SATuRN HIV Treatment Failure Clinic Model

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Southern African Treatment Resistance Network (SATuRN)

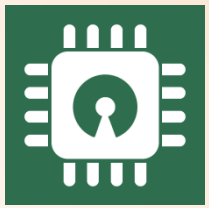
http://www.bioafrica.net/saturn/

wellcome trust

UNIVERSITY OF KWAZULU-NATAL

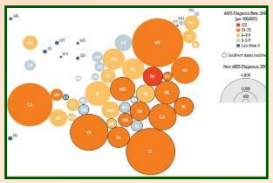
SATuRN Vision

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**.



ADVANACED DIAGNOSTICS

PHC CLINICS

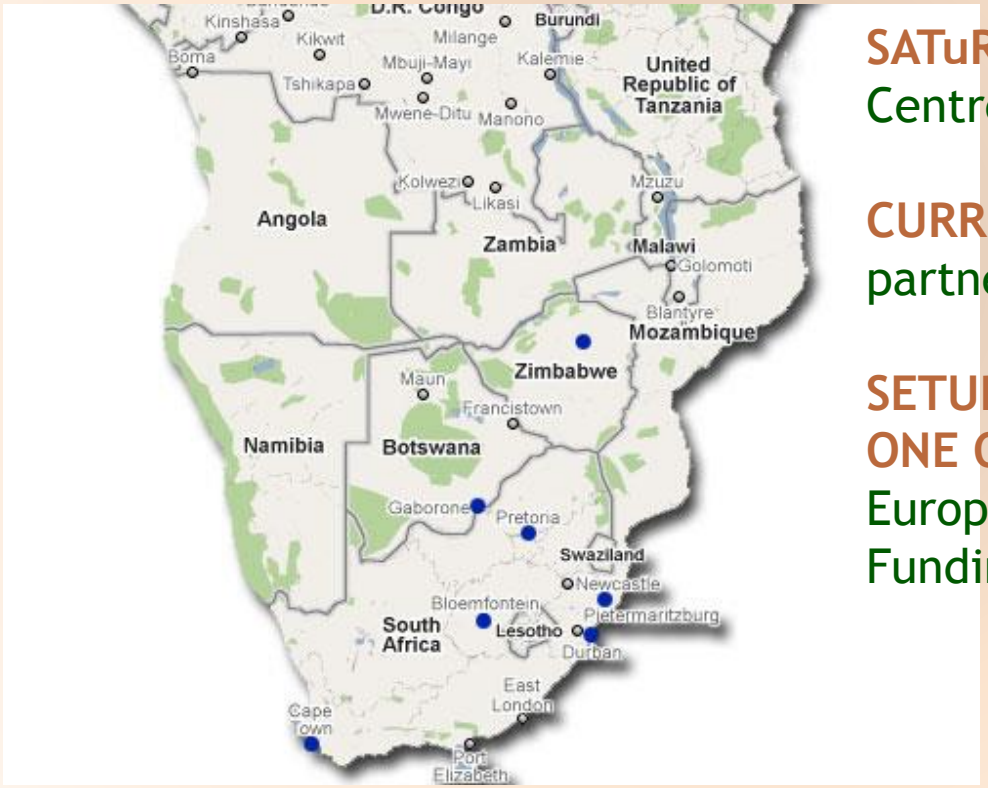


SURVEILLANCE & RESEARCH

COLLABORATION & CAPACITY BUILDING

What is the SATuRN?

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



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

SATuRN managed at the Africa Centre and and the SA-MRC

CURRENT PARTNERS includes 24 partners in southern Africa

SETUP A RESISTANCE NETWORK ONE OF THE OBJECTICES of the European Commission MRC funding. Funding complemented by US CDC

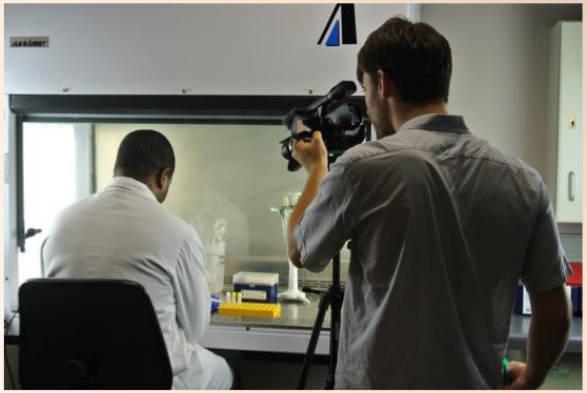
Research & Development: Diagnostics

3500 ABI Sanger DNA Analyzer

Genotyping system is the most accurate diagnostic test for HIV drug resistance. It was prohibited for national implementation due to its cost and complexity.

