Francois Venter

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Therapy success and failure: first, second and third line therapy
Why is South Africa important?

- Almost a fifth of global HIV-positive population
- Almost 5 million people on ART (95% on TDF/FTC (or 3TC)/EFV)
- Procurement giant: SA=PEPFAR=Global Fund for ART generics
- Sustainable programme – mostly funded off SA tax base
- Almost halving of incidence in last 5 years in some demographics – HSRC, July 2012
Challenges for SA - HIV

• Re-entry to system – drive NNRTI resistance – re-entry now > naives
• PEPFAR focus on last 90: massive mop up and attention to viral loads – more second, third line patients
• Large numbers – drug storage
• Stockout of singles
• Lots of pregnancies
• Patients getting older – increased co-morbidities
• (very small numbers of paeds)
SA guidelines (state)

TDF + FTC + EFV

≈ 5 /7.9 million people on first-line, 250 000-400 000/year starting/restarting
VL>1000 copies/ml

AZT + 3TC + PI (lopinavir)

Dolutegravir

Etravirine

Darunavir

XTC, other nukes
SA guidelines (state)

- TDF + FTC + EFV
- AZT + 3TC + PI (lopinavir/rit)

150-170 000 on 2nd line (should be more, likely to rise with PEPFAR focus) – suppression rates anecdotally poor

- Darunavir
- Dolutegravir
- Etravirine
SA guidelines (state)

TDF + FTC + EFV

AZT + 3TC + PI (lopinavir)

Almost 2000 on adult third-line (accelerating) - >80% suppression
Good outcomes

Darunavir  Dolutegravir  Etravirine
## When to check VL

<table>
<thead>
<tr>
<th></th>
<th>SA Dept. Health</th>
<th>SA HIV Clin. Soc.</th>
<th>DHHS (USA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At initiation</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Before 6 months</td>
<td>X</td>
<td>3 months</td>
<td>At 2-8 weeks, then every 4-8 weeks until suppressed</td>
</tr>
<tr>
<td>6 months</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>12 months</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Thereafter</td>
<td>Every 12 months</td>
<td>Every 6 (-12) months</td>
<td>Every 3-6 months</td>
</tr>
</tbody>
</table>

### Why check viral loads before 6 months?
- Enables early detection of virological failure (usually due to poor adherence), before resistance develops, or worsens.
- At 3 months, most patients will be virally suppressed, but a small group of people who started with a very high viral load may still have detectable viraemia... although they’ll still show at least a $2 \log_{10}$ drop from their initiation viral loads.
90-90-90 Cascade - Total Population (Jun 2018 - South Africa)

<table>
<thead>
<tr>
<th>Category</th>
<th>Actuals</th>
<th>90-90-90 Target</th>
<th>Progress against previous pillar</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLHIV</td>
<td>7,208,234</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PLHIV who know their status</td>
<td>6,487,411</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PLHIV On ART</td>
<td>5,838,670</td>
<td></td>
<td></td>
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<tr>
<td>Viral loads done</td>
<td>2,643,496</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Virologically Suppressed</td>
<td>2,346,015</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **83%** PLHIV who know their status
- **72%** PLHIV On ART
- **61%** Viral loads done
- **89%** Virologically Suppressed
% of HIV+ adults at different levels of engagement in HIV care

Thembisa version 4.1
~4 YEAR LAG BETWEEN SCALE UP OF ART AND DECLINE IN MTB INCIDENCE

Figure 1: Incidence of microbiologically-confirmed pulmonary tuberculosis (per 100,000 population) and antiretroviral treatment coverage rates in HIV-infected individuals nationally in South Africa nationally and provincially from 2004 to 2012

The solid black line represents the estimated trend in PTB incidence per 100,000 population over the study period and the dotted black line the corresponding 95% confidence interval. The overlaid dotted grey line is the ART coverage per 1000 HIV positive individuals based on data from the ASSA 2008 model.

Some interesting data...

• Men still grossly under-represented (African issue, but worse in South Africa)
• Young people under-represented
• Under-represented testing and linkage; over-represented in lack of adherence, late adherence and loss to follow-up
• Stock outs: Highly complex situation
Viral loads and other monitoring

- Crudely, \( \approx 0.8 \) tests/yr/per patient (but remember – some may be repeats)
- Bigger clinics do better than smaller clinics
- No data on creat clearance, CrAG action published yet
- ?creat really necessary
Summary Indicators for CCMT M&E in SA - Adults

**Period:** from Q1 2012 to Q1 2015

**Select Age Category:** Adults, Children <15 years

### # People on treatment (DHIS)
- **GP**
- FS
- **EC**
- **WC**
- NW
- **NC**
- **MP**
- KZN

**Total:** 2,836,866

### # People with a VL test done in the last 12 months
- **GP**
- FS
- **EC**
- **WC**
- NW
- **NC**
- **MP**
- KZN
- LP

**Total:** 2,146,853

### % People in care and on ART with a VL ≤ 1000 copies/ml
- **81.9%**

### % People in care and on ART, who have a VL done at least annually
- **75.7%**

### % People with CD4 tests done, with a CD4 count ≤ 500 cells/mm3
- **69.3%**

### % People with CD4 tests done, with a CD4 count ≤ 350 cells/mm3
- **47.4%**

### % People with CD4 tests done, with a CD4 count ≤ 200 cells/mm3
- **23.9%**

### % People with CD4 tests done, with a CD4 count ≤ 100 cells/mm3
- **11.5%**
Confidential data – Lucas Hermans, submission

