HIV Replication is a Major Predictor of Primary and Recurrent Pneumocystis Pneumonia - Implications for Prophylaxis Recommendations

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Introduction

- ***Background:*** Current guidelines state that primary and secondary prophylaxis against Pneumocystis Pneumonia (PcP) can be safely withdrawn once CD4 counts rise constantly above 200 cells/µL
- ***Previous work:*** An analysis in COHERE (Mocroft et al, CID 2010) showed that the incidence of primary PcP in patients
  - off prophylaxis
  - with CD4 of 100-200 cells/µL
  - with HIV RNA < 400 copies/mL

  is low (1.2 events per 1000 py, 95% CI 0.2-4.5) and concluded that primary prophylaxis is not needed in these patients

AIM

To evaluate the risk of primary and **secondary** PcP in patients

- on and **off** prophylaxis
- at different CD4 and HIV-RNA levels

Methods

- COHERE database (2014 data merger, 20 cohorts)
- Outcomes
  - Primary PcP – First PcP diagnosis in the database
  - Secondary PcP – Second PcP diagnosis
- Inclusion criteria
  - Periods after 1 January 1998, on and off cART, 16 years or older
  - Primary PcP – no previous PcP diagnosis
  - Secondary PcP – one previous PcP diagnosis
- Definitions
  - Primary/secondary PcP prophylaxis – TMP-SMX or dapsone or pentamidine or atovaquone (possibly in combination with other drugs)
- Safety margin
  - upper 95% CI of incidence calculation < 10/1000 person-years

Methods 2

Analyses

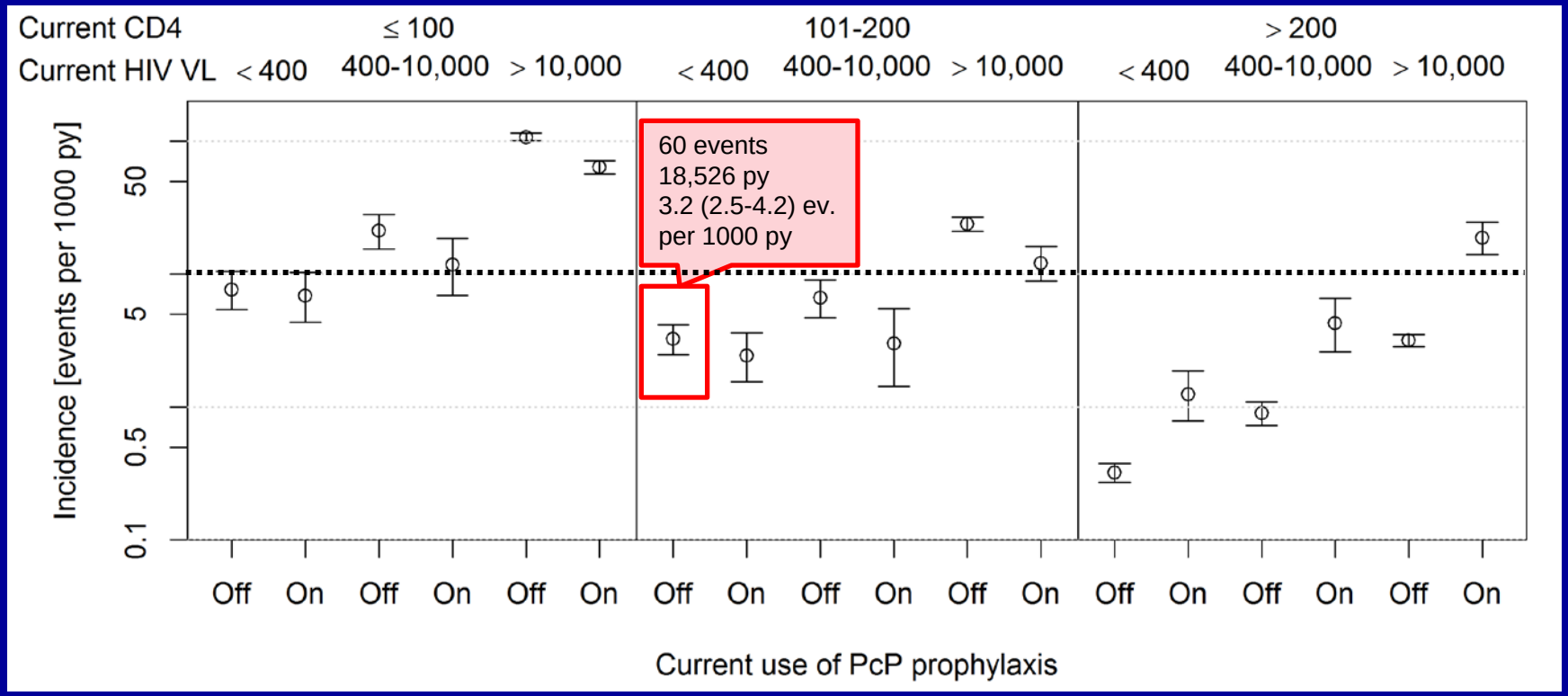
1. Incidence rate (events/1000 py) stratified by
   - current CD4 <100, 100-200, >200 /µL
   - HIV-RNA <400, 400-10’000, > 10’000 c/mL
   - use of prophylaxis