AFFORDABLE & OPEN ACCESS GENOTYPING

Genotyping price reduced from US$ 250 to Approx. US$ 50 per sample (Sanger ABI).



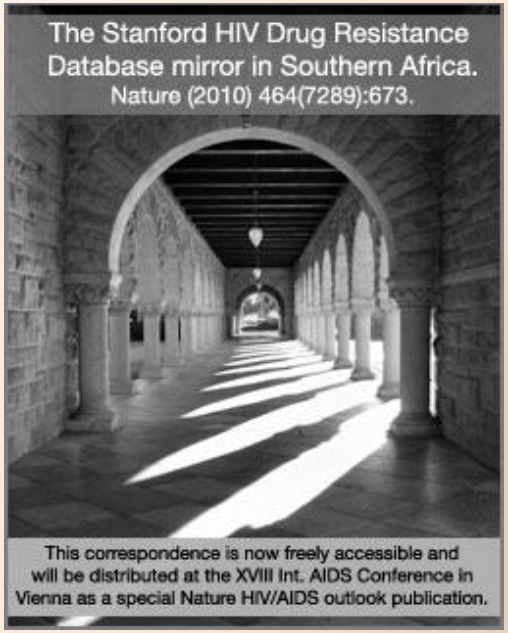
Filming of SATuRN/Life Open Access protocol (available at JOVE and Youtube)

Open Access protocol in VIDEO format.

All open accessible protocols curated at bioafrica.net website.

