The MACS is funded by the National Institute of Allergy and Infectious Diseases, with additional supplemental funding from the National Cancer Institute and the National Heart, Lung and Blood Institute. U01-AI-35039, U01-AI-35040, U01-AI-35041, U01-AI-35042, UM1-AI-35043, UL1-RR025005, (NCATS).
Multicenter AIDS Cohort Study (MACS)

- 7087 MSM enrolled in US
  - 4954 in 1984-85
  - 668 in 1987-90
  - 1350 in 2001-03
  - 115 in 2010+

- Study visits every 6 months
  - Standardized interviews, physical examination
  - Quality-controlled flow cytometry, HIV RNA quantification

- Storage of biospecimens in local/national repositories
MACS
Principal Investigators and Sites

Roger Detels, Los Angeles

Otto Martinez-Maza, Los Angeles

Lisa Jacobson, CAMACS

Charles Rinaldo, Pittsburgh

Joe Margolick, Baltimore

Steven Wolinsky, Chicago

December 2013
MACS Sites and Principal Investigators

Sites:
- Baltimore, MD (J. Margolick)
- Chicago, IL (S. Wolinsky)
- Los Angeles, CA (R. Detels, O. Martinez-Maza)
- Pittsburgh (C. Rinaldo)

Data Coordinating Center (CAMACS):
- Baltimore, MD (L. Jacobson)
MACS Working Groups

- Aging (J. Margolick)
- Behavioral (R. Stall)
- Biomarkers (J. Bream)
- Cardiovascular (W. Post)
- Clinical (F. Palella)
- Core Laboratory (B. Jamieson)
- Data (A. Abraham)
- Genetics (J. Martinson)
- Liver (C. Thio)
- Malignancy/Pathology (E. Breen)
- Metabolic (T. Brown)
- Neuropsychology (N. Sacktor)
- Renal (M. Estrella / F. Palella)
- Viral Immune Pathogenesis (J. Margolick)
Semiannual Visit

- Questionnaire / ACASI
  - Medical History, Health Services, Behavior
  - Medications: Antiretrovirals, OI-specific, Adherence

- Labs
  - T-cells, HIV RNA, HBV & HCV serology
  - Lipids, liver and kidney function tests / anal cytology

- Banked Specimens
  - Plasma, Serum, Cells
  - B-cell lines
  - PBMC pellets

- Demographics
- Physical Examination / Lipodystrophy / Frailty

- Psychosocial
  - Quality of Life (SF36)
  - Depression (CESD)
  - Activities of Daily Living (IADL)

- Neuropsychological Screening
Continuous Outcome Ascertainment

- Seroconversion

- Clinical Outcomes (medical records confirmation)
  - AIDS diagnoses
  - Non-AIDS diagnoses
    - Cardiovascular disease
    - Cerebrovascular disease
    - Kidney disease
    - Liver disease
    - Lung infection, bacterima, septicemia
    - Malignancies
    - Neurologic
  - Mortality

November 2004
Data Collection Forms

- Drug Form 1 (*anti-virals*)
- Antiretroviral Medication Adherence
- Section 2* (*demographics, depression (CESD]*)
- Physical Exam / Lipodystrophy Exam
- Section 4 (*medical history, health services, behavior*)
- Quality of Life* (SF36)
- Neuropsychological
- HIV Seroconversion
- Clinical Diagnostic Outcomes

* Administered using Audio Computer Assisted Structured Interview (ACASI)
Administrative Forms

- Data Set Transmission
- Study Investigator Registration for using MACS Specimens
- Restricted Use of MACS Specimens

May 2000
CAMACS

- Planning and design of studies
- Coordination of data acquisition
  - Form development
  - Codebooks
  - Data transfer
- Standardization and data management
  - Edits and updates
  - Data security
- Data analysis, statistical computing and methodological research

September 1995
MACS Database
(as of October 2013)

<table>
<thead>
<tr>
<th>Category</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Publications</td>
<td>1,306</td>
</tr>
<tr>
<td>Participants</td>
<td>7,087</td>
</tr>
<tr>
<td>Person-Years</td>
<td>93,710</td>
</tr>
<tr>
<td>Variables</td>
<td>12,357</td>
</tr>
<tr>
<td>Repository aliquots</td>
<td>1,743,937</td>
</tr>
<tr>
<td>(plasma, serum, cells, urine)</td>
<td></td>
</tr>
<tr>
<td>HIV+</td>
<td>HIV-</td>
</tr>
<tr>
<td>Person-Visits</td>
<td>61,357</td>
</tr>
<tr>
<td>CD4 Measurements</td>
<td>56,144</td>
</tr>
<tr>
<td>HIV RNA Measurements</td>
<td>38,503</td>
</tr>
</tbody>
</table>

November 2013
MACS Cohort

7087*

Seroprevalent: 2963 (41.8%)

AIDS: 1655 (55.9%)
- Alive: 161 (9.7%)
- Active: 126 (78.2%)
- Dead: 1494 (90.3%)
- Active: 784 (69.9%)

AIDS-Free: 1308 (44.1%)
- Alive: 1122 (85.8%)
- Active: 44 (77.2%)
- Dead: 186 (14.2%)
- Active: 247 (73.7%)

Seroconverter: 712 (17.3%)

AIDS: 333 (46.8%)
- Alive: 57 (17.1%)
- Active: 44 (77.2%)
- Dead: 276 (82.9%)
- Active: 247 (73.7%)

AIDS-Free: 379 (53.2%)
- Alive: 335 (88.4%)
- Dead: 44 (11.6%)
- Active: 1139 (72.88%)

Seronegative: 4124 (58.2%)

AIDS: 333 (46.8%)
- Alive: 1565 (91.3%)
- Active: 1139 (72.88%)
- Dead: 150 (8.7%)

AIDS-Free: 379 (53.2%)
- Alive: 150 (8.7%)
- Active: 1139 (72.88%)
- Dead: 150 (8.7%)

Not Censored: 1715 (50.3%)
- Alive: 1565 (91.3%)
- Active: 1139 (72.88%)

Censored: 1697 (49.7%)
- Alive: 150 (8.7%)
- Active: 1139 (72.88%)

* Includes 115 additional men (12 seronegatives, 103 seroprevalent, 24 with known seroconversion dates prior to entry) enrolled in the MACS per the 2010 recruitment protocol.

November 2013
Composition & Size of Cohort

* 1710 have been administratively censored
# Total # of CD4 and HIV RNA Measurements by Serostatus

<table>
<thead>
<tr>
<th># per individual</th>
<th>Seronegative</th>
<th>Seropositive (CD4 ; HIV RNA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5</td>
<td>6 ; 326</td>
</tr>
<tr>
<td>1 – 4</td>
<td>711</td>
<td>804 ; 1412</td>
</tr>
<tr>
<td>5 – 8</td>
<td>373</td>
<td>594 ; 499</td>
</tr>
<tr>
<td>9 – 12</td>
<td>579</td>
<td>476 ; 263</td>
</tr>
<tr>
<td>13 – 16</td>
<td>459</td>
<td>385 ; 222</td>
</tr>
<tr>
<td>17 – 20</td>
<td>336</td>
<td>402 ; 227</td>
</tr>
<tr>
<td>21 – 24</td>
<td>146</td>
<td>330 ; 254</td>
</tr>
<tr>
<td>25 – 28</td>
<td>82</td>
<td>72 ; 63</td>
</tr>
<tr>
<td>29 – 32</td>
<td>128</td>
<td>75 ; 61</td>
</tr>
<tr>
<td>33 – 36</td>
<td>185</td>
<td>75 ; 93</td>
</tr>
<tr>
<td>37 – 40</td>
<td>104</td>
<td>70 ; 119</td>
</tr>
<tr>
<td>41 – 44</td>
<td>70</td>
<td>64 ; 49</td>
</tr>
<tr>
<td>45 – 48</td>
<td>70</td>
<td>68 ; 33</td>
</tr>
<tr>
<td>49 – 52</td>
<td>61</td>
<td>81 ; 32</td>
</tr>
<tr>
<td>53 – 54</td>
<td>32</td>
<td>44 ; 13</td>
</tr>
<tr>
<td>55 – 56</td>
<td>48</td>
<td>62 ; 7</td>
</tr>
<tr>
<td>57 - 58</td>
<td>23</td>
<td>67 ; 2</td>
</tr>
</tbody>
</table>

November 2013
Incidence* of Seroconversion in the MACS by Center


* Incidence = # of seroconverters per 1,000 person-semesters

September 1995
Adjusted Time to HIV Seroconversion by Methamphetamine (M) and Popper Use (P)

Plankey, Ostrow,... Jacobson. JAIDS 2007;45:85-92
Adjusted Time to HIV Seroconversion by Methamphetamine (M) Use and Number of Unprotected Receptive Anal Sex (URAS) Partners

Plankey, Ostrow,... Jacobson. JAIDS 2007;45:85-92

June 2008
Adjusted Time to Recent HIV Seroconversion by Combinations of Sex-Drug Use

Ostrow, Plankey, ..., Stall. JAIDS 2009

Observation time (years)

% HIV-negative

N = None
S = Stimulant
P = Poppers
E = EDD

S+P+E
P+E
S+P
S+E
N = None

Observation time (years)

May 2010
T-Cell Subset Changes and Homeostasis in AIDS-Free MACS Seroconverters


![Graph showing changes in T-cell subsets over months from seroconversion](image-url)
Kaplan-Meier Survival Curve for Inversion of the CD4/CD8 Ratio after the Estimated Time of HIV-1 Seroconversion