2. Poisson generalized additive model
   - smooth effect of CD4 modelled by a spline
   - HIV-RNA stratified <400, 400-10’000, >10’000 c/mL

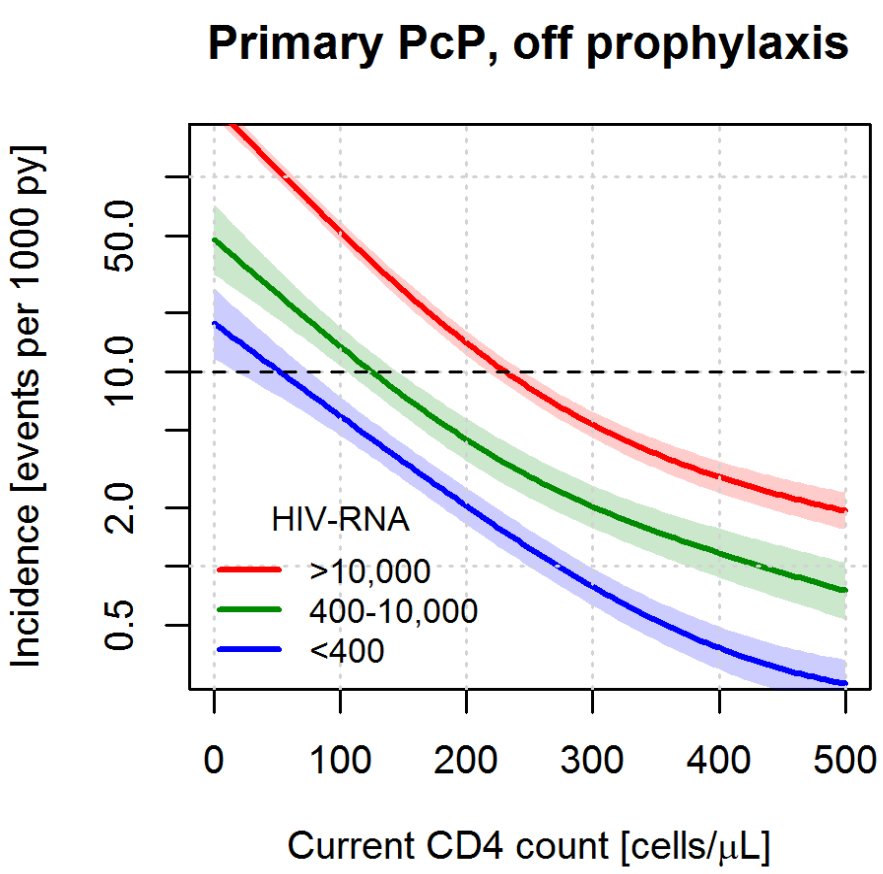
Patient and follow-up characteristics

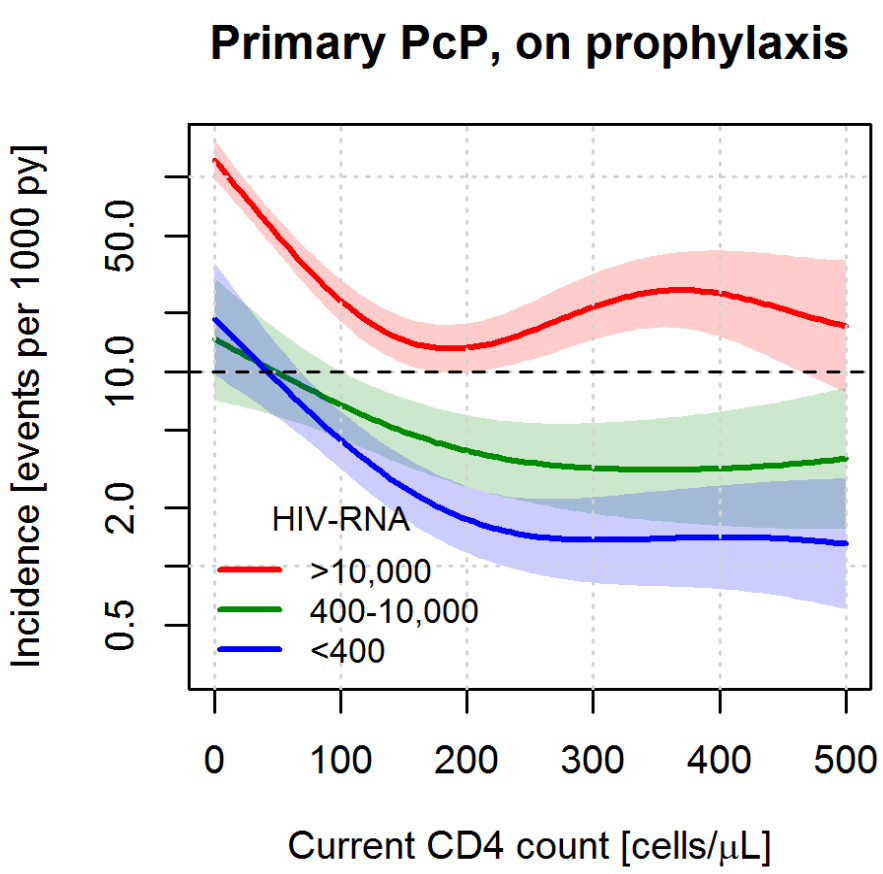
	Primary PcP	Secondary PcP
Number of patients	125,282	8,456
Male sex	76%	80%
Age (median, IQR)	37 (31-44)	40 (35-47
HIV transmission mode		
MSM	45%	44%
Heterosexual	33%	36%
IDU	18%	16%
FUP time per patient (median, IQR)	5.4 (2.2-10.2)	5.8 (2.3-10.6)
Total FUP time (median, IQR)	808,279	56,449
Number of events	2405	291
Incidence /1000 py (95% CI)	3.0 (2.9-3.1)	5.2 (4.6-5.8)

Incidence of primary PcP (crude incidence)
(re-analysis with 2014 data)