Manasa et al. J. Visual Exp. (JoVE) 2013
Manasa et al. PLoS On 2010

2- Research & Development: Bioinformtics Databases and Tools



Stanford HIVDB mirror in southern Africa

Bioinformatics system for HIV and other pathogens

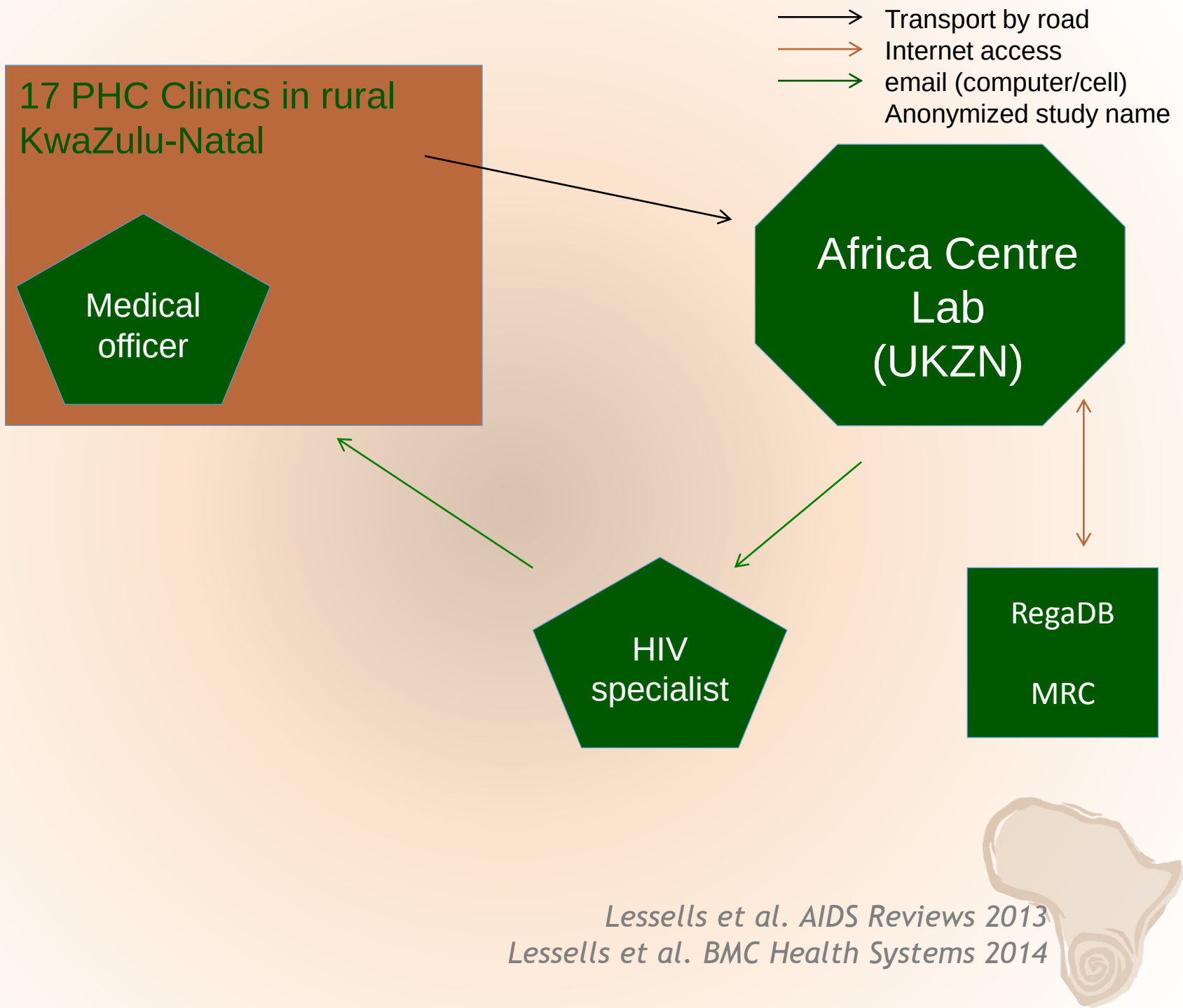
PUBLIC & FREE OPEN SOURCE SOFTWARE

Use of gold, standard, free open source software databases and tools.

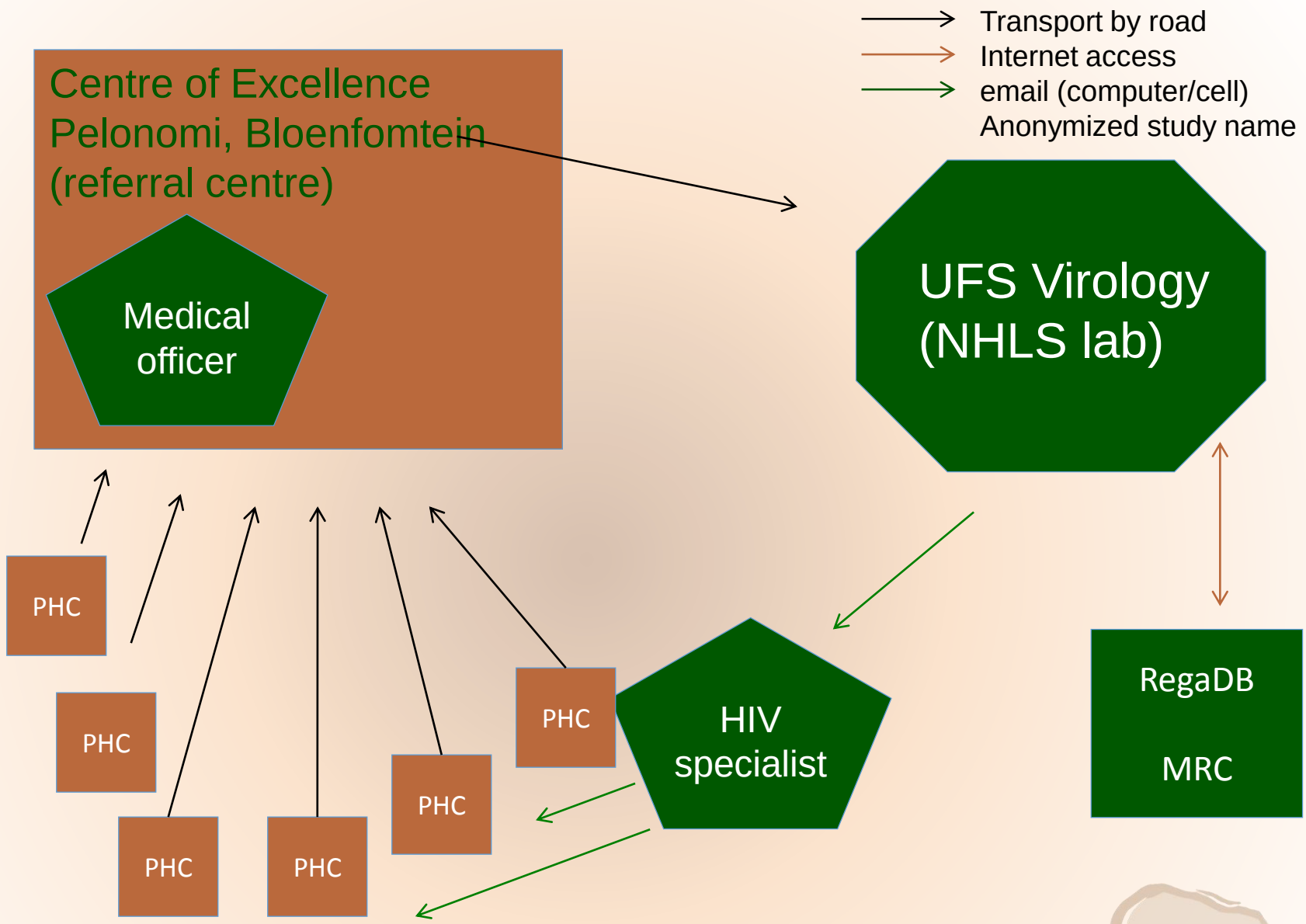
RegaDB for clinical management and Stanford HIVDB for genotypes after publication.

