Pandemia e HIV: cosa abbiamo imparato ?

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Offline: COVID-19 is not a pandemic

Richard Horton **The Lancet Vol 396 September 26, 2020**

…..These conditions are clustering within social groups according to patterns of inequality deeply embedded in our societies. The aggregation of these diseases on a background of social and economic disparity exacerbates the adverse effects of each separate disease. ***COVID-19 is not a pandemic. It is a syndemic.*** *The syndemic nature of the threat we face means that a more nuanced approach is needed if we are to protect the health of our communities.*

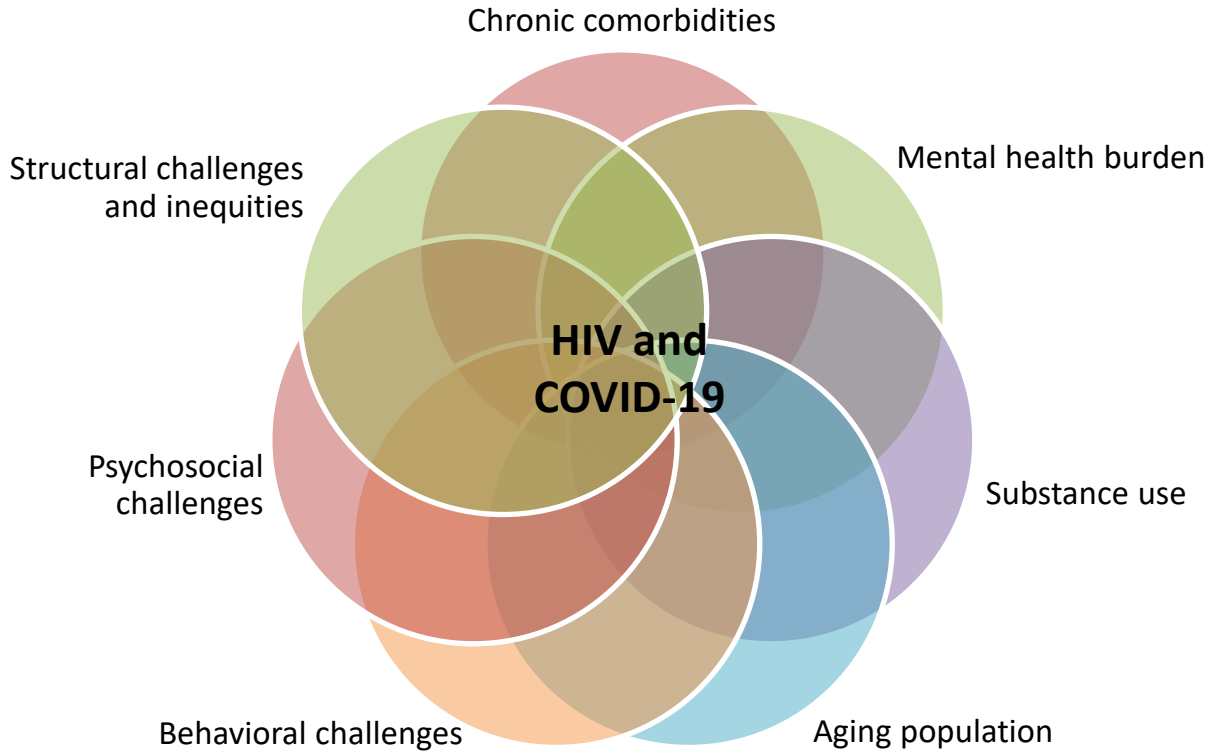
Offline: COVID-19 is not a pandemic

- The notion of a syndemic (from the greek συν and δήμος) was first conceived by Merrill Singer in the 1990s.
- **“a syndemic approach reveals biological and social interactions that are important for prognosis, treatment, and health policy.**
- Limiting the harm caused by SARS-CoV-2 will demand far greater attention to NCDs and socioeconomic inequality than has hitherto been admitted.
- **A syndemic is not merely a comorbidity**.
- Syndemics are characterised by biological and social **interactions** between **conditions** and **states**, **interactions that increase a person’s susceptibility to harm or worsen their health outcomes**.
- The total number of people living with chronic diseases is growing.

COVID-19 and HIV: a Syndemic Framework

A **syndemic** is 2 or more epidemics that **interact synergistically to increase the burden of disease in a population**.

"To understand the manifestation of COVID-19 in the lives of PLWH, it must be viewed alongside HIV and other health conditions that already exist in this population."



Shiau S et al. *AIDS Behav*. 2020;24(8):2244-2249. doi:10.1007/s10461-020-02871-9

Question 1

Are people living with HIV at increased risk for COVID-19?

Incidence of COVID-19 in PLWH May Be Comparable With the General Population

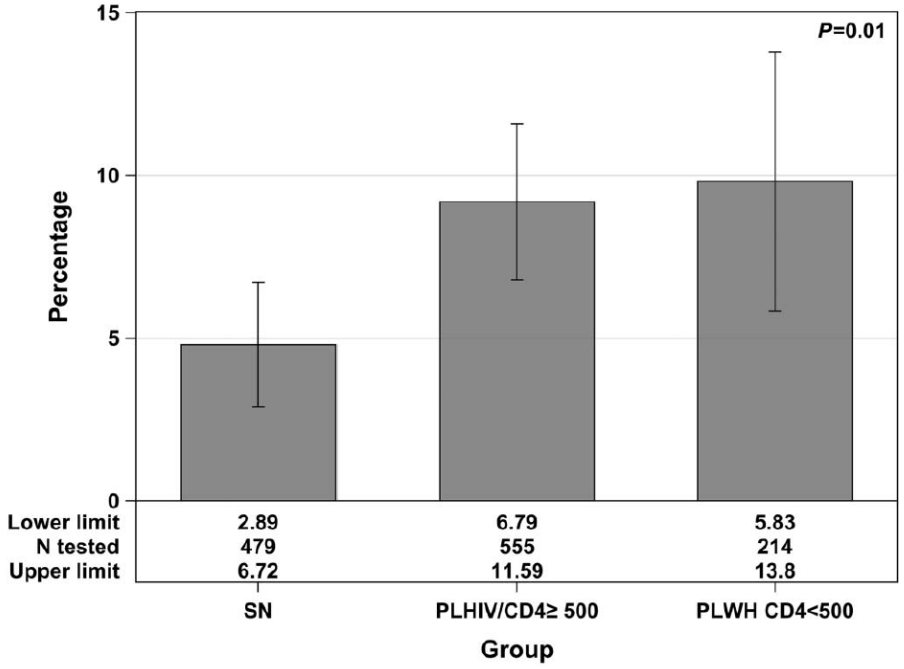
- Thus far, most evidence suggests that there is not an increased risk for COVID-19 among PLWH
  - Evidence from Spain, France, Boston, and Atlanta suggested no difference in COVID-19 risk among PLWH[1]

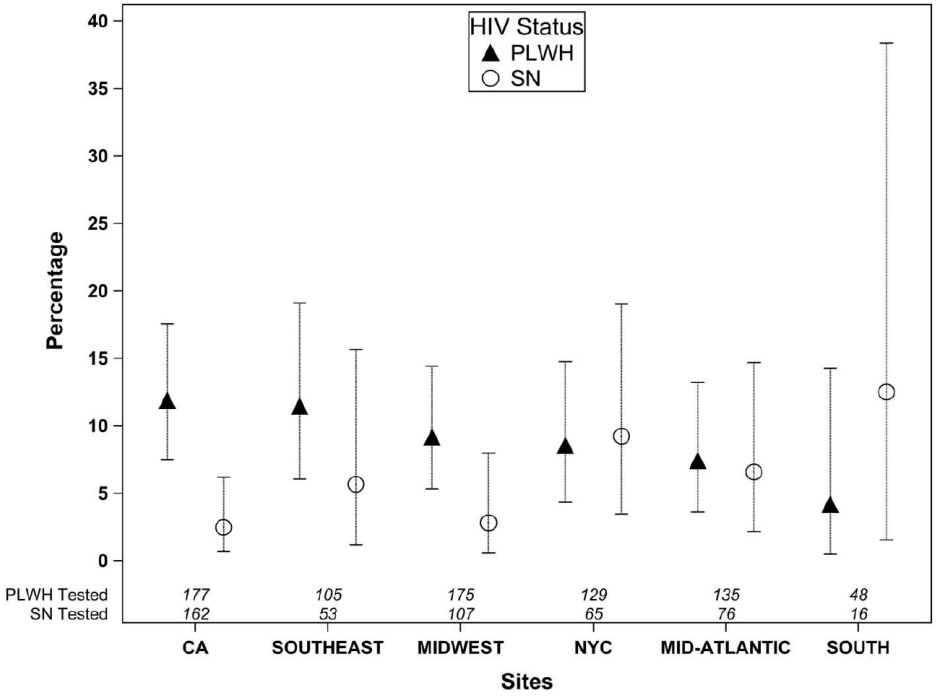
  However, in San Francisco, 4.5% of COVID-19 tests were positive among PLWH compared with 3.5% in the general population ($P < .001$)[2]

1. Saag M. *AIDS*. 2020;34(12):1755-1756.
2. Sachdev D et al. *J Acquir Immune Defic Syndr*. 2020;10.1097/QAI.0000000000002531.

Are people with HIV at higher risk of SARS-CoV-2infection?

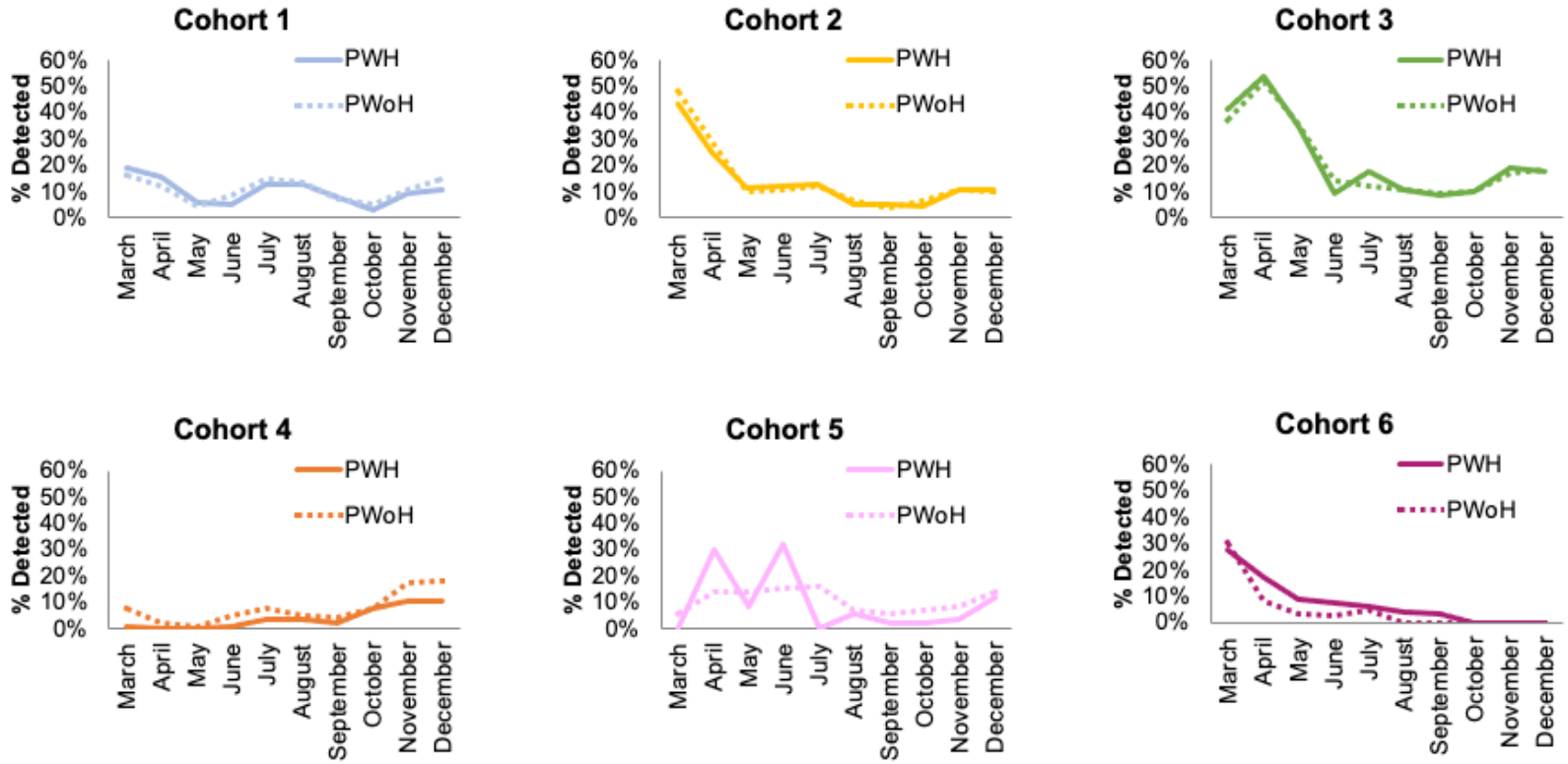
- In a study with the MACS-WIHS cohort, PHW were more likely to test + for SARS-CoV-2 than seronegative controls. *«Despite similar SARS-CoV-2 testing rates, a higher proportion of PLWH in our study tested positive for SARS-CoV-2 infection compared with SN participants. This suggests that PLWH may have increased susceptibility or have had greater non–HIV-related risks for SARS-CoV-2 infection»*





D'Souza G, et al. JAIDS 2022; 89(1): 1- 8

There was no evidence that PWH were at higher risk of infection with SARS-CoV-2 in a study that included 6 cohorts in the U.S.



Park LS, et al. JAIDS 2022.

Whom, among PWH is at increased risk of COVID?

