CD4 Count, Viral Suppression, Prophylaxis and the Risk of Primary Pneumocystis Pneumonia in the cART Era - the Collaboration of Observational HIV Epidemiological Research Europe (COHERE)

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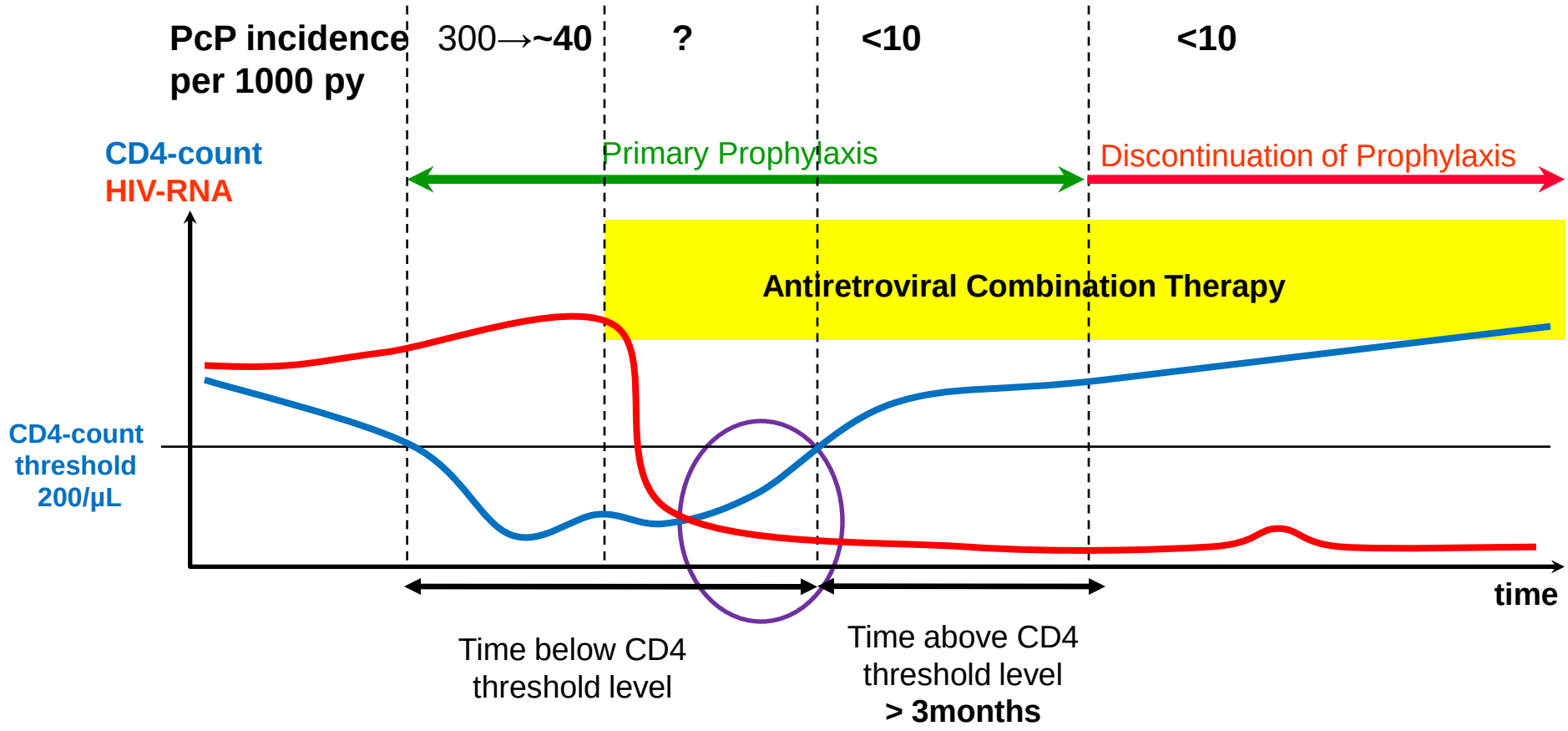
for the Opportunistic Infections Working Group of COHERE

