AETC AIDS Education & Training Center Program Mountain West

An Update on COVID-19 for People with HIV

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Project ECHO

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Disclaimer

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Learning Objectives

After attending this presentation, learners will be able to:

- Describe the characteristics and impact of COVID-19 among persons with HIV
- Describe the importance of COVID-19 vaccination in persons with HIV
- Understand COVID-19 treatment and prevention modalities for PWH

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COVID-19 Epidemiology Among People with HIV

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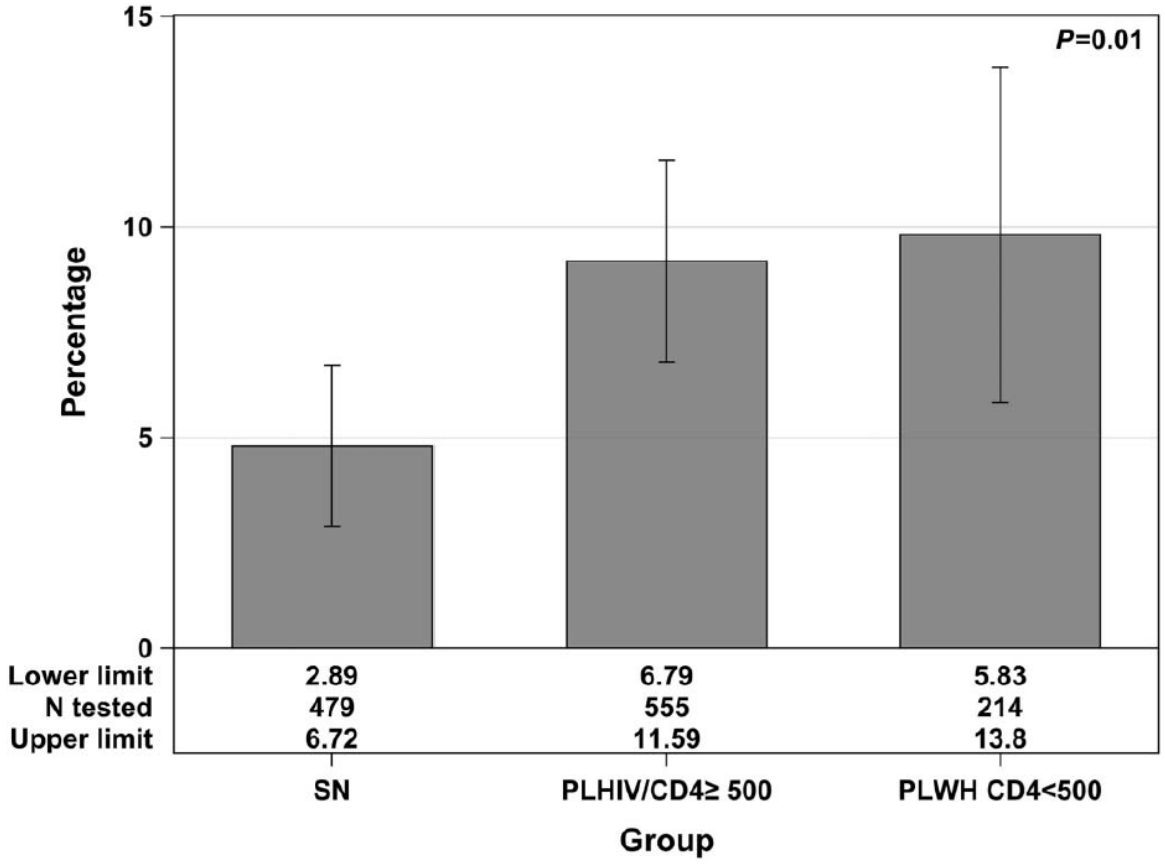
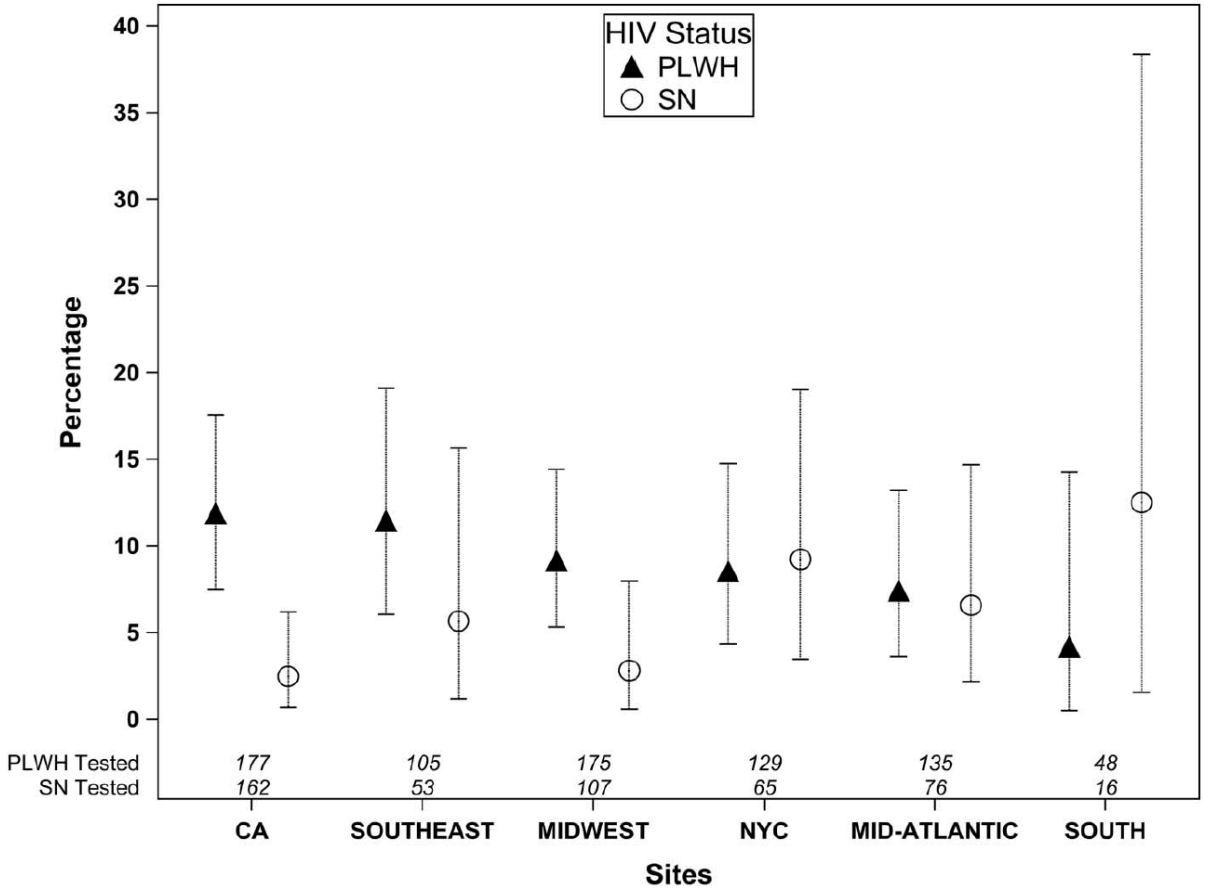
Are People with HIV at Higher Risk of SARS-CoV-2 Infection?

