

HIV and Covid-19: When two pandemics collide

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IMPAACT Annual Meeting 2021

Outline

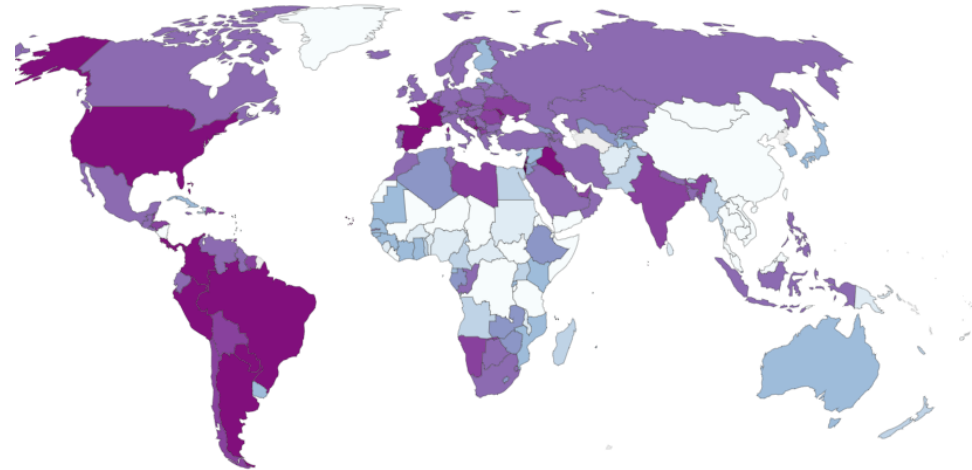
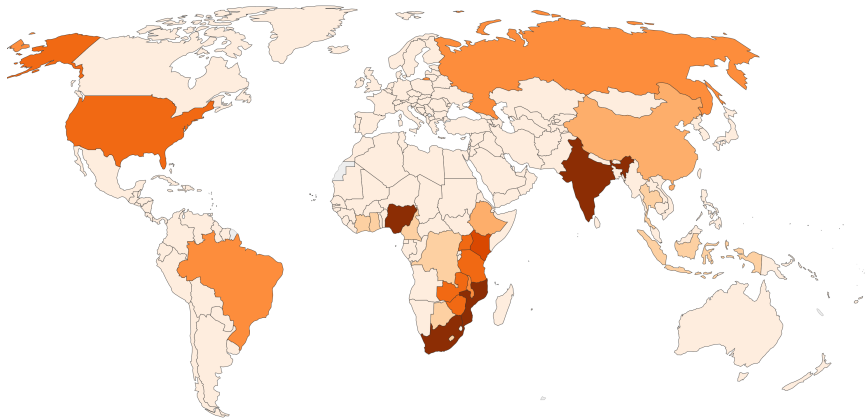
- ▶ **The HIV and Covid-19 pandemics at a glance**
- ▶ **The collisions occur at three levels:**
 - 1. Health services**
 - ◆ HIV services enhanced the Covid-19 response
 - ◆ Covid-19 impacted HIV services
 - 2. Clinical care and outcomes**
 - ◆ HIV affects Covid-19 clinical outcomes
 - 3. Immunology and virology impacting prevention**
 - ◆ HIV immunosuppression ↓ natural & vaccine immunity
 - ◆ HIV immunosuppression facilitates creation of variants
- ▶ **3 key lessons from HIV for the Covid-19 response**

HIV & Covid-19 pandemics at a glance



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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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**

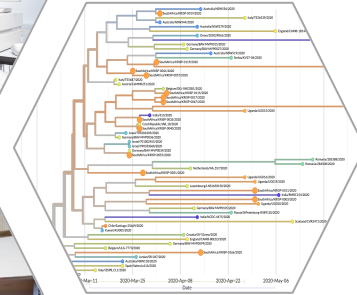
- PCR machines used for HIV viral load testing enabled rapid establishment of SARS-CoV-2 PCR testing

- **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



By Quarisha Abdoel Karim and Salim S. Abdoel Karim

Shortly after instituting coronavirus disease 2019 (COVID-19) mitigation measures, such as banning air travel and closing schools, the South African government implemented a national lockdown on 27 March 2020 when there were 402 cases and the number of cases was doubling every 2 days (2). This drastic step, which set out to curb viral transmission by restricting the movement of people and their interactions, has had several unintended consequences for the provision of health care services for other prevalent conditions, in particular the prevention and treatment of tuberculosis (TB) and HIV. Key resources that had been extensively built up over decades for the control of HIV and TB are now being redirected to control COVID-19 in various countries in Africa, particularly South Africa. These include diagnostic platforms, community outreach programs, medical care access, and research infrastructure. However, the COVID-19 response also provides potential opportunities to enhance HIV and TB control.

