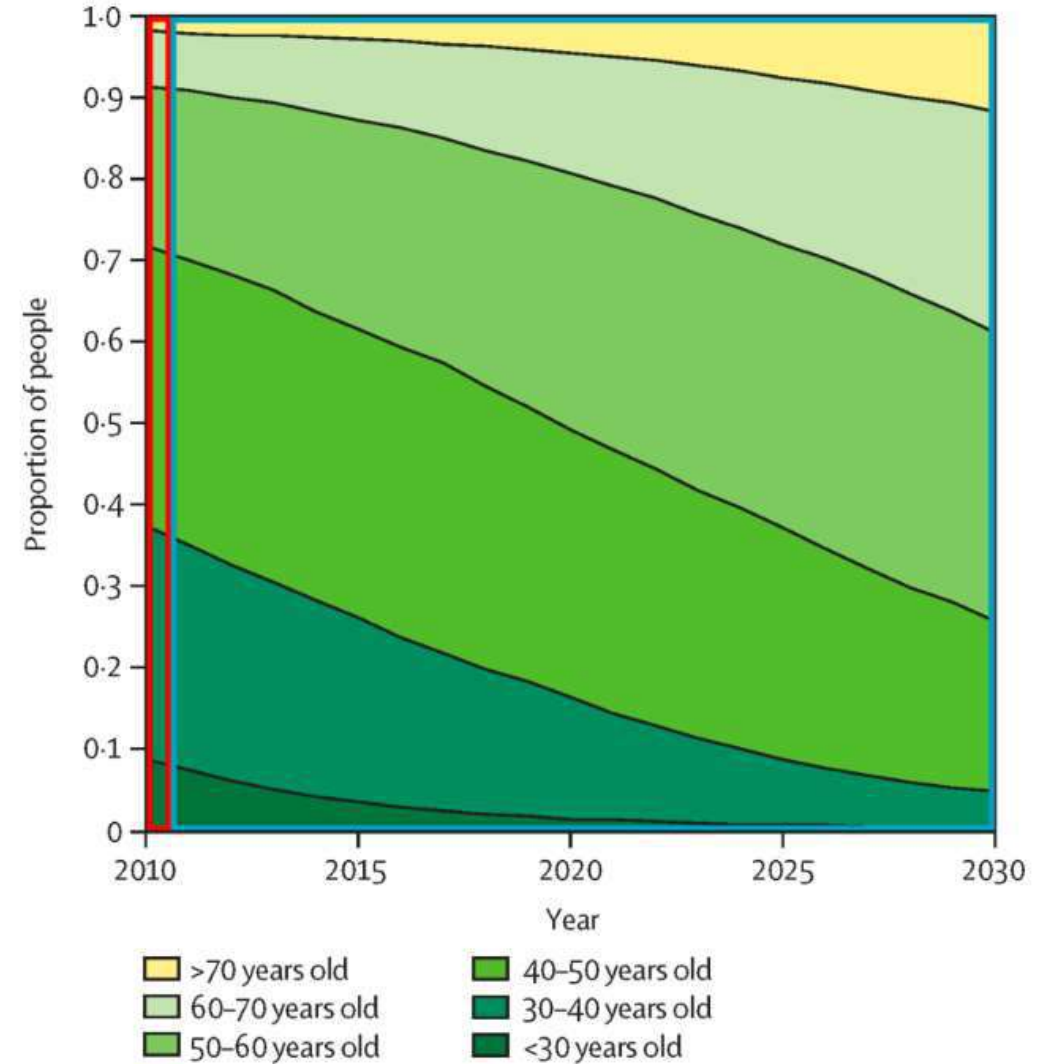
- **>50 yaş HİYB**

2010 → %28

2030 → %73

Modelleme çalışması →

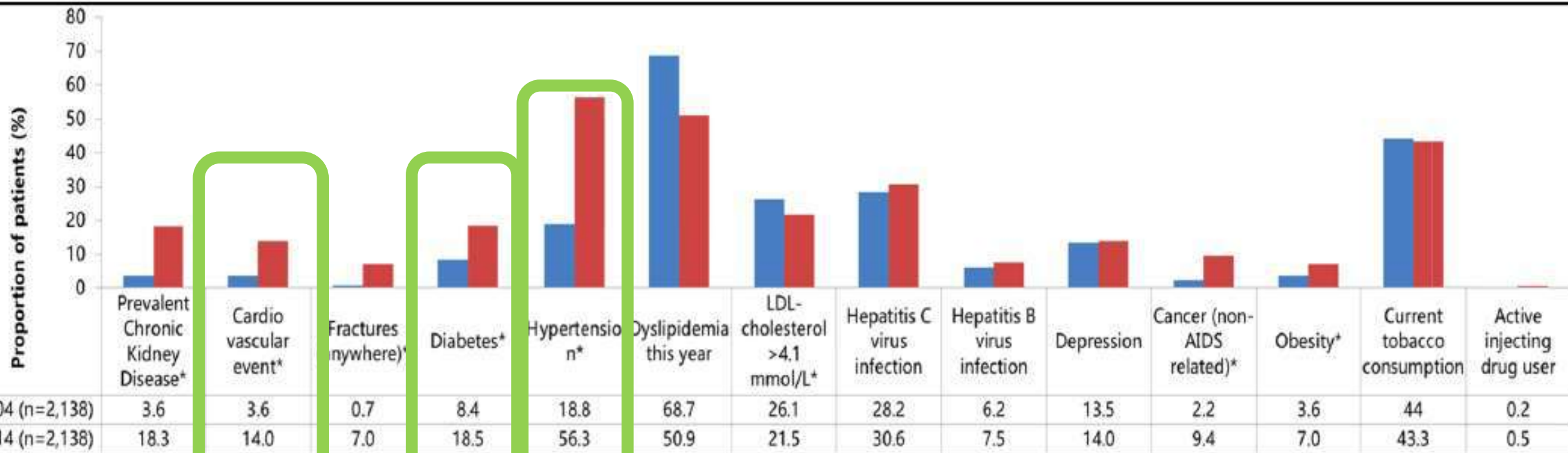
**2030 → HİYB ve KVH %78**





# Kronik Komorbiditeter 2004-2014

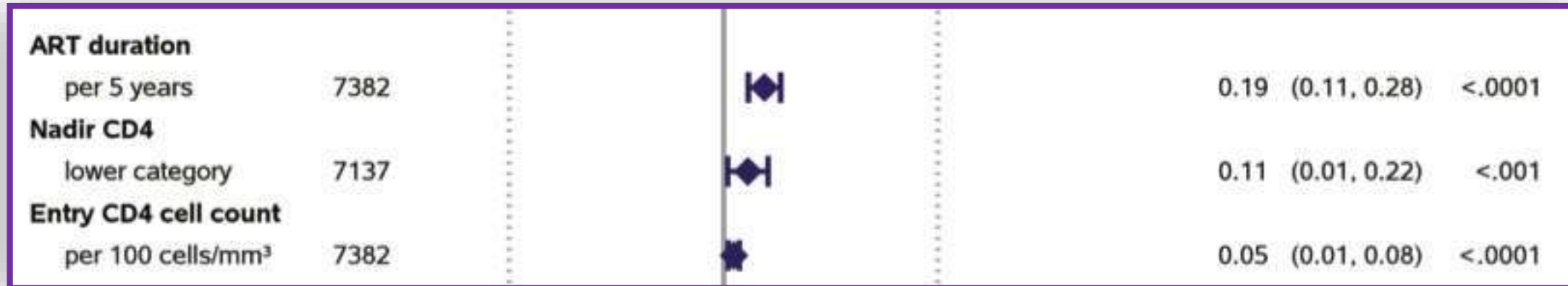
## ANRS CO3 Aquitaine Kohort



# Cardiovascular Risk and Health Among People With Human Immunodeficiency Virus (HIV) Eligible for Primary Prevention: Insights From the REPRIEVE Trial

*Clinical Infectious Diseases*

**MAJOR ARTICLE**



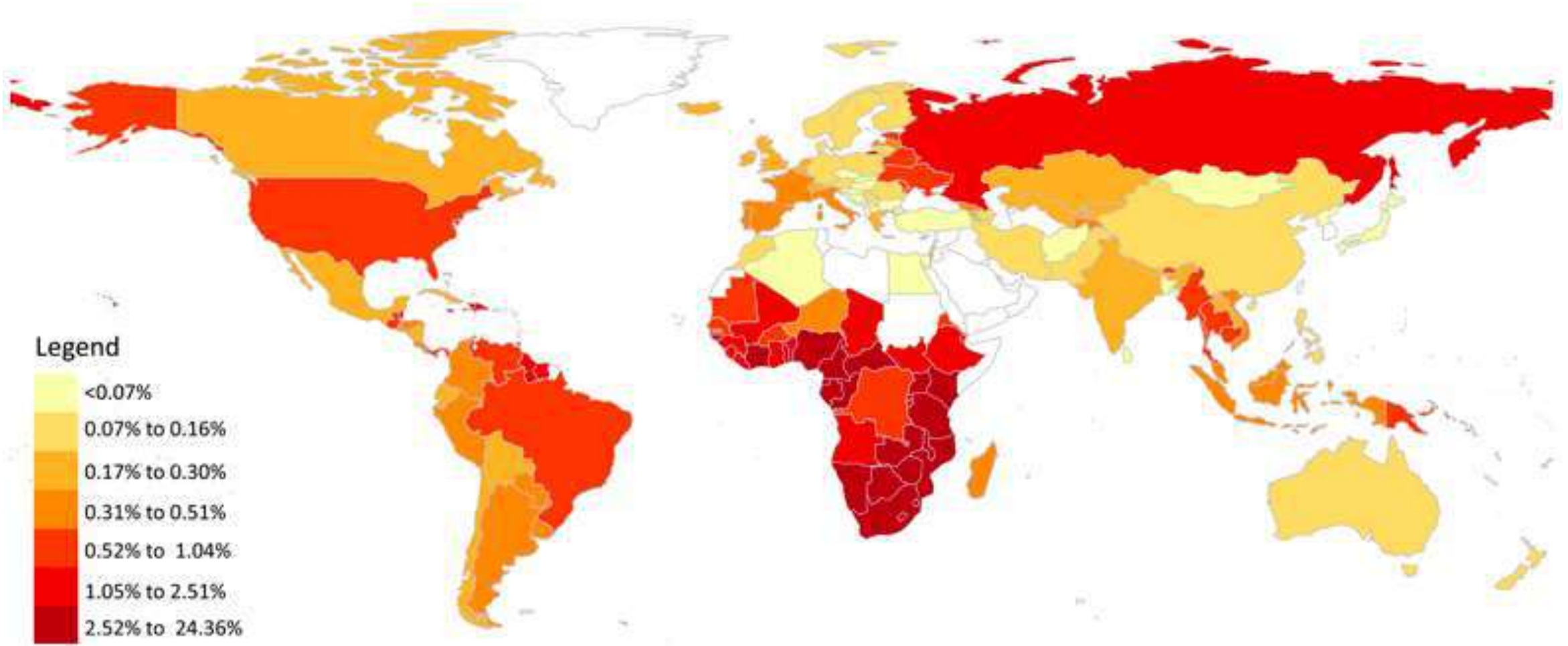
# Global Burden of Atherosclerotic Cardiovascular Disease in People Living with the Human Immunodeficiency Virus: A Systematic Review and Meta-Analysis

