HIV and Aging

Douglas G. Fish, MD
Albany Medical College
Cali, Colombia
March 25, 2010

Objectives

- Epidemiology of aging
- Immunology of aging
- Clinical effects
- Health screenings

National HIV/AIDS and Aging Awareness Day
September 18, 2009

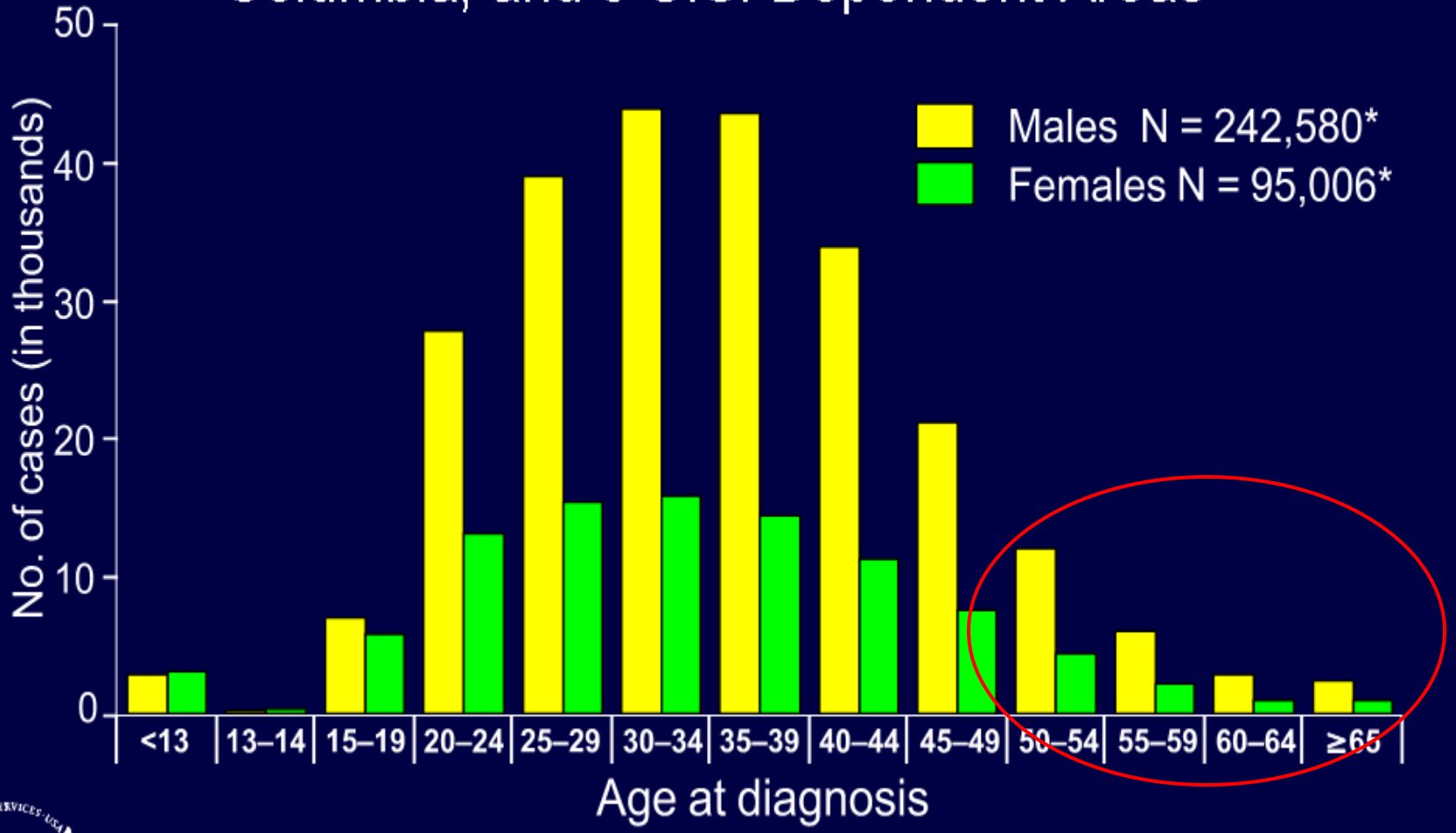
Statement of Anthony S. Fauci, M.D.
Director, National Institute of Allergy and Infectious Diseases
Richard J. Hodes, M.D.
Director, National Institute on Aging
and
Jack Whitescarver, Ph.D.
Director, NIH Office of AIDS Research
National Institutes of Health

Reported Cases of HIV Infection (not AIDS), by Age Group at Diagnosis, Cumulative through 2007—47 States, the District of Columbia, and 5 U.S. Dependent Areas

	HIV Infection (not AIDS)	
Age (years)	No.	%
<13	5,821	2
13–14	529	<1
15–24	53,579	16
25–34	114,163	34
35–44	103,080	30
45–54	44,938	13
55–64	12,120	3
>65	3,360	<1
Total	337,590	

Note. Data from 47 states, the District of Columbia, and 5 U.S. dependent areas with confidential name-based HIV infection reporting as of 2007.

