Insights from geospatial analysis of detectable HIV-1 viral loads and drug resistance amid dolutegravir rollout in KwaZulu-Natal, South Africa

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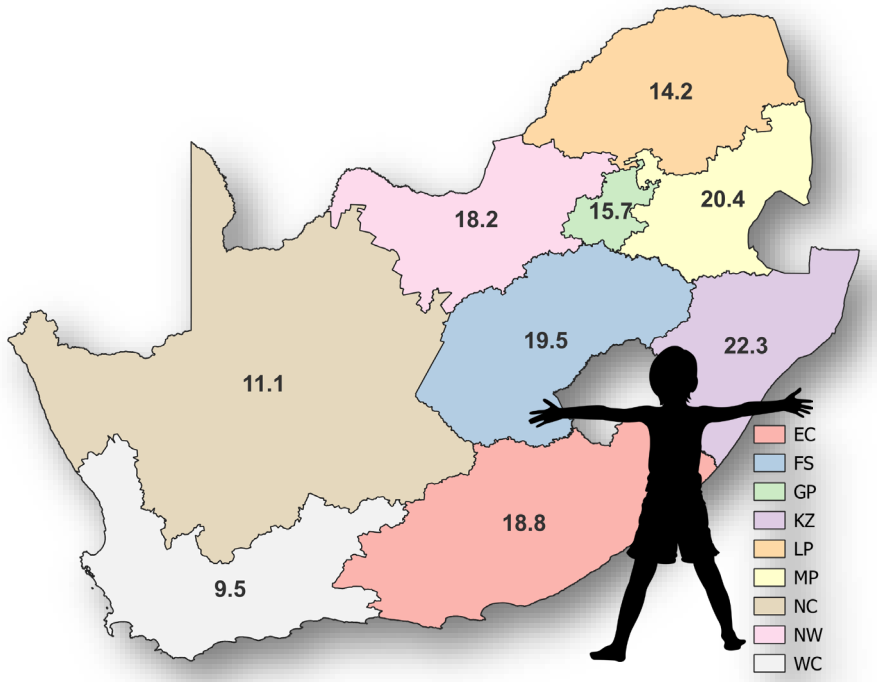
Outline

- Background and Research Problem
- Research Aims and Objectives
- Methods
- Results
- Key Messages

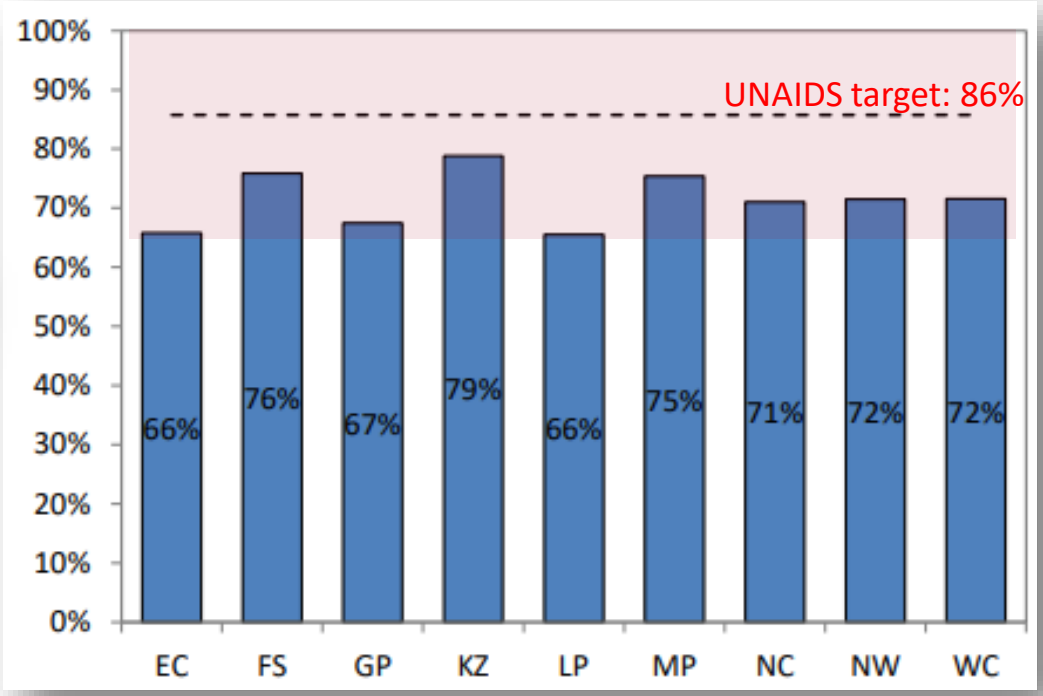
Photo by Lilishia Gounder on Unsplash

Background and Research Problem

- In 2024, 20% of all people living with HIV (PLWH) were in South Africa.
- Detectable viraemia ↑ risk of HIV drug resistance (HIVDR).
- Real-time geospatial monitoring of HIVDR is limited in our setting.



SA HIV prevalence: 2024



% of PLWH on ART and virally suppressed in 2024 per province in South Africa

Source: Modelling the impact of HIV in South Africa's provinces: 2025 update; Centre for Integrated Data and Epidemiological Research working paper - March 2025; Leigh F. Johnson, Cari van Schalkwyk, Rob E. Dorrington

Research aims and objectives

- Describe spatiotemporal changes in HIV viral loads (VLs) and HIVDR in KwaZulu-Natal (KZN), the epicentre of the HIV epidemic in South Africa, amid transition to dolutegravir-based regimens.
- Use geospatial analysis to advise on use of health resources for targeted HIV prevention and treatment.

Source: Kiepiela P, Manasa J, Moosa MY, et al. HIV drug resistance patterns at the epicentre of the HIV-1 epidemic in Kwazulu-Natal, South Africa 2003-2013. *J AIDS Clin Res*. 2014;5(5):299

Methods

- VL and HIVDR data was obtained from National Health Laboratory Service Central Data Warehouse, for the period January 2018 - June 2022, for all adult PLWH attending public-sector healthcare facilities in KZN who had VLs and genotypic resistance tests (GRTs) done.

