HIV and Aging: Overview and Future Opportunities

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Disclosures

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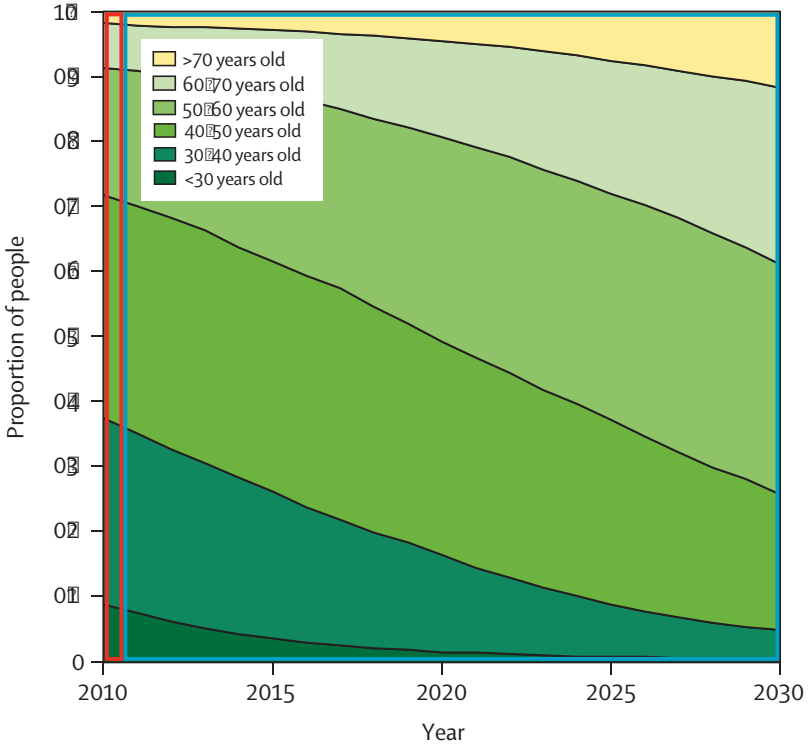
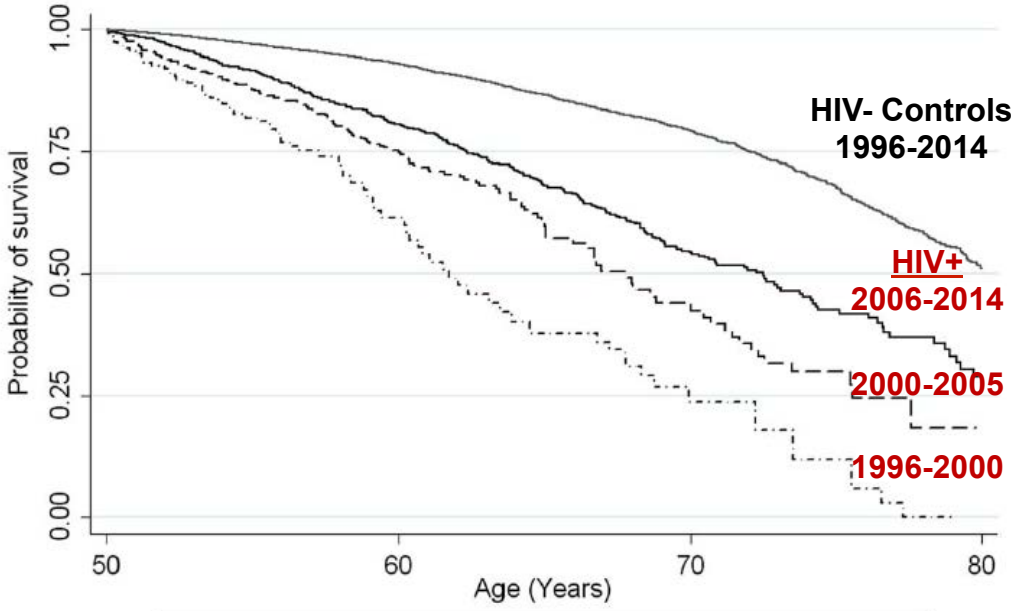
- None

HIV+ Adults Are Aging but Survival Has Not Yet Normalized



Smit, Lancet Inf Dis 2015, 15(7):810-8



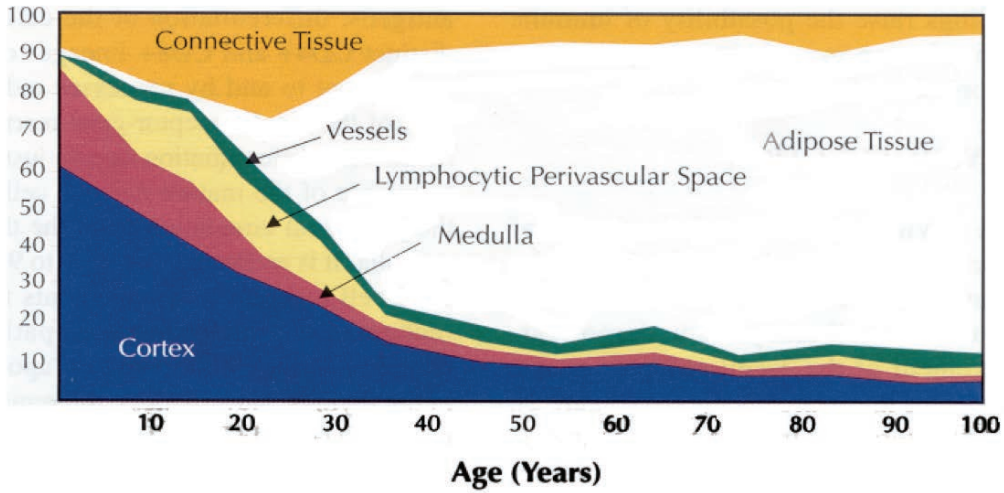
~9 years shorter life expectancy even among those with *no comorbidity*

Legarth et al, JAIDS 2016, 71(2):213-8

Graphs Courtesy Sara Gianella & Peter Hunt

Aging and HIV Affect the Immune System in Similar Ways

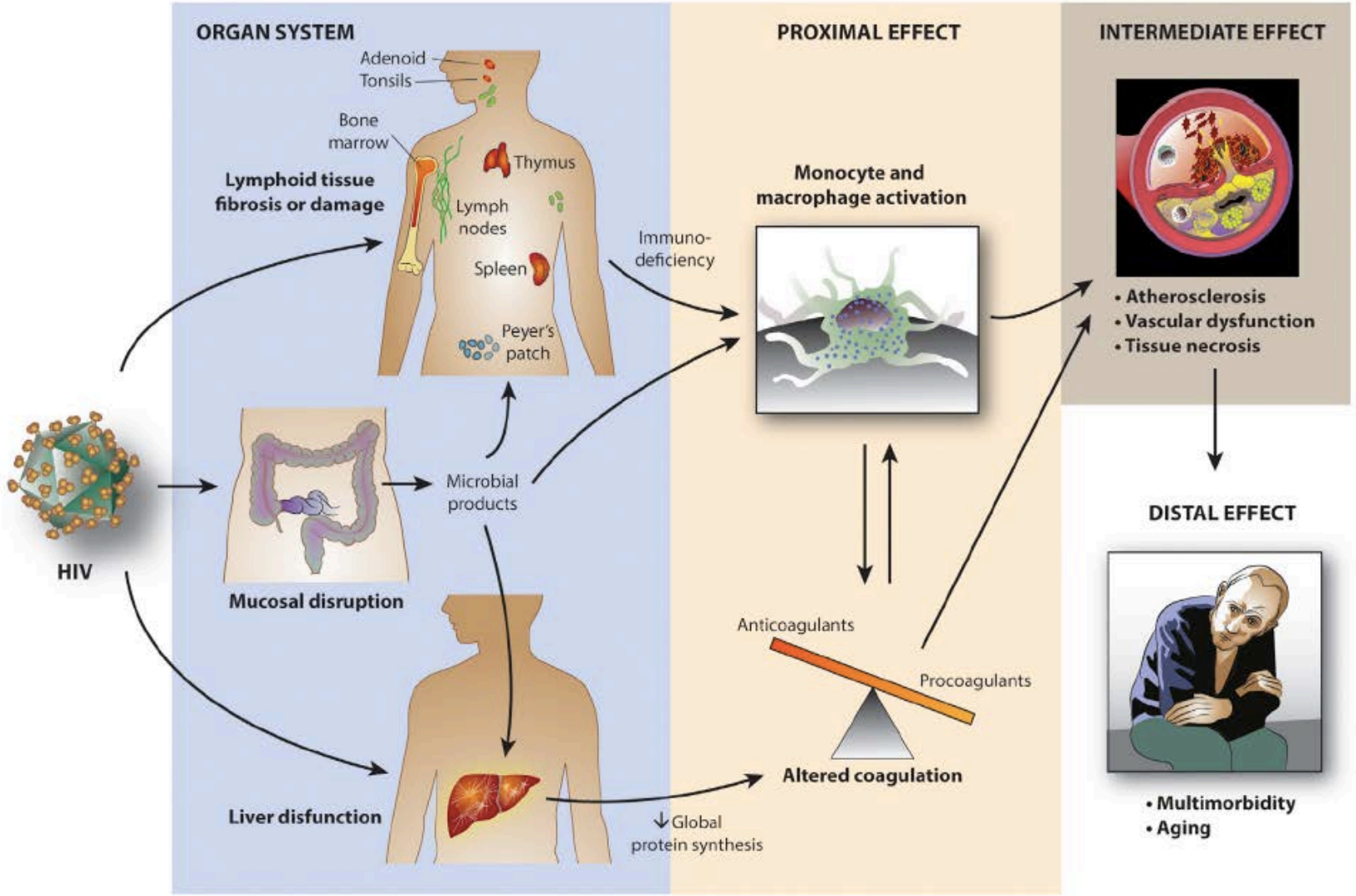
- **Aging associated with:**
  - Loss of thymus tissue
  - Decrease in the number of naive T-cells
  - Reduced T-cell responsiveness
  - B cell dysfunction



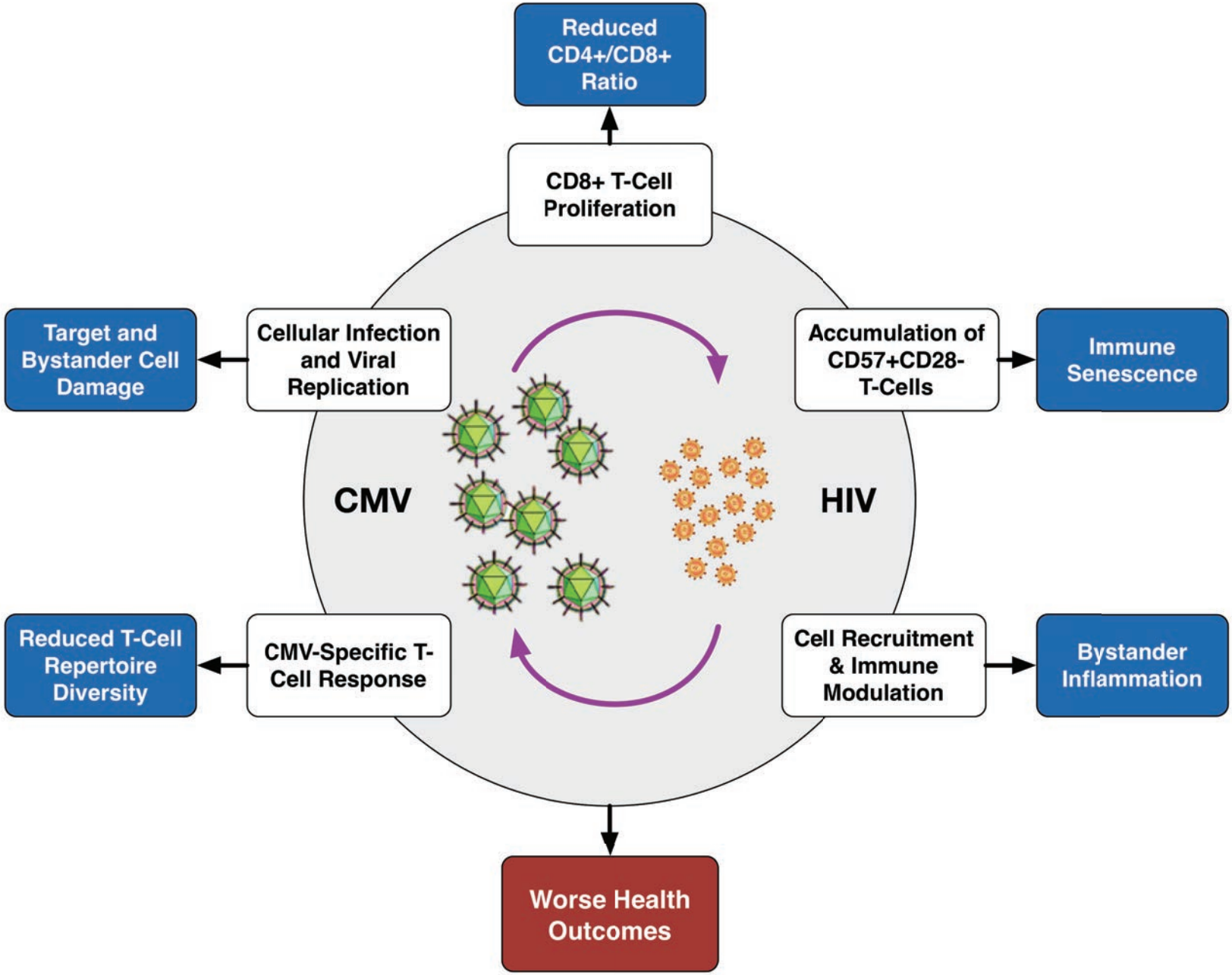
- **Immune senescence** in the general population has been linked to some of the same end-organ disorders that occur in aging HIV+ adults

Brooks et al, American Journal of Public Health 2012, 102(8): 1516-26
Effros RB, Clin Infect Dis. 2008;47(4):542-553; Kaplan et al, J Infect Dis. 2011; 203: 452-463

Unifying Hypothesis of Premature Aging of HIV+ Adults



Deeks, Tracy, & Douek, Immunity 2013, 39: 633-45



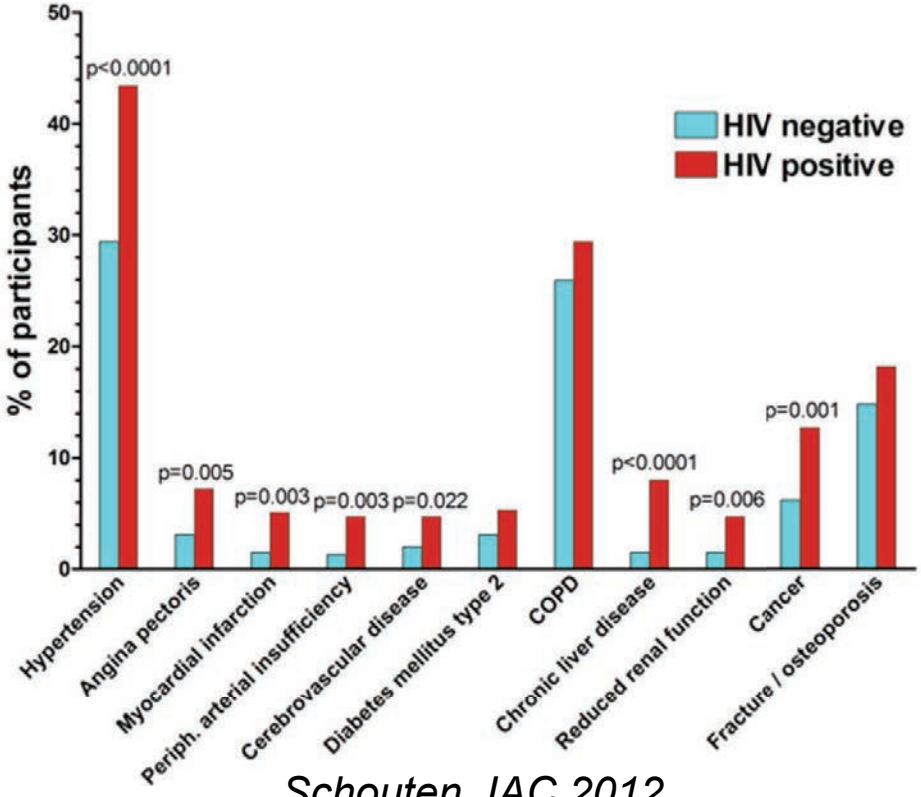
Gianella & Letendre, J Inf Dis 2016

Evidence of Premature Aging Has Been Found in Nearly Every Organ System

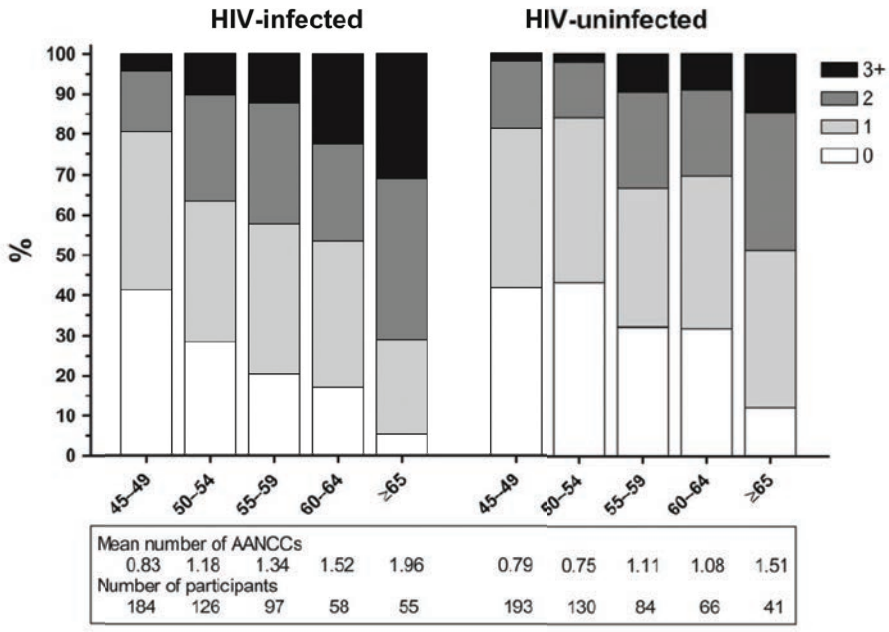
- **Nervous System**
  - Cognitive Disorders
  - Depression
  - Neuropathy
  - Sleep Disorders
- **Vascular System**
  - Cardiovascular
  - Cerebrovascular
- **Endocrine/Metabolic**
  - Diabetes
  - Hypogonadism
- **Liver**
  - ↓ Drug Metabolism
  - ↓ Synthetic Function
- **Kidney**
  - ↓ Drug Elimination
- **Musculoskeletal**
  - Osteoporosis
  - Frailty
- **Pulmonary**
- **Hematopoietic**
- **(Cancer)**

Brooks et al, American Journal of Public Health 2012, 102(8): 1516-26
Onen et al, HIV Clin Trials. 2010;11(2):100-109; Womack et al, PLoS ONE. 2011;6(2): E17217; Desquilbet et al, J Gerontol A Biol Sci Med Sci. 2007;62(11):1279---1286.