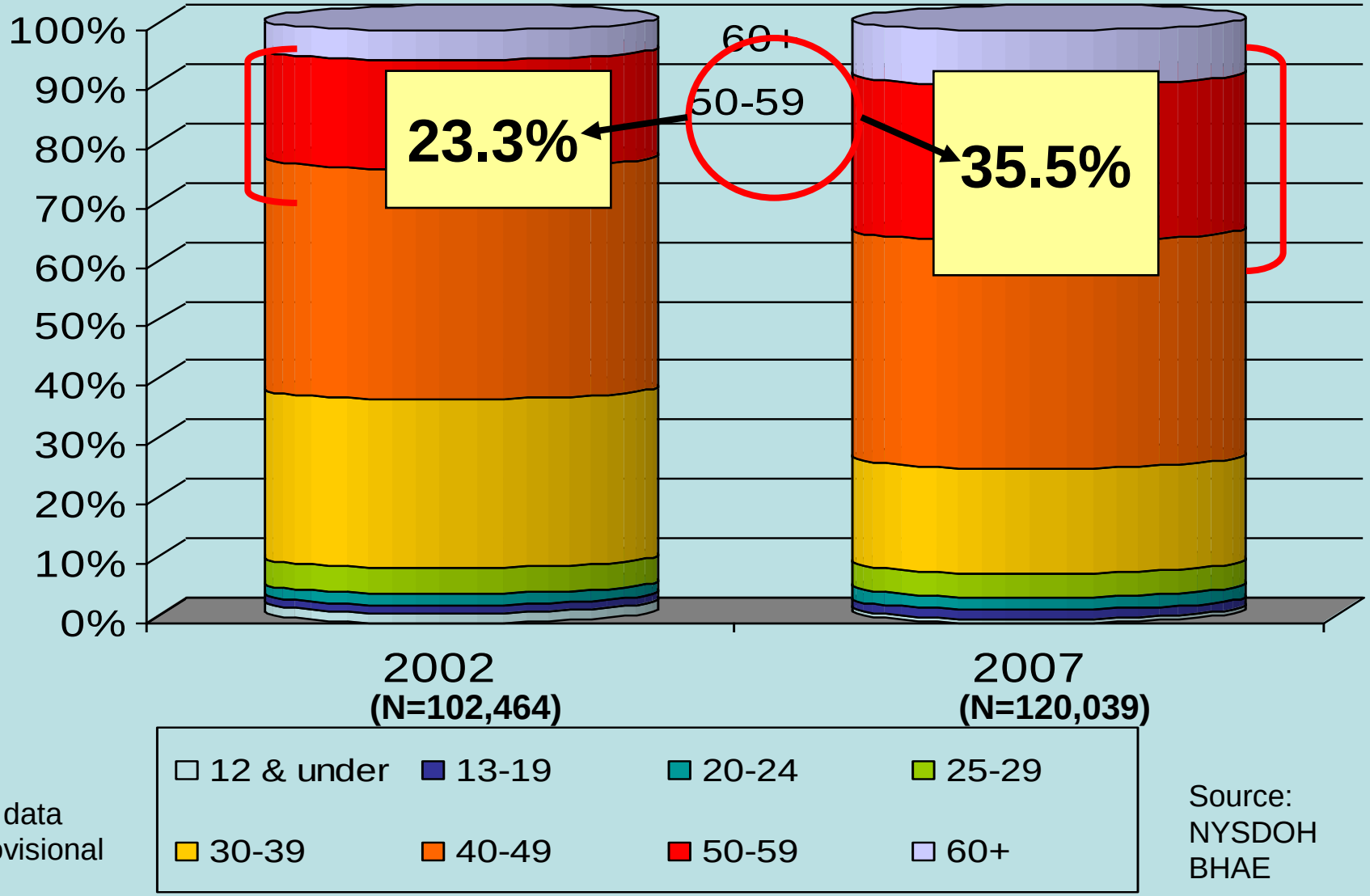
Reported Cases of HIV Infection (not AIDS), by Age Group and Sex, Cumulative through 2007—47 States, the District of Columbia, and 5 U.S. Dependent Areas



Note. Data from 47 states, the District of Columbia, and 5 U.S. dependent areas with confidential name-based HIV infection reporting as of 2007.
*Excludes 7 persons of unknown sex.

