

# SUMMARY OF RECOMMENDATIONS

The recommendations listed in these guidelines are categorized as follows:

## Existing recommendation (not changed in 2016)

The recommendation was published in previous WHO guidelines. The source of the guideline is provided with the recommendation. These recommendations have not been reviewed or changed in 2015. The evidence base for these recommendations is included in the original source document.

## Existing recommendation (reviewed and updated in 2016)

The recommendation was published in previous WHO guidelines, and evidence to inform the recommendation was reviewed for this edition. The supplementary web annexes of this guideline include evidence to support the recommendation. Where changes have been made to the strength of the recommendation, this is noted in the relevant chapter.

**NEW**

## New recommendation (2016)

The recommendation is new and published for the first time in these guidelines. These recommendations address new topic areas or replace previous recommendations. The supplementary web annexes of these guidelines provide evidence to support the recommendation.

The following table presents all recommendations included in these guidelines, including the strength of the recommendation and quality of the evidence.


Chapter	Recommendation
<b>2. HIV DIAGNOSIS</b>	
<b>2.2 Retesting prior to enrollment in care</b>	
WHO reminds national programmes to retest all newly diagnosed people with HIV. WHO information note – 22 October 2014. Geneva: World Health Organization; 2014 ( <a href="http://www.who.int/hiv/pub/vct/retest-newly-diagnosed-plhiv-full/en/">http://www.who.int/hiv/pub/vct/retest-newly-diagnosed-plhiv-full/en/</a> )	
	Retest all clients diagnosed HIV-positive with a second specimen and a second operator using the same testing strategy and algorithm before enrolling the client in care and/or initiating ART, regardless of whether or not ART initiation depends on CD4 count.
	Retesting people on ART is not recommended, as there are potential risks of incorrect diagnosis, particularly for in vitro diagnostics (IVDs) that use oral fluid specimens.
<b>2.3 Pre- and post-test services</b>	
Guideline on HIV disclosure counselling for children up to 12 years of age. Geneva: World Health Organization; 2011 ( <a href="http://www.who.int/hiv/pub/hiv_disclosure/en/">http://www.who.int/hiv/pub/hiv_disclosure/en/</a> )	
	Initiatives should be put in place to enforce privacy protection and institute policy, laws and norms that prevent discrimination and promote the rights of people living with HIV. This can help create environments where disclosure of HIV status is easier (strong recommendation, low-quality evidence).
<b>2.4 Principles and approaches for service delivery</b>	
Consolidated guidelines on HIV testing services. Geneva: World Health Organization; 2015 ( <a href="http://www.who.int/hiv/pub/guidelines/hiv-testing-services/en/">http://www.who.int/hiv/pub/guidelines/hiv-testing-services/en/</a> )	
Guidance on provider-initiated HIV testing and counselling in health facilities. Geneva: World Health Organization; 2007 ( <a href="http://www.who.int/hiv/pub/vct/pitc2007/en/">http://www.who.int/hiv/pub/vct/pitc2007/en/</a> ).	
<b>2.4.1 Improving quality and efficiency</b>	Lay providers who are trained and supervised can independently conduct safe and effective HIV testing using rapid diagnostic tests (RDTs) (strong recommendation, moderate-quality evidence).
<b>2.4.2 HIV testing approaches</b>	<i>Generalized HIV epidemic</i>
Facility-based HIV testing services and provider-initiated testing and counselling (PITC)	PITC should be offered for all clients and in all services (including services for sexually transmitted infections (STI), viral hepatitis, tuberculosis (TB), children under the age of 5 years, immunization, malnutrition, antenatal care and all services for key populations) as an efficient and effective way to identify people with HIV.
	<i>Concentrated HIV epidemic</i>
	PITC should be offered for clients (adults, adolescents and children) in clinical settings who present with symptoms or medical conditions that could indicate HIV infection, including presumed and confirmed TB cases.
	<i>Regardless of epidemic type</i>
	PITC should be considered for malnutrition clinics, STI, hepatitis and TB services, ANC settings and health services for key populations.
	For TB settings, routine HIV testing should be offered to all clients with presumptive and diagnosed TB; partners of known HIV-positive TB patients should be offered voluntary HTS with support for mutual disclosure (strong recommendation, low-quality evidence in accordance with the recommendation for the partners of all people living with HIV), and TB control programmes should mainstream provision of HTS in their operations and routine services.

Chapter	Recommendation
Community-based HIV testing services	<p><i>Generalized HIV epidemic</i></p> <p>WHO recommends community-based HIV testing services with linkage to prevention, treatment and care services in addition to routinely offering PITC for all populations, particularly key populations (strong recommendation, low-quality evidence).</p> <p><i>Concentrated HIV epidemic</i></p> <p>WHO recommends community-based HIV testing services, with linkage to prevention, treatment and care, in addition to PITC for key populations (strong recommendation, low-quality evidence).</p>
<p><b>2.5 HIV diagnosis in infants and children</b></p> <p>Consolidated guidelines on HIV testing services. Geneva: World Health Organization; 2015 (<a href="http://www.who.int/hiv/pub/guidelines/hiv-testing-services/en">http://www.who.int/hiv/pub/guidelines/hiv-testing-services/en</a>).</p> <p>Supplement to the 2013 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2014 (<a href="http://www.who.int/hiv/pub/guidelines/arv2013/arvs2013supplement_march2014/en">http://www.who.int/hiv/pub/guidelines/arv2013/arvs2013supplement_march2014/en</a>).</p> <p>WHO recommendations on the diagnosis of HIV infection in infants and children. Geneva: World Health Organization; 2010 (<a href="http://www.who.int/hiv/pub/paediatric/diagnosis/en">http://www.who.int/hiv/pub/paediatric/diagnosis/en</a>).</p>	
<b>2.5.1 Overview</b>	<p>It is strongly recommended that HIV serological assays used for the purpose of clinical diagnostic testing have a minimum sensitivity of 99% and specificity of 98% under quality assured laboratory conditions (strong recommendation, moderate-quality evidence).</p> <p>It is strongly recommended that HIV virological assays used for the purpose of clinical diagnostic testing (usually at or after 6 weeks of age) have a sensitivity of at least 95% and ideally greater than 98%, and specificity of 98% or more under quality-assured, standardized and validated laboratory conditions (strong recommendation, moderate-quality evidence).</p> <p>It is strongly recommended that HIV virological testing be used to diagnose HIV infection in infants and children below 18 months of age (strong recommendation, high-quality evidence).</p> <p>In infants and children undergoing virological testing, the following assays (and respective specimen types) are strongly recommended for use: HIV DNA on whole blood specimen or DBS; HIV RNA on plasma or DBS; Us p24 Ag on plasma or DBS (strong recommendation, high-quality evidence).</p> <p>It is strongly recommended that all HIV-exposed infants have HIV virological testing at 4–6 weeks of age or at the earliest opportunity thereafter (strong recommendation, high-quality evidence).</p> <p>In infants with an initial positive virological test result, it is strongly recommended that ART be started without delay and, at the same time, a second specimen is collected to confirm the initial positive virological test result. Do not delay ART. Immediate initiation of ART saves lives and should not be delayed while waiting for the results of the confirmatory test (strong recommendation, high-quality evidence).</p> <p>It is strongly recommended that test results from virological testing in infants be returned to the clinic and child/mother/caregiver as soon as possible, but at the very latest within four weeks of specimen collection. Positive test results should be fast-tracked to the mother–baby pair as soon as possible to enable prompt initiation of ART (strong recommendation, high-quality evidence).</p> <p>It is strongly recommended that all infants with unknown or uncertain HIV exposure being seen in health-care facilities at or around birth or at the first postnatal visit (usually 4–6 weeks) or other child health visit have their HIV exposure status ascertained (strong recommendation, high-quality evidence).</p> <p>It is strongly recommended that HIV-exposed infants who are well undergo HIV serological testing at around 9 months of age (or at the time of the last immunization visit). Infants who have reactive serological assays at 9 months should have a virological test to identify HIV infection and the need for ART (strong recommendation, low-quality evidence).</p>