Margolick, Gange, ..., Lai. JAIDS 2006
Histogram of 1222 CD4+ Regression Slopes Among HIV-1 Seropositive Men, 1984-1996

Muñoz, Kirby, . . ., Phair. JAIDS 1995 (update)

Slopes of CD4# (change per 6 months)

June 1997
A Seropositive Triplet with Distinct Profiles

Calendar Time (years)

CD4 Number

- Stable high CD4
- Moderate CD4 decline
- Rapid CD4 decline
- AZT
- AIDS
- Death
- September 1995
Disease Progression Among Triplets of HIV-Infected Men with Distinct CD4 Trajectories

Gange et al.    JAIDS 1997 (Update)

October 2000
Likelihood of Developing AIDS in HIV Infected Individuals with CD4 > 350 in the Non-HAART Era

Phair, Mellors,…, Muñoz - AIDS 2002

Graphical Reference: Li, Buechner, …, Muñoz - Am Statistician 2003
Likelihood of Developing AIDS in HIV Infected Individuals with 200 < CD4 < 350 in the Non-HAART Era

Phair, Mellors,..., Muñoz - AIDS 2002

Graphical Reference: Li, Buechner, ..., Muñoz - Am Statistician 2003
Recommend Viable Deferral

AIDS?
Yes No
CD4 count?
<200 201-350 >350

HIV-RNA?
>20,000 <20,000/14,000* >60,000 <60,000/30,000*

(30% of those with 201<CD4<350) (80% of those with CD4>350)

Source: Multicenter AIDS Cohort Study

Phair, Mellors,…,Muñoz. AIDS; 2002

October 2002
Estimated Long Term AIDS-Free Proportions Prior to Potent Antiretroviral Therapies

Muñoz, Kirby, . . ., Phair – JAIDS 1995
Progression of HIV-1 Infection Prior to Potent Antiretroviral Therapy


Graph showing the progression of HIV-1 infection with time in years and proportion. The graph illustrates the time it takes for various events to occur, such as CD4≤200, AIDS, and death. The median time for CD4≤200 is 8.9 years, while the median time for AIDS is 1.3 years. The 5 percent time for death is 10.3 years.

October 1998
Circulating T-Cell Lymphocyte Levels Relative to the Onset of AIDS

Margolick, Muñoz, . . ., Ferbas - Nat Med 1995

Months from AIDS

AIDS <= 3 years (N=20)
AIDS (3,4.5] years (N=22)
AIDS (4.5,6] years (N=22)
AIDS > 6 years (N=28)
HIV Markers after Seroconversion Prior to HAART

Lyles, Muñoz, . . ., Mellors - JID 2000

HIV RNA

CD4 Count

Years Since First HIV+ Visit

HIV RNA (log10 copies/mL)

CD4 Cell Count (cells/mm³)

December 2001
Decline in CD4 Count per Year by Plasma HIV-1 RNA

Plasma HIV-1 RNA copies/ml

Mean and 95% CI's for Decline per Year of CD4 Cell Count

## X4 Emergence Prior to Clinical Event According to Time of Events After Seroconversion

*Shepherd, Jacobson, . . ., Margolick - JID 2009*

<table>
<thead>
<tr>
<th>Progression Groups</th>
<th>Rapid</th>
<th>Moderate</th>
<th>Slow</th>
<th>Very Slow</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CD4 &lt; 200 cells/µl</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n (%)</td>
<td>7 (54%)</td>
<td>11 (79%)</td>
<td>4 (50%)</td>
<td>3 (19%)</td>
</tr>
<tr>
<td>OR</td>
<td>5.1</td>
<td>15.9</td>
<td>4.3</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>AIDS Illness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n (%)</td>
<td>4 (57%)</td>
<td>17 (77%)</td>
<td>4 (57%)</td>
<td>4 (25%)</td>
</tr>
<tr>
<td>OR</td>
<td>4.0</td>
<td>10.2</td>
<td>4.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>
HIV-1 Viremia after Seroconversion and Proximal to AIDS

Lyles, Muñoz, . . ., Mellors - JID 2000

AIDS Category

<table>
<thead>
<tr>
<th></th>
<th>&lt;3yrs</th>
<th>3-7yrs</th>
<th>&gt;7 yrs</th>
<th>No AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Level of HIV RNA (log_{10} copies/mL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3yrs</td>
<td>3.5</td>
<td>4.0</td>
<td>4.5</td>
<td>5.0</td>
</tr>
<tr>
<td>3-7yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;7 yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No AIDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- at 1st HIV+ (p<0.001)
- at AIDS (p=0.652)

<table>
<thead>
<tr>
<th></th>
<th>&lt;3yrs</th>
<th>3-7yrs</th>
<th>&gt;7 yrs</th>
<th>No AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slope of HIV RNA (log_{10} copies/mL) per Year</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3yrs</td>
<td>-0.2</td>
<td>-0.1</td>
<td>0.0</td>
<td>0.1</td>
</tr>
<tr>
<td>3-7yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;7 yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No AIDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- after 1st HIV+ (p=0.013)
- prior to AIDS (p=0.708)

October 2000
Estimates from Lognormal Model
Multicenter AIDS Cohort Study

Muñoz, Sabin, Phillips. AIDS 1997

- vanGriensven, et al, AJE 1996

Median Incubation of AIDS (years) and 90% C.B.
Likelihood of Developing AIDS in Three Years

Mellors, Muñoz, . . ., Rinaldo - Ann Int Med 1997

Plasma Viral Load (copies/ml in thousands)

CD4+ T-lymphocyte Count (cells/mm³)

- >30K
- 10K – 30K
- 3K – 10K
- 501 – 3K
- <500 bDNA
- >55K
- 20K – 55K
- 7K – 20K
- 1501 – 7K
- ≤1501 RT-PCR

June 1997
Likelihood of Developing AIDS in Three Years

*Mellors, Muñoz, ..., Rinaldo – Ann Int Med 1997*

Graphical Reference: *Li, Buechner, ..., Muñoz - Am Statistician 2003*
Likelihood of Developing AIDS in Six Years

Plasma Viral Load (copies/ml in thousands)

- > 30K
- 20K – 55K
- 7K – 20K
- 3K – 10K
- 1501 – 7K
- 501 – 3K
- ≤ 1500

CD4+ T-lymphocyte count (cells/mm³)

- > 750
- ≤ 500
- ≤ 1500

Graphical Reference: Li, Buechner, ..., Muñoz - Am Statistician 2003
Likelihood of Developing AIDS in Nine Years

Mellors, Muñoz, . . ., Rinaldo - Ann Int Med 1997

CD4+ T-lymphocyte Count (cells/mm³)

Plasma Viral Load (copies/ml in thousands)

>30K  10K – 30K  3K – 10K  501 – 3K  ≤500  bDNA
>55K  20K – 55K  7K – 20K  1501 – 7K  ≤1501  RT-PCR

June 1997
Likelihood of Developing AIDS in Nine Years

Mellors, Muñoz, ..., Rinaldo – Ann Int Med 1997

Graphical Reference: Li, Buechner, ..., Muñoz - Am Statistician 2003
Effect of HLA-B Alleles on AIDS Progression  
(N=1,089)

Gao, Bashirova, …, Carrington. Nat Med 2005

- B*27
- B*57
- B*35Px
- others

RH=0.4  
P=0.001

RH=0.5  
P=0.003

RH=1.63  
p<0.0001

RH=0.43  
p<0.0001

RH=0.71  
P=0.03

RH=1.92  
p<0.0001

May 2006
## HLA Allotypes are Distinct in Terms of the Timing at Which They Influence AIDS Progression

*Gao, Bashirova, …, Carrington. *Nat Med 2005

### All Races

<table>
<thead>
<tr>
<th></th>
<th>Serocon.→ CD4&lt;200</th>
<th>CD4&lt;200→ AIDS 87</th>
<th>AIDS 87→ death</th>
</tr>
</thead>
<tbody>
<tr>
<td>RH</td>
<td>p value</td>
<td>RH</td>
<td>p value</td>
</tr>
<tr>
<td>B27</td>
<td>0.77</td>
<td>0.55</td>
<td>0.77</td>
</tr>
<tr>
<td>B57</td>
<td>0.41</td>
<td>0.7</td>
<td>0.85</td>
</tr>
<tr>
<td>B35 Px</td>
<td>1.43</td>
<td>1.09</td>
<td>0.91</td>
</tr>
</tbody>
</table>

N = 1089, N = 1934, N = 1529

May 2006
Kaplan-Meier Survival Curves for Genotypes of SNP rs17762192, Representing a Haplotype Located 36kb Upstream of PROX1 and Chromosome 1, Showing Strong Associations with Differing Rates of Progression to Clinical AIDS

Herbeck, Gottlieb, ... Mullins. J Infect Dis 2010

A. Replication cohort (ALIVE, MACS, MHCS, SFCC, individuals genotyped by Steve O’Brien)
B. Combined analysis of replication and discovery cohorts (156 MACS individuals enriched with rapid progressors and long-term non-progressors.)
The bar graphs show the allelic distribution of the 4 variants that have a genome-wide significant association with HIV-1 set point and/or disease progression in subsets of the study population. Groups were defined according to HIV-1 set point (left-hand side graphs) and to progression time (right-hand side graphs).
The scatter plot shows the first two principal components from the multi dimensional scaling (MDS) procedure, performed on the ancestry informative markers (AIMs) data. Each dot represents an individual who was genotyped in the MACS cohort (n=1914). Colors represent self-reported race (SRR) (red = BnH, blue = WnH, green = other) and boundaries of biogeographical ancestry (BGA) populations (EA, AEA, and AsEA) were defined by a $k$-means clustering procedure.
Distribution of Mean HIV-1 Set Point According to Patient Genotype

