HIV and AGING

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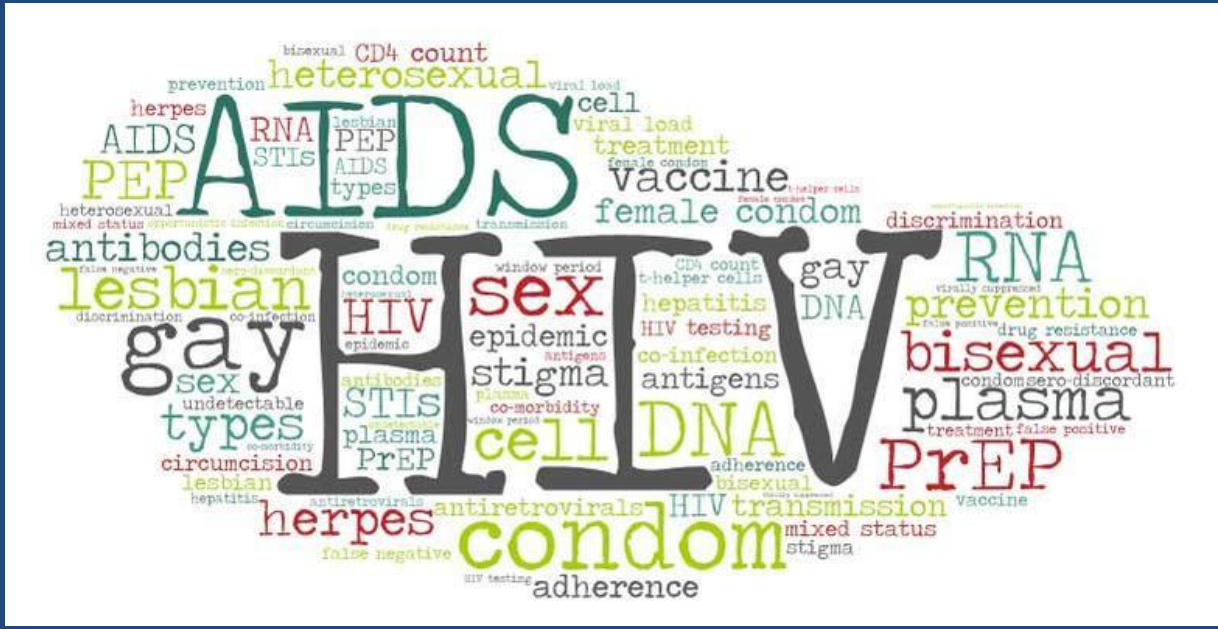
Disclosures

- I have no financial relationships to disclose.
- I will not discuss off-label and/or investigational medication use in my presentation.

Objectives

- Review and update HIV treatment
- Review aging in the general population
- Describe current prevalence of HIV among the senior population
- Discuss issues associated with treating older individuals with HIV infection

HIV

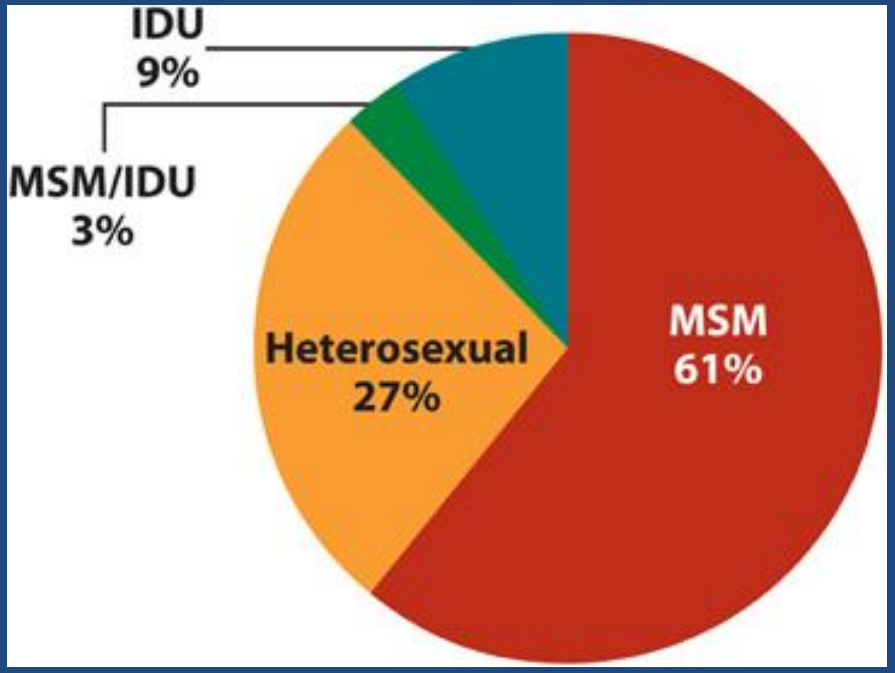

HIV
AIDS
sex
condom
gay
lesbian
antibodies
PEP
heterosexual
herpes
CD4 count
prevention
RNA
cell
viral load
treatment
vaccine
female condom
discrimination
bisexual
plasma
PrEP
DNA
hepatitis
HIV testing
co-infection
antigens
stigma
epidemic
window period
transmission
mixed status
adherence
antiretrovirals
drug resistance
false positive
false negative
circumcision
undetectable
types
STIs
PrEP
bisexual
vaccine

HIV: Important Terms

- Human Immunodeficiency Virus (HIV)
- Acquired Immune Deficiency Syndrome (AIDS)
- CD4 (T Cell) count
- Viral Load

Transmission

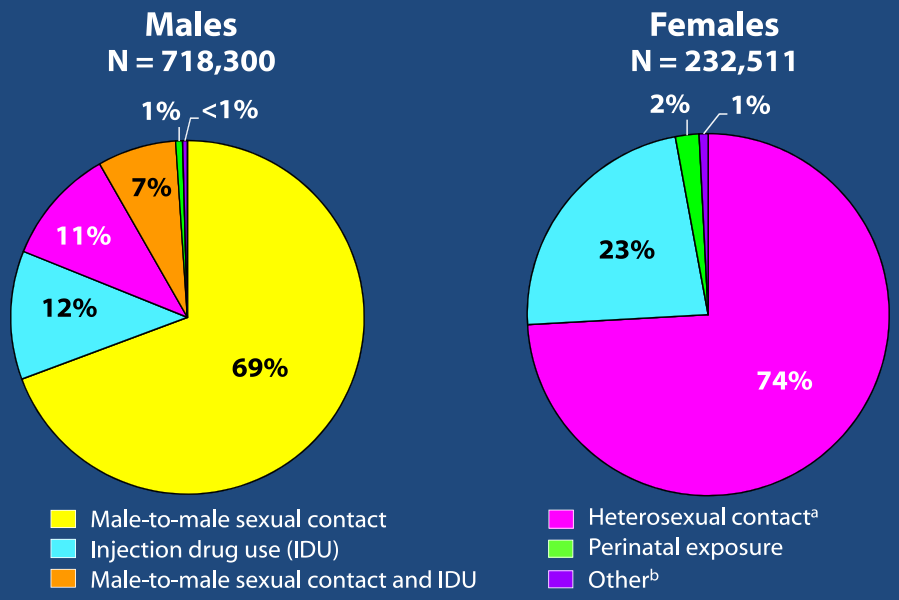
- Occurs via infected body fluids
  - Blood
  - Semen
  - Breast Milk
- Other body fluids have not been implicated in transmission
  - Tears
  - Saliva



