LIVING WELL WITH HIV

Dr Choy Chiaw Yee

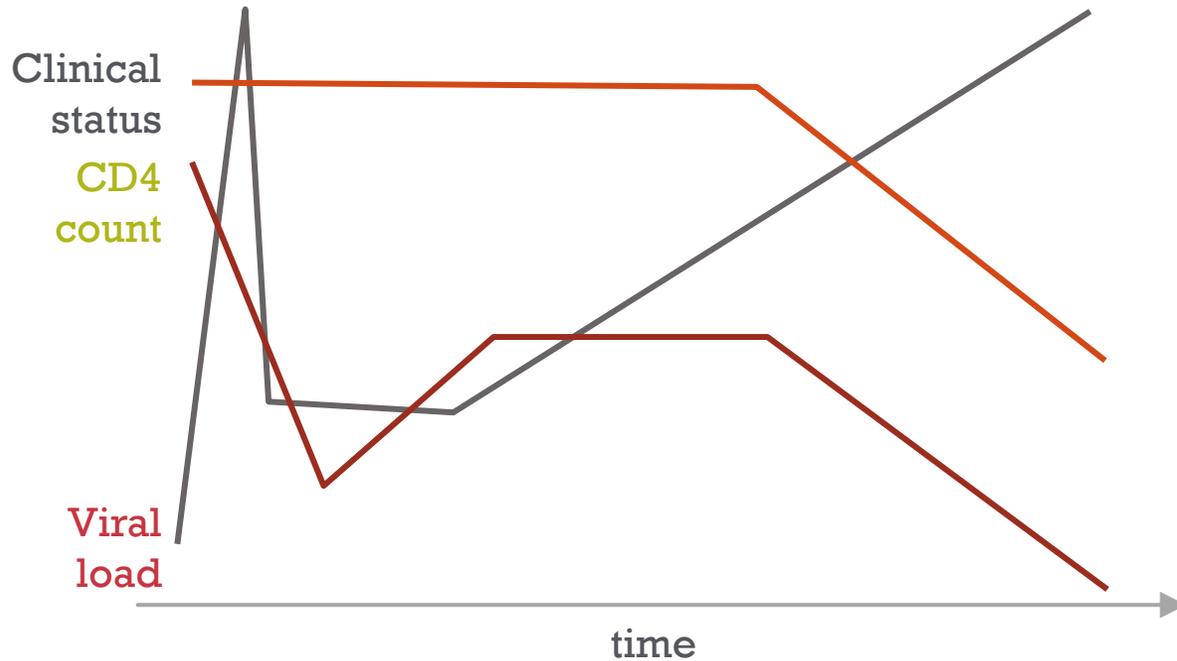National Centre for Infectious Diseases, Singapore

AGENDA

- How do people living with HIV age differently from others?

- What are the strategies we can use for better aging and living?
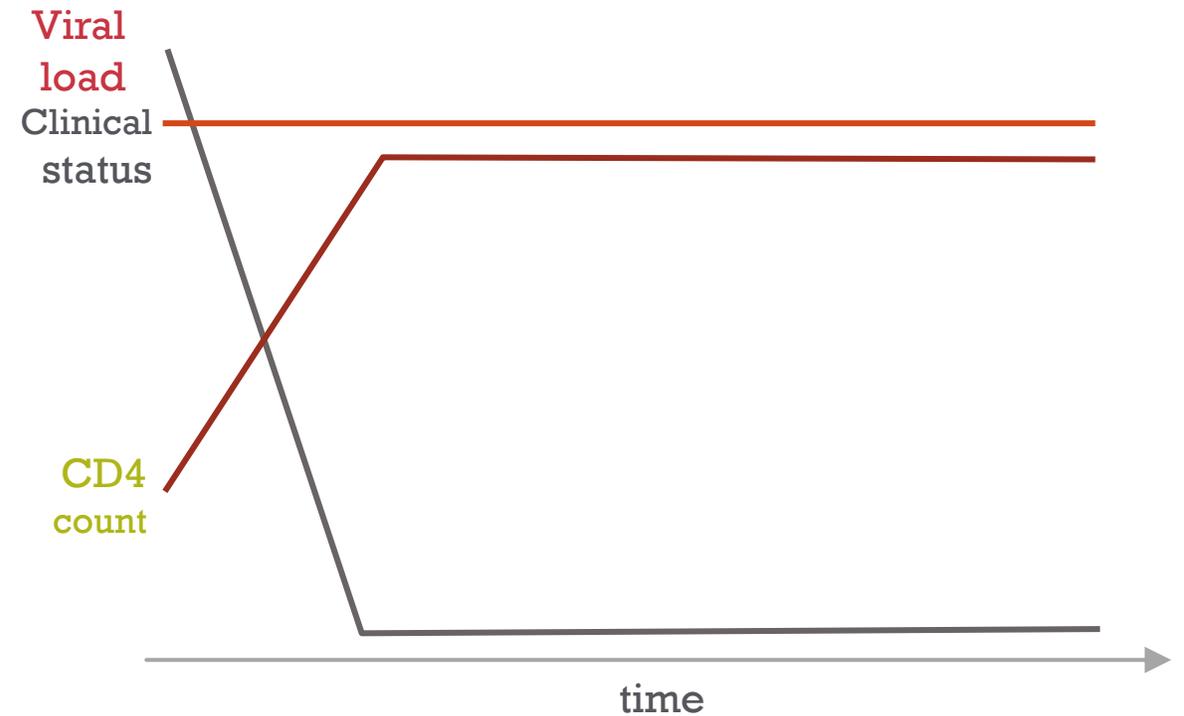
- Co-infections

TREATED HIV INFECTION

Untreated HIV Infection

With Rapid Therapy to Achieve Viral Suppression

Clinical status

CD4 count

Viral load

time

Viral load

Clinical status

CD4 count

time

Viral load — CD4 count — Clinical status

HIV TREATMENT LANDSCAPE: THEN AND NOW

	1996	2023
% 50 years or older	<15%[1]	53%[1]
Average Life Expectancy	39 years[2]	women 76-79 years[1] men 75-77 years[1]
Medication Burden	>12 tablets daily[3]	May be 1/day[4]
		2 injections every 2 month[4]

*Daily pill burden as low as 1 due to availability of single-tablet regimens
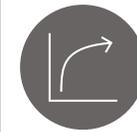
The life expectancy of people with HIV taking antiretroviral therapy (ART) has increased substantially over the past 25 years[5]

With advances in HIV treatment, people with HIV now **live almost as long as the general population**[5]

Prevention and/or management of **comorbidities** are key considerations when selecting HIV regimens, as PWH age[5]

HIV treatment success may be influenced by many factors. **Social Determinants of Health** have a huge impact on adherence [6]
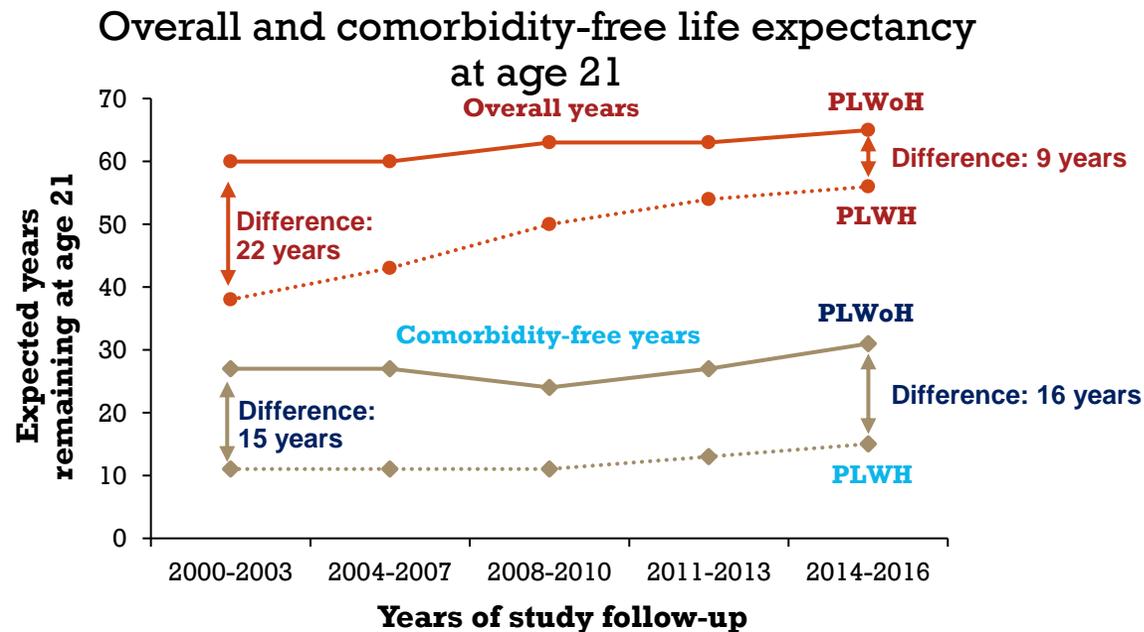
1. Lancet HIV 2023: 10; e295–307. Published Online. March 20, 2023. https://doi.org/10.1016/S2352-3018(23)00028-0 Accessed Dec. 8, 2023
2. Marcus JL et al. Narrowing the Gap in Life Expectancy Between HIV-Infected and HIV-Uninfected Individuals With Access to Care. *J Acquir Immune Defic Syndr*. 2016 Sep 1;73(1):39-46. Accessed December 6, 2023
3. krentz-et-al-2012-pill-burden-in-hiv-infection-20-years-of-experience.pdf. Accessed December 6, 2023
4. https://clinicalinfo.hiv.gov/sites/default/files/glossary/Glossary-English_HIVinfo.pdf
5. https://www.hiv.gov/hiv-basics/living-well-with-hiv/taking-care-of-yourself/aging-with-hiv/. Accessed December 6, 2023
6. Dominguez LW, et al. The Impact of Social Determinants of Health on Medication Adherence: J Gen Intern Med. https://pubmed.ncbi.nlm.nih.gov/33515188/. Accessed December 6, 2023

PREVENTION OF COMORBIDITIES IS AN UNMET NEED IN PLWH

Cohort analysis of comorbidities in PLWH (n = 39,000) and PLWoH (n = 387,767) in US, 2000–2016

