**Diplomarbeit**

# Leprosy Disabilities – Complications of the Poorest?

## Retrospective Analysis of Social Determinants of Health and Disability-Scores in Leprosy Affected Persons in Salem, Tamil Nadu, India


eingereicht von

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Graz, am 16.07.2019

# Eidesstaatliche Erklärung

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Graz, am 16.07.2019 *Martin Heidinger eh*

# Preface

Leprosy still accounts for over 210 000 new infections globally each year. The majority of these occur in India. An infection leads to skin changes, loss of sensibility and autonomous innervation as well as to immune reactions in parts of the affected persons, which can lead to disabilities. The latter disfigure the affected persons and may result in the near impossibility of activities of daily living. The disease itself, especially however the visible changes and disabilities often lead to the social exclusion of affected persons. Therefore, it is not without reason, that leprosy is frequently described as one of the most stigmatized diseases of all, which affects the poorest of the poor.

Since the 1980s a cooperation between der Medical University (former Medical Faculty of the Karl-Franzens University) of Graz and the Doctor Typhagne Memorial Charitable (DTMC) Trust exists. The revitalization of this cooperation was conducted with the project „Leprosy on the Road". In fall 2015 preparations commenced, including the intensified communication with the project partners as well as the exact elaboration of the project's goals within the program „FairYoung Styria – unsere globalen Ziele 2015+" of the Styrian federal government. In October and November 2016 necessary adaptions were coordinated and implemented together with the project partner. Thereafter the acquired data were analyzed, interpreted, and publications prepared.

The presented work is therefor the result of almost four years. I am pleased and proud to have contributed to the characterization of one of the poorest populations globally, as well as to have added to a continuous target-oriented cooperation.

# Vorwort

An Lepra, dem biblischen Aussatz erkranken auch heute noch jährlich über 210 000 Personen weltweit. Der Großteil der Neuinfektionen findet sich in Indien. Es kommt zu Hautveränderungen, Verlust der Sensibilität und vegetativen Innervierung und bei einem Teil zu Immunreaktionen, die in Behinderungen enden können. Letztere entstellen die betroffenen Personen und machen physische Aktivitäten in gewissen Fällen quasi unmöglich. Die Erkrankung selbst, speziell aber auch die sichtbaren Veränderungen und Behinderungen führen häufig zum Ausschluss dieser Person aus ihren sozialen Strukturen. Nicht ohne Grund wird Lepra daher häufig als eine der stigmatisierendsten Krankheiten bezeichnet und betrifft als solche die Ärmsten der Armen.

Bereits seit den 1980er Jahren bestand eine Kooperation der Medizinischen Universität (vormals Medizinische Fakultät der Karl-Franzens Universität) Graz und dem Indischen Doctor Typhagne Memorial Charitable Trust. Im Zuge der Revitalisierung dieser Zusammenarbeit entstand das Projekt „Lepra on the Road“. Bereits im Herbst 2015 starteten die Vorbereitungen mit der Kontaktaufnahme zu den Projektpartnern und der exakten Ausarbeitung der Fragestellungen im Zuge des Programms „FairYoung Styria – unsere globalen Ziele 2015+“ der Steiermärkischen Landesregierung. Im Oktober und November 2016 wurden vor Ort sämtliche Adaptationen gemeinsam mit dem Projektpartner abgestimmt und vorgenommen. Danach folgten die Datenauswertung, -interpretation und Verfassung daraus resultierender Schriftstücke.

Die vorliegende Arbeit spiegelt das Endprodukt einer beinah vier-jährigen Arbeit wieder. Ich bin froh und stolz, dadurch einen Beitrag zur Charakterisierung einer der ärmsten Populationen weltweit sowie meinen Anteil für weitere zielgerichtete Kooperationen geleistet zu haben.

# Danksagung | Acknowledgements

Such a work is never an individual's task. Therefore, I would like to thank all supporters, critics as well as sponsors, which have enabled and facilitated this project and made it to what it finally is. In case I do not mention someone within the following lines personally, please do excuse this and feel included in any case.