- KVH geliştirme olasılığı → X2
- HIV ile ilişkili KVH küresel yükü son yirmi yılda → X3



A

## HIV ile ilişkili kardiyovasküler hastalık



# HIV ile Yaşayan Bireylerde Kardiyovasküler Hastalıklar (KVH)

- Koroner Kalp Hastalığı
- Kalp Yetmezliği
- Ani Kardiyak Ölüm



# HIV ilişkili KVH'nin Olası Mekanizmaları

## Coronary Vascular Injury



## Structural & Functional Pathology



## Ischemic Phenotype

Co-Infections  
e.g., CMV



### Vessel Inflammation

- Cytokines, local & systemic
- Oxidative stress
- Cellular adhesion
- Increased permeability

### Endothelial Dysfunction

- Impaired vasodilation
- Increased thrombogenesis
- Vessel wall hypertrophy

### Atherogenesis

- Leukocyte migration
- oxLDL exposure
- Subendothelial foam cells and lipid accumulation



### Unstable Plaque

- Persistent intima T-cell and macrophage activation
- healing and maturation of fibrous cap

### Coronary Dysfunction

- Enhanced vasoconstriction
- Impaired vasodilation
- Demand mismatch

### Coagulopathy

- Pro-coagulant drive
- Platelet activation
- Reduced anti-coagulant response



### Myocardial Infarction (MI)

- Type 1 MI
- Type 2 MI

### Ischemic Heart Failure

### Sudden Cardiac Death

HIV Disease  
+/- ART toxicity



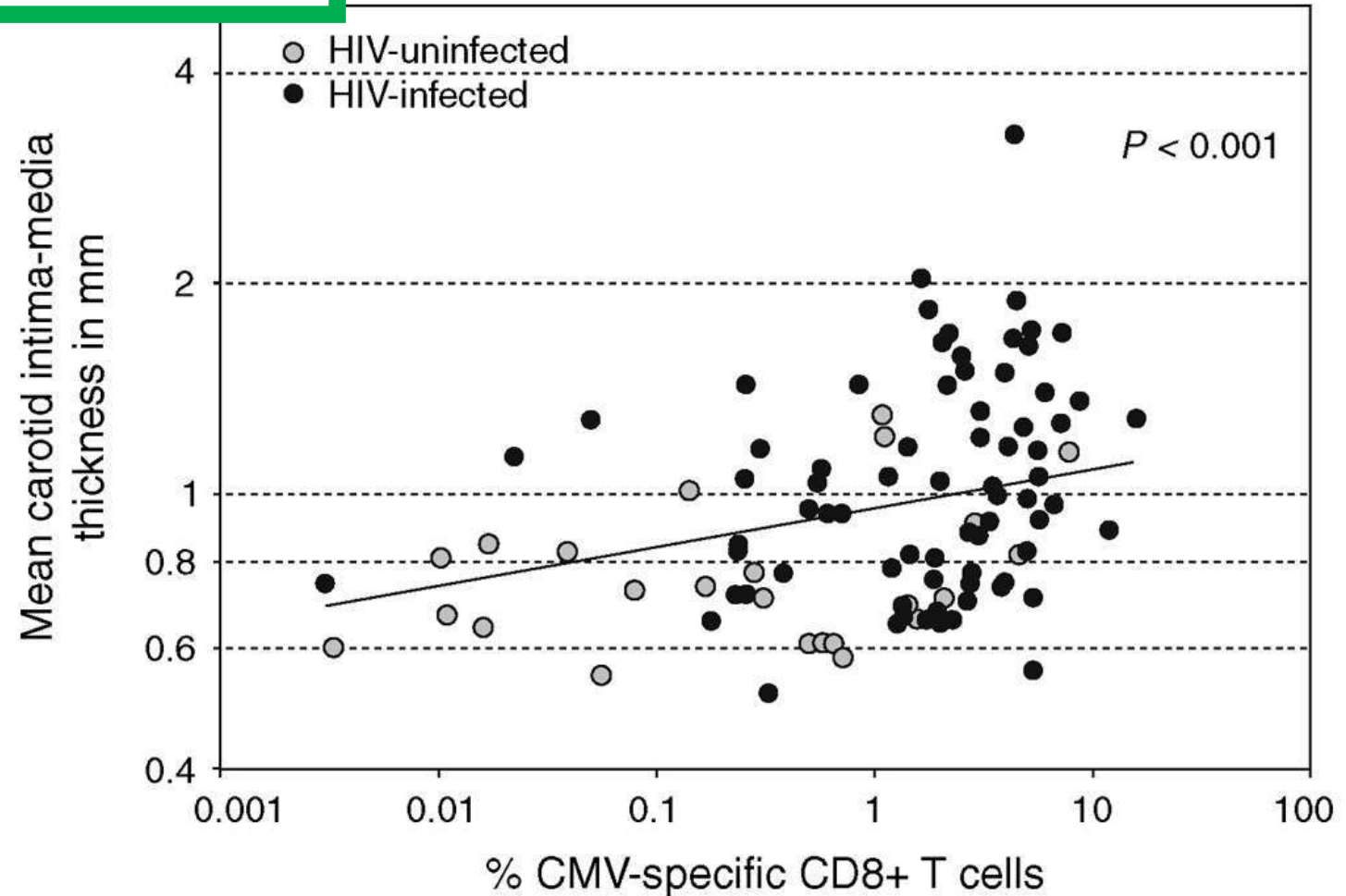
### Cardiometabolic Risk Factors

- Dyslipidemia
- Obesity
- Diabetes
- Hypertension
- Smoking

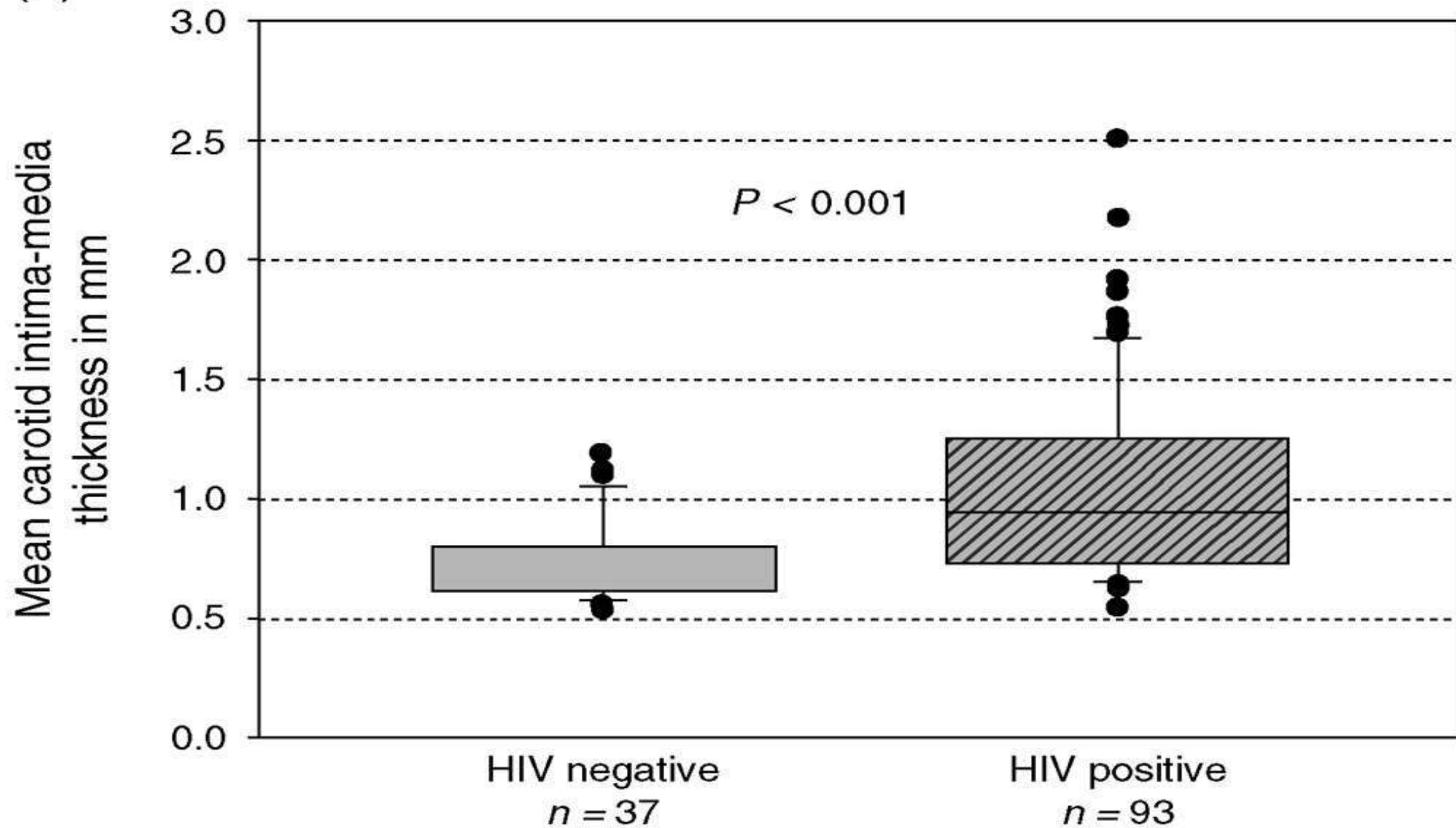


# Increased carotid intima-media thickness in HIV patients is associated with increased cytomegalovirus-specific T-cell responses

- HIV(+)/(-) karşılaştırmada, CMV'ye özgü T hücrelerinin yüzdesindeki her 10 katlık artış için karotis IMT'de %14'lük artış ( $P < 0,001$ ).

