How are we doing with Universal Test and Treat?

Francois Venter
October 2018

Thanks DoH, WHO, PEPFAR, CHAI, UCT, Joep Lange Institute, Celicia Serenata, Steve Smith, David Allen
Optimising ART Consortia

The USAID-funded OPTIMIZE consortium includes five leading private and public sector partners, and led by Wits RHI. OPTIMIZE leverages efforts by a wide range of donors and key stakeholders (e.g., Unitaid and its implementing partners, WHO and Global Fund).

OPTIMIZE operates under the assumption that aligning the collective power of scientists, regulators, drug companies, donors, programmers and advocates to achieve its singular goal -- accelerating access to simpler, safer and more affordable HIV treatment -- can rapidly advance ART optimization efforts.

Unitaid finds new and better ways to prevent, test and treat HIV, tuberculosis and malaria quickly and more affordably. It takes game-changing ideas and turns those into practical solutions that can help accelerate the end of the three diseases. Established in 2006 by Brazil, Chile, France, Norway and the United Kingdom, Unitaid plays an important part in the global effort to defeat HIV, tuberculosis and malaria. For more information, please visit: www.unitaid.org
Why is South Africa important?

• Almost a fifth of global HIV-positive population
• 5 of 7.9 million people on ART
• Sustainable programme – mostly funded off SA tax base
• Almost halving of incidence in last 5 years in some demographics – HSRC, July 2012
Why is test and treat so important?
More ART coverage = less death...
Number of AIDS-related deaths, by sex, sub-Saharan Africa, 1990–2017
Figure 3.1: Number of registered deaths by year of death, 1997–2016*

Data for 1997–2015 have been updated with late registrations/delayed death notification forms processed in 2016/2017.
Increases in Adult Life Expectancy in Rural South Africa: Valuing the Scale-Up of HIV Treatment

Jacob Bor,1,2* Abraham J. Herbst,1 Marie-Louise Newell,1,3 Till Bärnighausen1,2

Adult life expectancy has increased from 49.2 years in 2003 to 60.5 years in 2011

Trends of TB registration from 2005 to 2016

- 2005: 302,467
- 2006: 316,863
- 2007: 353,879
- 2008: 388,882
- 2009: 406,082
- 2010: 401,048
- 2011: 389,974
- 2012: 349,582
- 2013: 328,896
- 2014: 318,193
- 2015: 283,085
- 2016: 254,258

WITS RHI
And CD4 count is rising
FIGURE 3.9. TRENDS IN MEDIAN CD4 T-CELL COUNT AT ANTIRETROVIRAL THERAPY INITIATION, 10 COUNTRIES, 2004–2015

Changing disease severity over time

Adjusted proportion of patients started ART by CD4 category

Source: Consolidated National report covering monthly and quarterly ART data to end March 2014

Thanks: Andrew Boulle
### Change of treatment guidelines and evolution of ART initiation in rural South Africa: data of a large HIV care and treatment programme

Mélanie PLAZY, François DABIS, Kevindra NAIDU, Joanna ORNE-GUEIMANN, Till BARNIGHAUSEN and Rosemary DRAIY-SPIRA

*BMC Infectious Diseases* 2015 15:452

<table>
<thead>
<tr>
<th>Group–n (%)</th>
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<td>13,851</td>
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IQR: Inter-Quartile Interval

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IQR: Inter-Quartile Interval

But late presentation remains a problem

- % presenting < 200, 100 not significantly changed
- Cryptococcal meningitis levels
Persistent High Burden of Advanced HIV Disease Among Patients Seeking Care in South Africa’s National HIV Program: Data From a Nationwide Laboratory Cohort

Sergio Carmona,1,2 Jacob Bor,3,4,5 Cornelius Nattey,3 Brendan Maughan-Brown,6 Mhairi Maskew,3 Matthew P Fox,3,4,5 Deborah K Glencross,1,2 Nathan Ford,7 and William B MacLeod3,4
Cryptococcal antigen positivity combined with the percentage of HIV-seropositive samples with CD4 counts <100 cells/μl identifies districts in South Africa with advanced burden of disease
Less new infection
High Coverage of ART Associated with Decline in Risk of HIV Acquisition in Rural KwaZulu-Natal, South Africa

Frank Tanser,¹* Till Bärnighausen,¹,² Erofili Grapsa,³ Jaffer Zaidi,¹ Marie-Louise Newell¹,³
NB. The 2012 results were re-calculated using the 2017 test parameters.

The overall HIV incidence has significantly dropped by 44%.