Primär möchte ich mich ganz speziell bei Elisa Simonnet bedanken, die mir nicht nur in Indien, bei der Erhebung der Daten und Reflexion derer Bedeutung, sondern auch im Leben eine perfekte Partnerin ist.

Wolfdieter Sixl als meinem Mentor, Motivator und Freund möchte ich für die zahlreichen Besprechungen zu diesem und anderen Themen der globalen Gesundheit, für das Mitteilen seines erfahrenen und frischen Geistes und nicht zuletzt auch für seine Networking-Aktivitäten danken.

Ohne meine Betreuerin Andrea Grisold und meinem Betreuer Johann Pfeifer wäre diese Arbeit wohl gar nicht zustande gekommen. Von der ersten Stunde dieser Idee, über die Betreuung vor Ort in Indien, bis hin zu unzähligen Manuskripten, die ich Ihnen schicken durfte haben sie mich unterstützt und gefördert. Das weitere „Indien Team" setzte sich aus Anneliese Pfeifer, Angelika Schirnhofer, Claudia Wilfinger und Andreas Schöpfer zusammen, wodurch gerade die Wochen ihrer Anwesenheit sehr kurzweilig wurden. Die statistische Auswertung in dieser Qualität wurde durch Markus Puchinger ermöglicht. Und ohne die Kollegenschaft der GHD würde es solche Möglichkeiten für Studierende an unserer Universität wohl nicht in dieser Form geben.

Obviously, it was our project partners who enabled us to undertake such a project and supported us along the way. I want to thank Sister Dr. Francina Karrippadathu, Albert Kennedy and Anthony Chinnappan.

Mein Dank gilt auch Maria Elßer und Michael Kvas die dem Projekt gleich zu Beginn einen offiziellen Rahmen und Raum zur Entwicklung gaben. Sowie Martin Eberhart, der die Präsentation der Projektidee kurzerhand übernahm.

Um aber überhaupt erst zu der Person zu werden, die ich sein darf, gilt mein allergrößter Dank meiner Familie, die mich vor und während einer intensiven Studienzeit stets unterstützt hat, mit aufbauenden Worten zur Seite stand wenn es einmal zu viel wurde, und mit herzlichen, pragmatischen als auch strategischen Ratschlägen die Zeiten prägte in denen wichtige Entscheidungen getroffen werden mussten.

# Zusammenfassung

Lepra wurde beständig mit Ungleichheiten der sozialen Determinanten von Gesundheit und ihrem Einfluss auf die Wahrscheinlichkeit der Übertragung und Infektion, sowie der Wahrscheinlichkeit einer erfolgreichen Therapie assoziiert. Indien, als Land, in dem die präsentierte Studie durchgeführt wurde, zeigt weiterhin die weltweit höchste jährliche Detektionsrate von Lepra-Fällen. Salem, der Bezirk, in dem die präsentierte Untersuchung vorgenommen wurde, zeigt die höchste Rate an zweit-gradigen Behinderungen durch Lepra bei Diagnosestellung. Das Ziel dieser Studie war es, zu untersuchen, ob Ungleichheiten der strukturellen Mechanismen, eine niedrige sozioökonomische Position bzw. im weiteren Sinne Ungleichheiten der sozialen Determinanten von Gesundheit mit höheren Behinderungsschweregraden bei durch Lepra behinderten Personen korrelieren. Die Analyse basiert auf einer willkürlichen Stichprobe von Personen des lebenslangen Pflegeprogrammes des Doctor Typhagne Memorial Charitable (DTMC) Trust, die eine multidrug therapy (MDT) für Lepra abgeschlossen haben und/oder slit-skin smear negativ sind und mindestens eine erst-gradige Behinderung durch Lepra vorweisen. Eine deskriptive Analyse sowie eine multiple schrittweise lineare Regressionsanalyse wurden durchgeführt. Der Eyes-Hands-Feet (EHF) Score war die Ergebnisvariable, mit Geschlecht, Alter, Zeit seit Therapieabschluss, monatlichem Einkommen und Wohnfläche als erklärende Variablen. Es wurden 123 Personen in die Studie eingeschlossen, davon waren 41 (33.33%) weibliche und 82 (66.67%) männliche Studienteilnehmer. Alle Studienteilnehmerinnen und Studienteilnehmer waren Teil der indischen „Backward classes“; 81.30% waren Analphabeten und das durchschnittliche monatliche Einkommen belief sich auf 1252 Indische Rupie (INR) (US$19.08 bzw. €17.16). Der durchschnittliche EHF Score war 7.016 (95% CI, 6.595 – 7.437). Die schrittweise multiple lineare Regressionsanalyse resultierte in einem signifikanten Model, mit $F(2, 120) = 13.960$, $p \leq 0.001$, Effektgröße (Cohen’s f2) = 0.81, wodurch 18.9% der Varianz des EHF Scores erklärt werden kann ($R2 = 0.189$). Signifikante Prädiktoren eines höheren EHF Scores bei durch Lepra behinderten Personen waren höheres Alter (beta = 0.340, 95% CI, 0.039 – 0.111, $p < 0.001$), sowie geringerer