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BREC approved

NATIONAL HEALTH LABORATORY SERVICE

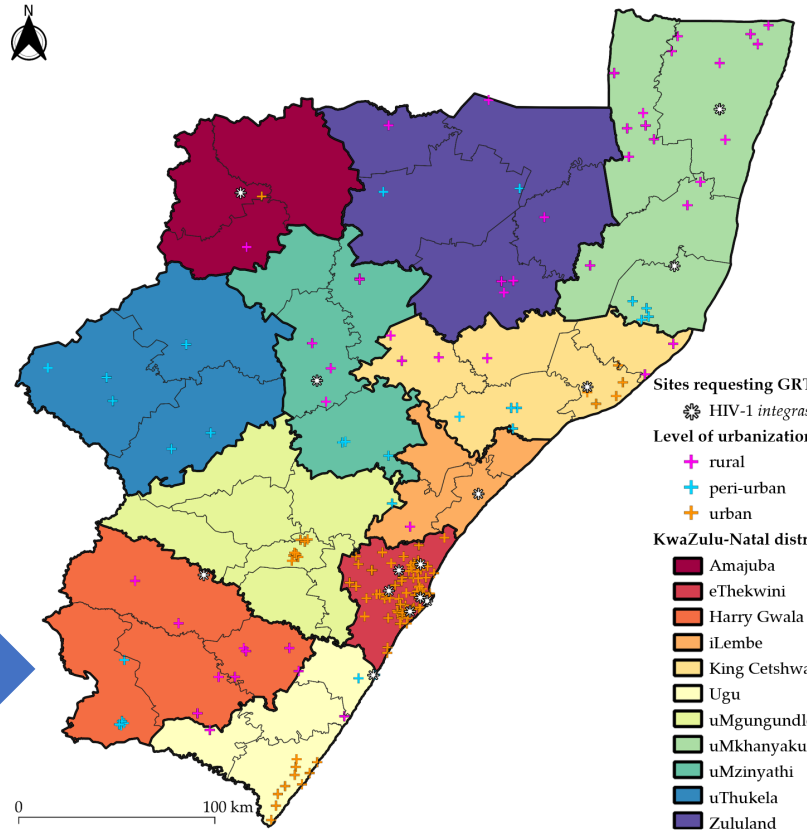
Data acquired from Central Data Warehouse

Power BI

QGIS

STATA

Database curation, data analysis & geospatial mapping



Data storage at Department of Virology

VL: Results

Unique HIV VL records obtained from NHLS CDW (n = 7 646 683)

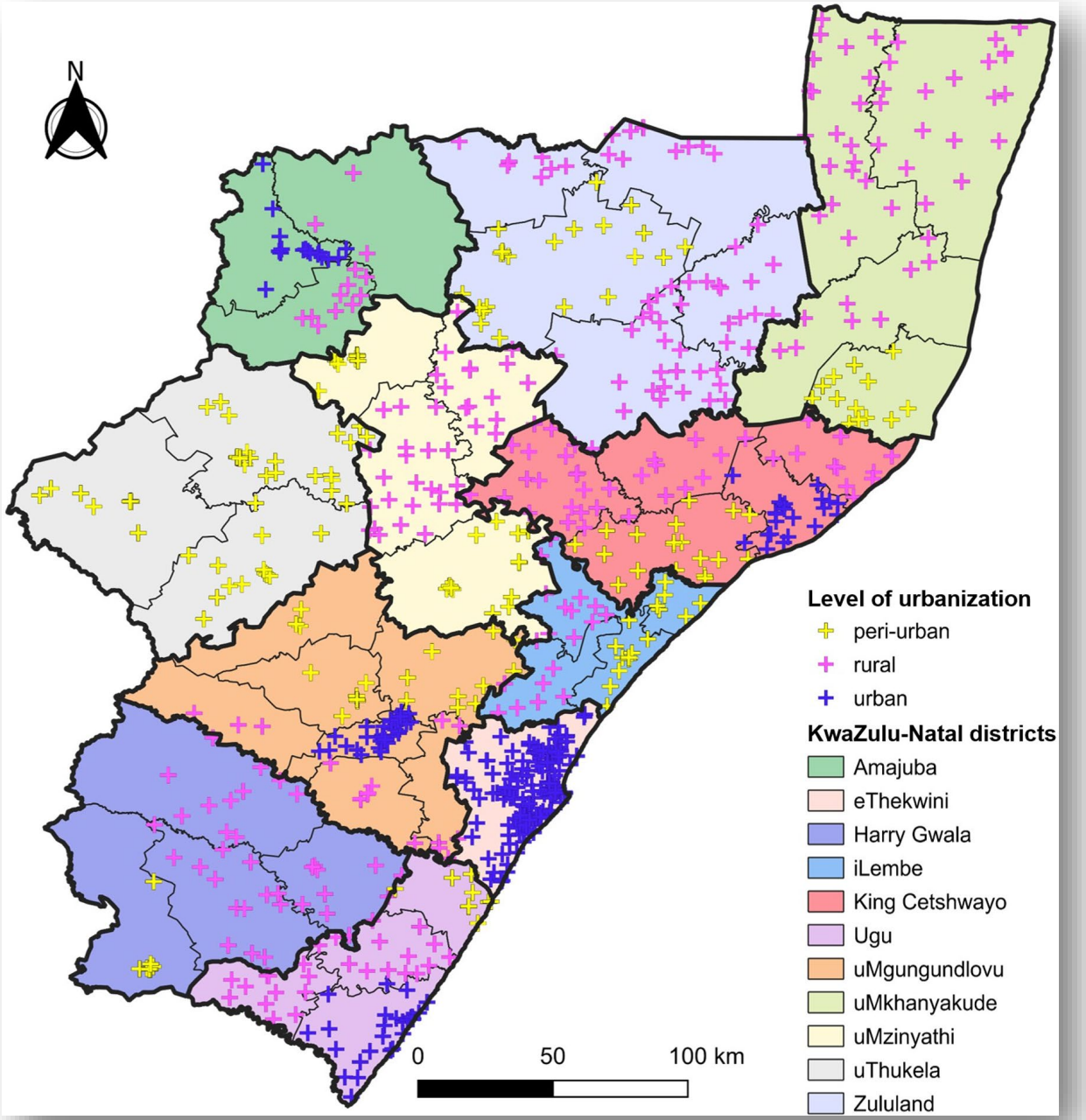
HIV VL records from outside KZN (n = 6 705)

HIV VL records from KZN (n = 7 639 978)

HIV VL records included in final analysis (n = 7 639 978)
HIV VLs <400 copies/mL (6 608 807)
HIV VLs 400 - 999 copies/mL (198 296)
HIV VLs ≥1 000 copies/mL (832 875)

Flow diagram of HIV VL records obtained and included in final analysis.

CDW, central data warehouse; HIV VL, HIV viral load; KZN, KwaZulu-Natal; mL, millilitre; NHLS, National Health Laboratory Service.



