The leaky cascade: where exactly are patients lost to follow-up

Andrew Boulle, 1,2

1) Health Impact Assessment, Department of Health, Western Cape Province of South Africa
2) School of Public Health and Family Medicine, University of Cape Town, South Africa
The cascade as a health system lens: USA 2010

- >1.1 million HIV-infected people in the USA
- 902,000 diagnosed as HIV+ (82%)
- 726,000 linked to HIV care (66%)
- 407,000 retained in HIV care (37%)
- 363,000 prescribed ART (33%)
- 275,000 with a suppressed viral load (<200 copies/ml) (25%)

Fauci, Nature Immunology 2013
The cascade in South Africa: 2012

100%

6.4 million living with HIV

67% of all South Africans had tested
But only 42 & 47% +/- knew status

Linked to care – not known

Retained in care

On ART

VLS

? 70%2,3

? 60%

? 50%

36%

>14%

1. Nat HIV survey 2012
2. Johnson p.c.
3. MSF Mbongalwane survey
4. SANAC annual report 2014
MSF Mbongolwane survey 2013

<table>
<thead>
<tr>
<th>Stage</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosed</td>
<td>74.8%</td>
</tr>
<tr>
<td>Linked to care</td>
<td>65.4%</td>
</tr>
<tr>
<td>Initiated on ART</td>
<td>57.1%</td>
</tr>
<tr>
<td>Remained on ART</td>
<td>52.1%</td>
</tr>
<tr>
<td>Virally suppressed</td>
<td>49.3%</td>
</tr>
</tbody>
</table>
Rosen, PLoS Medicine 2011
Components of the cascade for averting mortality

Proportion of deaths

- Improved wellness care
- More testing and linkage to care
- Clinical focus on advanced disease
- Retention
- Improved routine ART care
- Total

Category of potential preventive intervention

Boulle, World Congress of Epidemiology 2014
Key concepts in a dynamic system

- Incidence/eligibility
- Enrolment capacity
- Loss to ART
3 concepts – show mortality slide

Incidence/eligibility

Enrolment capacity

Fast-track or special vigilance

Loss to ART
3 concepts – show mortality slide

- Incidence/eligibility
- Enrolment capacity
- Fast-track or special vigilance
- Loss to ART

1. Enrolment ratio
<table>
<thead>
<tr>
<th>Year</th>
<th>Numbers initiating ART ('000)</th>
<th>ART enrolment ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Males 15+</td>
</tr>
<tr>
<td>2000/01</td>
<td>6.7</td>
<td>2.7</td>
</tr>
<tr>
<td>2001/02</td>
<td>10.4</td>
<td>4.3</td>
</tr>
<tr>
<td>2002/03</td>
<td>12.2</td>
<td>4.9</td>
</tr>
<tr>
<td>2003/04</td>
<td>24.7</td>
<td>8.4</td>
</tr>
<tr>
<td>2004/05</td>
<td>71.2</td>
<td>22.4</td>
</tr>
<tr>
<td>2005/06</td>
<td>139.9</td>
<td>43.1</td>
</tr>
<tr>
<td>2006/07</td>
<td>171.4</td>
<td>52.3</td>
</tr>
<tr>
<td>2007/08</td>
<td>242.2</td>
<td>74.5</td>
</tr>
<tr>
<td>2008/09</td>
<td>380.2</td>
<td>118.0</td>
</tr>
<tr>
<td>2009/10</td>
<td>453.1</td>
<td>137.5</td>
</tr>
<tr>
<td>2010/11</td>
<td>582.9</td>
<td>190.6</td>
</tr>
<tr>
<td>2011/12</td>
<td>681.4</td>
<td>207.5</td>
</tr>
</tbody>
</table>
3 concepts – show mortality slide

1. Enrolment ratio
   Enrolment capacity

2. Audit implementation of guidelines for priority patients at high risk of mortality
CD4 counts and ART initiation in the WC RSA, 2012

- **263,193** total CD4 tests
- **198,666** unique individuals
- **116,720** already on ART
- **81,946** pre-ART

**22,960** CD4 >=350

- **40,289** previously tested
- **17,329** with CD4<350 (43%)

**41,657** first ever CD4 count

- **22,447** with CD4<350 (54%)