Overall and comorbidity-free life expectancy at age 21

Repurposed from Marcus JB, et al, © 2020 The Authors, published by JAMA under a CC-BY-NC-ND License. Permission granted from Julia Marcus, on behalf of the coauthors
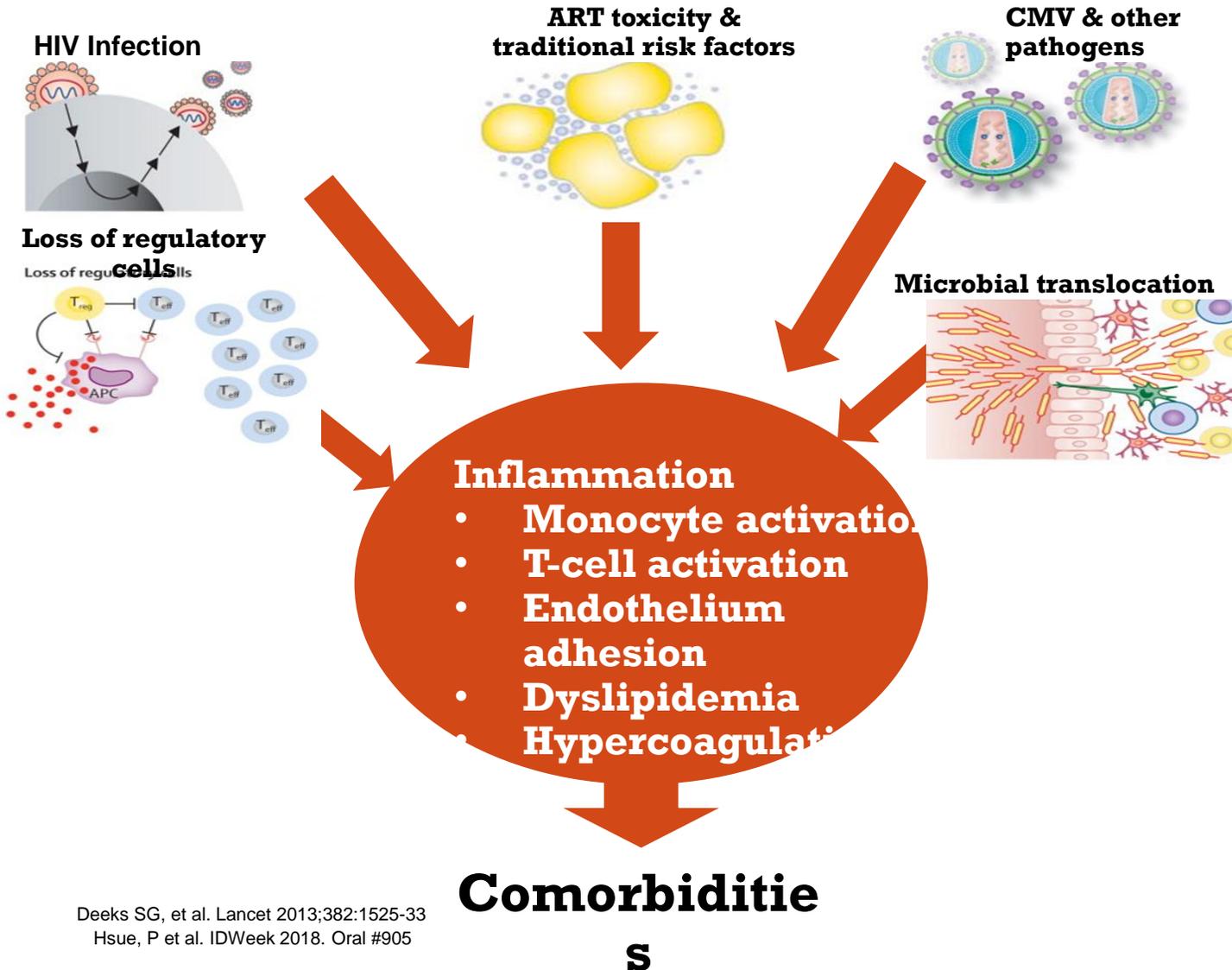
- PLWoH have an expected additional 16 comorbidity-free years versus PLWH
- For each separate comorbidity,* there was a persistent difference in comorbidity-free life expectancy between PLWH and PLWoH
- Initiating ART with a CD4 count >500/µL narrowed the difference in comorbidity-free life expectancy (difference of 9.5 years)

While overall life expectancy has greatly improved for PLWH, individuals still live substantially fewer healthy years than PLWoH

FACTORS CAUSING PERSISTENT INFLAMMATION DURING ANTIRETROVIRAL THERAPY

HIV Infection

Loss of regulatory cells

ART toxicity & traditional risk factors

CMV & other pathogens

Microbial translocation

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

Comorbidities

- Chronic inflammation persists in treated HIV and is a strong predictor of CVD, serious non-AIDS events and mortality

- HIV-related strategies including ART and early ART lower inflammatory markers, but additional agents will be needed

- Some inflammatory pathways may be unique to HIV

- The risks/benefits of anti-inflammatory therapies in the setting of HIV need exploration

Deeks SG, et al. Lancet 2013;382:1525-33
Hsue, P et al. IDWeek 2018. Oral #905

CMV, Cytomegalovirus; ART, antiretroviral therapy; CVD, cardiovascular disease

Italy

PRESENCE OF COMORBIDITIES IN PLWH AGED 40 YEARS AND OLDER

Persons With HIV

HIV negative

Comorbidities*
- 4
- 3
- 2
- 1
- 0

	≤ 40 Yrs (n = 542)	41-50 Yrs (n = 1724)	51-60 Yrs (n = 452)	> 60 Yrs (n = 136)	≤ 40 Yrs (n = 1626)	41-50 Yrs (n = 5172)	51-60 Yrs (n = 1356)	> 60 Yrs (n = 408)
Polypathology Prevalence, %	3.9	9.0	20.0	46.9	0.5	1.9	6.6	18.7
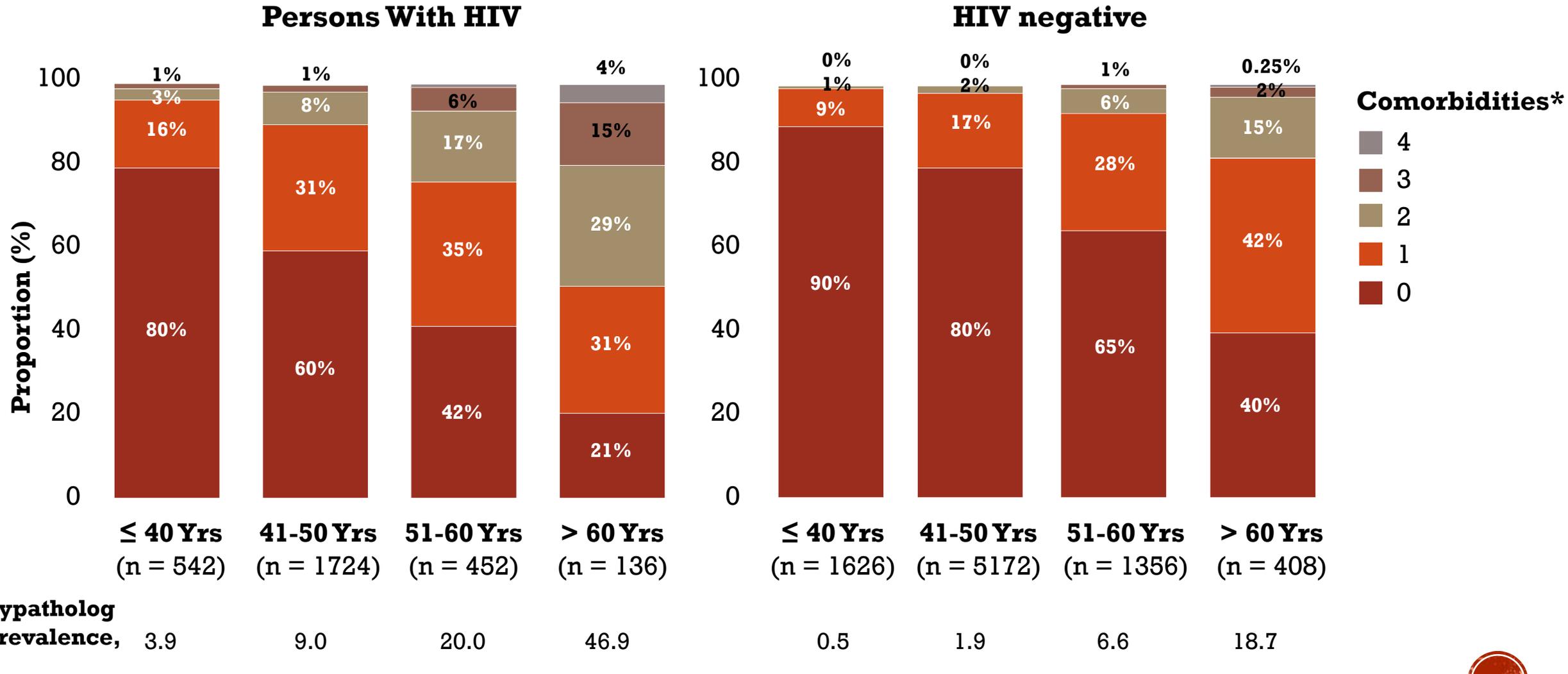
*Includes evaluation of HTN, diabetes, hypothyroidism, CVD, and bone fracture.

