


**19<sup>th</sup> Annual HIV CONFERENCE**  
May 14-15, 2010 • Orlando, FL

## Aging in HIV Infection

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### Disclosure of Financial Relationships

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## Aging in HIV Infection

- **Objectives**
  - Recognize issues associated with treating older individuals with HIV infection
  - Define health care issues related to HIV infected individuals including metabolic, renal, cardiovascular and non-AIDS defining malignancies
  - Implement strategies for treating older individuals with HIV infection

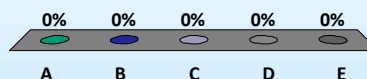


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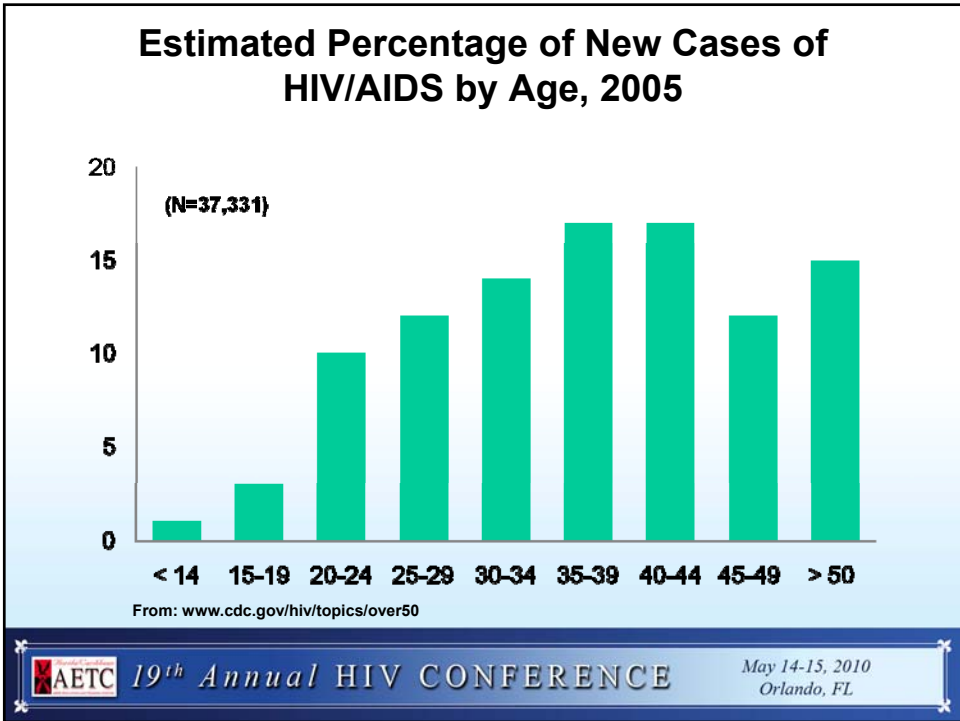
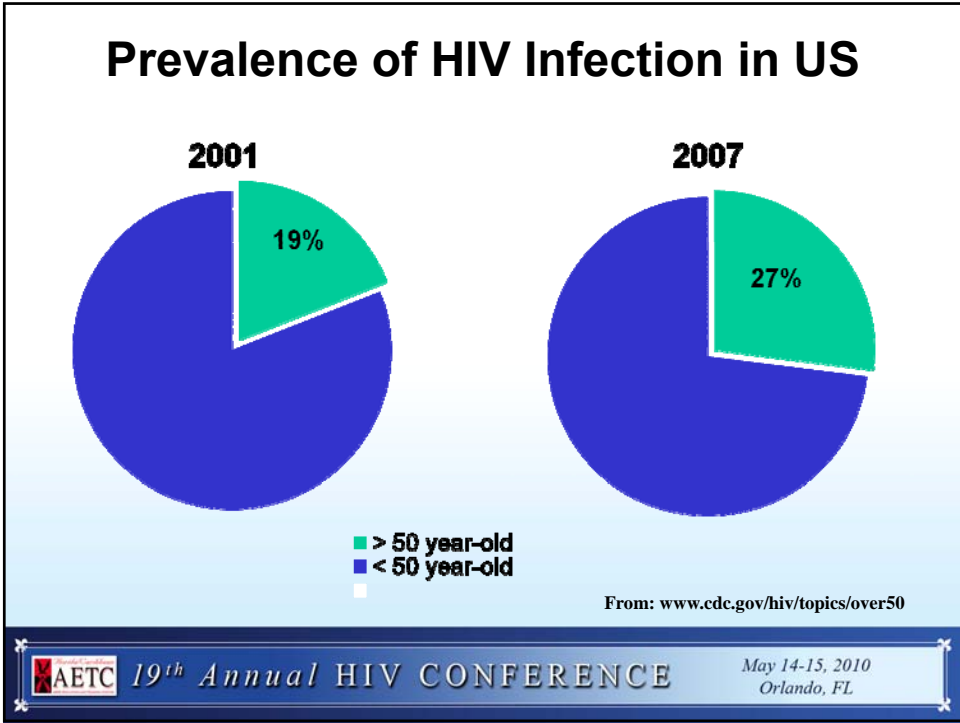
As estimated by the CDC: The percentage of HIV infected individuals older than 50 years, in the year 2015 will be:

