



FEEDBACK ON IAS 2022 CONFERENCE

HIV & CO-INFECTIONS



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3 DECEMBER 2022



HIV & CO-INFECTIONS

- **HIV... HBV...HCV**
 - Triple Elimination
 - Prof Marina Klein
 - McGill University Health Centre
- **HIV-associated TB**
 - What's new and topical
 - Prof Graeme Meintjes
 - Groote Schuur Hospital, University of Cape Town
- **HIV and COVID**
 - Dr N Kumarasamy
 - Infectious Disease Specialist-director
 - Chennai, India
- **HIV and Monkeypox**

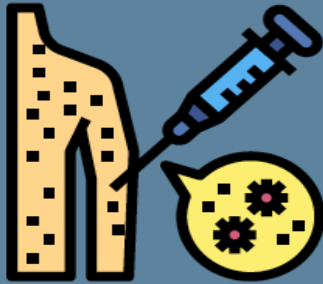


HIV...HBV...HCV Triple Elimination

What do we mean by Elimination?

Eradication

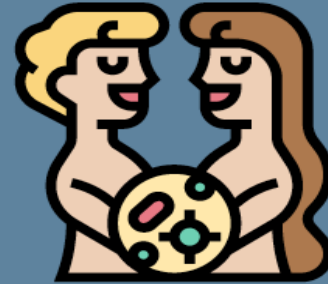
Smallpox



Permanent reduction to zero of the worldwide incidence of infection
Intervention measures are no longer needed

Elimination

Viral Hepatitis, HIV



Reduction of incidence of infection/disease to where **no longer a public health threat**
Continued measures required

Key ingredients for elimination



SIMPLE TESTS

That can detect active infection accurately and cheaply



TREATMENT

Ideally one that cures
available at an affordable cost



VACCINE

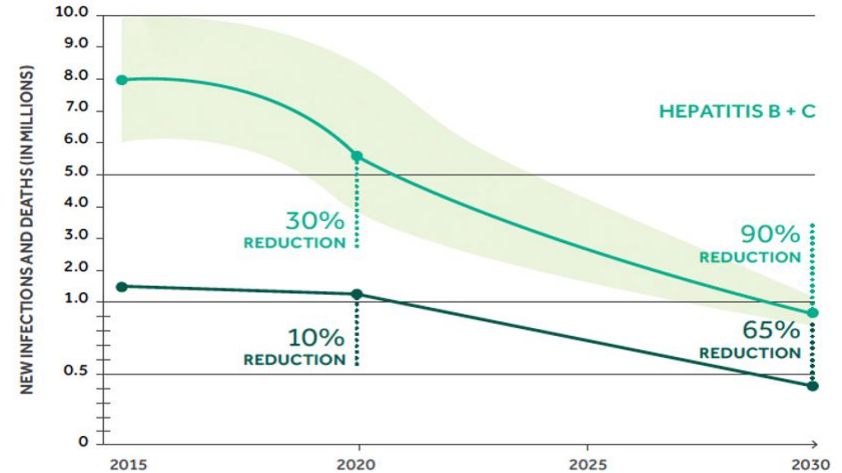
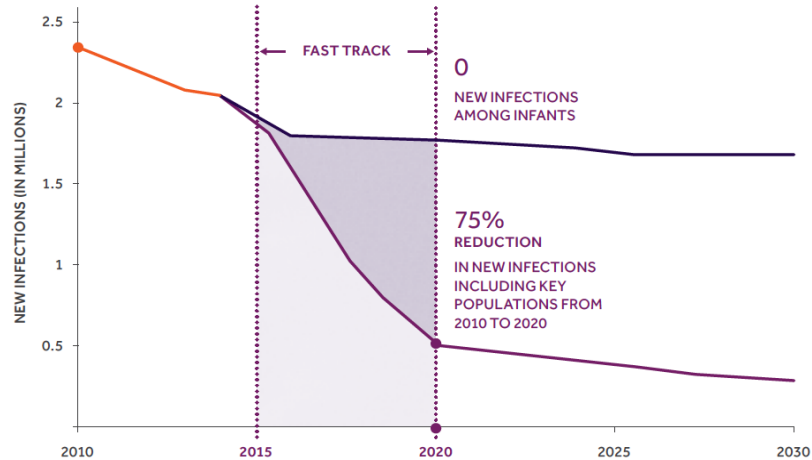
Preventative and/ or
therapeutic vaccine



PREVENTION

Accessible
Safe
Widely available

Elimination targets HIV & Viral hepatitis



HIV... HBV... HCV... What will it take?

	HIV	HBV	HCV
Test	<ul style="list-style-type: none">- Self testing- Reaching vulnerable populations	<ul style="list-style-type: none">- Complex phases of disease- Need for DNA testing	<ul style="list-style-type: none">- Need for RNA testing to confirm chronic infection
Treat	<ul style="list-style-type: none">- Life-long- Access to 2nd line	<ul style="list-style-type: none">- Life long therapy- Lack of TDF in many countries- Ongoing HCC risk	<ul style="list-style-type: none">- Reaching vulnerable populations- Expanding beyond speciality centers
Prevent	<ul style="list-style-type: none">- Prep for women- Prep fatigue- Access to long acting prep- No vaccine	<ul style="list-style-type: none">- Suboptimal MTCTP and birth dose vaccine	<ul style="list-style-type: none">- No vaccine- Inadequate harm reduction for many drugs- Criminalization of drug use
Cure	<ul style="list-style-type: none">- Complex regimes- Expensive- Scalability questionable	<ul style="list-style-type: none">- Complex regimes required- Expensive- Scalability questionable	<ul style="list-style-type: none">- Expensive

HIV Transmission Prevention

The science is clear.

HPTN 052

PARTNER

Opposites Attract

PARTNER 2

Combined data from 2008-2018 show that there were **ZERO** linked HIV transmissions after more than a hundred thousand condom-less sex acts within both heterosexual and male-male serodiscordant couples where the partner living with HIV had a durably undetectable viral load.



HIV & PrEP

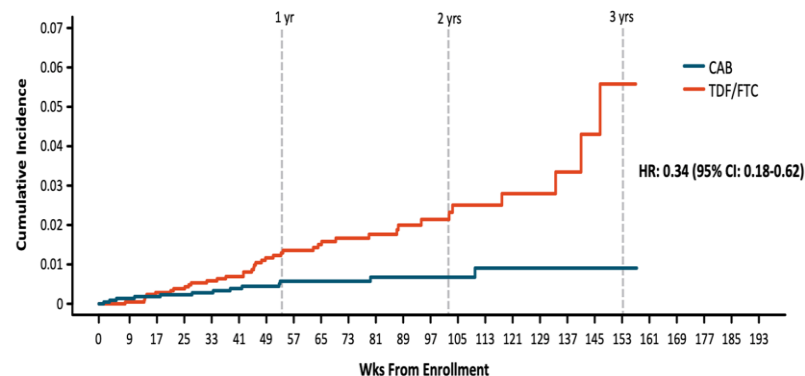
Treatment prevention:

- Therapeutic trials on oral and topical based prevention efficacy "prove" that PrEP is effective if taken consistently
- When used correctly, PrEP is 99% effective in preventing HIV
- PrEP drug preparations: oral tablet, TDF/FTC - PO Dly ; injectable agent e.g cabotegravir taken monthly/ every second month

HPTN 083 trial

- What is the HPTN 083 trial?: it is the first study to compare the efficacy of CAB LA to daily oral TDF/FTC for HIV PrEP. HPTN 083 enrolled 4,570 cisgender men who have sex with men (MSM) and transgender women (TGW) who have sex with men at 43 sites
- Why is it important: decrease pill burden, increase adherence, discrete
- Findings: The study results showed that CAB LA, administered every eight weeks, provided high efficacy compared to TDF/FTC

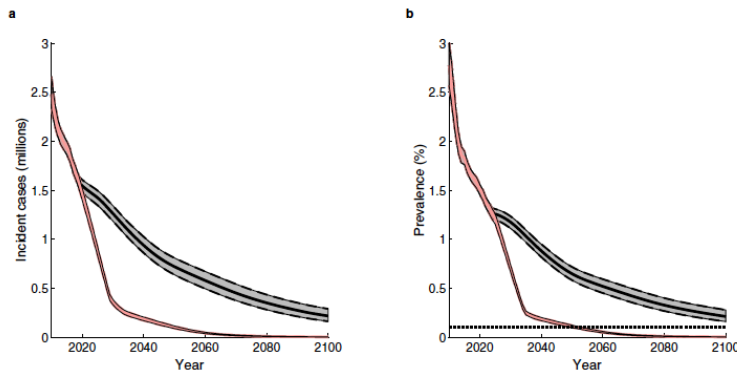
HPTN 083: HIV Incidence with LA Injectable CAB vs. Daily Oral TDF/FTC PrEP



HBV

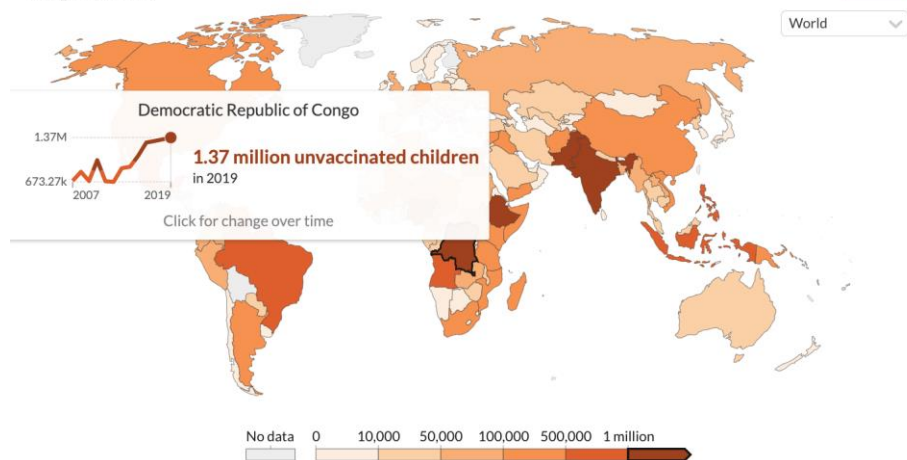
- HBV is preventable by vaccine
- Hep B vaccine recommended for all age groups
- Risk factors: sexual exposure, exposure to blood (health care workers, dialysis, IV drug use) , HCV, HIV
- Treatment of acute Hep B infection: none available
- Treatment of chronic HBV: Several medications have been approved to treat people who have chronic hepatitis B, and new drugs are in development. However, not every person with chronic hepatitis B needs medication, and the drugs may cause side effects in some patients. People who start hepatitis B treatment may need to take medication indefinitely because these medications do not lead to a cure.

HBV: A highly effective vaccine



Scaling up timely **HBV birth dose** vaccination to 90% of newborns in 110 low- and middle-income countries by 2030 could prevent 710,000 (580,000 to 890,000) deaths in the 2020 to 2030 birth cohorts compared to status quo, with the greatest benefits in Africa. additional deaths

Number of one-year-olds who did not receive the vaccine against hepatitis (HepB3), 2019








Source: World Health Organization (WHO); UNICEF
Note: Hepatitis B is a viral infection that attacks the liver and can cause both acute and chronic disease.

OurWorldInData.org/vaccination • CC BY

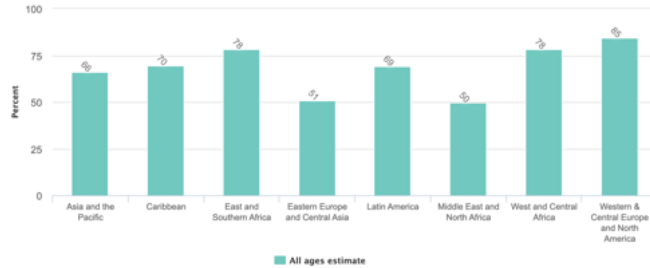
HCV

- No vaccine- ongoing trials in search of vaccine
- Current approach: reduce risk of infection
- 6 strains of HC virus
- Acute Hep C infection may not need treatment, can be cleared by immune system
- Chronic Hep C requires treatment
- Treatment for all genotypes:
 - Eplclusa: 98% overall cure, works in the presence of liver cirrhosis, one pill, 12 week duration
 - Maviret: 97% clearance with 8 weeks Rx, treatment lasts either 8/12/16 weeks depending on genotype, avoid if severe liver dysfunction present, active substances: glecaprevir/piibrentasvir
- Overall treatment can be simple: no genotyping required, 3 full months of sofosbuvir/velpatasvir, only 2 check ups, costs can be reduced

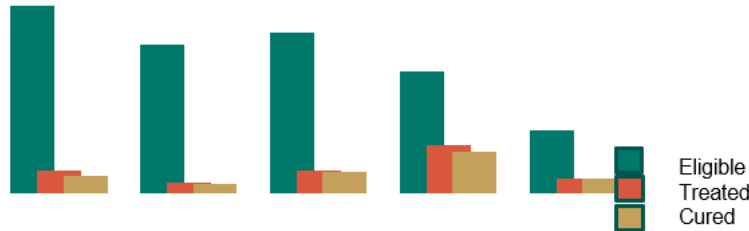
Brand name (generic name)	Genotypes	Image	Dosage schedule	Food requirements	Weeks of treatment
Treatments for all genotypes					
Eplclusa (velpatasvir + sofosbuvir) with or without ribavirin*	All				12
Maviret (glecaprevir + pibrentasvir)	All				8