HIV+ Adults are at Greater Risk for Multiple Diseases than the General Population



Schouten, IAC 2012, Abstract THAB0205



Schouten et al, Clin Infect Dis 2014; 59(12):1787–97

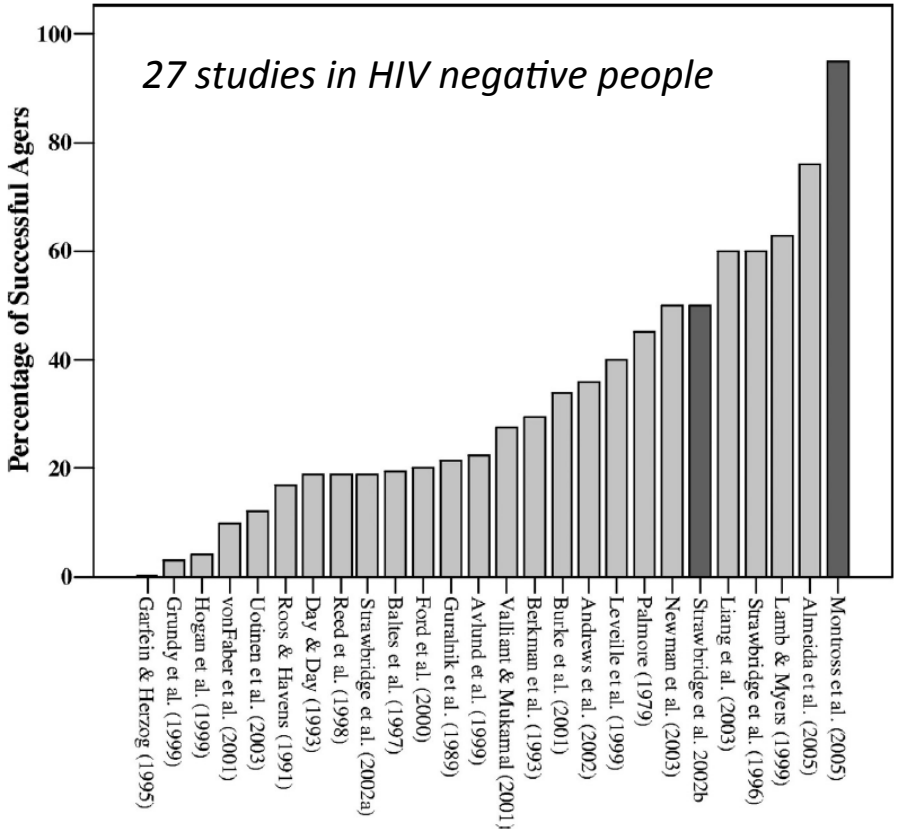
Adapted from Todd Brown, Johns Hopkins

Successful Aging is a Multidimensional Construct

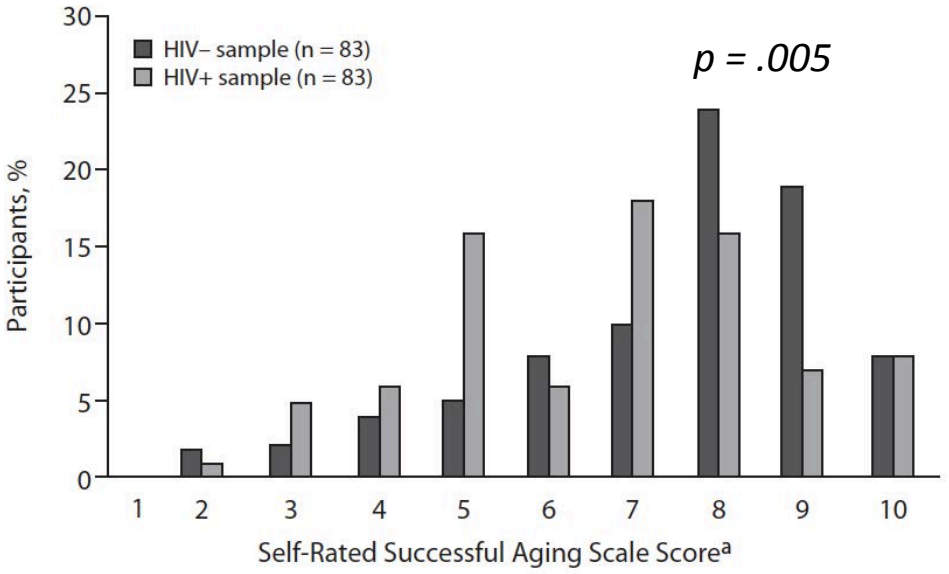
- **Typical elements of successful aging**
  - Avoidance of disease and disability
  - Maintenance of high physical and cognitive function
  - Sustained engagement in social and productive activities
- **Subjective quality of life** may be more important than the absence of disease

Rowe & Kahn, Gerontologist. 1997;37(4):433-40
http://en.wikipedia.org/wiki/Successful_Aging, Accessed 8 November 2013

36% of the Population Age Successfully: May be Lower in HIV+ Adults



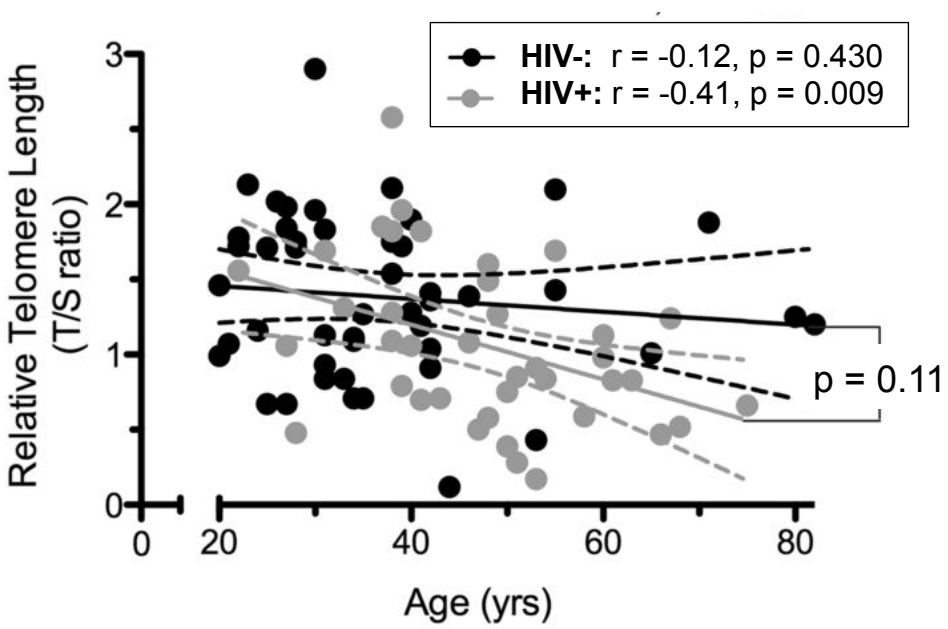
Most frequent correlates of SA: Nonsmoking and absence of disability, arthritis, and diabetes



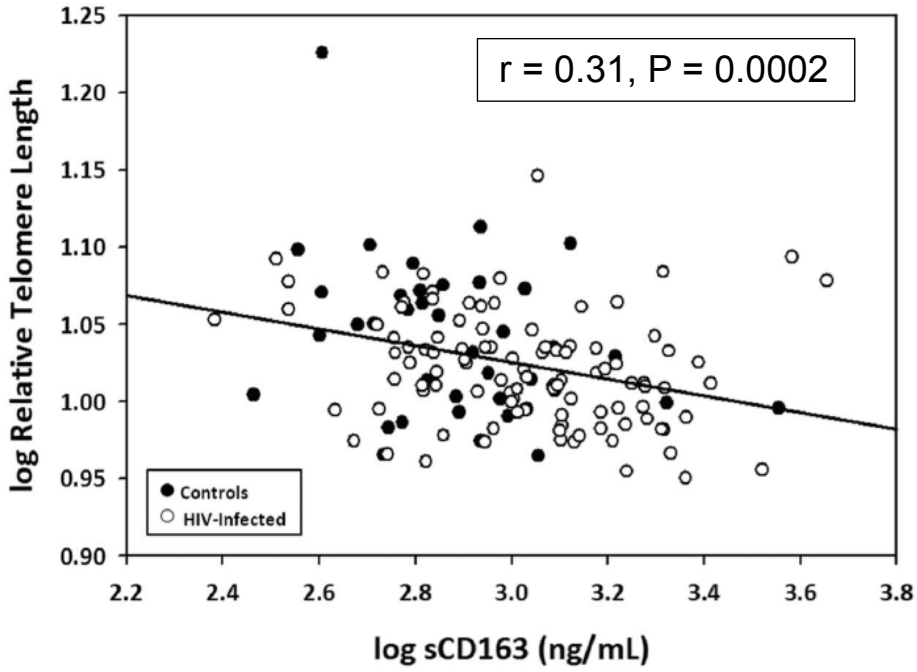
Higher self-rated SA in PLWH was associated with better physical and emotional functioning but not HIV disease or negative life events

Depp & Jeste, American Journal of Geriatric Psychiatry. 2006; 14: 6-20
Moore et al, J Clinical Psychiatry 2013, 74: e417-23

HIV and Inflammation Associated with Shorter Telomere Length



Leeansyah et al, JID 2013; 207:1157



Srinivasa et al, JAIDS 2014; 67: 414

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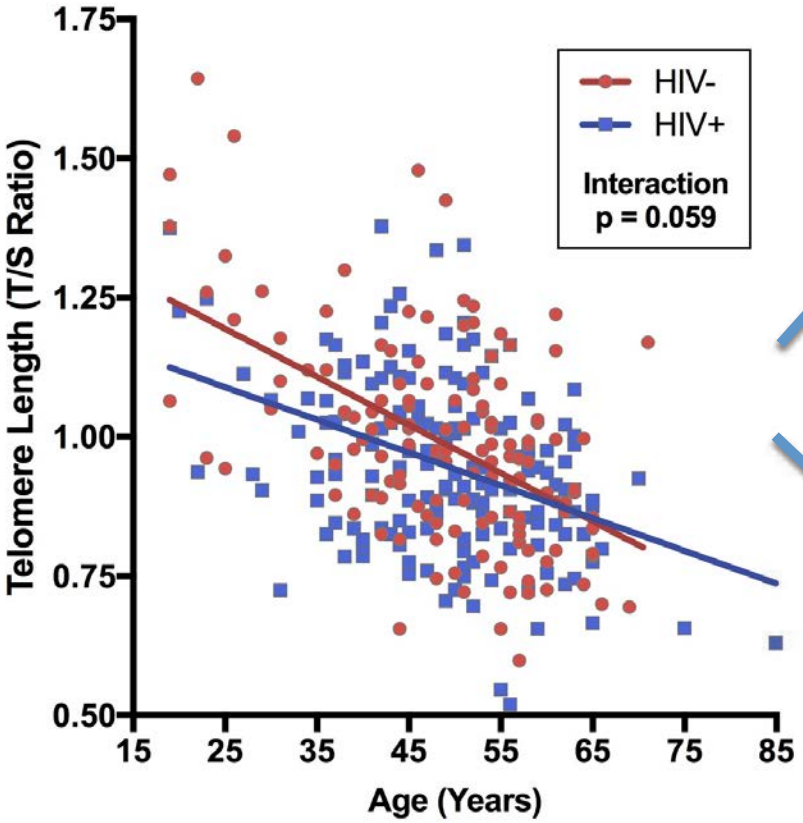
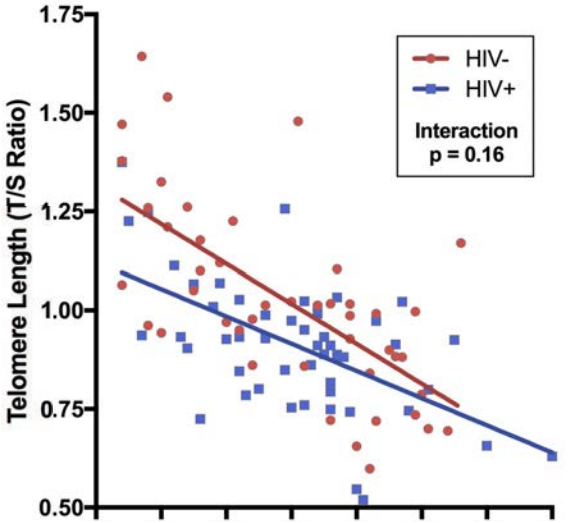
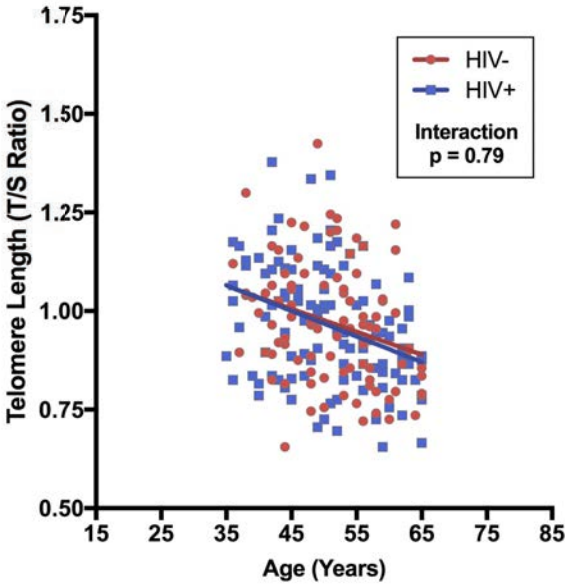
Telomere Data from 2 UCSD Cohorts



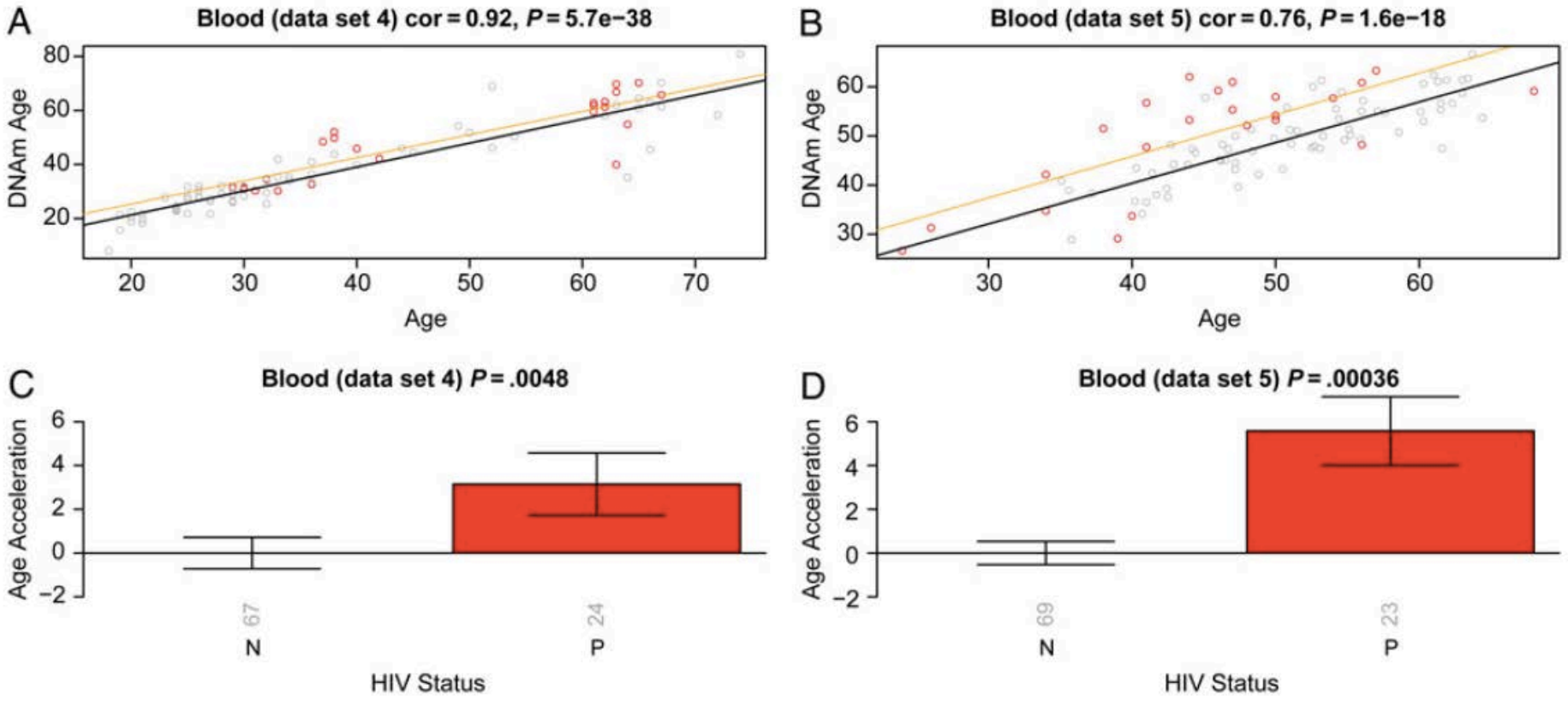


TMARC



SIRA

HIV Accelerates Aging of Blood Cells by ~5 Years by DNA Methylation

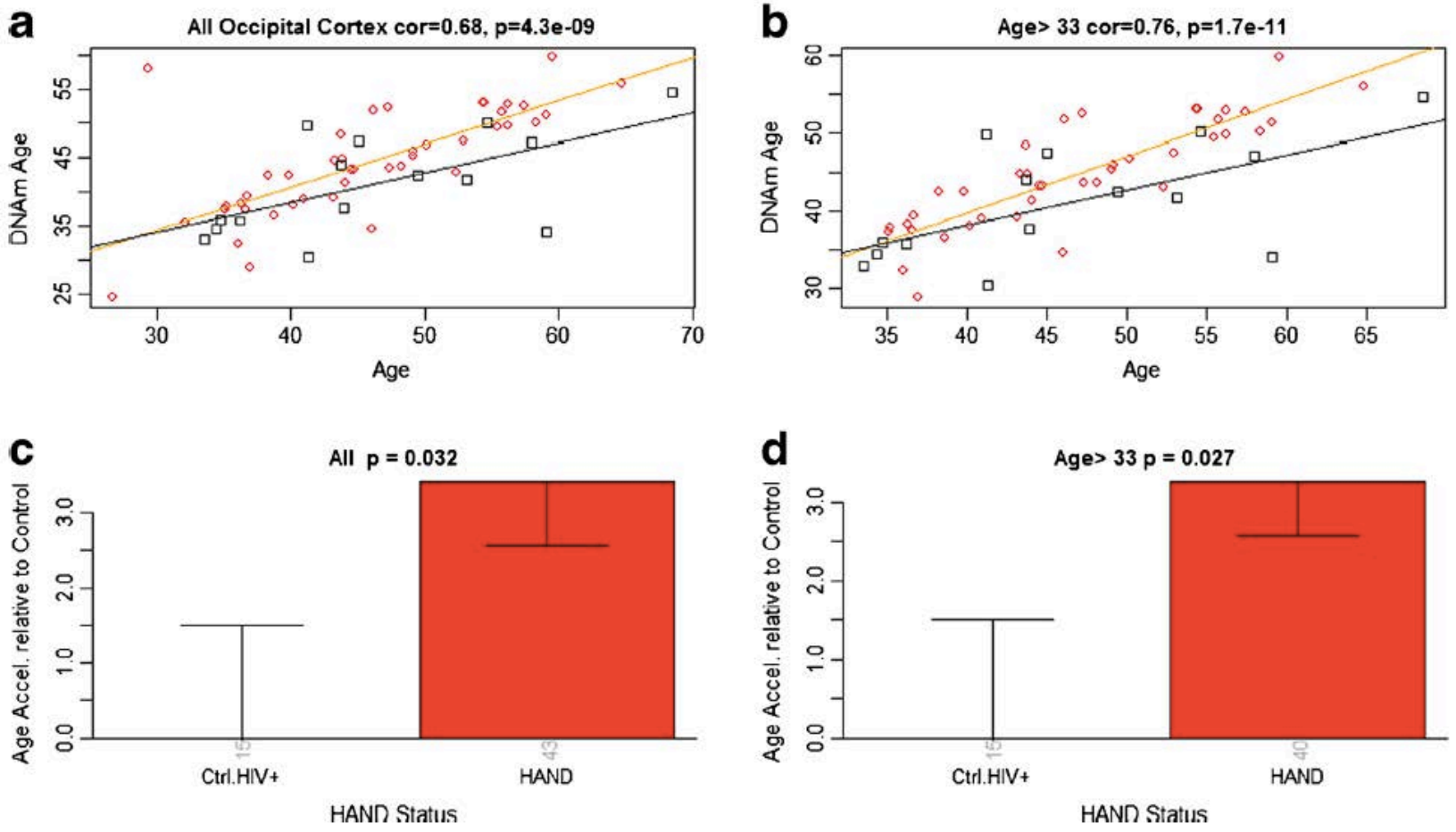


Horvath & Levine, J Infect Dis 2015, 212:1563–73

Multiple Mechanisms of Brain Injury

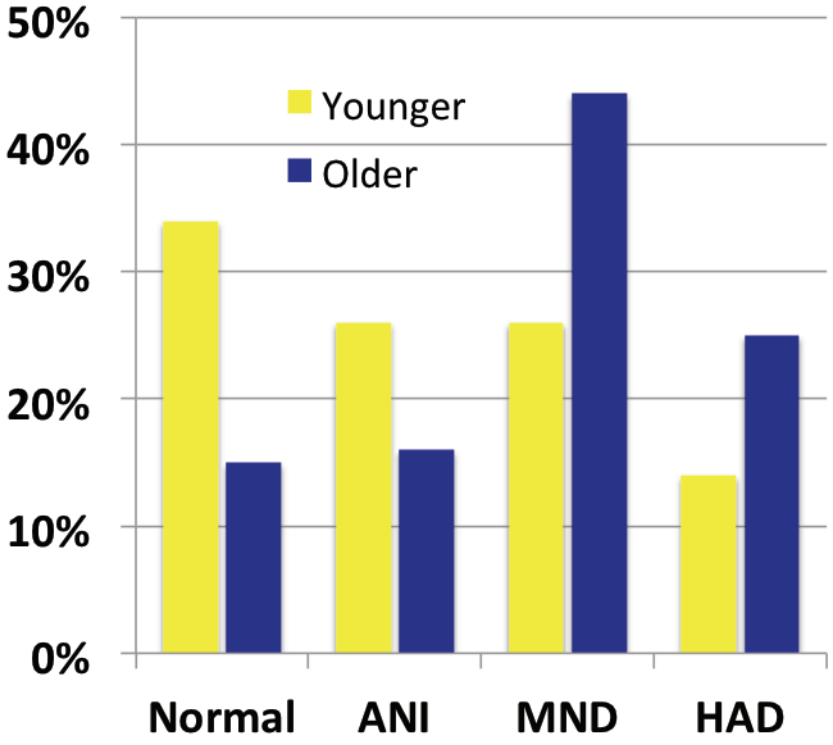
- **Comorbidities**
  - Vascular disease
  - Metabolic syndrome
  - Frailty and sarcopenia
  - Anemia and iron metabolism
  - Other neurodegenerative diseases
- **Cellular senescence**
  - Immune senescence
  - Telomere length
- **Neuronal vulnerability**
  - Mitochondria and oxidative stress
- **Polypharmacy and Drug interactions**
- **Drug metabolism and distribution**
  - Reduced elimination
  - Reduced drug binding proteins
  - Altered blood-brain barrier permeability and molecular drug transporter functioning