- A. 20%
- B. 25%
- C. 30%
- D. 40%
- E.  $\geq 50\%$



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## HIV/AIDS in 2005

CDC HIV/AIDS Topics. Feb 12, 2008

- **Persons aged 50 and older**
  - 15% of new HIV/AIDS diagnosis
  - 24% of PLWHA (up from 17% in 2001)
- **Racial/ethnic disparities among 50 and older**
  - Whites 4.2/100,000
  - Hispanic 21.4/100,000
  - Blacks 51.7/100,000



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## HIV/AIDS Symptoms

- **Older adults and risks**
- **AIDS related dementia vs. Alzheimer**
- **Fatigue and weight loss vs. aging**
- **Confusion, fatigue, memory loss vs. alcohol use**

El-Sadr & Gettler, 1995

Mack & Bland, 1997

Aupperle, 1996



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## HIV Diagnosis in Older Adult

- Physicians are less likely to discuss HIV related risk factors with older adults
- HIV-associated symptoms and other illnesses
- Late presentation for diagnosis and care
- CDC recommendations

Gebo KA. Drugs Aging 2006  
Lindau ST. NEJM 2007  
MMWR Recomm Rep. 2006



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## Late Diagnosis of HIV Infection

- Less common routine screening
- Poor awareness of the risk of HIV infection
- Poor awareness of safer sex practices
- Failure of physicians to consider HIV infection
- Confusion of symptoms between OIs and conditions associated with aging

Grabar,S: JAC; Jan 2006



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## Treatment and Prognosis

- Age as independent predictor on clinical progression on HAART
- Significantly slower CD4 cell reconstitution
- Better virological response
- Death and AIDS during first and fifth year of therapy
- Viral suppression and adherence

Hinkin, CH: AIDS 2001; 15:1576-9  
Grabar,S: JAC; Jan 2006; 57:4-7



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## Myth : HIV over 50

- Seniors don't have sex and therefore are not at risk for HIV

About.com AIDS/HIV



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## FACT

- **Sexual desire does not wane after age 50**
- **More than 50% of persons over 50 years old have sex twice a month**
- **In 1999 AARP survey (age 64-74%)**
  - 1/3 of men
  - 1/4 of women
- **Have sex at least once a week**