In Africa, the COVID-19 epidemic is unfolding against a backdrop of the longstanding TB and HIV epidemics. South Africa ranks among the worst-affected countries in the world for both diseases. Despite having just 0.7% of the world's population, South Africa is home to ~20% (1.7 to 7.5 million people) of the global burden of HIV infection (3) and ranks among the worst affected countries in the world for TB, with the fourth highest rate of HIV/TB co-infection (59%) (3). South Africa has made steady progress since 2010 in controlling both diseases. Increased access to antiretroviral drugs for treatment and for prevention of mother-to-child transmission of HIV has resulted in a 30% reduction in AIDS-related deaths between 2010 and 2018 (2). Similarly, the death rate among TB cases has declined from 224 per 100,000 population in 2010 to 130 per 100,000 population in 2018 (2). Have the strategies implemented for COVID-19 mitigation, particularly the lockdown, inadvertently threatened these gains in HIV and TB?

HIV and TB polymerase chain reaction (PCR) tests are key to treatment initiation and monitoring to achieve the United Nations goals for the control of HIV and TB. Disturbingly, these diagnostic tests declined during the lockdown. The 50% drop in the median number of daily GeneXpert TB tests—a cartridge-based PCR test capable of diagnosing TB within 2 hours while simultaneously testing for drug resistance—was

The GeneXpert cartridge-based platform is used routinely at the CAPRICA clinic in Durban, South Africa, to rapidly test for tuberculosis and HIV viral load. Such it is now also being used to test for COVID-19.

VIEWPOINT: COVID-19

COVID-19 affects HIV and tuberculosis care

The COVID-19 response should be balanced with the need to manage other diseases

Science
MAAAS

THE LANCET

"We estimate that vaccination against the ten selected pathogens will have averted 67.6 million deaths between 2000 and 2030, of which 37 million were averted between 2005 and 2025."

The impact of the COVID-19 lockdown on HIV care in 65 South African primary care clinics: an interrupted time series analysis

Jienchi Dorward, Thokozani Khubone, Kelly Gate, Hope Ngobese, Yuktshwar Sookraj, Siyabonga Mkhize, Aslam Jeeva, Christian Bottomley, Lara Lewis, Kathy Baisley, Christopher C Butler, Nomakhosi Gxagxisa, Nigel Garrett

- ▶ 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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Overview of SARS-CoV-2 infection in adults living with HIV

Juan Ambrosioni*, José Luis Blanco*, Juliana M Reyes-Urueña, Mary-Ann Davies, Omar Sued, Maria Angeles Marcos, Esteban Martínez, Silvia Bertagnolio, Jose Alcamí, Jose M Miro, COVID-19 in HIV Investigators†

	Hospitalisation	Intensive care unit admission	Mechanical ventilation	Mortality rate	Other relevant results and conclusions
Inciarte et al (2020) ⁵²	49%	8%	4%	4%	No HIV or ART role identified as prognostic factor
Vizcarra et al (2020) ⁴⁴	55%	12%	9-8%	4%	No differences in COVID-19 presentation due to HIV status
Sigel et al (2020) ⁴⁰	NA*	17%	18%	21%	Smoking and comorbidities more frequent in people living with HIV than in people who are HIV-negative, but both groups had similar outcomes
Ho et al (2021) ³⁷	NA*	26.4%	20.8%	26.4%	Higher inflammatory markers in people living with HIV with poor outcome
Etienne et al (2020) ⁵³	NR	9.3%	NR	2%	Sub-Saharan African ethnicity and metabolic disorders associated with critical outcome; CD4 cell count not related
Dandachi et al (2020) ⁴¹	57.3%	28.7%	22.6%	16.5%	CD4 counts of less than 200 cells per μ L was associated with intensive care unit admission, mechanical ventilation, or death
Boulet et al (2020) ⁴	20-75%	NR	NR	3.6%	Higher mortality in people living with HIV compared with people who are HIV negative
Miyashita et al (2021) ⁶⁴	NR	22%	12%	14%	Poor outcomes related to comorbidities
Del Amo et al (2020) ⁶⁵	64%	6.35%	NR	8.5%	Incidence of COVID-19 not higher than in the general population; tenofovir might be protective
Geretti et al (2020) ⁵	NA*	33%	16.4%	24%	After adjusting for age and other variables, higher mortality seen in people living with HIV
Cabello et al (2021) ³⁷	32.3%	3.2%	3.2%	3.2%	Prognosis related to age and comorbidities

ART=antiretroviral therapy. NR=not reported. NA=not applicable. *Studies included only hospitalised patients.

