

DISCIPLINE OF VIROLOGY

QUARTERLY NEWSLETTER Q4 OF 2022



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MESSAGE FROM OUR HOD

In this newsletter we focus on HIV drug resistance.

According to the WHO, **28.7 million people**, out of an estimated 38.4 million people living with HIV were receiving antiretrovirals globally at the end of 2021.

The relatively successful global rollout of antiretrovirals has led to the emergence of HIV drug resistance, which is steadily increasing.

Genetic mutations can confer survival advantages to viruses when faced with replication-blocking drugs. Every class of antiretroviral therapy (ART) is at risk of partial or full inactivity against HIV. Our greatest tool in the fight against this is to prevent it by proper adherence to prescribed antiretrovirals.

Where prevention has failed, and high levels of drug resistance are in circulation, changes such as the expansive introduction of dolutegravir have been required.

The WHO recommends surveillance to monitor the quality of ART and to minimize the emergence and spread of HIV drug resistance. Diagnostic virology laboratories have had to adapt their tests accordingly.

At our department, we have successfully expanded the HIV drug resistance test to include the integrase region. We have also successfully migrated from an in-house method to a commercial method of testing. Further plans in the pipeline include the fine-tuning our method of



NEWSLETTER

This issue of the newsletter was edited by Dr Kerusha Govender. Please email questions or comments to: govenderk7@ukzn.ac.za

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MESSAGE FROM OUR HOD

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surveying dried blood spot specimens and, excitingly, the introduction of next-generation sequencing which has a higher sensitivity for low-abundance variants – read more about this on page 8.

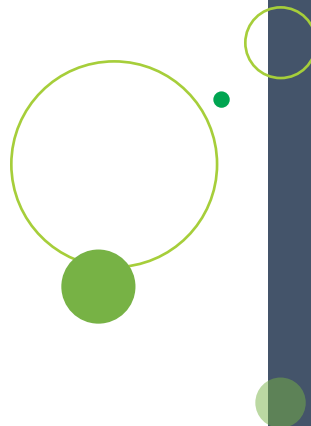
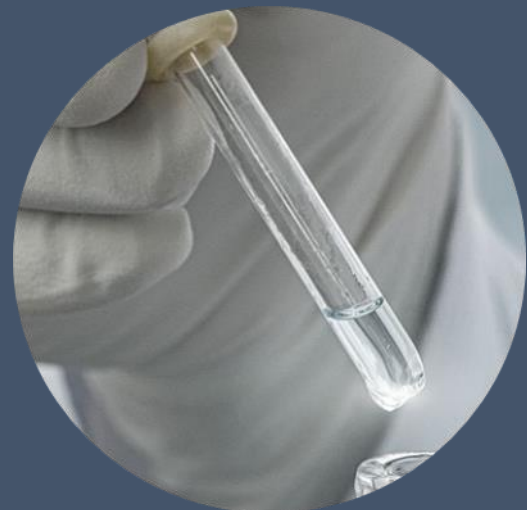
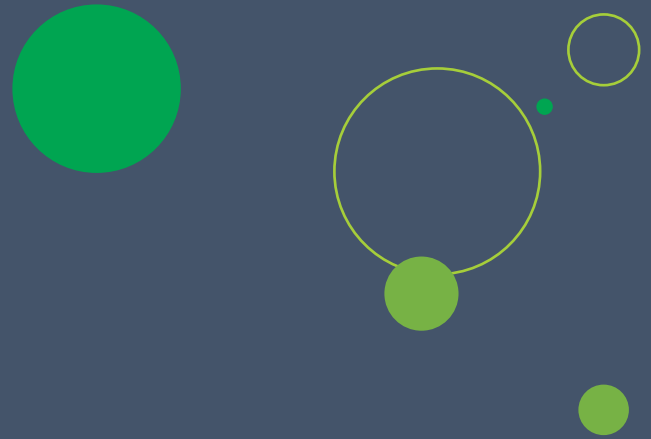
The virology diagnostic laboratory remains a key stakeholder in the battle against HIV drug resistance, and we are privileged to play our part in the global response.