We aim to **enhance the capacity of physicians and scientists to produce research** results and of **policy makers to use research evidence.**

De Oliveira et al. Nature 2010
Libin et al. Bioinformatics 2013
Manasa et al. Database 2013



Lessells et al. AIDS Reviews 2013
Lessells et al. BMC Health Systems 2014



Primary health care (PHC) clinics in the Free State

No clinical and laboratory information – no genotype.

Objective is to provide enough information to be used for clinical decision.

Laboratory tests: VL, CD4, HBV, Creatinine clearance

Treatment: current and previous regimens

Demographic: age, gender

Other OIs: TB and other Ois

Adherence: questions, social worker interview

Report 2-3 pages: drug resistance, interpretation & specialist suggestion

NATIONAL HEALTH LABORATORY SERVICE

Department of Virology
Level 5, Laboratory Building □ Inkosi Albert Luthuli Central Hospital
Private Bag X03, Mayville, 4058 □ 800 Bellair Road, Mayville, 4058
Tel: (031) 240- 2794 □ Fax: (031) 240-2797

24/02/2012

Dear Clinician,

I enclose the report of the genotyping that you requested

Patient ID on the SATuRN Rega database*: RES007 /
**Please notice that no patient personal identification information should be stored in this database, please use an sequential study number as patientID.*

Sample ID / Sample Date: ACRES007 - 19/01/2011
Antiretroviral experience: [D4T, 3TC, TDF, EFV, LPV/r]
Subtype: HIV-1 Subtype C

