

# Mortality following hospitalization for acute coronary syndrome among HIV+ and HIV- patients

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# Background

- HIV patients living longer as a result of effective combination antiretroviral therapy (ART)
- Medical care now focused more on non-AIDS-related morbidity, such as coronary artery disease including acute coronary syndrome (ACS)
- HIV patients have 40-50%<sup>1,2</sup> higher risk of myocardial infarctions (MI) or ACS compared with HIV- individuals
- Higher ACS risk may be due to use of specific antiretrovirals (i.e., protease inhibitors [PI]), higher smoking rates, chronic inflammation or immunodeficiency

1. Silverberg et al. *JAIDS*. 2013, in press. 2. Freiberg et al. *JAMA Intern Med*. 2013;173:614-622.

# Acute coronary syndrome in the setting of HIV

- Typically male, aged 40-50, smoker, dyslipidemic, ART-experienced
- More ST elevation MI (STEMI); less non-ST elevation MI (NSTEMI) or unstable angina<sup>1</sup>
- Few have evaluated differences by HIV status in mortality after an ACS hospitalization:

	HIV+ (n)	HIV- (n)	Methods	Results
<b>Lorgis et al.<sup>2</sup></b>	435	945	<b>1 year</b> follow-up; 2005-09 Matched: age, sex	<b>1.4% HIV+</b> <b>1.7% HIV-</b> ; p=0.64
<b>Boccarda et al.<sup>3</sup></b>	103	195	<b>1 year</b> follow-up; 2003-06 Matched: age, sex, ACS type	<b>0 deaths HIV+</b> <b>2 deaths HIV-</b>
<b>Boccarda et al.<sup>4</sup></b>	50	50	<b>20 months</b> follow-up; 2001-03 Matched: age, sex	<b>0 deaths HIV+</b> <b>0 deaths HIV-</b>
<b>Matetzky et al.<sup>5</sup></b>	24	48	<b>15 months</b> follow-up; 1998-00 Matched: age, sex, ACS type	<b>0 deaths HIV+</b> <b>2 deaths HIV-</b>

1. Boccarda et al. *JACC*. 2013;61:511-523. 2. Lorgis et al. *Circulation*. 2013; 2013;127:1767-1774. 3. Boccarda et al. *Eur Heart J*. 2011;32:41-50. 4. Boccarda et al. *Heart* 2006;92:543-544. 5. Matetzky et al. *Arch Intern Med*. 2003;163:457-460.

# Research question

**Does HIV status, immunodeficiency, or antiretroviral therapy use affect long-term survival following a hospitalization with acute coronary syndrome?**

# Methods

Study design and setting	Data	Analysis
<ul style="list-style-type: none"><li>■ Kaiser Permanente Northern California</li><li>■ Cohort study of all hospitalizations, 1996-2010, for ACS (STEMI; NSTEMI; unstable angina)</li><li>■ <b>226</b> HIV+ and <b>86,321</b> HIV- ACS patients followed from hospital discharge until death or 12/31/10</li></ul>	<ul style="list-style-type: none"><li>■ <u>Data sources</u>: HIV registry; electronic medical record; death certificates, Social Security Admin files</li><li>■ <u>Outcome</u>: all-cause mortality</li><li>■ <u>Exposures</u>:<ul style="list-style-type: none"><li>a. HIV</li><li>b. CD4</li><li>c. ART use</li></ul></li><li>■ <u>Confounders</u>: age, sex, race/ethnicity, diagnosis year, ACS type, smoking, cholesterol levels</li></ul>	<ul style="list-style-type: none"><li>■ Kaplan-Meier plots</li><li>■ Adjusted hazard ratios for death from Cox models:<ul style="list-style-type: none"><li>a. <b>HIV+</b> <b>HIV- (reference)</b></li><li>b. <b>CD4&lt;200</b> <b>CD4 200-499</b> <b>CD4≥500</b> <b>HIV- (reference)</b></li><li>c. <b>No ART</b> <b>PI-based ART</b> <b>PI-sparing ART</b> <b>HIV- (reference)</b></li></ul></li></ul>

