World Health Organization
www.who.int/tb/

Shorter treatment regimens for multi-drug-resistant tuberculosis (MDR-TB)

What are the standard MDR-TB regimens ?

The World Health Organization (WHO) currently recommends the use of at least four second line drugs which are effective, plus pyrazinamide, in the intensive phase, for a total treatment duration of 20 months in most cases, with pyrazinamide plus four effective anti-TB drugs during the intensive phase. This recommendation is based on pooled data from >9000 MDR-TB cases treated in observational studies (which also included data on patients treated with regimens lasting 9-15 months in Bangladesh). The recommendation on duration of treatment is subject to adaptation based on patient response to treatment.

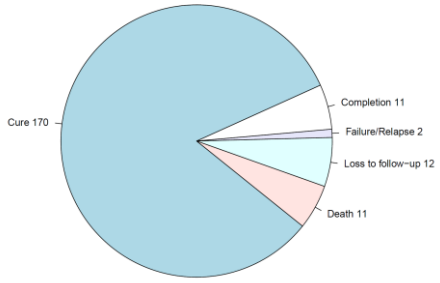
What are "shorter MDR-TB regimens" ?

These are regimens for MDR-TB patients which typically last 9-12 months and which differ from the standard WHO-recommended MDR-TB regimen in drug composition. Evidence on their use has been reported in Bangladesh, in one peer-reviewed publication that reported success rates comparable to those of treatment for drug-susceptible TB. These regimens are now also being introduced by National TB control programmes of a number of African countries (see map). These regimens are less costly than the standard 20-month treatment regimen and likely to be better tolerated by patients.

Treatment outcomes observed in Bangladesh for MDR-TB cases treated with a 9-month regimen

A regimen consisting of a minimum of 4 months of KmCfzGfxEHZPto, prolonged if necessary until conversion was achieved, followed by 5 months of GfxEZCfz, was reported to give high, relapse-free cure rate in MDR-TB patients [van Deun et al, 2010].

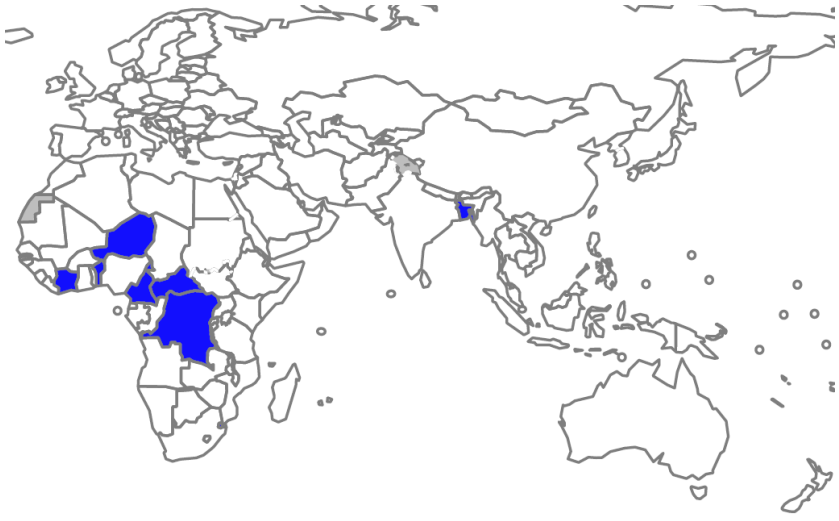
Completion 5.3%
Cure 82.5%
Death 5.35
Default 5.8%
Failure 0.5%
Relapse 0.5%



Km=kanamycin; Cfz=clofazimine; Gfx=gatifloxacin; E=ethambutol; H=high-dose isoniazid; Z=pyrazinamide; Pto=prothionamide

Source: van Deun A et al (2010); Short, highly effective, and inexpensive standardized treatment of multidrug-resistant tuberculosis. Am J Respir Crit Care Med 182(5):684–92.

Countries currently using or planning to use shorter treatment regimens for MDR-TB according to WHO policy, by June 2013



Bangladesh, Benin, Cameroon, Central African Republic, Côte d'Ivoire, Democratic Republic of Congo, Niger, Swaziland

For more information: www.who.int/tb/challenges/mdr

WHO CRITERIA TO BE APPLIED IN THE USE OF SHORTER REGIMENS FOR MDR-TB TREATMENT

WHO's current position is that regimens which are markedly different from those that make up the current norm should be used only within the context of research and under close monitoring of the response to treatment, for a period of at least 12 months after treatment completion. The major concerns are that patients who do well after 9–12 months of treatment, with less drugs in the continuation phase than in the longer regimen, may have a higher risk of acquiring resistance in while on treatment and subsequently relapsing with TB.

Until sufficient evidence is available to inform a change in policy, WHO advises countries on a case-by-case basis to introduce short MDR-TB regimens if

- the project is approved by a national ethics review committee, ahead of patient enrolment;
- treatment is delivered under operational research conditions following international standards to assess the safety and effectiveness of these regimens; and
- the programmatic management of drug-resistant TB and the research project are monitored by an independent monitoring board set up by, and reporting to, WHO.

Countries planning to use short regimens for MDR-TB treatment according to the criteria listed above will be offered assistance to develop the required operational research and programme management capacity if this is not yet available. Support from WHO for such assistance should be sought on a country-by-country basis prior to embarking on the use of short MDR-TB regimens.

ABOUT MDR-TB, XDR-TB AND PMDT

• **Multidrug-resistant TB (MDR-TB)** is caused by organisms that are resistant to the most effective anti-TB drugs (isoniazid and rifampicin). MDR-TB results from either infection with organisms which are already drug-resistant or may develop in the course of a patient's treatment.

• **Extensively drug-resistant TB (XDR-TB)** is a form of TB caused by organisms that are resistant to isoniazid and rifampicin (i.e. MDR-TB) as well as any fluoroquinolone and any of the second–line anti-TB injectable drugs (amikacin, kanamycin or capreomycin).

• These forms of TB do not respond to the standard six month treatment with first-line anti-TB drugs and can take two years or more to treat with drugs that are less potent, more toxic and much more expensive.

• **Programmatic management of drug-resistant TB (PMDT)** refers to the coordinated action of the different components of the national TB control programme (NTP) - including case detection, treatment, prevention, surveillance, and monitoring and evaluation of programme performance - which are essential to an effective handling of drug-resistant tuberculosis in a community.