WHO consolidated guidelines on tuberculosis

Module 5: Management of tuberculosis in children and adolescents

Web Annex 5. Overview of consolidated WHO recommendations

World Health Organization

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Design by Inis Communication

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Recommendations on TB screening and contact investigation relevant to children and adolescents

WHO consolidated guidelines on tuberculosis. Module 2: screening – systematic screening for tuberculosis disease *(1)*.
Screening for TB in targeted populations
Household contacts and other close contacts of individuals with TB disease should be systematically screened for TB disease. *(Strong recommendation, moderate certainty of evidence)*
People living with HIV should be systematically screened for TB disease at each visit to a health facility. *(Strong recommendation, very low certainty of evidence)*
Systematic screening for TB disease may be conducted among subpopulations with structural risk factors for TB. These include urban poor communities, homeless communities, communities in remote or isolated areas, indigenous populations, migrants, refugees, internally displaced persons and other vulnerable or marginalized groups with limited access to health care. (*Existing recommendation: conditional recommendation, very low certainty of evidence*)
Tools for screening for TB
Among individuals aged 15 years and older in populations in which TB screening is recommended, systematic screening for TB disease may be conducted using a symptom screen, chest X-ray or molecular WHO-recommended rapid diagnostic tests, alone or in combination. *(Conditional recommendation, very low certainty of evidence for test accuracy)*
Among individuals aged 15 years and older in populations in which TB screening is recommended, computer-aided detection software programmes may be used in place of human readers for interpreting digital chest X-rays for screening and triage for TB disease. *(Conditional recommendation, low certainty of evidence)*
Among adults and adolescents living with HIV, systematic screening for TB disease should be conducted using the WHO-recommended four symptom screen and those who report any one of the symptoms of current cough, fever, weight loss or night sweats may have TB and should be evaluated for TB and other diseases. *(Strong recommendation, moderate certainty of evidence)*

Among adults and adolescents living with HIV, C-reactive protein using a cut-off of >5mg/L may be used to screen for TB disease. (*Conditional recommendation, low certainty of evidence for test accuracy*)
Among adults and adolescents living with HIV, chest X-ray may be used to screen for TB disease. *(Conditional recommendation, moderate certainty of evidence for test accuracy*)
Among adults and adolescents living with HIV, molecular WHO-recommended rapid diagnostic tests may be used to screen for TB disease. *(Conditional recommendation, moderate certainty of evidence for test accuracy*)
Adult and adolescent inpatients with HIV in medical wards where the TB prevalence is > 10% should be tested systematically for TB disease with a molecular WHO-recommended rapid diagnostic test. *(Strong recommendation, moderate certainty of evidence for test accuracy*)
Among individuals younger than 15 years who are close contacts of someone with TB, systematic screening for TB disease should be conducted using a symptom screen including any one of cough, fever or poor weight gain; or chest radiography; or both. *(Strong recommendation, moderate to low certainty of evidence for test accuracy*)
Among children younger than 10 years who are living with HIV, systematic screening for TB disease should be conducted using a symptom screen including any one of current cough, fever, poor weight gain or close contact with a TB patient. *(Strong recommendation, low certainty of evidence for test accuracy*)
Guidance for national tuberculosis programmes on the management of tuberculosis in children. Second Edition *(2)*.
In settings of high HIV prevalence, all household and close contacts of people with TB should be counselled and tested for HIV. *(Strong recommendation, very low certainty of evidence)*
In settings of low HIV prevalence, all household members and close contacts of people with TB who have symptoms compatible with TB disease may be offered counselling and testing for HIV as part of their clinical evaluation. *(Conditional recommendation, very low certainty of evidence)*
All household contacts of an index case who is a person living with HIV should be counselled and tested for HIV. *(Strong recommendation, very low certainty of evidence)*

Recommendations on TB infection prevention and control, BCG vaccination and TB preventive treatment relevant to children and adolescents

TB infection prevention and control: WHO guidelines on tuberculosis infection prevention and control, 2019 update *(3)*.

Administrative controls

Triage of people with TB signs and symptoms, or with TB disease, is recommended to reduce *M. tuberculosis* transmission to health workers (including community health workers), persons attending health care facilities or other persons in settings with a high risk of transmission.

(Conditional recommendation based on very low certainty in the estimates of effects)

Respiratory separation / isolation of people with presumed or demonstrated infectious TB is recommended to reduce *M. tuberculosis* transmission to health workers or other persons attending health care facilities.

(Conditional recommendation based on very low certainty in the estimates of effects)

Prompt initiation of effective TB treatment of people with TB disease is recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

(Strong recommendation based on very low certainty in the estimates of effects)

Respiratory hygiene (including cough etiquette) in people with presumed or confirmed TB is recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

(Strong recommendation based on low certainty in the estimates of effects)

Environmental controls

Upper-room germicidal ultraviolet (GUV) systems are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

(Conditional recommendation based on moderate certainty in the estimates of effects)

Ventilation systems (including natural, mixed-mode, mechanical ventilation and recirculated air through high-efficiency particulate air (HEPA) filters) are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

(Conditional recommendation based on very low certainty in the estimates of effects)

Respiratory protection

Particulate respirators, within the framework of a respiratory protection programme, are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

(Conditional recommendation based on very low certainty in the estimates of effects)

BCG vaccination: Weekly epidemiological record. BCG vaccines: WHO position paper, 2018 *(4)*.

Bacillus Calmette-Guérin (BCG) vaccination at birth vs. at 6 weeks

In countries or settings with a high incidence of TB and/or leprosy, a single dose of BCG vaccine should be given to neonates at birth, or as soon as possible thereafter, for prevention of TB and leprosy disease. If it cannot be given at birth, it should be given at the earliest opportunity thereafter and should not be delayed. Any delay in vaccination may lead to opportunities for known or unknown exposure to TB or leprosy infected contacts.

Co-administration of BCG with the hepatitis B birth dose is safe and strongly recommended. In order to avoid missed opportunities for neonatal vaccination, BCG multi-dose vials should be opened and used despite any wastage of unused vaccine.

If the birth dose was missed, catch-up vaccination of unvaccinated older infants and children is recommended since evidence shows it is beneficial. Catch-up vaccination should be done at the earliest convenient encounter with the health-care system to minimize known or unknown exposure to TB or leprosy infected contacts.

Selective BCG vaccination

Countries with a low incidence of TB or leprosy may choose to selectively vaccinate neonates in recognized risk groups for developing disease. High-risk groups to be considered for BCG vaccination include the following:

- Neonates to parents (or other close contacts/relatives) with previous TB or leprosy
- Neonates in households with contacts to countries with high incidence of TB and/or leprosy
- Neonates in any other locally identified risk group for TB and/or leprosy

In a few countries with low TB incidence, BCG vaccination is largely replaced by intensified case detection, contact tracing and supervised early treatment.

