BHIVA
British HIV Association

BHIVA 'Best of CROI' feedback webinars 2023

Co-morbidities and ageing

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GILEAD Creating Possible
MSD
ViiV Healthcare

With thanks to those presenting research for permission to use slides for 'Best of CROI'

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Conflict of Interest

Caroline Sabin has received financial support for the membership of Data Safety and Monitoring Boards, Advisory Panels and for preparation of educational materials from Gilead Sciences, ViiV Healthcare and MSD.

Speakers are required by the Federation of the Royal Colleges of Physicians to disclose conflicts of interest at the beginning of their presentation, with sufficient time for the information to be read by the audience. They should disclose financial relationships with manufacturers of any commercial product and/or providers of commercial services used on or produced for patients relating to the 36 months prior to the event. These include speaker fees, research grants, fees for other educational activities such as training of health professionals and consultation fees. Where a speaker owns shares or stocks directly in a company producing products or services for healthcare this should also be declared.

Topics to be covered

- The first plenary on ageing at CROI…
- Choosing appropriate controls for studies of ageing in HIV
- Impact of INSTIs on CV events in people starting ART
  - target trial emulation approach
- Depression and anxiety associations with type 1/type 2 MI
- Gender-specific predictors of stroke
- Caution required…

The first plenary on ageing at CROI

- Most chronic diseases share a modifiable risk factor – ageing
- *Unitary theory of fundamental ageing mechanisms* - by targeting one fundamental ageing process, may impact several or all others
- *Precision Gerontology*: Multidisciplinary approach to better understand heterogeneity of ageing in all dimensions and thus develop precise and targeted effective interventions

Kuchel G. Plenary 38. The science of aging: lessons for HIV

The first plenary on ageing at CROI - reflections

- Very US-centric, little awareness of the published and ongoing research within the HIV context in Europe and elsewhere
- Importance of partnerships – community advocates, those working in geriatrics/gerontology/geroscience
- Lip service to the impact of non-biological factors on ageing process or the contribution of these to effects attributed to HIV
- Solutions primarily pharmacological - e.g. proposed trial of Dasatinib + Quercetin

Kuchel G. Plenary 38. The science of aging: lessons for HIV

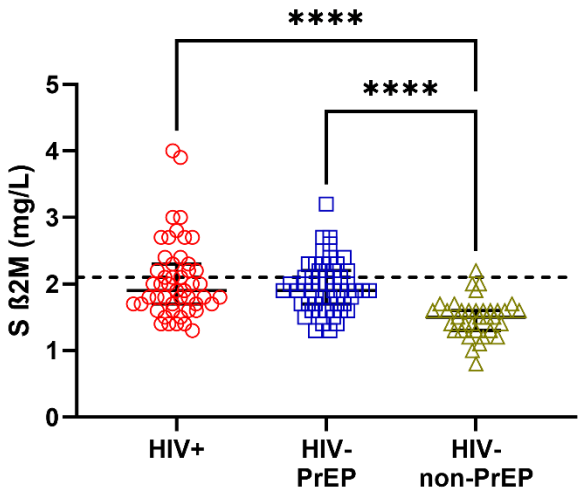
Choosing appropriate controls for studies of ageing in HIV

- Comparison of markers of immune activation and neuronal injury in ART-treated people with HIV compared to controls with similar lifestyles
- Three groups considered:
  - n=50 MSM receiving ART for >12 months (median age 37.8 years)
  - n=50 MSM without HIV on PrEP (median age 35.5 years)
  - n=35 volunteers without HIV not on PrEP (median age 44.8 years)
- Measured serum/CSF beta-2 microglobulin, serum/CSF neopterin, CSF/plasma albumin ratio and CSF neurofilament light ratio (NFL)