HIV may Accelerate Aging to a Greater Extent in the Brain

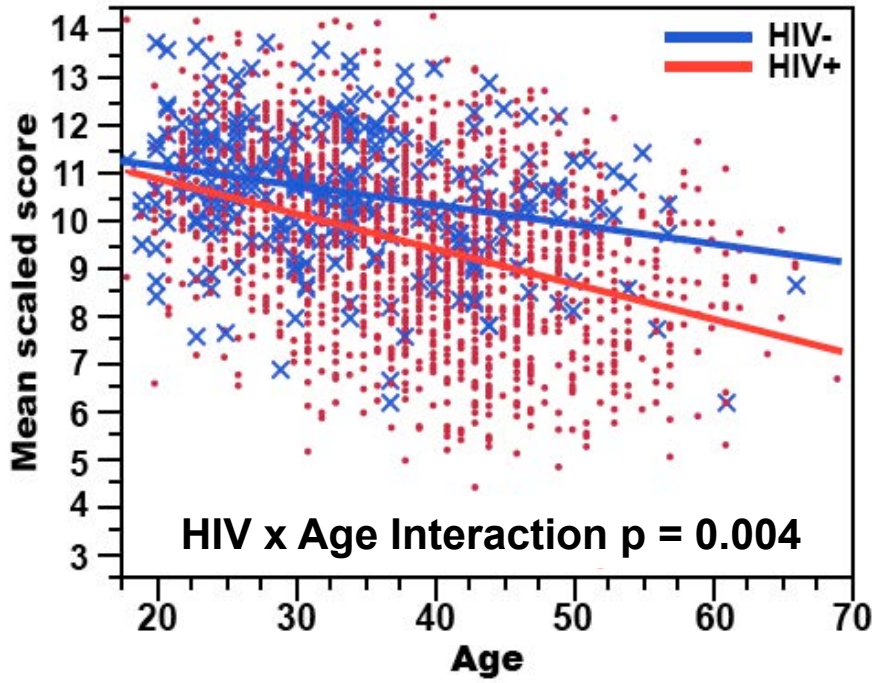


Levine et al, J Neurovirol 2015, Epub ahead of print

HIV May Cause Premature Neurocognitive Decline



Modified from Valcour et al, Neurology 2004;63:822–827



Heaton et al, J Neurovirology, 2012, 18(Suppl 1): S46

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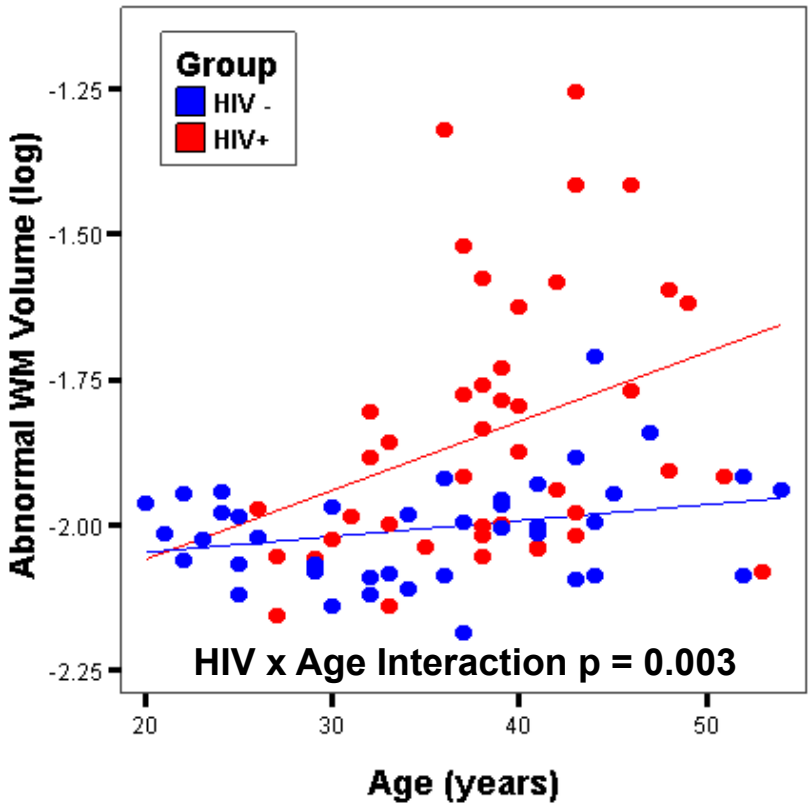
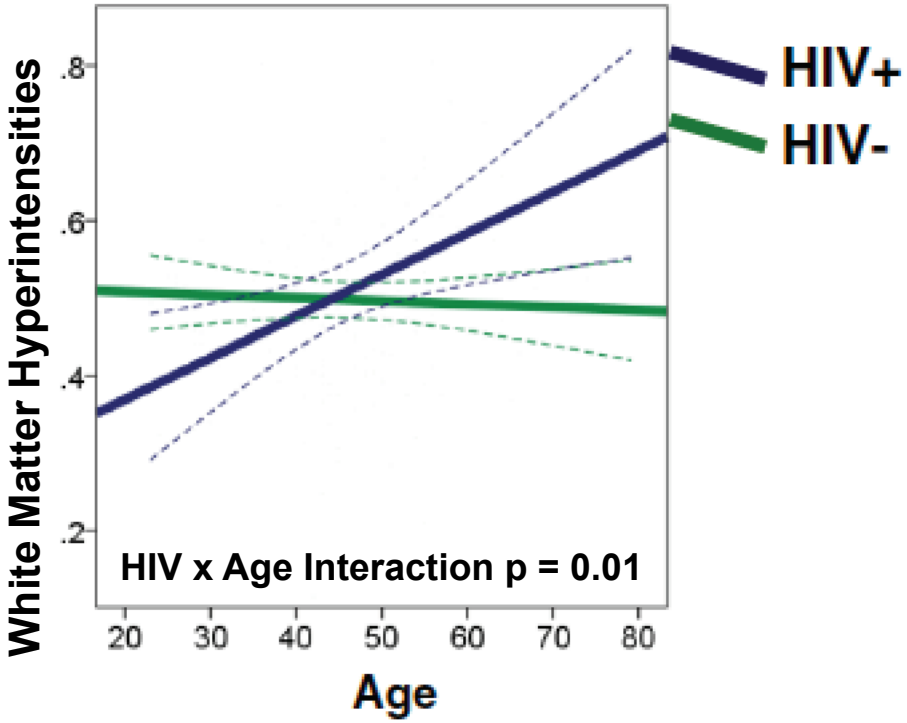
HIV May Accelerate White Matter Injury in the Brain

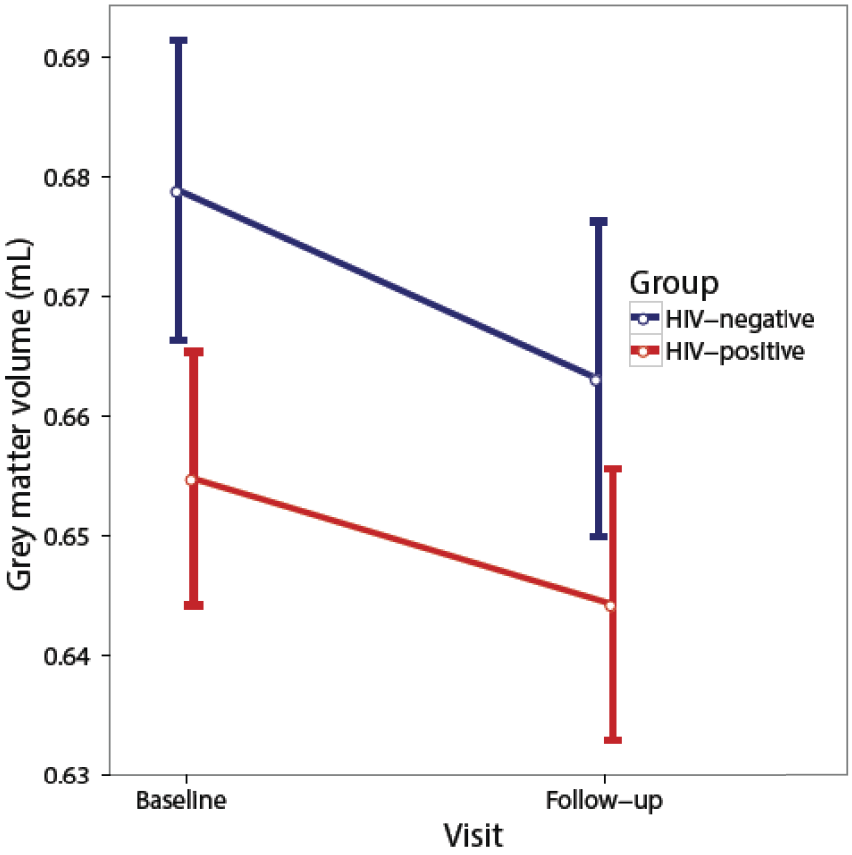


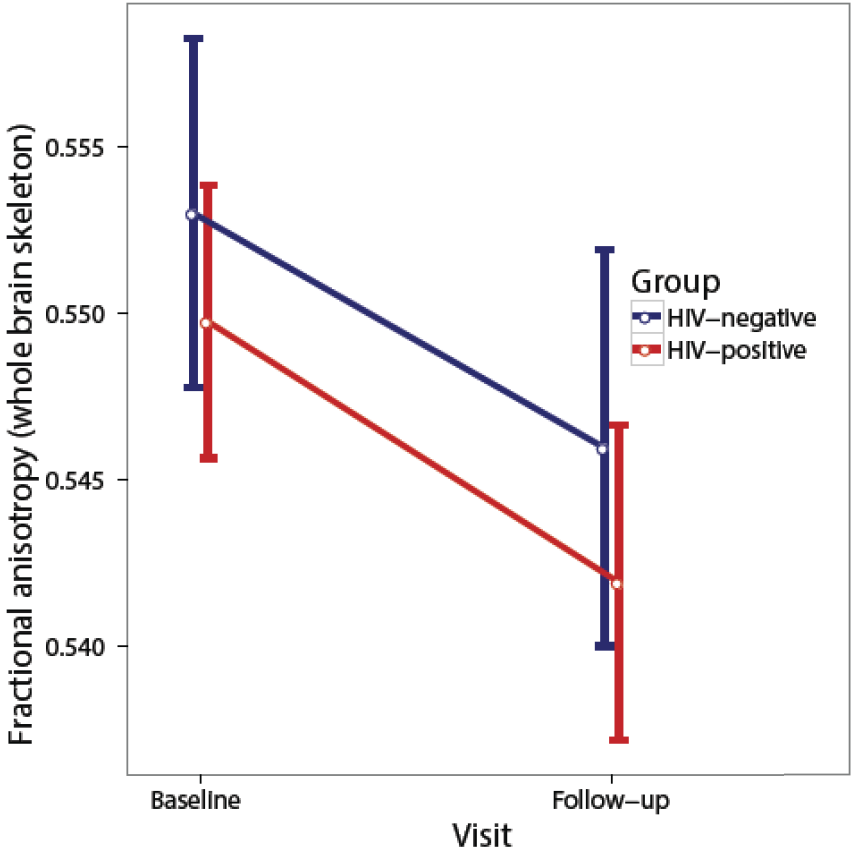
Unpublished CHARTER Data



Seider et al, J. Neurovirol. (2016) 22:201–212

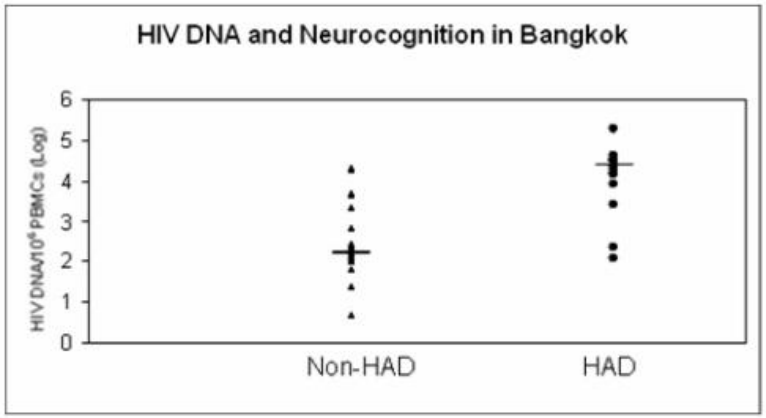
Recent Longitudinal Data Do Not Support Premature Brain Aging



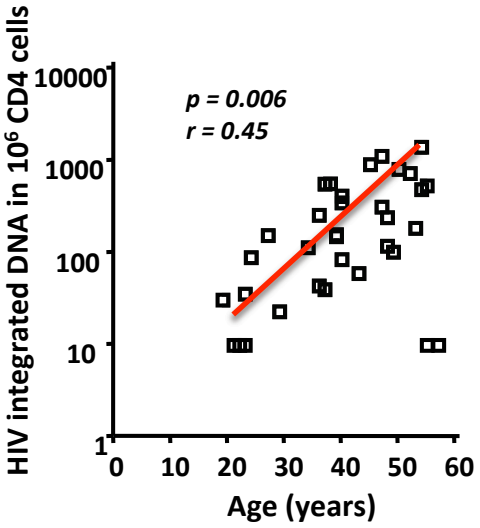


Cole et al, CROI 2017, Abstract 352LB

Other Biomarkers May Be More Sensitive to Accelerated Aging

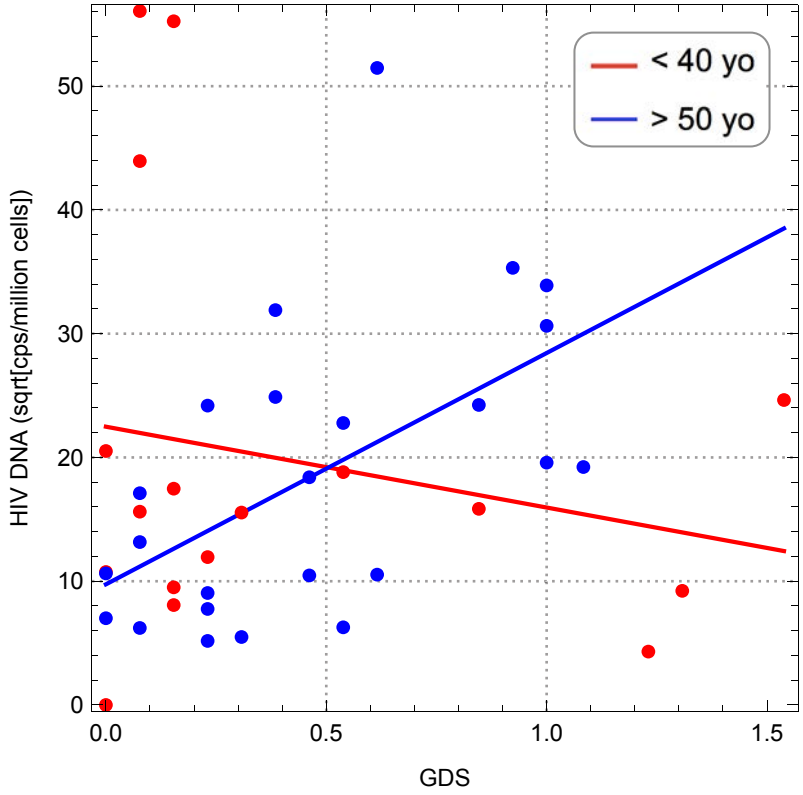


Shiramizu et al, Int J Med Sci 2006, 6;4(1):13-8



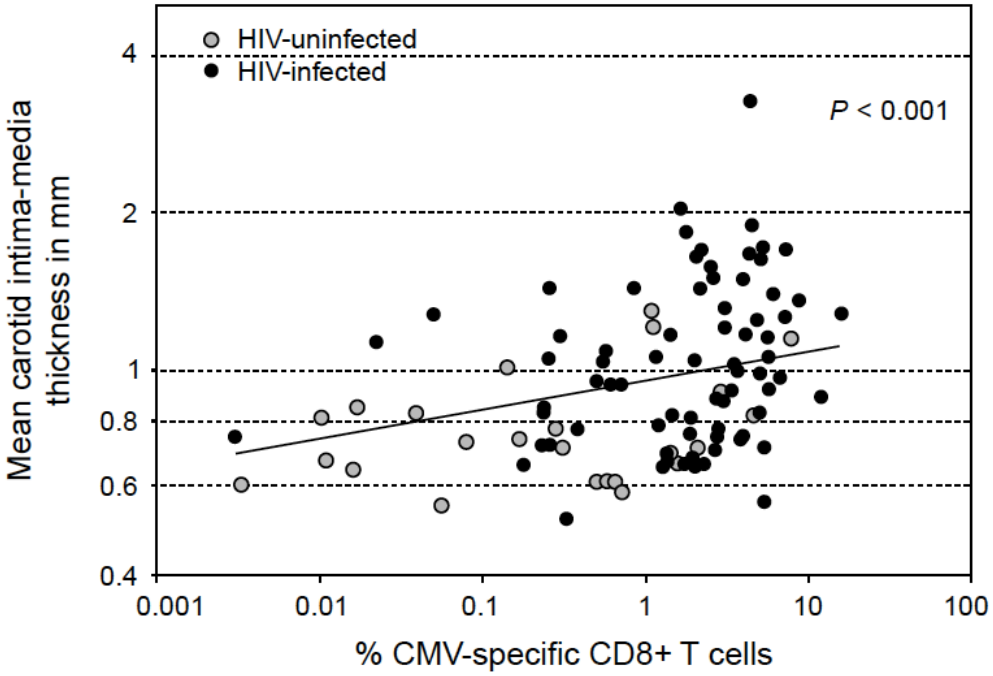
Boulassel, Routy et al. J Clin Virol 2012, 53: 29-32

	Statistic	*p* (after EDI control)
Younger	−0.200141	0.447789 (0.646705)
Older	0.546697	0.00492138 (0.0213879)

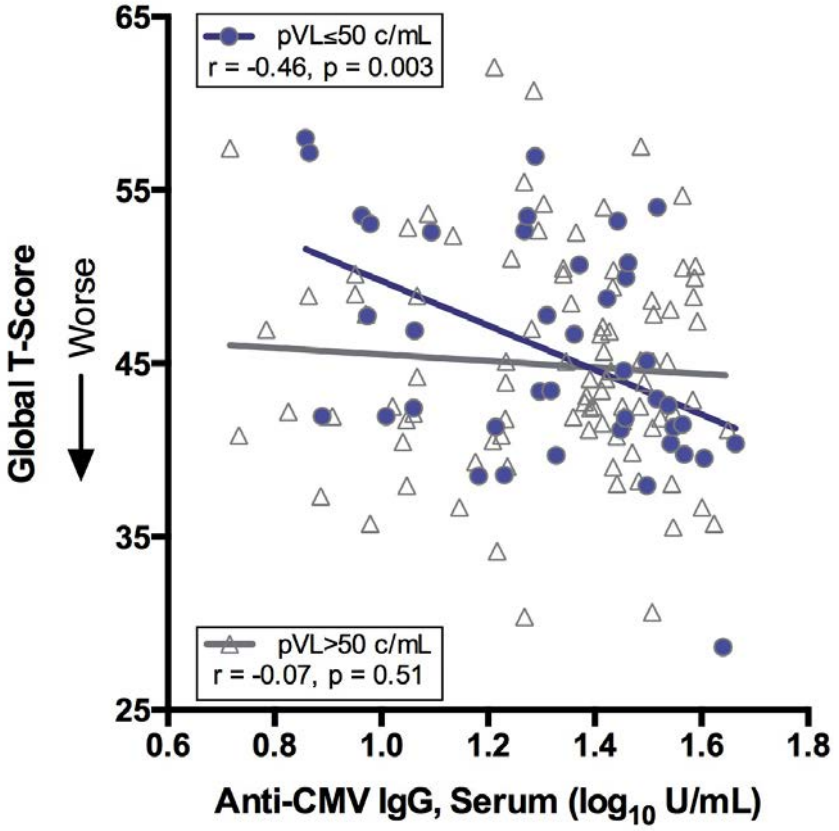


Oliveira et al, Sci Rep. 2015; 5: 17094

Immune Responses to CMV Are Associated with Atherosclerosis & HAND



Hsue et al, AIDS 2006, 20: 2275-83



Letendre, et al. J Infect Dis 2016, Submitted

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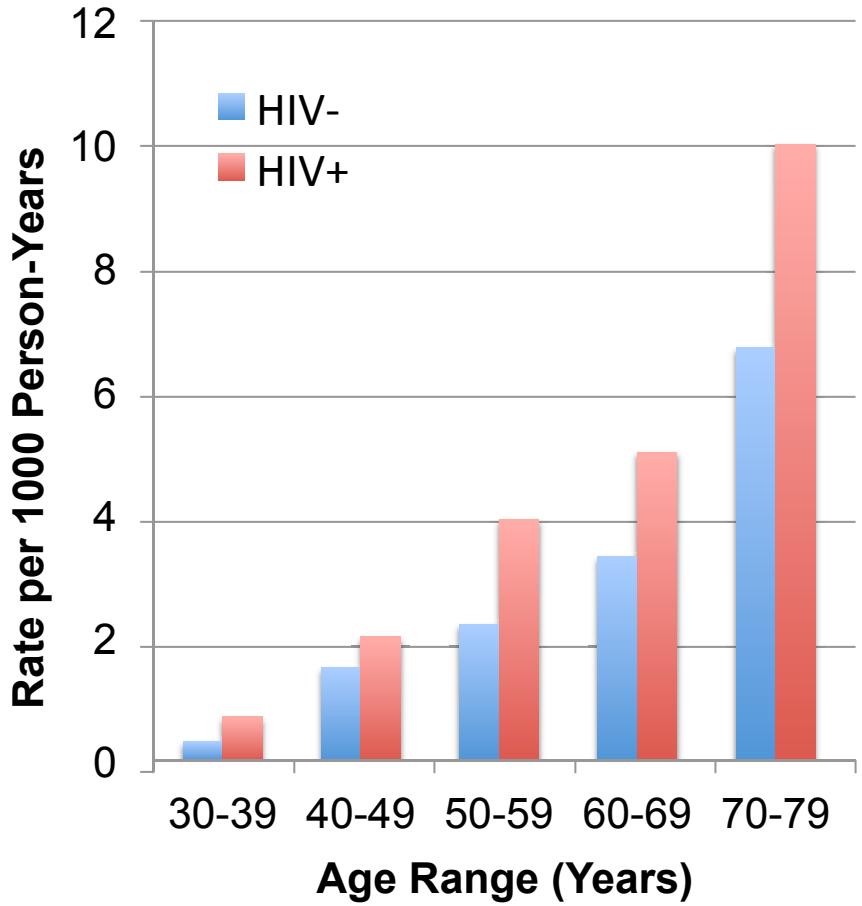
Multiple Studies Have Identified Increased Risk of Vascular Disease

