Envelhecer com o HIV

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Envelhecimento global

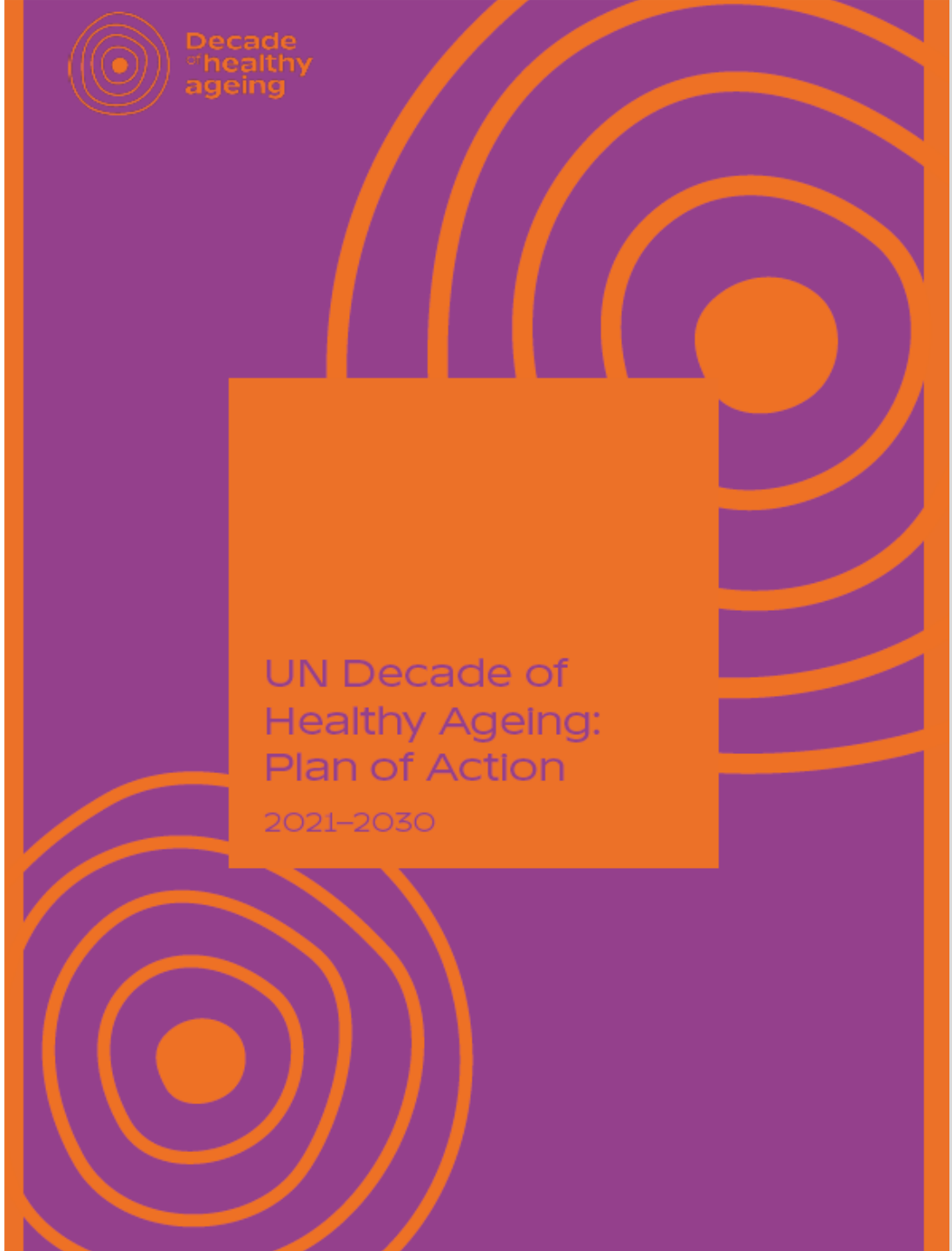
2020: o número de pessoas com 60 anos ou mais superou o número crianças menores de 5 anos

A estimativa para 2050, é de que esse grupo superará o de adolescentes e jovens de 15 a 24 anos.

A maioria das pessoas idosas vive em países em desenvolvimento. 8% na América Latina e no Caribe (2019)

O número de idosos cresce mais rapidamente na África, seguida pela América Latina, Caribe e Ásia.

Em 2050 quase 80% da população idosa do mundo viverá em países menos desenvolvidos



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PLOS ONE

RESEARCH ARTICLE

Global and regional trends of people living with HIV aged 50 and over: Estimates and projections for 2000–2020

Christine S. Autenrieth[1], Eduard J. Beck[1,2]*, Dominik Stelzle[1], Christoforos Mallouris[1], Mary Mahy[1], Peter Ghys[1]

1 UNAIDS, Programme Branch, Geneva, Switzerland, 2 UNAIDS, Latin American and Caribbean Regional Support Team, Georgetown, Guyana

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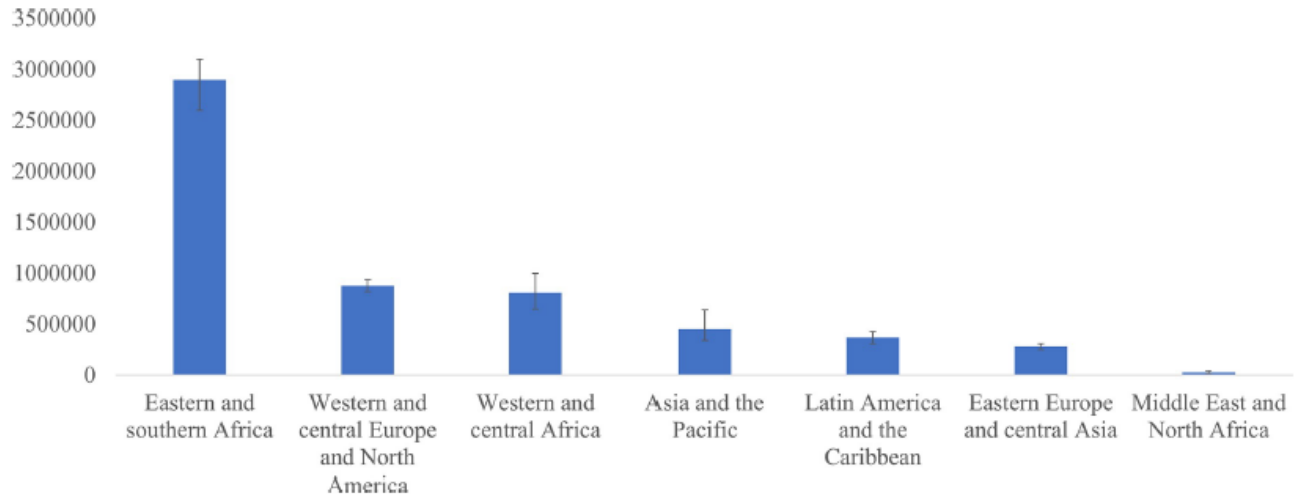
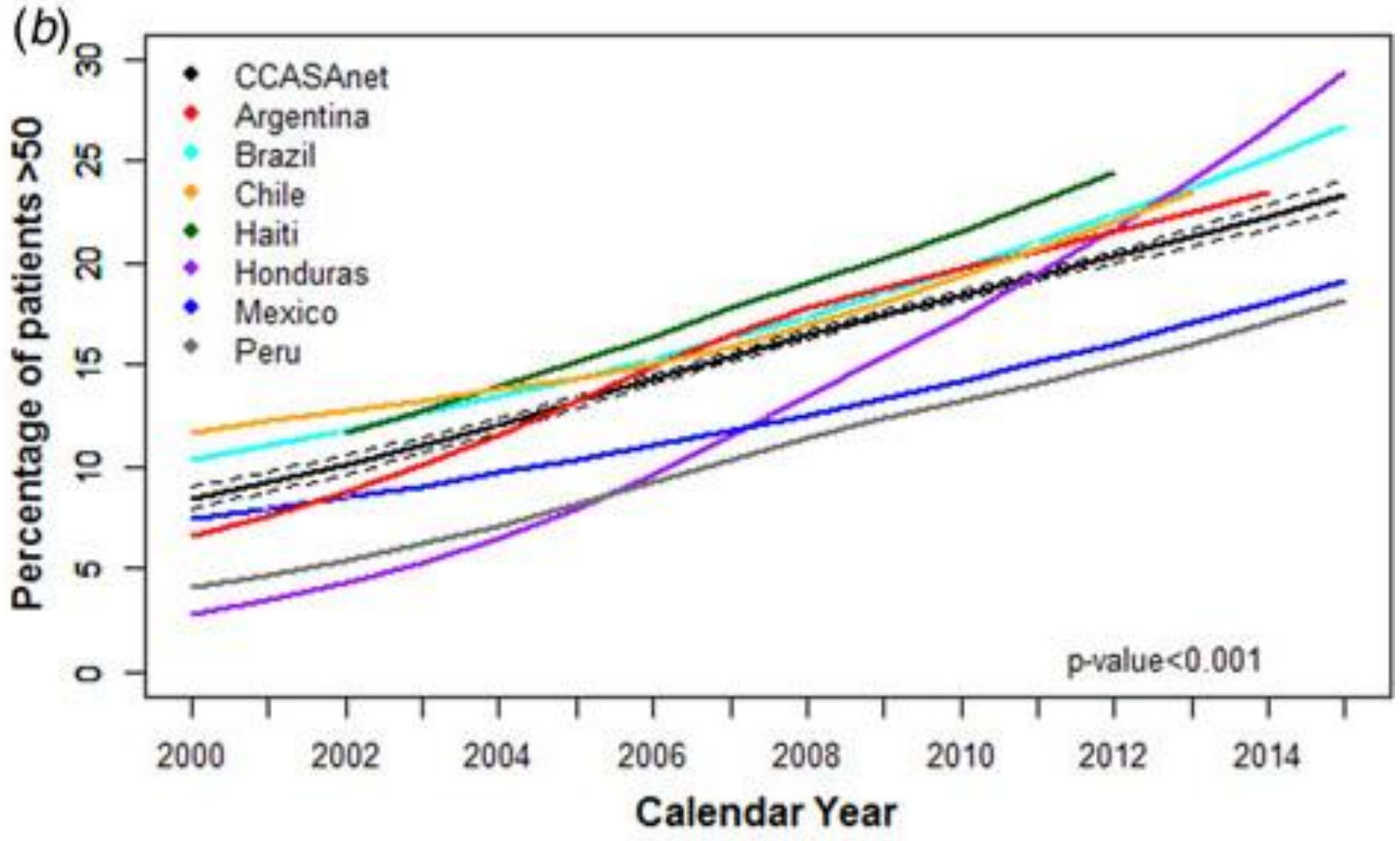
Envelhecimento & HIV