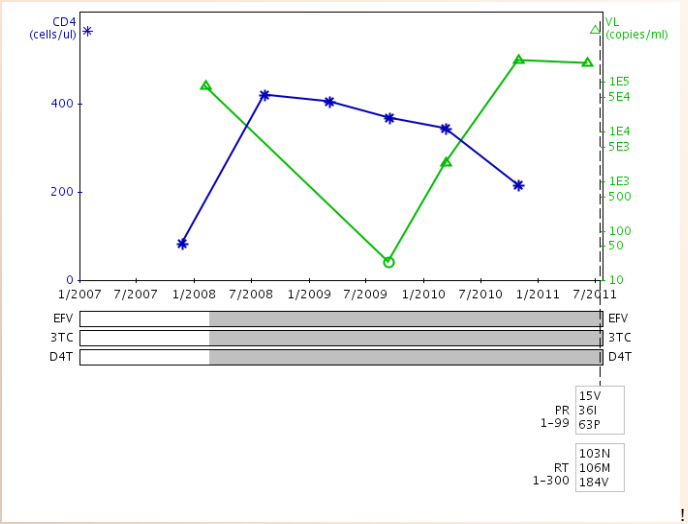
Resistance interpretations: HIVDB 6.0.5

HIVDB 6.0.5

Drug	Mutations	Description	Level	GSS
zidovudine	184V	Susceptible	1	1.0
zalcitabine	N/A	N/A	N/A	N/A
didanosine	184V	Susceptible	1	1.0
lamivudine	184V	High-level resistance	5	0.0
stavudine	184V	Susceptible	1	1.0
abacavir	184V	Potential low-level resistance	2	1.0
emtricitabine	184V	High-level resistance	5	0.0
tenofovir	184V	Susceptible	1	1.0
nevirapine	106M 190A	High-level resistance	5	0.0
delavirdine	106M	High-level resistance	5	0.0
efavirenz	106M 190A	High-level resistance	5	0.0
etravirine	106M 190A	Low-level resistance	3	0.5
saquinavir	N/A	N/A	N/A	N/A
saquinavir/r		Susceptible	1	1.0
ritonavir	N/A	N/A	N/A	N/A
indinavir	N/A	N/A	N/A	N/A
indinavir/r		Susceptible	1	1.0
nelfinavir		Susceptible	1	1.0
fosamprenavir	N/A	N/A	N/A	N/A
fosamprenavir/r		Susceptible	1	1.0
lopinavir/r		Susceptible	1	1.0
atazanavir	N/A	N/A	N/A	N/A
atazanavir/r		Susceptible	1	1.0
tipranavir/r		Susceptible	1	1.0
darunavir/r		Susceptible	1	1.0

Advice:
- Antiretrovirals for which the virus showed a reduced sensitivity, may still be partially active in a combination therapy. Antiretroviral agents against resistant virus are not recommended but may still exhibit a temporary activity when on HAART (> 3 Antiretrovirals).
- The interpretations of enfuvirtide (Envelope entry inhibitor) and tipranavir/r (boosted PI) are based on limited clinical information. These interpretations should be take with care.

List of all amino acid mutations observed in:



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Clinical chart and resistance interpretation:
This individual has resistance to two of the three ARVs that she currently on. She has High-level resistance to the NNRTI, EFavirenz (EFV) and the NRTI, Lamivudine (3TC). Her HIV population has the NNRTI mutation K103N and V106M. For resistance to NRTIs there is the 3TC specific mutation M184V. The currently circulating viral population is still susceptible to Tenofovir (TDF).

This patient's viral load has never fully suppressed in had a very good immunological response after the initiation of therapy. However this lasted for less than a year only and the CD4 count started on a downward trend. Her last three viral loads done in a space of fifteen months have all been above 2000 RNA copies/ml.

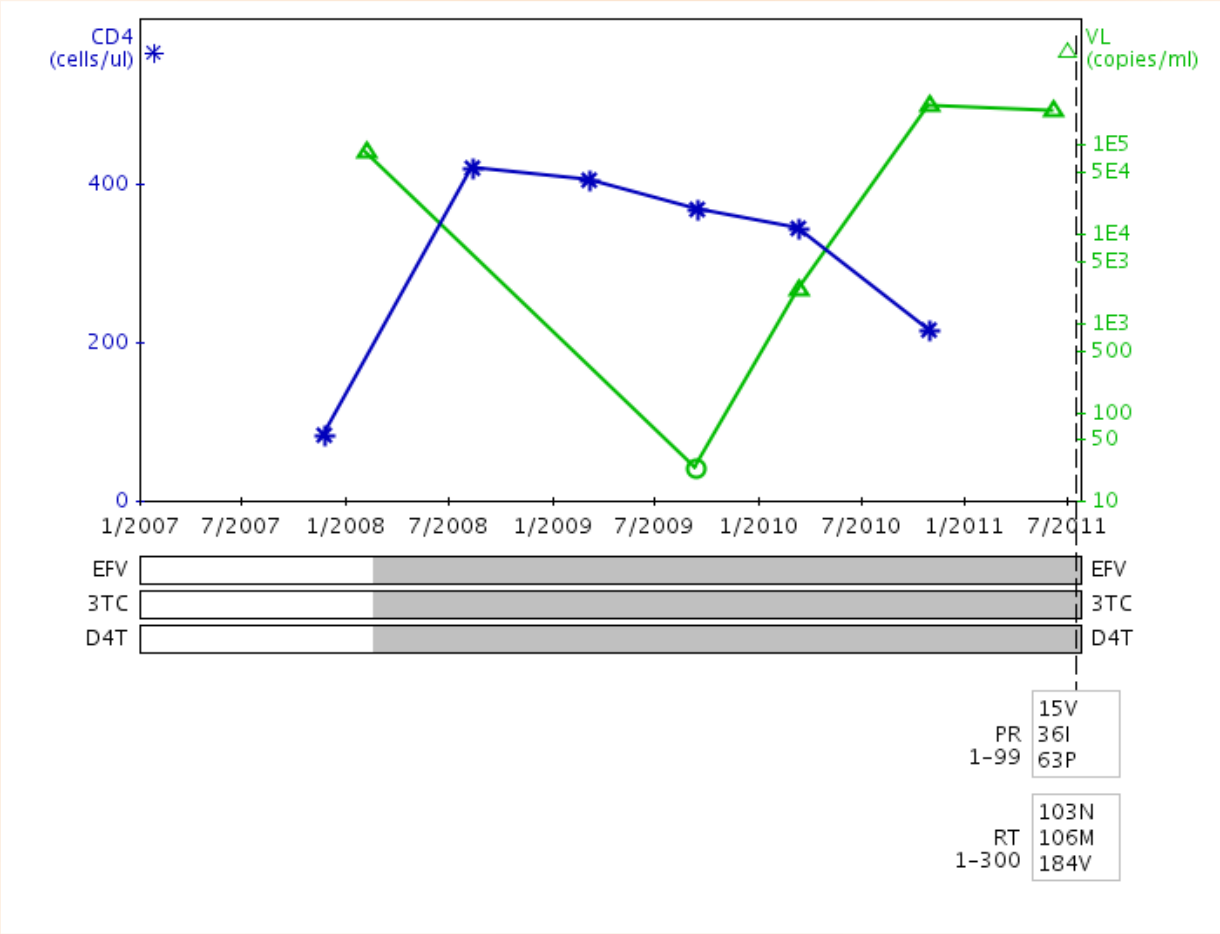
I.D. treatment switch suggestion: !
Interpretation of genotype: This patient has not accumulated any TAMs or TDF resistance, despite failing for quite some time.

