



**GUIDELINES FOR THE DIAGNOSIS, TREATMENT AND
PREVENTION OF LEPROSY**

EXECUTIVE SUMMARY

Background

Leprosy is a disease that predominantly affects the skin and peripheral nerves, resulting in neuropathy and associated long-term consequences, including deformities and disabilities. The disease is associated with stigma, especially when deformities are present. Despite the elimination of leprosy as a public health problem (defined as achieving a point prevalence of below 1 per 10 000 population) globally in 2000 and at a national level in most countries by 2005, leprosy cases continue to occur. Over 200 000 new leprosy cases were reported in 2016. Therefore, guidance on early diagnosis and treatment of leprosy is essential for reducing the burden of this disease.

Leprosy is classified as paucibacillary (PB) or multibacillary (MB), based on the number of skin lesions, presence of nerve involvement and identification of bacilli on slit-skin smear. The standard treatment for leprosy involves the use of multiple (two or three) drugs; the duration of treatment, dose and number of antibiotics depend on the type of leprosy (PB or MB) and age of the patient (adult or child). Strategies to prevent leprosy include vaccination or use of prophylactic antibiotics among persons with exposure.

Rationale and methods

The purpose of these WHO guidelines is to provide evidence-based recommendations on the diagnosis, treatment and prevention of leprosy, utilizing WHO guideline development methods based on the GRADE¹ process. Previous leprosy guidance documents were developed through Expert Committee meeting reports and/or through other technical documents, without a formal guideline development process. For prevention of leprosy, these guidelines focus on the use of antibiotics (chemoprophylaxis). Although vaccinations could also prevent leprosy, WHO regulations require that the Strategic Advisory Group of Experts on Immunization (SAGE) formulate all vaccination (immunoprophylaxis) recommendations. Therefore, the Guidelines Development Group (GDG) reviewed evidence on vaccinations but did not formulate recommendations; rather, findings on vaccinations were shared with the SAGE *bacille Calmette-Guérin* (BCG) working group to help inform its recommendations.

The primary audience for these WHO guidelines includes persons involved in leprosy policy formulation and clinicians who manage leprosy, particularly in low- and middle-income countries.

These guidelines were developed in accordance with procedures established by the WHO Guidelines Review Committee (GRC). The scope of the guidelines and associated systematic reviews was determined in October 2016. Systematic reviews were commissioned to address the key questions developed in the scoping process on diagnosis, treatment and prevention of leprosy.

Recommendations were formulated by a regionally representative and multidisciplinary GDG at a meeting held in May 2017 and in a subsequent meeting in October 2017 held upon availability of additional evidence. The GRADE approach was used to formulate and categorize the strength of recommendations (strong or conditional), and was adapted for questions related to diagnostic tests. GRADE includes an assessment of the quality of evidence (high, moderate, low or very low), consideration of the overall balance of benefits to harms (at individual and population levels),

¹ GRADE: Grading of Recommendations Assessment, Development and Evaluation

patient/health worker values and preferences, resource use, effects on equity, cost–effectiveness and consideration of feasibility and effectiveness across a variety of settings, including resource-limited settings and those in which access to laboratory infrastructure and specialized tests is limited. There was no evidence on benefits and harms of treatment for drug-resistant leprosy; therefore, recommendations for this topic were based on expert opinion. The process also identified other key research gaps to help inform the future research agenda for leprosy. These guidelines do not address the programmatic aspects of leprosy management, which is covered by the WHO *Global Leprosy Strategy 2016–2020 “Accelerating towards a leprosy-free world”* and its accompanying *Operational Manual* and *Monitoring and Evaluation Guide*.

Summary of recommendations

Table 1 summarizes the recommendations on diagnosis, treatment and prevention of leprosy with antibiotics (chemoprophylaxis).

Diagnosis of leprosy

The guidelines recommend no additional tests in addition to standard methods for diagnosis of leprosy: the diagnosis of leprosy remains based on the presence of at least one of three cardinal signs: (i) definite loss of sensation in a pale (hypopigmented) or reddish skin patch; (ii) thickened or enlarged peripheral nerve with loss of sensation and/or weakness of the muscles supplied by that nerve; or (iii) presence of acid-fast bacilli in a slit-skin smear. The clinical diagnosis of early leprosy and PB leprosy can be a challenge. Therefore, a number of serological and other laboratory assays have been developed to supplement clinical diagnostic methods. However, enzyme-linked immunosorbent assays (ELISA) and lateral flow assays are associated with low diagnostic accuracy for PB leprosy. Although some polymerase chain reaction (PCR)-based assays are associated with higher diagnostic accuracy, they lack standardization, are not commercially available, and would be difficult to perform in most primary health-care settings.

The guidelines also do not recommend any test for the diagnosis of leprosy in asymptomatic contacts. The predictive accuracy of diagnostic tests for identifying persons who will develop leprosy is low, with poor positive predictive values.

