Differences in response to antiretroviral therapy by sex and HCV status

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Background

- Liver disease is a leading cause of death among HIV+, with 25% of HIV+ coinfected with HCV
- HIV/HCV-coinfected individuals are considered a priority population for HCV treatment due to faster liver disease progression
- However, it is unclear if there are subgroups at particular risk of the negative effects of HCV on HIV outcomes
- One such subgroup may be biological sex
  - Women have a better HCV profile than men
  - Women also have a superior response to ART

There have been no studies examining response to ART with respect to both sex and HCV status over time

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Objective

To identify differences by sex and HCV status in response to ART among HIV+ individuals, as measured by:

1) Change in CD4 count over 5 years
2) Attaining HIV RNA <500 copies/mL within 1 year
3) Clinical AIDS diagnosis
4) Death

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Methods

- Study population
  - Kaiser Permanente (KP) California cohort during 1996-2011
  - HIV+ adults initiating combination ART
- Data sources
  - KP HIV registries (HIV status) and electronic health record (self-reported gender)
  - HCV status defined by laboratory data (ever Ab+ or RNA+)
- Analysis by gender and HCV status
  - Piecewise linear regression with generalized estimating equations to assess change in CD4 over 5 years
  - Cox regression to estimate hazard ratios (HR) for HIV RNA <500, AIDS, and death
  - Adjusted models included age, race/ethnicity, calendar era, KP region, prior ART use, HIV-transmission risk factor, years known to be HIV+, drug/alcohol abuse, smoking, and baseline CD4 and HIV RNA

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Cohort characteristics (N=12,865)

	Women		Men	
	HIV monoinfected	HIV/HCV coinfected	HIV monoinfected	HIV/HCV coinfected
N	1,088	154	10,623	1,000
Baseline age, mean	39	45	42	45
Years known HIV+, mean	4	6	5	6
Race/ethnicity, %				
White	34	43	57	58
Black/African-American	40	39	14	17
Hispanic	19	12	22	18
Other/unknown	8	6	8	7
Injection drug use, %	4	40	4	25
Ever smoking, %	41	72	49	62
Ever alcohol abuse, %	8	16	11	22
Ever drug abuse, %	13	34	16	32
Prior antiretroviral use, %	42	48	44	52
Baseline CD4, mean	341	392	362	354

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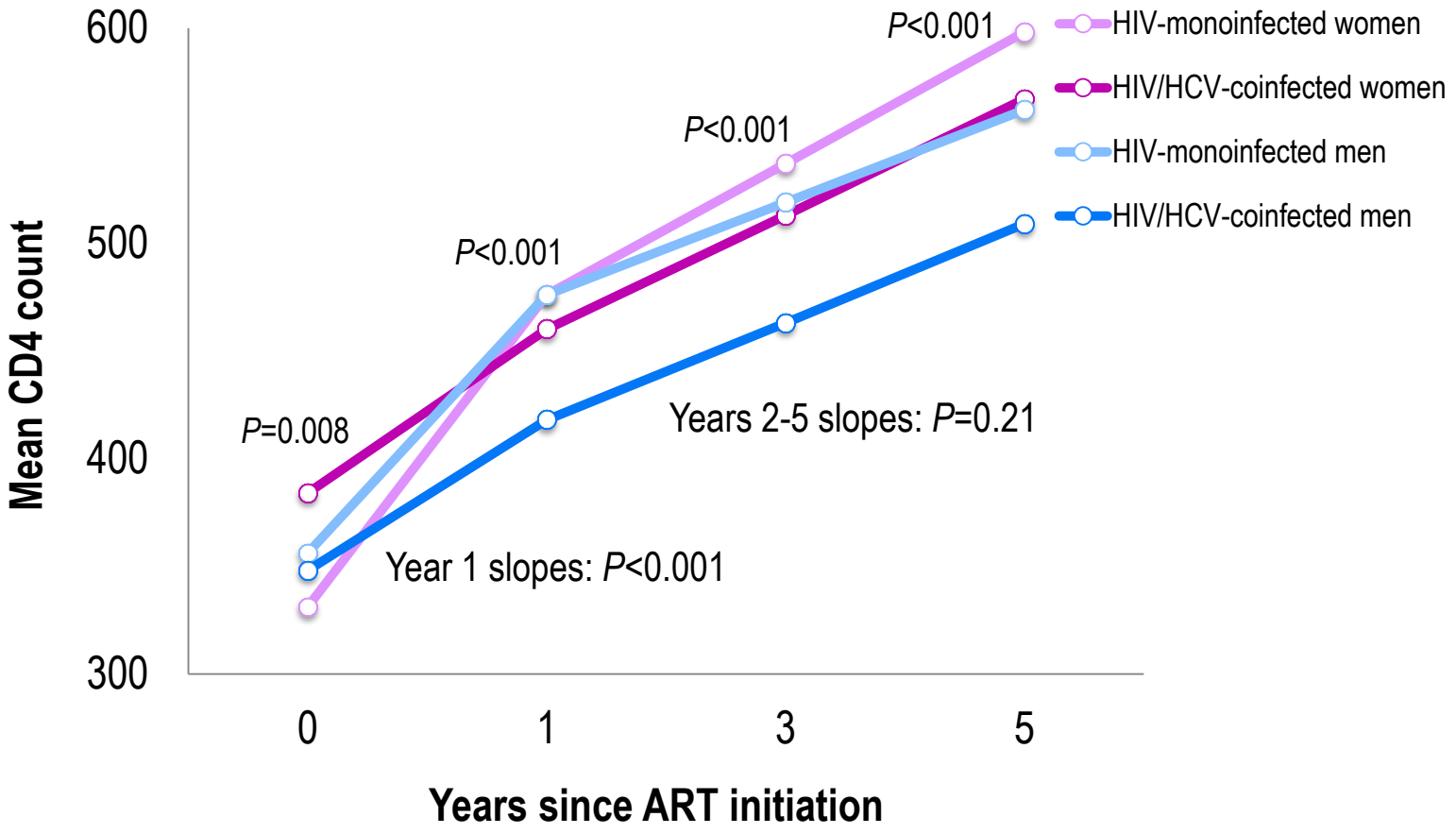
Change in CD4