VL: Results

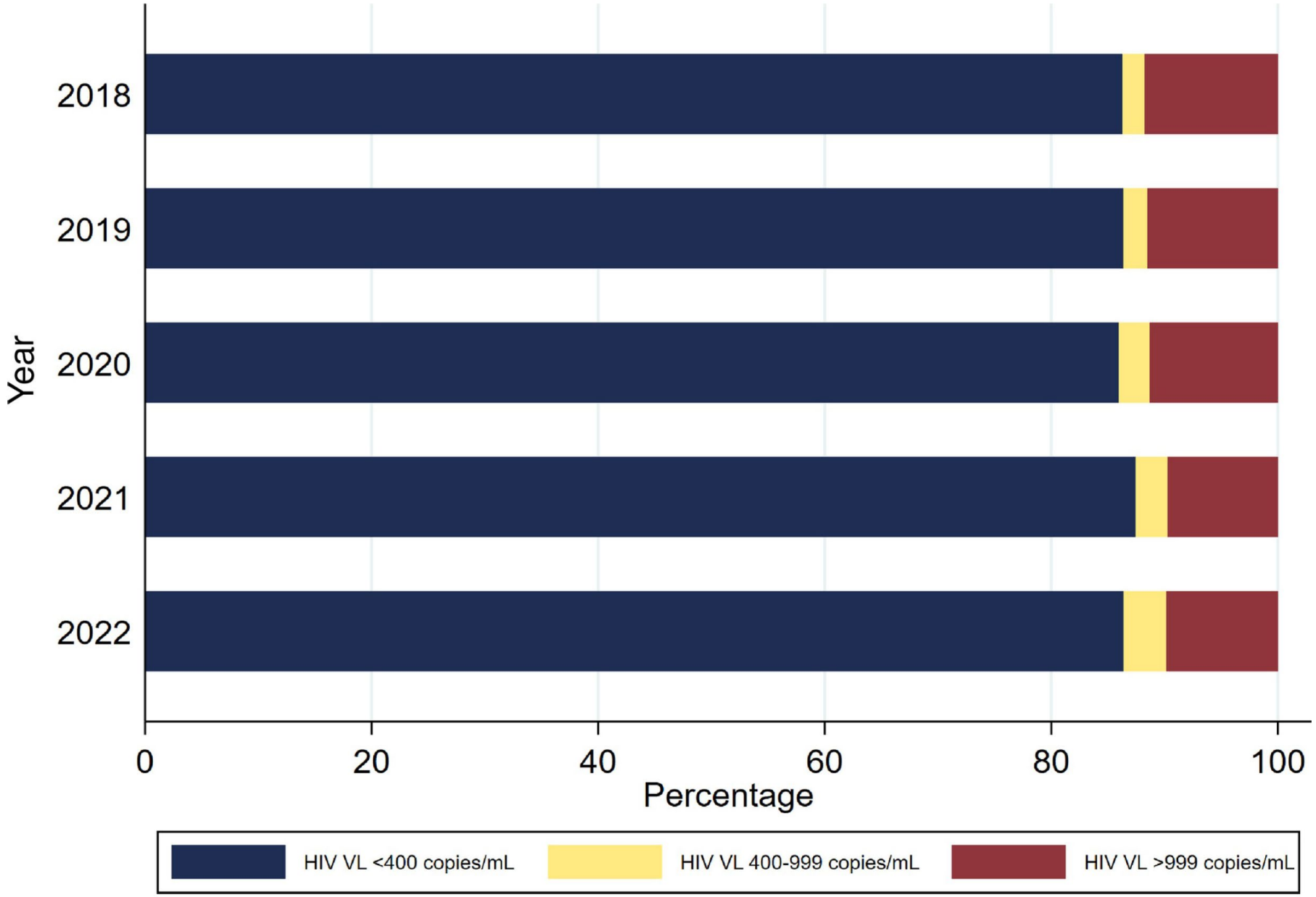
HIVVLs: 86.5% <400 c/mL; 2.6% 400-999 c/mL; 10.9% ≥1000 c/mL

Patient characteristics

	All n=7 639 978 (%)	VL <400 c/mL n=6 608 807 (%)	VL 400-999 c/mL n=198 296 (%)	VL ≥1000 c/mL n=832 875 (%)
Characteristics				
Female[a]	5 209 487 (68)	4 579 540 (88)	128 476 (2)	501 471 (10)
Male[a]	2 204 485 (29)	1 834 681 (83)	63 996 (3)	305 808 (14)
Median age[b] (IQR)	37 (29-45)	37 (30-46)	36 (27-44)	33 (24-41)
<5	37 833 (0.5)	21 262 (56.2)	2057 (5.4)	14 514 (38.4)
5-14	222 266 (2.9)	146 383 (65.9)	12 055 (5.4)	63 828 (28.7)
15-24	710 242 (9.3)	539 469 (75.9)	25 468 (3.6)	145 305 (20.5)
25-49	5 404 631 (70.7)	4 750 906 (87.9)	129 445 (2.4)	524 280 (9.7)
>50	1 210 106 (15.8)	1 105 594 (91.4)	27 686 (2.3)	76 826 (6.3)
Outpatients[c]	7 273 492 (95.2)	6 336 424 (87.1)	186 822 (2.6)	750 246 (10.3)
Inpatients[c]	333 743 (4.4)	242 672 (72.7)	10 949 (3.3)	80 122 (24)
Rural[d]	1 943 486 (25)	1 674 192 (86.1)	49 834 (2.6)	219 460 (11.3)
Peri-urban[d]	1 755 258 (23)	1 499 314 (85.4)	53 172 (3)	202 772 (11.6)
Urban[d]	3 941 234 (52)	3 435 301 (87.2)	95 290 (2.4)	410 643 (10.4)

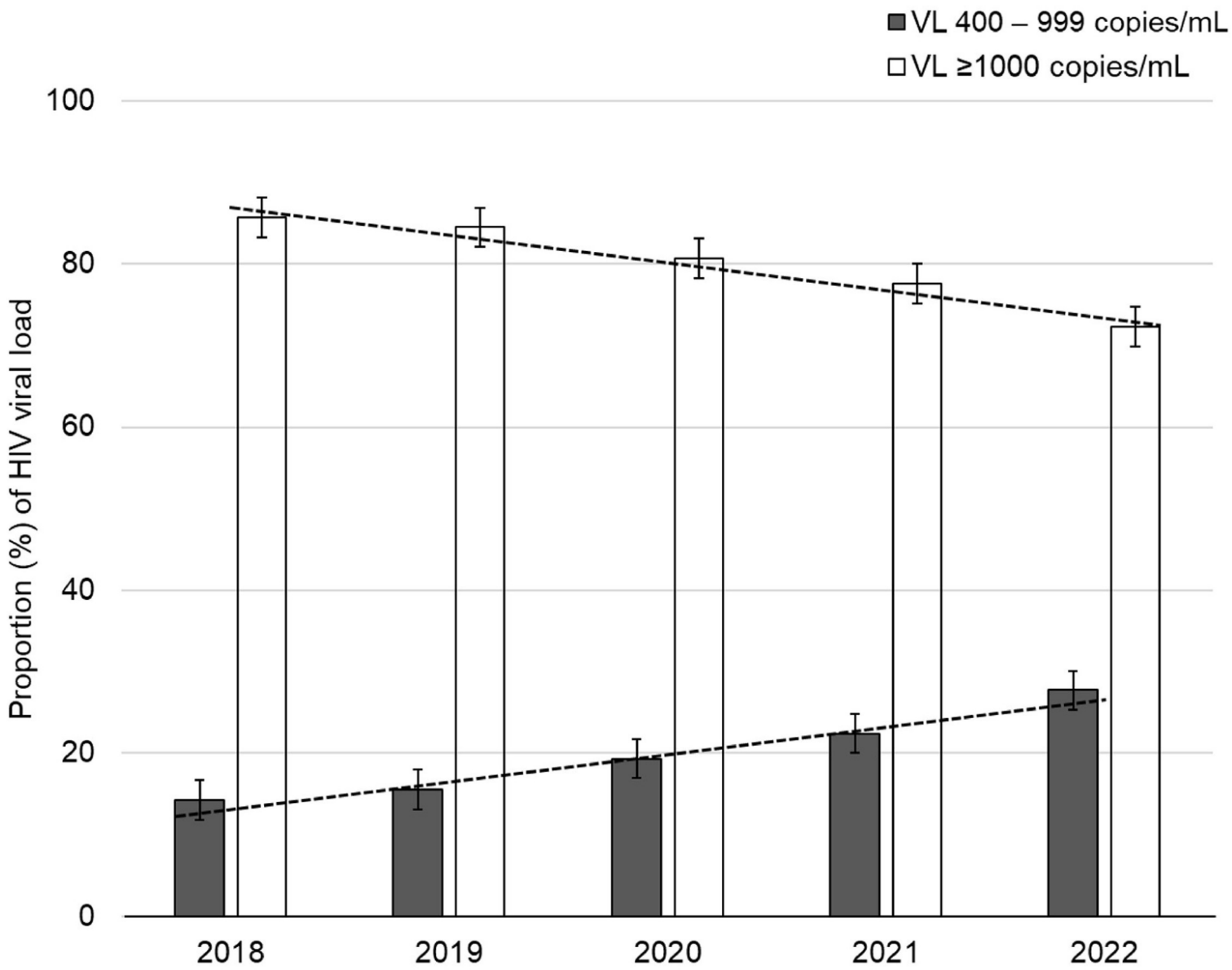
c/mL copies per millilitre, IQR interquartile range, VL viral load; [a] 226 006 (3%) missing data for sex, [b] 54 900 (0.7%) missing data for age, [c] 32 743 (0.4%) were institutionalized, [d] level of urbanization obtained from annual reports and integrated development plans for individual subdistricts

