

# WHO consolidated guidelines on tuberculosis

Module 4: Treatment

**Tuberculosis care  
and support**



World Health  
Organization



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WHO consolidated guidelines on tuberculosis. Module 4: treatment. Tuberculosis care and support

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Details of the participants and members of GDGs, external review groups, WHO steering groups, evidence review teams, individuals and partners who contributed to the 2011, 2017 and 2022 guideline updates are included in Annex 1.

The consolidation of recommendations and the production of this document – *WHO consolidated guidelines on tuberculosis. Module 4: Treatment. Tuberculosis care and support* – were coordinated by Fuad Mirzayev and Linh Nguyen, under the guidance of Matteo Zignol and the overall direction of Tereza Kasaeva, Director of the WHO Global Tuberculosis Programme. Colleagues from the Vulnerable Populations, Communities and Co-morbidities Unit, Global TB Programme, WHO, under the leadership of Farai Mavhunga, also contributed to the consolidation of these guidelines.

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# List of abbreviations

<b>AIDS</b>	Acquired immunodeficiency syndrome
<b>ART</b>	Antiretroviral treatment
<b>DALY</b>	Disability-adjusted life year
<b>DSD</b>	Differentiated service delivery
<b>DS-TB</b>	Drug-susceptible tuberculosis
<b>GDG</b>	Guideline Development Group
<b>GRADE</b>	Grading of Recommendations Assessment, Development and Evaluation
<b>GTB</b>	Global TB Programme
<b>HIV</b>	Human immunodeficiency virus
<b>iCCM</b>	Integrated community case management
<b>IMCI</b>	Integrated management of childhood illness
<b>MDR-TB</b>	Multidrug-resistant tuberculosis
<b>NGO</b>	Nongovernmental organization
<b>PHC</b>	Primary health care
<b>PICO</b>	Patients, Intervention, Comparator and Outcomes
<b>SAT</b>	Self-administered treatment or unsupervised treatment
<b>SMS</b>	Short Message Service or text message
<b>TB</b>	Tuberculosis
<b>The Union</b>	International Union Against Tuberculosis and Lung Disease
<b>TPT</b>	TB preventive treatment
<b>VST</b>	Video-supported treatment
<b>WHO</b>	World Health Organization



# Executive summary

WHO aims to use the best available evidence on interventions to ensure adequate patient care and support and in order to inform policy decisions made by national TB control programme managers, national policy-makers and medical practitioners in a variety of geographical, economic and social settings.

This module of the *WHO consolidated guidelines on tuberculosis* aims to provide a summary of existing valid WHO recommendations on care and support during tuberculosis treatment.

The recommendations included in this module were developed by three Guidelines Development Groups (GDGs) convened by the WHO Global Tuberculosis Programme in 2011, 2016 and 2021 (1–3) in order to review the evidence available on key aspects of TB care and support. The GDGs were composed of a multidisciplinary group of TB experts external to WHO.

The recommendations were formulated by the GDGs using the GRADE approach. The recommendations were then reviewed by external review groups which were composed of experts and end-users from all WHO regions.

The recommendations on TB care and support are as follows:

## 1. Care and support interventions for all people with TB

Recommendations:

**1.1. Health education and counselling on the disease and treatment adherence should be provided to patients on TB treatment (strong recommendation, moderate certainty of evidence).**

**1.2. A package of treatment adherence interventions<sup>1</sup> may be offered for patients on TB treatment in conjunction with the selection of a suitable treatment administration option<sup>2</sup> (conditional recommendation, low certainty of evidence).**

**1.3. 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<sup>3</sup> or digital medication monitor<sup>4</sup> (conditional recommendation, very low certainty of evidence);**

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<sup>1</sup> Treatment adherence interventions include social support such as: patient education and counselling; material support (e.g. food, financial incentive and transport fees); psychological support; tracers such as home visits or digital health communications (e.g. SMS, telephone calls); medication monitor; and staff education. The interventions should be selected on the basis of the assessment of the individual patient's needs, provider's resources and conditions for implementation.

<sup>2</sup> Suitable treatment administration options include various forms of treatment support, such as video-supported treatment and regular community or home-based treatment support.

<sup>3</sup> Tracers refer to communication with the patient including via SMS, telephone (voice) calls, or home visit.

<sup>4</sup> 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.

- b) material support to patient<sup>5</sup> (conditional recommendation, moderate certainty of evidence);*
- c) psychological support<sup>6</sup> to patient (conditional recommendation, low certainty of evidence);*
- d) staff education<sup>7</sup> (conditional recommendation, low certainty of evidence).*

**1.4. 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 unsupervised treatment (Conditional recommendation, moderate certainty of 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 of evidence).*
- c) Video-supported treatment (VST) can replace in-person 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 of evidence).*

## 2. Models of care for people with drug-resistant TB

Recommendations:

**2.1. 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 of evidence).**

**2.2. A decentralized model of care is recommended over a centralized model for patients on MDR-TB treatment (conditional recommendation, very low certainty of evidence).**

## 3. Models of care for children and adolescents exposed to TB or with TB disease

Recommendations:

**3.1. 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 (conditional recommendation, very low certainty of evidence).**

**3.2. 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 (conditional recommendation; very low certainty of evidence).**

It is critical that national TB programmes and public health leaders consider these recommendations in the context of countries' TB epidemics, the strengths and weaknesses of health systems, and the availability of financial, human and other essential resources. In adapting these guidelines, care must be exercised to protect access for the populations most in need in order to achieve the greatest

<sup>5</sup> 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.

<sup>6</sup> Psychological support can be counselling sessions or peer-group support.

<sup>7</sup> Staff education can be adherence education, chart or visual reminder, educational tools and desktop aids for decision-making and reminder.

impact for the greatest number of people and to ensure sustainability. It is similarly important to ensure that the adaptation of these guidelines does not stifle ongoing or planned research; the new recommendations reflect the current state of knowledge and new information will be needed for sustainability and future modifications of the existing guidelines.



# Introduction

The Global TB Programme (GTB) of the World Health Organization (WHO) has been combining all current recommendations into one overall set of consolidated guidelines on TB. The guidelines contain recommendations regarding all areas related to the programmatic management of TB (e.g. screening, preventive treatment, diagnostics, the treatment of drug-susceptible and drug-resistant TB, patient care and support). The consolidated guidelines contain modules specific to each programmatic area.

The consolidated WHO evidence-based guidelines for the treatment of drug-resistant TB (4), for the treatment of drug-susceptible TB (DS-TB) (5), and for the management of tuberculosis in children and adolescents (3) were published in 2020 and 2022. The recommendations on tuberculosis care and support contained in these guidelines were developed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method for assessment of the quality of evidence.

People-centred care is an important element of the End TB Strategy which recommends treatment and patient support for all people with TB. Several interventions to support patients in their adherence to TB treatment have been implemented by national TB programmes for many years (e.g. treatment support with observation of medicine intake and social support), while others have been introduced recently (e.g. digital health interventions such as SMS messages, telephone calls or other reminders, and video-supported treatment, or VST). These interventions and models of care have been assessed using the GRADE method and WHO has issued guidelines with evidence-based recommendations for a variety of interventions for TB care and support. This module presents all WHO's recommendations on TB care and support that are either newly developed or are existing recommendations that have been published previously in other WHO guidelines that applied the GRADE approach.

## Structure of the document

The Recommendations part of this document has three main sections on elements of TB care and support. The elements covered are:

1. Care and support interventions for all people with TB.
2. Models of care for people with drug-resistant TB.
3. Models of care for children and adolescents exposed to TB or with TB disease.

Each section starts with the current WHO recommendations for that element. It then gives information on the evidence used to inform the recommendations, summarizes the analyses that were carried out on the basis of the evidence, and describes considerations for specific subgroups, for monitoring and evaluation and for implementation. Research gaps that were identified for each of the sections are presented at the end of the document; online annexes provide more details on the methods, the Guideline Development Groups (GDGs), the reports of systematic reviews and data analyses, evidence profiles, unpublished data and statistical analysis plans. Each section reflects discussions held at GDG meetings. Additional information on the implementation of patient care interventions is presented in the relevant submodule of the WHO operational handbook on TB care and support which is, a separate document that is designed to aid implementation efforts.