Pelak, Goldstein,…, Weintrob. J Infect Dis 2010

A Mean setpoint by rs2523608 genotype African American ancestry

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Mean of log_{10} VL setpoint</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT</td>
<td>4.24</td>
<td>202</td>
</tr>
<tr>
<td>CT</td>
<td>4.07</td>
<td>249</td>
</tr>
<tr>
<td>CC</td>
<td>3.72</td>
<td>62</td>
</tr>
</tbody>
</table>

p=2.3E-06

B Mean setpoint by rs2523608 genotype European ancestry

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Mean of log_{10} VL setpoint</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT</td>
<td>4.18</td>
<td>904</td>
</tr>
<tr>
<td>CT</td>
<td>4.02</td>
<td>1094</td>
</tr>
<tr>
<td>CC</td>
<td>3.99</td>
<td>363</td>
</tr>
</tbody>
</table>

p=1.1E-06

C Mean setpoint by HLA-B*5703

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Mean of log_{10} VL setpoint</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA-B*5703 absent</td>
<td>4.19</td>
<td>262</td>
</tr>
<tr>
<td>HLA-B*5703 present</td>
<td>3.23</td>
<td>23</td>
</tr>
</tbody>
</table>

p=5.6E-10

May 2011
AIDS Prevented Fraction Among Seroconverters

Silverberg, Smith, . . ., Muñoz - AJE 2004

Fraction of AIDS prevented by nodes 1, 2, and 3: 0.30 (95% CI: 0.07, 0.47)

November 2004
Proportion Surviving AIDS by Year of Diagnosis
Assumed currently alive at 6/30/99 if contacted since 6/30/98

Jacobson, Kirby, . . ., Schrager - AJE 1993 (update)

Proportion Surviving AIDS

Years After Initial Clinical AIDS Diagnosis
Effect of HIV-1 RNA within CD4 Category Prior to HAART


Proportion AIDS-Free

Years after HIV-1 RNA

CD4: 0 to 200 (N = 100)
CD4: 201 to 350 (N = 231)
CD4: 351 to 500 (N = 403)
CD4 > 500 (N = 870)

<0.5K
0.5 - 3K
3 - 10K
10 - 30K
>30K

December 2001
Predictive Value of HIV RNA (copies/ml) by Time Since Seroconversion

Lyles, Muñoz, . . ., Mellors - JID 2000

LogRank Statistic = 25.1
LogRank Statistic = 33.8
LogRank Statistic = 48.4
LogRank Statistic = 50.0

Years from HIV RNA Quantification

Proportion AIDS-Free

October 2000
## Extension of Time to Events by Reducing HIV RNA Setpoint

*Gupta, Jacobson, ..., Straus. J Infect Dis 2007*

### Outcome

<table>
<thead>
<tr>
<th>HIV RNA copies/ml</th>
<th>Relative Time</th>
<th>Median Time (Years)</th>
<th>Relative Time</th>
<th>Median Time (Years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30,000</td>
<td>1</td>
<td>8.4</td>
<td>1</td>
<td>3.4</td>
</tr>
<tr>
<td>9,487 (0.5 log)</td>
<td>1.4</td>
<td>11.9</td>
<td>1.3</td>
<td>4.5</td>
</tr>
<tr>
<td>3,000 (1 log)</td>
<td>2.0</td>
<td>16.9</td>
<td>1.7</td>
<td>5.9</td>
</tr>
<tr>
<td>300 (2 log)</td>
<td>4.1</td>
<td>34.4</td>
<td>3.0</td>
<td>10.3</td>
</tr>
</tbody>
</table>

May 2007
Prognostic Value of HIV-1 RNA, CD4 Cell Count and CD4 Cell Count Slope for Progression to AIDS and Death in Untreated HIV-1 Infection

Mellors, Margolick, …, Jacobson.  JAMA 2007;297:2349-50

Percent (95% CI) Variability in Outcomes Explained by Predictor

<table>
<thead>
<tr>
<th>Baseline Predictors</th>
<th>AIDS</th>
<th>Death</th>
<th>CD4 cell count &lt;200/µL</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Events/Total N)</td>
<td>(598/1640)</td>
<td>(421/1640)</td>
<td>(648/1472)</td>
</tr>
<tr>
<td>HIV-1 RNA</td>
<td>47 (40-55)</td>
<td>50 (41-62)</td>
<td>34 (25-42)</td>
</tr>
<tr>
<td>CD4 cell count</td>
<td>29 (25-34)</td>
<td>26 (21-32)</td>
<td>26 (21-31)</td>
</tr>
<tr>
<td>Age</td>
<td>1 (0-2)</td>
<td>3 (1-5)</td>
<td>1 (0-3)</td>
</tr>
<tr>
<td>HIV-1 RNA and CD4 cell count</td>
<td>54 (47-61)</td>
<td>56 (48-67)</td>
<td>46 (37-52)</td>
</tr>
</tbody>
</table>
Prognostic Value of HIV-1 RNA, CD4 Cell Count and CD4 Cell Count Slope for Progression to AIDS and Death in Untreated HIV-1 Infection

*Mellors, Margolick, …, Jacobson. JAMA 2007;297:2349-50*

Percent (95% CI) Variability in Outcomes Explained by Predictor

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(Events/Total N)</td>
<td>(302/1303)</td>
<td>(285/1490)</td>
<td>(206/870)</td>
</tr>
<tr>
<td>Median HIV-1 RNA</td>
<td>51 (38-64)</td>
<td>58 (47-69)</td>
<td>39 (24-60)</td>
</tr>
<tr>
<td>Median CD4 cell count</td>
<td>29 (22-38)</td>
<td>35 (29-43)</td>
<td>24 (15-35)</td>
</tr>
<tr>
<td>CD4 cell count slope</td>
<td>3 (1-7)</td>
<td>7 (4-12)</td>
<td>4 (1-8)</td>
</tr>
<tr>
<td>Age in June 1988</td>
<td>1 (0-4)</td>
<td>2 (0-3)</td>
<td>2 (1-4)</td>
</tr>
<tr>
<td>Median HIV-1 RNA and CD4 cell count</td>
<td>58 (46-69)</td>
<td>63 (54-73)</td>
<td>48 (31-79)</td>
</tr>
</tbody>
</table>
Kaplan-Meier Estimates of the Time from Seroconversion to AIDS, CD4+ Lymphocyte Count <200 cells/mm³, Rapid TLC Decline, and CD4+ Lymphocyte Count <350 cells/mm³

Lau, Gange, …, Margolick - JAIDS 2005

Proportion Remaining Free of Event

Time from Seroconversion (years)

Rapid total lymphocyte count decline
CD4 < 200
AIDS
Rapid hemoglobin decline
CD4 < 350

October 2005
HIV Disease Progression to AIDS by CRP Level


May 2006

<table>
<thead>
<tr>
<th>CRP Level</th>
<th>Relative Time</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP ≤0.6 mg/l</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.6 &lt; CRP ≤1.2 mg/l</td>
<td>0.86</td>
<td>0.68-1.09</td>
<td>0.21</td>
</tr>
<tr>
<td>CRP &gt;2.3</td>
<td>0.63</td>
<td>0.51-0.79</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Adjusted for CD4, HIV RNA, and hemoglobin

- **CRP ≤0.6 mg/l**
- **0.6 < CRP ≤1.2 mg/l**
- **CRP >2.3**
Time to Death According to GBV-C Serostatus Early and Late in HIV Infection

Williams, Klinzman, …, Stapleton - N Engl J Med 2004

GBV-C 5-6 yr post HIV-SC

GBV-C 12-18 mo and 5-6 yr post HIV-SC

<table>
<thead>
<tr>
<th>GBV-C</th>
<th>No.</th>
<th>Deaths</th>
<th>RH</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNA+ at 5-6 yr, E2-</td>
<td>50</td>
<td>9</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>RNA- at 5-6 yr, E2+</td>
<td>59</td>
<td>23</td>
<td>2.38</td>
<td>(1.10, 5.15)</td>
</tr>
<tr>
<td>RNA- at 5-6 yr, E2-</td>
<td>29</td>
<td>14</td>
<td>3.85</td>
<td>(1.66, 8.95)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GBV-C</th>
<th>No.</th>
<th>Deaths</th>
<th>RH</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNA+ at both visits, E2-</td>
<td>49</td>
<td>9</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>RNA- at both visits, E2+</td>
<td>59</td>
<td>23</td>
<td>2.40</td>
<td>(1.11, 5.20)</td>
</tr>
<tr>
<td>RNA- at both visits, E2-</td>
<td>17</td>
<td>6</td>
<td>2.57</td>
<td>(0.91, 7.24)</td>
</tr>
<tr>
<td>RNA+ at 12-18 mo, RNA- at 5-6 yr</td>
<td>12</td>
<td>8</td>
<td>5.87</td>
<td>(2.24, 15.38)</td>
</tr>
</tbody>
</table>
Use of Antiretroviral Therapy by Seropositive MACS Participants without Clinical AIDS

Detels, Tarwater, . . ., Muñoz - AIDS 2001 (update)

Calendar Year

% Receiving Therapy

- NRTI Monotherapy
- NRTI Combination Therapy
- HAART with PI
- HAART no PI
- PCP Prophylaxis
- Candida Prophylaxis
- MAC Prophylaxis
- CMV Prophylaxis