Table 2: Summary of outcomes in studies reporting on more than 50 people living with HIV who have been infected with COVID-19

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

THE LANCET

"The British men with advanced prostate cancer they remain hope that alternative might be available to them, given the provisional nature of NHS guidance and the arrival of 200 million cancer drug fund that is available for such treatments for patients in England."

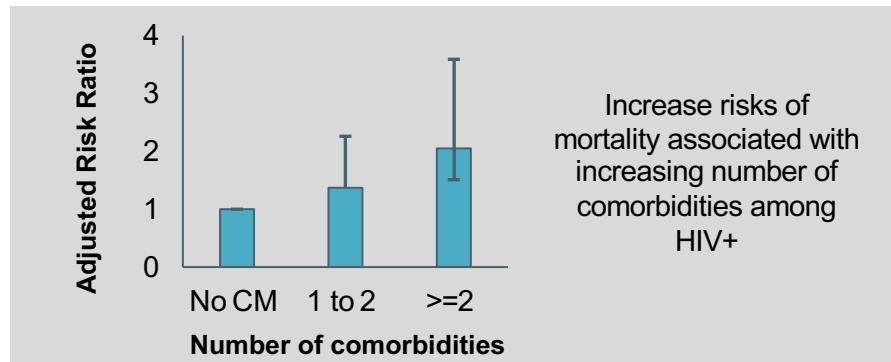
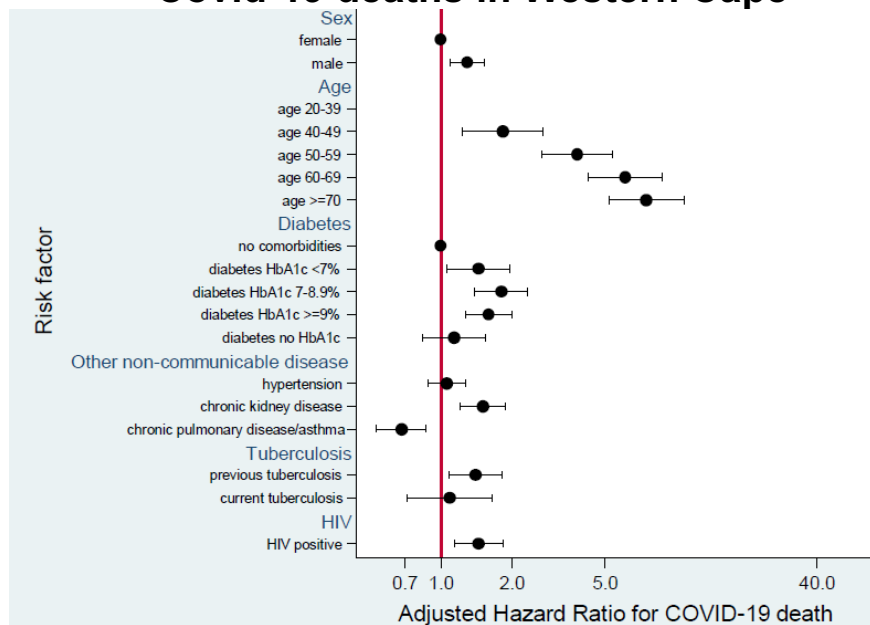
HIV infection and COVID-19 death: a population-based cohort analysis of UK primary care data and linked national death registrations within the OpenSAFELY platform

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**

- **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

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



Increase risks of mortality associated with increasing number of comorbidities among HIV+

- **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**

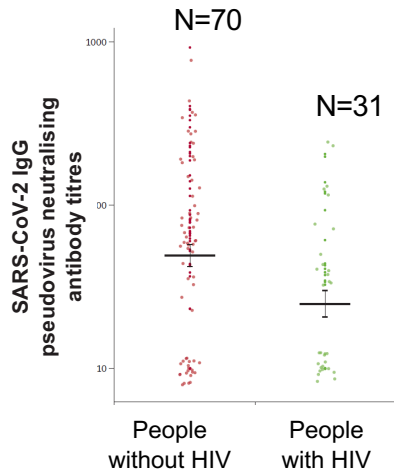
Source: Boule A et al. Clin Infect Dis. 2020; doi: 10.1093/cid/ciaa1198