Chapter	Recommendation
	<p>It is strongly recommended that infants with signs or symptoms suggestive of HIV infection undergo HIV serological testing and, if positive (reactive), virological testing (strong recommendation, low-quality evidence).</p> <p>It is strongly recommended that children (18 months or older) with suspected HIV infection or HIV exposure have HIV serological testing performed according to the standard diagnostic HIV serological testing algorithm used in adults (strong recommendation, high-quality evidence).</p>
<p><b>NEW</b> 2.5.2 Timing of virological testing</p>	<p>Addition of nucleic acid testing (NAT) at birth to existing early infant diagnosis (EID) testing approaches can be considered to identify HIV infection in HIV-exposed infants (conditional recommendation, low-quality evidence).</p>
<p><b>NEW</b> 2.5.3 Point-of-care technologies for the diagnosis of HIV infection in infants and children</p>	<p>Nucleic acid testing (NAT) technologies that are developed and validated for use at or near to the point of care can be used for early infant HIV testing (conditional recommendation, low-quality evidence).</p> <p>Rapid diagnostic tests (RDTs) for HIV serology can be used to assess HIV exposure only in infants less than 4 months of age. HIV-exposure status in infants and children 4–18 months of age should be ascertained by undertaking HIV serological testing in the mother (conditional recommendation, low-quality evidence).</p> <p>Rapid diagnostic tests for HIV serology can be used at 9 months to rule out HIV infection in asymptomatic HIV-exposed infants (conditional recommendation, low-quality evidence).</p> <p>Rapid diagnostic tests for HIV serology can be used to diagnose HIV infection in children older than 18 months following the national testing strategy (strong recommendation, moderate-quality evidence).</p>
<p><b>NEW</b> 2.5.4 Provider-initiated HIV testing and counselling for infants and children</p>	<p>In generalized epidemic settings, infants and children with unknown HIV status who are admitted for inpatient care or attending malnutrition clinics should be routinely tested for HIV (strong recommendation, low-quality evidence).</p> <p>In generalized epidemic settings, infants and children with unknown HIV status should be offered HIV testing in outpatient or immunization clinics (conditional recommendation, low-quality evidence).</p>
<p><b>2.6 Other priority populations</b></p> <p>Consolidated guidelines on HIV testing services. Geneva: World Health Organization; 2015 (<a href="http://www.who.int/hiv/pub/guidelines/hiv-testing-services/en">http://www.who.int/hiv/pub/guidelines/hiv-testing-services/en</a>).</p> <p>Guidance for HIV testing and counselling and care for adolescents living with HIV. Geneva: World Health Organization; 2013 (<a href="http://www.who.int/hiv/pub/guidelines/adolescents/en">http://www.who.int/hiv/pub/guidelines/adolescents/en</a>).</p> <p>Guidance on couples HIV testing and counselling, including antiretroviral therapy for treatment and prevention in serodiscordant couples. Geneva: World Health Organization; 2012 (<a href="http://www.who.int/hiv/pub/guidelines/9789241501972/en/index.html">http://www.who.int/hiv/pub/guidelines/9789241501972/en/index.html</a>).</p> <p>Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations Geneva: World Health Organization; 2014 (<a href="http://www.who.int/hiv/pub/guidelines/keypopulations/en">http://www.who.int/hiv/pub/guidelines/keypopulations/en</a>).</p>	
<p>2.6.1 Adolescents</p>	<p>HIV testing services, with linkages to prevention, treatment and care, should be offered for adolescents from key populations in all settings (strong recommendation, very low-quality evidence).</p> <p>Adolescents with HIV should 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).</p>

Chapter	Recommendation
	<p><i>Generalized HIV epidemic</i></p> <p>HIV testing services with linkage to prevention, treatment and care should be offered to all adolescents in generalized epidemics (strong recommendation, very low-quality evidence).</p> <p><i>Concentrated HIV epidemic</i></p> <p>HIV testing services with linkage to prevention, treatment and care should be <i>accessible</i> to adolescents in low-level and concentrated epidemics (conditional recommendation, very low-quality evidence).</p>
2.6.2 Pregnant women	<p><i>High-prevalence settings</i></p> <p>PITC for women should be considered a routine component of the package of care in all antenatal, childbirth, postpartum and paediatric care settings. In such settings, where breastfeeding is the norm, lactating mothers who are HIV negative should be retested periodically throughout the period of breastfeeding.</p> <p>All HIV-negative pregnant women should be retested in the third trimester, postpartum and/or during labour, because of the high risk of acquiring HIV during pregnancy.</p> <p><i>Low-prevalence settings</i></p> <p>PITC can be considered for pregnant women in antenatal care as a key component of the effort:</p> <ul style="list-style-type: none"> <li>• to eliminate mother-to-child transmission of HIV</li> <li>• to integrate HIV testing with other key testing (for viral hepatitis, syphilis, etc.) as relevant to the setting</li> <li>• to retest HIV negative pregnant women who are in a serodiscordant couple, from a key population group or have known ongoing HIV risk.</li> </ul>
2.6.3 Couples and partners	<p>Couples and partners should be offered voluntary HIV testing services with support for mutual disclosure. This applies also to couples and partners from key populations (strong recommendation, low-quality evidence).</p> <p>In antenatal care settings, couples and partners should be offered voluntary HIV testing services with support for mutual disclosure (strong recommendation, low-quality evidence).</p> <p>HIV testing services for couples and partners, with support for mutual disclosure, should be offered to individuals with known HIV status and their partners (strong recommendation, low-quality evidence for all people with HIV in all epidemic settings; conditional recommendation, low-quality evidence for HIV-negative people depending on country-specific HIV prevalence).</p>
2.6.5 Key populations	<p>HIV testing services should be routinely offered to all key populations in the community, in closed settings such as prisons and in facility-based settings.</p> <p>Community-based HIV testing services for key populations linked to prevention, treatment and care services are recommended, in addition to routine facility-based HIV testing services, in all settings (strong recommendation, low-quality evidence).</p>

Chapter	Recommendation
<b>2.7 Diagnostics</b> Consolidated guidelines on HIV testing services. Geneva: World Health Organization; 2015 ( <a href="http://www.who.int/hiv/pub/guidelines/hiv-testing-services/en">http://www.who.int/hiv/pub/guidelines/hiv-testing-services/en</a> ). Technical guidance update on quality assurance for HIV rapid diagnostic tests. Geneva: World Health Organization; 2015 ( <a href="http://apps.who.int/iris/bitstream/10665/181244/1/WHO_HIV_2015.28_eng.pdf?ua=1&amp;ua=1">http://apps.who.int/iris/bitstream/10665/181244/1/WHO_HIV_2015.28_eng.pdf?ua=1&amp;ua=1</a> ).	<p><i>High-prevalence settings</i></p> <p>In settings with greater than 5% HIV prevalence in the population tested, a diagnosis of HIV positive should be provided to people with two sequential reactive tests.</p> <p>For individuals with discrepant test results where Assay 1 is reactive, Assay 2 is non-reactive and Assay 3 is reactive, the results should be considered inconclusive and the client should be asked to return in 14 days for retesting.</p> <p>For individuals with discrepant test results where Assay 1 is reactive, Assay 2 is non-reactive and Assay 3 is non-reactive, the final result should be considered HIV negative.</p> <p><i>Low-prevalence settings</i></p> <p>In settings with less than 5% HIV prevalence in the population tested, a diagnosis of HIV positive should be provided to people with three sequential reactive tests.</p> <p>For individuals where Assay 1 result is reactive and Assay 2 result is non-reactive, the final result should be considered HIV negative. However, in the case of such results and where Assay 1 is a fourth-generation assay (antibody/antigen [Ab/Ag]) and Assay 2 is an Ab-only assay, the result should be considered inconclusive and the person should be retested after 14 days.</p> <p>For individuals with results in which Assay 1 is reactive, Assay 2 is reactive and Assay 3 is non-reactive, the result should be considered inconclusive and the client should be asked to return in 14 days for retesting.</p> <p><i>All settings</i></p> <p>HIV testing services may use combinations of RDTs or combinations of RDTs/enzyme immunoassays (EIAs)/supplemental assays rather than EIA/Western blot combinations.</p>