COVID-19 Incidence, hospitalization both ~2x in PWH in Kaiser Permanente SoCal

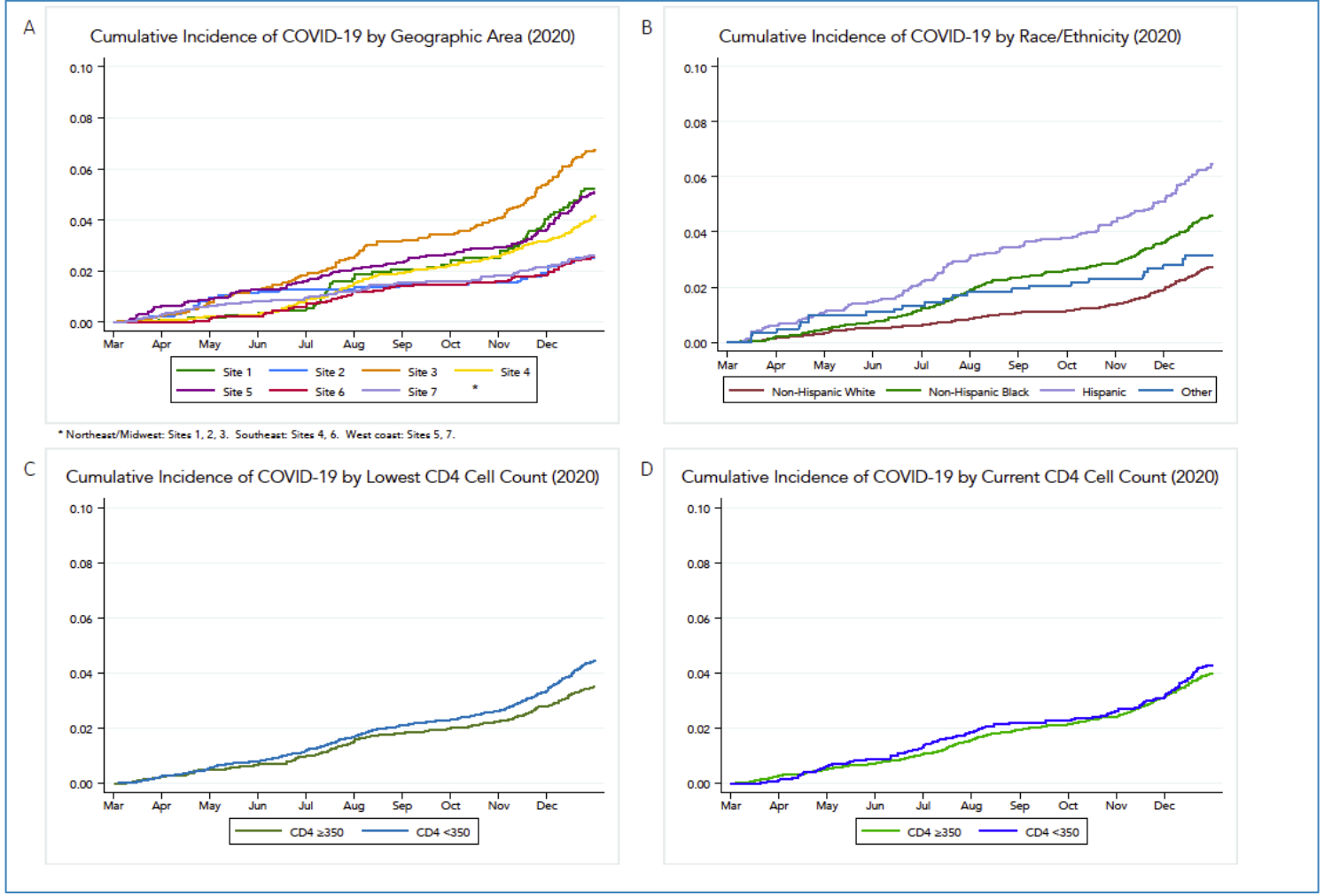
- PWH less comorbidities than general population
- Almost entire PWH pop with viral load suppression (>95%)

JJ Chang, JAIDS 2021

Black and Latinx PWH more likely to test COVID+ve after adjustment for age, comorbidity score- N3C

Islam, IJSTD AIDS 2022

CNICS multicenter US Cohort of PWH, 2020



Bender Ignacio and Shapiro, AIDS 2022

Question 2

Are people living with HIV at increased risk for hospitalization and death during acute COVID-19?

Potential Reasons Why PWH May Have Worse COVID-19 Outcomes

Immunodeficiency or immune dysregulation

- Patients with immunodeficiency, such as organ transplant recipients, are at increased risk for severe COVID-19
- Prolonged SARS CoV-2 replication reported in immunocompromised hosts
- Suggests PWH with low CD4 cell counts may be at increased risk for severe COVID (as they are for influenza)
- Residual inflammation in PWH on ART, most pronounced in PWH with low CD4 cell count nadirs, incomplete CD4 cell reconstitution, low CD4/CD8 ratio

Comorbidities

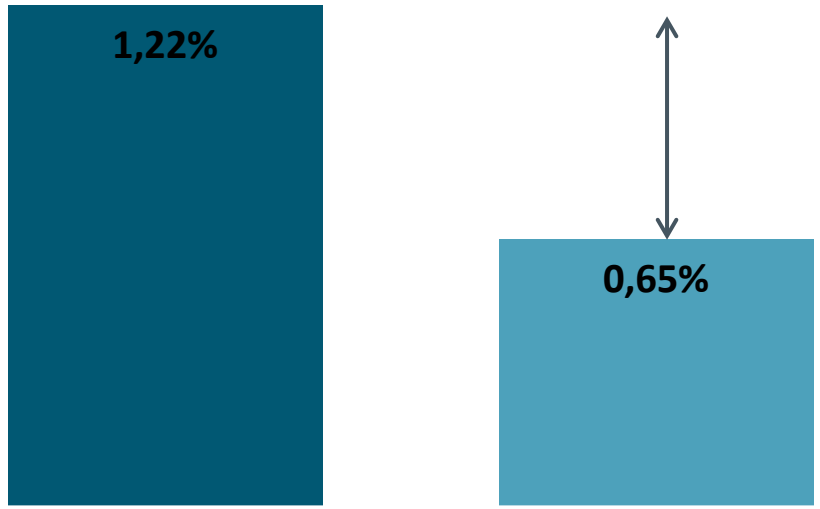
- PWH have high rates of comorbidities that are also risk factors for severe COVID-19

Social determinants of health

- PWH more likely to be racial/ethnic minorities, poor – risk factors for worse COVID-19 outcomes

PLWH May Have Increased Risk for Severe COVID-19

- In a meta-analysis of studies, PLWH **were 2-fold more likely** to be hospitalized with COVID-19[1]
- In a study of hospitalized participants with COVID-19 from the ISARIC WHO CCP, PLWH[2]:
  - Were younger at admission
  - Had higher lymphocyte counts and CRP levels
  - Had more systemic symptoms
  - Had comparable overall 28-day mortality (25.2% vs 32.1%; *P* = .12)
  - Had higher mortality risk for those aged <50 years after adjustment for severity at admission (adjusted HR, 1.63; *P* = .02)



1. Ssentongo P et al. Poster presented at IDWeek 2020. October 21, 2020. Accessed November 11, 2020. https://3002a505d4f8666b1f13-6d0524d9c8a5052ce15209ae3ecb39a3.ssl.cf1.rackcdn.com//1402743-1602880525.pdf
2. Geretti A et al. Presented at HIV Glasgow 2020. October 5, 2020. Accessed November 11, 2020. https://onlinelibrary.wiley.com/doi/10.1002/jia2.25616

Selected comparative 15 studies (n=11,797 PLWH) assessing the association between HIV and severe COVID-19 outcomes

Study	Month Published	Population	N HIV+ COVID	N COVID	Risk Increased	Effect Size	Outcome	Adjusted	Matched
Karmen-Tuohy[1]	June 2020	NYC hospitalized	21	42	No		ICU admission; mechanical ventilation; mortality	No	Yes
Sigel[2]	July 2020	NYC hospitalized	88	405	No		Mechanical ventilation; mortality	Yes	No
Stoeckle[3]	August 2020	NYC hospitalized	30	90	No		Mechanical ventilation; in-hospital mortality	No	Yes
Park[4]	July 2020 (IAS Conference)	US multicenter	253	504	No		Hospitalization; ICU admission; mechanical ventilation; mortality	Yes	No
Boulle[5]	August 2020	South Africa	3978	22,308	Yes	2.14	Mortality	Yes	No
Miyashita	August 2020	NYC	161	8,912	No		ICU admission; mechanical ventilation; mortality	No	No
Del Amo	October 2020	Spain	236	-	Yes	1.76	Mortality	No	No
Hadi[6]	November 2020	US multicenter	404	49,763	No		Mortality	No	Yes
Geretti[7]	October 2020	UK hospitalized	122	47,592	Yes	1.47	Mortality	Yes	No
Bhaskaran[8]	December 2020	UK OpenSafely			Yes	2.30	Mortality	Yes	No
Braunstein	December 2020	NYC	2410	204,583	Yes	1.63	Mortality	No	No
Tesoriero[9]	February 2021	NY state	2988	375,260	Yes	1.23	Mortality	Yes	No
Gagliardini[10]	May 2021	Italy hospitalized	43	1,604	No		Mortality, mechanical ventilation	Yes	No
Venturas[11]	May 2021	South Africa hospitalized	108	276	No		Mortality	Yes	No
Spinelli[12]	June 2021	San Francisco hospitalized	955	1,118	Yes	5.52	Severe COVID-19	Yes	Yes

[1]Matched on admission date, age, body mass index, gender, tobacco history, and a history of chronic kidney disease, hypertension, asthma, chronic obstructive pulmonary disease, and heart failure; [2]Adjusted for age, sex, race/ethnicity, COVID-19 severity on admission, COPD, smoking, baseline ferritin level, baseline white blood cell count; [3]Matched on age, sex, race/ethnicity; 4adjusted for age, race/ethnicity, sex; [5]Adjusted for age, sex, diabetes, hypertension, chronic kidney disease, chronic pulmonary disease/asthma, tuberculosis; [6]Matched on sex, BMI, diabetes, hypertension, chronic lung diseases, chronic kidney disease, race, history of nicotine dependence; [7]Adjusted for age, sex, ethnicity, baseline date, indeterminate/probable hospital acquisition of COVID-19, 10 comorbidities and hypoxia/receiving oxygen at presentation; [8]Adjusted for age, sex, index of multiple deprivation, ethnicity, smoking, obesity, diagnosed hypertension, chronic respiratory disease, asthma, chronic cardiac disease, diabetes, non-hematological cancer, hematological cancer, chronic liver disease, stroke and dementia, other neurological disease, reduced kidney function, organ transplant, asplenia, rheumatoid arthritis, lupus, and psoriasis, and other immunosuppressive conditions; [9]Adjusted for age, sex, region; [10]adjusted for age, gender, comorbidities, PaO2/FiO2 and pneumonia at admission to the hospital; [11]adjusted for demographics, clinical, complications, laboratory markers; [12]adjusted for age, sex.

modified from Triant VA & Gandhi RT. Clin Infect Dis, 2021

HIV infection and COVID-19 death: a population-based cohort analysis of UK primary care data and linked national death registrations within the OpenSAFELY platform

Krishnan Bhaskaran, Christopher T Rentsch, Brian MacKenna, Anna Schultze, Amir Mehrkar, Chris J Bates, Rosalind M Eggo, Caroline E Morton, Sebastian C J Bacon, Peter Inglesby, Ian J Douglas, Alex J Walker, Helen I McDonald, Jonathan Cockburn, Elizabeth J Williamson, David Evans, Harriet J Forbes, Helen J Curtis, William J Hulme, John Parry, Frank Hester, Sam Harper, Stephen J W Evans, Liam Smeeth*, Ben Goldacre*

Lancet HIV 2021; 8: e24–32
Published Online December 11, 2020

Summary

Background Whether HIV infection is associated with risk of death due to COVID-19 is unclear. We aimed to investigate this association in a large-scale population-based study in England.

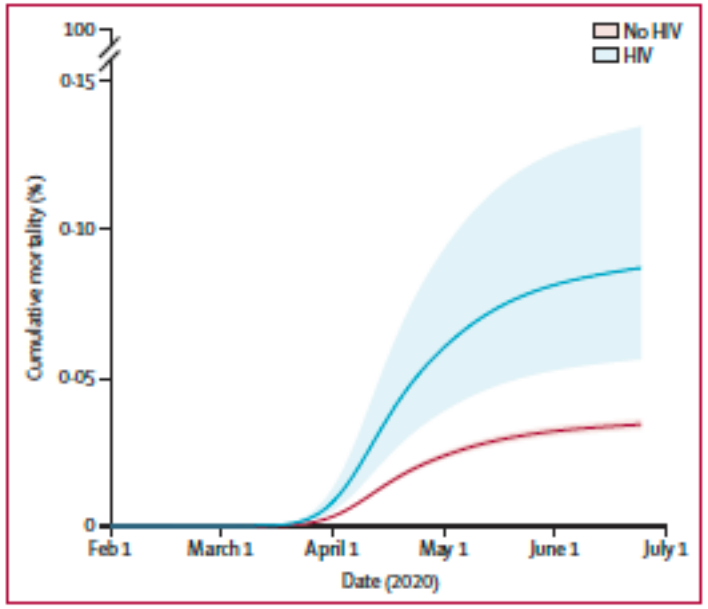


Figure 2: Cumulative COVID-19 mortality during the study period by HIV status with 95% CI, standardised to covariate distribution of the HIV group
Note that cumulative COVID-19 mortality is not restricted to individuals infected with severe acute respiratory syndrome coronavirus 2 but rather represents the cumulative incidence of acquiring infection and then progressing to death with COVID-19 listed as a cause. Cumulative mortality predicted from a Royston-Parmar model including age, sex, index of multiple deprivation, ethnicity, smoking, and obesity, with the baseline hazard parametrised as a three-degrees-of-freedom cubic spline; predictions standardised to the covariate distribution of the HIV group. This analysis was done for individuals with complete ethnicity data only, because computational limitations prevented implementation in the dataset with multiply imputed ethnicity.

Implications of all the available evidence
People with HIV in the UK seem to be at increased risk of COVID-19 mortality. Targeted policies should be considered to address this apparent raised risk as the pandemic response evolves. The monitoring and evaluation of the effects of HIV on COVID-19 outcomes in countries with a higher prevalence of HIV and lower levels of treatment and viral control should be prioritised.

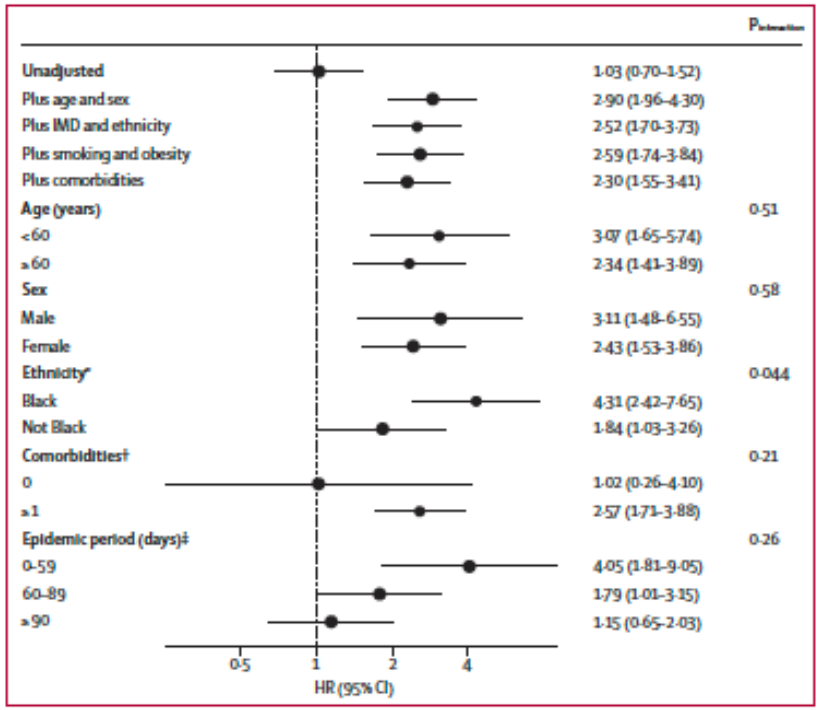
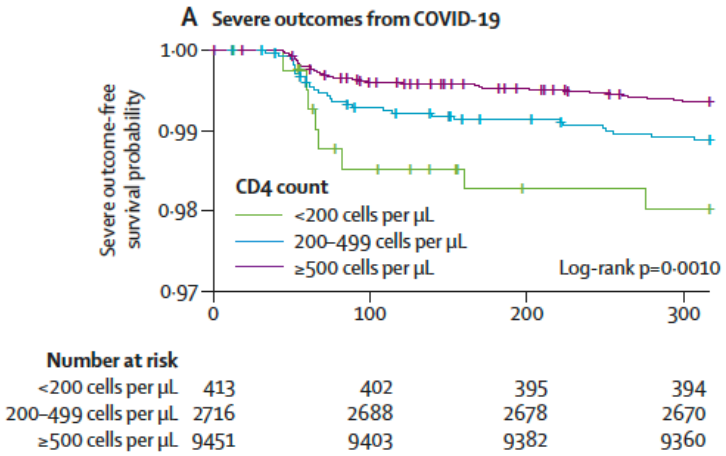
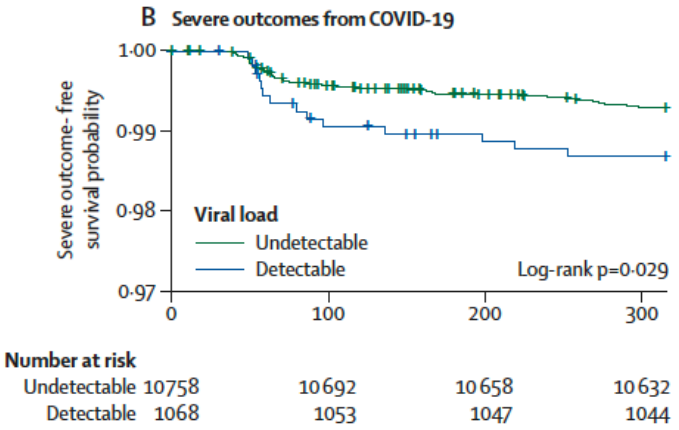


