18ª edición

POSTCROI 2021

Una actualización de la 28ª Conference on Retroviruses and Opportunistic Infections

16 de Marzo del 2021

Novedades del CROI 2021 sobre el COVID-19

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FUNDACIÓN LUCHA CONTRA EL SIDA Y LAS ENFERMEDADES INFECCIOSAS

FLS SCIENCE

CROI 2021 News on COVID-19 & HIV

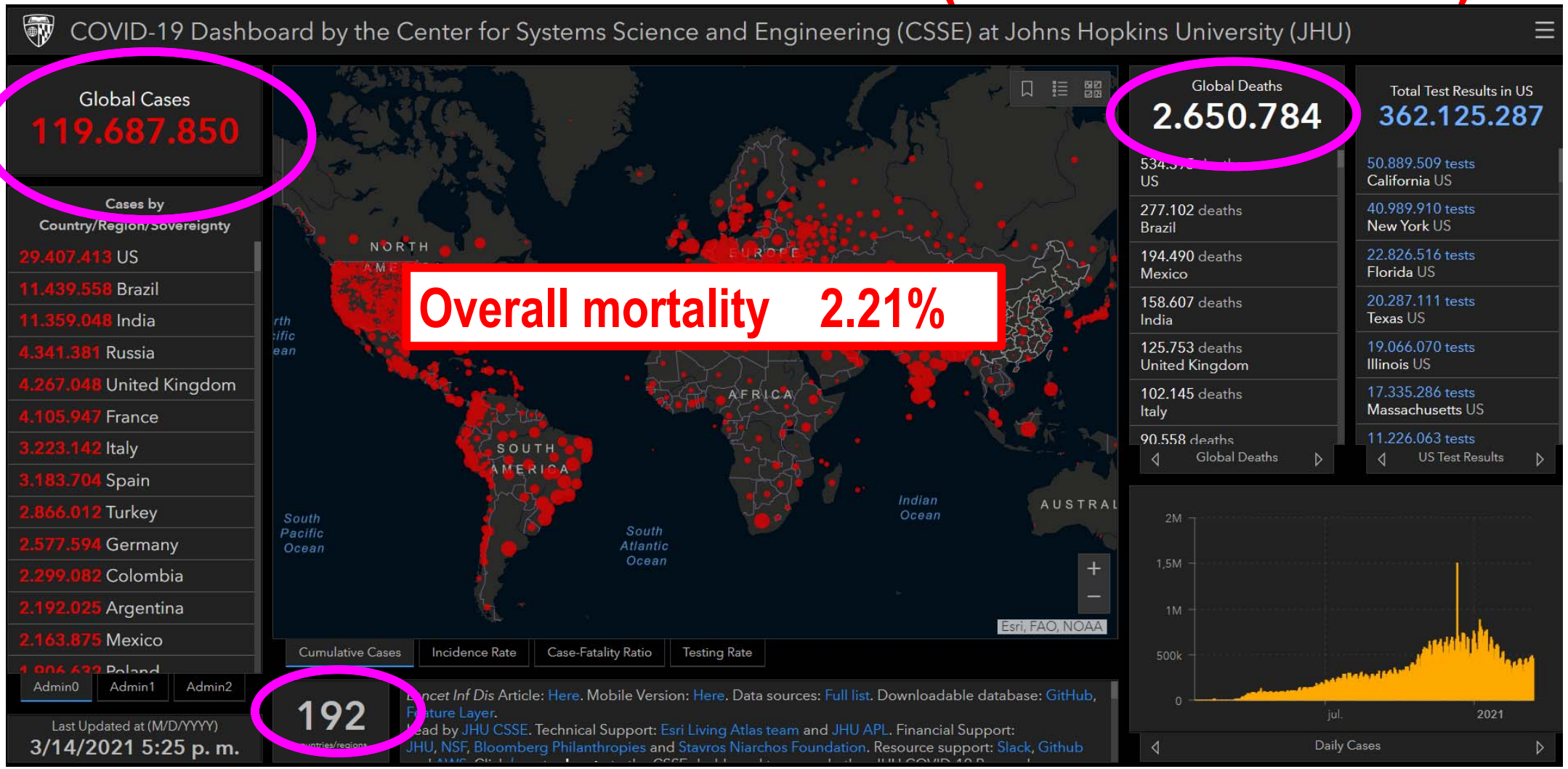
E-mail address: jmmiro@ub.edu

CROI 2021 News on COVID-19 & HIV

- **Current Epidemiology**
- A tale of two viruses: HIV & SARS-CoV-2
- Impact of COVID-19 in health care systems
- Hospitalization risk in HIV-infected patients
- Prognosis in HIV-infected patients
- Humoral response in HIV-infected patients
- Take-home messages

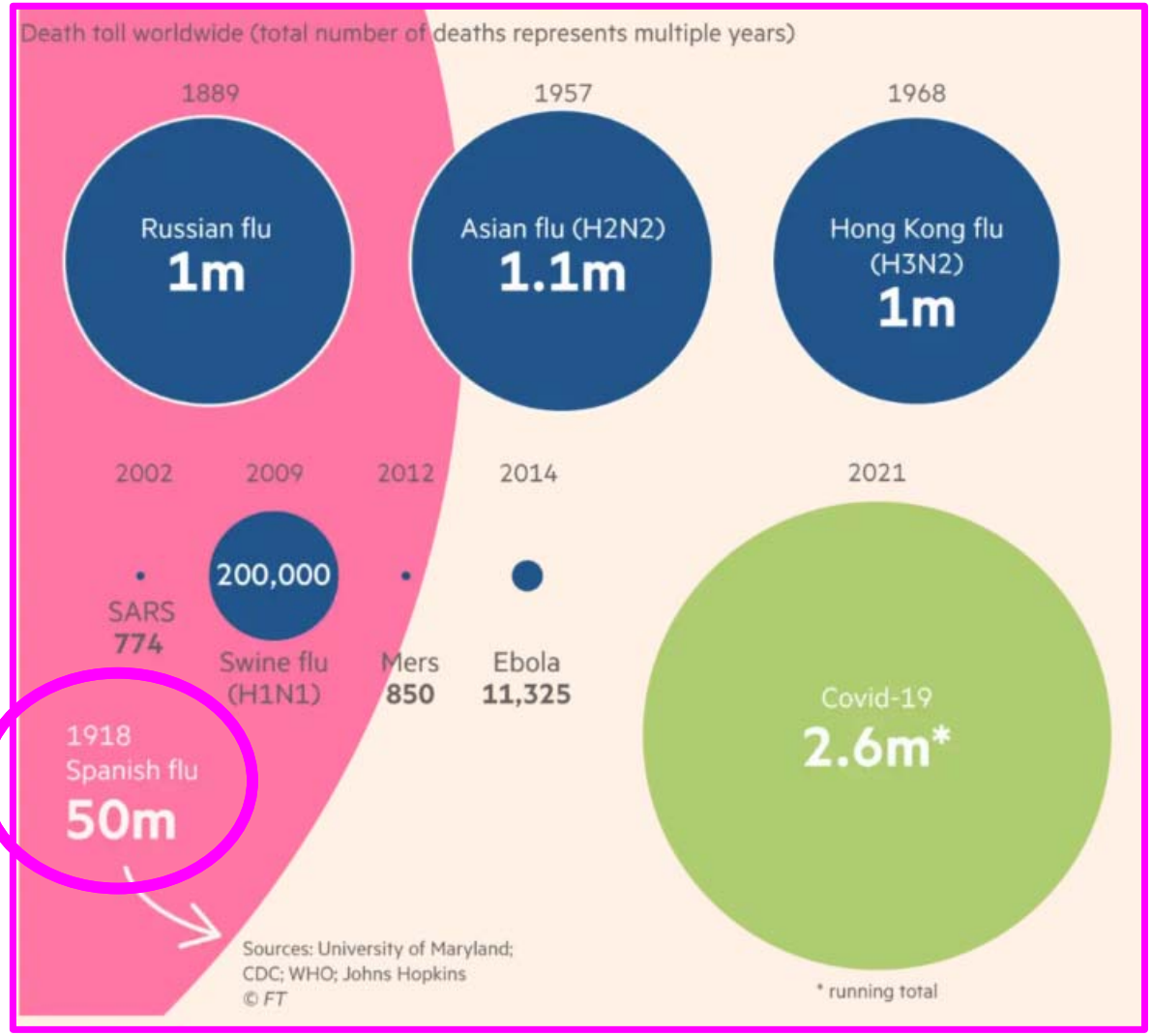
March 16th 2021

SARS-CoV-2 Global Cases (March 14th 2021)



https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6; accessed on March 14th 2021

Putting Coronavirus in Context: Flu *vs.* COVID-19



CROI 2021 News on COVID-19 & HIV

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- **A tale of two viruses: HIV & SARS-CoV-2**
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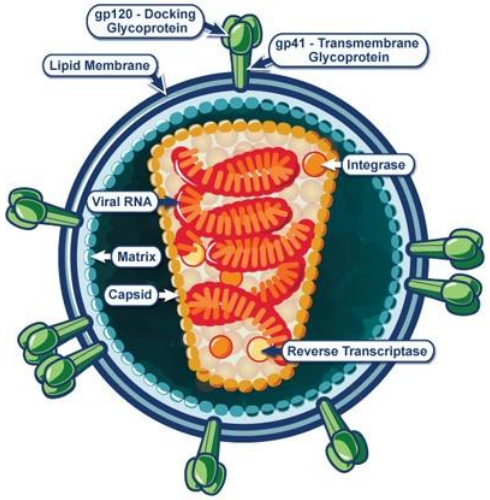
A tale of 2 viruses…

Dr. Galit Alter
Ragon Institute of MGH, MIT and Harvard

HIV

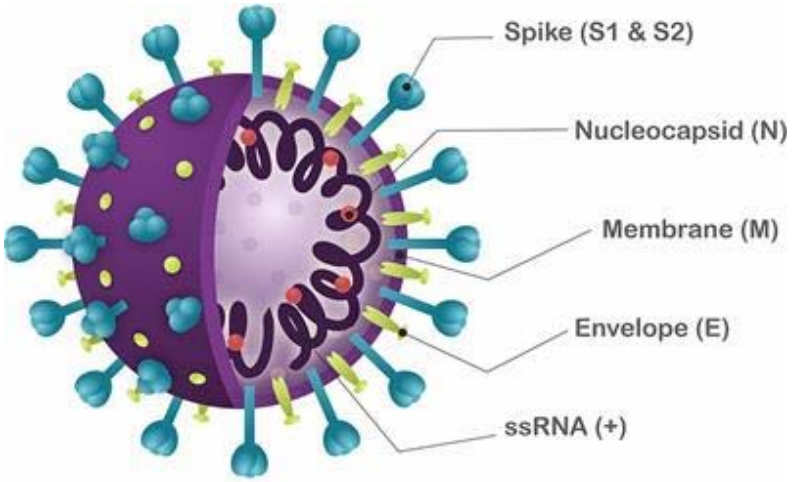
75 million cases
35 million deaths



Mortality without therapy: 95%

SARS-CoV-2

119 million cases
2.6 million deaths



Mortality without therapy: ~1%

https://www.bcm.edu/departments/molecular-virology-and-microbiology/emerging-infections-and-biodefense/specific-agents/hiv-aids

https://www.nphil.gov.lr/index.php/about-covid-19/

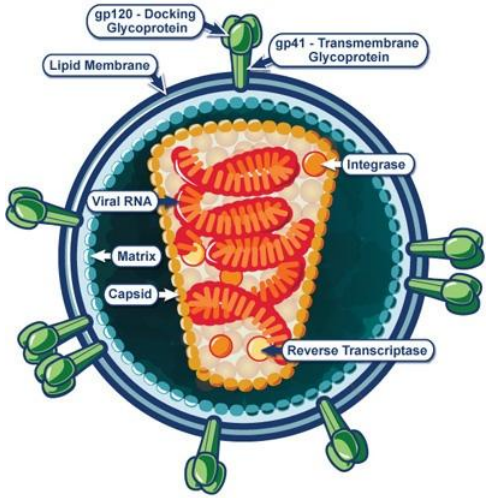
Both RNA, one sticks with us for life…

HIV

RNA

Sexual/parenteral transmission

Integrates

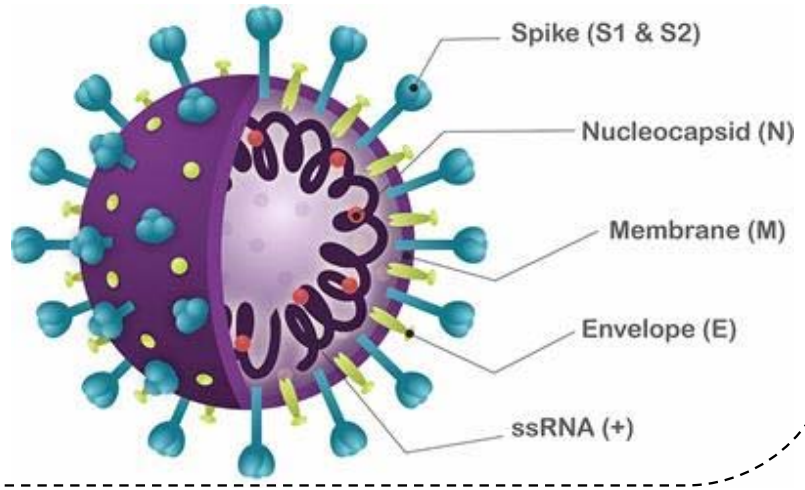


SARS-CoV-2

RNA

Respiratory/droplets

No integration



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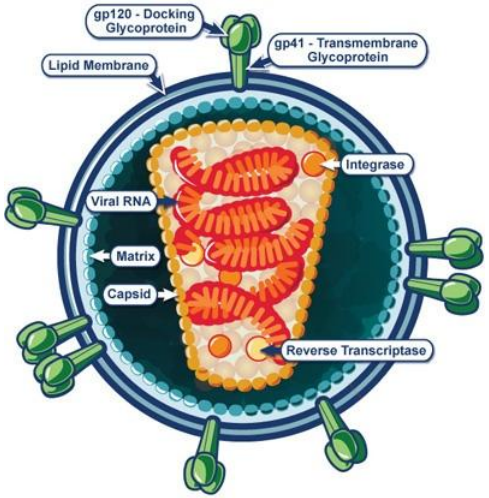
…but both target mucosal barriers!

