State of the Art for ART for Prevention

Wafaa El-Sadr, MD, MPH
ICAP-Columbia University
Global Scale-Up of HIV Treatment

End of 2002: 0.0
End of 2003: 0.0
End of 2004: 0.4
End of 2005: 0.7
End of 2006: 1.2
End of 2007: 2.0
End of 2008: 2.5
End of 2009: 4.0
End of 2010: 5.5

Millions of people on antiretroviral therapy at the end of each year.
Deaths in PEPFAR-Supported Countries in Africa

Mortality per 1,000 adults

- PEPFAR Supported

Adapted Bendavid et al. CROI2012
Deaths in PEPFAR-Supported Countries in Africa

Deaths per 1,000 adults


PEPFAR Supported

Other countries

Adapted Bendavid et al. CROI 2012
6-25 million

Additional people who need treatment
2.5 million people infected every year
7,000
New infections every day
1,000 in children
We can’t treat our way out of this epidemic
ART for Prevention: The Evidence

HPTN 052 Study
- 1,763 sero-discordant couples (97% heterosexual)
- HIV infected partners: 890 men, 873 women
- 39 HIV transmissions
  - 28 linked HIV transmissions
  - 11 unlinked

- Immediate ART: 1 transmission
- Deferred ART: 27 transmissions

☑️ 96% Protection
We can treat our way out of this epidemic
HIV Continuum

- Test
  - HIV Positive
- Link
- Engage, Counsel, Monitor, and Support
  - HIV Care (PRE-ART)
- ART Eligible
- Retain, Counsel, Monitor, and Support
  - ART
- Adherence and Viral Suppression

McNairy et al, AIDS 2012
Challenges in Achieving Potential of ART for Prevention

- Unaware of HIV Status
- Late Diagnosis of HIV Disease
- Failures in Linkage and Retention in Care
- Late Initiation of ART
- Inability to Achieve and Maintain Viral Suppression
HIV Testing - Kenya (15-64 yrs) 2007 & 2012

KAIS Preliminary Findings 2012
Awareness of HIV Positive Status -- Kenya (15-64 yrs)

- 2007:
  - 56% never tested
  - 28% reported HIV negative
  - 16% reported positive

- 2012:
  - 53% unaware of HIV Infection
  - 47% reported HIV positive
  - 37% reported HIV negative
  - 16% never received test result

84% Unaware of HIV Infection
56% never tested
28% reported HIV negative
16% reported positive
37% reported HIV negative
47% reported HIV positive
16% never received test result
Kais 2012
HIV Diagnosis, ART Coverage and Viral Suppression – MSM in UK

Brown et al. HIV Medicine 2013
Viral load <1500 copies/mL, 65%  
Undiagnosed  
62% (n=8700)  
Untreated CD4 count <350 cells/µL  
5% (n=700)  
Untreated CD4 count 350-500 cells/µL  
12% (n=1700)  
Untreated CD4 count >500 cells/µL  
16% (n=2300)  
Treated  
5% (n=700)  
Brown et al. HIV Medicine 2013
Lack of Awareness of HIV Infection: US MSM tested, by race/ethnicity
21 U.S. cities, 2008

<table>
<thead>
<tr>
<th>Race/ethnicity</th>
<th>Total Number</th>
<th>HIV-infected and unaware</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian/Pacific Islander</td>
<td>140</td>
<td>2.9%</td>
</tr>
<tr>
<td>Black, non-Hispanic</td>
<td>1,674</td>
<td>14.5%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1,850</td>
<td>6.7%</td>
</tr>
<tr>
<td>White, non-Hispanic</td>
<td>3,163</td>
<td>3.0%</td>
</tr>
<tr>
<td>Other</td>
<td>33</td>
<td>10.2%</td>
</tr>
</tbody>
</table>

CDC. National HIV Behavioral Surveillance. *MMWR 2011; 60:694-699*
Mean CD4+ Cell Count Over Time in Developed Countries