Chapter	Recommendation
<b>3. CLINICAL GUIDELINES: ANTIRETROVIRAL DRUGS FOR HIV PREVENTION</b>	
<b>3.1 Oral pre-exposure prophylaxis for preventing the acquisition of HIV</b>	
	Oral pre-exposure prophylaxis (PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk <sup>1</sup> of HIV infection as part of combination HIV prevention approaches (strong recommendation, high-quality evidence).
<b>3.2 Post-exposure prophylaxis</b>	
Guidelines on post-exposure prophylaxis for HIV and the use of co-trimoxazole prophylaxis for HIV-related infections among adults, adolescents and children: recommendations for a public health approach – December 2014 supplement to the 2013 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2014 ( <a href="http://www.who.int/hiv/pub/guidelines/arv2013/arvs2013supplement_dec2014/en">http://www.who.int/hiv/pub/guidelines/arv2013/arvs2013supplement_dec2014/en</a> ).	
	<p>A regimen for post-exposure prophylaxis for HIV with two drugs is effective, but three drugs are preferred (conditional recommendation, very low-quality evidence).</p> <p>Post-exposure prophylaxis ARV regimens for adults and adolescents:</p> <p>TDF + 3TC (or FTC) is recommended as the preferred backbone<sup>2</sup> regimen for HIV post-exposure prophylaxis in adults and adolescents (strong recommendation, low-quality evidence).</p> <p>LPV/r or ATV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for adults and adolescents (conditional recommendation, very low-quality evidence). Where available, RAL, DRV/r or EFV can be considered as alternative options.</p> <p>Post-exposure prophylaxis ARV regimens for children ≤10 years:</p> <p>AZT + 3TC is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis for children aged 10 years and younger. ABC + 3TC or TDF + 3TC (or FTC) can be considered as alternative regimens (strong recommendation, low-quality evidence).</p> <p>LPV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for children younger than 10 years (conditional recommendation, very low-quality evidence). An age-appropriate alternative regimen can be identified among ATV/r, RAL, DRV, EFV and NVP.<sup>3</sup></p> <p><i>Prescribing practices</i></p> <p>A full 28-day prescription of antiretroviral drugs should be provided for HIV post-exposure prophylaxis following initial risk assessment (strong recommendation, low-quality evidence).</p> <p>Enhanced adherence counselling<sup>4</sup> is suggested for all individuals initiating HIV post-exposure prophylaxis (conditional recommendation, moderate-quality evidence).</p>

<sup>1</sup> Provisional definition of substantial risk is defined as HIV incidence higher than 3 per 100 person-years in the absence of PrEP.

<sup>2</sup> Backbone regimen refers to the two-NRTI component of an ART regimen (normally comprising 3 ARV drugs).

<sup>3</sup> NVP should not be used in children above the age of two years.

<sup>4</sup> Enhanced adherence counselling includes baseline individual needs assessment, adherence counselling and education sessions and follow-up telephone calls.

Chapter	Recommendation
<b>4. CLINICAL GUIDELINES: ANTIRETROVIRAL THERAPY</b>	
<b>4.3 When to start ART</b>	
<b>NEW</b> 4.3.1 When to start ART in adults (>19 years old)	ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count (strong recommendation, moderate-quality evidence).
	As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with a CD4 count $\leq 350$ cells/mm <sup>3</sup> (strong recommendation, moderate-quality evidence).
<b>NEW</b> 4.3.2 When to start ART in pregnant and breastfeeding women	ART should be initiated in all pregnant and breastfeeding women living with HIV, regardless of WHO clinical stage and at any CD4 cell count and continued lifelong (strong recommendation, moderate-quality evidence).
<b>NEW</b> 4.3.3 When to start ART in adolescents (10–19 years of age)	ART should be initiated in all adolescents living with HIV, regardless of WHO clinical stage and at any CD4 cell count (conditional recommendation, low-quality evidence).
	As a priority, ART should be initiated in all adolescents with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adolescents with a CD4 count $\leq 350$ cells/mm <sup>3</sup> (strong recommendation, moderate-quality evidence).
4.3.4 When to start ART in children younger than 10 years of age	<b>NEW</b> ART should be initiated in all children living with HIV, regardless of WHO clinical stage or at any CD4 cell count:
	<ul style="list-style-type: none"> <li>• Infants diagnosed in the first year of life (strong recommendation, moderate-quality evidence).</li> </ul>
	<b>NEW</b> <ul style="list-style-type: none"> <li>• Children living with HIV 1 year old to less than 10 years old (conditional recommendation, low-quality evidence).</li> </ul>
	As a priority, ART should be initiated in all children <2 years of age or children younger than 5 years of age with WHO clinical stage 3 or 4 or CD4 count $\leq 750$ cells/mm <sup>3</sup> or CD4 percentage <25% and children 5 years of age and older with WHO clinical stage 3 or 4 or CD4 count $\leq 350$ cells/mm <sup>3</sup> (strong recommendation, moderate-quality evidence).
4.3.5 Timing of ART for adults and children with TB	ART should be started in all TB patients living with HIV regardless of CD4 count (strong recommendation, high-quality evidence). <sup>1</sup>
	TB treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment (strong recommendation, high-quality evidence). <sup>2</sup>
	HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts less than 50 cells/mm <sup>3</sup> ) should receive ART within the first two weeks of initiating TB treatment.
	ART should be started in any child with active TB disease as soon as possible and within 8 weeks following the initiation of antituberculosis treatment regardless of the CD4 cell count and clinical stage (strong recommendation, low-quality evidence).
Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 ( <a href="http://www.who.int/hiv/pub/guidelines/arv2013/download/en">http://www.who.int/hiv/pub/guidelines/arv2013/download/en</a> ).	

<sup>1</sup> The quality of evidence for this recommendation was upgraded to high in 2015.

<sup>2</sup> The quality of evidence for this recommendation was upgraded to high in 2015.





Chapter	Recommendation
<b>4.4 What to start: first-line ART</b>	
<b>4.4.1 First-line ART for adults</b>	<p>First-line ART for adults<sup>1</sup> should consist of two nucleoside reverse-transcriptase inhibitors (NRTIs) plus a non-nucleoside reverse-transcriptase inhibitor (NNRTI) or an integrase inhibitor (INSTI):</p> <ul style="list-style-type: none"> <li>• TDF + 3TC (or FTC) + EFV as a fixed-dose combination is recommended as the preferred option to initiate ART (strong recommendation, moderate-quality evidence).</li> <li>• If TDF + 3TC (or FTC) + EFV is contraindicated or not available, one of the following alternative options is recommended: <ul style="list-style-type: none"> <li>◦ AZT + 3TC + EFV</li> <li>◦ AZT + 3TC + NVP</li> <li>◦ TDF + 3TC (or FTC) + NVP (strong recommendation, moderate-quality evidence).</li> </ul> </li> </ul>
	<p><b>NEW</b></p> <p>TDF + 3TC (or FTC) + DTG or TDF + 3TC (or FTC) + EFV 400 mg/day may be used as alternative options to initiate ART (conditional recommendation, moderate-quality evidence).</p>
	<p>Countries should discontinue d4T use in first-line regimens because of its well-recognized metabolic toxicities (strong recommendation, moderate-quality evidence).</p> <p>Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 (<a href="http://www.who.int/hiv/pub/guidelines/arv2013/download/en">http://www.who.int/hiv/pub/guidelines/arv2013/download/en</a>).</p>
<b>4.4.2 Fixed-dose combinations</b>	<p><b>NEW</b></p> <p>Fixed-dose combinations and once-daily regimens are preferred for antiretroviral therapy (strong recommendation, moderate-quality evidence).</p>
<b>4.4.3 First-line ART for adolescents</b>	<p><b>NEW</b></p> <p>First-line ART for adolescents should consist of two NRTIs plus an NNRTI or an INSTI:</p> <p>TDF + 3TC (or FTC) + EFV as a fixed-dose combination is recommended as the preferred option to initiate ART (strong recommendation, low-quality evidence).</p> <p>TDF + 3TC (or FTC) + DTG or TDF + 3TC (or FTC) + EFV<sub>400</sub><sup>2</sup> may be used as alternative options to initiate ART (conditional recommendation, low-quality evidence).</p> <p>If preferred regimens are contraindicated or not available, one of the following alternative options is recommended (strong recommendation, moderate-quality evidence):</p> <p>ABC + 3TC + EFV  ABC + 3TC + NVP  AZT + 3TC + EFV  AZT + 3TC + NVP  TDF + 3TC (or FTC) + NVP</p>
<b>4.4.4 First-line ART for children aged 3 to 10 years of age</b>	<p>For children 3 to less than 10 years of age, the NRTI backbone<sup>3</sup> should be one of the following, in preferential order (conditional recommendation, moderate-quality evidence<sup>4</sup>):</p> <ul style="list-style-type: none"> <li>• ABC + 3TC</li> <li>• AZT or TDF + 3TC (or FTC)</li> </ul> <p>For children 3 years and older, EFV is the preferred NNRTI for first-line treatment and NVP is the preferred alternative (strong recommendation, low-quality evidence).</p>

