

Will Transmitted Drug Resistance Jeopardize the National HIV Drug Resistance Programme?

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HIV Clinicians Conference

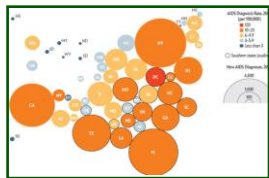
“14 April 2016”

<http://www.bioafrica.net/>

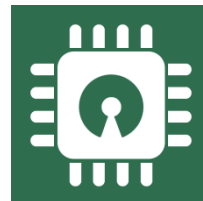


SATuRN Vision

Develop advanced yet affordable HIV & TB drug resistance diagnostics, implement it at primary health care clinics in resource limited settings and create a collaborative system for surveillance, research and capacity building.



**SURVEILLANCE
& RESEARCH**



**ADVANCED
DIAGNOSTICS**



**COLLABORATION &
CAPACITY BUILDING**



What is the SATuRN?

a network consisting of biomedical scientists, clinicians, epidemiologists and public health experts



SATuRN managed at the UKZN and and the SA-MRC

CURRENT PARTNERS includes 24 partners in southern Africa

OPEN ACCESS DIAGNOSTIC, DATABASE AND RESEARCH

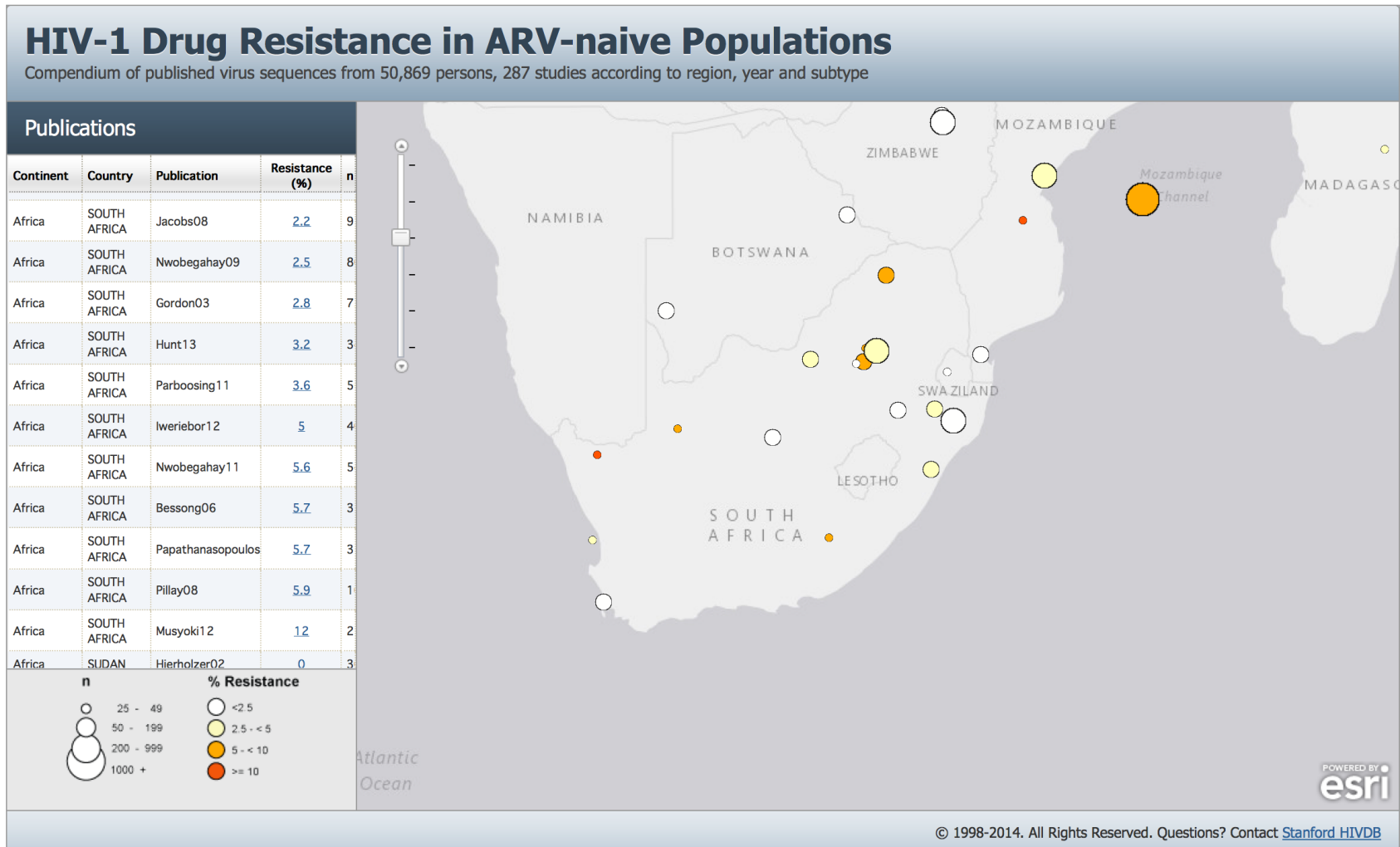
More info at www.bioafrica.net

Collaborators & implementation sites info at www.bioafrica.net/saturn/

De Oliveira et al. *Nature* 2010
Manasa et al. *Database* 2014



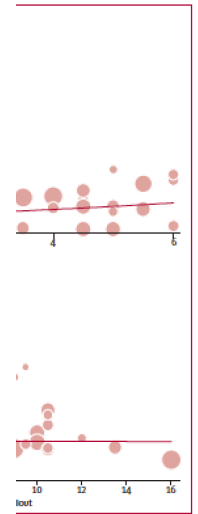
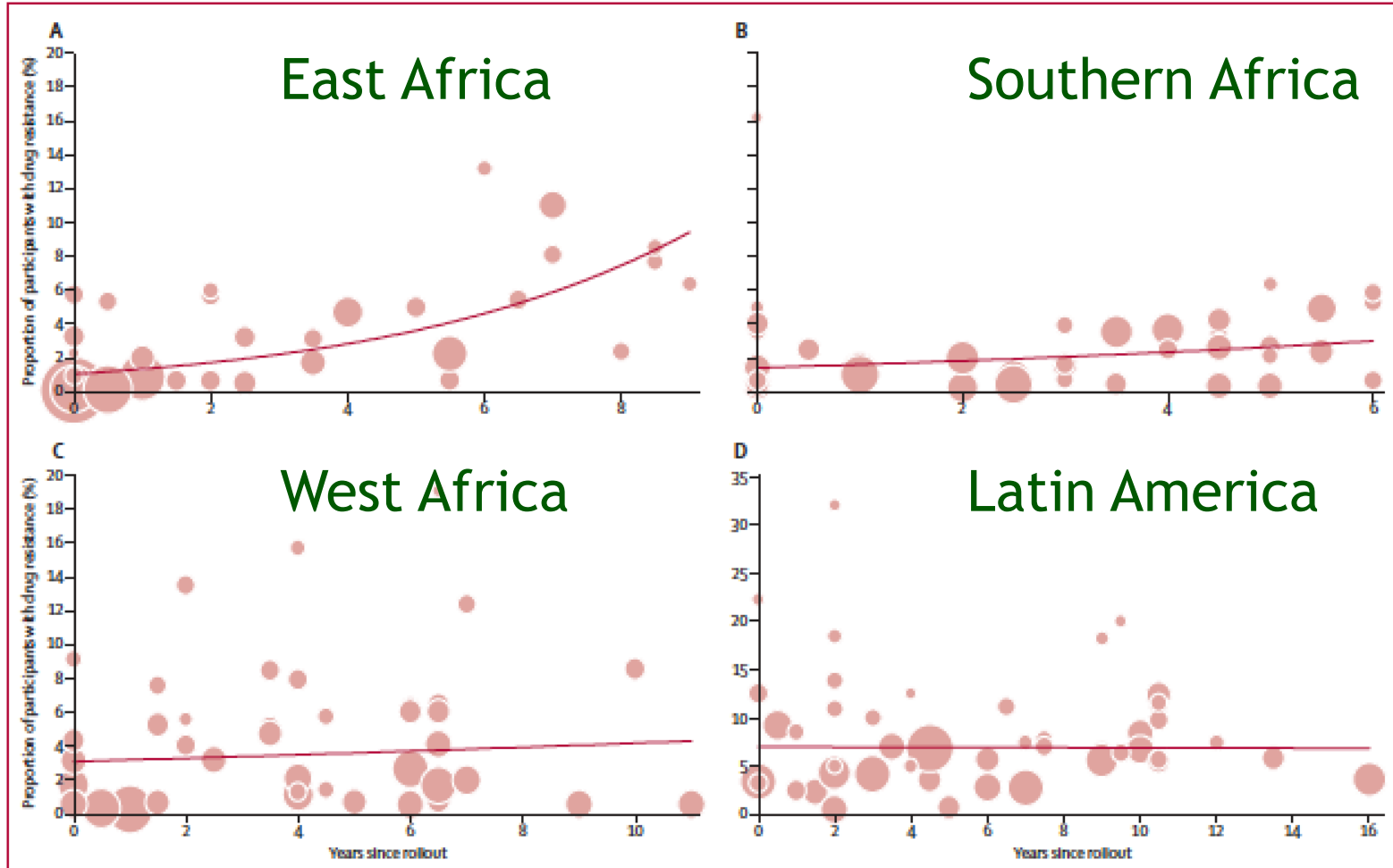
SATuRN & Stanford HIVDB: Public database to track drug resistance



