8th International Conference on HIV TREATMENT AND PREVENTION ADHERENCE

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National Institute of Mental Health

PIM
Postgraduate Institute for Medicine

- No Conflict of Interest

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Aging and HIV Co-Morbidities:

A Challenge for Engagement in Care

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Objectives

- Understand the aging of the Immune System in the HIV population and how it relates to development of Co-morbidities
- Discuss the Epidemiology of HIV in the aging population
- Discuss the Challenges in:
  - HIV diagnosis
  - HIV care
  - Management of Co-morbidities

AGING: Britanica Encyclopedia

"Gradual change in an organism that leads to increased risk of weakness, disease, and death. It takes place in a cell, an organ, or the total organism over the entire adult life span of any living thing... Changes in organs include the replacement of functional cardiovascular cells with fibrous tissue. Overall effects of aging include reduced immunity, loss of muscle strength, decline in memory and other aspects of cognition, and loss of colour in the hair and elasticity in the skin.

In women, the process accelerates after menopause."

How old is “aging” in HIV?

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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

The process of aging in HIV

Aging

HIV

Aging related Co-morbidities

HTN, DM, CVD, cancers, cognitive decline

Mechanisms

Persistent immune activation

Immune senescence

Microbial translocation

Chronic inflammation

Telomere length

Telomerase activity

OPEN ACCESS Freely available online

PLOS | ONE

Immune Activation in HIV-Infected Aging Women on Antiretrovirals—Implications for Age-Associated Comorbidities: A Cross-Sectional Pilot Study

Maria L. Alcaide[1☯], Anita Parmigiani[2☯], Suresh Pallikkuth[2], Margaret Roach[2], Riccardo Freguja[3], Marina Della Negra[4], Hector Bolivar[5], Margaret A. Fischl[5], Savita Pahwa[2*]

Aging + HIV

- State of immune activation, immune senescence, microbial translocation, inflammation
- Biomarkers of cardiovascular disease in HIV infected post-menopausal women on ART

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May 2013 | Volume 8 | Issue 5 | e63804

HIV infected post-menopausal women

	HIV– n=15	HIV+ n=27	P value
Age (years)	59 (53–63)	56.5 (48–66)	0.11
Time to menopause (years)	15 (3–29)	12 (2–22)	0.09
CD4 cell count (cells/mm^3)	n.a.	584 (144–1,144)	
CD4 nadir (cells/mm^3)	n.a.	147 (2–648)	
HIV RNA (copies/ml)	n.a.	undetectable–80	
Current smoking	13%	8%	0.61
Current illicit drug use	6%	4%	1.00
Body mass index (kg/m^2)	31.4 (21.5–38.1)	27.6 (20.1–38.3)	0.20

Alcaide et al. PLOS ONE 2013

Tcell cellular markers of IA

	HIV–	HIV+	P value
T cell activation			
CD38+ HLA-DR+ CD4 (%)	1.69±0.95	3.21±1.87	**0.0313**
CD38+ HLA-DR+ CD8 (%)	2.08±1.39	10.17±13.26	**<0.0001**
Ki-67+ CD4 (%)	0.39±0.22	0.63±0.29	**0.0260**
Ki-67+ CD8 (%)	0.32±0.09	0.34±0.18	0.6913
T cell exhaustion			
PD-1+ CD4 (%)	13.36±6.81	21.99±11.80	**0.0321**
PD-1+ CD8 (%)	16.72±9.86	20.50±7.34	0.2177
T cell senescence			
CD28– CD57+ CD4 (%)	2.22±2.61	9.43±12.24	**0.0390**
CD28– CD57+ CD8 (%)	16.07±10.40	24.59±13.88	**0.0481**

Alcaide et al. PLOS ONE 2013

Soluble markers of IA and MT

	HIV–	HIV+	P value
Monocyte/macrophage activation			
sCD14 (ng/ml)	1,537±253	2,113±426	**<0.0001**
sCD163 (ng/ml)	323±155	533±260	**0.0043**
T cell activation			
sCD25 (ng/ml)	387.3±151.2	590.1±425.6	**0.0423**
Microbial translocation			
LPS (pg/ml)	90.2±21.4	107.4±20.7	**0.0221**

Alcaide et al. PLOS ONE 2013

Inflammatory Cytokines

	HIV–	HIV+	P value
IL-6 (pg/ml)	0.89±0.17	1.86±0.44	0.0728
IL-8 (pg/ml)	4.38±0.52	6.57±1.26	0.1012
IL-10 (pg/ml)	3.31±1.58	19.74±4.85	**0.0124**
TNFα (pg/ml)	7.02±1.43	9.58±1.23	0.1359

Alcaide et al. PLOS ONE 2013

- **Tcell immune activation**
- **Tcell exhaustion**
- **Tcell senescence**
- **Microbial Translocation**
- **Soluble markers of IA**
- **Inflammatory Cytokines**

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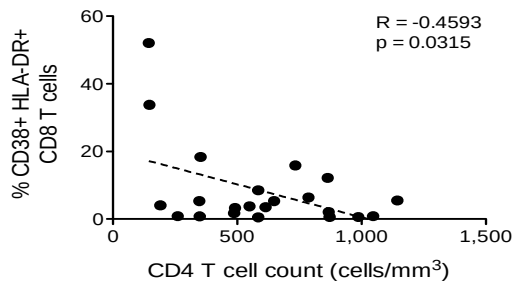
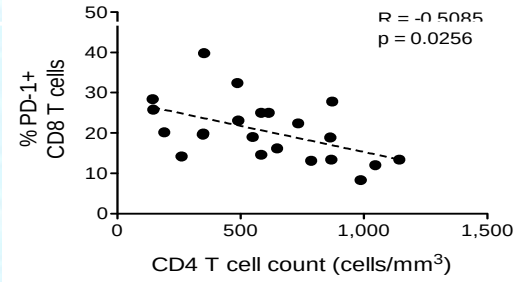
Alcaide et al. PLOS ONE

IA and senescence are associated with low CD4

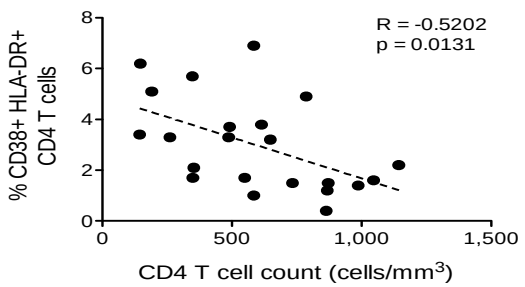
%CD38+HLA-DR+ CD8 Tcells/CD4



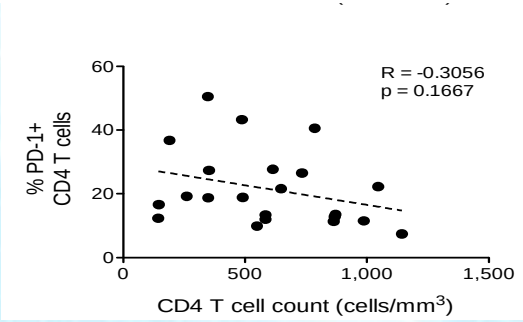
%PD-1+ CD8 Tcells/CD4



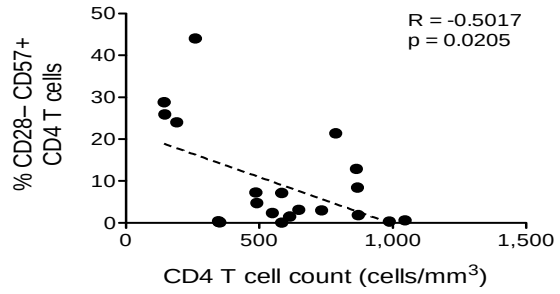
%CD38+HLA-DR+ CD4 Tcells/CD4



%PD-1+ CD4 Tcells/CD4



%CD28-CD57+ CD4 Tcells/CD4



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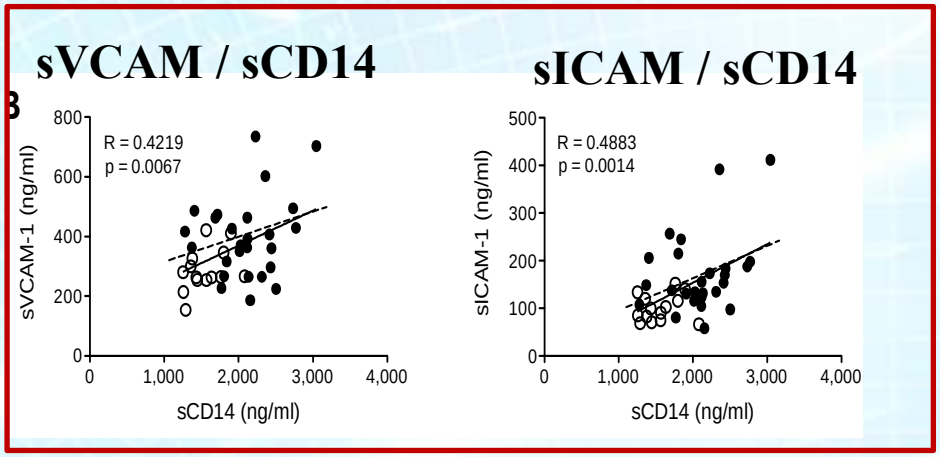
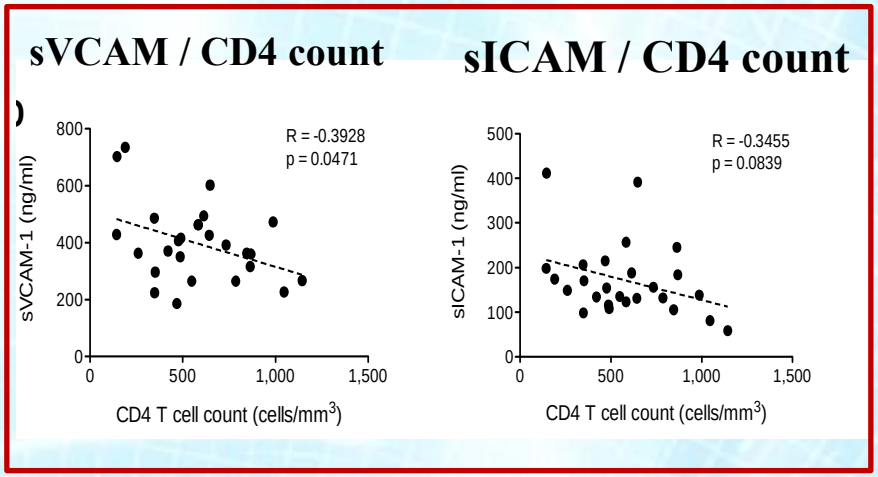
Biomarkers of CVD