2001-3 cohort added

2010

1987 1989 1991 1993 1995 1997 1999 2001 2003 2005 2007 2009 2011 2013

Based on November 2008 HAART definition

November 2013
Use of Antiretroviral Therapy by Seropositive MACS Participants with Clinical AIDS

Detels, Tarwater, . . ., Muñoz - AIDS 2001 (update)

* Based on November 2008 HAART definition

* Calendar Year

% Receiving Therapy

0 10 20 30 40 50 60 70 80 90 100

1987 1989 1991 1993 1995 1997 1999 2001 2003 2005 2007 2009 2011 2013

NRTI Monotherapy  NRTI Combination Therapy  HAART with PI  HAART no PI

PCP Prophylaxis  Candida Prophylaxis  MAC Prophylaxis  CMV Prophylaxis

November 2013
Use of ART by Participants with AIDS

**Schneider, Gange, …, Muñoz. AIDS 2005**

**Multicenter AIDS Cohort Study**

**A**

- **Monotherapy**
- **Combination Therapy**
- **PI-HAART**
- **Non PI-HAART**

**Study Began in October 1994**

**B**

**Women’s Interagency HIV Cohort Study**

- **Monotherapy**
- **Combination Therapy**
- **PI-HAART**
- **Non PI-HAART**

**Study Began in October 1994**

October 2005
HAART Use in the Multicenter AIDS Cohort Study

Jacobson, Li, ..., Muñoz - Am J Epidemiol 2002 [update]

Cumulative incidence of highly active antiretroviral therapy (HAART)

Period incidence of HAART

Incidence of HAART Use per 100 person-semesters

Calendar (Year-Semester)
## Adherence to HIV-Antiretroviral Therapies

*Kleeberger, Phair, . . ., Jacobson - JAIDS 2001*

<table>
<thead>
<tr>
<th>Adherence Level</th>
<th>% (N)</th>
<th>Percent with &lt;50 HIV RNA copies/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>100% Adherent</td>
<td>77.7 (419)</td>
<td>48.2</td>
</tr>
<tr>
<td>&lt;100% Adherent</td>
<td>22.3 (120)</td>
<td>33.7*</td>
</tr>
</tbody>
</table>

* *p=0.01*
CD4 Cell Count in HAART Initiation and Non-Initiation

Yamashita, Phair, . . ., Jacobson - AIDS 2001

* significant difference between HAART initiators and non-initiators (p<0.05)
Comparison of CD4 Slope Before and After HAART Use

Yamashita, Phair, . . ., Jacobson - AIDS 2001

I: Increased by $\geq 200$
II: Increased by 100-199
III: Increased by $< 99$
IV: Decreased

I: $N = 109$ (22%)
II: $N = 173$ (35%)
III: $N = 168$ (34%)
IV: $N = 47$ (9%)

May 2001
Trajectories of Median CD4 Cell Counts over 3.5 Years after Initiation of HAART

Tarwater, Margolick, . . ., Muñoz - JAIDS 2001

<table>
<thead>
<tr>
<th>Change*</th>
<th>Slope (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>78</td>
<td>44.0 (0.482)</td>
</tr>
<tr>
<td>152</td>
<td>-13.9 (0.736)</td>
</tr>
<tr>
<td>176</td>
<td>-12.6 (0.568)</td>
</tr>
<tr>
<td>187</td>
<td>-2.0 (0.923)</td>
</tr>
<tr>
<td>225</td>
<td>16.1 (0.330)</td>
</tr>
</tbody>
</table>

* test for trend (p<.001)
Individual Variation of CD4 T-Cell Trajectory among HIV+ on Long Term HAART

Chu, Gange, …, Jacobson - Am J Epidemiol 2005

Pre-HAART CD4

CD4 Cell Count (Log_{10} Scale)

Years Since HAART Initiation

October 2005
Individual Variation of CD4 T-Cell Trajectory among HIV+ on Long Term HAART

Chu, Gange, … , Jacobson - Am J Epidemiol 2005

<table>
<thead>
<tr>
<th>Pre-HAART CD4</th>
<th>≤ 100</th>
<th>≤ 200</th>
<th>≤ 350</th>
<th>≤ 500</th>
<th>&gt; 500</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Years Since HAART Initiation</th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 100</td>
<td>31(47%)</td>
<td>42(56%)</td>
<td>88(81%)</td>
<td>66(92%)</td>
</tr>
<tr>
<td>≤ 200</td>
<td>35(53%)</td>
<td>33(44%)</td>
<td>20(19%)</td>
<td>6(8%)</td>
</tr>
<tr>
<td>≤ 350</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 500</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 500</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total: 309(76%) Yes, 95(24%) No
Overall Cumulative Incidence of an Increase in CD4 Cells of ≥100 cells/mm³ in the First Two Years after HAART Initiation, by Age Group and Initial HAART Regimen Class

Althoff, Justice, . . . , Gebo. AIDS 2010
CD4 Cell Count 5-10 Years After HAART Initiation

Li, Margolick, ..., Jacobson. J Acquir Immune Defic Syndr 2011

Pre-HAART

CD4 cells:  <350
Age:  <35 years

<350  350-499  >500

>50 years
Mixture Model of Predicted HIV Viral Load Trajectory among HIV Positive on Long Term HAART

Chu, Gange, Li. Epidemiology 2010

MACS

WIHS

Log10 (HIV RNA)

Proportion of suppressed HIV RNA

Years since HAART initiation

May 2011
Longitudinal Measurement of HIV RNA

Chu, Gange, Li. Epidemiology 2010

MACS

WIHS

Proportion of undetectable HIV RNA

Years since HAART initiation

Log_{10} (HIV RNA)

Years since HAART initiation

May 2011
Use of Antiretroviral Therapy and Effectiveness at the Population Level

Tarwater, Mellors, . . ., Muñoz - AJE 2001
Detels, Muñoz, . . ., Phair - JAMA 1998 (update)

Relative Hazard of AIDS at equal infection duration:
1.52 1 0.91 0.30

Relative Hazard of AIDS at equal CD4 cell count and HIV RNA:
1.52 1 1.03 0.31

% Receiving Therapy

NRTI Monotherapy  NRTI Combination Therapy  HAART

May 2001
AIDS-Free Time by Calendar

Detels, Muñoz, . . ., Phair - JAMA 1998 (update)

Percent AIDS-Free

<table>
<thead>
<tr>
<th>Calendar</th>
<th>N</th>
<th>AIDS</th>
<th>RH</th>
<th>(p-value)</th>
<th>RT</th>
<th>(p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>86.0 to 89.5</td>
<td>341</td>
<td>36</td>
<td>1.48</td>
<td>(0.119)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>89.5 to 93.0</td>
<td>427</td>
<td>91</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>93.0 to 96.5</td>
<td>378</td>
<td>100</td>
<td>0.92</td>
<td>(0.626)</td>
<td>1.03</td>
<td>(0.690)</td>
</tr>
<tr>
<td>96.5 to 99.5</td>
<td>264</td>
<td>20</td>
<td>0.30</td>
<td>(&lt;.001)</td>
<td>2.11</td>
<td>(&lt;.001)</td>
</tr>
</tbody>
</table>

May 2000
Survival Time by Calendar

Detels, Muñoz, . . ., Phair - JAMA 1998 (update)

Years from Seroconversion

<table>
<thead>
<tr>
<th>Calendar</th>
<th>N</th>
<th>Death</th>
<th>RH</th>
<th>(p-value)</th>
<th>RT</th>
<th>(p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>86.0 to 89.5</td>
<td>341</td>
<td>26</td>
<td>3.17</td>
<td>(0.001)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>89.5 to 93.0</td>
<td>441</td>
<td>60</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>93.0 to 96.5</td>
<td>430</td>
<td>98</td>
<td>0.88</td>
<td>(0.496)</td>
<td>1.01</td>
<td>(0.895)</td>
</tr>
<tr>
<td>96.5 to 99.5</td>
<td>324</td>
<td>33</td>
<td>0.38</td>
<td>(&lt;.001)</td>
<td>1.55</td>
<td>(&lt;.001)</td>
</tr>
</tbody>
</table>

Percent Alive

May 2000
Lymphoma and Kaposi’s Sarcoma Incidence per 1000 Seropositive Person Years (1/98)

Jacobson, Yamashita, . . ., Muñoz - JAIDS 1999

Incidence Rate

Percent on Anti-Retroviral Therapy

Calendar Period

Kaposi’s sarcoma
Combination therapy with NRTIs
Non-Hodgkin’s lymphoma
Combination therapy with PIs and/or NNRTIs

October 1999
Incidence of HIV Dementia in the Multicenter AIDS Cohort Study

Sacktor, Lyles, …, McArthur - Neurology 2001
Time to AIDS by CD4 Cell Count at Time of Treatment Adjusting for Individual Lead Time

Ahdieh-Grant, Yamashita, ..., Jacobson - Am J Epidemiol 2003

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Percent with AIDS</th>
<th>RH</th>
<th>p-value</th>
<th>RH</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>350-499</td>
<td>92</td>
<td>12.0</td>
<td>1.0</td>
<td>---</td>
<td>1.0</td>
<td>---</td>
</tr>
<tr>
<td>200-349</td>
<td>130</td>
<td>21.5</td>
<td>1.05</td>
<td>0.897</td>
<td>1.0</td>
<td>---</td>
</tr>
<tr>
<td>&lt;200</td>
<td>127</td>
<td>50.4</td>
<td>2.68</td>
<td>0.003</td>
<td>2.56</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Years from Index Visit (Time when 350 ≤ CD4 < 500)
Percent AIDS-free after HAART Initiation (MACS & WIHS)