The largest decline (56%) in incidence was among females.

Among males the incidence declined by 18%.
South Africa: Decreasing Incidence, Increasing Treatment

- Total HIV infections
- Cumulative AIDS deaths
- Total number of ART patients
- Total new HIV infections
- Total new on Treatment

WITS RHI
Similar drops in...

- Botswana
- Zimbabwe
- Swaziland
- (Melbourne, San Francisco)
...making the treatment target in adults one of the first ones to be on trajectory to be attained by 2020.

Number of people living with HIV accessing antiretroviral therapy, global, 2000–2017 and 2020 target.

Test and treat is now the standard of care in most countries, increasing eligibility for ART.

1. CD4 ≤ 200
   Recommended since 2003

2. CD4 ≤ 350
   Recommended since 2010

3. CD4 ≤ 350
   + TB/HIV
   HBV/HIV

4. CD4 ≤ 500
   + TB/HIV
   HBV/HIV

5. All HIV+
   “Test and treat”

Initiate ART regardless of CD4 count for:
- Serodiscordant couples
- Pregnant women
- Children < 5 years

Estimated millions of people eligible for ART in LMIC in 2012:
- 11 m
- 15 m
- 17.6 m
- 28.6 m
- 33 m
The Evolving HIV Treatment Paradigm

- 3TC=lamivudine; ZDV=zidovudine

HIV-1 discovered

1983 WITS RHI

1987

1995

1996

2006

2012–2013

2017

2020

Long Acting Injectable?

The Integrase Era

Single-Tablet Regimens

Triple-Drug Therapy

ZDV/3TC

ZDV monotherapy

HIV-1 discovered

1983 WITS RHI

1987

1995

1996

2006

2012–2013

2017

2020

Long Acting Injectable?
WHO: new recommendations for first-line ART regimens

BOX 1. RECOMMENDATIONS: FIRST-LINE ARV DRUG REGIMENS

1. A DTG based regimen may be recommended as a preferred first-line regimen for people living with HIV initiating ART (conditional recommendation)

- Adults and adolescents (moderate-certainty evidence)

- Women and adolescent girls of childbearing potential\textsuperscript{a} (very-low-certainty evidence)

- Infants and children with approved DTG dosing\textsuperscript{b} (low-certainty evidence)

\textsuperscript{a} Possible pregnancy in the future

\textsuperscript{b} No approved dosing yet

WHO 2018
“Dolutegravir in first line therapy has by far the highest impact in getting to the last 90 for South Africa”

Professor Gesine Meyer-Rath - Boston University/HE²RO
<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimated number of people on ART (n)</th>
<th>Proportion of people living with HIV on ART (%) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>National</td>
<td>4,401,872</td>
<td>62.3 (59.2-65.2)</td>
</tr>
<tr>
<td>Female</td>
<td>2,998,170</td>
<td>65.5 (62.4-68.4)</td>
</tr>
<tr>
<td>Male</td>
<td>1,403,702</td>
<td>56.3 (51.0-61.5)</td>
</tr>
</tbody>
</table>
However, children lag far behind in ART treatment coverage...

Number of children (aged 0–14 years) accessing antiretroviral therapy, global 2000–2017 and 2018 target

...as do key populations

Antiretroviral therapy coverage, by population, select countries, 2014–2017

## ART exposure by age group, South Africa, 2017

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Estimated number of people on ART (n)</th>
<th>Proportion of people living with HIV on ART (%) 95% CI</th>
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</thead>
<tbody>
<tr>
<td>Total</td>
<td>4,401,872</td>
<td>62.3 (59.2-65.2)</td>
</tr>
<tr>
<td>0-14</td>
<td>131,052</td>
<td>50.0 (36.6-63.3)</td>
</tr>
<tr>
<td>15-24</td>
<td>273,981</td>
<td>39.9 (32.1-48.3)</td>
</tr>
<tr>
<td>25-49</td>
<td>3,243,819</td>
<td>63.1 (59.2-66.8)</td>
</tr>
<tr>
<td>50 and older</td>
<td>753,020</td>
<td>76.7 (71.3,81.4)</td>
</tr>
<tr>
<td>15-49</td>
<td>3,517,800</td>
<td>60.4 (57.0-63.6)</td>
</tr>
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Viral suppression among all PLHIV irrespective of treatment by age and sex, South Africa, 2017
Same-day initiation?
So Sydney did a study….
# Effect Modification by Site and by Age and Sex

