An Update on COVID-19 and People With HIV

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2021 Ryan White HIV/AIDS Program CLINICAL CONFERENCE

Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years

Dr Bender Ignacio has served as a consultant for AbbVie and Seagen. (Updated 9/23/21)

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Learning Objectives

After attending this presentation, learners will be able to:

- Describe COVID-19 risks in people with HIV (PWH)
- Describe vaccination and prevention measures for PWH
- Describe COVID-19 treatment considerations for PWH

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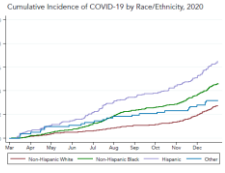
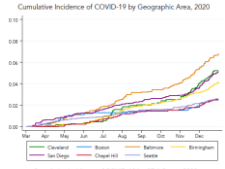
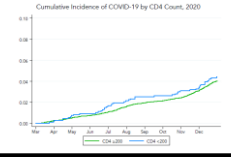
COVID-19 Epidemiology

Risk in PWH







CNICS Multisite US Cohort of PWH 2020
Cachay et al, IDWeek "San Diego" 2021

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

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

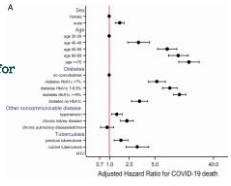
(JJ Chang, JAIDS 2021)

COVID RISK vs General population

No significant difference in risk of COVID-19 diagnosis in Western Cape, RSA, 2-fold risk of death (partially adjusted for comorbidities)

- WHO Data (IAS 2021) 15,522 PWH among 168k persons, 24 countries
- Among hospitalized COVID-19 cases, aOR severe/critical illness: 1.13
- aOR of in-hospital death 1.30 for PWH
- 60% had missing ART status, no stratification for ART, VL or CD4
- AHA COVID-19 Cardiovascular Disease Registry (IAS 2021)
- No significant difference in in-hospital mortality
- No stratification on CD4, ART
- Very little population data that takes incidence in PWH vs general population into account
- Disparities based on structural factors, allostatic load, access to care, substance use, smoking distributed differently for PWH vs general

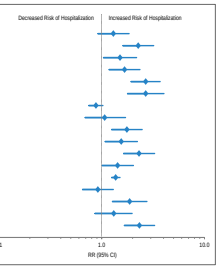
Bertagnolio, WHO, IAS 2021
Durstenfeld, IAS 2021



Comparison of adjusted HRs and 95% CIs for associations with COVID-19 death; WCDPHDC RSA, CID 2020

Risk Factors for COVID Severity among PWH

Characteristic*	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/mm³)	1.67 (1.18, 2.36)
Current CD4 count (≤350 vs. >350 cells/mm³)	2.68 (1.93, 3.71)
Current CD4 count (<200 vs. ≥200 cells/mm³)	2.68 (1.76, 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 m²)	2.31 (1.63, 3.28)
BMI (≥30 vs. ≤30 kg/m²)	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 (>2.45 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, CROI 2021 and manuscript under review

COVID 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 (eg WCDPH used data from hospitalization)
- Most large non-HIV specific datasets lack specificity on parameters of HIV treatment
- Most PWH 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, under review

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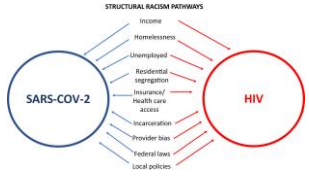
Impact of the Pandemic on PWH

Intersecting disparities affect both populations



1. Similar challenges facing EHE and COVID-19 response
   - Addressing structural disparities
2. COVID-19 competing with EHE priorities
   - Care & service interruption
   - Research funding rechanneled
3. Challenges to EHE unrelated to COVID-19
   - Rise of new disparities
   - New legislation that impairs provision of comprehensive care- especially sexual health + gender care

Millet JIAS, 2021

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Influence of pandemic on HIV incidence

- Models of service disruptions vs behavioral change/no change
  - In Baltimore MSM model, 25% reduction in partners without change in services ↓ new diagnoses by 12.2% over a year
- Care interruption sans behavior change ↑ incidence by up to10.5%
- Combination of 25% fewer partnerships + care changes:
  - Overall stable incidence
- Separate study- no change in capacity, less partnerships=> 50% reduction
- Could not rule out 9% increase in HIV
- Link SARS-COV-2 testing with opt-out HIV screening

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COVID prevention in PWH

Covid-19 Vaccines for PWH

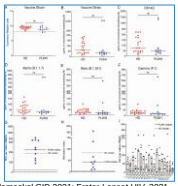
WHICH VACCINES: Vaccine with any EUA or approved vaccine (globally, WHO endorses + ChAdOx1 + Sinopharm, Sinovac)
-Preference for mRNA vaccine if possible given multiple doses likely more important if compromised response

