

Global Partnership on Zero Leprosy Research Agenda Working Group Subgroup on **Disability**

Prepared by

Liesbeth Mieras, Netherlands Leprosy Relief

In consultation with

Wim van Brakel, Netherlands Leprosy Relief

Cynthia Ferreira, FUAM team, Manaus, Brazil

Ana Paula Fontana, Universidade Federal do Rio de Janeiro, Brazil

Karthikeyan Govindasamy, The Leprosy Mission Trust India

Annamma John, (formerly) Research Resource Centre, The Leprosy Mission Trust India

Saba Lambert, London School of Hygiene & Tropical Medicine/ ALERT Hospital, Ethiopia

Diana Lockwood, London School of Hygiene and Tropical Medicine, United Kingdom

Sathish Kumar Paul, Schieffelin Institute of Health Research & Leprosy Centre, India

Maria Renata Sales Nogueira, Lauro de Souza Lima Institute, Department of Health of São Paulo, Brazil

Biliom Sangma, Christian Hospital Chandraghona & Christian Leprosy Centre, Bangladesh

Kelly Regina Dias Scipioni, Federal University of Paraná, Brazil

David Scollard, National Hansen's Disease Programs, United States (Retired)

Pushpendra Singh, Maharaja Sayajirao University of Baroda, India

Cairns Smith, University of Aberdeen, United Kingdom

James Staples, Brunel University, United Kingdom

Tantut Susanto, Faculty of Nursing, University of Jember, Indonesia

Susilene Maria Tonelli Nardi, Instituto Adolfo Lutz, São José do Rio Preto, Brazil

Steve Walker, London School of Hygiene and Tropical Medicine, United Kingdom

Cassandra White, Georgia State University, United States

Dhelya Widasmara, Saiful Anwar Hospital, Brawijaya University, Indonesia

Basudeve Yadav, READ Nepal

Summary

Leprosy is an important cause of preventable disability. Leprosy-related disability is not limited to physical dysfunction but includes activity limitations, stigma, discrimination, and social participation restrictions. Within the Research Agenda Working Group of the Global Partnership on Zero Leprosy (GPZL), two subgroups were formed to address these issues. The agenda for stigma and discrimination research was defined by the Subgroup on Stigma; the Subgroup on Disability focused their work in the following two areas:

- I. Preventing disabilities among persons affected by leprosy
- II. Minimizing the impact of living with impairments due to leprosy

Much is known on these two main components of leprosy-related disability. Early detection and treatment of both the disease and the reactions and nerve function impairment it causes are critical to prevent disabilities. Effective strategies for preventing disability and its worsening are known, and successful rehabilitation techniques are available. However, there is much room for improvement in areas such as accessibility of services, effectiveness (including cost effectiveness) of available services, and novel tools to improve current practices. Increased understanding of the causes of disabilities and ways to optimize disease management and improve inclusion is definitely needed to work towards zero leprosy.

The Subgroup identified several priority research topics under the two focus areas:

- I. *Preventing disabilities among persons affected by leprosy*
 - Early detection of leprosy to prevent disability
 - Assessing the impact of case finding/contact tracing strategies on the prevalence of leprosy-related disabilities among new cases.
 - Pathophysiology, detection, and management of reactions
 - Research on pathophysiological/immunological mechanisms of type 1 or type 2 reactions and nerve damage
 - Development and validation of diagnostic tools for the detection and measurement of nerve function impairment
 - Promotion and facilitation of the use of available treatment for reactions and nerve function impairment and identification of new treatment options
- II. *Minimizing the impact of living with impairments due to leprosy*
 - Number of people with disability due to leprosy and categorization and quantification of their needs
 - Estimating the burden of disability due to leprosy
 - Prevention of disability and its worsening (POD)
 - Research on the feasibility, effectiveness, and impact of POD strategies, including self-care, physiotherapy, occupational therapy, and combined approaches
 - Rehabilitation services
 - Assessing the accessibility and effectiveness of physical rehabilitation services and the provision of assistive devices
 - Community-based rehabilitation (CBR)
 - Research on the effectiveness, feasibility, and social and economic impact of CBR programs

Some of these research needs can be addressed by large, population-based surveys. Such surveys could be added to ongoing multicenter studies, if resources were added to ensure sufficient capacity. Studies of reactions and nerve function impairment would require basic pathophysiological/immunological lab research. Efforts to minimize the impact for people living with impairments would require a targeted approach in areas with large numbers of people affected by leprosy or where people are affected by multiple neglected tropical diseases (NTDs).