# WHO policy recommendations

## 1. Care and support interventions for all people with TB

### Recommendations:

- 1.1 **Health education and counselling on the disease and treatment adherence should be provided to patients on TB treatment**  
*(strong recommendation, moderate certainty of evidence).*
- 1.2 **A package of treatment adherence interventions<sup>8</sup> may be offered to patients on TB treatment in conjunction with the selection of a suitable treatment administration option<sup>9</sup>**  
*(conditional recommendation, low certainty of evidence).*
- 1.3 **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<sup>10</sup> and/or digital medication monitor<sup>11</sup>** *(conditional recommendation, very low certainty of evidence);*
  - b) **material support<sup>12</sup> to patient** *(conditional recommendation, moderate certainty of evidence);*
  - c) **psychological support<sup>13</sup> to patient** *(conditional recommendation, low certainty of evidence);*
  - d) **staff education<sup>14</sup>** *(conditional recommendation, low certainty of evidence).*

<sup>8</sup> Treatment adherence interventions include social support such as: informational or educational support (e.g. patient education or educational counselling), material support (e.g. food, financial incentives, transport fees) and psychological support; tracers such as home visits or digital health communications (e.g. SMS, telephone calls); medication monitor; and staff education. The interventions should be selected based on the assessment of the individual patient's needs, provider's resources and conditions for implementation.

<sup>9</sup> Suitable treatment administration options include various forms of treatment support, such as video-supported treatment and regular community or home-based treatment support.

<sup>10</sup> Tracers refer to the communication with the patient – including via SMS, telephone (voice) calls or home visits.

<sup>11</sup> 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 may send an SMS to remind the patient to take the medications, along with recording when the pill box is opened.

<sup>12</sup> Material support can be food or financial support: 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 accessing health services and, possibly, tries to mitigate the consequences of income loss related to the disease.

<sup>13</sup> Psychological support can be counselling sessions or peer-group support.

<sup>14</sup> Staff education can be adherence education, charts or visual reminders, educational tools and desktop aids for decision-making and reminder.

- 1.4 **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 of evidence*).
  - b) **Treatment support by trained lay providers or health-care workers is recommended over treatment support by family members or unsupported treatment** (*conditional recommendation, very low certainty of evidence*).
  - c) **Video-supported treatment (VST) may replace in-person treatment support when the video communication technology is available and it can be appropriately organized and operated by health-care providers and patients** (*conditional recommendation, very low certainty of evidence*).

## Justification

### **Treatment support**

Treatment support terminology in this document is used to describe an approach to supporting patients who are taking prescribed doses of TB medicines in order to help ensure adherence to treatment and maximize its efficacy. Treatment support needs to be provided in the context of people-centred care and should be based on the individual patient's needs, acceptability and preferences. It includes aspects of support, motivation and understanding of patients without coercion. Historically, this group of interventions were labelled as "directly observed treatment" or DOT. However, with a need to emphasize the need to support people in adhering to treatment, as recommended by the WHO TB ethics guidance of 2010 and 2017 (6, 7), this legacy terminology has been replaced by "treatment support" throughout this document in order to align the language with the essence of the recommendation of the WHO TB ethics guidance.

In the systematic review that led to the recommendations on treatment adherence, "treatment support" was defined as any person observing the patient taking medications in real time. The treatment supporter does not need to be a health-care worker, but could be a friend, a relative or a lay person who works as a treatment supporter.

Treatment support may also be achieved with real-time video feed and video recording which is referred to as video-supported treatment (VST). VST was analysed separately in this review.

Adherence definitions varied across the studies. In general, however, adherence was defined as taking > 90% of medications under conditions of observation by another person.

The systematic review conducted in support of this guideline was based on synthesis of data from randomized controlled trials (8–15) and from observational studies (16–29), with preference given to the results of randomized controlled trials. Outcomes from treatment support with observation were compared with outcomes from self-administered treatment (SAT) given under standard TB practice and without any additional support. Treatment support could be given by a health-care worker, a family member or a community member and could be done at home, in the patient's community or at a clinic. Treatment support was generally performed daily. The GDG focused preferentially on randomized controlled trial data from the systematic review. When the data from randomized controlled trials were limited or not available, observational data were examined and their results were presented. Interpretation of the associations, however, requires caution due to limitations of the observational data when the associations are confounded by different factors. In uncontrolled observational studies, for instance, patients with more severe disease or higher risk of non-adherence



are likely to be assigned treatment support and the less sick or, less likely, noncompliant patients are assigned SAT. The same may apply to the selection of treatment support location, treatment support provider or other interventions in cohort studies.

When treatment support alone was compared with SAT, patients who were on treatment support had better rates of treatment success, adherence and 2-month sputum conversion, and also had slightly lower rates of loss to follow-up and acquired drug resistance. However, patients on treatment support had a slightly higher relapse rate. The GDG considered that, overall, the evidence was inconsistent in showing clear advantages of treatment support alone over SAT or vice versa. However, the evidence showed that some subgroups of patients (e.g. TB patients living with HIV) with factors affecting treatment adherence are likely to benefit from treatment support more than other patients do, and that specific types of treatment support delivery (e.g. locations of treatment support or support providers) are likely to work better than others. The evidence also showed that, when patients received treatment adherence interventions (e.g. different combinations of patient education, staff education, material support, psychological support, tracers and use of medication monitor) in conjunction with treatment support or SAT, the treatment outcomes were significantly improved compared to treatment support with observation or SAT alone (see below).

Only cohort studies were available to examine treatment support and SAT in HIV-positive TB patients (30–46), and many of these studies were conducted in the pre-ART era prior to antiretroviral treatment (ART) or shortly after the introduction of this treatment for HIV-positive TB patients (42–45). As above, treatment support could have been administered by a variety of people in a variety of settings, including homes and clinics; occasionally, during initial intensive-phase treatment, the treatment support was hospital-based. A few studies provided incentives and enablers or provided treatment support only for persons considered to be at higher risk of loss to follow-up. HIV-positive TB patients on SAT had lower rates of treatment success, treatment completion and cure; they also had higher rates of mortality, treatment failure and loss to follow-up. The evidence showed that HIV-positive TB patients, as a subgroup, benefit more from treatment support than TB patients in general do and that SAT alone is not advisable in HIV-positive TB patients. Reasons such as increased rates of drug–drug interactions and more severe disease in this cohort may cause treatment support to offer a significant advantage over SAT.

Treatment support and SAT in MDR-TB patients were also examined in the systematic review. However, very limited data were available from a cohort study (32). There were higher rates of mortality and non-adherence and lower rates of treatment completion in MDR-TB patients on SAT compared with those on treatment support, although the differences were not significant.

### ***Treatment support provider***

Randomized controlled trials (10, 12–14) and observational studies (17, 18, 21, 23, 28, 31, 36, 38, 41, 42, 46) were available for examination of the effect of treatment support providers versus SAT. Providers were classed as health-care workers, lay providers or family members. The health-care worker group was varied and included personnel working at different levels of health-care systems and who had received health training. Health-care workers could be nurses, physicians or trained community health workers. Lay providers were also varied and could include teachers, community volunteers or traditional healers. Treatment support by lay providers had higher rates of treatment success and cure, and a slightly lower rate of loss to follow-up compared with SAT. However, in one cohort study there was a higher rate of treatment completion with SAT compared to treatment support with lay providers. Patients receiving treatment support from a family member had higher rates of treatment success and lower rates of loss to follow-up compared with patients using SAT. When treatment support provided by a health-care worker was compared to SAT, there were higher rates of cure and adherence and lower rates of relapse and acquisition of drug resistance with the treatment support provided by a health-care worker. However, there was a higher rate of treatment completion with SAT compared to treatment support provided by health-care workers in cohort studies.

The effect that different types of treatment support provider had on outcomes was also examined. Treatment support provided by health-care workers and treatment support provided by lay persons were compared. Only observational studies were available in the literature (18, 21, 38, 47–51). There were no significant differences although slightly higher rates of success – and lower rates of mortality, failure and loss to follow-up – were observed among patients who had received treatment support administered by a lay provider as opposed to a health-care worker.

