

THE LEPROSY MISSION GLOBAL RESEARCH

ADDRESSING CURRENT CHALLENGES

SDG 3.3



ZERO TRANSMISSION

- ▶ understanding and reducing transmission
- ▶ understanding and enabling early diagnosis (including early diagnostic tests)
- ▶ monitoring relapse and leprosy drug resistance

GOAL Earlier detection and treatment of new leprosy cases and strategies and trials to stop transmission

ZERO DISABILITY

- ▶ early detection and clinical trials for leprosy reactions and nerve damage
- ▶ improving reconstructive surgery
- ▶ innovating in ulcer care
- ▶ enhancing eye care
- ▶ strengthening inner wellbeing and mental healthcare

GOAL Reduced disability and transforming physical, mental, emotional and spiritual wellbeing

ZERO DISCRIMINATION

- ▶ reducing stigma
- ▶ engaging in community-based rehabilitation

GOAL Greater inclusion and justice and people affected by leprosy confidently standing up for their rights

 **The Leprosy Mission**
Leprosy defeated, lives transformed

WHO WE ARE

We are the world's largest leprosy-focused organisation; a key player in the fight against leprosy. Our Members from 30 countries work with people of all faiths and none to defeat leprosy and transform the lives of those affected. We work in partnership with governments, universities, local churches, people affected by leprosy and other stakeholders to achieve our vision.

Leprosy can affect anyone regardless of age, gender, nationality, class or religion. However, its severest impact is on people who are marginalised or living in poverty. It is these people, so often stigmatised and left dealing with disability, that we seek to serve.

As well as providing holistic treatment and care for people living with the effects of leprosy in 18 countries across Asia, Africa and the Pacific, we serve future generations so that they will be born into a world free from the oppression of this disease.

● Nearly every modern advance in leprosy prevention and treatment can be connected to Leprosy Mission Research contributions. ●

DR DEANNA A. HAGGE DIRECTOR OF RESEARCH AND LABORATORIES, TLM NEPAL AND SENIOR RESEARCH ADVISOR, THE LEPROSY MISSION

OUR LEPROSY RESEARCH

To defeat this disease in our lifetime, we need to invest in research to develop new tools in the fight against leprosy; and we have a proven track record.

The Leprosy Mission has been involved in research for more than 50 years from the testing of anti-leprosy drugs such as clofazimine in the 1960s and 1970s to the innovative surgical procedures pioneered by Dr Paul Brand.



Dr Paul Brand CBE (1914 – 2003) pioneered the tendon transfer techniques that are still used today.

In addition to undertaking field-based primary research, The Leprosy Mission has research facilities in Bangladesh, India and Nepal which conduct basic research and work with 17 hospitals in clinical research. Over the decades, our research centres have made a significant contribution to global knowledge on leprosy, how to manage the disease and its complications.

CURRENT RESEARCH FOCUS

Our current research is focused on:

- ▶ understanding and reducing transmission
- ▶ understanding and enabling earlier diagnosis (including early diagnostic tests)
- ▶ monitoring relapse and leprosy drug resistance
- ▶ early detection and clinical trials for leprosy reactions and nerve damage
- ▶ improving reconstructive surgery
- ▶ innovating in ulcer care
- ▶ enhancing eye care
- ▶ strengthening inner wellbeing and mental healthcare
- ▶ reducing stigma
- ▶ engaging in community-based rehabilitation

NEGLECTED TROPICAL DISEASES

Leprosy is one of the ten NTDs referred to in the 2012 London Declaration. Therefore, in addition to researching leprosy-specific approaches, we are implementing cross-NTDs research. Examples include the treatment and prevention of leprosy and Buruli ulcers, comorbidity of leprosy and soil-transmitted helminths and developing effective approaches to improving mental health in people with NTDs.