About.com HIV/AIDS  
Kaiser network.org



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## Older Adult and AIDS

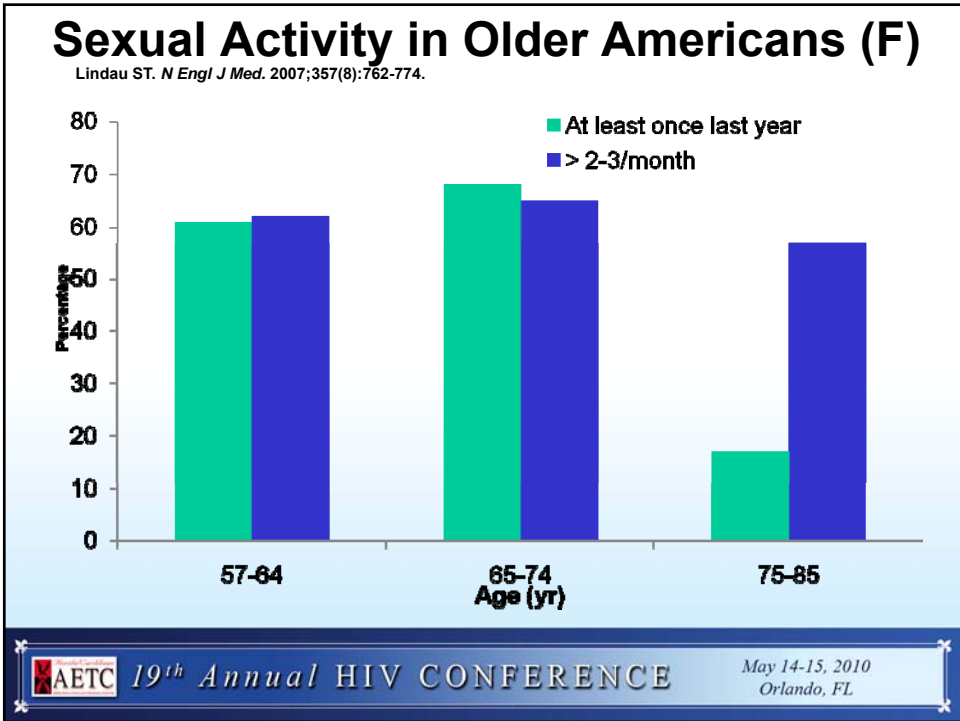
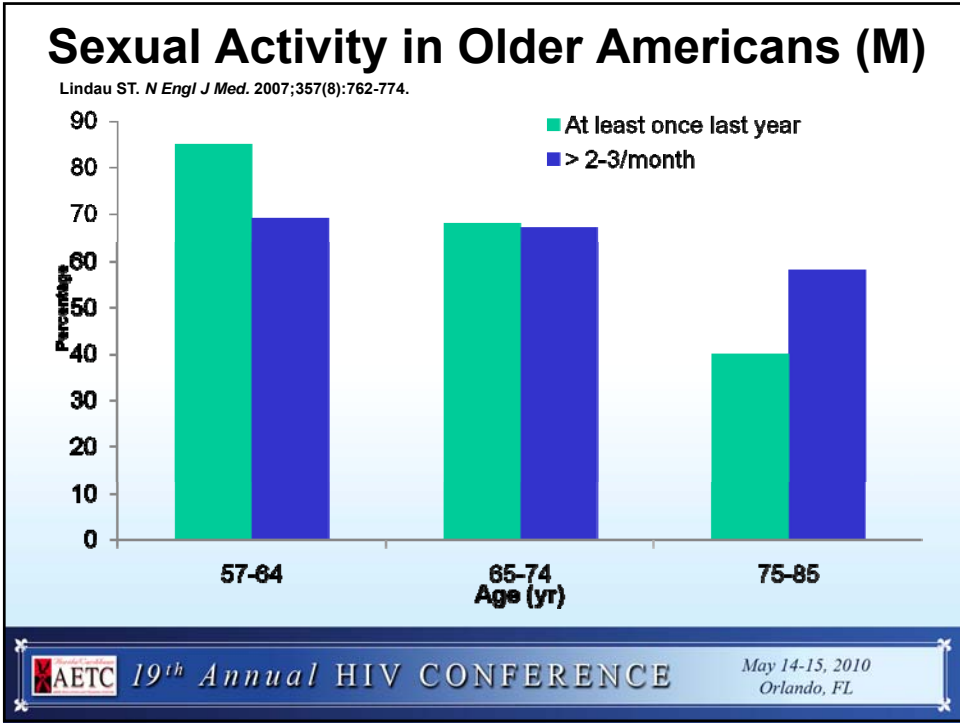
- **HIV/AIDS “is quieting down”**
- **“We can get it too, well not us-I don’t think, but other older people”**
- **“AIDS can be prevented by eating well and exercising; having a stable life”**
- **“We need to teach our children and grandchildren”**