When provision of treatment support by a family member was compared to health-care worker provision of treatment support, there were higher rates of mortality, loss to follow-up and failure, and lower rates of successful treatment, cure and treatment adherence among patients who had treatment support administered by a family member. Therefore, although treatment support by a health-care worker, trained lay provider and family member showed advantages compared to SAT, provision by trained lay providers and health-care workers are the preferred options for treatment support, with the least preferred treatment support provider being a family member.

### **Treatment support location**

Randomized controlled trials (10, 12, 14, 28, 52–55) and observational studies (16, 23, 36, 38, 41, 42, 56–89) examined how the location of treatment support affected the treatment outcome. Locations were grouped by community- or home-based treatment support and health facility-based treatment support. Community- or home-based treatment support was defined as treatment support delivered in the community that is close to the patient's home or workplace. In general, community- or home-based treatment support was provided close to the patients. Health facility-based treatment support was defined as treatment support delivered at a health centre, clinic or hospital, although there were some instances of community- or home-based treatment support being provided by health-care workers. When comparing treatment support locations, community- or home-based treatment support had higher rates of treatment success, cure, treatment completion and 2-month sputum conversion. Community- or home-based treatment support also had lower rates of mortality and lower rates of unfavourable outcomes compared with health facility-based treatment support.

When comparing community/home-based treatment support or health facility-based treatment support with SAT, there were no significant differences across the outcomes in randomized controlled trials. However, cohort studies showed higher rates of treatment success and adherence, and a lower rate of loss to follow-up, with community/home-based treatment support compared with SAT.

Observational data from cohort studies also showed lower rates of treatment completion and slightly higher rates of failure and loss to follow-up in health-facility treatment support compared to SAT.

Consequently, community- or home-based treatment support is the preferred option rather than health facility-based treatment support and SAT.

Combining the evidence on treatment support provider and treatment support location, treatment support should preferably be delivered at home or in the community by a health-care worker or trained lay provider. Treatment support that is delivered at a health facility or provided by a family member, and treatment that is unsupported are not preferable options.

### **Video-supported treatment (VST)**

For VST there were only two cohort studies from high-income countries and no data from low- and middle-income countries (90, 91). These studies compared in-person treatment support with VST done in real time. Patients given VST had no statistically significant difference in treatment completion and mortality compared to patients who had in-person treatment support.

Although there is some concern as to the indirectness of evidence for VST, given that the studies were conducted in high-income countries and there is uncertainty of evidence regarding the use of VST, the

results from the two cohort studies showed that in-person treatment support was not better than VST. Treatment support has been the standard of care that many programmes aim for, even if in practice they have to resort to SAT for many patients because of lack of resources. The advantages of using VST are its potential to observe adherence to treatment from a distance – even when people travel and cannot visit or be visited by a treatment support provider. VST is also more flexible with regard to people's schedules as it offers virtual observation at different times of the day. VST could help achieve better levels of patient interaction at a much lower cost and less inconvenience when compared with in-person treatment support. VST can be used in addition to, or may be interchangeable with, in-person treatment support or other treatment administration options. For instance, it is not expected that a patient receives VST as the sole option of supervision during the whole duration of treatment.

Furthermore, the technology required for VST (broadband Internet and smartphone availability) is becoming increasingly available in resource-constrained settings. Moreover, VST delivery options are evolving (e.g. enhanced possibility for real-time communication in addition to recorded video), and therefore evidence and best practices are likely to develop further in the coming years, especially from the ongoing randomized controlled trials. The benefits of VST may become more apparent as programmes are able to choose forms of VST that best meet their needs. In fact, VST may be particularly useful for easing the burden on the health-care system in low- and middle-income countries.

### ***Package of combined treatment adherence interventions***

Both randomized controlled trials (91–96) and observational studies (56–62, 97) examined the effects of combined treatment adherence interventions. When patients receiving combined treatment adherence interventions along with treatment support or SAT were compared to those receiving treatment support or SAT alone, the patients who received the combined treatment adherence interventions had higher rates of treatment success, treatment completion, cure and adherence, and lower rates of mortality and loss to follow-up. The mixture of types of adherence intervention was varied (Table 1). These included different combinations of patient education, staff education, material support (e.g. food, financial incentives, transport fees, bonuses for reaching treatment goals), psychological support and counselling. The treatment adherence interventions also included tracers such as home visits, use of digital health communication (e.g. SMS, telephone calls) or a medication monitor. Interventions should be selected on the basis of an assessment of individual patients' needs, providers' resources and conditions for implementation.

**Table 1. Treatment adherence interventions**

Treatment adherence intervention	Description
Patient education	Health education and counselling.
Staff education	Education, chart or visual reminder, educational tool and desktop aid for decision-making and reminder.
Material support	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 accessing health services and, possibly, tries to mitigate the consequences of income loss related to the disease.
Psychological support	Counselling sessions or peer-group support.
Tracer	Communication with the patient, including home visit or via mobile telephone communication such as SMS or telephone (voice) call.
Digital medication monitor	A digital medication monitor is a device that can measure the time between openings of the pill box. The medication monitor can give audio reminders or send an SMS to remind the patient to take medications, along with recording when the pill box is opened.

### ***Tracers and digital health interventions rather than VST***

Varied tracers were included in randomized controlled trials (98–105) and observational studies (90, 91, 106–110). These interventions included, for instance, SMS, telephone calls or automated telephone reminders. Patients who missed appointments or failed to collect their medication received reminder letters or home visits by health-care workers. Medication monitors or computer systems in the clinic were also used to aid health-care workers in tracing patients. Medication monitors can measure the time between openings of the pill box, give audio reminders, record when the pill box is opened or send SMS reminders to take medications.

There were higher rates of treatment success, treatment adherence and 2-month sputum conversion, and lower rates of mortality, loss to follow-up and drug resistance acquisition with tracers, either through home visits or mobile telephone communication (SMS or telephone call).

When mobile telephone interventions were examined separately, there were higher rates of treatment success, cure and 2-month sputum conversion and lower rates of treatment failure, loss to follow-up, poor adherence and unfavourable outcomes with mobile telephone reminders as opposed to no intervention.

Medication monitors had better rates of adherence and favourable outcomes, and combined interventions of SMS and medication monitors also showed better adherence compared to no intervention.

It should be noted, however, that only a small number of studies were available for all digital health interventions. There was only one small randomized controlled trial (99) on which these data are based. With all the digital interventions and tracers, including VST, it is important to preserve patient support and the ability of patients to interact with health-care workers. In fact, these digital interventions should be considered as tools to enable better communication with the health-care provider rather than as replacements for other adherence interventions. In practice, it is expected that SMS, telephone calls

and VST may replace in-person treatment support for certain periods of time rather than for the entire duration of treatment and that they promote patient-centered approaches to care.

Mobile telephone interventions, tracers and VST may also increase health equity if the need to travel to a health clinic or to a patient's home is reduced. However, the ability of patients to participate in these programmes depends on the patient living in an area with a good telecommunications infrastructure.

### ***Material support for patients***

The effects of material support were examined both with randomized controlled trials (69–72) and observational studies (78, 111–118). The interventions included giving meals with treatment support with observation, monthly food vouchers, food baskets, food supplements and vitamins. Food support for patients and family members is an important incentive for TB patients and also helps protect patients from the catastrophic costs associated with TB. Food may be an incentive but it may also improve the outcome biologically by reducing malnutrition and consequently improving immune function. Other material support could be in the form of financial incentives, transport subsidies, living allowance, housing incentives, or financial bonuses after reaching treatment targets.

There were higher rates of treatment success, completion and sputum conversion in patients who received material support, and lower rates of treatment failure and loss to follow-up compared with patients who did not receive material support. It is of note that all these studies were in low- and middle-income countries, so presumably these incentives were of significant value to the patients in these settings. However, the material support would also be of significant value to TB patients even in higher-income countries, especially in countries that do not have a good social welfare system, since TB is a disease of poverty.

The studies in this review found that material support was usually given to the most vulnerable groups, and therefore health equity was presumably improved by this intervention. However, if these incentives are not applied equitably, health disparities may be increased. The distribution of material support is likely to depend on the country context and may have different effects both within and between countries.

