Optimizing the HIV Treatment and Care Continuum

Meg Doherty, MD, MPH, PhD
Coordinator Treatment and Care
WHO HIV Department, HQ
How can we improve the treatment and care continua/um?

• Continua of Treatment, Care and Prevention

• Populations specific examples and interventions

• WHO approach to optimizing the treatment and care continuum

• How this translates into country level implementation and programming
Targets require innovations across the continuum of care

Drugs, diagnostics & service delivery optimization:

- New FDCs (Paeds), simplified second and third line
- Diagnostics for HIV rapid, CD4, and viral load testing
- Community ARV delivery
The Gardner Cascade for HIV in the United States


ART scale-up depends on improving every step of the cascade – SS Africa
The spectrum of engagement in HIV care in 4 countries

The cascade of HIV care in British Columbia, Canada (1996–2011)

Source: Nosyk et al, Lancet ID, Jan 2014
Challenges with the continuum of care

- Unaware of HIV Status
- Late Diagnosis of HIV Infection
- Failure of HIV-Positive Patients to Link to Care
- Late Initiation of ART
- Inability to Achieve and Maintain Viral Suppression

Source: Mc Nairy & El-Sadr, CID, Feb 2014
Treatment initiation still late in the large majority of countries

Median CD4 count at start in 2013 (data for some countries extrapolated)

*: extrapolated value

Courtesy: D Cooper, IAC 2014
HIV Testing → Linkage to pre-ART care → Treatment Initiation → Retention in Care

Observational processes, do the events match up?

Too many people are being lost to follow-up

ART retention rates (%) at 12, 24 and 60 months reported by selected low- and middle-income countries, 2013.

Too many people are being lost to follow-up: newer cohorts with worse retention.

**Percentage adults remaining on ART by duration**
(Data from 352 phase 6 sites)

- **40% LTFU at 36 months**

Source: Joint Review of HIV, TB and PMTCT, Programmes in South Africa, Main Report, April 2014, Department of Health, South Africa
Figure 2. Percentage of persons with HIV engaged in selected stages of the continuum of care, by race/ethnicity -- United States

BY GENDER: Although men are less likely to be retained in care, men and women are equally likely to be virally suppressed.

BY AGE: Younger Americans are least likely to be retained in care or have their virus in check; HIV care and viral suppression improve with age, except among those aged 65 and older.

BY RISK GROUP: Across all risk groups, fewer than half are in ongoing care and roughly a quarter have their virus in check.

Note: Although national data were not available to provide estimates of viral suppression for those under the age of 25, the data show that 13–24 year-olds are substantially less likely to have been diagnosed with HIV than other age groups (only 49 percent versus more than 79 percent for all other age groups).
Paediatric retention across the cascade

Testing at birth

- HIV+ Births: 100%
- Receive PCR: 70%
- Mother Receives Results: 40%
- Child Initiates Treatment: 30%

Double Dividend—integration testing and treatment into Child Survival work (ACT & PHTI)

1. Pneumonia and Diarrhea initiatives
2. Routine child health services – *EPI*
3. Nutrition Initiatives
4. Neonatal initiatives

5. National Post-natal care programs
6. eMTCT – *The Global Plan*
7. *Option B+

8. IATT Paediatric ART working group, simpler regimens – “Optimal Formulary”
9. WHO recommendations 2014 Supplement;
10. Improved SCM of ARTs

Action to improve survival of HIV exposed infected and uninfected children in the era of eMTCT and renewed child survival campaigns

World Health Organization
Unacceptable inequality: AIDS deaths rising among adolescents

Deaths in children aged 0 – 4 years
Deaths in children aged 5 – 9 years
Deaths in adolescents aged 10 - 19
Deaths in young people aged 20 - 24

Source: UNAIDS 2012 HIV and AIDS estimates
UNDIAGNOSED + LOST TO FOLLOW UP = INADEQUATE CARE

Acquire TB → Diagnosed with TB → Prescribed adequate TB treatment → Begin ART (within 2 weeks of TB diagnosis) → Complete TB regimen + ART Adherence → Transition to long-term HIV care
Xpert MTB/RIF in HIV settings – a vital opportunity

TUBERCULOSIS DIAGNOSTICS

Xpert MTB/RIF Test

ABOUT THE XPERT MTB/RIF TEST
The rapid TB test – known as Xpert MTB/RIF- is a fully automated diagnostic molecular test. It has the potential to revolutionize and transform TB care and control. The test:

• simultaneously detects TB and rifampicin drug resistance
• provides accurate results in less than two hours so that patients can be offered proper treatment on the same day
• has minimal bio-safety requirements and training needs, and can be housed in non-conventional laboratories.