Wohnraum (beta = -0.276, 95% CI, -0.041 – -0.011, p = 0.001). Unsere Resultate legen nahe, dass durch Lepra behinderte Personen in niedrigen Lebensverhältnis leben und das Ungleichheiten der sozialen Determinanten von Gesundheit mit höheren Behinderungsgraden durch Lepra korrelieren.(1)

# Abstract

Leprosy has consistently been associated with inequities in social determinants of health (SDH) concerning its transmission and infection, as well as its probability for a successful cure. India, the country in which this investigation took place still shows the highest Annual New Case Detection (ANCD) rate globally. Salem, the district in which this study took place shows the highest rate of grade-2 disabilities at diagnosis (G2D). The objective of this study was to determine whether unequal structural mechanisms, a lower socioeconomic status and therefore inequities in SDH correlate with higher severity of disabilities in persons affected by leprosy. This analysis was based on a sampled population of persons, who were enrolled in the lifelong-care program of the Doctor Typhagne Memorial Charitable (DTMC) Trust, had completed a multidrug therapy (MDT) for leprosy and/or were slit-skin smear negative and showed grade-1 disabilities or higher due to leprosy. A descriptive analysis as well as a multiple stepwise linear regression analysis was performed. The Eyes-Hands-Feet (EHF) score was the outcome variable, and gender, age, time after release from treatment, monthly income, and living space were explanatory variables. There were 123 participants, comprised of 41 (33.33%) women and 82 (66.67%) men. All study participants belonged to India's Backward classes; 81.30% were illiterate and the average monthly income was 1252 Indian rupee (INR) (US$19.08 or €17.16). The average EHF score was 7.016 (95% CI, 6.595 to 7.437). Stepwise multiple linear regression analysis built a significant model, where $F(2, 120) = 13.960$, $p \leq 0.001$, effect size (Cohen's f2) = 0.81, explaining 18.9% of the variance in EHF scores ($R2 = 0.189$). Significant predictors of a higher EHF score in persons affected by leprosy were found to be higher age (beta = 0.340, 95% CI, 0.039 to 0.111, $p < 0.001$), as well as less living space (beta = -0.276, 95% CI, -0.041 to -0.011, $p = 0.001$). Our results suggest, that persons affected by leprosy live in poor living standards and that inequities in SDH correlate with higher disabilities in persons affected by leprosy.(1)