HIV

Infects CD4+ immune cells

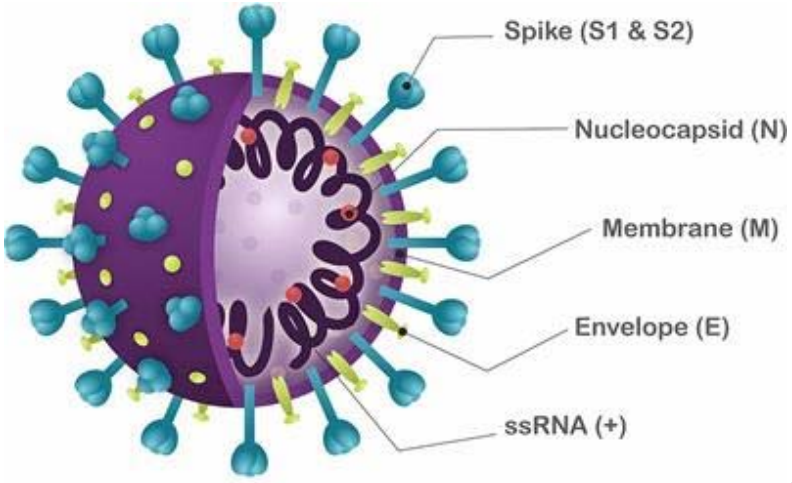
Enriched in mucosal tissues



SARS-CoV-2

Infects epithelial cells (ACE2)

Tropism for mucosa



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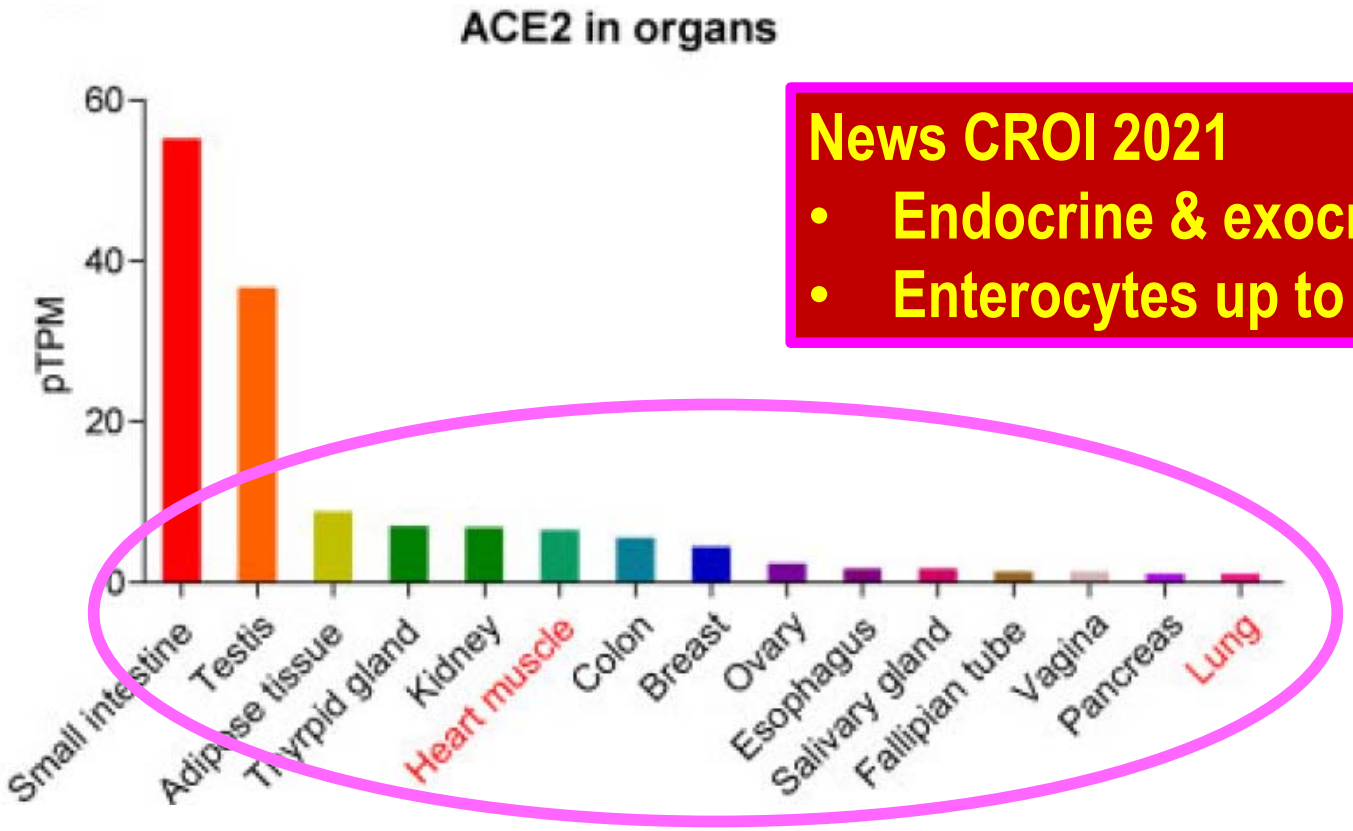
ACE2 mRNA Expression Level across Human Organs



News CROI 2021

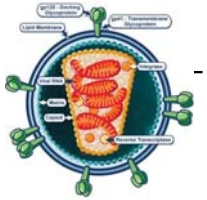
- **Endocrine & exocrine pancreas**
- **Enterocytes up to 7 months**

Chen L et al. Cardiovascular Research. 2020; 116, 1097–1100

* Li D et al. JAMA Network Open. May 7th 2020;3(5):e208292

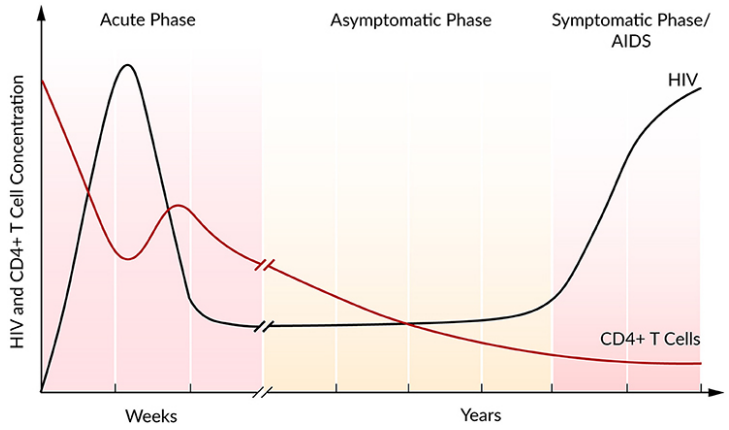
Müller CROI21 #213; Tokuyama CROI21 #115

Kinetics of diseases …

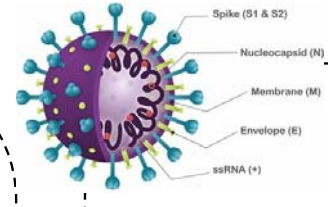


HIV

Years

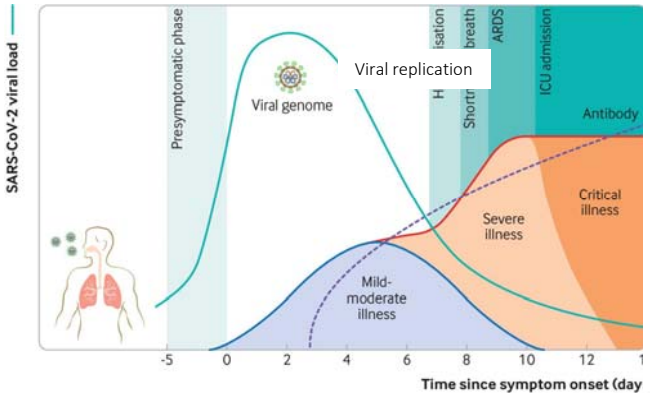


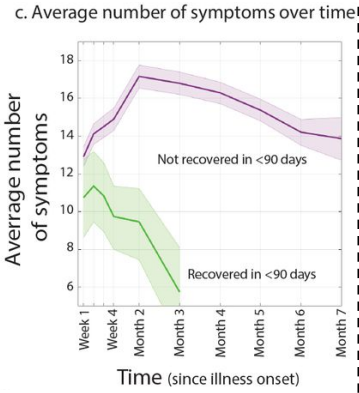
https://www.frontiersin.org/articles/10.3389/fmicb.2018.01546/full



SARS-CoV-2

Days





https://www.bmj.com/content/371/bmj.m3862

Comments (5)

Characterizing Long COVID in an International Cohort: 7 Months of Symptoms and Their Impact

Hannah E. Davis, Gina S. Assaf, Lisa McCorkell, Hannah Wei, Ryan J. Low, Yochai Re'em, Signe Redfield, Jared P. Austin, Athena Akrami

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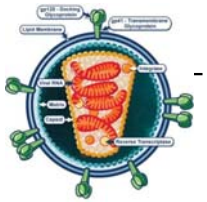
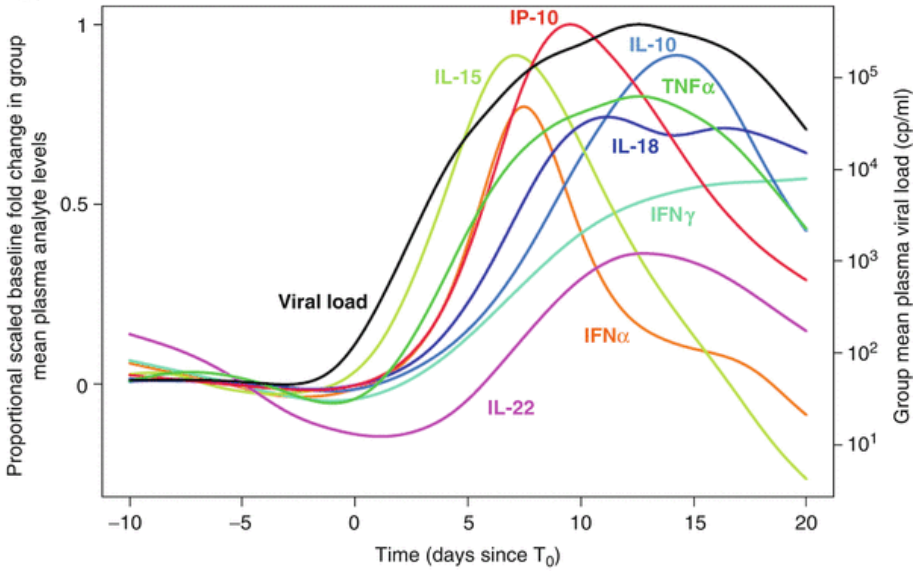
A cytokine storm is associated with both acute HIV and SARS-CoV-2 infection …

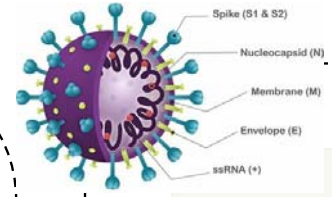


HIV

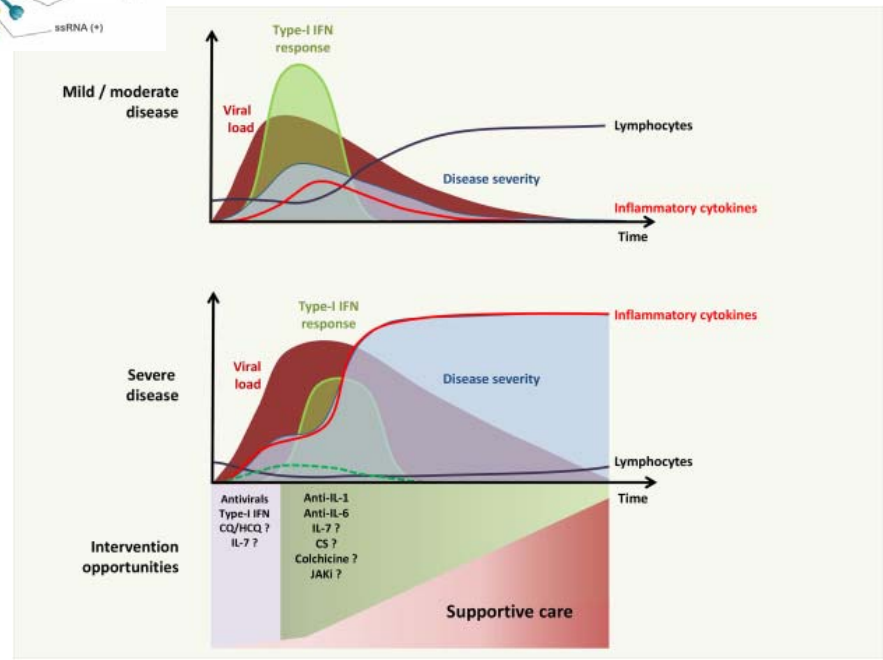


Induction of a Striking Systemic Cytokine Cascade prior to Peak Viremia in Acute Human Immunodeficiency Virus Type 1 Infection, in Contrast to More Modest and Delayed Responses in Acute Hepatitis B and C Virus Infections

Andrea R. Stacey, Philip J. Norris, Li Qin, Elizabeth A. Haygreen, Elizabeth Taylor, John Heitman, Mila Lebedeva, Allan DeCamp, Dongfeng Li, Douglas Grove, Steven G. Self, Persephone Borrow



SARS-CoV-2



Should we stimulate or suppress immune responses in COVID-19? Cytokine and anti-cytokine interventions

Yvan Jamilloux [a, b], Thomas Henry [b], Alexandre Belot [b, c, f], Sébastien Viel [b, d, f], Maxime Fauter [a, b], Thomas El Jammal [a], Thierry Walzer [b], Bruno François [e], Pascal Sève [a]

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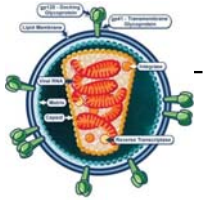
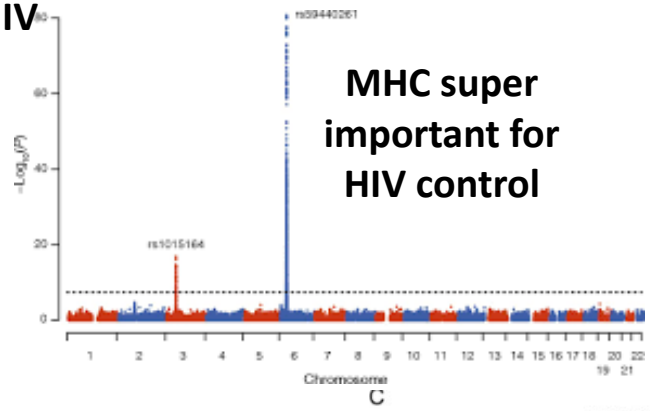
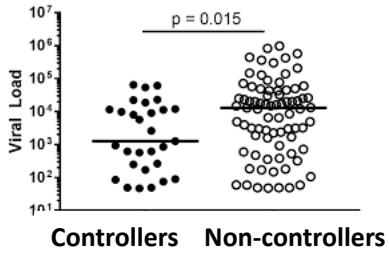
Critical role of T cells in both HIV and SARS-CoV2?