Until next time.

Dr Khanyi Msomi

Key references & resources

1. HIV drug resistance strategy, 2021 update. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO.
2. WHO HIVResNet HIV drug resistance laboratory operational framework, second edition. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO.
3. <https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hiv/treatment/hiv-drug-resistance>



FOCUS ON HIV DRUG RESISTANCE

*This section is a preliminary report done by clinical virologist, Dr Lilishia Gounder in fulfillment of a **CAPRISA & EDCTP-funded** career development fellowship project.*

HIV drug resistance is caused by changes in the genetic structure of HIV that affect the ability of drugs to block the replication of the virus.

Monitoring trends of HIV-1 drug resistance in KwaZulu-Natal amid dolutegravir rollout in South Africa

We aimed to describe preliminary study findings on HIV-1 drug resistance (HIVDR) amid dolutegravir (DTG) rollout in KwaZulu-Natal (KZN) province, South Africa. The project objectives were:

1. To develop a database for monitoring HIVDR using routine HIV genotypic testing data of ART-experienced patients with virological failure (i.e., VLs $\geq 1,000$ copies/mL) receiving HIV-care at public-sector facilities in KZN
2. To determine HIVDR hotspots and populations requiring priority interventions in HIV treatment care

We developed an **HIV drug resistance database** and conducted analysis of routine HIVDR genotypic results obtained from specimens collected in public-sector healthcare facilities across **11 districts in KZN**. We obtained and curated 2148 de-identified HIVDR genotypic results with linked data (collection date, age, sex, healthcare facility) processed at the National Health Laboratory Service (NHLS) Department of Virology, UKZN, Inkosi Albert Luthuli Central Hospital, for the period January 2018 to August 2020. Permission to access de-identified data was granted by the National Health Laboratory Service (NHLS) Central Data Warehouse (CDW).

Of 2148 patient genotypes obtained from 151 KZN facilities, 1846 (**85.9%**) had ≥ 1 HIVDR mutation, with only 5 (**0.2%**) having **INSTI-associated resistance**. Genotypes with drug resistance (n=1846) were categorized according to age and sex. The proportion of HIVDR mutations was significantly **higher among adult females** aged ≥ 20 years, $p=0.04$.

FOCUS ON HIV DRUG RESISTANCE

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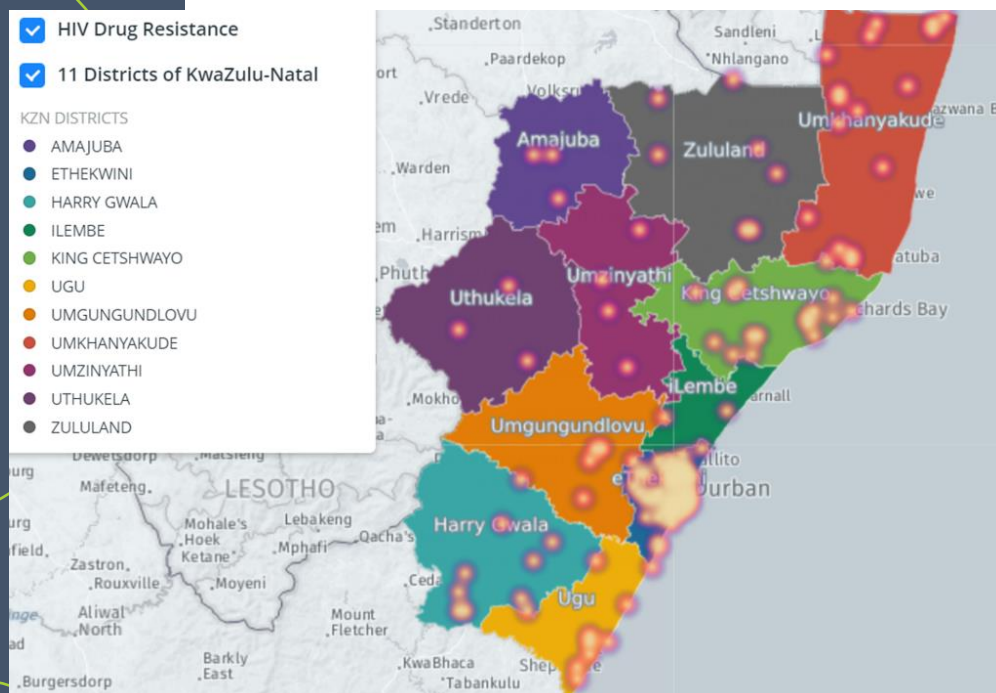