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Attainment of HIV RNA <500 within 1 year

Hazard ratios for HIV/HCV coinfection, overall and stratified by sex

	Unadjusted HR* (95% CI)	*P*	Adjusted HR† (95% CI)	*P*
Overall	0.9 (0.9-1.0)	0.07	1.0 (0.9-1.1)	0.99
Women	0.8 (0.6-1.0)	0.039	0.9 (0.7-1.1)	0.28
Men	1.0 (0.9-1.0)	0.26	1.0 (0.9-1.1)	0.7
P interaction	0.10		0.18	

* Reference group is HIV-monoinfected.

† Adjusted for age, race/ethnicity, calendar era, KP region, prior ART use, HIV-transmission risk factor, years known to be HIV+, drug/alcohol abuse, smoking, baseline CD4 and HIV RNA.

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AIDS

Hazard ratios for HIV/HCV coinfection, overall and stratified by sex

	Unadjusted HR* (95% CI)	*P*	Adjusted HR† (95% CI)	*P*
Overall	1.3 (1.1-1.6)	<0.001	1.1 (0.9-1.3)	0.27
Women	1.5 (1.0-2.4)	0.08	1.3 (0.7-2.2)	0.37
Men	1.3 (1.1-1.6)	0.002	1.1 (0.9-1.3)	0.39
P interaction	0.58		0.45	

* Reference group is HIV-monoinfected.

† Adjusted for age, race/ethnicity, calendar era, KP region, prior ART use, HIV-transmission risk factor, years known to be HIV+, drug/alcohol abuse, smoking, baseline CD4 and HIV RNA.

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Death

Hazard ratios for HIV/HCV coinfection, overall and stratified by sex

	Unadjusted HR* (95% CI)	*P*	Adjusted HR† (95% CI)	*P*
Overall*	1.8 (1.5-2.1)	<0.001	1.4 (1.2-1.6)	<0.001
Women	1.9 (1.2-3.0)	0.004	1.3 (0.7-2.4)	0.43
Men	1.8 (1.5-2.1)	<0.001	1.4 (1.2-1.6)	<0.001
P interaction	0.74		0.73	
Liver-related death			6.0 (3.9-9.0)	<0.001
AIDS-related death			0.9 (0.7-1.2)	0.41
Other deaths			1.4 (1.0-2.0)	0.045

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Strengths and limitations

- Strengths
  - Large, well-characterized, and generalizable cohort
  - Near-perfect case ascertainment for HIV, AIDS, and death
  - Adjustment for important covariates
  - Differences in outcomes unlikely to be attributable to differential access to care
- Limitations
  - Potential misclassification of HCV status as measured by lab data
  - Potential misclassification of sex as measured by self-reported gender
  - Unknown timing of HCV infection
  - Lack of detail on risk factors

Summary and conclusions

- Differences in immunologic response to ART by sex and HCV status
  - After 5 years, women attained higher CD4 than men regardless of HCV status
  - HIV/HCV-coinfected had slower CD4 recovery compared with HIV-monoinfected, especially in first year of ART
  - HIV/HCV-coinfected men achieved the lowest CD4 counts by 5 years
- No difference in virologic response or AIDS by sex or HCV status
- HIV/HCV-coinfected men and women had increased mortality compared with HIV-monoinfected, largely driven by liver-related causes

HCV infection should be aggressively treated in HIV/HCV-coinfected adults, regardless of sex

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Acknowledgments

- Kaiser Permanente Northern California

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