Persons Living with HIV/AIDS

By Age, New York State, end of year, 2002 and 2007*

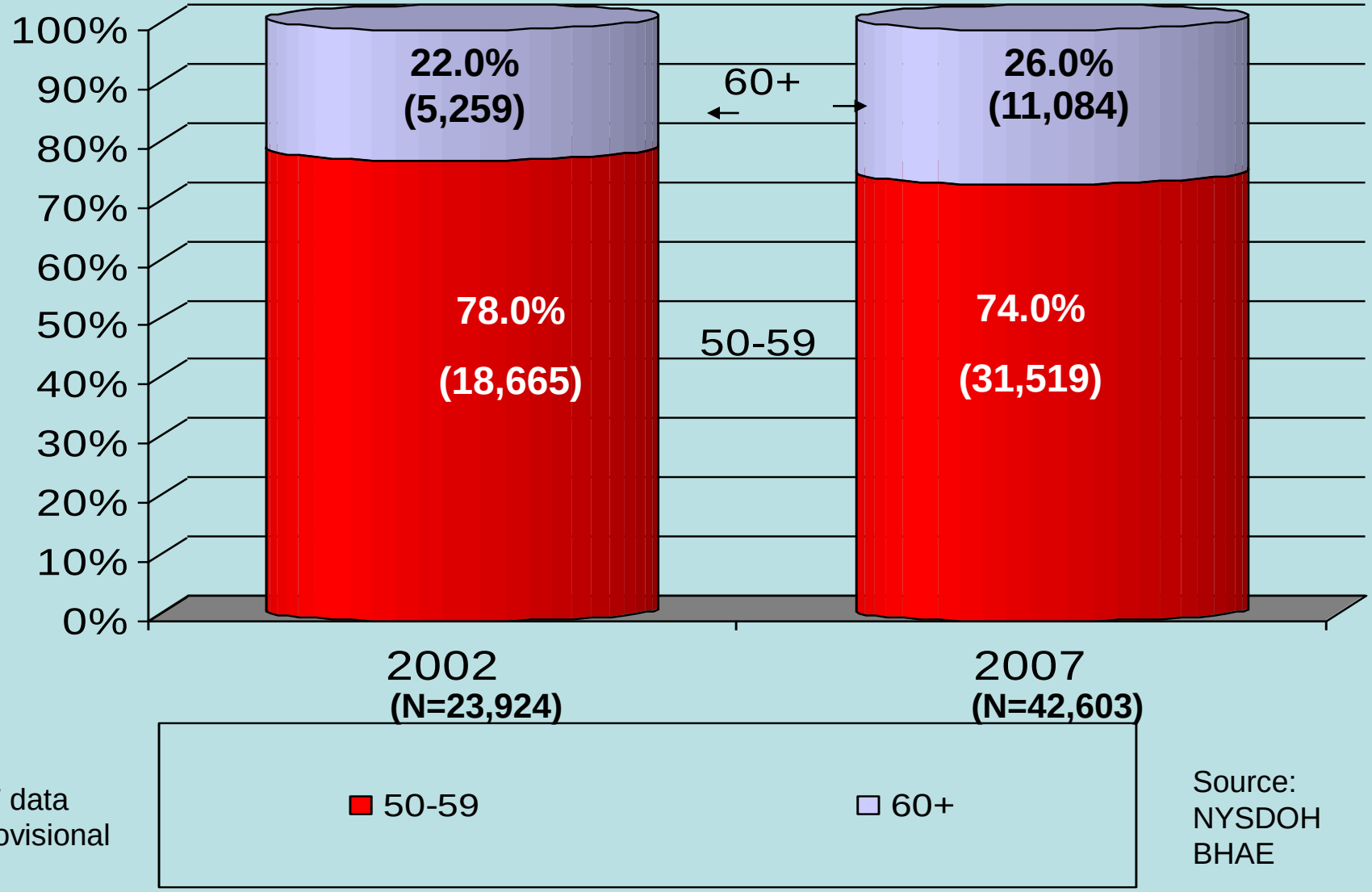


* 2007 data are provisional

Source: NYSDOH BHAE

Persons Living with HIV/AIDS Age ≥50

New York State, end of year, 2002 and 2007*



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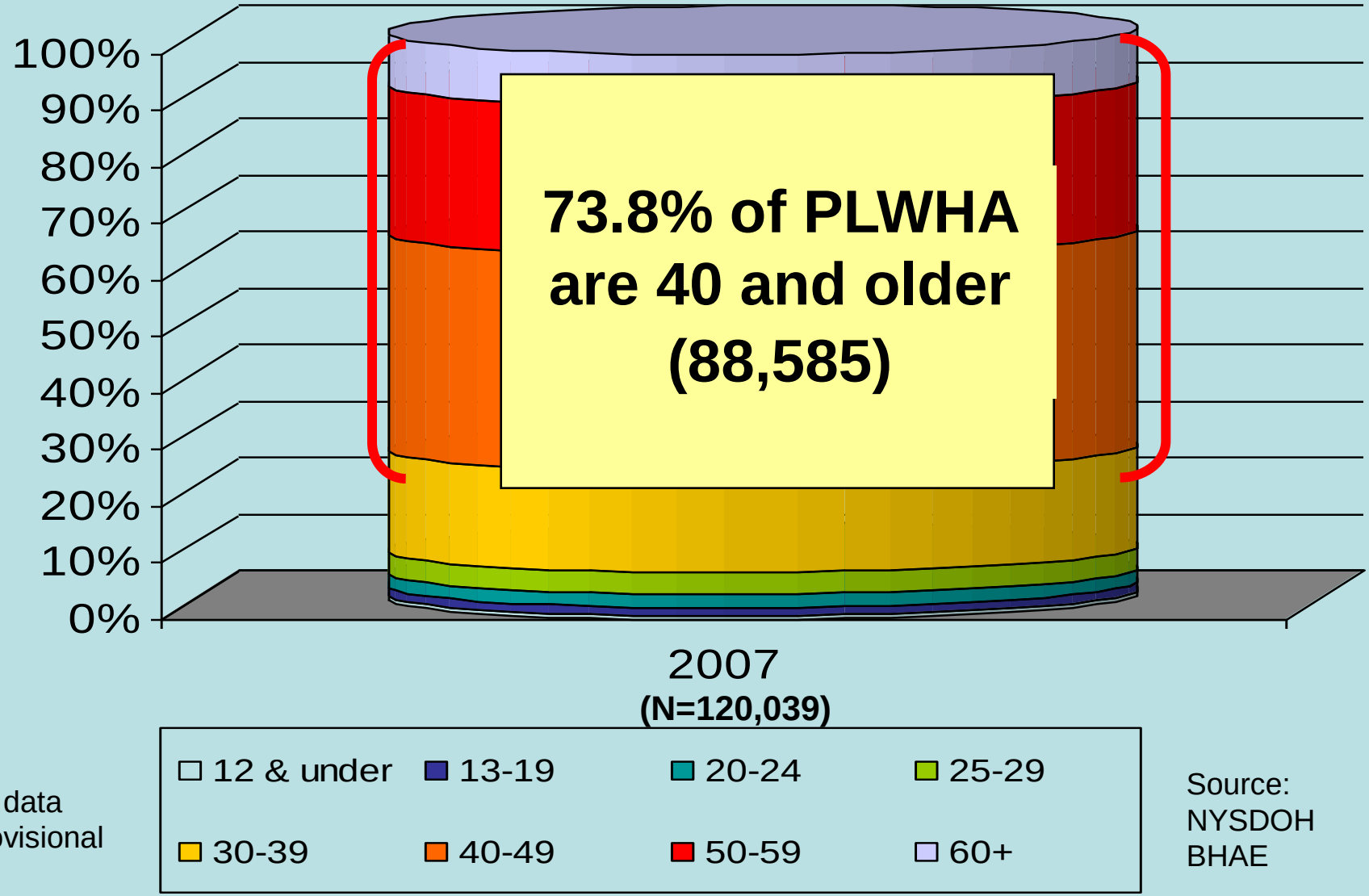


* 2007 data are provisional

Source: NYSDOH BHAE

Life Expectancy of Patients without AIDS

- Athena cohort – N = 4174; 1998-2007
  - 3700 were men in this Netherlands cohort
  - Compared to the general population
- Expected life years remaining at age 25 was:
  - 52.7 years for those with asymptomatic HIV infection;
  - 53.1 years for the general population.
- Modeled life expectancy of a patient presenting at an older age, for women and for those presenting with CDC B classification was slightly lower.

Van Sighem A *et al.* 17th CROI, 2010; Abstract 526.

HIV Effects and Aging of the Immune System

- Reduced capacity to renew T-helper cell populations
- Chronic inflammatory condition of HIV itself
- Persistence of replicating HIV in gut tissue

Deeks S. IDSA Philadelphia, PA;10/09.

Immune Systems of People with HIV…

- Age similarly to transplant patients.
- Age similarly to children born without a thymus.
- Age faster than those uninfected.

Deeks S. IDSA Philadelphia, PA;10/09.

Higher Risk of Clinical Progression in Patients Aged 50 Years or Older

- Prospective cohort study of 3015 treatment-naive patients initiating HAART
  - Aged ≥ 50 years: n = 401
  - Aged < 50 years: n = 2614
- Median follow-up: 31.5 months
- At BL, older patients more likely to have
  - AIDS-defining event (*P* = .0001)
  - Lower CD4+ cell count (*P* = .0002)
  - Higher HIV-1 RNA level (*P* = .0001)

- Patients 50 years of age or older have higher risk of clinical progression but improved virologic response vs patients younger than 50 years of age

Outcome	Adjusted HR	*P* Value
Progression to ADE or death	1.52	.0035
Progression to new ADE	1.50	.0087
HIV-1 RNA < 500 copies/mL	1.23	< .05

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

Immunologic Response Slower in Patients Aged 50 Years or Older

- Monthly CD4+ cell count increases significantly lower in patients aged 50 years or older

Mean CD4+ Cell Count Increase/Mo, cells/mm^3	Within First 6 Mos of HAART*		After 6 Months of HAART*	
	Age < 50 Yrs	Age ≥ 50 Yrs	Age < 50 Yrs	Age ≥ 50 Yrs
BL HIV-1 RNA < 5 log_{10} copies/mL	17.3	14.1	11.1	9.8
BL HIV-1 RNA ≥ 5 log_{10} copies/mL	42.9	36.9	17.9	15.6