Figure 1 Heatmap of genotypes with HIV drug resistance across KwaZulu-Natal

Approximately six in every seven genotypes had HIVDR mutations with minimal DTG-associated resistance, supporting use of DTG-based ART. The most common NNRTI mutation was K103N observed in 45% (838/1846) of genotypes with HIVDR, despite most patients (94%) being on PI-based ART. The most common major PI mutation was V82A observed in 27% (495/1846), and K65R NRTI mutation was observed in 5% (99/1846) of genotypes with HIVDR.

The largest proportion of genotype requests with HIVDR were from densely populated urban and peri-urban districts as shown in **Figure 1**. However, despite the lower number of genotype requests from rural district facilities, there were higher levels of HIVDR detected. This highlights the **need to strengthen HIV treatment monitoring and timely switching of suboptimal regimens in rural districts**. Findings from the ADRess study comparing HIV treatment outcomes between peri-urban and rural clinics in KZN, indicated that virological failure and drug resistance did not differ between

sites, however viral suppression was noted earlier in peri-urban sites, which likely reflected greater attention to monitoring patients on ART [Brijkumar J. et al., HIV Medicine, 2022].

In summary, using our database, we were able to identify facilities with high proportions of HIVDR, which is relevant to clinicians and policymakers. By incorporating **geospatial analyses** into our dashboard, we identified proportions of HIVDR in urban, peri-urban and rural districts. Moreover, we observed **higher proportions of HIVDR among adult women**, highlighting individuals needing priority HIV care. Ultimately, as DTG-use becomes more common, a trend towards decreased HIVDR prevalence is expected. However, near-real time HIVDR monitoring is required for optimization of HIV-1 treatment at public-health level, and for sustainable DTG use in first-line and subsequent ART regimens.

UPDATE ON HIV DRUG RESISTANCE

As an update to the presentation above, Dr Gounder has presented more recent data on the trends of HIV drug resistance (Figure 2). Note the trend of PI and INSTI resistance in 2021.