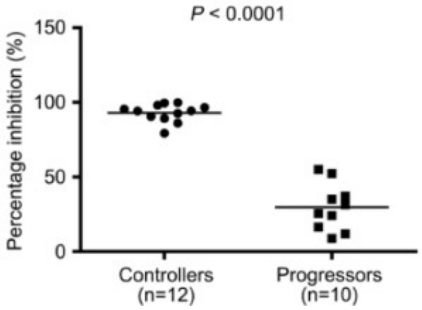


HIV



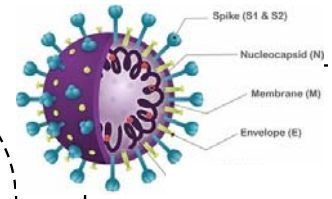
MHC super important for HIV control



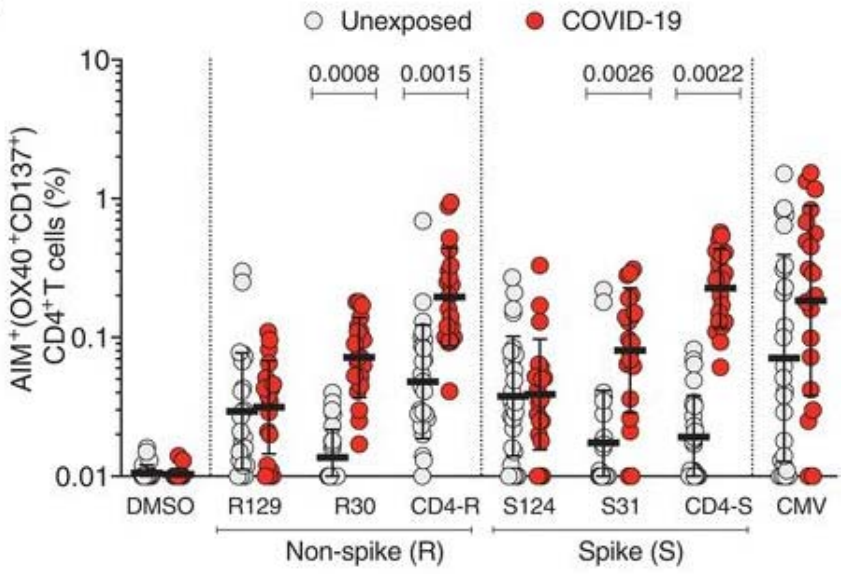


Polymorphisms of large effect explain the majority of the host genetic contribution to variation of HIV-1 virus load

Paul J. McLaren, Cedric Coulonges, István Bartha, Tobias L. Lenz, Aaron J. Deutsch, Arman Bashirova, Susan Buchbinder, Mary N. Carrington, Andrea Cossarizza, Judith Dalmau, Andrea De Luca, James J. Goedert, Deepti Gurdasani, David W. Haas, Joshua T. Herbeck, Eric O. Johnson, Gregory D. Kirk, Olivier Lambotte, Ma Luo, Simon Mallal, Daniëlle van Manen, Javier Martinez-Picado, Laurence Meyer, José M. Miro, James I. Mullins, Niels Obel, Guido Poli, Manjinder S. Sandhu, Hanneke Schuitemaker, Patrick R. Shea, Ioannis Theodorou, Bruce D. Walker, Amy C. Weintrob, Cheryl A. Winkler, Steven M. Wolinsky, Soumya Raychaudhuri, David B. Goldstein, Amalio Telenti, Paul I. W. de Bakker, Jean-François Zagury, and Jacques Fellay



SARS-CoV-2



SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls

Nina Le Bert, Anthony T. Tan, Kamini Kunasegaran, Christine Y. L. Tham, Morteza Hafezi, Adeline Chia, Melissa Hui Yen Chng, Meiyin Lin, Nicole Tan, Martin Linster, Wan Ni Chia, Mark I-Cheng Chen, Lin-Fa Wang, Eng Eong Ooi, Shirin Kalimuddin, Paul Anantharajah Tambyah, Jenny Guek-Hong Low, Yee-Joo Tan & Antonio Bertoletti

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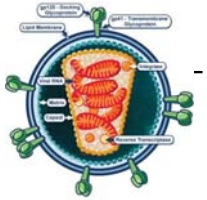
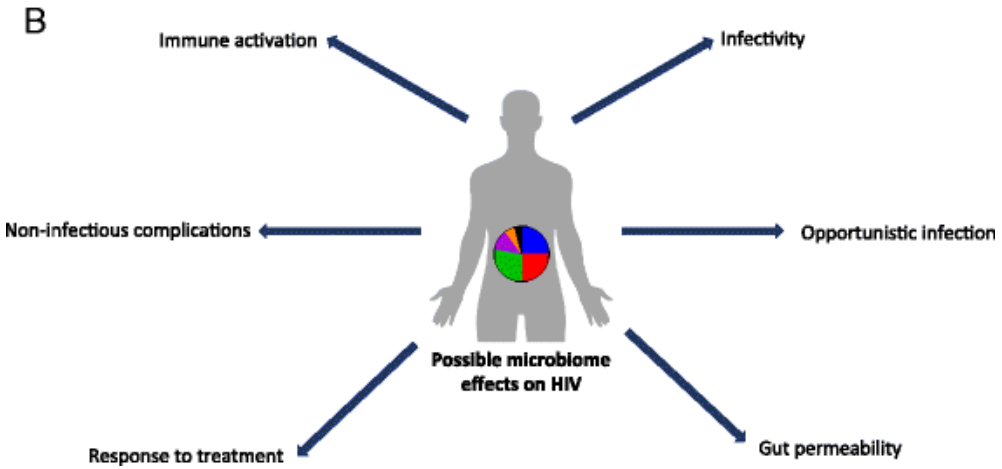
Role of the microbiome in modulating disease

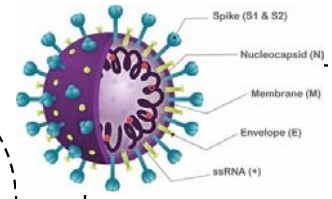


HIV

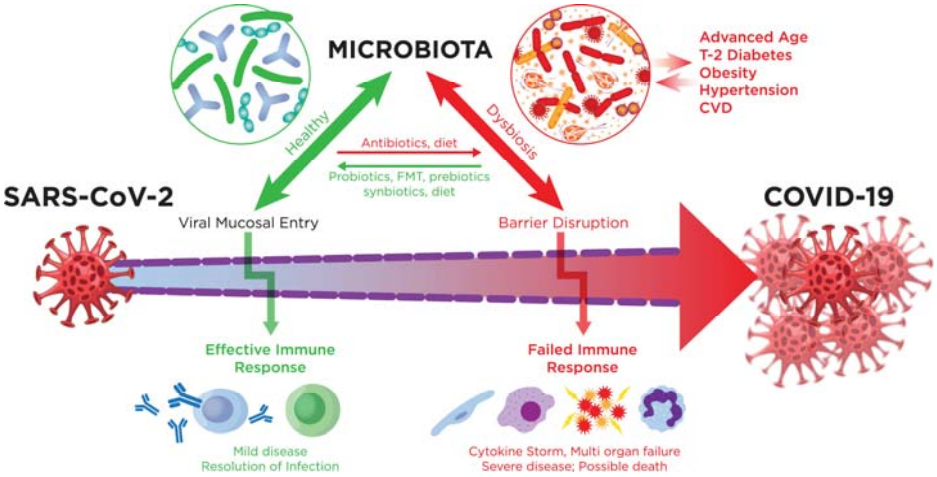


The gut microbiome in human immunodeficiency virus infection

Gili Zilberman-Schapira, Niv Zmora, Shlomik Itav, Stavros Bashiardes, Hila Elinav & Eran Elinav



SARS-CoV-2



Is Gut Microbiota Dysbiosis a Predictor of Increased Susceptibility to Poor Outcome of COVID-19 Patients? An Update

by Carolina Ferreira [1,2,3], Sofia D. Viana [1,2,3,4] and Flávio Reis [1,2,3,*]

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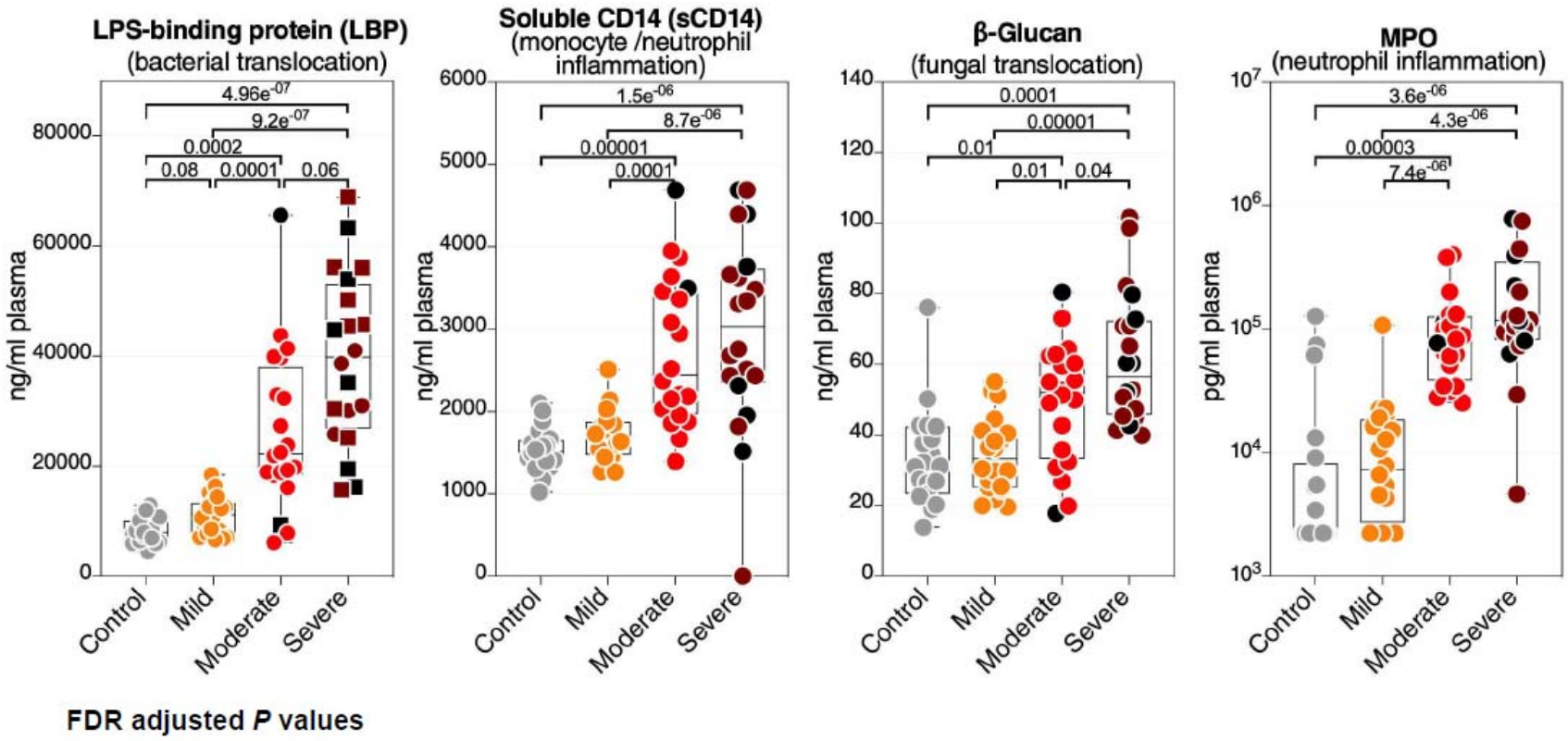
The role for the metagenome in the pathogenesis of COVID-19

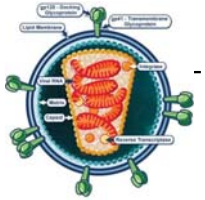
Robert P Friedland • Bodduluri Haribabu

Severe COVID-19 is Associated with Markers of Disrupted Gut Functions

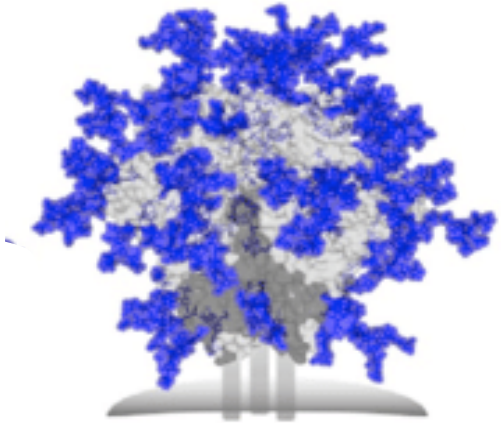


Giron LB CROI 2021 #114

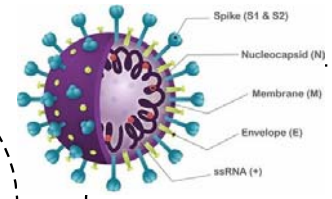
Equivalent level of glycan occlusion



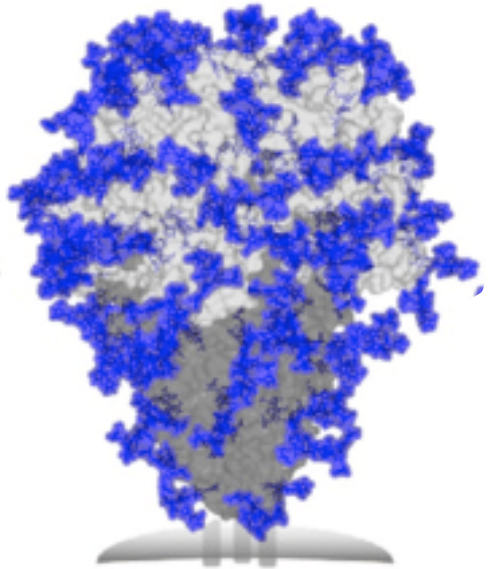
HIV



HIV-1 Env



SARS-CoV-2



Coronavirus
S protein

Exploitation of glycosylation in enveloped virus pathobiology

Yasunori Watanabe [a, b, c], Thomas A. Bowden [b], Ian A. Wilson [d, e], Max Crispin [a]