## Published Works

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# Table of Content

# List of Abbreviations

| | |
|---|---|
| AMFES | ALERT MDT Field Evaluation Study |
| BC | Before Christ |
| DP | Deformity Pension |
| DTMC Trust | Doctor Typhagne Memorial Charitable Trust |
| EHF Score | Eyes-Hands-Feet Score |
| ENL | Erythema Nodosum Leprosum; Type 2 leprosy reactions |
| G1D | Grade-1 disabilities at diagnosis |
| G2D | Grade-2 disabilities at diagnosis |
| GHD | Global Health and Development |
| HIV | Human Immunodeficiency Virus |
| ILEP | Indian Leprosy Elimination Plan |
| INR | Indian Rupee |
| MB | Multibacillary Leprosy |
| MPI | Multidimensional Poverty Index |
| MDT | Multidrug Therapy |
| MUG | Medical University of Graz |
| NLEP | National Leprosy Eradication Programme |
| PB | Paucibacillary Leprosy |

| | |
|---|---|
| POD | Prevention of Disabilities |
| SDH | Social Determinants of Health |
| SEAR | WHO’s South-East Asian Region |
| SMMI | Salesian Missionaries of Mary Immaculate |
| TB | Tuberculosis |
| WHO | World Health Organization |

# List of Figures

# List of Tables

# List of Photographs

# Introduction

Leprosy is a chronic, granulomatous infectious disease caused by *Mycobacterium (M.) leprae* or *M. lepromatosis*. It mainly affects nerves, skin, respiratory mucosa and eyes.(2)

Leprosy has consistently been associated with inequities in social determinants of health (SDH),(3–8) which comprise of contextual factors as well as the structural mechanisms within a society that result in an individual's socioeconomic position, that via intermediary determinants leads to inequities in health and well-being.(9) The quantitative power of each one or the combination of these parts of the SDH in the risk of infection with leprosy is however not yet elaborated in detail.(5–10) Disabled persons were generally shown to experience social- and health-status disparities,(11–15) however the relationship between disabilities due to leprosy, and SDH remains unclear.(1)

## Leprosy on the Road

The first partnership between the Medical Faculty of the Karl-Franzens University of Graz and the Doctor Typhagne Memorial Charitable (DTMC) Trust was already established in 1986 by Honorary-Doctor Prof. Wolfdieter Sixl and Dr. Sr. Francina Karippadathu in Kerala and later in Tamil Nadu, India. Initially, the work was focused on the sanitary and hygiene situation of social as well as healthcare centers, leprosy villages and living areas of indigenous tribes. More specifically, the measures taken throughout the 80s and 90s included recording the local sanitation surroundings as well as planning the creation of water wells and wastewater systems. Territories of the indigenous population were screened and appropriate measures to improve living standards put in place. Many practical projects are still functioning today, as for example the Trichoderma-project for pest-control, vermi-compost creation, quail and rabbit breeding as well as Anthurium plantations and the continuous financing of the Kolli Hill Educational Centre. In subsequent visits surgical interventions were carried

out, whereas Prof. Dr. Johann Pfeifer, former head of Global Health and Development (GHD) was already part of one excursion in 2005. This latter year also marks the last one of active cooperation of the Medical University of Graz (MUG) and the DTMC Trust until the reestablishment of the cooperation in October 2016. “Leprosy on the Road” was the title for a medical development cooperation program of GHD of the MUG and the DTMC Trust.

## Global Health and Development – Medical University of Graz

Global Health and Development (GHD) of the Medical University of Graz (MUG) resulted out of decade-long individual activities of doctors and professors of MUG in international projects. Fore-father and fore-thinker was Honorary-Doctor Prof. Wolfdieter Sixl, who was head of the department for geomedicine at the Medical Faculty in Graz and cooperated with partners in over thirty countries regarding medical development.

The team of GHD consists of experienced doctors, general practitioners and specialists in general surgery, plastic surgery, pediatric surgery, orthopedics, anaesthesia, hygiene and microbiology as well as geomedicine. Furthermore, nurses coming from various medical backgrounds as far as anaesthesia to surgery, internal medicine and finally, nursing as well medical students complete the team, which therefore covers great parts of various medical specialties.