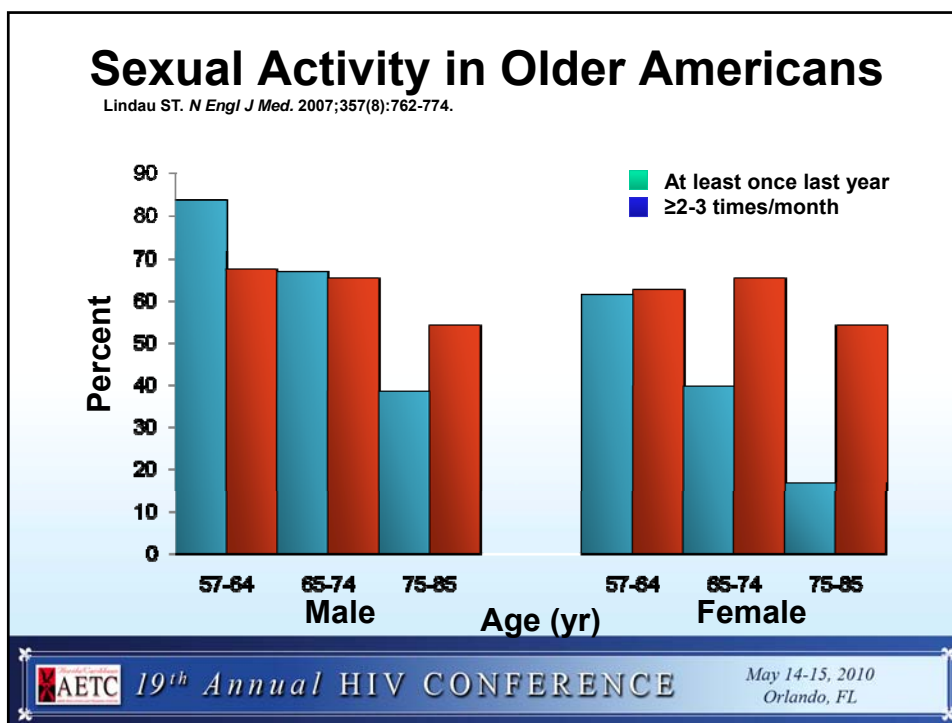
Rose, MR: J Geront Nurs, March 2004



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### PISCIS Cohort Study

Navarro G. et al. *J Infect.* 2008 Jul; 57(1):64-71

- **HIV-1 infected patients  $\geq 50$  years (n=493) vs. 18-49 years (n=4511)**
  - New HIV diagnosis since Jan 1, 1998
  - Males: 84% vs. 75%
  - Sexual transmission: 52% vs. 32%
  - AIDS at first visit: 38% vs. 22%
- **Follow-up for six years**
  - Lower CD4 on presentation
  - Mortality 9% vs. 4%

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## Aging with HIV

Orchi N, et al. AIDS Care. 2008 Apr; 20(4):419-25

- **Newly diagnosed older adults in Italy**
  - From Jan 2004 to Mar 2007: 11.6%
  - Males, heterosexual or unknown risk
  - Never tested before
  - More advanced stage of disease
  - More likely to have paid for sex, no use of drugs
  - Living with partners and children
  - No differences in condom use



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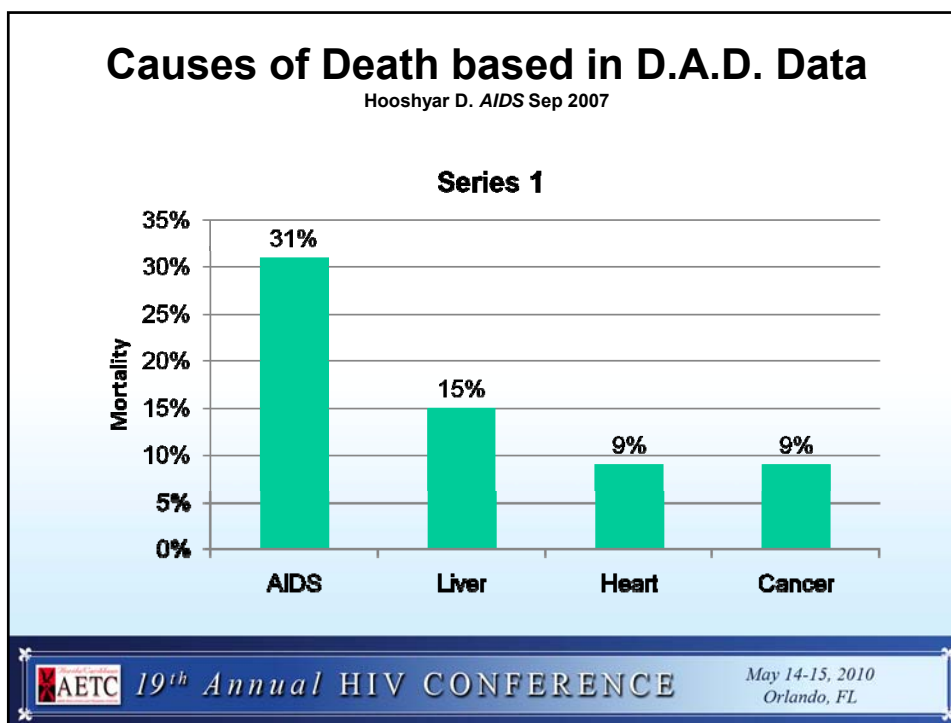
## Aging and Comorbidities