It depends on where and who you are

Coverage of people receiving ART (all ages) - by region



Source: Global AIDS Monitoring 2021; UNAIDS epidemiological estimates, 2021

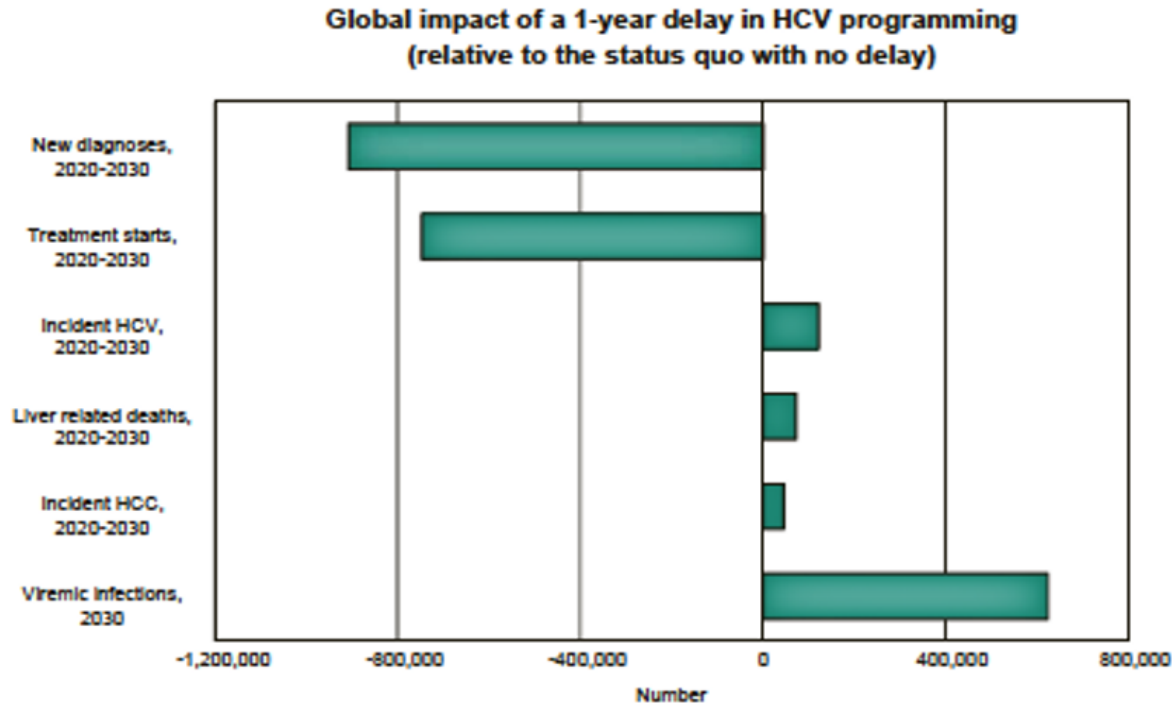


WHILE 25% OF PEOPLE ELIGIBLE FOR PREP WERE PRESCRIBED IT IN 2020, COVERAGE IS NOT EQUAL

PREP COVERAGE IN THE U.S. BY RACE/ETHNICITY, 2020



Impact of COVID-19



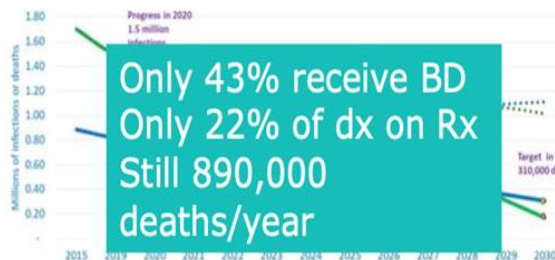
A 1-year delay could cause 72,000 excess deaths from HCV.

Can we leverage the hundreds of billions of dollars spent to tackle COVID-19 to strengthen surveillance, healthcare systems and enhance viral hepatitis services?

How are we doing?



HBV



HCV



HIV



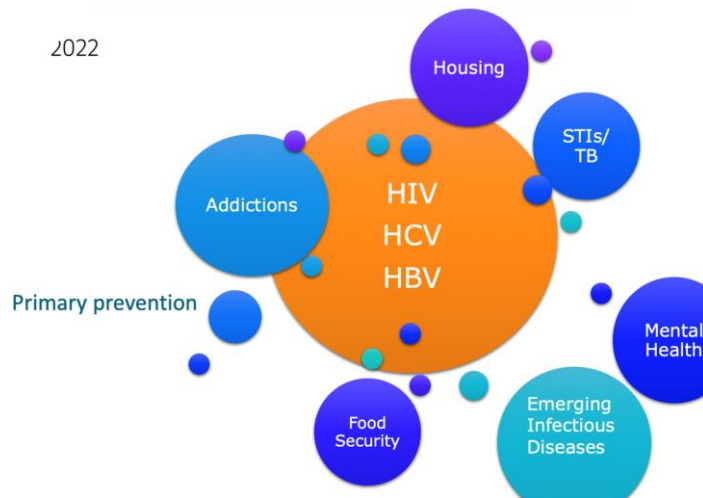
Elimination HIV/HBV/HCV

Elimination tools and targets are necessary but not sufficient:

- Strategy
- Commitment
- Sustained investment
- Reduce costs
- Equitable access
- Engagement with community
- Holistic approaches

Therefore important to focus on primary prevention as well

2022



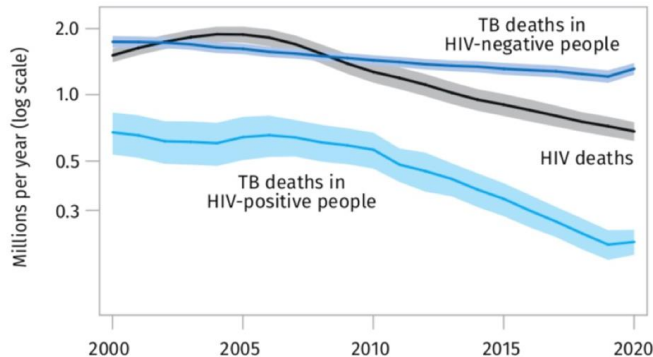
HIV - associated TB

Global epidemiology of HIV-TB

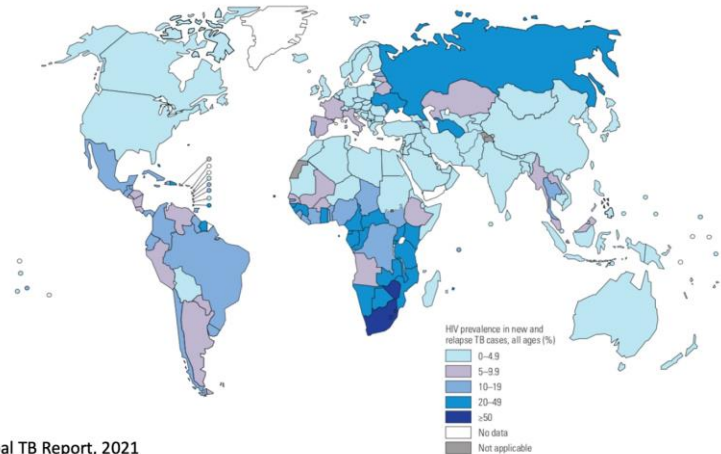
In 2020: 787 000 cases of TB in PLHIV with 214 000 TB deaths in PLHIV

Global trends in the estimated number of deaths caused by TB and HIV, 2000–2020^{a,b}

Shaded areas represent uncertainty intervals.