**P* < .0001 for younger than 50 years of age vs 50 years of age or older in all subgroups.

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

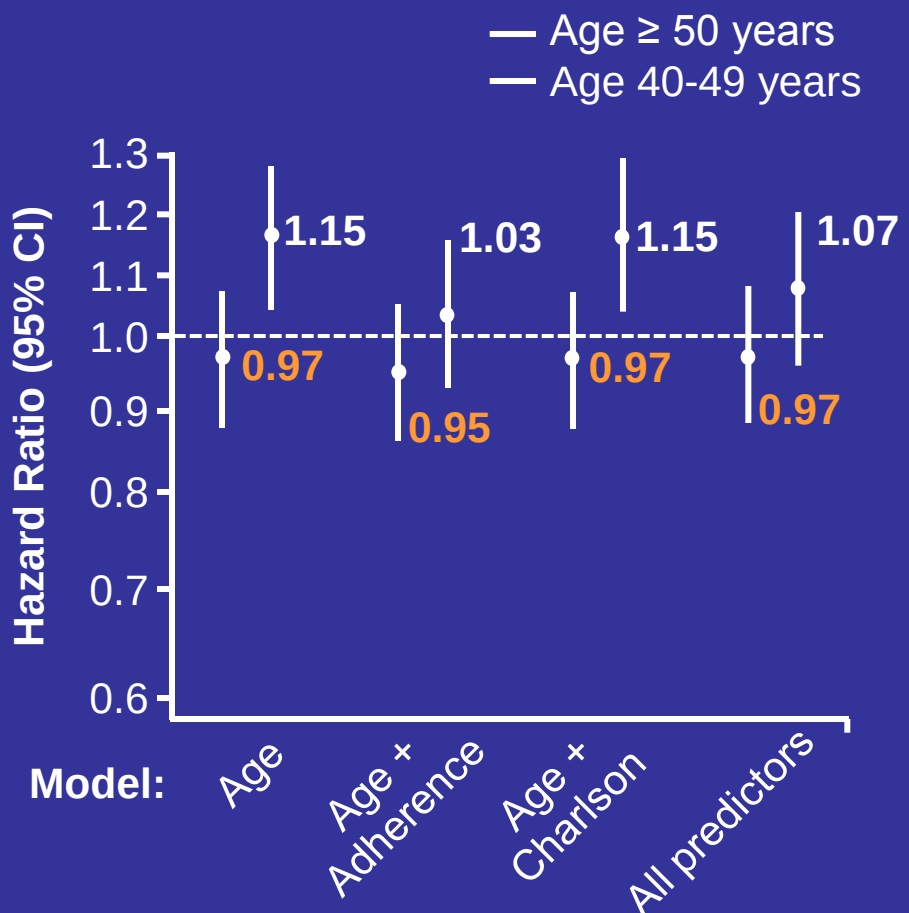
Younger Age Associated With Better Immunologic Recovery in ACTG 384

- Factors associated with significantly greater CD4+ cell count increases at Week 48 on HAART by multivariate analysis
  - Younger age (as continuous variable; *P* = .0014)
  - Female sex (*P* = .0004)
  - Higher BL $\log_{10}$ HIV-1 RNA (as continuous variable; *P* < .0001)
  - HIV-1 RNA ≤ 50 copies/mL at Week 48 (*P* = .0008)
- Both naive CD4+ cell percentage and naive:memory CD4+ cell count ratio associated with higher CD4+ cell count increases (r = 0.26 at Week 48 for both; *P* < .0001)
  - Naive CD4+ cell percentage and naive:memory CD4+ cell count ratio higher for younger (≤ 40 years) vs older (> 40 years) individuals (*P* < .0001 for both)

Gandhi RT, et al. J Acquir Immune Defic Syndr. 2006;42:426-434.

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

- Kaiser Permanente study compared patients 40-49 years of age and 50 years of age or older to younger patients (18-39 yrs of age)
- Patients older than 50 years of age more likely to achieve HIV-1 RNA < 500 copies/mL vs patients aged 18-39 years, even when adjusting for comorbidities
- Adherence major advantage for older patients



Silverberg M, et al. IAC 2006. Abstract TUPE0135.
Silverberg MJ, et al. Arch Intern Med. 2007;167:684-691.

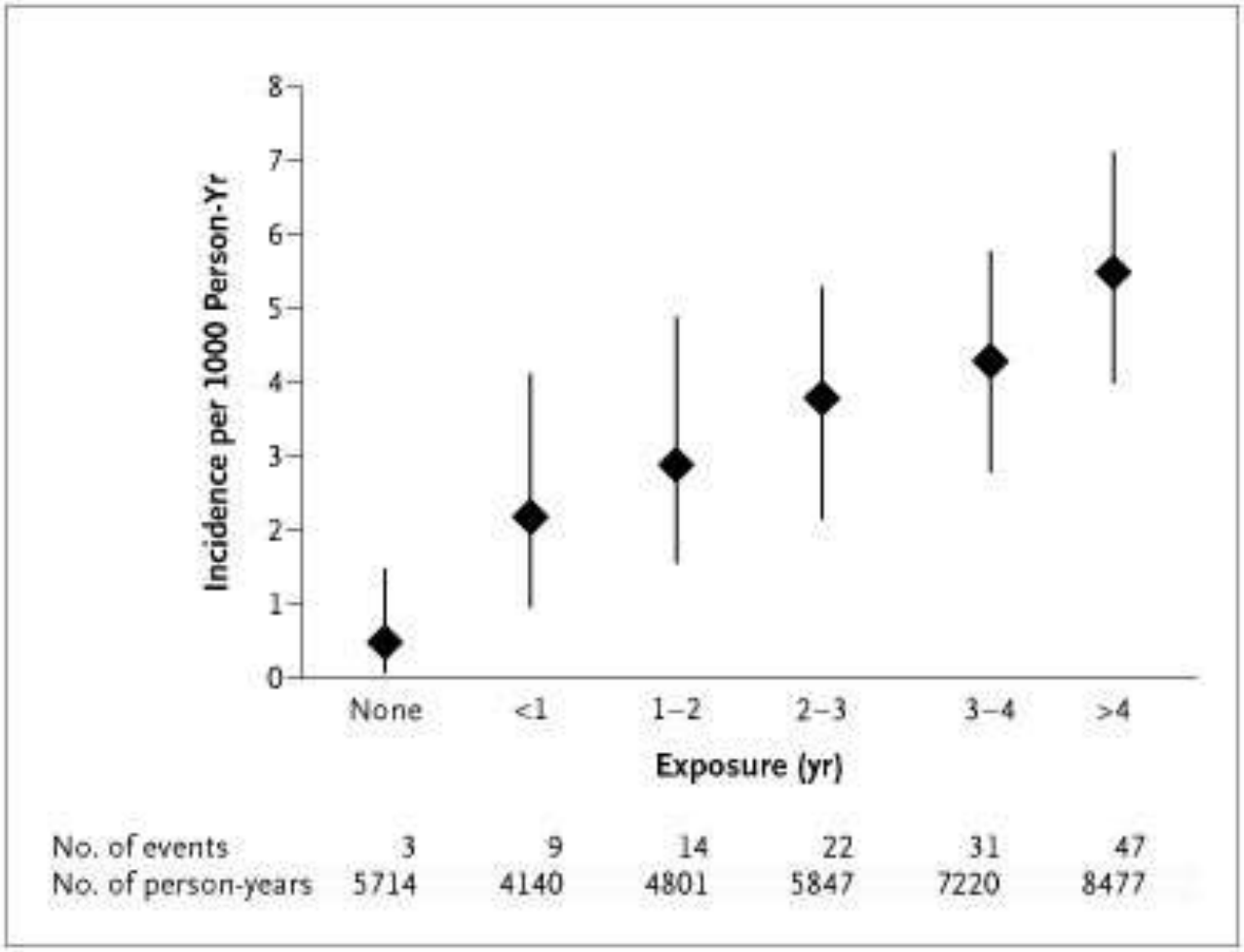
Clinical Effects of Aging

- Cardiovascular disease
- Pulmonary disease
- Malignancies in an aging population
- Endocrine disease
- Liver disease
- Aging effects on the brain & nervous system