Cole, Li,..., Muñoz - Stat Med 2004

Proportion AIDS-free

<table>
<thead>
<tr>
<th>CD4</th>
<th>Group</th>
<th>Leadtime</th>
<th>N</th>
<th>AIDS</th>
<th>RH</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>201-350</td>
<td>Immediate</td>
<td>NA</td>
<td>278</td>
<td>21</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>≤ 200</td>
<td>Deferred</td>
<td>Unadjusted</td>
<td>237</td>
<td>46</td>
<td>2.71</td>
<td>1.62, 4.54</td>
</tr>
<tr>
<td>≤ 200</td>
<td>Deferred</td>
<td>Adjusted</td>
<td>268.1</td>
<td>77.1</td>
<td>1.97</td>
<td>1.09, 3.54</td>
</tr>
</tbody>
</table>
### Percent AIDS-free after HAART Initiation (MACS & WIHS)

**Cole, Li,…, Muñoz - Stat Med 2004**

![Graph showing the proportion of AIDS-free individuals over time](image)

<table>
<thead>
<tr>
<th>CD4</th>
<th>Group</th>
<th>Leadtime</th>
<th>N</th>
<th>AIDS</th>
<th>RH</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>351-500</td>
<td>Immediate</td>
<td>NA</td>
<td>224</td>
<td>19</td>
<td>1</td>
<td>1.00</td>
</tr>
<tr>
<td>201-350</td>
<td>Deferred</td>
<td>Unadjusted</td>
<td>278</td>
<td>21</td>
<td>0.86</td>
<td>0.46, 1.60</td>
</tr>
<tr>
<td>201-350</td>
<td>Deferred</td>
<td>Adjusted</td>
<td>286.5</td>
<td>29.5</td>
<td>0.70</td>
<td>0.35, 1.42</td>
</tr>
</tbody>
</table>

May 2006
Individual Effect of HAART on AIDS or Death


Robust $p$ for interaction = 0.009

Baseline CD4 Cell Count

<table>
<thead>
<tr>
<th>Group</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 200</td>
<td>0.20 (0.125, 0.36)</td>
</tr>
<tr>
<td>200 - 350</td>
<td>0.27 (0.18, 0.36)</td>
</tr>
<tr>
<td>&gt; 350</td>
<td>0.82 (0.64, 1.00)</td>
</tr>
</tbody>
</table>

(n = 258) (n = 373) (n = 867)
Percent AIDS Free among HAART Users by CD4 T-cell Count and HIV RNA

Jacobson, Li, ..., Muñoz - Am J Epidemiol 2002 [update]

<table>
<thead>
<tr>
<th>CD4</th>
<th>N</th>
<th>AIDS</th>
<th>RH</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;=350</td>
<td>206</td>
<td>14</td>
<td>1</td>
<td>0.807</td>
</tr>
<tr>
<td>200-349</td>
<td>118</td>
<td>9</td>
<td>1.11</td>
<td>0.001</td>
</tr>
<tr>
<td>&lt;200</td>
<td>105</td>
<td>21</td>
<td>3.08</td>
<td>0.003</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>V load</th>
<th>N</th>
<th>AIDS</th>
<th>RH</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;=25000</td>
<td>202</td>
<td>12</td>
<td>1</td>
<td>0.122</td>
</tr>
<tr>
<td>25001-99999</td>
<td>127</td>
<td>14</td>
<td>1.84</td>
<td>0.003</td>
</tr>
<tr>
<td>&gt;=100000</td>
<td>89</td>
<td>16</td>
<td>3.18</td>
<td>0.003</td>
</tr>
</tbody>
</table>
Percent AIDS Free According to HAART Use and CD4 Tcell Count

Jacobson, Li, ..., Muñoz - Am J Epidemiol 2002

Percent AIDS-free

Years from 1/1/93 (non-users) or first HAART (users)

CD4  HAART  N  AIDS  Model 1  Model 2
350-500  NU (non-user)  239  57  1.90  <.001  0.34  0.001
200-349  NU (non-user)  181  72  6.45  <.001  0.26  0.002
<200    NU (non-user)  187  145  0.93  0.774  0.76  0.575
>=350   U (user)  194  13  0.34  0.001  1
200-349  U (user)  110  6  0.26  0.002  0.76  0.575
<200    U (user)  100  19  0.93  0.774  2.70  0.006

October 2002
Cumulative Mortality and Appropriateness of Weibull Model for Five Therapy Eras

Schneider, Gange, …, Muñoz. AIDS 2005

Years from AIDS diagnosis

Cumulative Mortality after AIDS (%)

June 1984 – Dec 1989
(β=0.55; σ=0.90)

Jan 1990 – Dec 1994
(β=0.70; σ=0.81)

(β=2.48; σ=1.53)

(β=2.96; σ=1.22)

July 2001 – Dec 2003
(β=3.25; σ=1.31)

Kaplan-Meier
Weibull

1st Quartile
Median
3rd Quartile
Corresponding Hazards of Death after AIDS Diagnosis from Weibull Models

Schneider, Gange, ..., Muñoz. AIDS 2005

Years from AIDS Diagnosis

Hazard of death after AIDS (%)
Risk of Death Associated with Deferral of Antiretroviral Therapy, According to CD4+ Count at Baseline, with Adjustment for HIV RNA Level, Age, and Sex*


<table>
<thead>
<tr>
<th>Variable</th>
<th>351 – 500 CD4+ Count</th>
<th>&gt; 500 CD4+ Count</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Relative Risk (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Without inclusion of HIV RNA data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deferral of antiretroviral therapy</td>
<td>1.69 (1.26-2.26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female sex</td>
<td>1.21 (0.89-1.64)</td>
<td>0.24</td>
</tr>
<tr>
<td>Older age (per 10-yr increment)</td>
<td>1.68 (1.48-1.91)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline CD4+ count (per 100 cells/mm³)</td>
<td>1.13 (0.72-1.78)</td>
<td>0.59</td>
</tr>
<tr>
<td>With inclusion of HIV RNA data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deferral of antiretroviral therapy</td>
<td>1.63 (1.21-2.19)</td>
<td>0.002</td>
</tr>
<tr>
<td>Female sex</td>
<td>1.47 (1.02-2.12)</td>
<td>0.04</td>
</tr>
<tr>
<td>Older age (per 10-yr increment)</td>
<td>1.89 (1.69-2.11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline CD4+ count (per 100 cells/mm³)</td>
<td>0.74 (0.55-1.00)</td>
<td>0.06</td>
</tr>
<tr>
<td>Baseline HIV RNA level (per log₁₀ copies/ml)</td>
<td>1.11 (0.96-1.28)</td>
<td>0.15</td>
</tr>
</tbody>
</table>

* The CD4+ count was measured in cells per cubic millimeter. Results were calculated with the use of Cox regression analyses with inverse probability-of-censoring weights.
Years since AIDS Diagnosis

(Hazard at 1, 2, 3 years for Period 1: 0.59, 0.71, 0.82)

Relative Hazards

Cox, Chu, ..., Muñoz. Stat Med 2007

Period 2 to Period 1

Period 3 to Period 1

Period 4 to Period 1

Period 2: Jan1990-Dec1994
Period 1: Jul1984-Dec1989

Period 3: Jan1995-Jun1998
Period 1: Jul1984-Dec1989

Period 4: Jul1998-Dec2003
Period 1: Jul1984-Dec1989
Cumulative Percent Deceased

Relative Time

Period 2 to Period 1
Period 2: Jan1990-Dec1994
Period 1: Jul1984-Dec1989

Period 3 to Period 1
Period 3: Jan1995-Jun1998
Period 1: Jul1984-Dec1989

Period 4 to Period 1
Period 4: Jul1998-Dec2003
Period 1: Jul1984-Dec1989

Cumulative Percent Deceased
(Deciles for Period 1: 0.23, 0.47, 0.72 years)
Prognostic Value of the CD4 Cell Count and HIV RNA attained by HAART-Treated Individuals

*Tarwater, Gallant, …Muñoz. AIDS, 2004*

<table>
<thead>
<tr>
<th>Attained CD4 cell count</th>
<th>Person-years at risk</th>
<th>Number of AIDS cases</th>
<th>Relative Hazard of AIDS</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;250 cells/μL</td>
<td>739</td>
<td>5</td>
<td>1</td>
<td>(1.5, 13.6)</td>
</tr>
<tr>
<td>≥100 cells/μL</td>
<td>295</td>
<td>9</td>
<td>4.6</td>
<td>(4.2, 34.5)</td>
</tr>
<tr>
<td>101–250 cells/μL</td>
<td>140</td>
<td>12</td>
<td>12.1</td>
<td>(11.2, 97.7)</td>
</tr>
<tr>
<td>≤100 cells/μL</td>
<td>44</td>
<td>10</td>
<td>33.1</td>
<td></td>
</tr>
</tbody>
</table>

November 2004
Effect of Interrupting and Discontinuing HAART on % CD4 Cell Count Increases in 6 months According to Prior HIV RNA Level

Li, Margolick, ..., Jacobson - JAIDS 2005
## Risk of AIDS or Death by CD4 Cell Count while Plasma Viral Load was <50 HIV RNA copies/mL