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

COMORBIDITY AND COMEDICATION BURDEN MEASURES FOR PLWH VS. PLWOH

Measure	PLWH (n=20,256)	PLWoH (n=40,512)
Baseline Charlson comorbidity score, mean (SD) [IQR]	0.9	0.6
Baseline Charlson comorbidity score category, n (%)		
0	12,416 (61.3)	29,194 (72.1)
1	2862 (14.1)	4894 (12.1)
3–4	1649 (8.1)	2164 (5.3)
5+	906 (4.5)	987 (2.4)
Comorbidity burden, n (%)		
0	6249 (30.9)	18,433 (45.5)
1	3741 (18.5)	5057 (12.5)
2	2737 (13.5)	4192 (10.4)
3+	7529 (37.2)	12,380 (31.7)

Percent of patients

Condition	PLWoH	PLWH
Liver disease	1.7%	3%
Cardiac dysrhythmia	6.1%	6.8%
Ischemic heart disease	7%	7.2%
Insomnia	7.6%	8.7%
Anxiety disorders	7.3%	11.2%
Depression	7.3%	13.1%
GI disorders	9.1%	12.6%
Obesity	13.9%	13.5%
CKD	9.4%	13.6%
T2DM	15.8%	13.9%
Dyslipidemia	24.6%	29.4%
Hypertension	32.2%	33.9%
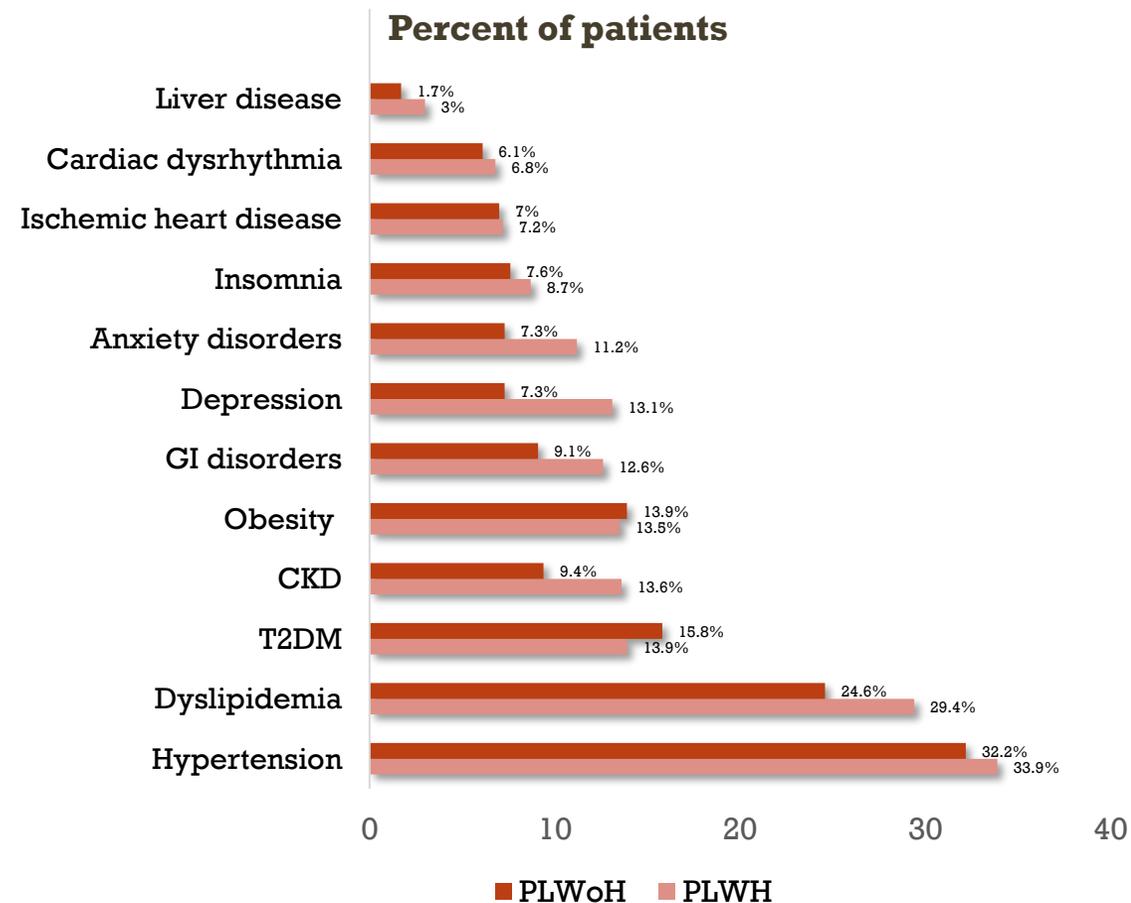
Patients with HIV have a higher prevalence of non-infectious comorbidities than individuals without HIV

Paudel M, et al. 2022:38:1443-1450

POLYPHARMACY AMONG PLWH AGED ≥ 50 YEARS OLD

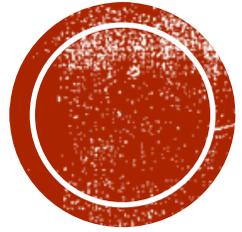| Reference	Age, years	Polypharmacy (At Least 5 Non-ARV Drugs)
Courlet P, et al. *CROI 2019; Poster 466*	≥ 65	46%
Guaraldi G, et al. *BMC Geriatr 2018;18(1):99*	≥ 65	37%
Justice A, et al. *AIDS 2018;32(6):739-749*	≥ 65	43%
Nuńez-Nuńez M, et al. *Farm Hosp 2018;42(4):163-167*	≥ 50	48%
Ssonko M, et al. *BMD Geriatr 2018;18(1):125*	≥ 50	15%
Krentz HB & Gill MJ *AIDS Patient Care STDs 2016;30(1):11-17*	≥ 50	43%
O'Halloran M, et al. *Antivir Ther 2019 (Epub ahead of print)*	≥ 50	30%
Ware D, et al. *PLoS One 2018;13(9):e0203890*	≥ 50	38.4-46.8%
Lopez-Centeno B, et al. *HIV Drug Therapy, Glasgow 2018;P211*	≥ 50	47%

Potential limitations: recall bias, under-reporting, OTC consistency, and different populations

Back D. CROI 2019 Seattle, WA. Oral 129

OTHER CONSIDERATIONS

Compared to their peers who are also above the age of 50:

Age related stigma ✚ HIV related stigma

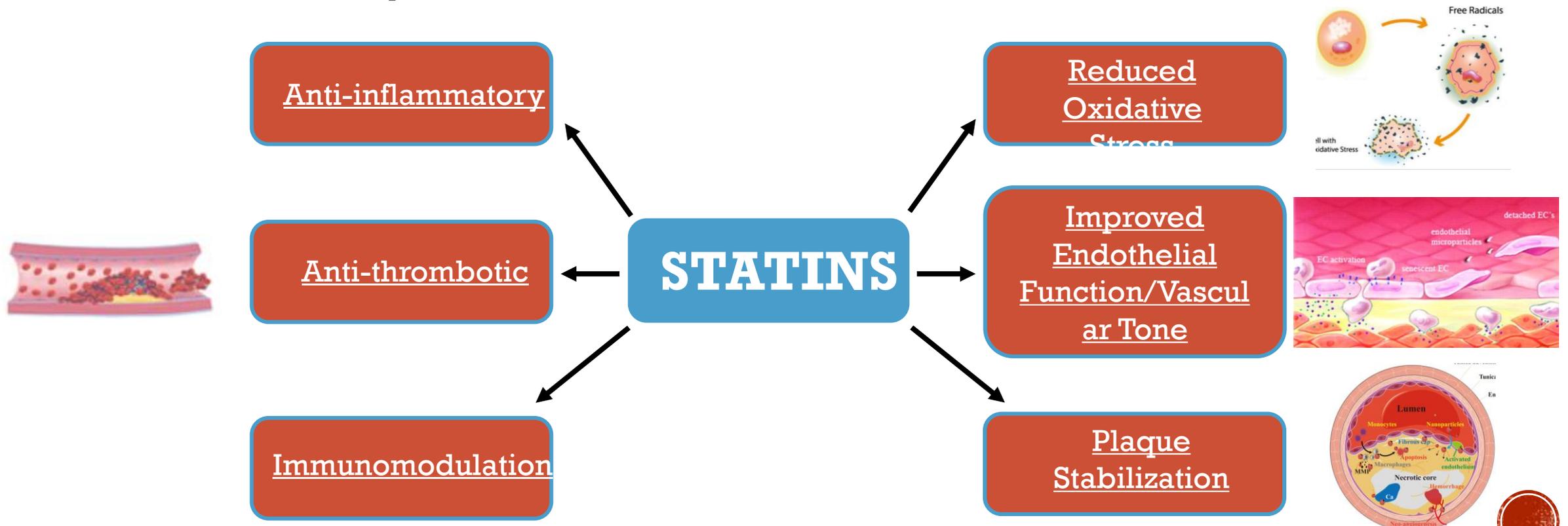Loneliness   Reduce cognition   Reduce energy
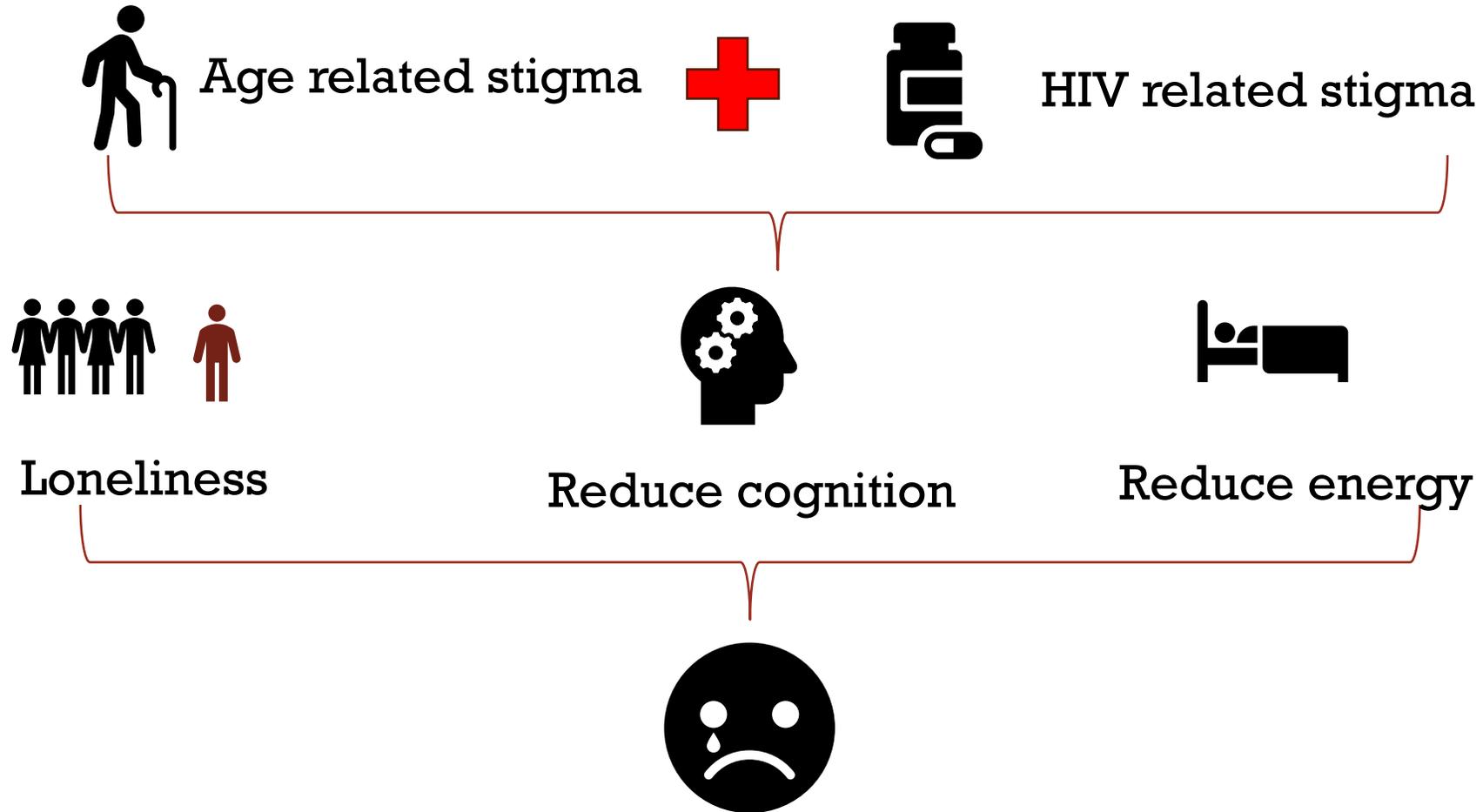
STRATEGIES

