VIRAL SUPPRESSION AND CANCER RISK

Long-term viral suppression predicts lower cancer incidence among HIV-infected veterans, but higher than among uninfected

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Outline

• Background
• Methods
  ◦ Viral suppression classification
  ◦ Cancer groups and types
• Results
  ◦ Age, race, sex-standardized IR, IRR
  ◦ Adjusted for additional confounders
• Conclusions
Background

- HIV viral suppression
  - treatment success
  - reduced morbidity
- ART reduces mortality, but HIV+ at increased risk of certain cancers

*Does long-term viral suppression reduce the risk of cancer?*
Veterans Aging Cohort Study (VACS)

- Prospective, observational cohort
- HIV+ and 1:2 age/race/site matched HIV- comparison
- Veterans Health Administration
  - Largest single provider of HIV care in US
- VACS Virtual Cohort
  - HIV+ N=44,782; HIV- N=95,039
- VA Central Cancer Registry (VACCR)
VACS database

VHA Health Information System

Electronic Medical Record
- Inpatient/Outpatient
- Laboratory Data
- Pharmacy Data (centralized)
- Pathology
- Radiology
- Progress Notes

Administrative Record (centralized)
- Diagnostic Codes
- Procedure Codes
- Utilization
- Mortality

VACS Database

Patient Survey
- Adherence
- Alcohol Use
- Drug Use
- Quality of Life
- Health Behaviors
- Provider Relationship

Substudies
- Telephone Interviews
- Blood Samples
- DNA Samples
- Neurocognitive
- Psychiatric Testing
- Focus Groups

Provider Surveys
- Adherence
- Comorbidity
- Health Behaviors
- Provider Characteristics
# VACS demographics

<table>
<thead>
<tr>
<th>Category</th>
<th>HIV+</th>
<th>HIV-</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=44,782</td>
<td>N=95,039</td>
</tr>
<tr>
<td>Age (Mean ± SD)</td>
<td>47.5 ± 10.5</td>
<td>48.1 ± 10.7</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>98</td>
<td>97</td>
</tr>
<tr>
<td>Female</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>39</td>
<td>40</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>49</td>
<td>48</td>
</tr>
<tr>
<td>Hispanic</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>5</td>
<td>5</td>
</tr>
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## VACS demographics, cont.

<table>
<thead>
<tr>
<th>Category</th>
<th>HIV+</th>
<th>HIV-</th>
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<tbody>
<tr>
<td><strong>Smoking</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>22</td>
<td>26</td>
</tr>
<tr>
<td>Current</td>
<td>47</td>
<td>45</td>
</tr>
<tr>
<td>Former</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>Unknown</td>
<td>19</td>
<td>13</td>
</tr>
<tr>
<td><strong>Alcohol abuse / dependence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>66</td>
<td>67</td>
</tr>
<tr>
<td>Yes</td>
<td>34</td>
<td>33</td>
</tr>
<tr>
<td><strong>Hepatitis C virus</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>54</td>
<td>54</td>
</tr>
<tr>
<td>Chronic</td>
<td>21</td>
<td>10</td>
</tr>
<tr>
<td>Exposed</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Unknown</td>
<td>17</td>
<td>32</td>
</tr>
</tbody>
</table>
Viral suppression categorization

Category (total obs time)

117,525 p-yrs

49,851 p-yrs

90,105 p-yrs

HIV-RNA (copies/mL)

Laboratory test date

Unsuppressed

Early suppressed

Long-term suppressed

Real laboratory test result

8
Methods

- Age-, race-, sex-, period-standardized IR
- IRR (HIV+ vs uninfected “in regular care”) 
- P-value for viral suppression trend
- Poisson regression to adjust for potential confounders
  - smoking, alcohol, HCV, HBV
## Cancer groups

<table>
<thead>
<tr>
<th>Cancer group</th>
<th>Cancer types</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any-cancer</td>
<td>First incident cancer of any type</td>
</tr>
<tr>
<td>AIDS-defining (ADC)</td>
<td>Invasive cervical cancer, non-Hodgkin lymphoma, Kaposi sarcoma</td>
</tr>
<tr>
<td>Virus-related non-AIDS-defining (NADC)</td>
<td>Oral cavity and pharynx, anal, liver, vulva, vagina, penis, Hodgkin lymphoma</td>
</tr>
<tr>
<td>Non-virus-related non-AIDS-defining</td>
<td>All other NADC</td>
</tr>
</tbody>
</table>
Standardized IR and IRR

