



Covid-19 & variants have made HIV control even more critical: Mapping a path forward

UNAIDS PCB – 8 November 2021

Salim S. Abdool Karim, FRS

Director: CAPRISA

CAPRISA Professor of Global Health, Columbia University

Adjunct Professor in Immunology and Infectious Diseases, Harvard University

Adjunct Professor of Medicine: Cornell University

Pro Vice-Chancellor (Research): University of KwaZulu-Natal

Director: DSI-NRF Centre of Excellence in HIV Prevention

Member: African Task Force for Coronavirus



CAPRISA hosts a
DST-NRF Centre of Excellence
in HIV Prevention



Overview

- **Key challenge in the HIV epidemic today...**
- **Importance and limitations of HIV treatment as prevention**
- **Challenges in HIV prevention – young girls in Africa**
- **Mapping a path forward**
- **Covid-19 – a new imperative for HIV control**
- **Omicron – a wake up call!**

The HIV epidemic today

In 2020, worldwide there were:

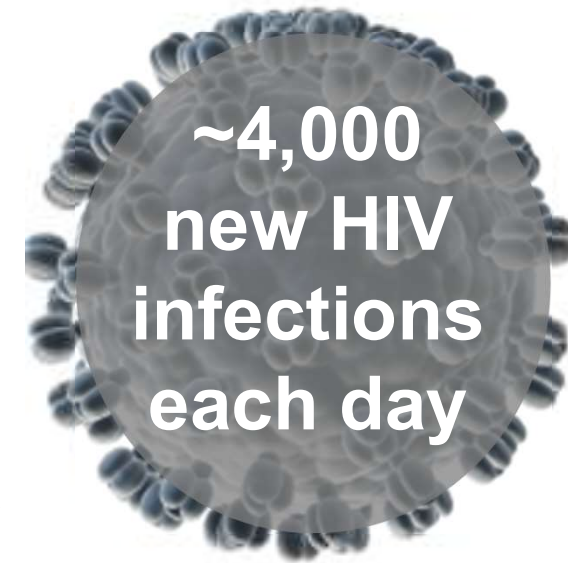
38 million living with HIV

690,000 HIV deaths

1.5 million new infections

Africa has \pm 70% of all the world's HIV

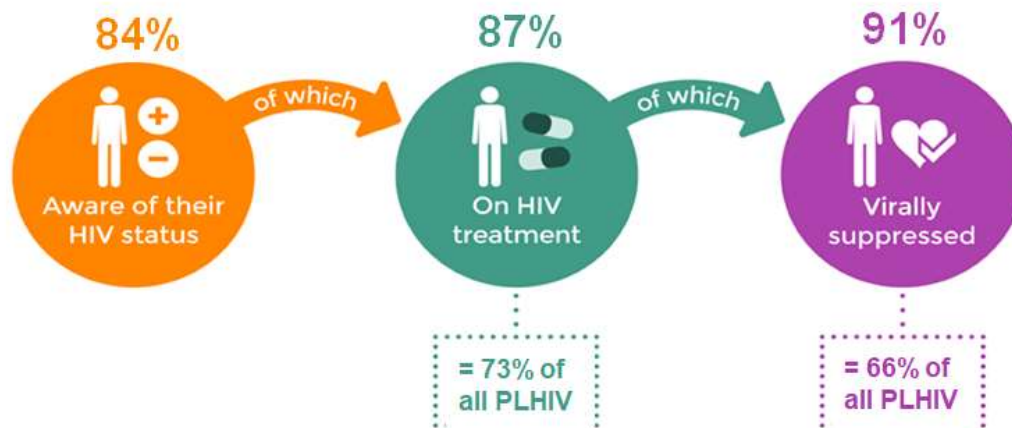
sub-Saharan Africa: Young women = ~25% of new infections



Global HIV strategy built on TasP – 2020 target: 90-90-90

Source: UNAIDS Global Report 2020

Progress with 90-90-90 with recent developments in simplifying HIV treatment



- Good global progress: 84-87-91
- 14 countries across 3 regions achieved the 73% target by 2020
- Uneven progress (2 regions <60%)
 - North Africa & Middle East: 36% → 73%
 - Eastern Europe & Central Asia: : 50% → 73%

New drugs with better safety profiles

Tenofovir
Alafenamide



Simplified Regimens using Dual-Therapy

Dolutegravir-based dual therapy



Long-acting monthly dual injectable

Cabotegravir + Rilpivirine (Cabenuva)



Source: UNAIDS 2021


Limitations in translating TasP to community impact



The NEW ENGLAND
JOURNAL of MEDICINE

HIV-1 Epidemic Control — Insights from Test-and-Treat Trials

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



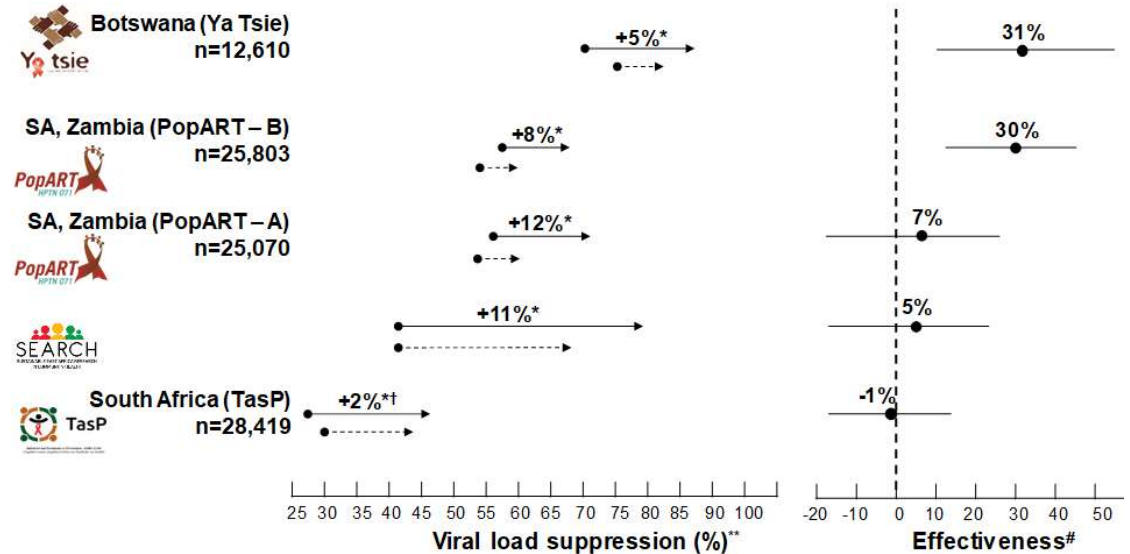
Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model

Reuben M Granich, Charles F Gilks, Christopher Dye, Kevin M De Cock, Brian G Williams



Prevention of HIV-1 Infection with Early Antiretroviral Therapy

Myron S. Cohen, M.D., Ying Q. Chen, Ph.D., Marybeth McCauley, M.P.H., Theresa Gamble, Ph.D., Mina C. Hosseinour, M.D.

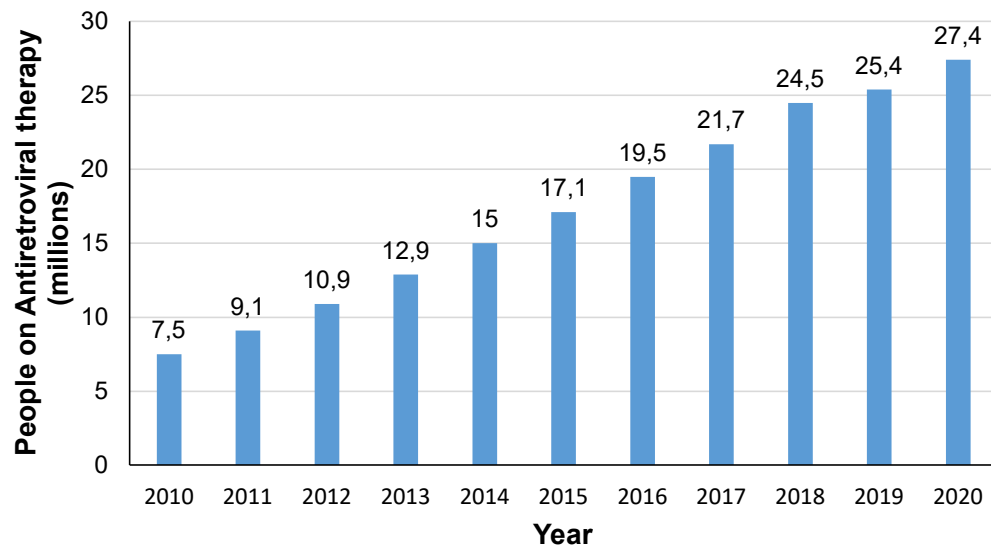


**4 large Universal Test & Treat trials:
Little / No impact on HIV incidence**

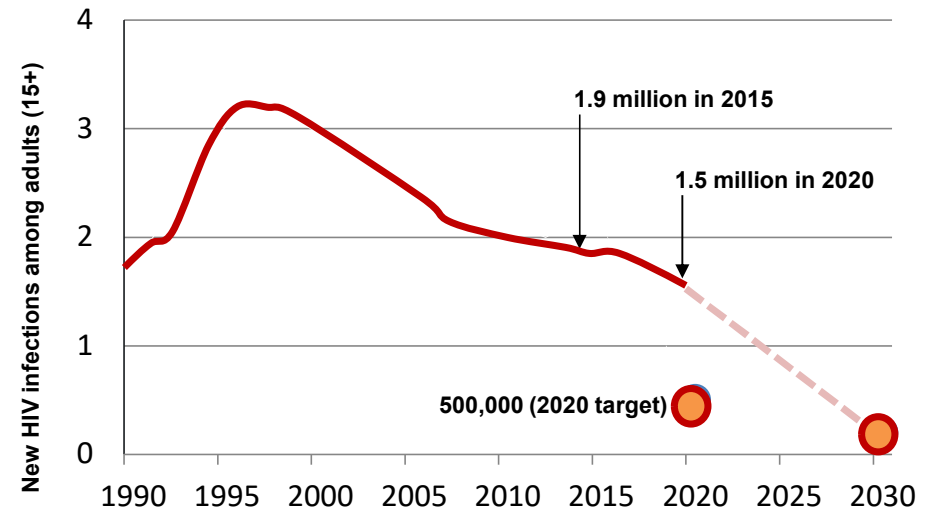
No silver bullet! ART scale-up essential but not sufficient for epidemic control – need to go beyond TasP