Estimated HIV prevalence in new and relapse TB cases, 2019



WHO Global TB Report, 2021

Diagnosis gap

Prior to COVID-19, WHO estimated that each year 1/3 of people who developed active TB disease were undiagnosed globally

TB case notifications declined 7.1 million (2019) to 5.8 million (2020)

WHO Global TB Report 2020
Trajman, Int J Tuberc Lung Dis 2022;26:710

Targeted universal testing for TB (TUTT)

Cluster randomized trial in SA- 62 primary clinics

TUTT= clinical attendees with HIV, recent TB contacts, prior TB (irrespective of symptoms)

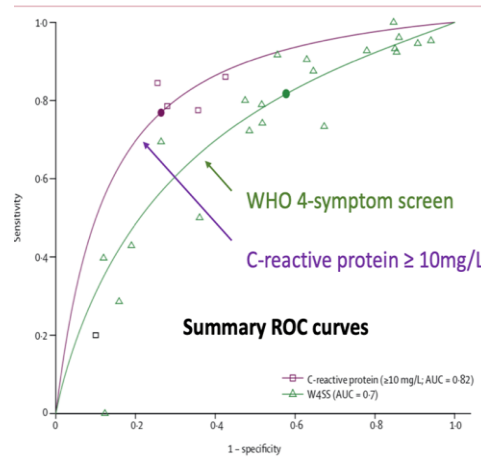
SoC= symptom-directed TB testing

In primary analysis, no difference in TB diagnosis between arms

Pre specified-in-difference analysis READ ARTICLE AND SUMMARISE PROPERLY

Main changed for adults living with HIV

- Screening with CXR improves sensitivity of 4-symptom screen for detecting TB
- Molecular WHO-recommended rapid diagnostics may be used for TB screening in high TB setting
- CRP (cut- off >5 mg/L) may be used for TB screening in addition to 4 symptom screen setting with high TB burden



- Individual patient meta-analysis
 - n = 15,666 from 22 studies
- **WHO 4-symptom screen**
 - Sensitivity = 82%
 - Specificity = 42%
- **C-reactive protein ≥ 10mg/L**
 - Sensitivity = 77%
 - Specificity = 74%
- Point-of-care CRP test available

Co-treatment with TB medication and ART

- Drug-drug interactions
- Shared toxicities
- Paradoxical TB-IRIS

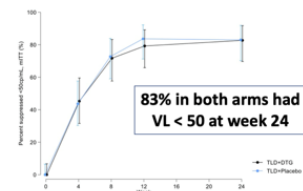
Drug-drug interactions

- Rifampicin reduces plasma exposure to TAF, NNRTIs, INSTIs, PIs, fostemsavir and maraviroc
- RADIANT-TB trial: dolutegravir with rifampicin

- 50mg daily vs 50mg twice daily dolutegravir with rifampicin-based TB treatment
- Phase 2 non-comparative RCT
- n=108 (re)initiating first line ART; CD4 > 100
- Randomised 1:1 to dolutegravir or placebo 12 hours after TLD

No emergent ART resistance

Figure 2: Virological suppression over time (HIV-1 RNA <50 copies/mL) by mITT analysis



Griesel, AIDS 2022, Poster EPLB01

Treatment initiation

Early ART in TB reduces mortality if CD4 <50, comparing starting ART ~2 weeks vs ~8 weeks on TB Rx. studies show that initiating patients on ART with CD4 <50, mortality decreases by 28% mortality; if CD4 >50 - no difference in mortality.

Early ART increases TB-IRIS risk, comparing starting ART ~2 weeks versus ~8 weeks on TB treatment. Early ART (~2 weeks): 17%, delayed ART (~8 weeks): 8%.

WHO guidance regarding ART timing:

- Should be started as soon as possible within two weeks of initiating TB Rx regardless of CD4

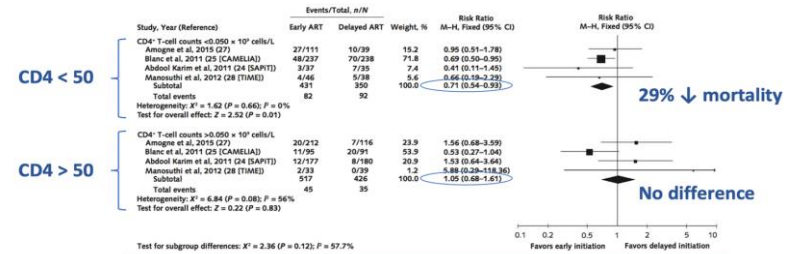
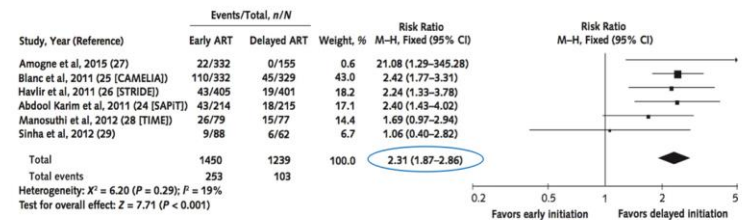


Figure 5. TB-IRIS comparing early versus delayed initiation of ART.



ART = antiretroviral therapy; CAMELIA = Cambodian Early Versus Late Introduction of Antiretrovirals; M-H = Mantel-Haenszel; SAPIT = Starting ART at Three Points in TB; STRIDE = Immediate Versus Deferred Start of Anti-HIV Therapy in HIV-Infected Adults Being Treated for Tuberculosis; TB-IRIS = tuberculosis-associated immune reconstitution inflammatory syndrome; TIME = Appropriate Timing of HAART in Co-infected HIV/TB Patients.

4 month regimens for drug-susceptible pulmonary TB

3-arm open-label non-inferiority RCT:

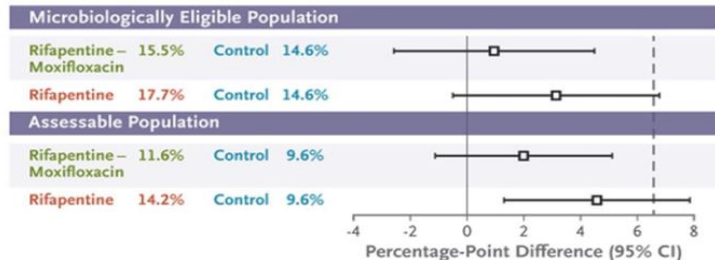
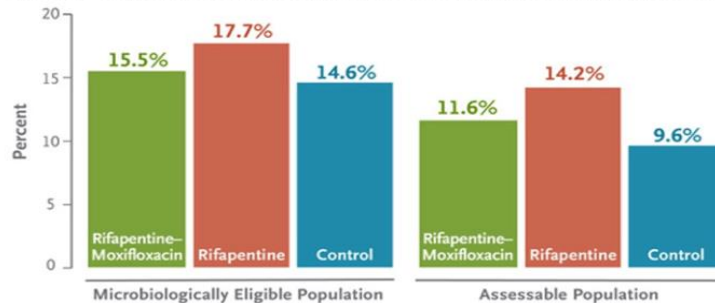
- **RIFAPENTINE (P)-MOXIFLOXACIN ARM**
2 months PHZM + 2 months PHM
- **RIFAPENTINE (P) ARM**
2 months PHZE + 2 months PH
- **CONTROL**
2 months RHZE + 4 months RH