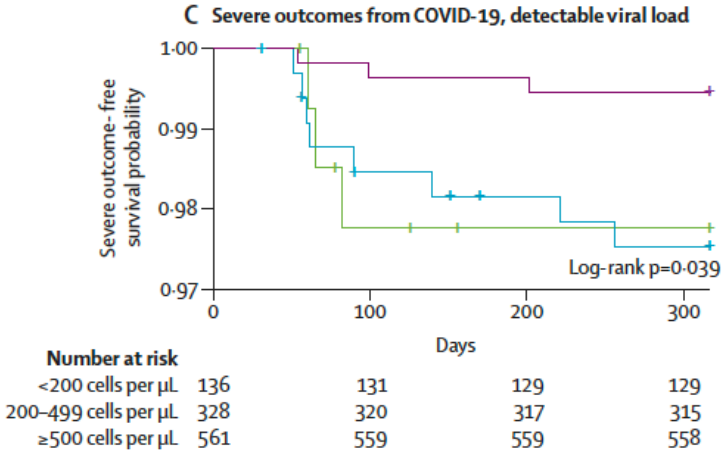
Figure 3: HRs for the association between HIV and COVID-19 mortality
All stratified models (by age, sex, ethnicity, comorbidities, epidemic period) were adjusted for age, sex, IMD, ethnicity. IMD=index of multiple deprivation. HR=hazard ratio. *Black is defined as self-report as African, Caribbean, or other Black; a similar pattern was seen in a direct comparison between Black (HR 4·81, 95% CI 2·63–8·80) and white (2·02, 1·05–3·89) among individuals with complete ethnicity data. †Comorbidities refers to diagnosed hypertension, chronic respiratory disease, asthma, chronic cardiac disease, diabetes, non-haematological cancer, haematological cancer, chronic liver disease, stroke and dementia, other neurological disease, reduced kidney function, organ transplant, asplenia, rheumatoid arthritis, lupus, and psoriasis, and other immunosuppressive conditions; the model stratified by comorbidities was additionally adjusted for these comorbidities as individual covariates; excluding hypertension from the list of comorbidities gave stratified HRs of 1·57 (0·59–4·20) for individuals without comorbidities and 2·52 (1·64–3·87) for those with comorbidities (p-interaction=0·39). ‡Days from Feb 1, 2020; the three categories were chosen to capture the period before social distancing policies in the UK would have affected mortality, the period of peak COVID-19 mortality, and the period during which restrictions began to be eased.

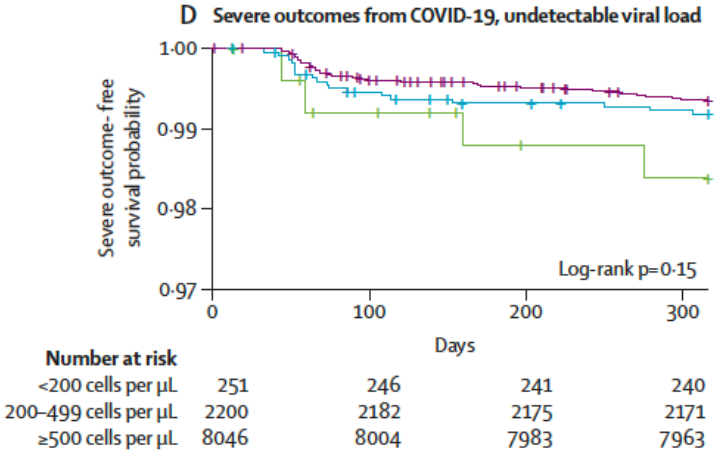
The PISCIS Cohort Group

People living with HIV with detectable HIV viremia, chronic comorbidities, and some subpopulations could be at increased risk of severe outcomes from COVID-19









We linked 20 847 (72·8%) of 28 666 participants in the PISCIS cohort with PADRIS data; **13 142 people had HIV. 749 (5·7%) people with HIV were diagnosed with SARS-CoV-2**: their median age was 43·5 years (IQR 37·0–52·7). **103 people with HIV (13·8%) were hospitalised, seven (0·9%) admitted to intensive care, and 13 (1·7%) died.**

Age at least 75 years (5·2, 1·8–15·3), non-Spanish origin (2·1, 1·3–3·4), and neuropsychiatric (1·69, 1·07–2·69), autoimmune disease (1·92, 1·14–3·23), respiratory disease (1·84, 1·09–3·09), and metabolic disease (2·59, 1·59–4·23) chronic comorbidities were associated with increased risk of severe outcomes.

A Kaplan-Meier estimator showed **differences in the risk of severe outcomes according to CD4 cell count in patients with detectable HIV RNA (p=0·039)** but **no differences were observed in patients with undetectable HIV RNA (p=0·15).**

Nomah DK, et al. *Lancet HIV* 2021; 8: e701–10. Published Online October 13, 2021

Risk of severe COVID-19 outcomes was increased in PLWH with uncontrolled HIV replication, low CD4 count, and prior AIDS diagnosis

The ATHENA cohort comprises **21,289 adult PWH**, median age 51.2 years, 96.8% had HIV-RNA <200 copies/ml, median CD4 cell count 690 (IQR 510–908) cells/ml. Primary **SARS-CoV-2 infections** were registered in **2,301 individuals**, of whom **157 (6.8%) required hospitalization** and **27 (1.2%) ICU admission**. **Mortality rates** were **13 and 0.4% among hospitalized and nonhospitalized** individuals, respectively.

Table 4. Independent predictors of mortality among people with HIV who were diagnosed with COVID-19.

	Multivariable model		Sensitivity analysis 1 Model limited to prevaccine period		Sensitivity analysis 2 Model including all ATHENA participants	
Risk factor	Odds ratio (95% CI)	*P*	Odds ratio (95% CI)	*P*	Odds ratio (95% CI)	*P*
Age (per 10 years increase)	5.01 (3.18–8.17)	<0.001	6.23 (3.14–12.3)	<0.001	4.03 (2.71–6.01)	<0.001
Region of birth						
Western	-ref		-ref-		-ref-	
Sub-Saharan Africa	−2.96 (0.72–12.1)	0.13	1.69 (0.17–16.5)	0.65	3.33 (0.89–12.4)	0.073
Latin America/Caribbean	3.32 (1.19–9.21)	0.021	4.48 (1.12–18.0)	0.034	6.7 (2.78–16.2)	<0.001
Other	0.66 (0.13–3.39)	0.61	0.66 (0.06–8.03)	0.75	1.19 (0.27–5.31)	0.82
Number of concomitantly diagnosed comorbidities (per one comorbidity increase)	2.11 (1.40–3.19)	<0.001	2.11 (1.40–3.18)	<0.001	1.93 (1.40–2.67)	<0.001
Current $CD4^+$ cell count						
0–199	6.48 (1.22–34.54)	0.029	12.7 (1.83–88.1)	0.010	4.54 (1.07–19.4)	0.041
200–499	2.80 (1.15–6.84)	0.024	4.14 (1.16–14.7)	0.028	2.49 (1.13–5.48)	0.024
500+	-ref-		-ref-		-ref-	

Western includes native Dutch people, and migrants from Western Europa, North America, Japan, Australia, and New Zealand. 95% CI, 95% confidence interval; ref, reference group.

CD4 count at COVID-19 diagnosis was **417 cells/mmc (316–789)** among PLWH who died of COVID-19 compared with **710 cells/mmc (529–900)** in those who survived.

Wit FWNM, et al. AIDS 2023, 37:1671–1681

ICONA Network

Association between the 6 level's exposure and in-hospital mortality in PLWH and general population

Restricted to subjects with pneumonia and/or P/F<300 at hospital admission*				
GenPop <65 years	1	-	1	-
GenPop ≥65 years	6·28	5·26-7·51	1·78	1·37-2·32
PLWH ≥65 years	7·79	4·06-14·95	2·80	1·43-5·46
PLWH <65 years and CD4 cell count ≤200 cell/mm^3	7·41	3·97-13·83	9·83	4·75-20·35
PLWH <65 years and CD4 cell count 201-350 cell/mm^3	5·69	2·47-13·12	4·41	1·74-11·18
PLWH <65 years and CD4 cell count >350 cell/mm^3	0·86	0·32-2·32	1·23	0·38-3·95
Restricted to centers able to provide both HIV exposed an unexposed*				
GenPop <65 years	1	-	1	-
GenPop ≥65 years	6·83	5·74-8·11	1·82	1·41-2·34
PLWH ≥65 years	4·00	1·48-10·78	1·75	0·64-4·75
PLWH <65 years and CD4 cell count ≤200 cell/mm^3	4·73	2·51-8·89	8·17	4·18-15·99
PLWH <65 years and CD4 cell count 201-350 cell/mm^3	3·95	1·62-9·62	5·45	2·29-13·00
PLWH <65 years and CD4 cell count >350 cell/mm^3	0·92	0·29-2·90	1·08	0·34-3·43

Unadjusted and adjusted Fine-Gray Cox regression model of the association between the 6 level's exposure and in-hospital mortality restricted to:

- subjects with pneumonia and/or P/F<300 at hospital admission;
- b) centers able to provide both HIV exposed and unexposed;
- c) after rerunning the model by adjusting for comorbidities.

Overall^	SHR	95% CI	aSHR	95% CI
GenPop <65 years	1	-	1	-
GenPop ≥65 years	6·83	5·75-8·11	1·86	1·44-2·39
PLWH ≥65 years	5·42	2·89-10·13	2·18	1·18-4·06
PLWH <65 years and CD4 cell count ≤200 cell/mm^3	5·08	3·01-8·57	8·65	4·91-15·22
PLWH <65 years and CD4 cell count 201-350 cell/mm^3	3·89	1·74-8·73	4·25	1·76-10·29
PLWH <65 years and CD4 cell count >350 cell/mm^3	0·86	0·32-2·32	1·04	0·39-2·78

Giacomelli A, et al. Int J Infect Dis, 2023

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Risk of COVID-19 in-hospital mortality in people living with HIV compared to general population according to age and CD4 strata: data from the ICONA network

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- PLWH <65 years with CD4 ≤350 cells/mm^3 are at higher risk of worse COVID-19 outcomes
- This risk is further increased in PLWH <65 years with CD4 count ≤200 cells/mm^3
- The evidence was insufficient for PLWH aged ≥65 years
- PLWH with low CD4 counts should be prioritized for preventive interventions.

Risk factors for COVID-19-related in-hospital mortality in a high HIV and tuberculosis prevalence setting in South Africa

219.265 individuals admitted to hospital with laboratory-confirmed SARS-CoV-2 infection and known in-hospital outcome data, 51.037 (23·3%) died. **Most commonly observed comorbidities** among individuals with available data were hypertension in 61.098 (37·4%) of 163.350, diabetes in 43.885 (27·4%) of 159.932, and **HIV in 13.793 (9·1%) of 151.779**.

Increasing age was the strongest predictor of COVID-19 in-hospital mortality. Other factors associated were **HIV infection (adjusted odds ratio 1·34, 95% CI 1·27–1·43)**, past tuberculosis (1·26, 1·15–1·38), current tuberculosis (1·42, 1·22–1·64), and both past and current tuberculosis (1·48, 1·32–1·67)

	Case fatality ratio unimputed	Case fatality ratio (95% CI) imputed	Unadjusted OR (95% CI) imputed	p value	Adjusted OR (95% CI) imputed*	p value	Adjusted OR (95% CI) imputed*	p value
ART status								
HIV negative	30 697/137 986 (22·2%)	23·1% (22·9–23·3)	1 (ref)	..	1 (ref)	..	0·77 (0·72–0·82)	<0·0001
HIV positive on ART	2046/7484 (27·3%)	24·6% (23·8–25·4)	0·85 (0·80–0·90)	<0·0001	1·30 (1·22–1·39)	<0·0001	1 (ref)	..
HIV positive not on ART	192/594 (32·3%)	28·1% (25·2–31·1)	0·99 (0·86–1·15)	0·98	1·89 (1·60–2·23)	<0·0001	1·45 (1·22–1·72)	<0·0001
CD4 count								
HIV negative	30 697/137 986 (22·2%)	23·1% (22·9–23·3)	1 (ref)	..	1 (ref)	..	1·06 (0·93–1·20)	0·37
HIV positive CD4 count, ≥200 cells per µL	368/1690 (21·8%)	19·7% (17·7–21·7)	0·64 (0·57–0·73)	<0·0001	0·95 (0·83–1·08)	0·37	1 (ref)	..
HIV positive CD4 count, <200 cells per µL	380/1080 (35·2%)	32·2% (29·9–34·5)	1·23 (1·09–1·38)	0·0023	2·19 (1·92–2·49)	<0·0001	2·31 (1·82–2·93)	<0·0001
Viral load								
HIV negative	30 697/137 986 (22·2%)	23·1% (22·9–23·3)	1 (ref)	..	1 (ref)	..	0·83 (0·76–0·90)	0·0002
HIV positive viral load, <1000 HIV RNA copies per mL	316/1273 (24·8%)	24·7% (23·0–26·4)	0·86 (0·78–0·94)	0·0029	1·21 (1·11–1·32)	0·0002	1 (ref)	..
HIV positive viral load, ≥1000 HIV RNA copies per mL	128/443 (28·9%)	25·2% (21·0–29·4)	0·85 (0·69–1·05)	0·13	1·88 (1·53–2·31)	<0·0001	1·55 (1·20–2·01)	0·0029

Model adjusted for age, sex, race or ethnicity, health sector, province, month of admission, non-communicable comorbidities, and past or current tuberculosis. ART=antiretroviral therapy. OR=odds ratio.
*Output from the same model but with different reference categories to assess the effect of the predictors compared with HIV-uninfected individuals (model 1) or individuals on ART, with high CD4 count, or with low viral load (model 2).