<sup>1</sup> Includes pregnant and breastfeeding women (further guidance in Box 4.3).

<sup>2</sup> EFV at a lower dose (400 mg/day).

<sup>3</sup> Backbone regimen refers to the two-NRTI component of an ART regimen (normally comprising 3 ARV drugs).

<sup>4</sup> Strength of evidence reviewed in 2015.

Chapter	Recommendation
4.4.5 First-line ART for children younger than 3 years of age	For infants and children younger than 3 years, the NRTI backbone for an ART regimen should be ABC or AZT + 3TC (strong recommendation, moderate-quality evidence <sup>1</sup> ).
	A LPV/r-based regimen should be used as first-line ART for all children infected with HIV younger than 3 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 EFV at 3 years of age after viral suppression is sustained (conditional recommendation, moderate-quality evidence).
	For infants and children infected with HIV younger than 3 years, 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).
4.4.7 Infant prophylaxis	 Infants born to mothers with HIV who are at high risk of acquiring HIV <sup>2</sup> should receive dual prophylaxis with AZT (twice daily) and NVP (once daily) for the first 6 weeks of life, whether they are breastfed or formula fed (strong recommendation, moderate-quality evidence).
	 Breastfed infants who are at high risk of acquiring HIV, including those first identified as exposed to HIV during the postpartum period, should continue infant prophylaxis for an additional 6 weeks (total of 12 weeks of infant prophylaxis) using either AZT (twice daily) and NVP (once daily) or NVP alone (conditional recommendation, low-quality evidence).
	Infants of mothers who are receiving ART and are breastfeeding should receive 6 weeks of infant prophylaxis with daily NVP. If infants are receiving replacement feeding, they should be given 4–6 weeks of infant prophylaxis with daily NVP (or twice-daily AZT) (strong recommendation, moderate-quality evidence for breastfeeding infants; strong recommendation, low-quality evidence for infants receiving only replacement feeding).
	Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 ( <a href="http://www.who.int/hiv/pub/guidelines/arv2013/download/en">http://www.who.int/hiv/pub/guidelines/arv2013/download/en</a> ).
4.4.8 Infant feeding in the context of HIV	National or subnational health authorities should decide whether health services will principally counsel and support mothers known to be HIV infected to either breastfeed and receive ARV <sup>3</sup> interventions or avoid all breastfeeding.  In settings where national authorities have decided that maternal and child health services will principally promote and support breastfeeding and antiretroviral interventions as the strategy that will most likely give infants born to mothers known to be HIV infected the greatest chance of HIV-free survival, mothers known to be infected with HIV 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. <sup>4</sup> Breastfeeding should then stop only 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).  Guidelines on HIV and infant feeding 2010. Principles and recommendations for infant feeding in the context of HIV and a summary of evidence. Geneva: World Health Organization; 2010 ( <a href="http://www.who.int/maternal_child_adolescent/documents/9789241599535/en">http://www.who.int/maternal_child_adolescent/documents/9789241599535/en</a> ).






<sup>1</sup> Strength of evidence reviewed in 2015.

<sup>2</sup> High-risk infants are defined as those:

- born to women with established HIV infection who have received less than four weeks of ART at the time of delivery; or
- born to women with established HIV infection with viral load >1000 copies/mL in the four weeks before delivery, if viral load measurement is available; or
- born to women with incident HIV infection during pregnancy or breastfeeding; or
- identified for the first time during the postpartum period, with or without a negative HIV test prenatally.



<sup>3</sup> All women living with HIV are eligible for initiation of ART regardless of CD4 count.

<sup>4</sup> Infants who are HIV infected will benefit from extended breastfeeding and should continue breastfeeding for as long as feasible and desired.

Chapter	Recommendation
<b>4.5 Monitoring the response to ART and diagnosing treatment failure</b>	
<b>4.5.1 Laboratory monitoring before and after initiating ART</b>	<p> Routine viral load monitoring can be carried out at 6 months, at 12 months and then every 12 months thereafter if the patient is stable on ART to synchronize with routine monitoring and evaluation reporting<sup>1</sup> (conditional recommendation, very low-quality evidence).</p> <p> In settings where routine viral load monitoring is available, CD4 cell count monitoring can be stopped in individuals who are stable on ART and virally suppressed<sup>2</sup> (conditional recommendation, low-quality evidence).</p> <p>Viral load is recommended as the preferred monitoring approach to diagnose and confirm treatment failure<sup>a</sup> (strong recommendation, low-quality evidence).</p> <p>Viral failure is defined by a persistently detectable viral load exceeding 1000 copies/ml (that is, two consecutive viral load measurements within a 3-month interval, with adherence support between measurements) after at least 6 months of starting a new ART regimen.</p> <p>Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 (<a href="http://www.who.int/hiv/pub/guidelines/arv2013/download/en">http://www.who.int/hiv/pub/guidelines/arv2013/download/en</a>).</p> <p> Dried blood spot specimens using venous or capillary whole blood can be used to determine the HIV viral load. A threshold of 1000 copies/mL can be used to determine virological failure when using dried blood spot samples, as defined for testing in plasma<sup>a</sup> (conditional recommendation, low-quality evidence).</p>
<b>4.8 What ART regimen to switch to (second and third line)</b>	
<b>4.8.1 Second-line ART for adults and adolescents</b>	<p>Second-line ART in adults should consist of two nucleoside reverse-transcriptase inhibitors (NRTIs) plus a ritonavir-boosted protease inhibitor (PI).</p> <p>The following sequence of second-line NRTI options is recommended:</p> <ul style="list-style-type: none"> <li>• After failure on a TDF + 3TC (or FTC)-based first-line regimen, use AZT + 3TC as the NRTI backbone in second-line regimens.</li> <li>• 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.</li> </ul> <p>Use of NRTI backbones as a fixed-dose combination is recommended as the preferred approach (strong recommendation, moderate-quality evidence).</p> <p>Heat-stable fixed-dose combinations of ATV/r and LPV/r are the preferred boosted PI options for second-line ART (strong recommendation, moderate-quality evidence).</p> <p> A heat-stable fixed-dose combination of DRV/r can be used as an alternative boosted PI option for second-line ART (conditional recommendation, low-quality evidence).</p> <p> A combination of RAL plus LPV/r can be used as an alternative second-line ART regimen (conditional recommendation, low-quality evidence).</p>

<sup>1</sup> Viral load testing should be performed early after initiating ART (within 6 months), at 12 months and then at least every 12 months to detect treatment failure. If viral load testing is not routinely available, CD4 count and clinical monitoring should be used to diagnose treatment failure, with targeted viral load testing to confirm viral failure where possible.