De Oliveira, Seebregts & Shafer *Nature* 2010
 Mulder et al. *PLoS Computational Biology* 2016



Large datasets are needed to test if drug resistance is increasing...

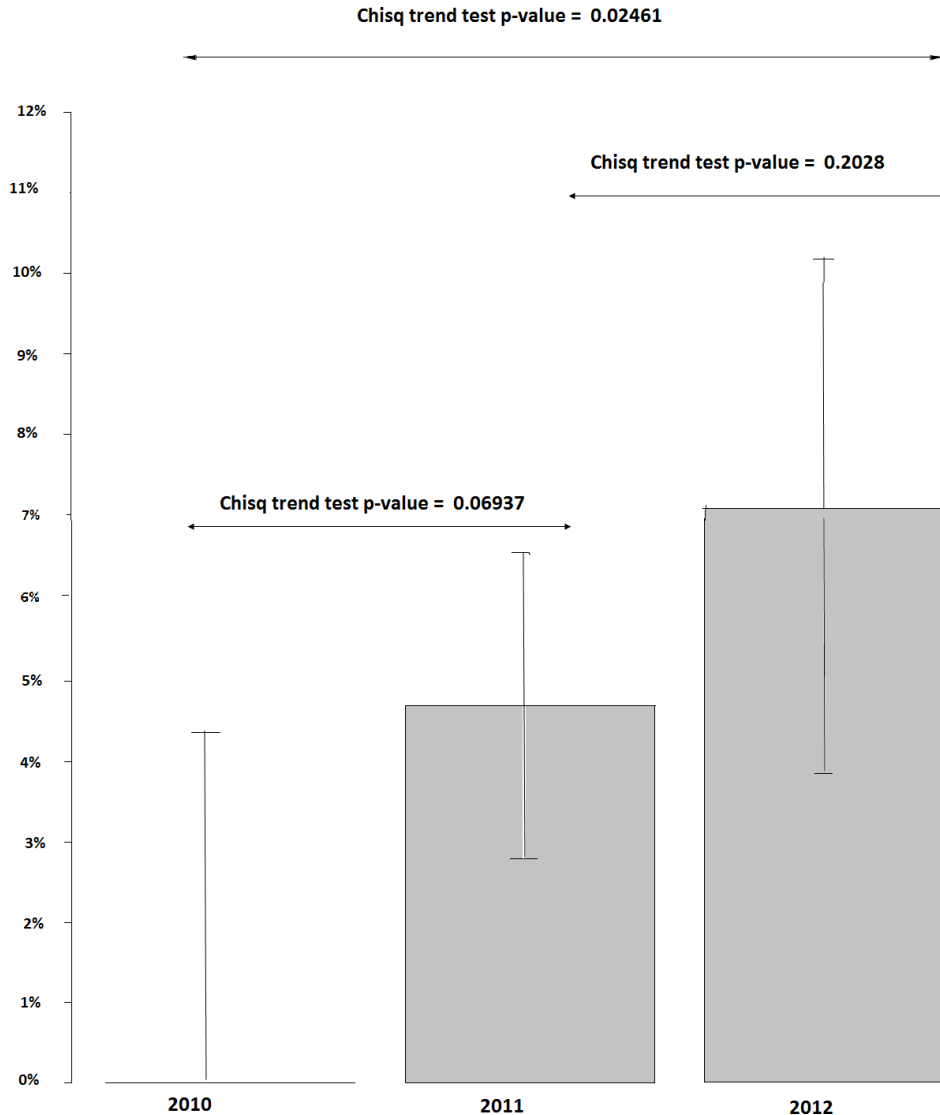


Manasa et al., ARHR 2012

Gupta et al., LID 2012



Is transmission of drug resistance increasing? Can we test this statistically?



701 genotypes from treatment naïve individuals were produced in a rural cohort in KZN.

No TDR was detected in 2010. 2011 and 2012 TDR levels were 4.7% and 7.1% respectively

The majority of the mutations were NNRTI (103, 106), which provide resistance to EFV.

Only 0.3% (2/701) had K65R, which is the main mutation to TDF.

- Manasa et al. *ARHR*, 2016



Do we need recent infections to accurately test transmitted drug resistance?