2016: 5,7 milhões [4,7 milhões – 6,6 milhões] de PVVIH50+

A proporção de PVHIV50+ passou de 8% em 2000 para 16% em 2016 com projeção de passar a 21% até 2020.



PVHI com ≥ 50 anos nos sites CCASAnet



Crescimento de 8% em 2000 para 24% em 2015

Caro-Vega et al. *Epidemiol Infect*. 2018 Jul;146(10):1308-1311.

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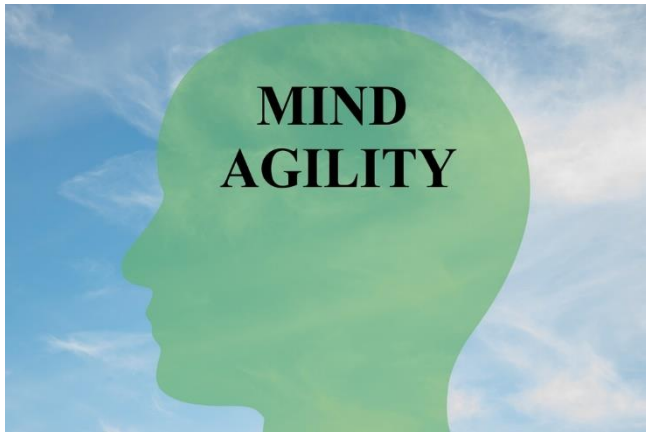
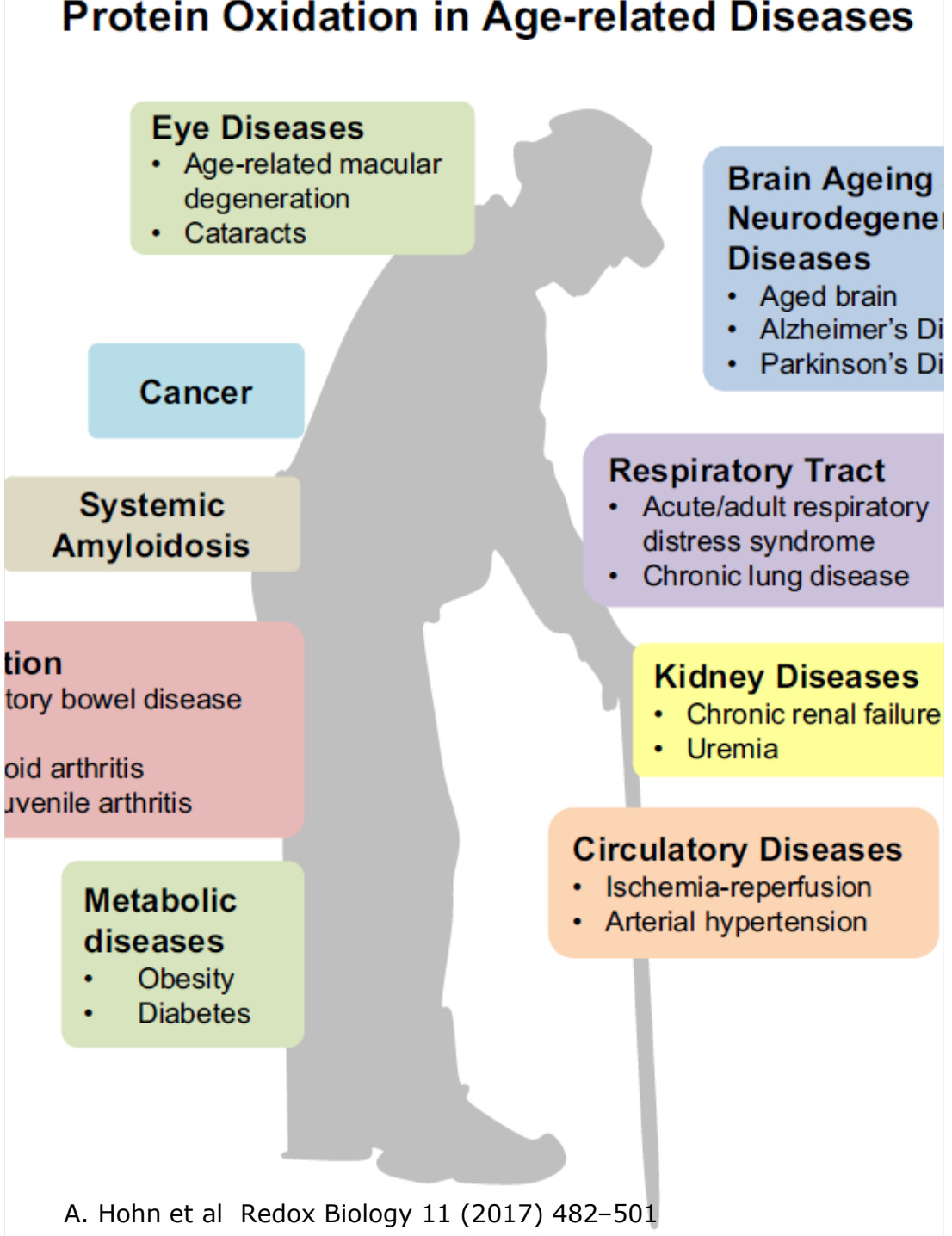
O que é envelhecimento?