http://www.cdc.gov/hiv/group/age/olderamericans/index.html

HIV: The Numbers

- 1.2 million cases of HIV in the U.S.
- ~37,000 new diagnoses each year



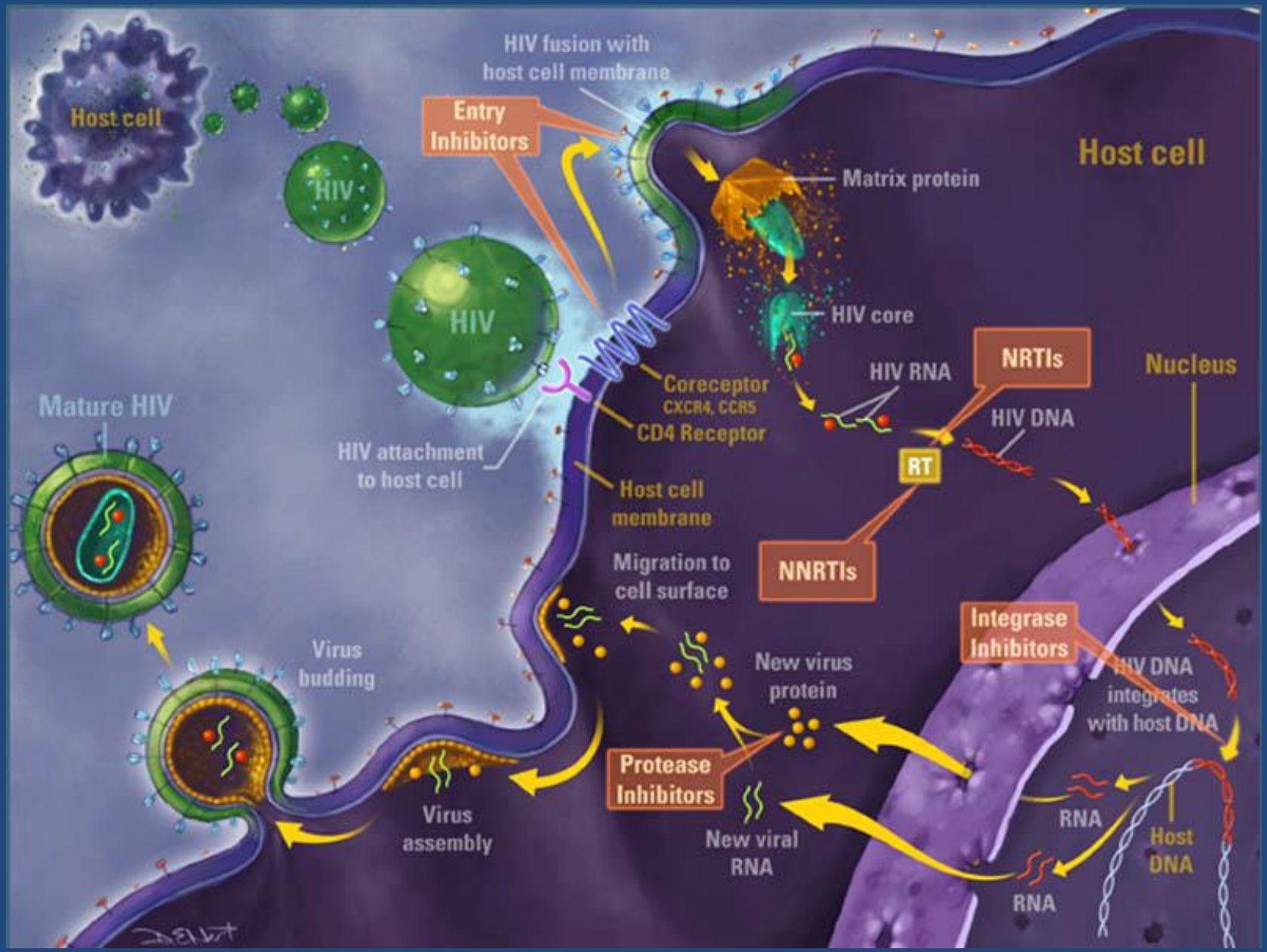
Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays and missing transmission category, but not for incomplete reporting.

[a] Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.

[b] Includes hemophilia, blood transfusion, and risk factor not reported or not identified.

http://www.cdc.gov/hiv/group/age/olderamericans/index.html

HIV Treatment


Host cell
HIV
HIV fusion with host cell membrane
Entry Inhibitors
Host cell
Matrix protein
HIV
HIV core
HIV RNA
NRTIs
Nucleus
Coreceptor CXCR4, CCR5
CD4 Receptor
HIV DNA
Mature HIV
HIV attachment to host cell
RT
Host cell membrane
NNRTIs
Migration to cell surface
Integrase Inhibitors
Virus budding
New virus protein
HIV DNA integrates with host DNA
Protease Inhibitors
Virus assembly
New viral RNA
RNA
Host DNA
RNA

NRTIs

Inhibit HIV reverse transcriptase by competing for incorporation into the still forming HIV DNA causing premature chain termination

- Backbone of antiretroviral therapy
- Renal Dosed (except abacavir)
- Class Side Effects: lactic acidosis and hepatomegaly

Generic	Brand	Abbr.	Dose	Combination Products
Abacavir	Ziagen®	ABC	600mg daily	Epzicom®, Triumeq®, Trizivir®
Tenofovir (TDF)	Viread®	TDF	300mg daily	Truvada®, Stribild®, Atripla®, Complera®
Tenofovir (TAF)	Combo only	TAF	25mg daily	Descovy®, Genvoya®, Odefsy®
Emtricitabine	Emtriva®	FTC	200mg daily	See 2 above cells
Lamivudine	Epivir®	3TC	300mg daily	See abacavir combos
Zidovudine	Retrovir®	AZT	300mg BID	Trizivir®, Combivir®

NNRTIs

Binds to and inhibits enzymatic activity of HIV reverse transcriptase

- Long drug half life
- Low barrier to resistance
- CYP3A4 inducers
- Class Side Effects: rash and hepatitis

Generic	Brand	Abbr	Dose	Combination Products
Efavirenz	Sustiva®	EFV	600mg daily	Atripla®
Nevirapine	Viramune®	NVP	200mg BID	n/a
Rilpivirine	Edurant®	RPV	25mg daily	Odefsy®, Complera®
Etravirine	Intelence®	ETV	200mg BID	n/a

Protease Inhibitors (PIs)

Inhibit protease enzyme preventing the cleavage of immature polyproteins into mature, functional HIV enzymatic and structural proteins

- High barrier to resistance
- Class Side effects: metabolic and GI
- CYP3A4 inhibitors
- Ritonavir used at as a “booster”

Generic	Brand	Abbr	Dose	Combination Products
Darunavir	Prezista®	DRV	800mg daily or 600mg BID	Prezcobix®
Atazanavir	Reyataz®	ATV	300mg daily with booster	Evotaz®
Lopinavir	n/a	LPV	400mg BID	Kaletra®
Ritonavir	Norvir®	RTV or /r	100mg with other PIs	Kaletra®

Integrase Inhibitors

Inhibits integrase enzyme activity preventing the integration of viral DNA into host cell DNA

- Well tolerated
- Few CYP3A4 interactions
- Separate for polyvalent cations
- cobicistat used at as a “booster” for EVG

Generic	Brand	Abbr	Dose	Combination Products
Raltegravir	Isentress®	RAL	400mg BID	n/a
Elvitegravir	Vitekta®	EVG	150mg daily (with booster)	Stribild®, Genvoya®
Dolutegravir	Tivicay®	DTG	50mg daily	Triumeq®
Bictegracir	n/a	BIC	50mg daily	Biktarvy®

Entry Inhibitors

- Maraviroc
  - MOA: CCR5 antagonist
  - Exclusively metabolized by CYP3A4
- Enfuvirtide
  - MOA: Prevents a change in the shape of the membrane protein and fusion of the virus and the CD4 cell membrane
  - Twice daily injection requiring reconstitution
  - Side effect: Injection site reactions

HIV: Goals of Treatment

1. Reduce HIV-associated morbidity and prolong the duration and quality of survival
2. Restore and preserve immunologic function
3. Maximally and durably suppress plasma HIV viral load (VL <50 copies/ml)
4. Prevent HIV transmission