# Baseline characteristics (1)

Characteristic	HIV+	HIV-	P-value
N	226	86,321	
Mean baseline age, years	54.3	66.8	<0.001
Men, %	94.3	63.0	<0.001
Year of ACS diagnosis, %			0.008
1996-2003	48.7	57.5	
2004-2010	51.3	42.5	
Race/ethnicity, %			<0.001
White	74.0	77.5	
Black	16.8	7.5	
Hispanic/Asian/Other	9.2	15.1	

## Baseline characteristics (2)

Characteristic	HIV+	HIV-	P-value
ACS type, %			<0.001
STEMI	36.7	24.8	
NSTEMI	33.6	33.4	
Unstable angina	29.7	41.8	
HDL<40 mg/dl, %	59.2	40.2	<0.001
LDL≥160 mg/dl %	13.2	13.3	0.95
Triglycerides≥150 mg/dl, %	73.3	49.8	<0.001
Ever smoking, %	69.9	55.2	<0.001

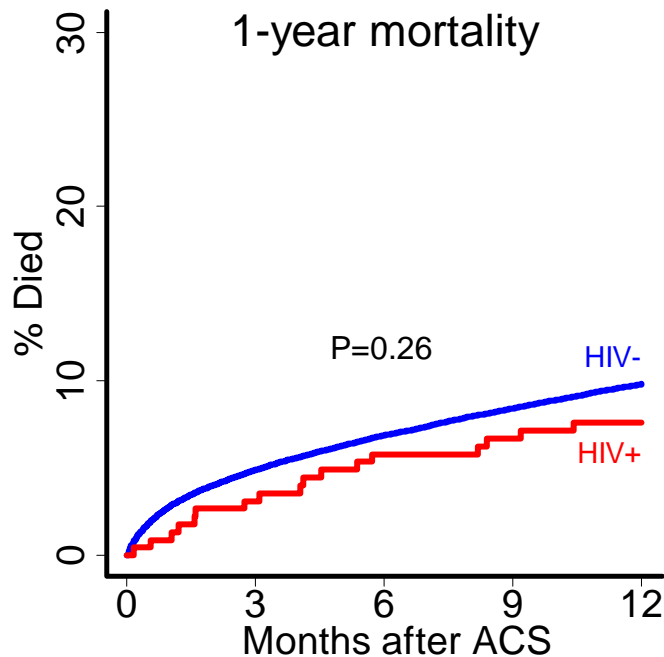
# Baseline characteristics (3)

Characteristic	HIV+
CD4 T-cell counts/ $\mu$ L, %	
<200	20.0
200-499	48.6
$\geq$ 500	31.4
Antiretroviral therapy class, %	
No ART	16.4
PI-based ART	58.0
PI-sparing ART	25.7