Need for revaccination

Studies show minimal or no evidence of any additional benefit of repeat BCG vaccination against TB or leprosy. Therefore, revaccination is not recommended even if the TST reaction or result of an IGRA is negative. The absence of a BCG scar after vaccination is not indicative of a lack of protection and is not an indication for revaccination.

BCG vaccination for HIV-infected infants

Children who are HIV-infected when vaccinated with BCG at birth are at increased risk of developing disseminated BCG disease. However, if HIV-infected individuals, including children, are receiving ART, are clinically well and immunologically stable (CD4 % >25% for children aged <5 years or CD4 count ≥200 if aged >5 years) they should be vaccinated with BCG.

- In general, populations with high prevalence of HIV infection also have the greatest burden of TB; in such populations the benefits of potentially preventing severe TB through vaccination at birth are outweighed by the risks associated with the use of BCG vaccine. Therefore, it is recommended that in such populations:
  - Neonates born to women of unknown HIV status should be vaccinated as the benefits of BCG vaccination outweigh the risks.
  - Neonates of unknown HIV status born to HIV-infected women should be vaccinated if they have no clinical evidence suggestive of HIV infection, regardless of whether the mother is receiving ART.
  - Although evidence is limited, for neonates with HIV infection confirmed by early virological testing, BCG vaccination should be delayed until ART has been started and the infant confirmed to be clinically and immunologically stable (CD4% >25%).

TB preventive treatment: WHO consolidated guidelines on tuberculosis. Module 1: prevention – tuberculosis preventive treatment, 2020 *(5)*.

Identifying populations for TB infection testing and TB preventive treatment – People living with HIV

Adults and adolescents living with HIV who are unlikely to have TB disease should receive TB preventive treatment as part of a comprehensive package of HIV care. Treatment should also be given to those on antiretroviral treatment, to pregnant women and to those who have previously been treated for TB, irrespective of the degree of immunosuppression and even if TB infection testing is unavailable.

(Strong recommendation, high certainty in the estimates of effect)

Infants aged < 12 months living with HIV who are in contact with a person with TB and who are unlikely to have TB disease on an appropriate clinical evaluation or according to national guidelines should receive TB preventive treatment.

(Strong recommendation, moderate certainty in the estimates of effect)

Children aged ≥ 12 months living with HIV who are considered unlikely to have TB disease on an appropriate clinical evaluation or according to national guidelines should be offered TB preventive treatment as part of a comprehensive package of HIV prevention and care if they live in a setting with high TB transmission, regardless of contact with TB.

(Strong recommendation, low certainty in the estimates of effect)

All children living with HIV who have successfully completed treatment for TB disease may receive TB preventive treatment.

(Conditional recommendation, low certainty in the estimates of effect)

Identifying populations for TB infection testing and TB preventive treatment – Household contacts (regardless of HIV status)

Children aged < 5 years who are household contacts of people with bacteriologically confirmed pulmonary TB and who are found not to have TB disease on an appropriate clinical evaluation or according to national guidelines should be given TB preventive treatment even if TB infection testing is unavailable.

(Strong recommendation, high certainty in the estimates of effect)

Children aged ≥ 5 years adolescents and adults who are household contacts of people with bacteriologically confirmed pulmonary TB who are found not to have TB disease by an appropriate clinical evaluation or according to national guidelines may be given TB preventive treatment.

(Conditional recommendation, low certainty in the estimates of effect)

In selected high-risk household contacts of patients with multidrug-resistant tuberculosis, preventive treatment may be considered based on individualized risk assessment and a sound clinical justification.

(Conditional recommendation, very low certainty in the estimates of effect)

Identifying populations for TB infection testing and TB preventive treatment – Other people at risk

(These populations may include children and adolescents)

People who are initiating anti-TNF[1] treatment, or receiving dialysis, or preparing for an organ or haematological transplant, or who have silicosis should be systematically tested and treated for TB infection.

(Strong recommendation, low to very low certainty in the estimates of effect)

[1] TNF: tumour necrosis factor

Systematic TB infection testing and treatment may be considered for prisoners, health workers, immigrants from countries with a high TB burden, homeless people and people who use drugs.

(Conditional recommendation, low to very low certainty in the estimates of effect)

Systematic TB infection testing and treatment is not recommended for people with diabetes, people who engage in the harmful use of alcohol, tobacco smokers and underweight people unless they also belong to other risk groups included in the above recommendations.

(Conditional recommendation, very low certainty in the estimates of effect)

Algorithms to rule out TB disease

Adults and adolescents living with HIV should be screened for TB according to a clinical algorithm. Those who do not report any of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have TB disease and should be offered preventive treatment, regardless of their antiretroviral treatment (ART) status.

(Strong recommendation, moderate certainty in the estimates of effect)

Adults and adolescents living with HIV who are screened for TB according to a clinical algorithm and who report any of the symptoms of current cough, fever, weight loss or night sweats may have TB disease and should be evaluated for TB and other diseases and offered preventive treatment if TB disease is excluded.

(Strong recommendation, moderate certainty in the estimates of effect)

Chest radiography may be offered to people living with HIV on ART and preventive treatment given to those with no abnormal radiographic findings.

(Conditional recommendation, low certainty in the estimates of effect)

Infants and children living with HIV who have poor weight gain, fever or current cough or who have a history of contact with a person with TB should be evaluated for TB and other diseases that cause such symptoms. If TB disease is excluded after an appropriate clinical evaluation or according to national guidelines, these children should be offered TB preventive treatment, regardless of their age.

(Strong recommendation, low certainty in the estimates of effect)

The absence of any symptoms of TB and the absence of abnormal chest radiographic findings may be used to rule out TB disease among HIV-negative household contacts aged ≥ 5 years and other risk groups before preventive treatment.

(Conditional recommendation, very low certainty in the estimates of effect)

Testing for TB infection

Either a tuberculin skin test (TST) or interferon-gamma release assay (IGRA) can be used to test for TB infection.

(Strong recommendation, very low certainty in the estimates of effect)

TB preventive treatment options

The following options are recommended for the treatment of TB infection regardless of HIV status: 6 or 9 months of daily isoniazid, or a 3-month regimen of weekly rifapentine plus isoniazid[2], or a 3 month regimen of daily isoniazid plus rifampicin.

(strong recommendation, moderate to high certainty in the estimates of effect).