HIV Treatment: The Rules

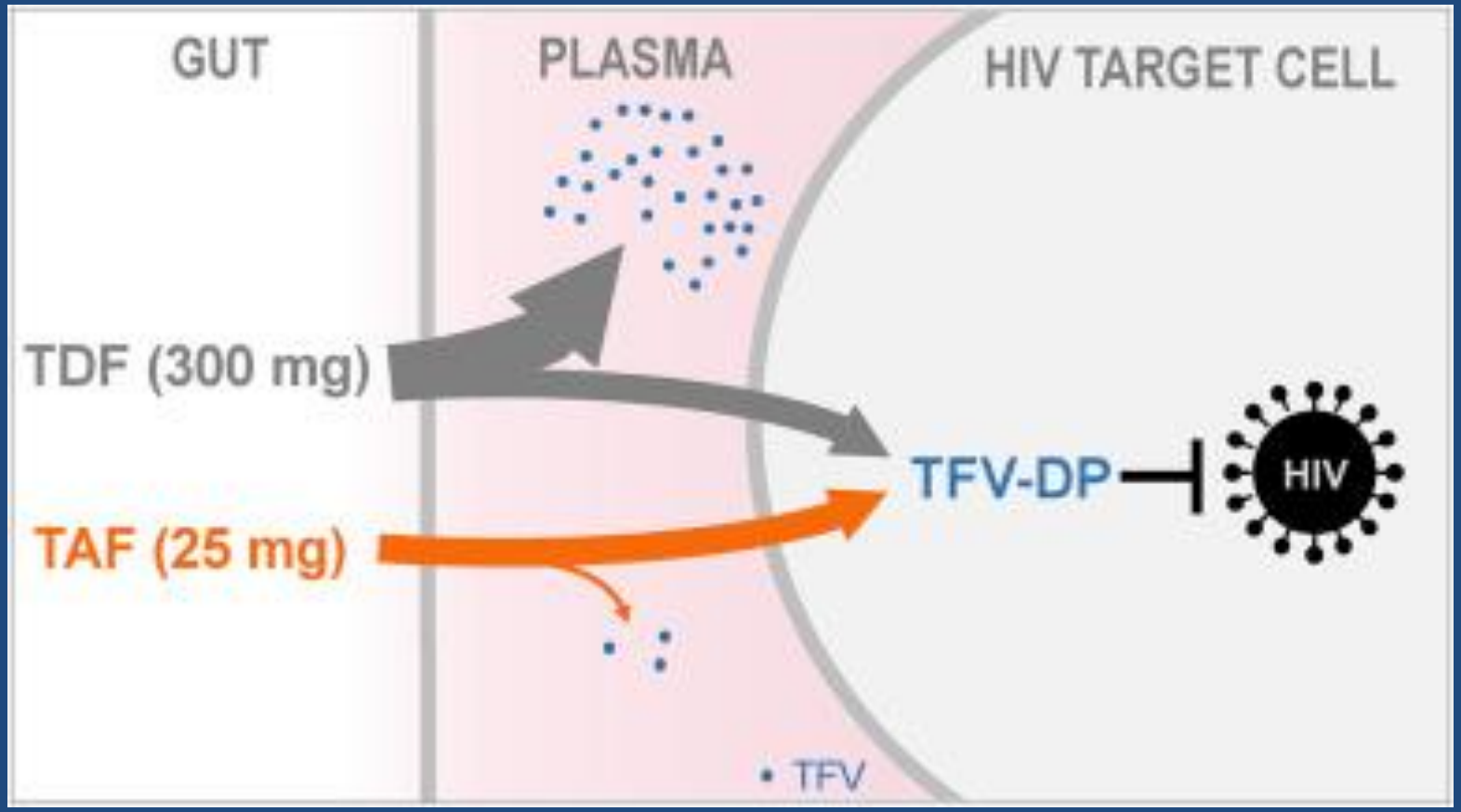
- Three **ACTIVE** medications
  - No resistance
  - Boosters do not count
- At least two different classes of medications
- Ideal characteristics
  - Safe/tolerable
  - Effective
  - Few drug interactions

First-Line Therapies

Integrase Strand Transfer Inhibitor-Based

- Dolutegravir/abacavir/lamivudine
- Dolutegravir plus Tenofovir/Emtricitabine
- Elvitegravir/cobicistat/Tenofovir/Emtricitabine
- Bictegravir/Tenofovir/Emtricitabine
- Raltegravir plus Tenofovir/Emtricitabine

First Line Therapies
Tenofovir DF vs. Tenofovir AF



Antiviral Research1 125, 1/2016: 63-70.

When to Start

- All patients with HIV should start ART regardless of:
  - CD4 count
  - Viral Load
- Initiating therapy is not an emergency
- Adherence is vital to virologic control

Adherence

- >95% adherence to achieve therapeutic goals
- 10% reduction in adherence = doubling of VL
- Result of non-adherence- RESISTANCE
- Reasons for poor adherence:

Knowledge/Understanding	Side Effects
Irregular schedules	Pill Fatigue
Memory	Access to meds/$$
Mental Health Issues	Illicit Drug Abuse
Issues swallowing	


PAUSE

AGING

‘You know you're getting old when you get that one candle on the cake. It's like, 'See if you can blow this out.'

-Jerry Seinfeld

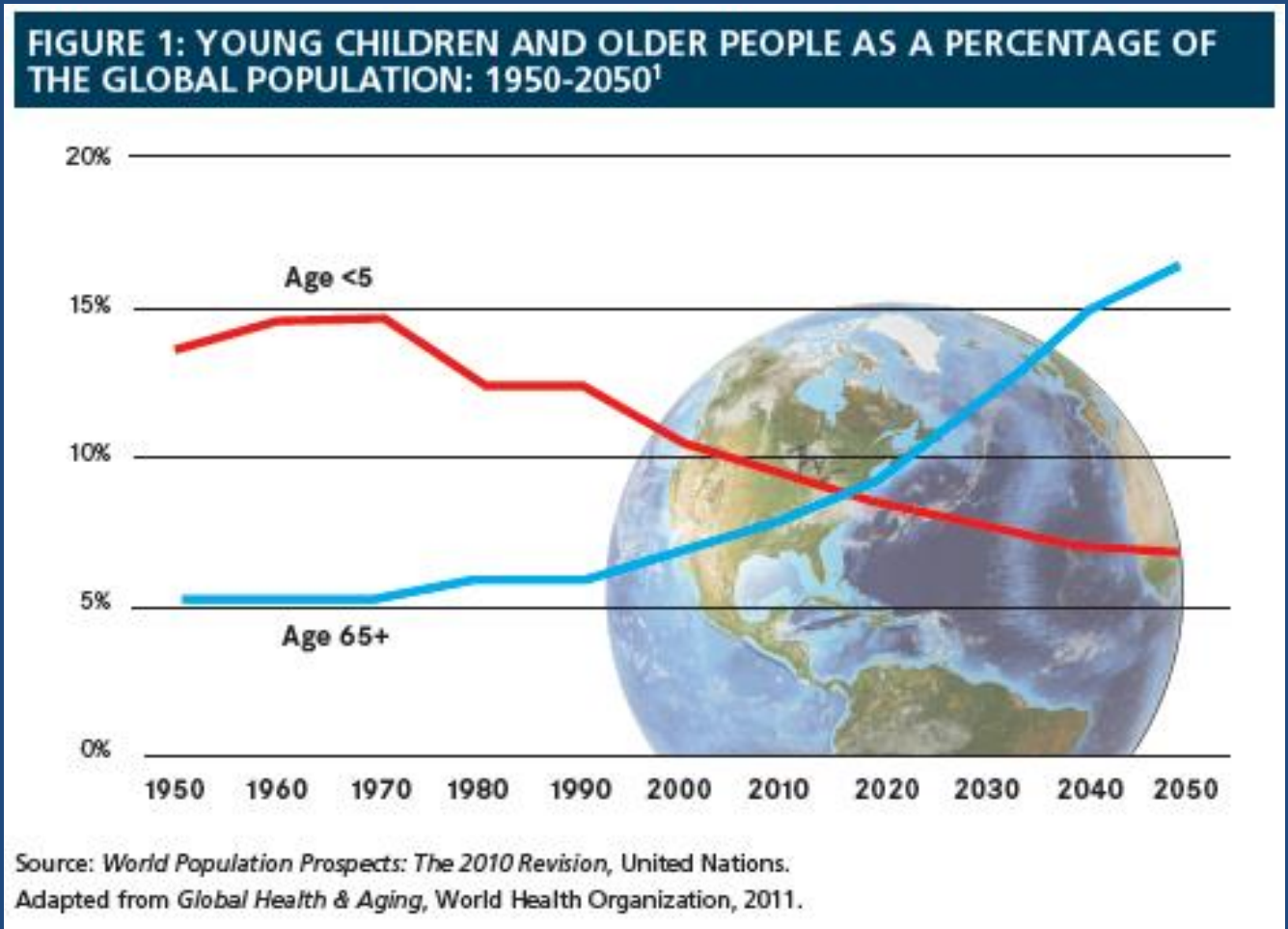
Aging: Defined

- Process of becoming older
- Age-dependent or age-progressive decline in intrinsic physiological function, leading to an increase in age-specific mortality rate
- Senescence