	HIV–	HIV+	P value
Cardiovascular disease			
sVCAM-1 (ng/ml)	287.0±71.3	397.8±136.0	**0.0073**
sICAM-1 (ng/ml)	100.4±28.1	171.5±82.9	**0.0037**

Alcaide et al. PLOS ONE

Biomarkers of CVD are associated with the state of immune activation and with low CD4 counts





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Alcaide et al. PLOS ONE

HIV infected post-menopausal women

Aging + HIV

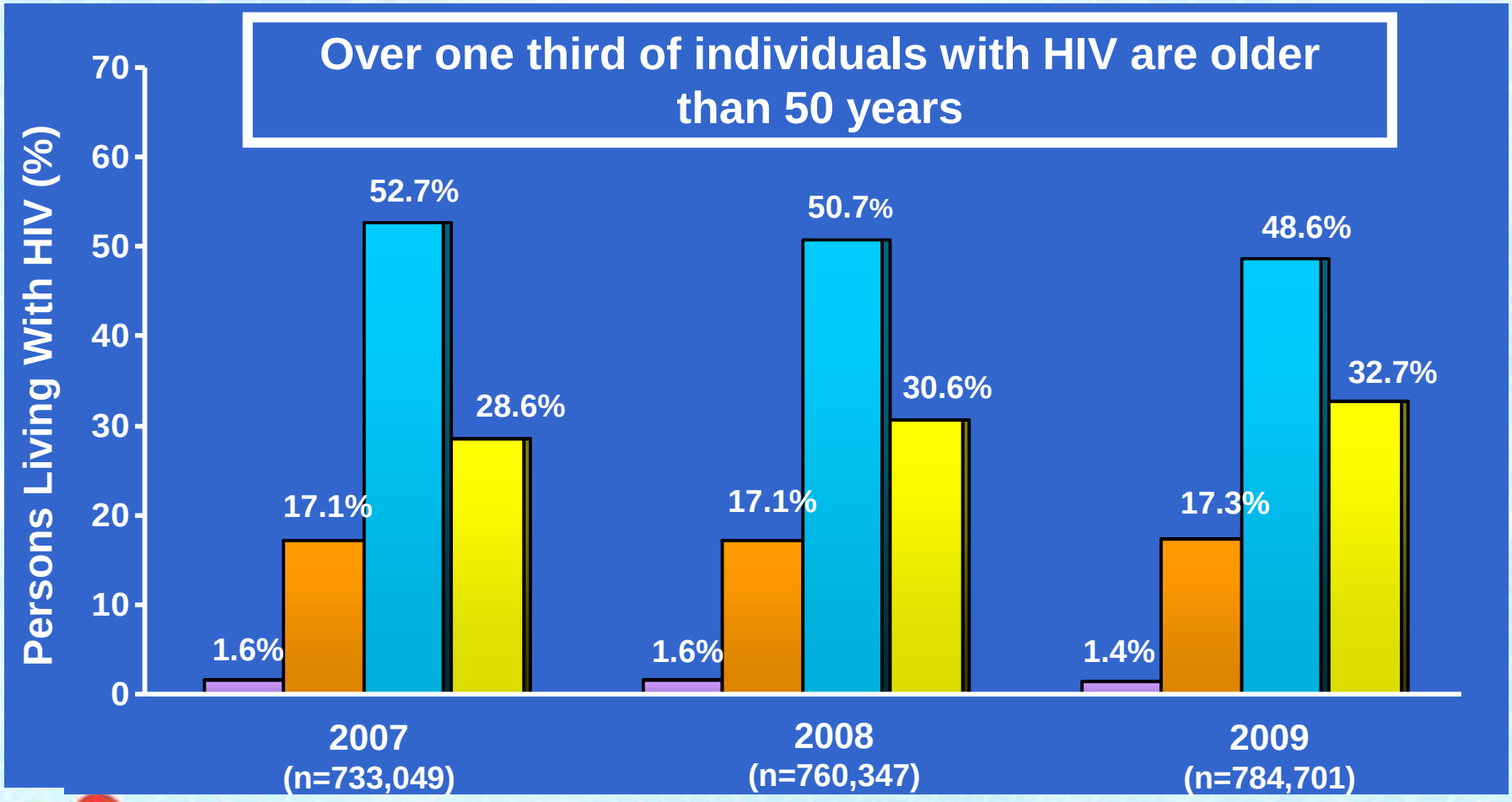
Despite appropriate immunological and virological response to ART:

- The immune system of HIV infected aging women is in a higher state immune activation
- The state of IA predispose them to develop CVD

IA and risk for CVD are associated with lower CD4 counts

Epidemiology of HIV in the aging population

People living with HIV



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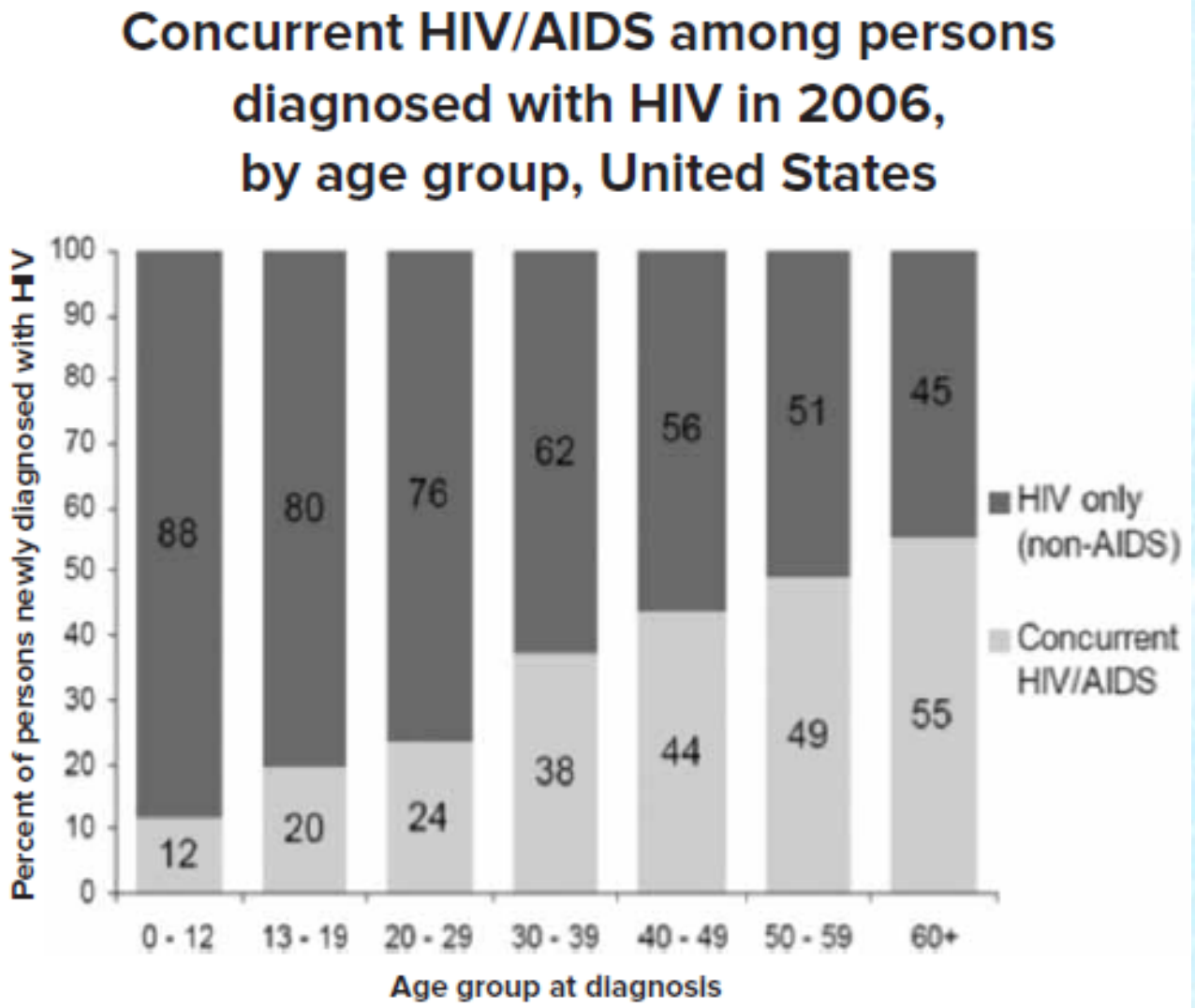
CDC. *HIV Surveillance Report, 2010*.
http://www.cdc.gov/hiv/pdf/statistics_2010_HIV_Surveillance_Report

By 2015, approximately 50% of people living with HIV will be older than 50 years of age.

NIH statement on National HIV/AIDS and Aging Awareness Day Sept. 18, 2010. Available at: http://www.nih.gov/news/health/sep2010/niaid-09.htm.