UPDATED WHO RECOMMENDATIONS
AS OF OCTOBER 2013

Strong recommendation:

• Xpert MTB/RIF should be used as the initial diagnostic test in adults and children presumed to have MDR-TB or HIV-associated TB
Integrate service delivery according to the setting

TB service
- HIV testing
- HIV prevention
- CPT
- ART
- Referral to HIV

One-stop service
- HIV testing
- ART
- CPT
- Condoms
- HIV and TB Services provided together
- ART
- TB diagnosis and treatment
- Partially integrated

HIV service
- TB screening
- IPT
- TB diagnosis
- TB treatment
- TB contact tracing
- Partially integrated
- Referral to TB

Co-located Adjacent

Partially integrated

Adjacent
Moscow MSM: HIV Diagnosis and Treatment

HIV prevalence  RDS adj: 12.4% (95%CI: 9.3 – 16.1)

HIV Care Cascade Among 1,146 HIV Positive MSM From 12 sites In India

**Prevalence**

Engagement in care was better in sites with established epidemics where there have been more government-led targeted interventions.

Awareness of status was better among individuals who had received other services (e.g., TB treatment and STI treatment).

**Solomon SS et al IAS 2014 MOPE1500**

**Mehta SH et al CROI 2014**

**Courtesey:** B Grinsztejn, IAC 2014
Continuum of Care Cascade for HIV+ MSM/TW in Peru (Est. N = 38,000)

The testing gap is most acute – once diagnosed relative success

Carlos F. Cáceres, Cayetano Heredia University, Lima
The treatment cascade in Swaziland

HIV Testing, Knowledge of Infection Status and ARV Use Among Enrolled FSW and MSM Living with HIV in Swaziland

- Tested in past 12 months
- Reported awareness of HIV Infection status
- On ARVs

**FSW**
- Tested in past 12 months: 78%
- Reported awareness of HIV Infection status: 29%
- On ARVs: 9%
- **Total n=223**

**MSM**
- Tested in past 12 months: 73%
- Reported awareness of HIV Infection status: 29%
- **Total n=55**
Access to prevention and ART

MSM (Global Men’s Health and Rights Study 2012)
New WHO recommendations on PrEP
WHO Consolidated Guidelines on HIV Prevention, Diagnosis, Treatment and Care for Key Populations 2014

- PrEP is effective and safe if taken as prescribed
- Effectiveness trials (Phase II b and III) conducted in MSM, higher risk women & PWID
- OLE in MSM PrEP sites show promising outcomes

Dose-response relationship between adherence and PrEP efficacy

<table>
<thead>
<tr>
<th>Study</th>
<th>Reported Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partners FTC/TDF</td>
<td>81%</td>
</tr>
<tr>
<td>Partners TDF</td>
<td>81%</td>
</tr>
<tr>
<td>TDF2</td>
<td>79%</td>
</tr>
<tr>
<td>Bangkok TDF</td>
<td>67%</td>
</tr>
<tr>
<td>iPrEx</td>
<td>51%</td>
</tr>
<tr>
<td>FEM-PrEP</td>
<td>26%</td>
</tr>
<tr>
<td>VOICE FTC/TDF</td>
<td>&lt;30%</td>
</tr>
<tr>
<td>VOICE TDF</td>
<td>50% never</td>
</tr>
</tbody>
</table>
Among men who have sex with men, PrEP is recommended as an *additional HIV prevention choice* within a comprehensive HIV prevention package.

No recommendation was made at this stage concerning the use of PrEP among people who inject drugs.

WHO 2012 PrEP conditional recommendation for other KP and people in SDC remains – *for consideration in demonstration projects*.
Review of 25 studies (including 13,583 HCV patients)
HCV treatment experience a clinical care setting

Hepatitis C patients

All patients 100%
(N=13,583)

Treatment eligible 39%

Started treatment 19%

Completed treatment 13%

SVR 3%

e.g. mild-to-moderate liver disease – made to wait until disease progresses

Only about 1 in 5 patients with HCV receive treatment

HIV-Hep Service Integration

- HIV is a service platform for supporting an emerging hepatitis agenda

*Share among 58 WHO HIV focus countries offering hepatitis services in ART clinics, June 2014*

- 41% HBV HCV testing
- 21% HBV vaccination
- 14% HCV treatment
Advantages of HIVST

• Convenience
• Privacy
• Autonomy
• Reduced stigma & normalization
• Less resource intensive for the health care system
WHO Innovations in Drugs