A. Hohn et al Redox Biology 11 (2017) 482–501

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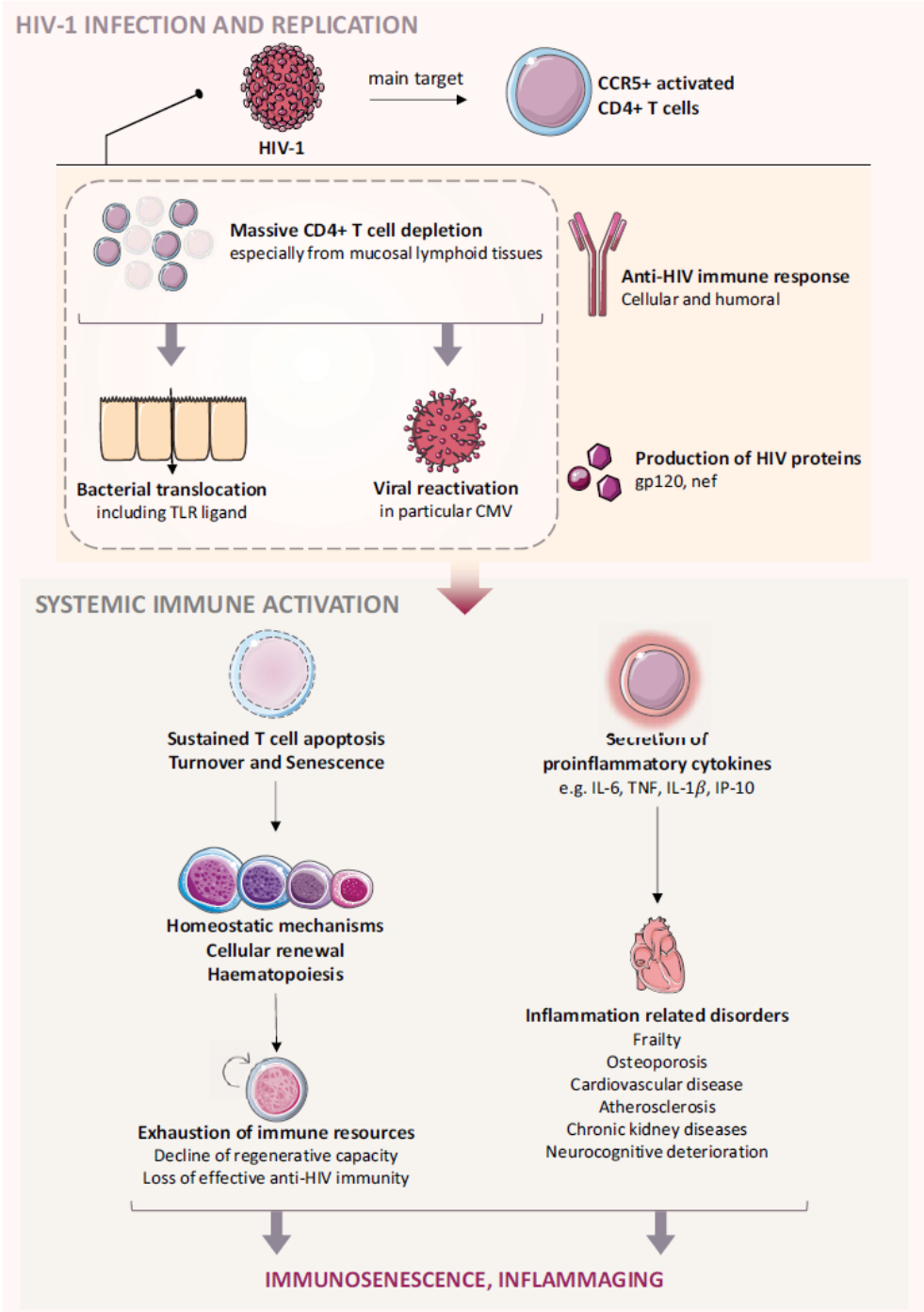
Envelhecimento com HIV: imunosenescência e inflamação

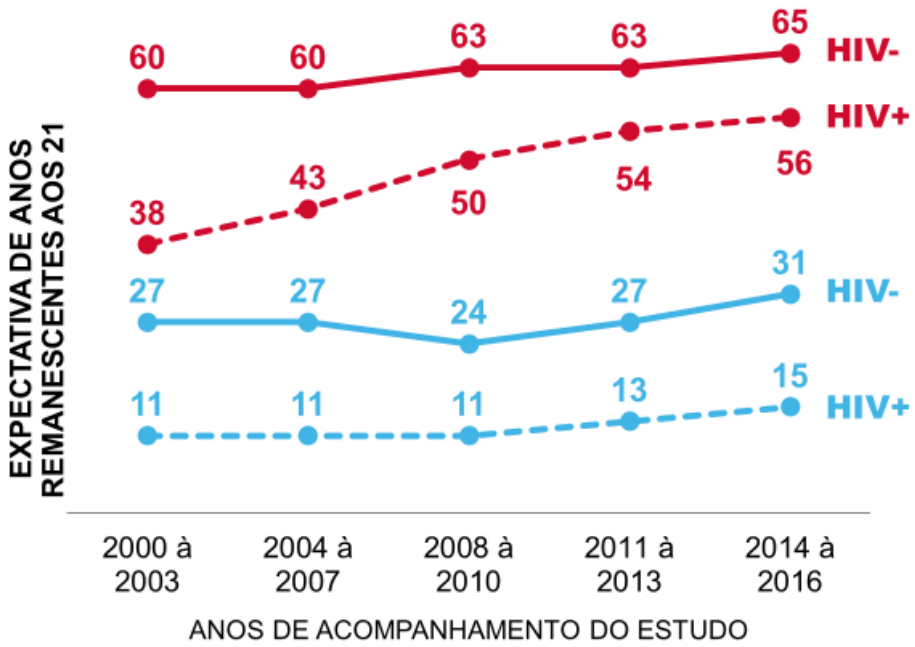


Clinical Science (2022) **136** 61–80 - https://doi.org/10.1042/CS20210344

EXPECTATIVA DE VIDA E TEMPO SEM COMORBIDADES POR STATUS DE HIV A PARTIR DOS 21 ANOS

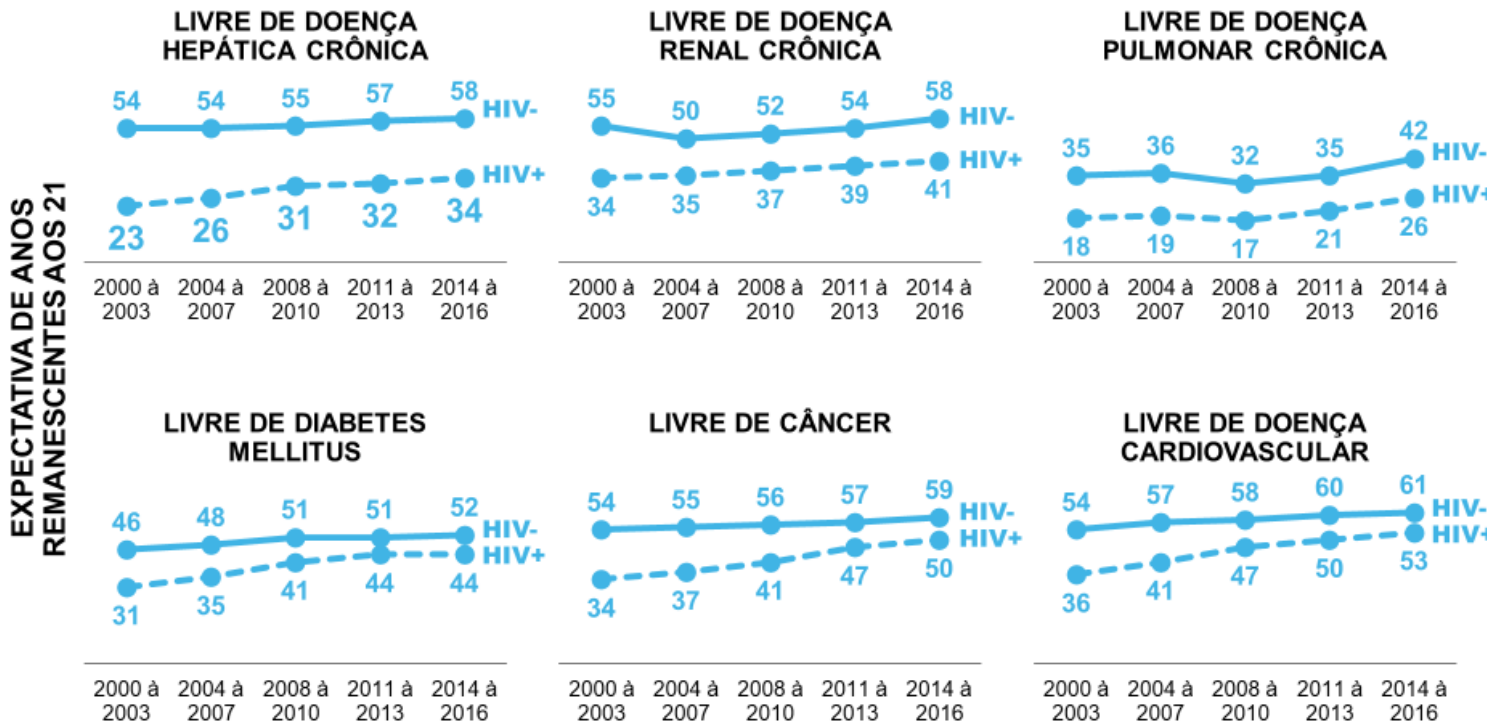
COMORBIDADES EM ADULTOS COM (N=39.000) E SEM HIV (N=387.767) NOS EUA, 2000-2016

Expectativa de vida com e sem comorbidades



Diferença cada vez menor na expectativa de vida, mas não no tempo sem comorbidades.