Great progress on increasing HIV treatment but we are lagging in prevention

Number of people receiving antiretroviral therapy: 2010–2020



1.5 million new infections in 2020 but target was 500,000

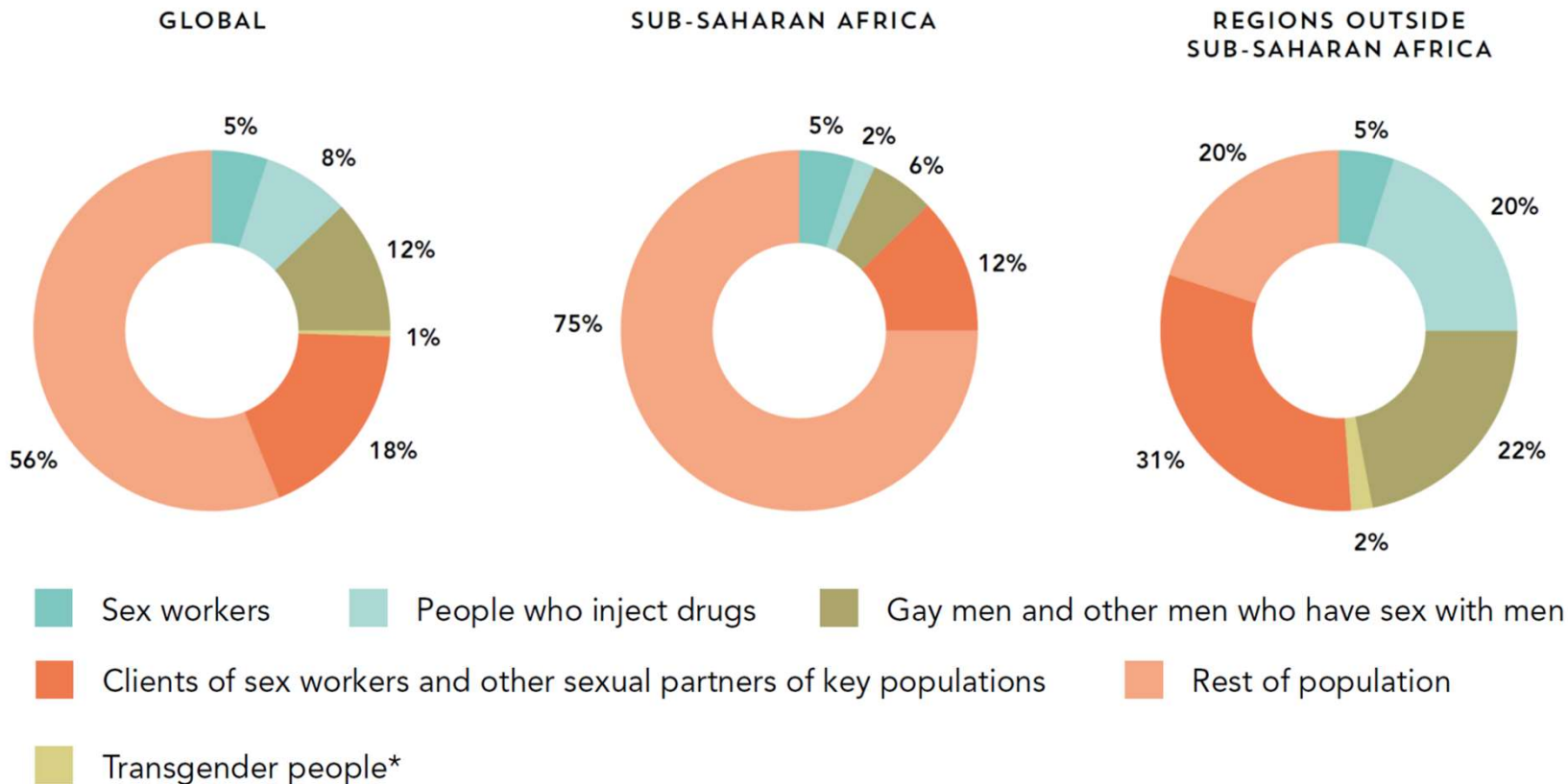


Source: UNAIDS reports

Overview

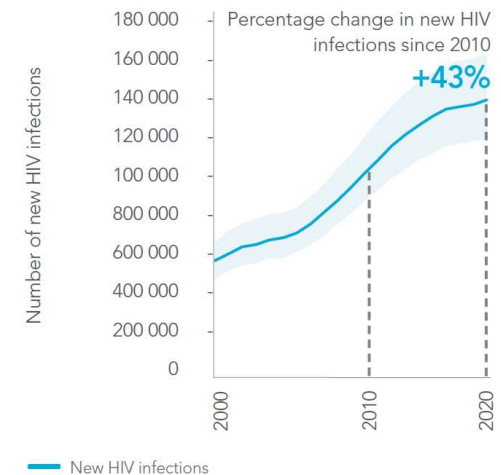
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Young women main contributors to new HIV infections in Africa, but key populations elsewhere

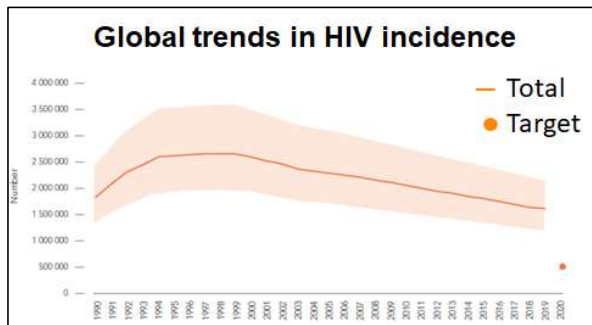


Source: UNAIDS

For example: New HIV infections in Eastern Europe & Central Asia: 1990–2019



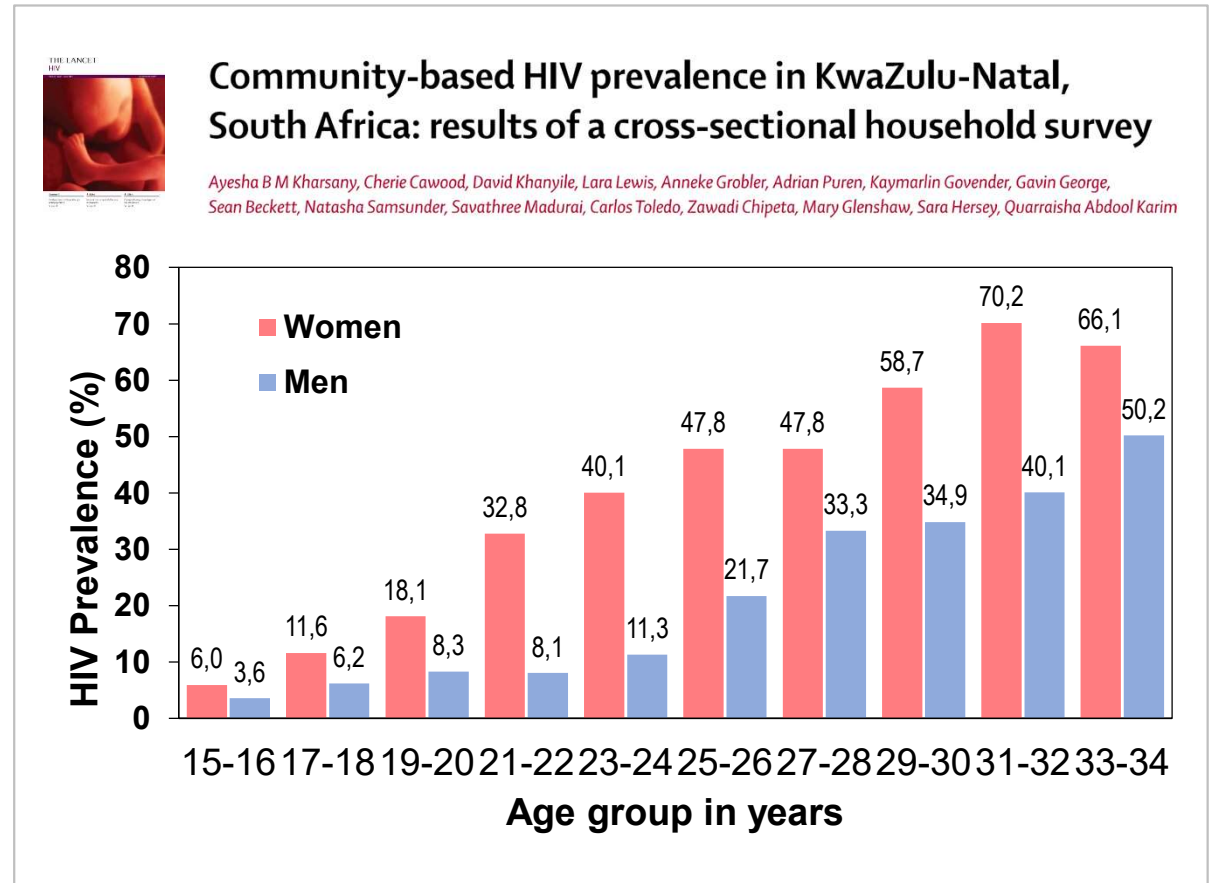
High global priority to reach 2030 UN goal... ...HIV prevention in young women in Africa