Aging: The Numbers

- Age 65 and older – 47.8 million (~14.9%)
- By 2030 estimated double in size and account for 1/5
- Everyday in the US 10,000 people celebrate their 65th birthday

Aging: The Numbers



Aging: Physiologic Changes

- Body Composition
- Cellular functionality
- CNS
- Endocrine
- Cardiovascular
- Immune system
- GI tract
- Kidneys
- Liver
- Pulmonary
- Otolaryngologic
- Peripheral Nervous System
- Musculoskelatal
- Opthalmalogic
- Skin

Aging

- Challenges among older patients
  - Multiple chronic diseases
  - Geriatric syndromes
  - Polypharmacy
- 65 and older medication use
  - Account for >30% of prescriptions
  - Account for >40% of OTCs

Aging

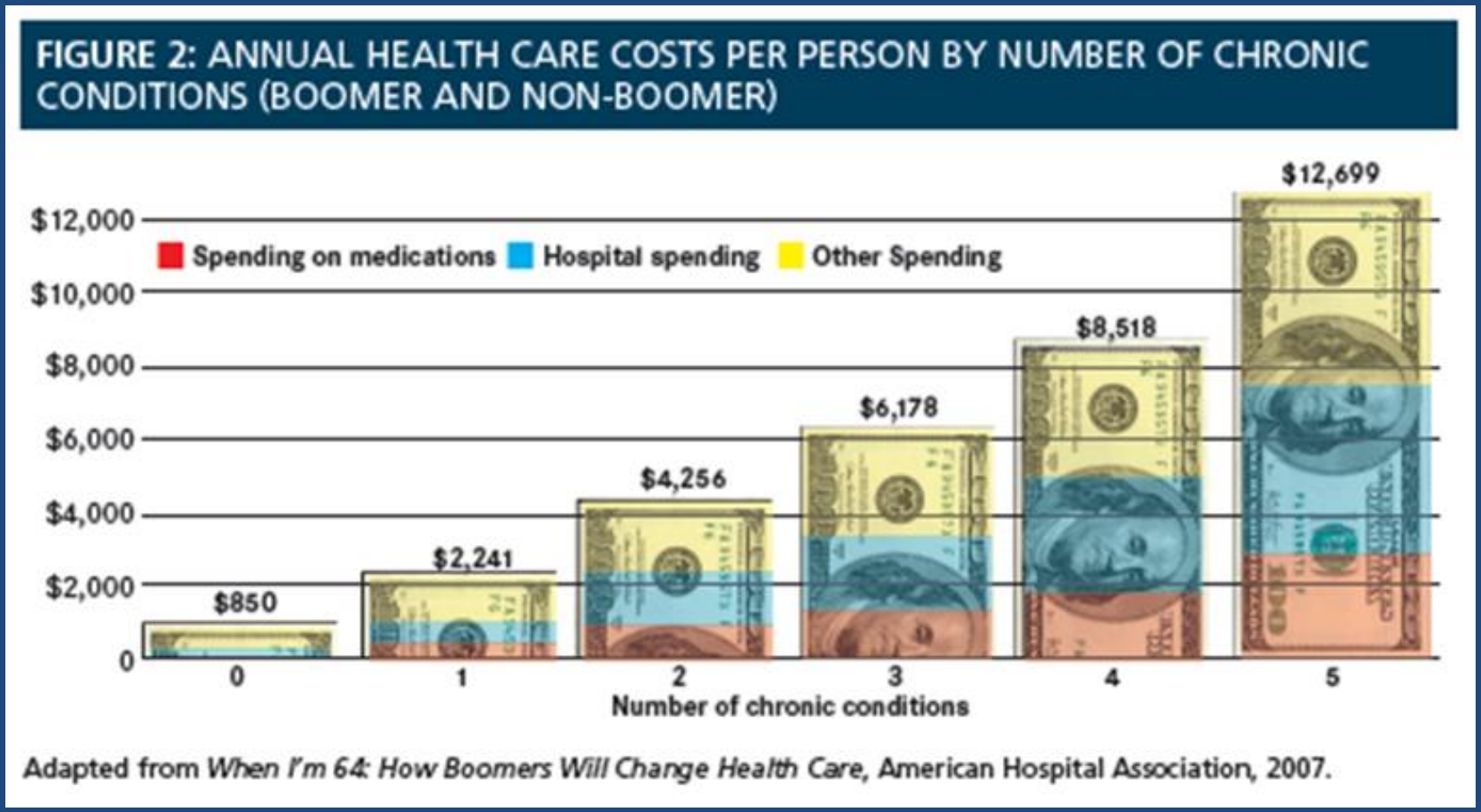
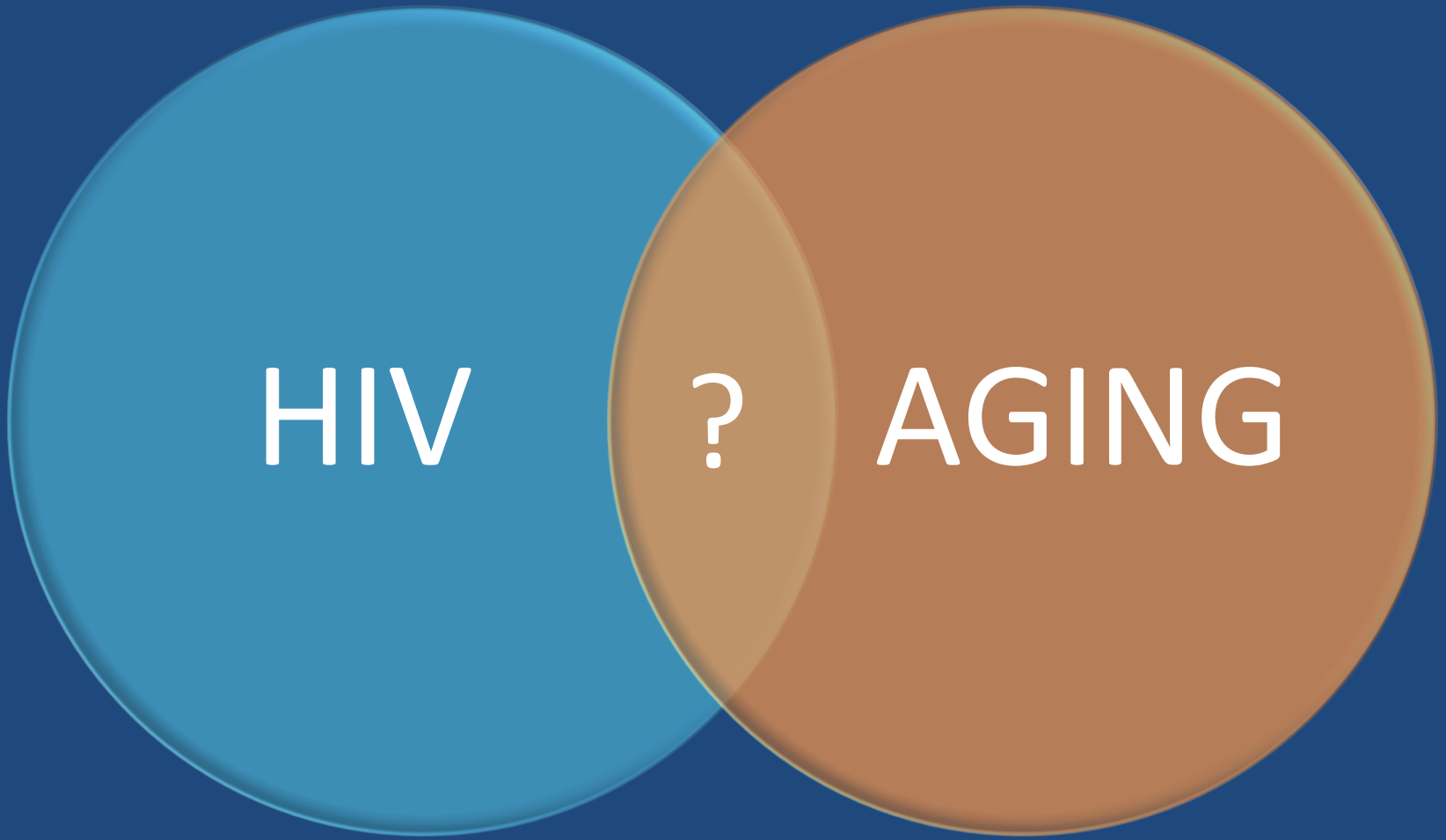