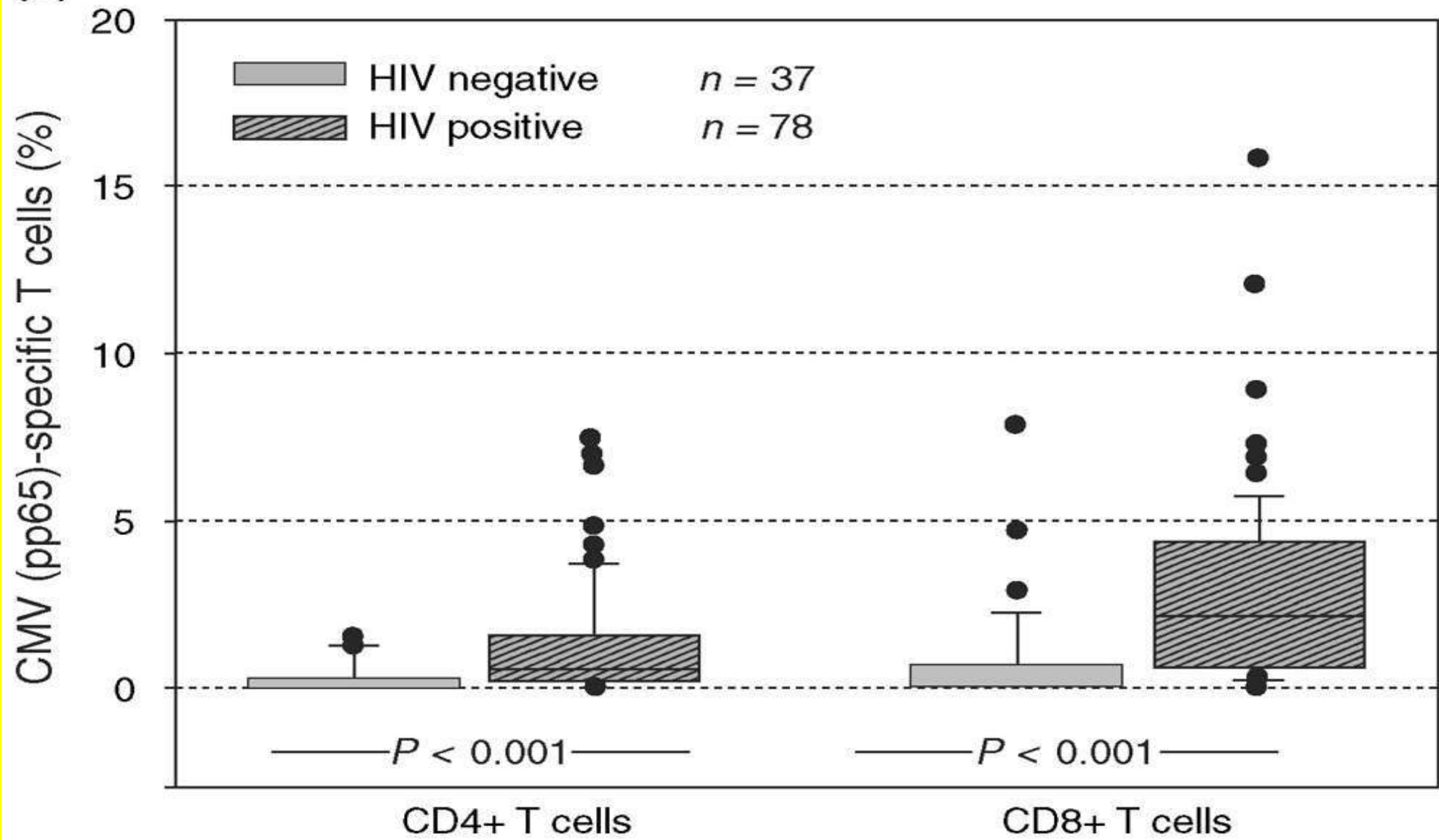


(a)

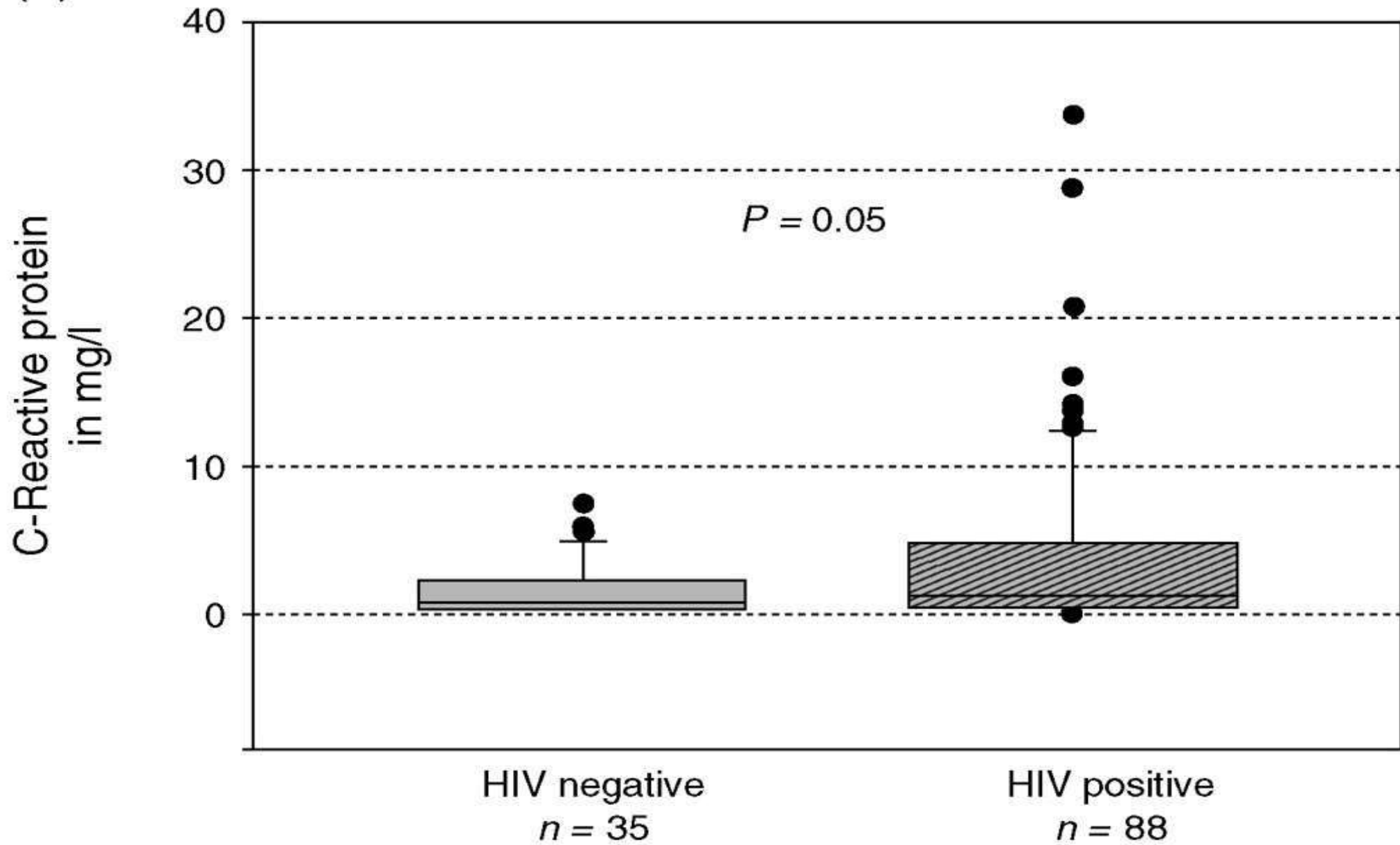




(d)

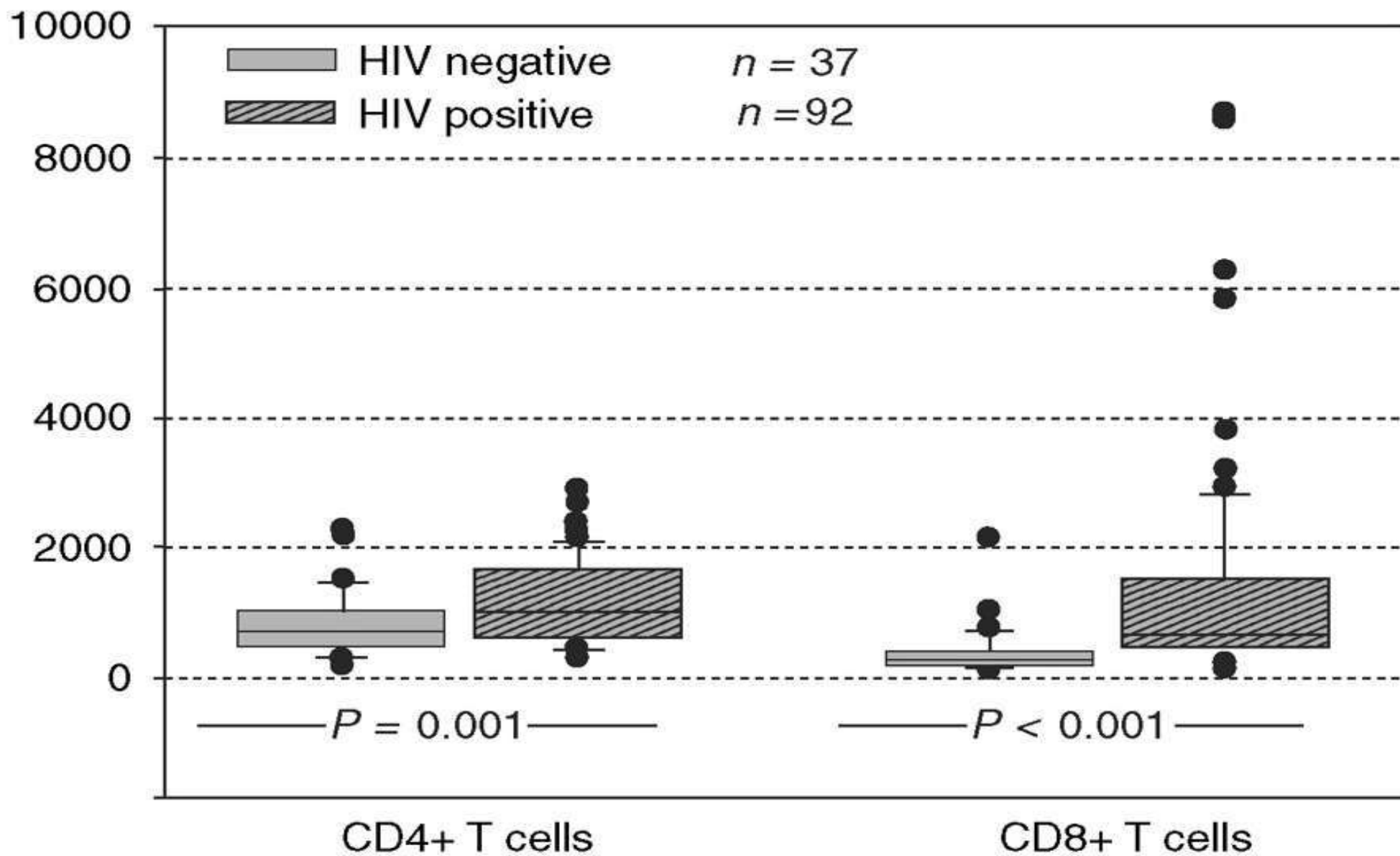


(b)