- **HIV+ adults have greater 10-year risk of cardiovascular events (CVEs) and higher rates of atherosclerosis than HIV- adults**
- **HIV disease itself is associated with greater risk of atherosclerosis independent of viral load, type of ART, or severity of immunodeficiency**
- **Whether the increased risk of cardiovascular disease can be modified by ART remains uncertain**
  - **We still need randomized clinical trial data**

Brooks et al, American Journal of Public Health 2012, 102(8): 1516-26; Hsue et al, IDS. 2009;23 :1059-1067; Kaplan et al, Clin Infect Dis. 2007;45(8):1074-1081; El-Sadr et al, Ann Intern Med. 2008;149(5):289-299; Triant et al, Clin Infect Dis. 2012; 54:408-413

Acute Myocardial Infarctions Are More Common in HIV+ Adults

- 871 acute MIs in ~80,000 veterans over ~6 years
- **Across 3 decades of age, mean acute MIs per 1000 person-years was consistently higher for HIV+ than HIV- adults**
- **Hazard ratio for acute MI: 1.5** after adjusting for Framingham risk factors, comorbidities, and substance use



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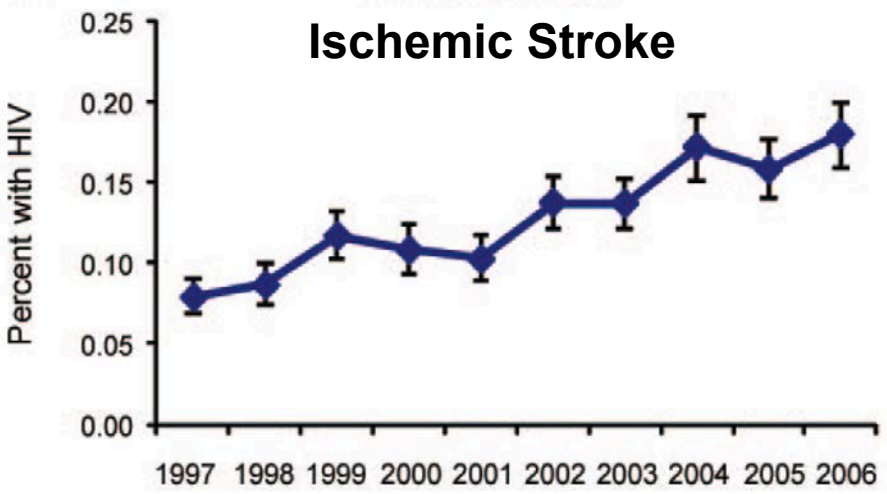
Freiberg et al, JAMA Intern Med. 2013;173(8):614-622

Stroke Risk is Also Higher in HIV+ Adults



- Using a hospital database of 9,664,892 people, US stroke hospitalizations declined 7% while **stroke hospitalizations with HIV rose 60%**

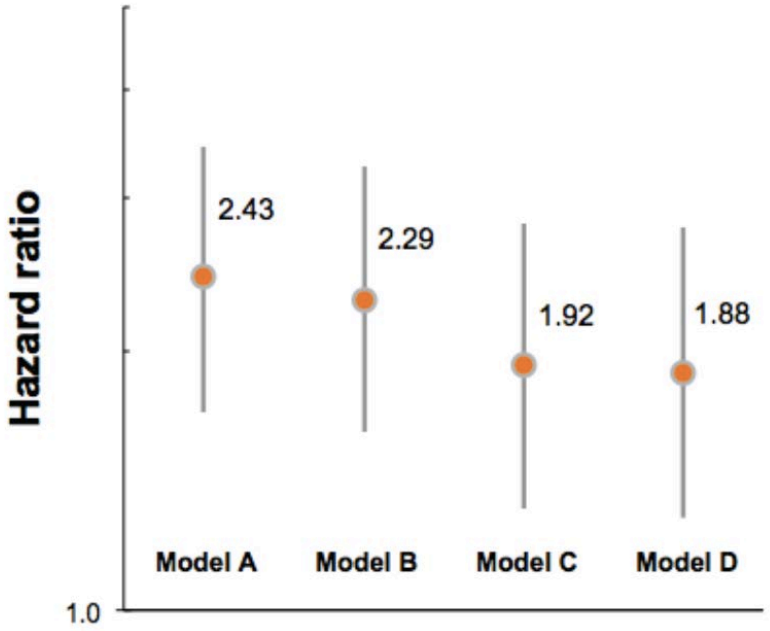
Ovbiagele, et al. Neurology 2011;76:444–450

Variable	HR	p Value
Age	1.06	< 0.001
Atrial fibrillation	3.15	0.01
NNRTI Use	0.38	0.006
HIV RNA	1.10	0.001
CNS Infection or Malignancy	2.75	0.01

- 4,308 people with HIV and 32,423 people without HIV
- **Incidence rate of ischemic stroke was 40% higher in people with HIV**
  - HIV: 5.27 per 1,000 PY
  - Non-HIV: 3.75 per 1,000 PY

Chow, et al. JAIDS 2012; 60:351–358

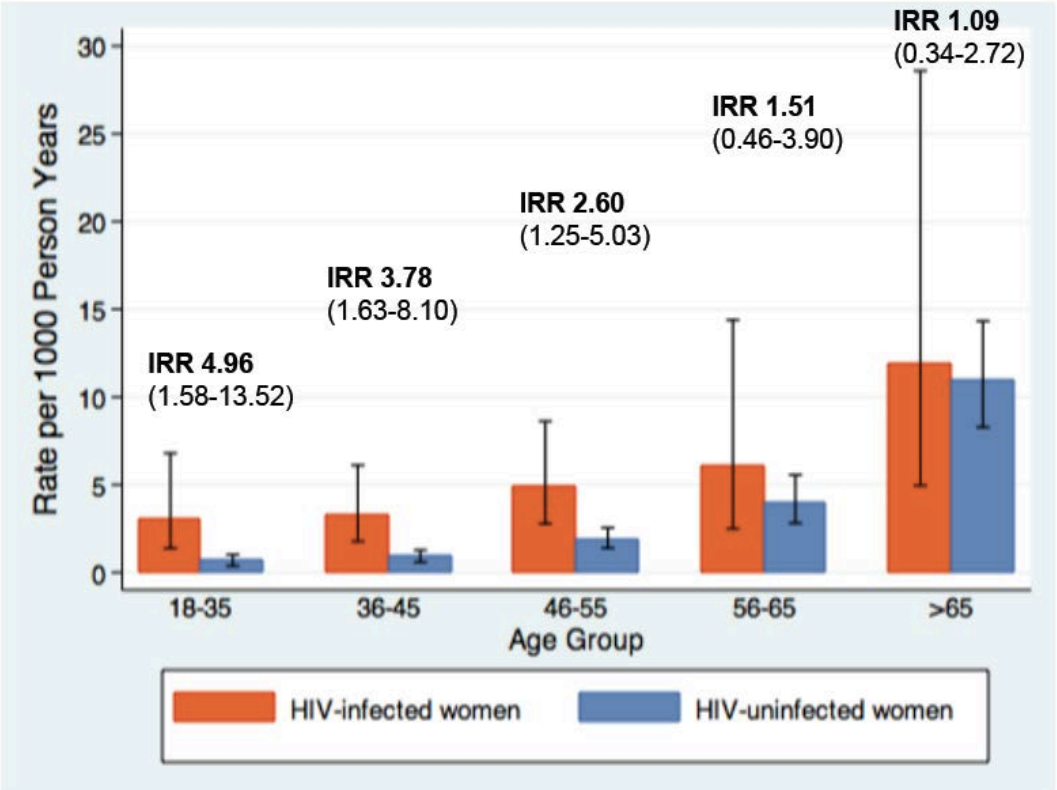
Persistently Increased Ischemic Stroke Risk in HIV-Infected Women



Model A: Unadjusted
Model B: Demographics
Model C: +Traditional Risk Factors
Model D: +Sex-specific Risk Factors

1,212 HIV+, 12,040 HIV- women

All	HIV-infected	HIV-uninfected	Incidence rate ratio (95% CI)
2.09	4.36	1.86	2.34 (1.60-3.35)



Chow et al, CROI 2016, Abstract 638

Mechanisms of Premature Aging May Differ Between Women and Men

- **Estrogen has neuroprotective effects so its loss may increase neuronal vulnerability**
  - Wallace et al, Synapse 2006, 59: 51-60
  - Dye et al, International Journal of Alzheimer's Disease 2012, doi:10.1155/2012/258454
- **Insulin resistance linked to cognitive impairment in women**
  - Gerena et al, PLoS ONE 2012; 7(5): e37358
- **Lower antioxidants in women**
  - Kraft-Terry et al, Proteomics Clin. Appl. 2010, 4, 706–714
- **Women more likely to have altered iron metabolism, which can affect the CNS**

Women May Have Different Exposure of Some Antiretrovirals Than Men

- **Reviews of ART pharmacokinetics indicate that women can have higher drug exposure**
- **Difference exists for:**
  - **Zidovudine**
  - **Lamivudine**
  - **Ritonavir-Boosted PIs**
- **Mixed data for non-nucleoside RTIs**

- Body weight and composition, blood and organ volumes (e.g. bone mass)
- Absorption, intestinal motility and secretions
- Transport and distribution
- Protein binding and tissue affinity
- Metabolism: phase I (hydrolysis, reduction, oxidation, cyclization, decyclization)
- Metabolism: phase II (conjugation)
- Excretion (glomerular filtration rate, renal clearance)
- Intracellular metabolism
- Activity of drug transporters
- Differential (hormone-mediated) gene expression

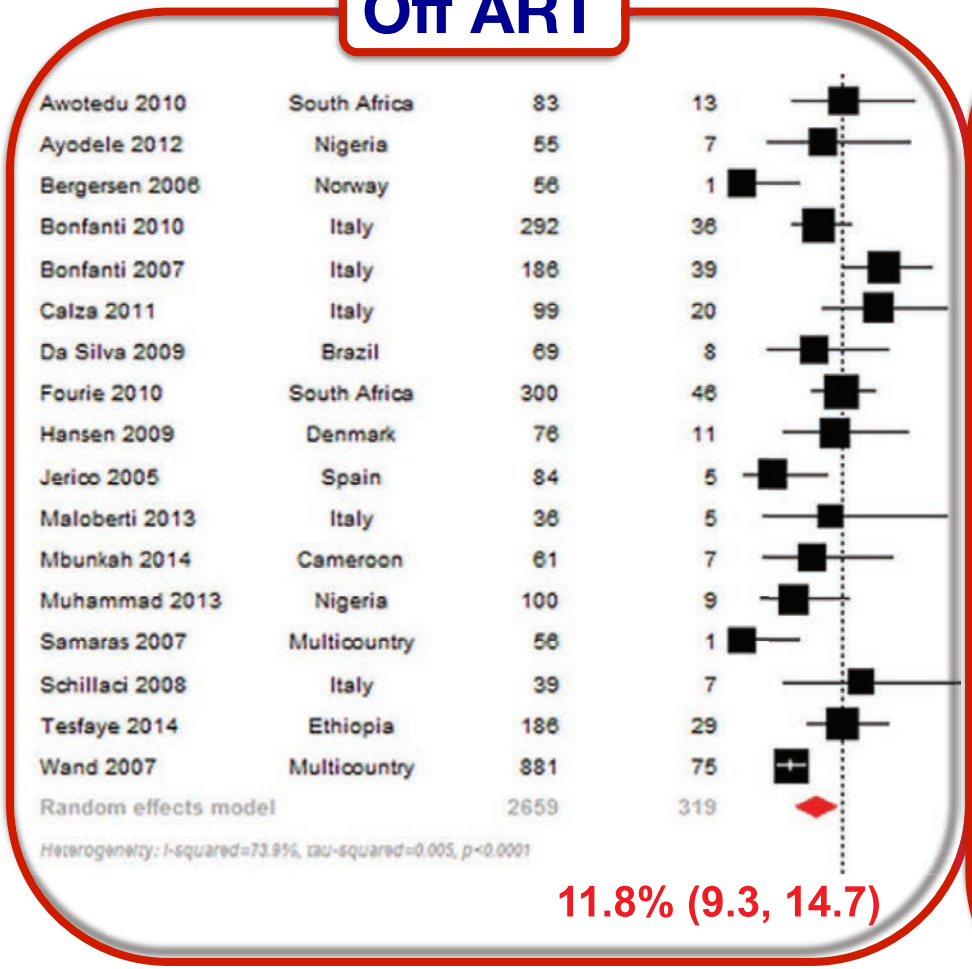
Effect modifiers:

- Adherence
- Diet and nutritional factors
- Nutritional status
- Concomitant treatments
- Hormonal environment
- Reproductive status
- Smoking

Floridia et al, Pharmacological Research 2008, 58:173–182
Ofotokun et al, Gender Medicine, 4(2):106-

Meta-Analysis of Prevalence of Metabolic Syndrome in HIV

Off ART

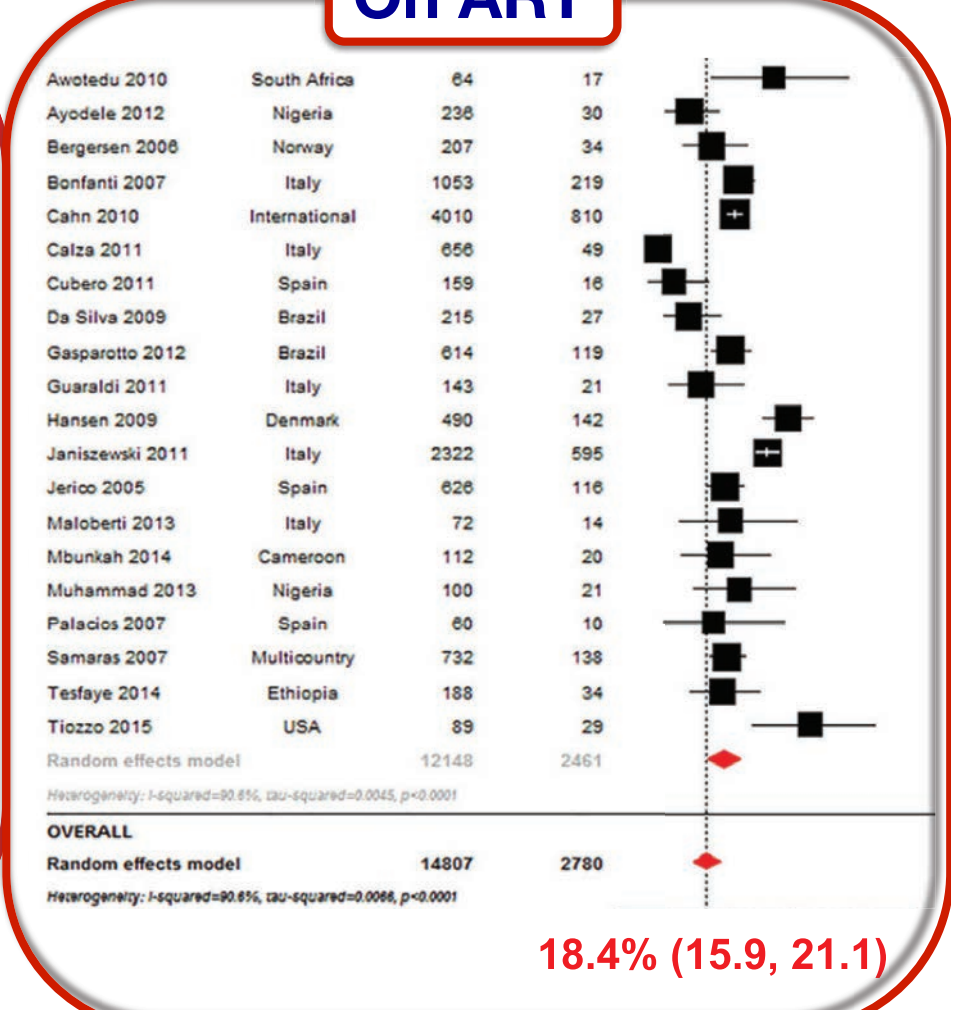


Awotedu 2010	South Africa	83	13
Ayodele 2012	Nigeria	55	7
Bergersen 2006	Norway	56	1
Bonfanti 2010	Italy	292	36
Bonfanti 2007	Italy	186	39
Calza 2011	Italy	99	20
Da Silva 2009	Brazil	69	8
Fourie 2010	South Africa	300	46
Hansen 2009	Denmark	76	11
Jerico 2005	Spain	84	5
Maloberti 2013	Italy	36	5
Mbunkah 2014	Cameroon	61	7
Muhammad 2013	Nigeria	100	9
Samaras 2007	Multicountry	56	1
Schillaci 2008	Italy	39	7
Tesfaye 2014	Ethiopia	186	29
Wand 2007	Multicountry	881	75
Random effects model		2659	319

Heterogeneity: I-squared=73.9%, tau-squared=0.005, p<0.0001

11.8% (9.3, 14.7)

On ART



Awotedu 2010	South Africa	64	17
Ayodele 2012	Nigeria	236	30
Bergersen 2006	Norway	207	34
Bonfanti 2007	Italy	1053	219
Cahn 2010	International	4010	810
Calza 2011	Italy	656	49
Cubero 2011	Spain	159	16
Da Silva 2009	Brazil	215	27
Gasparotto 2012	Brazil	614	119
Guaraldi 2011	Italy	143	21
Hansen 2009	Denmark	490	142
Janiszewski 2011	Italy	2322	595
Jerico 2005	Spain	626	116
Maloberti 2013	Italy	72	14
Mbunkah 2014	Cameroon	112	20
Muhammad 2013	Nigeria	100	21
Palacios 2007	Spain	60	10
Samaras 2007	Multicountry	732	138
Tesfaye 2014	Ethiopia	188	34
Tiozzo 2015	USA	89	29
Random effects model		12148	2461

Heterogeneity: I-squared=90.6%, tau-squared=0.0045, p<0.0001

OVERALL		
Random effects model	**14807**	**2780**

Heterogeneity: I-squared=90.6%, tau-squared=0.0068, p<0.0001

18.4% (15.9, 21.1)

Overall prevalence varied by definition:
16.7% - 31.3%

Nguyen et al, PLOS ONE 2016, 11(3):e0150970

Metabolic and Vascular Disease Increase Risk for Neurocognitive Impairment

CHARTER

	Risk	OR	p
AIDS	Yes	49.6	0.01
Diabetes	Yes	17.6	0.07
Waist circumference	Larger	1.3	0.001
Triglycerides	Lower	0.32	0.09
BMI	Smaller	0.69	0.04

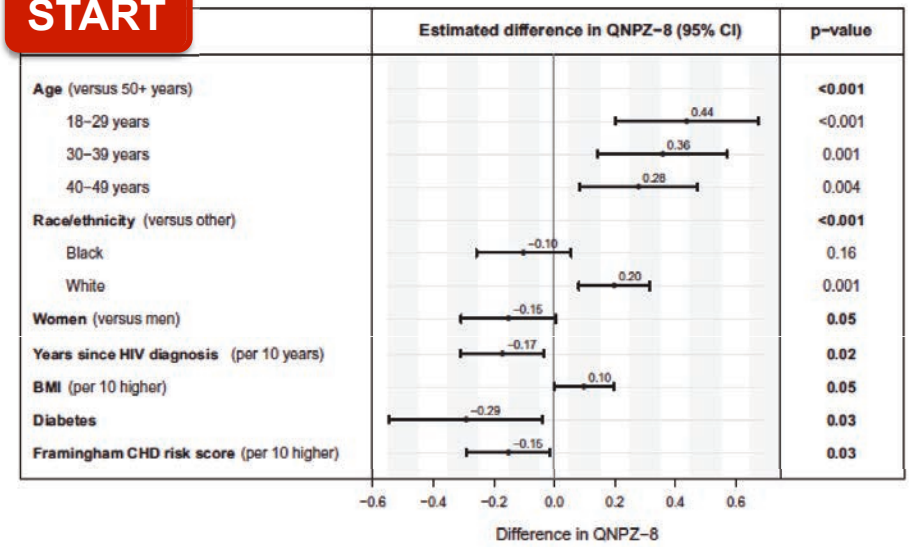
McCutchan et al. Neurology 2012. 78: 485