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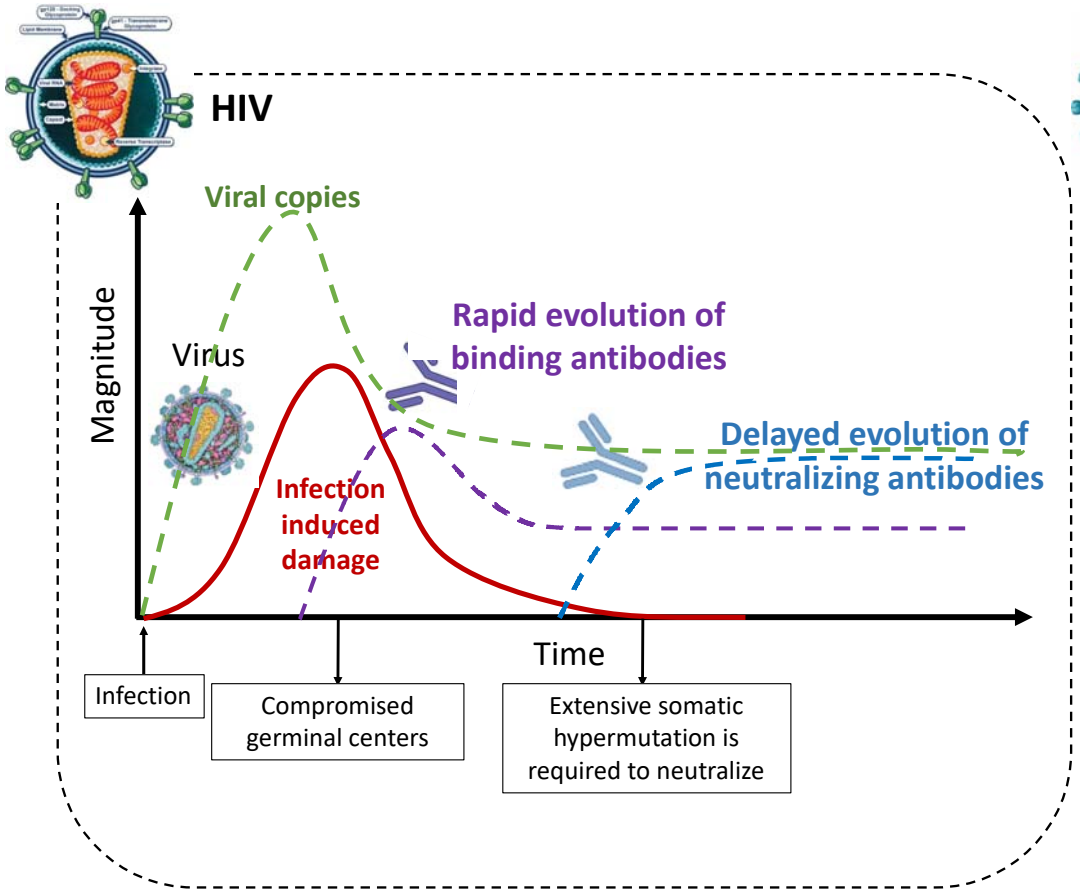
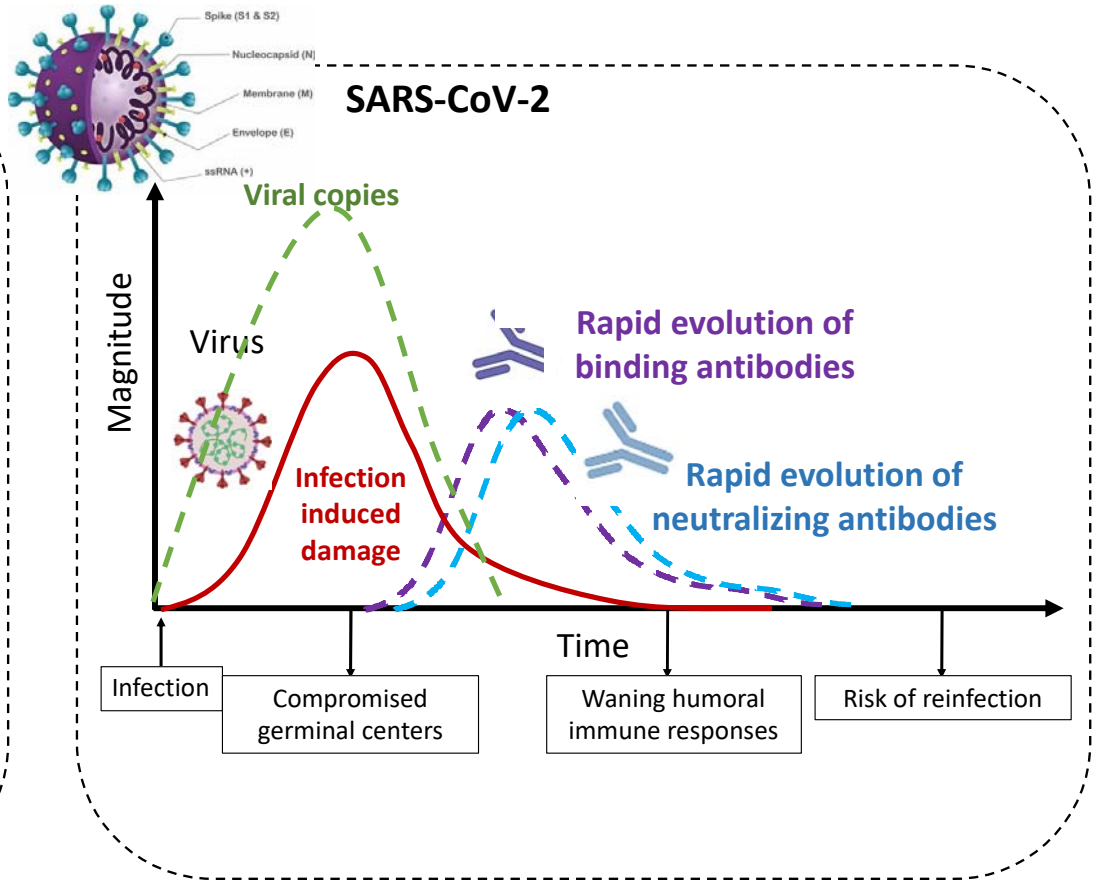
Evolution of antibodies





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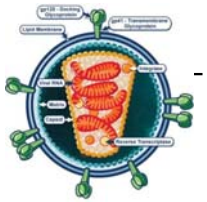
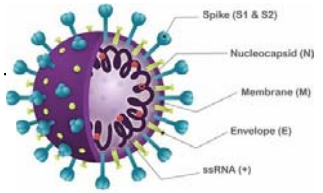
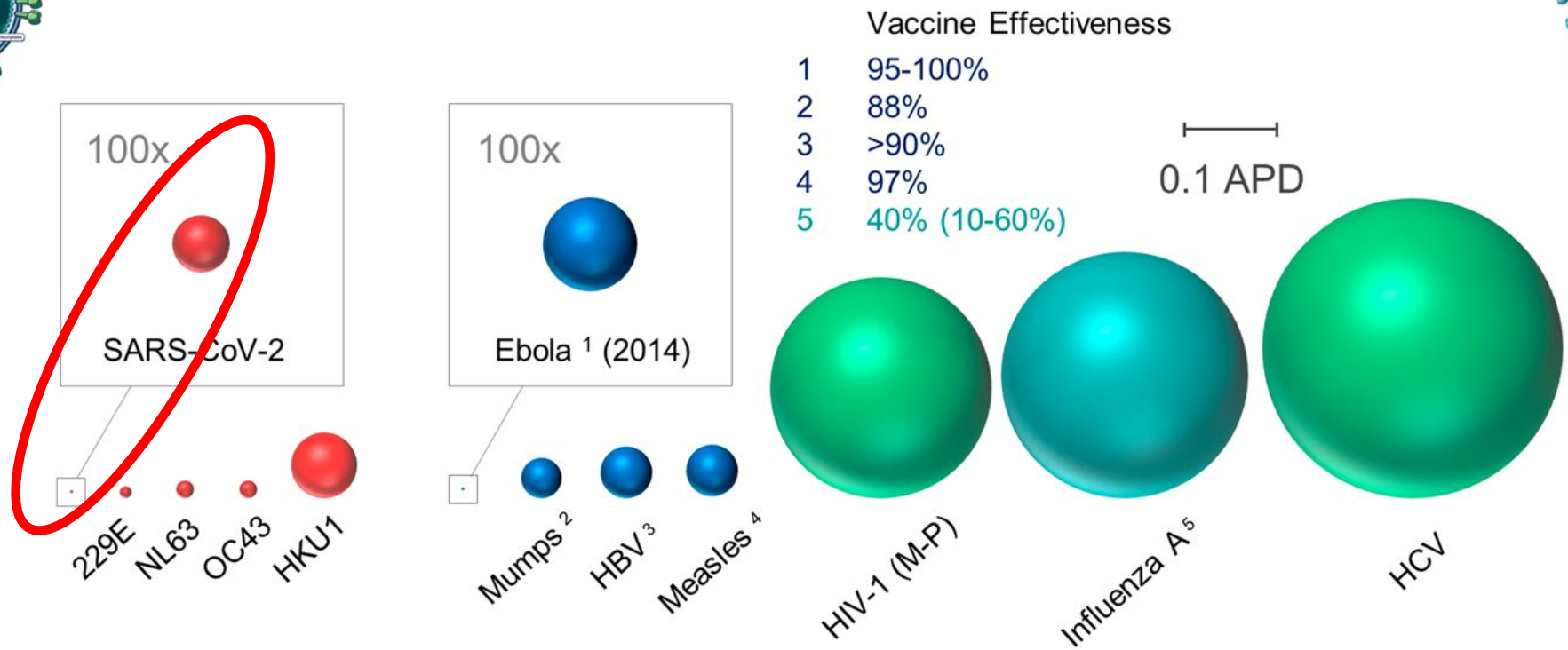
But massive differences in mutational rates







Low genetic diversity may be an Achilles heel of SARS-CoV-2

Jason W. Rausch, Adam A. Capoferri, Mary Grace Katusiime, Sean C. Patro, and Mary F. Kearney

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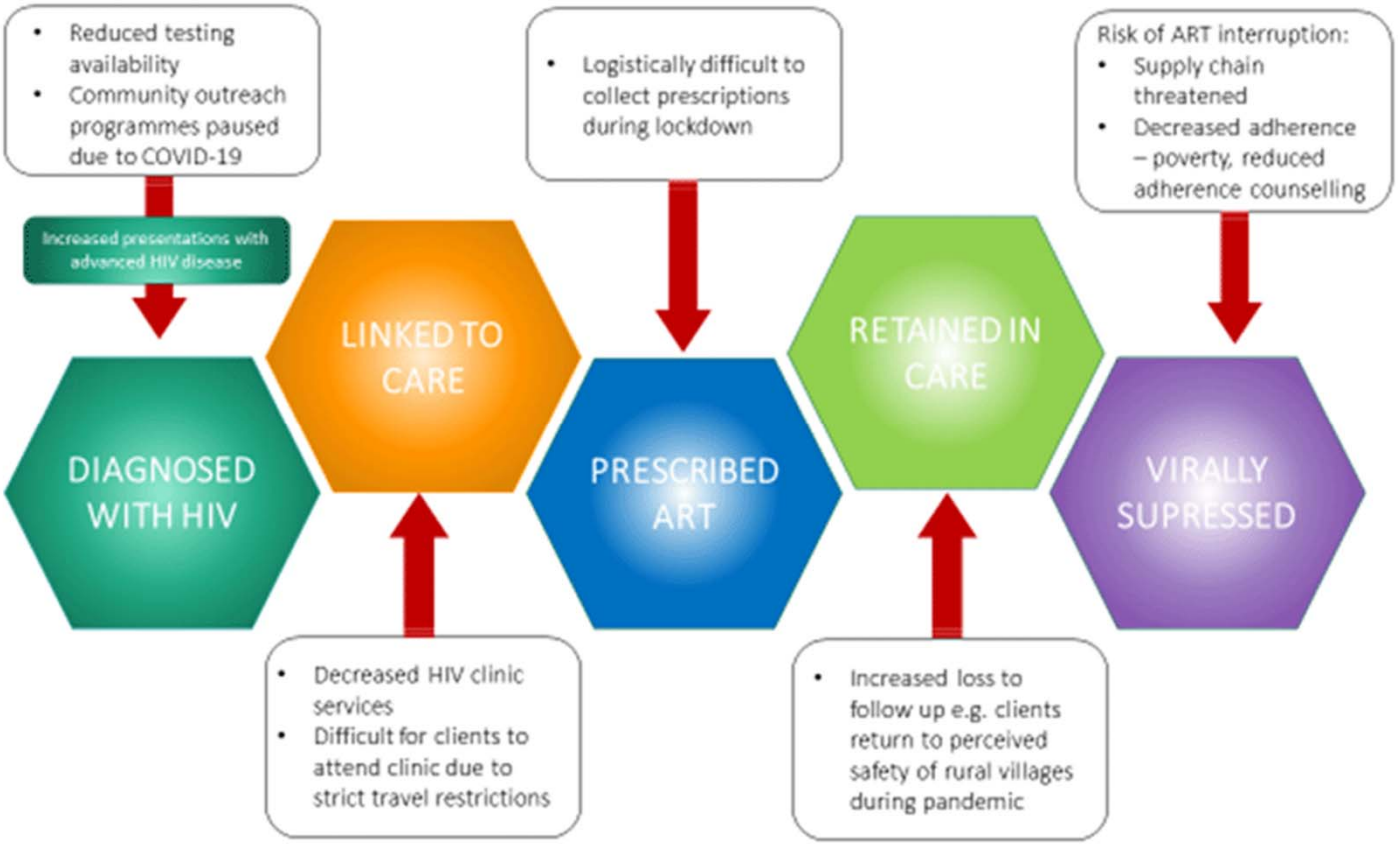
Specifics COVID-19 Disruptions in the HIV Cascade



→ In Africa, a 10% increase in deaths over 5 years compared to scenario without COVID-19!

Kambugu, CROI 2021; Kagimu E et al: AAS Open Research 2020, 3:28; Hogab A B et al: Lancet Glob Health 2020; 8: e1132–41

Impact of COVID-19 on HIV Care & Prevention in San Francisco, CA

Background & Methods

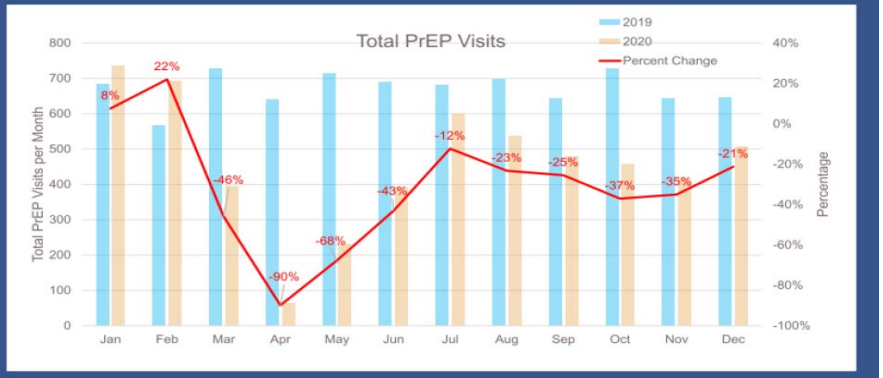
Background

- The COVID-19 pandemic has resulted in a disruptions in HIV prevention and care services throughout the US
- We sought to evaluate the impact of the COVID-19 pandemic on these metrics year-over-year in 2019 and 2020

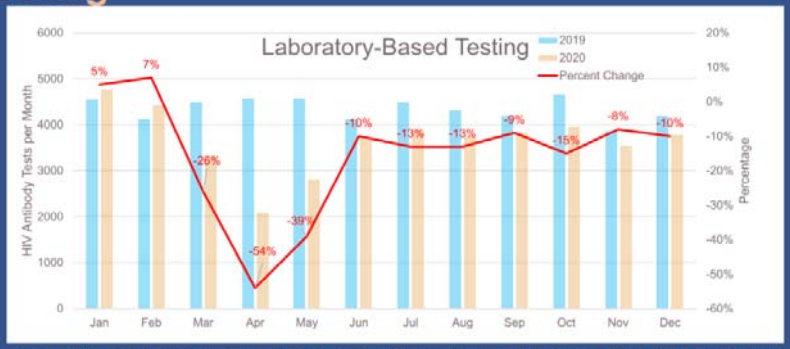
Methods

- We evaluated the following HIV prevention and care metrics in 2019 and 2020:
  1. HIV antibody/antigen tests from 4 laboratories and a large CTS
  2. Linkage to care and viral suppression among new diagnoses
  3. PrEP visits at the large CTS
  4. HIV viral load testing from 12 laboratories

HIV Prevention Indicator – PrEP Visits



HIV Prevention Indicator – Laboratory HIV Testing



- Proportion HIV positive remained stable (2020: Range 0.9-1.4%; 2019: Range 1.1-1.6%)
- New HIV Diagnoses: 75 from Jan-Jun 2020; 101 Jan-Jun 2019
- Linkage to care within 1 month was 93% in 2020 and 97% in 2019

HIV Care Indicator – HIV Viral Load

- Viral suppression within 6 months of diagnosis: 75% Jan-Jun 2020; 76% Jan-Jun 2019.

