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Clinical Outcome of COVID-19 in PLWH

Rakan Nasreddine

9th BREACH Symposium

November 30, 2021

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Disclosure

- No conflicts of interest to declare

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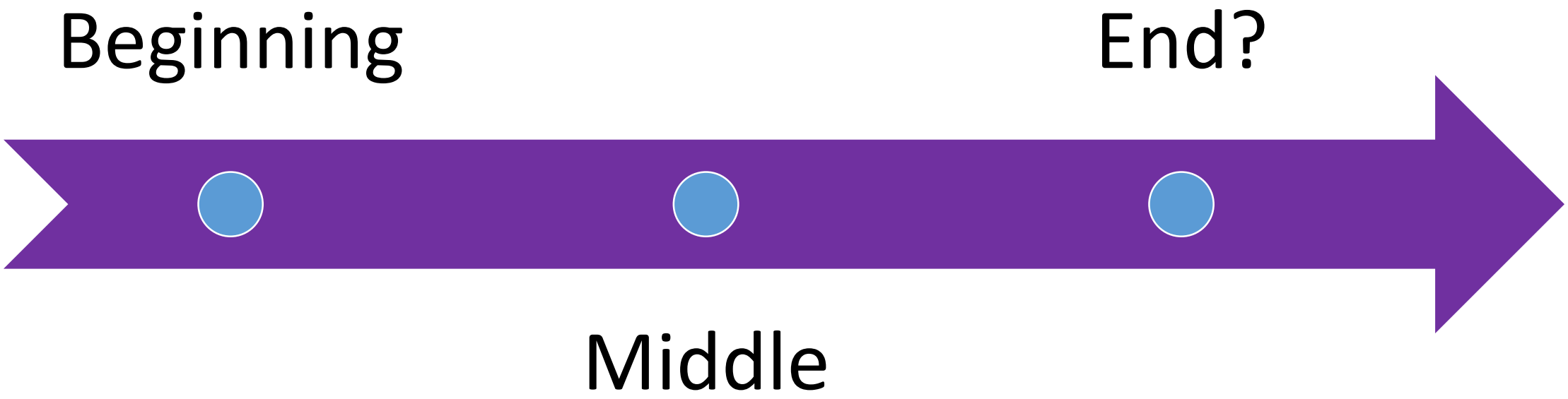
Outline



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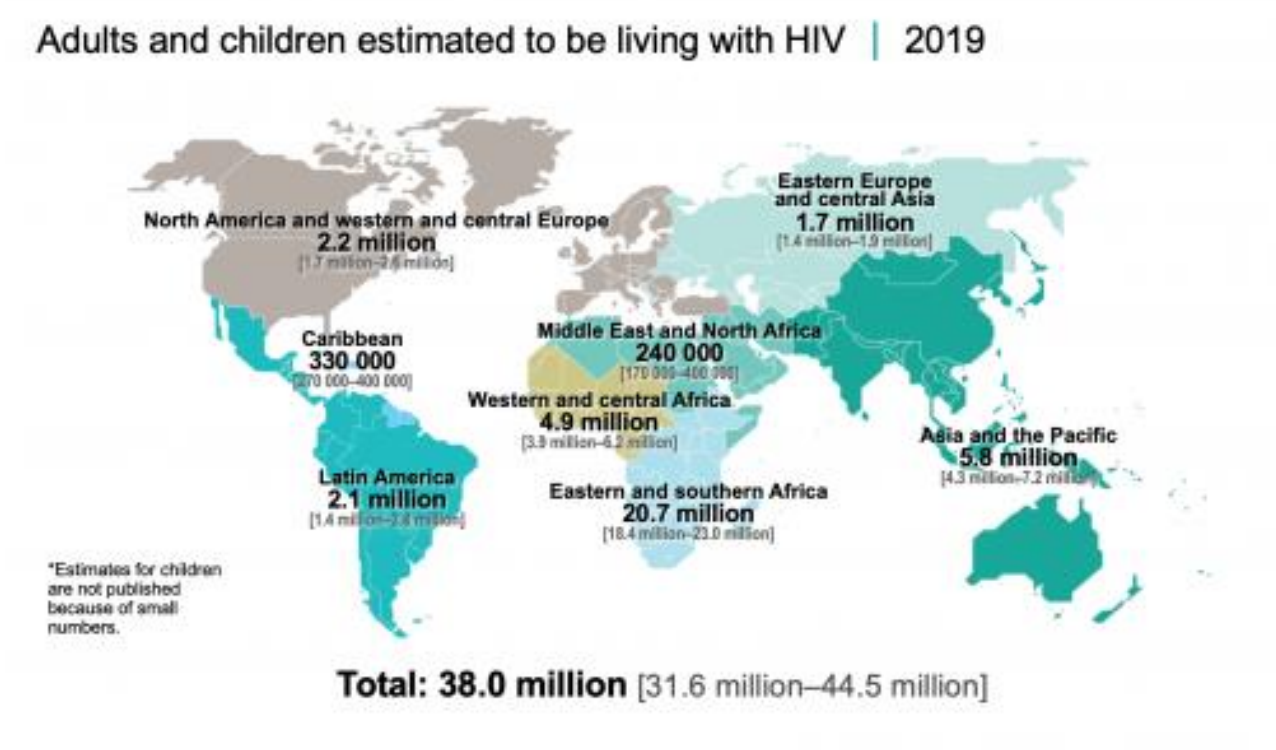
HIV and COVID-19 syndemic



Total Cases
255 160 888

UNAIDS 2020

Johns Hopkins Coronavirus Resource Center

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Impact of HIV on COVID-19

- Hypothesis 1: **HIV would have a deleterious effect**
  - HIV-related lymphopenia
  - Low $CD4^+$ cell counts and high viral loads
  - More co-morbidities in PLWH
  - Social vulnerabilities