<sup>2</sup> WHO defines people stable on ART according to the following criteria: on ART for at least 1 year, no current illnesses or pregnancy, good understanding of lifelong adherence and evidence of treatment success (two consecutive viral load measurements below 1000 copies/mL). For service delivery recommendations in these guidelines (see Chapter 6 "Service delivery"), an additional criterion is that there are no adverse drug reactions requiring regular monitoring, but this is not relevant to this recommendation.

Chapter	Recommendation
4.8.2 Second-line ART for children	 <p>After failure of a first-line LPV/r-based regimen, children younger than 3 years should be switched to a RAL-based second-line regimen (conditional recommendation, very low-quality evidence).</p>
	 <p>After failure of a first-line LPV/r-based regimen, children older than 3 years should be switched to a second-line regimen containing two NRTIs plus EFV or RAL (conditional recommendation, very low-quality evidence).</p>
	<p>After failure of a first-line NNRTI-based regimen, children should be switched to a boosted PI-based regimen. LPV/r or ATV/r are preferred (conditional recommendation, very low-quality evidence).</p>
	<p>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).</p>
	<p>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)</p>
4.8.3 Third-line ART	<p>National programmes should develop policies for third-line ART (conditional recommendation, low-quality evidence).</p> <p>Third-line regimens should include new drugs with minimal risk of cross-resistance to previously used regimens, such as INSTIs and second-generation NNRTIs and PIs (conditional recommendation, low-quality evidence).</p> <p>Patients on a failing second-line regimen with no new ARV options should continue with a tolerated regimen (conditional recommendation, very low-quality evidence).</p> <p>Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 (<a href="http://www.who.int/hiv/pub/guidelines/arv2013/download/en">http://www.who.int/hiv/pub/guidelines/arv2013/download/en</a>).</p>

Chapter	Recommendation
<b>5. CLINICAL GUIDELINES: PREVENTION, SCREENING AND MANAGEMENT OF COMMON COINFECTIONS AND COMORBIDITIES</b>	
<b>5.2 Prevention, screening and management of common coinfections</b>	
5.2.1 Co-trimoxazole prophylaxis	<p>Co-trimoxazole prophylaxis is recommended for adults (including pregnant women) with severe or advanced HIV clinical disease (WHO stage 3 or 4) and/or with a CD4 count <math>\leq 350</math> cells/mm<sup>3</sup> (strong recommendation, moderate-quality evidence).</p> <ul style="list-style-type: none"> <li>• In settings where malaria and/or severe bacterial infections (SBIs) are highly prevalent, co-trimoxazole prophylaxis should be initiated regardless of CD4 cell count or WHO stage (conditional recommendation, moderate-quality evidence).</li> <li>• Co-trimoxazole prophylaxis may be discontinued in adults (including pregnant women) with HIV who are clinically stable on ART, with evidence of immune recovery and viral suppression (conditional recommendation, low-quality evidence).</li> <li>• In settings where malaria and/or severe bacterial infections are highly prevalent, co-trimoxazole prophylaxis should be continued regardless of CD4 cell count or WHO clinical stage (conditional recommendation, moderate-quality evidence).</li> </ul> <p>Routine co-trimoxazole prophylaxis should be given to all HIV-infected patients with active TB disease regardless of CD4 cell count (strong recommendation, high-quality evidence).</p> <p>Co-trimoxazole prophylaxis is recommended for infants, children, and adolescents with HIV, irrespective of clinical and immune conditions. Priority should be given to all children less than 5 years old regardless of CD4 cell count or clinical stage, and children with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and/or those with CD4 <math>\leq 350</math> cells/mm<sup>3</sup> (strong recommendation, high-quality evidence).</p> <ul style="list-style-type: none"> <li>• In settings where malaria and/or severe bacterial infections are highly prevalent, co-trimoxazole prophylaxis should be continued until adulthood, irrespective of whether ART is provided (conditional recommendation, moderate-quality evidence).</li> <li>• In settings with low prevalence for both malaria and bacterial infections, co-trimoxazole prophylaxis may be discontinued for children 5 years of age and older who are clinically stable and/or virally suppressed on ART for at least 6 months and with a CD4 count <math>&gt;350</math> cells/mm<sup>3</sup> (strong recommendation, very low-quality evidence).</li> </ul> <p>Co-trimoxazole prophylaxis is recommended for HIV-exposed infants from 4 to 6 weeks of age and should be continued until HIV infection has been excluded by an age-appropriate HIV test to establish final diagnosis after complete cessation of breastfeeding (strong recommendation, very low-quality evidence).</p> <p>Guidelines on post-exposure prophylaxis and the use of co-trimoxazole prophylaxis for HIV-related infections among adults, adolescents and children: recommendations for a public health approach – December 2014 supplement to the 2013 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2013 (<a href="http://www.who.int/hiv/pub/guidelines/arv2013/arvs2013supplement_dec2014/en">http://www.who.int/hiv/pub/guidelines/arv2013/arvs2013supplement_dec2014/en</a>).</p>
5.2.2 Tuberculosis	<p>Xpert MTB/RIF should be used rather than conventional microscopy, culture and drug susceptibility testing (DST) as the initial diagnostic test in adults and children suspected of having HIV-associated TB or multidrug resistant TB (strong recommendation, adults: high-quality evidence; children: very low-quality evidence).</p> <p>Xpert MTB/RIF should be used in preference to conventional microscopy and culture as the initial diagnostic test for cerebrospinal fluid specimens from patients suspected of having TB meningitis (strong recommendation, very low-quality evidence).</p> <p>Xpert MTB/RIF may be used as a replacement test for usual practice (including conventional microscopy, culture or histopathology) for testing specific non-respiratory specimens (lymph nodes and other tissues) from patients suspected of having extrapulmonary TB (conditional recommendation, very low-quality evidence).</p> <p>Xpert MTB/RIF assay for the diagnosis of pulmonary and extrapulmonary TB in adults and children: WHO policy update. Geneva: World Health Organization; 2013 (<a href="http://www.who.int/tb/laboratory/xpert_policyupdate/en">http://www.who.int/tb/laboratory/xpert_policyupdate/en</a>).</p>

Chapter	Recommendation
	<p>Except as specifically described below for people with HIV infection with low CD4 counts or who are seriously ill,<sup>1</sup> urine lateral flow (LF)-LAM should not be used for the diagnosis of TB (strong recommendation, low-quality evidence).</p> <p>LF-LAM may be used to assist in the diagnosis of active TB in adult inpatients living with HIV, with signs and symptoms of TB (pulmonary and/or extrapulmonary), who have a CD4 cell count less than or equal to 100 cells/mm<sup>3</sup> or people living with HIV who are seriously ill regardless of CD4 count or with unknown CD4 count (conditional recommendation, low-quality evidence).<sup>2</sup></p> <p>LF-LAM should not be used as a screening test for active TB (strong recommendation, low-quality evidence).</p> <p>The use of lateral flow urine lipoarabinomannan assay (LF-LAM) for the diagnosis and screening of active tuberculosis in people living with HIV: Policy guidance. Geneva: World Health Organization; 2015 (<a href="http://apps.who.int/iris/bitstream/10665/193633/1/9789241509633_eng.pdf">http://apps.who.int/iris/bitstream/10665/193633/1/9789241509633_eng.pdf</a>).</p> <p>TB patients with known positive HIV status and TB patients living in HIV-prevalent settings should receive at least 6 months of a rifampicin-containing treatment regimen. The optimal dosing frequency is daily during the intensive and continuation phases (strong recommendation, high-quality evidence).</p> <p>WHO policy on collaborative TB/HIV activities: guidelines for national programmes and other stakeholders. Geneva: World Health Organization; 2012 (<a href="http://www.who.int/tb/publications/2012/tb_hiv_policy_9789241503006/en">http://www.who.int/tb/publications/2012/tb_hiv_policy_9789241503006/en</a>).</p>
Isoniazid preventive therapy (IPT)	<p>Adults and adolescents living with HIV should be screened with a clinical algorithm; those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered IPT (strong recommendation, moderate-quality evidence).</p> <p>Adults and adolescents living with HIV who have an unknown or positive tuberculin skin test (TST) status and are unlikely to have active TB should receive at least 6 months of IPT as part of a comprehensive package of HIV care. IPT should be given to such individuals regardless of the degree of immunosuppression and also to those on ART, those who have previously been treated for TB and pregnant women (strong recommendation, high-quality evidence).</p> <p>Adults and adolescents living with HIV who have an unknown or positive tuberculin skin test status and among whom active TB disease has been safely ruled out should receive at least 36 months of IPT. IPT should be given to such individuals regardless of whether or not they are receiving ART. IPT should also be given irrespective of the degree of immunosuppression, history of previous TB treatment, and pregnancy (conditional recommendation, moderate-quality evidence).</p> <p>Children living with HIV who do not have poor weight gain, fever or current cough are unlikely to have active TB. Children living with HIV who have poor weight gain, fever or current cough or contact history with a TB case may have TB and should be evaluated for TB and other conditions. If the evaluation shows no TB, they should be offered IPT preventive therapy regardless of their age (strong recommendation, low-quality evidence).</p> <p>Children living with HIV who are more than 12 months of age and who are unlikely to have active TB on symptom-based screening and have no contact with a TB case should receive 6 months of IPT (10 mg/kg/day) as part of a comprehensive package of HIV prevention and care (strong recommendation, moderate-quality evidence).</p>