Background
PcP Prophylaxis Guidelines



Objective

- To study the risk of primary Pneumocystis pneumonia in patients in the cART era with regards to
  - Current CD4 count
  - Current viral load
  - On or off prophylaxis
  - On or off cART
- Implications on indication of PcP prophylaxis

- COHERE collaboration among 33 cohorts representing 29 different European countries including 240’000 adults
- Current analysis: 12 cohorts with prospective data about
  - start and stop of specific therapeutic and prophylactic regimens against PcP
  - recurrences of opportunistic infections in adults

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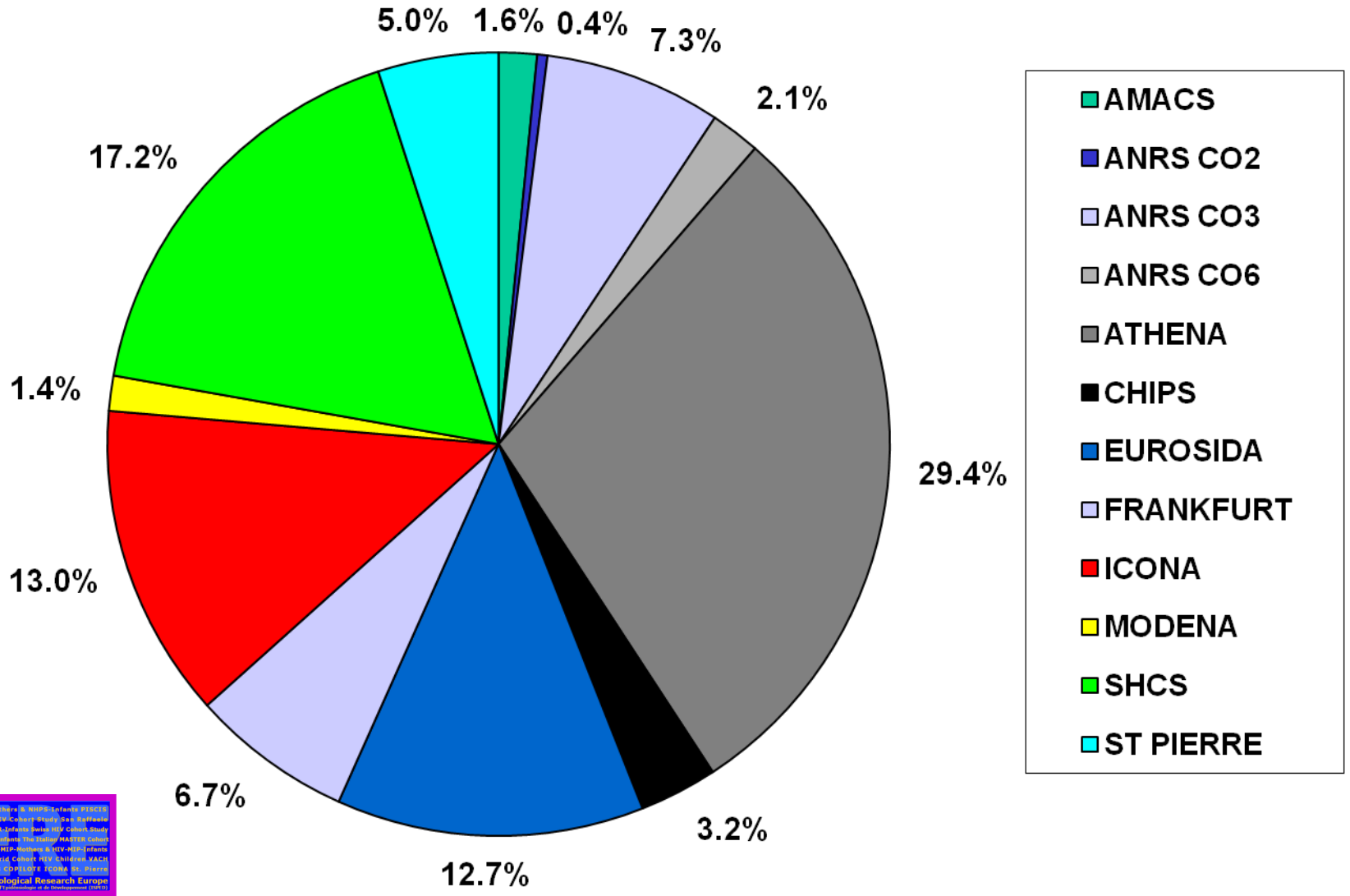
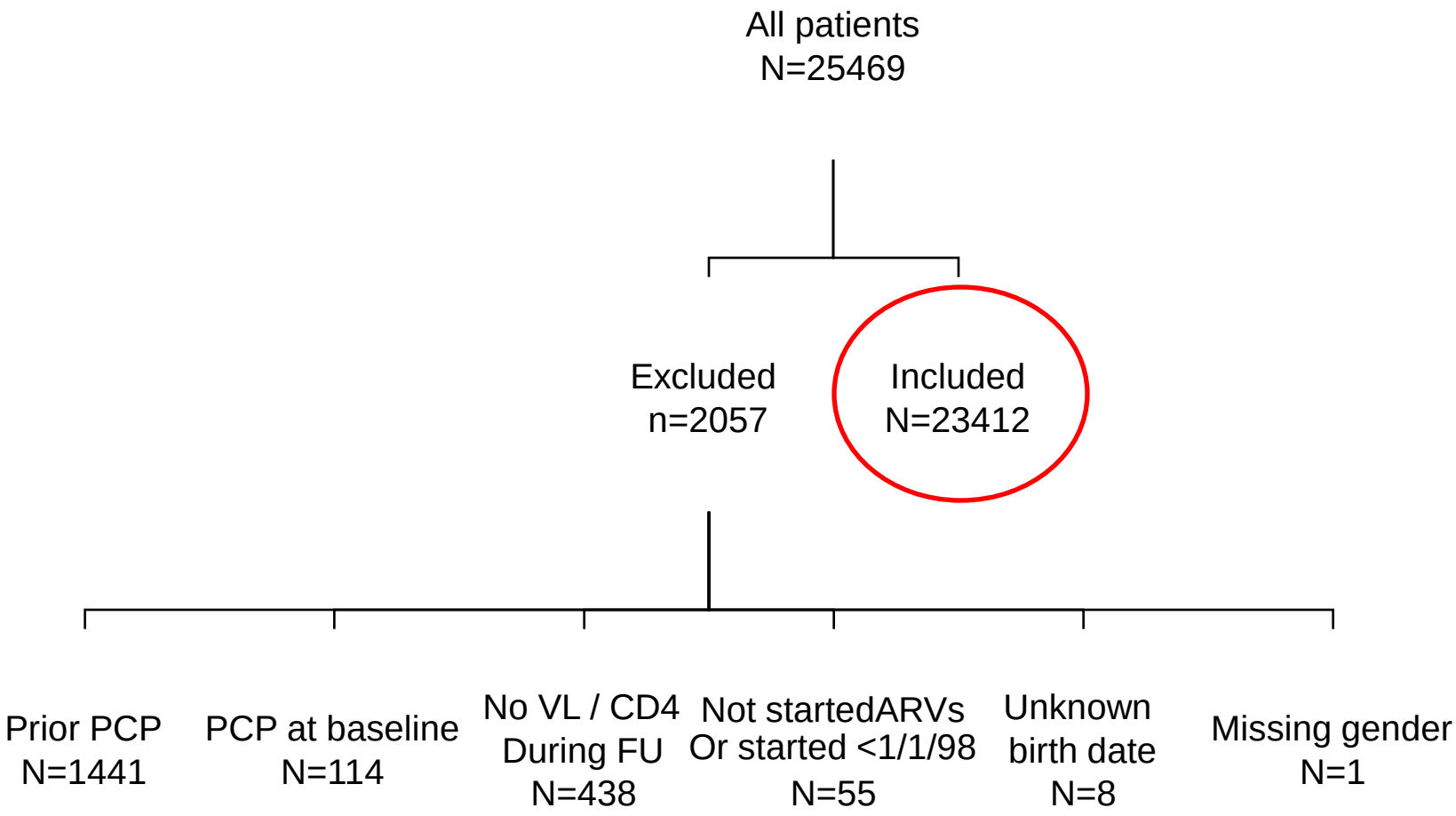
Contributing Cohorts N=23‘412