REPRIEVE TRIAL

- A phase 3, multinational, randomised, placebo controlled trial

- Assess the efficacy and safety of pitavastatin for the prevention of cardiovascular events in persons living with HIV infection and low to moderate

- 7769 participants were enrolled, between ages 40-75 years (median LDL cholesterol, 108mg/dl)

- 3888 received pitavastatin, 3881 received placebo

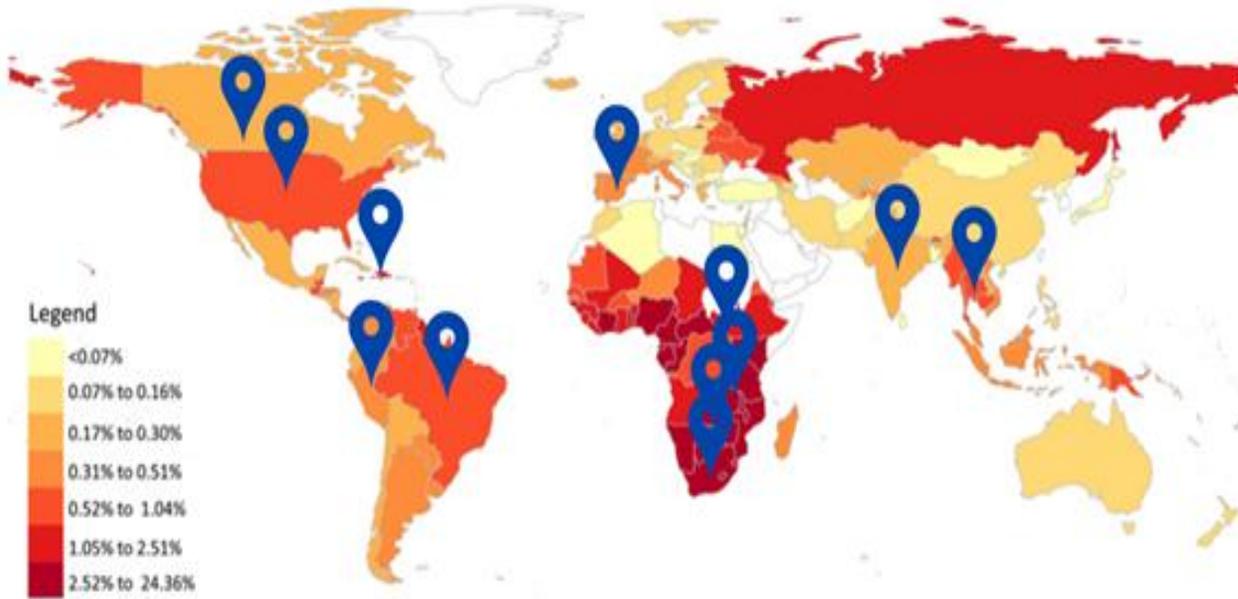- Primary outcome is major adverse cardiovascular event (MACE)
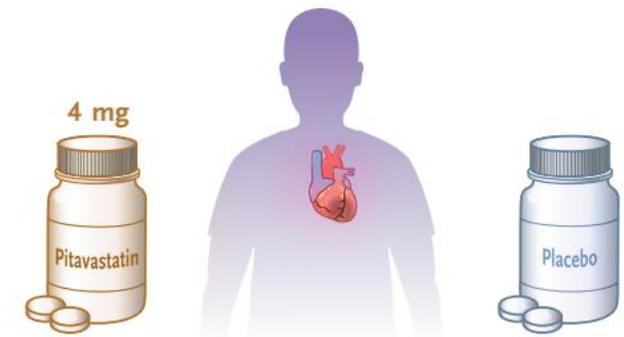
BEYOND LDL: PLEIOTROPIC EFFECTS OF STATINS

- Statins primary effect is to inhibit HMG-CoA reductase to lower LDL cholesterol

- Statins have many other beneficial effects to reduce vascular disease

STATINS

- Anti-inflammatory
- Anti-thrombotic
- Immunomodulation
- Reduced Oxidative Stress
- Improved Endothelial Function/Vascular Tone
- Plaque Stabilization

REPRIEVE Study Population

Study hypothesis: Pitavastatin would prevent MACE through statin effects in PWH, at low to moderate risk, for whom statins not typically prescribed under current guidelines

Inclusion Criteria

- Documented HIV
- Receiving stable ART
- CD4+ > 100 cells/mm3
- Age ≥ 40 years, ≤ 75 years
- No known atherosclerotic cardiovascular disease (ASCVD)
- 10-yr ASCVD risk score
  - <7.5% LDL < 190 mg/dL
  - ≥7.5% and ≤ 10% LDL, < 160 mg/dL
  - >10% and ≤15%, LDL < 130 mg/dL
- Certain laboratory parameters

Exclusion Criteria

- Current use of statins, gemfibrozil, or PCSK9 inhibitors
- Known decompensated cirrhosis

Slides from Dr Anchalee with thanks

Baseline Characteristics		Total (N=7769)	Pitavastatin (N=3888)	Placebo (N=3881)
Age (years)	Median (Q1 – Q3)	50 (45-55)	50 (45-55)	50 (45-55)
Sex at birth	Male	5350 (69%)	2677 (69%)	2673 (69%)
	Female	2419 (31%)	1211 (31%)	1208 (31%)
Gender identity	Cisgender	7367 (95%)	3687 (95%)	3680 (95%)
	Transgender spectrum	127 (2%)	63 (2%)	64 (2%)
	Not reported	275 (4%)	138 (4%)	137 (4%)
Race	White	2704 (35%)	1634 (35%)	1340 (35%)
	Black/African American	3208 (41%)	1569 (40%)	1639 (42%)
	Asian	**1138 (15%)**	**571 (15%)**	**567 (15%)**
CD4 count (cells/mm3)	Median (Q1 – Q3)	621 (448-827)	620 (449-832)	622 (445-824)
Nadir CD4 count (cells/mm3)	< 50	1409 (18%)	688 (18%)	721 (19%)
	50-199	2392 (31%)	1202 (31%)	1190 (31%)
	≥ 200	3706 (48%)	1859 (49%)	1847 (47%)
HIV RNA (Copies/mL)	< LLQ	5250 (88%)	2641 (88%)	2609 (87%)
	LLQ - < 400	617 (10%)	305 (10%)	312 (10%)
	400+	130 (2%)	63 (2%)	67 (2%)
	Missing	1772	879	893
ASCVD risk score, (%)	Median (Q1 – Q3)	4.5 (2.1-7.0)	4.5 (2.1-7.0)	4.5 (2.2-7.0)
LDL-C (mg/dL)	Median (Q1 – Q3)	108 (87-128)	109 (87-128)	108 (87-127)