A 1-month regimen of daily rifapentine plus isoniazid[3] or 4 months of daily rifampicin alone may also be offered as alternatives.

(Conditional recommendation, low to moderate certainty in the estimates of effect).

[2] In ages 2 years and above

[3] In ages 13 years and above

In settings with high TB transmission, adults and adolescents living with HIV who have an unknown or a positive TB infection test and are unlikely to have TB disease should receive at least 36 months of daily isoniazid preventive therapy (IPT). Daily IPT for 36 months should be given whether or not the person is on ART, and irrespective of the degree of immunosuppression, history of previous TB treatment and pregnancy in settings considered to have a high TB transmission as defined by national authorities.

(Conditional recommendation, low certainty in the estimates of effect)

Recommendations on TB diagnostics and diagnostic approaches relevant to children and adolescents

WHO consolidated guidelines on tuberculosis. Module 5: Management of tuberculosis in children and adolescents, 2022 *(6)*.

Diagnosis of pulmonary TB in children

In children with signs and symptoms of pulmonary TB, Xpert Ultra should be used as the initial diagnostic test for TB and detection of rifampicin resistance on sputum, nasopharyngeal aspirate, gastric aspirate or stool, rather than smear microscopy/culture and phenotypic drug susceptibility testing (DST).

*(**UPDATED**: Strong recommendation, moderate certainty of evidence for test accuracy in stool and gastric aspirate; low certainty of evidence for test accuracy in sputum; very low certainty of evidence for test accuracy in nasopharyngeal aspirate)*

In children with presumptive pulmonary TB attending healthcare facilities, integrated treatment decision algorithms may be used to diagnose pulmonary TB.

*(**NEW**: interim, conditional recommendation, very low certainty of evidence)*

- *Presumptive TB refers to a patient who presents with symptoms and/or signs suggestive of TB.*[4]
- *Bacteriological confirmation should be sought as part of the integrated treatment decision algorithms whenever possible, using WHO recommended rapid diagnostic tests and appropriate paediatric specimens (including stool, nasopharyngeal aspirate [NPA], induced or expectorated sputum or gastric aspirate).*
- *In follow-up to the GDG meeting, new integrated treatment decision algorithms for specific populations and settings, have been developed and internally validated. These algorithms are detailed with practical guidance on their use in the operational handbook on the management of tuberculosis in children and adolescents.*[5]
- *National TB and other health programmes are encouraged to use the evidence-based algorithms included in the operational handbook on the management of tuberculosis in children and adolescents, rather than alternative algorithms that have not been evaluated.*
- *This interim recommendation will remain valid for a period of 24 months after the publication of these guidelines, after which new evidence will be reviewed.*

WHO consolidated guidelines on tuberculosis. Module 3: diagnosis – rapid diagnostics for tuberculosis detection, 2021 update *(7)*.

Recommendations on Xpert MTB/RIF and Xpert Ultra as initial tests in adults and children with signs and symptoms of pulmonary TB (Note that in these guidelines, adults refer to persons aged 15 years and above and children aged below 15 years, therefore the adult population includes older adolescents)

In adults* with signs and symptoms of pulmonary TB, Xpert MTB/RIF should be used as an initial diagnostic test for TB and rifampicin-resistance detection in sputum rather than smear microscopy/culture and phenotypic DST.

(Strong recommendation, high certainty of evidence for test accuracy; moderate certainty of evidence for patient-important outcomes)

** Adults and adolescents from 15 years*

[4] World Health Organization. Definitions and reporting framework for tuberculosis – 2013 revision (updated December 2014 and January 2020). Geneva: World Health Organization; 2013.

[5] WHO operational handbook on tuberculosis. Module 5: management of tuberculosis in children and adolescents (https://apps.who.int/iris/bitstream/handle/10665/352523/9789240046832-eng.pdf).

In children with signs and symptoms of pulmonary TB, Xpert MTB/RIF should be used as an initial diagnostic test for TB and rifampicin-resistance detection in sputum, gastric aspirate, nasopharyngeal aspirate and stool rather than smear microscopy/culture and phenotypic DST.

(Strong recommendation, moderate certainty for accuracy in sputum; low certainty of evidence for test accuracy in gastric aspirate, nasopharyngeal aspirate and stool)

In adults* with signs and symptoms of pulmonary TB and without a prior history of TB (≤5 years) or with a remote history of TB treatment (>5 years since end of treatment), Xpert Ultra should be used as an initial diagnostic test for TB and for rifampicin-resistance detection in sputum, rather than smear microscopy/culture and phenotypic DST.

(Strong recommendation, high certainty of evidence for test accuracy)

** Adults and adolescents from 15 years*

In adults* with signs and symptoms of pulmonary TB and with a prior history of TB and an end of treatment within the last 5 years, Xpert Ultra may be used as an initial diagnostic test for TB and for rifampicin-resistance detection in sputum, rather than smear microscopy/culture and phenotypic DST.

(Conditional recommendation, low certainty of evidence for test accuracy)

** Adults and adolescents from 15 years*

Recommendations on Xpert MTB/RIF and Xpert Ultra as initial tests in adolescents and children with signs and symptoms of extrapulmonary TB

In adults and children with signs and symptoms of TB meningitis, Xpert MTB/RIF or Xpert Ultra should be used in cerebrospinal fluid (CSF) as an initial diagnostic test for TB meningitis rather than smear microscopy/culture.

(Strong recommendation, moderate certainty of evidence for test accuracy for Xpert MTB/RIF; low certainty of evidence for test accuracy for Xpert Ultra)

In adults and children with signs and symptoms of extrapulmonary TB, Xpert MTB/RIF may be used in lymph node aspirate, lymph node biopsy, pleural fluid, peritoneal fluid, pericardial fluid, synovial fluid or urine specimens as the initial diagnostic test for respective form of extrapulmonary TB rather than smear microscopy/culture.

(Conditional recommendation, moderate certainty of evidence for test accuracy for pleural fluid; low certainty for lymph node aspirate, peritoneal fluid, synovial fluid, urine; very low certainty for pericardial fluid, lymph nodes biopsy)

In adults and children with signs and symptoms of extrapulmonary TB, Xpert Ultra may be used in lymph node aspirate and lymph node biopsy as the initial diagnostic test for lymph nodes TB rather than smear microscopy/culture.

(Conditional recommendation, low certainty of evidence)

In adults and children with signs and symptoms of extrapulmonary TB, Xpert MTB/RIF or Xpert Ultra should be used for rifampicin-resistance detection rather than culture and phenotypic DST.