Concurrent HIV/AIDS



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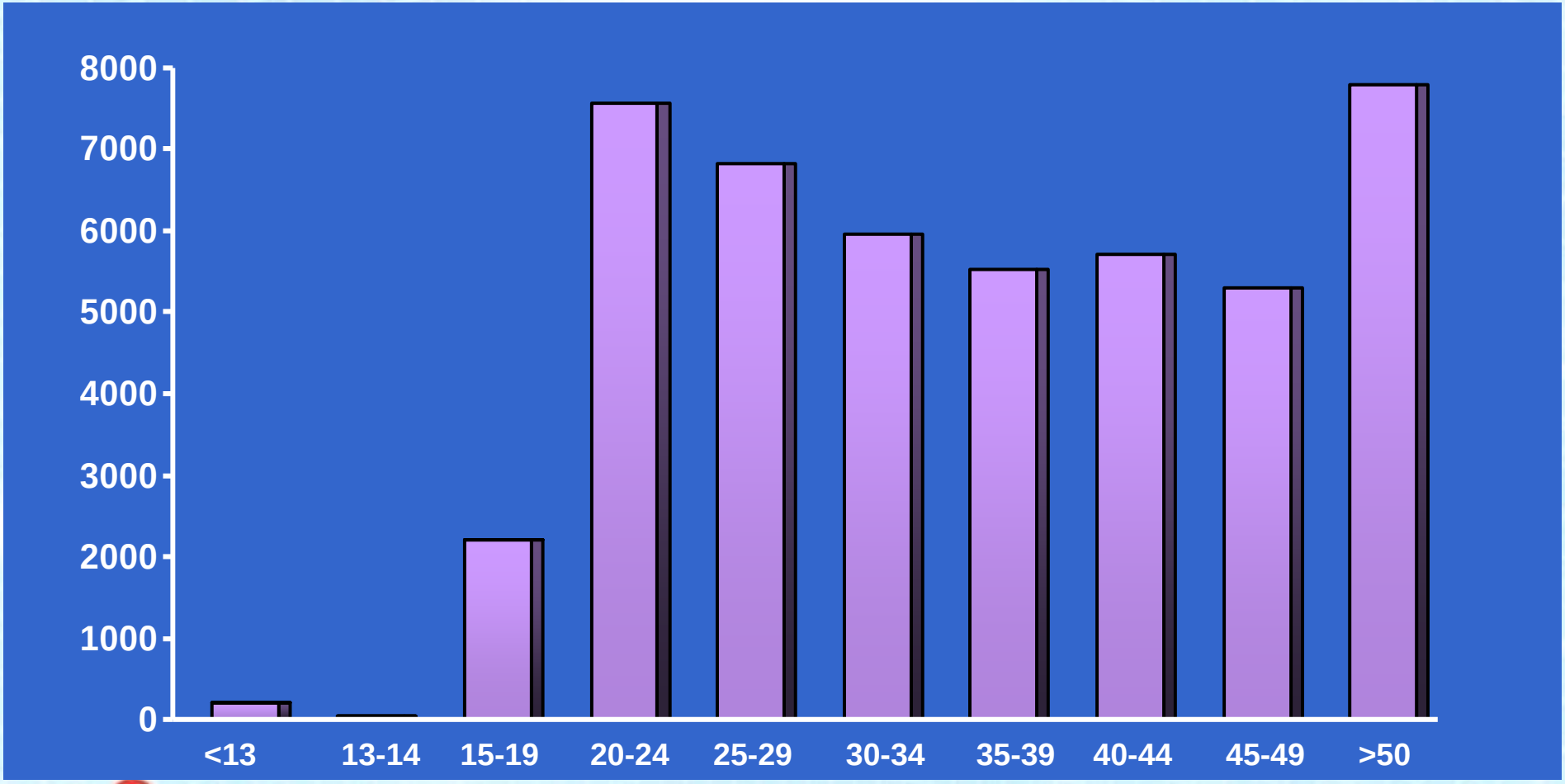
CDC. *HIV Surveillance Report, 2006*.

New HIV diagnosis 2011



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CDC. *HIV Surveillance Report, 2011*.
http://www.cdc.gov/hiv/pdf/statistics_2011_HIV_Surveillance_Report

Challenges in HIV diagnosis, HIV care and management of Co-morbidities in the aging population

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CHALLENGES IN DIAGNOSIS

63 yo male

DM

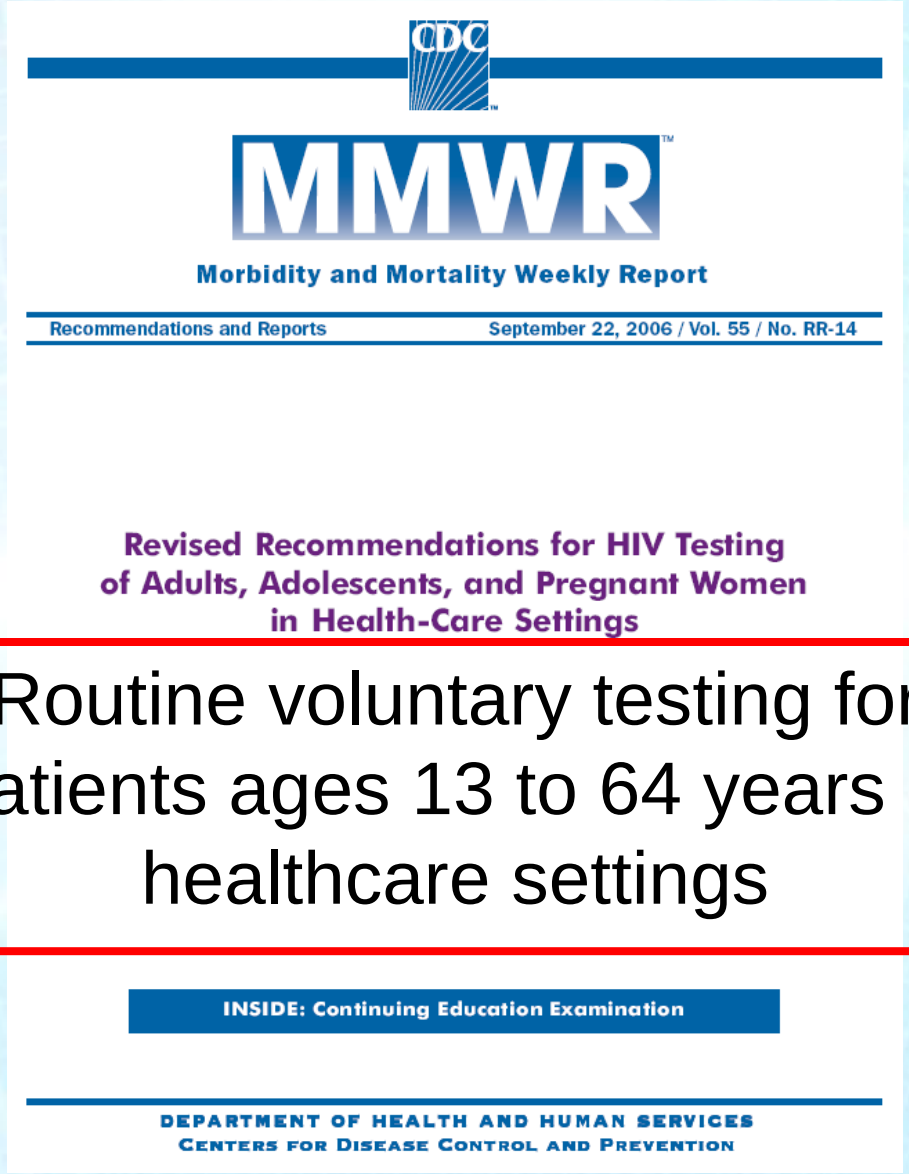
HTN

Married for 30 years

Diagnosed with HIV infection during labs done as part of a DM research study

CD4=537, VL=90,000

Challenges in HIV diagnosis



Routine voluntary testing for patients ages 13 to 64 years in healthcare settings

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Challenges in HIV diagnosis

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August 2012 | Volume 7 | Issue 8 | e43618

PLOS ONE

The New Invincibles: HIV Screening among Older Adults in the U.S.

Oluwatoyosi A. Adekeye[1]*, Harry J. Heiman[2], Onyekachi S. Onyeabor[2], Hyacinth I. Hyacinth[3]

- 2009 National Health Interview Survey (NHIS)
- 12,366 adults over 50 years
- 75% had never been tested for HIV
- 84% thought they had no chances of getting HIV
- The most common reason for testing was patient request
- No difference in testing rates by race

Late or Missed Diagnosis in Older Adults

- Poor awareness of HIV risk factors (including safe sex practices)
- Lack of HIV prevention education targeting older adults
- Health care provider belief that older adults are not sexually active
- Failure of some health care providers to consider HIV infection in this patient population

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Luther VP, et al. *Clin Geriatr Med*. 2007;23:567-583.
Illa L, et al. *AIDS Behav*. 2008;12:935-942.

Challenges in HIV diagnosis

CURRENT SEXUAL ACTIVITY AND RISKY SEXUAL BEHAVIOR IN OLDER MEN WITH OR AT RISK FOR HIV INFECTION

AIDS Educ Prev. 2007 August ; 19(4): 321–333.