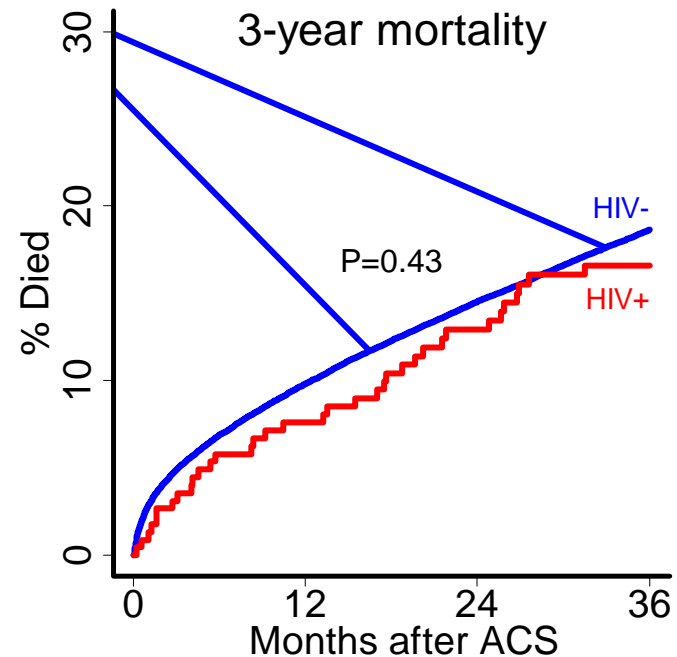


# Mortality after an ACS diagnosis

## By HIV status



	3-year mortality	Adjusted* hazard ratio	(95% CI)	P
<b>HIV+</b>	7.6%	2.2	(1.3-3.5)	0.001
<b>HIV- (ref)</b>	9.8%	1		

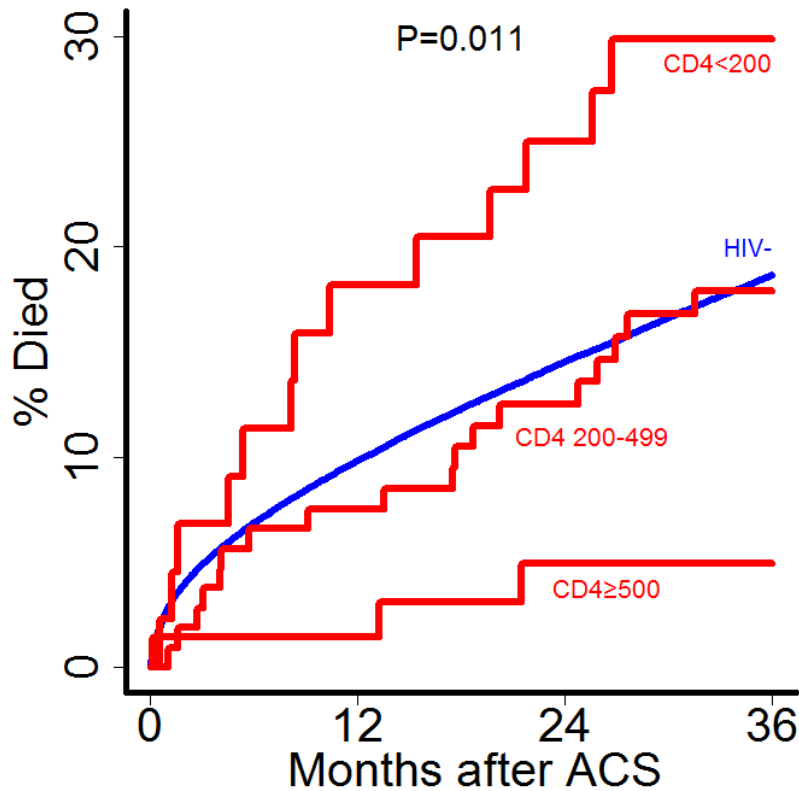


	3-year mortality	Adjusted* hazard ratio	(95% CI)	P
<b>HIV+</b>	16.6%	2.5	(1.8-3.5)	<0.001
<b>HIV- (ref)</b>	18.6%	1		

\* Adjusted for baseline age, sex, race, diagnosis year, ACS type, ever smoking status, and LDL, HDL, and triglyceride levels