- Hypothesis 2: **HIV may be paradoxically protective**
  - Less cytokine storm
  - ART as chemoprophylaxis
  - Adherence to COVID-19 regulations

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Infection of severe acute respiratory syndrome coronavirus 2 in a patient with AIDS

Junwei Su, Xiaomin Shen*, Qin Ni, Hong Zhao, Jieru Cai, Biao Zhu, Wenrui Wu, Guanjing Lang, Kaijin Xu*

Title: COVID-19 in HIV infected patients: A Case series and Literature Review

Authors: Neeraja Swaminathan, Peter Moussa, Nidhi Mody, Kevin Bryan Lo, Gabriel Aponte Pattaroyo

COVID-19 in HIV: a Review of Published Case Reports

Zoya Morani[1] · Saumil Patel[2] · Sudeshna Ghosh[3] · Falah Abu Hassan[4] · Shriya Doreswamy[5] · Sandeep Singh[6] · Venkata Neelima Kothapudi[7] · Rupak Desai[8]

COVID-19 in patients with HIV: clinical case series

*Jose L Blanco, Juan Ambrosioni, Felipe Garcia, Esteban Martínez, Alex Soriano, Josep Mallolas, *Jose M Miro, on behalf the COVID-19 in HIV Investigators†*

COVID-19 in people living with human immunodeficiency virus: a case series of 33 patients

Georg Härter[1] · Christoph D. Spinner[2] · Julia Roider[3,4] · Markus Bickel[5] · Ivanka Krznaric[6] · Stephan Grunwald[6] Farhad Schabaz[7] · Daniel Gillor[8] · Nils Postel[9] · Matthias C. Mueller[10,11] · Markus Müller[12] · Katja Römer[13] · Knud Schewe[14] · Christian Hoffmann[14,15]

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Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort

*Pilar Vizcarra, María J Pérez-Elías, Carmen Quereda, Ana Moreno, María J Vivancos, Fernando Dronda, José L Casado, on behalf of the COVID-19 ID Team**

Clinical characteristics, risk factors, and incidence of symptomatic coronavirus disease 2019 in a large cohort of adults living with HIV: a single-center, prospective observational study

Alexy Inciarte[a], Ana Gonzalez-Cordon[a], Jhon Rojas[a], Berta Torres[a], Elisa de Lazzari[a], Lorena de la Mora[a], Maria Martinez-Rebollar[a], Montserrat Laguno[a], Pilar Callau[a], Azucena Gonzalez-Navarro[c], Lorna Leal[a], Felipe Garcia[a], Josep Mallolas[a], Mar Mosquera[b], Maria A. Marcos[b], Juan Ambrosioni[a], Josep M. Miro[a,*], Esteban Martinez[a,*], Jose L. Blanco[a,*],

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COVID-19 in the largest US HIV cohort

Lesley S. Park[1], Christopher T. Rentsch[2], Keith Sigel[3], Maria Rodriguez-Barradas[4], Sheldon T. Brown[3,5]
Matthew Bidwell Goetz[6], Emily C. Williams[7], Keri Althoff[8], Norbert Bräu[3,5], Lydia Aoun-Barakat[9], Alice Tseng[10], Amy C. Justice[9,11], Janet P. Tate[9,11]

Outcomes Among HIV-Positive Patients Hospitalized With COVID-19

Savannah Karmen-Tuohy, BS,[a] Philip M. Carlucci, BS,[a] Fainareti N. Zervou, MD,[a] Ioannis M. Zacharioudakis, MD,[a] Gabriel Rebick, MD,[a] Elizabeth Klein, BS,[a] Jenna Reich, BS,[a] Simon Jones, PhD,[b,c] and Joseph Rahimian, MD[a]

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America
hivma hiv medicine association
OXFORD

Coronavirus 2019 and People Living With Human Immunodeficiency Virus: Outcomes for Hospitalized Patients in New York City

Keith Sigel,[1] Talia Swartz,[2] Eddye Golden,[3] Ishan Paranjpe,[3,4] Sulaiman Somani,[3,4] Felix Richter,[3,4] Jessica K. De Freitas,[3,4] Riccardo Miotto,[3,4] Shan Zhao,[3,5] Paz Polak,[6] Tinaye Mutetwa,[1] Stephanie Factor,[2] Saurabh Mehandru,[7] Michael Mullen,[2] Francesca Cossarini,[2] Erwin Bottinger,[3,8] Zahi Fayad,[9,10] Miriam Merad,[6,11,12] Sacha Gnjatic,[6,11,12] Judith Aberg,[2] Alexander Charney,[4,13,14] Girish Nadkarni,[3,11,15,a] and Benjamin S. Glicksberg[3,4,a]

Park et al. AIDS 2020. Poster LBPEC23
Karmen-Tuohy et al. J Acquir Immune Defic Syndr. 2020
Sigel et al. CID. 2020

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COVID-19 symptoms and SARS-CoV-2 infection among people living with HIV in the US: the MACS/WIHS combined cohort study

Gypsyamber D'Souza[1], Gayle Springer[1], Deborah Gustafson[2], Seble Kassaye[3], Maria L. Alcaide[4], Catalina Ramirez[5], Anjali Sharma[6], Frank J. Palella[7], Phyllis C. Tien[8], Roger Detels[9], Mirjam-Colette Kempf[10], Cecile D. Lahiri[11], Charles R. Rinaldo[12], Audrey L. French[13], Joseph B. Margolick[14] and Ada A. Adimora[5,15]

- The survey was completed by 3411 participants, including 2078 PLWH and 1333 HIV-seronegative participants from across the US

- In multivariable analysis, the odds of SARS-CoV-2 positivity were higher among PLWH than HIN-negative patients (aOR 2.22; 95%CI 1.01–4.85; *P* = 0.046)