Nina A. Cooperman, **Julia H. Arnsten**, and **Robert S. Klein**

- Sexual risk behaviors among 624 men over 50 years
- In the prior 6 months:
  - 75% sexually active (48% weekly or more)
  - 50% drug use
  - 18% use condoms
  - 24% more than one sex partner

CHALLENGES IN HIV CARE

60 yo female

HIV – 23 years

Nadir CD4=23

CD4=130, RNA<20

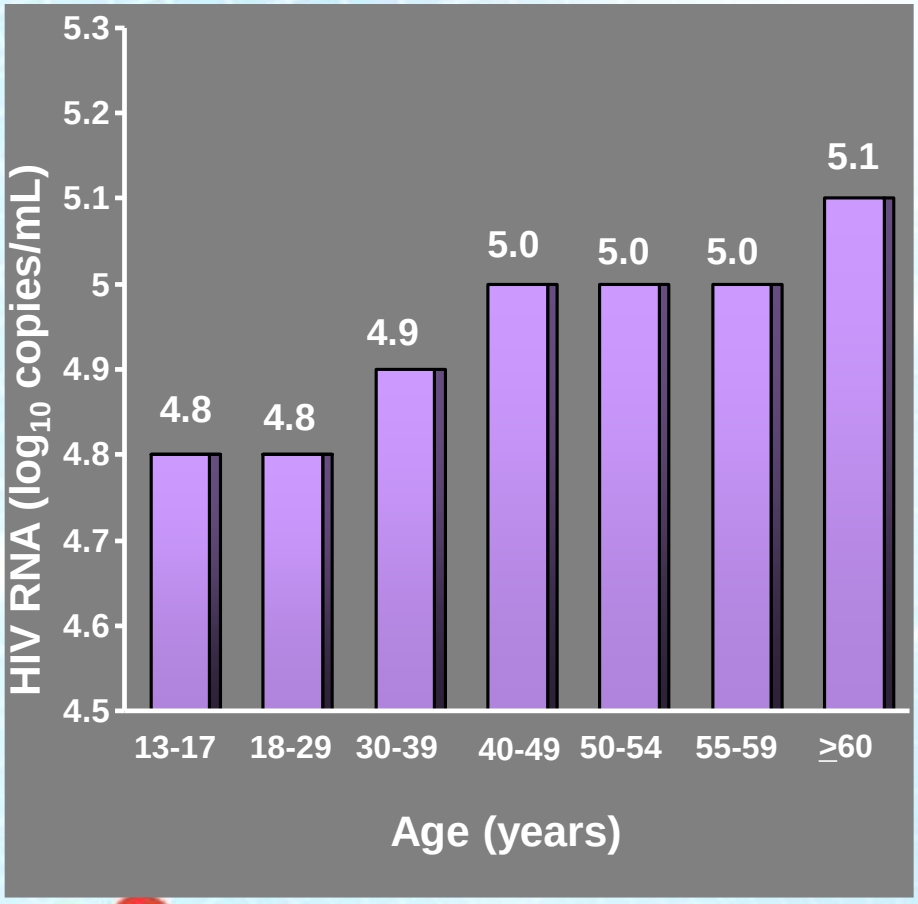
Cervical cancer

HTN

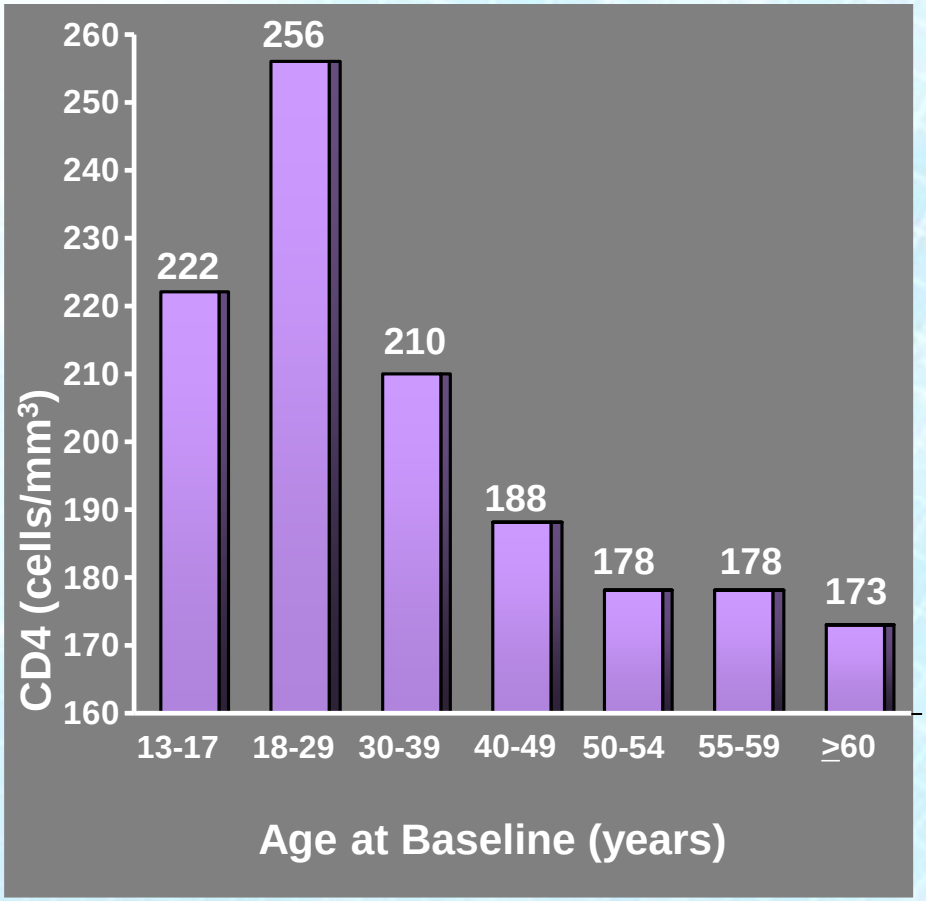
Unable to achieve CD>200 despite adherence to medication

Baseline viral load and CD4 counts

Baseline HIV RNA



Baseline CD4 Count



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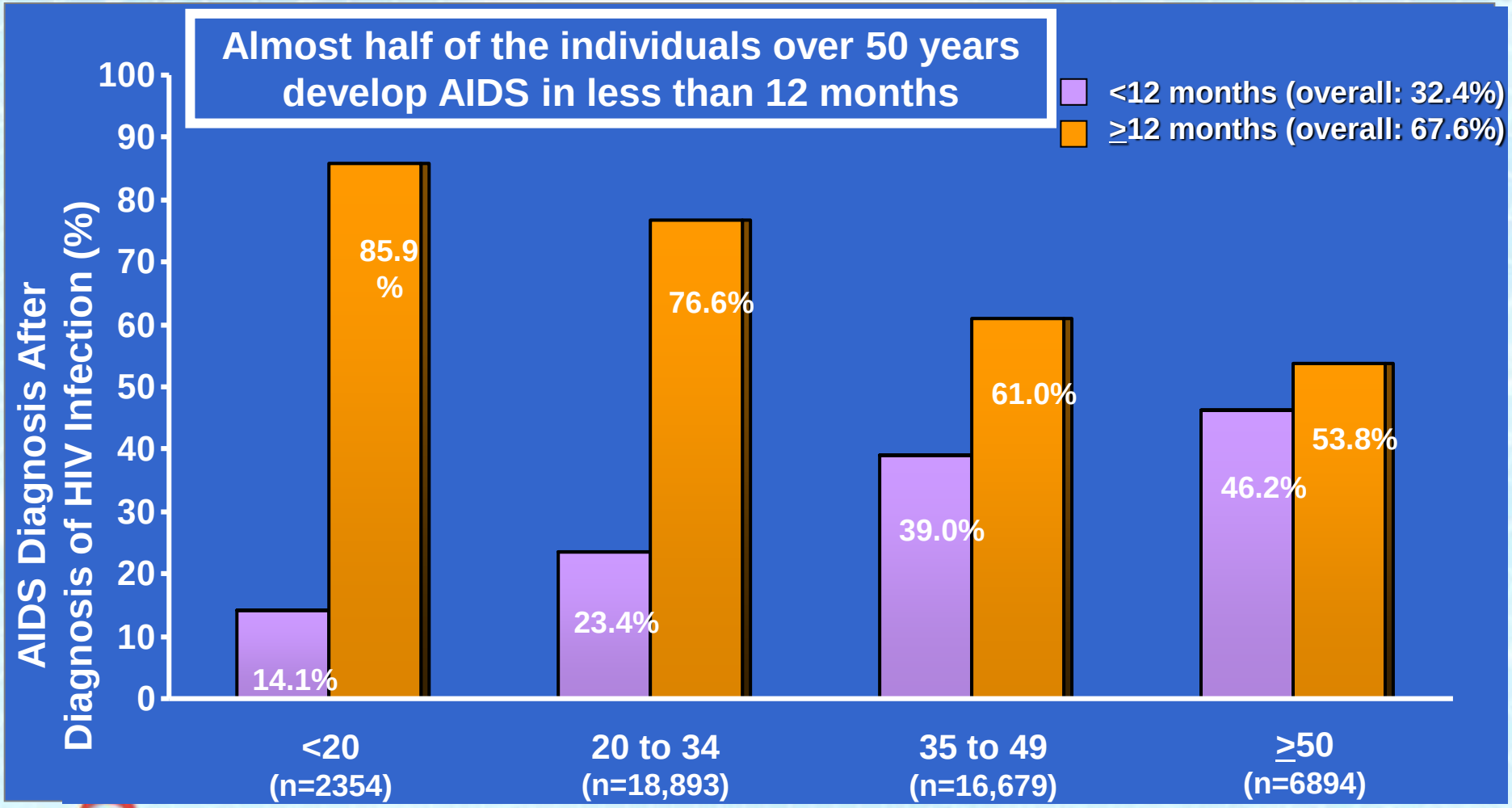
Lower CD4 counts and higher VL at baseline

COHERE Study Group. *AIDS.* 2008;22:1463-1473.

