Overview of 2013 WHO consolidated ARV guidelines and update plans

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Key aspects of 2013 WHO Consolidates Guidelines and development process
### Summary of WHO Guidelines Evolution

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<tbody>
<tr>
<td>When to start</td>
<td>CD4 ≤ 200</td>
<td>CD4 ≤ 200</td>
<td>CD4 ≤ 200 - Consider 350</td>
<td>CD4 ≤ 350 - Irrespective CD4 for TB and HBV</td>
<td>CD4 ≤ 500 - Irrespective CD4 for TB, HBV, PW and SDC - CD4 ≤ 350 as priority</td>
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<tr>
<td>1st Line</td>
<td>8 options</td>
<td>4 options</td>
<td>8 options - AZT or TDF preferred</td>
<td>6 options &amp; FDCs - AZT or TDF preferred - d4T phase out</td>
<td>1 preferred option &amp; FDCs - TDF and EFV preferred across all populations</td>
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<tr>
<td>3rd Line</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>DRV/r, RAL, ETV</td>
<td>DRV/r, RAL, ETV</td>
</tr>
<tr>
<td>Viral Load Testing</td>
<td>No</td>
<td>No (Desirable)</td>
<td>Yes (Tertiary centers)</td>
<td>Yes (Phase in approach)</td>
<td>Yes (preferred for monitoring, use of PoC, DBS)</td>
</tr>
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</table>

**Earlier initiation**: Earlier initiation of treatment has led to earlier CD4 thresholds for initiation.

**Simpler treatment**: Treatment options have become simpler, with fewer drug combinations and less toxicity.

**Less toxic, more robust regimens**: Regimens have become less toxic with better outcomes.

**Better monitoring**: Monitoring tools like viral load testing have been introduced to improve patient outcomes.
WHO Consolidated ARV Guidelines: an step towards the vision

Simplification and consolidation across:
- Continuum of HIV care
- Ages and populations
- Existing and new recommendations
The process of guideline development at WHO

- **Systematic reviews**
- **Mathematical Modelling**
- **ARV drug costs**
  - GPRM database (Global Price Reporting Mechanism)
- **Surveys of country experience**
- **2012 WHO Survey of ARV and lab use**

**QUALITY OF EVIDENCE (GRADE)**

**COST/COST-EFFECTIVENESS (RESOURCE USE)**

**VALUES & PREFERENCES**

**FEASIBILITY**

- Community & health worker consultations
**Clinically relevant**

- **Earlier initiation of ART** (CD4 count ≤ 500 cells/mm³) for adults & adolescents
- **Immediate ART for children below 5 years**
- **More potent regimens for children < 3 years** (LPV/r)
- **Immediate & lifelong ART for all pregnant and breastfeeding women** (Option B/B+)
- **Simplified, less toxic 1st-line regimens** (TDF/XTC/EFV)

**Operationally relevant**

- **Use of Fixed Dose Combinations (FDCs)**
- **Improved patient monitoring with increased use of viral load**
- **Recommend task shifting, decentralization, and integration**
- **Community based testing and ARV delivery**

The 2013 Consolidated ARV Guidelines: Key new recommendations
Estimated impact: implementing 2013 guidelines as compared to 2010

- Avert 3.0 m deaths (↓59%)
- Avert 3.1 m new infections (↓23%)
- Highly cost effective at QALY 350 USD

Adoption and Implementation challenges of 2013 WHO Consolidates Guidelines
Threshold for ART initiation

Uptake based on 58 WHO focus countries, by region

- CD4 <350: 20%
- CD4 <500: 63%
- Regardless of CD4: 30%

Total Uptake:
- CD4 <350: 43%
- CD4 <500: 54%
- Regardless of CD4: 3%

Uptake of 2013 recommendations as of July 2014

Uptake based on 58 WHO focus countries, by region.
Patterns of ARV use

Uptake based on 58 WHO focus countries, by region

Preferred 1st line TDF/3TC(FTC)/EFV

Countries with fixed dose preference

Total 71%

Total 81%

Uptake of 2013 recommendations as of July 2014
Global scale up progress is tempered by challenges: coverage, quality and focus

As of 2013, significant progress...

- 13 million people on ART in 2013
- One million women receiving ARVs for PMTCT
- 5.8 million males circumcised
- HIV Incidence ↓ 32% since 2001
- HIV mortality ↓ 30% since 2005

... yet major challenges

- 2.3 million, including 260,000 children, were newly infected with HIV in 2012
- 1.6 million people died from HIV in 2012 (adults and children)
- 1 in 2 new infections occur among KPs
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
Too many people are being lost to follow-up in some countries newer cohorts with worse retention.