2516 participants ≥ 12 years; 8% HIV-positive

Non-inferiority margin = 6.6%

RIFAPENTINE-MOXIFLOXACIN ARM NON-INFERIOR

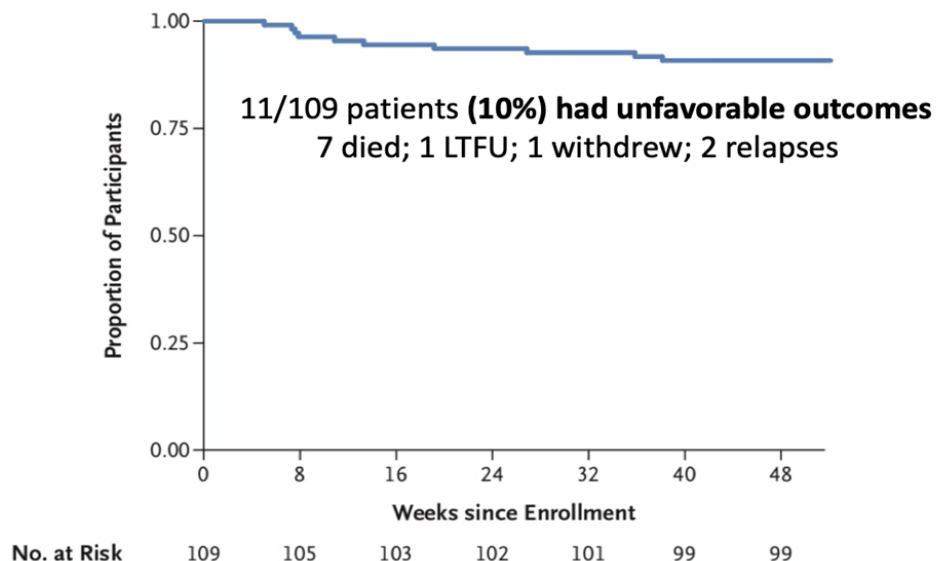
Absence of tuberculosis disease-free survival at 12 months after randomization



Nix-TB trial: Bedaquiline, pretomanid, linezolid

26 weeks treatment + 6 months follow-up

A Overall Time to Unfavorable Outcome



65% XDR-TB (others MDR)

51% HIV-positive

81% peripheral neuropathy

48% myelosuppression

Outcomes similar in
HIV positive & negative

ZeNix trial: Nix-TB regimen with variable LZD

- 181 participants (20% HIV positive) randomized to one of the 4 regimens
- All 6 months BPaL with varying linezolid (LZD) dose and duration
- Outcome evaluated 6 months after completing treatment
- Need for LZD dose modification less with lower dose and shorter duration

Linezolid dose & duration (# assessable)	1200mg 26 weeks (n=44)	1200mg 9 weeks (n=45)	600mg 26 weeks (n=44)	600mg 9 weeks (n=44)
Favorable outcome	41 (93%)	40 (89%)	40 (91%)	37 (84%)

TB-Practecal 6 month all oral regimens

- Open label RCT: Belarus, SA, Uzbekistan
- 23% HIV positive
- 30% cavitation
- 28% fluoroquinolone resistant
- BPaL= Bedaquiline, Pretomanid, Linezolid

	BPaL (n=60)	BPaL + Clofazimine (n=64)	BPaL + Moxifloxacin (n=62)	WHO SoC 36-96 weeks (n=66)
Unfavorable outcomes	23%	19%	11%	49%
SAE or new grade 3 AE	22%	32%	19%	59%

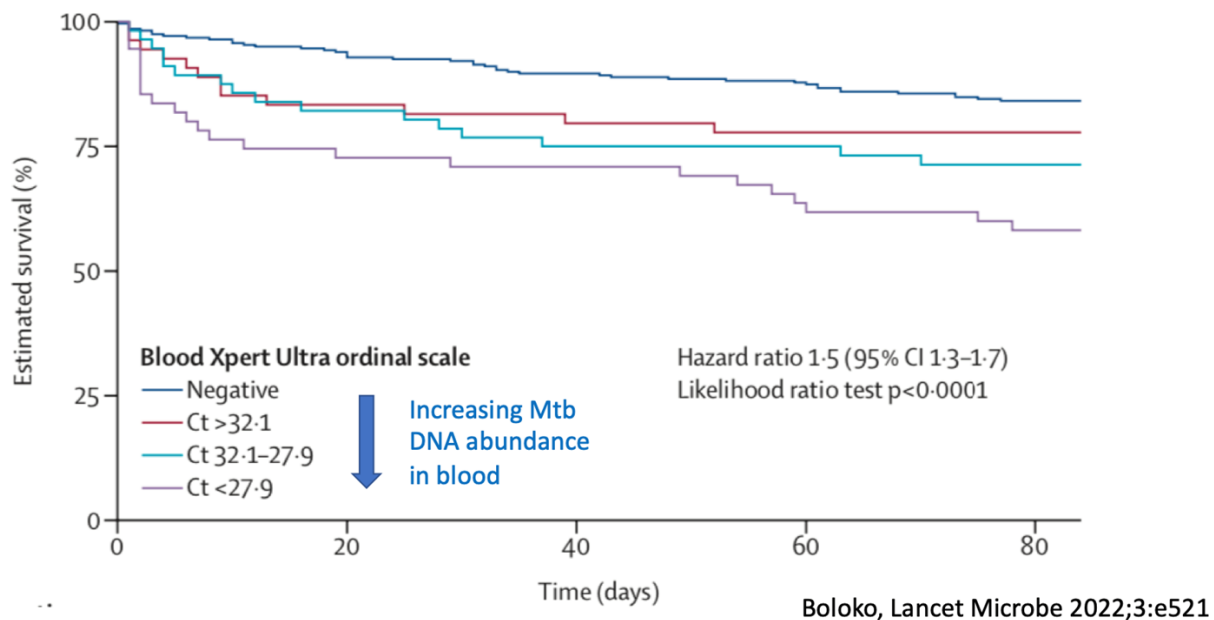
WHO rapid communication-May 2022:

The 6 month BPaLM regimen, comprising bedaquiline, pretomanid, linezolid (600mg) and moxifloxacin, may be used programmatically in place of 9-month or longer (>18 months) regimens, in patients (aged >15 years) with MDR/RR-TB who have not had previous exposure to bedaquiline, pretomanid and linezolid.