Time to AIDS Diagnosis



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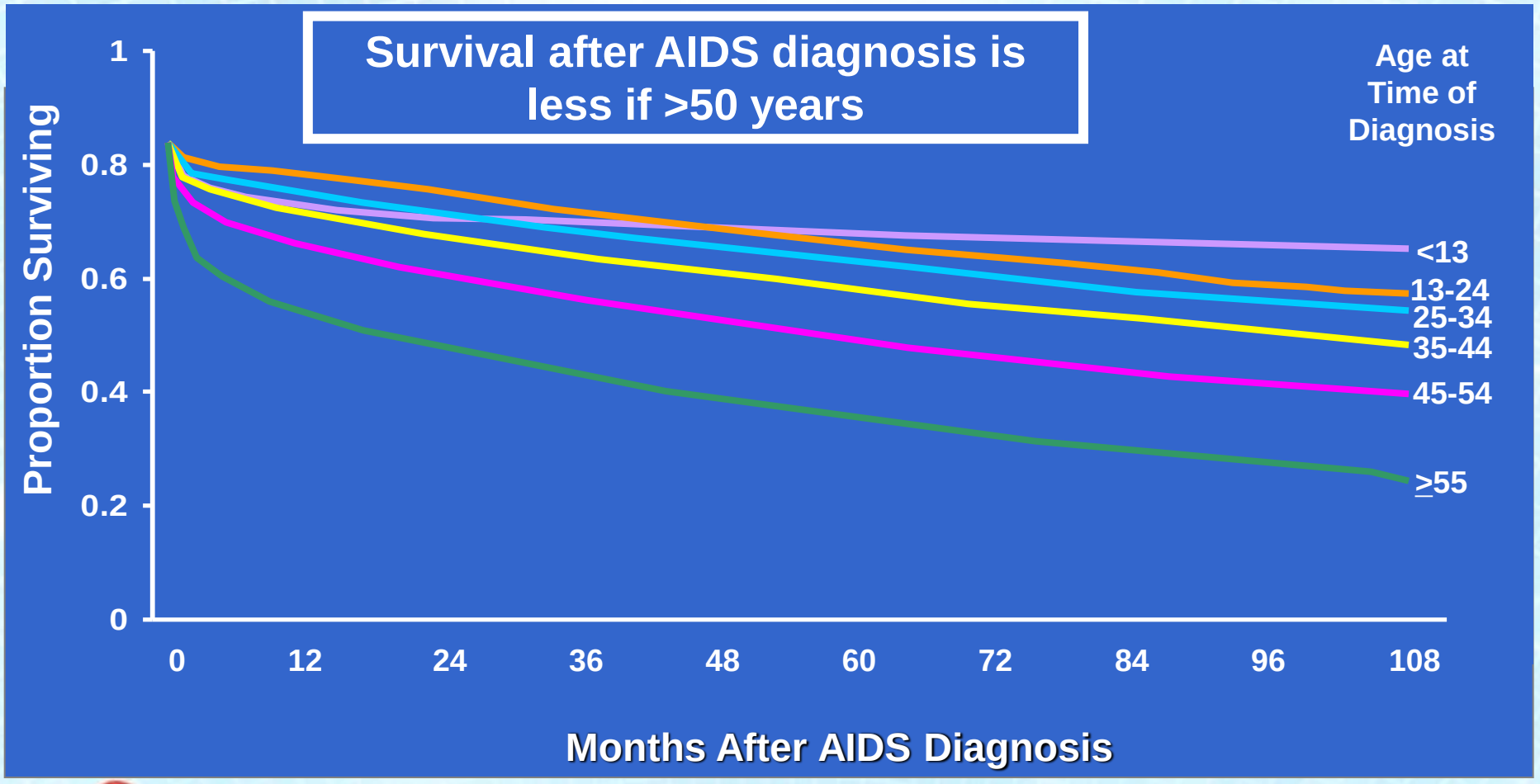
CDC. *HIV Surveillance Report, 2010*. http://www.cdc.gov/hiv/surveillance/resources/reports/2010report/.

Survival after AIDS Diagnosis



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CDC. *HIV Surveillance Report, 2010*. http://www.cdc.gov/hiv/surveillance/resources/reports/2010report/.

ART Response by Age: % of people who experience an event 12 months after ART (p<0.0001)

Age (ys)	Virological response	Discontinuation ART	CD4>200	AIDS event/death
18-29	50%	14.8%	86.7%	5.2%
30-39	51.6%	11.4%	80.6%	7.6%
40-49	57.5%	9.2%	76.3%	9.4%
50-54	61.4%	6.9%	75.2%	11.1%
55-59	60.3%	7.9%	73.9%	10.9%
>60	61.8%	7.3%	74.7%	11.7%
Total	53.7%	11.0%	80.1%	8.1%

BETTER

WORSE

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COHERE Study Group. *AIDS.* 2008;22:1463-1473.

CHALLENGES IN MANAGEMENT OF CO-MORBIDITIES

73 yo male

Smoker

HIV – 25 years

CD4=483, RNA<20

Nadir CD4= 190

HTN

DM

Erectile dysfunction

AMI and 3 vessel disease

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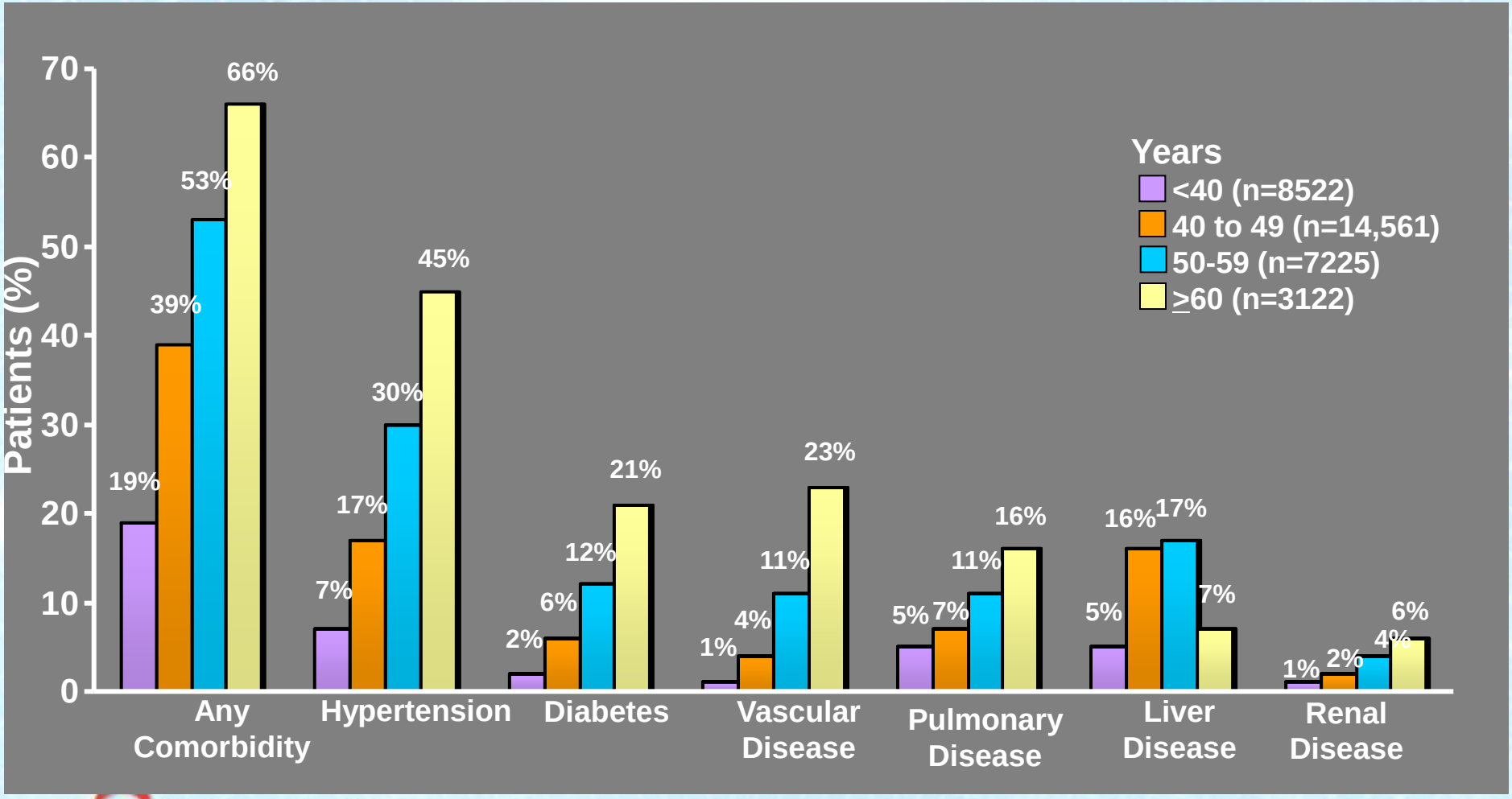
VACS: Comorbidities in HIV infection



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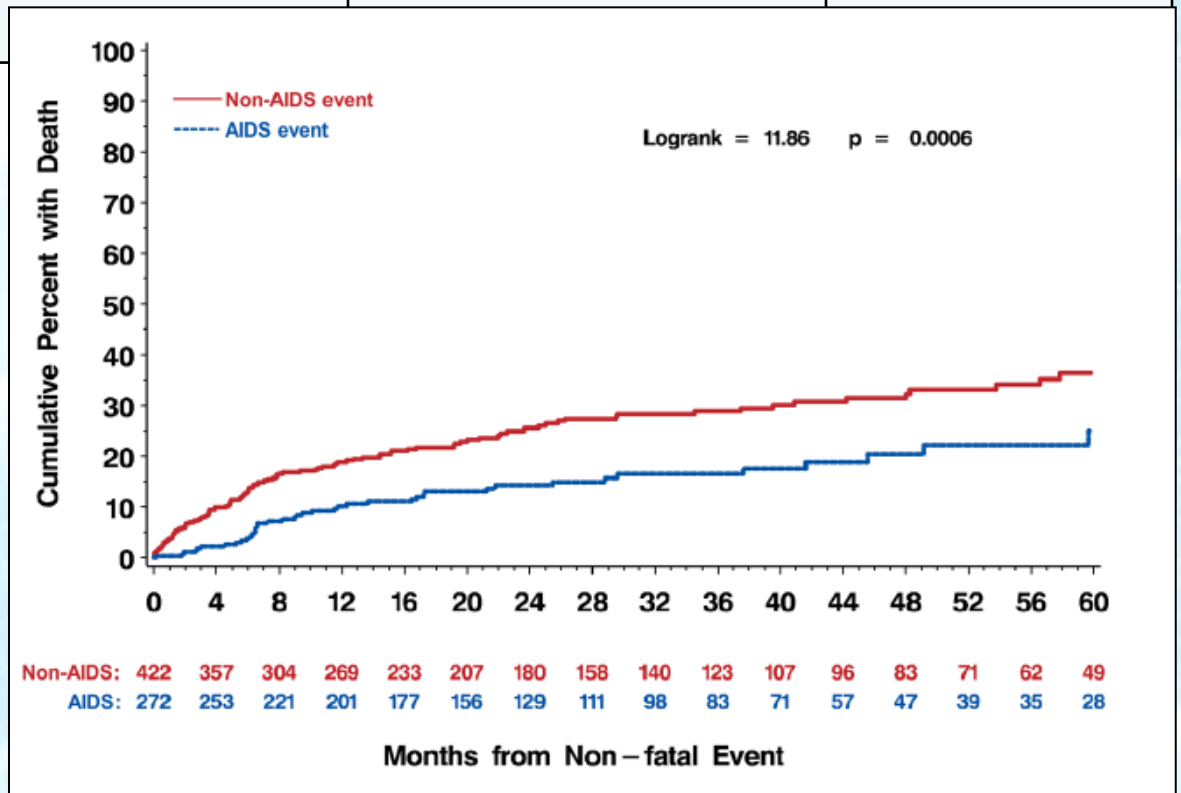
Goulet JL, et al. *Clin Infect Dis.* 2007;45:1593-1601.