Expectativa de vida livre de comorbidades



Diferença cada vez menor na expectativa de vida livre de comorbidades para:

- Diabetes, câncer e DCV para PVHIV
- Câncer e DCV para PVHIV que iniciaram ART com CD4 ≥500 células/μL

Kaiser Permanente (EUA)

EV, expectativa de vida; PVHIV, pessoas vivendo com HIV / Marcus J, et al. CROI 2020. Boston, MA. Oral 151

Received: 23 March 2022 | Accepted: 14 July 2022
DOI: 10.1111/hiv.13375

SHORT COMMUNICATION

A matched cohort study investigating premature, accentuated, and accelerated aging in people living with HIV

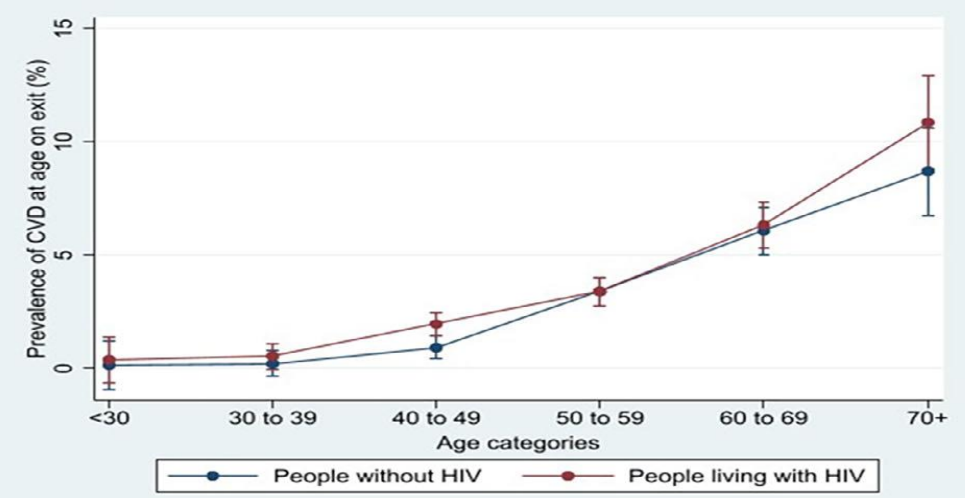
Tiffany E. Gooden[1] | Jingya Wang[1] | Dawit T. Zemedikun[1] | Stephen Taylor[1,2] | Sheila Greenfield[1] | Semira Manaseki-Holland[1] | Krishnarajah Nirantharakumar[1] | G. Neil Thomas[1]

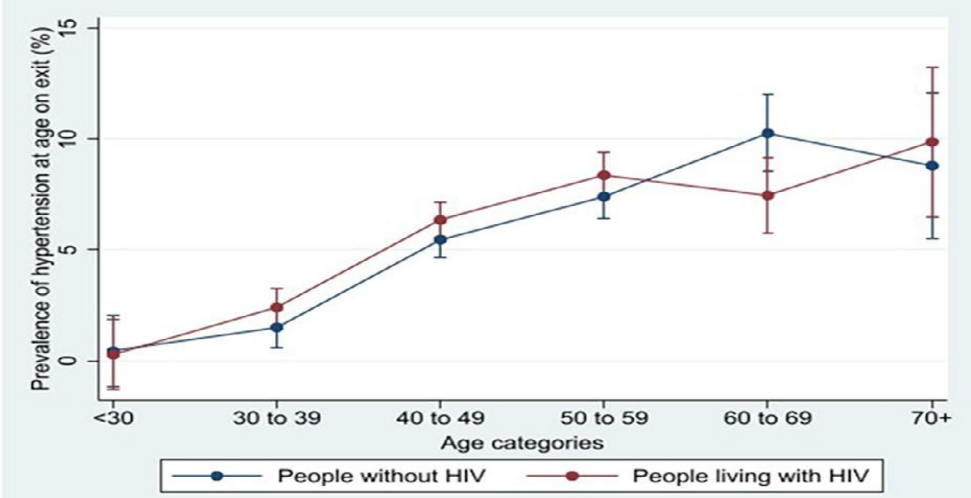
PVHIV foram diagnosticadas com DCV em uma idade mais jovem do que as pessoas sem HIV (54,5 vs. 56,8 anos, p ajustado = 0,002)

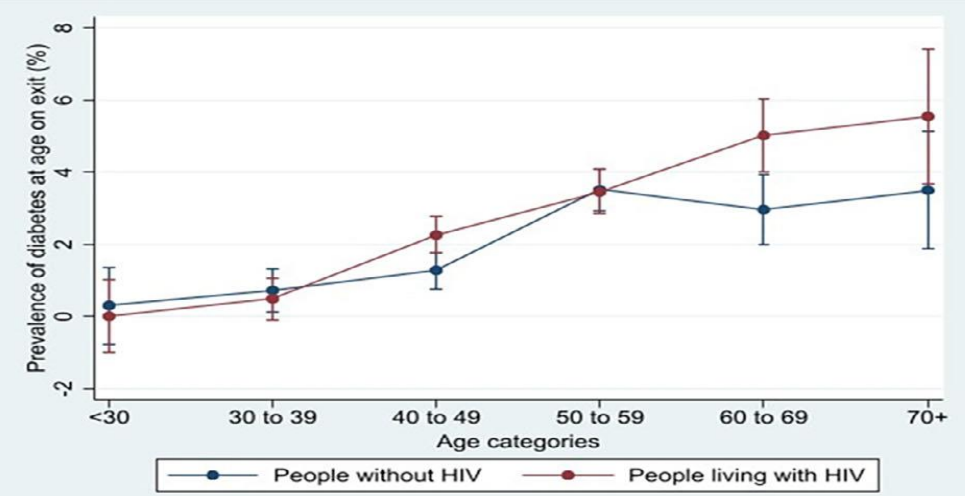
Isso também foi observado para hipertensão (49,7 vs. 51,4 anos, p ajustado = 0,002

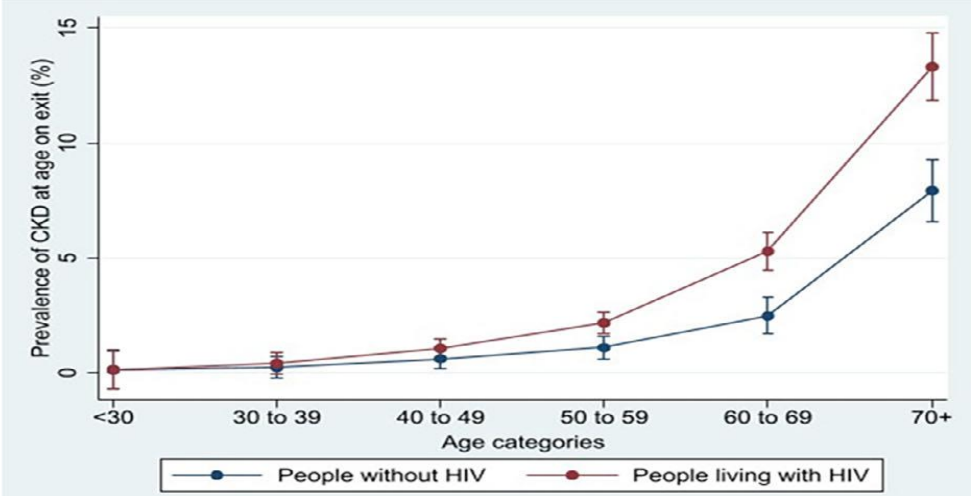
Não houve diferença na idade ao diagnóstico para DM2 (53,4 e 52,6 anos, ajustado p = 0,368) ou DRC (57,6 e 58,1 anos, p ajustado = 0,483.