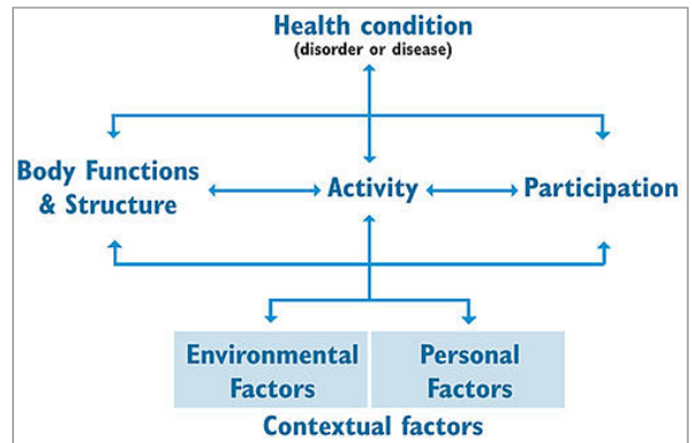
Introduction

Although most leprosy-related disabilities are preventable, an estimated 2-3 million people live with leprosy-related impairments. These impairments may or may not cause activity limitations or restrict

social participation, depending on the degree of severity and of social stigma. If the psychosocial consequences of leprosy, such as exclusion, anxiety, and depression were also considered, the number of persons affected could be much higher. This is certainly the case if the impact on family members is taken into account.

Disability is more than physical dysfunction; it includes activity limitations, stigma, discrimination, and social participation restrictions in interaction with contextual factors. This is reflected in the WHO International Classification of Functioning, Disability and Health (ICF) model of disability, which shows the relatedness of body structure and function (and impairment thereof), activity (and activity restrictions), and participation (and participation restrictions) (Figure). Future research therefore should address major challenges at the national and international levels to ensure prevention of disabilities and to minimize the impact of people living with disabilities by managing these in such a way that their participation and inclusion in society is optimized.

Figure. WHO ICF Model of Disability



The Subgroup on Disability identified key research areas related to disability that are needed to prevent and reduce leprosy and the consequences of the disease. As a basis of their work, the Subgroup reviewed multiple strategies, including the [Triple Zero Campaign of ILEP](#), the [ILEP Global Strategy](#), and the [WHO Global Leprosy Strategy 2016-2020](#), along with documents and developments in the field of neglected tropical diseases (NTDs) and disability. The developments in the various disability-related task groups of the [NNN Disease Management, Disability and Inclusion \(DMDI\) Working Group](#) were also considered. The Subgroup also examined the recent work done by the [Leprosy Research Initiative](#) (LRI) to draft an updated set of research priorities aligned with current developments in the field of leprosy. For this effort, the LRI completed an extensive exercise that involved an inquiry panel, focus group discussions, an e-survey, and a Delphi panel and included a wide range of stakeholders (e.g. persons affected by leprosy, organizations working in the field of leprosy, medical staff, policy makers, researchers etc.).

Goal of the Disability Subgroup

The goal of the research recommended by the Subgroup on Disability is to contribute to

- Preventing disabilities among persons affected by leprosy
- Minimizing the impact for people living with impairments due to leprosy by
 - Ensuring that persons with permanent impairments due to leprosy or other NTDs can effectively manage their impairments and disabilities and have access to medical, rehabilitation, and social services when needed
 - Improving social inclusion of all persons affected by leprosy through disability-inclusive development

Research Priorities

I. *Preventing Disabilities among Persons Affected by Leprosy*

- **Early Detection of Leprosy to Prevent Disability**

- *Assessing the impact of case finding/contact tracing strategies on the prevalence of leprosy-related disabilities among new cases*

The impairment status of a leprosy patient at diagnosis is known to be the most important determinant for future impairment (1). However, the extent to which different active case finding and contact tracing strategies contribute to a reduction of leprosy related disabilities is unknown.

- *Key question*

- What is the impact of case finding/contact tracing strategies on the prevalence of leprosy-related disabilities?