TABLE 3. PROPORTION OF PARTICIPANTS WITH SURVEILLANCE DRUG RESISTANCE MUTATIONS ACCORDING TO THREE DIFFERENT DEFINITIONS OF RECENT INFECTIONS

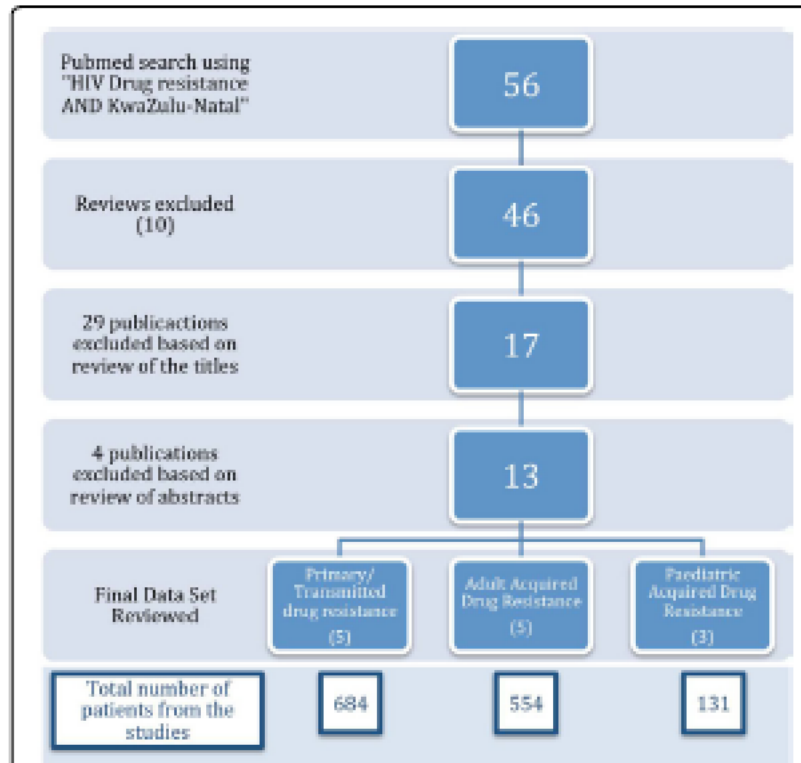
<i>Definition of recent infections</i>	<i>Proportion with SDRM in recently infected, % (n)</i>	<i>Proportion with SDRM in chronically infected, % (n)</i>	<i>Proportion with SDRM in patients with unknown duration infection, % (n)</i>	<i>p-Value^a</i>
≤12 months				
All	8 (79)	4 (472)	7 (150)	.289
2010	0 (17)	0 (50)	—	—
2011	11 (37)	4 (263)	5 (81)	.169
2012	8 (25)	6 (159)	9 (69)	.797
≤24 months				
All	7 (134)	4 (417)	7 (150)	.306
2010	0 (30)	0 (37)	—	—
2011	9 (68)	3 (232)	5 (81)	.133
2012	8 (36)	7 (148)	7 (69)	.748
≤36 months				
All	6 (179)	4 (372)	7 (150)	.515
2010	0 (44)	0 (23)	—	—
2011	7 (91)	4 (209)	5 (81)	.580
2012	9 (44)	4 (140)	9 (69)	.626

^a χ^2 p-values.