Slides from Dr Anchalee with thanks

STUDY PREMATURE DISCONTINUATION DUE TO MACE ENDPOINTS MET

Major Adverse Cardiovascular Events
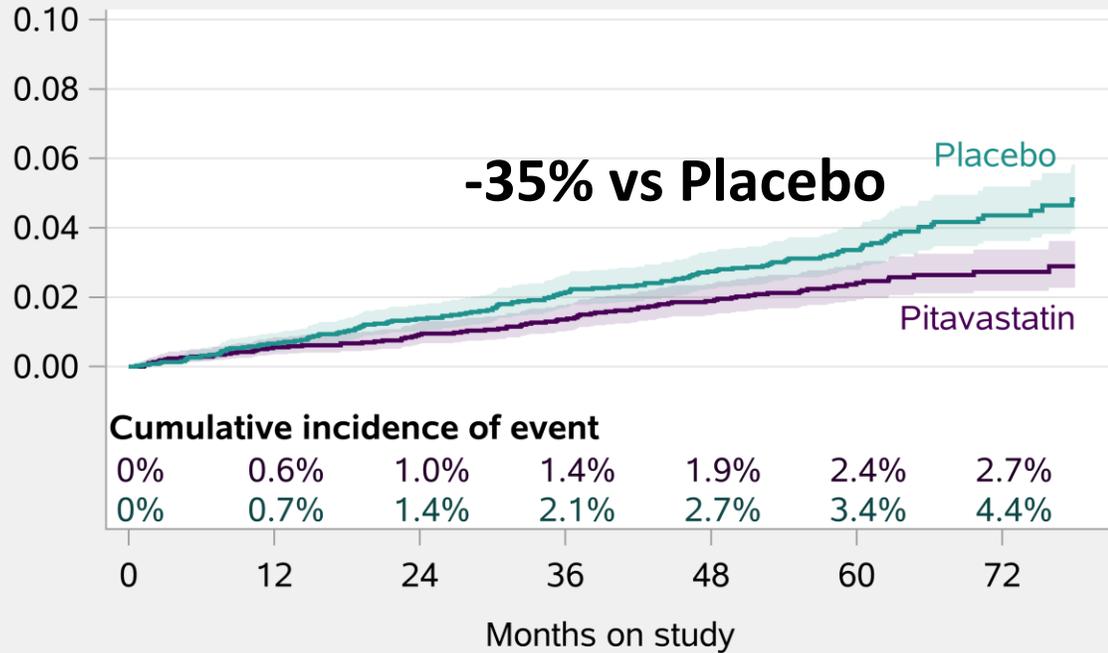
HR, 0.65 (95% CI, 0.48–0.90); P=0.002
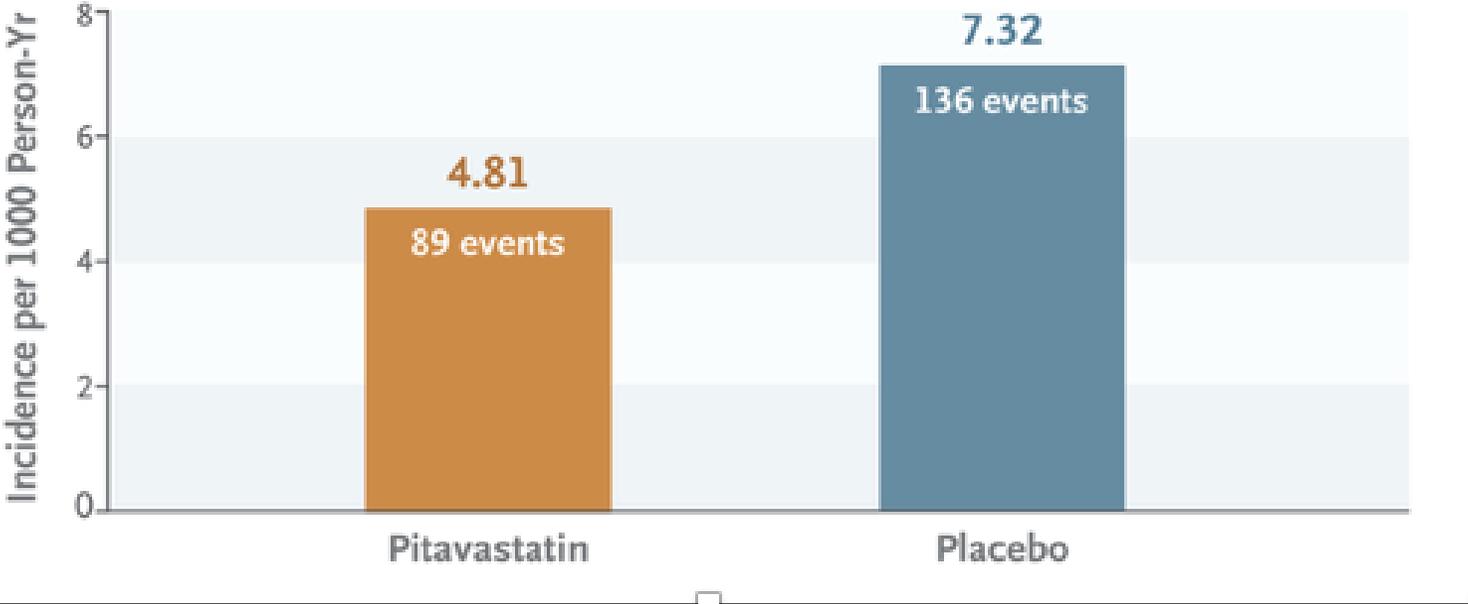
- An events driven trial with 85% power to detect a HR of 0.70 with 288 planned events

- After a median time of follow-up of 5.1 years, DSMB recommended early closure of the trial for efficacy

Grinspoon SK et al NEJM 2023;389:687-699

DSMB = data and safety monitoring board

REPRIEVE : Primary and Key Secondary Endpoints

median time of follow-up of 5.1 years
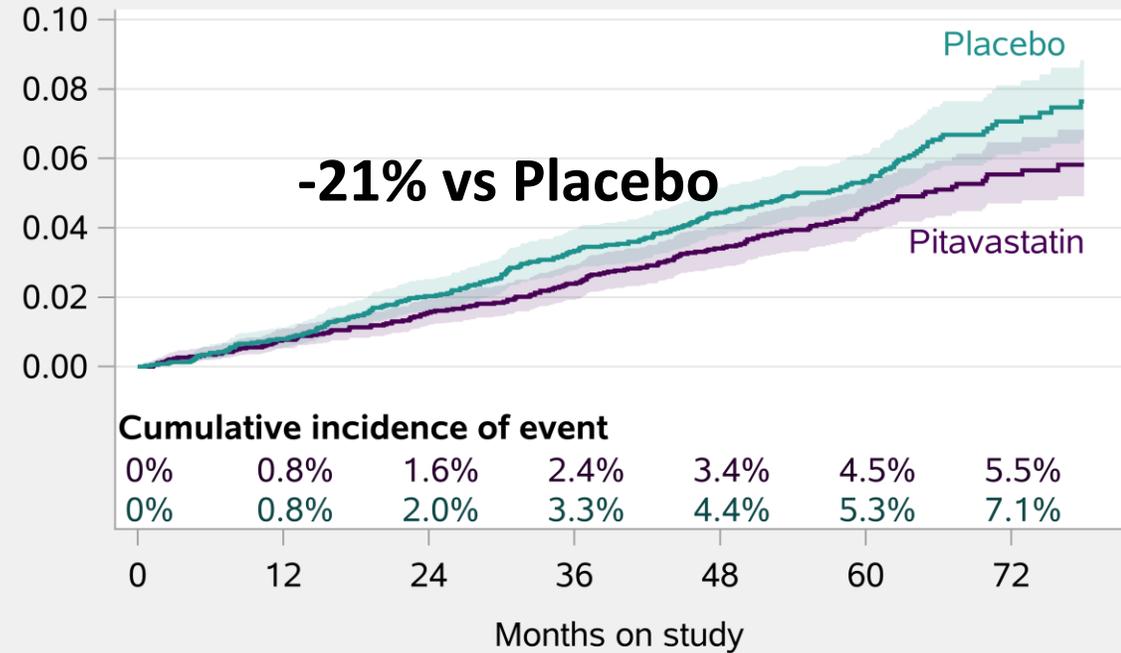
Grinspoon SK et al NEJM 2023;389:687-699

INCIDENCE OF ADVERSE EVENTS

Adverse Events

Incidence rate ratio, 1.01 (95% CI, 0.91–1.12)

4.16 **4.13**

Incidence rate ratio, 1.35 (95% CI, 1.09–1.66)

1.13 **0.84**

Incidence rate ratio, 1.74 (95% CI, 1.24–2.45)

0.49 **0.28**

Incidence per 100 Person-Yr

Nonfatal Serious Event

Diabetes Mellitus
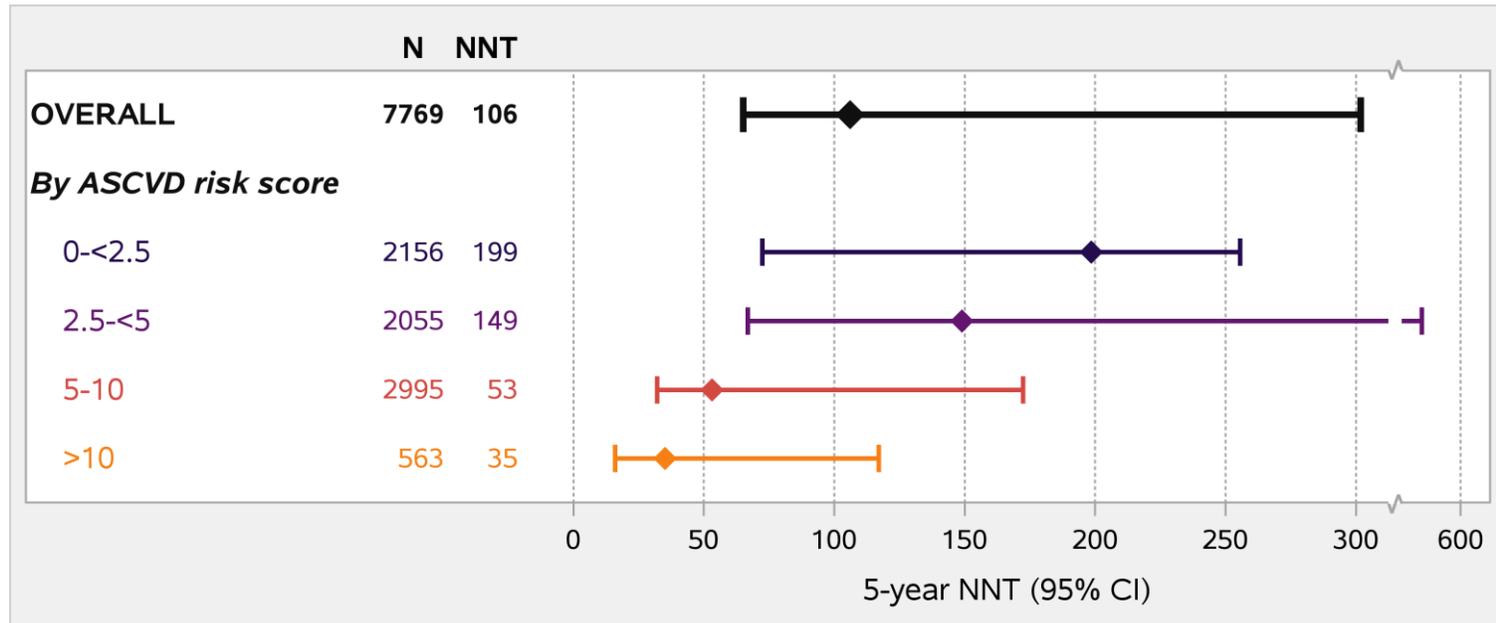
Grade ≥3 Myalgia, Muscle Weakness, or Myopathy
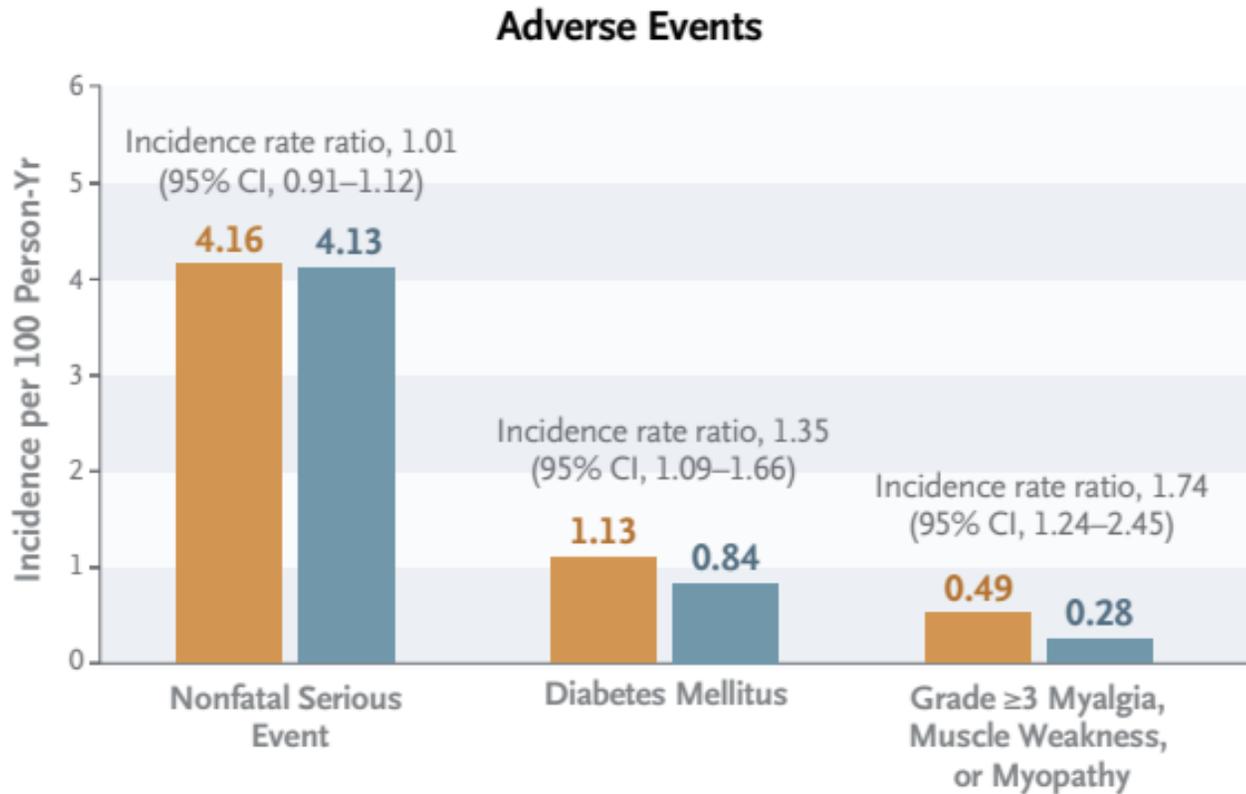
- Serious adverse events similar in each group
- ➤ Muscle-related symptoms higher in pitavastatin group but mostly mild (only 1% of withdrawal)
- ✓ Diabetes rates: 5.3% in pitavastatin group vs 4.0% in placebo group
- No effect on grade 3 ALT or