D'Souza et al. HIV Res Clin Pract. 2020

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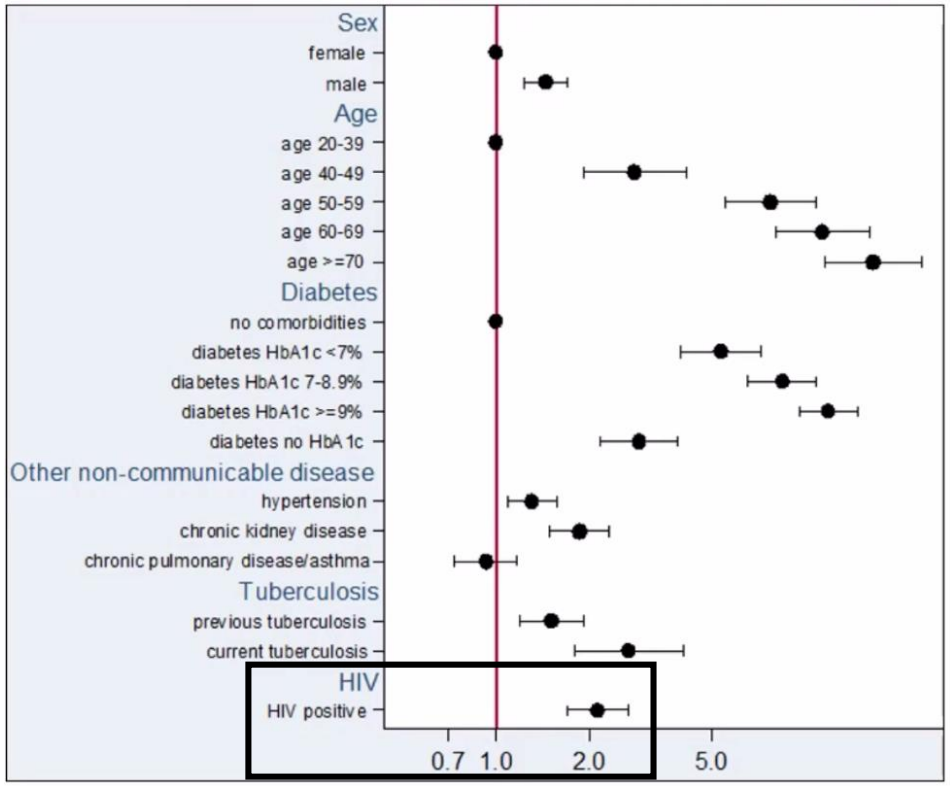
Risk Factors for Coronavirus Disease 2019 (COVID-19) Death in a Population Cohort Study from the Western Cape Province, South Africa

Western Cape Department of Health in collaboration with the National Institute for Communicable Diseases, South Africa

	No COVID-19	COVID-19 not deceased	COVID-19 deceased
n	3,438,624	21,683	625
Median age (IQR)	38 (29; 51)	37 (30; 48)	63; (54; 71)
Male	42%	31%	46%
Diabetes	8%	14%	60%
Hypertension	16%	23%	58%
Chronic kidney disease	2%	2%	18%
COPD / asthma	6%	7%	13%
Previous TB	8%	8%	14%
Current TB	2%	1%	4%
HIV	16%	18%	18%
Suppressed or recent ART	58%	71%	72%
Viraemic / CD4 <200	8%	5%	10%
Unknown	35%	24%	18%

*Adjusted for all variables in the table as well as Metro/rural location & subdistrict within Cape Town



VL ≥1000 copies/ml (last 12 mo) OR CD4⁺ <200 cells/µl (last 12 mo): HR 3.59; 95% CI 1.96-6.56; *P* <0.001

Boulle et al. CID. 2020

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Outcomes of Coronavirus Disease 2019 (COVID-19) Related Hospitalization Among People With Human Immunodeficiency Virus (HIV) in the ISARIC World Health Organization (WHO) Clinical Characterization Protocol (UK): A Prospective Observational Study

Anna Maria Geretti,[*,1,2] Alexander J. Stockdale,[*,1,2] Sophie H. Kelly,[1,2] Muge Cevik,[3] Simon Collins,[4] Laura Waters,[5,6] Giovanni Villa,[7] Annemarie Docherty,[8,9] Ewen M. Harrison,[8] Lance Turtle,[1,2,©] Peter J. M. Openshaw,[10] J. Kenneth Baillie,[9,11] Caroline A. Sabin,[12,13] and Malcolm G Semple[1,14]

- More severe clinical presentations in HIV patients
- Prolonged duration of symptoms (5 vs. 3 days, p = 0.002)

HIV-positive Versus HIV-negative	Hazard Ratio	95% CI	*P* value
Unadjusted	0.77	.54–1.11	.17
Adjusted for sex	0.76	.53–1.10	.15
Adjusted for ethnicity	0.88	.60–1.29	.52
Adjusted for age	1.47	1.01–2.14	.05
Adjusted for age and sex	1.45	1.00–2.12	.05
Adjusted for sex, ethnicity, age, baseline date, and indeterminate/probable hospital acquisition of COVID-19	1.49	1.01–2.20	.04
Adjusted for sex, ethnicity, age, baseline date, indeterminate/probable hospital acquisition of COVID-19, and 10 comorbidities[a]	1.50	1.02–2.22	.04
Adjusted for sex, ethnicity, age, baseline date, indeterminate/probable hospital acquisition of COVID-19, 10 comorbidities[a], and hypoxia/receiving oxygen at presentation[b]	1.69	1.15–2.48	.008
Adjusted for sex, ethnicity, age, baseline date, indeterminate/probable hospital acquisition of COVID-19, 10 comorbidities[a] and hypoxia/receiving oxygen at presentation[b] among individuals aged <60 years	2.87	1.70–4.86	<.001

Geretti et al. CID. 2020

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Epidemiology and outcomes of COVID-19 in HIV-infected individuals: a systematic review and meta-analysis

