Testing and treatment of HIV within 24 hours: is it viable?

Dr Nneka Nwokolo
56 Dean Street, Chelsea and Westminster Hospital
We make Virginia Slims especially for women because they are biologically superior to men.

That’s right, superior. Women are more resistant to starvation, fatigue, exposure, shock, and illness than men are. Women have two “X” chromosomes in their sex cells, while men have only one “X” chromosome and a “Y” chromosome... which some experts consider to be the inferior chromosome.

They are also less inclined than men to congenital baldness, Albright’s of the eyes, improperly developed sweat glands, color blindness of the red-green type, clay blindness, defective hair follicles, defective iris, defective tooth enamel, double eyelashes, skin cysts, shortsightedness, night-blindness, noma, drome, retinal detachment, and white or black locks of hair.

In view of these and other facts, the makers of Virginia Slims feel it highly inappropriate that women continue to use the fat, stubby cigarettes designed for men.

Virginia Slims.

Slimmer than the fat cigarettes men smoke.

With rich Virginia flavor women like.

You’ve come a long way, baby.
Proportion of people who accessed HIV care who are on treatment and virally suppressed, UK: 2015

- People who accessed HIV care (n=88,800): 100%
- On treatment (n=84,800): 96%
- Virally suppressed (n=79,800): 89%
How has this happened?

• Newer ARVs from existing classes with better tolerability
• Newer ARV classes
• Better evidence base (START, TasP and “Cure” studies)
• Better accessibility (generics)
• Life expectancy approaching normal
BHIVA monitoring guidelines 2016

Now

HIV diagnosis

Baseline tests appointment within 2 weeks:
VL, CD4, resistance test, HLA; hepatitis screens, haematology and biochemistry; vaccination status; STI screening

Adjustment period

Start treatment according to baseline bloods and guidelines
The patient says:

- I’m ready to start today
- I don’t want to be infectious
- I want modern once a day treatment
- I want to preserve my immune system
- Will this lead to cure?
But

I’m ready to start today

I don’t want to be infectious

I want modern once a day treatment

I want to preserve my immune system

Will this lead to cure?

Is it safe?

What about resistance?

Am I pressurizing the patient?
Aims of treatment

• Prevention of disease progression

• Reduction in onward transmission

• Better retention in care
challenging the STATUS QUO
Is it feasible to start ART within a day of diagnosis?

• Data from research studies suggest that it is (Ananworanich et al. 2013; Thumath et al. 2015; Rosen et al. 2015; Koenig et al. 2016)

• Virtually no “real world” data
What do we know?

• Haiti study

• “Real world” San Francisco RAPID programme

• “Real world” 56 Dean Street experience
Superior Outcomes with Same-Day HIV Testing and ART Initiation

Serena Koenig, MD, MPH
GHESKIO, Haiti
Brigham and Women’s Hospital, USA
Current Situation

• High attrition rates from HIV testing to ART initiation, resulting in delays in treatment
  – Increased mortality
  – Diminished recovery of CD4 cells
  – Higher cost of treatment for opportunistic infections (for those with access to advanced hospital care)
  – Ongoing HIV transmission

• Removal of requirements for multiple pre-ART visits may decrease pre-ART attrition
Objectives and Participants

- **Objective:** To compare standard vs. same-day ART

- **Inclusion criteria:**
  - Non-pregnant ART-naïve adults
  - WHO stage 1 or 2 disease
  - CD4 count ≤500 cells/mm³

- **Exclusion**
  - CXR consistent with TB or pneumonia
  - Failed ART readiness questionnaire
  - Planned to transfer care during study period
Schedule of Visits

- **Standard group**
  - Days 7, 14, and 21: Physician/social worker visits
  - Day 21: ART initiation
  - Week 5: Physician/social worker visits

- **Same-day ART group**
  - Day 1: Counseling and ART initiation
  - Days 3, 10, and 17: Physician/social worker visits
  - Day 24: Physician visit

- **Only difference was timing of ART initiation**
## 12 months

<table>
<thead>
<tr>
<th></th>
<th>Standard Group (n=285)</th>
<th>Same-Day ART Group (n=279)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiated ART</td>
<td>262 (92%)</td>
<td>279 (100%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Died</td>
<td>19 (7%)</td>
<td>8 (3%)</td>
<td>p=0.035</td>
</tr>
<tr>
<td>Alive and in care</td>
<td>201 (71%)</td>
<td>224 (80%)</td>
<td>p=0.007</td>
</tr>
<tr>
<td>In care with VL &lt;50 copies/ml</td>
<td>120 (42%)</td>
<td>151 (54%)</td>
<td>p=0.004</td>
</tr>
<tr>
<td>In care with VL &lt;1000 copies/ml</td>
<td>143 (50%)</td>
<td>171 (61%)</td>
<td>p=0.008</td>
</tr>
</tbody>
</table>
Conclusions