- **Common disorders in older adults**
  - Cardiovascular disease
  - Hypertension
  - Metabolic disorders, obesity
  - Neurocognitive decline
  - Hepatic and/or renal impairment
  - Bone fractures/Osteopenia/osteoporosis
  - Malignancies



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## CVD in Aging Patients with HIV

- **Microvascular risk factors for CVD increased by HIV infection**
  - Dyslipidemia
  - Endothelial dysfunction
  - Proinflammatory markers
- **Older age**
  - D:A:D Study
  - HOPS Cohort
  - SMART Study

## CVD Risk and ART

- **Potential Benefits of ART**
  - ACTG 5152s
  - MACS
  - SMART
- **Potential Negative Effects of ART**
  - D:A:D



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## Aging and ART in Comorbidities

- **Worsening of metabolic, renal, and hematologic abnormalities**
  - ? Toxicity
  - ? Worsening of pre-existing conditions
  - ? Less reserve
- **Close clinical and laboratory monitoring**



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## Drug-Drug Interactions

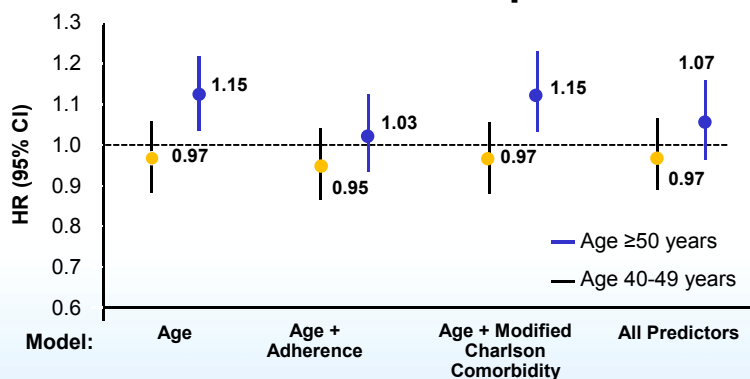
- HMG-CoA reductase inhibitors (statins)
- Antiarrhythmic agents (e.g. amiodarone)
- Drugs that inhibit gastric acidity
- Anticonvulsants
- Warfarin
- Selective serotonin reuptake inhibitors
- Erectile dysfunction agents



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## Older Patients More Likely to Achieve HIV-1 RNA <500 Copies/mL



- Adherence major advantage for older patients

Silverberg MJ. *Arch Intern Med.* 2007;167(7):684-691. Copyright ©2007 American Medical Association. All rights reserved.



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## CASCADE Collaboration. AIDS. 18(1):51-58, January 2, 2004

**Table 4. Predicted 6-month risk of AIDS according to age and current CD4 cell count and viral load, based on a Poisson regression model.**

Viral load (copies/ml)	Predicted risk (%) at current CD4 cell count ( $\times 10^6$ cells/l) <sup>a</sup>									
	50	100	150	200	250	300	350	400	450	500
<b>Age 25 years</b>										
3000	6.8	3.7	2.3	1.6	1.1	0.8	0.6	0.5	0.4	0.3
10000	9.6	5.3	3.4	2.3	1.6	1.2	0.9	0.7	0.5	0.4
30000	13.3	7.4	4.7	3.2	2.2	1.6	1.2	0.9	0.7	0.6
100000	18.6	10.6	6.7	4.6	3.2	2.4	1.8	1.4	1.1	0.8
300000	25.1	14.5	9.3	6.3	4.5	3.3	2.5	1.9	1.5	1.2
<b>Age 35 years</b>										
3000	8.5	4.7	3.0	2.0	1.4	1.0	0.8	0.6	0.5	0.4
10000	12.1	6.7	4.3	2.9	2.0	1.5	1.1	0.9	0.7	0.5
30000	16.6	9.3	5.9	4.0	2.8	2.1	1.6	1.2	0.9	0.7
100000	23.1	13.2	8.5	5.8	4.1	3.0	2.3	1.7	1.3	1.1
300000	30.8	18.0	11.7	8.0	5.7	4.2	3.1	2.4	1.9	1.5
<b>Age 45 years</b>										
3000	10.7	5.9	3.7	2.5	1.8	1.3	1.0	0.7	0.6	0.5
10000	15.1	8.5	5.4	3.6	2.6	1.9	1.4	1.1	0.8	0.7
30000	20.6	11.7	7.5	5.1	3.6	2.6	2.0	1.5	1.2	0.9
100000	28.4	16.5	10.6	7.3	5.2	3.8	2.9	2.2	1.7	1.3
300000	37.4	22.4	14.6	10.1	7.2	5.3	4.0	3.1	2.4	1.9
<b>Age 55 years</b>										
3000	13.4	7.5	4.7	3.2	2.3	1.7	1.2	0.9	0.7	0.6
10000	18.8	10.7	6.8	4.6	3.3	2.4	1.8	1.4	1.1	0.8
30000	25.4	14.6	9.4	6.4	4.6	3.3	2.5	1.9	1.5	1.2
100000	34.6	20.5	13.3	9.2	6.5	4.8	3.6	2.8	2.2	1.7
300000	44.8	27.5	18.2	12.6	9.1	6.7	5.0	3.9	3.0	2.4