The work of GHD is based on four pillars, namely:

- Education

  Elective courses cover basics on development cooperation, the Sustainable Development Goals and medical aspects in international cooperation. Furthermore, practical skills in hygiene, laboratory medicine and surgical procedures are trained.

- Public Events

  Events organized for a broad interested public, presenting aspects of medical development cooperation.

- International Projects

  The goal is to create a platform for individuals, especially in the medical fields, to be able and work internationally under the umbrella of GHD and a post-secondary institution. Currently three projects in two continents are directly supported.

- Research

  As one of the duties of post-secondary institutions, the GHD strives to combine its national and international activities in practical research projects.(16)

*Figure 1 – Logo of Global Health and Development (GHD)*


Source: (16)

## Doctor Typhagne Memorial Charitable Trust

The Doctor Typhagne Memorial Charitable (DTMC) Trust was founded in January 1999 under the Salesian Missionaries of Mary Immaculate (SMMI) Convent and is operating in the districts of Salem and Namakkal, which are both part of the province of Tamil Nadu in Southern India. Its head-office is located in Salem and two field-offices operate in Kakkaveri and Kolli Hills. The objectives of the charitable trust are the treatment of leprosy, tuberculosis (TB) and Human Immunodeficiency Virus (HIV) patients, the

empowerment of socially marginalized people, care for women and children in distress, protection of the environment and promotion of organic farming.(17)

*Figure 2 – Logo of the Doctor Typhagne Memorial Charitable (DTMC) Trust*


Source: (17)

In Salem, the DTMC Trust Headquarter is located on the Campus of the St. Mary's Hospital and the SMMI Convent Staff Quarters. Adjoined to the building is an inpatient department for males and females affected by leprosy, who are admitted for ulcer care and physiotherapy to treat deformities. Furthermore, around 40 patients are seen six days a week in the outpatient clinic and skin clinic, with lab facilities to test for leprosy, HIV and TB.

Kakkaveri, approximately 40 kilometers south of Salem, hosts a 60-bed hospital, which provides general medical, surgical and obstetric services with a focus on the inpatient treatment of persons affected by HIV, TB and leprosy. Additionally, pharmaceutical services, x-ray, lab, ultrasound and ecg facilities are available. Furthermore, a unit for drugless and Sujok therapy, a traditional medicine of South-East Asia, is available.

Furthermore, Kakkaveri is home to the Gertrude-Women-Training-Centre, which provides local women with educational opportunities for careers in textile and garment industries as well as one-year courses in nursing and patient management, which shows a 100% job-placement rate. In this respect the Vidivelli Community College for Women was founded. A women's shelter offers women and children in distress a rescue-shelter and regular support groups to foster self-sustainment, cooperation and help.

Within the district of Kolli Hills, south-east of Salem, the DTMC Trust runs organic farms, producing vegetables, fruits, bio-fertilisers and crops as part of a greater environment sanitation program. An anthurium cultivation unit and a biocontrol laboratory are also operated. Here the DTMC Trust offers women empowerment units and support groups for women as well as men, further educational opportunities in form of vocational schools for trades in agriculture as well as textile and garment industries and education for school dropouts. What is special about Kolli Hills are its inhabitants, who partly proceed the aboriginal tribal lifestyle, which the DTMC Trust is fostering through special tribal development and education of tribal children.(17)

## Leprosy Activities of the DTMC Trust

The SMMI sisters initiated their activities in the region in 1931, focusing on education (especially for girls) and health care. Leprosy attracted a lot of attention at that time with prevalence-rates estimated as high as 130 affected persons per 10 000 inhabitants and continued to be a focus ever since. Dr. Typhagne, a French doctor and name-patron of the DTMC Trust, started the leprosy eradication work with the SMMI sisters in 1960. Ever since the DTMC Trust and its predecessor organizations are actively engaged in the prevention, diagnostic and treatment of leprosy. In 1981 it was integrated as a non-governmental organisation into the national Anti-Leprosy Programme. 1986 not just marked the introduction of Multi-Drug-Therapy (MDT) with dapsone, clofazimine and rifampicin in Salem but also the integration of leprosy working institution into the National Leprosy Eradication Initiative.