Paddy Ssentongo[1,2✉], Emily S. Heilbrunn[1], Anna E. Ssentongo[1,3], Shailesh Advani[4,5], Vernon M. Chinchilli[1], Jonathan J. Nunez[6] & Ping Du[1,6]

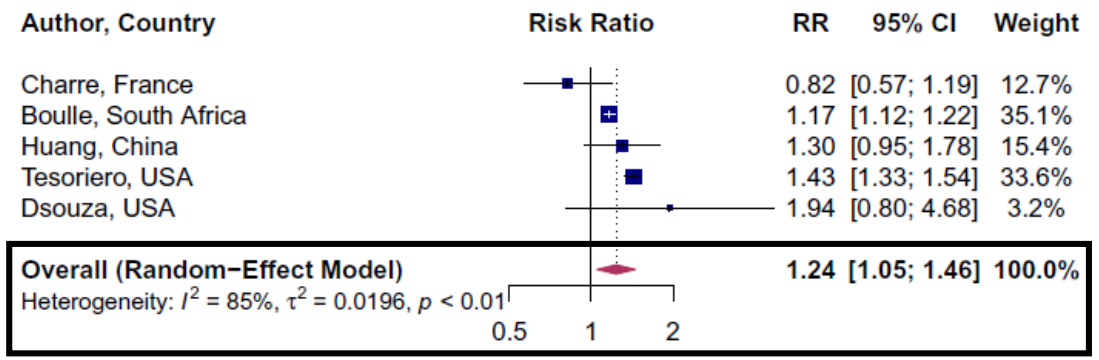

Figure 2. Association of HIV and attack rate of SARS-CoV-2. Blue squares and their corresponding lines are the point estimates and 95% confidence intervals from each study. Maroon diamond represents the pooled effect estimate.

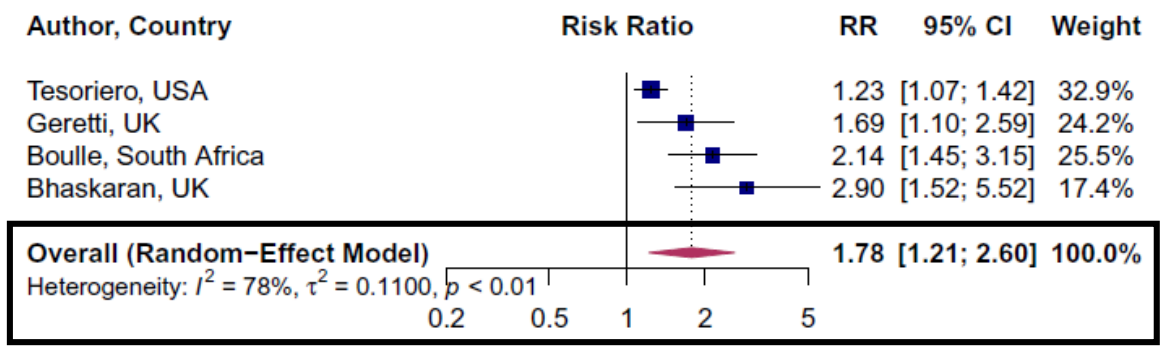

Figure 5. Association of HIV and mortality risk from COVID-19. Blue squares and their corresponding lines are the point estimates and 95% confidence intervals per each study. Maroon diamond represents the pooled effect estimate.

Ssentogo et al. Sci Rep. 2021

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WHO Global Clinical Platform for COVID-19

Data for public health response

Clinical features and prognostic factors of COVID-19 in people living with HIV hospitalized with suspected or confirmed SARS-CoV-2 infection

Fig. 5. HIV infection and risk of severe or critical illness of COVID-19 at hospital admission

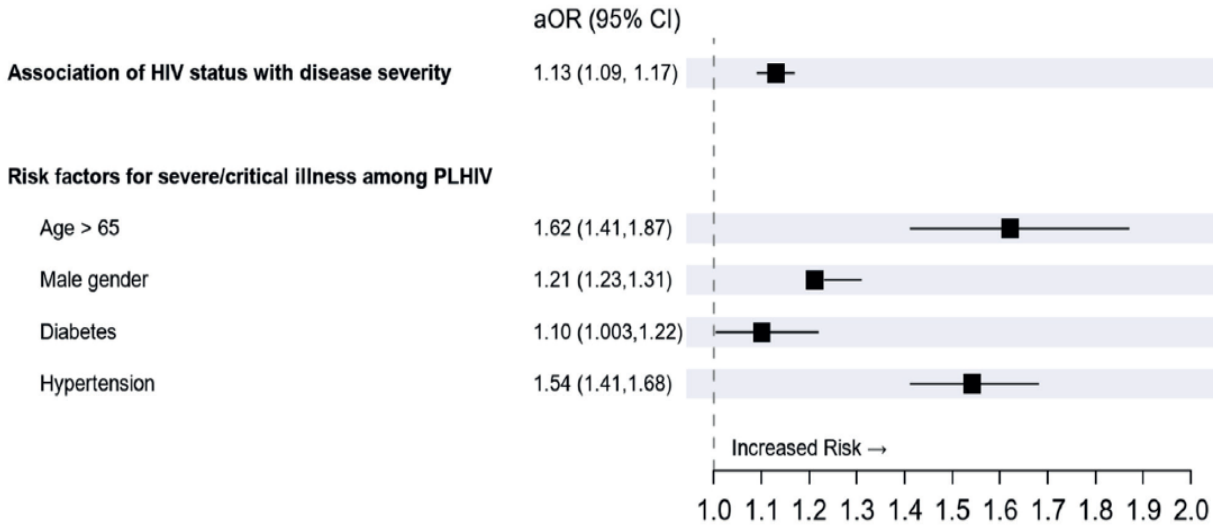
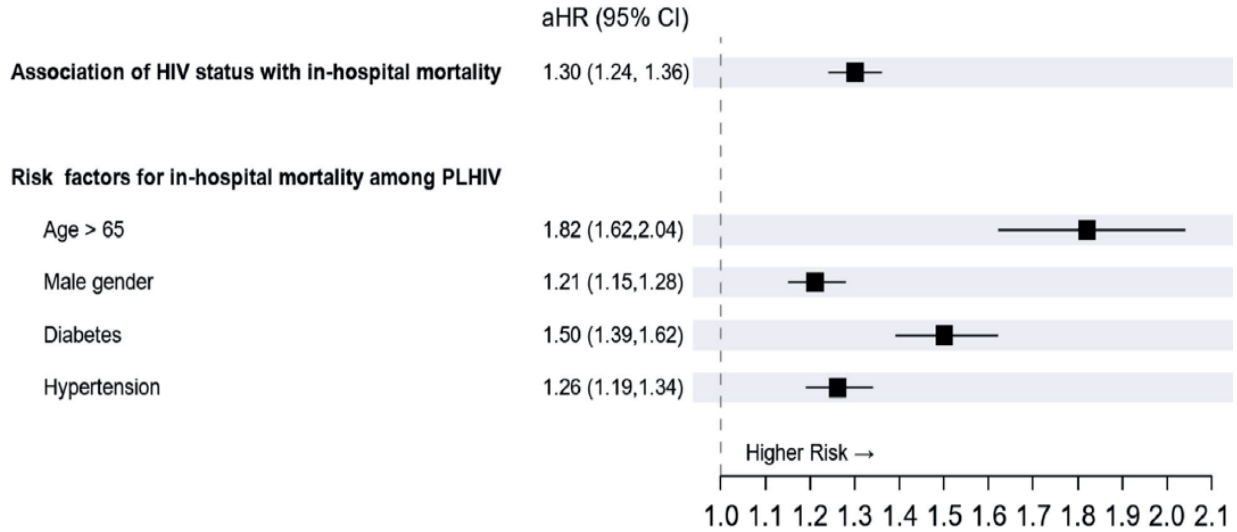