<sup>a</sup>Shading distinguishes risk: < 2%, no shading; 2–9.9%, light gray; 10–19.9%, mid-gray;  $\geq$  20%, darkest gray. AIDS

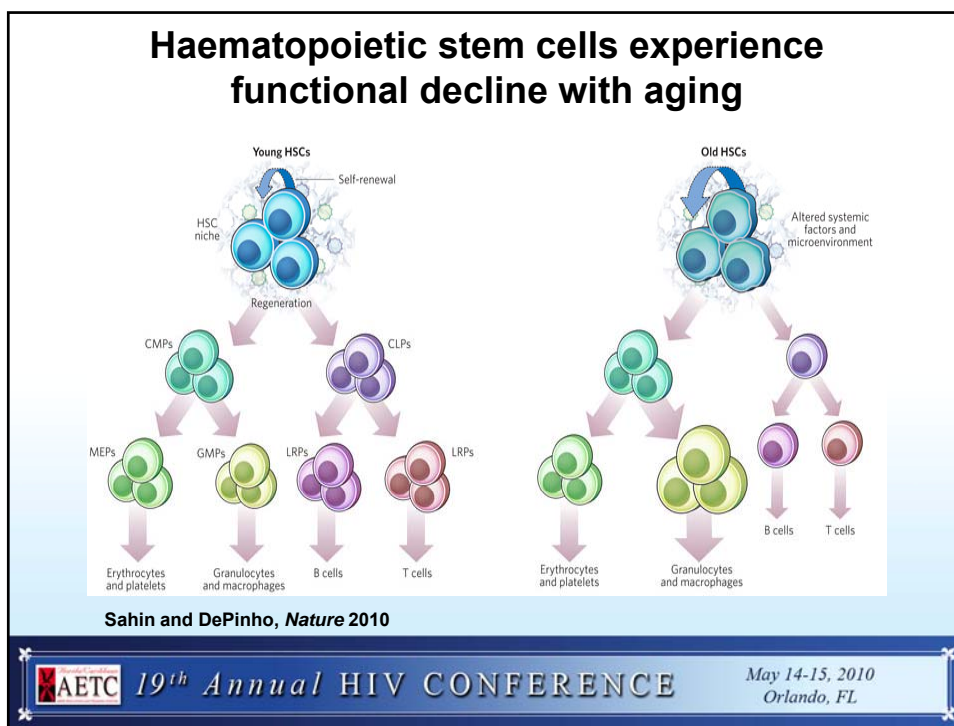
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## Immunologic Response to ART by Age

Viral Load Stratum	Mean CD4 Cell Count Increase per Month, cell/mm <sup>3</sup>			
	Within first 6 months of HAART		After 6 months of HAART	
	Age < 50 years	Age $\geq$ 50 years	Age < 50 years	Age $\geq$ 50 years
BL HIV-1 RNA < 5 log <sub>10</sub> copies/mL	17.3	14.1	11.1	9.8
BL HIV-1 RNA $\geq$ 5 log <sub>10</sub> copies/mL	42.9	36.9	17.9	15.6

Grabar S, et al. AIDS, 2004; 18(15):2029-2038

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### Age- and HIV-associated changes of immune response (B cells)

High, KP CID Aug 2008

Adaptive immune response	Change in HIV-infected compared to age-matched control	Change in aging persons, compared with young adults
Naïve cell number	Normal to low	Normal to low
Memory cell number	Increased	Increased
Resting activation	Increase	Normal
Cytokine production (unstimulated)	Increased	Normal
CD86 (costimulatory ligand) expression	Increased	Normal
Total IgG and IgA level	Polyclonal increase	Normal
V <sub>H</sub> gene use (naïve B cells)	Normal	Normal
V <sub>H</sub> gene mutation frequency	Few data	Normal
Primary responses	Decreased	Decreased
Memory responses	Low to normal	Normal