* Taiwo, Li, …, Phair. *HIV Med* 2009

<table>
<thead>
<tr>
<th>CD4 cell count</th>
<th>AIDS* (P value)</th>
<th>Death* (P value)</th>
<th>AIDS or Death* (P value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 200 cells/µL</td>
<td>5.96 (0.40, 87.8)</td>
<td>22.8 (1.89, 275)</td>
<td>10.7 (1.65, 70.0)</td>
</tr>
<tr>
<td></td>
<td>(0.194)</td>
<td>(0.014)</td>
<td>(0.013)</td>
</tr>
<tr>
<td>201-350 cells/µL</td>
<td>5.44 (0.47, 63.4)</td>
<td>10.8 (0.92, 127)</td>
<td>8.54 (1.54, 47.2)</td>
</tr>
<tr>
<td></td>
<td>(0.176)</td>
<td>(0.059)</td>
<td>(0.014)</td>
</tr>
</tbody>
</table>

* Compared to having CD4 cell count > 350 cells/µL while plasma viral load was <50 copies/mL:  

May 2010
Time to Viral Suppression Following HAART According to Selected Genotypings

Hendrickson, Jacobson, . . ., O’Brien - JAIDS 2008

感慨，对病毒抑制时间依赖于不同的基因分型。图中展示了CCR5-△32和CX3CR1-V249I基因型对病毒抑制时间的影响。在CCR5-△32基因型中，Δ32/+和+/+的抑制率分别用灰色和深蓝色的线表示，显示Δ32/+的抑制率更高。在CX3CR1-V249I基因型中，V/V、V/I和I/I的抑制率分别用灰色、浅蓝色和紫色的线表示，显示I/I的抑制率最低。图中还显示了统计结果，如RH=1.40，p=0.008，N=419/352，以及RH=1.27，p=0.01，N=403/310。
Time to AIDS Following HAART According to Selected Genotypings

Hendrickson, Jacobson, . . ., O’Brien - JAIDS 2008

![Graphs showing time to AIDS following HAART according to genotypings](image-url)
Lamivudine (LMV) Resistance in HIV-HBV Coinfected Cohort

Matthews, Bartholomeusz, …, Thio. AIDS 2006

Sequenced Pol in 53 viremic persons > 6 mos LMV

- 39 (74%) LMV-R HBV
- After 4 yrs, 94% with LMV-R HBV
- Factors associated with developing resistance
  - Longer LMV, HAART
  - Higher CD4 count at time of resistance testing
- 9 (17%) with triple mutant
  - 2x the prevalence of monoinfected persons
Pre- and On-HAART Biomarker Geometric Means and 95% Confidence Intervals Overall and Stratified by Cohort

Palella, Gange, . . ., Elion, AIDS 2010

Combined MACS and WIHS
MACS
WIHS

hsCRP (ug/ml)

D-dimer (ug/ml)

IL-6 (pg/ml)

Pre-HAART
On-HAART
Pre-HAART
On-HAART
Pre-HAART
On-HAART

Palella, Gange, . . ., Elion, AIDS 2010

May 2011
Effect of HAART on Biomarkers of Inflammation and Immune Activation

Regidor, Detels, . . . , Martinez-Maza. AIDS 2011

A) Total population; B) Stratified by viral load response (<50 copies within 1.5 years after HAART initiation and sustained 1.5 – 3 years post HAART, if measurement was available)
Infection of Dendritic Cells with HHV-8 is Blocked by anti-DC-SIGN mAb

Rappocciolo, Jenkins, ..., Rinaldo. J Immunol 2006
Infection of Macrophages with HHV-8 is Blocked by anti-DC-SIGN mAb

Rappocciolo, Jenkins, ..., Rinaldo. J Immunol 2006
Annual Mean Change over a 4-year Interval in BMI in 4 Groups

Brown, Wang, …, Dobs. JAIDS 2006

Years from baseline (1999)

BMI
Diabetes Mellitus and Hyperglycemia

Brown, Cole, ..., Dobs - Arch Intern Med 2005

RATE RATIO 1

<table>
<thead>
<tr>
<th>HIV-</th>
<th>HIV+</th>
<th>HIV+ HAART</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.4</td>
<td>1.7</td>
<td>4.7</td>
</tr>
<tr>
<td>15.3</td>
<td>11.1</td>
<td>21.4</td>
</tr>
<tr>
<td>(1.9, 9.2)</td>
<td>(1.2, 2.3)</td>
<td></td>
</tr>
</tbody>
</table>

RATE 2

1 Adjusted for age and BMI
2 Rate per 100 person-years

May 2007
### Mean Change in Blood Lipids Over Time for 50 Seroconverters Who Initiate HAART

*Riddler, Smit, …, Kingsley - JAMA 2003*

<table>
<thead>
<tr>
<th>Lipids, mg/dL:</th>
<th>Pre-seroconversion (n=50)</th>
<th>Last Visit before HAART (n=50)</th>
<th>1st Visit after HAART (n=49)</th>
<th>2nd Visit after HAART (n=49)</th>
<th>3rd Visit after HAART (n=43)</th>
<th>4th Visit after HAART (n=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>201 (179, 222)</td>
<td>-30 (-52, -9)</td>
<td>4 (-17, 25)</td>
<td>9 (-16, 34)</td>
<td>20 (-1, 41)</td>
<td>18 (-7, 42)</td>
</tr>
<tr>
<td>HDL-C</td>
<td>51 (46, 57)</td>
<td>-12 (-19, -6)</td>
<td>-11 (-16, -6)</td>
<td>-11 (-16, -6)</td>
<td>-9 (-16, -2)</td>
<td>-10 (-16, -3)</td>
</tr>
<tr>
<td>LDL-C</td>
<td>122 (102, 143)</td>
<td>-22 (-45, 1)</td>
<td>-6 (-29, 17)</td>
<td>-1 (-24, 22)</td>
<td>-1 (-25, 22)</td>
<td>5 (-20, 30)</td>
</tr>
</tbody>
</table>
Serum Lipids in HIV Seroconverters Who Initiated HAART

Riddler, Smit, ..., Kingsley - JAMA 2003

<table>
<thead>
<tr>
<th>N</th>
<th>TC</th>
<th>LDL</th>
<th>HDL</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>(50)</td>
<td>201</td>
<td>122</td>
</tr>
<tr>
<td>+</td>
<td>(50)</td>
<td>171</td>
<td>100</td>
</tr>
<tr>
<td>1</td>
<td>(49)</td>
<td>205</td>
<td>116</td>
</tr>
<tr>
<td>2</td>
<td>(49)</td>
<td>210</td>
<td>121</td>
</tr>
<tr>
<td>3</td>
<td>(43)</td>
<td>221</td>
<td>121</td>
</tr>
<tr>
<td>4</td>
<td>(38)</td>
<td>219</td>
<td>127</td>
</tr>
</tbody>
</table>

**Legend:**
- TC - total cholesterol
- LDL - low density lipids
- HDL - high density lipids

November 2004
Percent Difference in Lipoprotein Concentrations Among HAART Treated According to Clinical Status, Compared to Uninfected

Riddler, Li, . . ., Sharrett - JAIDS 2008

Percent Difference

Good (n=220)  Intermediate (n=160)  Poor (n=16)

Large LDL  Small LDL  VLDL  HDL

Percent Difference

May 2009
Distribution of Total Cholesterol and High-Density Lipid Levels in HIV-Infected Men

Abraham, Li, ..., Phair - AIDS Res Hum Retroviruses 2013;29:1346-52

Pre- and Post-ART Cholesterol (mg/dL)

Total Cholesterol

HDL

November 2013
Estimated GFR after cART Initiation According to Total Cholesterol Change

Abraham, Li, …, Phair - AIDS Res Hum Retroviruses 2013;29:1346-52

November 2013
Mean Serum Lipids Vary by Biogeographical Ancestry and HIV/HAART Status

Nicholaou, Martinson, ..., Kingsley - AIDS Res Hum Retroviruses 2013;29:871-9

A: Mean total cholesterol (TCHOL) by HIV/HAART status (-/- = HIV negative; +/- = HIV/HAART naïve, +/+ = HIV/HAART).

B: Mean low density lipoprotein cholesterol (LDL-C).

C: Mean high-density lipoprotein cholesterol (HDL-C).

D: Mean triglyceride (TRIG).

AEA = African/European ancestry population; EA = European ancestral populations. Raw calculated means are shown in blue and adjusted means are shown in red. Bars indicate 95% confidence intervals of the mean.
Prevalence of Systolic Hypertension (SH) and Diastolic Hypertension (DH) by HIV Sero-status and Therapy, and Relative to the Time of HAART Initiation

Seaberg, Muñoz, ..., Phair. AIDS 2005
### Multiple Regression Analyses:
**Systolic Hypertension and Diastolic Hypertension**