GLOBAL FELLOWSHIP FOR ZERO LEPROSY

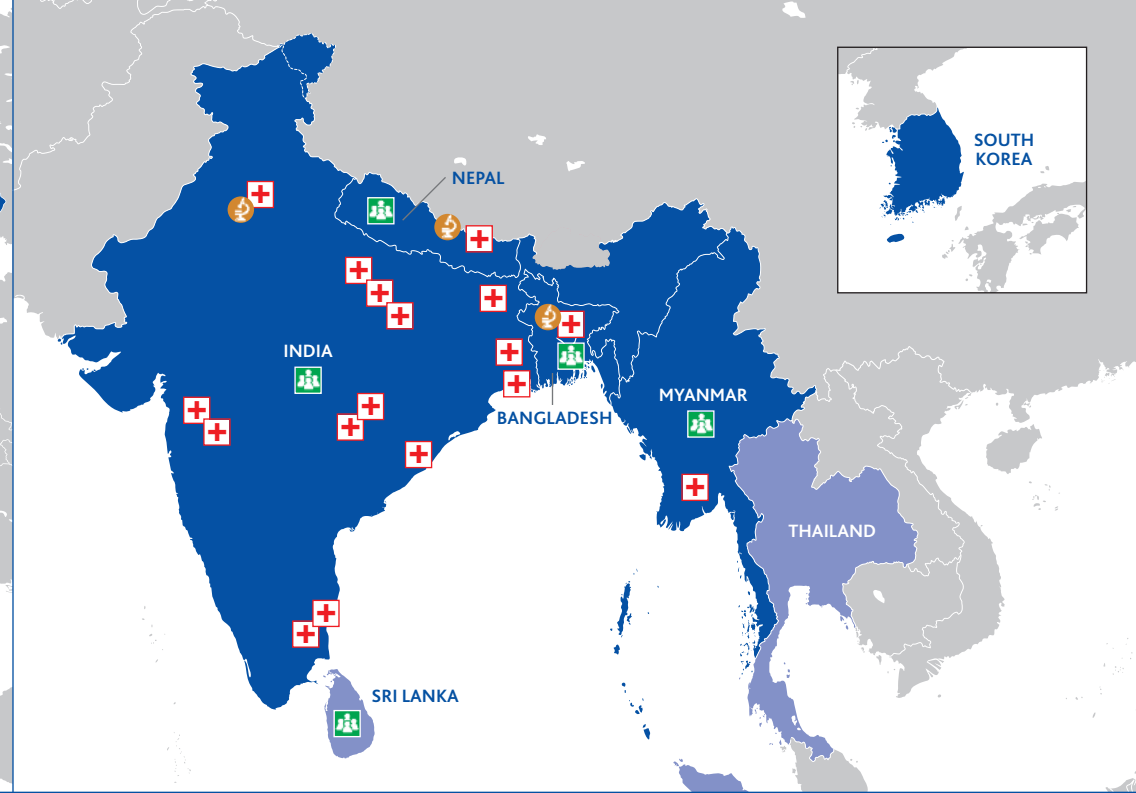
We are working with members of the Global Partnership for Zero Leprosy to share learning and research.



WHERE WE WORK

KEY

- Global Fellowship Members
- Other countries where we work
- Research centres (laboratories)
- TLM hospital research
- Primary field research countries



TOWARDS ZERO LEPROSY TRANSMISSION

- ▶ **Target: Stop transmission**
- ▶ **Tools under Research and Development: Contact screening + LPEP, *Mycobacterium leprae* environmental and drug resistance studies**

Until recently, there was no proven method to reduce leprosy transmission. Although contact screening is effective, people affected by leprosy can be hesitant to reveal their diagnosis to others, especially where stigma is prevalent.

In 2002, TLMi Bangladesh partnered with Erasmus University in the Netherlands to perform studies which combined contact screening with a single dose of rifampicin; one of the antibiotics used to treat leprosy. This type of drug treatment is called Leprosy Post-Exposure Prophylaxis (disease prevention) or LPEP.

After two years of follow-up, results showed that 57% of contacts had a combined lowered risk for developing leprosy sustained for four years afterwards.

However, people with least contact received greater protection and those with the highest level of contact, such as with household blood relatives, received less protection.

In addition, there was an important trend observed when health staff had LPEP in hand.

Leprosy patients were more likely to permit access to their household and other contacts for leprosy screening; and contacts were more receptive to treatment and learning about leprosy. This access enabled focused efforts for reducing stigma and discrimination.