- *Research to address the issue*

- Operational research to assess the (cost-) effectiveness of case finding strategies
- Mapping studies of leprosy patients and leprosy-related disabilities

- **Pathophysiology, Detection, and Management of Nerve Function Impairment and Reactions**

- *Pathophysiology of reactions and nerve function impairment*

Research is needed on the pathophysiological/immunological mechanisms of type 1 or type 2 reactions and nerve damage (as well as neuropathic pain) in leprosy, including the identification of factors associated with increased risk of reactions and nerve function impairment. Some of these factors are known, such as the type of leprosy and the time since completion of treatment (2,3). Still, a better and more specific understanding of mechanisms and risk factors is needed to improve management of reactions (4-6). In addition, as neuropathic pain also importantly contributes to disability, early recognition and improved management of such pain is needed.

- *Key questions*

- What are the pathophysiological/immunological mechanisms associated with increased risk of reactions, nerve function impairment, and neuropathic pain?
- What new and effective treatment options are available for the management of neuropathic pain?

- *Research to address the issue*

- Basic pathophysiological/immunological lab research to identify risk factors for reactions and nerve involvement

- *Detection of nerve function impairment*

Development and validation of diagnostic tools is needed to detect and measure nerve function impairment (including silent neuritis) and reactions. Detecting nerve damage as early as possible will greatly contribute to the prevention of disability. Nylon monofilaments (Semmes-Weinstein monofilaments) and voluntary muscle testing are current state-of-the-art tools that have been shown to correlate well with sophisticated neurophysiological measures (7-13). Newer instruments have recently been evaluated (14). Definitions for clinically relevant nerve function impairment are needed to determine meaningful change.

- *Key questions*

- How can the identification of type 1 and type 2 reactions be improved?

- Which simple, existing or new tools can provide the earliest detection of neurological signs of leprosy and/or measure nerve function impairment?
- How can the use of these tools best be promoted and the capacity of health care staff to use them be ensured?
- *Research to address the issue*
 - Clinical research to test and compare new and existing tools to detect nerve function impairment
 - Implementation research to ensure the use of tools to detect nerve function impairment by different health care providers
- *Management of reactions and nerve function impairment*

Efforts are needed to promote and facilitate the use of available treatment for reactions and nerve function impairment and to identify new treatment options. Given that reactions and neuropathy remain the leading cause of disability in leprosy, promoting and facilitating the use of available treatment (steroids) remains top priorities. Recent trials have established that a steroid regimen of 32 weeks to treat nerve damage does not give added benefit over a 20-week regimen (15,16). A parallel trial established that steroid treatment of newly diagnosed leprosy patients with sub-clinical, small fibre neuropathy at the time of diagnosis does not reduce the risk of long-term clinical nerve damage. Alternative drug treatments for type 1 and type 2 reactions may improve prognosis and reduce the risks inherent in long-term steroid treatment. Research has shown that households affected by erythema nodosum leprosum (ENL) face significant economic burden and are at risk of being pushed further into poverty (17). However, more research is needed to explore this area and identify solutions. Research on armadillos suggested that LepVax treatment might restore some early sensory axonal function: when used as post-exposure prophylaxis, it alleviates and delays the neurologic disruptions caused by *M. leprae* infection (18).

 - *Key questions*
 - What efforts are needed to ensure that steroids are available and used properly and in a timely manner for the treatment of reactions?
 - What are alternative, effective treatment options for the management of reactions?
 - What are mechanisms of increased financial burden on leprosy patients and their families due to reactions, and what are possible solutions to address them?
 - What could the role of LepVax be in the prevention and treatment of nerve function impairment?
 - *Research to address the issue*
 - A survey to assess 1) the (national) guidelines on steroid use and the steroid availability at national and peripheral levels and 2) the capacity of health workers to use them
 - Qualitative research to examine patient and health care provider behavior when treatment of reactions is needed
 - A new Cochrane review of steroid and other drug trials for management of reactions
 - An assessment on the benefits of alternatives to corticosteroids
 - Health economics research to determine the risks for an increased financial burden due to reactions

- Qualitative research to determine solutions to prevent an increase of the financial burden
- Clinical trials to learn more about the effects of LepVax

II. *Minimizing the impact of living with impairments due to leprosy*¹

- **Number of People with Disability due to Leprosy**

- *Estimating the burden of disability due to leprosy and other NTDs or other diseases that share cross-cutting issues with leprosy*

Efforts to improve disability prevention and management for persons affected by leprosy are hindered by the lack of data on the number of persons with disabilities in general as well as the number with disabilities related to leprosy or other NTDs. The disability grade at the time of diagnosis is usually the only disability factor that is recorded in leprosy control. The type of disability and the worsening of disability during and after treatment is usually not included in reports. A better understanding of the magnitude of the problem and the needs of the people living with impairments is required to properly address them through program planning, using baselines for monitoring outcome and impact of interventions as well as for advocacy and fundraising.