- Some studies suggest PWH are more likely to test positive for SARS-CoV-2.
- In a study with the MACS-WIHS cohort, PWH were more likely to test + for SARS-CoV-2 than seronegative controls.





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

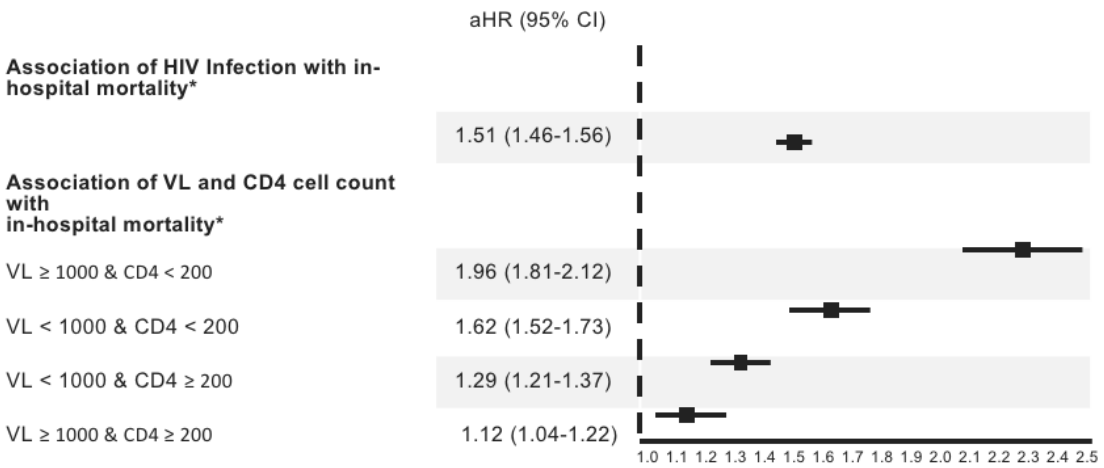
Are People with HIV at Higher Risk of Severe, Fatal COVID-19?

Objective: To assess clinical features and risk factors for severe/fatal COVID-19 among hospitalized individuals

Methods: Between January 2020 to May 2022 anonymized individual-level clinical data from 629,729 in-hospital COVID-19 cases in 50 countries across the world were reported to WHO

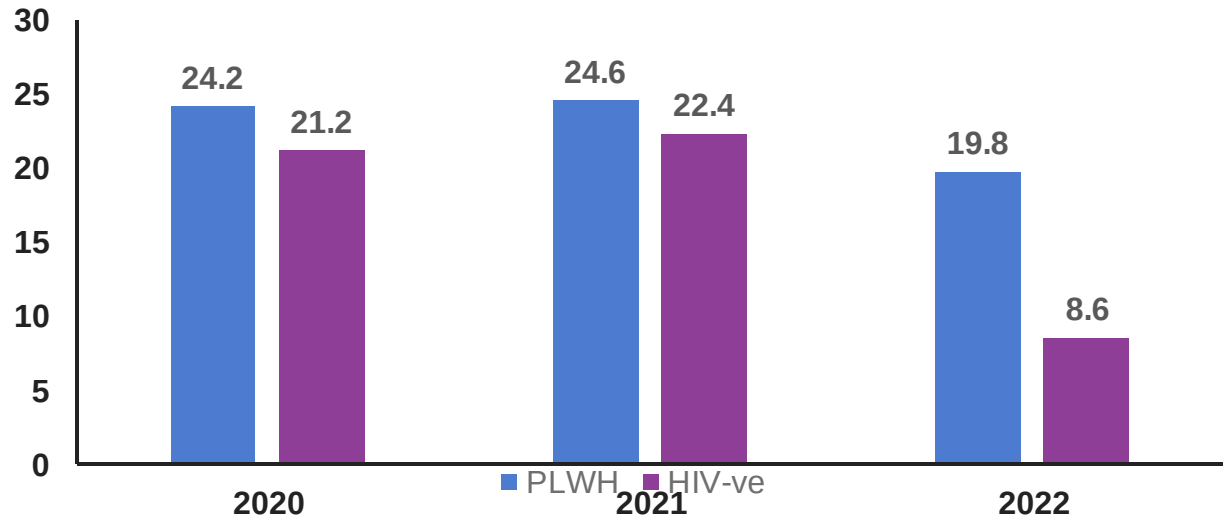
Results: The group included 362,941 people in 42 countries with known HIV status, of whom 29,530 (8.1%) were people with HIV

RESULTS (2): PWH have higher risk of in-hospital mortality compared to HIV-ve



*Adjusted for age, gender, co-morbidities including TB, cancer, diabetes, hypertension, pulmonary disease and chronic kidney failure

COVID-19 mortality over time by HIV status



Bertagnolio S, et al. AIDS 2022; Montreal, Canada; July 29-Aug 2, 2022; Abst. OAB0404.