VL: Results



Proportion of all HIV viral loads by year in KwaZulu-Natal province, South Africa

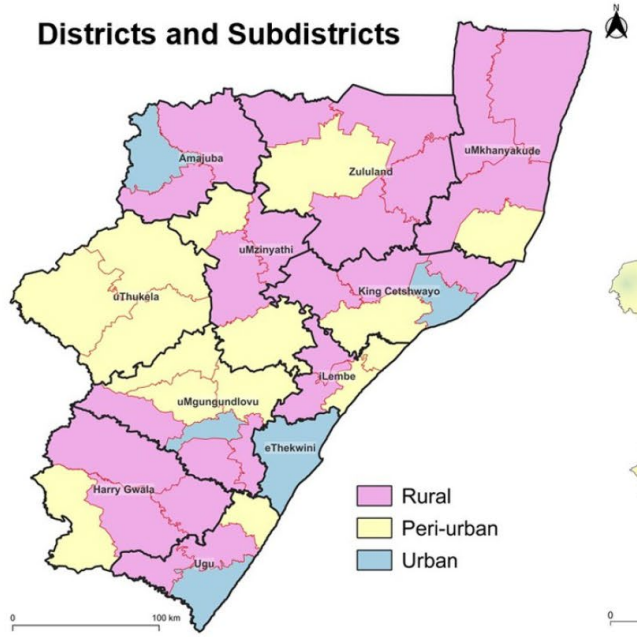
VL: Results

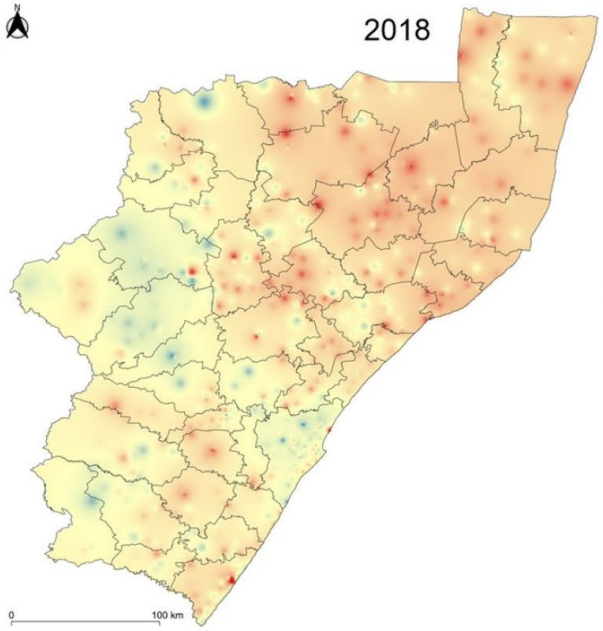


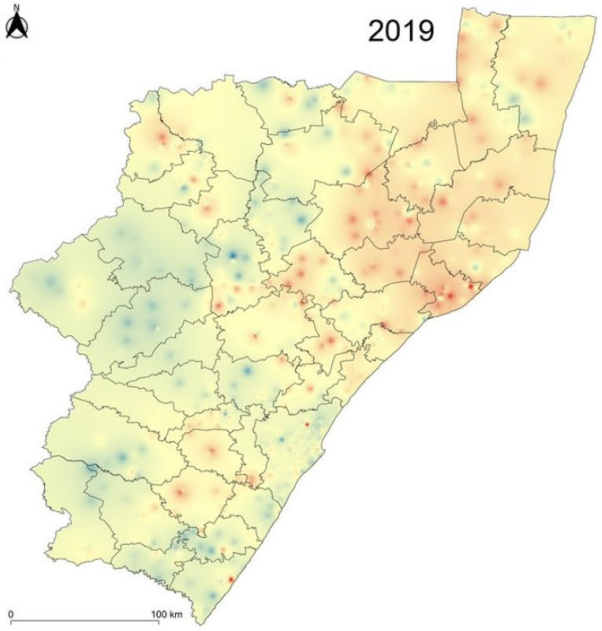
Trend analysis of detectable HIV viral loads by year in KwaZulu-Natal province, South Africa

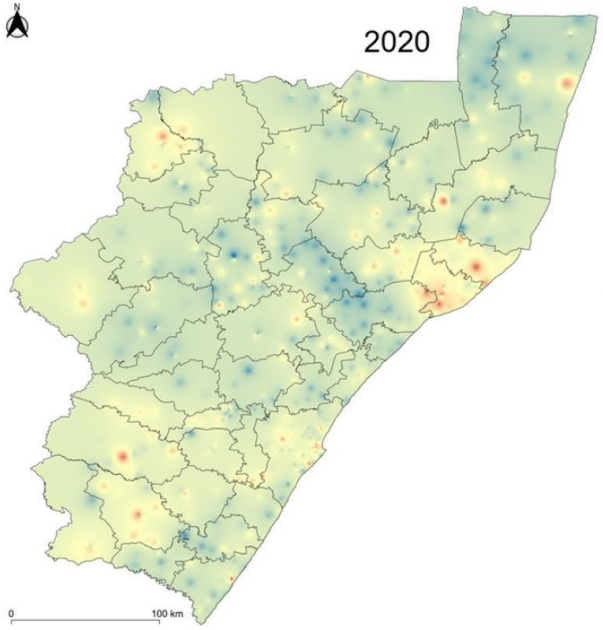
median log10 VLs ↓ from 4.093 $\log_{10}$ copies/mL (CI 4.087–4.100) in 2018 to 3.563 $\log_{10}$ copies/mL (CI 3.553–3.572) in 2022, $p<0.01$