Drug optimization agenda (CADO, PADO, PAWG, Peds Formulary, PHTI):

- Low-dose EFV / low-dose AZT
- Use of new drugs (e.g., dolutegravir, TAF)
- Heat stable FDC for DRV/r; single pill second line
- Paediatric formulations (pellets, injectables, long-acting)
## WHO leadership in Drug Optimization

<table>
<thead>
<tr>
<th>ART Optimization Strategy</th>
<th>Tolerability</th>
<th>Resistance</th>
<th>Convenience</th>
<th>PW, TB, children</th>
<th>Cost Reduction</th>
<th>What action are needed?</th>
<th>Expected Timeline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low dose EFV</td>
<td>✓</td>
<td>?</td>
<td>✓</td>
<td>?</td>
<td>✓</td>
<td>• pK studies (PW &amp; TB)</td>
<td>1-2 yrs</td>
</tr>
<tr>
<td>Low dose DRV/r (as FDC)</td>
<td>✓</td>
<td>?</td>
<td>✓</td>
<td>?</td>
<td>✓</td>
<td>• pK studies (DRV:RTV ratio) • RCT (standard vs low dose)</td>
<td>2-5 yrs</td>
</tr>
<tr>
<td>Use of DTG</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>?</td>
<td>✓</td>
<td>• Studies in PW, TB &amp; children • Comparative trials (TDF / TAF in 1st line) • RCT (DRV/r + DTG in 2nd line)</td>
<td>2-5 yrs</td>
</tr>
<tr>
<td>Use of TAF</td>
<td>✓</td>
<td>?</td>
<td>✓</td>
<td>?</td>
<td>✓</td>
<td>• Trials DTG • Studies in PW, TB &amp; children</td>
<td>2-5 yrs</td>
</tr>
<tr>
<td>Long-acting formulations</td>
<td>✓</td>
<td>?</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>• Phase II/III studies</td>
<td>&gt; 5 yrs</td>
</tr>
</tbody>
</table>
WHO Innovations in Service delivery

Bringing ARV services closer to the patient:

• Task Shifting / sharing
• Integration & Decentralisation
• Community based ARV delivery approaches
• Use of POC CD4 for rapid linkage / engagement
Uptake of 2013 WHO operational and Service Delivery Recommendations as of June 2014

ART and TB Service integration policies, percent (%) of 59 WHO focus countries, by region

- TB treatment in ART settings
- ART in TB clinics

AFRO

WHO region

- 63% (TB treatment in ART settings)
- 67% (ART in TB clinics)

Total

- 56% (TB treatment in ART settings)
- 44% (ART in TB clinics)

WHO region
**WHO consultation on Community ART Delivery (ICASA 2013)**

*Already happening: DRC, Mozambique, South Africa, Uganda, Zimbabwe*

- Models need to be flexible and adapted to context
- Referral mechanisms are critical
- Supportive policy needed, including for support of community health workers
- Simplified, integrated M&E critical

<table>
<thead>
<tr>
<th>Model of care</th>
<th>Country, implementer and year</th>
<th>Criteria for delivering ART</th>
<th>ART refill interval</th>
<th>Frequency of clinic visit</th>
<th>Patient–provider ratio, human resources used and organization</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community adherence groups (14,15)</td>
<td>Mozambique Ministry of Health 2011–present Lesotho, Malawi, South Africa and Zimbabwe</td>
<td>Stable on ART Piloting inclusion of pre-ART people living with HIV</td>
<td>Monthly (Lesotho and Mozambique), every 2 months (Malawi), every 3 months (Zimbabwe)</td>
<td>Every 6 months (Lesotho, Malawi and Mozambique), annually (Zimbabwe)</td>
<td>Self-forming groups of 6–10 people living with HIV rotate to collect ART for the group. Groups formed with support from clinic staff and local networks of people living with HIV</td>
<td>98% retention in care after 3 years; children in community adherence groups reporting 94% retention (11) Uptake around 50%</td>
</tr>
<tr>
<td>Community adherence groups – pilot for the above (15)</td>
<td>Mozambique Médecins Sans Frontières 2008–present</td>
<td>&gt;6 months on ART, absence of adverse drug events, no opportunistic infection, CD4 &gt;200 cells/mm³</td>
<td>Monthly</td>
<td>Every 6 months</td>
<td>Self-forming groups of six people living with HIV rotate to attend the clinic and collect ART for the group</td>
<td></td>
</tr>
</tbody>
</table>
Additional interventions to improve the treatment and care cascade