• Same-day ART initiation is feasible and beneficial
  – Improves retention with virologic suppression
  – Decreases mortality
• We believe same-day ART increases the sense of hope, optimism, and connectedness to health care providers
• The new WHO recommendations to provide universal ART should facilitate same-day test and treat
San Francisco RAPID programme

• Clinic cohort of newly diagnosed patients between June 2013 and December 2014

• Subset of individuals with acute or recent infection (<6m) or CD4 <200; OI or seronegative partner managed according to RAPID care initiation protocol

Pilcher et al. JAIDS 2016
RAPID programme (I)

- Same day access to HIV provider (doctor or nurse practitioner); taxi vouchers
  - HIV education
  - risk reduction and sexual health advice
  - discussion about benefits of ART/assessment of contraindications
  - offer of immediate start
RAPID programme (II)

- Baseline bloods (often no results prior to treatment)

- Accelerated insurance approval process

- Pre-approved regimens based on local transmitted resistance patterns (TDF/FTC and dolutegravir)

- 5-day starter pack while insurance being arranged

- DOT for 1st dose

- Telephone follow-up within 1st 7 days (lab results, adherence, side-effects)
## RAPID programme (III)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RAPID N=39</th>
<th>Non-RAPID N=47</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>31.6</td>
<td>34.8</td>
<td>0.14</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>39 (100)</td>
<td>44 (93.6)</td>
<td>0.11</td>
</tr>
<tr>
<td>Female</td>
<td>0</td>
<td>3 (6.4%)</td>
<td></td>
</tr>
<tr>
<td>Baseline CD4 (mean)</td>
<td>474 cells/mm³</td>
<td>417 cells/mm³</td>
<td>0.38</td>
</tr>
<tr>
<td>Baseline VL (mean) log10 (cpm)</td>
<td>4.89 (77,600)</td>
<td>4.49 (30,900)</td>
<td>0.082</td>
</tr>
<tr>
<td>Acute infection (RNA+/Ab-)</td>
<td>8/32 (25%)</td>
<td>2/32 (6.3%)</td>
<td>0.041</td>
</tr>
<tr>
<td>Recent infection (Ab- within 6/12)</td>
<td>24/32 (75%)</td>
<td>9/32 (28.1%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
## Rapid programme (IV)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RAPID</th>
<th>Non-RAPID</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transmitted resistance (any)</td>
<td>8/32 (25%)</td>
<td>18/43 (41.9%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Days to ART initiation (range)</td>
<td>1 (0-5)</td>
<td>10 (7-17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time from diagnosis to viral suppression &lt;200 cpm in days (range)</td>
<td>65 (52-119)</td>
<td>170 (79-363)</td>
<td>0.009</td>
</tr>
<tr>
<td>ART regimen initiated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INSTI</td>
<td>35/39 (89.7%)</td>
<td>32/38 (84.2%)</td>
<td>0.47</td>
</tr>
<tr>
<td>PI</td>
<td>5/39 (12.8%)</td>
<td>5/38 (13.2%)</td>
<td>0.97</td>
</tr>
<tr>
<td>NNRTI</td>
<td>0/39</td>
<td>3/38 (7.9%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Retention in care</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss to follow-up</td>
<td>4/39 (10.3%)</td>
<td>7/47 (14.9%)</td>
<td>0.52</td>
</tr>
</tbody>
</table>

Pilcher et al. JAIDS 2016
RAPID start

• Feasible
• Acceptable
• Well tolerated
• Shorter time to viral suppression
• No negative impact on engagement in care

Pilcher et al. JAIDS 2016
RAPID start

- Resource intensive
  - social/psychological (insurance, housing, substance use/mental health support)
  - medical (need for early review of regimens based on resistance test results etc. when available)

Pilcher et al. JAIDS 2016
“Real-life” experience from a Central London HIV clinic
56 Dean Street
56DS - Rapid start in AHI

All patients with AHI May 2014 – October 2015

AHI defined as:

A – Detectable plasma HIV RNA only

B – Detectable plasma HIV RNA + p24 antigen; negative HIV-EIA

C – HIV-EIA changing from negative to positive within 6 weeks

Girometti et al. Antivir ther 2016
## Results

<table>
<thead>
<tr>
<th>Total 113</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A (plasma RNA only)</td>
<td>7 (6%)</td>
</tr>
<tr>
<td>Group B (RNA + p24)</td>
<td>77 (68%)</td>
</tr>
<tr>
<td>Group C (evolving HIV EIA)</td>
<td>29 (26%)</td>
</tr>
</tbody>
</table>
Outcomes

• All patients seen in medical appointment within 2 weeks
• All patients offered ART at 1\textsuperscript{st} appointment
• 26 (23\%) did not start at 1\textsuperscript{st} visit
  - 18 declined immediate treatment
  - (6 lost to follow-up; no info on 2)
• Data on 87 (77\%)
### Demographics & outcomes according to regimen (I)

<table>
<thead>
<tr>
<th></th>
<th>All N=87</th>
<th>INI (%) N=36 (41.4)</th>
<th>PI (%) N=20 (23.0)</th>
<th>NNRTI (%) N=22 (25.3)</th>
<th>QUAD (%) N=9 (10.3)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years median (range)</strong></td>
<td>34 (28-40)</td>
<td>34 (28-43)</td>
<td>35 (31-43)</td>
<td>32 (27-37)</td>
<td>26 (33-39)</td>
</tr>
<tr>
<td><strong>p24Ag only</strong></td>
<td>56 (64.4%)</td>
<td>21 (58.3%)</td>
<td>12 (60%)</td>
<td>15 (68.2%)</td>
<td>8 (88.9%)</td>
</tr>
<tr>
<td><strong>CD4 count cells/mm³</strong></td>
<td>483 (351-701)</td>
<td>524 (385-698)</td>
<td>459 (319-700)</td>
<td>541 (306-702)</td>
<td>362 (319-559)</td>
</tr>
<tr>
<td><strong>HIV-1 RNA median log10 cpm (IQR)</strong></td>
<td>6.45 (5.87-6.83)</td>
<td>6.23 (5.42-6.75)</td>
<td>6.76 (6.04-7.08)</td>
<td>6.07 (5.57-6.75)</td>
<td>6.88 (6.69-7.57)</td>
</tr>
</tbody>
</table>

**QUAD** – regimen containing TDF/FTC + DRV/r + raltegravir

Girometti et al. Antivir ther 2016
### Demographics & outcomes according to regimen (I)

<table>
<thead>
<tr>
<th>Demographics/Outcome</th>
<th>All N=87</th>
<th>INI (%) N=36 (41.4)</th>
<th>PI (%) N=20 (23.0)</th>
<th>NNRTI (%) N=22 (25.3)</th>
<th>QUAD (%) N=9 (10.3)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td>34 (28-40)</td>
<td>34 (28-43)</td>
<td>35 (31-43)</td>
<td>32 (27-37)</td>
<td>26 (33-39)</td>
</tr>
<tr>
<td><strong>p24Ag only</strong></td>
<td>56 (64.4%)</td>
<td>21 (58.3%)</td>
<td>12 (60%)</td>
<td>15 (68.2%)</td>
<td>8 (88.9%)</td>
</tr>
<tr>
<td><strong>CD4 count cells/mm³</strong></td>
<td>483 (351-701)</td>
<td>524 (385-698)</td>
<td>459 (319-700)</td>
<td>541 (306-702)</td>
<td>362 (319-559)</td>
</tr>
<tr>
<td><strong>HIV-1 RNA median log10 cpm (IQR)</strong></td>
<td>6.45 (5.87-6.83)</td>
<td>6.23 (5.42-6.75)</td>
<td>6.76 (6.04-7.08)</td>
<td>6.07 (5.57-6.75)</td>
<td>6.88 (6.69-7.57)</td>
</tr>
</tbody>
</table>

**QUAD** – regimen containing TDF/FTC + DRV/r + raltegravir

Girometti et al. Antivir ther 2016
## Demographics & outcomes according to regimen (II)