(Strong recommendation, high certainty of evidence for test accuracy for Xpert MTB/RIF; low certainty of evidence for Xpert Ultra)

In HIV-positive adults and children with signs and symptoms of disseminated TB, Xpert MTB/RIF may be used in blood, as an initial diagnostic test for disseminated TB.

(Conditional recommendation, very low certainty of evidence for test accuracy)

Recommendations on Xpert MTB/RIF and Xpert Ultra repeated testing in children and adolescents with signs and symptoms of pulmonary TB

In adults* with signs and symptoms of pulmonary TB who have an Xpert Ultra trace positive result on the initial test, repeated testing with Xpert Ultra may not be used.

(Conditional recommendation, very low certainty of evidence for test accuracy)

Remark: *Xpert Ultra trace results in adolescents will require follow-up, including reassessing clinical symptoms and information on prior history of TB. In the case of suspected rifampicin resistance, repeated testing may provide additional benefit for detection as well as an initial attempt to assess rifampicin resistance. For interpretation of trace results in children, see section 4.1.3 in the main guideline*

** Adults and adolescents from 15 years*

In children with signs and symptoms of pulmonary TB in settings with pretest probability below 5% and an Xpert MTB/RIF negative result on the initial test, repeated testing with Xpert MTB/RIF in sputum, gastric fluid, nasopharyngeal aspirate or stool specimens may not be used.

(Conditional recommendation, low certainty of evidence for test accuracy for sputum and very low for other specimen types)

In children with signs and symptoms of pulmonary TB in settings with pretest probability 5% or more and an Xpert MTB/RIF negative result on the initial test, repeated testing with Xpert MTB/RIF (for total of two tests) in sputum, gastric fluid, nasopharyngeal aspirate and stool specimens may be used.

(Conditional recommendation, low certainty of evidence for test accuracy for sputum and very low for other specimen types)

In children with signs and symptoms of pulmonary TB in settings with pretest probability below 5% and an Xpert Ultra negative result on the initial test, repeated testing with Xpert Ultra in sputum or nasopharyngeal aspirate specimens may not be used.

(Conditional recommendation, very low certainty of evidence for test accuracy)

In children with signs and symptoms of pulmonary TB in settings with pretest probability 5% or more and an Xpert Ultra negative result on the first initial test, repeated one Xpert Ultra test (for a total of two tests) in sputum and nasopharyngeal aspirate specimens may be used.

(Conditional recommendation, very low certainty of evidence for test accuracy)

Recommendations on Xpert MTB/RIF and Xpert Ultra as initial tests for pulmonary TB in adults in the general population either with signs and symptoms of TB or chest radiograph with lung abnormalities or both

In adults* in the general population who had either signs or symptoms of TB or chest radiograph with lung abnormalities or both, the Xpert MTB/RIF or Xpert Ultra may replace culture as the initial test for pulmonary TB.

(Conditional recommendation, low certainty of the evidence in test accuracy for Xpert MTB/RIF and moderate certainty for Xpert Ultra)

** Adults and adolescents from 15 years*

In adults* in the general population who had either a positive TB symptom screen or chest radiograph with lung abnormalities or both, one Xpert Ultra test may be used rather than two Xpert Ultra tests as the initial test for pulmonary TB.

(Conditional recommendation, very low certainty of evidence for test accuracy).

** Adults and adolescents from 15 years*

Truenat MTB, MTB Plus and Truenat MTB-RIF Dx in adults and children with signs and symptoms of pulmonary TB (specimen type: sputum)

In children and adults with signs and symptoms of pulmonary TB, the Truenat MTB or MTB Plus may be used as an initial diagnostic test for TB rather than smear microscopy/culture.

(Conditional recommendation, moderate certainty of evidence for test accuracy)

In children and adults with signs and symptoms of pulmonary TB and a Truenat MTB or MTB Plus positive result, Truenat MTB-RIF Dx may be used as an initial test for rifampicin resistance rather than culture and phenotypic DST.

(Conditional recommendation, very low certainty of evidence for test accuracy)

Moderate complexity automated nucleic acid amplification tests (NAATs) for detection of TB and resistance to rifampicin and isoniazid

In people with signs and symptoms of pulmonary TB, moderate complexity automated NAATs may be used on respiratory samples for the detection of pulmonary TB, and of rifampicin and isoniazid resistance, rather than culture and phenotypic DST.

(Conditional recommendation; moderate certainty of evidence for diagnostic accuracy)

Loop-mediated isothermal amplification

TB-LAMP may be used as a replacement test for sputum-smear microscopy for diagnosing pulmonary TB in adults* with signs and symptoms consistent with TB.

(Conditional recommendation, very low certainty evidence)

** Adults and adolescents from 15 years*

TB-LAMP may be used as a follow-on test to smear microscopy in adults* with signs and symptoms consistent with pulmonary TB, especially when further testing of sputum smear-negative specimens is necessary.

(Conditional recommendation, very low certainty evidence)

** Adults and adolescents from 15 years*

Lateral flow urine lipoarabinomannan assay

In inpatient settings, WHO strongly recommends using LF-LAM to assist in the diagnosis of TB disease in HIV-positive adults and children:

a. with signs and symptoms of TB (pulmonary and/or extrapulmonary) *(strong recommendation; moderate certainty in the evidence about the intervention effects)* or
b. with advanced HIV disease or who are seriously ill *(strong recommendation; moderate certainty in the evidence about the intervention effects)*; or
c. irrespective of signs and symptoms of TB and with a CD4 cell count of less than 200 cells/mm^3 *(strong recommendation; moderate certainty in the evidence about the intervention effects)*.

In outpatient settings, WHO suggests using LF-LAM to assist in the diagnosis of TB disease in HIV-positive adults and children:

a. with signs and symptoms of TB (pulmonary and/or extrapulmonary) or seriously ill *(conditional recommendation; low certainty in the evidence about test accuracy)*; and
b. irrespective of signs and symptoms of TB and with a CD4 cell count of less than 100 cells/mm^3 *(conditional recommendation; very low certainty in the evidence about test accuracy)*.

In outpatient settings, WHO recommends **against** using LF-LAM to assist in the diagnosis of TB disease in HIV-positive adults and children:

a. without assessing TB symptoms *(strong recommendation; very low certainty in the evidence about test accuracy)*;

b. without TB symptoms and unknown CD4 cell count or without TB symptoms and CD4 cell count greater than or equal to 200 cells/mm^3 *(strong recommendation; very low certainty in the evidence about test accuracy)*; and

c. without TB symptoms and with a CD4 cell count of 100–200 cells/mm^3 *(conditional recommendation; very low certainty in the evidence about test accuracy)*.