Grinspoon SK et al NEJM 2023;389.687-699

REPRIEVE: 5-YR NUMBER NEEDED TO TREAT TO PREVENT ONE MACE EVENT

Estimated incidence of Major CV event/1000 PY (95% CI) in the placebo group
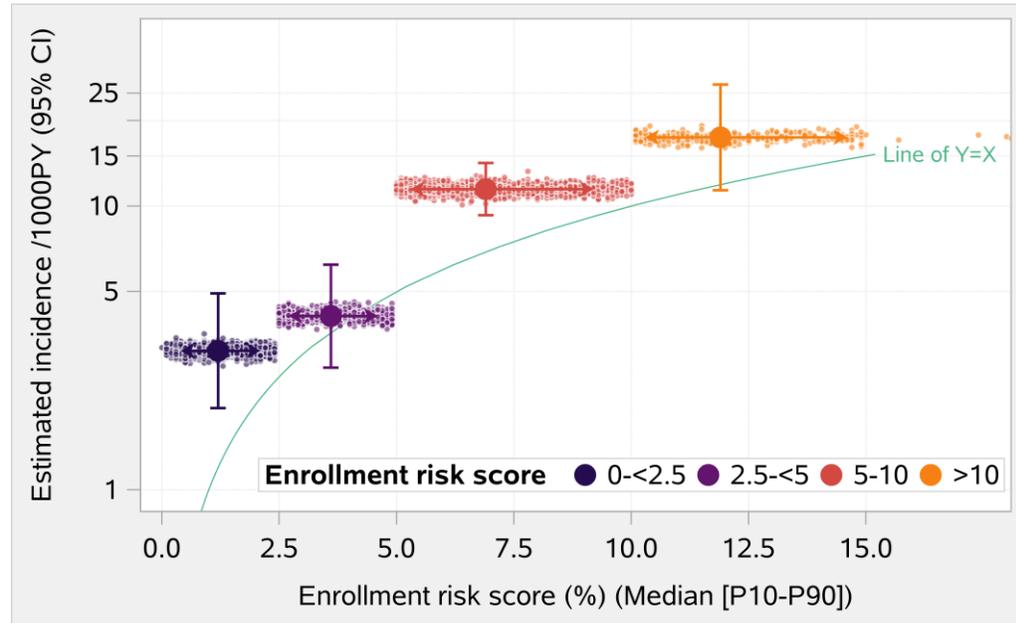
Increasing CVD with increasing ASCVD risk score

- **HIV increases CVD risk by ≠ 63 %**

Decreasing NNT with increasing ASCVD risk score

NNT = number needed to treat

Grinspoon S et al. 12th IAS 2023 ; abstr. SY0601, Grinspoon SK et al NEJM 2023;389:687-6

Conclusions: REPRIEVE (A5332)

Despite HIV being considered a risk equivalent, no prior trial has assessed a primary prevention strategy for this group, who would not typically be recommended for statin therapy

Among PWH 40-75, on ART, with low to moderate risk and normal range LDL, treatment with pitavastatin is effective and prevents MACE

Considerations should be given to expanding treatment guidelines in this regard

Grinspoon S et al. 12th IAS 2023 ; abstr. SY0601, Grinspoon SK et al NEJM 2023;389:687-6

Which statin ?

High Intensity statin therapy	Moderate Intensity	Low Intensity
Daily dose lower LDL on average ≥50%	Daily dose lower LDL on average by approximately 30%–49%	Daily dose lower LDL on average by <30%
Atorvastatin 40 - 80mg Rosuvastatin 20-40 mg	Atorvastatin 10 -20mg Rosuvastatin 5 -10 mg Simvastatin 20–40 mg Pravastatin 40-80 mg Lovastatin 40-80 mg Fluvastatin XL 80 mg Fluvastatin 40 mg BID **Pitavastatin 2–4 mg**	Simvastatin 10 mg Pravastatin 10–20 mg Lovastatin 20 mg Fluvastatin 20–40 mg

Atorvastatin, Pitavastatin and Rosuvastatin have potent pleiotropic effects
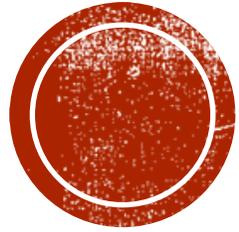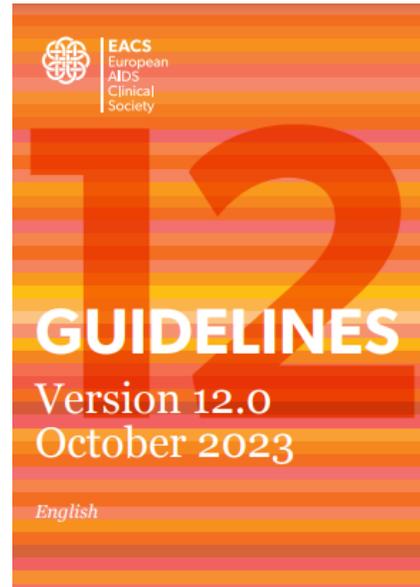
PRIMARY CARE RECOMMENDATIONS

Recommendation and Workgroup Processes

1. Review of select benchmark international and local guidelines and updates

RECOMMENDATION AND WORKGROUP PROCESSES

2. These recommendations are then discussed and adapted to the Singapore context with the Primary Care Recommendations Advisory Group via a consensus decision making process.

3. Consultation and feedback
   - ✓ Chapter of Infectious Disease Physicians, Academy of Medicine Singapore (AMS)
   - ✓ Chapter of Family Medicine Physicians, AMS Academy of Medicine, Singapore
   - ✓ College of Family Physicians Singapore (CFPS)
   - ✓ Community Advisory Board (CAB)

WHAT ARE THE SECTIONS OF THE RECOMMENDATION?

1. Introduction
2. Ageing and Geriatrics Syndromes
3. Renal care
4. Bone metabolism
5. Cardiovascular Risk factors
6. Liver and viral hepatitis
7. Mental health screening
8. Latent TB screening
9. STI management
10. Cancer screening
11. Vaccinations
12. Multidisciplinary care: Care and counselling, pharmacy, nursing care

SECTION 2: AGEING AND GERIATRIC SYNDROMES

Assessment/Screening tools	When to Screen and frequency	Additional Comments
General approach with focus on: • Frailty → Clinical Frailty Scale • Polypharmacy • Multi-morbidity • Falls • Cognitive impairment → MMSE, AMT and MoCA are available screening tools	• At age 50 years and older • If negative, repeat screen if patient develops multi-morbidity or geriatric syndrome	A holistic approach that is person-centric over a strict methodological adherence to multiple guidelines for each individual disease is preferred. Referral to geriatric and other specialists or allied health professionals including physiotherapists, occupational therapists, dieticians, speech therapists may be required if patients have geriatric syndromes reflecting accelerated ageing.