- *Key question*

- What is the burden of disability due to leprosy and other NTDs or other diseases that share cross-cutting issues with leprosy?

- *Research to address the issue*

- Cohort study to determine the quantity of the increase of disability during and after treatment
- Mapping studies of people with disabilities due to leprosy and other related diseases such as NTDs.

- **Prevention of Disability and Its Worsening (POD):**

- *Research on the feasibility, effectiveness, and impact of POD strategies (including self-care, physiotherapy, occupational therapy, and combined approaches)*

Limited evidence is available on the added value of self-care groups and family support for POD (19,20). More evidence, however, is needed on various POD approaches in different settings and with other disabling diseases, especially regarding feasibility and effectiveness, including cost-effectiveness. The local context, gender roles, living conditions, existing barriers, and other factors for persons affected by leprosy all determine the feasibility of disability prevention strategies. Novel techniques used in wound care in general and in diabetic foot-care specifically can be beneficial for persons with ulcers due to leprosy. Development of a protocol for combined self-care of persons with leprosy-related and diabetic neuropathy would be important.

- *Key questions*

- What are the most feasible, (cost-) effective strategies for POD in various settings?
- What new, effective treatment options for ulcers are available?

¹ Stigma and discrimination are addressed in the report from the Subgroup on Stigma

- Could alternative therapies contribute to increasing the quality of life for people with leprosy?
 - *Research to address the issue*
 - Operational research; piloting of best practices for combined skin and wound care, including M-Health approaches and self-management
 - Qualitative research on the application of alternative practices to alleviate pain symptoms and increase quality of life
 - Qualitative research on the perception and acceptability of POD strategies and ulcer treatment options
 - Health economics research to assess the cost-effectiveness of POD strategies
 - Operational research piloting different wound treatment
- **Inclusive Rehabilitation Services**
 - *Assessing the accessibility and effectiveness of physical rehabilitation services and the provision of assistive devices for persons with leprosy-related disabilities within a health system context*

Rehabilitation services and the provision of assistive devices for persons with leprosy-related disabilities are often organized in parallel to the existing general health services. Evidence showing the (cost-) effectiveness and feasibility of integrated services would help to convince stakeholders of the benefit of providing persons affected by leprosy with the services they need within the existing health system.

 - *Key question*
 - How can rehabilitation services for persons affected by leprosy be organized most effectively within the existing health system?
 - *Research to address the issue*
 - Health systems research to determine the best way to integrate rehabilitation services for persons affected by leprosy
 - Health economics research to determine the cost-effectiveness of integrated services
 - Mapping of rehabilitation services
- **Community-based Rehabilitation**
 - *Research on the effectiveness, feasibility, and social and economic impact of CBR programs*

The evidence base related to the impact of CBR remains limited, both in terms of quantity and strength of design (21).

 - *Key question*
 - What are the characteristics of sustainable, effective, feasible, and impactful CBR programs to address the needs of persons affected by leprosy?
 - *Research to address the issue*
 - Qualitative research to determine the needs of persons affected by leprosy
 - Operational research piloting different CBR approaches

Baseline Information Needed

An inventory of the existing leprosy research structures (e.g., the research groups involved in studies on leprosy, disability, and related issues) would help to clarify the capacity needed to address the research priorities on leprosy-related disability. It would also help identify ways to address various research needs through integrated studies.

Access to certain baseline data would be very useful for the research agenda on disability. To help attain these data, the GPZL's Operational Excellence Working Group could include the following issues in an assessment of leprosy control programs:

- Post-multi-drug treatment surveillance
- Availability of and accessibility to steroids; the use of thalidomide
- The use of nerve function assessment tools
- Geographic overlap with other NTDs
- The accessibility to and the use of devices, such as prosthetics, orthoses, and auxiliary devices
- Best practices to address POD and minimizing the impact of living with impairments due to leprosy

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