SMART

	Risk	OR	p
Prior CVD	Yes	6.2	0.01
Total cholesterol	Higher	1.1	0.06
AIDS	No	0.41	0.08
Race	Black	2.2	0.08

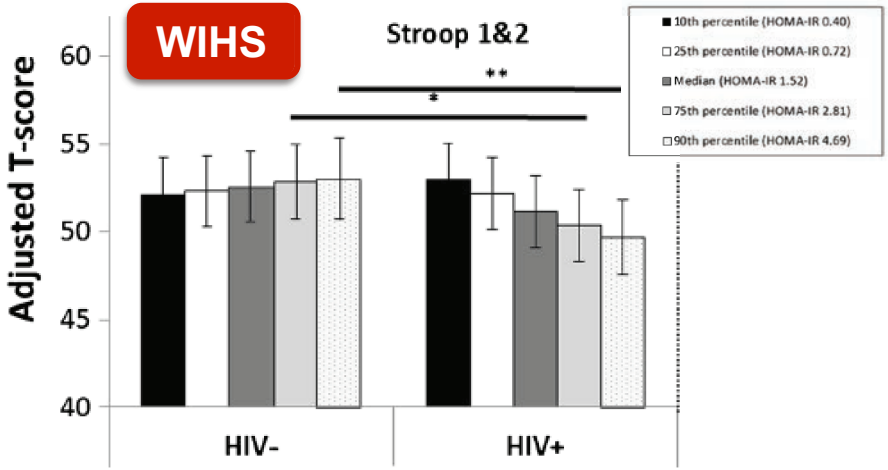
Wright et al. Neurology 2010; 75: 864

START



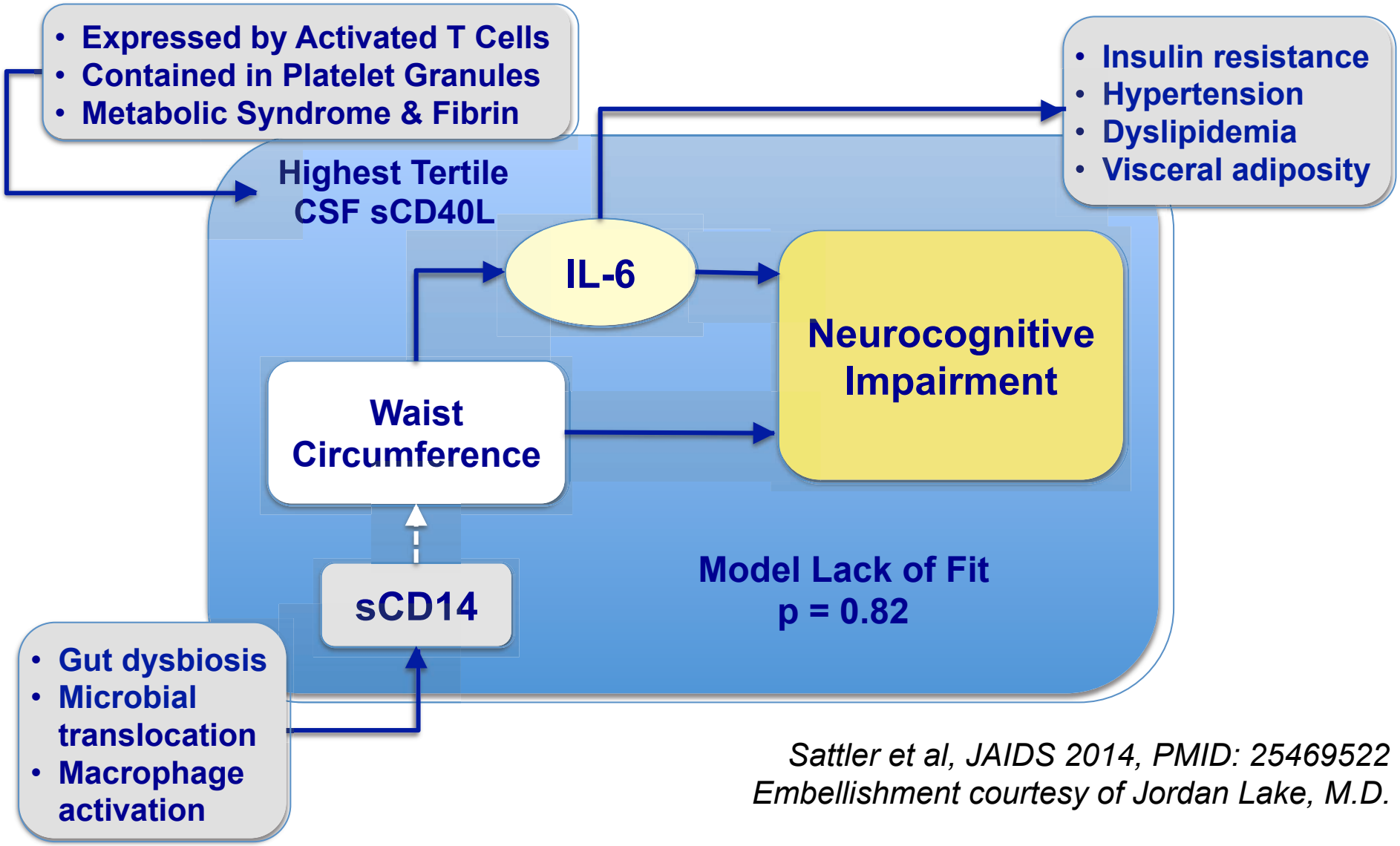
Wright et al, HIV Medicine 2015, 16 (S1), 97–108

WIHS

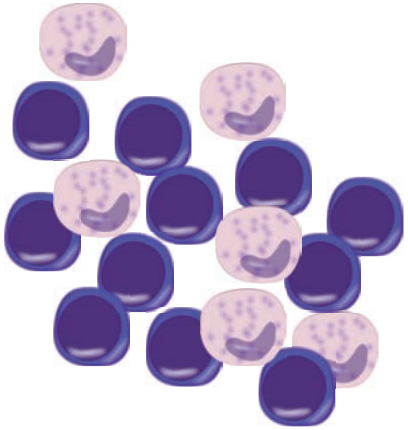


Valcour et al, J. Neurovirol. 2015, 21:415–421

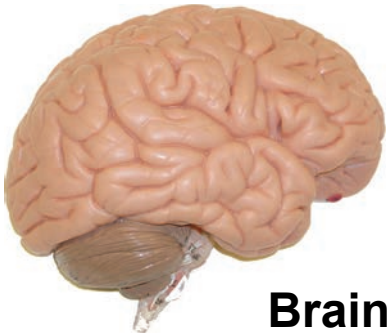
Path Analysis of Risk for Neurocognitive Impairment



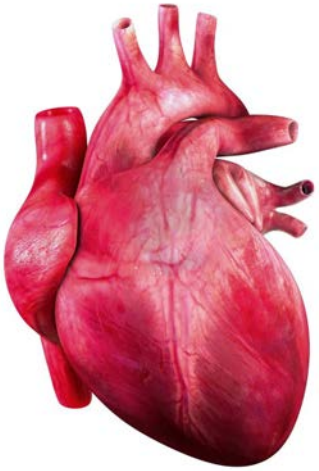
Sattler et al, JAIDS 2014, PMID: 25469522
Embellishment courtesy of Jordan Lake, M.D.



Persistent
Inflammation

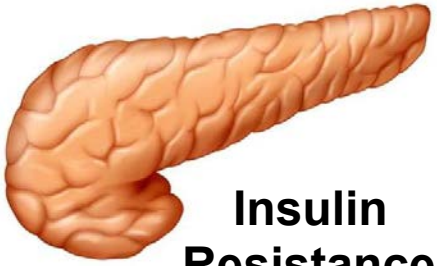


Brain
Disease

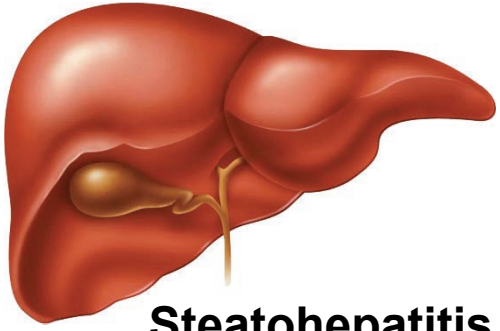


Vascular
Disease

Dyslipidemia
Visceral Fat

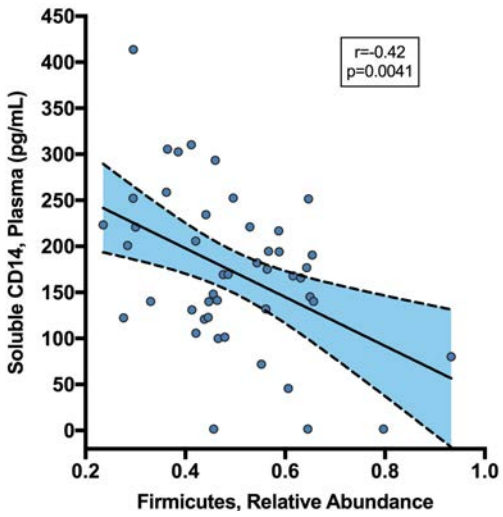


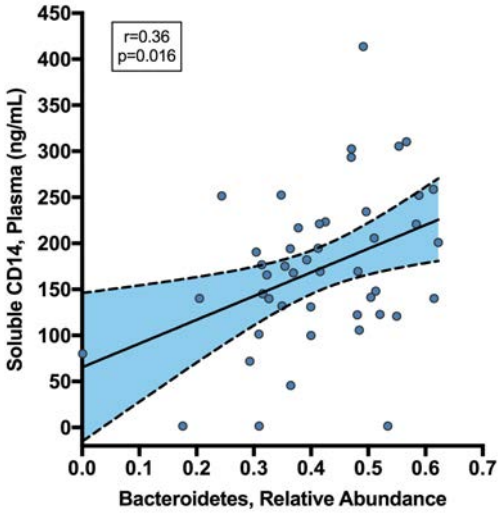
Insulin
Resistance

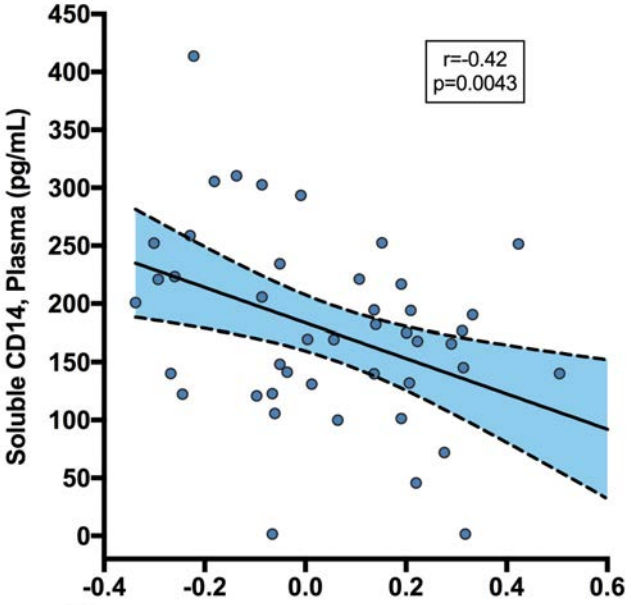


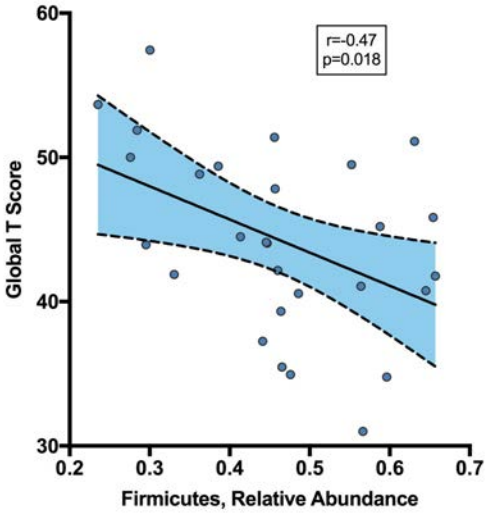
Steatohepatitis
Liver Fibrosis

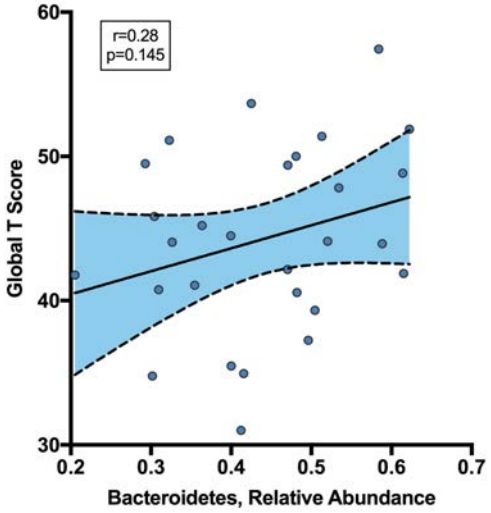
Gut Microbiome, sCD14, and HAND

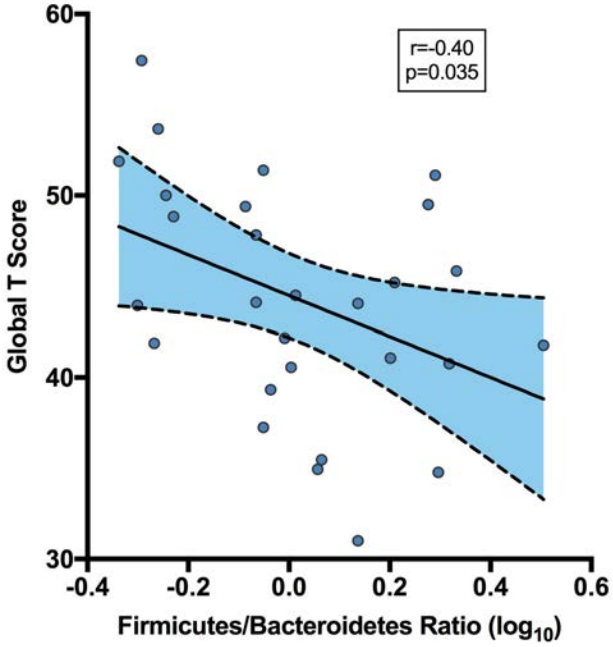








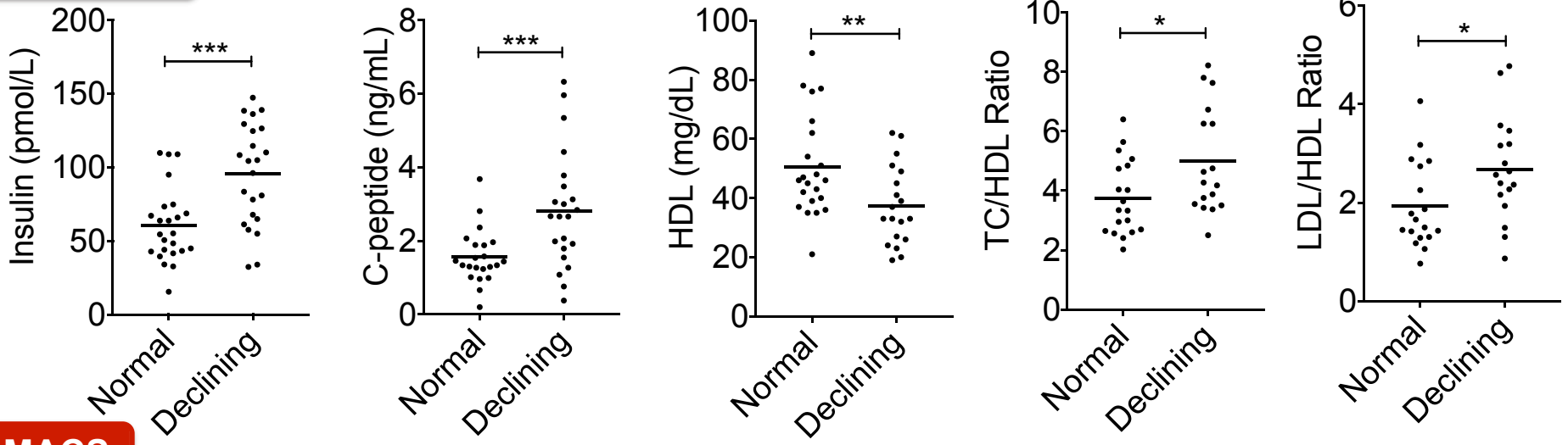




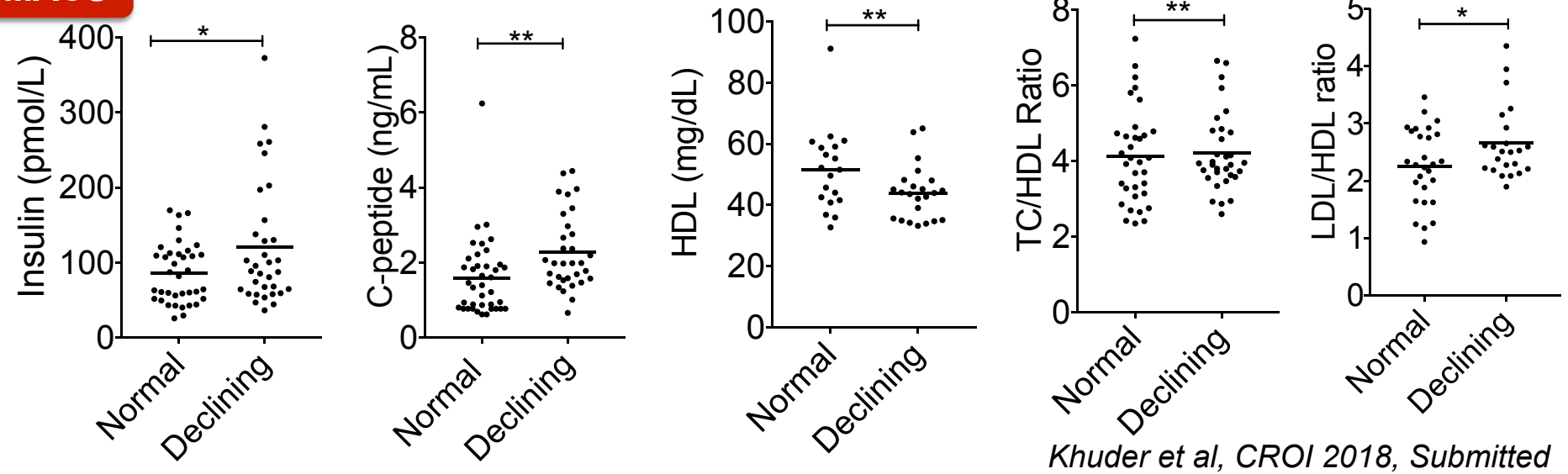
Perez Santiago et al, CROI 2017, Abstract 390