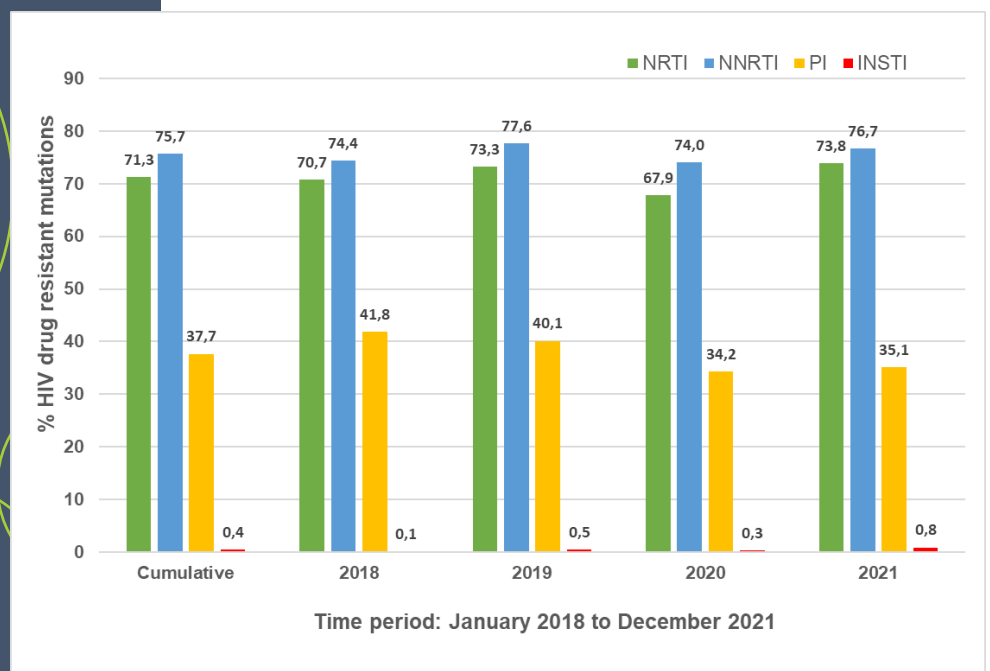


Figure 2 Genotypes with HIV drug resistance according to drug class and year

NEWS

1. New appointments

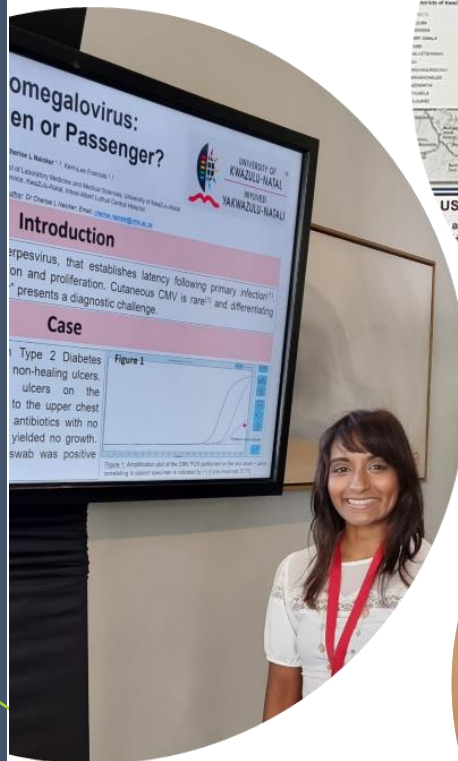
Mr Lunga Xaba has been appointed to our Research Laboratory, and has focused his efforts on the cell culture section. In the picture on the right, Mr Xaba is with Drs Moodley, Msomi and Govender, as well as Ms Rachel Kinloch, a representative from the Angel Network. They have supported his further career aspirations in Clinical Virology.

2. Events

Dr Lilishia Gounder attended and presented at the **Association of Medical Councils of Africa (AMCOA) International Conference**, hosted by the Health Professions Council of South Africa (HPCSA) and held at Sun City Resort in October 2022. She presented her dashboard showing trends of HIV-1 drug resistance in KwaZulu-Natal. Dr Gounder is pictured here at the conference, with her poster.

Our department had substantial presence at the **9th FIDSSA Congress** which was held in Durban in November this year. Pictured to the right is senior registrar, Dr Cherise Naicker presenting a case report on cytomegalovirus. Dr Lili Gounder presented on behalf of Dr Kerri-Lee Francois, an oral presentation about HIV-1 drug resistance among female sex workers in KwaZulu-Natal, South Africa. Drs Moodley and Msomi, pictured on the far right gave invited talks on Measles and SARS-CoV-2 respectively.

Dr Kerusha Govender gave an oral presentation on behalf of Dr Msomi at the **KZN Department of Health Research Day**, held on 7 December 2022. The presentation was entitled "Persistent Hepatitis B Viraemia with Polymerase Mutations among HIV/HBV Co-Infected Patients on HBV-Active ART in KZN, South Africa".



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Clinical Virologist, Dr Kerri-Lee Francois presented at the 9th Conference of the South African Immunology Society in October 2022, with a poster entitled "Seroprevalence of SARS-COV-2 IgG in HIV-Infected and Uninfected Individuals in Kwazulu-Natal Province, November 2020 - March 2021".