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## Age- and HIV-associated changes of immune response (T cells)

High, KP CID Aug 2008

Adaptive immune response	Change in HIV-infected compared to age-matched group	Change in aging persons, compared to young adults group
CD4 cells		
Naïve cell number	Low	Low
Memory cell number	Low	Normal to high
Resting activation	Highly increased	Increased
Cytokine production	Low	Low to normal
CD8 cells		
Naïve cell number	Low	Low
Memory cell number	Low	Normal to high
Resting activation	Highly increased	Increased
Cytokine production	Low	Normal to high
Senescent phenotype	Very high	High



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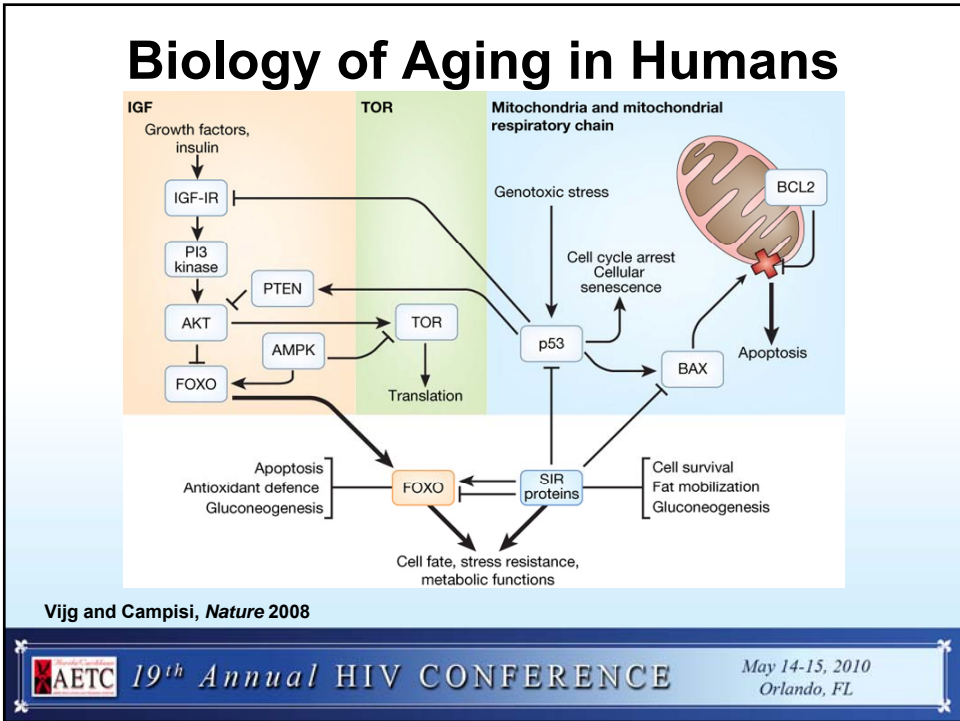
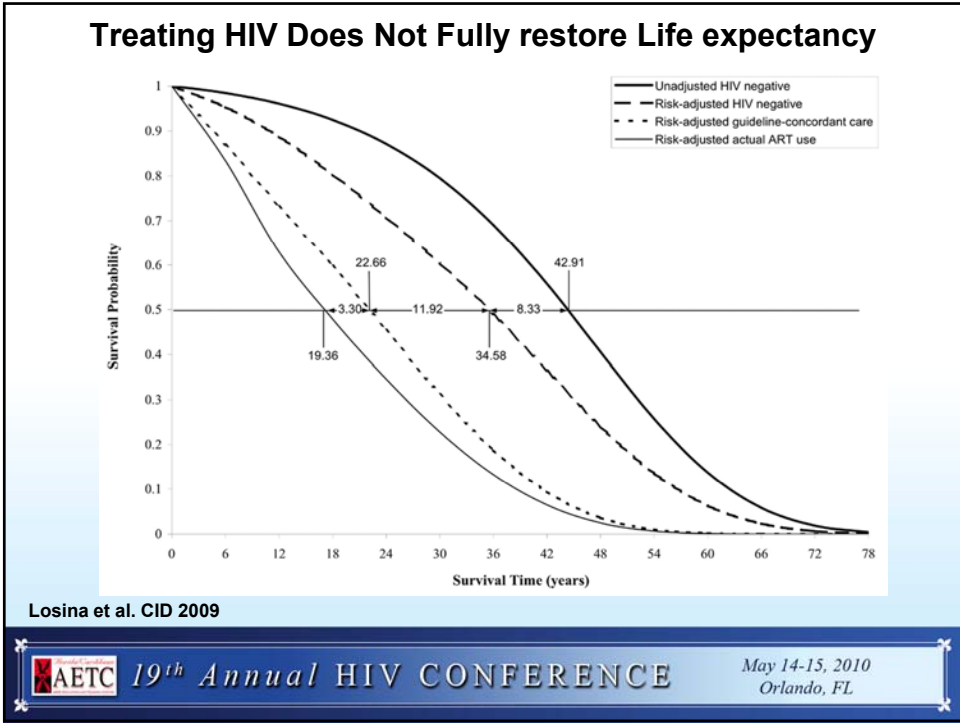
## T Cell Immunosenescence in Advanced Age Versus Long-Term HAART