By 2016, similar LPEP initiatives had been test launched with government health programmes in select districts of Indonesia, India, Nepal, Myanmar, Tanzania, Sri Lanka, Brazil and Cambodia.

In 2018, the WHO issued its updated *Guidelines for Diagnosis, Treatment and Prevention of Leprosy*, in which it cited TLMi Bangladesh's collaborative studies as part of the evidence-base for recommending contact screening with LPEP, as global policy for the prevention of leprosy and the reduction of its transmission.

TLM Trust India is a global leader in transmission studies in relation to the environment, to patients and households and to drug resistance. Since 2016, TLM Trust India has published 18 papers relevant to transmission and was first to publish rifampicin resistant patient cases.

TLM Trust India has improved PCR (DNA detection) tests by making the test sensitive for three gene sites instead of one. This means increased sensitivity when the test is used with slit skin smear, blood, nasal and saliva samples.

In 2019, TLM Trust India published field evidence confirming that leprosy bacteria can be associated with common amoeba found in soil; a single cell host potentially linked to persistence in environmental transmission.

MOVING FORWARDS

- ▶ BCG vaccination is being tested in combination with LPEP in Bangladesh.
- ▶ Both TLM Trust India and TLM Nepal participate in the WHO Global Surveillance Program which monitors rifampicin, ofloxacin and dapsone resistance.
- ▶ TLM Nepal is collaborating with the US Department of Health and Human Services, National Hansen's Disease Programs which is screening alternative LPEP drug regimens for better (100%) effectiveness.
- ▶ The Leprosy Mission is seeking additional funding to help scale up its LPEP programme.

MILLIONS
PEOPLE AFFECTED BY
LEPROSY – UNDIAGNOSED
AND AT RISK



TOWARDS ZERO LEPROSY **DISABILITY**

- ▶ **Target: Stop transmission and prevent disability**
- ▶ **Tools under Research and Development: Diagnostics to identify the missing millions and early leprosy**

Leprosy remains difficult to diagnose before symptoms start to appear, and these undetectable *missing millions* make it hard to stop transmission.

An early diagnosis can reduce the risks that lead to permanent physical problems: leprosy inflammatory reactions, nerve damage and disability development.

Dr Annemieke Geluk and her team at Leiden University Medical Centre in the Netherlands have developed field-friendly tools for early diagnosis of leprosy and reactions, partnering with global leprosy research field sites, including African countries, TLMI Bangladesh and TLM Nepal.

Their finger-prick blood test can detect multiple biomarkers that have been released into the blood stream by the body's immune response to leprosy exposure or infection. The different combinations create biomarker signatures that have the potential to differentiate between people exposed to leprosy, people with paucibacillary or multibacillary leprosy, and people at risk of developing inflammatory episodes.

Studies continue at TLM Nepal and TLMI Bangladesh to identify the best combination of biomarkers to maximise the application of global leprosy diagnostics.

- ▶ **Target: Prevent disability development**
- ▶ **Tools under Research and Development: Clinical trials to treat leprosy reaction and nerve damage**

30–50% of leprosy patients develop one or more inflammatory episodes, known as leprosy reactions, before, during or even years after multidrug therapy. Most reactions start within five years of leprosy diagnosis and can persist for many years.

Leprosy reactions are the primary cause of nerve damage and disability development. Many patients require repeated hospitalisation and long-term medical treatment before episodes cease. At any one time, 10–30% of leprosy hospital beds are occupied by reaction patients. Doctors have limited options for treating reaction patients, and no single drug completely stops nerve damage. Reactions can be long-term and the drugs can have serious side effects such as diabetes, blindness, fractures and joint issues. Due to a combination of stigma, duration of stay and poverty, leprosy patients can rarely find anywhere else for treatment.

TLM Trust India and TLM Nepal have performed studies that highlight how reactions affect households; casting families into catastrophic economic failure.

TLMI Bangladesh, TLM Trust India and TLM Nepal are involved in collaborative and individual clinical drug trials and participate in the Erythema Nodosum Leprosum International (ENLIST) Study Group along with other centres in South America, Africa, and Southeast Asia.