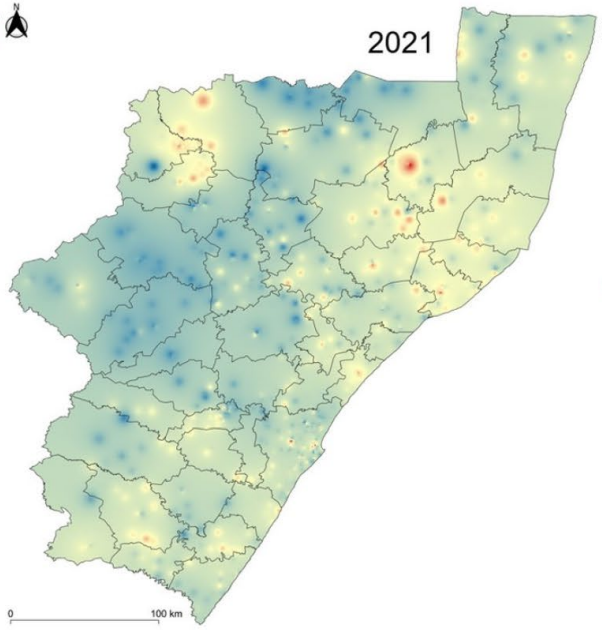
VL: Results

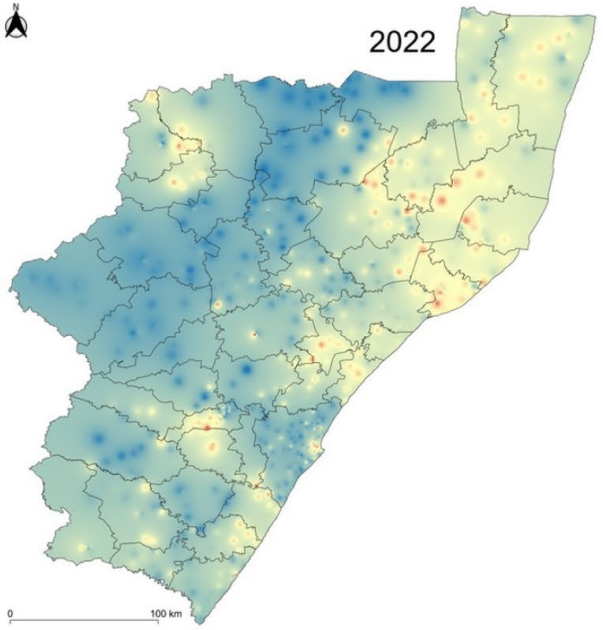




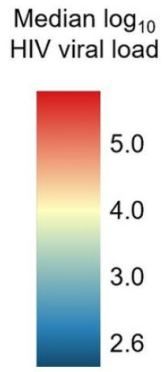




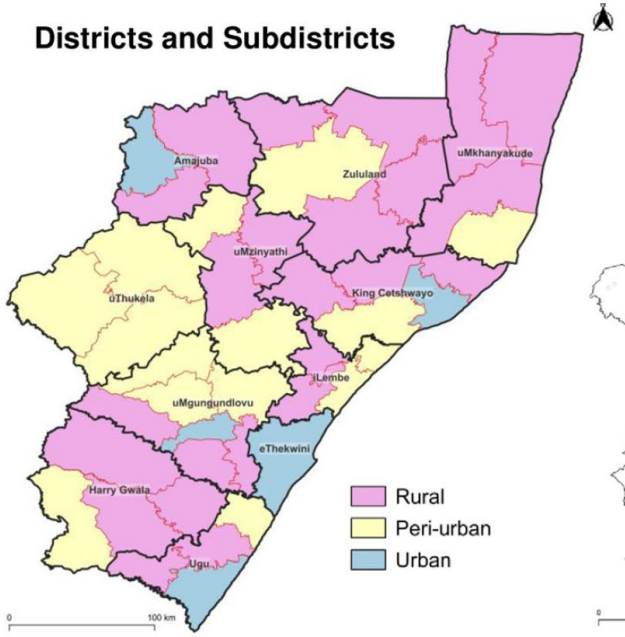


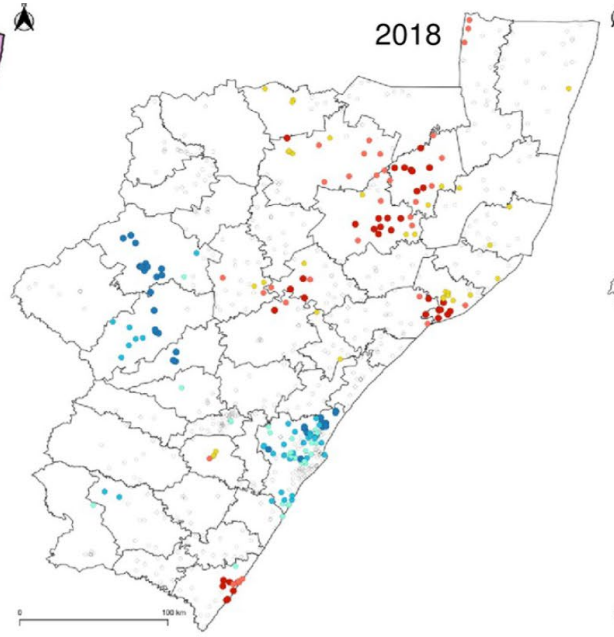


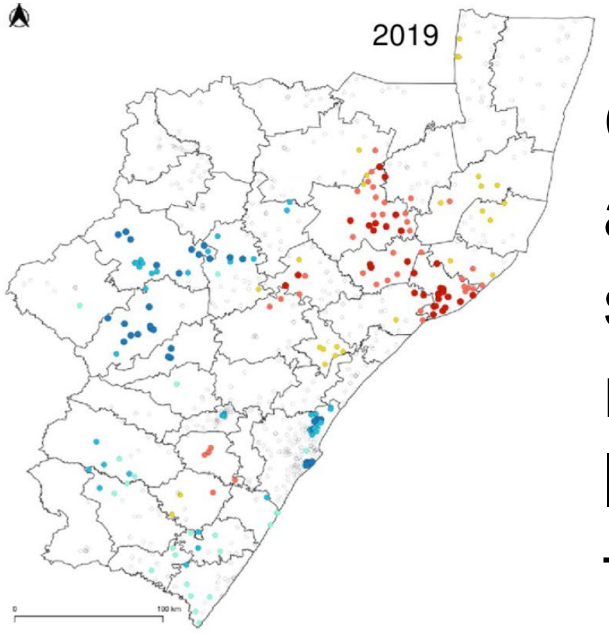
Inverse distance weighted interpolation maps from 2018 to 2022