SAFETY: No evidence of safety concerns with mRNA or inactivated viral-vector vaccines for PWH

EFFICACY: small studies show adequate response to mRNA and ChAdOx1 vaccine

BOOSTERS: for CD4 <200 or untreated only (more data pending)

- Following the change to the EUA, CDC updated its clinical COVID-19 vaccine guidance to recommend that individuals who are moderately to severely immunocompromised, including people with advanced or untreated HIV, who received either of the mRNA vaccines receive a third dose.
- Many experts consider people with HIV whose CD4 cell count is <200/mm3 or CD4 percentage is 14 or less to have advanced disease.
- People with HIV who are not receiving treatment for their HIV should start antiretroviral medications as soon as possible to protect themselves from complications from HIV. In addition to reducing the likelihood of medical problems related to HIV, antiretroviral therapy is expected to improve immune responses to the COVID-19 vaccine and to protect against severe COVID-19 in people with HIV.



hivma

COVID-19 Vaccines and People with HIV
Frequently Asked Questions

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Woldemeskel *CID* 2021; Frater *Lancet HIV*, 2021
https://www.hivma.org/globalassets/hivma/covid-19-vacines-hiv-8-19-21-faq.pdf

Post-exposure prophylaxis

FDA EUA for REGN –COV (casirivimab 600mg + imdevimab 600mg SQ or IV)

REGEN-COV may only be used as post-exposure prophylaxis for adults and pediatric individuals (12 years of age and older weighing at least 40 kg) who are:

- at high risk for progression to severe COVID-19, including hospitalization or death, **and**
- not fully vaccinated **or** who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, people with immunocompromising conditions, including those taking immunosuppressive medications), **and**
  - have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per Centers for Disease Control and Prevention (CDC), **or**

For PWH: Not fully vaccinated or CD4 <200, previously described comorbidities or age

FDA.org

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COVID-19 Treatment for PWH

Ambulatory Covid treatment for PWH

- **Not different from general population: Follow NIH and IDSA Guidelines**
- Consider early treatment for PWH with risks for severe outcomes
  - Unvaccinated
  - CD4 <200 or untreated: possible non-response to vaccine

Monoclonal Antibodies with EUA (REGN-COV or sotrovimab)
Clinical research opportunities

- Apart from mAb, no other authorized/approved treatments for COVID-19 in non-hospitalized patients
  - Discourage unproved therapies or ART change unless within a high-quality study

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Inpatient management of COVID-19

- Do not withhold immunomodulators or immunosuppressants (IL-6 antagonists, dexamethasone) in hospitalized PWH
  - These are being widely used in other immunocompromised populations
- Remdesivir for early-hospitalized (mod/severe)
- Add dexamethasone + baricitinib or anti-IL-6 for 02 requirement-> ICU
  - No RDV for critical illness
- May be indications for antithrombotics in some sub-populations
- No difference for hospitalized PWH

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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

- Do not change ART regimens for PWH with COVID-19 in most cases

New direct-acting SARS-CoV2 protease inhibitor antivirals include ritonavir boost
Singular consideration for amendment based on drug/drug interactions or duplication

- 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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COVID-19 studies inclusive of PWH (US)

- https://combatcovid.hhs.gov/clinicaltrials
- ACTIV-2: Monoclonal antibodies and other therapies
- ACTIV-6 Repurposed drugs: https://activ6study.org/
- MOVe-AHEAD Molnupiravir for post-exposure prophylaxis (PEP). NCT04939428

(list not exhaustive)

COMBATCOVID

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Current knowledge gaps

- Initial vaccine vaccine responses for mRNA and Ad-vectored vaccines (global) for PWH and unsuppressed VL or CD4 <200
- Real world effectiveness of COVID-19 vaccines in people with untreated/advanced HIV
  - Moving target with variants, geography, different vaccine types
- Real risks of COVID-19 severity in PWH not on ART, unsuppressed VL
  - Most analyses either include complete ascertainment of PWH retained in care vs incomplete data for general populations

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Innovations in HIV care during COVID-19

- Better access to care and ART
  - Much of insurance/ADAP renewal process streamlined
  - 90 day prescriptions for many insurance groups
  - Mail order med increase
  - Telehealth + across state lines
- CARES Fund
  - Improved funding for telehealth/connectivity tech
  - Co-pay coverage, safe transport, vouchers
- Many innovations already retreating
  - Advocate to keep telehealth reimbursement, improved ART delivery etc

Armstrong et al, CID 2020

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Helpful Resources

- Woldemeskel *CID* 2021; Frater *Lancet HIV*, 2021
- https://www.hivma.org/globalassets/hivma/covid-19-vacines-hiv-8-19-21-faq.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/
- Wendy S Armstrong, et al *Clinical Infectious Diseases*, 14, https://doi.org/10.1093/cid/ciaa1532

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Question-and-Answer Session
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