N= 44 studies

CD4-307.Q+1.5 (year)
CD4 + Cell Counts at HIV Diagnosis—US HIV Outpatient Study (HOPS), 2000-2009

Nationally representative sample of 18,169 adults (18-49 yrs)
Population CD4+ Count Distribution—Swaziland

Overall

- 0-199: 11%
- 200-349: 19%
- 350-499: 24%
- >500: 46%

Not on ART

- 0-199: 13%
- 200-349: 19%
- 350-499: 25%
- >500: 43%

Azih et al. CROI 2013
Median CD4+ Count and Late Enrollment in Care Over Time

Hoffman et al, CROI 2013

Median CD4 cell count at enrollment

Percent late

2006: CD4<350 or WHO 3/4

P trend < 0.0001

CD4<350 or WHO 3/4
Of 100 HIV+ patients, on average, 25 started ART.
Of ART-eligible patients 62% (95% CI 55.2-70.7%) started ART.

Mugglin et al. CROI 2012,
Patient Enrolment into HIV Care and Treatment within 90 Days of HIV Diagnosis in Eight Rwandan Health Facilities: A Review of Facility-Based Registers

- 8 health clinics
- 492 patients testing HIV+ from March-May 2009
- Testing sites: ANC, VCT, TB, OPD
- Median age 29 years, median CD4+ 387 cells/μL

![Bar chart showing patient enrollment data.](chart.png)
Retention in ART Programs

36 cohorts
226,307 patients
All losses except transfers

Retention:
- 6 months: 86.1%
- 12 months: 80.2%
- 24 months: 76.8%
- 36 months: 72.3%

Fox and Rosen, Trop Med Int Health 2010
## Barriers to Care and Predictor of Attrition: Systematic Review

Adapted Govindasamy et al. AIDS June 2012

<table>
<thead>
<tr>
<th>Factor</th>
<th>Predictor of Attrition</th>
<th>Barrier to Care</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Economical</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transport costs</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Distance</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Unable to make time (work)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Food Shortage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient time constraints</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td><strong>Psycho-Social</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stigma/fear of disclosure</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Fear of drug toxicities</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Perceived good health</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td><strong>Health Systems</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long clinic waiting times</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Poor service from HCWs</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Shortage of HCWs</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Inconvenient clinic hours</td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>
Retention in HIV Care (pre-ART) by Initial CD4+ Cell Count

- CD4+ 201-350
- CD4+ 351-500
- CD4+ >500

Proportion returning for CD4 Cell Count (%)

Adapted--Lessells et al, JAIDS 2011
LTF and mortality among pre-ART adult patients at 41 facilities in Rwanda (N=31,027)

<table>
<thead>
<tr>
<th></th>
<th>6 months</th>
<th>12 months</th>
<th>24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTF</td>
<td>6.6% (95%CI 6.3-6.9)</td>
<td>8.6% (95% CI 8.3-9.0)</td>
<td>11.2% (95%CI 10.9-11.6)</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.5% (95%CI 1.4-1.7)</td>
<td>2.1% (95%CI 1.9-2.2)</td>
<td>2.7% (95%CI 2.5-2.8)</td>
</tr>
</tbody>
</table>

Teasdale et al, CROI 2013
## Selected demographic and clinical characteristics and pre-ART LTF (N=31,027)

<table>
<thead>
<tr>
<th></th>
<th>aSHR*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>1.27</td>
<td>1.08-1.51</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21-30</td>
<td>1.46</td>
<td>1.30-1.64</td>
</tr>
<tr>
<td>31-40</td>
<td>1.09</td>
<td></td>
</tr>
<tr>
<td>41-50</td>
<td>0.84</td>
<td>0.73-0.95</td>
</tr>
<tr>
<td>Single vs. married</td>
<td>1.30</td>
<td>1.09-1.56</td>
</tr>
<tr>
<td>WHO Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>1</td>
<td>Ref.</td>
</tr>
<tr>
<td>II</td>
<td>0.69</td>
<td>0.55-0.87</td>
</tr>
<tr>
<td>III</td>
<td>0.64</td>
<td>0.48-0.85</td>
</tr>
<tr>
<td>IV</td>
<td>0.35</td>
<td>0.20-0.59</td>
</tr>
<tr>
<td>CD4+ count</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;100</td>
<td>0.19</td>
<td>0.13-0.30</td>
</tr>
<tr>
<td>100-199</td>
<td>0.20</td>
<td>0.15-0.27</td>
</tr>
<tr>
<td>200-349</td>
<td>0.35</td>
<td>0.28-0.45</td>
</tr>
<tr>
<td>≥350</td>
<td>1</td>
<td>Ref.</td>
</tr>
</tbody>
</table>