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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



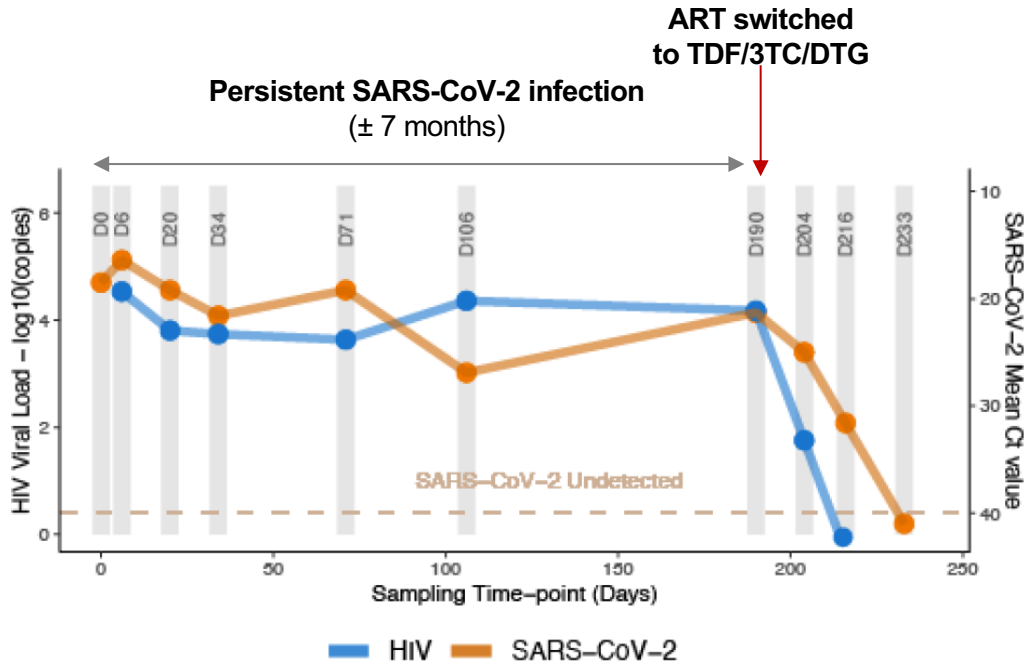
Failure to seroconvert after two doses of BNT162b2 SARS-CoV-2 vaccine in a patient with uncontrolled HIV

Emma Touizer, Aljawharah Alrubayyi, Chloe Rees-Spear, et al

- **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/ μ L
- 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

	Position	wildtype	Timepoint						
			D0	D6	D20	D34	D71	D106	D190
NTD	9	P					L		
	142	G	V						
	144	Y				-	-	-	-
	190	R					K		K
RBD	417	K					T		
	427	D							Y
	455	L						F	
	456	F						L	
	484	E		K	K	K			
	490	F					S	S	S
	501	N							Y
	614	D	G	G	G	G	G	G	G
796	D	Y				Y		Y	
1078	A		V						

SARS-CoV-2 aa substitutions and deletions over time

- 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)

Viral evolution in immunocompromised individuals with other conditions



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

medRxiv
THE PREPRINT SERVER FOR HEALTH SCIENCES

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

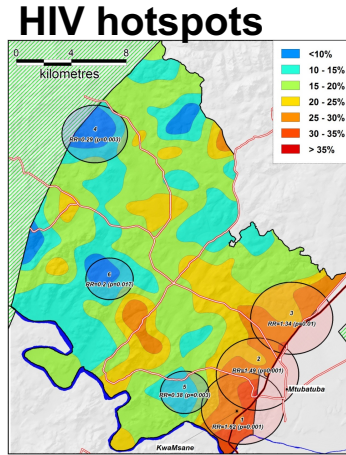
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1. “Know your epidemic – Know your response”

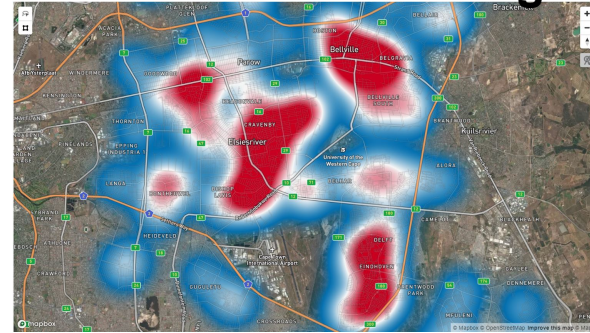
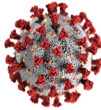


