CONSOLIDATED GUIDELINES ON
THE USE OF ANTIRETROVIRAL DRUGS FOR TREATING AND PREVENTING HIV INFECTION
SUMMARY OF KEY FEATURES AND RECOMMENDATIONS

JUNE 2013
ACRONYMS

- 3TC lamivudine
- ABC abacavir
- AIDS acquired immunodeficiency syndrome
- ART antiretroviral therapy
- ARV antiretroviral (drug)
- ATV/r atazanavir/ritonavir
- AZT azidothymidine (also known as zidovudine)
- DRV darunavir
- EFV efavirenz
- FTC emtricitabine
- HBV hepatitis B virus
- HCV hepatitis C virus
- HIV human immunodeficiency virus
- LPV/r lopinavir/ritonavir
- NNRTI non-nucleoside reverse transcriptase inhibitor
- NRTI nucleoside reverse transcriptase inhibitor
- NVP nevirapine
- PI protease inhibitor
- PMTCT prevention of mother-to-child transmission of HIV
- RAL raltegravir
- RTV ritonavir
- TB tuberculosis
- TDF tenofovir disoproxil fumarate
- WHO World Health Organization
1. WHAT ARE THE KEY FEATURES OF THE 2013 CONSOLIDATED GUIDELINES?

They respond to new science and emerging practice since 2010

- New and easy-to-use HIV testing technologies and approaches enable more people, especially those who are most vulnerable and marginalized, to learn their HIV status.
- Simpler, safer, once-daily, single-pill treatments that are suitable for use in most populations and age groups have become more affordable and more widely available in resource-limited countries.

- Programmes for preventing mother-to-child transmission of HIV (PMTCT) are promoting earlier and simpler treatments to improve the health of pregnant women and mothers living with HIV and to prevent HIV infection among their children and partners.
- In addition to improving health and prolonging lives, clear evidence indicates that antiretroviral therapy (ART) prevents the sexual transmission of HIV and that the use of ARV drugs by uninfected individuals can protect them from becoming infected.
- There is a trend towards starting treatment earlier among people with HIV to protect their own health and prevent HIV transmission to others.

Guidance is provided on ARV use along the continuum of care

For the first time, the 2013 guidelines combine recommendations across the continuum of HIV care, including recommendations on HIV testing and counselling, using ARV drugs for HIV prevention, linking individuals to HIV treatment and care services, providing general HIV care, initiating and maintaining ART and monitoring treatment. Guidance is provided on using ARV drugs across all age groups and populations of adults,
2. WHAT ARE THE NEW RECOMMENDATIONS?

New clinical recommendations for treating people with HIV

The 2013 guidelines are based on a public health approach to further expanding the use of ARV drugs for HIV treatment and prevention, with a particular focus on resource-limited settings. The new clinical recommendations in the guidelines include:

- treating adults, adolescents and older children earlier – starting ART in all individuals with a CD4 cell count of 500 cells/mm³ or less and giving priority to individuals with severe or advanced HIV disease and those with a CD4 cell count of 350 cells/mm³ or less;
- starting ART at any CD4 count for certain populations with HIV, including people with active TB disease, people with hepatitis B virus (HBV) co-infection with severe chronic liver disease, HIV-positive partners in serodiscordant couples, pregnant and breastfeeding women and children younger than five years of age;
- a new, preferred first-line ART regimen harmonized for adults, pregnant and breastfeeding women and children aged three years and older;
- support to actively accelerate the phasing out of stavudine (d4T) in first-line ART regimens for adults and adolescents;
- the use of viral load testing as the preferred approach to monitoring the success of ART and diagnosing treatment failure in addition to clinical and CD4 monitoring of people receiving ART; and
- community-based HIV testing and counselling and HIV testing of adolescents to diagnose people with HIV earlier and link them to care and treatment.

The guidelines provide advice on the clinical management of people living with HIV, make recommendations on how to improve the efficiency and effectiveness of HIV services and give guidance on how to plan HIV programmes and use resources most efficiently.