Heart & Vascular Disease and HIV Effects

- Small but real increased risk of myocardial infarction in patients on some HIV therapies
- Peripheral vascular disease
- Cerebrovascular disease

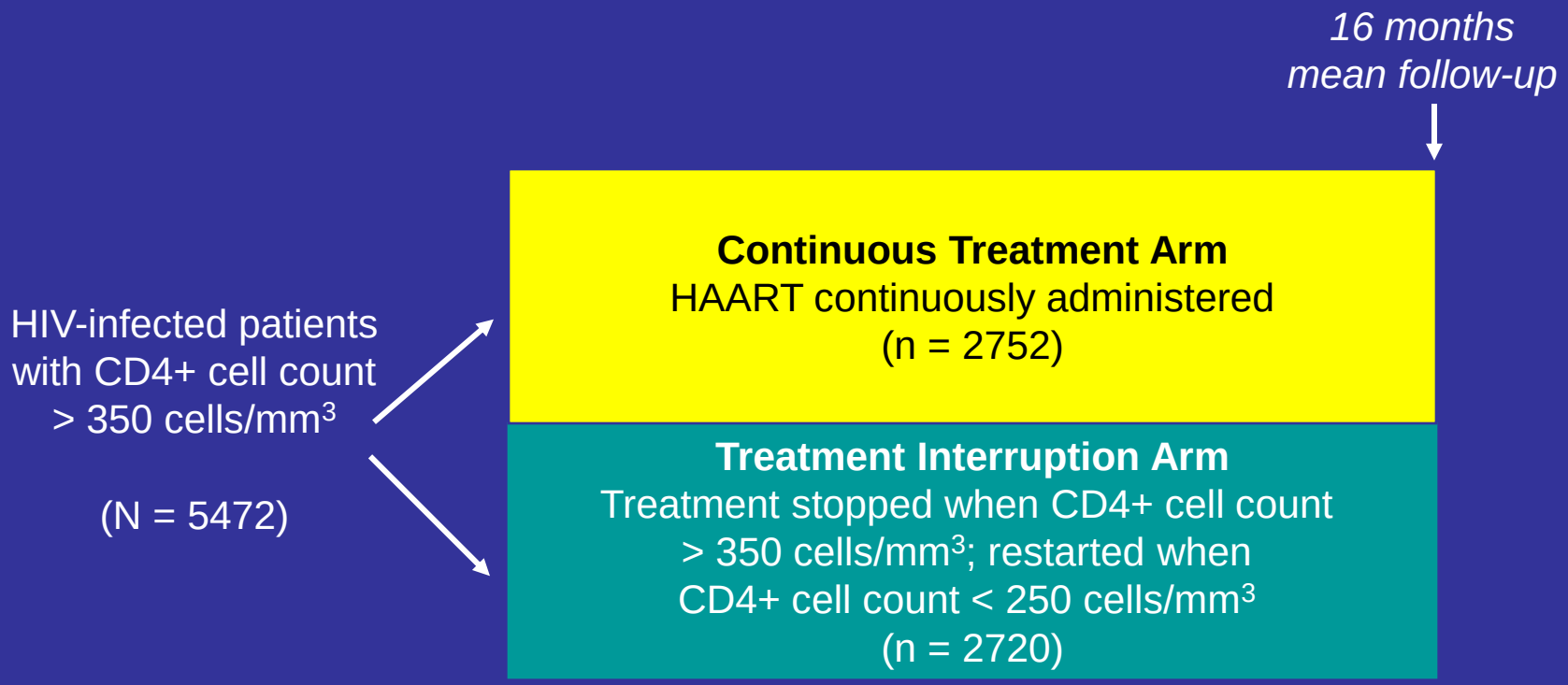
Incidence of Myocardial Infarction According to the Duration of Exposure to Combination Antiretroviral Therapy



The Data Collection on Adverse Events of Anti-HIV Drugs (DAD) Study Group *N Engl J Med* 2003;349:1993-2003.

The NEW ENGLAND JOURNAL of MEDICINE

SMART: Study Design



- Independent data and safety monitoring board reviewed interim study data annually
  - Board recommended that study enrollment halted on January 11, 2006
    - Significant safety risk in treatment interruption group

El-Sadr WM, et al. N Engl J Med. 2006;355:2283-2296.

SMART: Non-AIDS Event Rates With Continuous vs Intermittent Therapy

- Significantly more individuals in treatment interruption arm developed major cardiovascular, renal, or hepatic disease than individuals in viral suppression arm
- Significantly more individuals in treatment interruption arm experienced grade 4 event or death from any cause than individuals in viral suppression arm

Endpoint, n	Viral Suppression Arm (n = 2752)	Treatment Interruption Arm (n = 2720)	HR (95% CI)*	*P* Value
Major cardiovascular, renal, or hepatic disease	39	65	1.7 (1.1-2.5)	.009
• Fatal/nonfatal cardiovascular disease	31	48	1.6 (1.0-2.5)	.05
• Fatal/nonfatal renal disease	2	9	4.5 (1.0-20.9)	.05
• Fatal/nonfatal liver disease	7	10	1.4 (0.6-3.8)	.46
Grade 4 event or death from any cause	164	205	1.3 (1.0-1.6)	.03