Low complexity NAATs for detection of resistance to isoniazid and second-line anti-TB agents

In people with bacteriologically confirmed pulmonary TB, low complexity automated NAATs may be used on sputum for the initial detection of resistance to isoniazid and fluoroquinolones, rather than culture-based phenotypic DST.

(Conditional recommendation; moderate certainty of evidence for diagnostic accuracy)

In people with bacteriologically confirmed pulmonary TB and resistance to rifampicin, low complexity automated NAATs may be used on sputum for the initial detection of resistance to ethionamide, rather than DNA sequencing of the *inhA* promoter.

(Conditional recommendation; very low certainty of evidence for diagnostic accuracy)

In people with bacteriologically confirmed pulmonary TB and resistance to rifampicin, low complexity automated NAATs may be used on sputum for the initial detection of resistance to amikacin, rather than culture-based phenotypic DST.

(Conditional recommendation; low certainty of evidence for diagnostic accuracy)

First-line line-probe assay (LPAs)

For persons with a sputum smear-positive specimen or a cultured isolate of Mycobacterium tuberculosis complex (MTBC), commercial molecular LPAs may be used as the initial test instead of phenotypic culture-based DST to detect resistance to rifampicin and isoniazid.

(Conditional recommendation, moderate certainty in the evidence for the test's accuracy)

Second-line line-probe assays (SL-LPAs)

For patients with confirmed MDR/RR-TB, SL-LPA may be used as the initial test, instead of phenotypic culture-based DST, to detect resistance to fluoroquinolones.

(Conditional recommendation; moderate certainty in the evidence for test accuracy for direct testing of sputum specimens; low certainty in the evidence for test accuracy for indirect testing of Mycobacterium tuberculosis *cultures)*

For patients with confirmed MDR/RR-TB, SL-LPA may be used as the initial test, instead of phenotypic culture-based DST, to detect resistance to the second-line injectable drugs.

(Conditional recommendation; low certainty in the evidence for test accuracy for direct testing of sputum specimens; very low certainty in the evidence for test accuracy for indirect testing of Mycobacterium tuberculosis *cultures)*

High complexity reverse hybridization-based NAATs for detection of pyrazinamide resistance

In people with bacteriologically confirmed TB, high complexity reverse hybridization-based NAATs may be used on M. tuberculosis culture isolates for detection of pyrazinamide resistance rather than culture-based phenotypic DST.

(Conditional recommendation, very low certainty of evidence for diagnostic accuracy)

Commercial serodiagnostic tests for diagnosis of tuberculosis: policy statement, 2011 *(8)*.

Commercial serodiagnostics should not be used in children suspected of pulmonary or extrapulmonary TB, irrespective of their HIV status.

(Strong recommendation, very low certainty of evidence for the use of commercial serodiagnostics)

Recommendations on treatment of TB disease in children and adolescents

WHO consolidated guidelines on tuberculosis. Module 5: Management of tuberculosis in children and adolescents, 2022 *(6)*.

Treatment of drug-susceptible TB

In children and adolescents aged between 3 months and 16 years with non-severe TB (without suspicion or evidence of MDR/RR-TB), a 4-month treatment regimen (2HRZ(E)/2HR) should be used.

*(**NEW**: strong recommendation, moderate certainty of evidence)*

- *Non-severe TB is defined as: Peripheral lymph node TB; intrathoracic lymph node TB without airway obstruction; uncomplicated TB pleural effusion or paucibacillary, non-cavitary disease, confined to one lobe of the lungs, and without a miliary pattern.*
- *Children and adolescents who do not meet the criteria for non-severe TB should receive the standard 6-month treatment regimen (2HRZE/4HR), or recommended treatment regimens for severe forms of extrapulmonary TB.*
- *The use of ethambutol in the first two months of treatment is recommended in settings with a high prevalence of HIV[6], or of isoniazid resistance[7].*

Guidance for national tuberculosis programmes on the management of tuberculosis in children. Second Edition, 2014 *(2)*.

Treatment of drug-susceptible TB

Children with pulmonary TB or tuberculous peripheral lymphadenitis who live in settings with low HIV prevalence and/or low prevalence of isoniazid resistance and children who are HIV-negative, can be treated with a three-drug regimen (HRZ) for 2 months followed by a two-drug (HR) regimen for 4 months at standard dosages.

(Strong recommendation, moderate quality of evidence)

Children and adolescents with severe pulmonary disease should be treated with a four-drug regimen (HRZE) for 2 months followed by a two-drug regimen (HR) for 4 months at standard dosages.

(Strong recommendation, moderate certainty of evidence)

Infants aged 0–3 months with suspected or confirmed pulmonary TB or tuberculous peripheral lymphadenitis should be promptly treated with the 6-month treatment regimen (2HRZ(E)/4HR). Treatment may require dose adjustment to reconcile the effect of age and possible toxicity in young infants. The decision to adjust doses should be taken by a clinician experienced in managing paediatric TB.

(Strong recommendation, low certainty of evidence)

Streptomycin should not be used as part of first-line treatment regimens for children with pulmonary TB or tuberculous peripheral lymphadenitis.

(Strong recommendation, moderate certainty of evidence)

[6] Defined as countries, subnational administrative units, or selected facilities, where the HIV prevalence among adult pregnant women is ≥1% or among TB patients is ≥5% in the *Guidance for national tuberculosis programmes on the management of tuberculosis in children (second edition)* 2014.

[7] WHO does not intend to establish thresholds for low, moderate or high levels of prevalence of isoniazid resistance: NTPs will establish definitions for their own countries.

WHO consolidated guidelines on tuberculosis. Module 4: treatment – drug-susceptible tuberculosis treatment, 2022 update *(9)*.

Treatment of drug-susceptible TB

New patients with pulmonary TB should receive a regimen containing 6 months of rifampicin: 2HRZE/4HR.*

(Strong recommendation, high certainty of evidence)

** This recommendation is applicable to adolescents from 15 years of age*

In all patients with drug-susceptible pulmonary TB, the use of thrice-weekly dosing is not recommended in both the intensive and continuation phases of therapy, and daily dosing remains the recommended dosing frequency.

(Conditional recommendation, very low certainty in the evidence)

The use of fixed-dose combination (FDC) tablets is recommended over separate drug formulations in treatment of patients with drug-susceptible TB.

(Conditional recommendation, low certainty in the evidence)

Patients aged 12 years and older with drug-susceptible pulmonary TB, may receive a 4-month regimen of isoniazid, rifapentine, moxifloxacin and pyrazinamide.