Disseminated TB in hospitalised PLHIV

- Meta-analysis: predicted probability of MTB blood stream infection in inpatients with HIV-TB, WHO danger signs, and CD4=76 was 45%
- Mortality 21.5% in large inpatient cohort in SA; death associated with:
 - biomarkers of sepsis and organ dysfunction
 - markers of MTB disseminated in blood and urine
 - innate immune activation profile in blood
- Xpert ultra performed on lysed blood showed "dose response" relationship with mortality

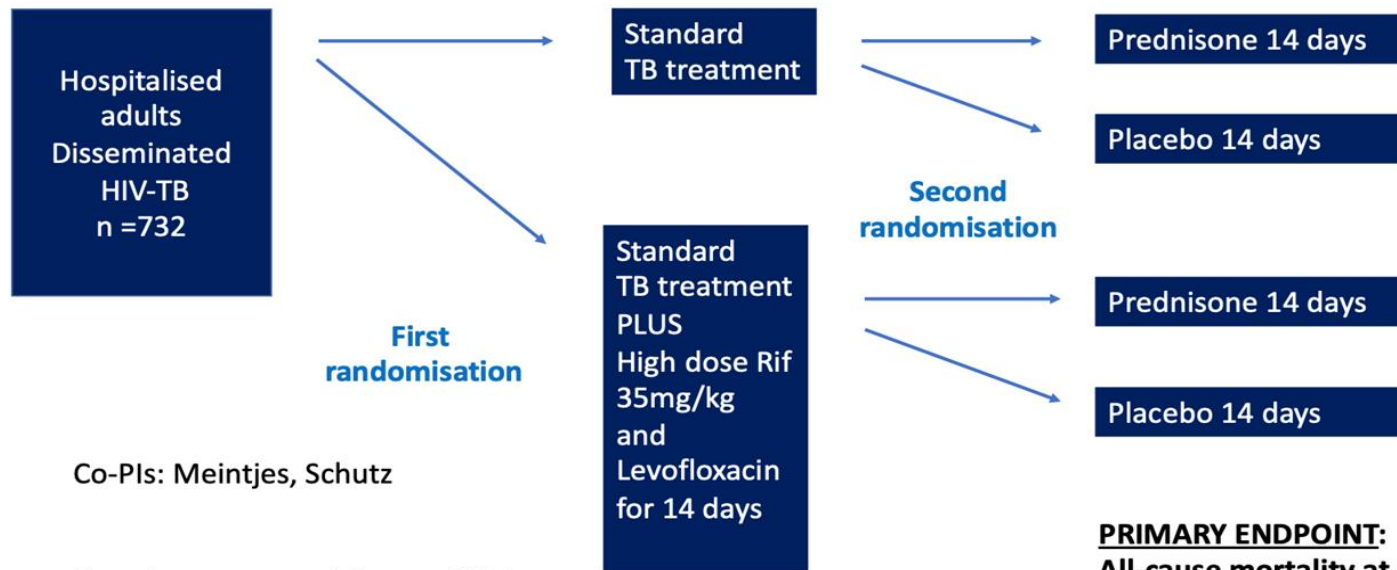
Xpert ultra on lysed whole blood



NEW-STRAT TB: Randomised controlled trial

- New STRAT TB= testing new strategies for patients hospitalised with HIV- associated disseminated tuberculosis
- Is a superiority phase III randomised control clinical trial with a 2x2 factorial design, CPT/UCT based
- Aim: to assess the efficacy and safety of high dose rifampicin and levofloxacin for 14 days in addition to standard TB therapy +/- steroids amongst adults with HIV- associated disseminated TB
- Hypothesis:
 - intensified treatment with increased rifampicin doses at 35 mg/kg plus levofloxacin will rapidly reduce mycobacterial load
 - Steroids will have an immune modulatory effect and dampen the activation of the innate immune system
 - Above strategies will improve survival in patients

NEW-STRAT TB: Randomized controlled trial



Co-PIs: Meintjes, Schutz

*Recruitment started August 2021
183/732 recruited*

PRIMARY ENDPOINT:
All-cause mortality at 12 weeks

TB meningitis

- Estimated that 0.3-4.9% of all TB pt.'s have TBM
- Mortality higher in PLGIV and exceeds 60% in some studies
- Standard TB Rx 9-12 months
- Dexamethasone improves survival; not specifically evaluated in PLHIV
- ART initiation delay of 4-8 weeks advised d/t risk of neurological IRIS
- Current and planned TBM trials :

	Title/Number	Phase	Intervention(s)	Setting
TB Rx	NCT03787940	3	High-dose INH (NAT2 stratified)	China
	HARVEST	3	High-dose Rifampicin	Indonesia, SA, Uganda
	TBM-KIDS	2	High-dose Rifampicin and Levofloxacin	India and Malawi
	ALTER	2	High-dose Rifampicin and Linezolid	Uganda
	SIMPLE	2	High-dose Rifampicin and Linezolid	Indonesia
Adjunct	LAST ACT	3	LTA4H-stratified Dexamethasone	Vietnam
	ACT HIV	3	Dexamethasone in HIV-associated TBM	Vietnam and Indonesia
	CTRI/2018/02/011722	NA	Indomethacin	India
TB Rx + Adjunct	INTENSE-TBM	3	High-dose Rifampicin and Linezolid <u>and</u> Aspirin	Cote d'Ivoire, Madagascar, SA, Uganda
	SURE	3	6-month intensified TB treatment <u>and</u> Aspirin	India, Uganda, Vietnam, Zambia, Zimbabwe
	LASER-TBM	2	High-dose Rifampicin and Linezolid <u>and</u> Aspirin	South Africa

TB preventive therapy: main options

- Isoniazid for 6 - 36 months (IPT)
- Isoniazid + Rifapentine weekly for 3 months (3HP)
- Isoniazid + Rifampicin daily for 3 months
- Isoniazid + Rifapentine daily for 1 month (1HP)

Currently limited access to Rifapentine in LMIC settings

Annual TB preventive therapy ?

- WHIP3TB trial compared 3 strategies: 3HP = INH + Rifapentine weekly for 3 months
 - Single-round 3HP
 - Annual 3HP
 - 6 months INH
- Completion rates: combined 3HP arms vs 6 months INH
 - 90% vs 51% (RR=1.78, p<0.001)
- TB incidence 0-24 months: annual vs single-round 3HP
 - 1.21 vs 1.26/100 person-years (HR=0.96, p=0.85)
- Annual 3HP did not reduce TB incidence over 2 years