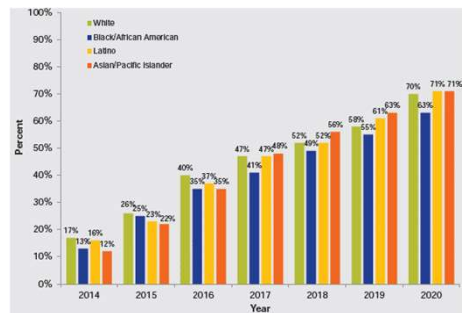
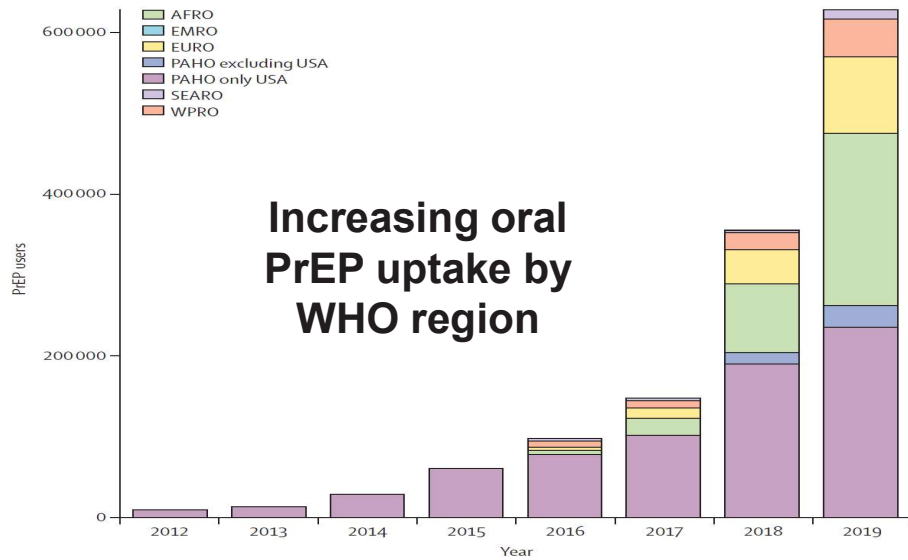
HIV incidence trends in Africa: young women at highest risk
*Salim S Abdool Karim, Cheryl Baxter

Age patterns of HIV incidence in eastern and southern Africa: a modelling analysis of observational population-based cohort studies
Kathryn A Risher, Anne Cori, Georges Reniers, Milly Marston, Clara Calvert, Amelia Crampin, Tawanda Dadirai, Albert Dube, Simon Gregson, Kobus Herbst, Tom Lutalo, Louisa Moorhouse, Baltazar Mtenga, Doreen Nabukalu, Robert Newton, Alison J Price, Malebogo Thajane, Jim Todd, Keith Tomlin, Mark Urassa, Alain Vandormael, Christophe Fraser, Emma Slaymaker, Jeffrey W Eaton, on behalf of the ALPHA Network

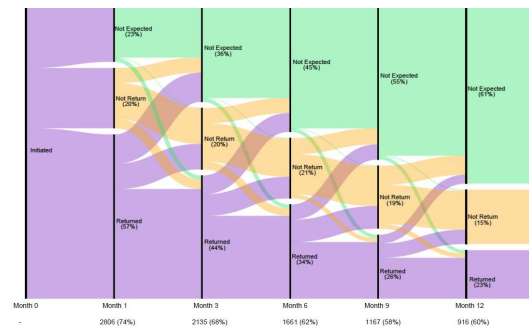
Recent levels and trends in HIV incidence rates among adolescent girls and young women in ten high-prevalence African countries: a systematic review and meta-analysis
Isolde Birdthistle, Clare Tanton, Andrew Tamita, Kristen de Graaf, Susan B Schaffnit, Frank Tanser, Emma Slaymaker



Scale up of PrEP and Implementation challenges



- 70% of all MSM in San Francisco on PrEP in 2020
- PrEP scale-up → 43% ↓ in new diagnoses in 3 years



High rates of PrEP uptake in HIV discordant relationships but not in many others

- High rates of discontinuation:
 - PrEP continuation was 57% at 1 month, 44% at 3 months & 34% at 6 months

PrEP needs to shift from a user-initiated service to a provider-initiated service (like pMTCT)

Sources: Shafer R et al. *Lancet HIV* 2021; 8: e502–10; Irungu EM, *Lancet Glob Health* 2021; 9: e1730–39; San Francisco Department of Public Health. *HIV epidemiology annual report, 2020*

Need new technologies for provider-initiated PrEP



Enhancing HIV Prevention with Injectable Preexposure Prophylaxis

Quarraisha Abdool Karim, Ph.D.

Daily oral PrEP

(1.5 million initiated on PrEP globally)

Oral TDF/FTC (Truvada) & Oral F/TAF (Descovy)



Long-acting 2-monthly injectable antiretrovirals

Cabotegravir



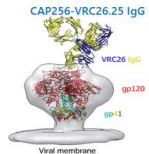
Antiretroviral-based monthly intravaginal ring

Dapivirine

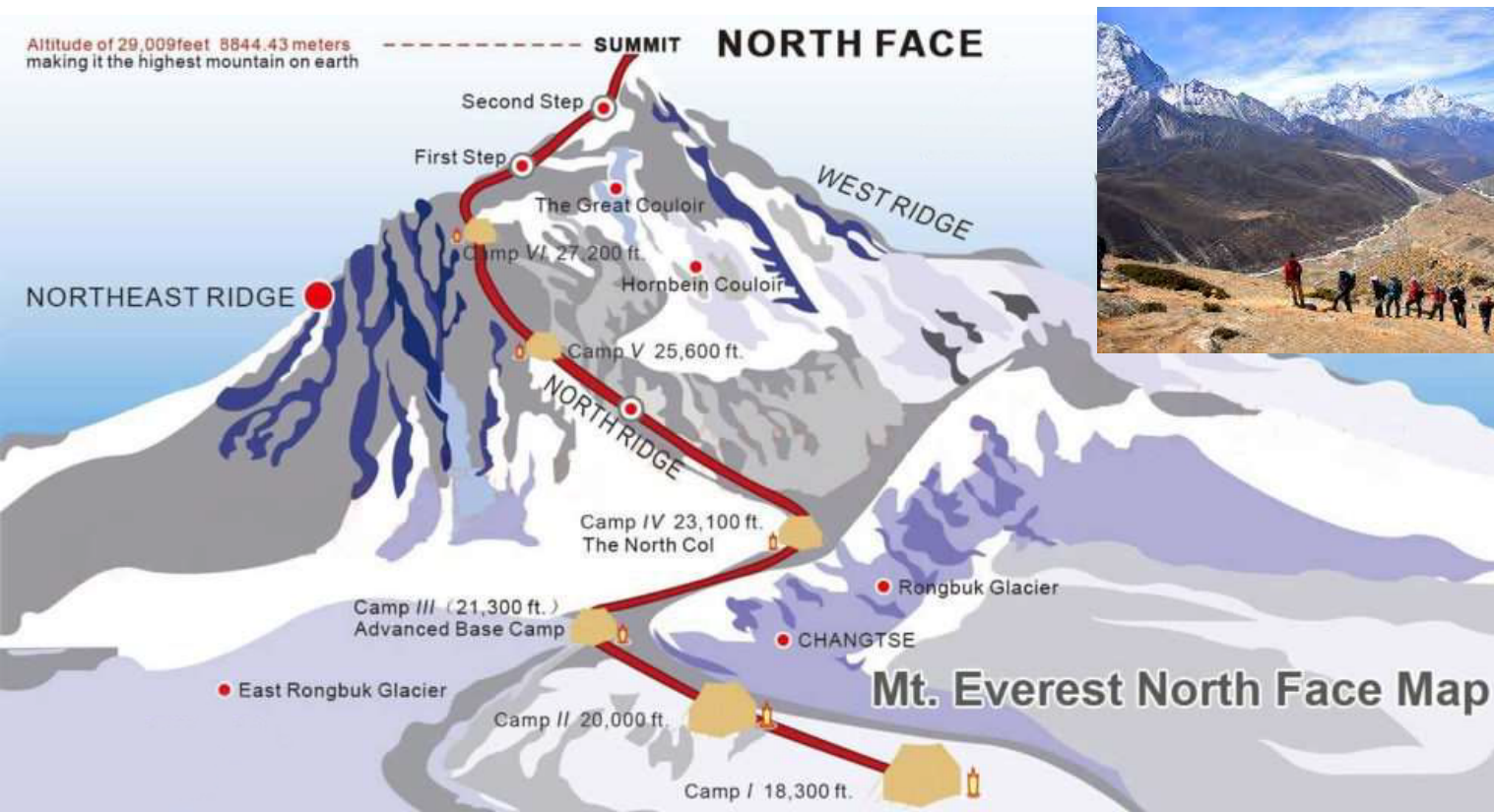


Promising new prevention technologies in clinical trials

- Monthly tablet – *Islatravir*
- 6-month injection – *Lenacapavir* or *bnAbs*
- Annual implant – *Islatravir* or *TAF*



Path Forward - Our chosen path to epidemic control: 90-90-90 is only base camp

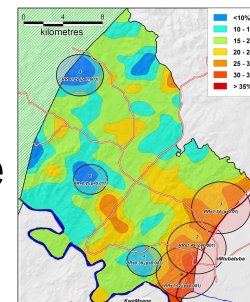


Need to stay focused on the SDG target of ending AIDS as a public health threat by 2030 – the path to endemic HIV infection