(**NEW in DS-TB guidelines**: *Conditional recommendation, moderate certainty evidence*)

Treatment of TB meningitis and osteoarticular TB in children and adolescents

In children and adolescents with bacteriologically confirmed or clinically diagnosed TB meningitis (without suspicion or evidence of MDR/RR-TB), a 6-month intensive regimen (6HRZEto) may be used as an alternative option to the 12-month regimen (2HRZE/10HR).

(***NEW***: *conditional recommendation, very low certainty of evidence)*

- *The shorter intensive regimen is suitable for children and adolescents who have no evidence of drug resistance and in children and adolescents who have a low likelihood of drug resistant TB, e.g. those without risk factors for any form of drug-resistant TB.*
- *The recommendation from the Guidance for national tuberculosis programmes on the management of tuberculosis in children (second edition, 2014) remains an option for the treatment of children and adolescents with suspected or confirmed TB meningitis (TBM): Children and adolescents with suspected or confirmed tuberculous meningitis (and children with suspected or confirmed osteoarticular TB) should be treated with a four-drug regimen (HRZE) for 2 months, followed by a two-drug regimen (HR) for 10 months, the total duration of treatment being 12 months. (Strong recommendation, low certainty of evidence).*
- *Due to a lack of data, the shorter intensive treatment regimen recommendation should not be used in children and adolescents living with HIV who are diagnosed with TB meningitis.*

Children and adolescents with suspected or confirmed osteoarticular TB should be treated with a four-drug regimen (HRZE) for 2 months, followed by a two-drug regimen (HR) for 10 months, the total duration of treatment being 12 months.

(Strong recommendation, low certainty of evidence)

WHO consolidated guidelines on tuberculosis. Module 4: treatment – drug-susceptible tuberculosis treatment, 2022 update *(9)*.

Treatment of TB meningitis children and adolescents

In patients with tuberculous meningitis, an initial adjuvant corticosteroid therapy with dexamethasone or prednisolone tapered over 6–8 weeks should be used.

(Strong recommendation, moderate certainty in the evidence)

WHO consolidated guidelines on tuberculosis. Module 5: Management of tuberculosis in children and adolescents, 2022 *(6)*.

Treatment of multi-drug and rifampicin resistant TB in children

In children with MDR/RR-TB aged below 6 years, an all-oral treatment regimen containing bedaquiline may be used *(conditional recommendation, very low certainty of the evidence)*.

This recommendation applies to and complements current WHO recommendations on shorter and longer regimens that contain bedaquiline *(10):*

- A shorter all-oral bedaquiline-containing regimen of 9–12 months duration is recommended in eligible patients with confirmed multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB) who have not been exposed to treatment with second-line TB medicines used in this regimen for more than 1 month, and in whom resistance to fluoroquinolones has been excluded. *(Conditional recommendation, very low certainty in the evidence)*
- Bedaquiline should be included in longer multidrug-resistant TB (MDR-TB) regimens for patients aged 18 years or more. *(Strong recommendation, moderate certainty in the estimates of effect)*
- Bedaquiline may also be included in longer MDR-TB regimens for patients aged 6–17 years. *(Conditional recommendation, very low certainty in the estimates of effect)*

In children with MDR/RR-TB aged below 3 years delamanid may be used as part of longer regimens *(conditional recommendation, very low certainty of evidence)*.

This recommendation complements the current WHO recommendation on longer regimens that contain delamanid *(10):*

- Delamanid may be included in the treatment of MDR/RR-TB patients aged 3 years or more on longer regimens *(conditional recommendation, moderate certainty in the estimates of effect)*.

WHO consolidated guidelines on tuberculosis. Module 4: treatment – drug-resistant tuberculosis treatment, 2020 update *(10)*.

Regimen for rifampicin-susceptible and isoniazid-resistant tuberculosis

In patients with confirmed rifampicin-susceptible, isoniazid-resistant tuberculosis (Hr-TB), treatment with rifampicin, ethambutol, pyrazinamide and levofloxacin is recommended for a duration of 6 months.

(Conditional recommendation, very low certainty in the estimates of effect)

In patients with confirmed rifampicin-susceptible, isoniazid-resistant tuberculosis, it is not recommended to add streptomycin or other injectable agents to the treatment regimen.

(Conditional recommendation, very low certainty in the estimates of effect)

Shorter all-oral bedaquiline-containing regimen for multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB)

A shorter all-oral bedaquiline-containing regimen of 9–12 months duration is recommended in eligible patients with confirmed multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB) who have not been exposed to treatment with second-line TB medicines used in this regimen for more than 1 month, and in whom resistance to fluoroquinolones has been excluded.

(Conditional recommendation, very low certainty in the evidence in adults and adolescents)

Longer regimens for MDR or RR-TB
In multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB) patients on longer regimens, all three Group A agents and at least one Group B agent should be included to ensure that treatment starts with at least four TB agents likely to be effective, and that at least three agents are included for the rest of treatment if bedaquiline is stopped. If only one or two Group A agents are used, both Group B agents are to be included. If the regimen cannot be composed with agents from Groups A and B alone, Group C agents are added to complete it. *(Conditional recommendation, very low certainty in the estimates of effect)*
Kanamycin and capreomycin are not to be included in the treatment of MDR/RR-TB patients on longer regimens. *(Conditional recommendation, very low certainty in the estimates of effect)*
Levofloxacin or moxifloxacin should be included in the treatment of MDR/RR-TB patients on longer regimens. *(Strong recommendation, moderate certainty in the estimates of effect)*
Linezolid should be included in the treatment of MDR/RR-TB patients on longer regimens. *(Strong recommendation, moderate certainty in the estimates of effect)*
Clofazimine and cycloserine or terizidone may be included in the treatment of MDR/RR-TB patients on longer regimens. *(Conditional recommendation, very low certainty in the estimates of effect)*
Ethambutol may be included in the treatment of MDR/RR-TB patients on longer regimens. *(Conditional recommendation, very low certainty in the estimates of effect)*
Pyrazinamide may be included in the treatment of MDR/RR-TB patients on longer regimens. *(Conditional recommendation, very low certainty in the estimates of effect)*
Imipenem–cilastatin or meropenem may be included in the treatment of MDR/RR-TB patients on longer regimens.[8] *(Conditional recommendation, very low certainty in the estimates of effect)*
Amikacin may be included in the treatment of MDR/RR-TB patients **aged 18 years or more** on longer regimens when susceptibility has been demonstrated and adequate measures to monitor for adverse reactions can be ensured. If amikacin is not available, streptomycin may replace amikacin under the same conditions. *(Conditional recommendation, very low certainty in the estimates of effect)*
Ethionamide or prothionamide may be included in the treatment of MDR/RR-TB patients on longer regimens only if bedaquiline, linezolid, clofazimine or delamanid are not used, or if better options to compose a regimen are not possible. *(Conditional recommendation against use, very low certainty in the estimates of effect)*
P-aminosalicylic acid may be included in the treatment of MDR/RR-TB patients on longer regimens only if bedaquiline, linezolid, clofazimine or delamanid are not used, or if better options to compose a regimen are not possible. *(Conditional recommendation against use, very low certainty in the estimates of effect)*

[8] Imipenem-cilastatin and meropenem are administered with clavulanic acid, which is available only in formulations combined with amoxicillin. Amoxicillin-clavulanic acid is not counted as an additional effective TB agent, and should not be used without imipenem-cilastatin or meropenem.