FIGURE 2: ANNUAL HEALTH CARE COSTS PER PERSON BY NUMBER OF CHRONIC CONDITIONS (BOOMER AND NON-BOOMER)
$12,000
$10,000
$8,000
$6,000
$4,000
$2,000
0
Spending on medications
Hospital spending
Other Spending
$850
$2,241
$4,256
$6,178
$8,518
$12,699
0
1
2
3
4
5
Number of chronic conditions
Adapted from When I'm 64: How Boomers Will Change Health Care, American Hospital Association, 2007.


PAUSE

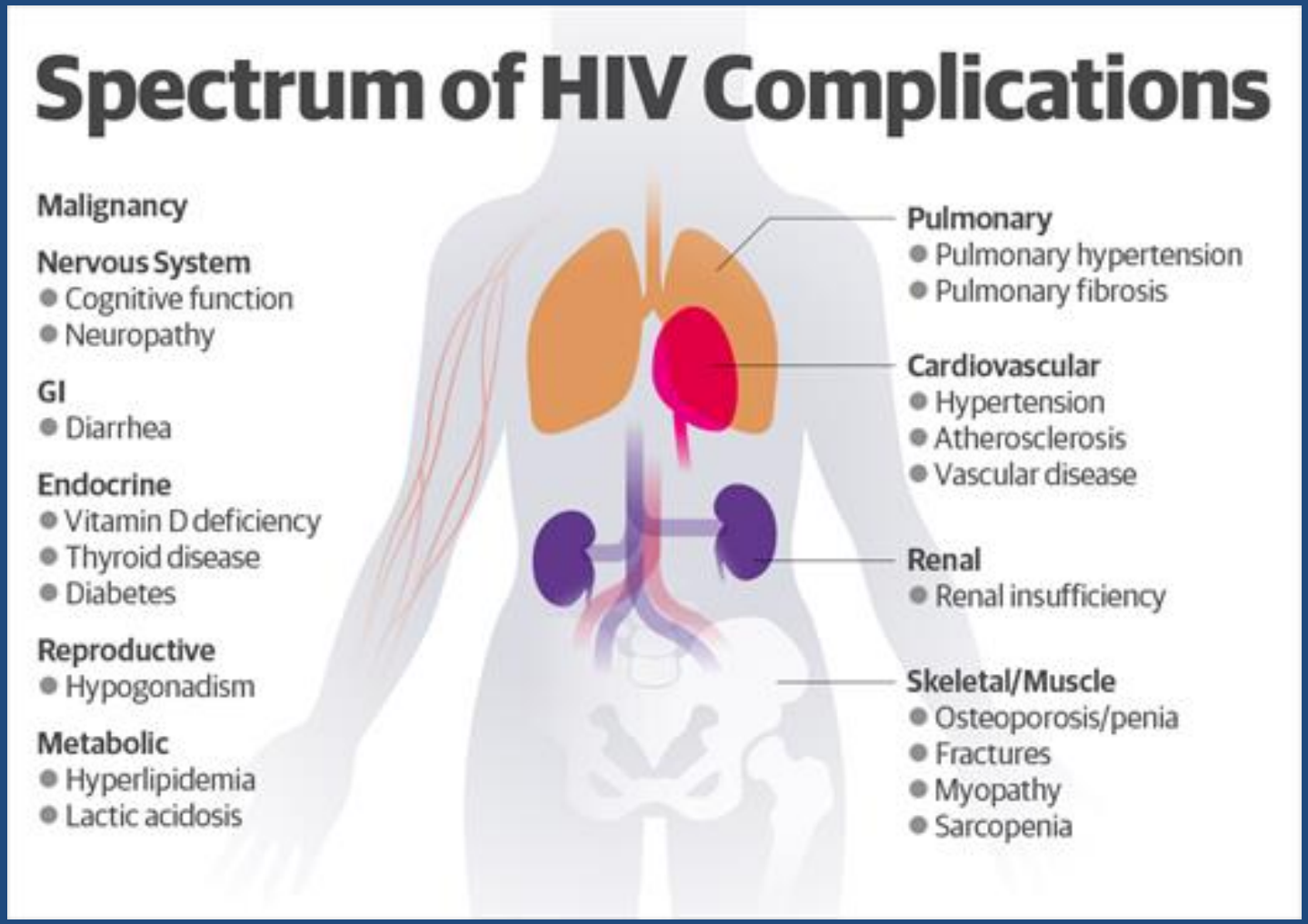

HIV
?
AGING

Aging with HIV

- HIV-positive patients have an increased risk for developing comorbidities

- Potential contributors to higher rates of comorbidities in HIV-positive patients
  - Risk factors that are more common in HIV-positive patients
  - Irreversible damage caused by HIV viremia
  - Chronic inflammation
  - Coinfections
  - Adverse effects of medications