Have to have flexibility – new challenges and benefits (technologies)

Successful climb to the summit needs 5 ingredients

1. Translating new science to community impact – know your epidemic, know your response



2. Community engagement – addressing inequalities:
“Do things *with* people - not *on* people”



3. Importance of committed leadership

4. Importance of global solidarity



Investing in our future
The Global Fund
To Fight AIDS, Tuberculosis and Malaria



UNAIDS



5. A bold evidence-based plan beyond 90-90-90 or 95-95-95 ...

A bold plan to move the global response beyond TasP

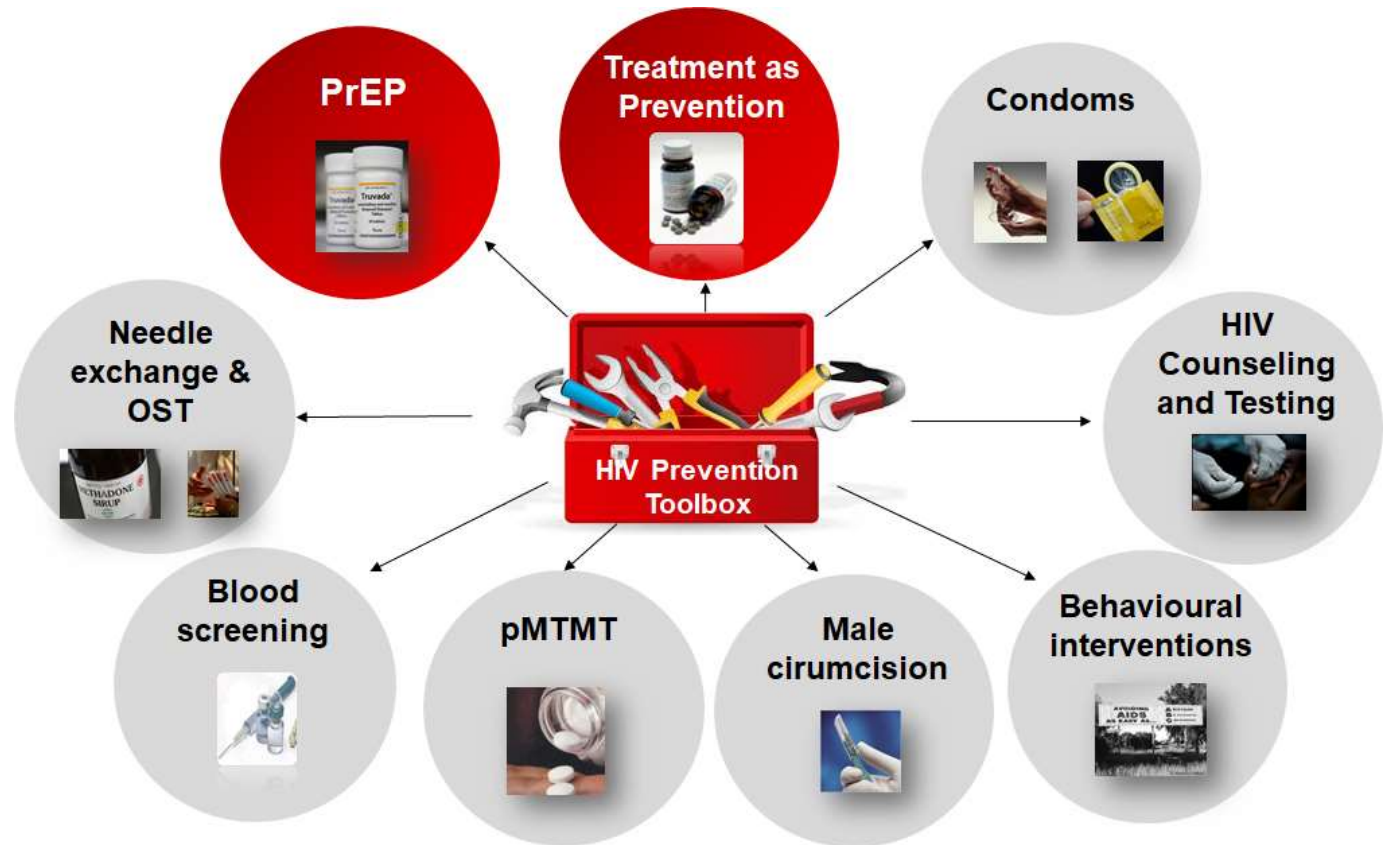
TasP + plan

3 Underlying principles:

1. Leave no one behind, fight stigma & inequality
2. Evidence-based strategy
3. Effective implementation targeted for priority areas

3 Key components:

1. Re-commit to TasP, but move beyond 95-95-95
2. Provider-initiated PrEP
3. Combination prevention using tools as needed



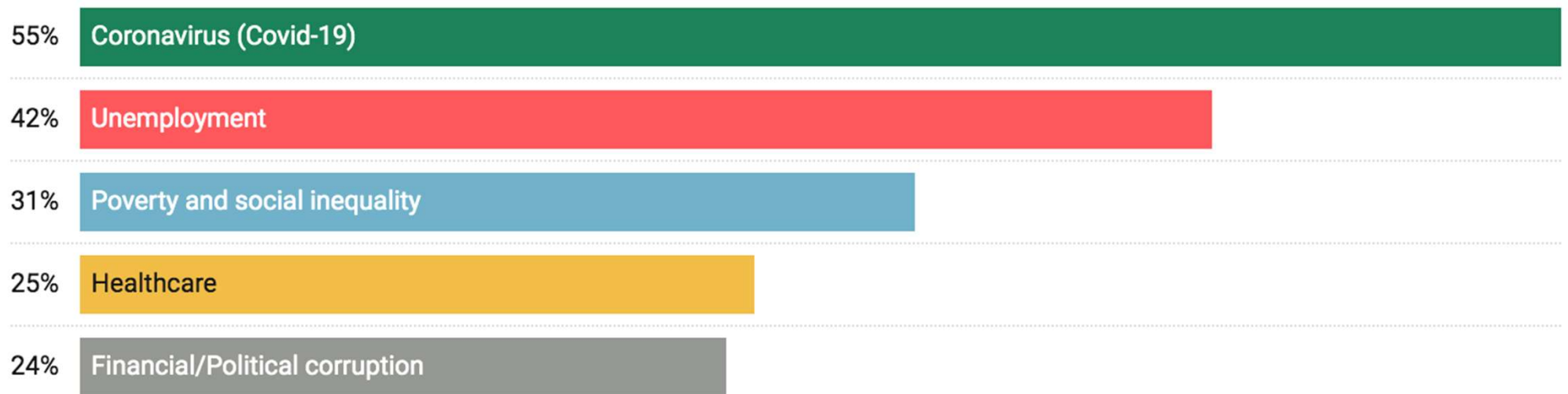
**Built on ART + Provider-initiated PrEP
while maximizing combination prevention**

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- Omicron – a wake up call!

Attention to HIV declines: Covid-19 tops the 5 biggest global concerns

Survey of 16-64 year participants in 27 countries in 2020



Research among adults aged 16-64 in 27 participating countries. c. 19,000 per month. (May 2020).

Source: Global Advisor • [Get the data](#) • Created with [Datawrapper](#)

Covid-19 impacted HIV services



INSIGHTS

PERSPECTIVES

Science
AAAS

Quaraisah Abdool Karim and Salim S. Abdool 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 (1). 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% (7.7 to 7.9 million people) of the global burden of HIV infection (2) and ranks among the worst-affected countries in the world for TB, with the fourth highest rate of HIV/TB coinfection (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 33% 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 110 per 100,000 population in 2018 (3). 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 59% 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 CAPRISA clinic in Durban, South Africa, to rapidly test for tuberculosis and HIV viral load, but it is now also being used to test for COVID-19.

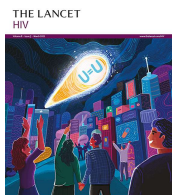
VIEWPOINT: COVID-19

COVID-19 affects HIV and tuberculosis care

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

366 24 JULY 2020 • VOL. 369 ISSUE 6002

sciencemag.org SCIENCE



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 Sookrajh, Siyabonga Mkhize, Aslam Jeewa, 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**

*The Ask Afrika COVID-19 Tracker

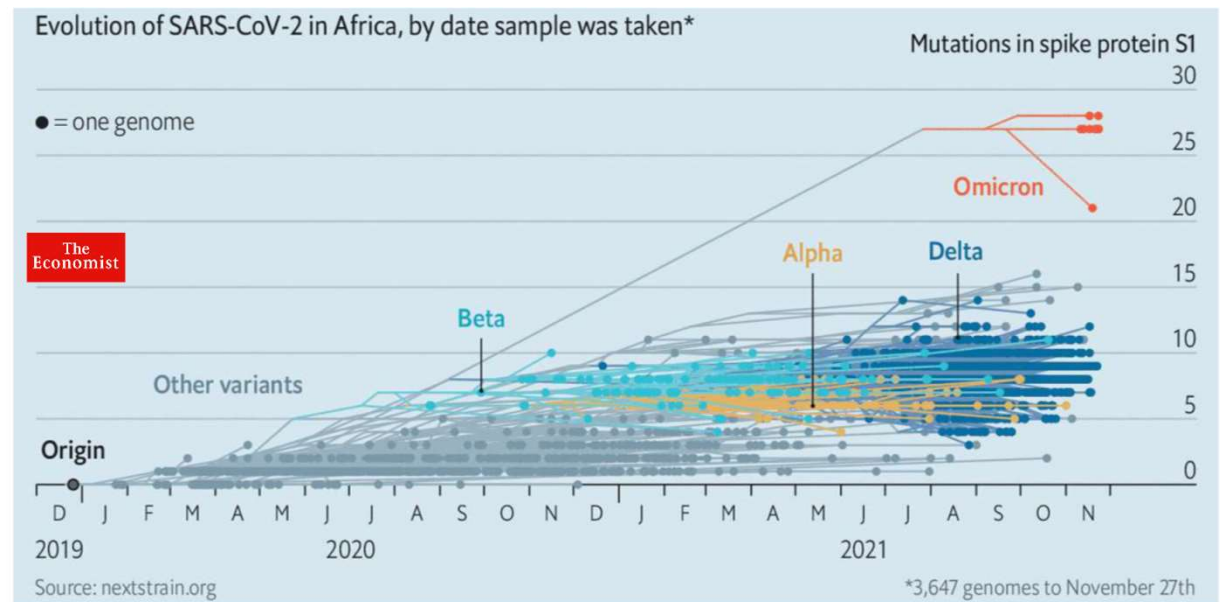
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How did Omicron come to exist?