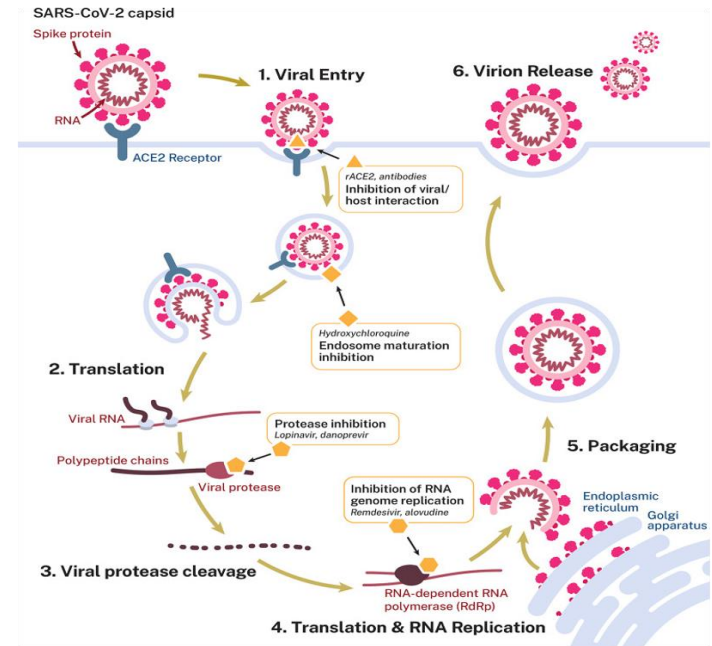
Key new developments

- New evidence and guidelines for systemic screening for TB
 - Role for CRP, CXR , molecular diagnostics
- Short course TB treatment
- Alternative 4-month regimen for drug susceptible TB
 - Including rifapentine and moxifloxacin
- Alternative 6-month regimens for drug resistant TB
 - BPaLM and BPal regimens

HIV and COVID

SARS-CoV-2

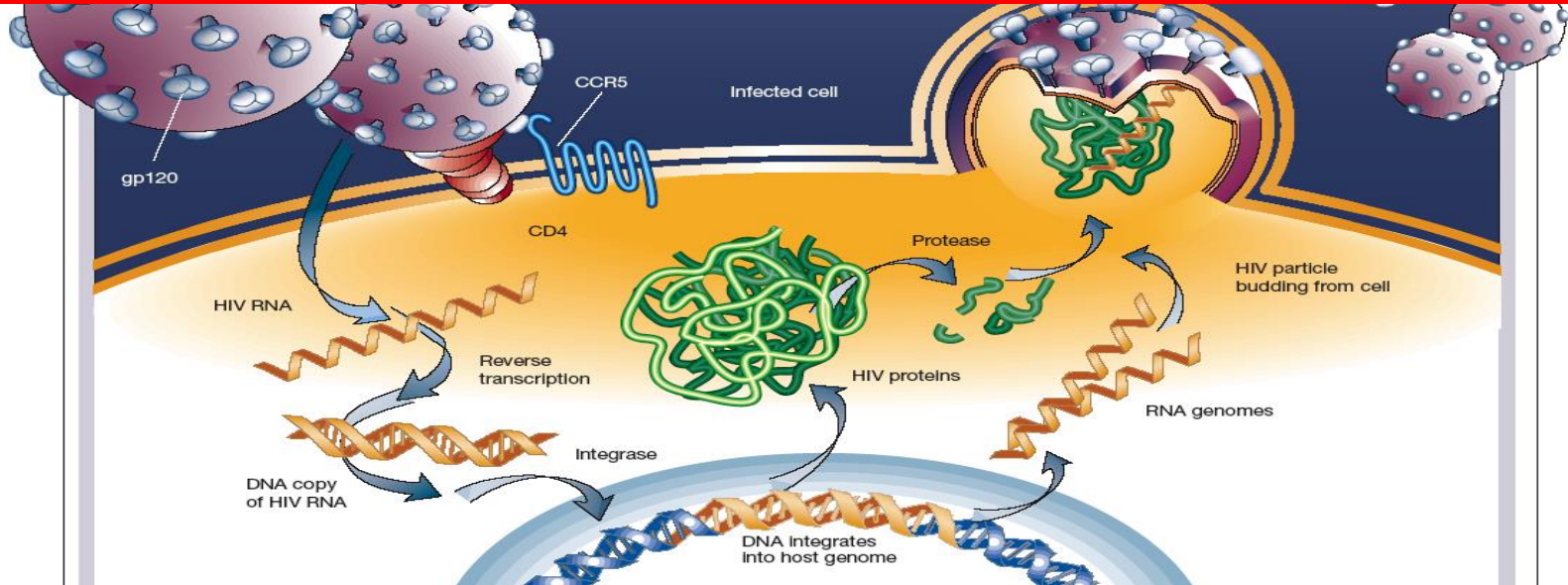
- Viral replication: [question to dad-> do you want my to wtype out all the steps?]
- Symptoms:
 - fever/cough/sore throat/malaise/myalgias
 - GIT: anorexia/nausea/diarrhea
 - Taste and smell disturbances
 - SOB
- Lab findings:
 - Lymphopenia
 - elevated : D-dimer, LDH, CRP, ferritin, liver enzymes, interleukin-6



Pathogenesis of HIV Infection

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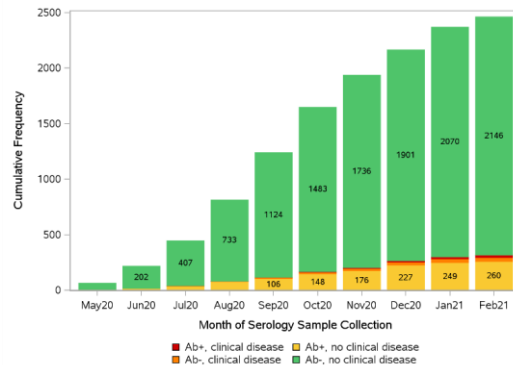
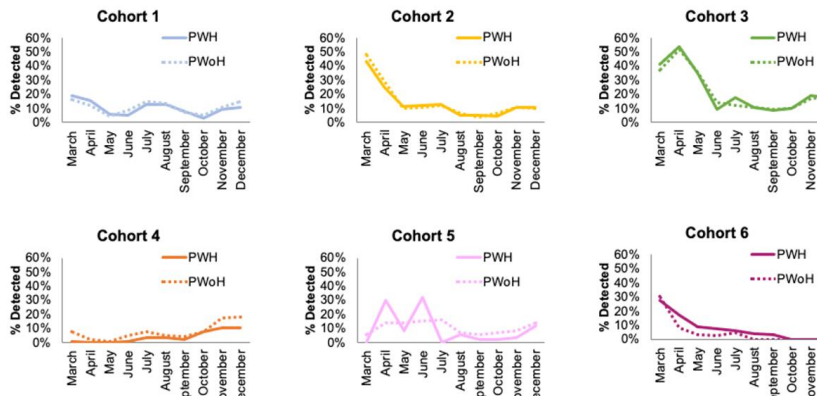
SARS- CoV-2 Viral pathogenesis and replication