Teasdale et al, CROI 2013
LTF and mortality among adults on ART at 41 facilities in Rwanda (N=17,212)

Loss to follow-up in ART patients

Mortality in ART patients

<table>
<thead>
<tr>
<th></th>
<th>6 months</th>
<th>12 months</th>
<th>24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTF</td>
<td>1.9% (95%CI 1.8-1.9)</td>
<td>2.9% (95%CI 2.8-2.9)</td>
<td>4.4% (95%CI 4.4-4.5)</td>
</tr>
<tr>
<td>Mortality</td>
<td>3.4% (95%CI 3.4-3.5)</td>
<td>4.7% (95%CI 4.7-4.8)</td>
<td>6.3% (95%CI 6.2-6.4)</td>
</tr>
</tbody>
</table>

Teasdale et al, CROI 2013
### Selected demographic and clinical characteristics and LTF among adults on ART (N=17,212)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>aHR(^*)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>1.39</td>
<td>1.17-1.67</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21-30</td>
<td>1.4</td>
<td>1.16-1.67</td>
</tr>
<tr>
<td>31-40</td>
<td>1</td>
<td>Ref.</td>
</tr>
<tr>
<td>41-50</td>
<td>0.81</td>
<td>0.72-0.92</td>
</tr>
<tr>
<td>Single vs. married</td>
<td>1.65</td>
<td>1.2-2.3</td>
</tr>
<tr>
<td>CD4 count</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;100</td>
<td>0.64</td>
<td>0.44-0.92</td>
</tr>
<tr>
<td>100-199</td>
<td>0.68</td>
<td>0.51-0.91</td>
</tr>
<tr>
<td>200-349</td>
<td>0.63</td>
<td>0.51-0.79</td>
</tr>
</tbody>
</table>
| >350                    | 1          | reference   

\(^*\)adjusted hazard ratio from Cox proportional hazards risk models

Teasdale et al, CROI 2013
Willingness to Initiate ART--SA

• 7287 adult patients HIV tested
  – 2,562 (35%) HIV-infected
    • 743 (29%) eligible for ART
  – 148 (20%) refused referral to initiate ART,
    • most (92%) refused again two months later

– Characteristics of those who refused:
  • Median CD4+ count: 110 cells/mm$^3$
  • Factors associated with refusal:
    – Single: AOR: 1.8 (1.06-3.06)
    – TB: AOR: 3.5 (1.55-6.61)

– Most common reason for refusal was feeling well (35%)

Katz et al AIDS 2011
HPTN 052: Reasons for Declining ART at 1 Year and 1.5 Years of Follow-up

<table>
<thead>
<tr>
<th>Reasons for Decline</th>
<th>N = 101 30 Jun 2012 (1 Year of Follow-up) [N (%)]</th>
<th>N = 73 31 Dec 2012 (1.5 Years of Follow-up) [N (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Believes CD4 is too high</td>
<td>58 (57%)</td>
<td>42 (58%)</td>
</tr>
<tr>
<td>Not ready to begin ART (including)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Feels healthy</td>
<td>28 (28%)</td>
<td>20 (27%)</td>
</tr>
<tr>
<td>• Doesn’t want to take/commit to ART</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Fear of side effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Family problems</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Mentally unprepared</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Mobile lifestyle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• In denial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wants to discuss decision with family/friends</td>
<td>5 (5%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Plans to begin at a later date</td>
<td>3 (3%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Still deciding</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Other/unknown reasons (including)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Lost-to-follow-up</td>
<td>6 (6%)</td>
<td>5 (7%)</td>
</tr>
<tr>
<td>• Religious belief</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Wants guaranteed drug supply after study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Spouse did not allow</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Gamble et al, CROI 2013
HOW?
Uptake of Community HIV Testing and Counseling