1. Human → animal → human
2. A multi-mutant circulating without detection
3. A new variant emerging from persistent infection - ?immunocompromised
4. Patient Zero? - not known
5. Country of origin?

- **Phylogenetic tree - separates in Q3 of 2020 (pre-vaccine)**
- **Likely evolved by persistent infection (~12 months) in immunocompromised person**
- **~50 mutations in SARS-CoV-2**



Variants evolving in an immuno-compromised HIV+ patient with a persistent 7-month infection

	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

- Started with a 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)

Source: Karim F et al. MedRxiv; 2021

Why the concern about variants?

Variants have changed the Covid-19 endgame



New SARS-CoV-2 Variants — Clinical, Public Health, and Vaccine Implications

Salim S. Abdool Karim, Tulio de Oliveira

THE LANCET



SARS-CoV-2 variants and ending the COVID-19 pandemic

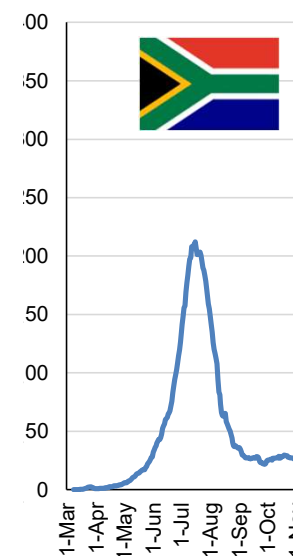
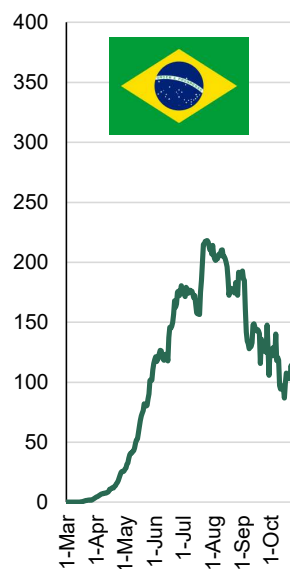
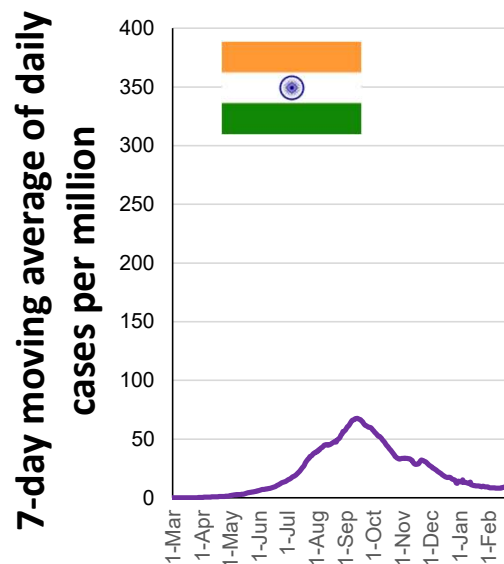
Arnaud Fontanet, Brigitte Autran, Bruno Lina, Marie Paule Kieny, Salim S Abdool Karim, Devi Sridhar

Vaccines and SARS-CoV-2 variants: the urgent need for a correlate of protection

Salim S Abdool Karim

Impact of Variants of Concern on the pandemic

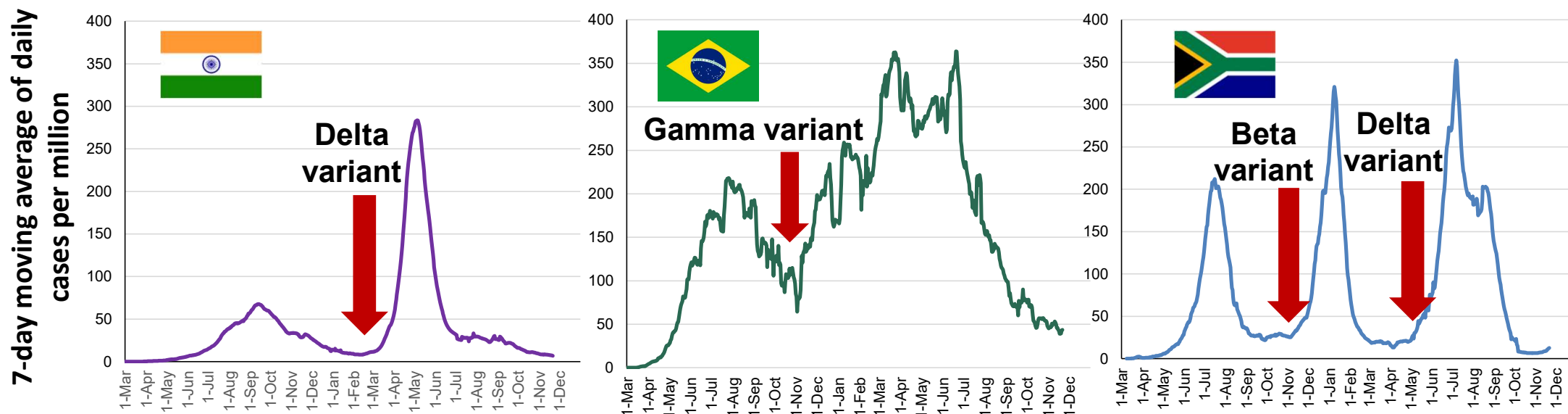
Covid-19 surges due to variants of concern in India, Brazil and SA