Mr Sontaga Manyana and Ms Lulama Mthethwa, pictured on the right, gave presentations at the **UKZN School of Laboratory Medicine and Medical Sciences Research Symposium** held in November 2022. The titles of their presentations were, respectively:

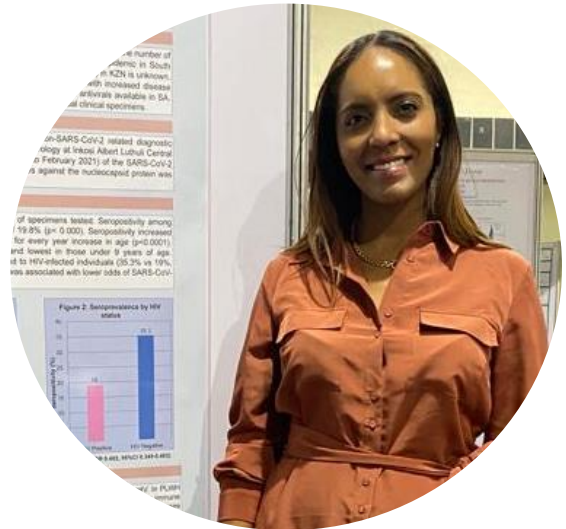
- Innovative and Affordable HIV-1 Drug Resistance Testing for Resource Limited Settings
- MicroRNA profiling in patients co-infected with chronic hepatitis B virus (CHBV) and human immunodeficiency virus (HIV) in a high prevalence setting

3. Department Plans

The department is setting up a next generation sequencing platform for HIV Drug Resistance. This is part of a national plan, in collaboration with the NHLS National Priority Programme (NPP) and the Global Fund. The WHO has identified several potential advantages, and has outlined a slow transition to this technology, to allow for adaptation of quality control procedures and interpretation of data. It is envisioned that this platform will further strengthen our research capacity across all focus areas in our department.

4. Achievements

Mr Sontaga Manyana and Dr Kerusha Govender graduated at the UKZN spring graduation ceremony in September 2022.



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Our department has once again maintained **SANAS accreditation**, and all the labs to which we provide **outreach** support have maintained accreditation for their NPP tests.

Pictured on the right are some of our laboratory staff enjoying a well-deserved end-of-year **Christmas dinner** to celebrate the close of 2022.

5. Training

Mr Melen Pillay is currently away at Prof Jon Li's Harvard/Brigham Virology Specialty Laboratory. Mr Pillay will be enhancing his sequencing skills, learning the Illumina and PacBio platforms and gene linkage analysis.



RESEARCH

NEW RESEARCH GRANTS

Dr Joedene Chetty was awarded an NHLS K-funding grant for her MMed Research project entitled "The prevalence of cytomegalovirus infection in HIV-exposed infants in Kwa-Zulu Natal, South Africa".

NEW COLLABORATIONS

Dr Kerri-Lee Francois is collaborating with the Siyaphambili study team, who are based mainly at TB HIV Care and Johns Hopkins Bloomberg School of Public Health. She will be studying HIV-1 drug resistance among female sex workers in KwaZulu-Natal, South Africa

RESEARCH

RECENT PUBLICATIONS

1. Bateman, M.; Wolf, A.; **Chimukangara, B.**; Brust, J.C.M.; Lessells, R.; Amico, R.; Boodhram, R.; Singh, N.; Orrell, C.; Friedland, G.; et al. Adherence Measured Using Electronic Dose Monitoring is Associated with Emergent Antiretroviral Resistance and Poor Outcomes in People with Human Immunodeficiency Virus/AIDS and Multidrug-Resistant Tuberculosis. *Clin Infect Dis* 2022, 75, 1489-1496, doi:10.1093/cid/ciac232.
2. Chen, J.; Hui, Q.; Liu, C.; Brijkumar, J.; Edwards, J.A.; Ordonez, C.E.; Dudgeon, M.R.; Sunpath, H.; Pillay, S.; **Moodley, P.** Associations of inflammation-related proteome with demographic and clinical characteristics of people with HIV in South Africa. *medRxiv* 2022.
3. **Chimukangara, B.**; Lessells, R.J.; Sartorius, B.; **Gounder, L.**; **Manyana, S.**; **Pillay, M.**; Singh, L.; Giandhari, J.; **Govender, K.**; Samuel, R.; et al. HIV-1 drug resistance in adults and adolescents on protease inhibitor-based antiretroviral therapy in KwaZulu-Natal Province, South Africa. *J Glob Antimicrob Resist* 2022, 29, 468-475, doi:10.1016/j.jgar.2021.10.023.