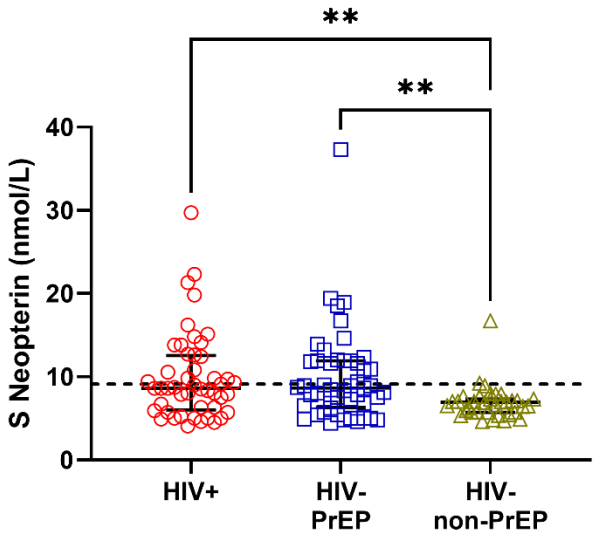
Gisslen M, et al. Abstract 184

Choosing appropriate controls for studies of ageing in HIV

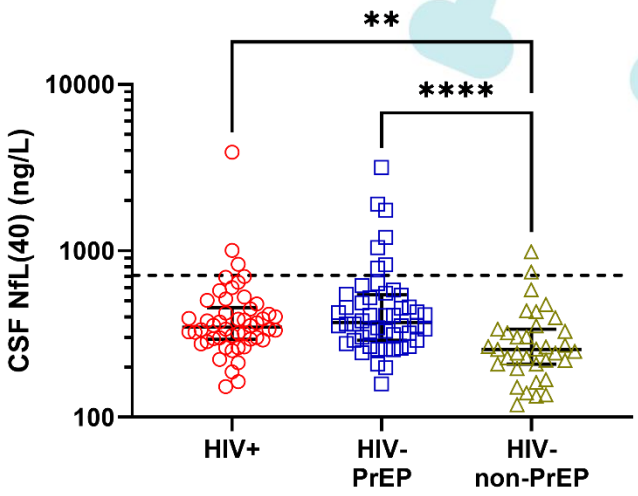
S beta2-microglobulin



S neopterin



CSF NfL (age adjusted)



No significant differences between groups in CSF B2M, CSF neopterin, blood CD8+ T-cells or CSF/P albumin ratio

Gisslen M, et al. Abstract 184 (with permission from author)

Impact of INSTIs on CV events in people starting ART

- Target trial emulation:
  - participants in Swiss HIV Cohort Study
  - treatment-naïve
  - detectable HIV RNA
  - starting ART after 1/5/2008
- Treatment comparison: started INSTI or started other regimen
- Follow-up to first CVD event (MI, stroke or invasive CV procedure)
- Pooled logistic regression with inverse probability of treatment and censoring weights