Aging with HIV

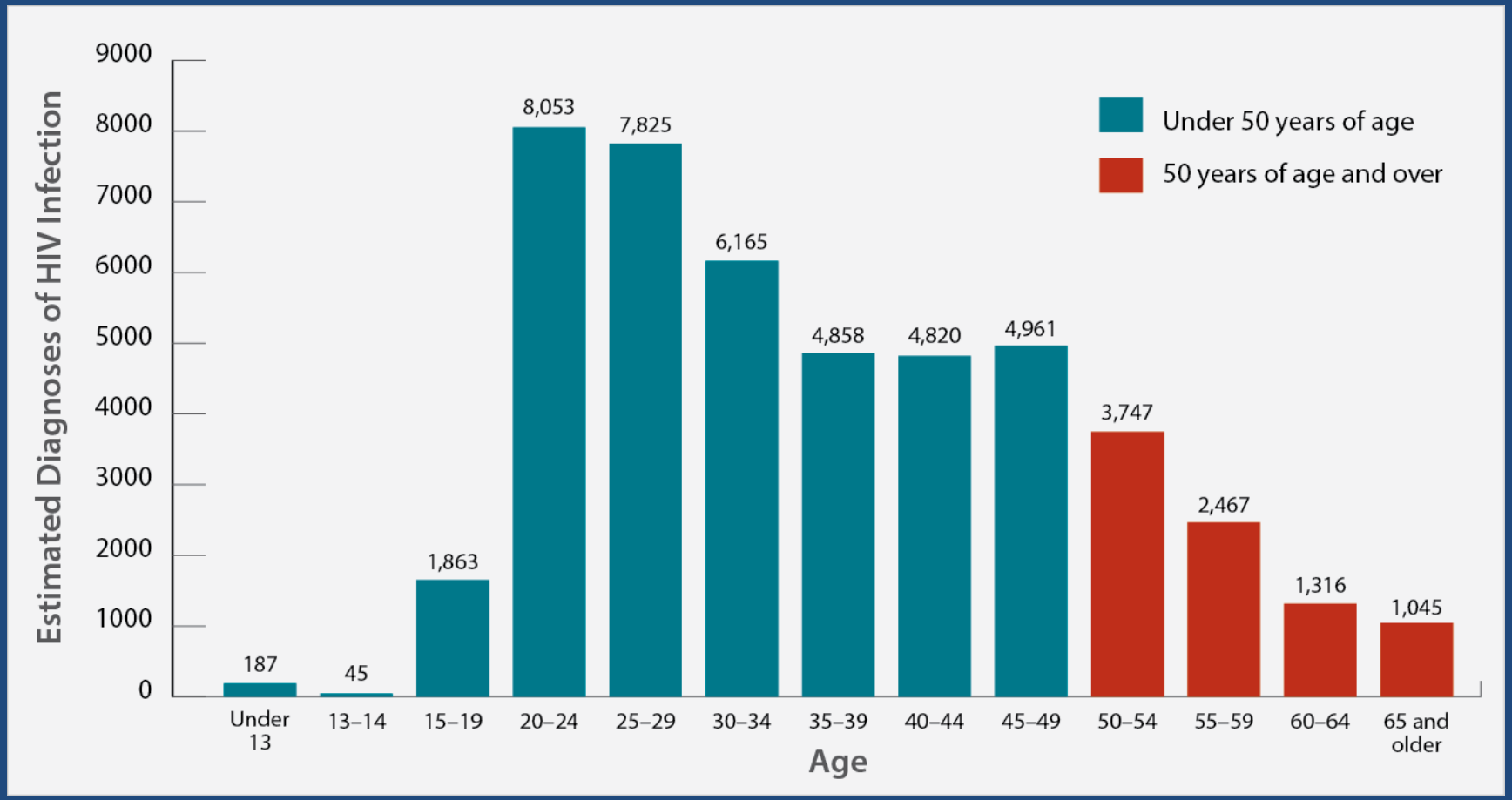


http://www.publichealth.org/public-awareness/hiv-aids/ accessed 9/18/2017.

Aging with HIV

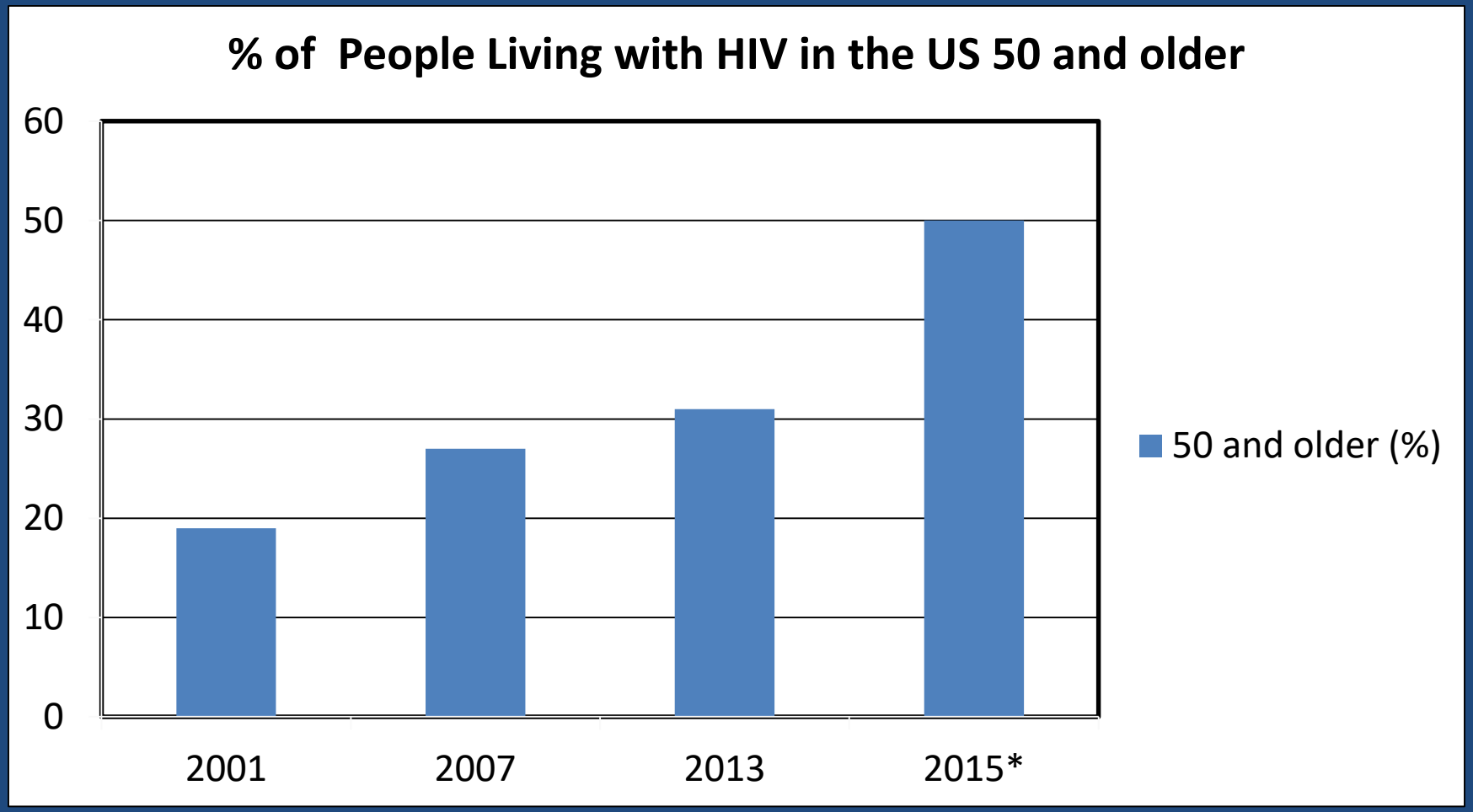
- The ‘double insult’ of aging and HIV infection to the hematopoietic system can contribute to many of the factors associated with immunosenescence: chronic inflammation, reduced ability of the immune system to mount effective response to infections, vaccines, other stressors

HIV: The Numbers
Diagnoses By Age (2015)