Risk of All-cause Mortality Associated with Non-fatal AIDS and Serious Non-AIDS Events among Adults Infected with HIV

Jacqueline NEUHAUS[1], Brian ANGUS[2], Justyna D. KOWALSKA[3], Alberto LA ROSA[4], Jim SAMPSON[5], Deborah WENTWORTH[1], and Amanda MOCROFT[6] for the INSIGHT SMART and ESPRIT Study Groups

AIDS. 2010 March 13; 24(5): 697–706.

n= 9,583	AIDS events	Non AIDS events	OR
Occurrence	16%	26%	
Cumulative mortality (6mo)	4.7%	13.4%	11.4



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HANA: HIV Associated Non AIDS comorbitidies

- Cardiovascular disease
- Cognitive decline
- Cancer
- Osteoporosis
- Frailty
- Hypertension
- Diabetes Mellitus type 2
- Hyperlipidemia
- Liver Failure
- Kidney Failure

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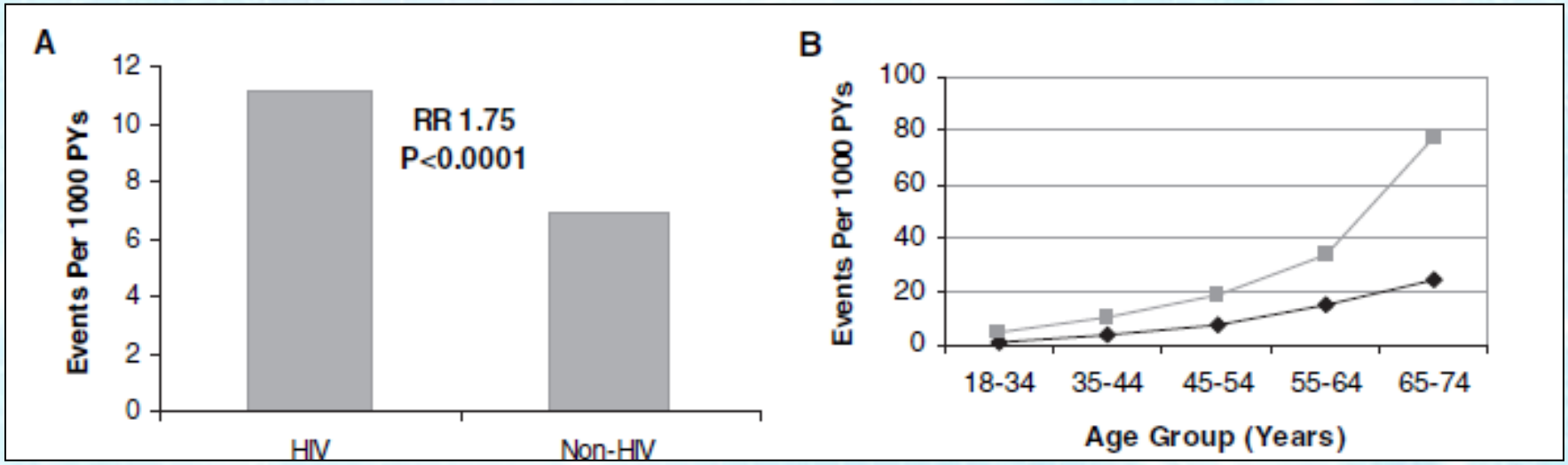
Challenges: Cardiovascular Disease

Increased Acute Myocardial Infarction Rates and Cardiovascular Risk Factors among Patients with Human Immunodeficiency Virus

Virginia A. Triant *J Clin Endocrinol Metab*. 2007 July ; 92(7): 2506–2512.



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Cardiovascular Disease is more common in HIV infected patients when compared with uninfected controls and the risk increases with age

HIV Infection and the Risk of Acute Myocardial Infarction

Matthew S. Freiberg, MD, MSc; Chung-Chou H. Chang, PhD; Lewis H. Kuller, MD, DrPH; Melissa Skanderson, MSW;

VACS Cohort

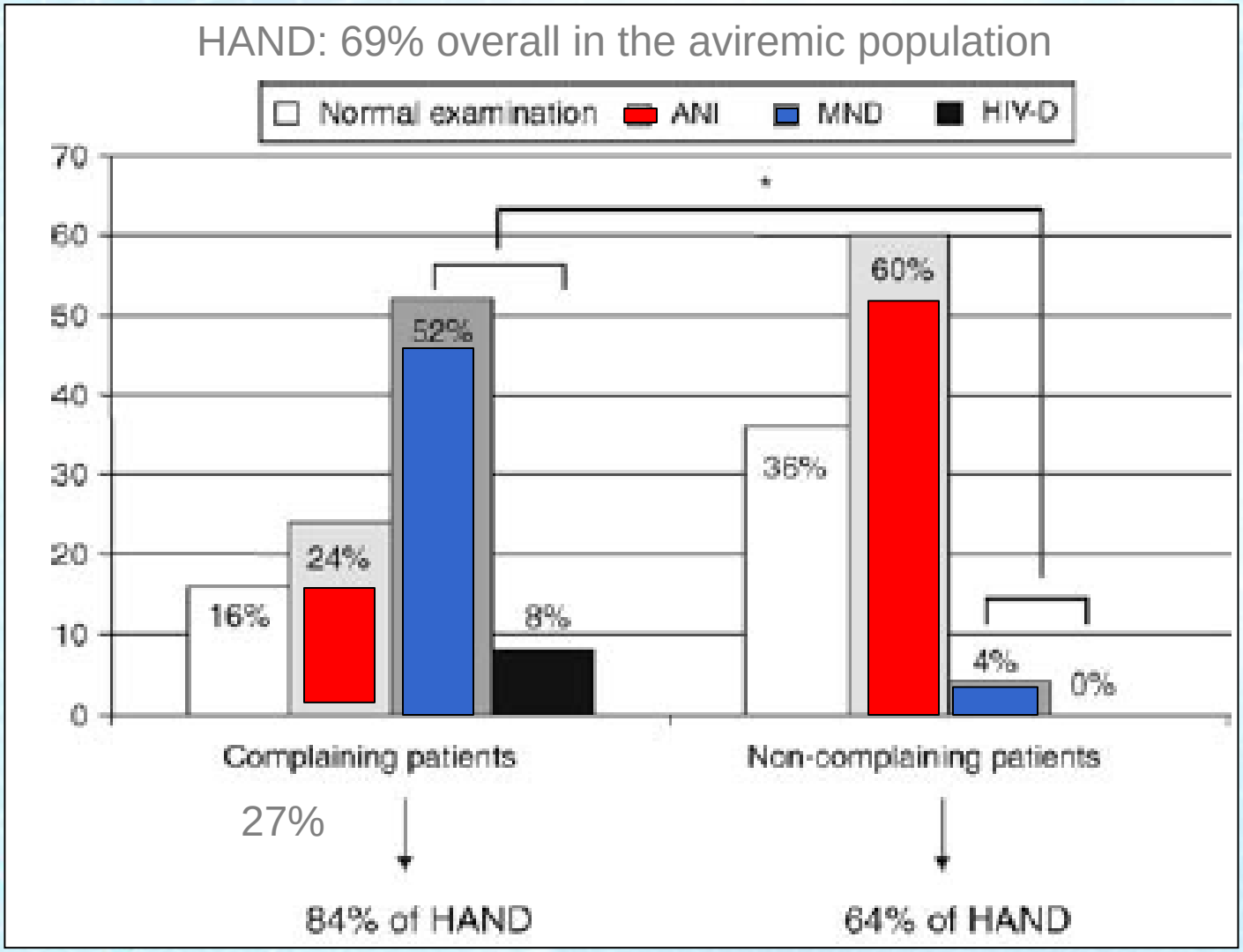
AMI events per 1000 person-years ($p<0.05$)

n = 83459	HIV infected	HIV uninfected
40 - 49 ys	2	1.5
50 - 59 ys	3.9	2.2
60 - 69	5	3.3

Adjusted for co-morbidities, substance abuse, Framingham risks

JAMA Intern Med. 2013;173(8):614-622.