Fig. 6. HIV infection and risk of in-hospital mortality for COVID-19



WHO Global COVID-19 Clinical Data Platform. July 2021

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Original Investigation | Infectious Diseases

COVID-19 Outcomes Among Persons Living With or Without Diagnosed HIV Infection in New York State

James M. Tesoriero, PhD; Carol-Ann E. Swain, PhD; Jennifer L. Pierce, BS; Lucila Zamboni, PhD; Meng Wu, PhD; David R. Holtgrave, PhD; Charles J. Gonzalez, MD; Tomoko Udo, PhD; Johanne E. Morne, MS; Rachel Hart-Malloy, PhD; Deepa T. Rajulu, MS; Shu-Yin John Leung, MA; Eli S. Rosenberg, PhD

Table 2. Factors Associated With Stages of COVID-19 Diagnosis, Hospitalization, and In-Hospital Death Among Persons Living With Diagnosed HIV Infection—New York State, March 1 to June 7, 2020[a]

Characteristic	Population size[b]	Diagnosed				Hospitalized				In-hospital death		
		No.	Rate per 1000 PLWDH	Rate ratio (95% CI)		No.	Rate per 1000 diagnoses	Rate ratio (95% CI)		No.	Rate per 1000 hospitalized	Unadjusted rate ratio (95% CI)
				Unadjusted	Adjusted[c]			Unadjusted	Adjusted[c]			
Stage of HIV Infection, at last test[f]												
Stage 1	63 712	1774	27.84	1 [Reference]	1 [Reference]	437	246.30	1 [Reference]	1 [Reference]	94	215.10	1 [Reference]
Stage 2	27 905	843	30.21	1.08 (0.99-1.18)	1.02 (0.94-1.11)	298	353.50	1.44 (1.24-1.66)	1.29 (1.11-1.49)	71	238.26	1.11 (0.81-1.51)
Stage 3	7498	270	36.01	1.29 (1.14-1.47)	1.22 (1.07-1.38)	126	466.70	1.89 (1.55-2.31)	1.69 (1.38-2.07)	34	269.84	1.26 (0.85-1.86)
Viral suppression, at last test[f]												
Yes	87 480	2628	30.04	1 [Reference]	NA	756	287.70	1 [Reference]	NA	180	238.10	1 [Reference]
No	12 027	267	22.20	0.74 (0.65-0.84)	NA	105	393.30	1.37 (1.11-1.68)	NA	21	200.00	0.84 (0.54-1.32)