(c)

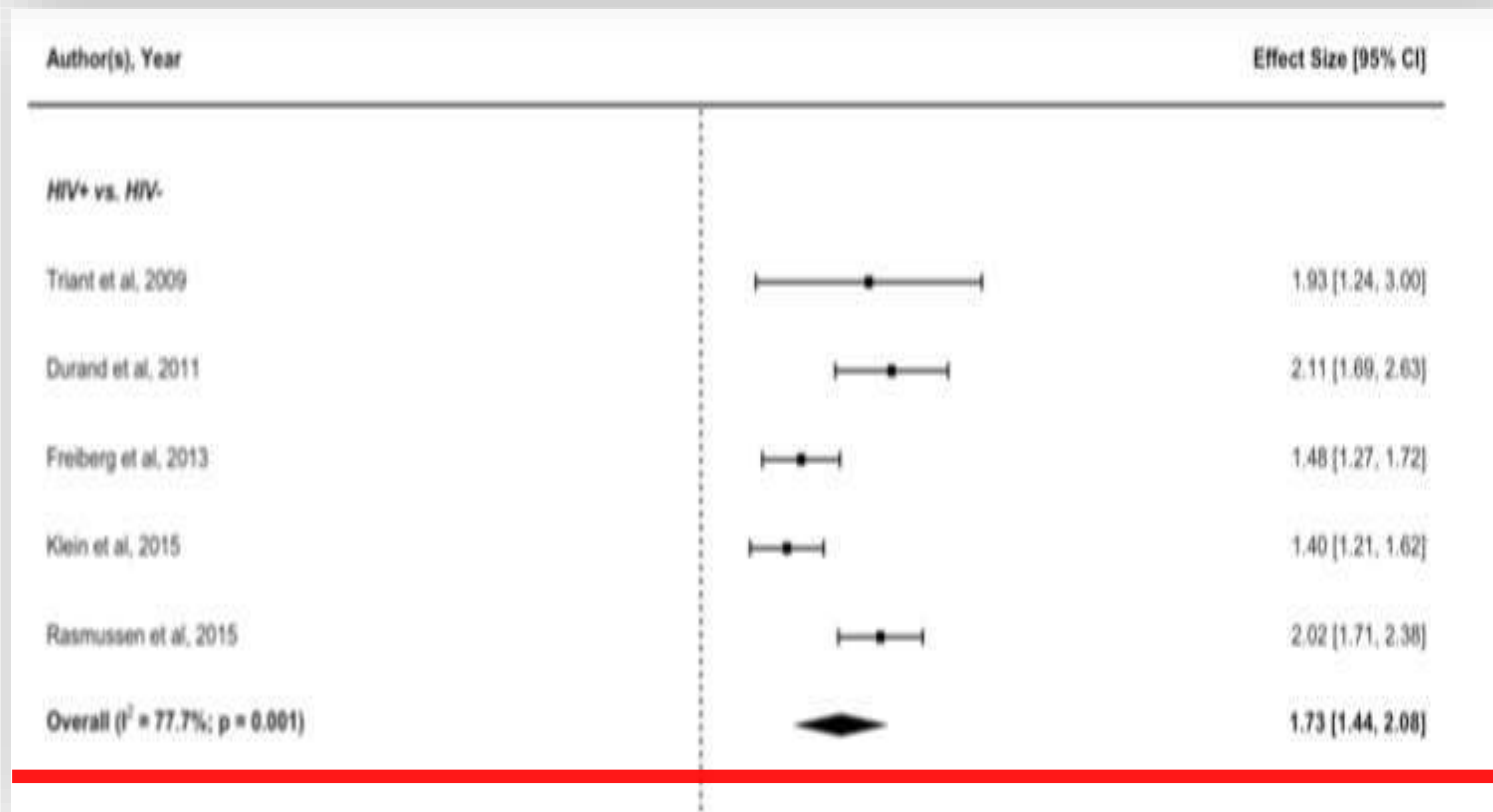
Median anti-CD38 antibodies  
bound / T cell



## HIV ve Tip 1 ve Tip 2 MI Farkı

- Tip 1 MI → Plak rüptürü ve aterotrombozla karakterize %50 HIV risk
- Tip 2 MI → Altta yatan ateroskleroz Ø
  - Uyuşturucu kullanımı vs nonkardiyojenik nedenler
  - Koroner mikrovasküler disfonksiyon
    - Kronik inflamasyon
    - Endotel aktivasyonu ve disfonksiyonu

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



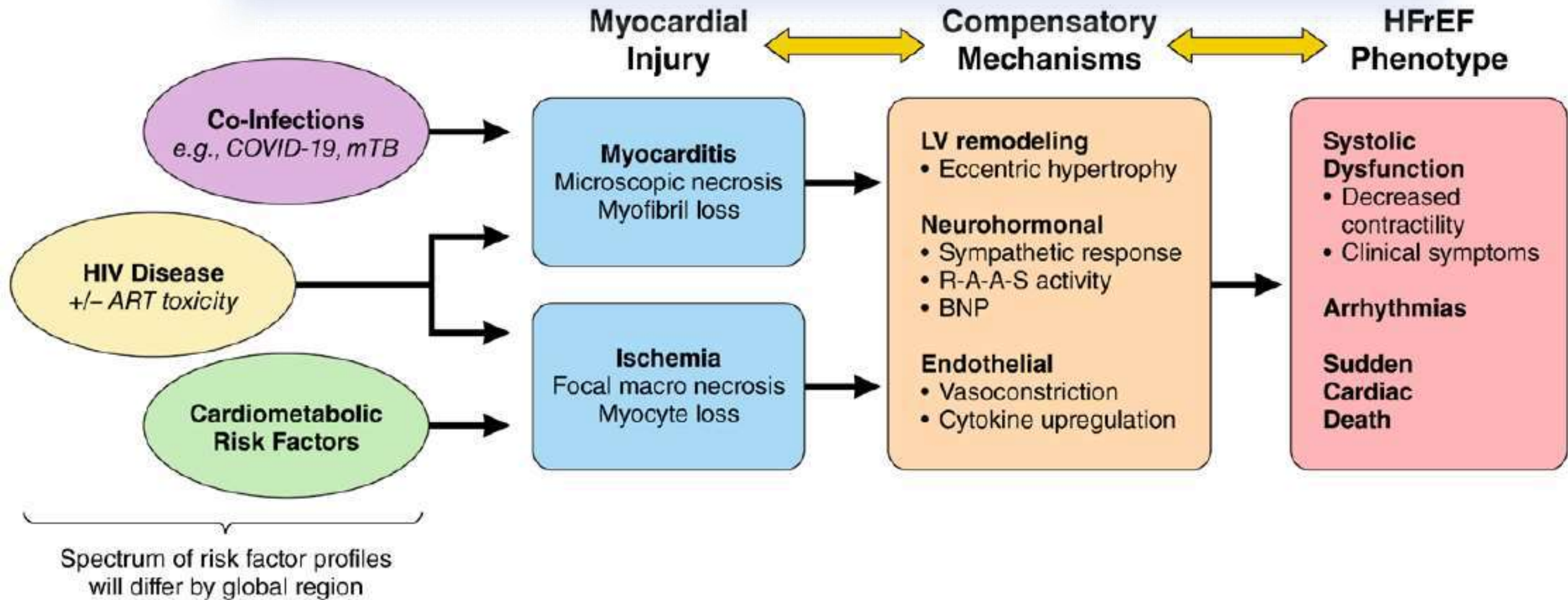
HIV (+) → 1,4-2,1 MI riski



## HIV ve Tip 1 ve Tip 2 MI Farkı

- ART öncesi dönemde HIV ilişkili KY sist. disfonk.
- Düşük CD4 düzeyi
- ART sonrası HIV ilişkili diast. disfonk.