Scott CROI21 #730 & #729-752

Structured COVID-19 Mitigation Approach

Kambugu, CROI 2021; Kagimu E et al: AAS Open Research 2020, 3:28; CROI21 #729-752

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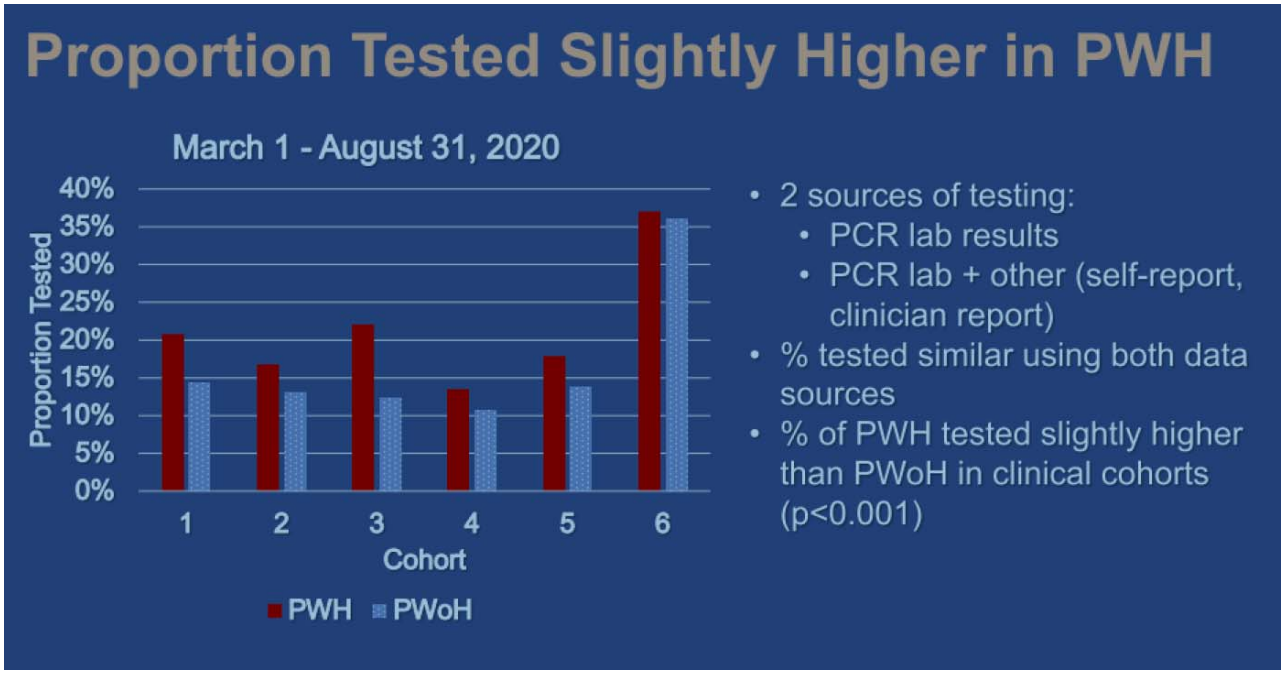
March 16th 2021

Proportion of SARS-CoV2 PCRs Higher in PLHIV in Six US Cohorts



Outcomes	PWH, N (%)	Non-PWH, N (%)	Tested aOR* (95% CI)	Positive aOR* (95% CI)
At risk patients	3,609	235,609		
Total Tested	1,232 (34%)[a]	22,483 (10%)[a]		
Diagnosis	104 (8%)[b]	603 (3%)[b]	3.41 (2.65, 4.39)	

- **Similar SARS-CoV-2 PCR positivity rates** in PLHIV and in the general population in the six cohorts.

- **Estimated cumulative incidence COVID-19 diagnosis (95%CI):**
  - PLHIV: 2.88% (2.34 to 3.43)
  - Non-PLHIV: 0.26% (0.24 to 0.28)

Park on behalh CIVET coolaboration within NA-ACCORD. CROI 2021 #626; Tang. CROI 2021; #542

Covid-19 Hospitalization among people with HIV or SOT in the USA

OUTCOMES	Overall	HIV- / SOT-	HIV+ only	SOT+ only	HIV+ / SOT+
Total, N	N=509,092	N=501,416	**N=2,932**	N=4,633	**N=111**
Hospitalization, N (%)	157,765 (31)	153,310 (30.6)	**1,421 (48.5)**	2,956 (63.8)	**78 (70.3)**
Invasive ventilation, N (%)	10,300 (2)	9,659 (1.9)	**162 (5.5)**	460 (9.9)	**≤20**

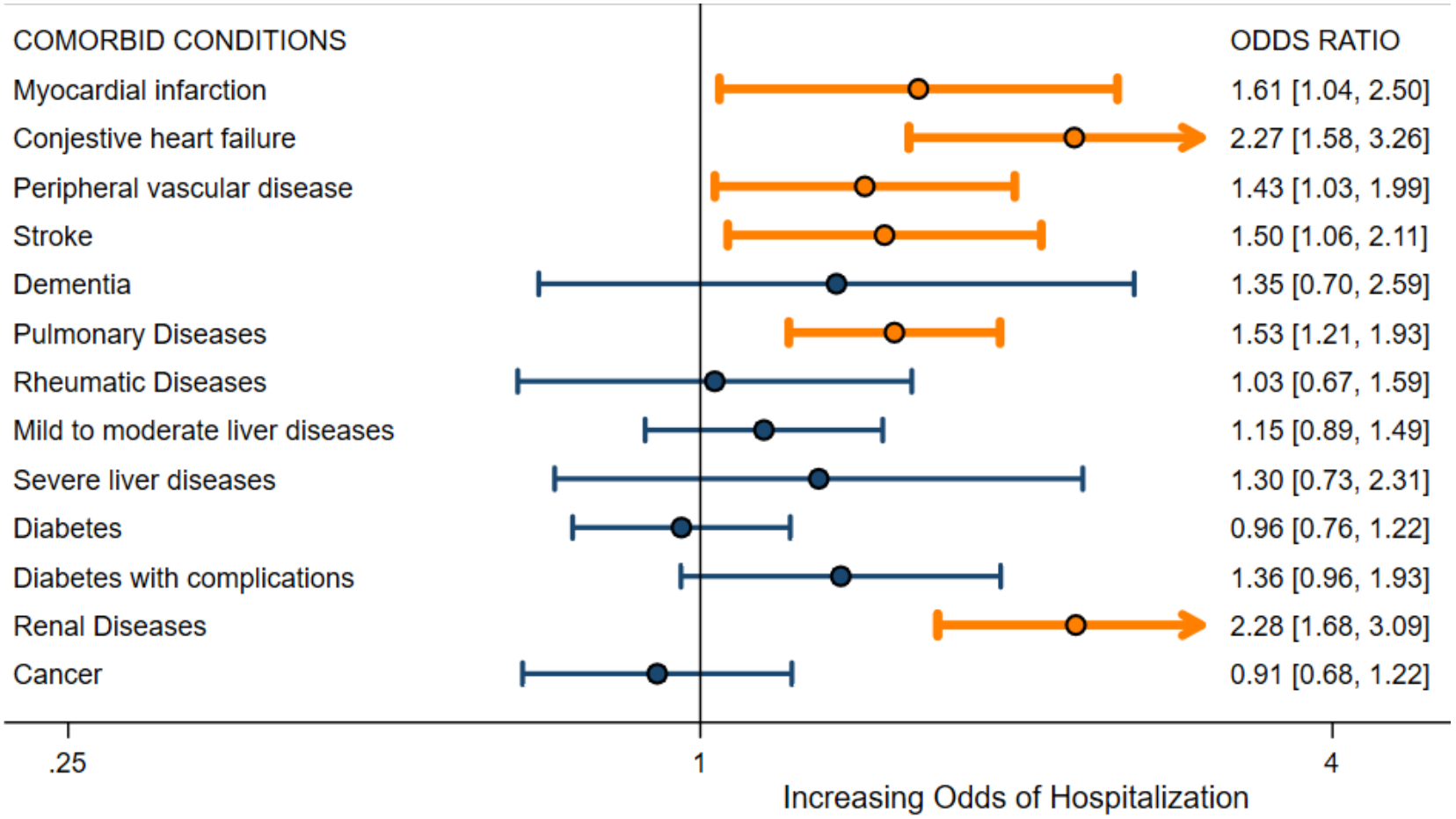
Odds of hospitalization

Immunosuppression groups	Crude estimates		Adjusted estimates [a]		Adjusted estimates [b]	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
HIV- / SOT- (N=501,416)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
HIV+ alone (N=2,932)	**2.14 (1.99, 2.30)**	**<0.01**	**1.63 (1.5, 1.76)**	**<0.01**	**1.32 (1.22, 1.43)**	**<0.01**
SOT+ alone (N=4,633)	4.00 (3.77, 4.25)	<0.01	3.07 (2.88, 3.27)	<0.01	1.69 (1.58, 1.81)	<0.01
HIV+ / SOT+ (N=111)	**5.37 (3.57, 8.06)**	**<0.01**	**3.50 (2.27, 5.42)**	**<0.01**	**1.65 (1.06, 2.56)**	**0.03**

Sun CROI 2021 #103

Covid-19 Hospitalization among people with HIV or SOT in the USA

Risk of hospitalization by comorbidities among PLHIV



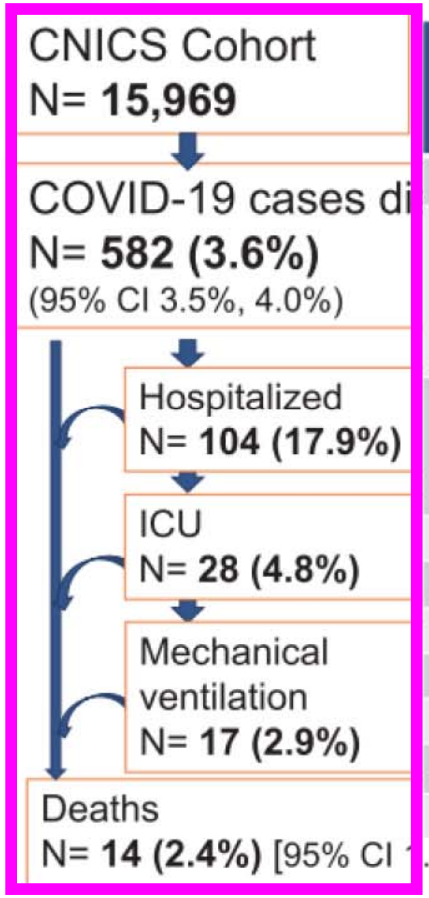
- PLHIV with history of cardiopulmonary or renal diseases had higher odds of hospitalization with COVID-19

- Associations were independent of demographics, study sites, and number of comorbidities.

Sun CROI 2021 #103

Risk Factors for Hospitalization in 582 PLHIV with COVID-19 in USA

COVID-19 in the CNICS cohort



	Total Cohort N=15,969	COVID-19 Case 582 (3.6%)	p-value	Adjusted RR	95% CI	p-value
Female	3,336 (20.9%)	164 (28.2%)	<0.001	1.41	1.19, 1.68	<0.001
Age <30	898 (6.1%)	46 (7.9%)	0.19	aRR (≥60 vs. <60)		
30-39	2,625 (18.0%)	107 (18.5%)				
40-49	2,975 (20.4%)	127 (21.9%)				
50-59	4,739 (32.4%)	182 (31.4%)				
≥ 60	3,377 (23.1%)	118 (20.3%)		0.89	0.73, 1.09	0.26
Race/ethnicity Black	7,095 **(44.4%)**	280 **(48.1%)**	<0.001	aRR (Black vs non-Black)		
White	6,077 (38.1%)	151 (26.0%)				
Hispanic	1,991 **(12.5%)**	125 **(21.5%)**				
Other	806 (5.1%)	26 (4.5%)		1.04	0.89, 1.22	0.62
Current ART	13,912 (95.2%)	554 (95.4%)	0.85	1.02	0.70, 1.49	0.93
Undetectable VL	13,598 (85.4%)	496 (85.7%)	0.86	1.10	0.87, 1.39	0.42
CD4+ count <350	2,754 (17.4%)	100 (17.3%)	0.97	1.04	0.84, 1.28	0.71
HCV	2,511 (15.8%)	81 (14.8%)	0.51	1.05	0.84, 1.32	0.66
Diabetes	2,995 (18.8%)	2,853 (18.5%)	<0.001	1.25	1.04, 1.51	0.016
eGFR <60	2,055 (12.9%)	80 (13.8%)	0.49	0.92	0.73, 1.17	0.50
BMI ≥ 30	4,865 (32.1%)	256 (45.6%)	<0.001	1.5	1.27, 1.76	<0.001

CFAR Network Of Integrated Clinical Systems

Shapiro on behalf CNICS cohort. CROI 2021 #543

Risk Factors for Hospitalization in 582 PLHIV with COVID-19 in USA

Predictors of hospitalization for PWH with COVID-19

Characteristic	Total COVID-19	Not Hospitalized	Hospitalized	aRR (95% CI)	p-value
	N = 582	N = 478 (82.1%)	N= 104 (17.9%)		
Female	164 (28.2%)	126 (26.4%)	38 (36.5%)	1.23 (0.86, 1.76)	0.25
Age ≥ 60	118 (20.3%)	82 (17.2%)	**36 (34.6%)**	**1.78 (1.25, 2.54)**	**0.001**
Black vs. non-Black	280 (48.1%)	220 (46.0%)	60 (57.7%)	1.24 (0.88, 1.74)	0.23
CD4+ ≤ 350	100 (17.3%)	66 (13.9%)	**34 (33.0%)**	**2.29 (1.63, 3.22)**	**<0.001**
On ART	554 (95.4%)	454 (95.2%)	100 (96.2%)	--	
Undetectable VL	496 (85.7%)	410 (86.3%)	86 (82.7%)	0.75 (0.48, 1.16)	0.19
Hepatitis C	81 (14.8%)	61 (13.5%)	**20 (20.8%)**	**1.53 (1.04, 2.25)**	**0.03**
ASCVD risk score, median (IQR)	5.5% (2.1%-13.0%)	5.0% (1.9%-12.1%)	**9.4% (3.8%-18.3%)**	**Per 10% increase: 1.41 (1.25, 1.60)**	**<0.001**
Diabetes	142 (26.0%)	101 (22.4%)	**41 (42.7%)**	**1.45 (1.02, 2.06)**	**0.038**
Anti-hypertensive use	225 (41.0%)	166 (36.6%)	**59 (61.5%)**	**1.69 (1.17, 2.42)**	**0.005**
eGFR < 60	80 (13.8%)	47 (9.9%)	**33 (31.7%)**	**2.28 (1.61, 3.24)**	**<0.001**
BMI ≥ 30	256 (45.6%)	196 (42.5%)	60 (59.4%)	1.32 (0.92-1.89)	0.126
COPD	39 (7.1%)	27 (6.0%)	12 (12.5%)	1.61 (0.98, 2.65)	0.062