Source: *Our World in Data*

Impact of Variants of Concern on the pandemic

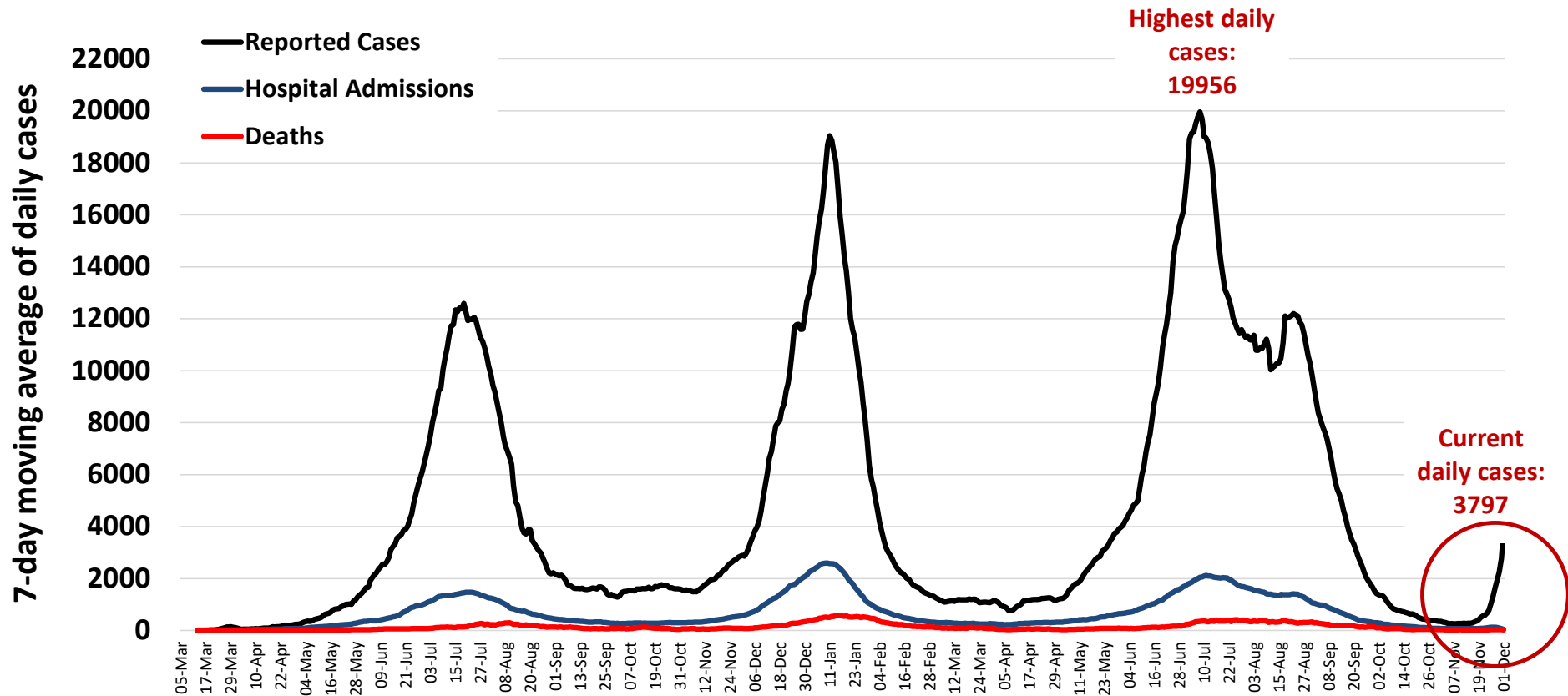
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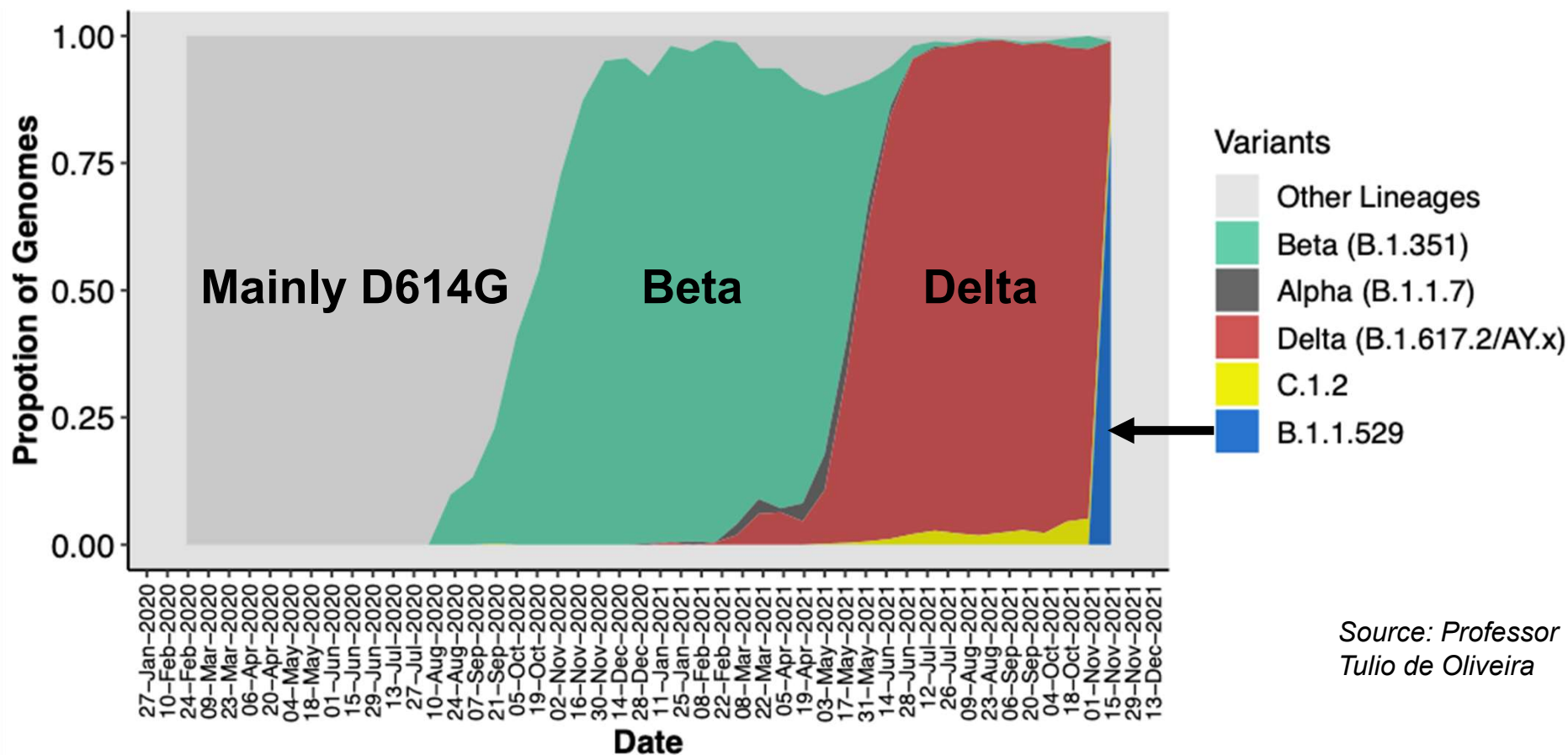
Covid-19 in South Africa

7-day moving average of new cases, hospital admissions and in-hospital Covid-19 deaths – 01 December 2021



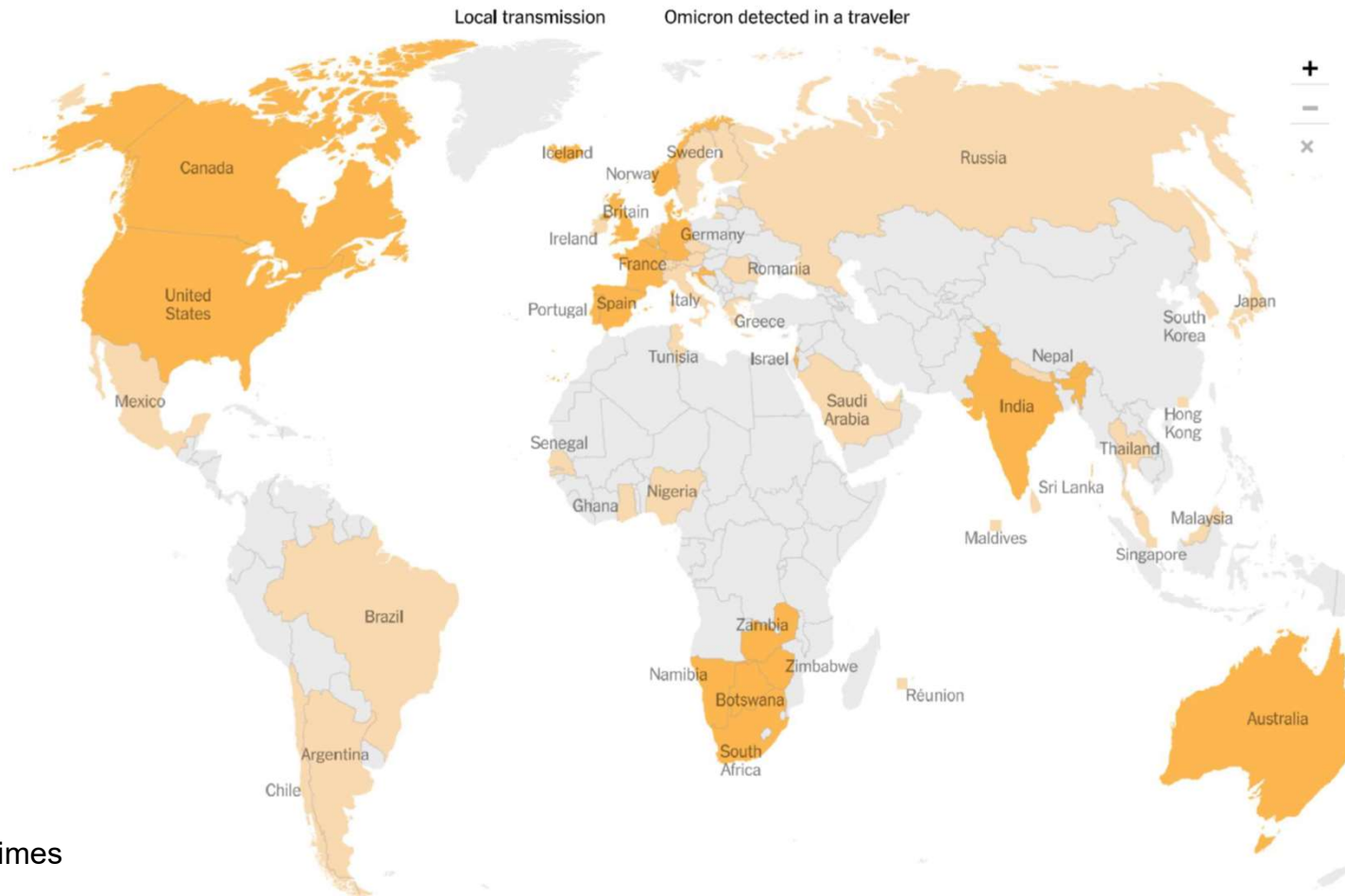
Source of hospital admissions data: Lucille Blumberg, Richard Welch and Waasila Jassat – DATCOV, NICD

Omicron is dominating South Africa's 4th wave



Source: Professor Tullio de Oliveira

Geographical distribution of Omicron – 5 Dec 2021



Source: New York Times

Geographical distribution of travel bans – Dec 2020

The **United States** announced travel restrictions from eight countries in southern Africa.

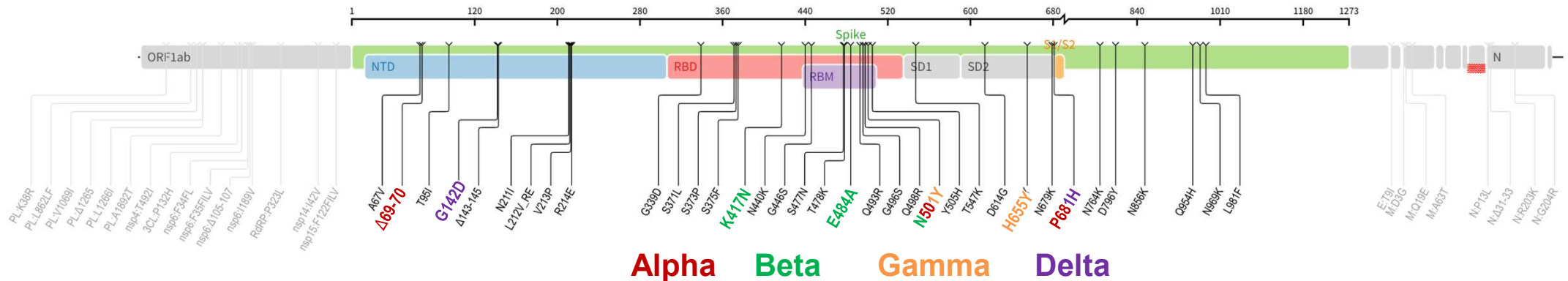


Britain announced restrictions from two additional countries. The European Union is also considering restrictions.