http://www.cdc.gov/hiv/group/age/olderamericans/index.html

HIV: The Numbers



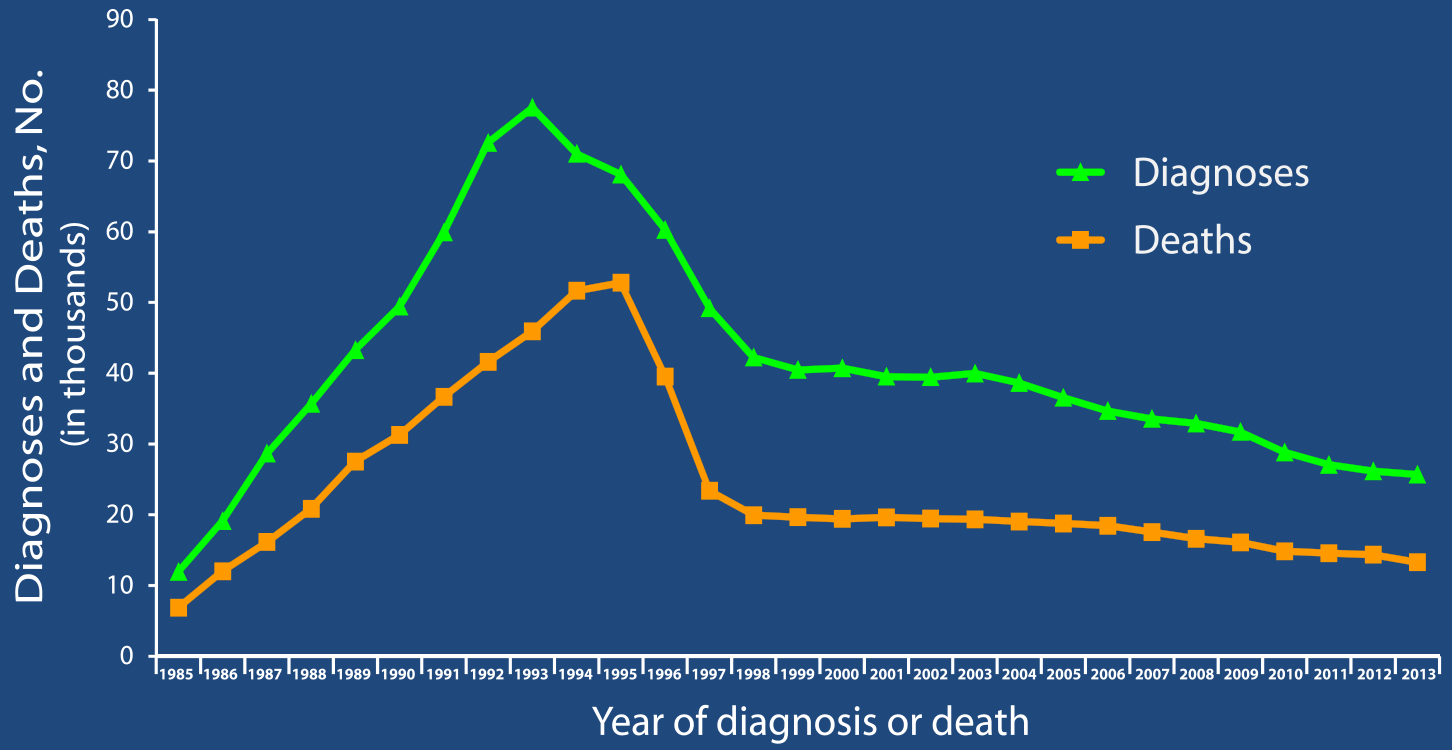
*estimate

http://www.cdc.gov/hiv/group/age/olderamericans/index.html

HIV: The Numbers

Why the Increase in 50 and older?

Antiretrovirals work!!!



http://www.cdc.gov/hiv/group/age/olderamericans/index.html

HIV: The Numbers

Why the Increase in 50 and older?

Other explanations

- Less condom use
- Erectile Dysfunction medications
- Post menopausal vaginal dryness – more tearing/abrasions
- Lack of education/information on transmission risks
- Lack cognitive ability to say “no”
- More “opportunities” in retirement communities
- Symptoms of HIV may be confused as signs of aging

HIV and Age Related Issues

Drug-Drug Interactions

- Polypharmacy: Definitions
  - Use of 6 or more medications
  - Use of a potentially inappropriate drug for which the medication does not match the diagnosis
- Polypharmacy repeatedly linked to:
  - Increase falls
  - Increased ADEs
  - Increased drug-drug interactions
  - Increased cost for patient and healthcare system
  - Older age

Drug-Drug Interactions

- HIV and polypharmacy
  - >50 significantly more likely to be taking additional meds
  - >50 significantly more likely to have potential drug-drug interactions
- Pharmacokinetic causes
  - Protease Inhibitors: CYP3A4 inhibitors
  - NNRTIs: CYP3A4 inducers
  - Atazanavir and rilpivirine: need acid for absorption
  - Tenofovir DF and cobicistat affect renal function

Ageing with HIV: medication use and risk for potential drug–drug interactions. *J Antimicrob Chemother. 2011;66(9):2107–2111.*

Drug-Drug Interactions

Table 4. Common Drug Interactions Between Antiretroviral and Other Prescribed Medications

Class of Interacting Medication	Interaction With NNRTIs	Interaction With Protease Inhibitors	Comment
Cardiovascular agents (eg, calcium channel blockers, amiodarone)		Increased calcium channel blocker exposure, amiodarone exposure, and potential PR interval prolongation	Use calcium channel blockers and protease inhibitors with caution; Avoid coadministration of amiodarone and protease inhibitors
Cardiovascular agents (eg, lipid-lowering agents)	Decreased statin exposure with selected NNRTIs	Increased statin exposure with selected protease inhibitors	Lovastatin and simvastatin contraindicated with concurrent protease inhibitor use; Use minimally effective doses of atorvastatin (maximum 20 mg/d) with protease inhibitors; Use lowest effective dose of pravastatin with darunavir
Benzodiazepines	Increased midazolam and triazolam effect with efavirenz; Increased diazepam exposure with etravirine	Increased benzodiazepine effect	Do not administer midazolam, alprazolam, diazepam and triazolam with protease inhibitors and efavirenz; Lorazepam, oxazepam and temazepam have less interaction potential with protease inhibitors
Proton pump inhibitors	Decreased rilpivirine absorption	Decreased atazanavir absorption	Proton pump inhibitors contraindicated with rilpivirine, atazanavir (without use of ritonavir); Proton pump inhibitors should not exceed a dose equivalent to omeprazole (20 mg/d) in protease inhibitor–naïve patients receiving ritonavir-boosted atazanavir; Proton pump inhibitors are not recommended in protease inhibitor–experienced patients receiving ritonavir-boosted atazanavir
Opiates	Decreased methadone exposure with efavirenz and nevirapine	Decreased methadone exposure with ritonavir-boosted protease inhibitors	Opiate withdrawal may occur with methadone and concurrent ritonavir-boosted protease inhibitor, efavirenz, or nevirapine use
Corticosteroids (systemic, inhaled, or intranasal)	Dexamethasone can decrease NNRTI levels, especially rilpivirine	Increased fluticasone and budesonide exposure with ritonavir; decreased protease inhibitor levels with dexamethasone	Cushing syndrome and adrenal insufficiency reported with fluticasone and budesonide coadministration with ritonavir; Beclomethasone preferred alternative Avoid dexamethasone and rilpivirine coadministration
Antiplatelet and anticoagulant agents (eg, clopidogrel, warfarin, rivaroxaban)	Decreased clopidogrel exposure with etravirine; Increased or decreased warfarin effect with NNRTIs	Increased or decreased warfarin effect with protease inhibitors; Increased rivaroxaban exposure with protease inhibitors	Avoid clopidogrel and etravirine coadministration if possible; Monitor international normalized ratio closely when stopping or starting protease inhibitors and NNRTIs and adjust warfarin dose accordingly; Avoid rivaroxaban and protease inhibitor coadministration
Phosphodiesterase type 5 inhibitors (sildenafil, tadalafil, vardenafil, avanafil)	Decreased phosphodiesterase type-5 inhibitor effect with etravirine	Increased phosphodiesterase type-5 inhibitor exposure with ritonavir-boosted protease inhibitors	Start with lowest effective dose with ritonavir-boosted protease inhibitors; Avoid coadministration of avanafil with NNRTIs or protease inhibitors
Antidepressants	Decreased bupropion and sertraline exposure with efavirenz	Decreased SSRI and bupropion exposure with selected protease inhibitors; Increased trazodone and tricyclic antidepressant effect with selected protease inhibitors	Titrate SSRI and bupropion doses based on clinical response in patients receiving protease inhibitors; Use lowest dose of trazodone and tricyclic antidepressants and monitor for central nervous system and cardiovascular adverse events in patients receiving protease inhibitors; Use of trazodone and saquinavir contraindicated

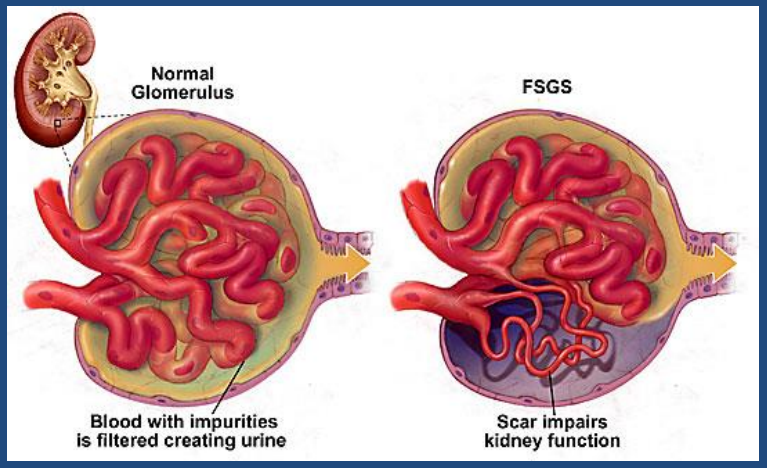
Abbreviations: NNRTI, nonnucleoside reverse transcriptase inhibitor; SSRI, selective serotonin reuptake inhibitor.
Derived from 2013 US Department of Health and Human Services guidelines, the HIV InSite website, and the University of Liverpool Drug interaction website (see Resources, available at http://www.jama.com).