**19,210** CD4 >=350

**Combined 39,776** eligible* for ART (48.5%)

<table>
<thead>
<tr>
<th>CD4</th>
<th>N (%)</th>
<th>ART</th>
<th>Days to ART – median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>3807</td>
<td>63%</td>
<td>33 (20-69)</td>
</tr>
<tr>
<td>50-99</td>
<td>4157</td>
<td>68%</td>
<td>42 (23-92)</td>
</tr>
<tr>
<td>100-199</td>
<td>10,650</td>
<td>65%</td>
<td>51 (28-126)</td>
</tr>
<tr>
<td>200-349</td>
<td>21,162</td>
<td>62%</td>
<td>63 (33-155)</td>
</tr>
<tr>
<td>350-499</td>
<td>19,221</td>
<td>30%</td>
<td>309 (181-465)</td>
</tr>
<tr>
<td>&gt;=500</td>
<td>22,949</td>
<td>14%</td>
<td>397 (237-538)</td>
</tr>
</tbody>
</table>

* Still need to account for patients with TB and pregnant with CD4 counts >=350 cells/µl
3 concepts – show mortality slide

1. Enrolment ratio

2. Audit implementation of guidelines for priority patients at high risk of mortality

3. Aggressive focus on ART retention
Typical output on temporal trends in loss to follow-up

(b) LTFU by year of ART initiation 0-5 years follow-up

Cornell, AIDS 2010
Returning to care after loss to follow-up

Time to returning to care in patients LTF

Based on 6,000 patients lost to follow-up for at least 6 months in Khayelithsa, South Africa
Simulating cumulative LTF with constant loss and re-entry rates

Cumulative loss to follow-up

Time since first starting ART (years)

- Started ART 2003-4
- Started ART 2005-6
- Started ART 2007-8
- Started ART in 2009
- Started ART in 2010

Johnson, AJE, in press
Comparing trends to first versus current loss to care status

Loss to follow-up or death by calendar period

Time to death or first LTF

Time to death or LTF as defined mid-2012

Based on 30,000 patients from Khayelithsa, South Africa
## South African national

<table>
<thead>
<tr>
<th>Reporting year&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Adults FY 2008/09</th>
<th>Adults FY 2012/13</th>
<th>Children FY 2008/09</th>
<th>Children FY 2012/13</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients evaluated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 year</td>
<td>61731</td>
<td>177301</td>
<td>4462</td>
<td>7681</td>
</tr>
<tr>
<td>2 years</td>
<td>40206</td>
<td>114973</td>
<td>3104</td>
<td>7322</td>
</tr>
<tr>
<td>3 years</td>
<td>26695</td>
<td>70958</td>
<td>2360</td>
<td>4957</td>
</tr>
<tr>
<td>4 years</td>
<td>14997</td>
<td>54460</td>
<td>1352</td>
<td>3930</td>
</tr>
<tr>
<td>5 years</td>
<td>6019</td>
<td>34929</td>
<td>489</td>
<td>2581</td>
</tr>
<tr>
<td>Retention in care</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 year</td>
<td>74.9%</td>
<td>71.7%</td>
<td>83.7%</td>
<td>79.3%</td>
</tr>
<tr>
<td>2 years</td>
<td>67.6%</td>
<td>58.1%</td>
<td>82.1%</td>
<td>71.6%</td>
</tr>
<tr>
<td>3 years</td>
<td>64.0%</td>
<td>50.6%</td>
<td>84.0%</td>
<td>67.7%</td>
</tr>
<tr>
<td>4 years</td>
<td>64.5%</td>
<td>46.6%</td>
<td>86.2%</td>
<td>65.7%</td>
</tr>
<tr>
<td>5 years</td>
<td>64.1%</td>
<td>42.2%</td>
<td>83.5%</td>
<td>68.2%</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reporting year refers to the year in which patients reach a duration on treatment. Patients reaching 1 year on treatment in a given reporting year will have started ART in the previous year, whereas those who could have reached 5 years on ART will have started ART 5 years previously.
Summary

- Moving target and both cross-sectional and longitudinal perspectives are needed
- Disjuncture between routine program and survey data
- Interventions to increase enrolment require concomitantly increases in enrolment capacity
- Interventions may be more effective if focussed on patients at high risk of clinical events
- Losses to care on ART probably already account for more morbidity and mortality than for patients who have never been enrolled onto ART
Acknowledgements

- CIDER colleagues
- Provinicial and National DoH HAST & M&E teams
- SANAC and HST
- Staff and patients of the programs who’s data are included
Western Cape Government
Health

Thank you
Impact of known transfers on ART-mortality estimates

Cornell, JAIDS, in press

<table>
<thead>
<tr>
<th>Number at risk</th>
<th>Crude</th>
<th>With LTF</th>
<th>With TFO</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>19481</td>
<td>1675</td>
<td>1716</td>
</tr>
<tr>
<td>12</td>
<td>(969)</td>
<td>(11504)</td>
<td>(1675)</td>
</tr>
<tr>
<td>24</td>
<td>(11404)</td>
<td>(11504)</td>
<td>(6115)</td>
</tr>
</tbody>
</table>

Cornell, JAIDS, in press