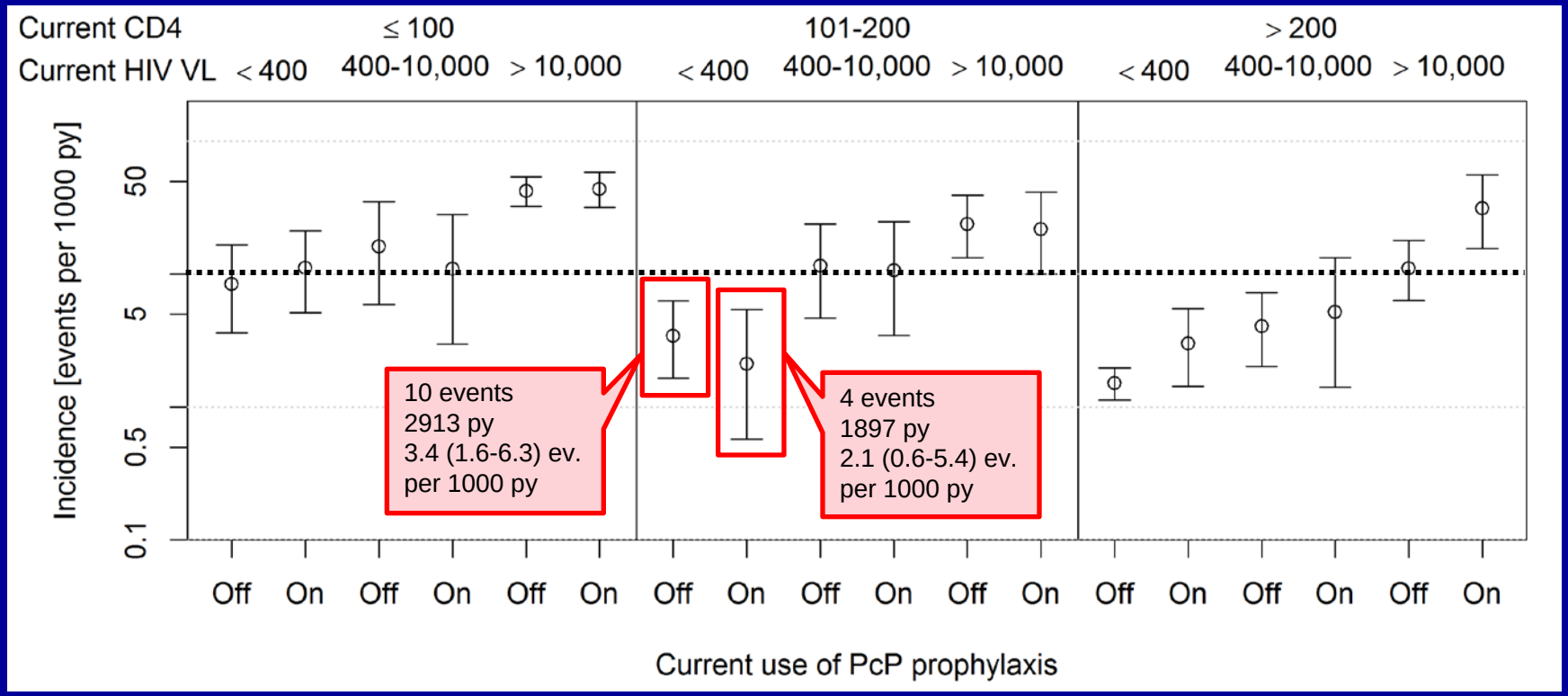


Incidence of primary PCP off and on prophylaxis





Incidence of secondary PcP
(crude incidence)