Neurocognitive Decline Associated with Evidence of Insulin Resistance

CHARTER

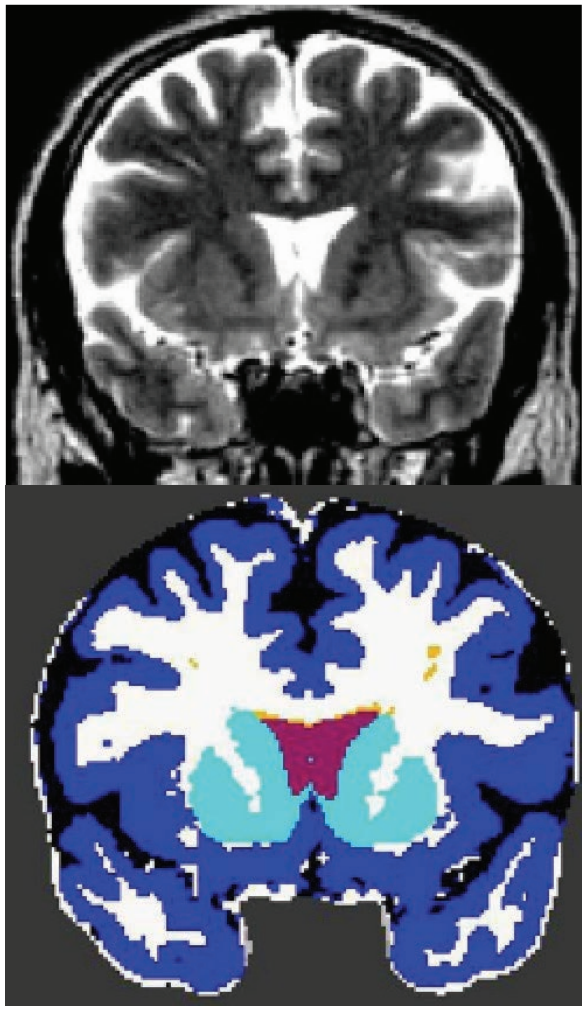


MACS

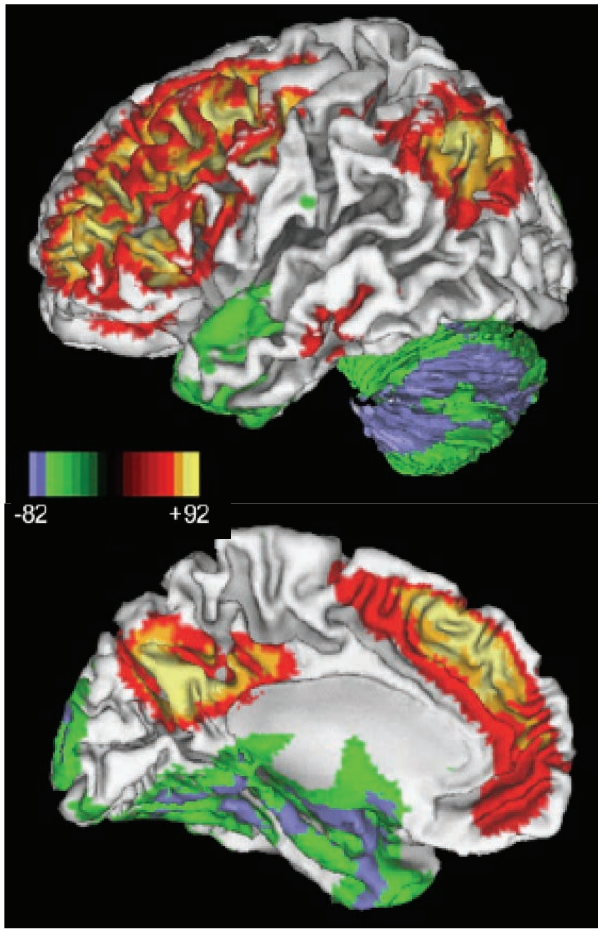


Khuder et al, CROI 2018, Submitted

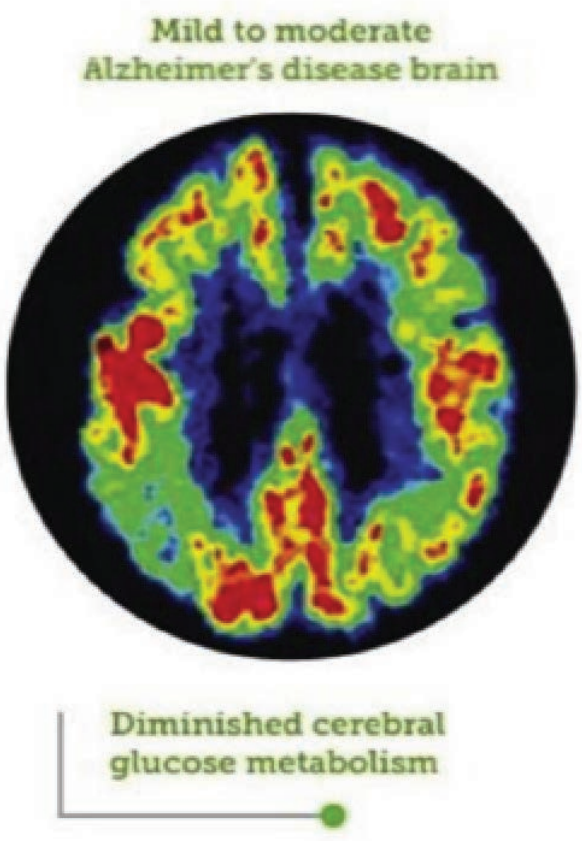
White Matter Abnormalities and Glucose Metabolism



Archibald et al, J. Neurovirol. 2014 20: 603–611

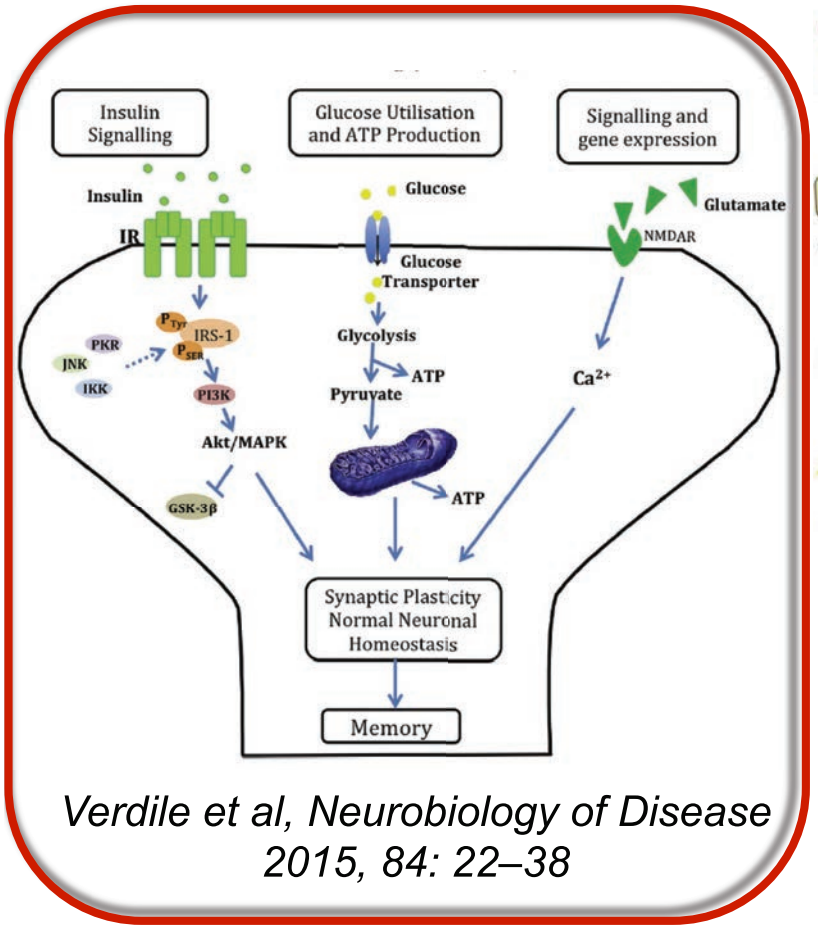


Vaishnavi et al, PNAS 2010; 107(41): 17757–17762

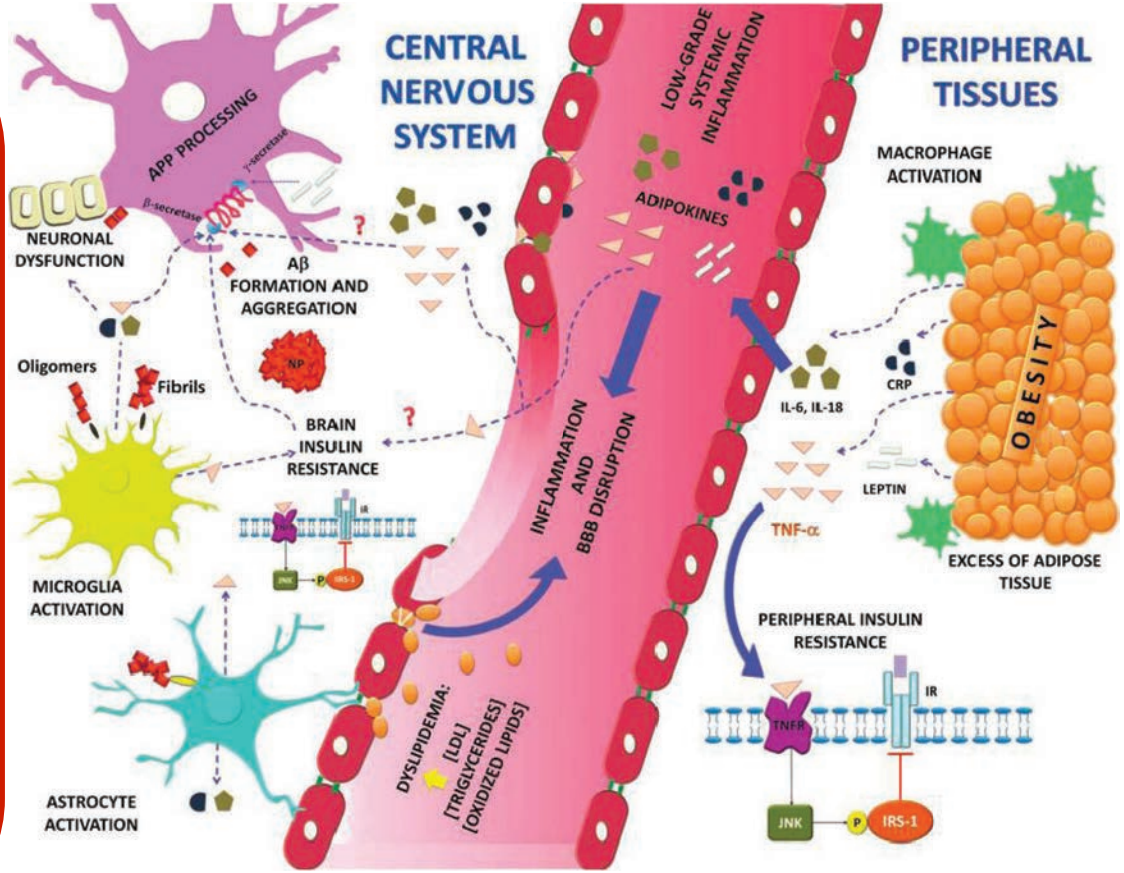


Non et al, Translational Research 2017;183:41–56

Interactions Between Insulin Resistance, Amyloid, & Neurodegeneration

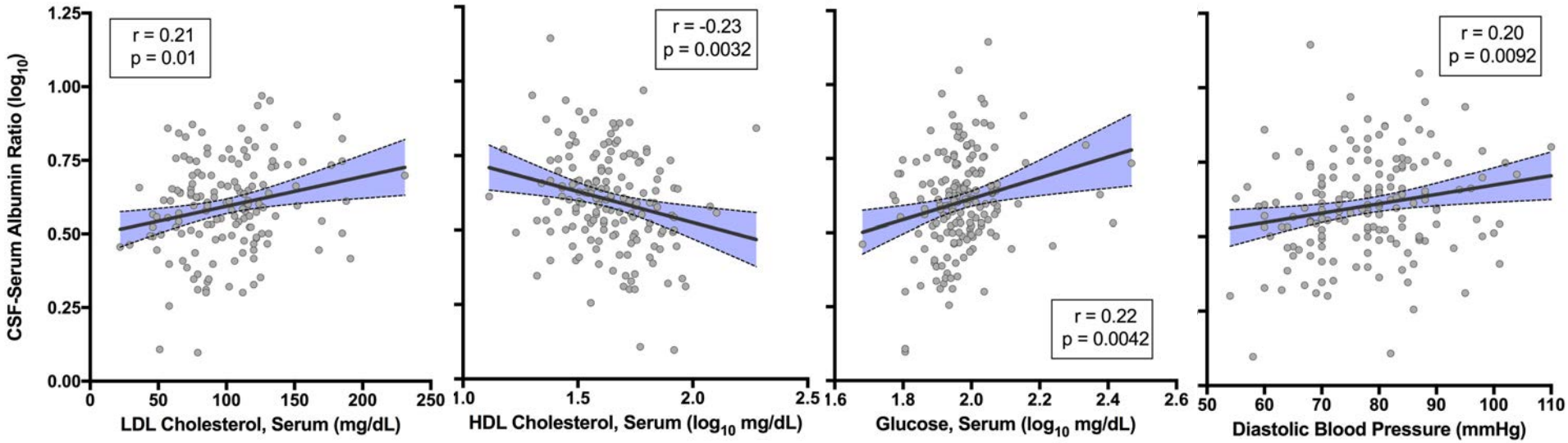


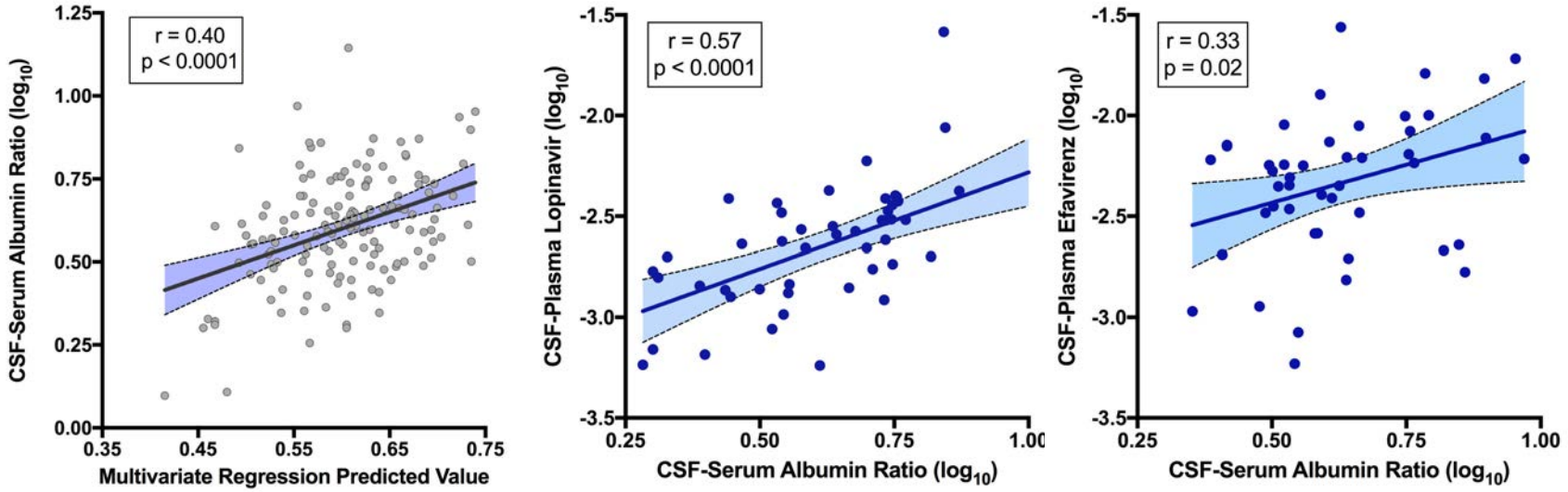
Verdile et al, Neurobiology of Disease 2015, 84: 22–38



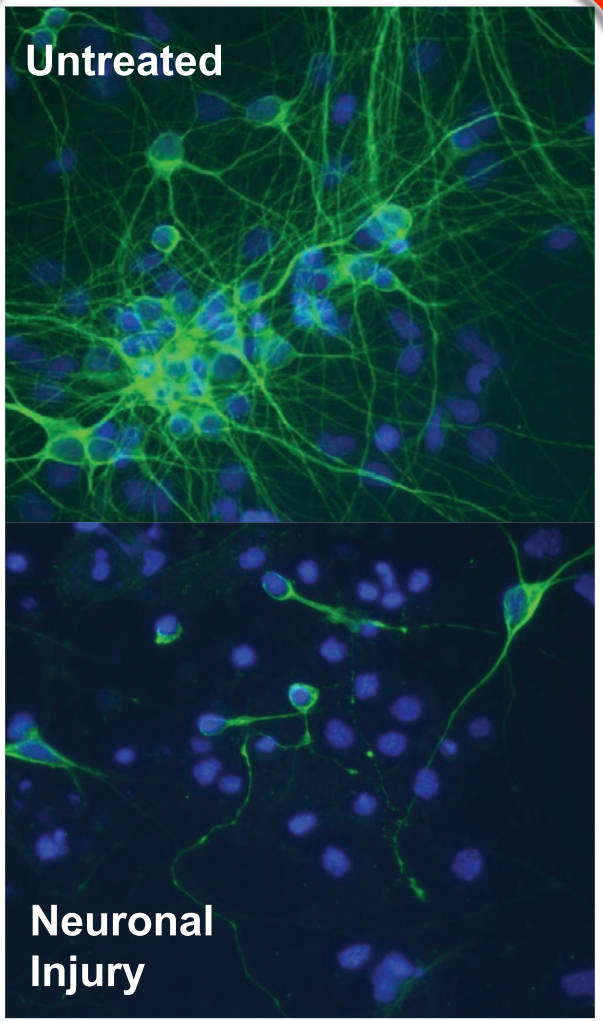
Campos Peña et al, Antioxidants & Redox Signaling 2017, 26 (10): 542-60

Metabolic Syndrome Components Influence BBB Permeability

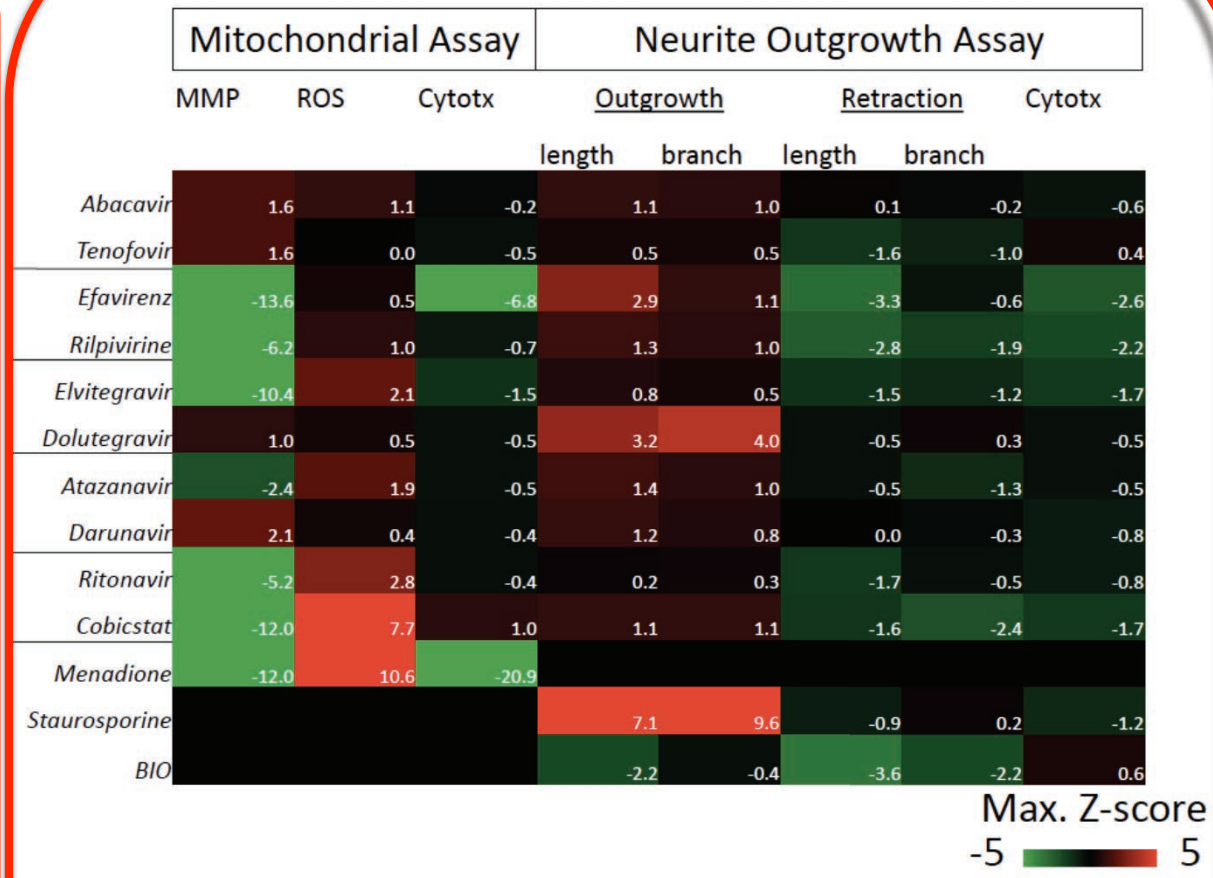




Higher Concentrations of ART Drugs Can Injure Neurons *in vitro*



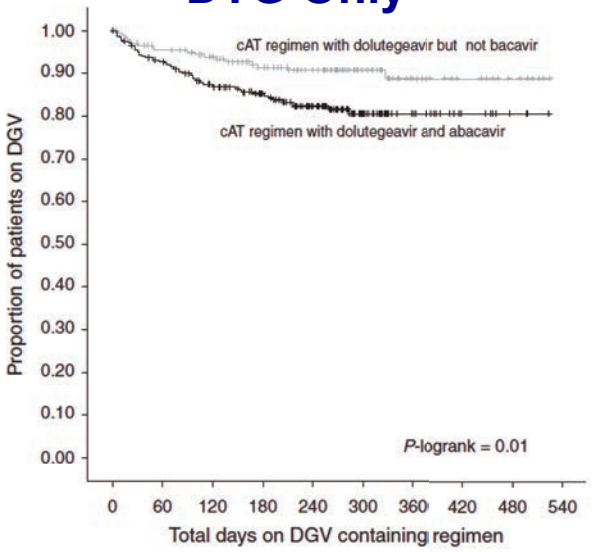
Robertson et al, J Neurovirol 2012, 18: 388-299