SECTION 3: RENAL HEALTH

Assessment/Screening tools	When to Screen and frequency	Additional Comments
Renal panel	Every 3-6 months	Avoid nephrotoxic ART e.g. tenofovir disoproxil fumarate (TDF) in patients with risk factors for kidney disease
Urinalysis	Annual	
Urine albumin/creatinine ratio or urine protein/creatinine ratio	• if abnormal urinalysis • at least annually for patients with existing chronic kidney disease • at least every 6-months for patients with diabetes	Dolutegravir, bictegravir, rilpivirine, cobicistat and boosted protease inhibitors are associated with an increase in serum creatinine/eGFR reduction (10-15 ml/min or up to 25%) due to inhibition of proximal tubular creatinine transporters without impairment of actual glomerular infiltration
• Serum bicarbonate and urinary pH • Blood phosphate and urinary phosphate excretion • Blood glucose and glucosuria • Blood uric acid level and urinary uric acid excretion • Serum potassium and urinary potassium excretion	If proximal tubulopathy is suspected for patients on tenofovir disoproxil fumarate	

SECTION 4: BONE METABOLISM

Assessment/Screening tools	When to Screen and frequency	Additional Comments
Dual-energy X-ray absorptiometry (DXA)	• At age 50 years and older • If T-score is normal, rescreening can be done in 3-5 years	For patients on TDF-based regimen who are at risk of osteoporosis or have been diagnosed with osteoporosis, consider switching to another NRTI or consider NRTI-sparing regimen If osteopenia is present, consider the secondary risk factors, and use of the (FRAX^{TM}) tool to estimate fracture risk in post-menopausal women and men > 65 years of age. If the risk for fragility fracture is high, consider referral to an endocrinologist
Vitamin D	Consider routine screen at age 40 years and older	If vitamin D is < 10 ng/ml, consider doing DXA. Consider Vitamin D supplementation if Vitamin D < 20ng/ml

SECTION 5: CARDIOVASCULAR RISK FACTOR (GENERAL CARE)

Assessment/Screening tools	When to Screen and frequency	Additional Comments
General Lifestyle Intervention	As clinically indicated	150 to 300 minutes per week of moderate-intensity aerobic activity spread out over 5 to 7 days per week should be undertaken Smoking cessation should be advised A maximum of 2 standard drinks per day for women and 3 per day for men is recommended Weight reduction through diet modification and exercise is recommended if body mass index > 23 kg/m²

SECTION 5: CARDIOVASCULAR RISK FACTOR

Assessment/Screening tools	When to Screen and frequency	Additional Comments
Blood pressure monitoring	At least annually or at every physical visit Home BP monitoring should be done for any person ≥ 50 years	The recommended target BP treatment levels are: • < 80 years old: BP < 140/90 mmHg • ≥ 80 years old: BP < 150/90 mmHg
Fasting plasma glucose ≥ 7.0 mmol/l, OR Random plasma glucose ≥ 11.1 mmol/l, OR 2-hour post-oral glucose tolerance test plasma glucose ≥11.1 mmol/l	At initial visit, then annually if normal	HbA1c has been found to underestimate the level of glycaemia in people living with HIV. This is due to several reasons, including macrocytosis (for patients on thymidine analogues) and NRTI (particularly abacavir) use, which affect HbA1c values and underestimates the level of glycaemia Dolutegravir may increase the concentration of metformin. US Prescribing Information suggests limiting the total daily dose of metformin to 1000 mg when starting metformin or dolutegravir
Fasting lipid panel	At initial visit, then annually if normal Every 6-12 months if initial screen abnormal	Primary prevention of CAD for patients more than 40 years old • Patients should be offered a statin irrespective of lipid profile or estimated CAD risk; those with an estimated 10-year CAD risk of 5% or greater should be prioritised • Atorvastatin 20 mg daily can be used with titration of dose as necessary For patients <40 years old Target LDL cholesterol levels: Without DM, high-risk of CAD <2.6mmol/L With DM, very high-risk of CAD <1.8 mmol/L When possible, consider switching ART regimens for patients on PI-based regimens

SECTION 6: LIVER AND VIRAL HEPATITIS (HIV-HBV CO-INFECTION)

Assessment/Screening tools	When to Screen and frequency	Additional Comments
Ultrasound hepatobiliary system (US HBS)	Every 6 months	
Alpha-fetoprotein (AFP)	Every 6 months	
Liver function test (LFT)	• At initiation of antiretroviral therapy (ART) • 1 month after initiation of ART • Every 3-6 months after	• Tenofovir-containing regimen is preferred ART regimen • For patients with contraindications to tenofovir, entecavir is recommended together with fully active ART
HBV DNA	• At initiation of treatment • Every 3-6 months after initiation of treatment • Annually if undetectable	
Transient elastography (e.g., FibroScan®)	At baseline upon diagnosis	

SECTION 6: LIVER AND VIRAL HEPATITIS (HIV-HCV CO-INFECTION)

Assessment/Screening tools	When to Screen and frequency	Additional Comments
US HBS	Every 6 months in patients with HCV-related cirrhosis or F3/bridging fibrosis	Treatment with direct-acting antivirals should be offered and initiated by experienced HIV physician/hepatologist
AFP	Every 6 months patients with HCV-related cirrhosis or F3/bridging fibrosis	
LFT	• At initiation of treatment • 4 weeks after initiation of treatment • Every 3-6 months as per routine once normalized	
HCV RNA	• Baseline • At 12 weeks, 24 weeks and 1 year after treatment cessation • Annually for at risk populations (MSM, PWIDs*)	
Transient elastography (e.g., FibroScan®)	At initiation of treatment	
Genotype testing	Prior to initiation of treatment	

SECTION 6: LIVER AND VIRAL HEPATITIS (NON-ALCOHOLIC FATTY LIVER (NAFL) / NON-ALCOHOLIC STEATOHEPATITIS (NASH)

Assessment/Screening tools	When to Screen and frequency	Additional Comments
General Care		Lifestyle modification and weight reduction should be advised Management of NASH should be in conjunction with an experienced hepatologist
US HBS	As clinically indicated	Preferred first-line imaging modality
FIB-4	As clinically indicated	• FIB-4 = Age ([years] x AST [U/L]) / (platelet count [10^9/L] x ALT [U/L]) to determine risk of fibrosis • A FIB-4 score of ≥ 2.67 has an 80% positive predictive value for advanced fibrosis. However, caution should be used for patients ≤ 35 years or ≥ 65 years of age
Transient elastography (e.g., FibroScan®)	As clinically indicated	Used with FIB-4 to determine risk of fibrosis

SECTION 7: MENTAL HEALTH SCREENING

Assessment/Screening tools	When to Screen and frequency	Additional Comments
PHQ-2	Baseline, then at least annually	Proceed to PHQ-9 if screen positive
GAD-2	Baseline, then at least annually	Proceed to GAD-7 if screen positive
General care		• Medical social worker support to support if mild depression or anxiety • Refer to psychiatrist if moderate/severe depression or anxiety or suicidal or reports history of concomitant substance use

SECTION 8: LATENT TB SCREENING

Assessment/Screening tools	When to Screen and frequency	Additional Comments
IGRA-QuantiFERON-TB Gold test, OR TB T-spot test	Baseline, unless previously tested positive or had documented TB

Repeat in patients with initial CD4 < 200 cells/µL and negative IGRA who subsequently immune reconstitute with CD4 > 200 cells/µL on ART | Active TB must be excluded with symptom screening and plain chest radiograph in patients with positive interferon gamma release assay (IGRA) |
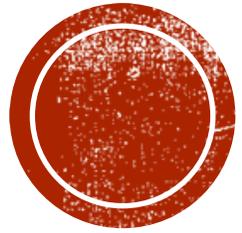
WHERE TO FIND THE FULL TEXT GUIDELINES

The full text Primary Care Recommendations can be found at the CDA website under National Recommendations and Guidelines:

https://wwme.cda.gov.sg/professionals/national-hiv-hepatitis-c-and-sti-programmes/

CO-INFECTIONS

Case 3

- 25-year-old business student lives with parents, no past medical history

- 2/52 rash (some pustules) on both palms and soles

- No other symptoms/ findings

Syphilis - Presentation

- **1°** - (10-90 days, mean 3/52) infection site ulcer or chancre

- **2°** - mucocutaneous lesions, rash, lymphadenopathy, gastric/ renal/ liver disease, meningitis, cranial nerve palsy, CVA

- **3°** (4-40 years) - aortic regurgitation, aortic aneurysm, meningovascular disease, General Paralysis of Insane, Tabes Dorsalis, dementia, CVA, granulomata in skin and bone

- **Latent** syphilis - Asymptomatic, positive serology; early latent or late latent determined by acquisition point (cut-off is one year)

SYPHILIS - MANAGEMENT

- Stage dictates treatment

   1° and 2 ° - benzathine penicillin single dose intramuscular

   Late latent or latent syphilis of unknown duration - 3 weekly doses benzathine penicillin intramuscular

   3 ° neurosyphilis - 14/7 IV aqueous penicillin 2.4 U per day in 4-hourly dosing

- Adequate treatment dictated by clinical and serological (4 fold RPR titre decline) and CSF WCC check at 6/12 and 12/12 and 24/12 in CNS disease: persistence indicates failure or re-infection

French P et al. IUSTI: 2008 European Guidelines on the Management of Syphilis. Int J STD AIDS May 2009; 20 (5): 300-309

HIV AND HBV CO-INFECTION

- HIV, HBV and HCV share common modes of transmission- sexual transmission, IVDU and transfusion of blood. Individuals can be co-infected with 2 or even 3 viruses

- Prior to ART, individuals with HIV-HBV co-infection are **19 more times** than mono-infected individuals to die from liver related complications[1]

- In NCID, estimated 7.2% are co-infected with HIV-HBV[2]

- Factors associated with HIV-HBV co-infection includes: Aged 30–49 years and 50–69 years at HIV diagnosis, male gender, and HIV transmission through intravenous drug use (IDU) [2]

1. Singh K.P., Crane M., Audsley J., Avihingsanon A., Sasadeusz J., Lewin S.R. HIV-Hep B Virus Coinfection: Epidemiology, Pathogenesis, and Treatment. *AIDS.* 2017;31:20 2052. doi: 10.1097/QAD.0000000000001574.
2. Trop Med Infect Dis. 2019 Jun; 4(2): 87.

TRANSMISSION ROUTES OF HIV AND HBV

- **HIV and HBV infection have similar routes of transmission[1]**

- **Population groups with greatest prevalence of HIV/HBV coinfection[2]**

  - Men who have sex with men (MSM)

  - Injection drug users

  - People coming from HBV endemic areas (eg, Sub-Saharan Africa, Asia)

Relative Efficiency of HBV and HIV Transmission by Exposure Type[3]

Type of exposure	HBV	HIV
Transfusion	++++	++++
Injection drug use	++++	++++
Perinatal	++++	+++
Sexual	+++	+++
Unsafe injections	+++	+
Needlestick	+++	<+

1. Sherman KE, et al. Epidemiology, clinical manifestations, and diagnosis of hepatitis B in the HIV-infected patient. In: UpToDate, Mitty J (Ed), UpToDate, Waltham, MA. (Accessed on Sep 13, 2022) 2. Puoti M, et al. AIDS Rev. 2002;4:27-35.
3. Centers for Disease Control and Prevention. Epidemiologic Update: Hepatitis C. http://slideplayer.com/slide/9039512/ (Accessed on Sep 13, 2022).