# HIV ve Tip 1 ve Tip 2 MI Farkı





# HIV ve Tip 1 ve Tip 2 MI Farkı

**Chronic Condition(s)** ↔ **Systemic Inflammation** ↔ **Structural Changes** ↔ **HFpEF Phenotype**

**Co-Infections**  
*e.g., COVID-19, mTB*

**HIV Disease**  
• Immune depletion  
• Immune activation  
• Co-pathogens  
• ART toxicity

**Comorbidities**  
• Hypertension  
• Obesity  
• Diabetes  
• Lung disease  
• Iron deficiency

**Coronary Microvascular Inflammation**

- ROS
- Endothelial injury

**Endothelial Dysfunction**

- Decreased NO
- Less responsive

**Monocyte Activation**

- Subendothelial migration
- Cytokine, TGF- $\beta$

**Tissue Damage**

- Oxidative stress
- Mitochondrial dysfunction

**LV Remodeling**

- Eccentric hypertrophy
- Myocyte hypertrophy

**Myocardial Stiffness**

**Myocardial Fibrosis**

**Myocardial Steatosis**

**Diastolic Dysfunction**

- Impaired relaxation
- Clinical symptoms

**Reduced Coronary Flow Reserve**

- Reduced exertional capacity

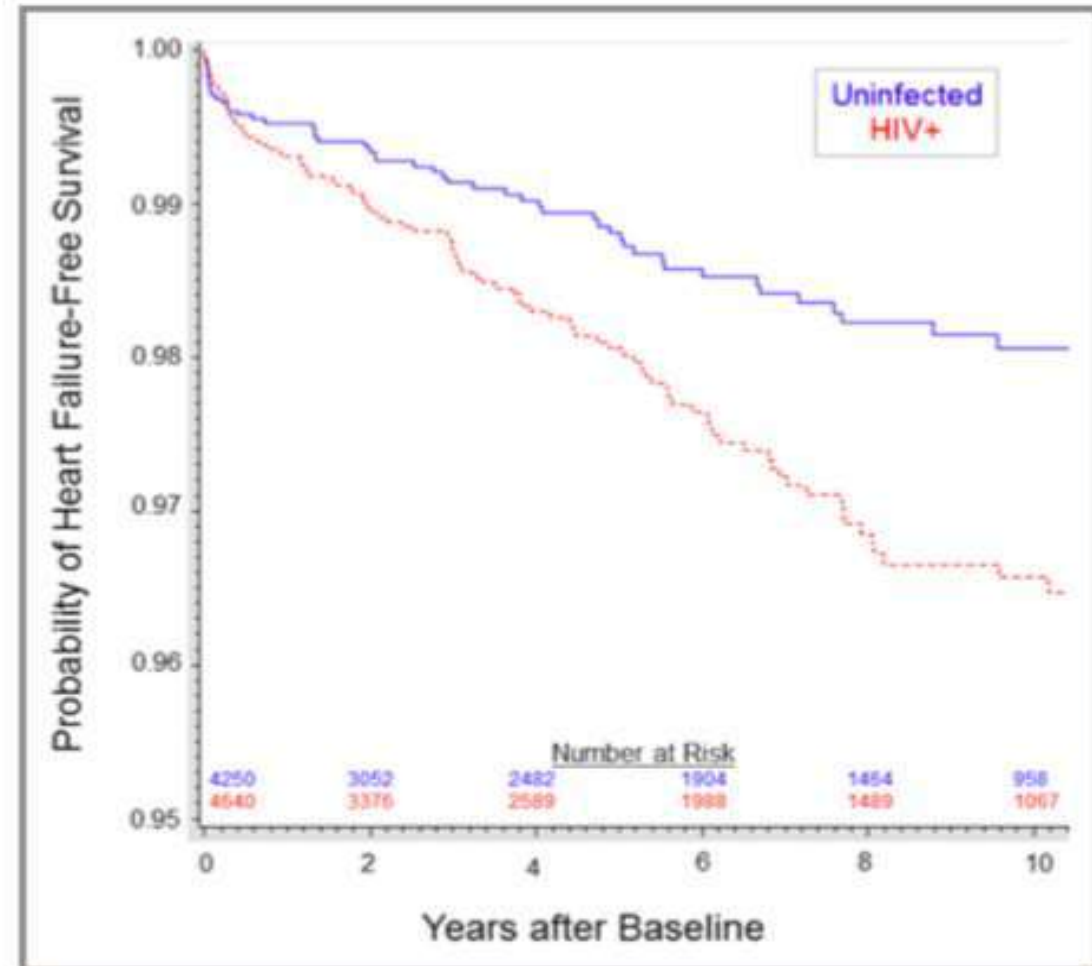
**Sudden Cardiac Death**

Spectrum will differ globally

# Adjudicated Heart Failure in HIV-Infected and Uninfected Men and Women



- HIV ilişkili KY  $\uparrow$
- $\uparrow$ HIV RNA ve  $\downarrow$  CD4
- KY  $\rightarrow$  97/ 4640 HIV (%2.1)
- Kontrol  $\rightarrow$  55/4250 (%1.3)
- HR  $\rightarrow$  2.10 (CI %95-1.38–3.21)

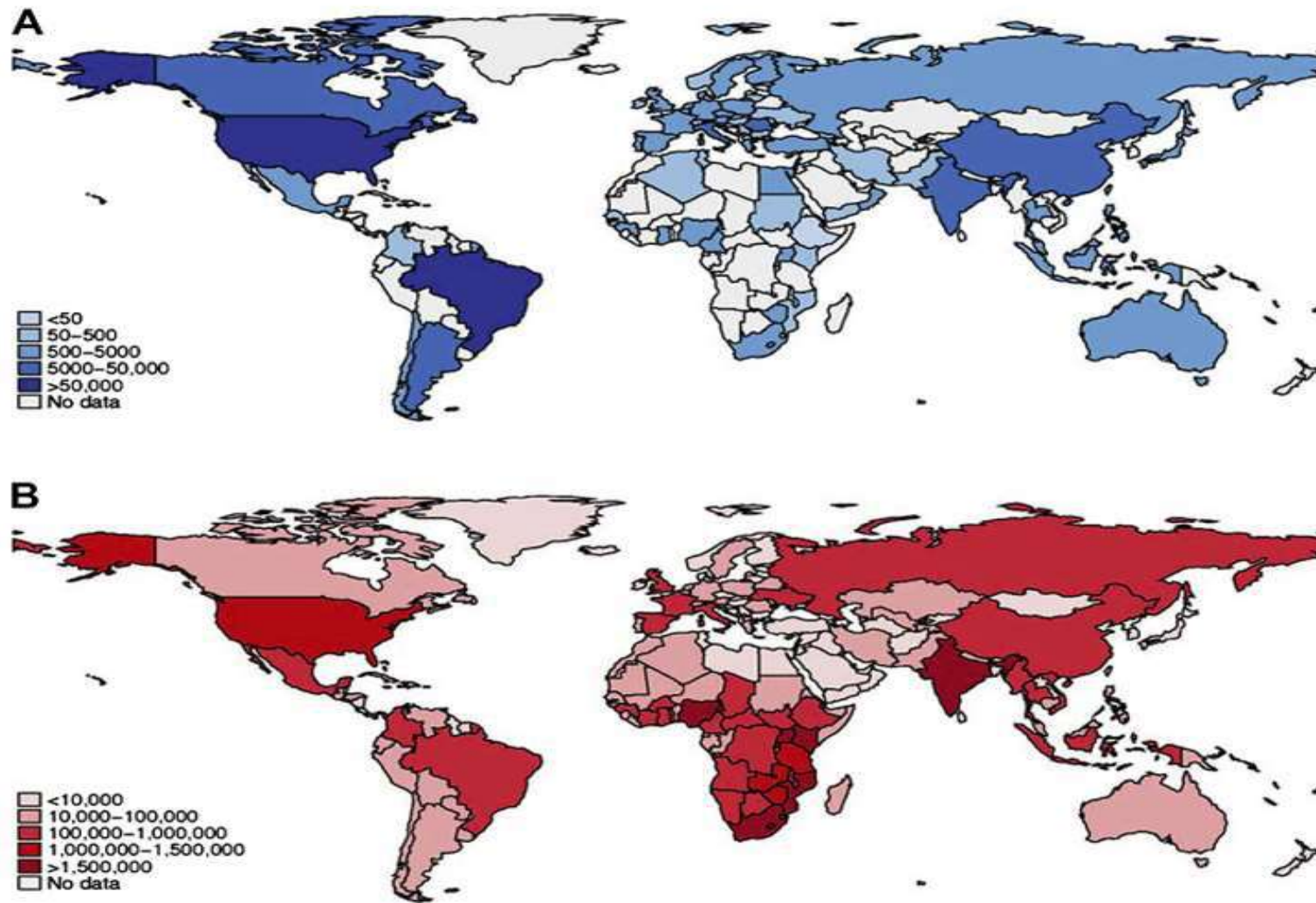




# Human Immunodeficiency Virus and Heart Failure in Low- and Middle-Income Countries

JACC: HEART FAILURE VOL. 3, NO. 8, 2015

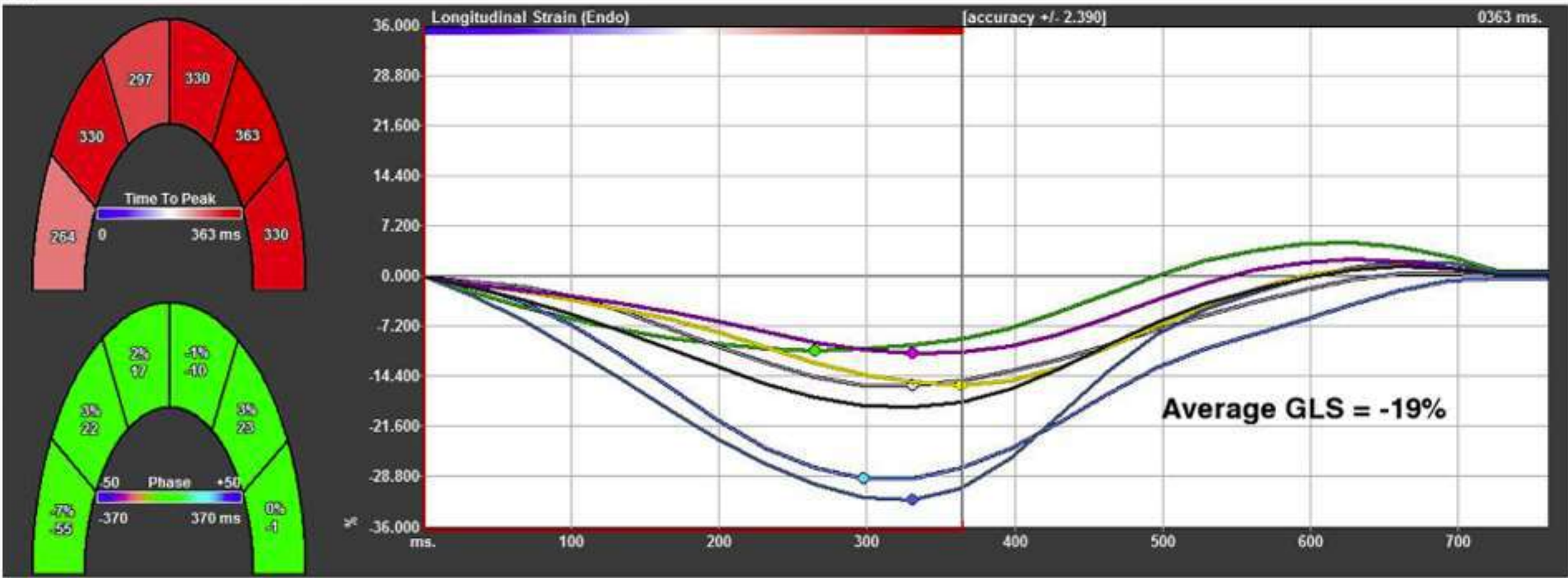
**FIGURE 1** Worldwide Distribution of Studies of HF and Burden of HIV





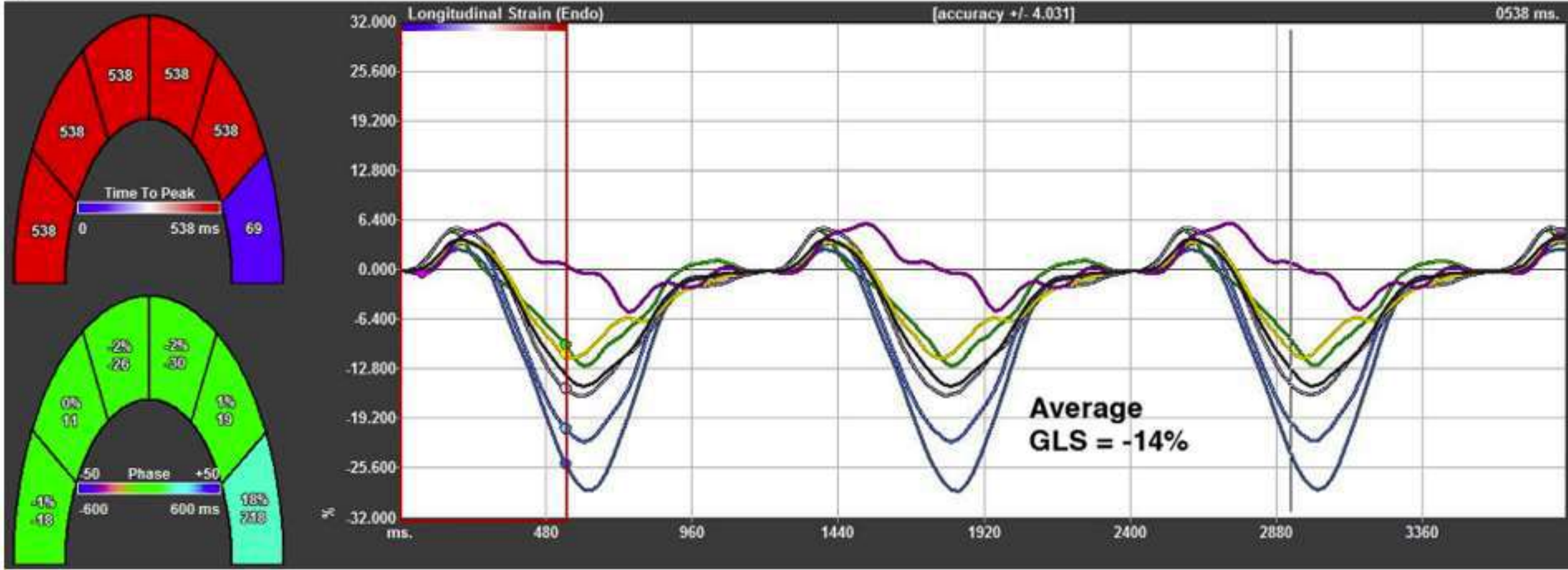
**FIGURE 3 Myocardial Deformation Tracings in HIV-Infected Individuals With Normal LVEF**