Table 3: **Effect of ART, CD4 cell count, and HIV viral load on COVID-19 in-hospital mortality among people with HIV admitted to hospital with laboratory-confirmed SARS-CoV-2 infection, South Africa**

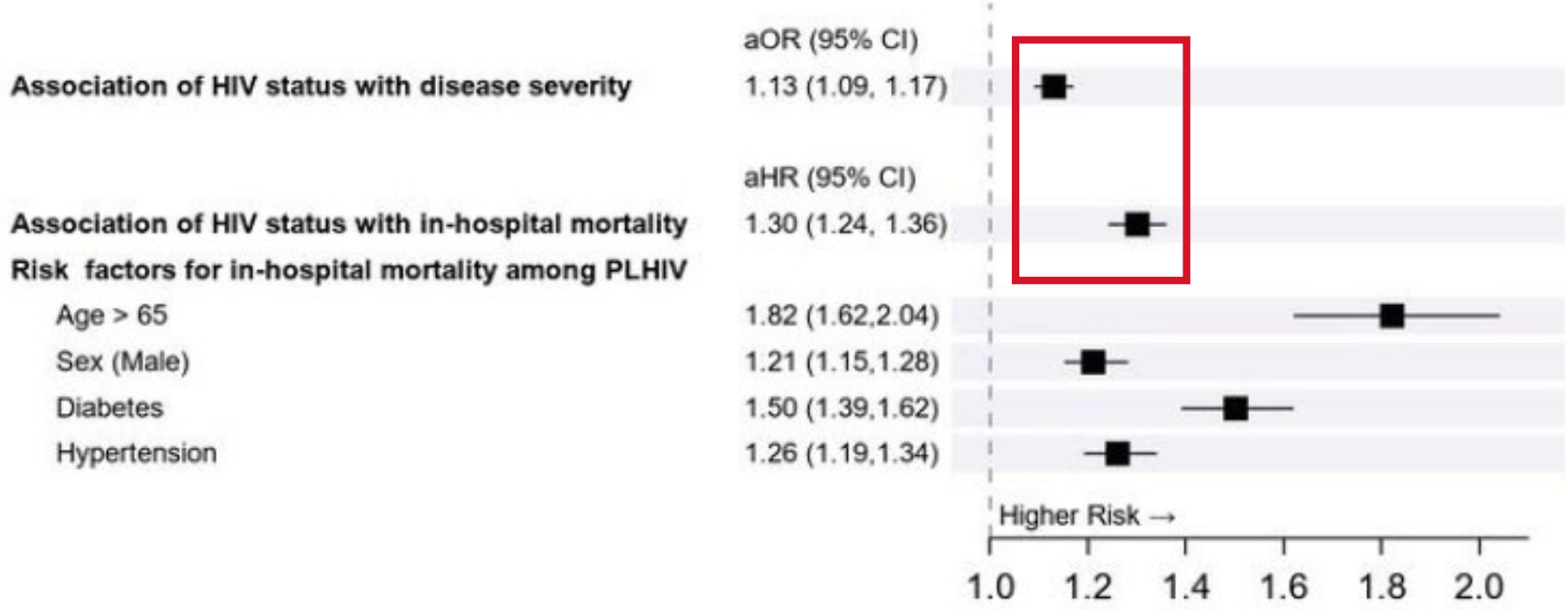
After adjusting for other factors, **people with HIV not on antiretroviral therapy (ART; adjusted odds ratio 1·45, 95% CI 1·22–1·72)** were **more likely to die in hospital than were people with HIV on ART.**

Jassat W, et al. Lancet HIV 2021; 8: e554–67

WHO Global Clinical Platform

Clinical characteristics and prognostic factors in PLWH hospitalized with COVID-19

Data from **15.522 PLHIV out of 168.649 hospitalized individuals** were reported from 24 countries.
Among PLHIV, 37.1% were male, mean age was 45.5 years, **91.8% received ART** and **36.2% had severe/critical illness**.



Individual clinical data from 37 countries reported to the WHO Global Clinical Platform for COVID-19 indicate that **HIV** infection is a significant **independent risk factor** for both **severe illness at hospital admission** and **in-hospital mortality**

Bertagnolio S, et al. IAS 2021; PEBLB20; Lancet HIV; 2022; 9: e486–95

Factors that increase risk for poor outcomes during *acute* COVID-19 in PWH

- Classical COVID-19 risk factors:
  - Age, diabetes, obesity, kidney disease, COPD, hypertension, male sex, race, ethnicity
- CD4 < 200-350
- CD4 nadir < 200
- In some analyses, unsuppressed HIV viral load

https://www.who.int/publications/i/item/WHO-2019-nCoV-Clinical-HIV-2021.1

N3C: Yang, X, et al. Lancet HIV. November 2021. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8514200/

CNICS: Shapiro, A, et al. JAIDS. April 2022. https://journals.lww.com/jaids/Abstract/9900/Factors_associated_with_severity_of_COVID_19.19.aspx

COVID-19 Real-Time Learning Network, HIV topic. https://www.idsociety.org/covid-19-real-time-learning-network/special-populations/hiv/#

Question 3

Are people living with HIV at increased risk for long COVID?

Long-COVID among people with HIV

- A preprint study from UCSF suggests that HIV infection is strongly associated with PASC (OR = 4.01),

- In models adjusting for HIV status, higher PD-1+ expression on total non-naïve CD4+ T-cells was independently predictive of PASC.

- Some inflammatory markers were also associated with increased risk of PASC including IL-6, TNF-alpha, and IP-10.

MedRxIV. https://doi.org/10.1101/2022.02.10.22270471

Long-COVID among people with HIV

- Study from Padua, Italy (Feb 2020 – March 2021) among PWH, all unvaccinated on ART with HIV VL < 40 cp/ml.
- 123 PWH w/ COVID-19 (median age = 51; median CD4 = 560).
- 35% had asymptomatic COVID; 48% mild COVID; 17.1% moderate to severe COVID and 4.1% died.
- Among 75 patients who survived COVID-19, 26.7% reported PACS at a median follow up of 6 months.
- Asthenia, shortness of breath and headaches were most common symptoms.
- Only the severity of COVID predicted PASC.

viruses Viruses 2022, 14, 493. https://doi.org/10.3390/v14030493 MDPI

Article

Factors Associated with Severe COVID-19 and Post-Acute COVID-19 Syndrome in a Cohort of People Living with HIV on Antiretroviral Treatment and with Undetectable HIV RNA

Maria Mazzitelli [1,*], Mattia Trunfio [2], Lolita Sasset [1], Davide Leoni [1], Eleonora Castelli [1], Sara Lo Menzo [1], Samuele Gardin [1], Cristina Putaggio [1], Monica Brundu [1], Pietro Garzotto [1] and Anna Maria Cattelan [1]

Postacute sequelae and adaptive immune responses in people with HIV recovering from SARS-COV-2 infection

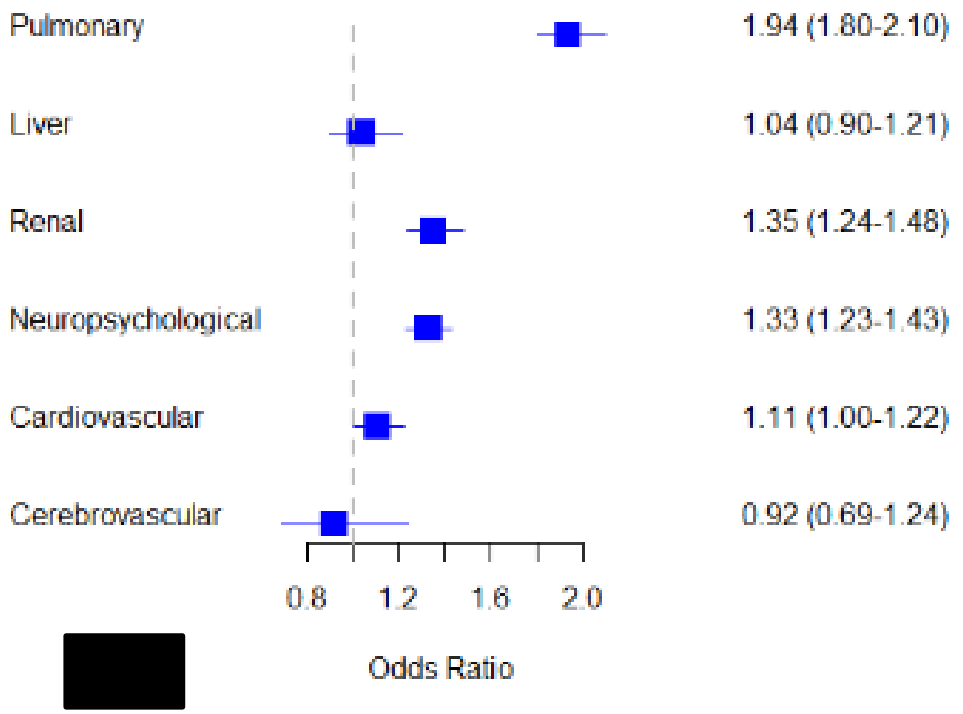
Michael J. Peluso[a,*], Matthew A. Spinelli[a,*], Tyler-Marie Deveau[b], Carrie A. Forman[a], Sadie E. Munter[b], Sujata Mathur[c], Alex F. Tang[a], Scott Lu[c], Sarah A. Goldberg[c], Mireya I. Arreguin[a], Rebecca Hoh[a], Viva Tai[a], Jessica Y. Chen[a], Enrique O. Martinez[a], Brandon C. Yee[d], Ahmed Chenna[d], John W. Winslow[d], Christos J. Petropoulos[d], Alessandro Sette[e,f], Daniella Weiskopf[e], Nitasha Kumar[b], Kara L. Lynch[g], Peter W. Hunt[b], Matthew S. Durstenfeld[h], Priscilla Y. Hsue[h], J. Daniel Kelly[c], Jeffrey N. Martin[c], David V. Glidden[c], Monica Gandhi[a], Steven G. Deeks[a], Rachel L. Rutishauser[b,*] and Timothy J. Henrich[b,*]

Conclusion: We identified potentially important differences in SARS-CoV-2-specific $CD4^+$ and $CD8^+$ T cells in PWH and HIV-negative participants that might have implications for long-term immunity conferred by natural infection. HIV status strongly predicted the presence of PASC. Larger and more detailed studies of PASC in PWH are urgently needed.

AIDS 2022, **36**:F7–F16

EletronicMedicalRecord Study: Increased risk of multi-organ dysfunction in PWH 12 months post-COVID

- NC3 study, USA
- ~5,600 PWH with COVID-19 before Jan 2021 compared to ~41,700 PWH without COVID-19
- Followed up at 12 months



Yue, Y, Liang, C, et al. CROI 2023 Poster #884

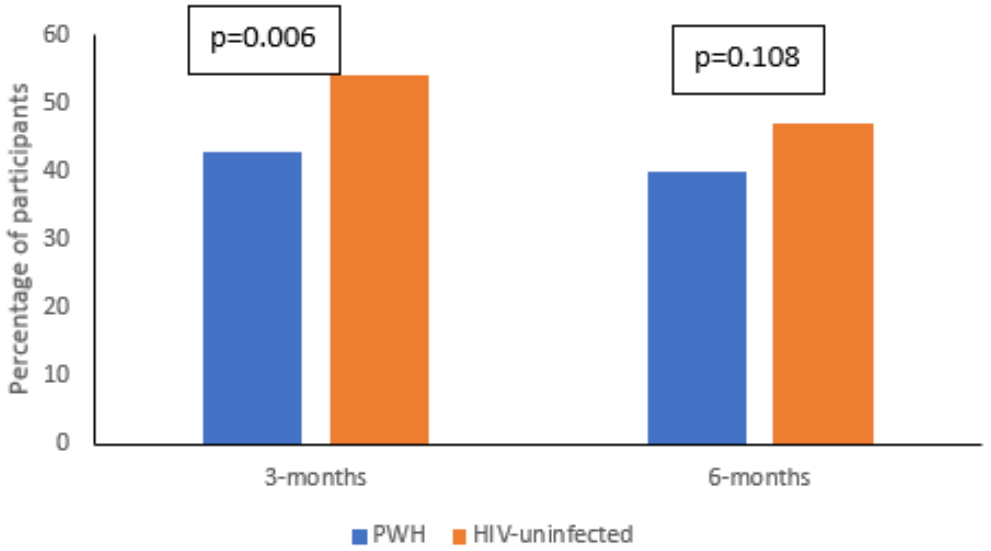
EletronicMedicalRecord Study : Increased risk of long COVID in PWH compared to HIV-negative people

	PASC risk		
Outcomes	**HIV +**	**HIV -**	**OR (CI)**
Mortality	597 (2%)	31411 (1%)	**2·01** (1·85, 2·18)
Diabetes	598 (3%)	33668 (1%)	**2·61** (2·40, 2·83)
Heart Disease	763 (5%)	55872 (2%)	**2·44** (2·27, 2·62)
Malignancy	517 (3%)	29644 (1%)	**3·15** (2·89, 3·45)
Thrombosis	699 (3%)	32612 (1%)	**3·04** (2·82, 3·28)
Mental Disorders	681 (9%)	72369 (3%)	**2·79** (2·58, 3·02)

- Electronic medical record study – TriNetX, USA. Data through Sept 2022.
- ~28,000 PWH compared to ~28,000 propensity-matched HIV-negative people
- PWH were also more likely to complain of 6 symptoms including fatigue, cognitive impairment, and body aches in the post-acute period than people without HIV.

Yendewa, G, et al. CROI 2023 Poster #724

HIV not a risk factor for long COVID in one South African survey study

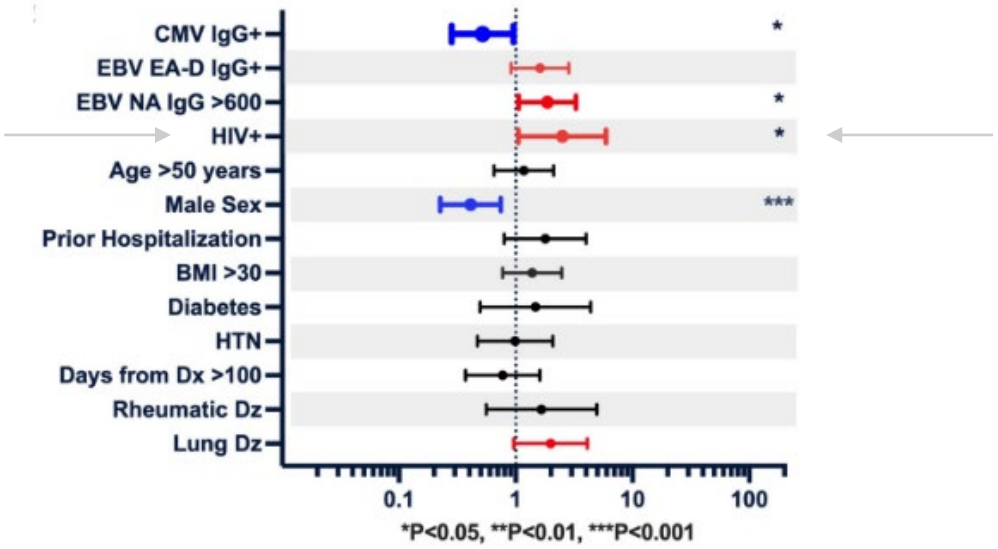


- Large survey study in South Africa of hospitalized and non-hospitalized people with confirmed COVID-19.
- ~3,700 participants surveyed. 151 PWH. Participants got COVID-19 during the beta, delta, or omicron waves.
- PWH were less likely to report persistent symptoms 3 months post-COVID, with no difference at 6 months.