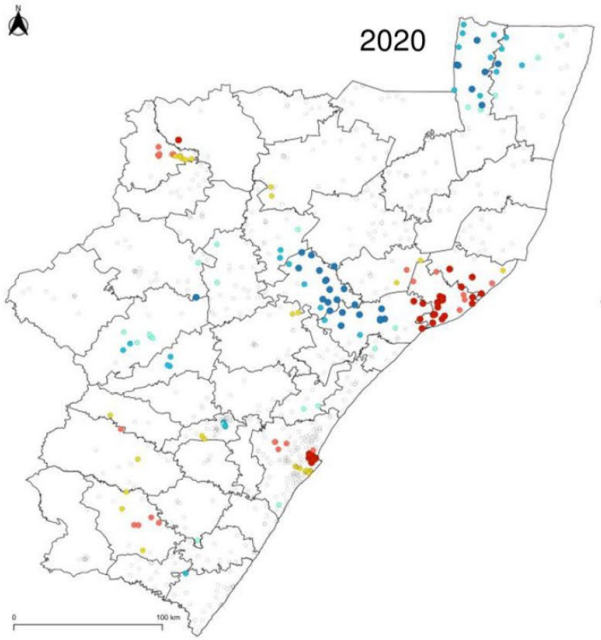


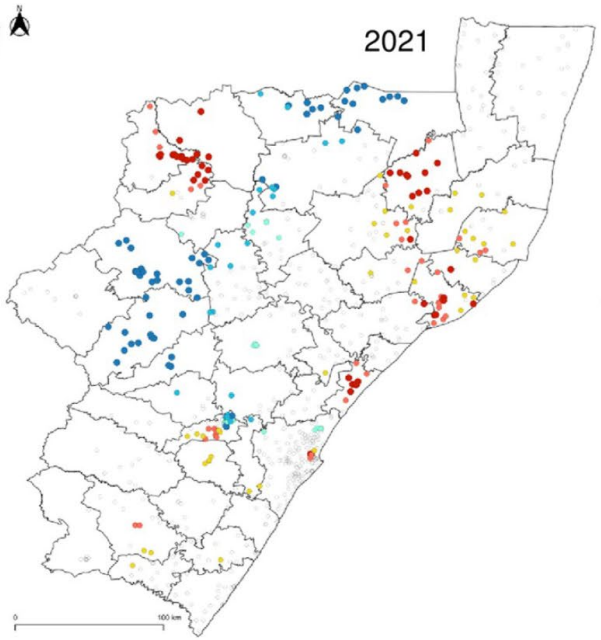
VL: Results

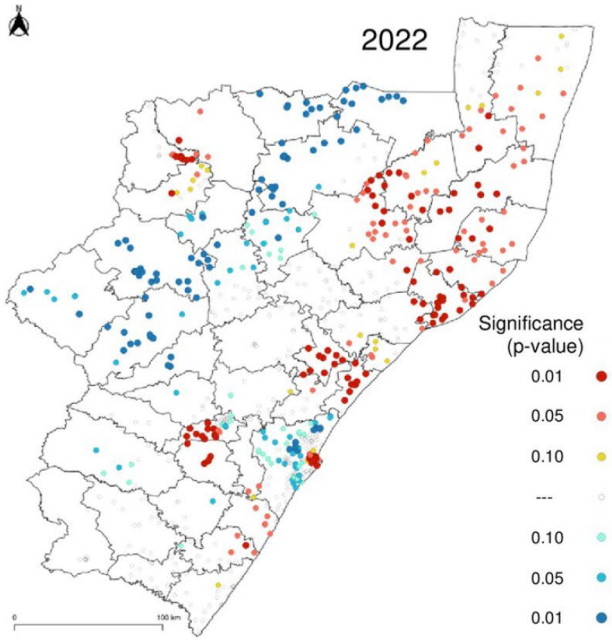


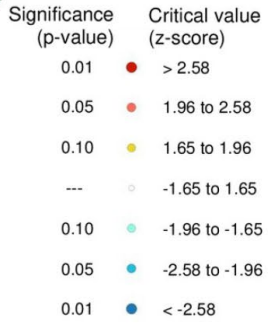












Getis-Ord Gi* hot- and coldspot statistical analysis of median $\log_{10}$ viral load mapped per facility

VL: Key Messages

- Upward trend in the proportion of low-level viraemia – could compromise DTG-based ART. Need to closely monitor low-level viraemia in PLWH.
- Geospatial analysis showed northern and coastal districts had higher HIVVLs – targeted interventions to support existing treatment programmes.
- Emerging hotspots amid DTG rollout – temporary disruptions in HIV treatment services during COVID-19 pandemic. Need prospective geospatial studies to assess if hotspots were related to pandemic, or trend continues.
- Limitations: facility-based VLs, testing practices differ, lab-based–no clinical history.
- Urgent need to develop systems that collect locally relevant data, to create geospatial models that can be accurately applied to the HIV epidemic.