Cognitive dysfunction in HIV patients despite long-standing suppression of viremia



ANI: Asymptomatic Neurocognitive Impairment

MND: mild neurocognitive disorder

HIV-D: HIV dementia

Nadir CD4 was associated with HAND

AIDS 2010, **24**:1243–1250

Malignancies in ART treated patients

AIDS-related malignancies

↓ Kaposi sarcoma

↓ CNS lymphoma

Non-AIDS defining malignancies

↑ Liver

↑ Larynx

↑ Anal

↑ Lung

Nadir Low CD4 associated with Non-AIDS malignancies

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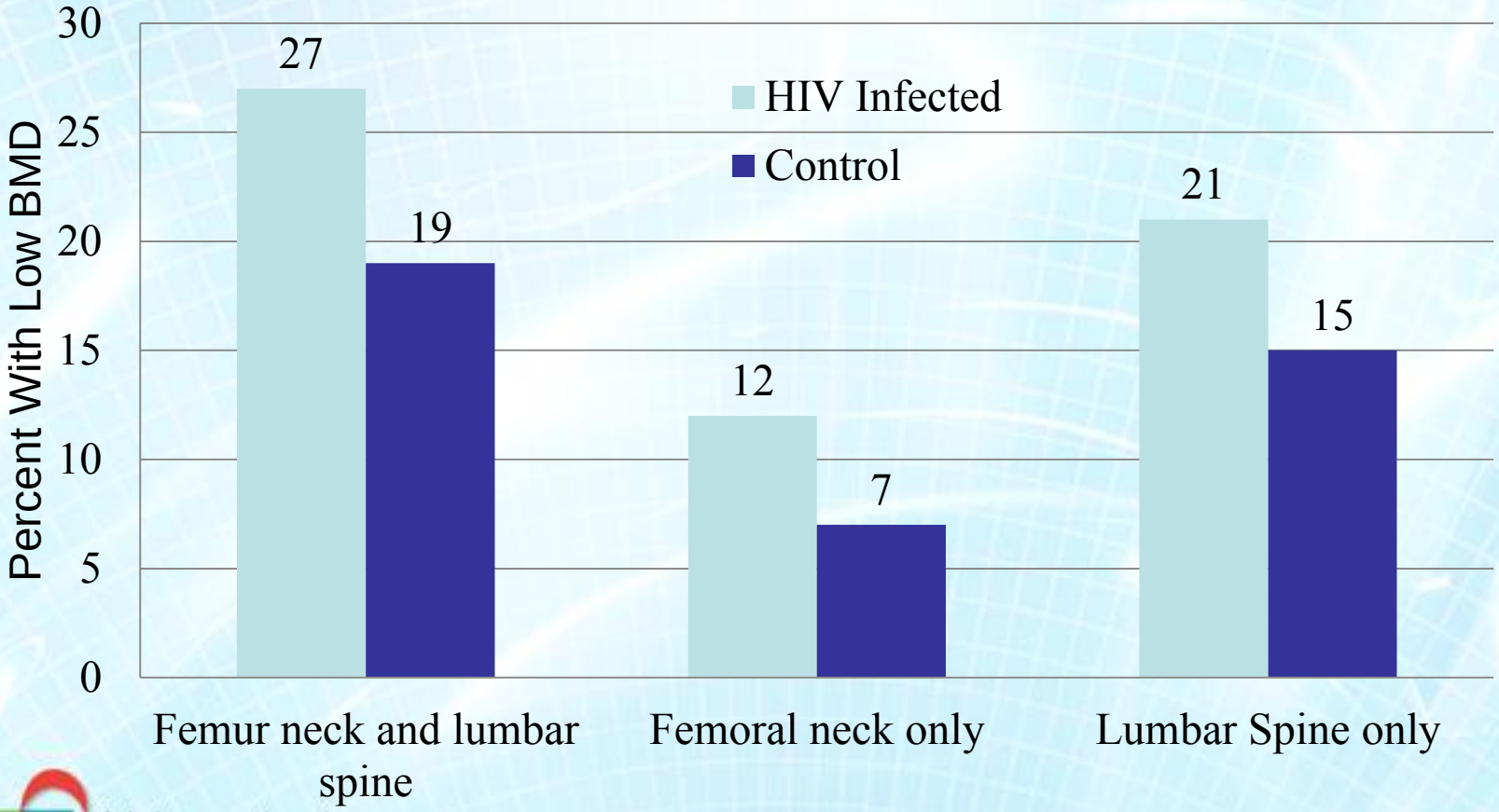
Mitsuyasu RT. *Top HIV Med*. 2008;16:117-121.
Engels EA, et al. *Int J Cancer.* 2008;123:187-194.
Patel P, et al. *Ann Intern Med.* 2008;148:728-736.

Osteopenia

BMD is Lower in HIV-Infected Women ≥ 40 Years of Age



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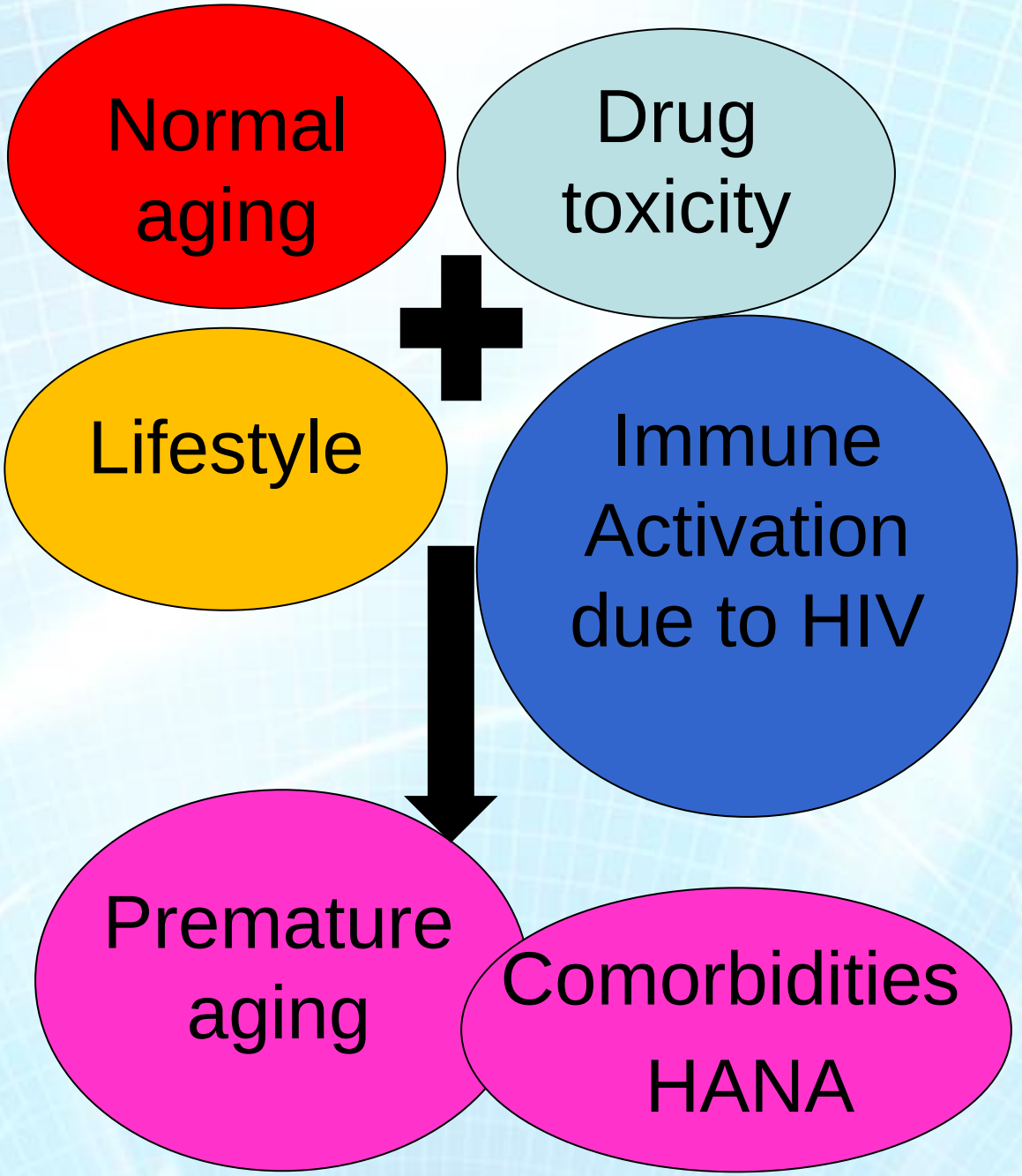
Arnsten JH, et al. Clin Infect Dis. 2006;42:1014-1020



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Deeks S G , Phillips A N BMJ 2009;338:bmj.a3172