- **Next guidelines**
  - Evidence of WHAT
  - Greater focus on the HOW to deliver ARVs and context

- **Optimized Care Package of interventions to improve continua:**
  - **Early**
    - Adherence & retention support
  - **Late**
    - Interventions to reduce mortality and morbidity
  - **Stable**
    - Community ART delivery
  - **Failing**
    - Second and third line support
WHO Innovations in Diagnostics

Diagnostics optimization agenda:

• Viral Load implementation guidance with CDC & PEPFAR
• Quality of Care for POCT
• Technical lead to the Diagnostics Access Initiative (DAI)
Impact of Point of care CD4 on linkage/retention in HIV care

Odds of linking to care increased
- Time to testing reduced by 9 days
- Time from testing to receiving the result was reduced by 17 days
Strategic Use of ARVs - SUFA3 (the WHAT and the HOW)

2011 SUFA 1
- Clinical science map
- Roadmap to consolidated ARV guidelines

2012 SUFA 2
- HIV programming: from clinical recommendations into policy and practice

2013
- Major capacity building
- Policy dialogue in countries

2014 SUFA 3
- Roadmap to the next generations of WHO ARV guidance
- Clinical and Implementation Science research agenda
### Distribution of Intervention Approaches at Each Step of the Cascade

**Geng, Feb 2014**

<table>
<thead>
<tr>
<th>Service Delivery Approach</th>
<th>Testing</th>
<th>Linkage</th>
<th>Staging</th>
<th>Pre-ART retention</th>
<th>ART initiation</th>
<th>Retention on ART</th>
<th>Adherence</th>
<th>Viral suppression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery Architecture</td>
<td>47%</td>
<td>64%</td>
<td>73%</td>
<td>56%</td>
<td>58%</td>
<td>64%</td>
<td>38%</td>
<td>63%</td>
</tr>
<tr>
<td>Counseling</td>
<td>10%</td>
<td>13%</td>
<td>4%</td>
<td>6%</td>
<td>10%</td>
<td>9%</td>
<td>29%</td>
<td>10%</td>
</tr>
<tr>
<td>Demand Creation</td>
<td>18%</td>
<td>13%</td>
<td>12%</td>
<td>31%</td>
<td>17%</td>
<td>13%</td>
<td>19%</td>
<td>15%</td>
</tr>
<tr>
<td>Management</td>
<td>28%</td>
<td>23%</td>
<td>29%</td>
<td>25%</td>
<td>37%</td>
<td>26%</td>
<td>21%</td>
<td>29%</td>
</tr>
<tr>
<td>Social</td>
<td>28%</td>
<td>13%</td>
<td>15%</td>
<td>13%</td>
<td>18%</td>
<td>17%</td>
<td>31%</td>
<td>15%</td>
</tr>
<tr>
<td>Technology</td>
<td>9%</td>
<td>16%</td>
<td>21%</td>
<td>19%</td>
<td>10%</td>
<td>14%</td>
<td>13%</td>
<td>13%</td>
</tr>
<tr>
<td><strong>Total studies</strong></td>
<td>125</td>
<td>64</td>
<td>52</td>
<td>16</td>
<td>109</td>
<td>115</td>
<td>68</td>
<td>52</td>
</tr>
</tbody>
</table>

*White = More Studies  Red = Fewer Studies*

- Service delivery approaches are most studied within each step.
- Differences by approach seemed largest for linkage interventions and smallest for adherence interventions.
Retention and the Leaky PMTCT & Paeds Cascade

Among infants testing HIV positive via EID, an estimated 38% will initiate treatment, and an estimated 28% will be retained and alive on treatment after 12 months.

Cascade based on Data from Lesotho, Malawi, South Africa, Uganda, Zambia, & Zimbabwe

Cascade Targets Addressed by Interventions for Children

<table>
<thead>
<tr>
<th>Service Delivery</th>
<th>Testing</th>
<th>Linkage</th>
<th>Staging</th>
<th>ART initiation</th>
<th>Pre-ART retention</th>
<th>Retention on ART</th>
<th>Adherence</th>
<th>Viral suppression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Counseling</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Demand Creation</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Management</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Social support</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Technology</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

White=More Studies

Red=Fewer Studies

- Service delivery approaches were the most common with retention on ART as the most examined outcome
- Overall there is a paucity of approaches and steps in the cascade
**Implementation Science Research Priorities/Gaps**

**Adults**
- ART Retention & reengagement
- Pre-ART Retention
- Linkage to care
- Adherence and VL suppression

**PMTCT**
- How to find those not in ANC
- How to retain mothers starting in B+/B programs
- Retesting late in pregnancy and BF
- Demand creation
- Special management for “high risk” mothers (infants) identified HIV+ at delivery

**Children / Youth**
- Strategies to target children/adolescents to test, link to care, create demand, promote adherence
- Tracing LTFU
- Reduction of social/structural barriers for youth testing/care
- Optimal models to deliver care and transition adolescents
Threshold for ART initiation

Uptake based on 58 WHO focus countries, by region

- CD4 <350
- CD4 <500
- Regardless of CD4

Total 43%
Total 54%
Total 3%

Uptake of 2013 recommendations as of July 2014
Will the funding be there?