Prevalência de DCV, HAS, DM-2 e DRC por idade para pessoas com e sem HIV

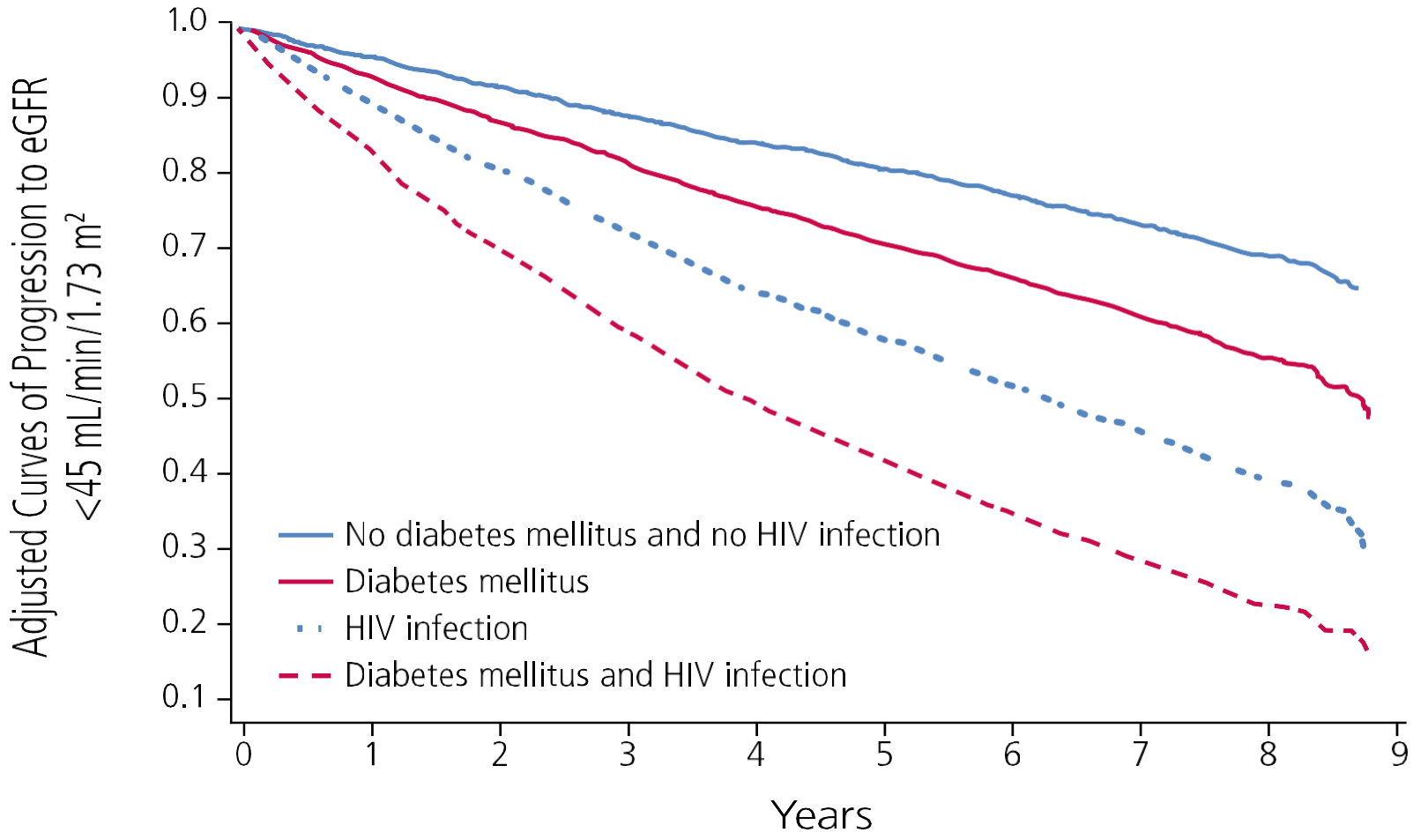








Efeito aditivo da infecção pelo HIV e DM na progressão da DRC



JAIDS. 2012;60(4): 393-399

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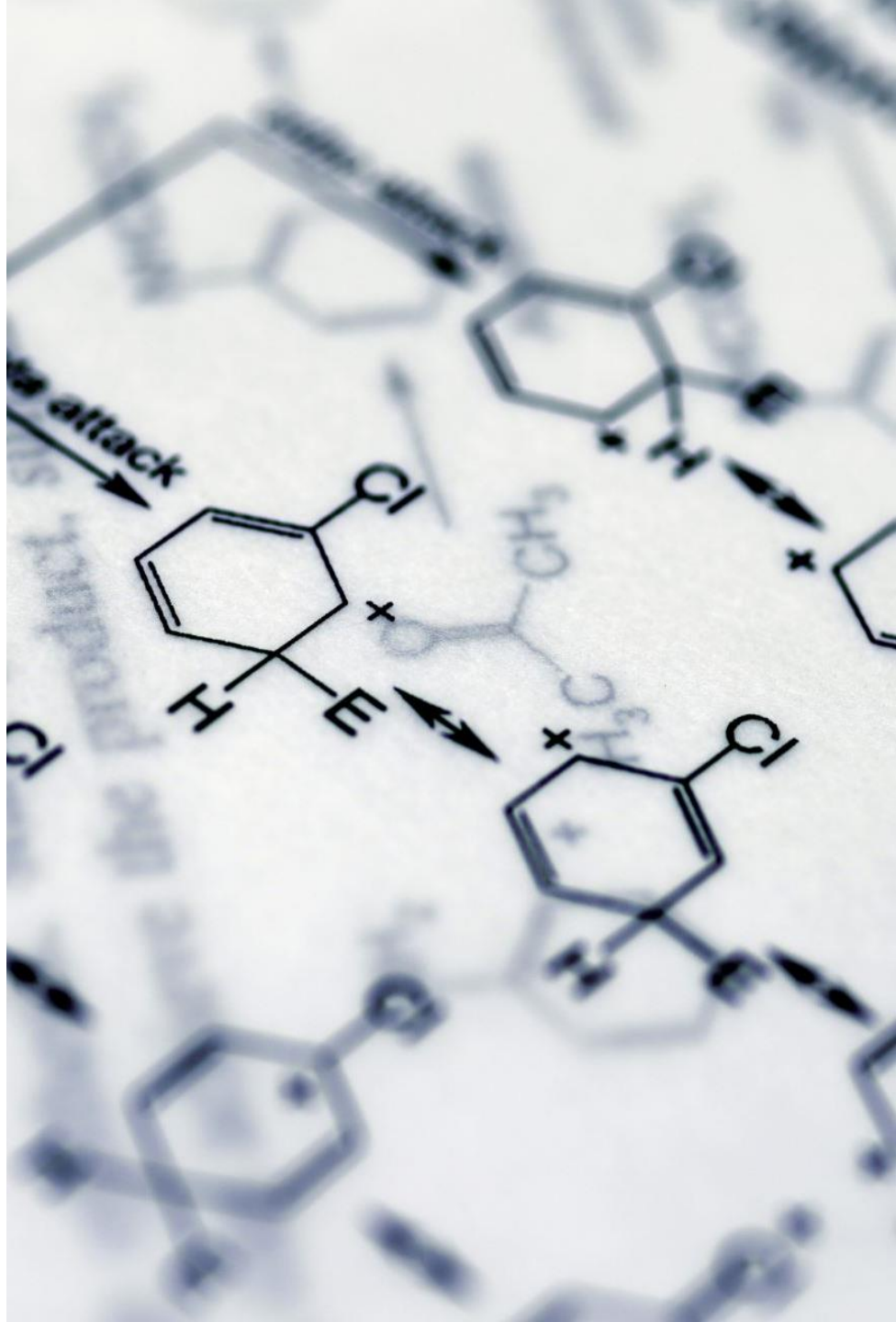
Envelhecer com HIV