They combine new and existing recommendations

WHO has been producing guidance on the use of ARV drugs since 2002, producing a range of guidelines on various aspects of HIV diagnosis, treatment and care. The 2013 guidelines aim to combine and harmonize new and existing recommendations, including updated recommendations from the 2010 guidelines on ART for adults, adolescents and children and ARV treatment and prophylaxis for pregnant and breastfeeding women living with HIV. They also include existing WHO guidance on HIV testing and counselling, HIV prevention, general care for people living with HIV, managing common coinfections and other comorbidities and monitoring and managing drug toxicities.
New operational guidance and recommendations

Expanding the use of ARV drugs provides new opportunities to save lives, improve the health of people living with HIV and reduce the number of people becoming newly infected with HIV. With these opportunities come challenges – policy-makers and implementers need to determine how best to implement the recommendations to achieve greatest impact. Guidance is provided on enhancing the efficiency and effectiveness of HIV interventions, strengthening the continuum of HIV care and improving linkages across the health system. This guidance focuses on:

• strategies to improve retention in HIV care and adherence to ART;
• task-shifting to address human resource gaps;
• decentralizing delivery of ART to primary health care and integrating ART services within maternal and child health clinics, tuberculosis (TB) clinics and drug dependence treatment services; and
• the implications of new clinical recommendations for laboratory services and procurement and supply systems for ARV drugs and other commodities.

New guidance for programme managers

The document aims to assist countries in decision-making and programme planning, to adapt the recommendations for their epidemic and health systems contexts. The guidance developed for HIV programme managers outlines fair, inclusive and transparent decision-making processes at the country level on the strategic use of ARV drugs. Consideration is given to national planning processes, HIV epidemiology, health system capacity, available financial resources and ethical and human rights considerations. Tools for costing and planning are also suggested. Implementation considerations especially relevant to programme managers are provided for all major new recommendations.

New guidance on monitoring and evaluation

Guidance is provided on monitoring the implementation of new recommendations, including potential indicators for monitoring the performance of programmes across the continuum of care.

3. COMPONENTS OF THE CONSOLIDATED GUIDELINES

What to do

• HIV testing and counseling
• Prevention based on ARV drugs
• General HIV care
• When to start ART (first-line ART)
• What ART to start with
• How to monitor (ART response and toxicity)
• What ART to switch to (second-line ART)
• Management of coinfections and comorbidities

How to do it

• Adherence to ART
• Retention in care
• Innovative models of service delivery (integration, decentralization and task shifting)
• Human resources
• Laboratory and diagnostic services
• Procurement and supply management systems

How to decide what to do, where and when

• Decision-making (process, data required and key parameters)
• Implementation considerations
• Useful tools for costing and planning

Monitoring and evaluation

• Monitoring implications of new recommendations
• Monitoring outputs and outcomes of scaling up ARV access
• Other monitoring considerations (HIV drug resistance and ARV toxicity monitoring)
• Strengthening monitoring and evaluation systems
4. WHAT IS THE EXPECTED IMPACT OF THE GUIDELINES?

Globally, an estimated 26 million people living with HIV in low- and middle-income countries will be eligible for ARV drugs under the new guidelines compared with the previous close to 17 million people eligible for them in accordance with the 2010 guidelines. Progressive full implementation of the guidelines could avert as many as 3 million AIDS-related deaths and 3.5 million new HIV infections between 2013 and 2025 over and above those averted by implementing the 2010 WHO treatment guidelines. Realizing these benefits will require an estimated 10% increase in the total annual investment in the global HIV response.
5. SUMMARY OF NEW RECOMMENDATIONS

The tables below summarizes the new WHO recommendations formulated for the 2013 guidelines. The table is not comprehensive and does not include recommendations drawn from other existing WHO guidelines.