<table>
<thead>
<tr>
<th>Initiated ≤ 90 days and retained and suppressed by 10 months</th>
<th>Standard arm</th>
<th>Rapid arm</th>
<th>Crude relative risk [95% CI]*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full sample</td>
<td>96/190 (51%)</td>
<td>119/187 (64%)</td>
<td>1.26 (1.05-1.50)</td>
</tr>
<tr>
<td>Site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary health clinic</td>
<td>46 (43%)</td>
<td>67 (64%)</td>
<td>1.50 (1.15-1.95)</td>
</tr>
<tr>
<td>Hospital-based HIV clinic</td>
<td>50 (61%)</td>
<td>52 (63%)</td>
<td>1.04 (0.82-1.32)</td>
</tr>
<tr>
<td>Age and sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male &lt; 35</td>
<td>12/32 (38%)</td>
<td>32/45 (71%)</td>
<td>1.90 (1.17-3.08)</td>
</tr>
<tr>
<td>Male ≥ 35</td>
<td>31/53 (58%)</td>
<td>28/45 (62%)</td>
<td>1.06 (0.77-1.47)</td>
</tr>
<tr>
<td>Female &lt; 35</td>
<td>28/60 (47%)</td>
<td>32/53 (60%)</td>
<td>1.29 (0.91-1.83)</td>
</tr>
<tr>
<td>Female ≥ 35</td>
<td>25/45 (56%)</td>
<td>27/44 (61%)</td>
<td>1.10 (0.78-1.57)</td>
</tr>
</tbody>
</table>

*Effect observed in study; p-values for interaction terms for absolute risk differences were not significant*
Conclusions

It is possible to initiate nearly all eligible patients on ART (75% on the same day) and improve overall health outcomes.

36% ART Initiation

26% Viral Suppression
## South Africa ART Surge Targets

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>FY 17/18</th>
<th>FY 18/19</th>
<th>FY 19/20</th>
<th>FY 19/20</th>
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<tr>
<td></td>
<td>Sep-17</td>
<td>Mar-18</td>
<td>Sep-18</td>
<td>Mar-19</td>
<td>Sep-19</td>
</tr>
<tr>
<td>Baseline (No Surge)</td>
<td>3,960,000</td>
<td>4,100,000</td>
<td>4,240,000</td>
<td>4,350,000</td>
<td>4,520,000</td>
</tr>
<tr>
<td>Baseline + Acceleration + Surge</td>
<td>3,960,000</td>
<td>4,280,000</td>
<td>4,600,000</td>
<td>5,000,000</td>
<td>5,400,000</td>
</tr>
<tr>
<td>Baseline + Surge + Private sector</td>
<td>4,356,000</td>
<td>4,708,000</td>
<td>5,060,000</td>
<td>5,500,000</td>
<td>5,940,000</td>
</tr>
<tr>
<td>27 Districts</td>
<td>Baseline + Surge [27 Districts]</td>
<td>3,168,000</td>
<td>3,424,000</td>
<td>3,680,000</td>
<td>4,000,000</td>
</tr>
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- **Increase of 2.1M on ART**
- **6.1M: 90-90-90**
- **6.7M: 95-95-95**

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**ART SURGE TARGETS**
In summary:
South Africa Progress to 90-90-90 (public sector)

90-90-90 Cascade - Total Population
(Nov 2017 - South Africa)

1st 90 (90%) 75%
2nd 90 (81%) 56%
3rd 90 (73%)* 26%

* Suppressed and recorded in HIS

Including private sector: 60% PLHIV on ART
BUT! A strong caution...

• Most patient who interrupt therapy do NOT do so for side effects

• Life challenges:
  • Stockouts, healthcare inaccessibility
  • Depression/anxiety
  • Relationship breakdown
  • Changing/losing jobs
  • Alcohol use
  • Inability to pay

• Poverty and healthcare access remain a major challenge
Conclusions

• South Africa is a mature programme – reaping large prevention and morbidity/mortality benefits
• Close to 90-90-90 but key people left behind
• CD4 at initiation rising – but getting complex to interpret
• DTG introduction is important but complex
• System failures huge risk – poor linkage, drug stockouts, poor attention to clinical monitoring, M&E dependent on lab
• Attention to drug supply security and adherence vital for epidemic control
• Social context needs loud voices
Thank you
27th International Workshop on HIV Drug Resistance and Treatment Strategies

Monday, 22 October to Tuesday, 23 October 2018
Gallagher Convention Centre, Midrand, Johannesburg, South Africa

www.hivresistance2018.co.za