Among PWH, Who is at Increased Risk of COVID-19?

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

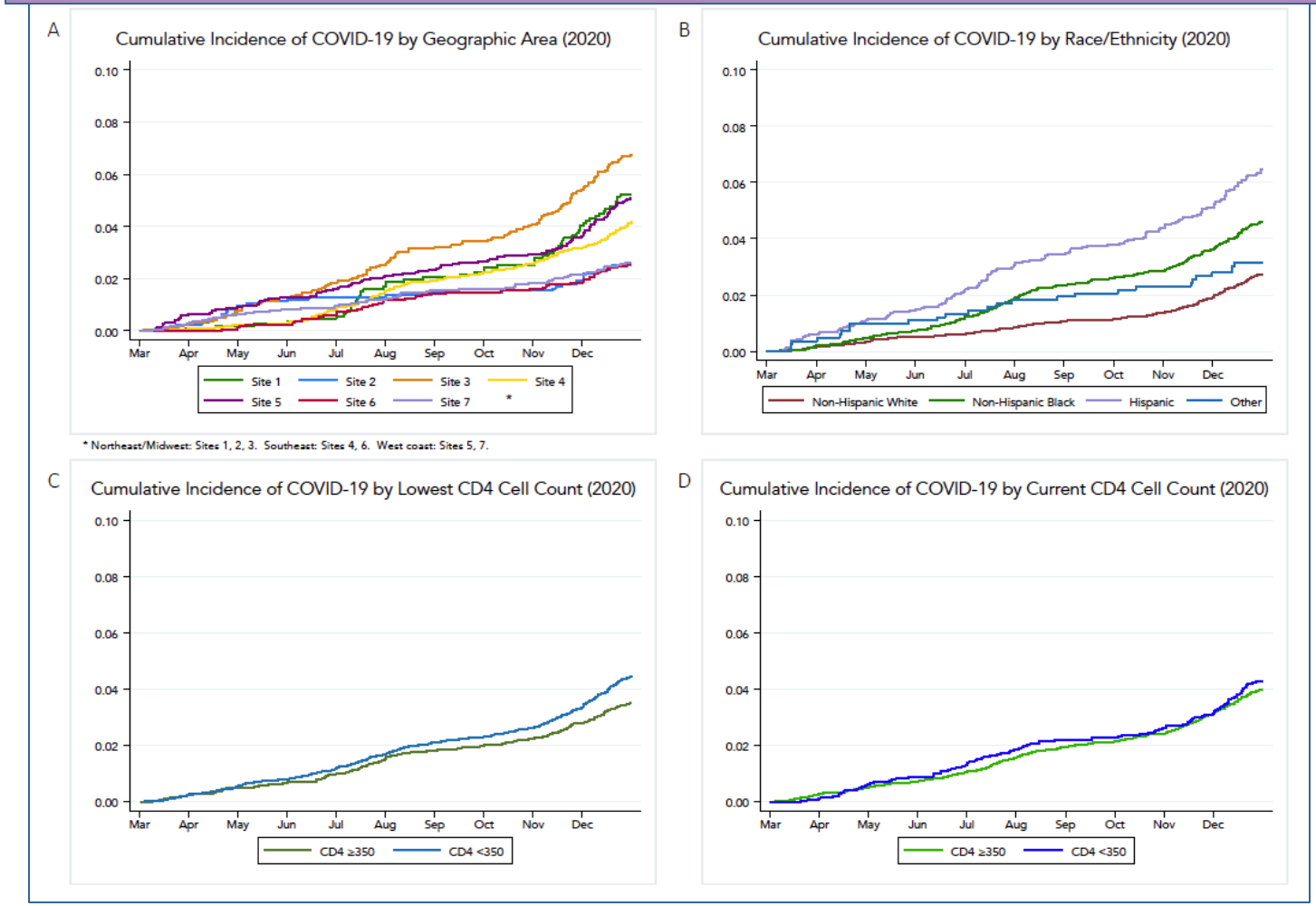
- PWH fewer comorbidities than general population
- Almost entire PWH pop with viral load suppression (>95%)