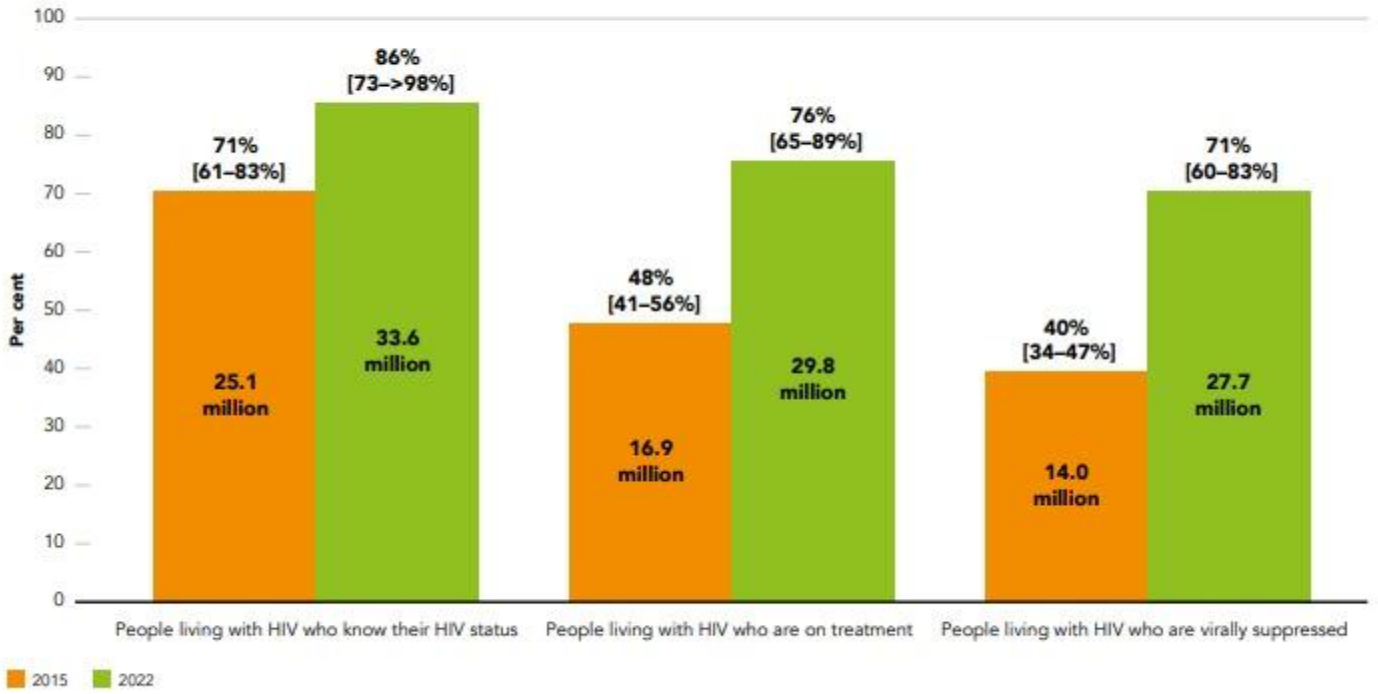
- ✓ Será que o diagnóstico precoce e tratamento imediato muda o cenário do envelhecimento com HIV?
- ✓ Temos novos esquemas com medicamentos mais bem tolerados. Isso fará diferença?



Aumento do conhecimento do status do HIV, tratamento e supressão viral

Knowledge of HIV status, treatment and viral load suppression levels have risen substantially

Figure 1.2 Percentage and number of people living with HIV who know their HIV status, are receiving antiretroviral therapy and are virally suppressed, global, 2015 and 2022



Source: UNAIDS special analysis of epidemiological estimates, 2023.

Delayed presentation of HIV among older individuals: a growing problem

Amy C Justice, Matthew B Goetz, Cameron N Stewart, Brenna C Hogan, Elizabeth Humes, Paula M Luz, Jessica L Castilho, Denis Nash, Ellen Brazier, Beverly Musick, Constantin Yiannoutsos, Karen Malateste, Antoine Jaquet, Morna Cornell, Tinei Shamu, Reena Rajasuriar, Awachana Jiamsakul, Keri N Althoff

	Range of the number of people with late presentation (CD4 count <350 cells/µL)	Proportion of people aged <50 years with late presentation (%)	Proportion of people aged 50–64 years with late presentation (%)	Proportion of people aged ≥65 years with late presentation (%)
North America (2018)	500–1000	38%	42%	47%
Central and South America and the Caribbean (2019)	1–500	49%	61%	60%
Central Africa (2019)	1–500	52%	57%	25%
East Africa (2019)	1500–2000	54%	67%	50%
West Africa (2017)	500–1000	63%	62%	64%
Asia-Pacific (2019)	1–500	69%	81%	75%
Southern Africa (2017)	4500–5000	55%	62%	50%

Estimates of CD4 at presentation for HIV care are not presented for the Australia subcohort of the IeDEA Asia-Pacific region. Participants were recruited to replenish the subcohort in 2016; the median age at presentation for HIV care is based on a relatively small subpopulation (<20 participants) of those presenting for HIV care at participating clinics. Presenting estimates would involve subgroups of less than five participants, which breaches confidentiality arrangements. In the IeDEA Southern Africa regional cohort, participants were observed from ART initiation (not from presentation for HIV care); age at ART initiation is believed to be reflective of age at presentation for HIV care as of 2017, when the Treat All guidelines were adopted in Southern Africa. ART=antiretroviral therapy. IeDEA=International epidemiology Databases to Evaluate AIDS.

Table 2: **People with late presentation (CD4 <350 cells per µL) for HIV care, by age, in the most recent complete calendar year of data available in IeDEA regions**

cells

MDPI

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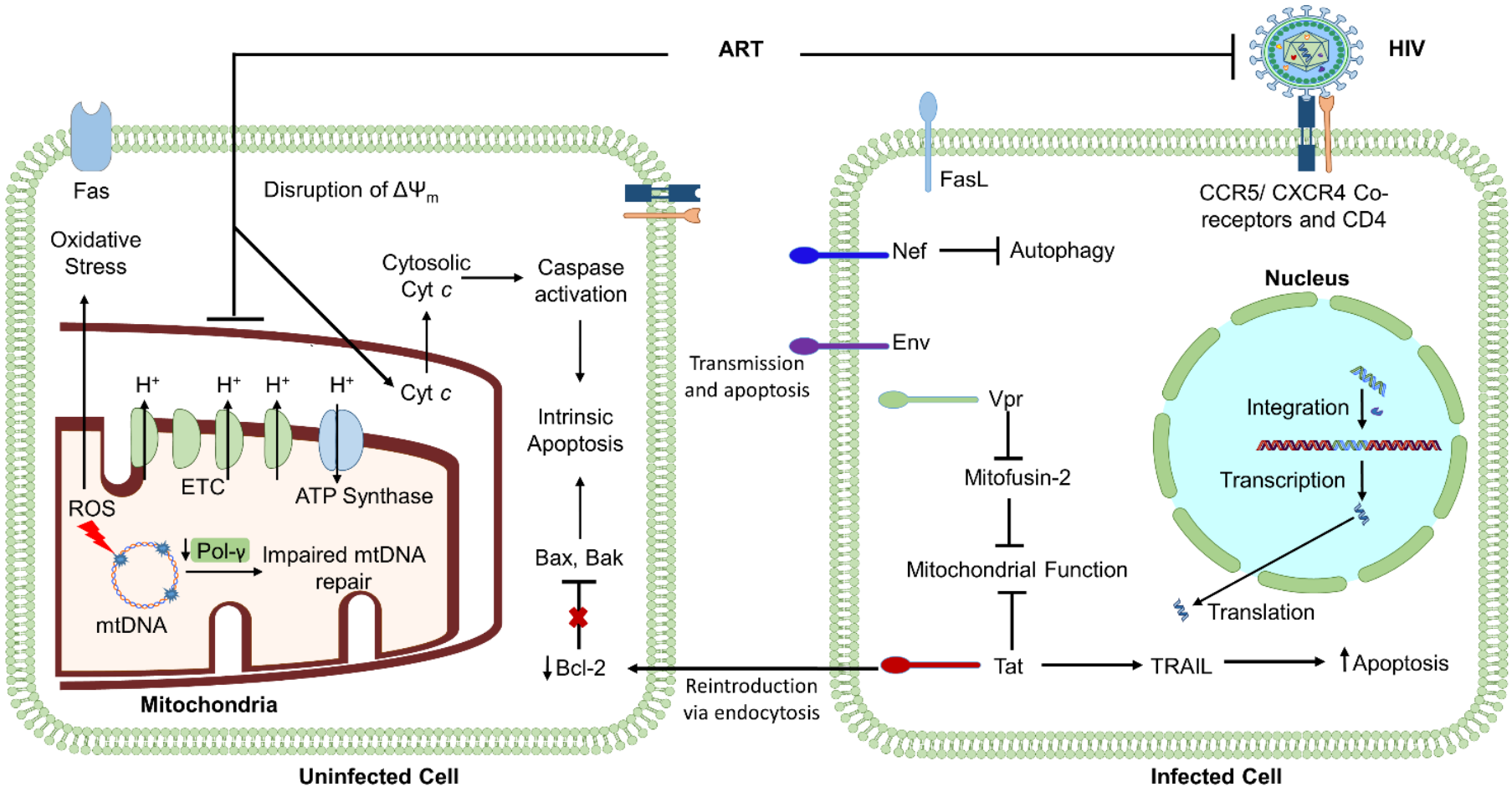
Review

The Impact of HIV- and ART-Induced Mitochondrial Dysfunction in Cellular Senescence and Aging

Madison Schank [1,2], Juan Zhao [1,2], Jonathan P. Moorman [1,2,3] and Zhi Q. Yao [1,2,3,*]



IAS As funções mitocondriais são interrompidas mesmo em pacientes clinicamente estáveis

Table 1. Pharmacology of antiretroviral therapy and reported effect on mitochondria [105,109,110].