Polypharmacy in the HIV-infected older adult population. *Clinical Interventions in Aging* 2013(8): 749-763

Renal Disease

Disease effects

- Increased risk of renal disease progression/ mortality
- HIVAN – focal segmented glomerulosclerosis



http://www.mayoclinic.org/~/media/kcms/gbs/patient%20consumer/images/2013/12/13/16/07/fsgs-lg-enlgjpg.ashx

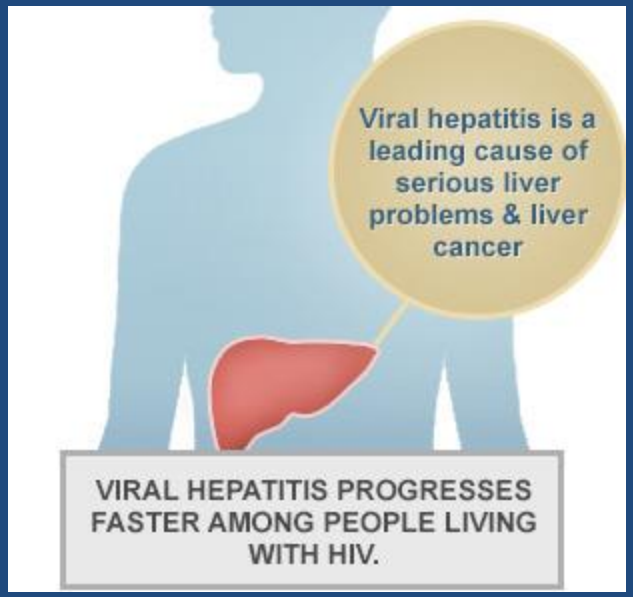
Medication effects

- Tenofovir DF increases CKD risk (Fanconi's)
- Cobicistat decreases apparent eGFR
- Renal stones with indinavir (common) or atazanavir (rare)

Liver Disease

Disease Effects

- Increasing liver-related mortality in HIV cohorts
- Increased risk of Hepatitis B & C infections



http://aids.gov/images/aids-infographics/hepatitis-2.jpg

Medication Effects

- NNRTIs- hepatoxicity
- NRTIs- steatosis, mitochondrial toxicity
- PIs- hepatotoxicity

Bone Mineral Density

Disease Effects

- Increased risk of fragility fractures, osteopenia, and osteoporosis in HIV cohorts
- Increased risk of osteonecrosis

Medication Effects

- PIs some NNRTIs decrease BMD
- Tenofovir DF decreases BMD

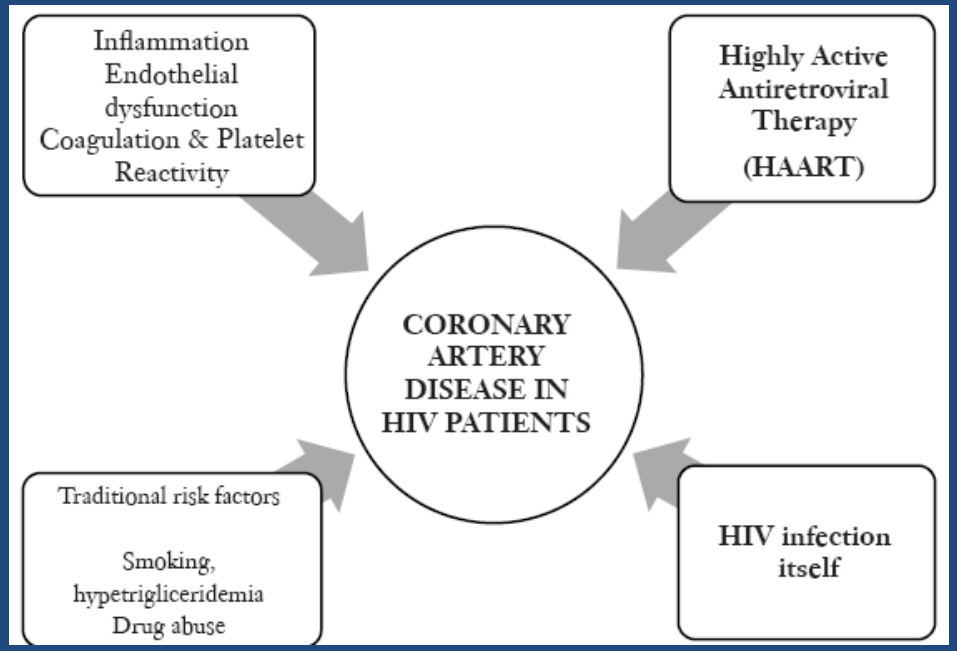
Cardiovascular Disease

Disease Effects

- Increased risk of fatal and nonfatal cardiovascular events
- Increased markers of atherosclerosis

Medication Effects

- PIs increase triglycerides
- Efavirenz increases LDL
- Abacavir possible increases risk of CV event

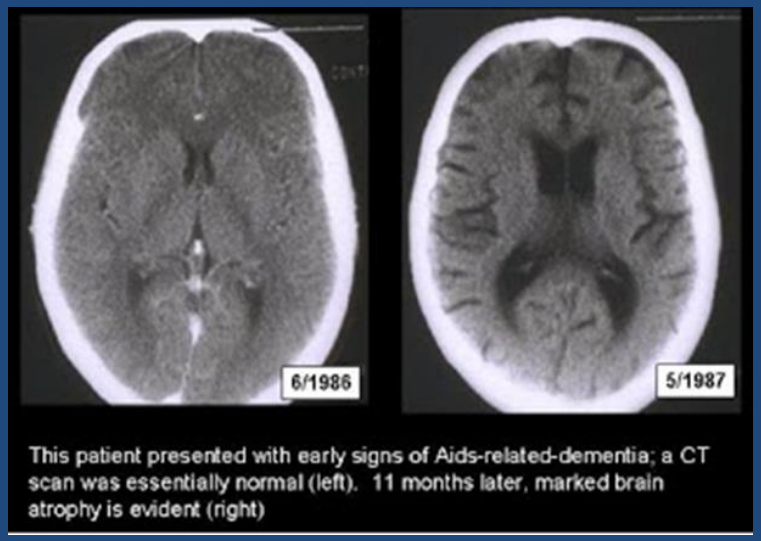


http://www.thecdt.org/article/viewFile/129/164/6654

Mental Health/Cognitive Disease

Disease Effects(?)

- Higher rates of mental health disease among HIV infected patients
- HAND



Medication Effects

- Significant number of drug-drug interactions!!!
- Efavirenz - increased risk of depression/suicidality

Malignant Diseases

- AIDS defining – opportunistic infections
  - Kaposi's Sarcoma
  - Non-Hodgkin's Lymphoma
  - Cervical Cancer
- Non-AIDS Defining
  - Hodgkin lymphoma (HL)
  - Hepatocellular carcinoma
  - Lung cancer
  - Head and neck squamous cell carcinoma
  - Anal cancer

Conclusion/Summary

- Population in America is aging (HIV population too!)
- With the aging comes new challenges for healthcare professionals caring for patients
- HIV and the medications used to treat HIV contribute to some age-related complication

Questions


THE BEST THING ABOUT BEING 104?
"There's no peer pressure."
-Marge Jetton