**A**



HIV → Longitudinal systolic cardiac strain ile myocardial deformasyon  
MR → Subklinik miyokard fibrosis ve steatosis  
Erken miyokard disfonksiyon tespiti → ↑ risk vaka tanımı

B

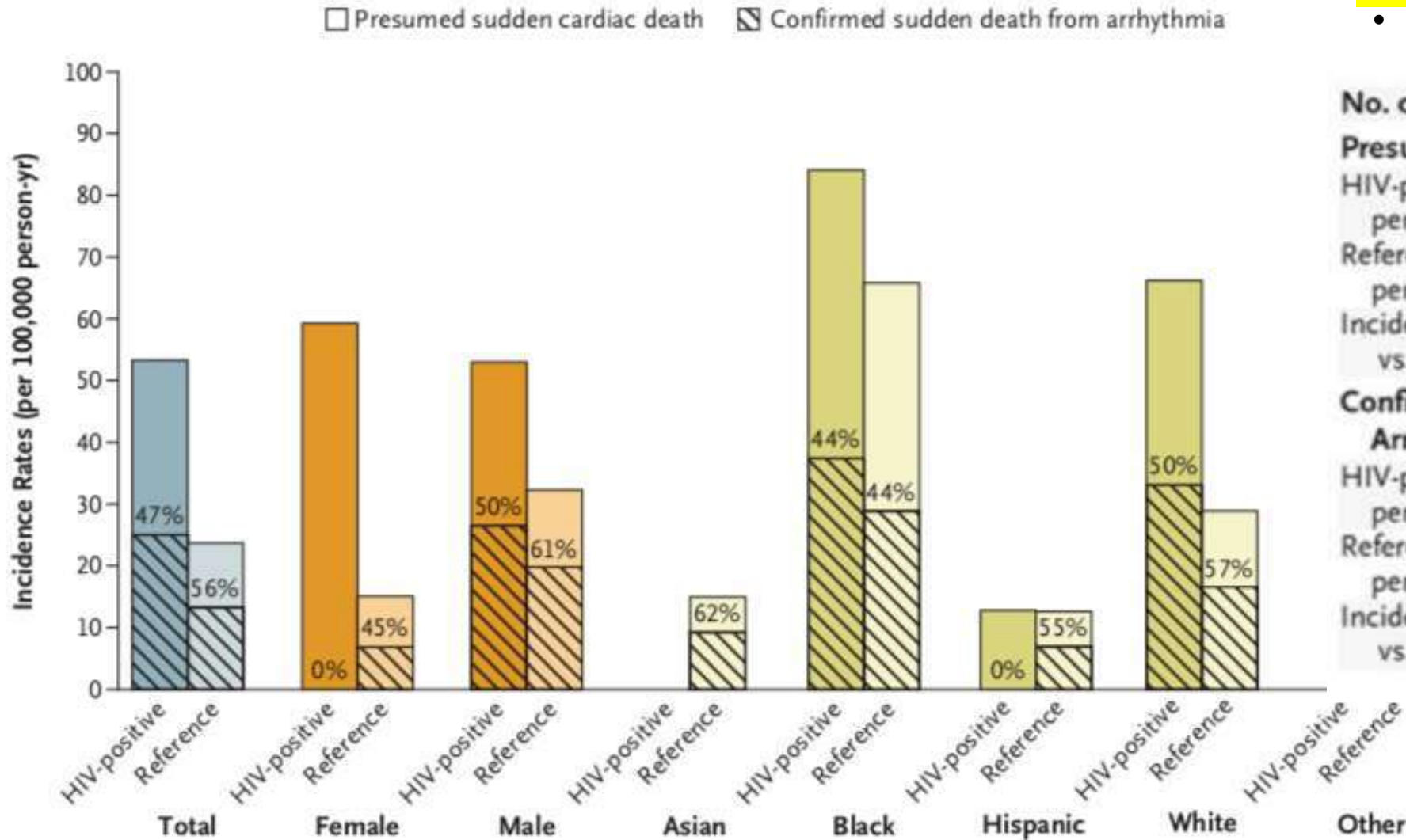


# HIV ve Ani Kardiyak Ölüm



# Sudden Cardiac Death and Myocardial Fibrosis Determined by Autopsy, in Persons with HIV

- San Francisco 2011-2016 HIV
- 2011-2014 Kontrol
- 100.000 kişi/yılı
- Aritmi ve ani ölüm
- İrk, etnik grup, cinsiyet



No. of Patients	47	505
<b>Presumed Sudden Cardiac Death</b>		
HIV-positive incidence rates —	53.3	
per 100,000 person-yr	(39.2–70.1)	
Reference incidence rates —	23.7	
per 100,000 person-yr	(21.7–25.9)	
Incidence rate ratio for HIV-positive vs. reference	2.25	(1.37–3.70)
<b>Confirmed Sudden Death from Arrhythmia</b>		
HIV-positive incidence rates —	25	
per 100,000 person-yr	(15.6–37.8)	
Reference incidence rates —	13.3	
per 100,000 person-yr	(11.8–15.0)	
Incidence rate ratio for HIV-positive vs. reference	1.87	(0.93–3.78)

N Engl J Med 2021;384:2306-16.



## HIV-Positive Group

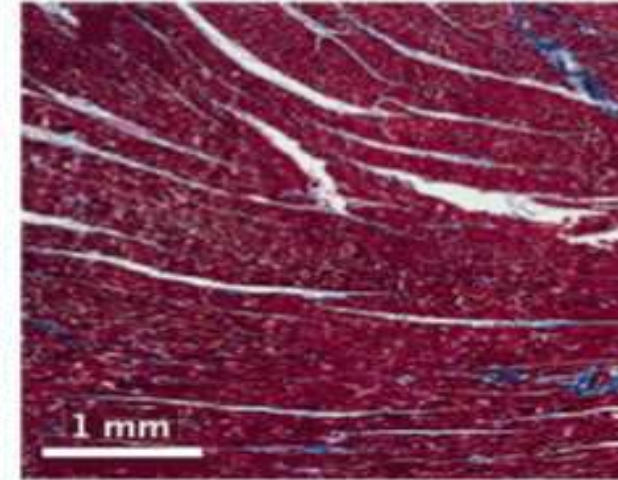
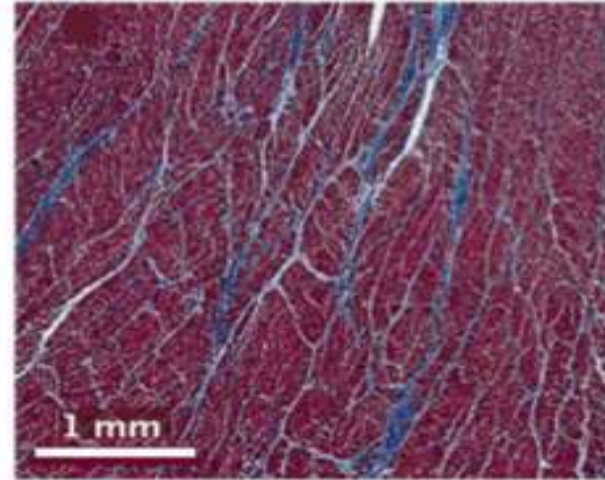
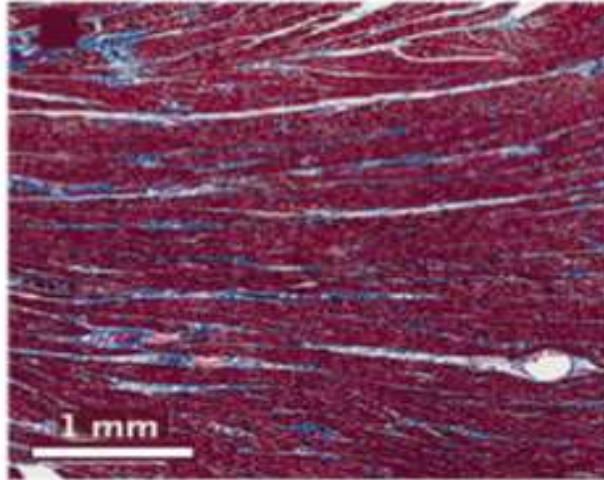
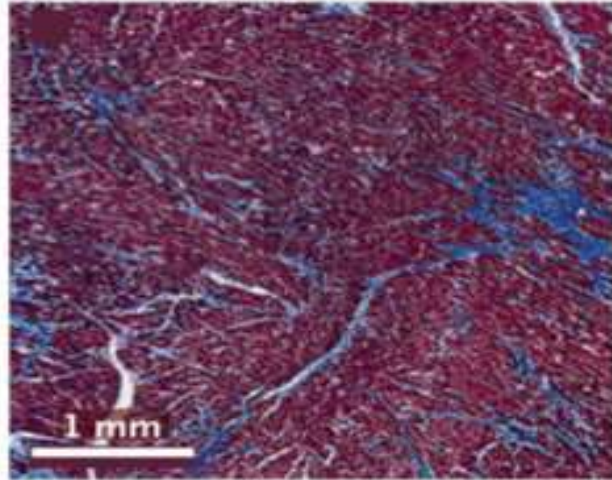
## Reference Group

Sudden death from arrhythmia

Sudden death from nonarrhythmic cause

Sudden death from arrhythmia

Sudden death from nonarrhythmic cause



HIV-Positive Group, Presumed Sudden Cardiac Death (N=24)

Reference Group, Presumed Sudden Cardiac Death (N=164)

HIV-Positive Group vs. Reference Group, Presumed Sudden Cardiac Death

	Sudden death from arrhythmia (N=12)	Sudden death from nonarrhythmic cause (N=12)	Sudden death from arrhythmia (N=100)	Sudden death from nonarrhythmic cause (N=64)	Sudden death from arrhythmia	Sudden death from nonarrhythmic cause
	<i>mean percent fibrosis</i>				<i>percent difference (95% CI)</i>	
<b>Total Fibrosis</b>	12.5±6.4	13.8±7.1	8.7±7.5		72 (23 to 142)	(7 to 198)
<b>Interstitial and Perivascular Fibrosis</b>	11.9±5.4					(8 to 185)
<b>Replacement Fibrosis</b>	1.9±3.4					(-20 to 75)

Presumed sudden cardiac deaths  
HIV+/- → (34% vs. 13%).