<sup>1</sup> Seriously ill is defined as four danger signs: respiratory rate >30/min, temperature >39°C, heart rate >120/min and unable to walk unaided.

<sup>2</sup> This recommendation also applies to adults living with HIV who are outpatients with signs and symptoms of TB (pulmonary and/or extrapulmonary) who have a CD4 cell count less than or equal to 100 cells/mm<sup>3</sup>, or who are seriously ill regardless of CD4 count or with unknown CD4 count, based on the generalization of data from inpatients. This recommendation also applies to children living with HIV, with signs and symptoms of TB (pulmonary and/or extrapulmonary) based on the generalization of data from adults, while acknowledging that data are very limited and that there are concerns regarding low specificity of the LF-LAM assay in children.



Chapter	Recommendation
	<p>In children living with HIV who are less than 12 months of age, only those who have contact with a TB case and who are evaluated for TB (using investigations) should receive 6 months of IPT if the evaluation shows no TB disease (strong recommendation, low-quality evidence).</p> <p>All children living with HIV, after successful completion of treatment for TB, should receive IPT for an additional 6 months (conditional recommendation, low-quality evidence).</p> <p>Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings. Geneva: World Health Organization; 2011 (<a href="http://apps.who.int/iris/bitstream/10665/44472/1/9789241500708_eng.pdf">http://apps.who.int/iris/bitstream/10665/44472/1/9789241500708_eng.pdf</a>).</p>
Infection control	<p>Administrative (facility-level infection control committee and protocols)</p> <ul style="list-style-type: none"> <li>• A triage system should be in place to identify people suspected of having TB and minimize diagnostic delays with rapid diagnostics e.g. Xpert MTB/RIF.</li> <li>• Separate people with suspected or confirmed TB</li> <li>• Ensure cough etiquette and respiratory hygiene</li> <li>• Minimize the time spent in health-care facilities (e.g. through community-based approaches)</li> </ul> <p>(all administrative recommendations: strong recommendation, low-quality evidence).</p> <p>Health workers and caregivers</p> <ul style="list-style-type: none"> <li>• Inform and encourage health workers with TB symptoms to undergo TB diagnostic investigation as well as HIV testing and counselling.</li> <li>• Provide a package of care for HIV positive-workers (ART and isoniazid preventive therapy).</li> <li>• Relocation for health workers living with HIV to a lower-risk area.</li> </ul> <p>(all health worker recommendations: strong recommendation in settings with a high prevalence of HIV and conditional with a low prevalence, high-quality evidence).</p> <p>Use of particulate respirators</p> <ul style="list-style-type: none"> <li>• Protective equipment (particulate respirator masks that meet or exceed N95 standards set by the CDC/NIOSH or the FFP2 standards that are CE certified) should be provided for health workers caring for patients with infectious TB (suspected or confirmed) (strong recommendation, low-quality evidence).</li> </ul> <p>Environmental</p> <ul style="list-style-type: none"> <li>• Ventilation (i.e. natural and/or mechanical) (strong recommendation, low-quality evidence)</li> <li>• Upper-room ultraviolet germicidal irradiation (conditional recommendation, low-quality evidence).</li> </ul> <p>WHO policy on TB infection control in health-care facilities, congregate settings and households. Geneva: World Health Organization; 2009 (<a href="http://www.who.int/tb/publications/2009/9789241598323/en">http://www.who.int/tb/publications/2009/9789241598323/en</a>).</p>
Multidrug-resistant TB and HIV	<p>Antiretroviral therapy is recommended for all patients with HIV and drug-resistant TB requiring second-line antituberculosis drugs irrespective of CD4 cell count, as early as possible (within the first 8 weeks) following initiation of antituberculosis treatment (strong recommendation, very low-quality evidence).</p> <p>Guidelines for the programmatic management of drug-resistant tuberculosis: 2011 update. Geneva: World Health Organization; 2011 (<a href="http://apps.who.int/iris/bitstream/10665/445971/9789241501583_eng.pdf">http://apps.who.int/iris/bitstream/10665/445971/9789241501583_eng.pdf</a>).</p>
5.3.2 Cryptococcal disease  Diagnosis of cryptococcal disease	<p>Prompt lumbar puncture with measurement of CSF opening pressure and rapid CSF cryptococcal antigen (CrAg) assay or rapid serum CrAg (either LA or LFA) is the preferred diagnostic approach. (strong recommendation, moderate-quality evidence).</p>

Chapter	Recommendation
Prevention of cryptococcal disease	<p>The routine use of antifungal primary prophylaxis for cryptococcal disease in HIV-infected adults, adolescents and children with a CD4 count less than 100 cells/mm<sup>3</sup>, and who are CrAg-negative or where CrAg status is unknown, is not recommended prior to ART initiation, unless a prolonged delay in ART initiation is likely (strong recommendation, high-quality evidence).</p> <p>The use of routine serum or plasma CrAg screening in ART-naïve adults, followed by pre-emptive antifungal therapy if CrAg-positive to reduce the development of cryptococcal disease, may be considered prior to ART initiation in:</p> <ol style="list-style-type: none"> <li>patients with a CD4 count less than 100 cells/mm<sup>3</sup>; and</li> <li>where this population also has a high prevalence (&gt;3%)<sup>1</sup> of cryptococcal antigenaemia (conditional recommendation, low-quality evidence).</li> </ol> <p>The use of routine CrAg screening in ART-naïve adolescents and children with pre-emptive antifungal therapy if CrAg positive, prior to ART initiation is not recommended (conditional recommendation, low-quality evidence).</p>
Induction, consolidation, and maintenance antifungal treatment regimens	<p>For the induction phase of treatment in HIV-infected adults, adolescents and children with cryptococcal disease (meningeal and disseminated non-meningeal), the following two-week antifungal regimens are recommended in order of preference:</p> <ol style="list-style-type: none"> <li>Amphotericin B + flucytosine (strong recommendation, high-quality evidence).</li> <li>Amphotericin B + fluconazole (strong recommendation, moderate-quality evidence).</li> <li>Amphotericin B short course (5–7 days) + high dose fluconazole (to complete 2 weeks of induction) when a minimum package of pre-emptive hydration and electrolyte replacement and toxicity monitoring and management cannot be provided for the full 2-week induction period (conditional recommendation, low-quality evidence).</li> <li>Fluconazole high dose + flucytosine, when amphotericin B is not available (conditional recommendation, low-quality evidence).</li> <li>Fluconazole high dose alone, when amphotericin B is not available (conditional recommendation, low-quality evidence).</li> </ol> <p>For the consolidation phase treatment of HIV infected adults, adolescents and children with cryptococcal meningitis or disseminated non-meningeal disease, the following 8-week antifungal regimen is recommended:</p> <p>Fluconazole 400–800mg/day after a two-week induction with amphotericin B regimen (6–12 mg/kg/day up to 400–800 mg/day if below 19 years).</p> <p>Fluconazole 800 mg/day after induction treatment with short-course amphotericin B or fluconazole-based induction regimen (fluconazole 12 mg/kg/day up to 800 mg/day if below 19 years) (strong recommendation, low-quality evidence).</p> <p>For maintenance treatment of cryptococcal disease in HIV-infected adults, adolescents and children, oral fluconazole 200 mg daily (6 mg/kg/day up to 200 mg/day if below 19 years) is recommended (strong recommendation, high-quality evidence).</p> <p>For localized non-meningeal disease, or in patients with isolated serum CrAg positivity (where active cryptococcal meningitis has been excluded). Fluconazole 800 mg/day (or 12 mg/kg/day if below 19 years) for two weeks, then 400 mg/day (or 6 mg/kg/day up to 400–800 mg/day if below 19 years) for 8 weeks, and continued maintenance with fluconazole 200 mg/day is recommended. The optimal antifungal regimen in this population remains to be determined (conditional recommendation, low-quality evidence).</p>