Patients included
if started cART after 1997



Methods

- Calculation of incidence rates (per 1000 person-years) in different strata
  - Current CD4 count
  - Current viral load
  - Use of prophylaxis
  - Use of cART
- Baseline defined as first study visit within the cohort
- Poisson regression to model incidence rate ratios of progression to primary PCP

Baseline characteristics

		N	%
All patients		23412	100
Gender	Male	16303	69.6
HIV Exposure Group	Homosexual	8428	36.0
	IDU	3030	12.9
	Heterosexual	9271	39.6
	Other	1545	6.6
	Unknown	1138	4.9
Prior AIDS		3014	12.9
VL < 400		4675	22.5
On cART		8145	34.8
		Median	IQR
CD4		320	170 – 500
Viral load	Log_{10}copies/ml	4.4	2.8 – 5.1
Age		36	30 - 43

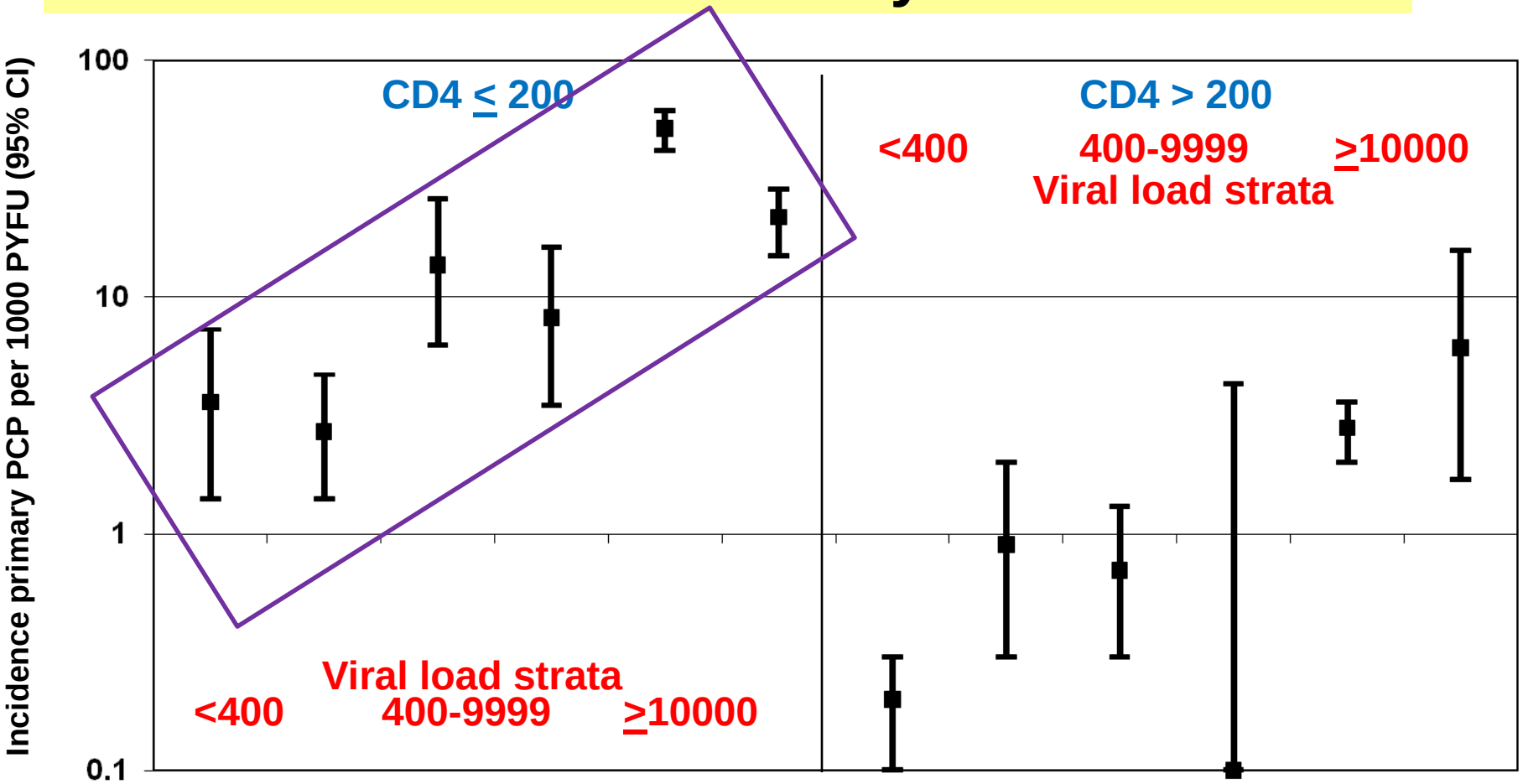
Results

	Person-years of follow-up	Events	Incidence /1000y (95% CI)
All patients	**107‘016**	**253**	**2.4 (2.1-2.7)**
CD4 count ≤ 200/µL	**11’932**	**181**	**15.1 (13.0– 17.4)**
CD4 count >200/µL	**95’084**	**72**	**0.76 (0.58 – 0.93)**

Non-Adherence to Guidelines

During 39% of follow-up time, patients with CD4 counts ≤ 200 were not on PcP prophylaxis.

Incidence Primary PCP



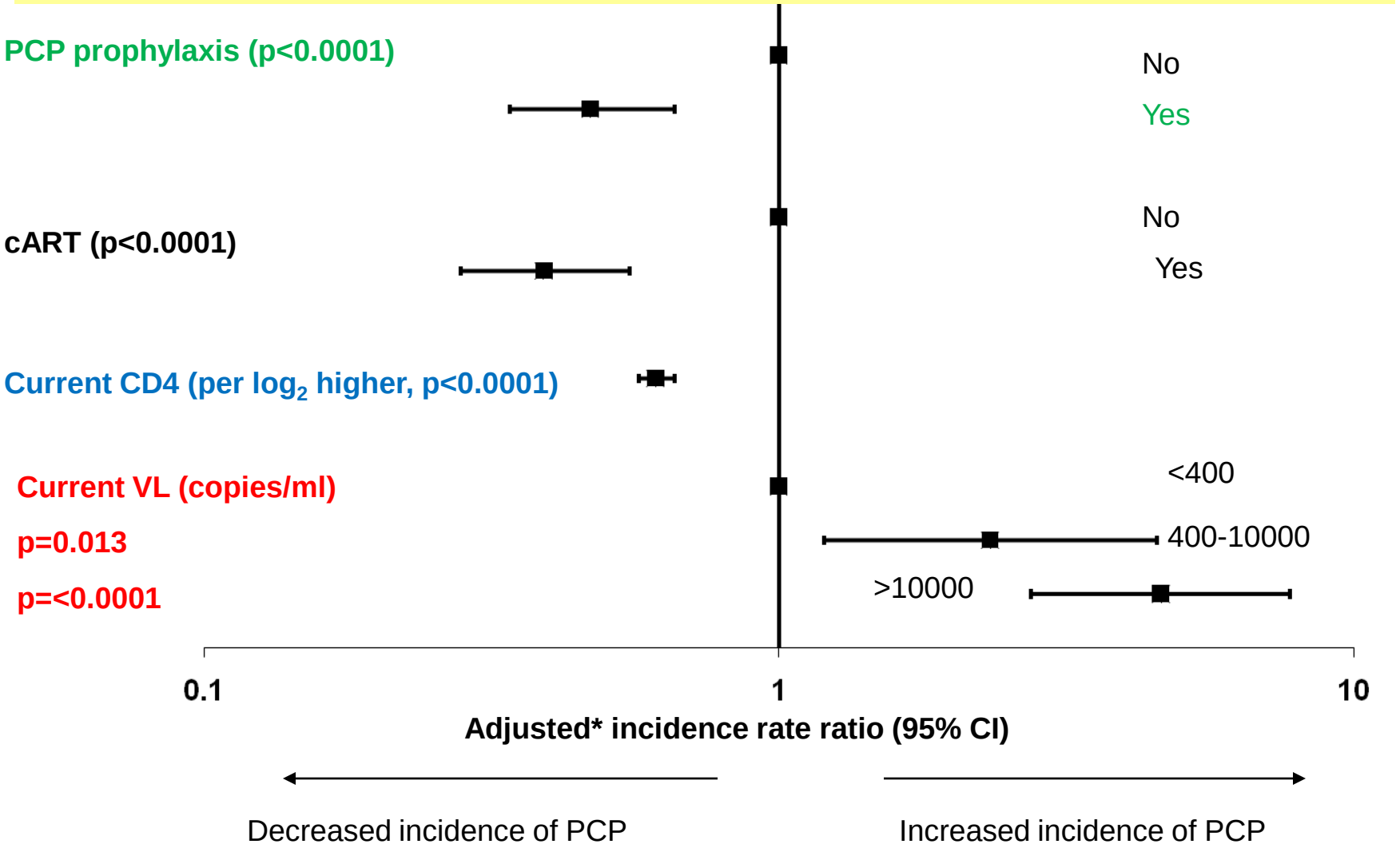
Proph	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
Events	7	12	9	8	106	39	11	5	8	0*	44	4
Median CD4[!]	160	140	154	126	133	90	530	320	489	300	415	300
Median VL!	2.6	2.6	3.4	3.2	5.0	5.0	2.6	2.6	3.4	3.2	4.6	4.7