Clavulanic acid should not be included in the treatment of MDR/RR-TB patients on longer regimens.

(Strong recommendation against use, low certainty in the estimates of effect)

The bedaquiline, pretomanid and linezolid (BPaL) regimen for multidrug-resistant tuberculosis with additional fluoroquinolone resistance

A treatment regimen lasting 6–9 months, composed of bedaquiline, pretomanid and linezolid (BPaL), may be used under operational research conditions in multidrug-resistant tuberculosis (MDR-TB) patients with TB that is resistant to fluoroquinolones, who have either had no previous exposure to bedaquiline and linezolid or have been exposed for no more than 2 weeks.

(Conditional recommendation, very low certainty in the estimates of effect)

Note: this recommendation concerns patients aged 14 years and above

Monitoring patient response to MDR-TB treatment using culture

In multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB) patients on longer regimens, the performance of sputum culture in addition to sputum smear microscopy is recommended to monitor treatment response.

(Strong recommendation, moderate certainty in the estimates of test accuracy). It is desirable for sputum culture to be repeated at monthly intervals.

Subgroup considerations: Patients <15 years of age with MDR/RR-TB comprised less than 2% of the IPD-MA analysed for PICO question 11 (MDR/RR-TB, 2018). Younger children usually cannot produce sufficient sputum spontaneously to allow a bacteriological diagnosis (many are typically sputum smear-microscopy negative). In these patients, culture may be a more sensitive means to detect viable TB bacilli even if very few organisms are present in the sputum or other samples, below the detection threshold of direct microscopy. However, in children who are unable to expectorate, gastric aspirates or induced sputa may be possible but the repetition of such tests at monthly frequency may not be acceptable.

Recommendations on models of TB care relevant to children and adolescents

WHO consolidated guidelines on tuberculosis. Module 5: Management of tuberculosis in children and adolescents, 2022 *(6)*.

In TB high burden settings, decentralized models of care may be used to deliver TB services to children and adolescents with signs and symptoms of TB and/or those exposed to TB

*(**NEW**: conditional recommendation, very low certainty evidence)*.

Family-centred, integrated models of care to deliver TB services may be used in children and adolescents with signs and symptoms of TB and/or those exposed to TB, in addition to standard models of care

*(**NEW**: conditional recommendation; very low certainty evidence)*.

WHO consolidated guidelines on tuberculosis. Module 4: treatment – care and support during tuberculosis treatment *(11)*.

Health education and counselling on the disease and treatment adherence should be provided to patients on TB treatment.

(Strong recommendation, moderate certainty in the evidence)

A package of treatment adherence interventions[9] may be offered for patients on TB treatment in conjunction with the selection of a suitable treatment administration option.[10]

(Conditional recommendation, low certainty in the evidence)

One or more of the following treatment adherence interventions (complementary and not mutually exclusive) may be offered to patients on TB treatment or to health care providers:

a. tracers[11] or digital medication monitor[12] *(Conditional recommendation, very low certainty in the evidence);*

b. material support to the patient[13] *(Conditional recommendation, moderate certainty in the evidence);*

c. psychological support to the patient[14] *(Conditional recommendation, low certainty in the evidence);*

d. staff education[15] *(Conditional recommendation, low certainty in the evidence)*.

[9] Treatment adherence interventions include social support such as patient education and counselling, material support (e.g. food, financial incentive, and transport fee); psychological support; tracers such as home visit or digital health communication (e.g. SMS, telephone call); medication monitor; and staff education. The interventions should be selected on the basis of the assessment of individual patient's needs, provider's resources and conditions for implementation.

[10] Treatment administration options include various forms of treatment support, video supported treatment, non-daily treatment support (e.g. treatment support provided weekly or a few times per week), or unsupported treatment.

[11] Tracers refer to communication with the patient including via SMS, telephone (voice) calls, or home visit.

[12] A digital medication monitor is a device that can measure the time between openings of the pill box. The medication monitor may have audio reminders or send an SMS to remind patient to take medications, along with recording when the pill box is opened.

[13] Material support can be food or financial support such as: meals, food baskets, food supplements, food vouchers, transport subsidies, living allowance, housing incentives, or financial bonus. This support addresses indirect costs incurred by patients or their attendants in order to access health services, and possibly tries to mitigate consequences of income loss related to the disease.

[14] Psychological support can be counselling sessions or peer-group support.

[15] Staff education can be adherence education, chart or visual reminder, educational tools and desktop aids for decision-making and reminder.

The following treatment administration options may be offered to patients on TB treatment:

a. Community- or home-based treatment support is recommended over health facility-based treatment support or unsupported treatment *(conditional recommendation, moderate certainty in the evidence);*

b. Treatment support administered by trained lay providers or health care workers is recommended over treatment support administered by family members or unsupported treatment *(conditional recommendation, very low certainty in the evidence);*

c. Video supported treatment (VST) can replace treatment support when the video communication technology is available and can be appropriately organized and operated by health-care providers and patients *(conditional recommendation, very low certainty in the evidence).*

Patients with multidrug-resistant TB (MDR-TB) should be treated using mainly ambulatory care rather than models of care based principally on hospitalization.

(Conditional recommendation, very low certainty evidence)

A decentralized model of care is recommended over a centralized model for patients on MDR-TB treatment.

(Conditional recommendation, very low certainty in the evidence)

Recommendations on TB/HIV co-infection and nutrition relevant to children and adolescents

WHO policy on collaborative TB/HIV activities: guidelines for national programmes and other stakeholders, 2012 *(12)*.

Routine HIV testing should be offered to all patients, with presumptive and diagnosed TB.

(Strong recommendation, low certainty of evidence)

Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach, July 2021 *(13)*.

Co-trimoxazole prophylaxis for infants, children and adolescents living with HIV

Co-trimoxazole prophylaxis is recommended for infants, children and adolescents with HIV, regardless of clinical and immune conditions. Priority should be given to all children younger than five 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 cell count ≤350 cells/mm^3.