Adherence: Intensive adherence support is needed and the use of alternative remedies and social deterrents to adherence should be thoroughly explored.

Treatment recommendation: Since the virus is still susceptible to TDF, the patient should do well on a standard second line consisting of TDF, 3TC and LPV/r.

General comments: The renal function should be monitored before initiation and again at three months. If the patient has a high risk if renal disease, pre-existing renal compromise (especially HT and DM patients)

CLINICAL information



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Can our clinical management model be replicated nationally?

MINISTRY of HEALTH
REPUBLIC OF BOTSWANA

Suggested by the South African HIV Clinician Society Guidelines as the database and failure system to be used for national implementation.

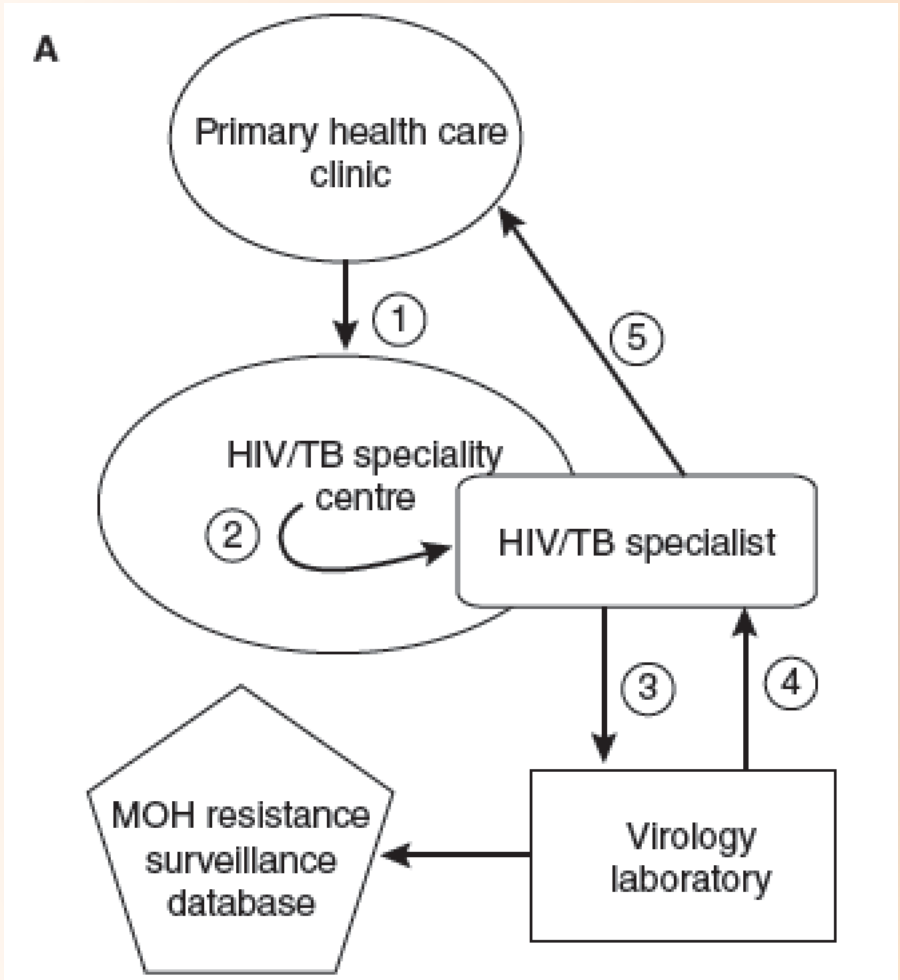
South Africa Department of Health (DoH) has SATuRN executive members to take part in the National HIV Drug Resistance Work Group.