Drug Class	Mechanism of Action	Mitochondrial Dysfunction	Species and Cell Type Models
NRTIs (Abacavir, Tenofovir)	Prevents viral replication by inhibiting HIV reverse transcriptase	Inhibition of Pol-γ [111] Reduction of mtDNA copy number/mitochondrial encoded proteins [106] Reduced lymphocyte proliferation Respiratory chain deficiency Inhibition of ETC complexes [113] ATP reduction [30,114] Increased oxidative stress Decrease in Ψ_m [112]	Human fibroblasts [111,112], PBMCs [106], CD4, and CD8 cells [113], and rat liver cells [30,114]
NNRTIs (Rilpivirine, Efavirenz, Nevirapine)	Prevents viral replication by noncompetitively binding to HIV reverse transcriptase	Respiratory chain deficiency ATP reduction Increased oxidative stress [109] Decrease in Ψ_m Apoptosis [110,115–117]	Human hepatic cells [109], PBMCs [110,115], coronary artery endothelial cells [116], and hepatoma cells [117], and Jurkat T cell line [115]
PIs (Ritonavir, Darunavir, Atazanavir, Indinavir, Saquinavir)	Prevents viral replication by inhibiting HIV protease	Increased oxidative stress [118] Reduced mtDNA copy number Respiratory chain deficiency Reduced ATP [64,119] Apoptosis [119,122,123]	Human CD4, CD8 [64], macrophage-derived foam cells [119], endothelial [118], hepatoma [117], and hepatic cells [120], and Huh-7.5, 293T, HeLa, and Hepa RG cell lines [121]
INIs (Raltegravir, Dolutegravir, Elvitegravir)	Prevents integration of viral DNA into the host genome by inhibiting HIV integrase enzyme	Respiratory chain deficiency Increased oxidative stress Increased cytoplasmic mtDNA copy number [64]	Human CD4 and CD8 [64]
Fusion Inhibitors (Leronlimab, Ibalizumab, Enfuvirtide)	Prevents viral fusion with target cell membrane by binding to the viral envelope protein gp41	Not identified	N/A
Coreceptor Antagonists (Aplaviroc, Maraviroc, Vicriviroc)	Prevent viral infection by interfering with viral entrance into the cell by blocking the coreceptors, such as CCR5 or CXCR4, on the surface of target immune cells	Not identified	N/A

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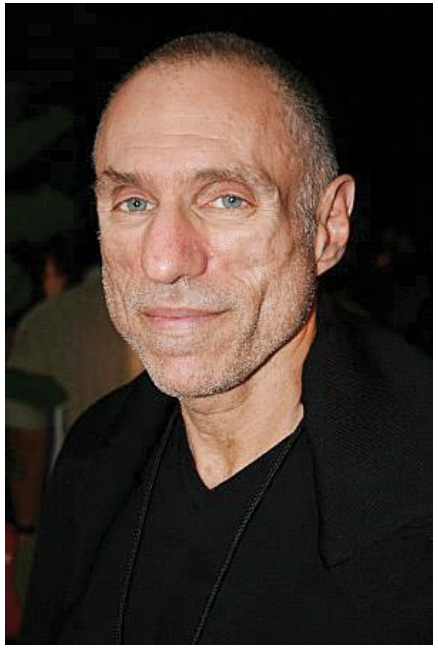
Envelhecer com HIV

- ✓ O que pode ser feito para melhorar a qualidade de vida das PVHIV que estão envelhecendo?
- ✓ Que tipo de preocupação ou atitude o clínico precisa ter?

Envelhecer com HIV: Vozes da comunidade



Jules Levin
NYC

Marc Thompson
London

Venita Ray
Houston

"Uma coisa que todos nós que estamos aqui hoje partilhamos é que estamos todos envelhecendo. Não podemos escapar disso. É um processo e uma jornada inevitável. Mas para aqueles de nós que têm HIV, há muitas camadas e dimensões adicionais a considerar… Não nos basta apenas estarmos gratos por ainda estarmos aqui." –Marc Thompson, CROI 2022

Frailty and health-related quality of life among older people living with HIV pre- and post-COVID-19 pandemic onset: A cross-sectional study

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Beatriz Grinsztejn
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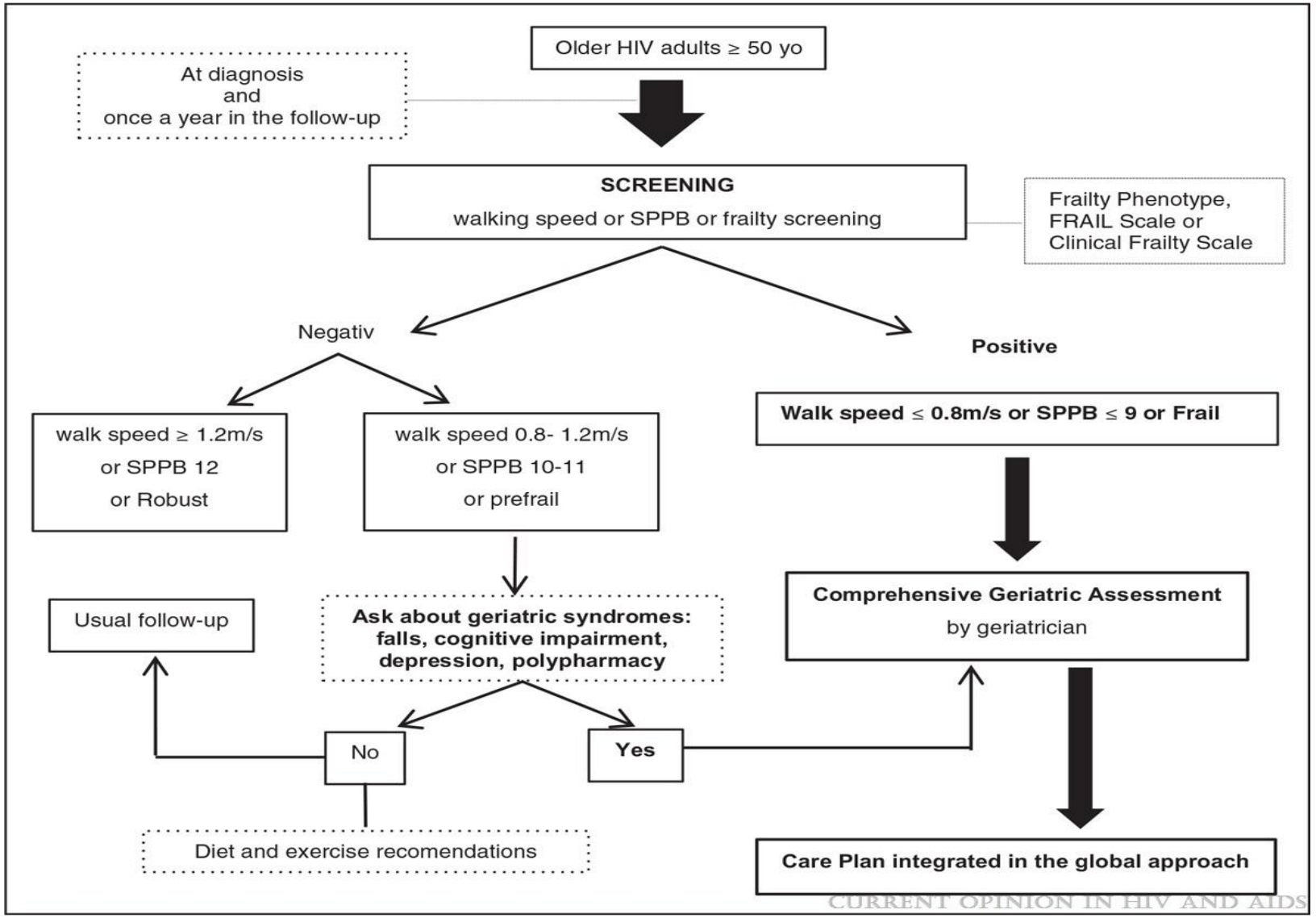
Sandra W. Cardoso
Oswaldo Cruz Foundation