Incidence of secondary PcP
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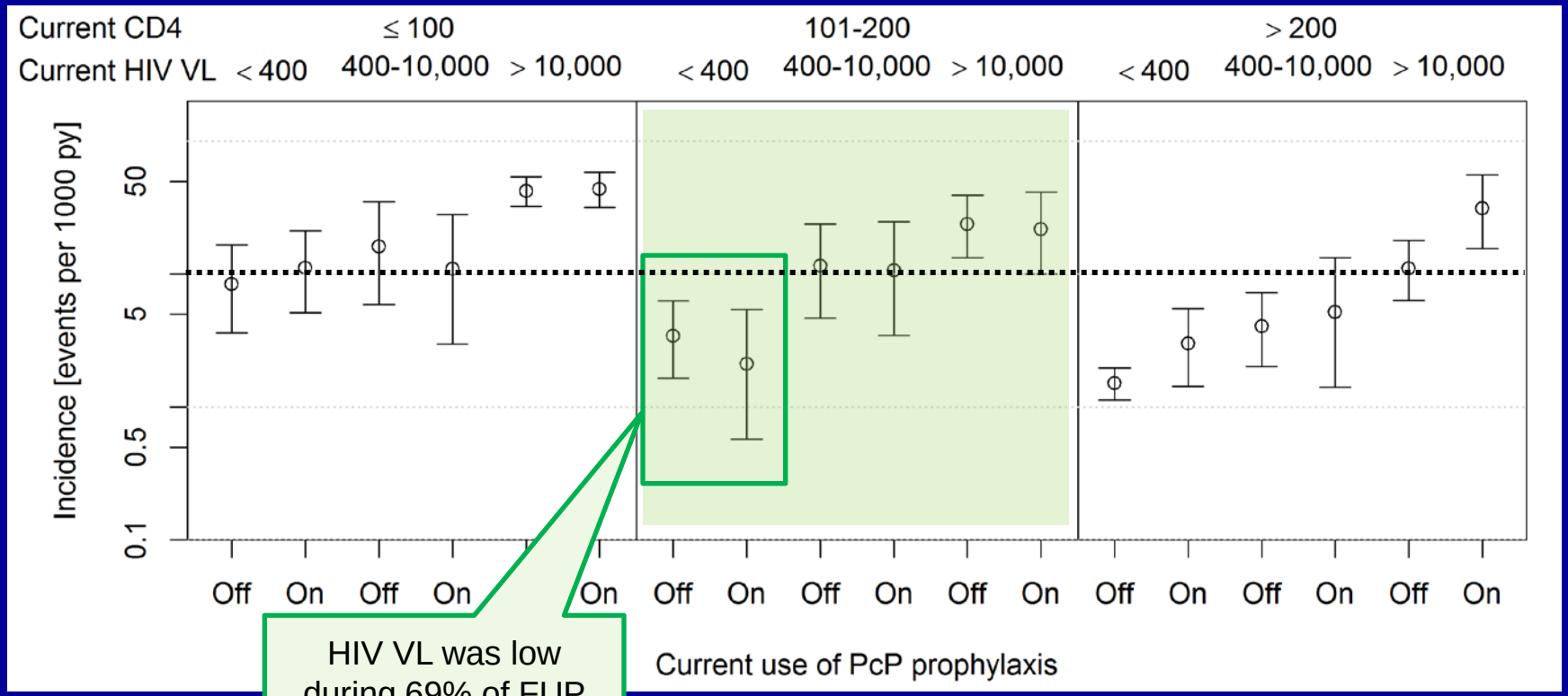
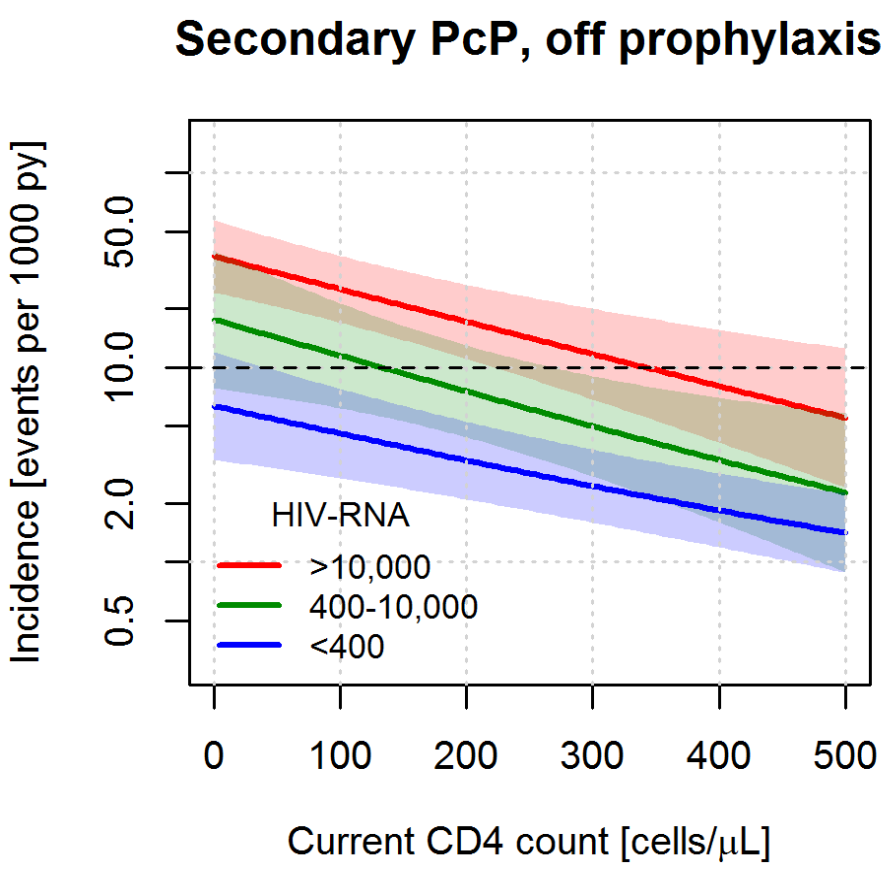