Operation and inclusion in the functioning of the provincial ART program

Databases and resistance genotyping implemented as part of National programme

Conradie et al SAHIVClinicians 2012
Lessells et al. AIDS Reviews 2013

National HIV/TB Drug Resistance Model in Botswana.



1. Patient identitied with HIV virological failure at Primary Health Care Clinic is referred to Specialist HIV/TB Centre (national or regional) for evaluation by HIV/TB specialist clinician.
2. Resistance test request (with full clinical history) is approved by the HIV/TB specialist clinician.
3. Specimen and resistance test request is submitted to virology laboratory.
4. Resistance test results are sent back to HIV/TB specialist clinician for interpretation.
5. Final resistance report with interpretation and treatment recommendations are documented and acted upon at the Specialist HIV Centre and once stabilized patient is returned to the Primary Health Care Clinic.

Lessells, Avalos, de Oliveira. AIDS Reviews 2013

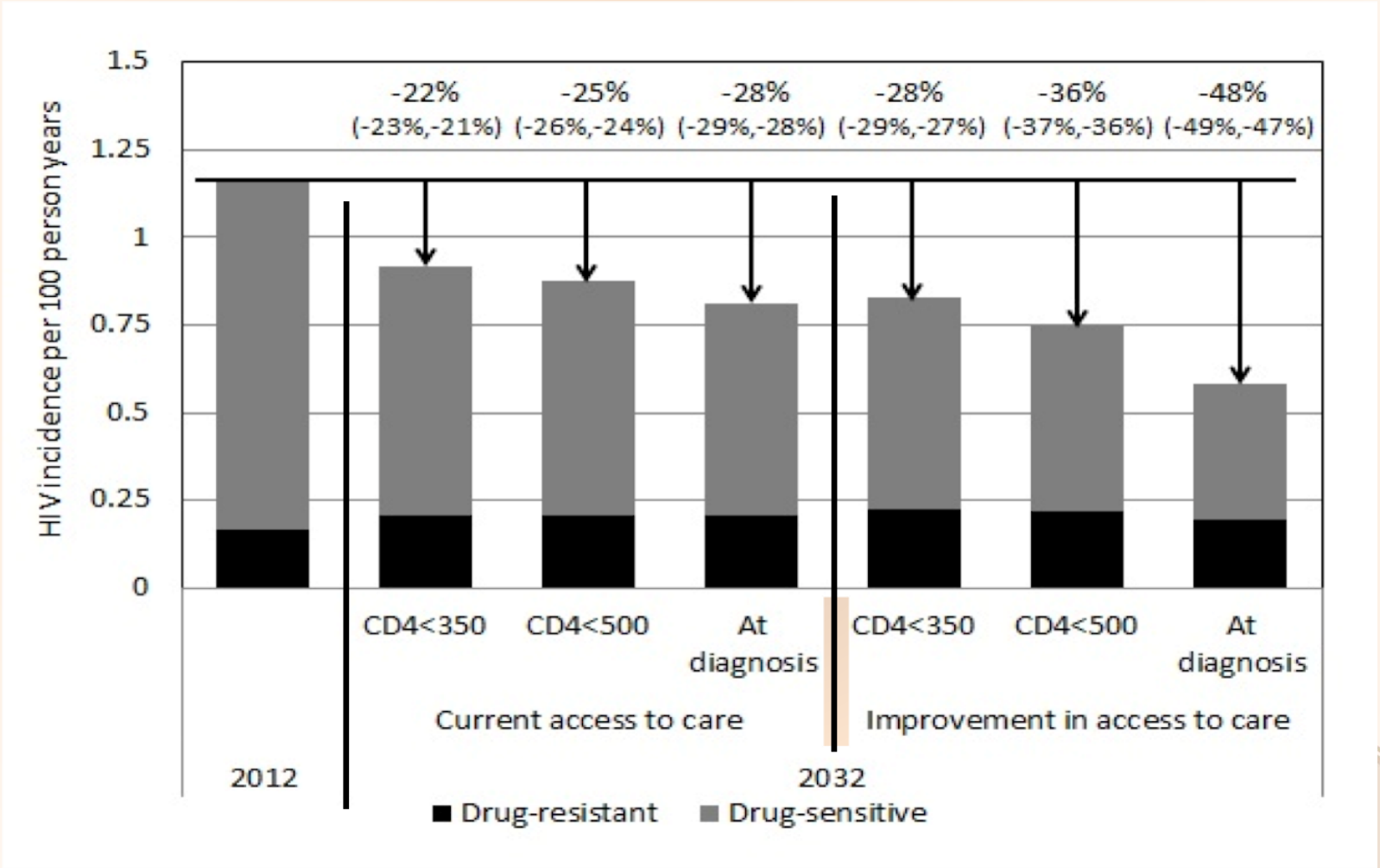
Surveillance: Primary & Acquired Drug Resistance