### ***Patient education or educational counselling***

Analysis of the benefit of patient education included randomized controlled trials (64–67) and observational studies (75). Patients who received education or educational counselling had better rates of treatment success, treatment completion, cure and treatment adherence, and had lower rates of loss to follow-up. It should be noted in this case that “counselling” refers to educational counselling and not psychological counselling. Patient education could include oral or written education via health-care workers or pharmacists. The education could be a one-time session at discharge from the intensive phase of therapy or at each presentation for follow-up care. The educational session might include only the health-care worker and patient, or it could involve the patients' social network and family members. It is important to make sure that education and counselling are done in a culturally appropriate manner. Additionally, specific marginalized populations may require special educational efforts.

### ***Staff education***

Staff education may include peer training, visual aids to help initiate conversations with patients, other tools to aid in decision-making and as reminders, as well as the education of laboratory staff. This intervention was examined in both randomized controlled trials (68, 69, 118) and observational studies (119). Staff education led to higher rates of treatment success and slightly lower rates of mortality and loss to follow-up. With better staff education, treatment for patients is likely to improve. Any stigma

that health-care workers may hold towards patients would decrease as the health-care workers better understand TB disease and TB treatment.

### ***Psychological support***

Psychological support was varied and could include self-help groups, alcohol cessation counselling and TB clubs (56, 74, 120). Patients who had access to psychological support had higher rates of treatment completion and cure, as well as lower rates of treatment failure and loss to follow-up. However, the GDG expressed concerns about confounding in these studies due to the severity of illness in the groups receiving support. Additionally, allocation of patients to the support groups was not always randomized.

When considering these data, it should also be noted that types of psychological support are very broad and may not be adequately represented in this review. To maximize health equity, psychological support should be targeted at the most marginalized populations.

## **Subgroup considerations**

The evidence that was reviewed did not allow for conclusions about the advantages of treatment support over SAT or vice versa for TB patients; however, in a subgroup analysis of TB patients living with HIV, treatment support showed clear benefit with significantly improved treatment outcomes. It is probable that treatment support may not be beneficial for all patients but that it is likely to have more benefit in certain subgroups of TB patients. Apart from HIV-positive TB patients, other factors or groups of patients that were more or less likely to result in treatment adherence (and therefore require treatment support) were not examined in the scope of the systematic review.

## **Implementation considerations**

### ***Treatment adherence interventions***

As treatment support alone is not likely to be sufficient to ensure good TB treatment outcomes, additional interventions for treatment adherence need to be provided. Patient education should be provided to all patients on TB treatment. A package of the other treatment adherence interventions also needs to be offered to patients on the basis of an assessment of individual patients' needs, providers' resources and conditions for implementation.

With regard to telephone or video-assisted interventions, there may be reluctance to use new technology, making implementation more difficult. There may be privacy concerns regarding the security of telephone data, so encryption and other measures to safeguard privacy will need to be considered. The feasibility of implementing these types of interventions depends on telecommunications infrastructure, telephone availability and connection costs. Multiple organizations have initiated programmes such as these, so TB programmes may find it helpful to collaborate and communicate with other medical service delivery programmes that have already set up such infrastructure.

There may be reluctance on the part of implementers (e.g. national or local governments, health partners) to pay for incentives. Implementers may be more willing to pay for material support for smaller subgroups at particularly high risk (e.g. patients with MDR-TB). However, one of the components of the End TB Strategy (121) is to provide "social protection and poverty alleviation" for patients with TB. The strategy specifically calls for measures to "alleviate the burden of income loss and non-medical costs of seeking and staying in care". Included in the suggested measures are social welfare payments, vouchers and food packages. The benefit of material support found in this review supports these components of the End TB Strategy (121).

In order to distribute the material support, a government or nongovernmental organization (NGO) infrastructure would need to be in place, including anti-fraud mechanisms (e.g. reliable unique personal identifiers) and appropriate accounting to ensure that incentives are distributed equitably and to the people who need them most. Countries should choose incentives that are the most appropriate for their situation.

### ***Treatment administration***

Community-based or home-based treatment support has more advantages than health facility-based treatment support, although family members should not be the first or only option for administering treatment support. Treatment support is better provided at home or in the community by trained lay providers or health-care workers. However, there may be challenges in providing community- or home-based treatment support by health-care workers because of the increased number of health-care workers required and the increased costs for staff time and daily travel to the community or to a patient's home. Treatment support provided in the community or at home by trained local lay persons is more feasible. A combination of lay provider and health-care worker for provision of community- or home-based treatment support is also an option. Community-based or home-based treatment support is more likely to be acceptable and accessible to patients than other forms of treatment support. Nevertheless, stigma may continue to be a concern with community- or home-based treatment support. Having a health-care worker coming regularly to a patient's house may be stigmatizing, and the feeling of being "watched over" may be disempowering to patients. Other forms of treatment support (e.g. administered by an emotionally supportive relative or close friend) may be more acceptable but may still be stigmatizing.

Given complex family social dynamics, family members may not always be the best people to supervise treatment, so the suitability of such treatment adherence supervisors needs to be carefully analysed in each national or local context. If family members are already providing treatment support, careful identification and training of those persons is required. Additional supervision of local supporters or health-care workers is still needed, as family members cannot be depended on as the only option for care. Patients will continue to need social support, even if family members are providing treatment support.

Assessment of potential risk factors for poor adherence must be taken into account by health-care workers at the start of a patient's treatment in order to decide which treatment administration option should be selected for that patient. Some groups of patients who are less likely to adhere to treatment may gain more benefit from treatment support than others do. Another factor to consider when selecting options for treatment administration is that some patients with inflexible work or family responsibilities may not be able to provide treatment support. Any treatment administration option offered to a patient must also be provided in conjunction with proper medical care, including regular pick-up of TB drugs, consultations with a physician or other health-care workers when necessary, TB treatment that is free of charge, and provision to the patient of essential information on TB treatment.

### **Monitoring and evaluation**

Programmes should attempt to measure whether the provision of incentives improves programme performance.



## 2. Models of care for people with drug-resistant TB

### Recommendations:

- 2.1 **Patients with MDR-TB should be treated using mainly ambulatory care rather than models of care based principally on hospitalization**  
(conditional recommendation, very low certainty of evidence).
- 2.2 **A decentralized model of care is recommended over a centralized model for patients on MDR-TB treatment**  
(conditional recommendation, very low certainty of evidence).

### Justification

**Ambulatory care:** Outcomes from models of MDR-TB care based mainly on clinic-based ambulatory treatment were compared with those using mainly hospital-based inpatient treatment. The data used came from cost-effectiveness studies in four countries, namely: Estonia and the Russian Federation [Tomsk oblast] (122), Peru (123) and Philippines (124). The design of these observational studies did not allow direct comparison of effects between models of care. Because none of the studies were randomized controlled trials, the evidence was considered to be of very low quality. Cost-effectiveness was modelled for all possible WHO Member States in a probabilistic analysis of the data from the four countries (125).

**Decentralized care:** As the use of Xpert® MTB/RIF expands, more patients will be diagnosed and enrolled on MDR-TB treatment. Having treatment and care provided in decentralized health-care facilities is a practical approach for scaling up treatment and care for patients who are eligible for MDR-TB treatment. Therefore, a systematic review of the treatment and care of bacteriologically confirmed or clinically diagnosed MDR-TB patients in decentralized versus centralized systems was conducted to gather evidence on whether the quality of treatment and care is likely to be compromised with a decentralized approach. Data from both randomized controlled trials and observational studies were analysed, with the majority being from low- and middle-income countries (120, 121, 126–133). The review provided additional value to the recommendation in the previous guidelines on ambulatory over hospitalized models of care for MDR-TB patients for which the evidence was examined only for treatment and care of patients outside or inside hospitals (4).

In the review, decentralized care was defined as care that is provided in the local community where the patient lives at non-specialized or peripheral health centres, by community health workers or nurses, non-specialized doctors, community volunteers or treatment supporters. Care could also occur at local venues or at the patient's home or workplace. Treatment and care included treatment and patient support plus injections during the intensive phase. In this group, a brief phase of hospitalization of less than one month was accepted for patients who were in need during the initial phase of treatment or when they had any treatment complications.