JJ Chang, JAIDS 2021

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

Islam, IJSTD AIDS 2022

CNICS Multicenter US Cohort of PWH, 2020



Bender Ignacio and Shapiro, AIDS 2022

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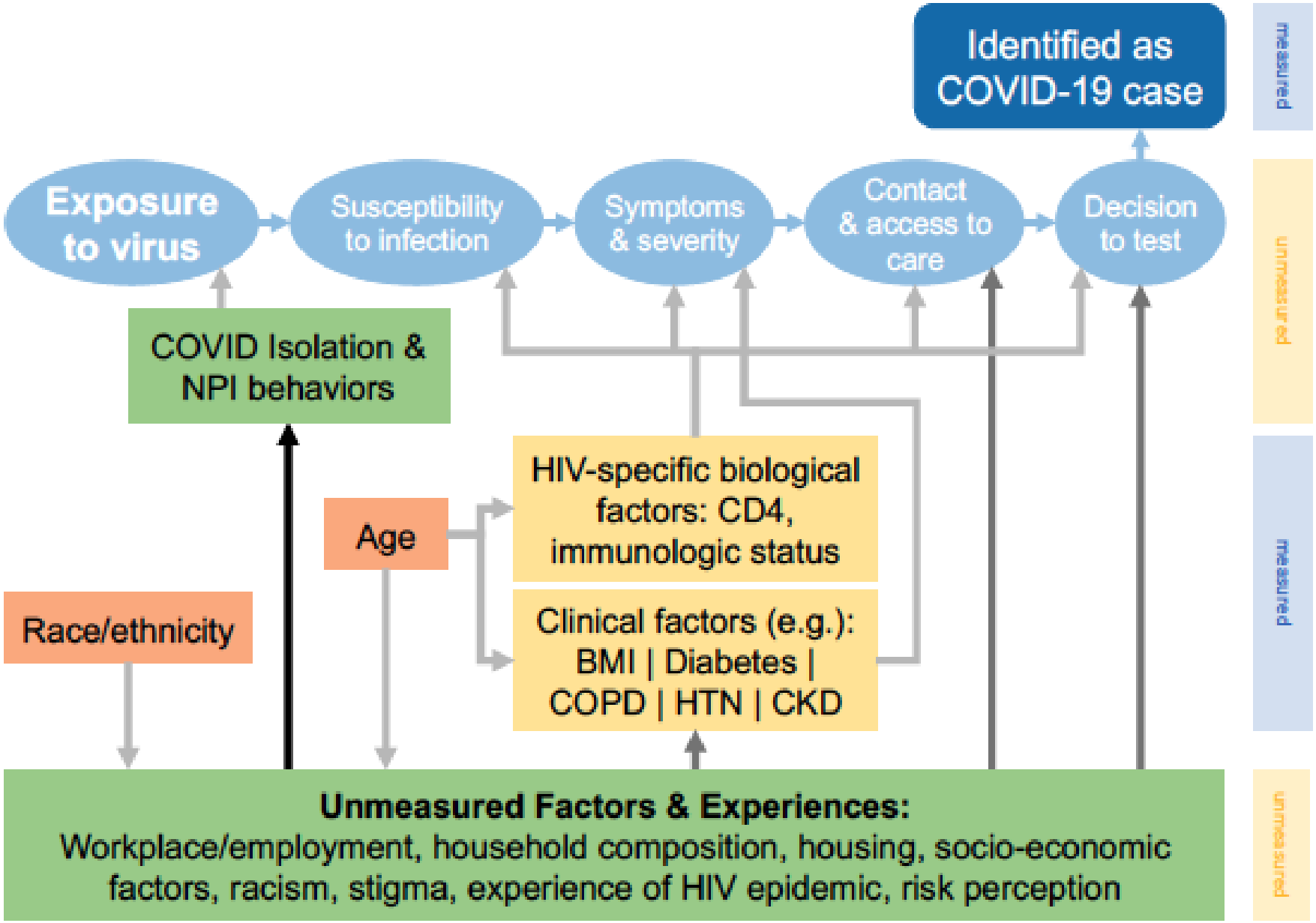
Risk of COVID-19 Incidence ≠ Risk of Comorbidities on COVID-19 Severity



Bender Ignacio, Shapiro, Cachay, *AIDS* 2022

Potential Reasons Why PWH May Have Worse COVID-19 Outcomes

- 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
- PWH with low CD4 cell counts may be at increased risk for severe COVID-19 (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
- PWH have high rates of comorbidities that are also risk factors for severe COVID-19
- PWH more likely to be racial/ethnic minorities, poor – risk factors for worse COVID-19 outcomes

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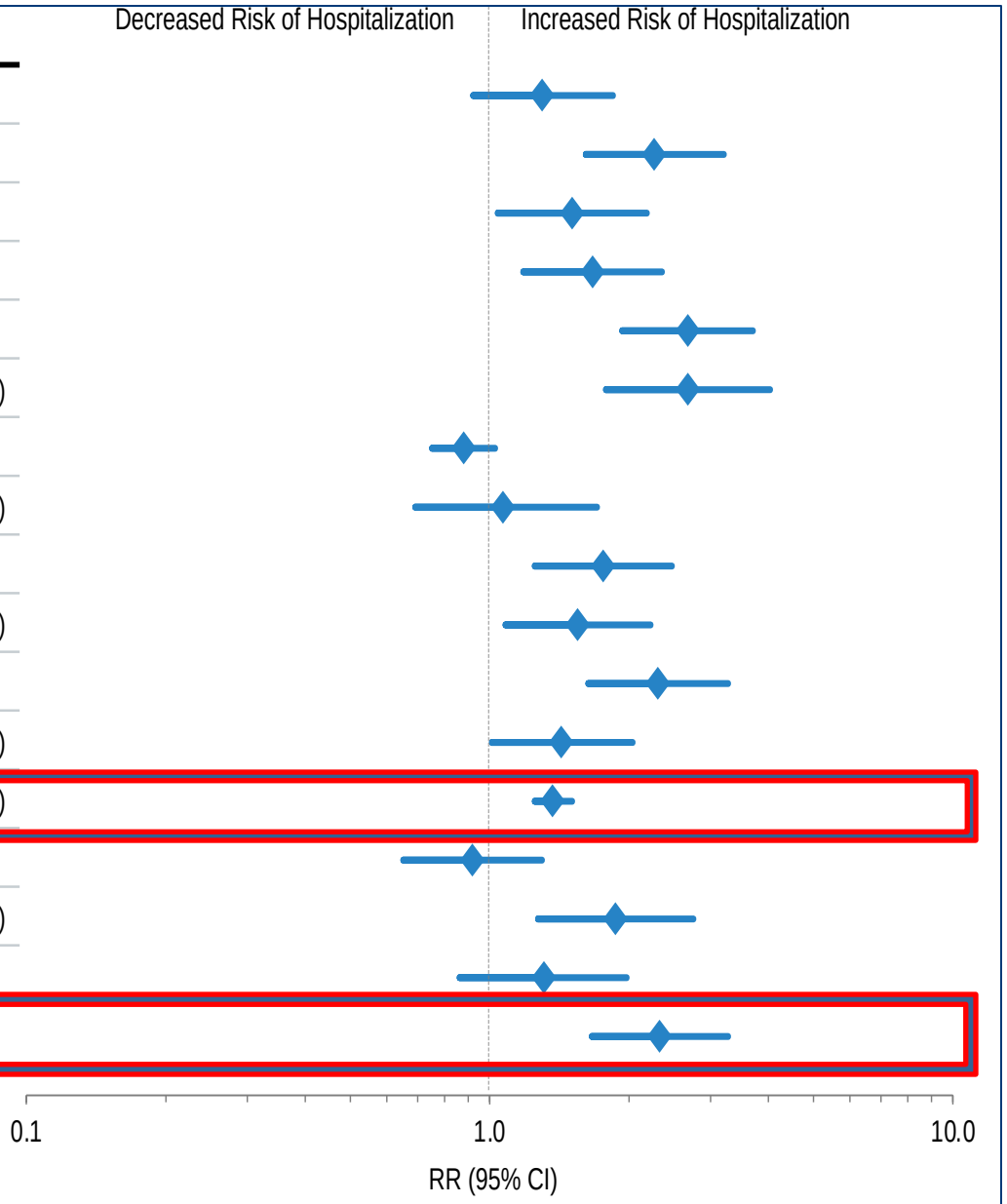
Are People with HIV at Higher Risk of Severe COVID-19?