Shapiro on behalf CNICS cohort. CROI 2021 #543

Risk Factors for Hospitalization in 94 PLHIV with COVID-19 in USA

Characteristics	N=94 (100%)
Male*	76 (81)
Mean age	46 years (SD 13.5)
Race/Ethnicity	
White/Caucasian	43 (46)
Hispanic/Latin-X	32 (34)
Black/African American	18 (19)
Average Length of Stay	10 days (SD 16.9)
HIV-1 RNA levels ≤200 copies/mL	79 (84)
CD4 count >500 cells/mm^3	50 (53)
≥1 comorbidity	71 (76)
Diabetes	15 (16)
Hypertension	25 (27)
Chronic kidney disease	13 (14)
Chronic pulmonary disease	9 (10)
Cardiac disease	6 (6)
Mental health	40 (43)
Obesity/morbid obesity	21 (22)
BMI ≥ 26	59 (63)
Tobacco use	
Current smoker	15 (16)
Former smoker	24 (26)
Never smoker	55 (59)
Admitted to the hospital	36 (38)
Admitted to ICU	6 (6)

Results

Univariate Analysis for Odds of Hospitalization

Model	OR (95% CI)
Age	**1.54 (1.09, 2.17)**
CD4 Count (cells/mm^3)	**1.32 (1.11, 1.56)**
Comorbidity Count	**1.77 (1.23, 2.56)**
Sex (female vs male)	1.03 (0.36, 2.96)
Primary language (English vs other)	1.97 (0.64, 6.05)
Race (White vs other)	2.30 (0.97, 5.45)
BMI (≥ 26 vs other)	0.66 (0.28, 1.58)
HIV-1 RNA (>200 vs ≤200 copies/mL)	2.55 (0.74, 8.78)
Tobacco use (current vs former/never smoker)	0.74 (0.23, 2.38)

*Gender as documented in the EMR which may not be up to date or accurate

- Length of stay was correlated with age

Barbera CROI 2021 #546

Risk Factors for Hospitalization in 180 PLHIV with COVID-19 in USA

N=180
Mean age: 49 years
Gender: 78% cisgender male, 20% cisgender female, 2% transgender female
Race/ethnicity: 78% Black, 14% Hispanic/Latinx

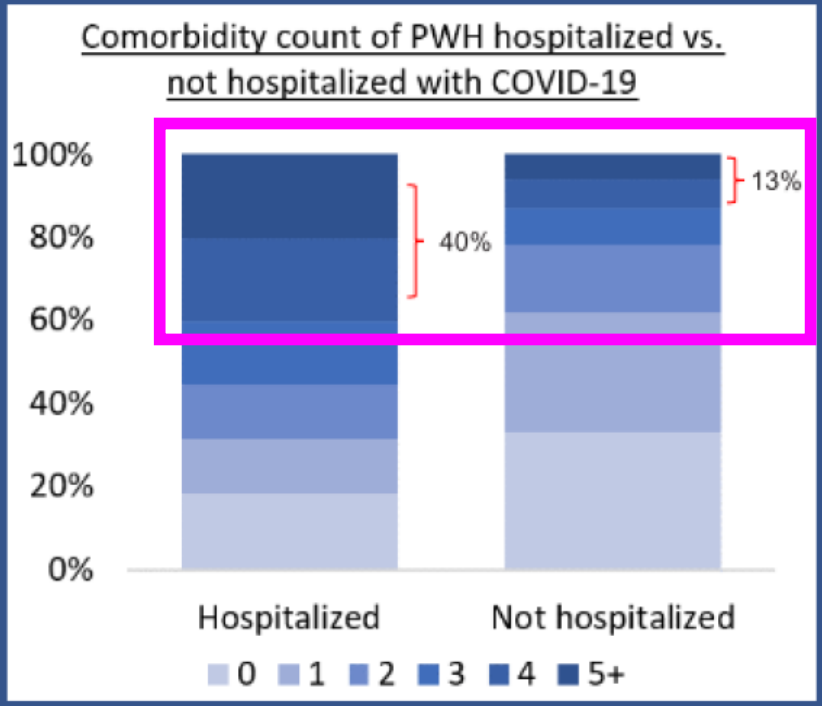
HIV Characteristics:

On ART: 97%
HIV-1 RNA <200 cop/ml: 91%
Mean CD4 count: 527 cells/ mm^3

Non-AIDS comorbidities (NACM):

≥1 NACM: 130 (72%)
≥4 NACM: 40 (22%)

Outcomes:
Hospitalization: 60 (33%)
Overall Mortality: 1.63%
Hospitalized mortality: 5%



Most prevalent comorbidities: hypertension (46%), dyslipidemia (34%), obesity (31%), diabetes mellitus (22%)

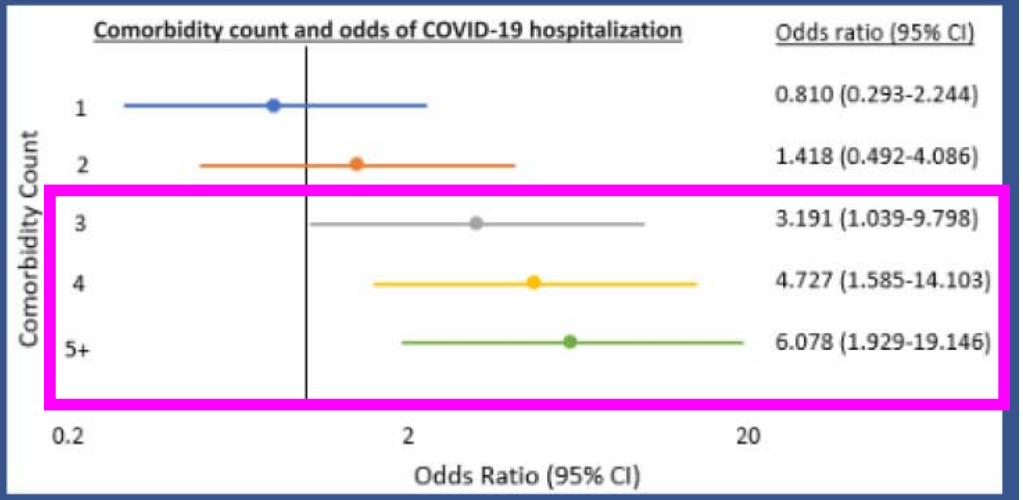
Moran CROI 2021 #547

Risk Factors for Hospitalization in 180 PLHIV with COVID-19 in USA

Table. Association of baseline characteristics with COVID-19 hospitalization among PWH

Characteristic	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
Age	**1.08 (1.05-1.11)**	**1.07 (1.04-1.11)**
Cisgender female (vs. cisgender male)	1.34 (0.63-2.87)	
Black race (vs. white)	0.96 (0.27-3.35)	
Site (VA vs. safety net)	2.32 (1.16-4.62)	1.44 (0.64-3.26)
Current smoking	0.69 (0.31-1.54)	
Hypertension	2.33 (1.24-4.39)	0.78 (0.33-1.85)
Dyslipidemia	2.47 (1.29-4.70)	0.77 (0.30-1.95)
Diabetes mellitus	**3.77 (1.81-7.82)**	**2.65 (1.03-6.85)**
Obesity	1.15 (0.59-2.24)	
Heart disease	3.30 (1.41-7.74)	2.02 (0.71-6.85)
Chronic kidney disease	2.55 (1.16-5.59)	0.99 (0.36-2.75)
Asthma/COPD	1.79 (0.58-5.60)	
Any antiretroviral therapy use	0.24 (0.04-1.33)	
Tenofovir use	0.50 (0.25-0.99)	0.51 (0.22-1.16)
CD4 count (<200 vs ≥200)	1.69 (0.63-4.54)	
HIV viral load (detectable vs. undetectable)	0.70 (0.25-1.93)	

*For age, site, hypertension, dyslipidemia, diabetes mellitus, heart disease, chronic kidney disease, and tenofovir use

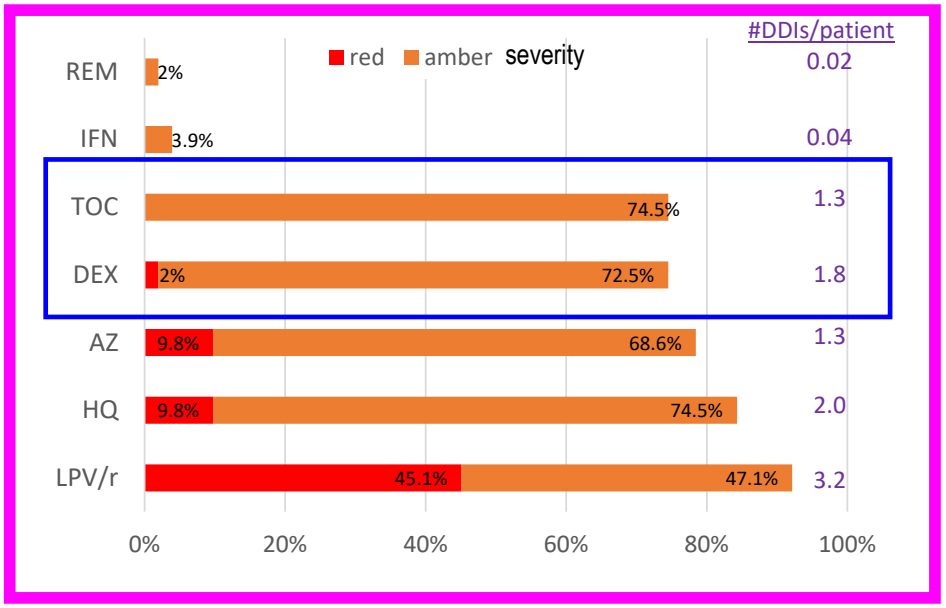


- Age-adjusted OR (95% CI) of each additional comorbidity with COVID-19 hospitalization: 1.25 (1.01-1.53)
- No association with hospitalization and HIV parameters when analysis was restricted to CD4 <200 or HIV RNA ≥200

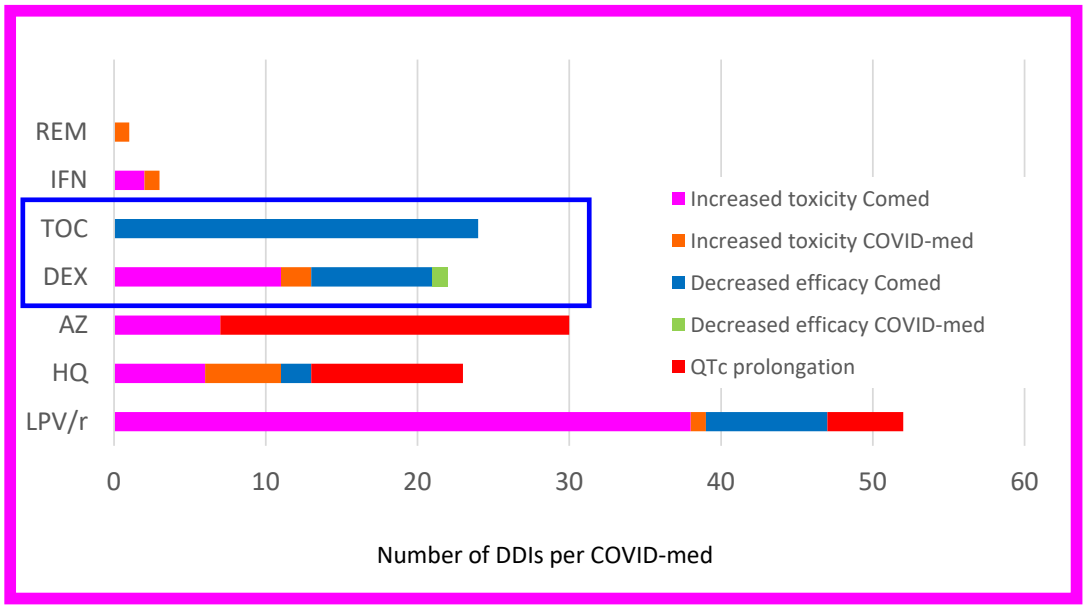
Moran CROI 2021 #547

Potential Drug-Drug Interactions in Hospitalized Covid-19 Patients in Canada (CATCO-DDI)

Proportion of patients with potential COVID-med/comed DDIs



Potential clinical impact of COVID-med/comed DDIs



DDIs with potential clinical impact:

- Increased comedication toxicity (LPV/r, **DEX,** AZT, HCQ)
  → Psychotropics, anticoagulants/antiplatelets
- Decreased comedication efficacy (**TOC, DEX**, LPVr, HCQ)
- QTc prolongation (AZT, HCQ).

Tseng CROI 2021 #372

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March 16th 2021

Prognosis of COVID-19 in PLHIV in Western countries

Country	Author (# Poster)	N. Cases/Controls	Outcomes
Italy	Gagliardini (#545)	31/1,044	• Less severe disease • No worse outcome
USA	Yendewa (#548LB)	1,638/295,556	• More severe disease • No worse outcome
USA	Tang (#542)	3,609/235,609	• Increased risk of diagnosis • No worse outcome
Spain	Diez (#544)	21/105	• No more severe disease • No worse outcome
Spain	**Blanco (#641LB)**	**204/204**	• **Worse outcome**

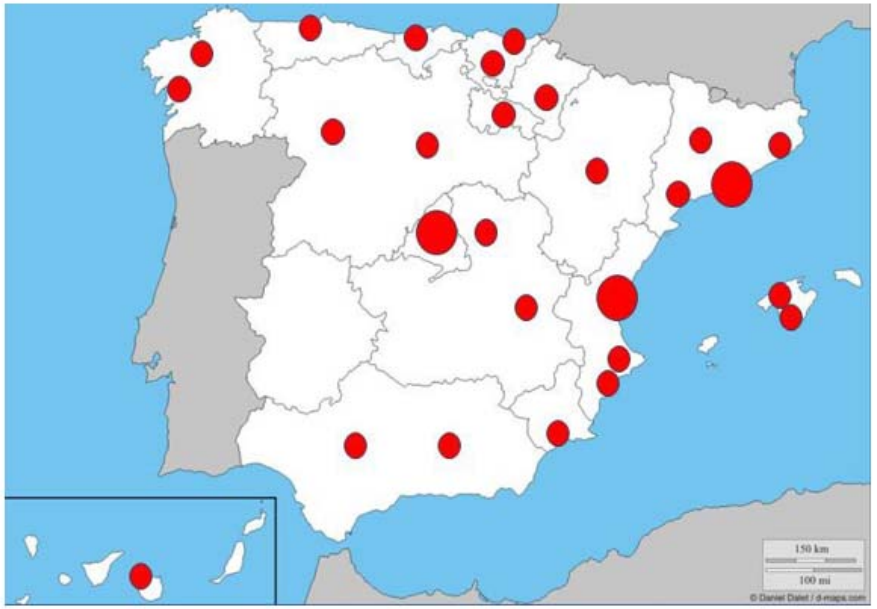
A Prospective Case-Cohort study of COVID-19 in PLHIV in Spain

Introduction

- Several large cohort studies have shown that **persons living with HIV (PWH) may have worse COVID-19 outcomes** than non-HIV-infected persons[1-6].
- Whether it may be due to a higher frequency of co-morbidities or to a direct HIV (e.g. viral load or CD4 counts) or ART effect is currently unclear[7].
- Advanced (e.g. >65 years) age is likely the strongest factor for worse outcomes in the general population[8], but the proportion of PLW with advanced age is small[9,10].