Results	Primary 2012 (n=377)	Adult* 2010-2013 (n=491)	Children* 2011-2012 (n=90)
Estimates of HIVDR prevalence	6%	82%	83%
Estimates of HIVDR to >= 2 drugs	2%	74%	71.8%
GSS for the standard second-line regimen was <2, suggesting a significantly compromised standard regimen	0%	17%	7%
Average time on therapy		47 months	39 months
Average time on failing regimen		27 months	20 months

- Approximately 15% of Adults and 25% of children have a viral load > 1,000 on failing regimen.

Manasa et al. ARHR 2012, Manasa et al. PLoS One 2013, Danaviah et al. JAIDS 2013

Will drug resistance jeopardize the elimination of HIV?



Cambiano et al. AIDS, 2014

SATuRN education and capacity building

We have organized and presented in > 20 workshops, including 7 annual workshops, which we have **trained > 2,500 participants** (mostly physicians, health care workers and researchers trained).

SATuRN/PASER 8th annual workshop, Bloemfontein, 20-22 November 2013.

Open access books and reports produced by SATuRN:

SATuRN Life Technologies Discounted genotyping manual

HIV/TB Drug Resistance & Clinical Management Case Book

Newsletters and annual report

Website: www.bioafrica.net

Popular website with >1,000 pages visited per day.

Interaction with the community by blogs, news, twitter.

SATuRN HIV & TB Drug Resistance Case Book

Roland van Geer Ambassador of the EU to South Africa, authors and Ronnie Anderson of University of Pretoria.

10,000 copies being distributed to health care workers, book used at medical schools and NGOs

The book is linked to a capacity building program, which we have **trained > 2,500 participants** (mostly physicians, health care workers and researchers trained).

Conclusion

Presented about the 4 pillars of SATuRN:

- Advanced diagnostics
- Implementation at PHC clinics
- Surveillance and research
- Education, collaboration and capacity building.

We believe that our system has the potential to be implemented at national and continental scale. It has also great potential to be a national strategic resource for drug resistance diagnostic and surveillance.

bioafrica.net

Bio = Greek bios 'human life'
Bioafrica = 'Bioinformatics for human life in Africa'

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Introduction

BioAfrica presents the research, software and publications of Prof. Tulio de Oliveira and members of his research group.

Prof. Tulio de Oliveira research team is based the Wellcome Trust Africa Centre for Health and Population Studies, University of KwaZulu-Natal with some of its bioinformatics servers hosted at the South African Medical Research Council. Our molecular violorogy laboratory is based at the DDMRI building, Nelson R Mandela School of Medicine, University of KwaZulu-Natal. BioAfrica also hosts the Southern African Treatment and Resistance Network (SATuRN) website.

Databases & Software	Software & Resources	Viruses Subtyping Tools	Featured News:
Mirror Stanford HIV Drug Resistance Database and SATuRN	BlastAlign Web Server Tool	REGA HIV-1 Subtyping Tool	
SATuRN RegaDB a collaborative clinical HIV Drug Resistance database	HIV-1, HCV & HBV Blast Servers Tool	Hepatitis C Subtyping Tool	
RNA Virus Database an international database to all RNA virus genomes.	HIV-1 Subtype C Molecular Epidemiology	LASP HTLV-1 Subtyping Tool	
HIV-1 Quality Analysis Tool	HIV-1 Proteomics Resources	Hepatitis B Subtyping Tool	
HIV-1 Epitope Analysis Tool	Virus Genotyping Tools Version 2.0	Human Papillomavirus Subtyping Tool	

Previous featured news

Bioafrica.net, Science 2005