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

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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.
What is the SATuRN?

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

SATuRN managed at the UKZN 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

HIV-1 Drug Resistance in ARV-naive Populations
Compendium of published virus sequences from 50,869 persons, 287 studies according to region, year and subtype

De Oliveira, Seebregts & Shafer *Nature* 2010
Large datasets are needed to test if drug resistance is increasing...

- East Africa
- Southern Africa
- West Africa
- Latin America

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

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

<sup>a</sup>χ² p-values.

SDRM, surveillance of drug resistance mutation.
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
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.

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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!