# Mortality after an ACS diagnosis

By HIV status and immunodeficiency

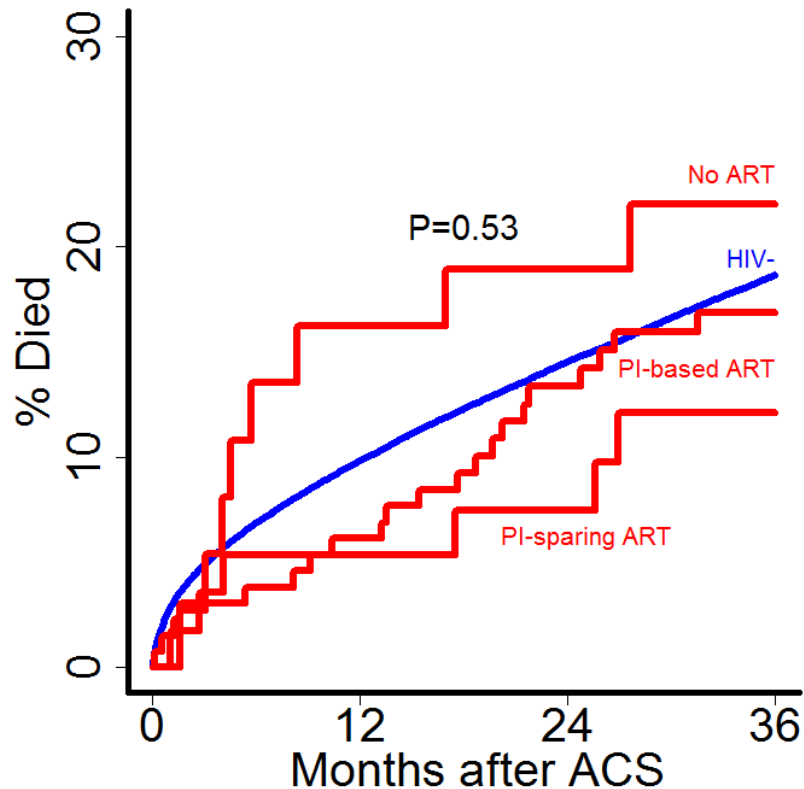


	3-year mortality	Adjusted* hazard ratio	(95% CI)	P
<b>CD4 &lt; 200</b>	29.8%	5.6	(3.2-9.7)	<0.001
<b>HIV- (ref)</b>	18.6%	1		
<b>CD4 200-499</b>	17.9%	2.5	(1.6-4.0)	<0.001
<b>CD4 ≥ 500</b>	4.9%	0.7	(0.2-2.1)	0.52

\* Adjusted for baseline age, sex, race, diagnosis year, ACS type, ever smoking status, and LDL, HDL, and triglyceride levels

# Mortality after an ACS diagnosis

By HIV status and antiretroviral therapy use



	3-year mortality	Adjusted* hazard ratio	(95% CI)	P
<b>No ART</b>	22.0%	3.4	(1.7-6.9)	0.001
<b>HIV- (ref)</b>	18.6%	1		
<b>PI-based ART**</b>	16.9%	2.5	(1.6-3.8)	<0.001
<b>PI-sparing ART**</b>	12.1%	1.8	(0.8-4.1)	0.14

\* Adjusted for baseline age, sex, race, diagnosis year, ACS type, ever smoking status, and LDL, HDL, and triglyceride levels

\*\* P >0.05 comparing PI-based and PI-sparing ART

# Summary

- HIV patients, in adjusted models, had higher all-cause mortality at 1 and 3 years after an ACS hospitalization
- No mortality difference at 3 years for HIV+ ACS patients with CD4 $\geq$ 500 compared with HIV- patients
- HIV patients without ART at ACS diagnosis had highest 3-year mortality
- HIV patients on PI-based and PI-sparing ART had similar mortality

# Strengths and Limitations

## Strengths

- Large N and extended follow-up
- Population-based
- Complete ascertainment of ACS, HIV status, and mortality

## Limitations

- Did not evaluate cause-specific mortality, recurrent ACS, or post-diagnosis treatments (e.g., medication and revascularization)
- Imperfect measurement of some risk factors (e.g., smoking) and no data for others (e.g., cocaine use)

# Conclusions

- The observed higher mortality after an ACS hospitalization for HIV patients appears to be driven by HIV-related factors, including low CD4 and lack of ART use
- These results strengthen recommendations for earlier initiation of ART
- Additional research is needed to investigate cardiovascular-specific mortality and ACS recurrence

# Thank you!