Tesoriero et al. JAMA Netw Open. 2021

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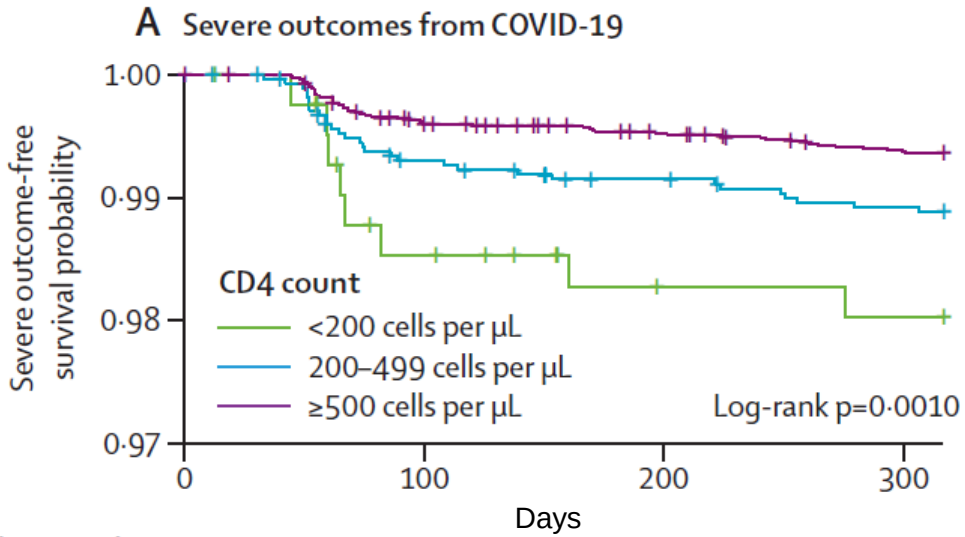
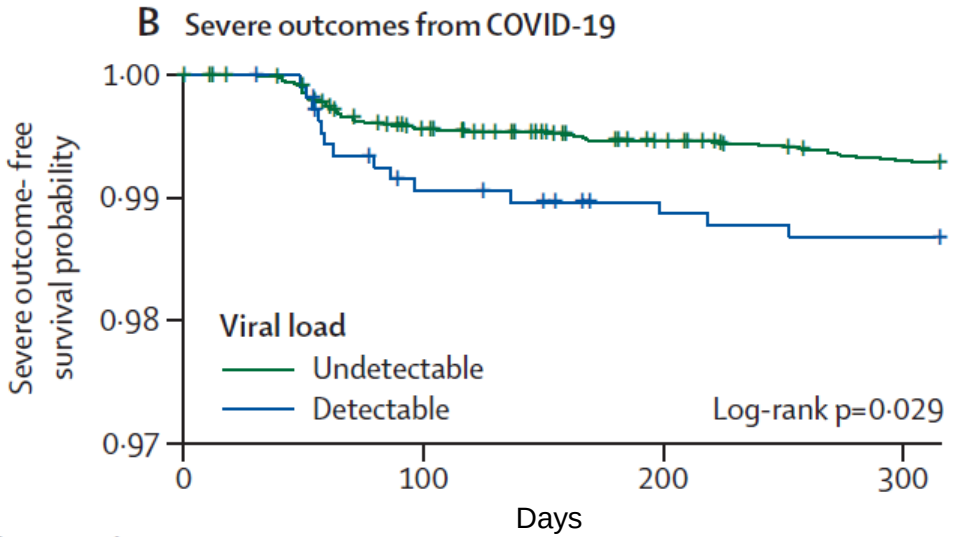
Sociodemographic, clinical, and immunological factors associated with SARS-CoV-2 diagnosis and severe COVID-19 outcomes in people living with HIV: a retrospective cohort study

Daniel K Nomah, Juliana Reyes-Urueña*, Yesika Díaz, Sergio Moreno, Jordi Aceiton, Andreu Bruguera, Rosa M Vivanco-Hidalgo, Josep M Llibre, Pere Domingo, Vicenç Falcó, Arkaitz Imaz, Cristina Cortés, Lluís Force, Emili Letang, Ingrid Vilaró, Jordi Casabona, Jose M Miro, and the PISCIS study group*



Number at risk				
<200 cells per µL	413	402	395	394
200–499 cells per µL	2716	2688	2678	2670
≥500 cells per µL	9451	9403	9382	9360



Number at risk				
Undetectable	10758	10692	10658	10632
Detectable	1068	1053	1047	1044

Nomah et al. Lancet HIV. 2021

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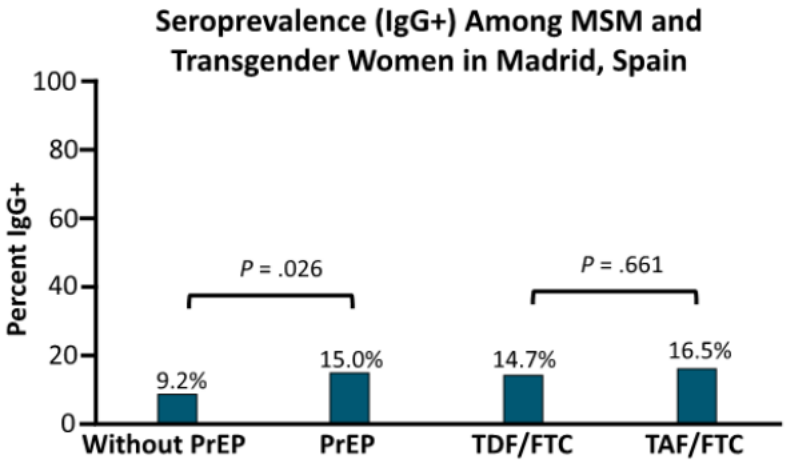
Preventive Efficacy of Tenofovir/Emtricitabine Against Severe Acute Respiratory Syndrome Coronavirus 2 Among Pre-Exposure Prophylaxis Users

Oskar Ayerdi,[1] Teresa Puerta,[1] Petunia Clavo,[1] Mar Vera,[1] Juan Ballesteros,[1] Manuel Enrique Fuentes,[2] Vicente Estrada,[3] Carmen Rodríguez,[1] and Jorge Del Romero[1]; Sandoval Study Group[1]

- Observational study of MSM and transgender women without (n = 250) and with (n = 500) PrEP use: TDF/FTC (n = 409); TAF/FTC (n = 91)



COVID-19 Outcome	PrEP Use		P Value	PrEP Type		P Value
	No	Yes		TDF/FTC	TAF/FTC	
Median symptom duration, days (IQR)	7 (4-14)	7 (4-13)	.41	7 (4-13)	10 (4-14)	.27
Required treatment, %	2	2.4	.73	2.7	1.1	.70