Pooled percentage accepting testing

- Index: N=12,052
- Self: N=1,839
- Mobile: N=79,475
- Door-to-door: N=555,267
- Workplace: N=62,406
- School: N=2,593

Suthar et al PLoS 2013
Novel Approaches for Linkage & Retention

• **Novel Interventions:** POC CD4\(^1-2\), case manager\(^3\), SMS, care bags, financial/transport incentive\(^4\)

• **Need for combination interventions:**
  – Use of multiple biomedical, structural and psychosocial barriers to testing and care

2. Faal et al. JAIDS 2011
3. Gardner et al. AIDS 2005
4. Emenyonu et al. CROI 2010
8. Van Rooyan CROI 2012
The HIV care continuum: no partial credit given

Margaret L. McNairy\textsuperscript{a,b,c} and Wafaa M. El-Sadr\textsuperscript{a,b}

McNairy et al, AIDS 2012
WHAT?
Efficacy to Effectiveness
Contribution by Key Populations to the HIV Epidemic

Proportion of new infections by group

---

UNAIDS, 2010
<table>
<thead>
<tr>
<th>Scenario</th>
<th>Mean Incidence 2006-2010/100pyr</th>
<th>% difference Versus actual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actual</td>
<td>0.53</td>
<td>---</td>
</tr>
<tr>
<td>No ART</td>
<td>0.89</td>
<td>+68%</td>
</tr>
<tr>
<td>No condoms</td>
<td>2.78</td>
<td>+425%</td>
</tr>
<tr>
<td>ART at diagnosis</td>
<td>0.36</td>
<td>-32%</td>
</tr>
<tr>
<td>Higher test rate</td>
<td>0.40</td>
<td>-25%</td>
</tr>
<tr>
<td>Higher test rate &amp; ART at diagnosis</td>
<td>0.20</td>
<td>-62%</td>
</tr>
</tbody>
</table>
Discordancy between Plasma and Seminal HIV Levels

Politch et al. AIDS 2012
Proportion of New Infections Caused by Early Infections

Population

Sub-Saharan Africa (heterosexuals)
U.S. (heterosexual or MSM)
U.S. (MSM)
Europe (MSM)

Proportion of New Infections Caused by Early Infections

Hayes and White, 2006
Salomon and Hogan, 2008
Powers et al., 2010
Jacquez et al., 1994
Pinkerton, 2007
Prabhu et al., 2009
Koopman et al., 1997
Xiridou et al., 2004
Kretzschmar and Dietz, 1998
Pinkerton and Abramson, 1996
Abu-Raddad and Longini, 2008
Hollingsworth et al., 2008

Cohen et al. NEJM 2011
Studies in Key Populations

PARTNER Study (MSM)

- International, observational multi-center study in 75 European sites from 2010 to 2014 (Phase 1) and 2014-2017 (Phase 2)
- Sero-different MSM partnerships (+ve partner on ART) who had condomless penetrative sex in the past 4 weeks in order to study:
  - Risk of HIV transmission to partners, in partnerships that do not use condoms consistently and the HIV-positive partner on ART with viral load < 50 copies/mL
  - Reasons for lack of condom use and adoption of consistent condom use
- > 1000 couples enrolled so far

HPTN 074

- Vanguard study
- Network-based randomized trial PWID and partners
- Integrated treatment and prevention
  - Facilitated ART
  - Substance use treatment
  - Behavioral counseling
- Sites under consideration: Eastern Europe and Asia
ART for Prevention is a Multi-component Integrated Strategy or Prevention and Treatment

Conclusions

Access

Acceptability

Quality

Coverage

Effectiveness
Thank you