HIV and Covid-19: When two pandemics collide

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The HIV and Covid-19 pandemics at a glance

The collisions occur at three levels:
1. Health services
   - HIV services enhanced the Covid-19 response
   - Covid-19 impacted HIV services

2. Clinical care and outcomes
   - HIV affects Covid-19 clinical outcomes

3. Immunology and virology impacting prevention
   - HIV immunosuppression decreases natural & vaccine immunity
   - HIV immunosuppression facilitates creation of variants

3 key lessons from HIV for the Covid-19 response
In 2020, worldwide there were:
38 M PLHIV | 690,000 HIV deaths | 1.5 M new infections

1 Jan 2020 – 14 June 2021, worldwide there were:
176 M Covid-19 cases | 3.8 M deaths
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3 key lessons from HIV for the Covid-19 response
HIV services enhanced the Covid-19 response – 3 examples

Key resources used for control of HIV were rapidly redirected to control Covid-19:

• **Diagnostic platforms**
  • PCR machines used for HIV viral load testing enabled rapid establishment of SARS-CoV-2 PCR testing

• **Whole genome sequencing / Phylogenetics**
  • Gene sequencing platforms established for HIV resistance testing enabled variant identification

• **Vaccine research infrastructure**
  • Clinical trial infrastructure for HIV vaccines pivoted to undertake Covid-19 vaccine trials
Covid-19 impacted HIV services

Lockdown reduced patient attendance at health facilities in South Africa:

- 57% (n=339) apprehensive to visit clinics/hospital during lockdown
- HIV testing ↓ 47.6% in April 2020
- ART initiations ↓ 46.2% in April 2020
- No marked change in ART medicine collections
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3 key lessons from HIV for the Covid-19 response
Most studies show PLHIV have similar clinical outcomes, but a few suggest that PLHIV have a more severe clinical course than HIV-negative patients.

Smaller studies on individual outcomes tended to find no difference.
Covid-19 outcomes in HIV-infected individuals: UK

- Retrospective cohort: 17,282,905 adults (27,480 (0.16%) had HIV)
- PLHIV ↑ male, ↑ Black and ↑ from deprived geographical area
- Of 14,882 Covid-19 deaths, 25 among people with HIV
- PLHIV - ↑ Covid-19 deaths [age/sex adjusted HR: 2.9 (CI 2.0–4.3)]
- HR for Blacks: 4.3 compared to HR for non-Black: 1.8
How HIV affects Covid-19 clinical outcomes in SA

- HIV increased risk of Covid-19 mortality **2-fold** (HR: 2.1; 95%CI: 1.7 - 2.7)
- No difference in outcome based on viral suppression
- About 8% of Covid-19 deaths related to HIV

**Associations with 2,978 in-hospital Covid-19 deaths in Western Cape**

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**Source:** Boulle A et al. Clin Infect Dis. 2020; doi: 10.1093/cid/ciaa1198
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3 key lessons from HIV for the Covid-19 response
Natural and vaccine-immunity compromised in HIV-positive patients

Diminished serological response in PLHIV to natural SARS-CoV-2 infection - lower IgG and neut antibody titres

- Patient with uncontrolled HIV replication (HIV VL: 831,764 copies; CD4: 20 cells)
- No immune response after 2 Pfizer vaccine doses
  - No IgG reactivity against S1 subunit of spike protein
  - No SARS-CoV-2-specific neut antibodies
  - No ELISpot spike protein-specific T cells

Source: Spinelli MA et al Lancet HIV 2021
Persistent SARS-CoV-2 replication in immunocompromised HIV+ patient

- Patient with uncontrolled HIV (low ARV adherence)
- CD4: 6 cells/μL
- HIV VL: 34,151 copies/mL
- SARS-CoV-2 Ct: 18.5
- Effective ART regimen at day 190 → HIV suppression, immune-reconstitution and SARS-CoV-2 clearance

Source: Karim F et al. MedRxiv 2021
Variants evolving in an immunocompromised HIV-positive patient

- Initial virus D614G variant
- 11 new mutations / deletions in spike protein (7 in RBD)
- E484K at day 6
- K417T at day 71
- N501Y at day 190
- Patient recreated the 3 key RBD mutations of Beta variant (501Y.V2)
- HIV resistance to TDF (K70KQ), FTC (M184V) and EFV (K103R/V179D)

### SARS-CoV-2 aa substitutions and deletions over time

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**Source:** Karim F et al. MedRxiv; 2021
### Persistence and Evolution of SARS-CoV-2 in an immunocompromised Host

**Choi B, Choudhary MC, Regan J, et al**

- Patient with antiphospholipid syndrome on anticoagulation, glucocorticoids & rituximab
- Remdesivir and anti-spike Regeneron mAbs
- Many mutations, incl. 8 in RBD – E484K, N501Y

### SARS-CoV-2 evolution during treatment of chronic infection

**Steven A. Kemp, Dami A. Collier, Rawlings P. Datir, et al**

- Patient with B cell lymphoma on chemotherapy and anti-CD20 B cell depletion with rituximab
- SARS-CoV-2 convalescent plasma
- Virus evolved with ↓ sensitivity to neut Abs

### Emergence of multiple SARS-CoV-2 antibody escape variants in an immunocompromised host undergoing convalescent plasma treatment

**Liang Chen, Michael C Zody, Jose R Mediavilla, et al**

- Renal transplant patient on steroids and rejection suppressant tacrolimus
- SARS-CoV-2 convalescent plasma
- Multiple NTD and RBD mutations, incl. E484K and Q493K
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3 key lessons from HIV for the Covid-19 response
1. “Know your epidemic – Know your response”

Data-driven plan for the response

HIV hotspots

South Africa: SARS-CoV-2 Hotspot identification and mitigation

Hlabisa district, KwaZulu Natal

Tanser et al IJE; 2009

Khayelitsha Township in Cape Town, Cloete et al, 2020

Guidelines for second generation HIV surveillance: an update: Know your epidemic

Covid-19 epidemic in South Africa
Does HIV cause AIDS? Can a virus cause a syndrome? How? It can’t, because a syndrome is a group of diseases resulting from acquired immune deficiency. 

Thabo Mbeki

"We bought a tremendous amount of... hydroxychloroquine, ...And there are signs that it works on [coronavirus], some very strong signs."

Donald Trump
3. Importance of mutual interdependence in HIV

“The AIDS movement demonstrates that with a shared vision, shared responsibility and through global solidarity and leadership of people living with HIV, affected communities and individual action, we can change the course of history.” – UNAIDS 2015

- **Global solidarity** – essential for access to life-saving medication, e.g. Global Fund, UNITAID, PEPFAR
3. Importance of mutual interdependence in Covid-19

**Initial - government action**
- Anxiety
- Institutional power over people
- Stay-at-home orders / Lockdown

**Pivot – prevention approach**
- Agency
- Individuals power within people
- Public health interventions

**Subsequent - Individual action**
- Self-efficacy
- Motivated individuals power to act for prevention

**To reach – collective community action**
- Collectivism
- Motivated communities power for collective action
- “I am, because you are” Ubuntu