<sup>1</sup> The prevalence threshold above which screening is cost-effective was 1% using LFA (Meya D, Rajasingham R, Rolfes M, Birkenkamp K, Boulware D. Cost benefit of integrating cryptococcal antigen screening and preemptive treatment into routine HIV care. In: International AIDS Conference, Washington, DC, 22–27 July 2012 [Abstract MOAB0102]). The prevalence cost-effectiveness threshold is likely to vary depending on the cost of the antigen assay used (latex agglutination [LA] vs. LFA) and cost of drug treatment.



Chapter	Recommendation
Prevention, monitoring and management of amphotericin B toxicity	In HIV-infected adults receiving amphotericin B-containing regimens for treatment of cryptococcal disease, a minimum package of toxicity prevention, monitoring and management is recommended to minimize the serious amphotericin B-related toxicities of hypokalaemia and nephrotoxicity (strong recommendation, moderate-quality evidence).
Timing of ART initiation	<p>Immediate ART initiation is not recommended in HIV-infected patients with cryptococcal meningitis due to the high risk of IRIS, which may be life-threatening (conditional recommendation, low-quality evidence)</p> <p>In HIV-infected adults, adolescents and children with a recent diagnosis of cryptococcal meningitis, ART initiation should be deferred until there is evidence of a sustained clinical response to antifungal therapy, and after 4 weeks of induction and consolidation treatment with amphotericin B-containing regimens combined with flucytosine or fluconazole, or after 4–6 weeks of treatment with a high-dose oral fluconazole induction and consolidation regimen (conditional recommendation, low-quality evidence)</p>
Discontinuation of azole maintenance treatment (secondary prophylaxis)	<p>In HIV-infected adults and adolescents with successfully treated cryptococcal disease (meningeal and non-meningeal), discontinuation of antifungal maintenance treatment is recommended based on the following criteria:</p> <p>a. If HIV viral load monitoring is available: when patients are stable and adherent to ART and antifungal maintenance therapy for at least 1 year and have a CD4 cell count of greater than or equal to 200 cells/mm<sup>3</sup> (two measurements 6 months apart) (strong recommendation, low-quality evidence).</p> <p>b. If HIV viral load monitoring is available: when patients are stable and adherent to ART and antifungal maintenance treatment for at least one year and with CD4 cell count of greater than or equal to 100 cells/mm<sup>3</sup> (two measurements 6 months apart) and a suppressed viral load (conditional recommendation, low-quality evidence).</p> <p>In children aged less than two years with successfully treated cryptococcal disease, antifungal maintenance treatment should NOT be discontinued (strong recommendation, low-quality evidence).</p> <p>In HIV-infected children aged between 2 and 5 years with successfully treated cryptococcal disease (meningeal and non-meningeal), discontinuation of antifungal treatment maintenance is recommended if the child is stable and adherent to ART and antifungal maintenance treatment for at least one year and with a CD4 cell count percentage greater than 25% or absolute count greater than 750 cells/mm<sup>3</sup> (two measurements 6 months apart) (strong recommendation, low-quality evidence).</p> <p>Maintenance therapy for cryptococcal disease should not be discontinued in children less than two years (strong recommendation, low-quality evidence).</p> <p>Maintenance treatment for cryptococcal disease should be restarted if CD4 count drops to 100 cells/mm<sup>3</sup>, or below in HIV-infected adults and adolescents (or CD4 cell count less than or equal to 25% or 750 cells/mm<sup>3</sup> in children aged between 2 and 5 years), or if a WHO stage 4 clinical event occurs, irrespective of patient age (strong recommendation, low-quality evidence).</p> <p>Rapid advice: diagnosis, prevention and management of cryptococcal disease in HIV-infected adults, adolescents and children. Geneva: World Health Organization; 2011 (<a href="http://www.who.int/hiv/pub/cryptococcal_disease2011/en">www.who.int/hiv/pub/cryptococcal_disease2011/en</a>).</p>

Chapter	Recommendation
<b>5.3 Prevention, screening and management of other comorbidities and chronic care for people living with HIV</b>	
 <p>5.3.1 Assessment and management of noncommunicable diseases</p>	<p>Assessment and management of cardiovascular risk should be provided for all individuals living with HIV according to standard protocols recommended for the general population<sup>1</sup> (conditional recommendation, very low-quality evidence).</p>
 <p>5.3.2 Assessment and management of depression in people living with HIV</p>	<p>Assessment and management of depression should be included in the package of HIV care services for all individuals living with HIV (conditional recommendation, very low-quality evidence).</p>

<sup>1</sup> The WHO PEN protocol targets the following populations for CVD screening: age >40 years, smokers, people with known hypertension or diabetes mellitus, waist circumference >90 cm in women and >110 cm in men, and family history of diabetes mellitus or premature CVD ([www.who.int/cardiovascular\\_diseases/publications/pen2010/en](http://www.who.int/cardiovascular_diseases/publications/pen2010/en)).

Chapter	Recommendation
<b>6. SERVICE DELIVERY</b>	
<b>6.4 Linkage from HIV testing to enrolment in care</b>	
<p><b>NEW</b></p> <p><b>6.4.1 Interventions to ensure timely linkage</b></p>	<p>Following an HIV diagnosis, a package of support interventions should be offered to ensure timely linkage to care for all people living with HIV (strong recommendation, moderate-quality evidence).</p> <p>The following interventions have demonstrated benefit in improving linkage to care following an HIV diagnosis:</p> <ul style="list-style-type: none"> <li>streamlined interventions to reduce time between diagnosis and engagement in care including (i) enhanced linkage with case management; (ii) support for HIV disclosure; (iii) patient tracing; (iv) training staff to provide multiple services, and (v) streamlined services (moderate-quality evidence);</li> <li>peer support<sup>1</sup> and navigation approaches for linkage (moderate-quality evidence); and</li> <li>quality improvement approaches using data to improve linkage (low-quality evidence).</li> </ul>
<p><b>NEW</b></p> <p><b>6.4.2 CD4 cell count testing at the point of care</b></p>	<p>CD4 cell count testing at the point of care can be used to prioritize patients for urgent linkage to care and ART initiation (conditional recommendation, low-quality evidence).</p>
<p><b>NEW</b></p> <p><b>6.4.3 Laboratory connectivity</b></p>	<p>Electronic communication can be considered to transfer test results and reduce delays in acting on the results of early infant diagnosis and other essential laboratory tests (conditional recommendation, low-quality evidence).</p>
<p><b>NEW</b></p> <p><b>6.5 Retention in care</b></p>	<p>Programmes should provide community support for people living with HIV to improve retention in HIV care (strong recommendation, low-quality evidence).</p> <p>The following community-level interventions have demonstrated benefit in improving retention in care:</p> <ul style="list-style-type: none"> <li>package of community based interventions<sup>2</sup> (children low-quality and adults very low-quality evidence)</li> <li>adherence clubs<sup>3</sup> (moderate-quality evidence)</li> <li>extra care for high-risk people (very low-quality evidence).</li> </ul>
<p><b>NEW</b></p> <p><b>6.6 Adherence</b></p>	<p>Adherence support interventions should be provided to people on ART (strong recommendation, moderate-quality evidence).</p> <p>The following interventions have demonstrated benefit in improving adherence and viral suppression:</p> <ul style="list-style-type: none"> <li>peer counsellors (moderate-quality evidence)</li> <li>mobile phone text messages (moderate-quality evidence)</li> <li>reminder devices (moderate-quality evidence)</li> <li>cognitive-behavioural therapy (moderate-quality evidence)</li> <li>behavioural skills training/medication adherence training (moderate-quality evidence)</li> <li>fixed-dose combinations and once-daily regimens (moderate-quality evidence)</li> </ul>
<p><b>NEW</b></p> <p><b>6.7 Frequency of visits</b></p>	<p>Less frequent clinical visits (3–6 months) are recommended for people stable on ART (strong recommendation, moderate-quality evidence).<sup>4</sup></p> <p>Less frequent medication pickups (3–6 months) are recommended for people stable on ART (strong recommendation, low-quality evidence).<sup>5</sup></p>