Any-cancer

- HIV+ unsuppressed
- HIV+ early suppressed
- HIV+ long-term suppressed
- HIV+ unknown
- HIV- unknown

# ca: 1,579 497 965 410 15 5,271

p<0.0001
Cancer group results

AIDS-defining

Virus-related NADC

Non-virus NADC

- HIV+ unsuppressed
- HIV+ early suppressed
- HIV+ long-term suppressed
- HIV-
- IRR

p<0.0001

p=0.0008

p=0.0008
AIDS-defining cancers

Non-Hodgkin lymphoma

Kaposi sarcoma

- HIV+ unsuppressed
- HIV+ early suppressed
- HIV+ long-term suppressed
- HIV-
- IRR

p<0.0001
Virus-related NADC

**Anal SCC**
- Bar graph showing IR vs. IRR.
- Significant difference with p=0.0016.

**Liver HCC**
- Bar graph showing IR vs. IRR.
- Significant difference with p=0.080.

**Hodgkin lymphoma**
- Bar graph showing IR vs. IRR.
- Significant difference with p=0.011.
Select non-virus-related NADC

Larynx

- IRR: 30, 40
- IR: 0, 10, 20, 30
- p-value: 0.0045

Lung

- IRR: 300, 400
- IR: 0, 100, 200, 300
- p-value: <0.0001

Melanoma skin

- IRR: 20, 30
- IR: 0, 10, 20, 30
- p-value: 0.094

Leukemia

- IRR: 2, 3
- IR: 0, 1, 2, 3
- p-value: 0.0008
Prostate cancer

- Androgen levels
- PSA testing
- Screening rates in HIV+

![Prostate cancer chart]
## Fully-adjusted IRR

- Elevated risk persisted: smoking, alcohol abuse  
  - all cancer groups, oral cavity & pharynx, lung cancer
- Hepatocellular carcinoma:

<table>
<thead>
<tr>
<th></th>
<th>Base model</th>
<th>Base + HCV, HBV, alcohol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IRR (95% CI)</td>
<td>IRR (95% CI)</td>
</tr>
<tr>
<td>HIV+ unsuppressed</td>
<td>3.3 (2.6, 4.2)</td>
<td>1.4 (1.1, 1.8)</td>
</tr>
<tr>
<td>HIV+ early suppressed</td>
<td>2.4 (1.7, 3.4)</td>
<td>1.2 (0.9, 1.7)</td>
</tr>
<tr>
<td>HIV+ long-term suppressed</td>
<td>2.2 (1.7, 2.7)</td>
<td>1.1 (0.8, 1.3)</td>
</tr>
<tr>
<td>HIV-</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
</tr>
</tbody>
</table>

*Evidence of confounding by HCV, HBV*
## CD4+ cell count IRRs

<table>
<thead>
<tr>
<th></th>
<th>ADC</th>
<th>Virus NADC</th>
<th>Non-virus NADC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Base</td>
<td>+ CD4</td>
<td>Base</td>
</tr>
<tr>
<td>Unsuppressed</td>
<td>7.5*</td>
<td>5.7*</td>
<td>1.5*</td>
</tr>
<tr>
<td>Early suppressed</td>
<td>2.8*</td>
<td>2.3*</td>
<td>1.0</td>
</tr>
<tr>
<td>Long-term suppressed (ref)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- After adjusting for CD4, IRRs decreased modestly for all cancer group outcomes
- All cancer group viral suppression p-trend < 0.05

*Decreasing viral suppression trend remained, and elevated cancer risk persisted*
Conclusions

• Limitations
  ◦ Long-term suppressed=healthier?
  ◦ HIV-RNA<500 cutoff

• Compared to HIV- patients seen at the VA, cancer risk:
  HIV+ unsuppressed > early suppressed > long-term suppressed

• Novel exploration: association between long-term viral suppression and cancer risk

*Potential cancer prevention effect of ART*
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