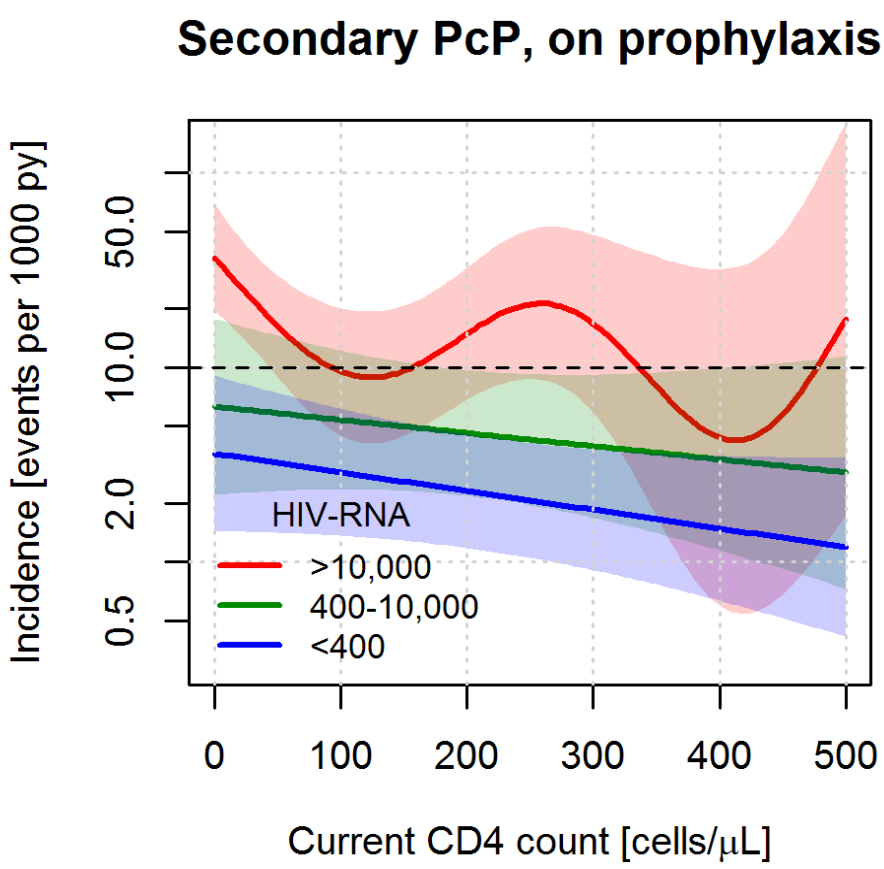
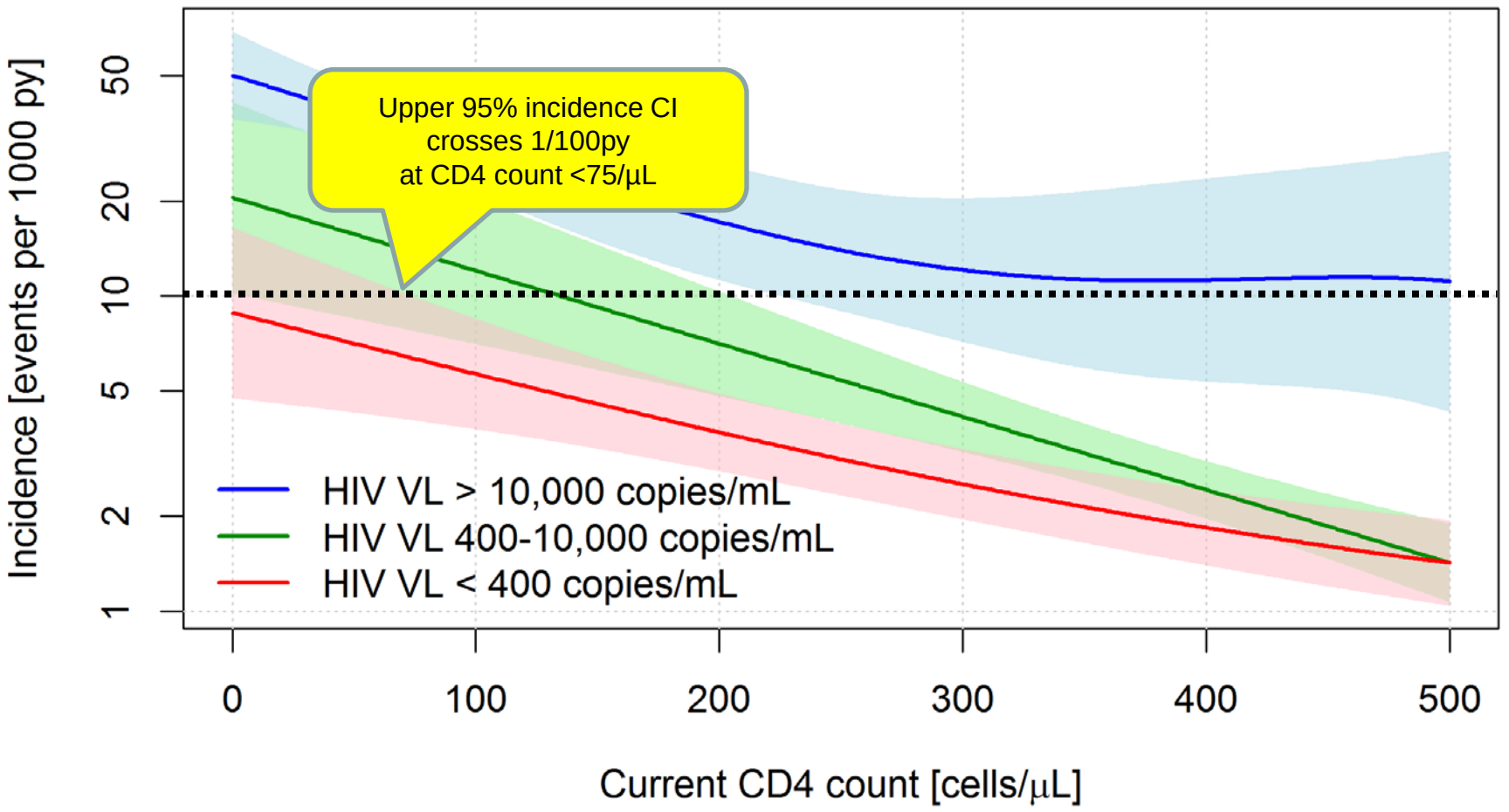