Centralized care was defined as inpatient treatment and care provided solely by centres or teams specialized in drug-resistant TB for the duration of the intensive phase of therapy or until culture or smear conversion. Afterwards, patients could have received decentralized care. Centralized care was usually delivered by specialist doctors or nurses and could include centralized outpatient clinics (i.e. outpatient facilities located at or near the site of the centralized hospital).

Analysis of the data showed that treatment success and loss to follow-up improved with decentralized care versus centralized care. However, the risk of death and treatment failure showed minimal difference



between patients undergoing decentralized care and those receiving centralized care. There were limited data on adverse reactions, adherence, acquired drug resistance and cost.

Both HIV-negative and HIV-positive persons were included in the reviewed studies although the studies did not stratify patients on the basis of HIV status.

There was some discussion regarding the quality of the data. The GDG expressed concerns that health-care workers may have selected for the centralized care groups those patients who they thought might have a worse prognosis. None of the studies controlled for this risk of bias.

## Subgroup considerations

Decentralized care may not be appropriate for patients with severe TB disease, extremely infectious forms of the disease, serious comorbidities or patients for whom treatment adherence is a concern.

Measures to protect the safety of patients on MDR-TB regimens – especially those containing new or novel medicines – need to be maintained in outpatient settings.

These recommendations for decentralized care should not preclude hospitalization if appropriate. This review did not include patients requiring surgical care.

## Implementation considerations

**Ambulatory care:** The cost varied widely across the modelled settings. The cost per disability-adjusted life year (DALY) averted by an ambulatory model in one setting was sometimes higher than the cost per DALY averted by a hospitalization model in another setting. However, cost per DALY averted was lower under outpatient-based care than under inpatient-based care in the vast majority (at least 90%) of settings for which cost–effectiveness was modelled. The variation in cost–effectiveness among settings correlated most strongly with the variation in the cost of general health-care services and other non-drug costs. Despite the limitations in the data available, there was no evidence that conflicted with the recommendation or which indicated that treatment in a hospital-based model of care leads to a more favourable treatment outcome.

The overall cost–effectiveness of care for a patient receiving treatment for MDR-TB can be improved with an ambulatory model. The benefits include reduced use of resources, and at least as many deaths avoided among primary and secondary cases as with hospitalization models. This result is based on clinic-based ambulatory treatment (i.e. patients attended a health-care facility); in some settings, home-based ambulatory treatment (provided by a health worker in the community) might improve cost–effectiveness even further. The benefit of reduced transmission can be expected only if proper infection control measures are in place in both the home and the clinic. Potential exposure to people who are infectious can be minimized by reducing or avoiding hospitalization where possible, reducing the number of outpatient visits, avoiding overcrowding in wards and waiting areas, and prioritizing community-care approaches for TB management (134). The regimen used in one of the studies on ambulatory care derived from a period when the combinations of medicines were not yet optimized, so the outcomes achieved were probably inferior to those that can be obtained with the regimens in use today. Admission to hospital for patients who do not warrant it may also have important social and psychological consequences that need to be taken into account.

There may be some important barriers to accessing clinic-based ambulatory care, including distance of travel and other costs to individual patients. Shifting costs from the service provider to the patient must be avoided, and implementation may need to be accompanied by appropriate enablers. While placing patients on adequate therapy would be expected to decrease the bacterial load and transmission of DR-TB, infection control measures for home-based and clinic-based measures will need to be part of an ambulatory model of care in order to decrease the risk of transmission in households, the community and clinics. TB control programmes will have to consider whether they are capable

of reallocating resources from hospital care to ambulatory care support in order to undertake the necessary changes in patient management. The choice between these options will affect the feasibility of implementing the recommendation in a particular programme.

A high value was placed on conserving resources and on patient outcomes such as preventing death and transmission of MDR-TB as a result of delayed diagnosis and inpatient treatment. There should always be provision for a back-up facility to manage patients who need inpatient treatment. This may be necessary in certain groups of patients at particular risk, such as children during the intensive phase, among whom close monitoring may be required for a certain period of time.

**Decentralized care:** National TB programmes should have standardized guidelines regarding which patients are eligible for decentralized care. Patient preference should be given a high value when choosing between centralized or decentralized care.

Decentralized care for MDR-TB patients requires appropriate treatment supervision, patient education and social support, staff training, infection control practices and quality assurance. The optimal treatment supervision options and treatment adherence interventions recommended in section 2.1 should be considered for MDR-TB patients on decentralized care.

Several of the studies in the review addressed treatment costs. However, cost estimates were found to vary widely and no concrete recommendations could be made on that basis. Resource requirements are likely to vary because TB treatment programmes are highly variable and costs vary across different countries. The GDG raised several issues for TB programmes to consider. Although hospitalization is generally thought to be more expensive than outpatient care, the costs of good outpatient programmes can also be significant. Additionally, outpatient costs may vary significantly according to the services provided. One cost-saving measure to consider in decentralized care is that patients may be able to receive treatment faster. The financial benefits of decentralized care would include finding patients before they become very ill and require more medical care, while treating people before TB can be transmitted to contacts would be a public health benefit.

If a patient is living with a person from a high-risk group (i.e. HIV-positive or a young child), there may be complications in sending the patient home for treatment. However, the risk posed to high-risk groups varies significantly, depending on whether the TB programme gives preventive treatment to high-risk persons. Studies involving preventive therapy for MDR-TB are ongoing.

An additional implementation concern is that in some places it may be illegal to treat MDR-TB patients in a decentralized setting, especially when the treatment involves injections. Such legal concerns need to be addressed.

### 3. Models of care for children and adolescents exposed to TB or with TB disease

This section contains two new recommendations on the implementation of decentralized models of care and integrated family-centred models of care to improve both case detection and the provision of TB preventive treatment (TPT).

Capacity for paediatric TB is often highly centralized at secondary/tertiary levels, where children may present as seriously ill, after delays in accessing care. At higher levels of care services are often managed in a vertical, non-integrated way (135, 136). Health-care workers at the primary health care (PHC) level may have limited capacity for and confidence in managing paediatric TB, although this is the level at which most children with TB or at risk of TB seek care (136). In addition, TB screening is often not systematically part of clinical algorithms for child health – such as integrated management of childhood illness (IMCI) or integrated community case management (iCCM). Private-sector providers play an increasing role as the first point of care in many countries (137). Nevertheless, there are many

missed opportunities for contact-tracing, as well as for TB prevention, detection and care, because of weak integration of child and adolescent TB services with other programmes and services.

Decentralization and provision of family-centred, integrated care are highlighted as one of 10 key actions in the 2018 *Roadmap towards ending TB in children and adolescents* (136). The Roadmap highlights that consistently and systematically addressing gaps and bottlenecks along children's and adolescents' pathway through TB exposure, infection and disease can lead to reduced transmission of TB, expanded prevention of TB infection and earlier TB diagnosis with better outcomes. Achieving this continuum of care requires collaboration across service areas, practice disciplines and sectors, and community engagement, as well as decentralization and integration of service delivery at the PHC level (136).

The Roadmap suggests actions to integrate child and adolescent TB into family- and community-centred care, including by:

- strengthening country-level collaboration and coordination across all health-related programmes engaged in woman, adolescent and child health – especially reproductive health, maternal, neonatal, child and adolescent health (MNCAH), nutrition, HIV, primary and community health – with clearly defined roles, responsibilities and joint accountability;
- decentralizing and integrating successful models of care for TB screening, prevention and diagnosis with other existing service delivery platforms for maternal and child health – such as antenatal care, iCCM and IMCI – as well as other related services (e.g. HIV, nutrition, immunization);
- ensuring that children and adolescents with other common co-morbidities (such as meningitis, malnutrition, pneumonia, chronic lung disease and HIV infection) are routinely evaluated for TB;
- ensuring that community health strategies integrate child and adolescent TB education, screening, prevention and case-finding into training and service delivery activities; and
- increasing awareness of and demand for child and adolescent TB services in communities and among health workers (136).