HIV + → ↑ histolojik intertisyel miyokard fibrosis

# Kardiyovasküler Risklerin Belirlenmesi

<40 yaş ise  
kardiyovasküler  
risklerin varlığını  
tespit et

≥40 yaş ise 5-10 yıllık  
kardiyovasküler  
hastalık riskini  
belirle

Risk modifikasyonu  
yap



Resources > Clinical risk scores

Welcome to the Risk Assessment Tool System (RATS). Please select the desired values from the list below.

## General

- EuroSida AIDS/Death risk score
- FENCE score
- <sup>CSR</sup>FENCE Score

## Cardiovascular

- D:A:D (R) CVD 5 and 10 year risk score
- D:A:D (F) CVD 5 and 10 year risk score
- Framingham CVD 5 and 10 year risk score
- MI Number needed to harm

Build form

Rigshospitalet, University of Copenhagen  
CHIP, Section 2100  
Blegdamsvej 9, DK-2100 Copenhagen, Denmark

CVR no.: 29190623  
VAT no.: DK29765790  
Follow us on:



1. Age:  yr

2. Gender:  Male  Female

3. Previous smoker?  Yes  No

4. Smoker?  Yes  No

5. Family CVD history?  Yes  No

6. Diabetes?  Yes  No

7. Abacavir treatment?  Yes  No

8. PI exposure:  yr



# ASCVD Risk Estimator Plus

## Estimate Risk

Current Age ⓘ \*

Age must be between 20-79

Sex \*

Male	Female
------	--------

Race \*

White	African American	Other
-------	------------------	-------

Systolic Blood Pressure (mm Hg) \*

Value must be between 90-200

Diastolic Blood Pressure (mm Hg) \*

Value must be between 60-130

Total Cholesterol (mg/dL) \*

Value must be between 130 - 320

HDL Cholesterol (mg/dL) \*

Value must be between 20 - 100

LDL Cholesterol (mg/dL) ⓘ ○

Value must be between 30-300

History of Diabetes? \*

Yes	No
-----	----

Smoker? ⓘ \*

Current ⓘ	Former ⓘ	Never ⓘ
-----------	----------	---------

On Hypertension Treatment? \*

Yes	No
-----	----

On a Statin? ⓘ ○

Yes	No
-----	----

On Aspirin Therapy? ⓘ ○

Yes	No
-----	----

Do you want to refine current risk estimation using data from a previous visit? ⓘ ○

Yes	No
-----	----



Risk of geographic region ⓘ

Low risk

Moderate risk

High risk

Very high risk

Gender

Male

Female

Age

40 - 69

years

Current smoking



Systolic blood pressure ⓘ

100 - 200

mmHg

mmol/L

mg/dL

Total cholesterol

3 - 9

mmol/L

HDL-cholesterol ⓘ

0.7 - 2.5

mmol/L

LDL-cholesterol ⓘ

0.1 - 9

mmol/L

Risk of geographic region ⓘ

Low risk

Moderate risk

High risk

Very high risk

Gender

Male

Female

Age

70 - 90

years

Current smoking



Diabetes mellitus ⓘ



Systolic blood pressure ⓘ

100 - 200

mmHg

mmol/L

mg/dL

Total cholesterol

3 - 9

mmol/L

HDL-cholesterol ⓘ

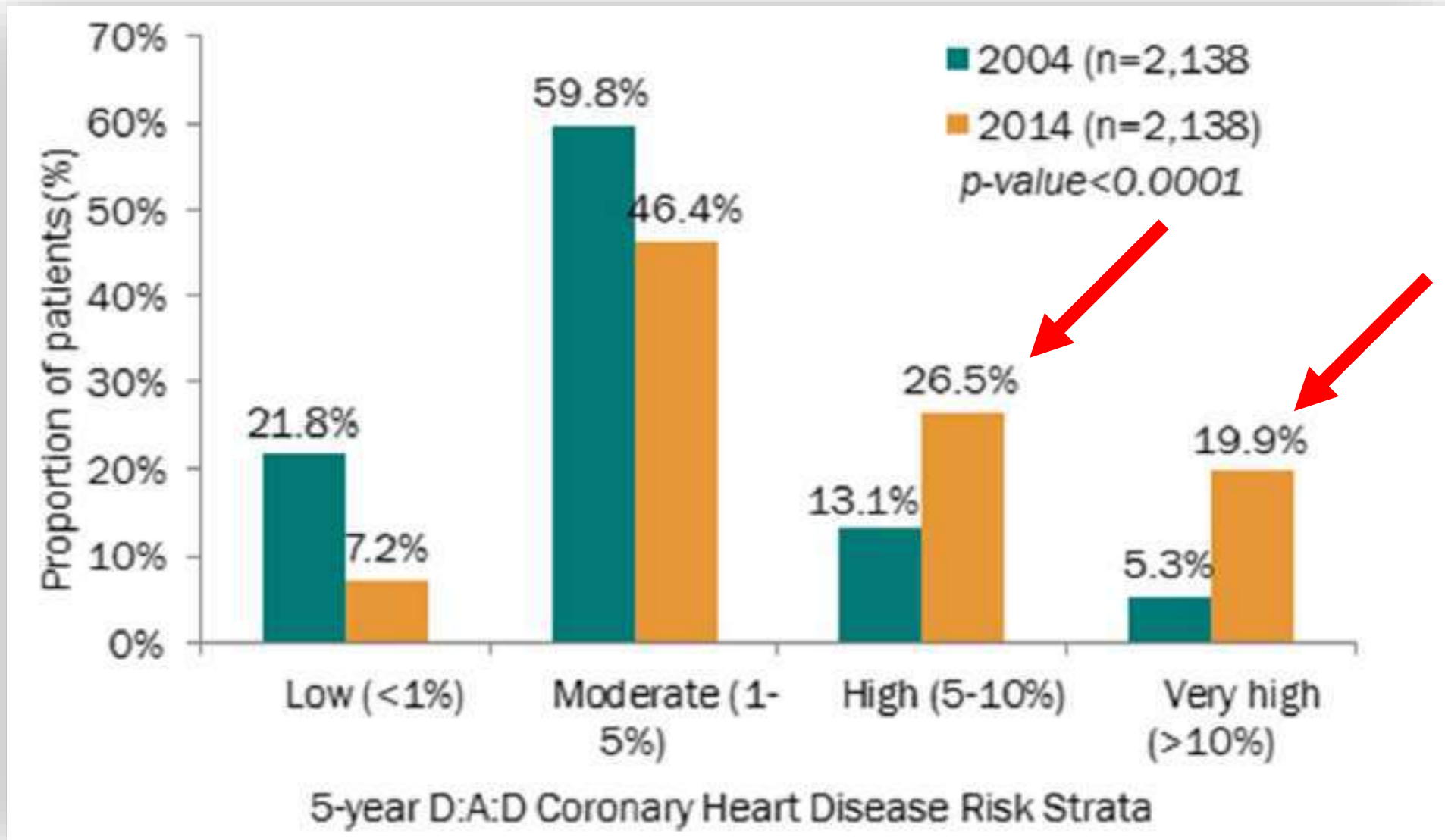
0.7 - 2.5

mmol/L

LDL-cholesterol ⓘ

0.1 - 9

mmol/L



# Comparison of Risk Category Predictions of Framingham Risk Score (FRS), Atherosclerotic Cardiovascular Disease Risk Score (ASCVD), Systematic Coronary Risk

576

## Evaluation (SCORE) and Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) Score in HIV-Infected Patients

Korten V<sup>1</sup>, Gökengin D<sup>2</sup>, Yıldırım T<sup>3</sup>, Inkaya AC<sup>4</sup>, Fincancı M<sup>5</sup>, Yagcı Caglayık D<sup>1</sup>, Mermut G<sup>2</sup>, Sirmsek F<sup>3</sup>, Eren G<sup>6</sup>, Unal S<sup>4</sup>

<sup>1</sup>Infectious Diseases, Marmara University Hospital, Istanbul, Turkey, <sup>2</sup>Infectious Diseases, Ege University Hospital, Izmir, Turkey, <sup>3</sup>Infectious Diseases and Clinical Microbiology, Okmeydanı Training and Research Hospital, Istanbul, Turkey, <sup>4</sup>Infectious Diseases, Hacettepe University, Ankara, Turkey, <sup>5</sup>Infectious Diseases and Clinical Microbiology, Istanbul Education and Research Hospital, Istanbul, Turkey

FRAMINGHAM - CVD (N=527)	Low Risk (≤10%) n (%)	Moderate Risk (>10% - ≤20%) n (%)	High Risk (>20%) n (%)	
Framingham score	273 (51.8)	173 (32.8)	81 (15.4)	
Framingham score with ARF*	268 (50.9)	152 (28.8)	107 (20.3)	
SCORE (N=527)	Low Risk (<1%) n (%)	Moderate Risk (≥1% - <5%) n (%)	High Risk (≥5% - <10%) n (%)	Very High Risk (≥10%) n (%)
Score	88 (16.7)	192 (36.4)	182 (34.5)	65 (12.4)
Score with ARF*	81 (15.4)	162 (30.7)	192 (36.4)	92 (17.5)
ASCVD (N=527)	Low Risk (≤7.5%) n (%)	High Risk (≥7.5%) n (%)		
ASCVD score	365 (69.3)	162 (30.7)		
ASCVD score with ARF*	335 (63.6)	192 (36.4)		
DAD-Full (N=527)	Low Risk (≤5%) n (%)	High Risk (≥5%) n (%)		
DAD-F score	387 (73.4)	140 (26.6)		
DAD-Reduced (N=527)	(≤5%) n (%)	(≥5%) n (%)		
DAD-R	381 (72.3)	146 (27.7)		

Çok merkezli kesitsel çalışma

Temmuz 2016- Şubat 2017, 5 merkez, 40-74 yaş arasında KVH olmayan, statin almayan hastalar