Incidence of secondary PcP off and on prophylaxis





Incidence of secondary PcP off prophylaxis



Conclusion 1

HIV replication
is an independent major risk factor for primary and secondary PcP

- In patients iwith suppressed viral load and off prophylaxis the risk for primary and secondary PcP is <10/1000 py if their CD4–count rises above 75 cells/uL

- In patients with high HIV-RNA risk for secondary PcP remains >10/1000 py even at CD4 counts above 200/cells/uL

Conclusion 2

Implication for Prophylaxis Recommendations

- We confirm the COHERE data from 2010 that **primary PcP prophylaxis** is not needed in patients with suppressed HIV load and CD4 counts > 100 cells/µL

- Our results suggests that **secondary PcP prophylaxis** can be safely withdrawn in patients with suppressed HIV load and CD4 counts > 100 cells/µL

  - This would allow to stop secondary prophylaxis in > 2/3 of European patients with CD4 counts between 100 and 200 cells/µL

IMIT AMACS ECS-Mothers & ECS-Infants NSHPC-Mothers & NHPS-Infants PISCIS KOMPNET CASCADE ANRS CO2 SEROCO Frankfurt HIV Cohort Study San Raffaele ANRS CO1/CO10 EPF UK CHIC Athena ITLR-Mothers & ITLR-Infants Swiss HIV Cohort Study ICC ANRS CO6 PRIMO Co-RIS MOCHIV-Mothers & MoCHIV-Infants The Italian MASTER Cohort CHIPS ANRS CO4 French Hospital's Database on HIV HIV-MIP-Mothers & HIV-MIP-Infants GEMES-Haemo ANRS CO3 AQUITAINE EuroSIDA Madrid Cohort HIV Children VACH Modena Cohort Study Danish HIV Study ANRS CO8 COPILOTE ICONA St. Pierre

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