Ayerdi et al. OFID. 2020

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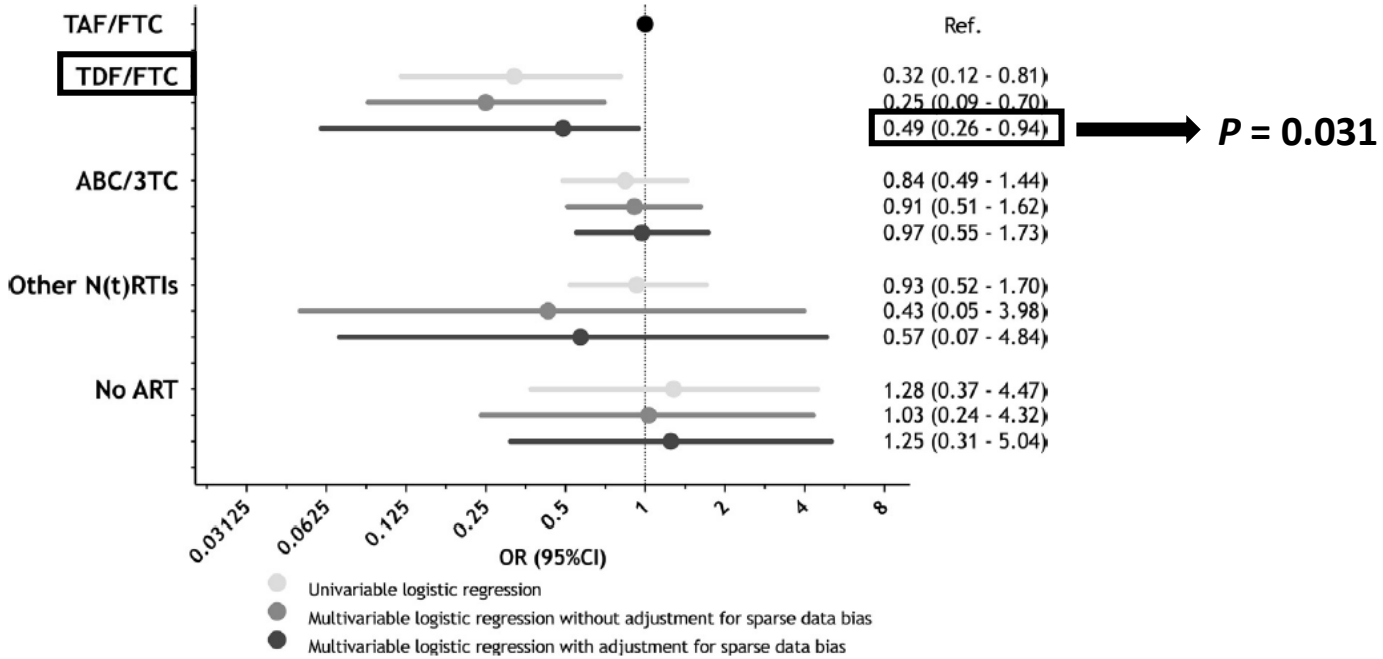
Prevalence and factors associated with SARS-CoV-2 seropositivity in the Spanish HIV Research Network Cohort

Juan Berenguer [1,*], Cristina Díez [1], María Martín-Vicente [2], Rafael Micán [3], María J. Pérez-Elías [4], Lucio J. García-Fraile [5], Francisco Vidal [6], Inés Suárez-García [7], Daniel Podzamczer [8], Jorge Del Romero [9], Federico Pulido [10], José A. Iribarren [11], Félix Gutiérrez [12], Eva Poveda [13], Carlos Galera [14], Rebeca Izquierdo [15], Víctor Asensi [16], Joaquín Portilla [17], Juan C. López [1], José R. Arribas [3], Santiago Moreno [4], Juan González-García [3], Salvador Resino [2,†], Inmaculada Jarrín [15,†]



***P* = 0.031**

Fig. 1. Association of the nucleoside/nucleotide reverse transcriptase inhibitors (N(t)RTI) backbone with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seropositivity by logistic regression analysis. Multivariable models were adjusted by sex, age, country of birth, education level, comorbidities, route of HIV acquisition, prior AIDS, CD4+ cell count, HIV viral load, type of third antiretroviral drug used, and month of sample collection. To avoid sparse data bias, we used penalization through data augmentation to perform multivariate logistic regression. TAF, tenofovir alafenamide; FTC, emtricitabine; TDF, tenofovir disoproxil fumarate; ABC, abacavir; 3TC, lamivudine; ART, antiretroviral therapy; OR, odds ratio; CI, confidence interval.

Berenguer et al. Clin Microbiol Infect. 2021

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Incidence and Severity of COVID-19 in HIV-Positive Persons Receiving Antiretroviral Therapy

A Cohort Study

Julia del Amo, MD, PhD; Rosa Polo, MD, PhD; Santiago Moreno, MD, PhD; Asunción Díaz, MD, PhD; Esteban Martínez, MD, PhD; José Ramón Arribas, MD, PhD; Inma Jarrín, PhD; and Miguel A. Hernán, MD, DrPH; for The Spanish HIV/COVID-19 Collaboration*

Table 2. Risk per 10 000 Persons for PCR-Confirmed COVID-19 Diagnosis, Hospital Admission, ICU Admission, and Death Among 77 590 HIV-Positive Persons Receiving ART, 1 February to 15 April 2020, Spain