Source: New York Times

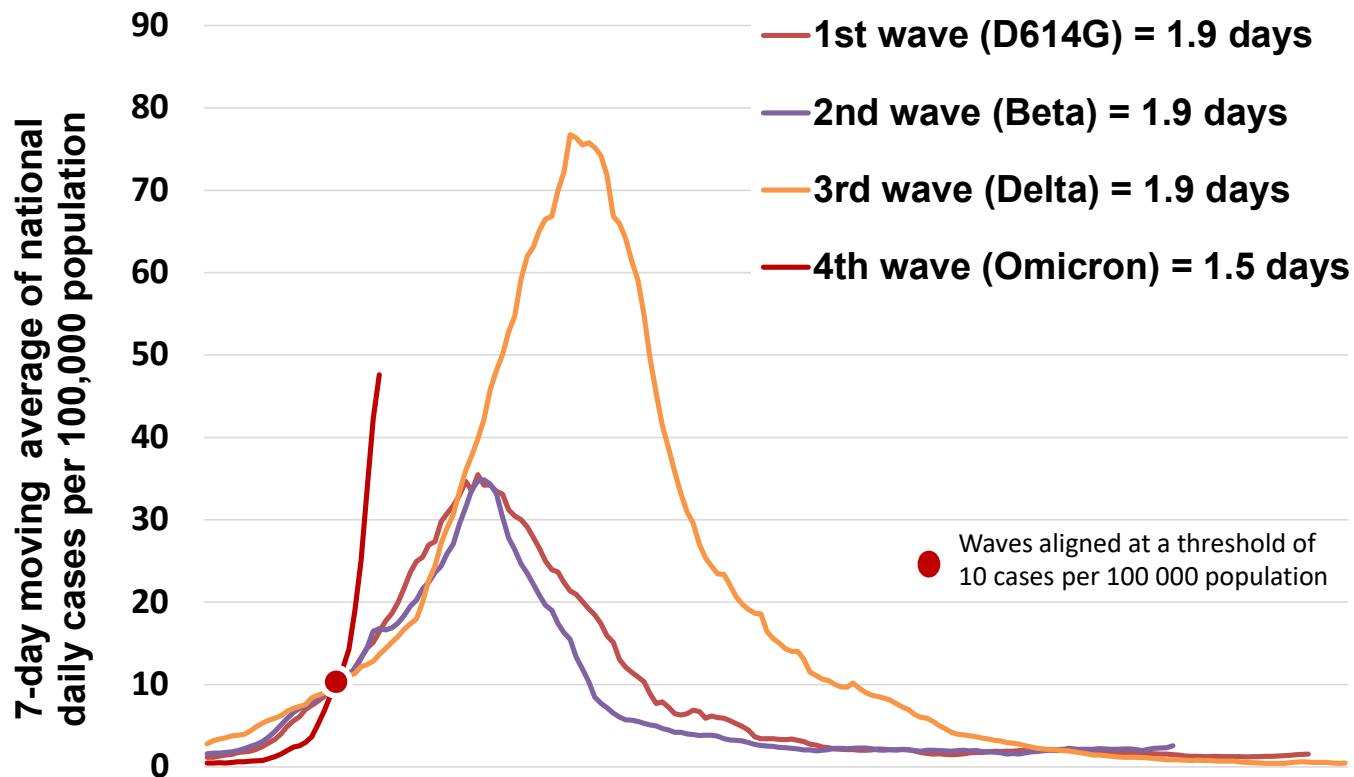
Omicron (B.1.1.529) – mutation profile



- **Overlapping mutations with Alpha, Beta, Gamma & Delta associated with:**
(Δ 69-70; T95I; G142D/ Δ 143-145; K417N; T478K; N501Y; N655Y; N679K; P681H)
 - impact one particular PCR test by S-gene target failure
 - increase transmissibility & improve binding affinity - easier for virus to attach to cells
 - enable the virus to partially escape antibodies
- **Some mutations not in other VOCs but we know some of what they do:**
A67V; Δ 211/L212I; ins214EPE; N440K; G339D; S371L; S373P; S375F; S477N; Q498R; E484A
 - help the virus to become more infectious & harder for antibodies to attach and/or kill
- **The remaining mutations are largely unknown:**
G446S; Q493K; G496S; Y505H; T547K; N764K; D796Y; N856K; Q954H; N969K; L981F

Transmissibility? – Covid-19 cases in 1st, 2nd, 3rd & 4th waves:

(7-day moving average cases per 100,000 population in Gauteng province, SA – up to 5 Dec 2021)



*doubling time for the first seven days following the wave threshold of 10 cases per 100 000 population.

Data source: Department of Health – sacoronavirus.co.za, Data analysis: Marothi Letsoalo

Clinical profile? – % with severe COVID-19 by age in Tshwane metro of Gauteng province 5 Mar 2020 – 4 Dec 2021

Age group	Total % severe* (n/N)	Nov 2021 % severe (n/N)
<20 years	28% (291/1039)	17% (24/139)
20-34 years	36% (750/2108)	13% (15/8114)
35-59 years	65% (6347/9704)	23% (35/154)
≥60 years	78% (5889/7563)	51% (45/88)
All ages	65% (13277/20414)	24% (119/495)

*Severity based on whether oxygen or assisted respiration required, ICU or death

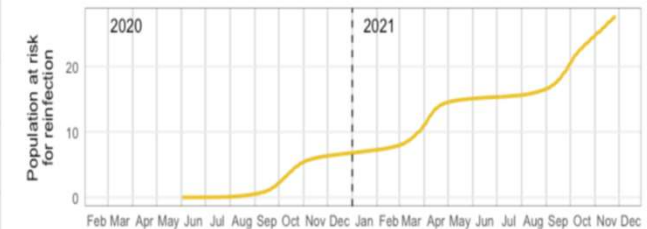
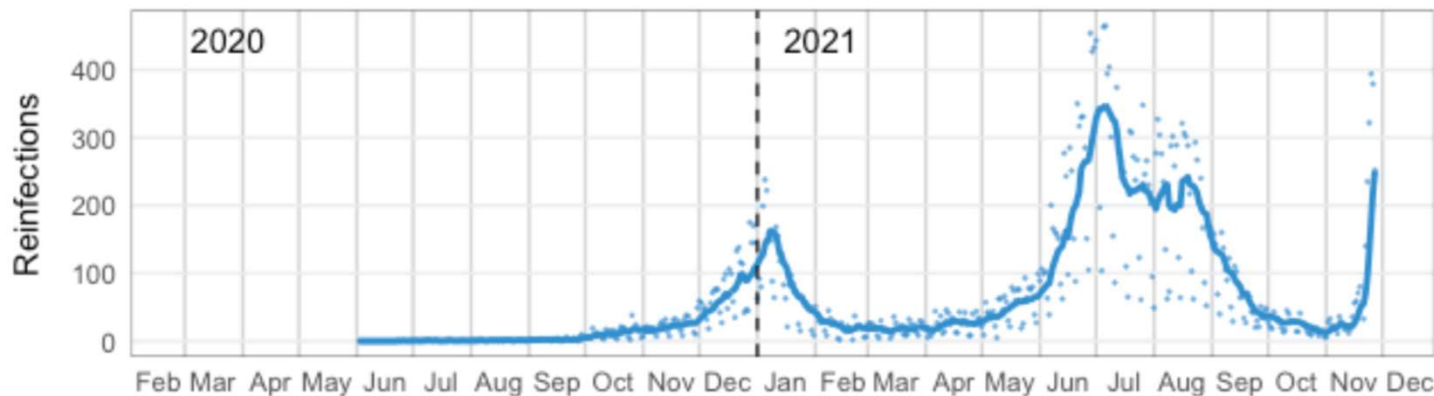
Caveat: early admissions may be biased to less severe cases & more likely to admit mild patients

Immune escape? – Reinfections rising in SA

medRxiv
THE PREPRINT SERVER FOR HEALTH SCIENCES

Increased risk of SARS-CoV-2 reinfection associated with emergence of the Omicron variant in South Africa

Juliet R.C. Pulliam^{1,*}, Cari van Schalkwyk¹, Nevashan Govender², Anne von Gottberg^{2,3}, Cheryl Cohen^{2,4}, Michelle J. Groome^{2,3}, Jonathan Dushoff^{1,5}, Koleka Mlisana^{6,7,8}, Harry Moultrie^{2,3}



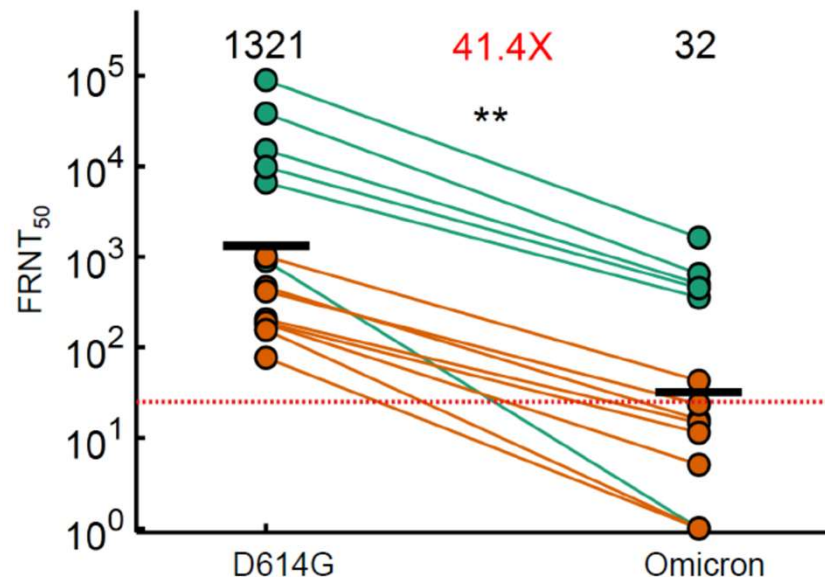
- Reinfections increasing rapidly in SA's 4th wave
- Reinfections 2.4 times higher than 1^o infection in 4th wave vs past waves