Characteristic[a]	RR (95% CI)
Female	1.30 (0.92, 1.85)
Age (≥60 vs. <60)	2.27 (1.61, 3.21)
Race (Black vs. non-Black)	1.51 (1.04, 2.19)
Lowest CD4 count (<200 vs. ≥200 cells/mm^3)	1.67 (1.18, 2.36)
Current CD4 count (≤350 vs. >350 cells/mm^3)	2.68 (1.93, 3.71)
Current CD4 count (<200 vs. ≥200 cells/mm^3)	2.68 (1.78, 4.04)
CD4:CD8 ratio (per 1 standard deviation increase)	0.88 (0.75, 1.03)
Detectable viral load (≥50 vs. <50 copies/mL)	1.07 (0.69, 1.71)
Diabetes	1.76 (1.25, 2.48)
Hypertension	1.55 (1.08, 2.23)
CKD (eGFR, <60 vs. ≥60 mL/min/1.73 m^2)	2.31 (1.63, 3.28)
BMI (<30 vs. ≥30 kg/m^2)	1.43 (1.01, 2.04)
ASCVD risk score (per 10% increase)	1.37 (1.25, 1.51)
Cigarette smoker (ever)	0.92 (0.65, 1.30)
COPD	1.87 (1.27, 2.76)
HCV	1.31 (0.86, 1.98)
FIB-4 score (>1.45 vs. ≤1.45)	2.33 (1.66, 3.28)



Most studies recapitulate non-HIV specific risks in PWH:

- HTN
- DM
- Age
- BMI

Shapiro & Bender Ignacio et al, *JAIDS*, 2022

COVID-19 Severity Risk: CD4 & VL

- Across cohorts from early pandemic through the present, clear trends toward increased risk of severe outcomes with low CD4
- Some cohorts suggest current CD4 <350 as threshold, others at 200, but analysis dependent
  - Concern for confounding by test date & SARS CoV-2 effect on lymphopenia (e.g. WCDPH used data from hospitalization)
- Most large non-HIV specific datasets lack specificity on parameters of HIV treatment
- Most PWH are on ART in these cohorts
- CNICS: History of CD4 <200 RR 1.67 and current CD4 <350 RR 2.68 for hospitalization, low CD4/CD8 ratio increases risk

WCDPH CID 2020; Vizcarra Lancet HIV 2020; Shapiro & Bender Ignacio, *JAIDS* 2022

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Long-COVID-19 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 out of 1800 PWH had COVID-19 (median age = 51; 79.7% males; median CD4 = 560).
- 35% had asymptomatic COVID-19; 48% mild COVID-19; 17.1% moderate to severe COVID-19 and 4.1% died.
- Among 75 patients who survived COVID-19, 26.7% reported PASC at a median follow up of 6 months.
- Asthenia, shortness of breath and headaches were most common symptoms.
- Only the severity of COVID-19 predicted PASC.

Viruses 2022; 14, 493

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Preventing and Treating COVID-19 in People with HIV

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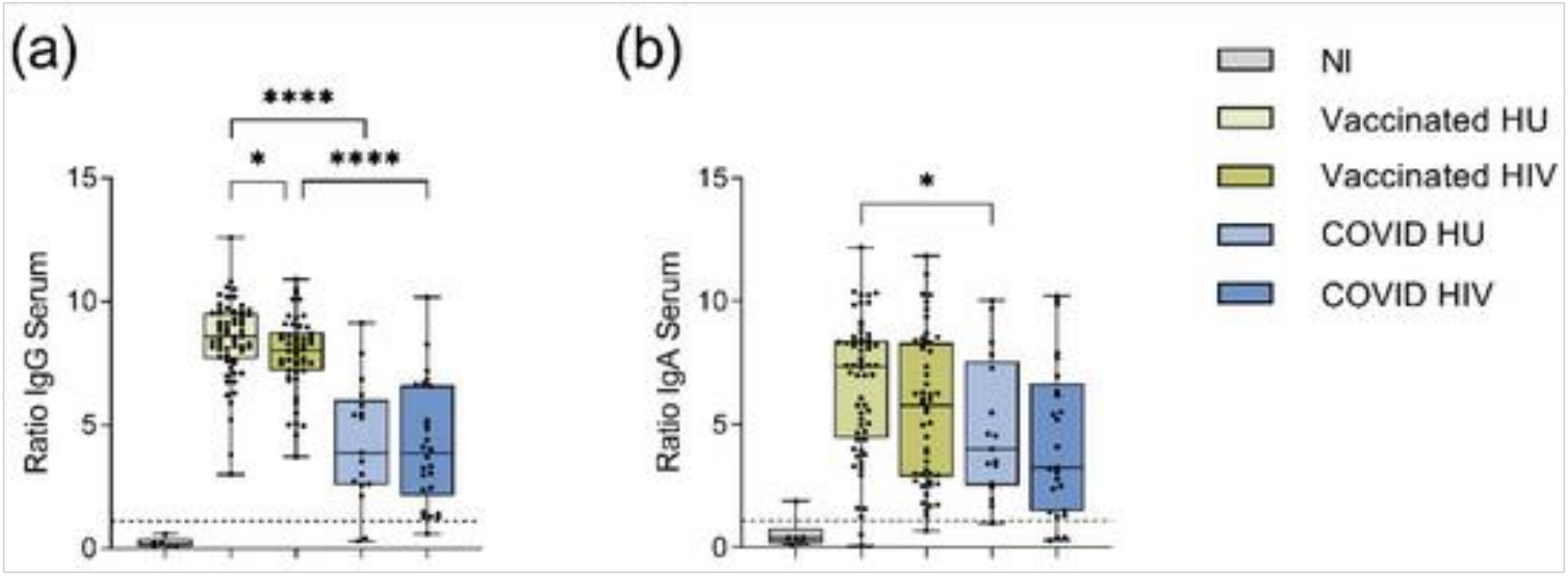
How Effective are mRNA COVID-19 Vaccines in PWH?