ENLIST is spearheaded by Dr Steve Walker and Dr Diana Lockwood of the London School of Hygiene and Tropical Medicine. In the quest for steroid sparing drugs, LSHTM also partnered with TLM Trust India in a clinical trial using azathioprine to treat type 1 reactions and neuritis. This AZALEP study was conducted at four hospital sites.

- The world class facilities of The Leprosy Mission and the number of people affected by leprosy which are served, provides a unique opportunity for researchers to collaborate in the global fight against leprosy. ●

**PROFESSOR DIANA LOCKWOOD BSC, MD, FRCP,
PROFESSOR OF TROPICAL MEDICINE, LSHTM**

A further collaboration between Dr Annemieke Geluk and TLM Nepal has identified evidence that urine contains biomarkers that may lead to the development of early diagnostic tests for reactions.

TLM Nepal is undertaking a clinical trial with a new drug for treating erythema nodosum leprosum and has published studies that have linked intestinal worm infections with the development of leprosy reactions.

30–50%
**LEPROSY PATIENTS
DEVELOP AT LEAST ONE
LEPROSY REACTION**



TOWARDS ZERO LEPROSY **DISABILITY**

- ▶ **Target: Prevent disability**
- ▶ **Tools under Research and Development: Surgery and wound management**

Leprosy can cause permanent peripheral nerve damage with devastating consequences, leaving eyes, hands or feet without motor movement or pain sensation.

While in some patients, damaged nerves can generate feelings of constant pain. Those who lack pain, however, are at high risk for the development of pressure ulcers which can lead to severe tissue damage. Recurrent ulcers can lead to disability and amputation.

Self-care is critical in this context but putting it into practice may be challenging. Daily physical labour or walking long distances may be a necessary fact of life to provide for a family with few or no other options.

Approximately 20% of leprosy patients are at risk of developing ulcers. On average, people affected by leprosy develop their first ulcer four to five years after diagnosis. After their first ulcer, a patient is at high risk for recurrence, which can eventually lead to amputation.

50–90%

**LEPROSY HOSPITAL BEDS IN
CONTINUAL USE BY PATIENTS
WITH ULCERS**



50–90% or more leprosy hospital beds are in continual use by patients with ulcers. 80% of these patients have foot ulcers. The average hospital stay can last five to six weeks and up to ten or more months.

A person affected by leprosy may experience a downward spiral of losses; their employment, their limbs and their home. Very often, they are abandoned by their family.

In early 2018, TLM Nepal began a study using a new technique for healing ulcers called Leukocyte Platelet Rich Fibrin (L-PRF). The patient's blood samples are collected and spun in a centrifuge to separate and concentrate the white blood cells and growth factors. The separated cells and growth factors are applied directly to the debrided wound which then heals more rapidly than conventional ulcer treatment.

Senior surgeon Dr Indra Napit, TLM Nepal applying L-PRF to a patient affected by leprosy.
Copyright: The Leprosy Mission



TLM Nepal, TLM Trust India and TLM Nigeria are collaborating on a research project to further investigate and improve leprosy ulcer care.

In 2016, surgeons from TLM Trust India and TLM Nepal served as part of an expert group to publish a *Protocol for a Randomised Controlled Trial Investigating Decompression for Leprous Neuropathy**.

TLM Trust India is improving standardised methods in reconstructive surgery to repair hand contractures with faster recovery rates and advanced techniques to correct grip weakness.

TOWARDS ZERO LEPROSY DISCRIMINATION

- ▶ **Target: Prevent discrimination**
- ▶ **Tools under Research and Development: community-based rehabilitation, surveys, interviews, tools and methods**

Although the prevention, diagnosis and treatment of leprosy are vital in stopping this disease, no strategy or holistic approach will succeed while leprosy stigma and discrimination still exist.