Biological Parameter	Aging (> 70 years)	Long-term treated HIV Infection
Low CD4/CD8 ratio	Yes	Yes
Low naïve T cell %	Yes	Yes
Low T cell proliferation	Yes	Yes
Increased T cell activation	Yes	Yes
Expansion of CMV-specific T cells	Yes	Yes
Reduced T cell repertoire	Yes	Probable
Reduced T cell telomeres/telomerase	Yes	Unknown
Reduced regenerative potential (HSM, thymus)	Yes	Probably



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## Aging of the Immune System “Immunosenescence”

### T cell characteristics that predict morbidity/mortality in the very old

- Reduced regenerative capacity (stem cells, thymus)
- Low naïve/memory T cell ratios
- Low CD4/CD8 ratio
- Increased T cell activation
- Increased inflammatory markers (IL-6, CRP)
- Clonal expansion of CD28-CD57+ T cells
- Expanded CMV specific T cell responses
- Reduced T cell proliferation

Weng N. *Immunity*, 2006;24:495-499

Linton PJ. *Nat Immunol*. 2004; 2:133-139



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## Inflammation and Aging: Therapeutic Strategies

- **Reduce inflammation**
  - Residual HIV replication (ART intensification?)
  - Prednisone, HU, cyclosporine, mycophenolic acid
  - Chronic/persistent co-infections (HCV, CMV)
  - Microbial translocation (sevelamer, colostrum)
  - CCR5 inhibitors
  - Chloroquine (reduced PDC mediated IFN $\alpha$ )
  - NSAIDs (COX-2 inhibitors)



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## Inflammation and Aging: Therapeutic Strategies

- **Enhance T-cell renewal**
  - GH, IL-7, stem cell transplant, perfenidone, lupron
- **Anti-aging interventions**
  - Caloric restrictions
  - Sirtuin activators, Telomerase activators
  - Vitamin D, omega-3 fatty acids, rapamycin



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## Management of Older Patient with HIV Infection

- **Optimizing Adherence to Care**
- **Cancer Screening**
  - PAP smear, skin exam
  - Prostate exam, colonoscopy
  - HCC, lung cancer
- **Women's health**
  - Mammogram
  - HRT



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## Management of Older Patient with HIV Infection

- **Cardiac evaluation**
  - HTN and CAD management
  - Use of selected ART
- **Osteoporosis**
  - Evaluation, diagnosis
  - Use of selected ART
  - Vitamin D supplementation
- **Renal disease**
- **Diabetes, hyperlipidemia**



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## Prevention

- **Sexual Risk Factors**
  - Discussed sex with their doctor: 38% of men and 22% of women
  - Age-related vaginal thinning and dryness
- **Drug Use**
  - Recreational drugs
  - IVDU
  - Tobacco



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## Prevention Challenges

- Sexually active but no safer sex.
- Use of drugs and behavior
- Knowledge about HIV, use of condoms, testing
- Discrimination and stigma: later testing and diagnosis
- Health care: opportunities missed



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## Summary

- Life expectancy is shorter than normal despite optimal ART. It appears to be predicted by lower CD4 and higher inflammation.
- Markers of inflammation and T cell activation remain higher in ART than non-HIV infected
  - Prevented by early therapy?



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## Summary

- **Management of older HIV-infected patients may be complicated by comorbidities**
- **Comorbidities attributed to increasing age may overlap with morbidity from HIV disease and toxicity from ART**
- **Early diagnosis, and probably early therapy initiation, may improve outcomes in this population.**



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