Table 4
Median quality of life scores (IQR) according to frailty status. Rio de Janeiro, Brazil (2019–2022)

	Non-Frailty N = 73 (29.2%)	Pre-frailty N = 154 (61.6%)	Frailty N = 23 (9.2%)	p-value[a]
General Health Perception	75 (75-91.7)	75 (58.3–75)	50 (25-66.7)	**< .001**
Physical Functioning	87.5 (75–100)	75 (53.1–100)	37.5 (31.2–50)	**< .001**
Labor Functioning	100 (100–100)	100 (75–100)	50 (50–100)	**< .001**
Social Functioning	100 (100–100)	100 (88.9–100)	66.7 (38.9–100)	**< .001**
Cognitive Functioning	93.3 (73.3–100)	86.7 (73.3–100)	66.7 (50-93.3)	**< .001**
Pain	77.8 (66.7–100)	72.2 (55.6–100)	55.6 (22.2–61.1)	**< .001**
Mental Health	86.7 (73.3–100)	80 (60-93.3)	60 (30–80)	**< .001**
Energy	90 (70–100)	80 (60–100)	40 (20–70)	**< .001**

IQR: interquartil range; [a] Kruskal-Wallis

Algoritmo/Screening para plano integrado de cuidado



Frailty: the current challenge for aging people with HIV Falutz, Julian; Brañas, Fátima; Erlandson, Kristine M. Current Opinion in HIV and AIDS16(3):133-140, May 2021. doi: 10.1097/COH.0000000000000677

Current HIV/AIDS Reports
https://doi.org/10.1007/s11904-023-00677-7

Pharmacological and Behavioral Interventions to Mitigate Premature Aging in Patients with HIV

Roxane Rohani[1,2] · Jacob Malakismail[3] · Emmanuel Njoku[4,5]

Accepted: 18 October 2023

Abstract

Purpose of Review We sought to review pharmacological and behavioral interventions that have been publicly presented, published, or are currently ongoing to prevent or mitigate the effect of premature HIV-associated comorbidities.

Recent Findings Multiple studies have been conducted in hopes of finding an effective intervention. While the choice of antiretroviral regimen influences recovery of immune function, several drugs used as adjunct treatments have proven effective to mitigate premature aging. Additionally, few behavioral interventions have exhibited some efficacy.

Summary Statins, angiotensin-receptor blockers, and anti-hyperglycemic agents as well as optimal adherence, exercise, and intermittent fasting among others have had beneficial impact on markers of immune activation and levels of inflammatory biomarkers. However, several investigations had inconclusive outcomes so further studies with larger sample sizes are warranted.

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Pitavastatin to Prevent Cardiovascular Disease in HIV Infection

Grinspoon SK et al. DOI: 10.1056/NEJMoa2304146

CLINICAL PROBLEM

In persons with HIV infection, the risk of atherosclerotic cardiovascular disease is twice that in the general population. Randomized studies of primary prevention strategies in this population are needed.

CLINICAL TRIAL

Design: A phase 3, multinational, randomized, placebo-controlled trial assessed the efficacy and safety of pitavastatin for the prevention of cardiovascular events in persons with HIV infection and low-to-moderate risk of atherosclerotic cardiovascular disease.

Intervention: 7769 participants between the ages of 40 and 75 years (median screening LDL cholesterol, 108 mg/dl) receiving stable antiretroviral therapy were assigned to receive oral pitavastatin calcium (4 mg) (3888 participants) or placebo (3881 participants) daily. The primary outcome was the occurrence of a major adverse cardiovascular event — cardiovascular death, myocardial infarction, hospitalization for unstable angina, stroke, transient ischemic attack, peripheral arterial ischemia, revascularization, or death from an undetermined cause, as measured in a time-to-event analysis.

RESULTS

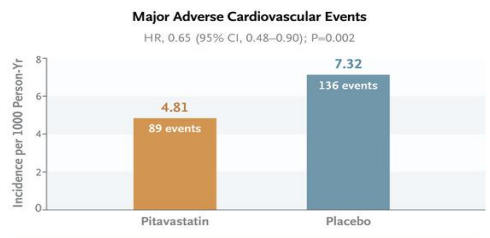
Efficacy: During a median follow-up of 5.1 years, the incidence of major adverse cardiovascular events was significantly lower in the pitavastatin group than in the placebo group.

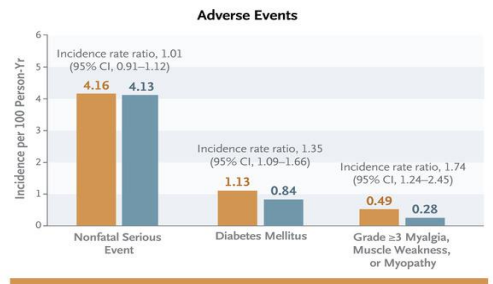
Safety: The incidence of nonfatal serious adverse events was similar in the two groups. Participants in the pitavastatin group were more likely than those in the placebo group to have newly diagnosed diabetes mellitus and grade ≥3 myalgia, muscle weakness, or myopathy.

LIMITATIONS AND REMAINING QUESTIONS

- Although other statins that do not interact with HIV medications may have similar protective effects, the results reported are specific to pitavastatin.
- Other strategies that lower LDL cholesterol may be useful in this population and need to be compared with statin therapy with respect to efficacy, safety, and cost.

Links: Full Article | NEJM Quick Take | Editorial

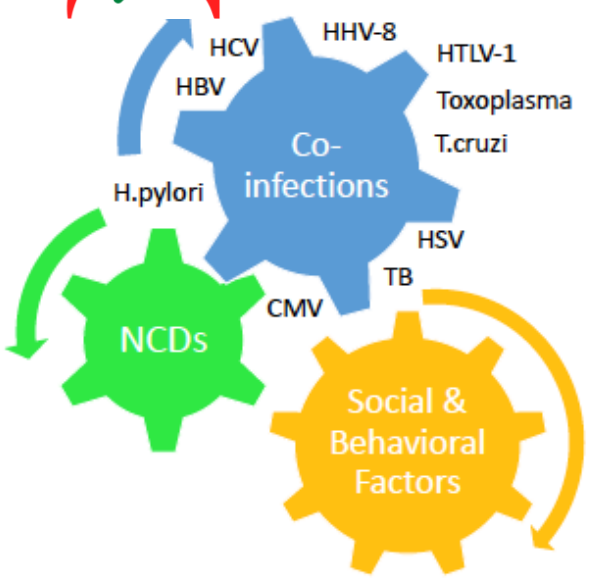




CONCLUSIONS

In persons with HIV infection receiving stable antiretroviral therapy and at low-to-moderate cardiovascular risk, daily treatment with pitavastatin resulted in a significantly lower risk of major adverse cardiovascular events than placebo over approximately 5 years of follow-up.

Estudo Longitudinal HIV & envelhecimento no Brasil



PWH
N=700
50-64 years: n=360
≥65 years: n=340

Prevalent epidemiology
AIM 1 outcomes:
1. Cardiometabolic syndemics
2. Geriatric syndromes

Comprehensive study visit

6 months

≥65 years sub-cohort
N=340

12 months | 24 months | 36 months

Mechanisms of Aging
AIM 3 outcomes:
1. IL-32 isoforms, TRAIL
2. Atherosclerosis progression

Prospective clinical assessments
AIM 2 outcomes:
1. Incident frailty and geriatric syndromes
2. Falls, hospitalizations, new dependency, death

R01AG071439 (Castilho & Grinsztejn)

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T. Waterboer

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C. Tremblay

M. El-Far

Aging research network STUDY

- ✓ Estudo prospectivo n=200 PVHIV ≥50 anos nos sites CCASAnet
- ✓ Avaliações de baseline e longitudinais para:
  - Fragilidade
  - Declínio Cognitivo
  - Osteoporose
  - Polyfarmácia
  - Multimorbidades
  - Insegurança alimentar
  - Isolamento social

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BRAZIL

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PERU

G. Carriquiry

ARGENTINA

C. Cesar

Obrigada!

- ✓Agradecimento a Jessica Castilho e Emilia Jalil pela ajuda com alguns slides para essa apresentação e ao Thiago Torres pela parceria nos estudos de envelhecimento & HIV.

- ✓Tenho um agradecimento especial a Beatriz Grinsztejn nossa presidente eleita da IAS não só por ser a pessoa que enxergou em mim parte do que sou hoje mas também pelo privilégio de, de certa forma estarmos “envelhecendo” juntas nos últimos 20 anos.

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