### HIV testing and counselling

<table>
<thead>
<tr>
<th>Topic and population</th>
<th>Recommendations</th>
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| Community-based testing                     | - In generalized HIV epidemics, community-based HIV testing and counselling with linkage to prevention, care and treatment services is recommended, in addition to provider-initiated testing and counselling (strong recommendation, low-quality evidence).  
- In all HIV epidemic settings, community-based HIV testing and counselling for key populations, with linkage to prevention, care and treatment services is recommended, in addition to provider-initiated testing and counselling (strong recommendation, low-quality evidence). |
| HIV testing and counselling of adolescents* | - HIV testing and counselling, with linkages to prevention, treatment and care, is recommended for adolescents from key populations in all settings (generalized, low and concentrated epidemics) (strong recommendation, very-low-quality evidence).  
- HIV testing and counselling with linkage to prevention, treatment and care is recommended for all adolescents in generalized epidemics (strong recommendation, very-low-quality evidence).  
- We suggest that HIV testing and counselling with linkage to prevention, treatment and care be accessible to all adolescents in low and concentrated epidemics (conditional recommendation, very-low-quality evidence).  
- We suggest that adolescents be counselled about the potential benefits and risks of disclosure of their HIV status and empowered and supported to determine if, when, how and to whom to disclose (conditional recommendation, very-low-quality evidence). |
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| **When to start ART in adults and adolescents**<sup>a</sup> | - As a priority, ART should be initiated in all individuals with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and individuals with CD4 count ≤350 cells/mm³ (strong recommendation, moderate-quality evidence).  
- ART should be initiated in all individuals with HIV with CD4 count >350 cells/mm³ and ≤500 cells/mm³ regardless of WHO clinical stage (strong recommendation, moderate-quality evidence).  
- ART should be initiated in all individuals with HIV regardless of WHO clinical stage or CD4 count in the following situations:  
  - Individuals with HIV and active TB disease (strong recommendation, low-quality evidence).  
  - Individuals coinfected with HIV and HBV with evidence of severe chronic liver disease (strong recommendation, low-quality evidence).  
  - Partners with HIV in serodiscordant couples should be offered ART to reduce HIV transmission to uninfected partners (strong recommendation, high-quality evidence). |
| **When to start ART in pregnant and breastfeeding women** | - All pregnant and breastfeeding women with HIV should initiate triple ARVs (ART), which should be maintained at least for the duration of mother-to-child transmission risk. Women meeting treatment eligibility criteria should continue lifelong ART (strong recommendation, moderate-quality evidence).  
- For programmatic and operational reasons, particularly in generalized epidemics, all pregnant and breastfeeding women with HIV should initiate ART as lifelong treatment (conditional recommendation, low-quality evidence).  
- In some countries, for women who are not eligible for ART for their own health, consideration can be given to stopping the ARV regimen after the period of mother-to-child transmission risk has ceased (conditional recommendation, low-quality evidence). |
| **ARVs and duration of breastfeeding** | The key principles and recommendations established in 2010 remain, including:  
National or subnational health authorities should decide whether health services will mainly counsel and support mothers known to be infected with HIV to either breastfeed and receive ARV interventions or avoid all breastfeeding given their particular context.  
In settings where national authorities have decided that maternal and child health services will mainly promote and support breastfeeding and ARV interventions as the strategy that will most likely give infants born to mothers known to be infected with HIV the greatest chance of HIV-free survival:  
- Mothers known to be infected with HIV (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first 6 months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life. Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast-milk can be provided (strong recommendation, high-quality evidence for the first 6 months; low-quality evidence for the recommendation of 12 months). |
| **When to start ART in children** | - ART should be initiated in all children infected with HIV below five years of age, regardless of WHO clinical stage or CD4 count.  
  - Infants diagnosed in the first year of life (strong recommendation, moderate-quality evidence)  
  - Children infected with HIV one year to less than five years of age (conditional recommendation, very-low-quality evidence).  
- ART should be initiated in all children infected with HIV five years of age and older with CD4 cell count ≤500 cells/mm³, regardless of WHO clinical stage.  
  - CD4 count ≤350 cells/mm³ (strong recommendation, moderate-quality evidence)  
  - CD4 count between 350 and 500 cells/mm³ (conditional recommendation, very-low-quality evidence).  
- ART should be initiated in all children infected with HIV with severe or advanced symptomatic disease (WHO clinical stage 3 or 4) regardless of age and CD4 count (strong recommendation, moderate-quality evidence).  
- ART should be initiated in any child younger than 18 months of age who has been given a presumptive clinical diagnosis of HIV infection (strong recommendation, low-quality evidence). |

<sup>a</sup> An adolescent is a person aged 10 to 19 years inclusive.
## What ART regimens to start