Jassat, W et al. 2023. Int. J. Infect. Dis.

LIINC cohort: HIV, CMV, and EBV reactivation are associated with neurocognitive long COVID

Figure 3. Associations between demographic and clinical factors and odds of neurologic Long COVID symptoms.



- San Francisco-based post-COVID cohort.
- 327 participants. 63 are PWH. Median age 44. 53% male sex at birth. 60% with obesity. >70% with long COVID.

Peluso, M et al. 2022. JCI. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9888380/
Peluso, M et al. CROI 2023 Poster #273

Question 4

What about impact of COVID-19 on HIV?

HIV Service Disruptions due to COVID-19

- The COVID-19 epidemic has the potential to cause severe disruptions in health services due to several factors:
  - Closing of facilities or cessation of services
  - Shortage of health care workers
  - Over-burdening of health care staff
  - Disruptions in supplies for commodities and person protection equipment
  - Travel restrictions
  - Fear of accessing health facilities
- **The effects of these disruptions on HIV testing, new infections, deaths will depend on the duration and severity of the disruptions and the program responses to them**

Effects of COVID-related Service Disruptions

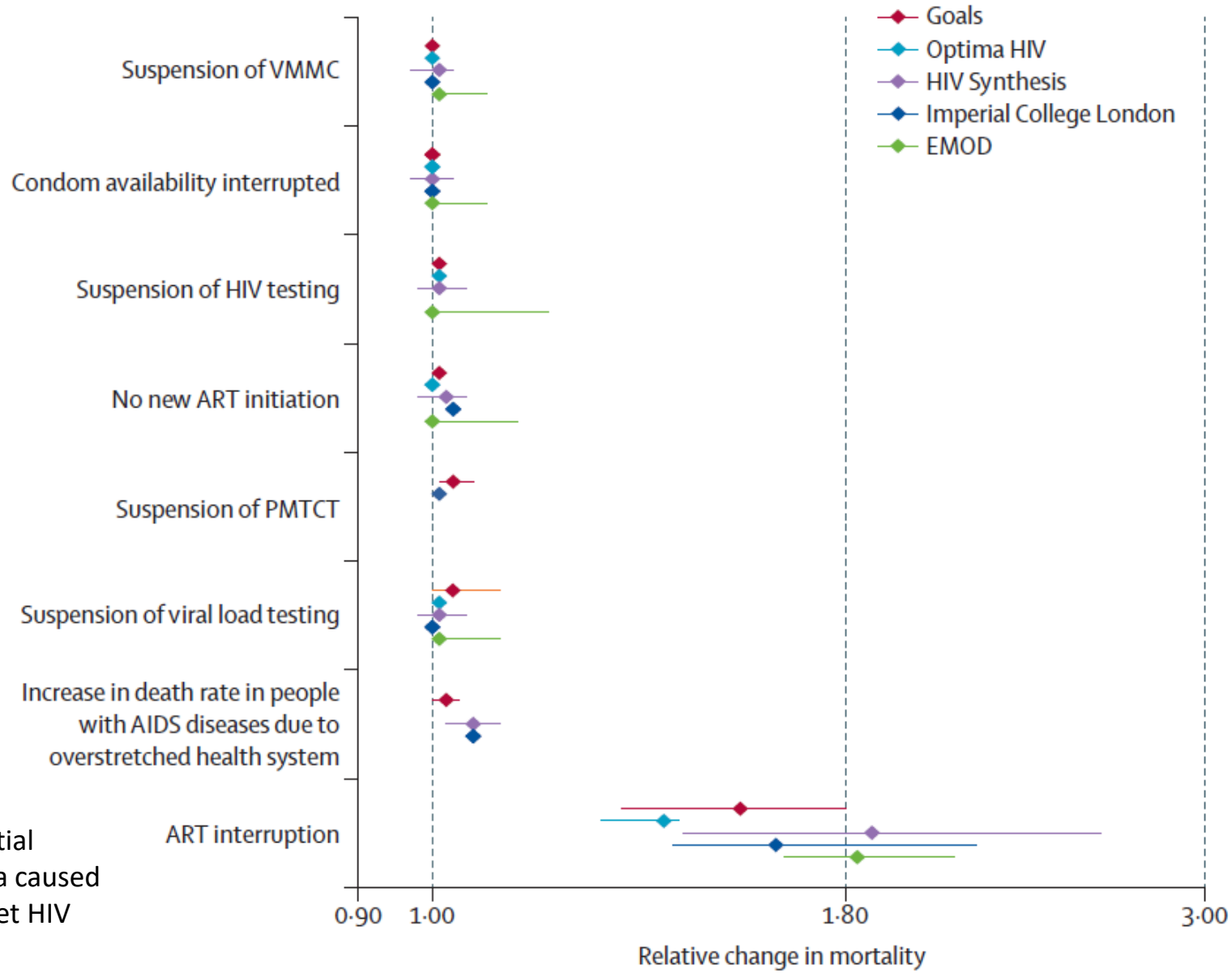
Multi-model analysis organized by the HIV Modeling Consortium found .

(Five different modeling groups applied their models to this question. We examine the potential impact of disruptions)

- Short-term disruptions in prevention services would have limited impact on HIV-related mortality
- Short-term disruptions of ART services could lead to 39-87% increase in HIV-related mortality in 2020 and 15-29% increase over 2020-2025

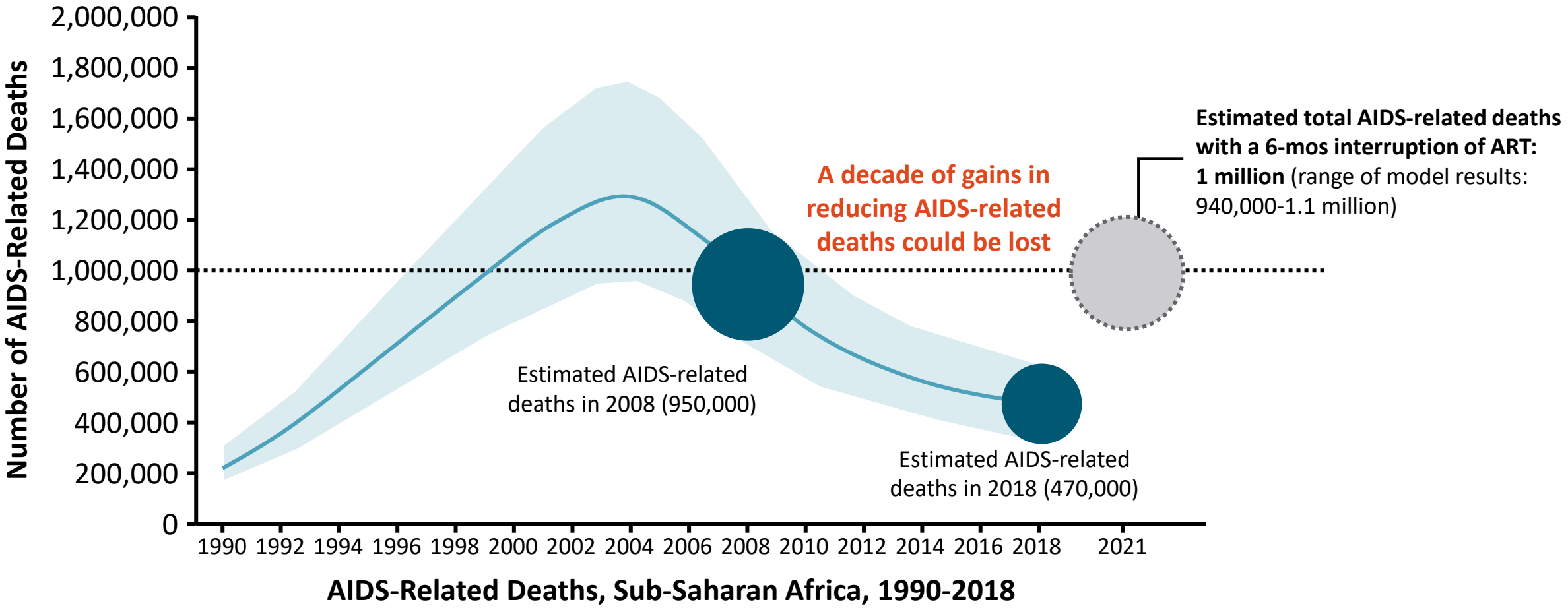
Assumptions

- Service disruption lasting 6 months
- Disruption affects 50% of the population
- Relative change in mortality is over 12 months (April 2020-March 2021)



Source: Jewel, Mudimu, Stover, ten Brink, Philipps *et al*. Potential effects of disruptions to HIV programmes in sub-Saharan Africa caused by COVID-19: result from multiple mathematical models, Lancet HIV 2020, doi.org/10.1016/S2352-3018(20)30211-3

Potential Cost of Interruption of HIV Services in Sub-Saharan Africa



UNAIDS. Modelling the extreme—COVID-19 and AIDS-related deaths. May 25, 2020. Jewell. Lancet HIV. 2020;[Epub].

ART provision was generally maintained during the 2020 COVID-19 lockdown, but HIV testing and ART initiations were heavily impacted

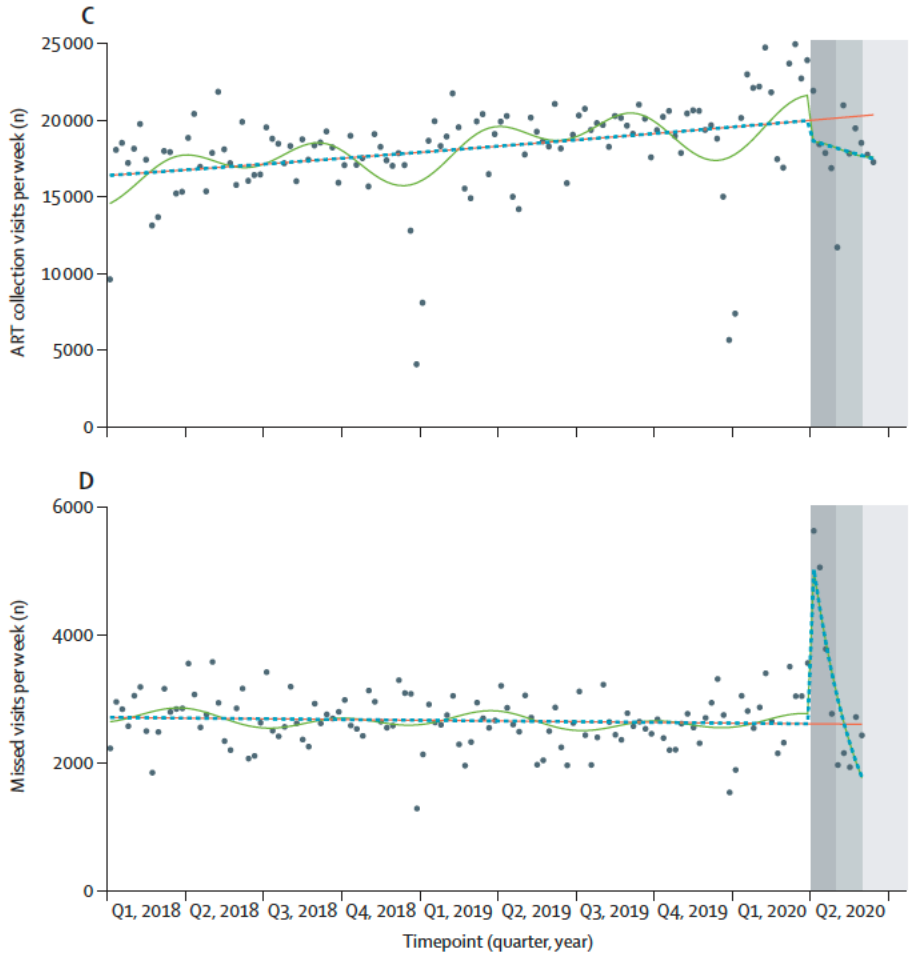
Between Jan 1, 2018, and July 31, 2020, we recorded 1 315 439 HIV tests. Between Jan 1, 2018, and June 15, 2020, we recorded 71 142 ART initiations and 2 319 992 ART collection visits. **We recorded a median of 41 926 HIV tests per month before lockdown (January, 2018, to March, 2020; IQR 37 838–51 069) and a median of 38 911 HIV tests per month after lockdown (April, 2020, to July, 2020; IQR 32 699–42 756).** In the Poisson regression model, taking into account long-term trends, **lockdown was associated with an estimated 47·6% decrease in HIV testing in April, 2020** (incidence rate ratio [IRR] 0·524, 95% CI 0·446–0·615). **ART initiations** decreased from a median of 571 per week before lockdown (IQR 498–678), to 375 per week after lockdown (331–399), **with an estimated 46·2% decrease** in the Poisson regression model in the first week of lockdown (March 30, 2020, to April 5, 2020; IRR 0·538, 0·459–0·630).

There was no marked change in the number of ART collection visits (median 18 519 visits per week before lockdown [IQR 17 074–19 922] *vs* 17 863 visits per week after lockdown

	Incidence rate ratio at lockdown	Incidence rate ratio at study end	Pre-lockdown trend*	Post-lockdown trend*
HIV testing†	0·475 (0·404–0·559)	0·741 (0·631–0·872)	1·018 (1·012–1·023)	1·180 (1·090–1·279)
ART initiation‡	0·496 (0·411–0·598)	0·798 (0·645–0·987)	1·000 (0·991–1·004)	1·225 (1·113–1·352)
ART collection visits‡	0·859 (0·733–1·007)	0·852 (0·745–0·975)	1·009 (1·004–1·013)	1·004 (0·924–1·090)
Missed ART collection visits‡	1·812 (1·494–2·197)	0·693 (0·459–1·048)	1·000 (0·996–1·004)	0·595 (0·451–0·783)

Data are rate (95% CI) or trend (95% CI). ART=antiretroviral therapy. *Slope change per month. †Autocorrelation addressed using Newey–West standard errors to calculate CI, with lag up to 2. ‡Autocorrelation addressed using Newey–West standard errors to calculate CI, with lag up to 3.