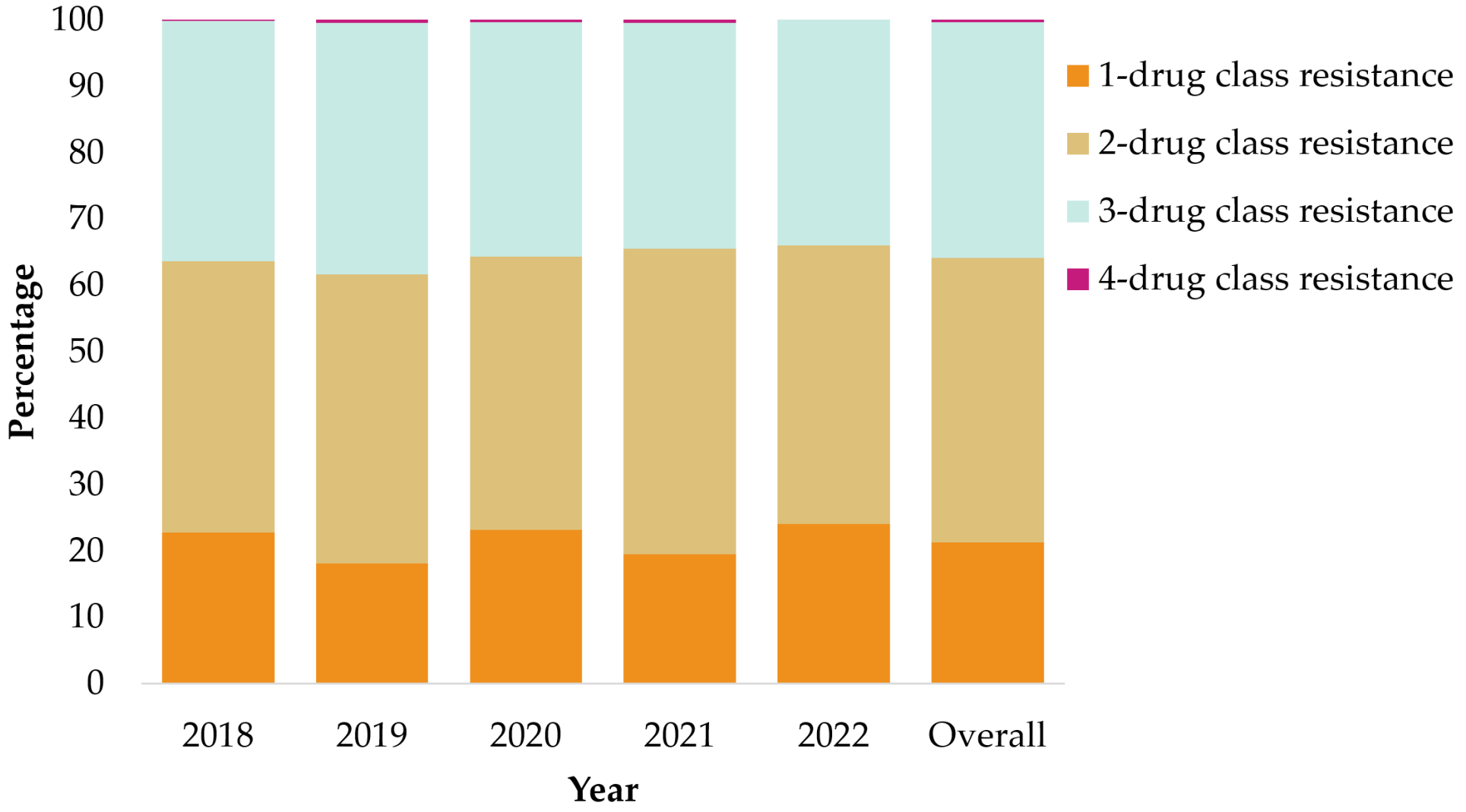
HIVDR: Results

Patient characteristics

	All; n=3,133 (100.00%)	No HIVDR; n=398 (12.70%)	HIVDR; n=2,735 (87.30%)
Characteristics			
Female[a]	1,982 (63.26%)	266 (13.42%)	1,716 (86.58%)
Male[a]	1,126 (35.94%)	130 (11.55%)	996 (88.45%)
Median age (IQR)	39 (30-46)	36 (22-43)	39 (32-46)
18-29	750 (23.94%)	156 (20.80%)	594 (79.20%)
30-59	2,284 (72.90%)	237 (10.38%)	2,047 (89.62%)
≥60	99 (3.16%)	5 (5.05%)	94 (94.95%)
ARV drug regimen			
LPV/r or ATV/r-based	2,830 (90.33%)	362 (12.79%)	2,468 (87.21%)
DRV/r-based[b]	30 (0.96%)	1 (3.33%)	29 (96.67%)
RAL-based[c]	14 (0.45%)	1 (7.14%)	13 (92.86%)
DTG-based[d]	46 (1.47%)	8 (17.39%)	38 (82.61%)
NNRTI-based[e]	36 (1.15%)	5 (13.89%)	31 (86.11%)
Not documented	177 (5.65%)	21 (11.86%)	156 (88.14%)

ARV, antiretroviral; ATV/r, ritonavir-boosted atazanavir; DRV/r, ritonavir-boosted darunavir; DTG, dolutegravir; HIVDR, human immunodeficiency virus drug resistance; INSTI, integrase strand transfer inhibitor; IQR, interquartile range; LPV/r, ritonavir-boosted lopinavir; NNRTI, non-nucleoside reverse transcriptase inhibitor; RAL, raltegravir; [a]Not documented in 25 genotypes; [b]Etravirine included in 4 regimens containing ritonavir-boosted darunavir; [c]Darunavir included in 9 regimens; [d]Darunavir included in 10 regimens; [e]Etravirine included in 1 NNRTI-based regimen