- Analysed >95 000 patients in NHLS database
- 34.9% (1 273/3 649) were switched to second-line ART. Patients were switched after a median of 58 weeks
- Young adults and men highest risk for viraemia
- 45% re-suppressed on NNRTI – huge implications for DTG

![Graph showing viral load over time and treatment switching]

- Treatment monitoring: actual situation
- Treatment monitoring: according to WHO guidelines (optimal situation)

Solid line represents viral load during rebound, shaded area represents time spent with a viral load >1000 copies/mL
And second line?

• Anecdote from 052: Those on PIs suppress!
Second-line antiretroviral therapy: long-term outcomes in South Africa

Richard A. Murphy, #1 Henry Sunpath, #2 Carmen Castilla, #3 Shameez Ebrahim, #2 Richard Court, #4 Hoang Nguyen, #5 Daniel Kuritzkes, #6 Vincent C. Marconi, #7 and Jean B. Nachega #5

The switch to second-line ART in South Africa was associated with an improvement in adherence, however a moderate ongoing rate of virologic failure – among approximately 25% of patients receiving second-line ART patients at each follow-up interval – was a cause for concern. Adherence level was
RESULTS: A total of 1236 patients switched to second-line treatment in a median (IQR) of 1.9 (0.9-4.6) months after first-line virologic failure. Approximately 13% and 45% of patients were no longer in care at 1 year and at the end of follow-up, respectively. Patients with low CD4 counts (<50 vs. ≥200, aHR: 1.85; 95% CI: 1.03-3.32) at second-line switch were at greater risk for attrition by the end of follow-up. About 75% of patients suppressed by 1 year, and 85% had ever suppressed by the end of follow-up.

CONCLUSIONS: Patients with poor immune status at switch to second-line ART were at greater risk of attrition and were less likely to
Sustained Virological Response on Second-Line Antiretroviral Therapy following Virological Failure in HIV-Infected Patients in Rural South Africa

Annelot F. Schoffelen, Annemarie M. J. Wensing, Hugo A. Tempelman, Sibyl P. M. Geelen, Andy I. M. Hoepelman, Roos E. Barth

![Graph showing virological response percentages](image-url)
Third-line antiretroviral therapy programme in the South African public sector: cohort description and virological outcomes

Michelle Moorhouse MBCh (Wits), DA (SA), FRSPH\textsuperscript{1}, Gary Maartens, MBChB, MMed\textsuperscript{2}, Willem Daniel Francois Venter, MBCh, MMed, FCP (SA), DTM\&H, Dip HIV Man (SA)\textsuperscript{1}, Mahomed-Yunus Moosa, MBChB, FCP (SA), PhD\textsuperscript{3}, Kim Steegen, BSc, MSc, PhD\textsuperscript{4}, Khadija Jamaloodien, BPharm, BCom (Law), MSC Clin Epi\textsuperscript{5}, Matthew P Fox, DSc, MPH\textsuperscript{6}, Francesca Conradie, MBCh, DTM\&H, Dip HIV management\textsuperscript{7}

Among those with at least one viral load at least six months after third-line approval (n=118), a large proportion (83\%, n = 98) suppressed to $<1000$ copies/mL, and 79\% (n=93) to $<400$ copies/mL.
How do we make sense of this?

• Simply paying attention to adherence may make a huge difference
• But how do we package it?
In summary:

- Prevention: Large decrease in new infections
- Diagnosis: Holes in testing, still substantial % testing late
- Linking to care: Biggest problem at the moment
- First line: Suppression rates 80-90% (but poor in adolescents, smaller and more rural clinics); success with CCMDD
- Second line: Switching rates and time to switch poor; Data not fantastic – but suppression rates seem low
- Third line – referral rate probably too low, but they do well
What can we see?

• South Africa is a mature programme – reaping large prevention and morbidity/mortality benefits
• Distraction to other health issues
• Cash crunch
• System failures in stark display – poor linkage, drug stock outs, poor attention to monitoring, M&E dependent on lab
• Huge implications for any drug changes – DTG introduction likely to be complex
• Attention to drug supply security and adherence vital for the last 90
Thank you
XXVII INTERNATIONAL WORKSHOP ON HIV DRUG RESISTANCE AND TREATMENT STRATEGIES
22 - 23 October 2018 Johannesburg, South Africa

27th International Workshop on HIV Drug Resistance and Treatment Strategies

www.hivresistance2018.co.za

4th Southern African HIV Clinicians Society Conference 2018
Wednesday, 24 October to Saturday, 27 October 2018
Gallagher Convention Centre, Midrand, Johannesburg, South Africa

www.sahivsoc2018.co.za