(Strong recommendation, high certainty evidence)

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 certainty evidence)

In settings with low prevalence for both malaria and bacterial infections, cotrimoxazole prophylaxis may be discontinued for children five years of age and older who are clinically stable and/or virally suppressed on ART for at least six months and with a CD4 count > 350 cells/mm^3.

(Strong recommendation, very low certainty evidence).

Co-trimoxazole prophylaxis is recommended for HIV-exposed infants from four to six 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-certainty evidence)

Routine co-trimoxazole prophylaxis should be given to all people living with HIV with TB disease regardless of CD4 cell count.

(Strong recommendation, high-certainty evidence)

General recommendations on eligibility for ART

ART should be initiated for all people living with HIV regardless of WHO clinical stage and at any CD4 cell count.

- Pregnant and breastfeeding women *(strong recommendation, moderate-certainty evidence)*
- Adolescents *(conditional recommendation, low-certainty evidence)*
- Children living with HIV one year old to less than 10 years old *(conditional recommendation, low-certainty evidence)*
- Infants diagnosed in the first year of life *(strong recommendation, moderate-certainty evidence)*

Rapid ART initiation should be offered to all people living with HIV following a confirmed HIV diagnosis and clinical assessment. *(strong recommendation: high-certainty evidence for adults and adolescents; low-certainty evidence for children).*

Rapid initiation is defined as within seven days from the day of HIV diagnosis; people with advanced HIV disease should be given priority for assessment and initiation.

ART initiation should be offered on the same day to people who are ready to start.

(strong recommendation: high certainty evidence for adults and adolescents; low-certainty evidence for children)

Timing of ART for children and adolescents with TB

ART should be started as soon as possible within two weeks of initiating TB treatment, regardless of CD4 count, among adolescents and children living with HIV (except when signs and symptoms of meningitis are present). *(Adolescents: strong recommendation, low- to moderate-certainty evidence; Children and infants: strong recommendation, very low certainty evidence)*

ART should be delayed at least four weeks (and initiated within eight weeks) after treatment for TB meningitis is initiated.

First-line ART regimens

Dolutegravir (DTG) in combination with a nucleoside reverse-transcriptase inhibitor (NRTI) backbone is recommended as the preferred first-line regimen for people living with HIV initiating ART

- Adolescents *(strong recommendation, moderate-certainty evidence)*
- Infants and children with approved DTG dosing *(conditional recommendation, low-certainty evidence)*

A raltegravir (RAL)-based regimen may be recommended as the preferred first-line regimen for neonates.

(Conditional recommendation, very-low-certainty evidence)

Second-line ART regimens

DTG in combination with an optimized NRTI backbone may be recommended as a preferred second-line regimen for people living with HIV for whom non-DTG-based regimens are failing.

- Adolescents *(conditional recommendation, moderate-certainty evidence*)
- Children with approved DTG dosing *(conditional recommendation, low-certainty evidence)*

Boosted protease inhibitors in combination with an optimized NRTI backbone are recommended as a preferred second-line regimen for people living with HIV for whom DTG-based regimens are failing.

(Strong recommendation, moderate-certainty evidence)

Guidelines: updates on the management of severe acute malnutrition in infants and children, 2013 *(14).*

Infants with severe acute malnutrition who are admitted for inpatient care should be given parenteral antibiotics to treat possible sepsis and appropriate treatment for other medical complications such as tuberculosis, HIV, surgical conditions or disability.

(Strong recommendation, very low certainty evidence)

Guideline: Nutritional care and support for patients with tuberculosis, 2013 *(15)*.

Management of severe acute malnutrition

School-age children and adolescents (5 to 19 years), and adults, including pregnant and lactating women, with TB disease and severe acute malnutrition (very low BMI-for-age) should be treated in accordance with the WHO recommendations for management of severe acute malnutrition.

(Strong recommendation, very low certainty evidence)

Children who are less than 5 years of age with TB disease and severe acute malnutrition (mid-upper arm circumference more than 115 mm or weight-for-height/length more than 3 z-scores below the WHO child growth standards median, or with any degree of bilateral pitting oedema) should be treated in accordance with the WHO recommendations for the management of severe acute malnutrition in children who are less than 5 years of age.

(Strong recommendation, very low certainty evidence)

Management of moderate undernutrition

School-age children and adolescents (5 to 19 years), and adults, including lactating women, with TB disease and moderate undernutrition, who fail to regain normal body mass index after 2 months' TB treatment, as well as those who are losing weight during TB treatment, should be evaluated for adherence and comorbid conditions. They should also receive nutrition assessment and counselling and, if indicated, be provided with locally available nutrient-rich or fortified supplementary foods, as necessary to restore normal nutritional status.

(Conditional recommendation, low certainty evidence)

Children who are less than 5 years of age with TB disease and moderate undernutrition should be managed as any other children with moderate undernutrition. This includes provision of locally available nutrient-rich or fortified supplementary foods, in order to restore appropriate weight-for-height.

(Strong recommendation, very low certainty evidence)

Patients with multidrug-resistant TB and moderate undernutrition should be provided with locally available nutrient-rich or fortified supplementary foods, as necessary to restore normal nutritional status.

(strong recommendation, very low certainty evidence)

A daily multiple micronutrient supplement at 1× recommended nutrient intake should be provided in situations where fortified or supplementary foods should have been provided in accordance with standard management of moderate undernutrition,[16] but are unavailable.

(conditional recommendation, very low certainty evidence)

[16] Pyridoxine supplementation is recommended along with isoniazid treatment for all pregnant (or breastfeeding) women, as well as for people with conditions such as HIV infection, alcohol dependency, malnutrition, diabetes, chronic liver disease or renal failure. Pyridoxine provision together with isoniazid treatment was not analysed for the 2013 nutrition guideline.

Nutritional screening as part of contact investigation

In settings where contact tracing is implemented, household contacts of people with TB disease should have a nutrition screening and assessment as part of contact investigation. If malnutrition is identified, it should be managed according to WHO recommendations.

(Conditional recommendation, very low certainty evidence)

Remarks:

- *There is no evidence that nutritional management of acute malnutrition of patients with TB disease should be different than for those without TB disease.*
- *Concerns about weight loss or failure to gain weight should trigger further clinical assessment (e.g. resistance to TB drugs, poor adherence, comorbid conditions) and nutrition assessment, in order to determine the most appropriate interventions.*
- *Closer nutritional monitoring and earlier initiation of nutrition support (before the first 2 months of TB treatment are completed) should be considered if the nutritional indicator is approaching the cut-off value for a diagnosis of severe undernutrition.*

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