RESEARCH

RECENT PUBLICATIONS

continued

4. Reynolds, Z.; McCluskey, S.M.; Moosa, M.Y.S.; Gilbert, R.F.; Pillay, S.; Aturinda, I.; Ard, K.L.; Muyindike, W.; Musinguzi, N.; Masette, G.; **Moodley P.**; Siedner M. Who's slipping through the cracks? A comprehensive individual, clinical and health system characterization of people with virological failure on first - line HIV treatment in Uganda and South Africa. *HIV medicine* 2022, 23, 474-484

5. Scheepers, C.; Everatt, J.; Amoako, D.G.; Tegally, H.; Wibmer, C.K.; Mnguni, A.; Ismail, A.; Mahlangu, B.; Lambson, B.E.; Martin, D.P.; **Msomi, N.** et al. Emergence and phenotypic characterization of the global SARS-CoV-2 C.1.2 lineage. *Nat Commun* 2022, 13, 1976, doi:10.1038/s41467-022-29579-9.

6. Subramoney, K.; Mtileni, N.; Bharuthram, A.; Davis, A.; Kalenga, B.; Rikhotso, M.; Maphahlele, M.; Giandhari, J.; Naidoo, Y.; Pillay, S.; **Network for Genomics Surveillance in South Africa**; et al. Identification of SARS-CoV-2 Omicron variant using spike gene target failure and genotyping assays, Gauteng, South Africa, 2021. *J Med Virol* 2022, 94, 3676-3684, doi:10.1002/jmv.27797.

7. Valley-Omar, Z.; Marais, G.; Iranzadeh, A.; Naidoo, M.; Korsman, S.; Maponga, T.; Hussey, H.; Davies, M.A.; Boule, A.; Doolabh, D.; **Msomi, N.** et al. Reduced amplification efficiency of the RNA-dependent-RNA-polymerase target enables tracking of the Delta SARS-CoV-2 variant using routine diagnostic tests. *J Virol Methods* 2022, 302, 114471, doi:10.1016/j.jviromet.2022.114471.

8. Viana, R.; Moyo, S.; Amoako, D.G.; Tegally, H.; Scheepers, C.; Althaus, C.L.; Anyaneji, U.J.; Bester, P.A.; Boni, M.F.; Chand, M.; **Msomi, N.** et al. Rapid epidemic expansion of the SARS-CoV-2 Omicron variant in southern Africa. *Nature* 2022, 603, 679-686, doi:10.1038/s41586-022-04411-y.

9. Wolter, N.; Jassat, W.; Walaza, S.; Welch, R.; Moultrie, H.; Groome, M.; Amoako, D.G.; Everatt, J.; Bhiman, J.N.; Scheepers, C.; **Parboosing R** et al. Early assessment of the clinical severity of the SARS-CoV-2 omicron variant in South Africa: a data linkage study. *Lancet* 2022, 399, 437-446, doi:10.1016/S0140-6736(22)00017-4.

10. Wolter, N.; Jassat, W.; Walaza, S.; Welch, R.; Moultrie, H.; Groome, M.J.; Amoako, D.G.; Everatt, J.; Bhiman, J.N.; Scheepers, C.; **Parboosing, R.** et al. Clinical severity of SARS-CoV-2 Omicron BA.4 and BA.5 lineages compared to BA.1 and Delta in South Africa. *Nat Commun* 2022, 13, 5860, doi:10.1038/s41467-022-33614-0.