SDRM, surveillance of drug resistance mutation.



Review on drug resistance levels in KZN



Transmitted drug resistance (TDR) to NNRTIs in adults is increasing to moderate levels as defined by WHO (5-15%). Important to track transmission, specially TDF, EFV and PI.

- Kiepiela, Manasa et al. AIDS & Clinical Research 2014

Study Period	Patient Population	N	Any mutation (%)	NNRTI (%)	NRTI (%)	PI (%)	Reference
2011	Treatment naïve women	351	7.4	5.7	2.0	0.6	Parikh et al. [13]
2010	HIV surveillance	72	0.0	0.0	0.0	0.0	Manasa et al. [17]
2009	ANC Survey	47	<5.0	<5.0 (2.1)	<5.0	<5.0	Parboosing et al. [14]
2009	ANC Survey	47	5-15	5-15	<5.0	<5.0	Hunt et al. [15]
2008*	ANC Survey	37	13.5	8.1	5.4	2.7	Hunt et al. [15]
2007	ANC Survey	34	<5.0	<5.0	<5.0	<5.0	Hunt et al. [15]
2005*	ANC Survey	40	2.5	2.5	ND	ND	Hunt et al. [15]
2003	Treatment naïve adults	56	<5.0	<5.0 (2.1)	<5.0	<5.0	Gordon et al. [16]

* The threshold level could not be determined because of insufficient numbers of samples genotyped.

N - number of patients genotyped; NNRTI - Non-nucleoside reverse transcriptase inhibitor; ND - not determined; NRTI - nucleoside reverse transcriptase inhibitor; PI - protease inhibitor;

Table 1: Surveillance of transmitted drug resistance (TDR) studies from KwaZulu-Natal (KZN), South Africa.

Concerns have been raised about the high levels of the K65R mutation associated with tenofovir regimens in adults and children failing ART.

Can this mutation be transmitted?