Methods: Centers

- **Nation-wide multicenter prospective case-cohort study**
- 39 Spanish centers



1. Hadi YB, *et al.* AIDS 2020 [Epub ahead of print]; 2. Karmen-Tuohy S, *et al.* J Acquir Immune Defic Syndr 2020 [Epub ahead of print]; 3. Boulle A, *et al.* Clin Infect Dis 2020 [Epub ahead of print]; 4. Geretti AM, *et al.* 2020 [Epub ahead of print]; 5. Bhaskaran K, *et al.* Lancet HIV 2021; 8: e24-e32; 6. Tesoriero JM, et al. JAMA Network Open 2021; 4: e2037069 7. Waters LJ, Pozniak AL. Lancet HIV 2021; 8: e2-e3 8. Berenguer J, *et al.* Clin Microbiol Infect 2020; 26: 1525-1536 9. National HIV surveillance data tables. In: https://www.gov.uk/government/statistics/hiv-annual-data-tables 10. HIV Monitoring Report 2020. In: https://www.hiv-monitoring.nl/application/files/7716/0571/6500/Netherlands_HIV_Monitoring_Report_2020.pdf .

Blanco CROI 2021 #641LB

A Prospective Case-Cohort study of COVID-19 in PLHIV in Spain

- **Consecutive COVID-19-confirmed PWH requiring hospital admission (cases)**
- Each case was **matched 1:1 to COVID-19-confirmed non-HIV-infected adults (controls)** for:
  - **Center**
  - **Calendar week (+5days)**
  - **Age (+/- 5 years)**
  - **Gender**
- **Clinical symptoms** & **laboratory parameters** at admission, and **co-morbidities** were collected:

Fever	Leukocytes/ Lymphocytes	Race
Cough	Haemoglobin	Tobacco
Anosmia/ageusia	Platelets	Alcohol
Headache	Creatinine	Hypertension
Nausea/vomiting	LDH	Diabetes
Diarrhea	AST/ALT	Cardiovascular disease
Abdominal pain	CRP/IL-6	Chronic kidney disease
Odinophagia	D-dimer	Chronic liver disease
Asthenia	Ferritin	COPD
Dyspnea	Procalcitonin	NON-HIV immune depression
	Troponin I	Neoplasia
		BMI

- **Informed consent** granted
- Principal outcome was **death**:
  - Contribution of HIV adjusted for comorbitities (whole population)
  - Contribution of immunological, virological, and antiretroviral factors (PWH cohort only)
- **Statistical analyses:**
  - Conditional logistic regression models
  - Mixed-effects logit regression models
  - Fine-Gray competing-risks regression models
  - Mutistate models

Blanco CROI 2021 #641LB

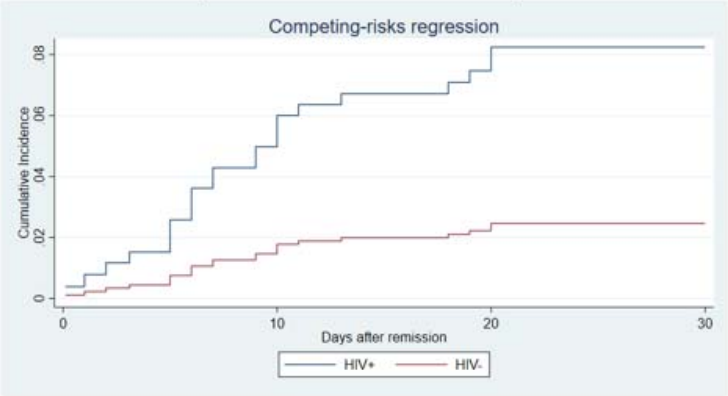
A Prospective Case-Cohort study of COVID-19 in PLHIV in Spain

- **From 26/Feb to 21/Sep 2020**, 204 cases and 204 controls were included:
  - Median (IQR) age **54 (47-60) years**
  - **85% were men**.
- **Among PWH:**
  - 33% prior AIDS events
  - Median (IQR) current CD4 cells/mm^3 521 (310-756)
  - 14% had CD4<200/mm^3
  - 90% HIV suppressed
  - Antiretrovirals: 17% NNRTI, 23% PI, 70% INSTI, 89% NRTI (6% TDF, 45% TAF, and 31% ABC)
- **Cases and controls significantly differed on:**
  - **Chronic liver disease** (aOR 8.7, 95%CI 1.5-50.0, P=0.0156)
  - **Cardiovascular disease** (aOR 2.09, 95%CI 1.19-3.68, P=0.0103)
  - **Obesity** (aOR 0.30, 95%CI 0.19-0.49, P<0.0001)

- **Twenty (9.8%) cases and 7 (3.4%) controls died.**
- **HIV infection** was associated with a **higher risk of death** after adjustment for chronic liver disease, cardiovascular disease, and obesity:

  aOR 5.27, 95%CI 1.00-27.72, P=0.0499
- **HIV infection** was associated with a higher incidence of death:

  subHR 3.45, 95%CI 1.47-8.11, P=0.0045



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A Prospective Case-Cohort study of COVID-19 in PLHIV in Spain

- **Factors associated with death in cases:**
  - **Age:** OR 1.12 (95%CI 1.07; 1.18) P<0.0001
  - **Hypertension:** OR 6.31 (95%CI 1.66-24.05) P=0.007
  - **Diabetes:** OR 4.39 (95%CI 1.39-13.80) P=0.011
  - **COPD:** OR 3.82 (95% 1.06-13.69) P=0.040
  - **Haemoglobin:** OR 0.95 (95%CI 0.92-0.98) P=0.0007
  - **CKD-EPI** (eGFR ≤90 mL/min/1.73 m²) OR 7.14 (95%CI 1.47-35.71) P=0.015

- **Factors associated with death in controls:**
  - **Age:** OR 1.09 (95%CI 1.01; 1.16) P=0.0213
  - **Neoplasia:** OR 34.68 (95%CI 4.99-241.12) P<0.0001

- **Adjusted logistic regression:**
  - **Cases:**
    Age: Adjusted OR 13.72 (95%CI 3.24; 58.03) P=0.0004
    COPD: Adjusted OR 4.06 (95%CI 1.26; 13.13) P=0.0192
  - **Controls:**
    Neoplasia: Adjusted OR 8.81 (95%CI 1.28; 60.44) P=0.0268

- **Not associated with death:**
  - Current CD4 count
  - Nadir CD4 count
  - Current CD4/CD8 ratio
  - Nadir CD4/CD8 ratio
  - Detectable HIV RNA
  - Specific antiretroviral agents (TDF, TAF)

CONCLUSIONS

-In this cohort of COVID-19 in-patients, risk of death was higher in PWH than in non-HIV-infected controls

-Several co-morbidities through increasing age, but not immunological, virological, or antiretroviral factors, were associated with a higher risk of death in PWH.

Blanco CROI 2021 #641LB

Long COVID-19 symptoms persists up to 6 mo. in NYC (N=570)

Characteristic	Initial Hospitalization N = 570 (%)	3 months N = 488 (%)	6 months N = 364 (%)	3 and 6 months N = 282 (%)
Cardiopulmonary Symptoms	**496 (87.0%)**	**174 (35.7%)**	**102 (28.0%)**	**37 (13.1%)**
Dyspnea	354 (62.1%)	108 (22.1%)	58 (15.9%)	28 (9.9%)
Generalized Symptoms	**468 (82.1%)**	**124 (25.4%)**	**96 (26.4%)**	**27 (9.6%)**
Fever	441 (77.4%)	42 (8.6%)	13 (3.6%)	3 (1.1%)
Fatigue	31 (5.4%)	44 (9.0%)	38 (10.4%)	7 (2.5%)
Myalgias or Arthralgias	164 (28.8%)	54 (11.1%)	64 (17.6%)	18 (6.4%)
Neuropsychiatric Symptoms	**112 (19.6%)**	**98 (20.1%)**	**88 (24.2%)**	**21 (7.4%)**
Weakness	21 (3.7%)	41 (8.4%)	34 (9.3%)	11 (3.9%)
Altered Mentation	32 (5.6%)	28 (5.7%)	20 (5.5%)	4 (1.4%)
Headache	62 (10.9%)	26 (5.3%)	21 (5.8%)	2 (0.7%)
Depression or Anxiety	0 (0%)	17 (3.5%)	18 (4.9%)	3 (1.1%)
Gait Instability	1 (0.2%)	9 (1.8%)	18 (4.9%)	3 (1.1%)
Gastrointestinal Symptoms	**239 (41.9%)**	**80 (16.4%)**	**75 (20.6%)**	**13 (4.6%)**

[1] Persistent symptoms = symptoms that did not resolve during each three-month follow-up period

Shoucri CROI 2021 #554

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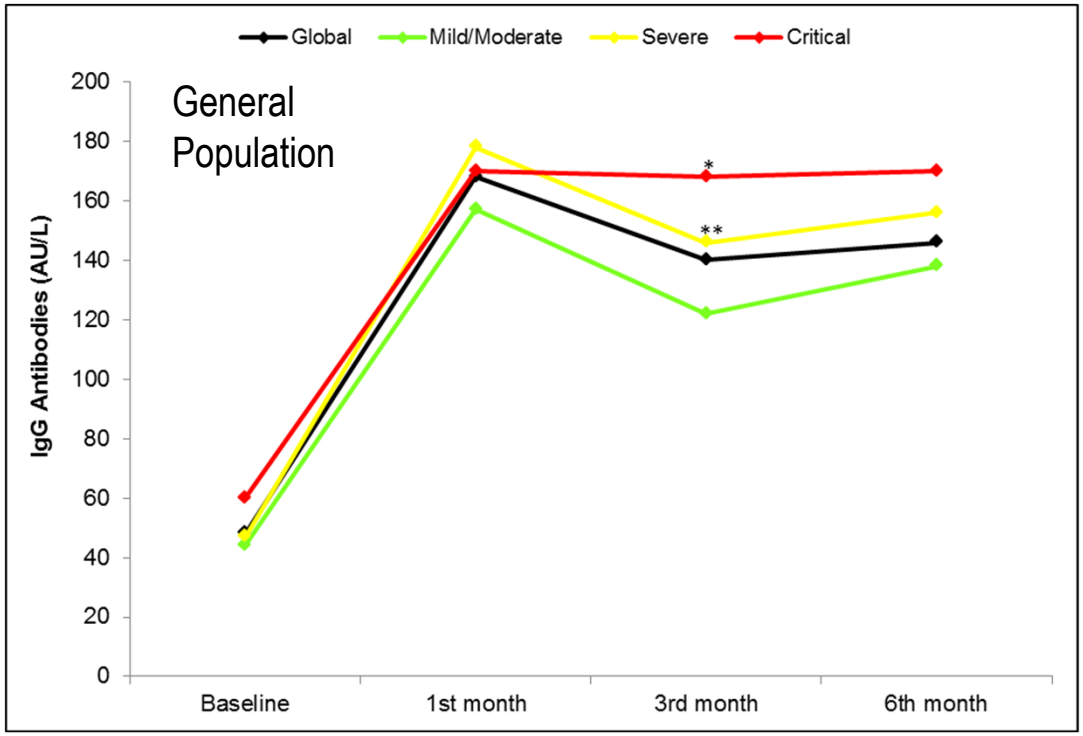
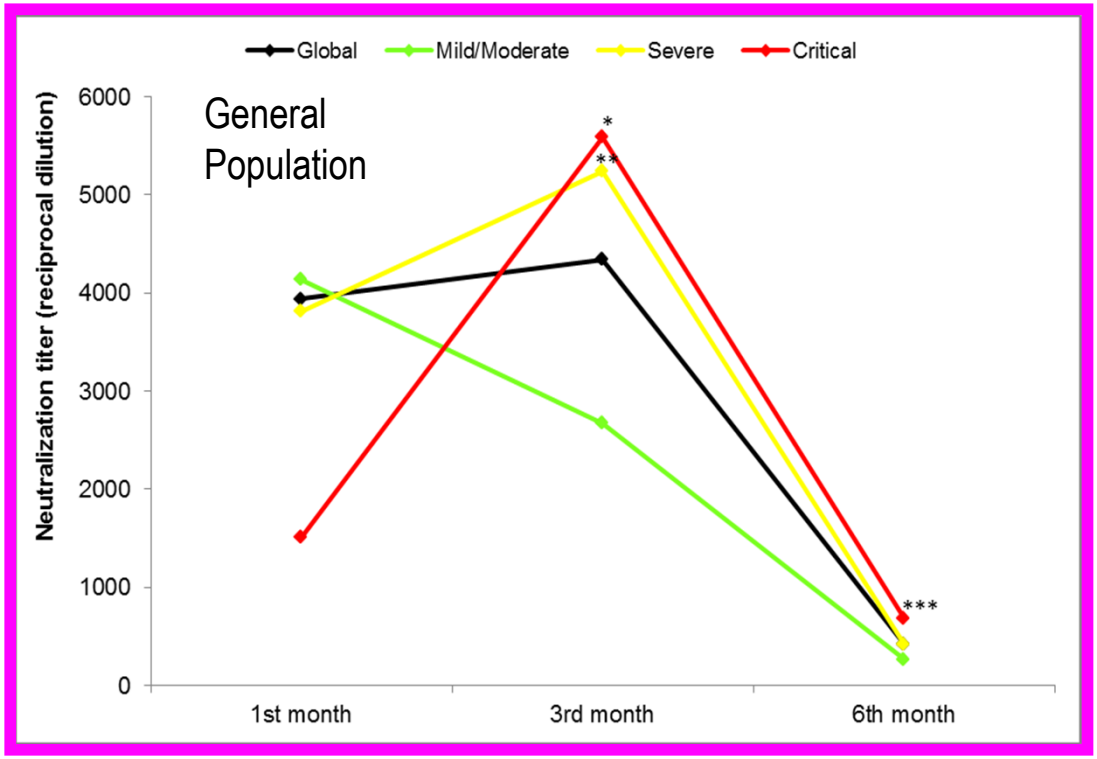
Neutralizing Antibody Responses after SARS-CoV-2 Infection at 6 mo. (Spain)

- No significant differences were observed in median IgG fold change values up to month 6 among severity groups.
- NAbs changes decreased at month 6 without differences among severity groups.