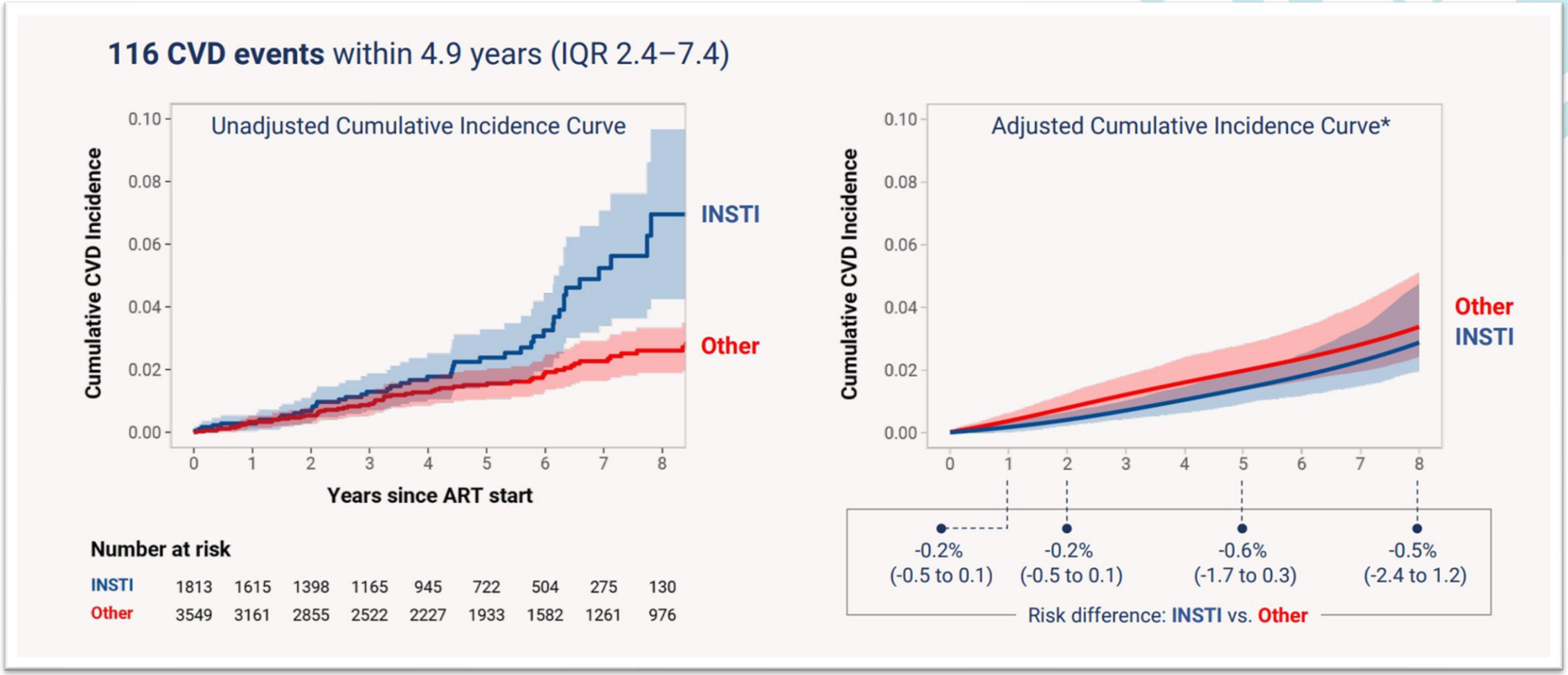
Surial B, et al. Abstract 149

Impact of INSTIs on CV events in people starting ART

- **13,767** in cohort, **6027** started ART after May 08, **5362** with detectable HIV RNA and known ART drugs included in analysis
- 1837 started INSTIs (53% DTG, 18% BIC, 16% EVG, 13% RAL)
- 3525 started other regimens (52% bPI, 43% NNRTI, 5% other)
- Some differences between groups (INSTI vs other):
  - nadir CD4+ T-cell count (330 vs 278)
  - female gender (16% vs 24%)
  - African ethnicity (11% vs 18%)
  - use of ABC (23% vs 12%)
  - use of TAF (40% vs 1.4%)

Surial B, et al. Abstract 149

Impact of INSTIs on CV events in people starting ART



Surial B, et al. Abstract 149 (with permission from author)

Depression and anxiety associations with type 1/type 2 MI

- NA-ACCORD network (7 clinical cohorts)
- Depression and anxiety based on time-varying, ICD-9/10 diagnoses; follow-up censored at death, loss to follow-up or first MI (if not the type of interest)
- N=33,071 people followed for 168,846 person-years
- 16351 (49%) had diagnosis of depression or anxiety; 33% of this group had both diagnoses
- 869 MIs: 495 (57%) T1, 374 (43%) T2

Hyle E, et al. Abstract 145

Depression and anxiety associations with type 1/type 2 MI

- Depression/anxiety associated with non-Hispanic white race, tobacco/cocaine use, HTN, diabetes, dyslipidaemia and CKD

RH (95% CI)*	T1 MI	T2 MI
Anxiety	0.92 (0.74, 1.16)	1.42 (1.10, 1.83)
Depression	1.23 (1.02, 1.49)	1.20 (0.96, 1.51)

* Adjusted for sex at birth, age, race/ethnicity, HIV risk acquisition group, substance use, traditional and HIV-related risk factors for CVD

- No significant interaction between anxiety and depression for either outcome
- No data on psychiatric medications or control of CVD risk factors

Hyle E, et al. Abstract 145

Gender-specific predictors of stroke

- 5 sites from the CNICS network, follow-up from 2005-2020
- 162 strokes (41 women, 121 men) among 13,573 participants
- Stroke risk factors generally as expected, but….
- Women had higher risk of stroke than men at younger ages but lower risk than men at older ages (p_{int}: 0.001)
  - Age 40: RH 2.05
  - Age 50: RH 1.10
  - Age 60: RH 0.60
- Higher risk of stroke among those with detectable viral load in women (RH 4.66) but not men (RH 1.30, p_{int}: 0.001)

Chow F, et al. Abstract 183

Sleep disturbances and cognitive function in women with HIV

- 337 women (WIHS) who completed Pittsburgh Sleep Quality Index (PSQI, 9 components) *and* had cognitive testing (12 domains)
- Associations between each cognitive and each sleep domain, after stratification by global cognitive impairment
- 132 statistical tests, 18 significant
- *'Distinct measures of poor sleep were associated with diminished working memory, processing speed and executive function among WLWH demonstrating global impairment.....targeted interventions that improve these potentially modifiable aspects of sleep may prevent worsening of cognitive function...'*

Dastgheyb R, et al. Abstract 473

Effect of common ART regimens on depressive symptoms

- Analysis of effect of 19 ART regimens on somatic and non-somatic depressive symptoms among women with HIV, stratified by:
  - High depressive symptoms: CES-D ≥16 on ≥50% visits
  - Low depressive symptoms: CES-D ≥16 on <50% visits
  - No depressive symptoms: CES-D <16 at all visits
- Among those with *high depressive symptoms only:*
  Higher risk of *somatic* symptoms: TAF/FTC/DRV/c, TAF/FTC/EVG/c, TAF/FTC/EVG/DRV/c
  No association (although risk WAS raised): TDF/FTC/DRV/c, TDF/FTC/EVG/c
  Lower risk of somatic symptoms: TDF/FTC/EFV, TDF/FTC/RPV
- No associations in those with low/no depressive symptoms or with non-somatic symptoms (not shown)

Parra-Rodriguez L, et al. Abstract 469

Summary

- Somewhat under-whelmed!
- Few high quality studies and many that were presented were plagued with methodological issues:
  - missing data/residual confounding
  - failure to account for multiple testing
  - unknown direction of cause and effect
- Hopeful that CROI 2024 will feature more better quality presentations on ageing and comorbidities