The set of PICO questions examined the impact of decentralization<sup>15</sup> and of family-centred, integrated approaches<sup>16</sup> of child and adolescent TB services on case detection in children and adolescents who present with signs and symptoms of TB. The questions also examined the impact of these approaches on coverage of TPT among children and adolescents.

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<sup>15</sup> **Decentralization:** Depending on the standard in the research settings used for the comparator, decentralization includes the provision of, access to or capacity for child and adolescent TB services at a lower level of the health system than the lowest level at which this is currently routinely provided. In most settings, decentralization would apply to the district hospital (first referral level hospital) and/or the primary health care level and/or community level. Interventions for decentralization can include capacity-building of various cadres of health-care workers, expanding access to diagnostic services.

<sup>16</sup> **Family-centred, integrated care:** Family-centred models of care refer to interventions selected on the basis of the needs, values and preferences of the child or adolescent and his or her family or caregiver. This can include health education, communication and material or psychological support. Integrated services refer to approaches to strengthen collaboration, coordination, integration and harmonization of child and adolescent TB services with other child health-related programmes and services. This can include integration of models of care for TB screening, prevention, diagnosis and treatment with other existing service delivery platforms for maternal and child health (such as antenatal care, integrated community case management, integrated management of childhood illnesses) and other related services (e.g. HIV, nutrition, immunization). Other examples include the evaluation of children and adolescents with common co-morbidities (e.g. meningitis, malnutrition, pneumonia, chronic lung disease, diabetes, HIV infection) for TB, as well as community health strategies to integrate child and adolescent TB awareness, education, screening, prevention and case-finding into training and service delivery activities.

## Recommendations:

- 3.1 **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**  
(conditional recommendation, very low certainty of evidence).
- 3.2 **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**  
(conditional recommendation, very low certainty of evidence).

## Remarks:

- These recommendations relate to TB services along the full range of care with a focus on case detection and provision of TPT.
- The recommendations apply to children and adolescents with signs and symptoms of TB in terms of the impact on case detection. They also concern children and adolescents who are exposed to TB (i.e. TB contacts), and who are eligible for TPT, in terms of the impact on provision of TPT. Children and adolescents with signs and symptoms who need evaluation for TB disease may also have a history of exposure to TB (i.e. TB contacts). Children and adolescents who are TB contacts and who do not have signs and symptoms should be evaluated for TPT eligibility.
- The recommendation on decentralized services refers to enhancing child and adolescent TB services at peripheral levels of the health system where they are closer to the community, and not to replacing specialized paediatric TB services at higher levels of the health system.
- Decentralization should be prioritized for settings and populations with poor access to existing services and/or in high TB-prevalence areas.
- Family-centred, integrated approaches are recommended as an additional option to standard TB services (e.g. alongside specialized services that may have a limited level of integration with other programmes or links to general health services).
- Family-centred care is a cross-cutting principle of child care at all levels of the health system.

## Justification and evidence

### PICO questions:

- a. In children and adolescents with signs and symptoms of TB, should the decentralization of child and adolescent TB services versus centralized child and adolescent TB services (at referral or tertiary hospital level) be used?
- b. In children and adolescents exposed to TB, should the decentralization of child and adolescent TB prevention and care services versus centralized prevention and care services (at referral or tertiary hospital level) be used to increase coverage of TPT in eligible children and adolescents?
- c. In children and adolescents with signs and symptoms of TB, should family-centred, integrated services versus standard, non-family-centred, non-integrated services be used?
- d. In children and adolescents exposed to TB, should family-centred, integrated services versus standard, non-family-centred, non-integrated services be used to increase TPT coverage in eligible children and adolescents?

**Evidence:** A systematic review of studies assessing the impact of decentralized, integrated or family-centred care models on TB diagnosis, treatment or prevention outcomes in children and adolescents with TB between 0 and 19 years of age, comprising both children (0–9 years of age) and adolescents (10–19 years of age), was conducted to answer this group of PICO questions. The PubMed, Embase, Web of Science, Global Index Medicus, Global Health and Cochrane Central databases were searched in February 2021, as were the references of 17 related reviews. A total of 3265 abstracts from databases and 129 additional references from related reviews were identified and assessed. Of these, 516 full-text articles were assessed for eligibility, from which 25 comparative studies (7 randomized, 18 observational) were identified; one unpublished observational study was added, making a total of 26 studies. Four studies (1 randomized, 3 observational) were excluded after review because the care model described was community-based treatment support, for which a WHO recommendation already exists (138). Of the remaining studies that were included, 16 had elements of decentralization, five had elements of integration, and three had elements of family-centred care. Four studies had elements of more than one care model of interest but were included only on the basis of their main model – such as either decentralization or family-centred, integrated care. Most studies focused on the 0–14-year age group.

Studies in which the primary intervention was decentralization chiefly assessed diagnosis or case notification outcomes (n=16) (139–154), with fewer assessing TPT outcomes (n=3) (59, 145, 155). In general, interventions that included both strengthening of diagnostic capacity in primary care settings and strengthening links between communities and facilities consistently showed an increase in case notifications and TPT initiations, while interventions that involved only community-based activities did not.

Two studies of service integration were identified (156, 157) as showing limited impact on case notifications of screening in IMCI clinics or co-location of TB and ART services. The two studies of family-centred care (158, 159) showed that the provision of socioeconomic support packages to families affected by TB was associated with increased TPT initiation and completion.

The reviewers noted that, while substantial wider literature on integration and family-centred care is available, evidence for the specific impact on child and adolescent TB outcomes is limited. Some overlap was noted between the integration of TB services into non-specialized settings such as general outpatient or primary care services or decentralization. This was a slightly artificial separation for the evidence review since in practice decentralization and integration into PHC may occur together.

**GDG considerations:** With regard to the evidence reviewed on the impact of decentralization on TB case detection, the GDG observed that two trials (148, 150) and one observational study of home-based screening (without facility-based strengthening) (153) had fewer diagnoses or notifications among children aged below 15 years in the intervention group compared to the control group, but that none of these differences were statistically significant. The GDG considered that, while there may be a reduction in case notifications at higher levels of care, TB detection may improve if children are seen by a competent clinician at the first point of access (such as at PHC level). The evidence overall was recognized as uncertain. The benefit of increased case-finding and an increased number of children with TB who are initiated on TB treatment was considered to outweigh the concern for overtreatment. Therefore, the undesirable effects of case detection were considered trivial. The GDG discussed the potential risks of provision and management of TPT at the peripheral level, including undetected drug-related adverse events such as hepatotoxicity and insufficient capacity to manage these events. In addition, there may be a risk of TB disease being treated with a course of TPT rather than with a complete treatment regimen. All these undesirable events can potentially happen but were considered rare and not of major concern. Therefore, the undesirable effects for TPT provision were also considered trivial. Overall, the GDG agreed that the balance of desirable and undesirable effects probably favours decentralized TB services for case detection and provision of TPT to children and adolescents. The panel noted that differences in the setting and the availability of adequate resources are important considerations.

The GDG also discussed the fact that family-centred, integrated care includes interventions at the household level to identify members of the household who require evaluation for TB disease, TPT, treatment support etc. Some overlap between the integration of TB services into non-specialized settings – such as general outpatient or primary care services and decentralization – was noted. However, this was considered to be a somewhat artificial separation since in practice decentralization and integration into PHC may occur at the same time. Overall, despite a lack of evidence on undesirable effects and low quality of the data, the panel agreed that there is evidence of positive effects of family-centred integrated care. It was suggested that family-centred, integrated care could be an addition to both the standard of care and specialized services which do not have an integration component. Family-centred care (in the sense of family involvement) was highlighted as a core principle of child health care.

The GDG noted that setting-specific factors related to the TB burden or the organization of health services may have an impact on feasibility, acceptability and equity. GDG members also pointed out that the initial health system costs for establishing decentralized and family-centred, integrated services may be relatively high (e.g. for infrastructure, human resources, training, equipment, community engagement), but that costs are likely to decrease over time – assuming that people with TB are effectively managed and that TPT is provided at the peripheral level, leading to a reduction in TB incidence. Decentralized and family-centred, integrated services may result in important savings for affected families. Equity was considered an important cross-cutting issue that also has an impact on cost. The GDG highlighted that TPT implementation can be very challenging with high levels of loss to follow-up in programmes implemented at higher levels of the health system, considering that children who are eligible for TPT are not sick. The panel agreed that the decentralization and integration of services can potentially increase equity and enhance the success of the programme and judged that cost-effectiveness probably favours decentralized and family-centred, integrated approaches to both case-finding and the provision of TPT.