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| **First-line ART regimens for adults** | • First-line ART should consist of two nucleoside reverse-transcriptase inhibitors (NRTIs) plus a non-nucleoside reverse-transcriptase inhibitor (NNRTI).  
  • TDF + 3TC (or FTC) + EFV as a fixed-dose combination is recommended as the preferred option to initiate ART (strong recommendation, moderate-quality evidence).  
  • If TDF + 3TC (or FTC) + EFV is contraindicated or not available, one of the following options is recommended:  
    - AZT + 3TC + EFV  
    - AZT + 3TC + NVP  
    - TDF + 3TC (or FTC) + NVP (strong recommendation, moderate-quality evidence).  
  • Countries should discontinue d4T use in first-line regimens because of its well-recognized metabolic toxicities (strong recommendation, moderate-quality evidence). |
| **First-line ART for pregnant and breastfeeding women and their infants** | • A once-daily fixed-dose combination of TDF + 3TC (or FTC) + EFV is recommended as first-line ART in pregnant and breastfeeding women, including pregnant women in the first trimester of pregnancy and women of childbearing age. The recommendation applies both to lifelong treatment and to ART initiated for PMTCT and then stopped (strong recommendation, low- to moderate-quality evidence: moderate-quality evidence for adults in general but low-quality evidence for the specific population of pregnant and breastfeeding women and infants).  
  • Infants of mothers who are receiving ART and are breastfeeding should receive six weeks of infant prophylaxis with daily NVP. If infants are receiving replacement feeding, they should be given four to six weeks of infant prophylaxis with daily NVP (or twice-daily AZT). Infant prophylaxis should begin at birth or when HIV exposure is recognized postpartum (strong recommendation, moderate-quality evidence for breastfeeding infants; strong recommendation, low-quality evidence for infants receiving only replacement feeding). |
| **First-line ART for children younger than 3 years of age** | • A LPV/r-based regimen should be used as first-line ART for all children infected with HIV younger than three years (36 months) of age, regardless of NNRTI exposure. If LPV/r is not feasible, treatment should be initiated with an NVP-based regimen (strong recommendation, moderate-quality evidence).  
  • Where viral load monitoring is available, consideration can be given to substituting LPV/r with an NNRTI after virological suppression is sustained (conditional recommendation, low-quality evidence).  
  • For infants and children younger than three years infected with HIV, ABC + 3TC + AZT is recommended as an option for children who develop TB while on an ART regimen containing NVP or LPV/r. Once TB therapy has been completed, this regimen should be stopped and the initial regimen should be restarted (strong recommendation, moderate-quality evidence).  
  • For infants and children younger than three years infected with HIV, the NRTI backbone for an ART regimen should be ABC + 3TC or AZT + 3TC (strong recommendation, low-quality evidence). |
| **First-line ART for children 3 years of age and older (including adolescents)** | • For children infected with HIV three years of age and older (including adolescents), EFV is the preferred NNRTI for first-line treatment and NVP is the alternative (strong recommendation, low-quality evidence).  
  • For children infected with HIV three years to less than 10 years old (and adolescents weighing less than 35 kg), the NRTI backbone for an ART regimen should be one of the following, in preferential order:  
    - ABC + 3TC  
    - AZT or TDF + 3TC (or FTC) (conditional recommendation, low-quality evidence).  
  • For adolescents infected with HIV (10 to 19 years old) weighing 35 kg or more, the NRTI backbone for an ART regimen should align with that of adults and be one of the following, in preferential order:  
    - TDF + 3TC (or FTC)  
    - AZT + 3TC  
    - ABC + 3TC (strong recommendation, low-quality evidence). |
### Monitoring ART response and diagnosis of treatment failure

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<th>Topic and population</th>
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| All populations | - Viral load is recommended as the preferred monitoring approach to diagnose and confirm ARV treatment failure *(strong recommendation, low-quality evidence)*.  
- If viral load is not routinely available, CD4 count and clinical monitoring should be used to diagnose treatment failure *(strong recommendation, moderate-quality evidence)*. |

### Second-line ART: what ARV regimen to switch to

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<th>Topic and population</th>
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| What ARV regimen to switch to in adults and adolescents *(includes pregnant and breastfeeding women)* | - Second-line ART for adults should consist of two nucleoside reverse-transcriptase inhibitors (NRTIs) + a ritonavir-boosted protease inhibitor (PI).  
  - The following sequence of second-line NRTI options is recommended:  
    - After failure on a TDF + 3TC (or FTC)-based first-line regimen, use AZT + 3TC as the NRTI backbone in second-line regimens.  
    - After failure on an AZT or d4T + 3TC-based first-line regimen, use TDF + 3TC (or FTC) as the NRTI backbone in second-line regimens.  
    - Use of NRTI backbones as a fixed-dose combination is recommended as the preferred approach *(strong recommendation, moderate-quality evidence)*.  
  - Heat-stable fixed-dose combinations ATV/r and LPV/r are the preferred boosted PI options for second-line ART *(strong recommendation, moderate-quality evidence)*. |
| What ARV regimen to switch to in children *(including adolescents)* | - After failure of a first-line NNRTI-based regimen, a boosted PI plus two NRTIs are recommended for second-line ART; LPV/r is the preferred boosted PI *(strong recommendation, moderate-quality evidence)*.  
  - After failure of a first-line LPV/r-based regimen, children younger than 3 years should remain on their first-line regimen, and measures to improve adherence should be undertaken *(conditional recommendation, very-low-quality evidence)*.  
  - After failure of a first-line LPV/r-based regimen, children 3 years or older should switch to a second-line regimen containing an NNRTI plus two NRTIs; EFV is the preferred NNRTI *(conditional recommendation, low-quality evidence)*.  
  - After failure of a first-line regimen of ABC or TDF + 3TC (or FTC), the preferred NRTI backbone option for second-line ART is AZT + 3TC *(strong recommendation, low-quality evidence)*.  
  - After failure of a first-line regimen containing AZT or d4T + 3TC (or FTC) the preferred NRTI backbone option for second-line ART is ABC or TDF + 3TC (or FTC) *(strong recommendation, low-quality evidence)*. |
### Third-line ART