COVID in PWH

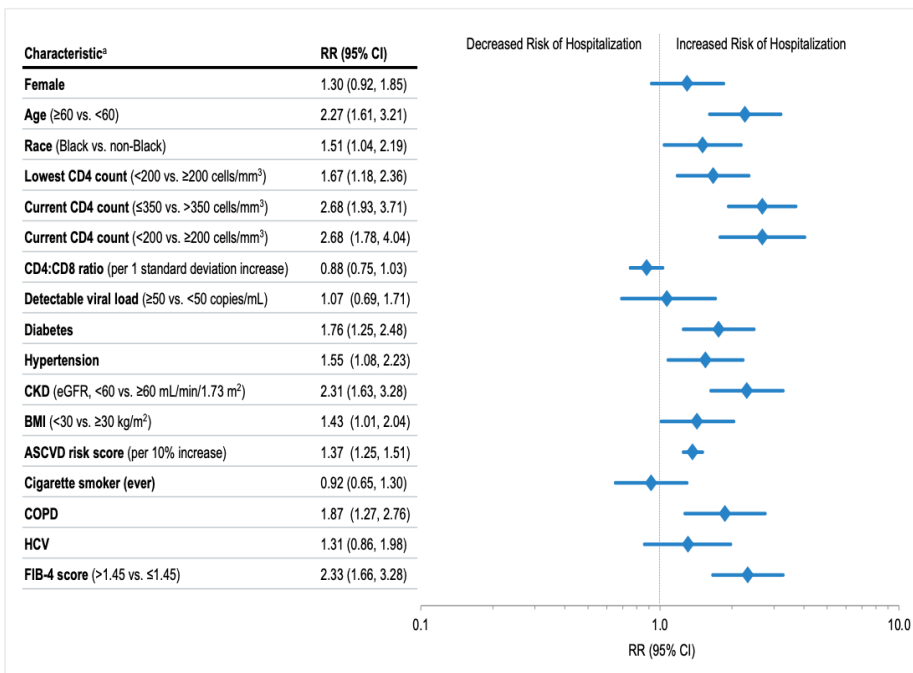
There was no evidence that PWH were at higher risk of infection with SARS-CoV-2 in a study that included 6 cohorts in the US

In the REPRIEVE study participants, asymptomatic SARS-CoV-2 infection was PWH. 60% of infections detected through antibody testing were asymptomatic



COVID in PWH

- There has been limited evidence in indicate that PWH with a low CD4 count have a higher risk of covid infections
- COVID19 in Chennai CART cohort showed no difference in disease progression as compared to non HIV (2022)
- Most studies recapitulate non-HIV specific risks in PWH : HTN, DM, age, BMI





Contents lists available at [ScienceDirect](#)

Journal of Virus Eradication

journal homepage: www.viruseradication.com



Review

Impact of COVID-19 on people living with HIV: A review

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ARTICLE INFO

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COVID-19

HIV

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Pathogenesis

ABSTRACT

There is great concern about the impact of COVID-19 among the nearly 40 million people living with HIV (PLWH) worldwide. In this review, we surveyed current literature and found no evidence of higher prevalence of COVID-19 among PLWH but equivocal data on increased mortality and worse clinical outcomes. Having HIV does not confer protection against severe manifestations of COVID-19. Several studies looking at antiretroviral drugs against HIV to treat SARS-CoV-2 have shown no mortality benefit. Thus, there is no indication to change antiretroviral therapy (ART) regimens among virologically suppressed PLWH to prevent COVID-19. HIV care delivery has been adversely impacted in several countries during this pandemic but has created an opportunity for accelerating effective strategies like multi-month ART. Decentralizing HIV care in low-resource settings and incorporating telemedicine in high-resource settings will be critical in mitigating shocks to healthcare systems in the future.

NIH-guidelines: COVID characteristics + Rx

Treatment options: steroids, antivirals, monoclonal antibodies

	Asymptomatic	Mild illness	Moderate illness	Severe illness	Critical illness
Characteristics	+ve test for sSARS-CoV-2 but no symptoms	Varied (fever/cough/malaise etc.) but no SOB/ dyspnea/ abnormal imaging	SpO2 >94% and lower respiratory disease on C/E or imaging	SpO2 >94%, PaO2/FiO2 <300, RR>30 or lung infiltrates >50%	Resp failure, septic shock, and/or multiorgan dysfunction
Treatment options	80-85% of them can progress to moderate and severe disease. Early anti-viral/monoclonal antibody therapy can halt disease progression		Antiviral treatment + monoclonal antibodies		

NIH-Recommended Treatment in Order of Preference by Efficacy and Ease of Use: April 8, 2022

Nirmatrelvir/Ritonavir

- Oral medication twice daily for 5 days
- Must be given within 5 days of symptom onset

Remdesivir

- 3 IV infusions over 3 days (30-120 mins for each infusion)
- Must be given within 7 days of symptom onset

Bebtelovimab

- Single IV infusion over 30 seconds
- Must be given within 7 days of symptom onset

Molnupiravir

- Oral medication for twice daily 5 days
- Must be given within 5 days of symptom onset

Drug Interactions

No interactions expected

- TLD + Molnupiravir
- TLD+ Nirmatrelvir/Ritonavir
- TLD+ Remdesivir- monitor creatinine

- Atazanavir/Darunavir+ Molnupiravir-No interactions expected
- Atazanavir/Darunavir+ Nirmatrelvir/Ritonavir- **Potential interaction**
- Atazanavir/Darunavir+ Remdesivir- **monitor creatinine**

Post COVID Sequelae (Long COVID) in HIV

- Fatigue, Arthralgia, Myalgia
- Persistent Cough,Dyspnea
- Sleep disturbance,Anxiety/Depression/Mood disorders
- Worsening of comorbidities
- Tuberculosis,
- Mucormycosis
- Higher PD-1+ expression and raised inflammatory markers were also associated with increased risk of PASC including IL-6, TNF-alpha, and IP-10.

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

CDC and HIVMA vaccination recommendation

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.

Impact of the COVID Pandemic on HIV incidence and continuation of care

- Service disruptions vs behavioral change/no change
- Disruptions in ART refill reported from all LMIC
- Multi-month prescriptions recommended-90 pill pack
- Telemedicine and Courier agencies to dispense ART

Immunosuppression and SARS-CoV-2 Variants

Beta and Omicron variants likely arose in SSA (Botswana or South Africa), among people with prolonged infection due to immunosuppression

Largest global population with immunosuppression is HIV in sub-Saharan Africa

- 50% of 37.7mill PWH are optimally treated

- 8million PWH in SSA are not receiving ART, more since COVID-19 interruptions

Discussion around COVID-19 mortality and global vaccine equity has largely ignored risk of variant generation potentially attributable to HIV

- PWH can have long duration of shedding without progressive illness

ART in COVID-19 Treatment & Prevention

- No clinical evidence of benefit of LPV/r, TDF or other ARVs against SARS-CoV-2
- Hospitalised COVID-19 patients:
 - Continue ART without change
 - Initiate ART once clinically stabilised, prior to hospital discharge
 - Similar to ART initiation during OI management

Advice for PLHIV related to COVID19?

- Hand washing
- Mask
- Avoid gatherings and public places
- **Strictly adhere to ART and other OI meds**
- Don't change current effective non PI based ART regimen to PI based therapy
- **Adhere to medications for co-morbidities-Diabetes, hypertension, etc**
- COVID Vaccination, Booster

HIV & MONKEYPOX

Monkeypox declared global health emergency by WHO as cases surge

Declaration is strongest call to action agency can make, with most recent such announcement being for Covid



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WHO declares monkeypox a global health emergency - video