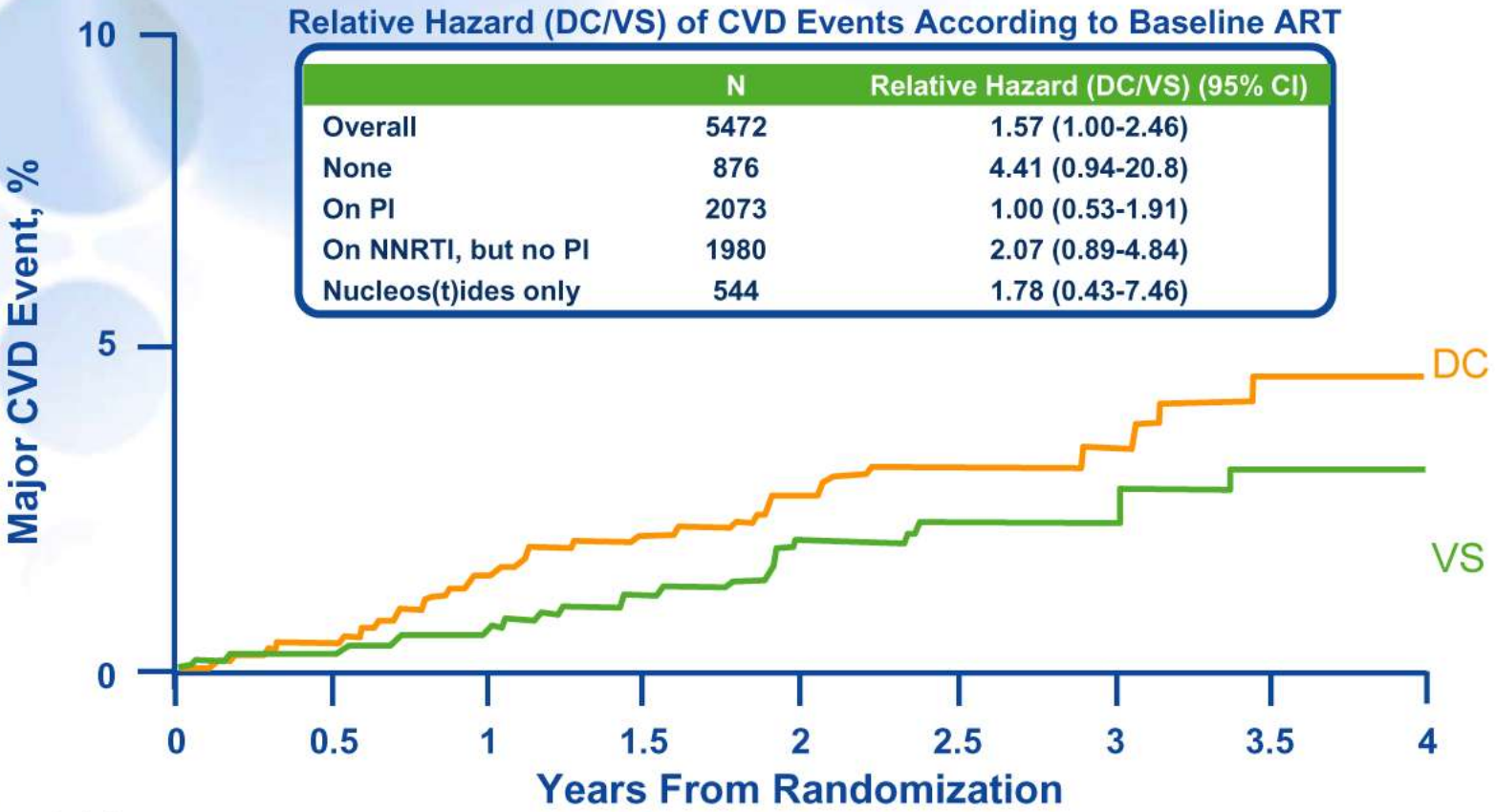
*Treatment interruption group vs viral suppression group.

El-Sadr WM, et al. N Engl J Med. 2006;355:2283-2296.

Treatment Interruption and CVD Risk

Relative Hazard (DC/VS) of CVD Events According to Baseline ART

	N	Relative Hazard (DC/VS) (95% CI)
Overall	5472	1.57 (1.00-2.46)
None	876	4.41 (0.94-20.8)
On PI	2073	1.00 (0.53-1.91)
On NNRTI, but no PI	1980	2.07 (0.89-4.84)
Nucleos(t)ides only	544	1.78 (0.43-7.46)



No. at risk

DC	2752	1306	713	379	10
VS	2720	1292	696	377	10

Relative hazard 1.57 (1.00-2.46); *P* = 0.05.

DC = drug conservation; VS = viral suppression.

Reproduced with permission from Phillips et al.

D:A:D Study: Recent Use of ABC, Didanosine Associated With Increased Risk of MI

- Thymidine analogs not associated with ↑ risk of MI
- Current or recent (within 6 months) use of ABC or ddI associated with ↑ relative risk of MI
  - Overall predicted rate of MI
    - Recent ddI: ~ 5/1000 PY
    - Recent ABC: ~ 6/1000 PY
  - Risk most prominent in individuals with underlying CVD risk factors
- ↑ risk no longer observed in patients who had discontinued ABC or ddI for > 6 months

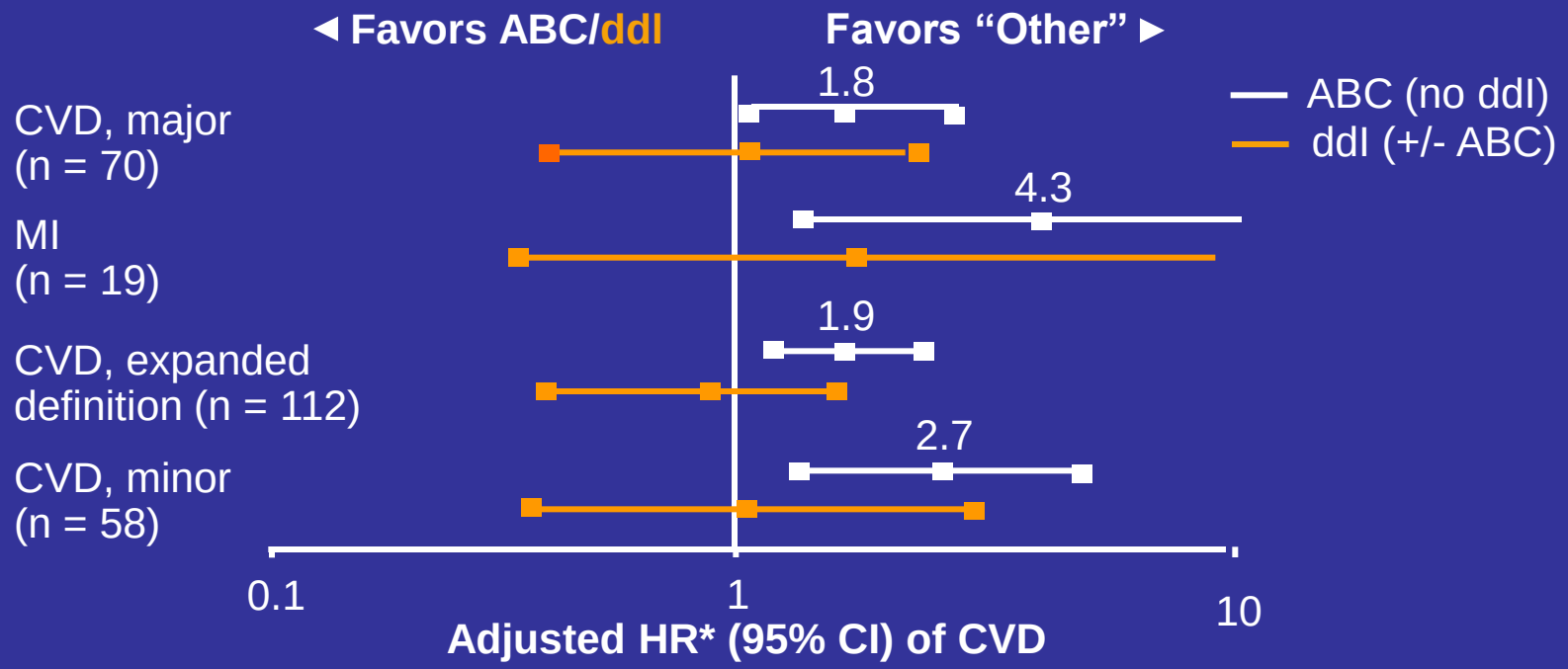
NRTI	Risk of MI With Recent Exposure (95% CI)	*P*
ZDV	0.97 (0.76-1.25)	.82
d4T	1.00 (0.76-1.32)	.98
3TC	1.25 (0.96-1.62)	.10
ddI	1.49 (1.14-1.95)	.003
ABC	1.90 (1.47-2.45)	.0001

Sabin C, et al. Lancet. 2008;371:1417-1426.