Since 2016, TLM Trust India and TLMI Bangladesh have performed 22 research studies on discrimination with topics including:

- ▶ access to disability entitlements;
- ▶ empowerment through adult literacy;
- ▶ inclusive education for disabled children;
- ▶ social participation;
- ▶ stakeholders' perceptions;
- ▶ healthcare providers' perceptions and participation;
- ▶ development of the Child Attitude Towards Illness Scale (CATIS) to measure children's and adolescent's attitudes towards leprosy

These studies not only highlight the continued need for such initiatives but provide evidence-based solutions that policy makers can adopt at a national and international level.

TLM Trust India's CREATE project (Civil Society Organisations for Resource Mobilisation, Empowerment, Advocacy, Training and Employment) developed a stigma tool kit that can be used in any stigmatising disease with minimal modifications.



Hawa, 70 years old, has regained her confidence after suffering from years of disability and discrimination. Due to the stigma and ignorance surrounding leprosy, she was thrown out of her community in eastern Niger. She once had to beg for food but now she is earning a living and can feed and clothe herself.

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Funded by the Leprosy Research Initiative (LRI), TLM Niger, IDEA Niger, AIFO Mozambique, IDEA Mozambique and IDEA Nigeria are researching the development and use of participatory methods for people affected by leprosy to understand their rights and increase dignity and inclusion in their communities.

Also funded by LRI, TLM Nigeria, the University of Jos and the not-for-profit company, Enablement Ltd, are studying how faith groups can affect perception to leprosy.



LEPROSY RESEARCH INITIATIVE

The Leprosy Research Initiative was launched in 2013 to establish a joint fund to support leprosy research and mechanisms to access external funding. The Leprosy Mission is one of the funding members.

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RESEARCH STUDIES
PERFORMED BY TLM
ON DISCRIMINATION



OUR PARTNERSHIPS

We conduct innovative research in collaboration with universities, research groups, governments and Ministries of Health worldwide. Our thanks go to all our research partners including:

All India Institute for Medical Sciences, India
Armauer Hansen Research Institute, Ethiopia
Ashiyan Medical College, Bangladesh
Bombay Leprosy Project, India
Colorado State University, USA
Erasmus MC, the Netherlands
Foundation for Medical Research, India
Global Leprosy Programme, WHO SE Asia, India
Griffith University, Australia
Indian Council of Medical Research, India
Indian Institute of Public Health, India
Institute of Himalayan Bioresource Technology, Palampur, India
Instituto Lauro de Souza Lima, Brazil
JALMA Institute, India
Khulna University, Bangladesh
Leiden University Medical Center, the Netherlands
Leonard Wood Memorial Center, Philippines
Lepra Blue Peter Public Health & Research Centre, India
London School of Hygiene & Tropical Medicine, UK
National Hansen's Disease Programs, USA
National Institute for Mental Health and Neurosciences, India
Oswaldo Cruz Institute, Brazil
Post Graduate Institute for Medical Education and Research, Chandigarh and Delhi, India
Royal Tropical Institute, the Netherlands
Schieffelin Institute of Health, India
The Maharaja Sayajirao University, India
University College of Medical Sciences, Delhi, India
University of Jos, Nigeria
University of Kelaniya, Sri Lanka
University of Leeds, UK
University of Warwick, UK
Vardhman Mahavir Medical College, India

We acknowledge that there are gaps in our toolkit including an urgent need to develop an early diagnostic test; a game changer in our quest to end leprosy.

We also need new tools to manage leprosy complications and improve the treatment of leprosy reaction. If we are to prevent disability and enhance the quality of life of those affected, we need tools to strengthen their physical, social and inner wellbeing.

We cannot develop all the tools that we need to achieve our vision. Our highly prized partnerships enable us to develop the evidence-base and obtain the funding we require to defeat leprosy and transform lives.

Could you partner with us? We are actively looking for partnerships with universities, other research institutions and research donors.



For general research information please check our website: www.leprosymission.org/our-work/research

For enquiries about research in India please contact: joydeepa.darlong@leprosymission.in

For enquiries about research in other countries or general research enquiries please contact: deanna.hagge@leprosymission.org

Left: Women affected by leprosy at Nilphamari Hospital, northern Bangladesh.

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Front cover photograph: Diagnosing, treating and raising awareness of leprosy, Kushtia, Bangladesh.

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