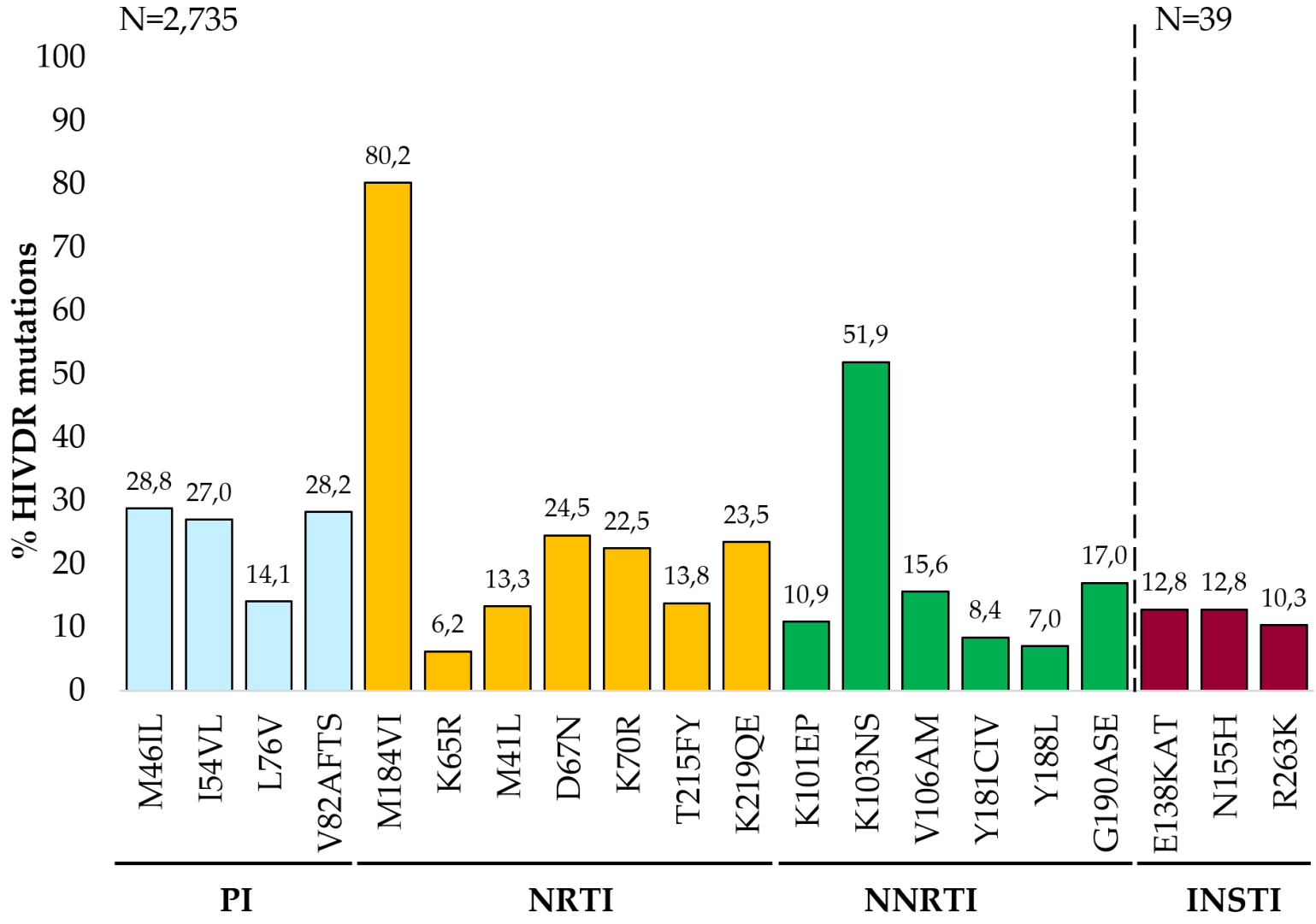
HIVDR: Results



Patterns of antiretroviral drug class resistance

Patterns of antiretroviral drug class resistance observed in 2,735 genotypes with HIVDR obtained from KwaZulu-Natal province, South Africa. Please note that 41 genotypes included HIV-1 integrase testing, of which only 9 met the definition for 4-drug class resistance.

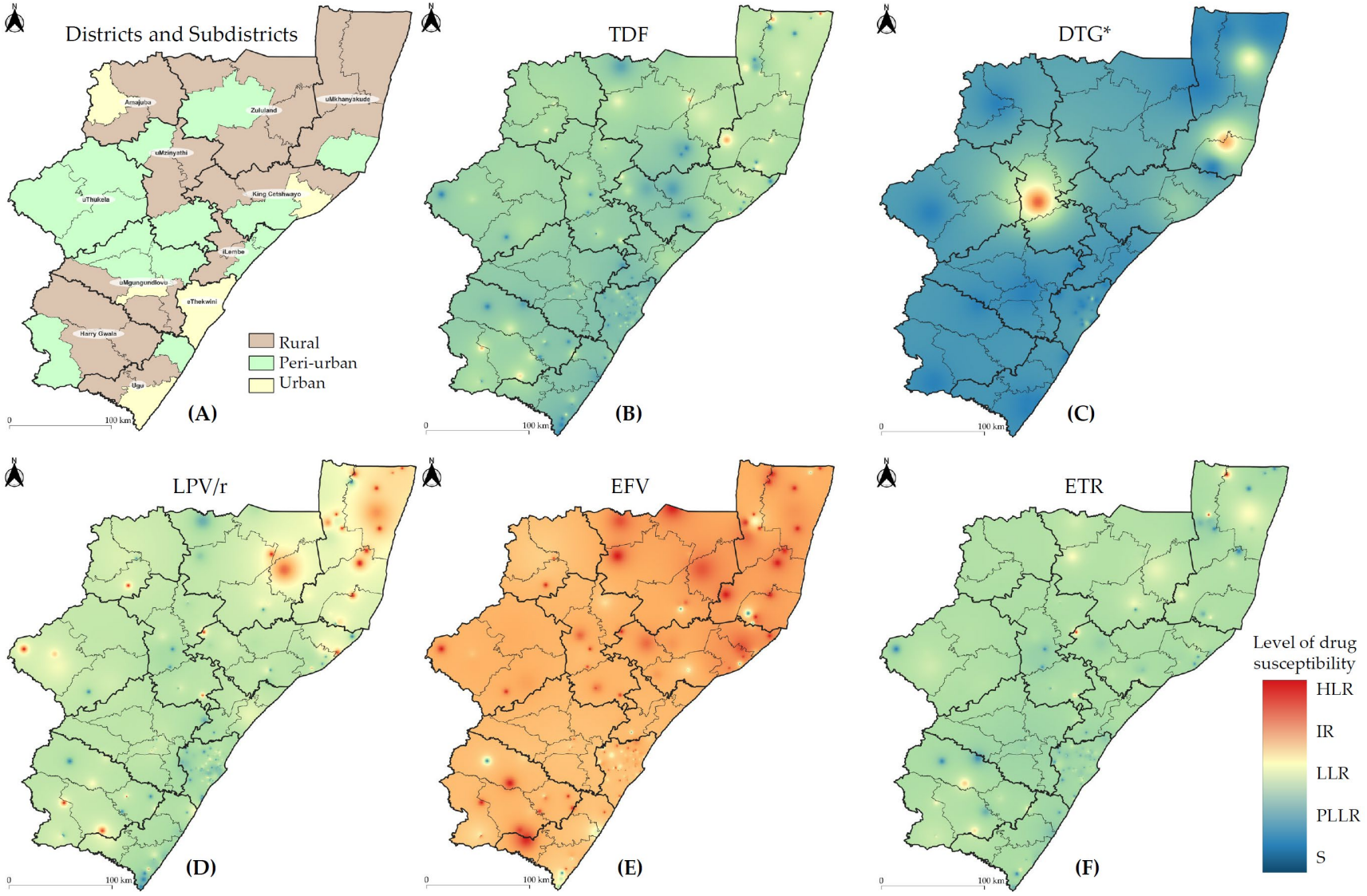
HIVDR: Results



Specific mutations detected in 2,735 genotypes with HIVDR

Mutations shown on the horizontal axis include “major” mutations observed in >6% of the genotypes with HIV-1 drug resistance, “major” as defined by Stanford HIV Drug Resistance Database or 2022 edition IAS–USA drug resistance mutations list. HIVDR, HIV-1 drug resistance; INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

HIVDR: Results



Antiretroviral drug susceptibility levels across KwaZulu-Natal

Districts and subdistricts are categorized by: (A) level of urbanization. Inverse distance weighted interpolation maps cumulatively reflect the drug susceptibilities for: (B) TDF, tenofovir; (C) DTG, dolutegravir; (D) LPV/r, lopinavir with boosted ritonavir; (E) EFV, efavirenz and (F) ETR, etravirine. Spectral colour change from blue to red reflects the drug susceptibility level as follows: S, susceptible; PLLR, potential low-level resistance; LLR, low-level resistance; IR, intermediate resistance; HLR, high-level resistance.

HIVDR : Key Messages

- Temporal trends of HIVDR similar, with dual- or triple-class resistance observed in 4 out of every 5 patients.
- Of 26 patients on DTG with an INSTI genotype, ~35% (9/26) had DTG-associated resistance mutations.
- Higher levels of HIVDR particularly in northern rural KZN, highlighting the need for targeted intensified HIV-1 treatment monitoring.
- This study serves as a proof of concept that geospatial analysis could potentially be used for data-driven public health decision making.
- Population-level analyses of impact of specific mutations were limited, (<2% of patients on INSTI-based regimens) - need to assess current prevalence of HIVDR to determine programmatic outcomes.

Acknowledgements

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