**Yüksek KVH skor prevelansı %20.3 ile %36.3**

607 hastanın 527 si değerlendirilmiş

%82'si erkek, ortanca yaş: 48

%11 erken başlangıçlı KVH aile öyküsü

%50 sigara içici

%22 HT

%8 DM

\* ARF= Additional Risk Factors: Framingham (DM), ASCVD (LDL cholesterol ≥ 190 mg/dL or DM), SCORE (DM or GFR < 60 ml/min or total cholesterol > 310 mg/dL or blood pressure ≥ 160/110 mmHg)



# Prevalence of cardiovascular disease (CVD) and Comparison of risk category predictions of Systemic Coronary Risk Evaluation Score-2 (SCORE2) and four other CVD risk calculators among people living with HIV(PLWH) in Türkiye

Tukenmez Tigen, E<sup>1</sup>; Gökengin, D<sup>2</sup>; Özkan Özdemir, H<sup>3</sup>; Akalın, H<sup>4</sup>; Kaya, B<sup>5</sup>; Deveci, A<sup>6</sup>; İnan, A<sup>7</sup>; İnan, D<sup>8</sup>; Altunsoy, A<sup>9</sup>; Özel, A.S<sup>10</sup>; Karaoğlan, İ<sup>11</sup>; Eraksoy, H<sup>12</sup>; Demirdal, T<sup>13</sup>; Yıldırım, T<sup>14</sup>; Birengel, S<sup>15</sup>; İnci, A<sup>16</sup>; Nazlı, A<sup>17</sup>; Kayaaslan, B<sup>9</sup>; Sayın Kutlu, S<sup>18</sup>; Ataman Hatipoğlu, Ç<sup>19</sup>; Esen, Y<sup>20</sup>; Koç, T<sup>20</sup>; Korten, V<sup>1</sup>; and HIV-TR Study Group

- Çok merkezli kesitsel çalışma, 2019-2021
- **20 merkez, 1425 hasta**, %82.7 erkek, >40 yaş, ortalama yaş 51
- **%10.6 tanılı KVH**
- Ortalama CD4 : 696 h/μl



Participant Characteristics	Median (IQR) or proportion (n=1425)
Age, y, median (IQR)	51 (45-58)
Male, Sex	1178 (82.7)
Smoking (current smoker)	651 (45.7)
Alcohol use (1-7 or >7 drinks/week)	411 (28.9)
IV non-prescription drug use	35 (2.5)
Exercise & physical activity	248 (17.4)
Body mass index	
Obese (≥30 kg/m <sup>2</sup> )	258 (18.3)
Diabetes mellitus	242 (17)
Hypertension	420 (29.5)
Hypercholesterolemia	498 (34.9)
Family history of premature cardiovascular disease	102 (7.2)
Family history of CAD (In parents)	310 (21.1)
Years since HIV diagnosis, median (IQR)	5.0 (2.0-9.0)
Cumulative months of ART use, median (IQR)	
Protease Inhibitor	218 (15.3)
Nucleoside Reverse Transcriptase Inhibitor	1390 (97.5)
Others	1325 (93)
Nadir CD4 <sup>+</sup> cell count, cells/μL, median (IQR)	318 (168-480)
Nadir CD4 <sup>+</sup> <200 cells/μL	424 (29.8)
Current CD4 <sup>+</sup> cell count, cells/μL, median (IQR)	696 (479-920)
Viral load, <200 copies/mL	1345 (94.4)

## Kardiyovasküler Risk Hesaplayıcıları:

- Framingham Risk Skoru (FRS)
- Modifiye Framingham Risk Skoru (Modified FRS)
- Avrupa Kardiyovasküler Risk Değerlendirme Skoru 2 (SCORE2\*)
- Data Collection on Adverse Effects of Anti-HIV Drugs Cohort (D:A:D)
- Aterosklerotik kardiyovasküler risk skoru (ASCVD)

### KVH risk faktör prevalansı:

- %50 sigara kullanımı
- %26 Hiperlipidemi,
- %22 Hipertansiyon,
- %16.5 obezite,
- %8 DM
- %11 ailesel KVH öyküsü

Korten et al 2017

### Lipid düşürücü ajan için uygun kişiler:

- ESC--> %21.8
- AHA--> %36.4

### KVH Risk faktör prevalansı:

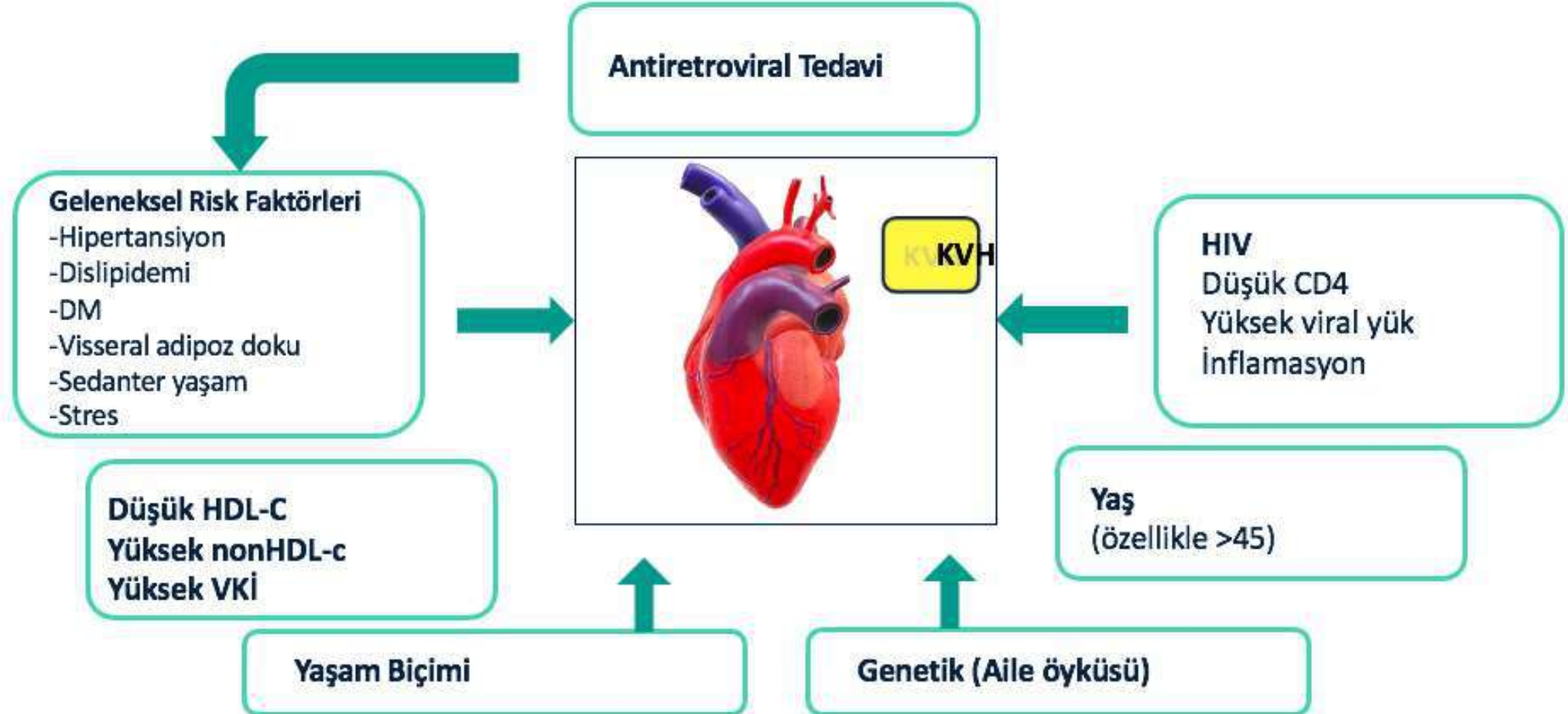
- %45.7 sigara kullanımı
- **%34.9 Hiperlipidemi,**
- **%29.5 Hipertansiyon,**
- **%18.3 obezite,**
- **%17 DM**
- %7.2 ailesel KVH öyküsü

Tigen et al 2021

### Lipid düşürücü ajan için uygun kişiler

- ESC--> %75.3
- AHA--> %47.1

# HIV ve Kardiyovasküler Hastalık için Risk Faktörleri





# **HIV ile Yaşayan Bireyde Kardiyovasküler Risk yönetimi**



10 yıllık kardiyovasküler hastalık riski hesapla

Tüm kişilere yaşam tarzı değişiklikleri öner,  
10 yıllık KVH riski  $\geq 10$  olanlarda ART modifikasyonu

Modifiye edilebilecek risk faktörlerini belirle

**Sigara**

Sigarayı bırak  
Davranışçı  
tedavi  
Farmakoterapi

**Kan basıncı**

KB  $\geq 140/90$   
mmHg ise (öz.  
KVH riski  $> 10$ )  
ilaç tedavisi

Hedef SKB  $< 130$ ,  
DKB  $< 80$  mmhg

**Koagülasyon**

Bilinen KVH  
varsa, DM + yüksek  
KVH riski varsa

75-150 mg ASA

**Kan şekeri**

DM tanısını  
doğrula ve tedavi  
et

Hedef  
AKŞ 80-130  
mg/dL  
HbA1c  
 $< 6.5-7$

**Lipidler**

KVH riski  $\geq 10$  veya  
Tip 2 DM veya bilinen  
KVH varsa ilaç  
tedavisi

Hedef :  
LDL-K  $< 70$ , Non-HDL  $< 100$   
Çok yüksek risk LDL-K  $< 55$ ,  
Non-HDL  $< 85$

# DHHS Güncellemesi – 27 Şubat 2024

**Date:** February 27, 2024

**Source** ClinicalInfo

The Department of Health and Human Services Guidelines Panel for the Use of Antiretroviral Agents in Adults and Adolescents with HIV (the Panel) has developed recommendations for the use of statin therapy in people with HIV, in collaboration with representatives from the American College of Cardiology (ACC), the American Heart Association (AHA), and the HIV Medicine Association.

With continuous antiretroviral therapy (ART) and viral suppression, most people with HIV achieve a life expectancy close to that of people without HIV. However, there remains a mortality gap primarily due to cardiovascular disease and cancer. REPRIEVE, a large randomized controlled trial among people with HIV aged 40 to 75 years who were receiving ART and had low-to-intermediate risk of atherosclerotic cardiovascular disease (ASCVD), showed that when compared to placebo, pitavastatin 4 mg daily was associated with a 35% reduction in major adverse cardiovascular events over a median follow-up duration of 5 years. The recommendations below are endorsed by the organizations listed above.

For people with HIV who have low-to-intermediate (<20%) 10-year ASCVD risk estimates:

- Age 40–75 years
  - When 10-year ASCVD risk estimates are 5 to <20%, the Panel recommends initiating at least moderate intensity statin therapy **(AI)**.
    - Recommended options for moderate intensity statin therapy include:
      - Pitavastatin 4mg once daily **(AI)**
      - Atorvastatin 20mg once daily **(AII)**
      - Rosuvastatin 10mg once daily **(AII)**