Hinckley et al, CROI 2016, Abstract 395

DTG and CNS Adverse Events

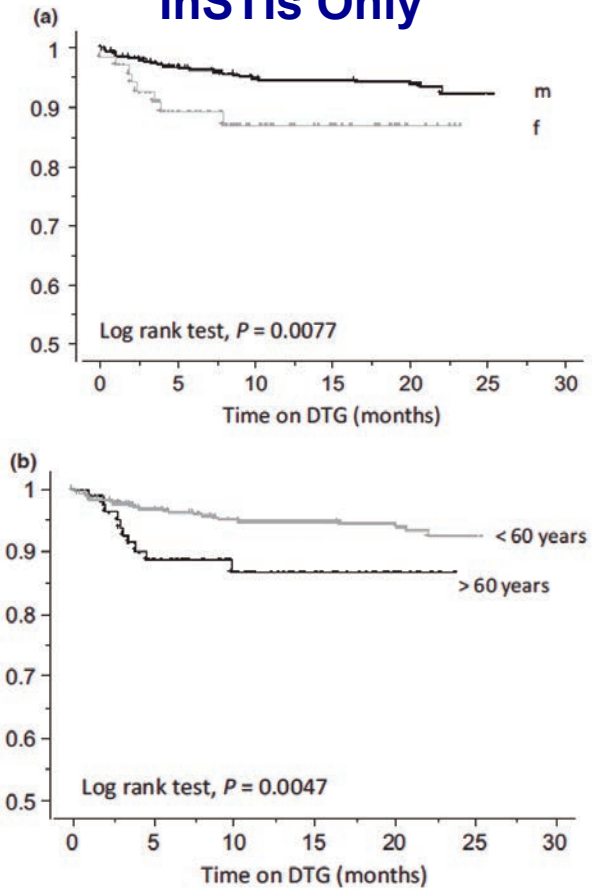
N=565
DTG Only



Adverse drug reaction	*n* (%)
Sleep disturbance, insomnia	31 (5.6)
Gastrointestinal complaints	21 (3.8)
Joint, tendon and/or muscle pain	11 (2.0)
Psychological/psychiatric symptoms[b]	14 (2.5)
Neurologic symptoms	10 (1.8)
General malaise (headache and severe fatigue)	24 (4.3)
Respiratory tract complaints	5 (0.9)
Other	9 (1.6)

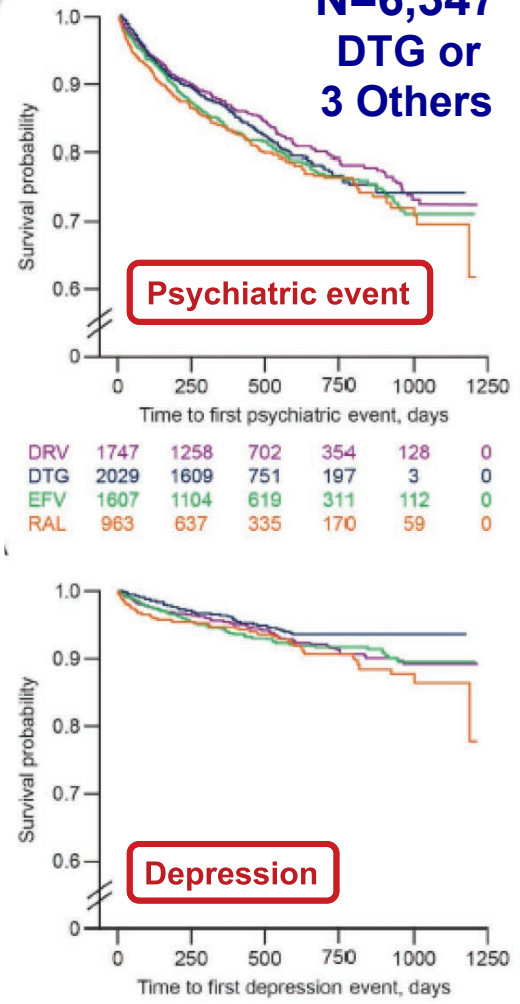
de Boer et al, AIDS 2016, 30:2831–2834

N=1,950
InSTIs Only



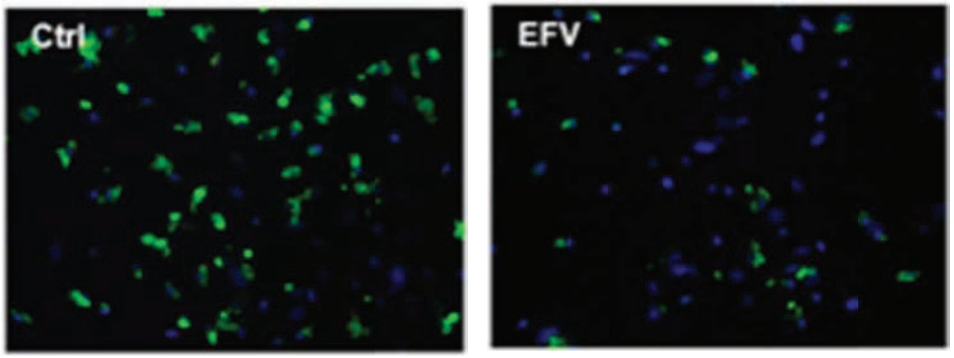
Hoffmann et al, HIV Medicine 2017, 18, 56--63

N=6,347
DTG or 3 Others

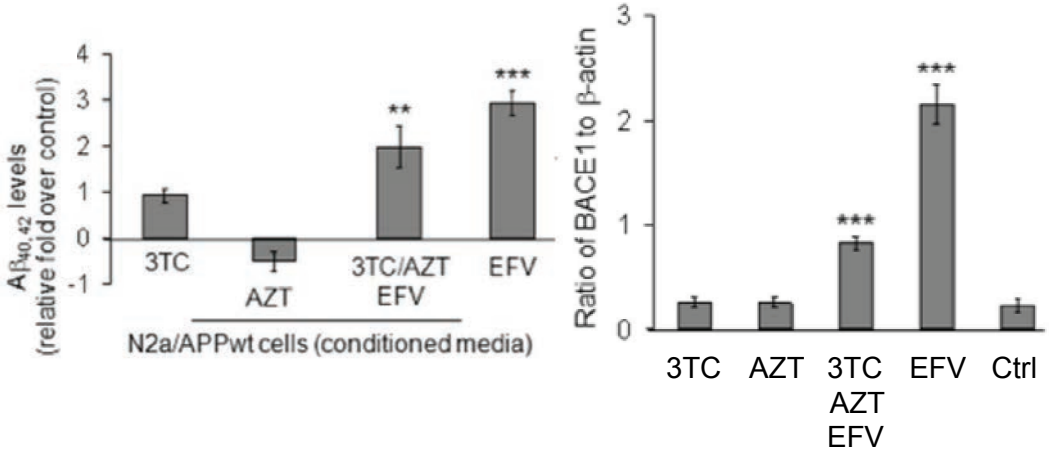


Fettiplace et al, J AIDS 2017;74:423–431

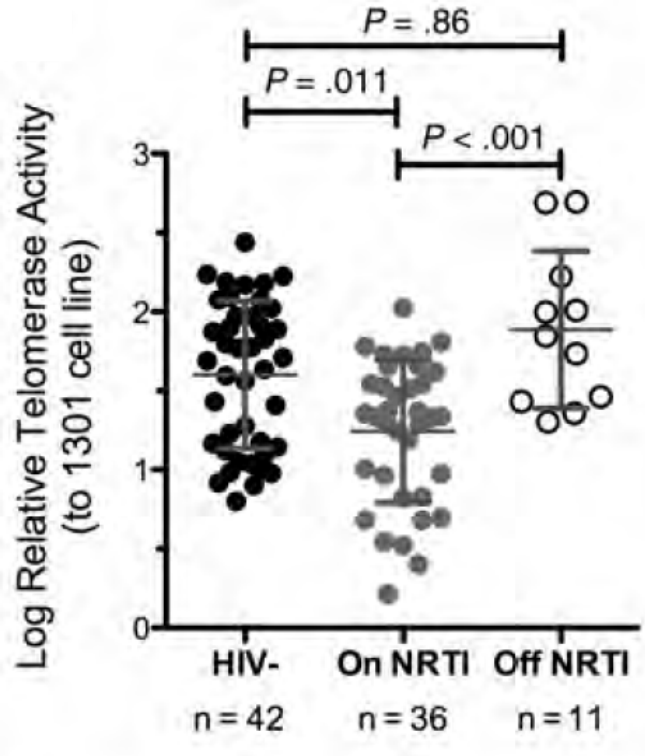
ART Drugs May Alter Other Aging-Related Biological Processes



EFV Reduces Microglial Phagocytosis of $A\beta_{1-42}$

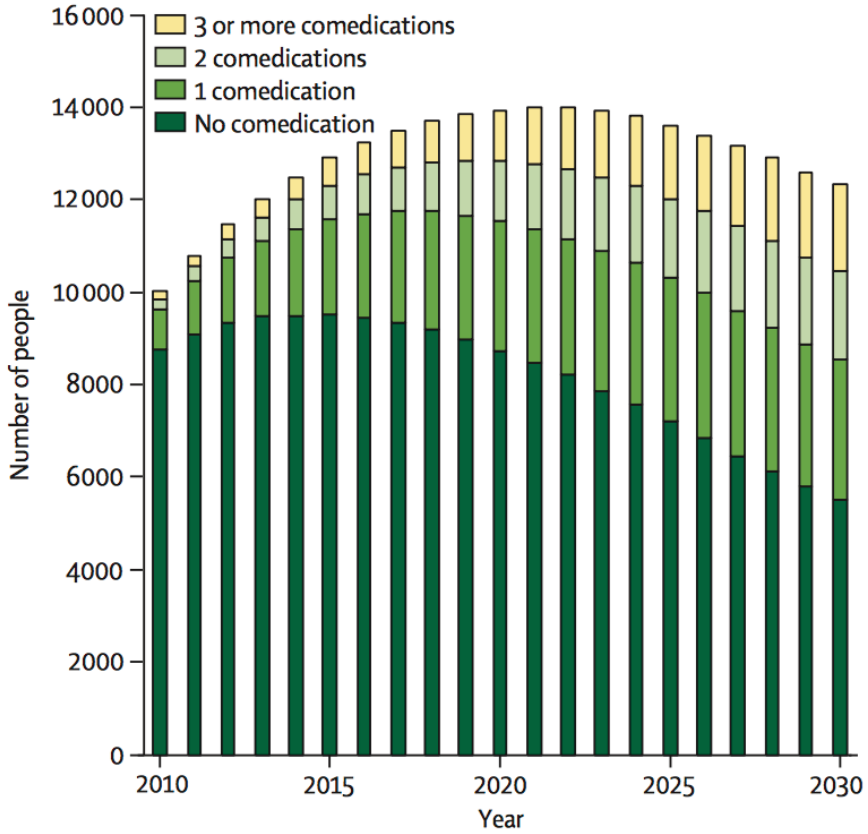


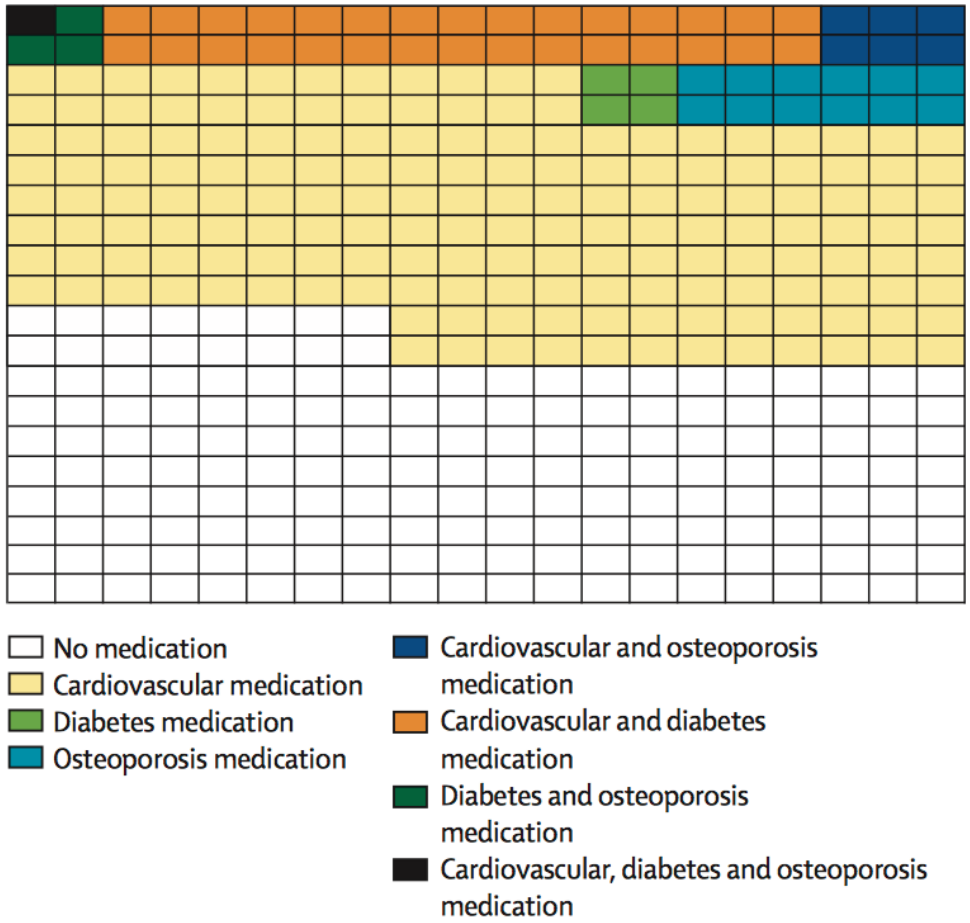
Brown et al, PLoS ONE 2014, 9(4): e95500



Leeansyah et al, J Infect Dis 2013; 207:1157

Increasing Polypharmacy in Aging HIV+ Adults





Smit, Lancet Inf Dis 2015, 15(7):810-8

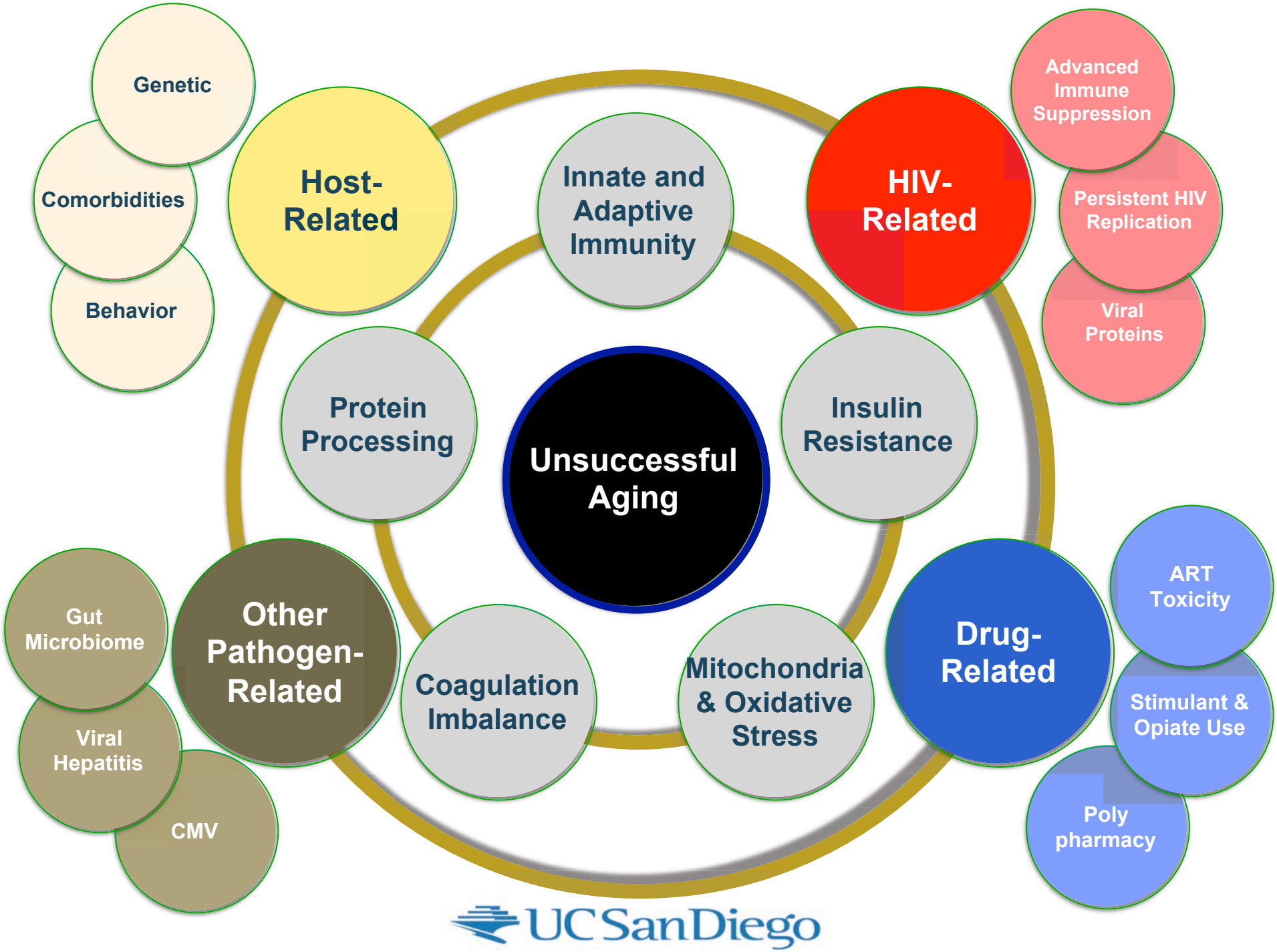
Concomitant Medications May Also Influence Risk for Metabolic Syndrome

Metabolic variable	MAP	TG[a]	DM
SGA	0.28*** (0.08, 0.49)	0.28** (0.06, 0.50)	2.28*** (1.29, 4.02)
Age[b]	0.11*** (0.04, 0.19)		1.62*** (1.30, 2.03)
Male	0.28*** (0.13, 0.44)	0.28*** (0.12, 0.44)	
Ethnicity[c]			
White	−0.26*** (−0.40, −0.12)	0.36*** (0.22, 0.51)	
Hispanic	−0.36*** (−0.55, −0.18)	0.50*** (0.31, 0.69)	
Other	−0.40** (−0.73, −0.06)	0.22 (−0.15, 0.60)	
Hepatitis C virus status			1.97** (1.23, 2.15)
Estimated HIV duration (years)[d]	0.05** (0, 0.10)		
CD4 Nadir[d]		−0.05* (−0.1, 0)	
CD4[e]		0.04*** (0.02, 0.06)	1.06* (1.00, 1.13)
Detectable plasma viral load			
Protease inhibitor-based regimen	−0.18*** (−0.31,−0.06)	0.19*** (0.06, 0.32)	
Lifetime substance dependence diagnosis			

SGA = Second generation antipsychotic, BMI = Body mass index, MAP = Mean arterial pressure, TG = Triglycerides, DM = Diabetes mellitus

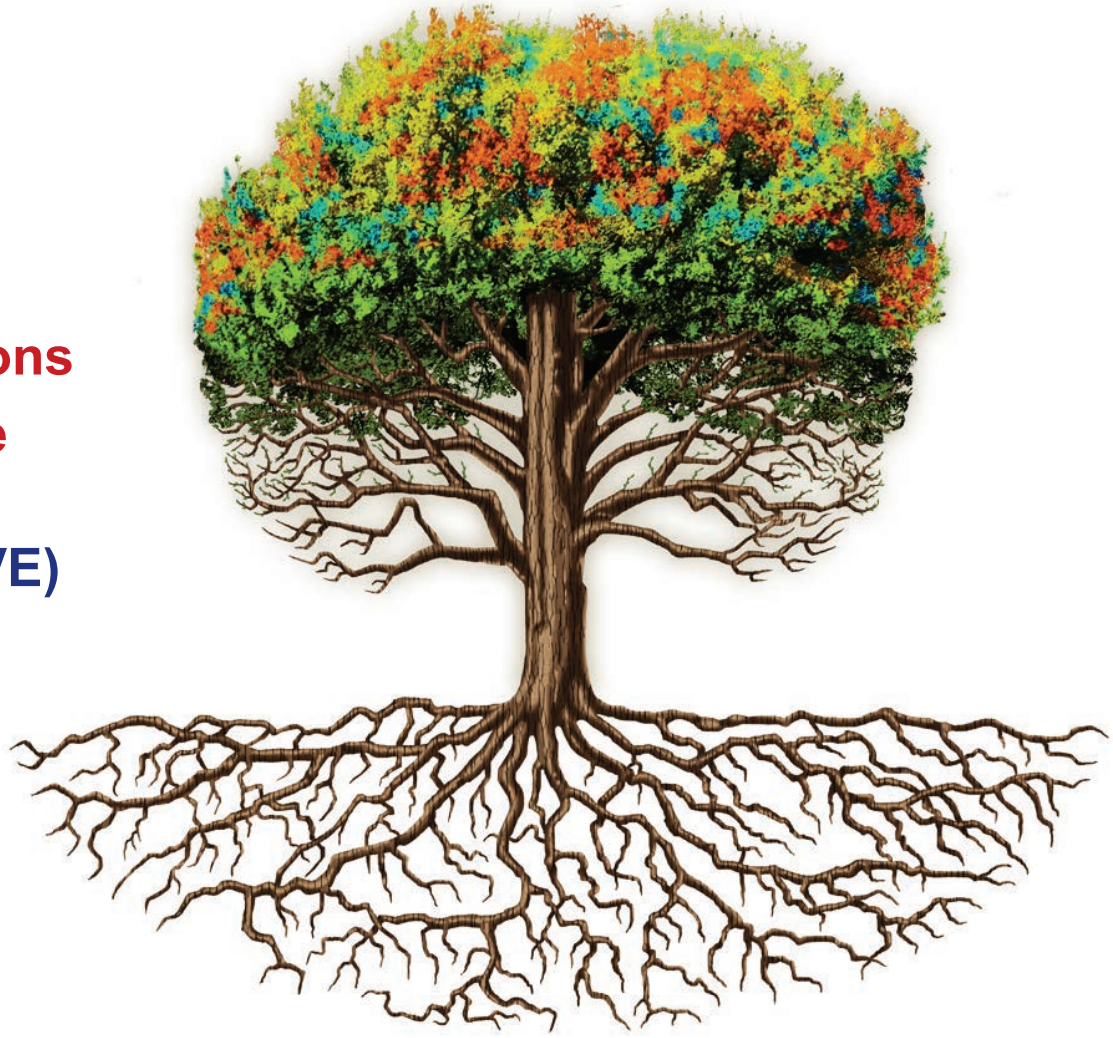
* $p < 0.10$, ** $p < 0.05$, ***$p < 0.01$