Successful aging with HIV infection

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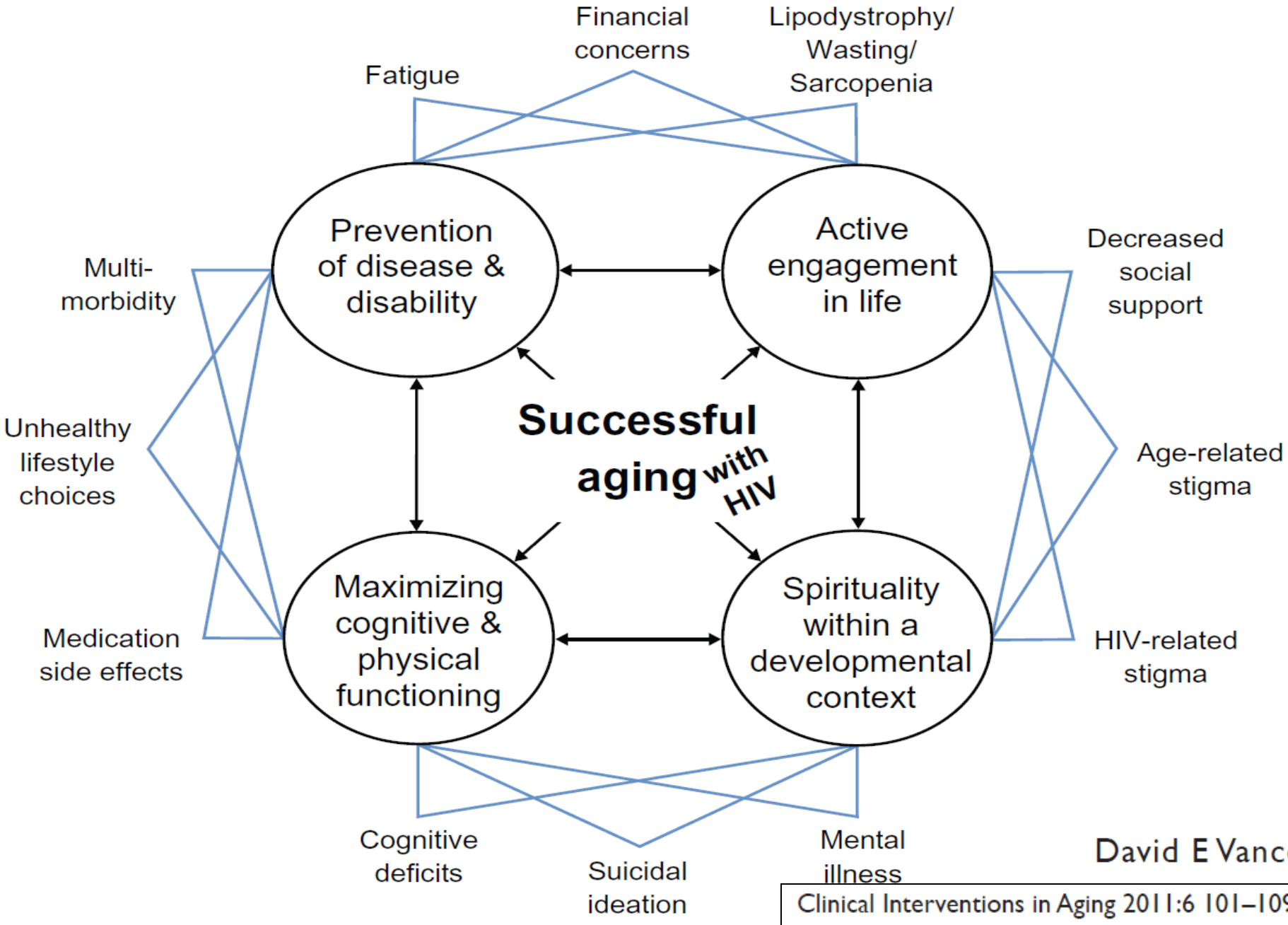
Barriers and components of successful aging with HIV



David E Vance

Clinical Interventions in Aging 2011:6 101–109

Summary

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What we know

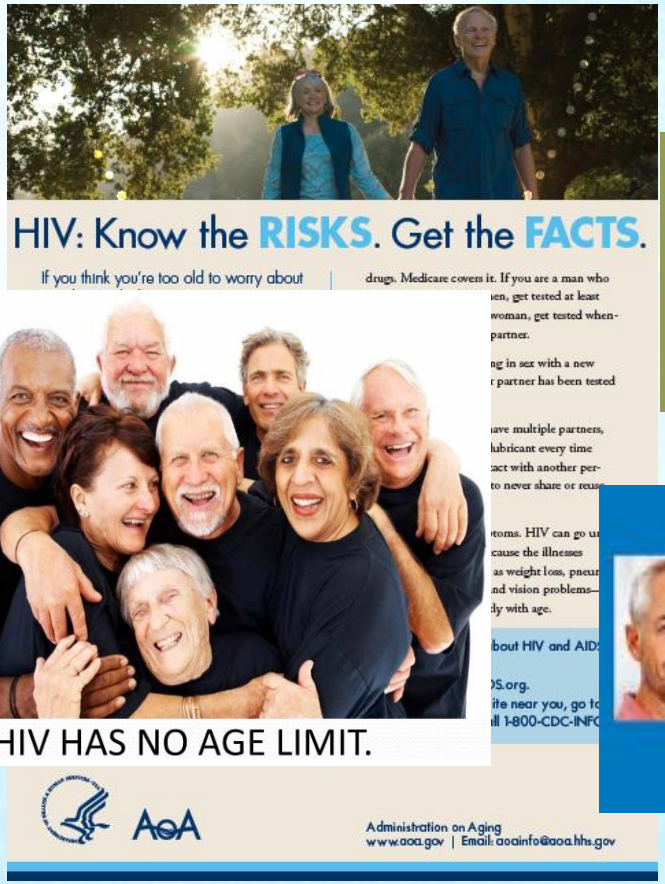
- HIV population is aging
- Aging of the immune system is enhanced by HIV infection despite ART
- Aging individuals engage in HIV risk behaviors but providers fail to identify those and adhere to screening guidelines
- Comorbidities attributed to increasing age overlap with morbidity from HIV disease and are predicted by lower CD4 counts

New directions: Pathogenesis

Understand the mechanisms that drive IA and aging in HIV infection (HIV reservoirs, viral co-infections, telomere length and telomerase activity,…)

New directions - Diagnosis

- Expand testing to all at risk
- PrEP in the aging population



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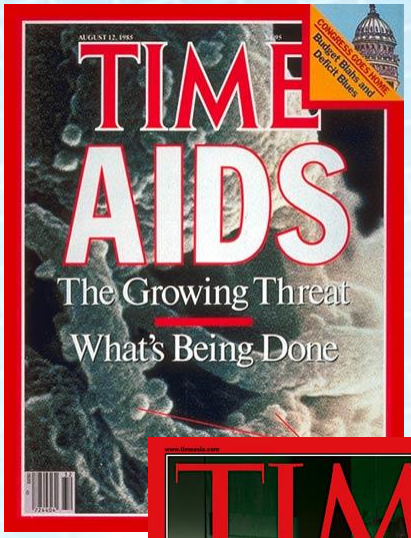
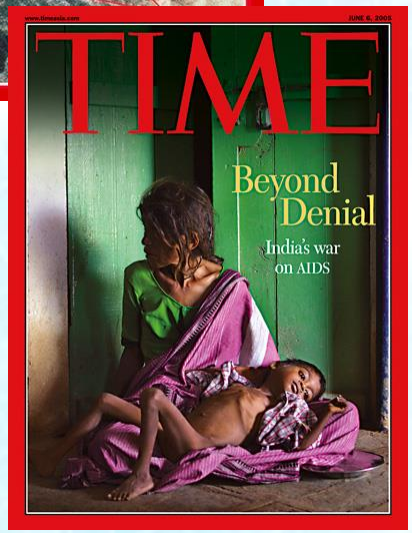
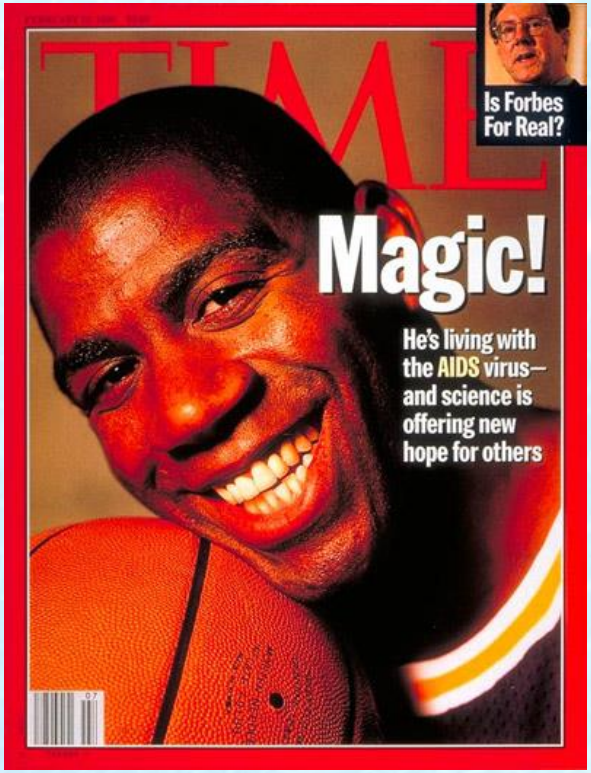
New directions - HIV care





- Early initiation of ART
- Strategies to improve immune recovery (intensification treatment, other immune therapies)



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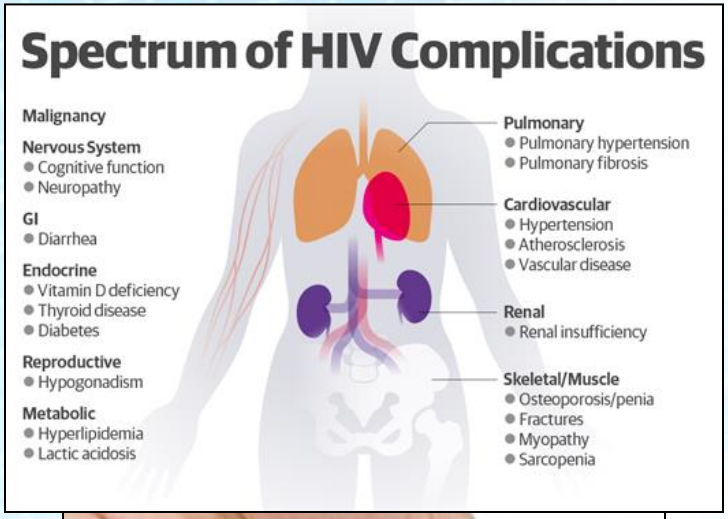
New directions - Comorbidities



- Guidelines for diagnosis and management of comorbidities
- Strategies to decrease inflammation and IA
- Anti-aging interventions
- Psychosocial management (HAND)

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http://www.aoa.gov/AoARoot/AoA_Programs/HPW/HIV_AIDS/toolkit.aspx

New directions – Successful Aging

Bio-behavioral interventions to promote successful aging

Deborah Jones

Allan Rodriguez

Anita Parmigiani

Stephen Weiss

Margaret Fischl

Suresh Pallikkuth

Michael Kolber

Mario Stevenson

Savita Pahwa

OUR PATIENTS

Jackson MEMORIAL HOSPITAL Jackson Health System

PUBLIC HEALTH TRUST

MIAMI CFAR

MIAMI CENTER FOR AIDS RESEARCH

8th International Conference on HIV TREATMENT AND PREVENTION ADHERENCE

UHealth UNIVERSITY OF MIAMI HEALTH SYSTEM

UNIVERSITY OF MIAMI MILLER SCHOOL of MEDICINE