*No events; incidence and lower bound of 95% CI=0.0; [!]During follow-up in strata; VL in log_{10}copies/ml

Incidence of PcP if CD4 ≤ 200

VL	Prophylaxis	Person-years of follow-up	events	Incidence/1000y (95% CI)
<400	no	1944	7	3.6 (1.4-7.3)
<400	yes	4444	12	2.7 (1.4-4.7)
400-9999	no	657	9	13.7 (6.3-26.1)
400-9999	yes	976	8	8.2 (3.5-16.2)
>10000	no	2046	106	51.8 (41.9-61.6)
>10000	yes	1789	39	21.8 (15-28.6)

Progression to primary PCP : CD4 ≤ 200



*Adjusted additionally for gender, prior AIDS, ethnic origin, HIV exposure group, race, hepatitis B and C status, age, first visit, and date of first starting ARVs. Prophylaxis, cART and CD4 are included as time-updated (current) values.

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Factors associated with primary PcP risk
(multivariate Poisson model)

Time updated (current values)		CD4 ≤200			CD4 >200		
		IRR	95% CI	P	IRR	95% CI	p
PcP prophylaxis		0.47	0.34 – 0.66	<0.0001	1.53	0.71 – 3.28	0.28
On cART		0.39	0.28 – 0.55	<0.0001	0.35	0.17 – 0.70	0.0030
CD4	per doubling	0.61	0.57 – 0.66	<0.0001	0.24	0.15 – 0.40	<0.0001
Viral load	<400	1.00			1.00		
	400-10000	2.33	1.20 – 4.54	0.013	4.61	0.84 – 2.37	0.31
	>10000	4.62	2.75 – 7.76	<0.0001	4.98	2.31 – 10.74	<0.0001

*Adjusted additionally for gender, prior AIDS, ethnic origin, HIV exposure group, race, hepatitis B and C status, age, first visit, and date of first starting ARVs. Prophylaxis, cART and CD4 are included as time-updated (current) values.

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Conclusions

- Non-adherence to guidelines regarding primary PcP prophylaxis is frequent
- Patients virologically suppressed on cART have a markedly decreased incidence of PcP even at CD4-counts ≤200 cells/mm^3 and irrespective of prophylaxis
- The incidence in virologically suppressed patients with CD4 ≤200 and off prophylaxis is lower than in historical controls on prophylaxis in the pre-cART era
- However, prophylaxis remains associated with lower incidence in patients with CD4 ≤200 in the multivariate model including plasma HIV RNA

Outlook

- Is there a subgroup of patients with CD4-counts ≤200 cells/mm^3 in whom primary PcP prophylaxis may be safely discontinued ?
  - Evaluation of incidence in different strata of CD4 <200
  - Evaluation of incidence in virologically suppressed patients who discontinued prophylaxis

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