IMPACT OF HIV/HBV COINFECTION IN DISEASE PROGRESSION

Impact of HIV on HBV Natural History[1,2]

- Increases risk of
  - Cirrhosis
  - Hepatocellular carcinoma
  - End-stage liver disease related to chronic HBV
  - Death
  - HBV reactivation
- Lower rate of spontaneous HBeAg or HBsAg seroconversion
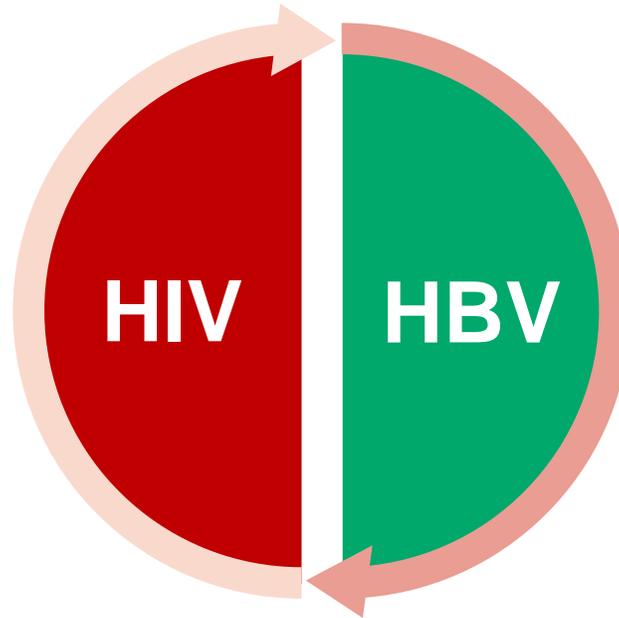
Impact of HBV on HIV Natural History[3, 4]

- HBV infection does NOT
  - Substantially alter HIV progression
  - Influence HIV suppression or CD4 counts following ART initiation

HIV **HBV**

- **HIV coinfection adversely affects the natural history of HBV infection at every stage and accelerates the progression of HBV disease**
- **Conversely, the impact of HBV in the natural history of HIV does not appear to be significant**
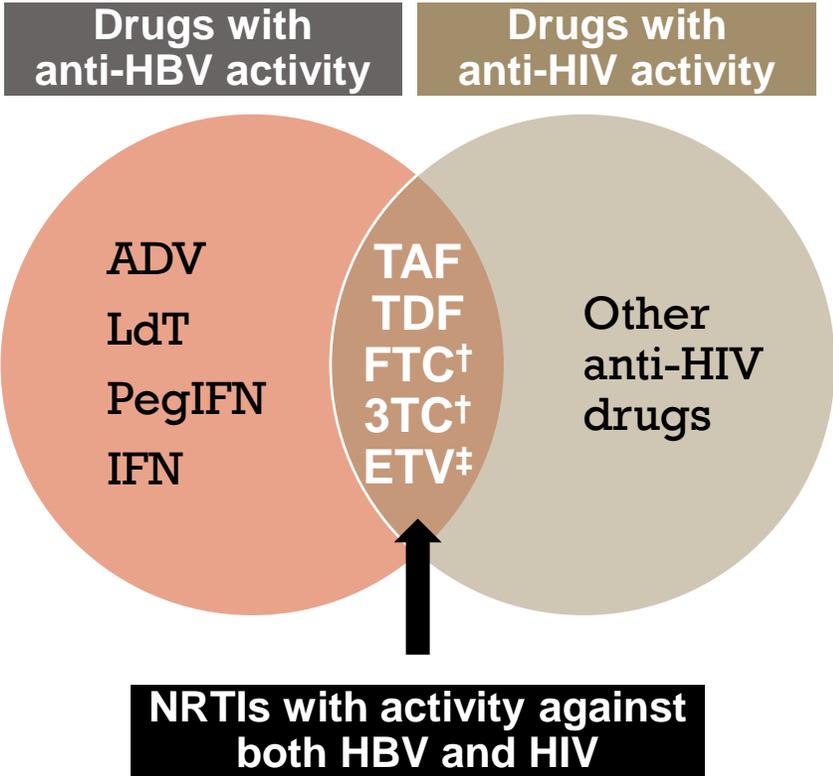
SCREENING, INITIATION, AND TREATMENT REGIMENS

Screening for HIV or HBV

- HBV (and HIV) patients should be screened for coinfection during their initial patient evaluation[1-3]

- The USPSTF recommends screening for HBV infection in persons at high risk* for infection[§6]

Treatment

- HIV/HBV therapy is indicated for coinfected patients[4,5,7]
- Therapy should have activity against both HBV and HIV[3,4,5]
- Conduct HIV resistance testing to guide ARV selection[3]

Drugs with anti-HBV activity

Drugs with anti-HIV activity

ADV
LdT
PegIFN
IFN

TAF
TDF
FTC[†]
3TC[†]
ETV[‡]

Other anti-HIV drugs

NRTIs with activity against both HBV and HIV

* high risk for infection includes important risk groups having a CHB prevalence of ≥ 2%, including HIV-positive patients
† resistance to LAM and FTC is high; ‡When used in HBV/HIV-coinfected patients, ETV must be used in addition to a fully suppressive ARV regimen due to risk of resistance selection
§ Grade B recommendation
ADV, adefovir; ETV, entecavir; IFN, interferon; FTC, emtricitabine; LAM, lamivudine; LdT, Telbivudine; pegIFN, pegylated interferon; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; USPSTF, U.S. Preventive Services Task Force
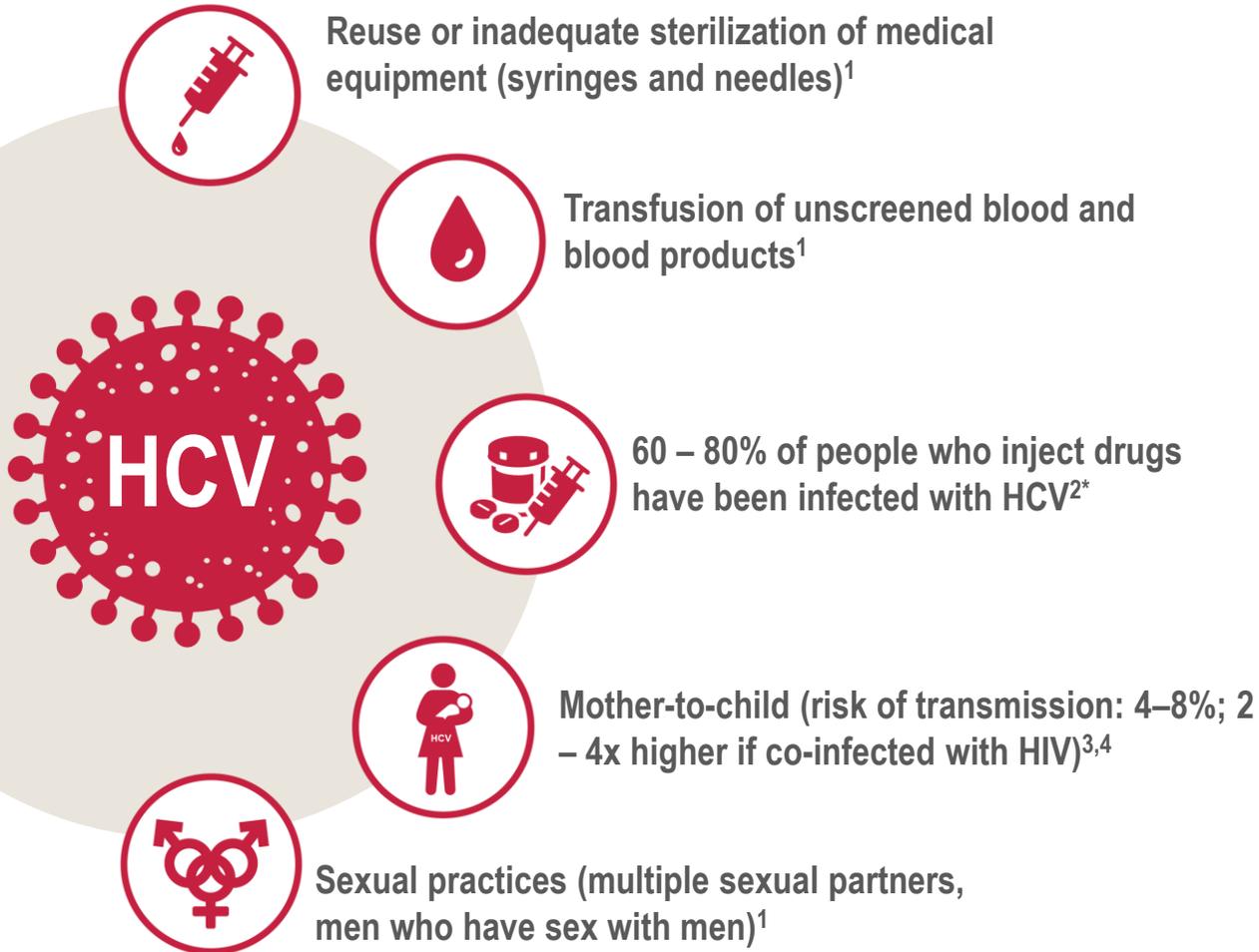
1. Terrault NB et al. Hepatology 2015; Published online November 13, 2015: doi:10.1002/hep.28156; 2. Martin P, et al. Clin Gastroenterol Hepatol 2015; Published online July 15, 2015: http://dx.doi.org/10.1016/j.cgh.2015.07.007;
3. DHHS Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. December 18 2019. Available at: http://www.aidsinfo.nih.gov/Guidelines; 4. DHHS Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-infected Adults and Adolescents. August 18 2020. Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf. 5. Gunthard H, et al. JAMA. 2016;316(2):191-210; 6. LeFevre ML, et al. Ann Intern Med. 2014; 27 May 2014; 7. EASL Clinical Practice Guidelines on the management of HBV infection. J Hepatol 2017; doi: 10.1016/j.jhep.2017.03.021

HCV IS TRANSMITTED THROUGH INFECTED BLOOD

Reuse or inadequate sterilization of medical equipment (syringes and needles)[1]

Transfusion of unscreened blood and blood products[1]

60 – 80% of people who inject drugs have been infected with HCV[2]*

Mother-to-child (risk of transmission: 4–8%; 2 – 4x higher if co-infected with HIV)[3,4]

Sexual practices (multiple sexual partners, men who have sex with men)[1]

HCV

HCV **does NOT** spread through[1]:

- Breast milk
- Food
- Water
- Casual contact with an infected person

THE END