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| All populations      | • National programmes should develop policies for third-line ART *(conditional recommendation, low-quality evidence).*  
• Third-line regimens should include new drugs with minimal risk of cross-resistance to previously used regimens, such as integrase inhibitors and second-generation NNRTIs and PIs *(conditional recommendation, low-quality evidence).*  
• Patients on a failing second-line regimen with no new ARV options should continue with a tolerated regimen *(conditional recommendation, very-low-quality evidence).* |
| Special considerations for children | Strategies that balance the benefits and risks for children need to be explored when second-line treatment fails. For older children and adolescents who have more therapeutic options available to them, constructing third-line ARV regimens with novel drugs used in treating adults such as ETV, DRV and RAL may be possible. Children on a second-line regimen that is failing with no new ARV drug options should continue with a tolerated regimen. If ART is stopped, opportunistic infections still need to be prevented, symptoms relieved and pain managed. |

### Operations and service delivery

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<th>Topic</th>
<th>Recommendations</th>
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<td>Interventions to optimize adherence to ART</td>
<td>• Mobile phone text messages could be considered as a reminder tool for promoting adherence to ART as part of a package of adherence interventions <em>(strong recommendation, moderate-quality evidence).</em></td>
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</tbody>
</table>
| Service integration and linkage | • In generalized epidemic settings, ART should be initiated and maintained in eligible pregnant and postpartum women and in infants at maternal and child health care settings, with linkage and referral to ongoing HIV care and ART, where appropriate *(strong recommendation, very-low-quality evidence).*  
• In settings with a high burden of HIV and TB, ART should be initiated for an individual living with HIV in TB treatment settings, with linkage to ongoing HIV care and ART *(strong recommendation, very-low-quality evidence).*  
• In settings with a high burden of HIV and TB, TB treatment may be provided for an individual living with HIV in HIV care settings where TB diagnosis has also been made *(strong recommendation, very-low-quality evidence).*  
• ART should be initiated and maintained in eligible people living with HIV at care settings where opioid substitution therapy (OST) is provided *(strong recommendation, very-low-quality evidence).* |
| Decentralization of treatment and care | The following options should be considered for decentralization of ART initiation and maintenance.  
• Initiation of ART in hospitals with maintenance of ART in peripheral health facilities *(strong recommendation, low-quality evidence).*  
• Initiation and maintenance of ART in peripheral health facilities *(strong recommendation, low-quality evidence).*  
• Initiation of ART at peripheral health facilities with maintenance at the community level (that is, outside health facilities in settings such as outreach sites, health posts, home-based services or community-based organizations) between regular clinical visits *(strong recommendation, moderate-quality evidence).* |
| Task-shifting | • Trained non-physician clinicians, midwives and nurses can initiate first-line ART *(strong recommendation, moderate-quality evidence).*  
• Trained non-physician clinicians, midwives and nurses can maintain ART *(strong recommendation, moderate-quality evidence).*  
• Trained and supervised community health workers can dispense ART between regular clinical visits *(strong recommendation, moderate-quality evidence).* |
**Guidance for programme managers**

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| Guidance for programme managers | For deciding on the implementation of the clinical and operational recommendations, it is recommended that:  
  - The national authorities do so using a transparent, open and informed process. This process should have broad stakeholder engagement, including meaningful participation from the affected communities, and take into account the specifics of the recommendations under discussion.  
  - The decision-making process take into account data on the national and local HIV epidemiology, current ART programme performance and the socioeconomic, policy and legal context, including the budgetary, human resource requirements and other health system implications. The latter would identify which inputs and systems are currently available and which areas require additional investment.  
  - The decision-making process take into account the ethics, equity and human rights, the impact and cost-effectiveness and the opportunity and risk dimensions of alternative implementation options. |
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