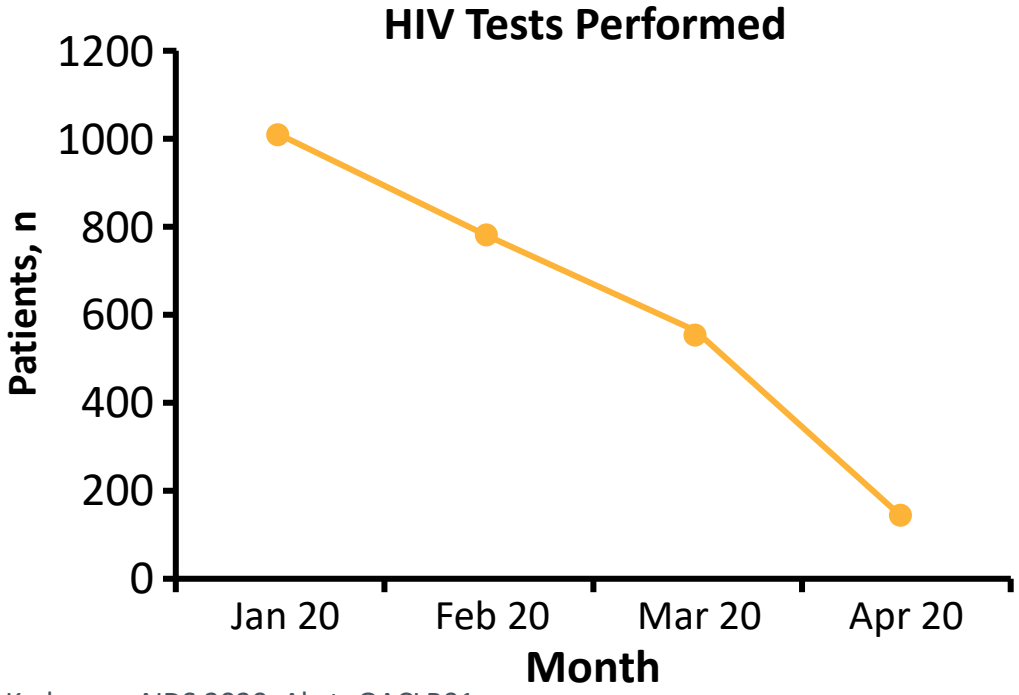
Table 3: **Sensitivity analyses taking account of seasonality using two Fourier pairs in Poisson segmented regression models of the impact of COVID-19 lockdown on HIV services in KwaZulu-Natal, South Africa**

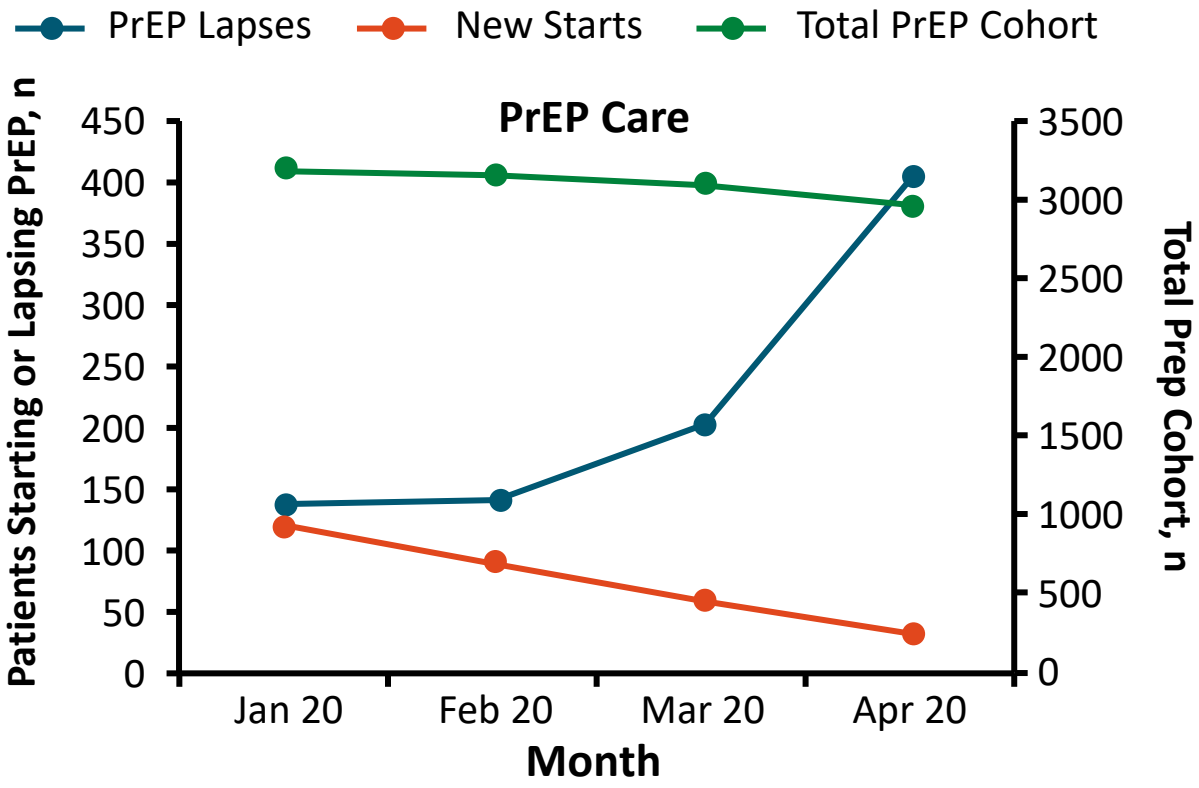


Dorward J, et al. Lancet HIV, 2021

Access to HIV Testing and PrEP Care in Boston

- Analysis of electronic health records data from January 2020 through April 2020 at Fenway Health, a community health center in Boston specializing in LGBTQIA+ healthcare
  - HIV tests decreased by 85.1%; total number of patients with an active PrEP prescription decreased by 18.3%





Krakower. AIDS 2020. Abstr OACLB01.

ICONA cohort

Impact of COVID-19 pandemic on retention in care of native and migrant people with HIV

PWH in ICONA Cohort in follow-up in each of the study periods were included: **01/09/2019-29/02/2020 (pandemic period) and 01/03/2018-31/08/2018 (historical period).** The risk of temporary **loss to follow-up (LTFU) was analyzed** by logistic regression, with migrant status as the main exposure variable. Difference in difference (DID) analysis was applied to evaluate the effect of COVID-19 pandemic on the different risks of LTFU between natives and migrants.

8,864 (17.1% migrants) and 8,071 (16.8% migrants) PWH constituted the pandemic and the historical period population, respectively.

The proportion of PWH defined as **LTFU in the pandemic period was 10.5% in native and 19.6% in migrant PWH**.

After controlling for age, sex, and geographical location of the enrolling site, the **risk of temporary LTFU was higher for migrants than native PWH [adjusted odds ratio 1.85 (95%CI 1.54-2.22)] in the pandemic period.**

	OR of temporary LTFU					
	Unadjusted OR (95% CI)	p-value	Adjusted1* OR (95% CI)	p-value	Adjusted2& OR (95% CI)	p-value
Natives	1		1		1	
Migrants	2.08 (1.79, 2.41)	<.001	1.93 (1.65, 2.26)	<.001	1.85 (1.54, 2.22)	<.001

*adjusted for gender, age and geographical location of site

&adjusted for gender, age, geographical location of site, AIDS diagnosis, maximum level of education and employment

Gagliardini R, et al. Manuscript submitted.

Health services disruption

Global pulse survey on continuity of essential health services during the COVID-19 pandemic

1 May 2023

Round 4

Key informant findings from 139 countries, territories and areas

Quarter 4 2022

World Health Organization

Three years into the COVID-19 pandemic, essential health service disruptions are still reported in majority of countries across all regions

On average, countries report disruptions to about a quarter of tracer services

World Health Organization

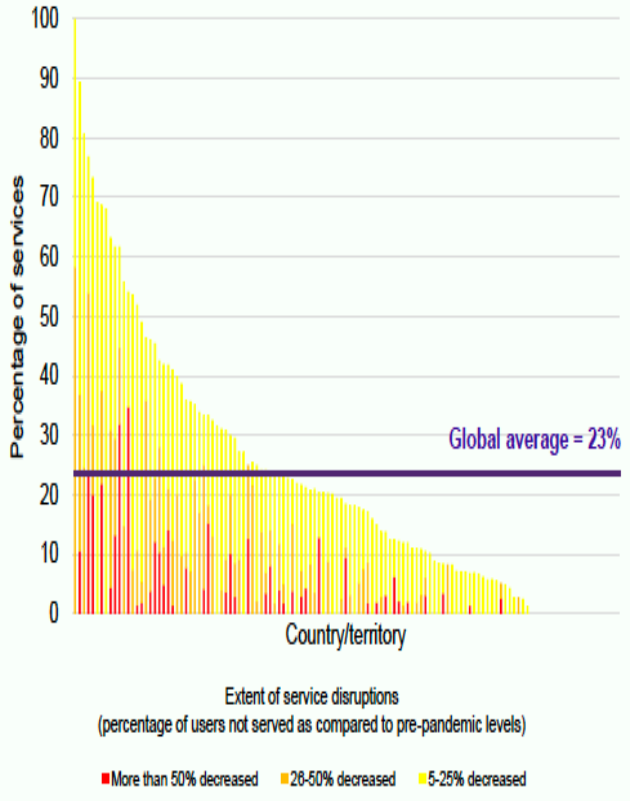
84% (105 of 125) countries reported some extent of disruptions in at least one essential health service

Note: The designations employed and the presentation of material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Denominator: represents responses from countries/territories/areas that responded to at least one survey section and consented to data sharing agreement.

Source: Round 4 Global pulse survey on continuity of essential health services, Nov 2022-Jan 2023 (reflecting situation at time of survey completion)

Countries reported continued disruptions to 23% of tracer health services (maximum number of services = 79)



The extent and magnitude of service disruptions has decreased compared to previous 2020-2021 reporting

World Health Organization

Demonstrating the first signs of recovery since reporting at the start of the pandemic

While service disruptions persist across most settings, countries reported the first signs of service recovery since 2020

- Fewer countries reported essential health service disruptions in 2022 compared to previous country reporting
- The magnitude of disruptions reported within countries has decreased

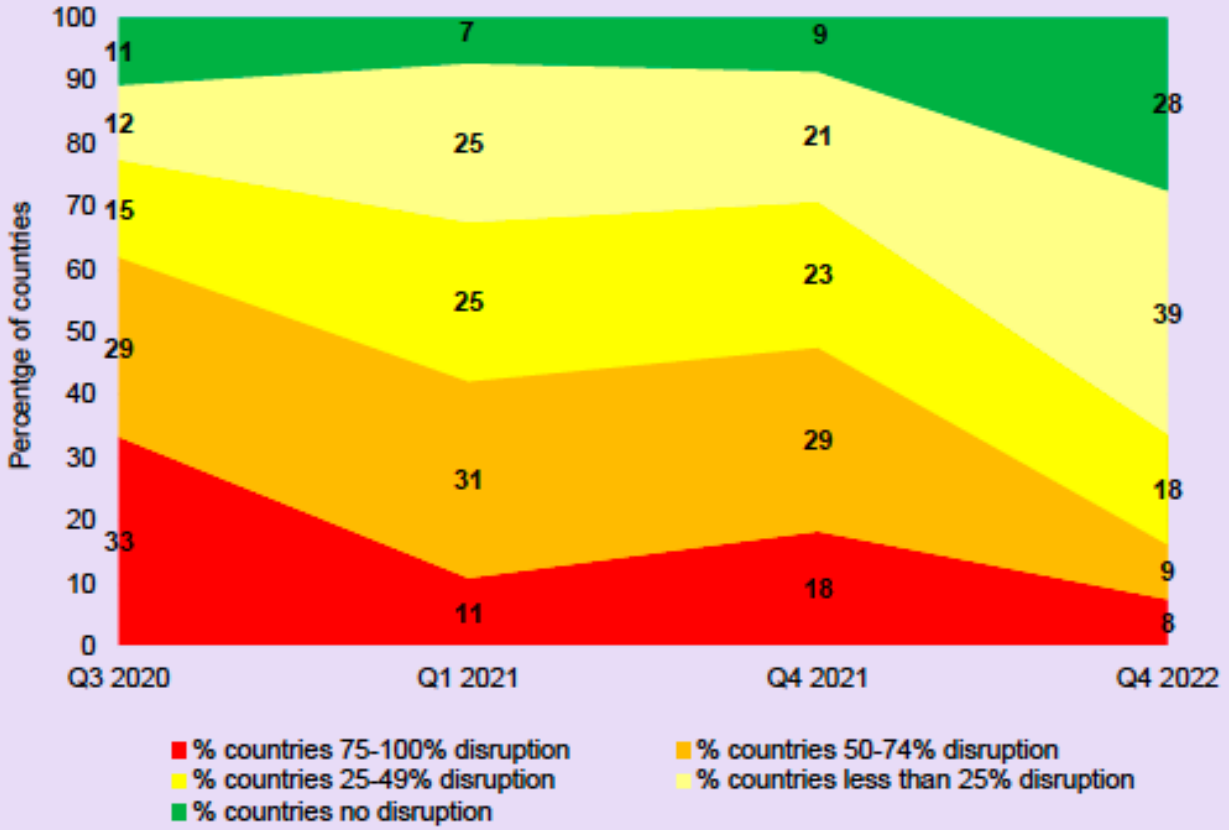
	Q3 2020 Round 1	Q1 2021 Round 2	Q4 2021 Round 3	Q4 2022 Round 4	Trajectory R1 R2 R3 R4
Percentage of countries reporting disruptions to at least one service	89%	93%	91%	84%	
Average percentage of services disrupted within country	56%	41%	46%	23%	

(n=84 countries that responded to all 4 survey rounds)

(n=27 services included in all 4 survey rounds)

Comparison of extent of service disruptions reported

by 84 countries that responded to all four survey rounds: Q3 2020 (Round 1), Q1 2021 (Round 2), Q4 2021 (Round 3) and Q4 2022 (Round 4)



Denominator: represents *84* countries, territories and areas that responded to all four survey rounds and consented to data sharing agreement. 27 tracer services were included in all four rounds of the survey.

Source: Round 4 Global pulse survey on continuity of essential health services, Nov 2022-Jan 2023 (reflecting situation at time of survey completion)

Disruptions in services for communicable diseases: TB, HIV, hepatitis and malaria

World Health Organization

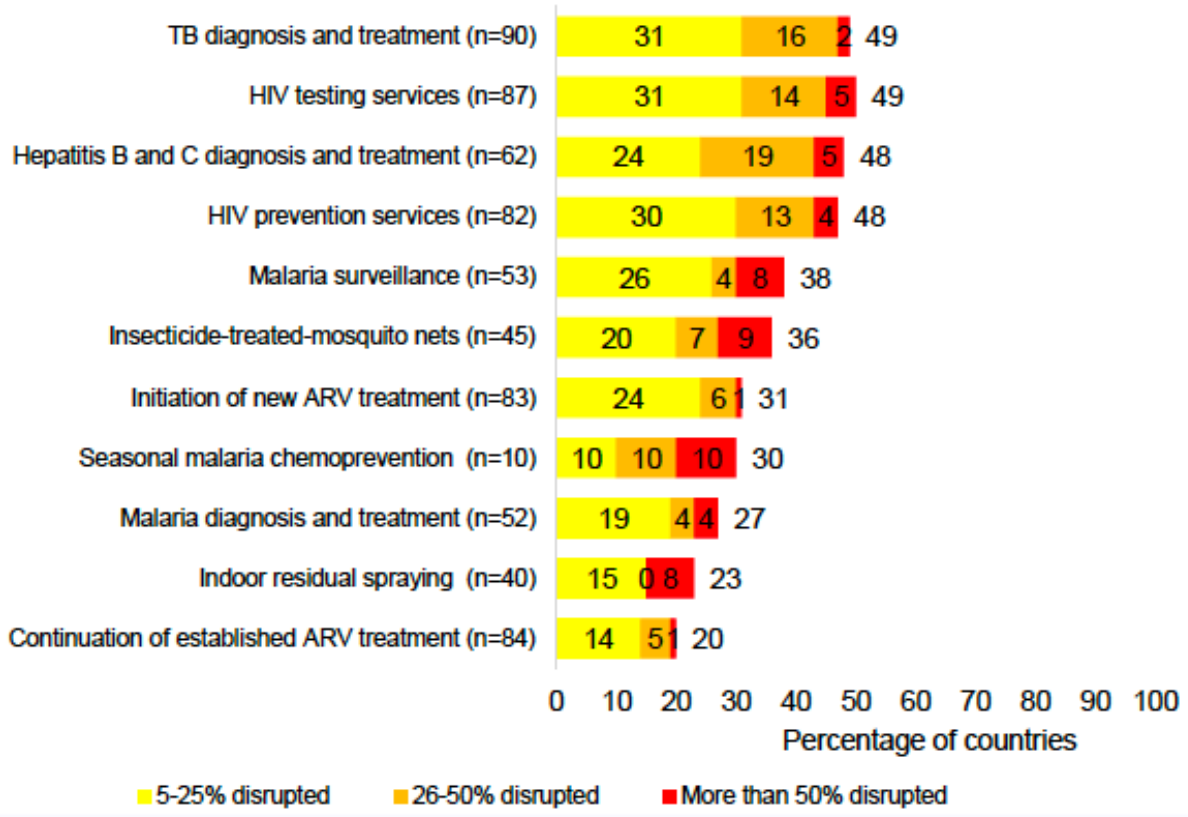
1/2

About half of countries report disruptions to TB diagnosis and treatment, HIV testing and prevention services, and hepatitis B & C diagnosis and treatment

1/3

About 1/3 of countries report disruptions to one or more malaria services (including diagnosis and treatment services and prevention campaigns)

Percentage of countries reporting disruptions in communicable disease (TB, HIV, hepatitis and malaria) services in Q4 2021



Denominator: excludes "Not applicable" or "Do not know" responses. Cumulative percentages may vary due to rounding.