Ferrara et al, Psychiatry Research 2014, 218: 201–208


Genetic
Comorbidities
Behavior
Host-Related
Innate and Adaptive Immunity
HIV-Related
Advanced Immune Suppression
Persistent HIV Replication
Viral Proteins
Protein Processing
Unsuccessful Aging
Insulin Resistance
Gut Microbiome
Viral Hepatitis
CMV
Other Pathogen-Related
Coagulation Imbalance
Mitochondria & Oxidative Stress
Drug-Related
ART Toxicity
Stimulant & Opiate Use
Poly pharmacy
UC San Diego

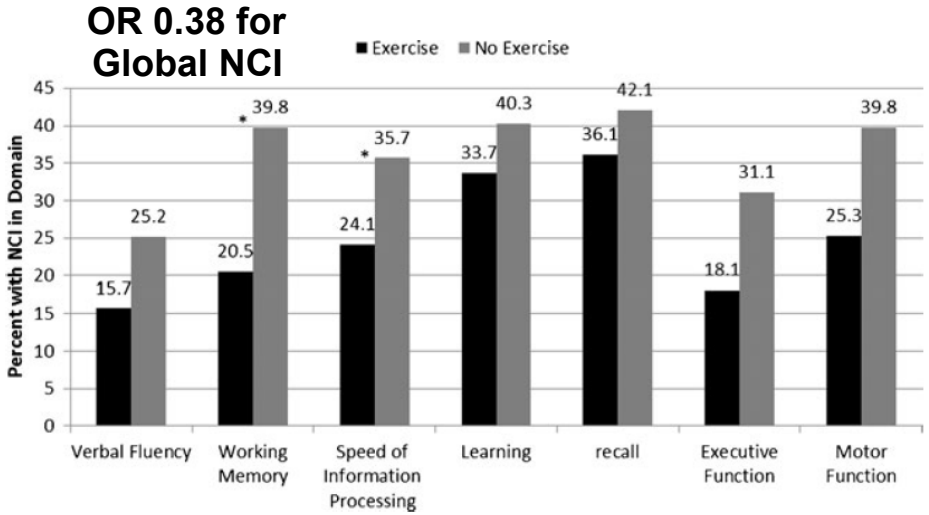
Possible Interventions

- "Lifestyle" modification
  - Exercise, Weight loss
  - Smoking Cessation
  - Moderate Alcohol Use
  - Alter Microbiome
- Modify Existing Medications
- Target components of the metabolic syndrome
  - Pitavastatin (REPRIEVE)
  - Metformin
- Treat coinfections
  - HCV
- Adjunctive therapy
  - Tesamorelin
  - Intranasal insulin
  - Intranasal IGF-1



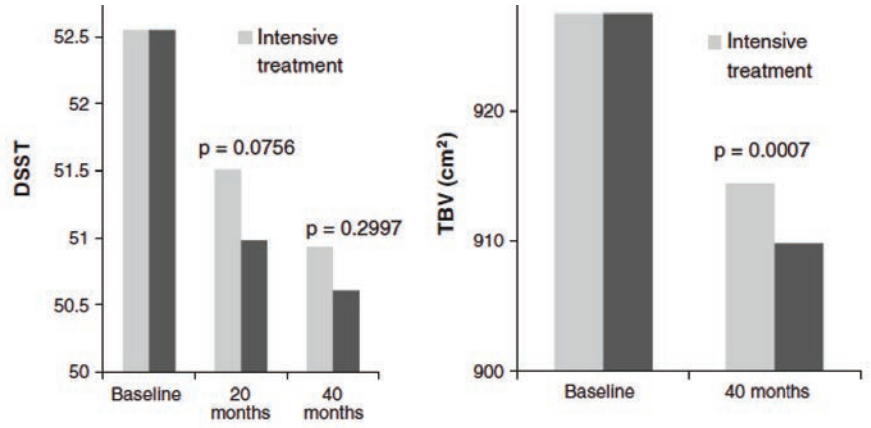
Graphic courtesy of Peter Hunt, UCSF (and ulead.org)

Benefits of Exercise, Diabetes Management, & Probiotics

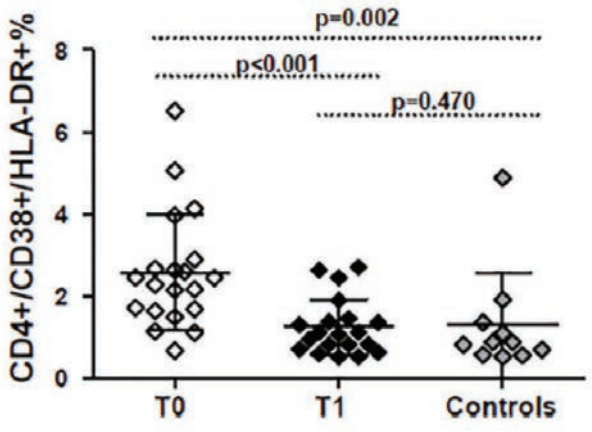


Dufour et al, J Neurovirol 2013, 19(5):410-7

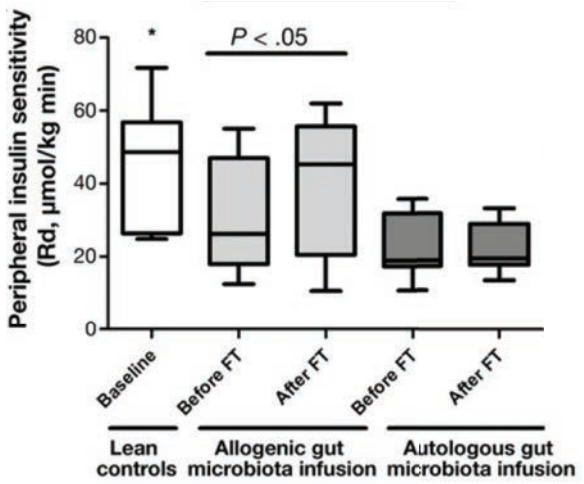
DSST = Digit Symbol Substitution Test
TBV = Total Brain Volume



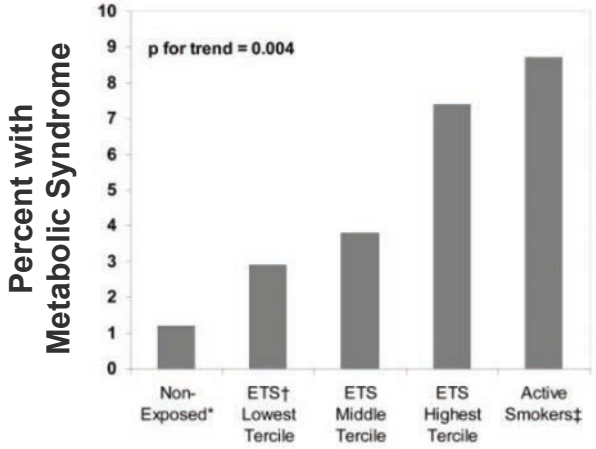
Bornstein et al, Neurol Sci (2014) 35:995–1001



d'Ettorre et al, PLoS ONE 2015, 10(9): e0137200



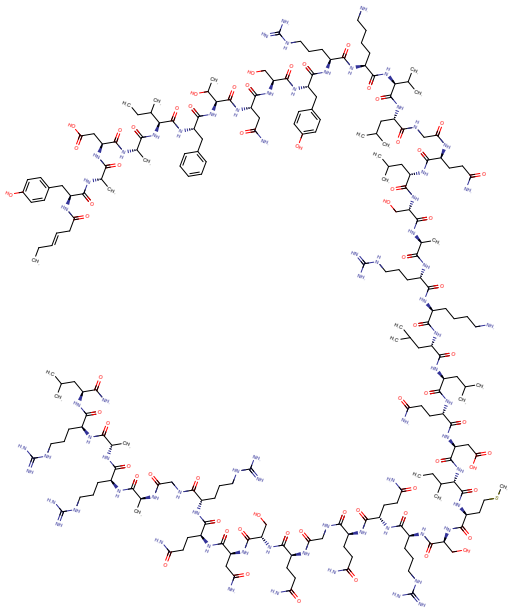
Vrieze et al, Gastroenterology 2012;143:913–916

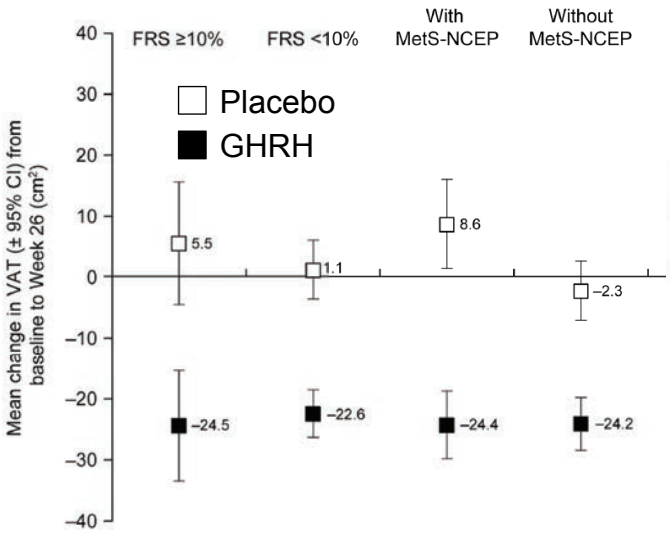


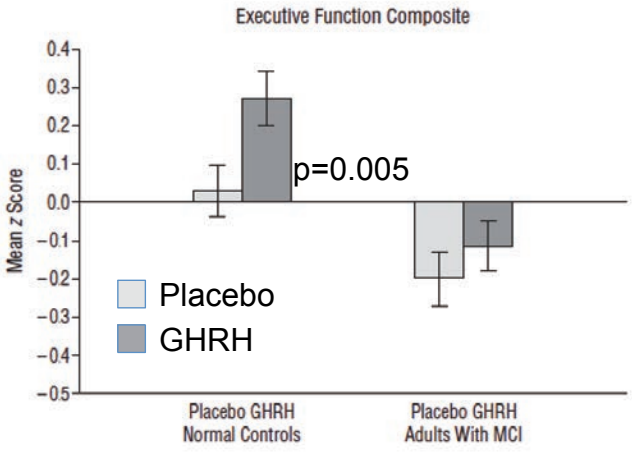
Weitzman et al, Circulation. 2005;112:862-869

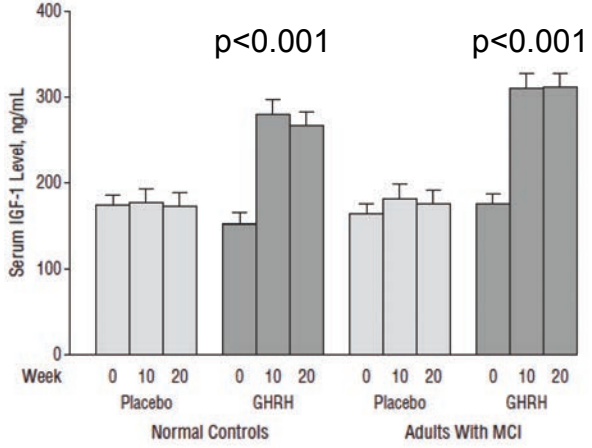
Tesamorelin

- **Synthetic growth hormone releasing factor analogue (GHRH) that stimulates in the pituitary production and pulsatile release of endogenous GH, which also stimulates IGF-1 production**
- **Selectively reduces visceral fat, intima media thickness and triglycerides, and improves cognitive function in older persons**



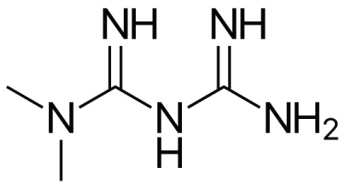






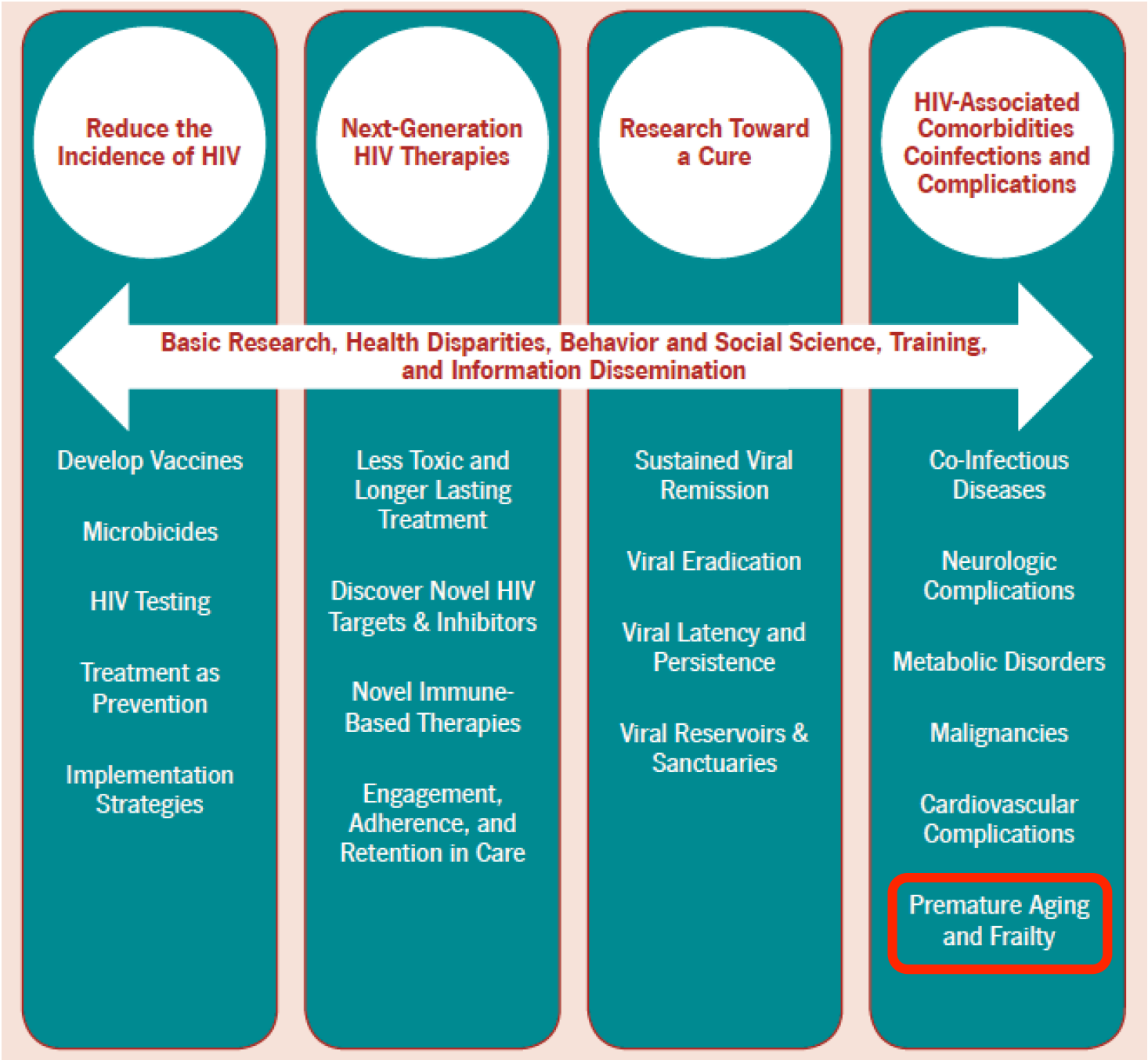
Mangili et al, PLoS ONE 2015, 10(10): e0140358
Baker et al, Arch Neurol. 2012;69(11):1420-1429
Sattler F. Best Practice & Research Clinical Endocrinology & Metabolism 27 (2013) 541–555

Metformin



- **Oral biguanide that has multiple effects on IR:**
  - Activates AMPK in liver, brain, and other tissues
  - Decreases hepatic gluconeogenesis production
  - Decreases intestinal absorption of glucose, increases peripheral glucose uptake, and reduces weight
- **Improves endothelial function**
- **Neurologic effects:**
  - Reduces BACE1 activity and amyloid β production
  - Antioxidant and anti-inflammatory effects in brain
  - May reduce acetylcholinesterase activity
  - May promote tau dephosphorylation
- **May also improve gut dysbiosis**

Lake & Currier, Lancet Infect Dis 2013; 13: 964–75
G. Verdile et al., Neurobiology of Disease 84 (2015) 22–38
Markowicz-Piasecka et al, Pharm Res, 2017, DOI 10.1007/s11095-017-2199-y


Reduce the Incidence of HIV
Next-Generation HIV Therapies
Research Toward a Cure
HIV-Associated Comorbidities Coinfections and Complications
Basic Research, Health Disparities, Behavior and Social Science, Training, and Information Dissemination
Develop Vaccines
Microbicides
HIV Testing
Treatment as Prevention
Implementation Strategies
Less Toxic and Longer Lasting Treatment
Discover Novel HIV Targets & Inhibitors
Novel Immune-Based Therapies
Engagement, Adherence, and Retention in Care
Sustained Viral Remission
Viral Eradication
Viral Latency and Persistence
Viral Reservoirs & Sanctuaries
Co-Infectious Diseases
Neurologic Complications
Metabolic Disorders
Malignancies
Cardiovascular Complications
Premature Aging and Frailty

Questions Guiding Future Research

- **Is premature aging a biological condition or an artifact of study design?**
  - Is evidence of premature aging from cross-sectional studies confirmed in longitudinal ones?
- **Is there a unifying hypothesis of the pathogenesis of premature aging?**
  - Immune senescence/inflammation, microbiome, coinfections, coagulation, genetic
  - Is it due to HIV, associated conditions, or both?
- **What are the best methods for assessing aging?**
  - Successful aging, Frailty, Multimorbidity, Quality of life
  - Ecological momentary assessment
  - Biological indicators of aging
  - NP testing, mood, imaging, CSF biomarkers

Questions Guiding Future Research

- **What are the best approaches for managing premature aging in the clinic?**
  - **Antiretroviral therapy**
  - **Treatment of multimorbid conditions**
    - **Metabolic syndrome, dyslipidemia, vascular disease, depression, addictive drugs**
  - **Limit polypharmacy**
  - **Nutrition, Microbiome, Exercise, Smoking cessation**
- **What support structures do aging people living with HIV require?**
  - **Case managers, Housing, Healthcare, Social**

Funding Opportunities

- **PAR-17-321: Multidisciplinary Studies of HIV-AIDS and Aging (R01)**
- Encourages applications at the intersection of HIV and aging by addressing two overarching objectives:
  1) To improve understanding of ***biological, clinical, and sociobehavioral aspects*** of aging through the lens of HIV infection and its treatment;
  2) To improve approaches for ***testing, prevention, and treatment of HIV infection, and management of HIV-related comorbidities, co-infections, and complications*** in different populations and cultural settings by applying our current understanding of aging science

Funding Opportunities

- **PAR-17-321: Multidisciplinary Studies of HIV-AIDS and Aging (R01)**
- Encourages applications with the following characteristics:

  1) Clinical orientation
  2) Focus on aging or the aged
  3) Attention to geriatric outcomes
  4) Leveraging existing resource where possible
  5) Selection of appropriate controls
  6) Characterization of phenotypes

Funding Opportunities

- **PA-17-088: Secondary Analyses of Existing Cohorts, Data Sets, and Stored Biospecimens to Address Clinical Aging Research Questions (R01)**
- Invites applications to address clinically related issues on aging changes influencing health across the lifespan, or on diseases and disabilities in older persons.
  - Use of cohorts that are linked to electronic health record systems or Centers for Medicare and Medicaid Services (CMS) administrative data are ***especially welcome***.

Funding Opportunities

- **PA-17-088: Secondary Analyses of Existing Cohorts, Data Sets, and Stored Biospecimens to Address Clinical Aging Research Questions (R01)**
- … to address clinically related issues on aging…:
  - –Will support activities addressing specific hypotheses in clinical aging research or to inform the design and implementation of future epidemiologic or human intervention studies, or current geriatric practice in maintenance of health, management of disease, and prevention of disability.
  - –Existing data sets may also be used to develop and test new analytical approaches.
  - –Costs for archiving of data to be made publicly available and those associated with data harmonization or assay refinement/validation may be included in the budget…

Funding Opportunities

- **RFA-AG-023: Pathogenesis of Age-Related HIV Neurodegeneration (R01)**
- **Due 9 February 2018**
- Encourages basic and clinical research to study the molecular and cellular mechanisms underpinning neurodegenerative diseases, particularly Alzheimer's disease, and neurological disorders associated with HIV infection and AIDS.
  - –Particularly encourages research to explore the causal role of Alzheimer's and other related proteinopathies in HIV+ older adults.
  - –Envisages cross-disciplinary, multi-PI, and integrative approaches. It will encourage development of both animal and human research to study whether, and how, different neuropathological processes interact with one another, as well as to understand how these interactions lead to neurodegeneration

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NIH

- …Mental Health
- …Drug Abuse
- …Allergy and Infectious Diseases

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