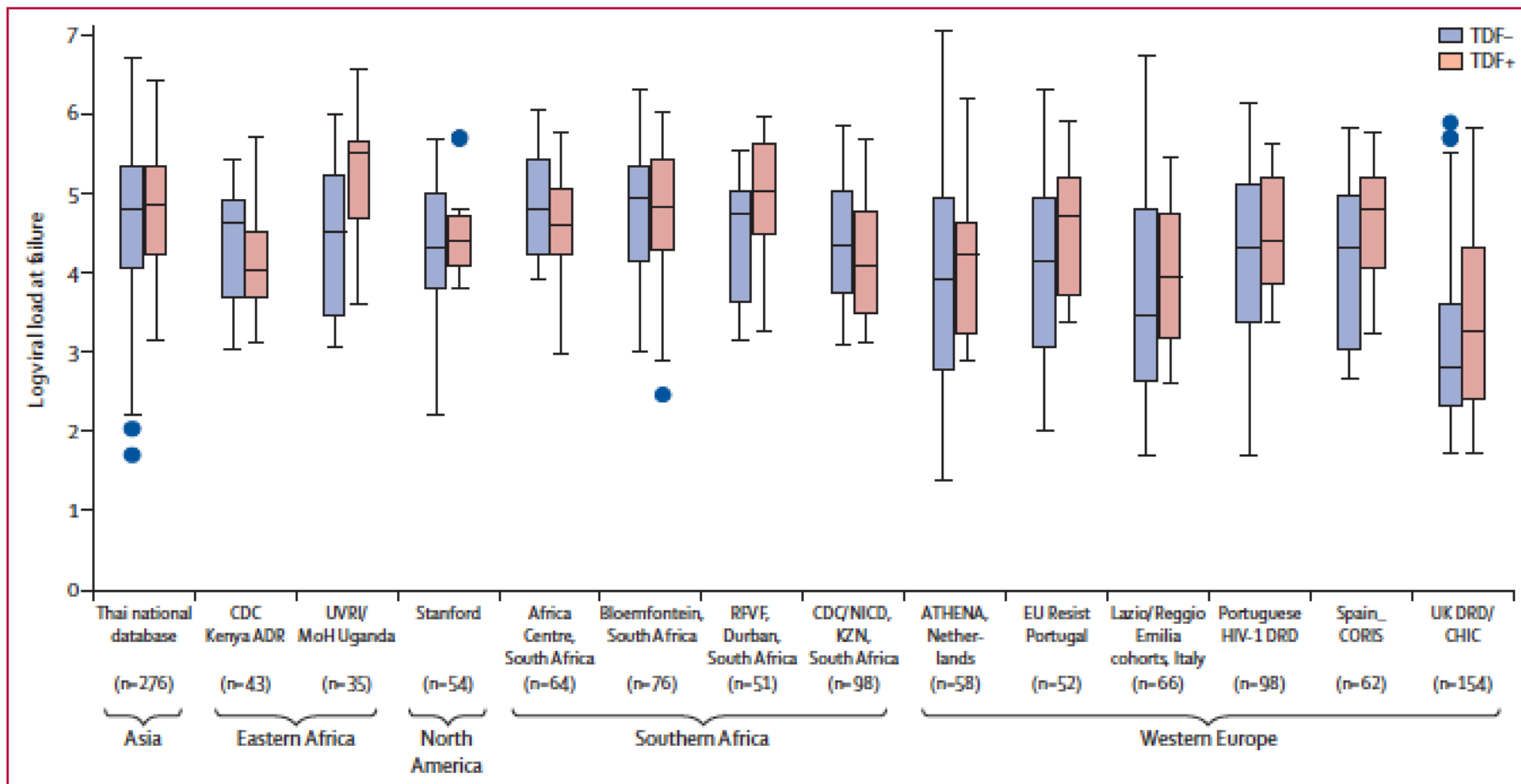


Figure 4: Boxplot of log viral load by presence (TDF-positive) or absence (TDF-negative) of tenofovir resistance at viral failure in studies with at least ten patients with TDF resistance and a viral load measurement at treatment failure

We restricted to studies with at least ten TDF-resistant mutations to help with graphical clarity, although the pattern of similar distributions of failure viral load in the presence or absence of TDF resistance was true for all studies. TDF=tenofovir disoproxil fumarate. Blue dots represent outliers.



Conclusion

There is a need to make data public and analyze it together to track resistance over time in order to inform the NDoH.



Transmitted drug resistance seems to be increasing over time.

Still low levels of TDF transmitted resistance.

The National HIV Drug Resistance Workplan aim to produce a public dashboard using South African mirror of Stanford HIVDB to track drug resistance over time in South Africa.





Foreword:

The concept behind this newsletter is that anyone with 15 minutes to spare can learn about the work of SATuRN.

In this first 2016 issue of our newsletter we have included interesting news, blogs, reports, tweets, publications and training information produced by our network.

We hope you enjoy it and find it informative. We welcome any feedback about content or format.

Produced by: Tulio de Oliveira, Richard Lessells, Justen Manasa, Jennifer G, Benjamin Chimukangara, Jennifer Giandhari, Nicolette Crozier

Highlights:

News: SATuRN and CAPRISA Advanced Clinical Care Workshop, 6-7 July 2016

Publication: Global epidemiology of drug resistance after failure of WHO recommended first-line regimens for adult HIV-1 infection

Publication: Increasing HIV-1 drug resistance between 2010 and 2012 in adults participating in population-based HIV surveillance in rural KwaZulu-Natal South Africa

Publication: Understanding Specific Contexts of Antiretroviral Therapy Adherence in Rural South Africa

Web Resource: BioAfrica and ViralZone HIV-1 proteome resource: summarizes all HIV protein functions and drug resistance mutations!

More info & Open
Access manuscripts:

SATuRN newsletter

www.bioafrica.net