Source: Round 3 Global pulse survey on continuity of essential health services, Nov-Dec 2021 (reflecting situation during previous 6 months)

Question 5

How effective are mRNA COVID-19 Vaccines in PWH?

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Review

Immunogenicity and efficacy of COVID-19 vaccines in people living with HIV: a systematic review and meta-analysis

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ABSTRACT

Objectives: Available data show that COVID-19 vaccines may be less effective in people living with HIV (PLWH) who are at increased risk for severe COVID-19. This meta-analysis aimed to compare the immunogenicity and efficacy of COVID-19 vaccines in PLWH with healthy individuals.

Methods: Pubmed/Medline, EMBASE, and the Cochrane Library were searched. Risk ratios of seroconversion were separately pooled using random-effects meta-analysis, and a systematic review without meta-analysis of SARS-CoV-2 antibody titer levels was performed after the first and second doses of a COVID-19 vaccine.

Results: A total of 22 studies with 6522 subjects met the inclusion criteria. After the first vaccine dose, seroconversion in PLWH was comparable to that in healthy individuals. After a second dose, seroconversion was slightly lower in PLWH compared with healthy controls, and antibody titers did not seem to be significantly affected or reduced among participants of both groups.

Conclusion: COVID-19 vaccines show favorable immunogenicity and efficacy in PLWH. A second dose is associated with consistently improved seroconversion, although it is slightly lower in PLWH than in healthy individuals. Additional strategies, such as a booster vaccination with messenger RNA COVID-19 vaccines, might improve seroprotection for these patients.

Table 1
Characteristics of included studies.

Source	Vaccine	n, Population(s) of interest	Age[a]	Gender[b]	Country/ Region	n, Comparison	Immunoassay	Threshold for positive response	Endpoints of data collection
Zou *et al.* (2022)	WIBP-CorV (inactivated)	46, HIV patients	Patients: 36 (31, 42) Controls: 31(27, 39)	Patients: 40/46 (87%) Controls: 19/38 (50%)	China	38, healthy controls	The serum levels of nAbs against the S protein RBD determined by SARS-CoV-2 nAbs assay kit by surrogate virus neutralization test (Zhuhai Livzon Diagnostics Inc, Zhuhai, China)	Positive serology: RBD: ≥10 BAU/ml	Day 28 after 2nd dose
Zeng *et al.* (2022)	BIBP-CorV or CoronaVac (inactivated)	132, HIV patients	Patients: 32 (28, 39) Controls: 34 (29, 39)	Patients: 119/132 (90.2%) Controls: 115/130 (75.5%)	China	130, healthy controls	S-RBD-IgG detected by magnetic particle chemiluminescence kits (Shengxiang Biotechnology, Changsha, China)	Positive serology: RBD: ≥1.0	Day 28 and 180 after 2nd dose
Madhi *et al.* (2022)	NVX-CoV2373 (recombinant protein nanoparticle)	122, HIV patients	Patients: 39 (34, 44) Controls: 32 (26, 38)	Patients: 37/122 (30.3%) Controls: 1217/2089 (58.3%)	South Africa	2089, healthy controls	Anti-S-IgG antibodies	Positive serology: > 95% participants in the placebo group	Day 14 after 2nd dose
Huang *et al.* (2022)	Sinopharm and Sinovac CoronaVac (inactivated)	129, HIV patients	Patients: 34 (28, 38) Controls: 34 (29, 47)	Patients: 128/129 (99.2%) Controls: 40/53 (75.5%)	China	53, healthy controls	SARS-CoV-2 specific total antibody and S-IgG antibodies using Chemiluminescence assay (CLIA) kits (Beijing Wantai Biological Pharmacy Enterprise Co., Ltd., Beijing, China)	Positive serology: > 30 pg/ml	Day 15–28 after 2nd dose
Antinori *et al.* (2022)	BNT162b2 or mRNA-1273 (mRNA)	166, HIV patients	Patients: 55 (46, 59) Controls: 42 (32, 53)	Patients: 27/166 (16.3%) Controls: 48/169 (28.4%)	Italy	169, healthy controls	The SARS-CoV-2 specific anti-N, and the anti-S/RBD tests (ARCHITECT SARS-CoV-2 IgG, and ARCHITECT SARS-CoV-2 IgG II) Quantitative, Abbott Laboratories, Wiesbaden, Germany respectively)	Positive serology: nAB ≥10	Day 28 after 2nd dose
Lombardi *et al.* (2022)	mRNA-1273 (mRNA)	71, HIV patients	Patients: 47 (39, 55) Controls: 58 (50, 66)	Patients: 60/71 (84.5%)Con-trols: 7/10 (70%)	Italy	10, healthy controls	Electrochemi Luminescent Immuno Assay (ECLIA)	Not explicitly stated	Day 28 from first dose and day 28 after 2nd dose
Schmidt *et al.* (2022)	BNT162,b2 (mRNA)	50, HIV patients	Patients: 55 (46–60) Controls: 42 (30–53)	Patients: 34/50 (68%)Con-trols: 32/60 (53.3%)	Germany	60, healthy controls	CE certified commercial ELISA (Euroimmun, Lübeck, Germany)	Positive serology: RBD: >1.1	7–155 days after the second dose (median of 37 days for people living with HIV and 26 days for controls)
Ogbe *et al.* (2022)	AZD1222 (Viral vector)	54, HIV patients	Patients: 42.5 (37.2–49.8) Controls: 38.5 (29.2–45.0)	Patients: 54/54 (100%) Controls: 36/50 (72%)	UK	60, healthy controls	Standardized total IgG ELISA against trimeric SARS-CoV-2 S protein	Seropositive: >3-fold increase	Day 42 and day 182 after 2nd dose
Brumme *et al.* (2022)	BNT162b2, mRNA-1273, AZD1222 (Viral vector)	100, HIV patients	Patients: 54 (40–61) Controls: 47 (35–70)	Patients: 88/100 (88%) Controls: 50/152 (33%)	Canada	152, healthy controls	Electro-chemiluminescence sandwich immunoassays	Not explicitly stated	One month after the first dose, and at 1 and 3 months after 2nd dose
Heftdal *et al.* (2022)	BNT162,b2 (mRNA)	269, HIV patients	Patients: 56.0 (49–64) Controls: 56 (49–63)	Patients: 242/269 (90.0%) Controls: 73/538 (13.6%)	Denmark	538, healthy controls	An in-house ELISA that detects IgG antibodies against the RBD of SARS-CoV-2	Positive serology: >150 AU/ml	Three weeks and 2 months after the first dose

(*continued on next page*)

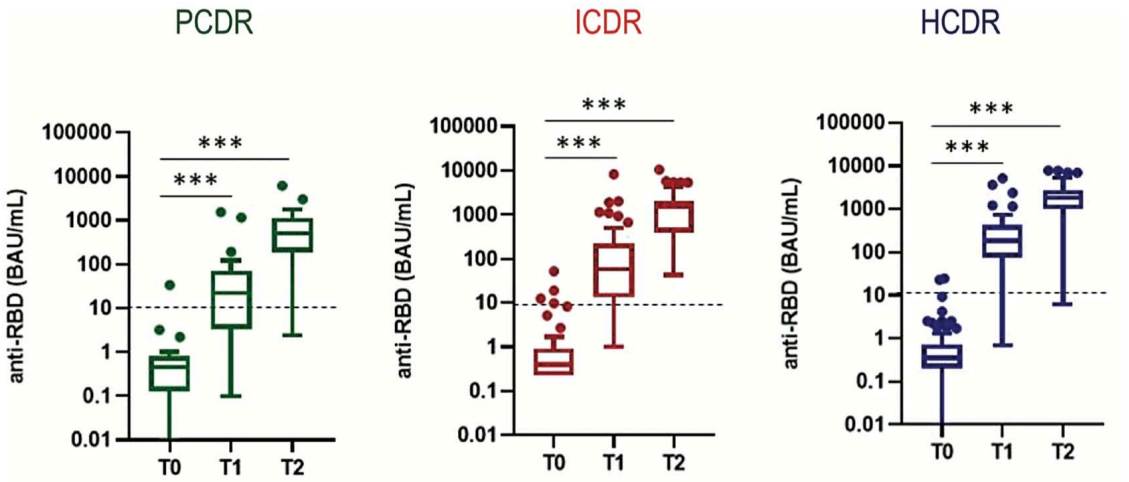
Clinical Infectious Diseases

MAJOR ARTICLE

Humoral and Cellular Immune Response Elicited by mRNA Vaccination Against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in People Living With Human Immunodeficiency Virus Receiving Antiretroviral Therapy Based on Current CD4 T-Lymphocyte Count

Andrea Antinori,[1] Stefania Cicalini,[1] Silvia Meschi,[2] Veronica Bordoni,[3] Patrizia Lorenzini,[1] Alessandra Vergori,[1] Simone Lanini,[1] Lidya De Pascale,[1] Giulia Matusali,[2] Davide Mariotti,[3] Alessandro Cozzi Lepri,[4] Paola Gallì,[5] Carmela Pinnetti,[1] Roberta Gagliardini,[1] Valentina Mazzotta,[1] Ilaria Mastrorosa,[1] Susanna Grisetti,[1] Francesca Colavita,[2] Eleonora Cimini,[3] Elisabetta Grilli,[1] Rita Bellagamba,[1] Daniele Lapa,[2] Alessandra Sacchi,[3] Alessandra Marani,[5] Carlo Cerini,[1] Caterina Candela,[1] Marisa Fusto,[1] Vincenzo Puro,[6] Concetta Castilletti,[2] Chiara Agrati,[3] Enrico Girardi,[7] and Francesco Vaia[5]; for the HIV-VAC Study Group[a]

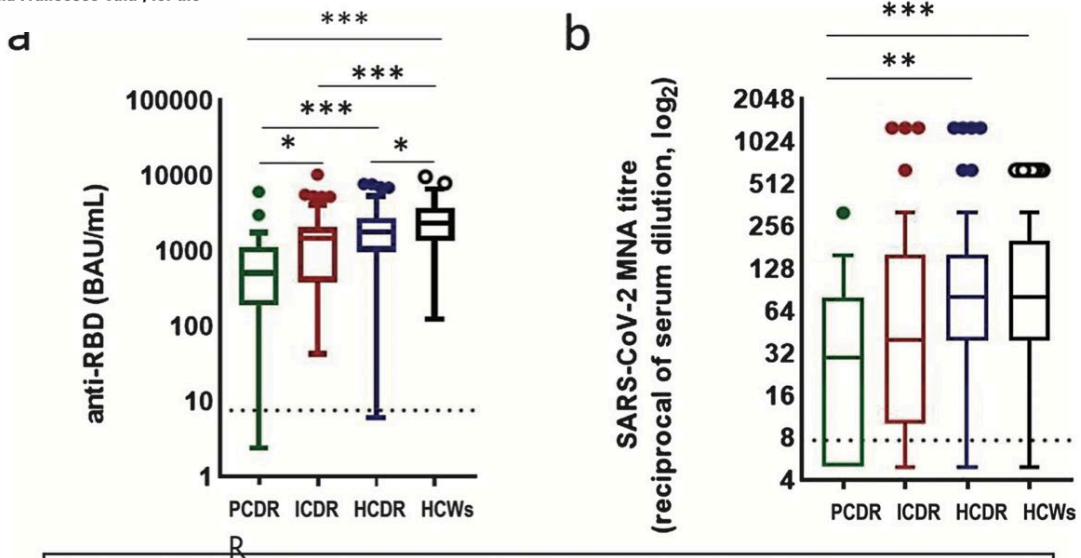
This study showed that humoral and T-cell responses to mRNA vaccination are significantly impaired in PLWH with CD4+ T-cell counts <200/µL, but comparable to those of the general population in PLWH with good CD4+ T-cell counts.