Characteristic	COVID-19 Diagnosis (95% CI)	COVID-19 Hospital Admission (95% CI)	COVID-19 ICU Admission (95% CI)	COVID-19 Death (95% CI)
Risk				
Overall	30.4 (26.7–34.6)	19.5 (16.5–22.8)	1.9 (1.1–3.2)	2.6 (1.6–4.0)
Standardized*	30.0 (29.8–30.2)	17.8 (17.7–18.0)	2.5 (2.4–2.6)	3.7 (3.6–3.8)
Sex				
Men	35.1 (30.4–40.3)	23.4 (19.6–27.7)	2.1 (1.1–3.6)	2.8 (0.6–4.5)
Women	16.4 (11.2–23.2)	7.7 (4.3–12.7)	1.5 (3–4.5)	2.1 (0.6–5.3)
Age				
20–39 y	28.3 (20.3–38.3)	10.3 (5.8–17.6)	0.7 (0–3.8)	0 (–2.9)†
40–49 y	27.9 (20.9–36.4)	20.1 (14.3–27.5)	0.5 (0–2.9)	1.0 (0.1–3.7)
50–59 y	26.3 (21.0–32.5)	16.7 (12.6–21.8)	2.2 (0.9–4.5)	2.2 (0.9–4.5)
60–69 y	38.8 (26.9–54.2)	27.4 (17.6–40.8)	4.6 (1.2–11.7)	4.6 (1.2–11.7)
70–79 y	83.7 (52.4–126.7)	72.3 (43.5–112.9)	7.6 (0.9–27.5)	26.6 (10.7–54.9)
NRTI				
TDF/FTC	16.9 (10.5–25.9)	10.5 (5.6–17.9)	0 (–2.9)†	0 (–2.9)†
TAF/FTC	39.1 (31.8–47.6)	20.3 (15.2–26.7)	2.7 (1.1–6.5)	3.9 (1.9–7.2)
ABC/3TC	28.3 (21.5–36.7)	23.4 (17.2–31.1)	3.0 (1.1–6.5)	4.0 (1.7–7.8)
Other regimens	29.7 (22.6–38.4)	20.0 (14.2–27.3)	1.0 (0.1–3.7)	1.0 (0.1–3.7)

3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; COVID-19 = coronavirus disease 2019; FTC = emtricitabine; ICU = intensive care unit; NRTI = nucleos(t)ide reverse transcriptase inhibitor; PCR = polymerase chain reaction; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate.

* Standardized to the age and sex of the general population of Spain aged 20 to 79 y.

† One-sided 97.5 CI.

Del Amo et al. Ann Intern Med. 2020

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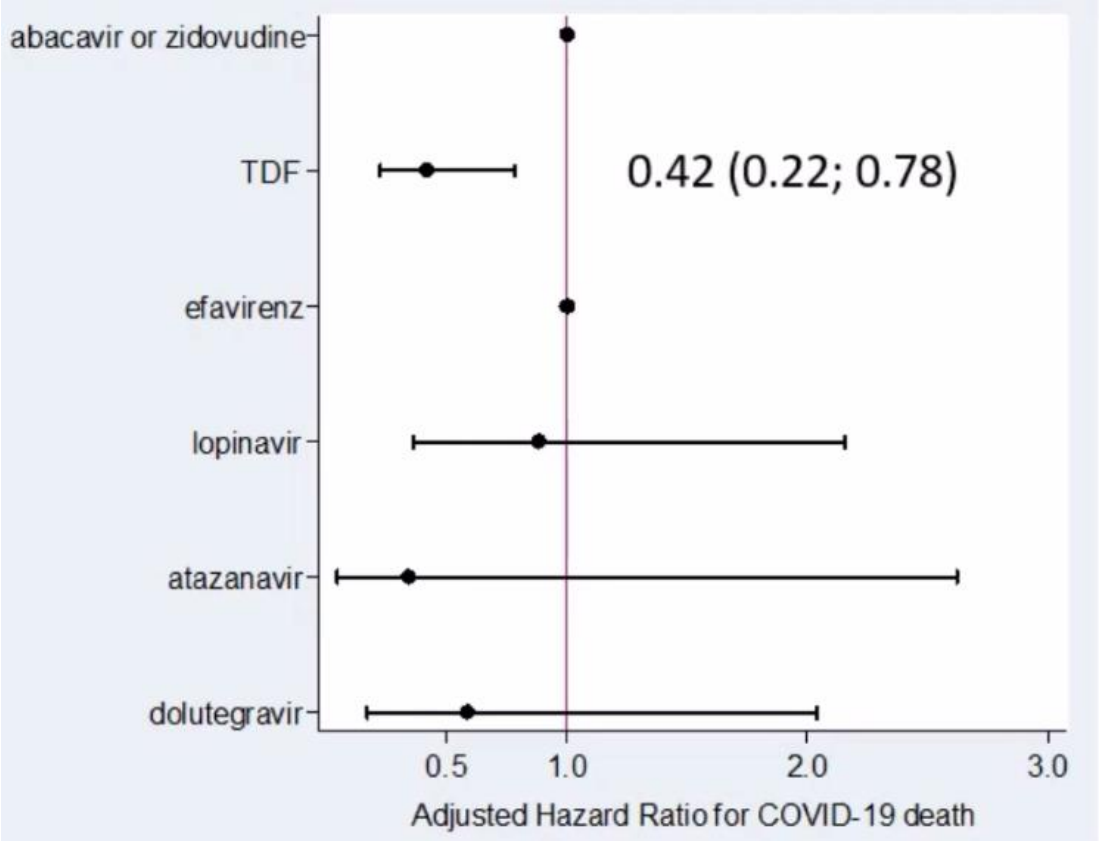
Risk Factors for Coronavirus Disease 2019 (COVID-19) Death in a Population Cohort Study from the Western Cape Province, South Africa

Western Cape Department of Health in collaboration with the National Institute for Communicable Diseases, South Africa



Reference

***P* = 0.007**

Reference

p = 0.846

p = 0.352

p = 0.380

Boulle et al. CID. 2020

Conclusion

- Risk of acquiring COVID-19 seems to be slightly higher in PLWH as compared to the general population, particularly in patients with lower $CD4^+$ cell counts

- HIV itself is an independent risk factor for poorer outcomes however severe COVID-19 disease is mostly driven by two factors:
  - Presence of comorbidities
  - Low $CD4^+$ cell counts / untreated HIV infection

- Protective role of TDF
  - Association or Causation?

- There is still a lot we don’t know
  - Thrombotic events during illness, long covid syndrome etc.

It is my 41st birthday today so I consider this symposium my birthday party 😉