<table>
<thead>
<tr>
<th></th>
<th>All N=87</th>
<th>INI (%) N=36 (41.4)</th>
<th>PI (%) N=20 (23.0)</th>
<th>NNRTI (%) N=22 (25.3)</th>
<th>QUAD (%) N=9 (10.3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median days from diagnosis to 1st med appt (IQR)</td>
<td>14.2 (7-17)</td>
<td>16.1</td>
<td>10.3</td>
<td>14.4</td>
<td>14.8</td>
</tr>
<tr>
<td>Median days from diagnosis to ART start (IQR)</td>
<td>20 (13-29)</td>
<td>21.5 (14-35)</td>
<td>11.5 (p=0.003) (6.2-18.7)</td>
<td>23.5 (15.7-30)</td>
<td>17 (14-24)</td>
</tr>
<tr>
<td>Median days to VL &lt;200cpm (IQR)</td>
<td>74 (35-106)</td>
<td>41 (p&lt;0.05) (28.5-68.5)</td>
<td>106 (84-134)</td>
<td>77 (49-116)</td>
<td>81.5 (63.7-95.2)</td>
</tr>
</tbody>
</table>

QUAD – regimen containing TDF/FTC + DRV/r + raltegravir

Girometti et al. Antivir ther 2016
Outcomes (II)

- No discontinuations at 24 weeks
- 85% VL <200 at 16 weeks
- 99% VL <200 at 24 weeks (1 individual with baseline VL $7.15 \log_{10}$ (14m cpm)
56DS Rapid Start pilot

• Can we offer treatment within 48 hours?
• All new diagnoses
• 1\textsuperscript{st} July – 2\textsuperscript{nd} September 2016
• 53 new diagnoses
• (2 DNAs; 4 moved abroad)
First appointment n=47

• Mean 7 days (range 0-20 days)
• All offered ART
• 12 did not start at first appointment
  - 4 wanted to reflect
  - 2 baseline resistance – referred to Virtual Clinic
  - 6 waited for resistance test
• 10/35 (29%) started within 48 hours
## 56DS Rapid Start pilot

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Within 48 hours</th>
<th>&gt; 48 hours</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=10</td>
<td>N=25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (mean)</td>
<td>32.7</td>
<td>34.3</td>
<td>0.62</td>
</tr>
<tr>
<td>Sex (%)</td>
<td>100</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline CD4 (mean) cells/mm³</td>
<td>359</td>
<td>521</td>
<td>0.06</td>
</tr>
<tr>
<td>Baseline VL (mean) cpm log10</td>
<td>6.07 (1,170,000)</td>
<td>5.22 (167,000)</td>
<td>0.08</td>
</tr>
<tr>
<td>Recent infection (RITA) %</td>
<td>56% (5/9*)</td>
<td>42% (10/24*)</td>
<td>0.48</td>
</tr>
</tbody>
</table>

*RITA not sent in one patient from each group
## 56DS Rapid Start pilot

<table>
<thead>
<tr>
<th></th>
<th>Within 48 hours N=10</th>
<th>&gt;48 hours N=25</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transmitted resistance (any)</td>
<td>3/10 (30%)</td>
<td>7/24** (29%)</td>
<td>0.96</td>
</tr>
<tr>
<td>Mean days to start (range)</td>
<td>1 (0-2)</td>
<td>9 (3-20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ART regimen initiated</td>
<td>0</td>
<td>9 (36%)</td>
<td>0.026</td>
</tr>
<tr>
<td>INSTI</td>
<td>10 (100%)</td>
<td>13 (52%)</td>
<td></td>
</tr>
<tr>
<td>PI</td>
<td>0</td>
<td>3 (12%)</td>
<td></td>
</tr>
<tr>
<td>NNRTI</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Retention in care</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Loss to follow-up</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

**One resistance test failed to amplify
Challenges to same-day ART initiation

• Service capacity

• Acceptability to clinicians

• Acceptability to patients

• Infrastructure – pharmacy capacity, health adviser support
Summary

- International guidelines recommend treatment for all individuals with HIV

- Early treatment particularly valuable in limiting reservoir in acute infection and preventing transmission

- In some settings early treatment associated with significant improvements in linkage to care
Conclusions

• Starting ART at diagnosis is challenging but feasible
• Acceptable to patients
• Parallel rather than serial interventions
• Retention in care in UK is excellent, early treatment may reinforce this
• Optimal regimen needs to be identified PI vs INI
Final thoughts

Much more research needed into test and treat within 24 hours
90-90-90
An ambitious treatment target to help end the AIDS epidemic

#PrEPWORKS
The time for debate on the effectiveness of PrEP is over.
Acknowledgments

• Dr Gary Whitlock
• Dr Chloe Orkin
• Dr Nicolo Girometti
• Dr Sarah Fidler
• Dr Alan McOwan
• 56 Dean Street staff
• Our patients