Immune escape? – Yes, Pfizer Abs ↓ neutraliation

medRxiv
THE PREPRINT SERVER FOR HEALTH SCIENCES

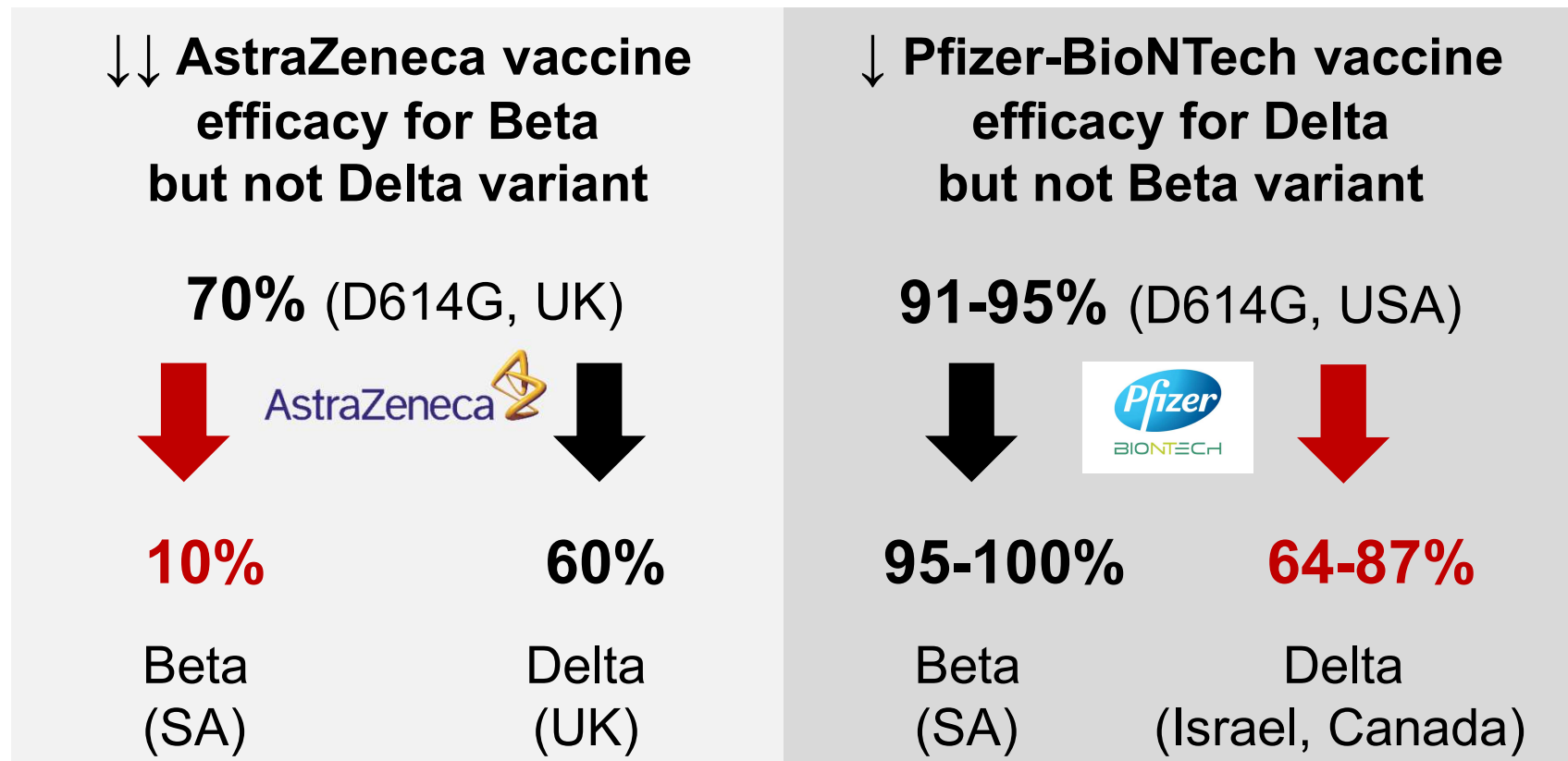
SARS-CoV-2 Omicron has extensive but incomplete escape of Pfizer BNT162b2 elicited neutralization and requires ACE2 for infection

Sandile Cele^{1,2}, Laurelle Jackson¹, Khadija Khan^{1,2}, David Khoury³, Thandeka Moyo-Gwete^{4,5}, Houriiyah Tegally^{6,7}, Cathrine Scheepers^{4,5}, Daniel Amoako⁴, Farina Karim^{1,2}, Mallory Bernstein¹, Gilai Lustig⁸, Derseree Archav⁸, Muneerah Smith⁹, Yashica Ganga¹, Zesuliwe Iule¹, Kaial Reedov¹, James



- Pfizer vaccinee sera had 41-fold lower neutralization of Omicron versus D614G
- Breakthrough infections (mostly mild) are occurring and increasing in SA's 4th wave
- Implications for clinical efficacy of vaccines for mild & severe infections unclear...

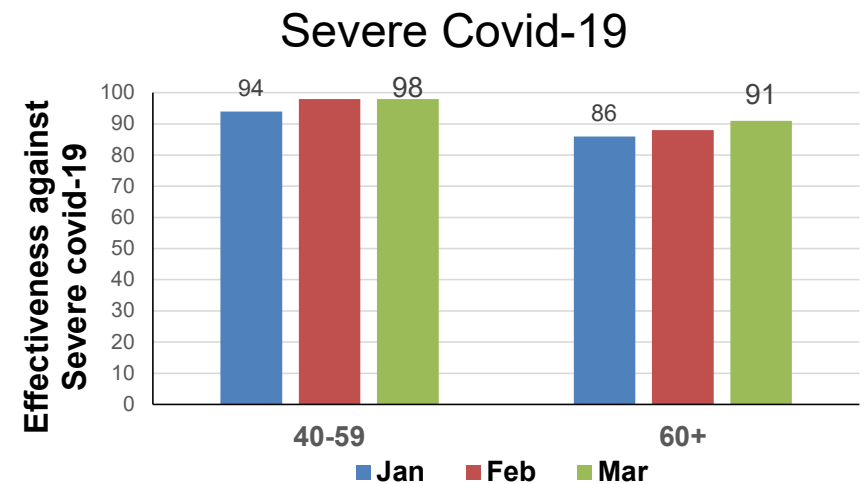
Omicron has ↑ risk of immune escape – likely to impact clinical efficacy of Covid-19 vaccines like past variants



Sources: Abdool Karim SS, et al. *NEJM*; 2021:10.1056/NEJMc2100362; Sheikh et al. *Lancet* (2021); Lopez Bernal et al. *medRxiv preprint*; Stowe et al. *PHE preprint*; Nasreen et al. *medRxiv preprint*

Vaccines remain effective over time for all past variants for severe Covid-19 / hospitalization

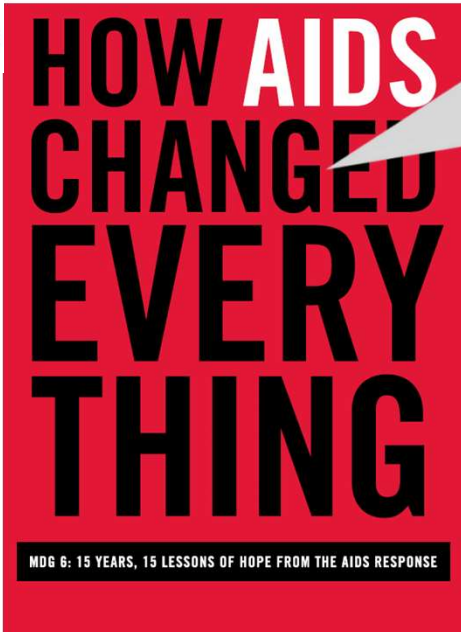
- While may see more mild infections from Omicron due to Ab escape, there is likely to be less impact on severe disease as it depends more on T-cells
- Matched test-negative, case-control study in Qatar (n=231,826):
 - VE against any severe, critical, or fatal Covid-19: **96%** (up to 6 months)
- Kaiser Permanente (n=3,436,957)
 - VE for hospital admissions (delta): **93%** (up to 6 months)
- New York State (n=8,834,604)
 - For ≥ 65 years, VE \downarrow May to August from **95%** to **89%** for Pfizer-BioNTech, from **97%** to **94%** for Moderna and from **86%** to **83%** for J&J



Earlier vaccinees (Jan-Feb) in Israel at similar risk of severe disease within their age groups

Sources: Thomas SJ et al. *NEJM* 2021; DOI: 10.1056/NEJMoa2110345; Chemaitelly, H, et al. *NEJM*. 2021; DOI: 10.1056/NEJMoa2114114; Goldberg Y, et al. *medRxiv*. Preprint: 2021:2021.08.24.21262423; Tartof SY et al. *Lancet* 2021; [https://doi.org/10.1016/S0140-6736\(21\)02183-8](https://doi.org/10.1016/S0140-6736(21)02183-8); Rosenberg ES et al *medRxiv* preprint doi: <https://doi.org/10.1101/2021.10.08.21264595>.

A key lesson from HIV for Covid-19: Importance of mutual interdependence



“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