	PCDR			ICDR			HCDR		
Median	0.5	21.9	507	0.4	59	1477	0.4	183	1782
	0.2;	3.7;	212;	0.3;	15;	471;	0.2;	77;	989;
IQR	0.8	68.5	1143	0.9	214	2056	0.7	421	2769

***p<0.001 by paired Wilcoxon test

Abbreviations: PCDR, poor CD4 recovery:current CD4 T cell count <200 cell/mm³; ICDR: intermediate CD4 recovery: current CD4 T cell count 200-500 cell/mm³; HCDR, high CD4 recovery: current CD4 T cell count >500 cell/mm³



	PCDR	ICDR	HCDR	HCWs	PCDR	ICDR	HCDR	HCWs
Median	507	1477	1782	2353	30	40	80	80
	212;	471;	989;	1378;	5;	10;	40;	40;
IQR	1143	2056	2769	3758	80	160	160	160

P<0.001 at Kruskall-Wallis test; *p<0.05; **p<0.01; ***p<0.001

Abbreviations: PCDR, poor CD4 recovery:current CD4 T cell count <200 cell/mm³; ICDR: intermediate CD4 recovery: current CD4 T cell count 200-500 cell/mm³; HCDR, high CD4 recovery: current CD4 T cell count >500 cell/mm³; HCWs, health care workers

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Analysis of Postvaccination Breakthrough COVID-19 Infections Among Adults With HIV in the United States

Sally B. Coburn, PhD, MPH; Elizabeth Humes, MPH; Raynell Lang, MD, MSc; Cameron Stewart, MS; Brenna C. Hogan, MPH; Kelly A. Gebo, MD, MPH; Sonia Napravnik, PhD; Jessie K. Edwards, PhD, MSPH; Lindsey E. Browne, BA; Lesley S. Park, PhD, MPH; Amy C. Justice, MD, PhD; Kirsha S. Gordon, PhD, MS; Michael A. Horberg, MD, MAS; Julia M. Carta, MPH; Eric Watson, BA; Caleena R. Jefferson, MIT; Michael J. Silverberg, PhD, MPH; Jacek Skarbinski, MD; Wendy A. Leyden, MPH; Carolyn F. Williams, PhD; Keri N. Althoff, PhD, MPH; for the Corona-Infectious-Virus Epidemiology Team (CIVETs) of the NA-ACCORD of IeDEA

RESULTS Among 113 994 patients (33 029 PWH and 80 965 PWoH), most were 55 years or older (80 017 [70%]) and male (104 967 [92%]); 47 098 (41%) were non-Hispanic Black, and 43 218 (38%) were non-Hispanic White. The rate of breakthrough infections was higher in PWH vs PWoH (55 [95% CI, 52-58] cases per 1000 person-years vs 43 [95% CI, 42-45] cases per 1000 person-years). Cumulative incidence of breakthroughs 9 months after full vaccination was low (3.8% [95% CI, 3.7%-3.9%]), albeit higher in PWH vs PWoH (4.4% vs 3.5%; log-rank $P < .001$; risk difference, 0.9% [95% CI, 0.6%-1.2%]) and within each vaccine type. Breakthrough infection risk was 28% higher in PWH vs PWoH (adjusted hazard ratio, 1.28 [95% CI, 1.19-1.37]). Among PWH, younger age (<45 y vs 45-54 y), history of COVID-19, and not receiving an additional dose (aHR, 0.71 [95% CI, 0.58-0.88]) were associated with increased risk of breakthrough infections. There was no association of breakthrough with HIV viral load suppression, but high CD4 count (ie, ≥500 cells/mm^3) was associated with fewer breakthroughs among PWH.

Key Points

Question Are the rate and risk of COVID-19 breakthrough infections higher among vaccinated people with vs without HIV in the United States through December 31, 2021?

Findings In this cohort study of 113 994 patients, risk of breakthrough infection was low overall (3.8%) but 28% higher in people with vs without HIV. The breakthrough rate was also higher in people with vs without HIV (55 cases per 1000 person-years vs 43 cases per 1000 person-years).

Meaning The higher rate and risk of infection in people with HIV observed in this study suggests comprehensive inclusion of this population in recommendations for additional primary doses in immunocompromised groups.

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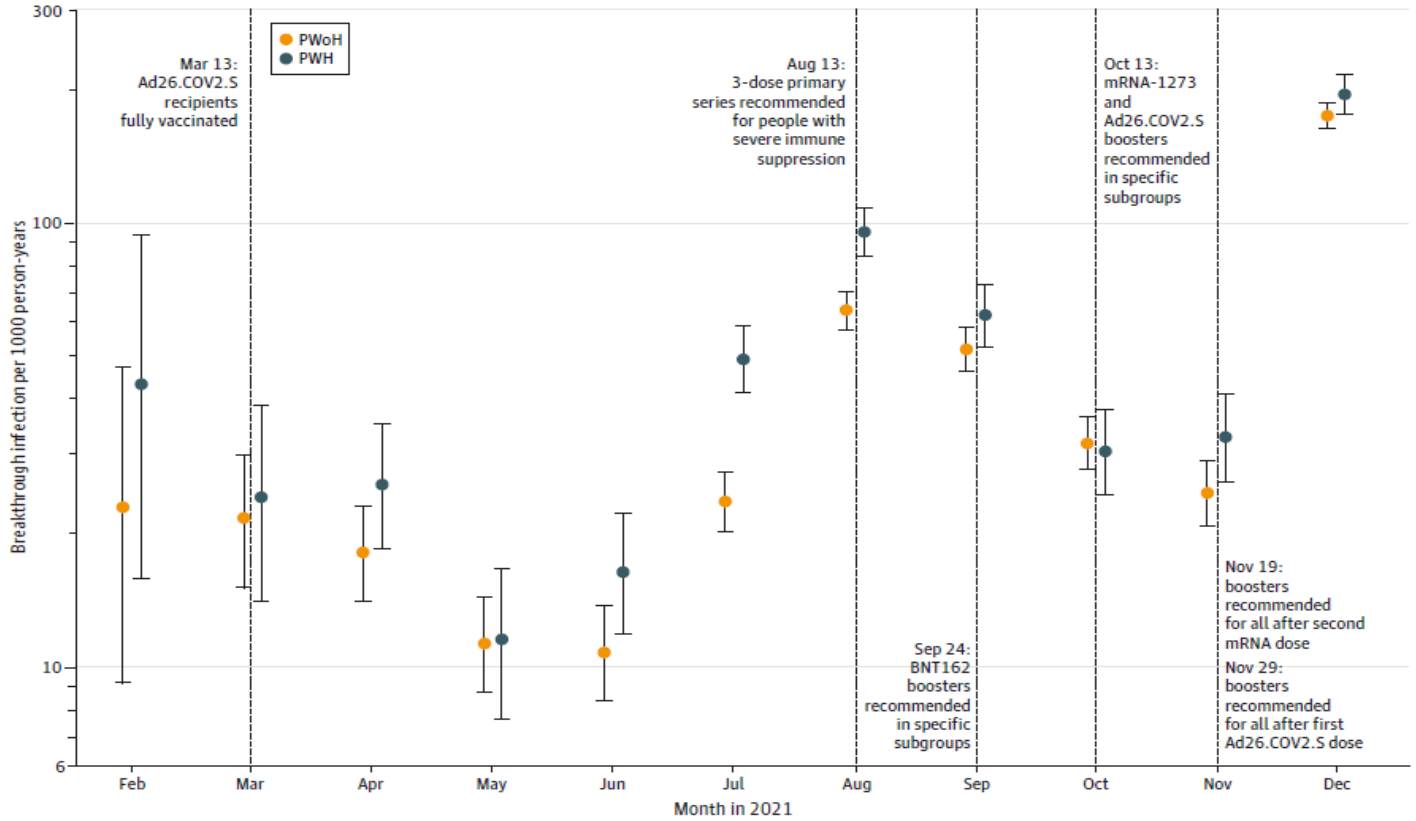
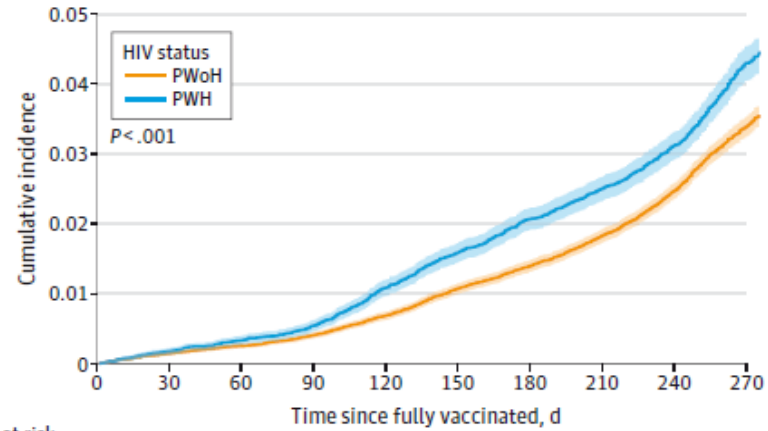
Figure 1. Trends in SARS-CoV-2 Vaccine Breakthrough Incidence Rates Among People With HIV (PWH) and People Without HIV (PWoH)



Overall, 113 994 individuals were included. The incidence rate estimates for January 2021 were 0 (95% CI, 0.0-492.3) cases per 1000 person-years for PWH and 57.0 (1.4-317.8) cases per 1000 person-years in PWoH; these estimates are not included in the plot due to small numbers.

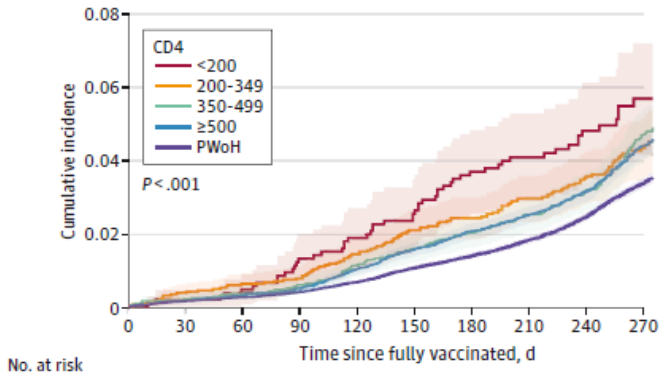
A Cumulative incidence of SARS-CoV-2 vaccine breakthrough by HIV status



No. at risk

PWoH	80965	80678	80394	80071	79601	79046	78550	74674	61777	32305
PWH	33029	32904	32768	32588	32305	32034	31762	30073	25171	13637

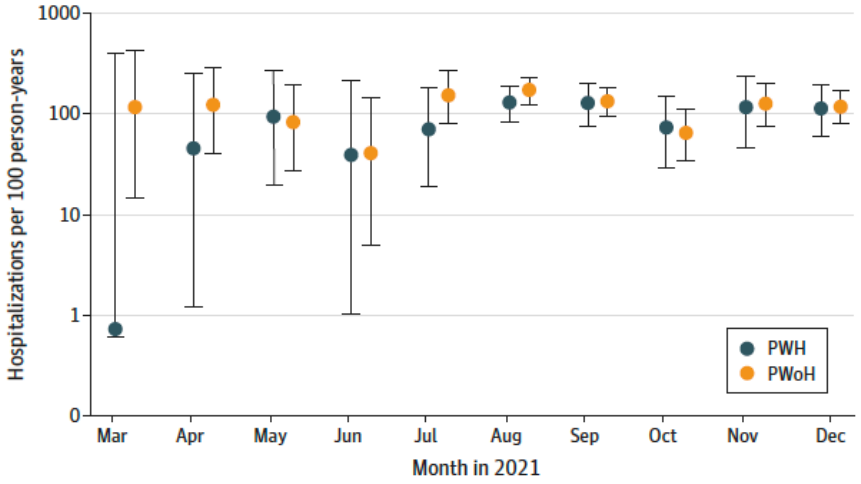
B Cumulative incidence of SARS-CoV-2 vaccine breakthrough by CD4 cell count and HIV status



No. at risk

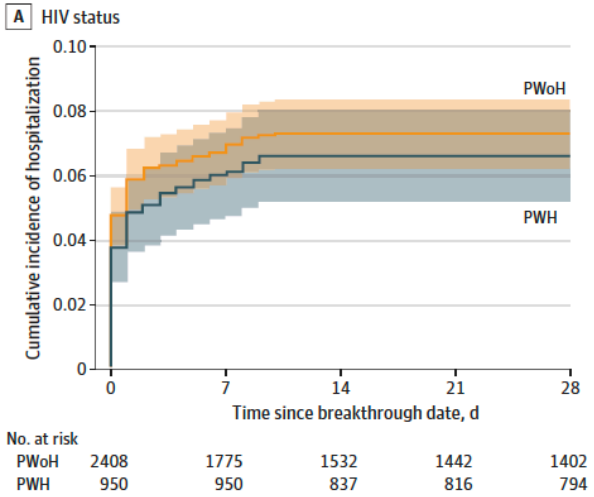
<200	1086	1080	1067	1047	1037	1017	998	915	720	409
200-349	2753	2734	2718	2703	2677	2652	2632	2470	2021	1143
350-499	4488	4467	4439	4413	4377	4338	4303	4071	3467	1960
≥500	18309	18242	18186	18107	17953	17806	17649	16752	13997	7321
PWoH	80965	80678	80394	80071	79601	79046	78550	74674	61777	32305

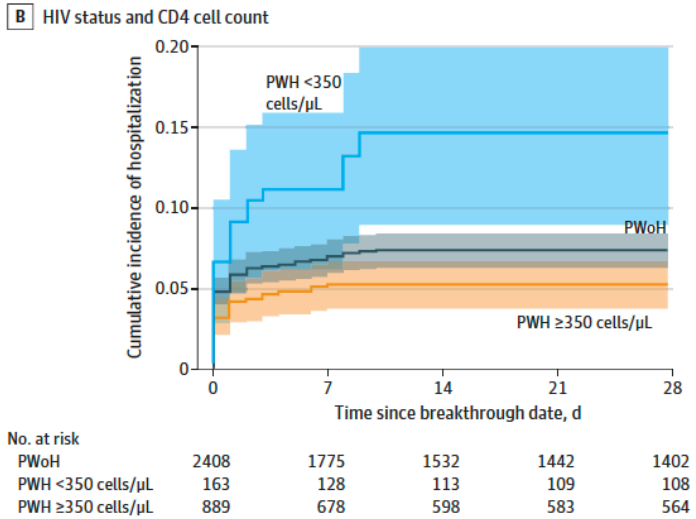
Risk of severe COVID-19 breakthrough illness was low among vaccinated PWH and PWoH

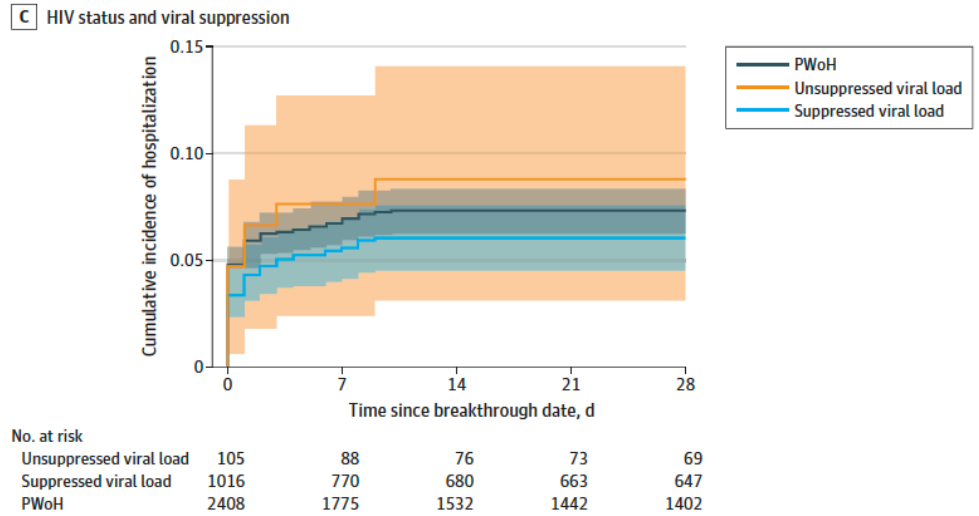


Among 3649 patients with breakthrough COVID-19 (1241 PWH and 2408 PWoH), the **cumulative incidence of severe illness in the first 28 days was low** and **comparable between PWoH and PWH (7.3%vs 6.7%; risk difference, −0.67%; 95%CI, −2.58%to 1.23%).**

The risk of **severe breakthrough illness** was 59% higher in PWH with CD4 cell counts less than 350 cells/μL compared with PWoH (aHR, 1.59; 95%CI, 0.99 to 2.46; P = .049). In multivariable analyses among PWH**, being female, older, having a cancer diagnosis, and lower CD4 cell count were associated with increased risk of severe breakthrough** illness, whereas previous COVID-19 was associated with reduced risk.







Lang R, et al. JAMA Network Open. 2022;5(10):e2236397

grazie per l'attenzione