Observational Analysis of SMART Study to Confirm/Refute D:A:D Results

- Analysis of SMART participants in 3 post hoc subgroups by NRTI use
  - Patients receiving ABC and not ddI
  - Patients receiving ddI, with ABC or other NRTIs
  - Patients receiving NRTIs other than ABC and ddI
- CV endpoints
  - MI
  - Major CVD events: clinical and silent MI, stroke, surgery for CAD, and CVD death
  - Expanded major CVD events: major CVD events plus peripheral vascular disease, CHF, pharmacotherapy for CAD, and unwitnessed deaths
  - Minor CVD events: CHF, peripheral vascular disease, or CAD requiring pharmacotherapy

SMART: Current Use of Abacavir but Not Didanosine Associated With Increased CV Risk



Increased risk of CVD events with use of ABC driven entirely by patients with ≥ 5 CV risk factors at BL (adjusted HR: 3.1)

No increased risk observed in patients without ≥ 5 risk factors, though difference in risk between patients with vs without these risk factors not statistically significant

Lundgren J, et al. IAC 2008. Abstract THAB0305.

Smoking

"Cigarette smoking is the most important modifiable cardiovascular risk factor among HIV-infected patients."

Greenspoon S, Carr A. Cardiovascular risk and body-fat abnormalities in HIV-infected adults. N Engl J Med 2005; 352:48–62.

Smoking

"Cessation of smoking is more likely to reduce cardiovascular risk than either the choice of antiretroviral therapy or the use of any lipid-lowering therapy."

Greenspoon S, Carr A. Cardiovascular risk and body-fat abnormalities in HIV-infected adults. N Engl J Med 2005; 352:48–62.

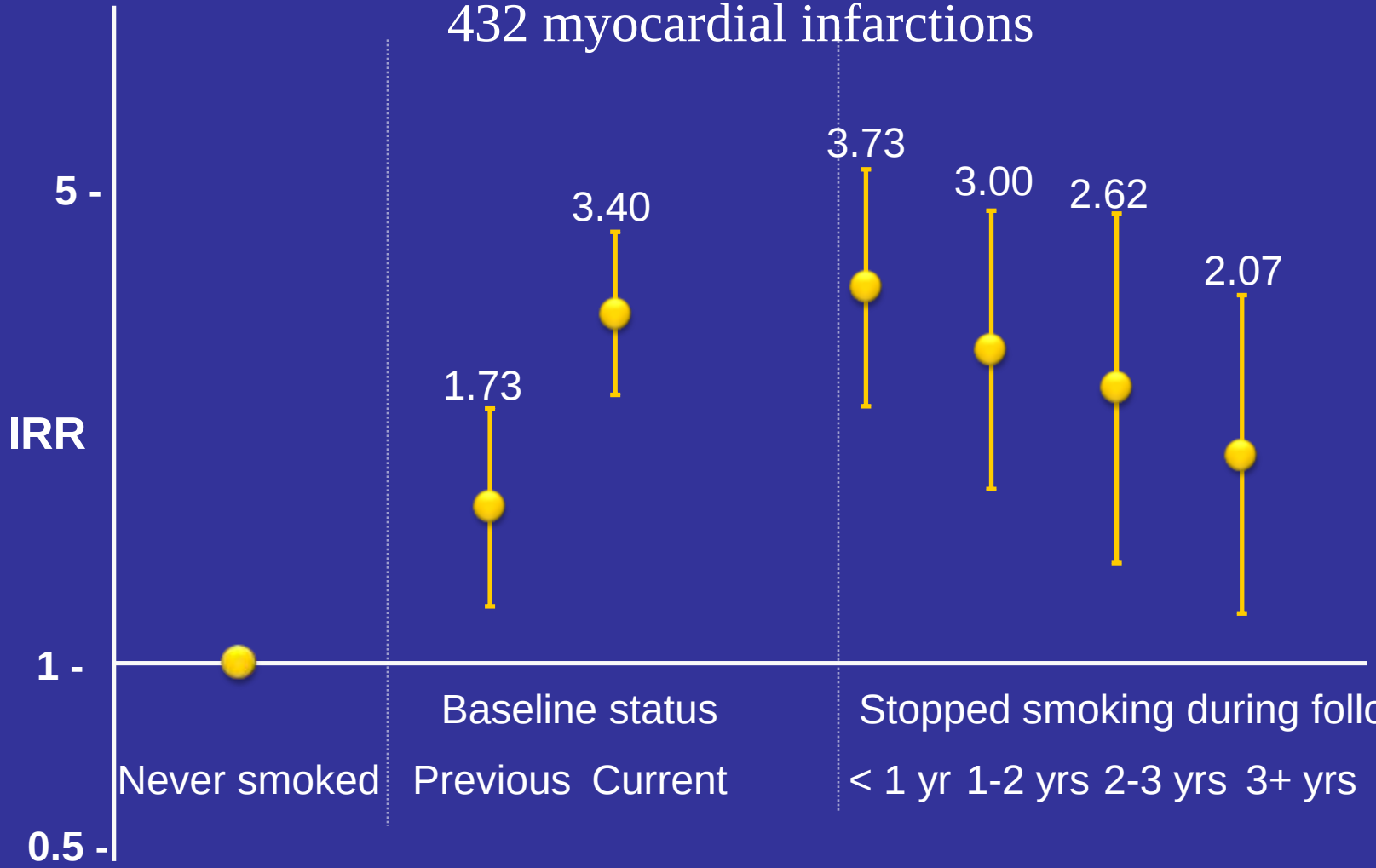
Smoking Prevalence among PLWHA Receiving Care in NYS: 2005

Use Status	N	%
Currently Use	**638**	**59.2**
Used in the Past	264	24.5
Never Used	175	16.3
Total	1077	100

NYS DOH AIDS Institute, OMD/OPER.