<sup>1</sup> Peer support includes peer counselling.

<sup>2</sup> Patient advocates, treatment and peer support interventions providing adherence and psychosocial support in the community.

<sup>3</sup> Peer support, distribution of ARV drugs and assessment by non-clinical or lay providers.

<sup>4</sup> When routine clinical consultations are due, they should be coordinated with planned medication pick-up to reduce visit frequency.



<sup>5</sup> ARV supply management should be strengthened to ensure the availability of ARV medicines and prevent stock-outs in the context of less frequent medication pickup.

Chapter	Recommendation
6.8 Task shifting and sharing	 Trained and supervised lay providers can distribute ART to adults, adolescents and children living with HIV (strong recommendation, low-quality evidence).
	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).
Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 ( <a href="http://www.who.int/hiv/pub/guidelines/arv2013/download/en">http://www.who.int/hiv/pub/guidelines/arv2013/download/en</a> ).	
6.9 Decentralization	<p>Decentralization of HIV treatment and care should be considered as a way to increase access to and improve retention in care:</p> <ul style="list-style-type: none"> <li>• initiation of ART in hospitals with maintenance of ART in peripheral health facilities (strong recommendation, low-quality evidence);</li> <li>• initiation and maintenance of ART in peripheral health facilities (strong recommendation, low-quality evidence);</li> <li>• initiation of ART at peripheral health facilities with maintenance at the community level (strong recommendation, moderate-quality evidence).<sup>1</sup></li> </ul> <p>Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 (<a href="http://www.who.int/hiv/pub/guidelines/arv2013/download/en">http://www.who.int/hiv/pub/guidelines/arv2013/download/en</a>).</p>
<b>6.10 Integrating and linking services</b>	
6.10.1 Delivering ART in maternal and child health-care settings	<p>In generalized epidemic settings, ART should be initiated and maintained in eligible<sup>2</sup> 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).</p> <p>Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 (<a href="http://www.who.int/hiv/pub/guidelines/arv2013/download/en">http://www.who.int/hiv/pub/guidelines/arv2013/download/en</a>).</p>
6.10.2 Delivering ART in TB treatment settings and TB treatment in HIV care settings	<p>In settings with a high burden of HIV and TB, ART should be initiated for people living with HIV in TB treatment settings, with linkage to ongoing HIV care and ART (strong recommendation, very low-quality evidence).</p> <p>In settings with a high burden of HIV and TB, TB treatment may be provided for people living with HIV in HIV care settings where a TB diagnosis has also been made (strong recommendation, very low-quality evidence).</p> <p>Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 (<a href="http://www.who.int/hiv/pub/guidelines/arv2013/download/en">http://www.who.int/hiv/pub/guidelines/arv2013/download/en</a>).</p>
6.10.3 ART in settings providing opioid substitution therapy	<p>ART should be initiated and maintained in eligible<sup>3</sup> people living with HIV at care settings where opioid substitution therapy (OST) is provided (strong recommendation, very low-quality evidence).</p> <p>Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 (<a href="http://www.who.int/hiv/pub/guidelines/arv2013/download/en">http://www.who.int/hiv/pub/guidelines/arv2013/download/en</a>).</p>

<sup>1</sup> Community level includes external outreach sites, health posts, home-based services or community-based organizations. The frequency of clinical visits will depend on health status.

<sup>2</sup> All people living with HIV are now eligible for initiating ART at any CD4 cell count.

<sup>3</sup> All people living with HIV are now eligible for initiating ART at any CD4 cell count.

Chapter	Recommendation
 6.10.4 STI and family planning in HIV care settings	Sexually transmitted infection (STI) and family planning services can be integrated within HIV care settings (conditional recommendation, very low-quality evidence).
6.11 Adolescent-friendly health services	 Adolescent-friendly health services should be implemented in HIV services to ensure engagement and improved outcomes (strong recommendation, low-quality evidence).  Community-based approaches can improve treatment adherence and retention in care of adolescents living with HIV (conditional recommendation, very low-quality evidence).  Training of health-care workers can contribute to treatment adherence and improvement in retention in care of adolescents living with HIV (conditional recommendation, very low-quality evidence).  Adolescents should be counselled about the potential benefits and risks of disclosure of their HIV status to others and empowered and supported to determine if, when, how and to whom to disclose (conditional recommendation, very low-quality evidence).  HIV and adolescents: guidance for HIV testing and counselling and care for adolescents living with HIV. Geneva: World Health Organization; 2013 ( <a href="http://www.who.int/hiv/pub/guidelines/adolescents/en">http://www.who.int/hiv/pub/guidelines/adolescents/en</a> ).

## Good practice statements

The table includes good practice statements made by the 2015 Guideline Development Groups.

Chapter	Good practice statement
<p><b>NEW</b></p> <p>2.5.4 Provider-initiated HIV testing and counselling</p>	In all settings, children with a parent living with HIV should be routinely offered HIV testing and, if found to be either infected or at high risk of infection through breastfeeding, should be linked to services for treatment or prevention.
<p><b>NEW</b></p> <p>4.3.6 Accelerated ART initiation</p>	Efforts should be made to reduce the time between HIV diagnosis and ART initiation based on an assessment of a person's readiness.
<p><b>NEW</b></p> <p>4.4.6 Infant prophylaxis</p>	In settings with a high risk of mother-to-child transmission, in addition to providing enhanced infant prophylaxis, ART should be initiated urgently in all pregnant and breastfeeding women, even if they are identified late in pregnancy or postpartum, because the most effective way to prevent mother-to-child HIV transmission is to reduce maternal viral load. <sup>1</sup>
<p><b>NEW</b></p> <p>5.3.1 Assessment and management of cardiovascular diseases</p>	Strategies for the prevention and risk reduction of cardiovascular diseases by addressing modifiable factors such as blood pressure, smoking, status obesity, unhealthy diet and lack of physical activity should be applied to all people living with HIV.
<p><b>NEW</b></p> <p>6.8 Task shifting and task sharing</p>	Trained and supervised non-laboratory staff including lay people can undertake blood finger-prick for sample collection.
<p><b>NEW</b></p> <p>6.12 Improving the quality of HIV care services</p>	<p>HIV programmes should:</p> <ul style="list-style-type: none"> <li>• provide people-centred care that is focused and organized around the health needs, preferences and expectations of people and communities, upholding individual dignity and respect, especially for vulnerable populations, and engage and support people and families to play an active role in their own care by informed decision-making;</li> <li>• offer safe, acceptable and appropriate clinical and non-clinical services in a timely fashion, aiming to reduce morbidity and mortality associated with HIV infection and to improve health outcomes and quality of life in general;</li> <li>• promote efficient and effective use of resources.</li> </ul>

<sup>1</sup> Whenever possible, all efforts should be made to identify pregnant women living with HIV early enough to avoid the need for high-risk prophylaxis.