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

40% LTFU at 36 months

2013 WHO ARV guidelines: Key Challenges

- Policy adoption translated into implementation
- Equity
  - Earlier care; key populations, young people
- Focused implementation
  - Areas with the greatest needs; greatest impact
- Beyond the treatment-prevention dichotomy
  - Smarter combination prevention
What is planned for 2015 update and future reviews
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
- Simplified Service Delivery and Care packages that improve the leaky cascade
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 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)
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
Additional interventions to minimize HIV-related mortality/morbidity

- **Package of care interventions** for patients at different stages:
  - **Late**
    - Interventions to reduce morbidity & mortality
  - **Early**
    - Adherence & retention support
  - **Stable**
    - Community ART delivery
  - **Failing**
    - Second and third line support

- Greater attention to **co-infections/co-morbidities** (including NCDs & mental health disorders)
- New strategies to improve **Cascade (Implementation Science)**
- **Quality** of treatment, care and prevention
**Roadmap of WHO ARV Consolidated Guidelines Updates**

**2014**

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

**JULY**
- **CO-MORBIDITIES & PEP**
  - Skin and oral manifestations
  - Cryptococcosis
  - CTX prophylaxis
  - HIV-PEP

**SEPT/OCTOBER**
- **CLINICAL & SERVICE DELIVERY**
  - Infant triple prophylaxis
  - Adolescent Treatment
  - HIV care packages
  - Quality Care
  - Diagnostics

**DECEMBER**
- Technical and operational considerations for implementing viral load testing
- Guidance for Improving the Quality of HIV-related Point-of-Care Testing
- Assessment of challenges and implementation of new recommendations
GDG format and proposed work plan

Clinical GDG
WHAT (chapters 5, 6, 7 and 8)
- When to start
- What to start
- option B/B+
- etc

Operational GDG
HOW (chapters 9, 10 and 11)
- SD, quality, HSS,
- Economics,
- Models,
- IS, M&E

Subgroup Scoping Meetings
- HIV & NCDs
- Quality T&C
- Adolescent Treatment

Revised scoping document (GRC submission)
First core group GDG meeting
Simplified Care Packages
- Treatment adherence
- Lab (EID, VL, CD4)
- Infant Prophylaxis & EID

WHO Steering Group
Systematic reviews and other assessments
Second GDG meeting to make recommendations

E-survey assess country uptake previous GL
Establishment of GDGs & methodologists
Develop overall scoping document

Core Guideline Development Group

Mar-May /2014
Apr- June/2014
Jun- Sept/2014
Oct/14- Jun/15
Aug-Dec/15
### Potential Topics to be evaluated in 2015 Update

<table>
<thead>
<tr>
<th>WHO Guidelines Area</th>
<th>Potential topics to be discussed</th>
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| **When to Start ART** | • CD4 threshold to initiate ART in adults (TEMPRANO study)  
• Immediate ART initiation in children between 5-15 yrs  
• EID and birth testing |
| **What ARV Regimens to use in 1st and 2nd lines** | • Dose optimization of EFV, AZT and DRV/r  
• Role of integrase inhibitors  
• What preferred NRTI backbone to start in children (AZT vs ABC)  
• Use of triple ART post natal prophylaxis in high risk exposed babies |
| **How to monitor ART efficacy and toxicity** | • Optimization of CD4 /VL strategy (including PoC)  
• VL threshold for failure criteria (standard techniques vs PoC)  
• Renal and CNS dysfunction with ARV regimens containing TDF and EFV  
• Surveillance of HIV drug resistance |
| **Management of co-morbidities** | • Earlier ART initiation (regardless of CD4) in presence of HBV, HCV, some chronic NCDs & non-AIDS cancers  
• What regimen to switch in presence of TB and Hep B & C co-infections |
| **Optimization of programmatic packages** | • Care packages for early and late presenters  
• Frequency, location and intensity of care services (adaptive approach in service delivery)  
• Use of option B+ as universal PMTCT approach  
• Adherence monitoring and support strategies for prevent and detect failure  
• Retention using decentralized/integrated care models  
• Community models of ART delivery  
• Quality of Care & Treatment  
• Procurement and supply chain management |
What we expect in 2015 review:

- Consolidation of evidence-based guidelines on ARV for treatment and prevention (more programmatic guidance)
- Optimization and innovation for efficient and effective use of resources
- More intersection with other areas