Treatment of leprosy

The guidelines recommend a 3-drug regimen of rifampicin, dapson and clofazimine for all leprosy patients, with a duration of treatment of 6 months for PB leprosy and 12 months for MB leprosy. This represents a change from the current standard treatment for PB leprosy, which is rifampicin and dapson for 6 months, due to some evidence indicating better clinical outcomes with a 3-drug, 6-month regimen over a 2-drug, 6-month regimen. A potential advantage of using the same three drugs for PB and MB leprosy is simplification of treatment (i.e. the same blister pack could be used for treating both types of leprosy) and reduced impact of misclassification of MB leprosy as PB leprosy, since all patients will receive a 3-drug regimen. For MB leprosy, the current standard

treatment is a 3-drug regimen for 12 months. Evidence on the potential benefits and harms of a shorter (6-month) 3-drug regimen was limited and inconclusive, with a potential increase in the risk of relapse. Therefore, the GDG determined that there was not enough evidence of equivalent outcomes to support a recommendation to shorten the treatment duration for MB leprosy.

For rifampicin-resistant leprosy, the guidelines recommend treatment with at least two second-line drugs (clarithromycin, minocycline or a quinolone) plus clofazimine daily for 6 months, followed by clofazimine plus one of these drugs for an additional 18 months. When ofloxacin resistance is also present, a fluoroquinolone should not be used as part of second-line treatment. The regimen of choice in such cases shall consist of 6 months of clarithromycin, minocycline and clofazimine followed by clarithromycin or minocycline plus clofazimine for an additional 18 months.

Resistance has been reported from several countries, although the number of patients is small. Evidence on the potential benefits and harms of alternative regimens for drug-resistant leprosy was not available. Therefore, recommendations for second-line regimens are based on expert opinion and the known activity of alternative drugs, including the likelihood of cross-resistance.

Prevention of leprosy through chemoprophylaxis

The guidelines recommend the use of SDR as preventive treatment for adult and child (2 years of age and above) contacts of leprosy patients, after excluding leprosy and TB disease and in the absence of other contraindications. The COLEP² randomized controlled trial found SDR in leprosy contacts associated with a 57% reduction in the risk of leprosy after 2 years and 30% after 5–6 years; SDR also appears highly cost effective, with an incremental cost–effectiveness ratio of US\$ 158 per additional prevented leprosy case.

The ability of programmes to adequately identify and manage contacts of leprosy cases is a prerequisite for successful implementation of the recommendation. Because leprosy is highly stigmatized, caution must be exercised when implementing SDR, particularly for contacts outside the patient's family. Programmes must respect the wish of patients to disclose or not disclose their diagnosis. When patients do not authorize disclosure, the GDG does not recommend identification or screening of contacts, which is a prerequisite for prescribing preventive treatment. In hyperendemic settings, a blanket approach (i.e. treatment of all community members without identifying contacts) might be more feasible and reduce potential harms related to disclosure of a leprosy diagnosis.

² COLEP: prospective sero-epidemiological study on contact transmission and chemoprophylaxis in leprosy

Table 1: Recommendations on diagnosis, treatment and chemoprophylaxis of leprosy (summary)

AREA OF THE RECOMMENDATION	RECOMMENDATION	STRENGTH	QUALITY OF EVIDENCE
DIAGNOSIS			
Diagnosis of leprosy	The diagnosis of leprosy may be based on clinical examination, with or without slit-skin smears or pathological examination of biopsies.	Conditional	Low
Diagnosis of leprosy infection	There is currently no test recommended to diagnose leprosy infection (latent leprosy) among asymptomatic contacts.	Conditional	Low
TREATMENT			
Treatment of leprosy	The same 3-drug regimen of rifampicin, dapsone and clofazimine may be used for all leprosy patients, with a duration of treatment of 6 months for PB leprosy and of 12 months for MB leprosy.	Conditional	Low
Treatment of drug-resistant leprosy	Leprosy patients with rifampicin resistance may be treated using at least two of the following second-line drugs: clarithromycin, minocycline or a quinolone (ofloxacin, levofloxacin or moxifloxacin), plus clofazimine daily for 6 months, followed by clofazimine plus one of the second-line drugs daily for an additional 18 months. Leprosy patients with resistance to both rifampicin and ofloxacin may be treated with the following drugs: clarithromycin, minocycline and clofazimine for 6 months followed by clarithromycin or minocycline plus clofazimine for an additional 18 months.	Conditional	No evidence retrieved (based on expert opinion)
PREVENTION			
Chemoprophylaxis for contacts of leprosy cases	Single-dose rifampicin (SDR) may be used as leprosy preventive treatment for contacts of leprosy patients (adults and children aged 2 years and above), after excluding leprosy and tuberculosis (TB) disease, and in the absence of other contraindications. This intervention shall be implemented only by programmes that can ensure: (a) adequate management of contacts, and (b) consent of the index case to disclose his/her disease.	Conditional	Moderate