While the GDG stressed the importance of taking into consideration the potential impact of stigma when decentralizing TB services for children and adolescents to lower levels, the panel judged that decentralized approaches are probably acceptable to key stakeholders. Overall, decentralized and family-centred, integrated approaches were judged to be feasible to implement, although feasibility may vary depending on factors such as infrastructure, availability of funding and the structure of the national TB programme. However, adequate investment is critical to enable the acceptability, equity and feasibility of decentralized approaches.

## Subgroup considerations

**Adolescents** have a disease presentation that is similar to that of adults and therefore may need different interventions than those for young children. Additional subgroup considerations for adolescents are included in the WHO operational handbook, taking into account their specific health-seeking behaviour and the need for adolescent-friendly services.

**TB contacts:** Provision of TPT has for many years focused mainly on children under five years of age. In 2018, target groups for the provision of TPT were expanded to include contacts of all ages (160). Available data from the global TB database (161) show that coverage of TPT in household contacts is poor – especially in contacts over five years of age.

In children with common illnesses with overlapping signs and symptoms of TB, approaches that integrate TB services in their care can improve case detection and provision of TPT.

These subgroups include:

- children with SAM;
- children with severe pneumonia;
- children living with HIV; and
- children with other chronic diseases.



## Implementation considerations

**Health system requirements:** Training of health-care workers at peripheral levels of the health system is a critical requirement for ensuring that decentralized approaches are implemented adequately. Similarly, resources are needed at the peripheral level – especially initially to establish services. It is expected that, as services are established and effectively implemented, the long-term impact will result in a decrease in TB incidence with an associated reduction in resource requirements. A phased approach may be applied if this is most appropriate in the country or area, depending on the local burden of TB, the availability of domestic or donor funding and the amount of technical and programmatic support.

Factors to consider in decentralizing child and adolescent TB services include: the existing infrastructure (such as baseline health infrastructure, needs for expansion or upgrading); an applicable regulatory framework; financing; the choice between an operational research setting or programmatic implementation; human resource issues (including staffing requirements and human resources development, such as capacity-building/training and consultation skills); monitoring and evaluation; qualitative research into community needs; perceptions (including views on stigma); and suggestions. Decentralization of services to the PHC level requires that child and adolescent TB services are integrated within general PHC services, resulting in possible significant overlap between decentralization and family-centred, integrated approaches.

**Contact investigation:** Active contact investigation at community and household level is a critical intervention for enhancing both case-finding and the provision of TPT to children and adolescents.

**Task-shifting:** Decentralization not only concerns the levels of the health system but should ideally also take place within the same structure, by training all health-care providers of all child and adolescent care services in the recognition and management of TB. This so-called task-shifting was mentioned by the GDG as an important implementation factor.

**Family-centred and integrated care:** Although in child health, care evolves around the family, the concept of family-centred care has not been well defined. Family-centred care is related to the more common concept of patient-centred care. The End TB Strategy (762) states: “Patient-centred care involves systematically assessing and addressing the needs and expectations of patients. The objective is to provide high-quality TB diagnosis and treatment to all patients – men, women and children – without their having to incur catastrophic costs. Depending on patients’ needs, educational, emotional and economic support should be provided to enable them to complete the diagnostic process and the full course of prescribed treatment.” Multiple descriptions exist that include components of support and education based on individual needs, building a patient–provider partnership and participatory decision-making. Family-centred care also includes interventions at household level to identify members of the household requiring evaluation for TB disease, TPT, treatment support and so on. As the concept of family-centred, integrated care may be specific to the setting, one of the first steps in implementation includes clarifying which definition applies to the setting in which the care is to be implemented. Similarly, the implementation strategy varies by setting and needs to be country- or region-specific and informed by social, cultural and societal values.

The package of TB services to be provided should be defined and developed by the national TB programme in close coordination with other relevant programmes, such as through an existing child and adolescent TB technical working group. This package should seek to identify and address capacity needs for national programmes interested in the uptake of proposed interventions, and should ideally be based on family and community perceptions of the ideal family-centred model of care. The package could include community-based models for active contact investigation, identifying children with TB signs and symptoms or exposure as part of routine growth-monitoring services, or an integrated model for IMCI integration, starting with the sick child and identifying signs and symptoms pointing to a high likelihood of TB.

Integration can start within the family by equipping family members with the knowledge to recognize signs and symptoms in order to understand the importance of a history of contact, to know when to seek help at the health-care facility and how to minimize stigma related to TB. High-yield entry points provide a good place to start within the health system. For instance, child and adolescent TB services can be integrated with malnutrition clinics, ANC, the Expanded Programme on Immunization, inpatient sites, adult TB and chest clinics, HIV and general paediatric clinics. TB care should ideally be integrated into general health services rather than being limited to enhanced coordination between two programmes. However, defining an optimal patient flow between services and creating strong links between child health entry points and TB clinics remains essential, especially in facilities where services are physically separated. This is critical for enhancing the quality of services, including the follow-up of persons with TB during the diagnostic evaluation, and also for ensuring the accuracy of recording and reporting. In the early phase, pilot programmes could be considered, and should be evaluated and adjusted as needed and then scaled up.

Factors to consider in designing an integrated approach to child and adolescent TB care include: the existing infrastructure (e.g. baseline health infrastructure, need for expansion or upgrading); the applicable regulatory framework; financing; the choice between an operational research setting or programmatic implementation; human resource issues (including staffing requirements and human resources development such as capacity-building/training and consultation skills); monitoring and evaluation; qualitative research into community needs; perceptions (including views on stigma; and suggestions.

***Differentiated service delivery (DSD):*** DSD is a person-centred approach developed in the HIV programme that simplifies and adapts HIV services across the range of care in ways that both serve the needs of people living with and vulnerable to HIV and optimize the available resources in health systems. The principles of DSD can be applied to prevention, testing, linkage to care, ART initiation and follow-up, as well as to the integration of HIV care, co-infections and co-morbidities (163). This approach is based on the principle that when families are given the choice to interact with the health system, this provides a possible mechanism for integration of child and adolescent TB services within PHC or other programmes. Examples of implementing DSD for children and adolescents with or at risk of TB are provided in WHO's operational handbook.

## Monitoring and evaluation

The move to decentralized, family-centred, integrated services requires careful planning and regular monitoring of implementation against the plan. The capacity needs of national TB programmes for implementing the proposed interventions need to be identified and addressed.

Enhanced data collection on child and adolescent TB potentially takes a substantial amount of additional time, and detailed data collection may be feasible only in specific operational research settings. Programmes generally have registers in place for contact investigation, treatment registration and outcomes, as well as TPT registers. The use of these (preferably electronic) tools is important for ensuring comprehensive management and treatment as programmes move to a more decentralized and family-centred, integrated approach. The use of the tools should be evaluated and enhanced, including through operational research.

It will be important to monitor the number of children diagnosed at different levels of the health system – including the proportion of children who have bacteriological confirmation, the proportion who were clinically diagnosed and the number of children initiated on and completing TPT. Disaggregation of data by sex will be important to evaluate the impact on gender equity. Evaluating the quality of services (covering the quality of all steps in the patient pathway, from screening to diagnosis and treatment) as well as client satisfaction are also important components.



# Research priorities

The GDGs discussed research priorities and highlighted a number of priorities.

## The effectiveness of different forms of interventions to improve treatment adherence

- The interventions for patient support and treatment supervision that are best suited to particular populations.
- The interventions for patient support that are most effective in low- and middle-income countries.
- Analysis of the cost-effectiveness of different types of incentives.
- Research into the effectiveness of VST in low- and middle-income countries, as the current available data are from high-income countries.
- The types of psychological support that are most appropriate.