BNT162b2 (Pfizer) post 2nd dose vs COVID-19 infection (n=153)



Schmidt et al, *Viruses* 2022

Lower neutralization response, trend toward lower IgG

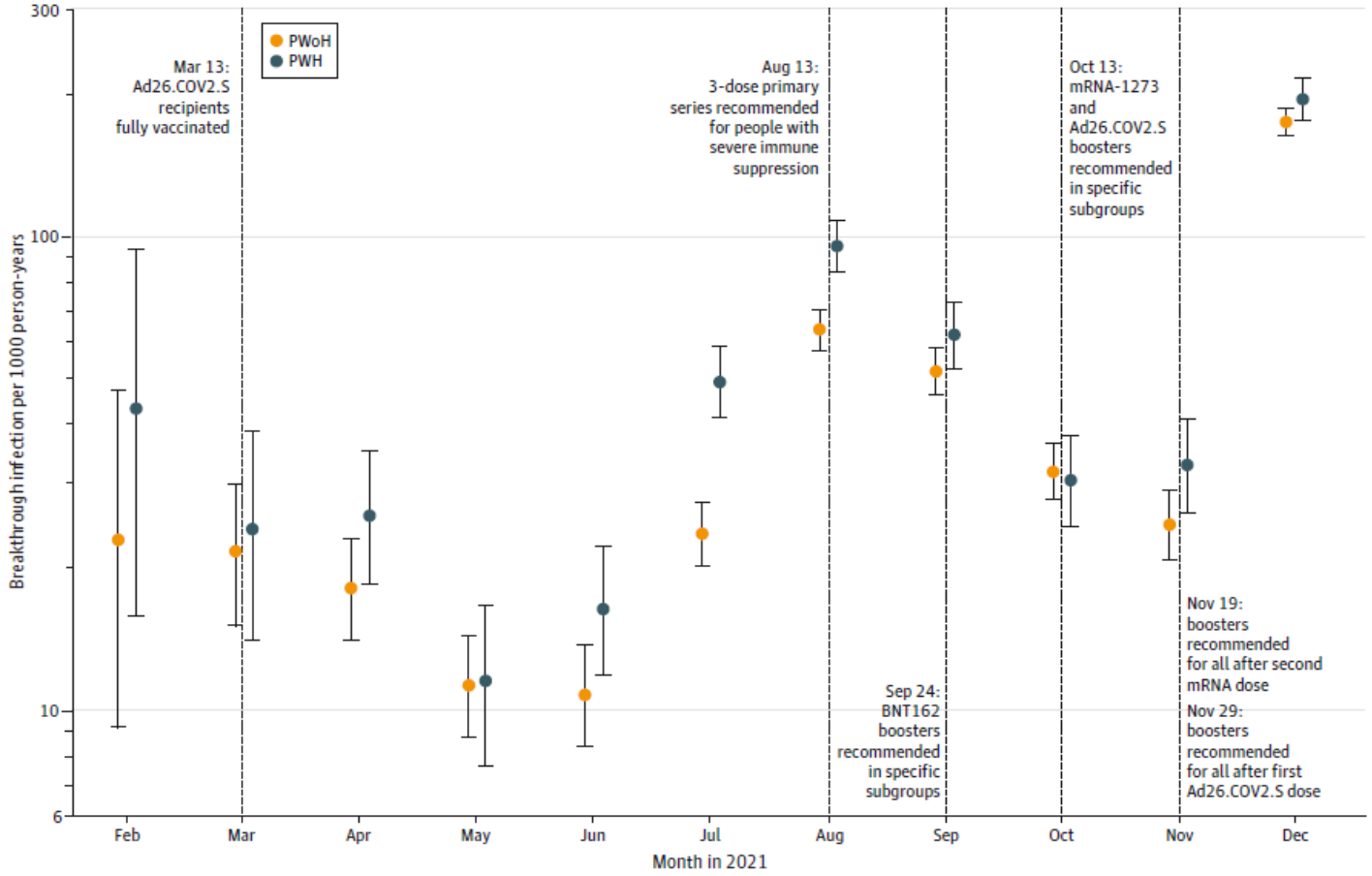
Especially among those with lower CD4 or receipt of BNT162b2 vs mRNA1273

-Spinelli CID 2021

33-44% higher breakthrough post-vaccination

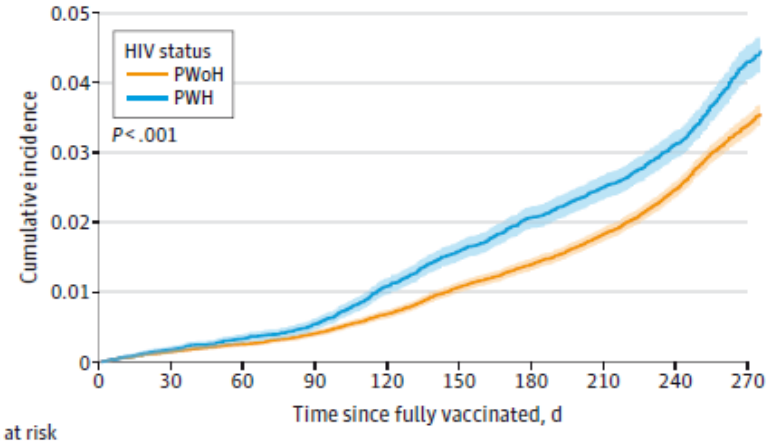
N3C Sun, JAMA 2021; CIVETs Coburn *Jama Network Open 2022*

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.