**Seaberg, Muñoz, …, Phair. AIDS 2005**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>OR</th>
<th>95% CI</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>1.21</td>
<td>1.06, 1.37</td>
<td>1.67</td>
<td>1.47, 1.90</td>
</tr>
<tr>
<td>40-49</td>
<td>1.69</td>
<td>1.46, 1.96</td>
<td>2.36</td>
<td>2.05, 2.73</td>
</tr>
<tr>
<td>&gt;50</td>
<td>3.23</td>
<td>2.73, 3.82</td>
<td>3.05</td>
<td>2.58, 3.62</td>
</tr>
<tr>
<td><strong>Race/ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>1</td>
<td></td>
<td>1.67</td>
<td>1.40, 1.99</td>
</tr>
<tr>
<td>African-American</td>
<td>1.42</td>
<td>1.16, 1.72</td>
<td>1.01</td>
<td>0.79, 1.29</td>
</tr>
<tr>
<td>All others</td>
<td>0.90</td>
<td>0.68, 1.18</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Body mass index (kg/m²)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>20-24.9</td>
<td>1.66</td>
<td>1.36, 2.01</td>
<td>1.46</td>
<td>1.23, 1.74</td>
</tr>
<tr>
<td>25-29.9</td>
<td>2.83</td>
<td>2.31, 3.47</td>
<td>2.46</td>
<td>2.05, 2.96</td>
</tr>
<tr>
<td>&gt;30</td>
<td>5.20</td>
<td>4.15, 6.51</td>
<td>4.43</td>
<td>3.62, 5.43</td>
</tr>
<tr>
<td><strong>Cigarette Smoking history</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoked</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Former smoker</td>
<td>1.21</td>
<td>1.08, 1.35</td>
<td>1.04</td>
<td>0.93, 1.15</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1.17</td>
<td>1.03, 1.33</td>
<td>0.93</td>
<td>0.82, 1.05</td>
</tr>
<tr>
<td><strong>HIV / ART / HAART (years since HAART initiation)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- no</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>+ no</td>
<td>0.79</td>
<td>0.70, 0.89</td>
<td>0.84</td>
<td>0.76, 0.94</td>
</tr>
<tr>
<td>+ yes naive</td>
<td>0.69</td>
<td>0.59, 0.80</td>
<td>0.73</td>
<td>0.63, 0.84</td>
</tr>
<tr>
<td>+ yes yes (&lt;2 years)</td>
<td>1.06</td>
<td>0.87, 1.30</td>
<td>0.84</td>
<td>0.68, 1.03</td>
</tr>
<tr>
<td>+ yes yes (2-5 years)</td>
<td>1.51</td>
<td>1.25, 1.82</td>
<td>0.78</td>
<td>0.63, 0.96</td>
</tr>
<tr>
<td>+ yes yes (&gt;5 years)</td>
<td>1.70</td>
<td>1.34, 2.16</td>
<td>1.21</td>
<td>0.94, 1.56</td>
</tr>
<tr>
<td>+ discontinued HAART</td>
<td>1.32</td>
<td>0.91, 1.90</td>
<td>1.02</td>
<td>0.69, 1.49</td>
</tr>
</tbody>
</table>
Association between CD4+ T-cell Count (cells/µl) and Prevalence of Carotid Lesions among Participants in Men (MACS) and Women (WIHS)

Kaplan, Kingsley, . . ., Hodis - AIDS 2008

Prevalence ratio

0.5 1.0 1.5 2.0 2.5 3.0 3.5

HIV- HIV+ HIV+ HIV+ HIV+ HIV+ HIV+ HIV+ HIV+ HIV+
CD4>500 350-500 200-349 <200 CD4>500 350-500 200-349 <200
N=325 N=303 N=147 N=100 N=50 N=496 N=487 N=269 N=288 N=187

Men Women

May 2009
Association of Subclinical Atherosclerosis with Presence of Plasma CMV DNA, and Antibodies to HSV-1, HSV-2 and HHV-8 in HIV-Infected Men Who have Sex with Men

Hechter, Budoff, …, Detels - Atherosclerosis 2012;223:433-6

![Graph showing adjusted odds ratios for CMV, HSV-1, HSV-2, and HHV-8](image-url)
Coronary Artery Disease (CAD) Variability Explained by Traditional Risk Factors, HIV-Related Factors and Genetic Background

Rotger, Glass, ..., Tarr - Clin Infect Dis 2013;57:112-21

November 2013

% of explained variability

Clinical
Genetic
HIV Related

Age
Current smoking
Family history of CAD
High cholesterol
Hypertension
Diabetes
Past smoking
Low HDL cholesterol
Genetic score
LPV, ≥1 year
on ABC
IDV, ≥1 year
on ART
RNA
CD4

November 2013
Agreement Between GFR and Observed GFR

Bias Ratio: 1.004
Ratio of SDs: 1.005
Correlation: 0.996
RMSE: 1.46

Bias Ratio: 1.005
Ratio of SDs: 0.987
Correlation: 0.980
RMSE: 4.59

Ng, Schwartz, ..., Muñoz. Kidney Int 2011

May 2012
Categorization of Hepatic Fibrosis by HIV and Viral Hepatitis Disease Category

*Price, Seaberg, ..., Thio. J Infect Dis 2012*

- **No/Mild Fibrosis (APRI <0.5)**
- **Intermediate Fibrosis (APRI 0.5-1.5)**
- **Significant Fibrosis (APRI >1.5)**

<table>
<thead>
<tr>
<th>Condition</th>
<th>No Infection</th>
<th>HIV Monoinfected</th>
<th>Hepatitis Monoinfected</th>
<th>Co-infected</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Infection</td>
<td>91.5</td>
<td>64.2</td>
<td>62.2</td>
<td>48.5</td>
</tr>
<tr>
<td>HIV Monoinfected</td>
<td>8.2</td>
<td>32.2</td>
<td>33.8</td>
<td>30.3</td>
</tr>
<tr>
<td>Hepatitis Monoinfected</td>
<td>0.3</td>
<td>3.5</td>
<td>4.1</td>
<td>21.2</td>
</tr>
<tr>
<td>Co-infected</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

May 2012
Increased Liver Mortality in HIV-HBV Co-infected Men: MACS

Thio, Seaberg, ..., Thomas - Lancet 2002

- 5293 men (326 HBsAg+ baseline) followed 10.5 years
- RR of liver death 18.7 in coinfected vs. only HBsAg+

Liver MR/1000 PYs

HIV-/HBV- 0.0
HIV-/HBV+ 0.8
HIV+/HBV- 1.7
HIV+/HBV+ 14.2

November 2004
Kaplan-Meier Curve of Non-AIDS Mortality by Hepatitis B Virus Status as Determined at Time of HAART Initiation

**Number at Risk**

<table>
<thead>
<tr>
<th>Status</th>
<th>Time (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never infected</td>
<td>350 326 250 191 125</td>
</tr>
<tr>
<td>Past infection</td>
<td>357 324 278 246 193</td>
</tr>
<tr>
<td>Chronic hepatitis B</td>
<td>45 41 31 27 16</td>
</tr>
<tr>
<td>Isolated core</td>
<td>64 53 35 31 23</td>
</tr>
</tbody>
</table>
Time Trend in Liver-Related Mortality Rates by Hepatitis and HIV-1 Status


IRR=1.6

HIV negative

1984-2010

IRR=3.0

2.9 (HBV) 1.0 (HCV)

1984-1996

IRR=2.1

13.1 (HBV) 6.7 (HCV)

1997-2001

IRR=24.4

24.4 (HBV) 14.9 (HCV)

2002-2010

IRR=1.2

8.1 (HBV) 6.7 (HCV)

HIV positive
Infectious and Non-Infectious Respiratory Complications in HIV-Infected Compared to Uninfected Persons

Gingo, Balasubramani, …, Morris - PLoS ONE 2013;8:e58812

Any Infectious Diagnosis (Odds Ratios)

Any Non-Infectious Diagnosis (Hazard Ratios)

Cohort: MACS Pre-HAART, MACS HAART, WIHS HAART

November 2013
Proportion of Participants HBV DNA Undetectable by HBV Regimen

Matthews, Seaberg, …, Thio - Clin Infect Dis 2013;56:e87-e94

Proportion of individuals coinfected with HIV and HBV with undetectable HBV DNA by HBV active regimen.

Abbreviations: FTC = emtricitabine; LMV = lamivudine; TDF = tenofovir
HCV incident rate per 1000 PY: 4.22 for HIV+ and 0.50 for HIV-
Oral HPV Prevalence (Unadjusted) by HIV Status and Current CD4 T-cell Count Among 370 HIV-Positive Individuals


* $P_{\text{trend}} \leq 0.001$
Oral HPV Prevalence (Unadjusted) by HIV Status and Current CD4 T-cell Count Among 370 HIV-Positive Individuals


* $P_{\text{trend}} \leq 0.001$
Cancer Incidence among HIV-infected vs. HIV-uninfected MACS Participants in the HAART Era


Cancer

AIDS-defining malignancies

Kaposi's Sarcoma
Non-Hodgkin's Lymphoma

Non-AIDS-defining malignancies

Anus
Hodgkin's Lymphoma
Lung *
Melanoma
Prostate

Incidence Rate Ratio

* Among participants with a history of smoking.
** Adjusted for age and race.

May 2011
Cancer Incidence in the HAART Era vs. the Pre-HAART Era among HIV-infected MACS Participants


Cancer

AIDS-defining malignancies
- Kaposi's Sarcoma: 0.13
- Non-Hodgkin's Lymphoma: 0.23

Non-AIDS-defining malignancies
- Anus
- Hodgkin's Lymphoma
- Lung *: 0.42
- Melanoma: 0.40
- Prostate: 1.72

* Among participants with a history of smoking.
** Adjusted for age and race.