Data-driven plan for the response

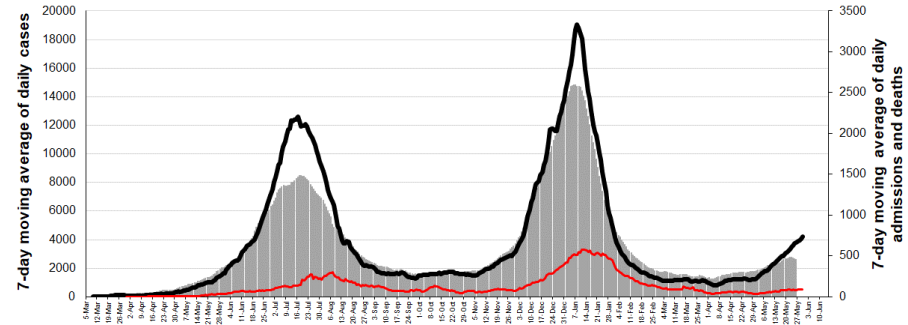


Hlabisa district, KwaZulu-Natal Tanser et al IJE; 2009

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



Khayelitsha Township in Cape Town, Cloete et al, 2020



Covid-19 epidemic in South Africa International Maternal Pediatric Adolescent AIDS Clinical Trials Network

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

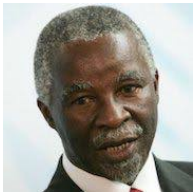
2. Centrality of scientific evidence in the response



07 UNAIDS Annual Report
Knowing your epidemic

LET OUR ACTIONS COUNT

SOUTH AFRICA'S NATIONAL STRATEGIC PLAN ON HIV, TB and STIs 2017-2022



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

The NEW ENGLAND JOURNAL of MEDICINE

The South African Response to the Pandemic

Salim S. Abdool Karim, M.B., Ch.B., Ph.D.

The first person with confirmed Covid-19 in South Africa was a traveler who had returned from Italy and was diagnosed on March 5, 2020. When 402 cases had been identified after 18 days, the government announced a national lockdown, which was implemented 4 days later when the doubling time was 2 days and there were 1170 identified cases (Fig. 1A). During 35 days of strict lockdown, the doubling time slowed to 15 days, and there were 5647 cases (including 109 deaths) by April 30. As of May 19, when a less strict lockdown was in place, South Africa had recorded 12,200 cases and 312 deaths and had conducted 488,609 tests (www.gov.za/Coronavirus). South Africa's national Covid-19 response has

During Stage 4, the government hi community health communities to ur case finding. Sout tracing teams, est been used for Covi toring of compliz highest HIV burden a network of pro As of May 19, when a less strict lockdown was in place, South Africa had recorded 12,200 cases and 312 deaths and had conducted 488,609 tests (www.gov.za/Coronavirus). South Africa's national Covid-19 response has

A. Cases and Stages of Response

The graph shows cumulative cases (blue line) and active cases (orange bars) of Covid-19 in South Africa from March to May 2020. The y-axis represents the number of cases (0 to 16,000). The x-axis shows dates from March 1 to May 21. The graph is divided into stages: Stage 1: Preparation; Stage 2: Primary prevention; Stage 3: Strict lockdown; Stage 4: Active case finding; Stage 5: Identification of hot spots; Stage 6: Medical care and Stage 7: Death and bereavement; Stage 8: Lockdown Easing Starts; Stage 9: Vigilance. Key events marked include 'State of Disaster' (March 15), 'National Lockdown' (March 27), and 'Lockdown Easing Starts' (May 19).



"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**



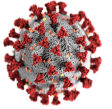
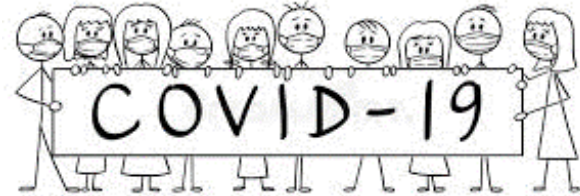
**Pivot –
prevention
approach**



**Subsequent -
Individual
action**



**To reach –
collective
community action**



Anxiety

**Institutional
power
over people**
Stay-at-home
orders /
Lockdown

Agency

**Individuals
power within
people**
Public health
interventions

Self-efficacy

**Motivated
individuals
power to act
for
prevention**

Collectivism

**Motivated communities
power for collective action**
“I am, because you are”
Ubuntu