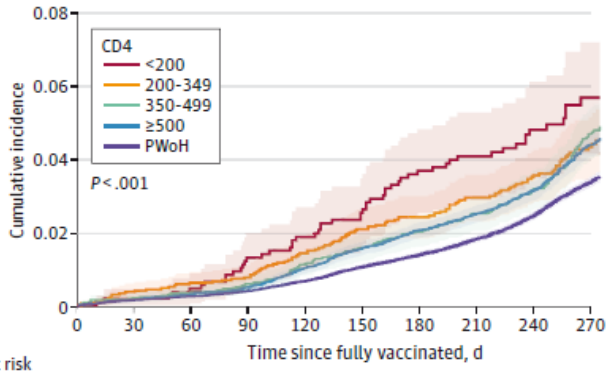
A Cumulative incidence of SARS-CoV-2 vaccine breakthrough by HIV status



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

Coburn SB, et al. JAMA Network Open 2022

Primary Series Recommendations for Adults with HIV Who Are Immunocompromised (CD4 ≤ 200 or Not Suppressed on Antiretroviral Therapy) *See the above recommendations plus an additional dose as recommended below and see notes.*		
Population	**Vaccine**	**Recommendation**
A person (16 years and older) with advanced HIV (CD4 cell count ≤ 200, CD4% < 14) or with untreated HIV who received two doses of the Pfizer/BioNTech vaccine	Pfizer/ BioNTech	Should receive a third dose of Pfizer/BioNTech vaccine at least 28 days after their second dose
A person (18 years and older) with advanced HIV (CD4 cell count ≤ 200, CD4% < 14) or with untreated HIV who received two doses of Moderna vaccine	Moderna	Should receive a third dose of Moderna vaccine at least 28 days after their second dose The third dose should also be a full (100 micrograms) dose.
A person (18 years and older) with advanced HIV (CD4 cell count ≤ 200, CD4% < 14) or with untreated HIV who received a single dose of the J&J/Janssen vaccine	J&J/Janssen	Should receive a second dose **with an mRNA vaccine** at least 4 weeks after their first dose.

Sept 2022: All >12yrs old should receive the Omicron bivalent booster following primary series
***Number of prior vaccinations (post primary dose) unimportant**
***Bivalent booster 2 months after last booster or Omicron infection**

CDC recommendations

https://www.hivma.org/globalassets/idsa/public-health/covid-19/covid-19-vaccines-pwh-table.pdf

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COVID-19 Vaccines for PWH – Summary

- Vaccine efficacy against SARS-CoV-2 infection was 72% in PWH with CD4 > 450 cells/uL but only 59% with lower counts (ancestral/Beta variants)
- COVID-19 vaccination is recommended for all PWH.
- There are no safety concerns that are specific for PWH.
- PWH with CD4 < 500 cells/uL may have a weaker response to vaccination.

Pooled meta-analysis, prior to Omicron: Tamuzi JL, et al. MedRxiv.

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COVID-19 PrEP for High-Risk Individuals

Tixagevimab/Cilgavimab 600 mg IM

Figure 2. FDA EUA criteria for the use of tixagevimab/cilgavimab for pre-exposure prophylaxis of COVID-19 in moderately or severely immunocompromised patients [1]

According to the FDA Emergency Use Authorization of Evusheld, medical conditions or treatments that may result in moderate to severe immune compromise include but are not limited to:

- Active treatment for solid tumor and hematologic malignancies
- Receipt of solid-organ transplant and taking immunosuppressive therapy
- Receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Advanced or untreated HIV infection (people with HIV and CD4 cell counts <200mm^3, history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV)
- Active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, chancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory (e.g., B-cell depleting agents)

FDA EUA Criteria
Via IDSA Guidelines
14 Mar 2022

**Concern about less efficacy vs BA.4 and BA.5, especially BA.4.6

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Among PWH, Who Should be Treated for COVID-19?

- Consider all risk factors, including age, medical comorbidities and disease stage, not just HIV immune and virologic status

- No differential recommendation for treatment modality: follow NIH guidelines for disease stage and EUA/approved agents

- IDSA: guidance on use of nirmatrelvir/r and HIV/HCV proteases continue both without interruption; ok for co-use

https://www.idsociety.org/globalassets/covid-19-real-time-learning-network/patient-populations/hiv/oral-covid-tx-considerations-for-people-with-hiv-and-hcv.pdf

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ART in COVID-19 Treatment & Prevention

- No clinical evidence of benefit of LPV/r, TDF, or other ARVs against SARS-CoV-2
  - Observational data from Spain on TAF or TDF not sufficiently replicated without confounding by indication
  - Focus on attaining viral suppression with any appropriate regimen

- Hospitalized COVID-19 patients:
  - Continue ART without change
  - Initiate ART once clinically stabilized, prior to hospital discharge
  - Similar to ART initiation during OI management

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Which of the Following Persons with HIV should be Considered for Anti-SARS-CoV-2 Therapies if Presenting with Mild Symptoms?

A. 67yo vaccinated PWH, suppressed, CD4 470, CKD III and CHF

B. 47yo unvaccinated PWH, suppressed CD4 260, CKD II

C. 41yo vaccinated PWH with recent diagnosis, ART naïve and CD4 38

D. 27yo pregnant PWH, suppressed, CD4 700

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Which of the Following Persons with HIV Should be Considered for Anti-SARS-CoV-2 Therapies if Presenting with Mild Symptoms?