## Models of care for all people with TB

- Evaluation of the risk of TB transmission in different settings – i.e. does treatment centered on hospital care or outpatient clinics pose a higher risk of transmission?
- Additional cost-effectiveness studies of decentralized versus centralized care.
- Many programmes are providing decentralized care, but very few have published the data. Programmes should be encouraged to publish – or at least systematically collect – their data.

## Models of TB care for children and adolescents

### ***Decentralization of TB services for children and adolescents with signs and symptoms of TB and for children and adolescents exposed to TB***

- The cost-effectiveness of decentralization/integration for case detection and provision of TPT.
- The impact of decentralization of services on health equity.
- The acceptability and feasibility of decentralized approaches to child and adolescent TB care for case detection and for TPT provision.

### ***Family-centred, integrated services for children and adolescents with signs and symptoms of TB and for children and adolescents exposed to TB***

- A detailed description of currently operating family-centred and integrated services, with associated costs and cost-effectiveness.
- Implementation research on the components of the interventions, and assessment of real-world implementation of the programmes.
- The acceptability and feasibility and of family-centred, integrated and/or decentralized approaches to child and adolescent TB care for case detection and TPT provision in different settings, from the perspectives of the persons with TB, the caregivers and providers.

- Costs and catastrophic costs.
- Cost-effectiveness evaluations of family-centred, integrated and/or decentralized approaches, considering currently available resources (N.B. some models assume that these interventions are built on existing structures that may not be available).
- Outcomes of interest: initiation of TPT; number of additional children and adolescents diagnosed; delay, retention in care, treatment completion, clinical outcomes (such as treatment success); qualitative research related to stigma, mental health outcome, school interruption, equity.
- Evaluation of outcomes of interest using randomized/non-randomized designs and qualitative designs.
- A baseline needs assessment in the community, community perceptions of TB care and prevention for children and adolescents.
- Research on the quality of TB diagnosis in children – addressing both under-diagnosis and over-diagnosis.

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163. Updated recommendations on service delivery for the treatment and care of people living with HIV. Geneva: World Health Organization; 2021.



# Annexes



# Annex 1. Experts involved in the development of the guidelines

## Annex 1.1. Experts participating in the guideline update, 2017

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The following persons participated as observers during the GDG meeting: Draurio Barreira Cravo Neto (Unitaid, Switzerland); Charlotte Colvin (USAID, United States of America); Anne Detjen (UNICEF, United States of America); Thomas Gradel (Unitaid, Switzerland); Brian Kaiser (Stop TB Partnership Global Drug Facility, Switzerland); Michael McCaul (Stellenbosch University, South Africa); Lawrence Mbuagbaw (St Joseph's Healthcare, Canada); Celeste Naude (Stellenbosch University, South Africa); Oxana Rucsineanu (TB Community Advisory Board); Anna Scardigli (Global Fund to Fight AIDS, Tuberculosis and Malaria, Switzerland); Cherise Scott (Unitaid, Switzerland).

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## WHO Steering Group

The WHO guidelines Steering Group comprised: Annabel Baddeley, Lice Gonzalez Angulo, Ernesto Jaramillo, Avinash Kanchar, Charalambos Sismanidis (WHO Global Tuberculosis Programme); Martina Penazzato (WHO Global HIV, Hepatitis and Sexually Transmitted Infections Programme); Bernadette Cappello, Lorenzo Moja (WHO Department of Health Products, Policy and Standards); Marie Valentin (WHO Department of Regulation and Prequalification); Corinne Simone Collette Merle (WHO Special Programme for Research and Training in Tropical Diseases); Valentina Baltag, Wilson Milton Were (WHO Department of Maternal, Newborn, Child & Adolescent Health & Ageing); Lina Mahy (WHO Department of Nutrition and Food Safety); Chiara Servili (WHO Department of Mental Health and Substance Use); Sarah Rylance (WHO Department of Noncommunicable Diseases Management); Ogtay Gozalov (WHO Regional Office for Europe); Mukta Sharma (WHO Regional Office for South-East Asia); Kyung Hyun Oh (WHO Regional Office for the Western Pacific Region); Pedro Avedillo (Pan American Health Organization); Kenza Bennani, Martin van den Boom (WHO Regional Office for the Eastern Mediterranean Region); André Ndongosieme (WHO Regional Office for Africa).

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# Annex 2. PICO questions

## Care and support interventions for all people with TB (Guideline update 2017)

**1. In patients with TB, are any interventions to promote adherence to TB treatment more or less likely to lead to the outcomes listed below?**

Population	Intervention	Comparator	Outcome
Patients on treatment for DS-TB Patients on treatment for MDR-TB Children (0–14 years) and adults HIV-infected and HIV-uninfected TB patients	Any intervention to promote treatment adherence <ul style="list-style-type: none"><li>• Supervision of treatment (treatment support, virtual (video-) supported therapy)</li><li>• Measures to improve treatment adherence (e.g. medication monitors and/or SMS or telephone call reminders)</li><li>• Social support (educational, psychological, material)</li><li>• Combinations of the above interventions</li></ul>	Routine practice <sup>17</sup>	<ul style="list-style-type: none"><li>• Adherence to treatment (or treatment interruption due to non-adherence)</li><li>• Conventional TB treatment outcomes: cure or treatment completion, failure, relapse, survival/death</li><li>• Adverse reactions from TB drugs (severity, type, organ class)</li><li>• Cost to the patient (including direct medical costs as well as others such as transportation, lost wages due to disability)</li><li>• Cost to health services</li></ul>

## Models of care for people with drug-resistant TB (Guideline updates 2011 and 2017)

**2. Among patients with MDR-TB, is ambulatory therapy compared with inpatient treatment, more or less likely to lead to better outcomes?**

**3. Is decentralized treatment and care for MDR-TB patients more or less likely to lead to the outcomes listed below?**

<sup>17</sup> Routine practice: regular TB drugs pick-up and consultations with physician or other health-care workers are available when necessary; TB treatment is free of charge; essential information/health education in relation to TB treatment is provided.

Population	Intervention	Comparator	Outcome
Patients on treatment for MDR-TB	Decentralized treatment and care (provided by non-specialized or periphery health centres; by community health workers, community volunteers or treatment supporters) <ul style="list-style-type: none"> <li>• Treatment and patient support</li> <li>• Injection during the intensive phase</li> <li>• Specialist care for co-morbidities (e.g. HIV, diabetes, chronic lung diseases, or other conditions such as auditory function, renal function, liver function, neurology, ophthalmology)</li> </ul>	Treatment and care provided solely by centres or teams specialized in drug-resistant TB	<ul style="list-style-type: none"> <li>• Adherence to treatment (or treatment interruption due to non-adherence)</li> <li>• Conventional TB treatment outcomes: cure or treatment completion, failure, relapse, survival/death</li> <li>• Adverse reactions from TB drugs (severity, type, organ class)</li> <li>• Acquisition (amplification) of drug resistance</li> <li>• Cost to the patient (including direct medical costs as well as others such as transportation, lost wages due to disability)</li> <li>• Cost to health services</li> </ul>

## Models of care for children and adolescents (Guideline update 2022)

### 4. Models of care for TB case detection and TB prevention settings with a prevalence of TB in the general population of 100 per 100 000 or more:

- In children and adolescents with signs and symptoms of TB, should the decentralization of child and adolescent TB services versus centralized child and adolescent TB services (at referral or tertiary hospital level) be used?
- In children and adolescents exposed to TB, should the decentralization of child and adolescent TB prevention and care services versus centralized prevention and care services (at referral or tertiary hospital level) be used to increase coverage of TB preventive treatment in eligible children and adolescents?
- In children and adolescents with signs and symptoms of TB, should family-centred, integrated services versus standard, non-family-centred, non-integrated services be used?
- In children and adolescents exposed to TB, should family-centred, integrated services versus standard, non-family-centred, non-integrated services be used to increase coverage of TB preventive treatment in eligible children and adolescents?



# Web Annexes

**Web Annex 1. GRADE evidence profiles**

**Web Annex 2. Evidence-to-decision tables**

**Web Annex 3. Reports of the systematic reviews**

<https://apps.who.int/iris/bitstream/handle/10665/352904/9789240047754-eng.pdf>







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