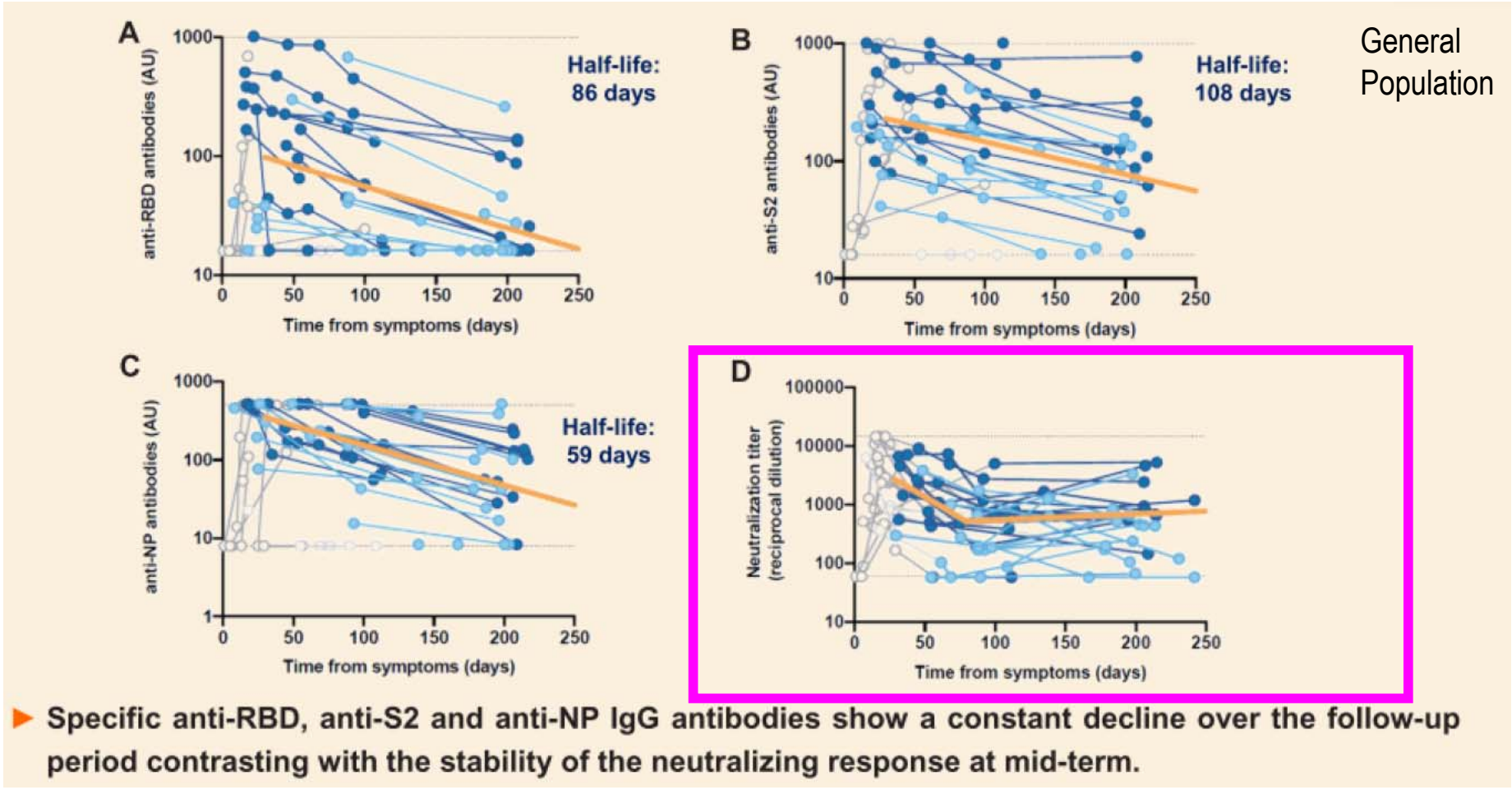
*: Significant differences between patients with mild/moderate and patients with critical signs (p=0.002)
**: Significant differences between patients with mild/moderate and patients with severe signs (p=0.002)
P: Mann-Whitney U test



*: Significant differences between patients with mild/moderate and patients with critical signs (p=0.002)
**: Significant differences between patients with mild/moderate and patients with severe signs (p=0.004)
***: Significant differences between patients with severe and patients with critical signs (p=0.035)
P: Mann-Whitney U test

Tiraboschi CROI 2021 #502

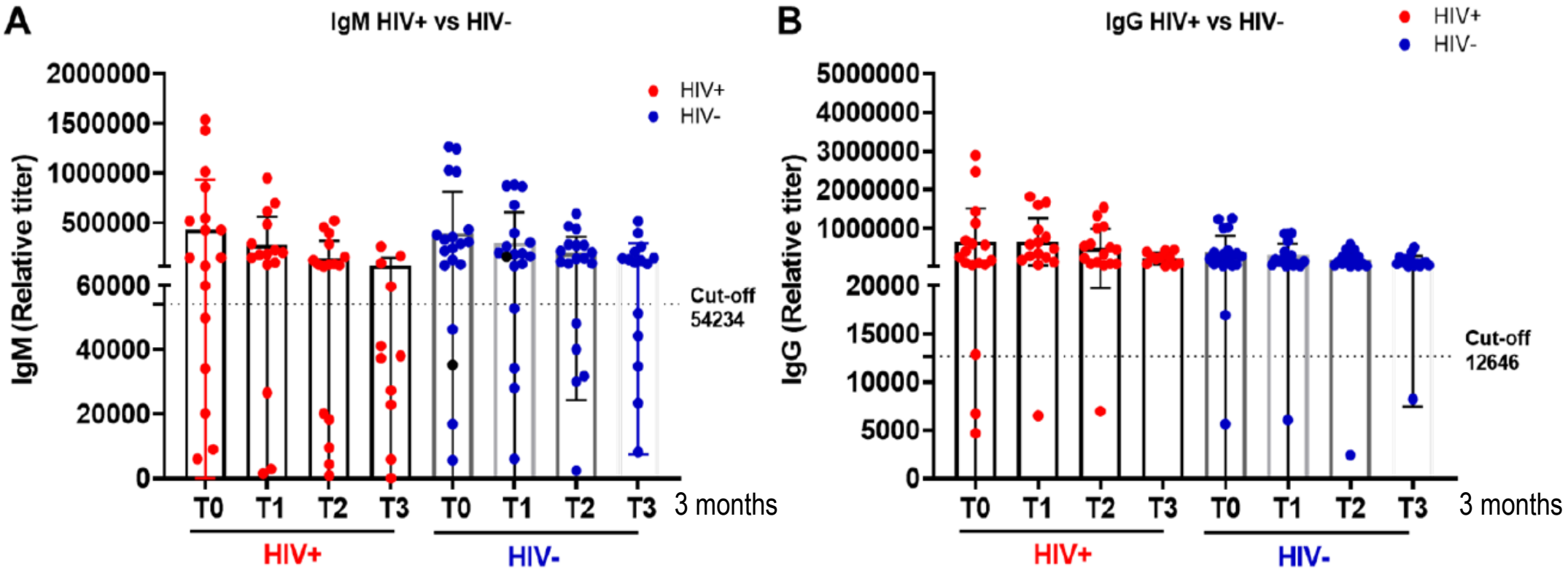
Stable Neutralizing-Antibody Levels 6 Months After Covid-19 at 6 mo. (Spain)



- Specific anti-RBD, anti-S2 and anti-NP IgG antibodies show a constant decline over the follow-up period contrasting with the stability of the neutralizing response at mid-term.

Pradenas CROI 2021 #259

RBD Specific IgM and IgG responses did not differ by HIV status in USA



- There was a trend of lower IgM/IgG responses at 3-months in both groups compared to entry level
- RBD specific IgM and IgG responses did not correlate with absolute CD4 count (data not shown)
- RBD specific IgG responses correlate with age

Pallikkuth CROI 2021 #260

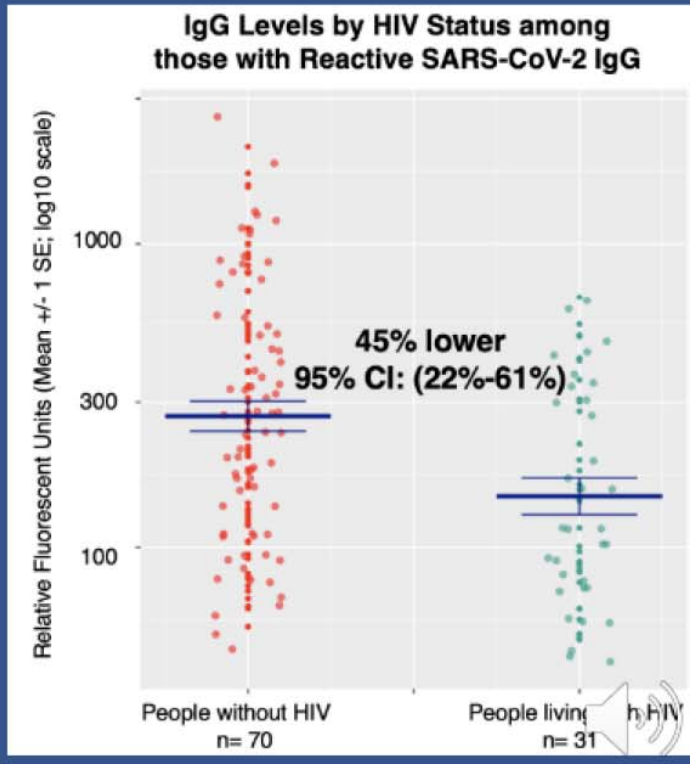
Lower IgG and neutralizing Ab levels inn PLHIV in USA

Results: Lower IgG Levels and Neutralizing Ab Titers among PLWH exposed to COVID-19

IgG Levels: 45% lower among PLWH vs. those without HIV with past infection (95% CI: 22%-61% lower)

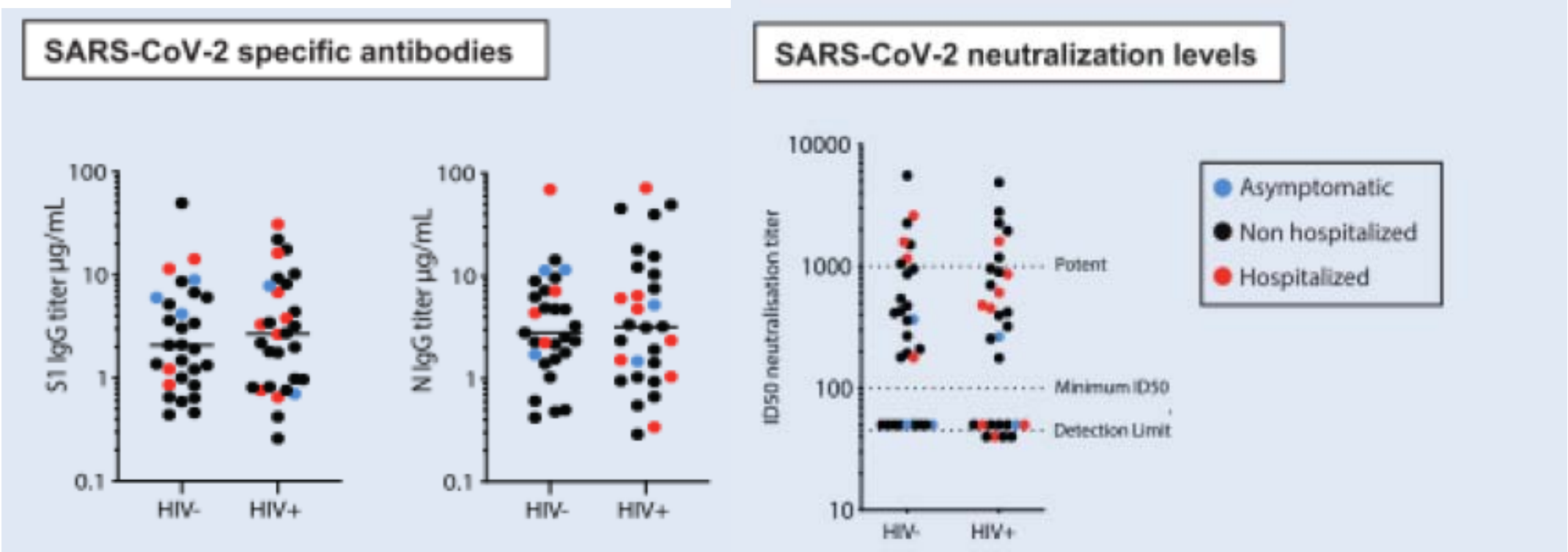
Neutralizing Ab titers: 63% lower among PLWH vs. those without HIV with past infection (95% CI: 2%-78% lower)

Avidity: No difference (+7.9%; 95% CI: -4%; +20%)



Spinelli CROI 2021 #627

RBD Specific IgM and IgG responses did not differ by HIV status in UK



- Memory responses were detected between **5-7 months post infection**.
- **Low CD4:CD8 ratio could impact SARS-CoV-2 immune responses**.
- These findings can have **implications for vaccination** against SARS-CoV-2 of PLWH.

Alrubayyi CROI 2021 #262LB

Prevalence and factors associated with SARS-CoV-2 antibodies in a Spanish HIV Cohort

- During the study period, blood samples were taken from 1,076/16,178 (6.7%) PWH in CoRIS
- **Seroprevalence = 8.5% (95%CI: 6.9% - 10.3%).** SARS-CoV-2 Ab were detected in 91/1,076 PWH.

Variables independently associated with COVID-19 seropositivity among 1,076 PWH

	Ab⁺/Total (%)	Crude OR (95% CI)	*P*	Adjusted OR (95% CI) †	*P*
Country of birth					
Spain	54/753 (7.2)	Ref		Ref	
Lat. Am. Countries	**33/231 (14.3)**	**2.16 (1.36; 3.42)**	**.001**	**2.34 (1.42; 3.85)**	**.001**
Other	4/91 (4.4)	0.60 (0.21; 1.68)	.328	0.64 (0.22; 1.88)	.419
Hypertension					
No	56/748 (7.5)	Ref		Ref	
Yes	**35/328 (10.7)**	**1.48 (0.95; 2.30)**	**.086**	**1.63 (1.00; 2.67)**	**.050**
NRTI ART backbone					
TAF/FTC	40/416 (9.6)	Ref		Ref	
TDF/FTC	**5/154 (3.2)**	**0.32 (0.12; 0.81)**	**.017**	**0.32 (0.12; 0.84)**	**.021**
ABC/3TC	23/279 (8.2)	0.84 (0.49; 1.44)	.537	0.86 (0.49; 1.50)	.588
Other	17/188 (9.0)	0.93 (0.52; 1.70)	.824	0.87 (0.46; 1.63)	.667
No ART	3/25 (12.0)	1.28 (0.37; 4.47)	.697	1.41 (0.37; 5.39)	.620

† Adjusted by sex at birth, age, mechanism of HIV acquisition, level of education, other comorbidities (chronic heart disease, diabetes, non-AIDS related cancer, chronic kidney disease, cirrhosis), prior AIDS-defining conditions, last CD4+ cell count, and last HIV-RNA detectability.

Berenguer CROI 2021 #549

CROI 2021 News on COVID-19 & HIV

- Current Epidemiology
- A tale of two viruses: HIV & SARS-CoV-2
- Impact of COVID-19 in health care systems
- Hospitalization risk in HIV-infected patients
- Prognosis in HIV-infected patients
- Humoral response in HIV-infected patients
- **Take-home messages**

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Take-home Messages

- COVID-19 has deeply disrupted the health care system in general and the HIV care in particular. Community engagement, strengthening the health care system with more investment and innovation and epidemic preparedness are the tools to overcome this pandemic.
- PLHIVs are screened more frequently than the general population but are not more infected. Hospital admission rates are higher and independent risk factors are age, comorbidities, and, in some studies, a low CD4 count (<350 cells/mm3).
- Most case-control studies conducted in Western countries have not shown that HIV-infected patients have a worse prognosis.
- In general, the IgG and IgM antibodies and neutralizing antibodies responses against the SARS-CoV-2 RBD of PLHIV do not differ from the general population.

Acknowledgements

Alter G
Berenguer J
Blanco JL
Coll O
Del Amo J
Kamburu A
To my colleagues
Moreno A
Rockstroh J
Sun S
Tang ME
Tiraboschi J
Tseng A
To our patients

CROI 2022 – February 13-16, 2022 – Denver, Colorado

THANKS A LOT!

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March 16th 2021