A. 67yo vaccinated PWH, suppressed, CD4 470, CKD III and CHF
   NIH Tier 3 for age and cardiorenal risk factors
B. 47yo unvaccinated PWH, suppressed CD4 260, CKD II
   NIH Tier 2 based on being unvaccinated with risk factors
C. 41yo vaccinated PWH with recent diagnosis, ART naïve and CD4 38
   NIH Tier 1 for immunosuppression
D. 27yo pregnant PWH, suppressed, CD4 700
   NIH Tier 4 for pregnancy + priority population

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Impact of COVID-19 on Delivery of HIV care

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Innovations in Human Immunodeficiency Virus (HIV) Care Delivery During the Coronavirus Disease 2019 (COVID-19) Pandemic: Policies to Strengthen the Ending the Epidemic Initiative—A Policy Paper of the Infectious Diseases Society of America and the HIV Medicine Association FREE

- Increased telemedicine access
- Longer ART fills (90 days) and mail delivery
- Flexibility in administering Ryan White programs
  - Easier enrollment, income verification etc.
- Funding, support for unstably housed PWH
- Much of these innovations were temporary; flexibilities have already lapsed

Armstrong…Bender Ignacio, et al CID, 2021

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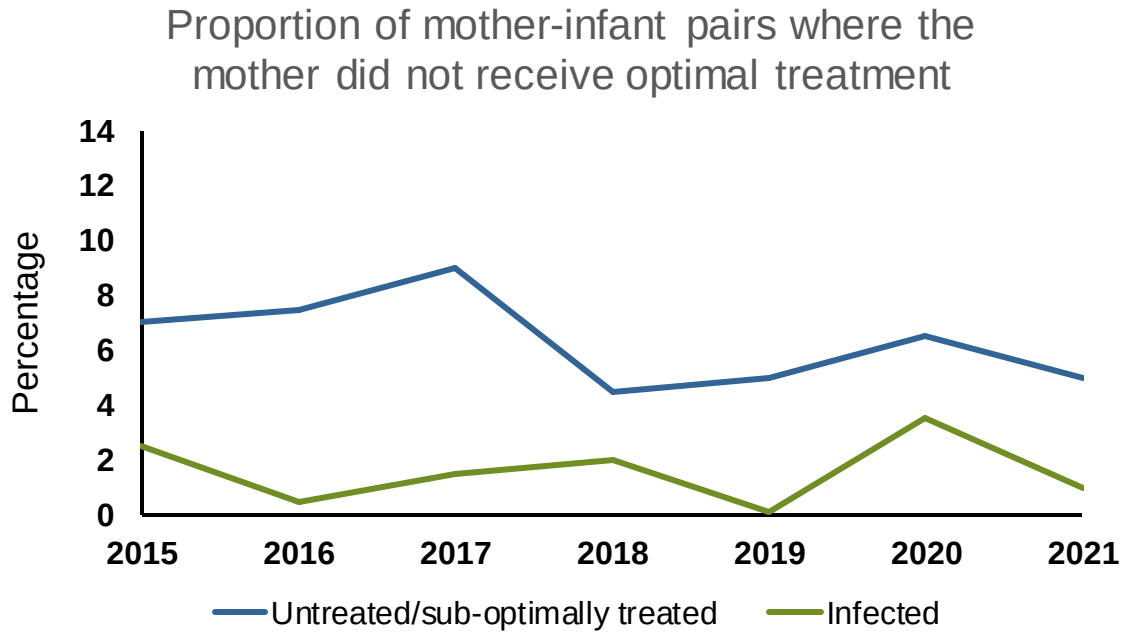
The Effect of the COVID-19 Pandemic on Access to HIV Treatment and Vertical Transmission

Objective: Study from 22 Canadian pediatric and HIV centers which assessed the effect of the COVID-19 pandemic on access to optimal therapy and perinatal transmission in the Canadian perinatal HIV surveillance cohort of births to WWH.

To compare the vertical transmission rate in the 5 years preceding the SARS-CoV-2 pandemic with the rates in May–December, 2020 and subsequently 2021 and then do a similar comparison of the suboptimal treatment rates.



	2015-2019	2020 May-Dec	2021
Untreated/ sub-optimally treated	87/1301 (6.7%)	12/157 (7.6%)	10/210 (4.8%)
Infected	18/1301 (1.4%)	5/157 (3.2%)	2/210 (1.0%)

Sauve L, et al. AIDS 2022; Montreal, Canada; July 29-Aug 2, 2022; Abst. OAC0204.

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Conclusions: COVID-19 in HIV

- Address vaccine hesitancy and access

- 3-dose primary series for CD4 <200 or unsuppressed, and boosters!
- Omicron Bivalent boosters for everyone

- Consider COVID-19 PrEP if advanced immunosuppression

- Most PWH's main COVID-19 risk is less attributable to HIV than metabolic, CVD comorbidities
  - Address with counseling
  - Prioritize treatment for folks meeting any guidelines criteria

- Access to both COVID-19 and HIV care need addressing with creative solutions, many of which should **not** be pandemic limited & focus on leveling disparities

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Questions?

Contact Information

Please feel free to follow up at rbi13@uw.edu

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- UW Positive Research/ACTU's CAB, which has given me so much perspective on living through a 2nd pandemic

CNICS
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Helpful Resources

https://www.idsociety.org/globalassets/idsa/public-health/covid-19/covid-19-vaccines-pwh-table.pdf

https://combatcovid.hhs.gov/clinicaltrials

https://www.idsociety.org/covid-19-real-time-learning-network/special-populations/hiv/#KL

https://www.covid19treatmentguidelines.nih.gov/

Armstrong, et al *Clinical Infectious Diseases*, 14, https://doi.org/10.1093/cid/ciaa1532

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