May 2011
Mean Serum Levels of Several B Cell Activation-associated Molecules are Consistently Elevated More than 3 Years Preceding AIDS-associated Lymphoma Diagnosis

Breen, Hussain, …, Martínez-Maza. Cancer Epidemiol Biomarkers Prev 2011

Natural log-transformed mean values (± s.e.m.) for HIV-infected subjects who went on to develop AIDS-NHL (▲) and HIV-infected controls without lymphoma (▲)
Elevated Levels of B Cell Activation Markers Prior to AIDS-NHL are Seen Only in Those Subjects Who Develop Systemic Lymphoma

_Breen, Hussain, …, Martínez-Maza. Cancer Epidemiol Biomarkers Prev 2011_

CD4-adjusted odds ratios (OR) ± 95% confidence intervals (CI) for increased serum cytokine levels are shown for AIDS-NHL cases compared to matched HIV+ controls, stratified according to primary tumor location outside of the central nervous system (systemic, □) or within the central nervous system (CNS, ■). For all markers except IL10, ORs are in terms of one unit increase in natural log-transformed values; for IL10, ORs are in terms of detectable vs. undetectable. ORs are missing for IL10 for CNS tumors at two time-points (>3 years and 0-1 year) due to failure of the logistic regression model to converge on account of sparse data.
CXCL13 Levels in HIV-Positive Non-Hodgkin Lymphoma Cases and Controls


<table>
<thead>
<tr>
<th>Years Prior to NHL</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;3 years</td>
<td>3.24</td>
<td>(1.90-5.54)</td>
</tr>
<tr>
<td>1-3 years</td>
<td>3.39</td>
<td>(1.94-5.94)</td>
</tr>
<tr>
<td>0-1 year</td>
<td>3.94</td>
<td>(1.98-7.81)</td>
</tr>
</tbody>
</table>

Note: p < 0.001 for all comparisons.
CXCL13 Levels by CXCL13 and CXCR5 tagSNPs


---

**CXCL13 Levels (pg/mL)**

<table>
<thead>
<tr>
<th></th>
<th>CXCL13 rs355689</th>
<th>CXCL13 rs17002733</th>
<th>CXCR5 rs630923</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT</td>
<td>112</td>
<td>110</td>
<td>109</td>
</tr>
<tr>
<td>TC</td>
<td>108</td>
<td>104</td>
<td>105</td>
</tr>
<tr>
<td>CC</td>
<td>94</td>
<td></td>
<td>62</td>
</tr>
<tr>
<td>CC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TT</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**MR**

- MR$_{CC \text{vs} \ TT} = 0.82$ (0.68-0.99)
- MR$_{TT \text{vs} \ CC} = 0.82$ (0.39-1.00)
- MR$_{AA \text{vs} \ CC} = 2.40$ (1.43-4.50)

---

November 2013
Time Free of Anal Cancer
HIV+ Men Pre-HAART and HAART Era vs HIV- Men


![Graph showing probability of anal cancer free over age for HIV-negative and HIV-positive men](image)

- HIV-negative
  - N: 3384
  - RH: 1.0

- HIV-positive 1984-1995
  - N: 2795
  - RH: 4.4

- HIV-positive 1996-2006
  - N: 1871
  - RH: 7.3

May 2009
Anal Cancer Incidence Rates by Calendar Era for HIV+ Men Who have Sex with Men, Other Men, and Women, NA-ACCORD, Years 1996-2007


MSM  Other men  Women

Global p-value=0.078  Global p-value=0.655  Global p-value=0.126

Infection Rate (per 100,000 person-years)

November 2013
Frailty-Related Phenotype (FRP) by Duration of HIV Infection (Pre-HAART)

Desquilbet, Jacobson, …, Margolick.


- Same FRP prevalence between a 55-year old man infected < 4 years and a >65-year old uninfected man

![Graph showing odds ratio for FRP by duration of HIV infection](image-url)
Estimated Prevalence of Frailty Phenotype (FRP) According to CD4+ Cell Count and Calendar Period (Age = 45 years)

Desquilbet, Margolick, . . ., Jacobson - JAIDS 2009

% FRP (95% CI)

CD4 cell/μl

1994-1995
1996-1999
2000-2005
Prognostic Effect of Persistent Frailty-related Phenotype (FRP) per-HAART on AIDS/Death Following HAART Initiation


% Alive and AIDS-free

RH (95% CI) = 3.83 (1.86-7.92)

N men at risk

<table>
<thead>
<tr>
<th>Years from HAART Initiation</th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;25% of FRP visits</td>
<td>454</td>
<td>401</td>
<td>353</td>
<td>287</td>
<td>127</td>
</tr>
<tr>
<td>&gt;25% of FRP visits</td>
<td>18</td>
<td>13</td>
<td>8</td>
<td>7</td>
<td>3</td>
</tr>
</tbody>
</table>
Distribution of Grip Strength in HIV-Infected Men with and without Lipodystrophy, and HIV-Uninfected Controls

Crawford, Li, …, Brown - AIDS Res Hum Retroviruses 2013;29:1138-45

P=0.004

(value >75th percentile + [1.5 x interquartile range])
Mean Trail-Making B Scores Around HIV-1 Seroconversion

Vo, Cox, ..., Miller - J Neurovirol 2013;19:24-31

Trailmaking Part B

Score in Seconds

Years Since HIV-1 Seroconversion

November 2013
Mental and Physical Health Summary Score Change over the Course of HIV Disease Progression

Liu, Ostrow, ..., Jacobson. Qual Life Res 2006

**Clinical Groups**
- Pre_SC (npv=235)
- No HAART (npv=242)
- HAART<2 yrs (npv=163)
- 2<HAART<4 yrs (npv=103)
- HAART≥4 yrs (npv=102)

**Graph**
- Physical Health Summary Score
- Mental Health Summary Score

**Mean and 95% CI**

May 2007
Longitudinally Preserved Psychomotor Performance in Long-Term Asymptomatic HIV-Infected Individuals


Long-term Disease Non-progressors
HAART, HIV RNA <50c/mL
Healthy CD4/ AIDS-free
HIV-negative

Visit

June 2008
Trail Making Performance Over Time by HIV Status and Age HAART Era

Sacktor, Skolasky,…, Miller. J NeuroVirol 2010
Incidence of Neurologic Events in the MACS by HIV and HAART Status

Mateen, Shinohara, …, Sacktor - Neurology 2012;79:1873-80
Adjusted Associations of Internalized Homophobia Resolution and Health Outcomes Among Men Who had Early Internalized Homophobia

Herrick, Stall, …, Plankey - AIDS Behav 2013;17:1423-30

November 2013
Goodness of Fit for $\log_{10}(\text{HIV RNA})$ as a Mixture of Two Normal Distributions - MACS

Li, Chu, …, Muñoz. J Epidemiol Community Health 2006

May 2006
Goodness of Fit for $\log_{10}(\text{HIV RNA})$ as a Mixture of Two Normal Distributions - WIHS

Li, Chu, …, Muñoz. *J Epidemiol Community Health* 2006

May 2006
Bimodel Distributions of $\log_{10}(\text{HIV RNA in copies/ml})$ for the MACS and WIHS

Li, Chu, …, Muñoz. *J Epidemiol Community Health* 2006

May 2006
Bimodal Mixture Distributions Summarizing the HIV-1 RNA Distributions Derived from 2 Assays Used to Measure HIV-1 RNA

Schneider, Margolick, …, Muñoz. J Acquir Immune Defic Syndr 2012

TaqMan

Amplicor

Predicted Cumulative Percentage

Plasma HIV-1 RNA

May 2012
Risk and Survival Attributable to an Exposure

Cox, Chu, Muñoz. Stat Med 2009

Attributable Risk

\[ AR(t) = \frac{S_0(t) - S(t)}{1 - S(t)} \]

Attributable Survival

\[ AS(t) = \frac{S_0(t) - S(t)}{S_0(t)} \]

\( S_0(t) \) = survival unexposed; \( S_1(t) \) = survival exposed

\( S(t) = \Pi S_1(t) + (1-\Pi)S_0(t) \) = survival in population

\( \Pi = \) proportion exposed; 

May 2010
Risk and Survival Attributable to the Absence of HAART

Cox, Chu, Muñoz. Stat Med 2009

Attributable Risk/Survival, $\pi = 0.7$

Attributable Risk/Survival, $\pi = 0.3$

Years from AIDS

May 2010
Number of Pre-2010 Participants with Specimens Available* in the National Repository Relative to the Time of Seroconversion**

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Last Seronegative Visit</th>
<th>First Seropositive Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma</td>
<td>472</td>
<td>515</td>
</tr>
<tr>
<td>Serum</td>
<td>496</td>
<td>493</td>
</tr>
<tr>
<td>Cells</td>
<td>455</td>
<td>450</td>
</tr>
</tbody>
</table>

* 2 or more tubes according to repository inventory as of 10/1/13
** A total of 651 pre-2010 participants have a known seroconversion date
Number of Pre-2010 Participants with Specimens Available* in the National Repository Relative to the Development of AIDS**

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Within 1 Year Pre-AIDS</th>
<th>Within 6 Months Post AIDS</th>
<th>After 6 Months Post AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma</td>
<td>1268</td>
<td>640</td>
<td>641</td>
</tr>
<tr>
<td>Serum</td>
<td>1205</td>
<td>553</td>
<td>594</td>
</tr>
<tr>
<td>Cells</td>
<td>808</td>
<td>296</td>
<td>386</td>
</tr>
</tbody>
</table>

* 2 or more tubes according to repository inventory as of 10/1/13
** A total of 1988 pre-2010 participants have developed AIDS

November 2013
### Number of Pre-2010 Participants with Specimens Available* in the National Repository Relative to HAART Use**

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Within 1 Year Prior to HAART</th>
<th>Within 6 Months Post HAART</th>
<th>After 6 Months Post HAART</th>
<th>All 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma</td>
<td>813</td>
<td>673</td>
<td>1368</td>
<td>532</td>
</tr>
<tr>
<td>Serum</td>
<td>781</td>
<td>642</td>
<td>1367</td>
<td>481</td>
</tr>
<tr>
<td>Cells</td>
<td>643</td>
<td>525</td>
<td>1266</td>
<td>366</td>
</tr>
</tbody>
</table>

* 2 or more tubes according to repository inventory as of 10/1/13
** A total of 1530 pre-2010 participants have initiated HAART