Current Global Fund CN applications & TRP feedback to countries:

- Expanding eligibility—
  - countries are phasing in eligibility to 500 (Moz, Tanz at 350)
  - going to 500 only if extra resources available (e.g. Zim)
  - Choosing non-FDC ARVs or non-recommended first line (Ukraine, Zimbabwe)

- Treatment/prevention balance (e.g. Zambia)
  - are investments well balanced?
  - has the prevention been fully maximized prior to expanding ARVs in high incidence areas

- Routine VL
  - Lower priority in many country CN as counties prioritizing ARVs
Updates to WHO ARV Guidelines: current and future plans

**MARCH**
- INNOVATIONS
  - HIV self-testing
  - EID
  - Optimized drugs adults & children
  - Monitoring (toxicity, CD4, VL, HIVDR)

**JULY**
- INNOVATIONS
  - HIV self-testing
  - EID
  - Optimized drugs adults & children
  - Monitoring (toxicity, CD4, VL, HIVDR)

**SEPT/OCT**
- COMORBITIES
  - Skin and Oral OIs
  - Cryptococcal dz
  - CTX Use
  - HIV-PEP

**DECEMBER**
- CLINICAL & SD
  - Infant triple prophylaxis
  - Adolescent Treatment
  - HIV comorbidities
  - Quality Care
  - Tiered service delivery
  - Diagnostics

1. Technical and operational considerations for implementing viral Load testing
2. Guidance for Improving the Quality of HIV-related Point-of-Care Testing

Assessment of challenges and implementation of new recommendations
Take home messages

• The treatment, care and prevention continuum is a data use approach to analyze gaps to by populations and location

• Optimization / solutions may need to be locally driven and focus on the intermediary hand-offs between each step (quality improvement of care and services)

• WHO committed to continue to lead on:
  • Drugs, Diagnostics & Service Delivery optimization/innovation
  • Guidelines that address the ‘HOW’
  • Promotion Implementation & improvement science research agenda to fill knowledge gaps
Acknowledgements

WHO HIV/Hep Department
• Gottfried Hirnschall
• Rachel Baggaley
• Michel Beusenberg
• Nathan Ford
• Cadi Irvine
• Eyerusalem Negussie
• Lisa Nelson
• Martina Penazzato
• Fintan Thompson
• Marco Vitoria
• Gundo Weiler
• Philippa Easterbrook
• Stefan Wiktor

Partners
• Haileyesus Getahun
• Annabel Baddeley
• Bruce Agins, HealthQual
• IAPAC
• ICAP
• PEPFAR
• Global Fund
• UNAIDS
• CHAI
• DNDI
• MMP
• UNITAID
• EGPAAF
Rationale for recommendations

**MSM**

- Efficacy
- Ongoing high incidence in almost all setting
- Current prevention interventions insufficient
- Values and preferences supporting PrEP as an additional prevention choice consistent
- Increasing experience from pilot and OLE studies

**PWID**

*Despite efficacy from 1 RCT*

- Only 1 trial site
- Alternative effective HIV prevention interventions available (incl. OST & NSP) with current poor global coverage and reach
- Limited values and preferences – much unfavourable
Paediatric ART Age Initiation

Uptake based on 58 WHO focus countries, by region

- Age < 2 yrs: 22%
- Age < 5 yrs: 48%
- Other: 21%

Total: 22% for Age < 2 yrs
Total: 48% for Age < 5 yrs
Total: 21% for Other

Uptake of 2013 recommendations as of July 2014
Option B / B+

Uptake based on 58 WHO focus countries, by region

Total
9%

Total
33%

Total
58%

Uptake of 2013 recommendations as of July 2014
Patterns of ARV use

- Preferred 1st line TDF/3TC(FTC)/EFV
- Countries with fixed dose preference

Uptake based on 58 WHO focus countries, by region

Total 71%

Total 81%

Uptake of 2013 recommendations as of July 2014