D-A-D Cohort Study: Smoking & MIs

33,308 HIV-positive pts in 212 clinics in Europe, the US and Australia
432 myocardial infarctions



Adjusted for: age, sex, cohort, calendar year, ART, FH of CVD, DM, and time-updated lipids and BP assessments. No start/stop dates, pack-yr data,other lifestyle factors

Petoumenos CROI 2010 #124

Lung Disease & Effect of HIV

- Recurrent pneumonias
- Asthma
- Smoking-related lung disease
  - Emphysema
  - Chronic obstructive pulmonary disease (COPD)
  - Chronic bronchitis
- Pulmonary hypertension
- Lung cancer

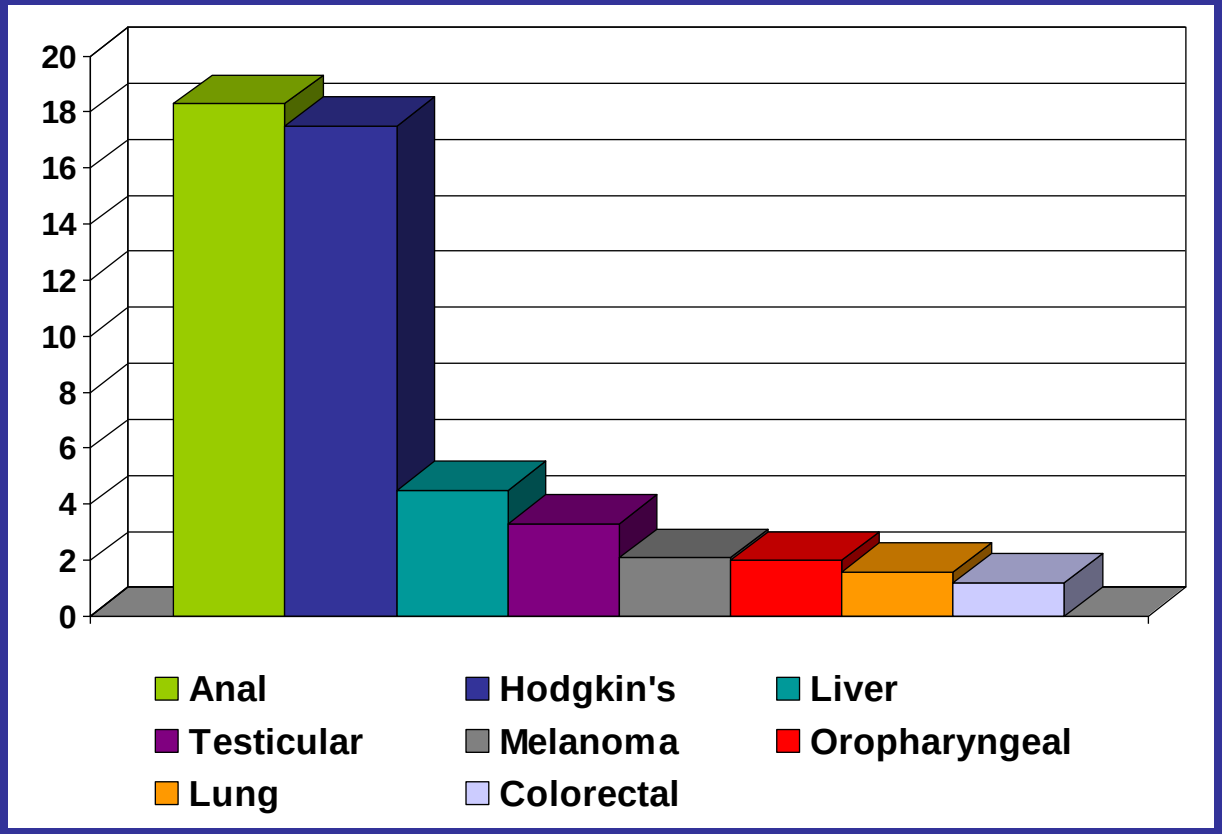
Non-AIDS Defining Malignancies

Increased Incidence of Non-AIDS–Defining Cancers Over Time

- In HIV-infected population in HAART era
  - Relative incidence of Kaposi's sarcoma and non-Hodgkin's lymphoma significantly decreased over time
  - Relative incidence of anal cancer, Hodgkin's lymphoma, melanoma, prostate cancer, and colorectal cancer increased significantly over time
    - Based on $P < .05$ for average change in incidence rates from 1992-1995 to 1996-1999 and 1996-1999 to 2000-2003.

Patel P, et al. Ann Intern Med. 2008;148:728-736.

Incidence Rate Ratios of Non-AIDS Defining Malignancies: 1992-2002



Incidence rate ratio
Standardized HIV: Observed SEER

HOPS and Adult/Adolescent Spectrum of Disease prospective cohorts

Patel P et al. Incidence of AIDS-defining and non-AIDS defining malignancies among HIV infected persons. CROI 2006

Endocrine (Hormonal) Disorders with HIV & Aging

- Insulin resistance and diabetes
- Thyroid disease
- Menopausal changes
- Bone metabolism

Factors Associated with Insulin Resistance & Diabetes

Physical Inactivity[1]
Abdominal Obesity[1,2]
Family History[1]
Non-White Race[1]
Dyslipidemia[1]
Other Risk Factors
Some Antiretroviral Therapies[3,4]
HIV & Hepatitis C Coinfection[5]

1. Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults.
2. Danoff *et al.* 3. Noor *et al.* 4. FDA “Dear Health Care Professional” Letter. 5. Duong *et al.*

Liver Disease & HIV Effects

- **Liver Diseases**
  - Chronic hepatitis B or C
  - Past or current alcohol dependence
  - Fatty liver
  - Can each lead to cirrhosis
- **Clinical presentation**
  - Fatigue
  - Encephalopathy
  - Bleeding
  - Liver cancer

Aging & HIV Effects on the Nervous System

- Memory impairment
  - Neuro-cognitive testing
- Peripheral neuropathy
- Vascular disease
  - Effects on carotid arteries and small vessels of the brain

Medication Effects

- Medication side effects and tolerability
- Drug-drug interactions
- Previous medications or doses no longer as well tolerated as we grow older
- Poly-pharmacy

Health Screens

- Blood pressure
- Cholesterol & triglycerides
- Blood glucose
- Colonoscopy if 50 or older
- Mammograms
- Pelvic and rectal exams
  - Anal PAP smears for MSM
- Prostate specific antigen for prostate cancer?
- Vitamin D level/calcium for bone health
  - DEXA scans?

Summary

- Aging is a natural part of living

- Presentation of some medical conditions may be accelerated in patients with HIV
  - Effects of the disease itself
  - Lesser effects due to antiretroviral therapy

- Benefits of antiretroviral therapy significantly outweigh potential, long-term side effects

Special Thanks to…

- Dr. Alvaro Carrascal, NY State Department of Health
- NY State Department of Health's Bureau of HIV/AIDS Epidemiology
- Centers for Disease Control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