Today, the DTMC Trust is integrated in the Indian Leprosy Elimination Plan (ILEP) as a referral centre for ulcer care, prevention of disabilities through early diagnosis and patient-assistance with welfare activities. Therefore, the organisation is involved in the stages of education, prevention and diagnostics as well as treatment of complications, management of disabilities, follow-up and lifelong-care of leprosy affected persons.

With over 85 years of experience in treating leprosy patients, the DTMC Trust today has an integrative and comprehensive approach to achieve its goals in the respective

fields. Five permanent health-workers and medical professionals are covering the primary line of representatives together with one lab-technician. Two accountants, one Managing Director and Dr. Sr. Francina build the institutional foundation. The concrete objectives of the project as well as the activities for a comprehensive leprosy care are the following:

- Information, Education, Communication (IEC) & Training Programs

  Public training activities as well as work with focus-groups towards knowledge about leprosy and steps to eliminate the disease.

- Deformity Prevention & Medical Rehabilitation (DPMR) Programs

  Prevention of Disability (POD) Camps are carried out monthly on an outpatient basis with around 85% of 50-80 invited patients attending. Patients and family members undergo IEC and group education, create networks. Community volunteers, who are themselves affected by leprosy are part of the network, and receive basic training as well as equipment for ulcer care, physiotherapy and counselling. Microcellular Rubber (MCR) Footwear is distributed and repaired. Patients are assisted in applying for government welfare schemes.

  Additionally, the above-mentioned activities are carried out in in-field activities, referring urgent cases to the referral centres and providing surrounding areas with IEC.

- Nutritional Assistance to Leprosy patients

  Provided for the neediest amongst patients, based on financial, social and nutritional assessments, and consisting of 10kg of rice and 2kg of nutritional powder per month.

- Medical Care for Leprosy Patients

Outpatient care is assigned bi-weekly for each patient undergoing leprosy and/or leprosy reaction treatment. Furthermore, patients are screened during in-field activities as well as POD Camps and referred from District Health Centres, which serve as public health-centres. The services provided by the DTMC Trust include:

- the care for persons affected by leprosy, both under treatment as well as with complications
- laboratory services to detect new cases
- family and neighbourhood surveys of multibacillary cases
- teaching of self-care
- ulcer care and reaction management
- physiotherapy including wax baths
- supply of MCR footwear
- referral services to higher-care centres

In 2015, 9630 cases were reviewed at the Outpatient Department, which included 4319 diagnosed leprosy cases (see Table 1). Furthermore, 44 new leprosy patients were identified as such in 2015.

Inpatient care is provided for ulcer cases, patients with deformities, for reaction cases and for post-operative care. General wound care with daily dressings is carried out as well as antibiotic treatment for infected wounds. Physiotherapy includes wax baths and exercises, which are both instructed as well as supervised. The psychosocial treatment is administered through voluntary occupational therapy. MCR footwear is distributed and patients referred to higher centres for special care. In 2015, 5938 dressings were applied in the Inpatient Department.

- Rehabilitation of persons affected by leprosy & affected families

To address the issue of social exclusion of people affected by leprosy, the DTMC Trust focuses on reducing the stigma by educating patients, families and the broad public and assisting persons affected by leprosy in applying for government welfare schemes.(17)

*Table 1 – Medical and nutritional activities of the DTMC Trust in 2015*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Annual number of patients consulted in Outpatient Department of the DTMC Trust** | | | | | | | |
| TOTAL | 9630 | *100%* | | | | | |
| Leprosy | 4913 | *51%* | | | | | |
| Respiratory/TB | 3732 | *39%* | | | | | |
| Skin Disease | 985 | *10%* | | | | | |
| **Annual number of new leprosy cases diagnosed in the Outpatient Department of the DTMC Trust** | | | | | | | |
| | **PB** | | **MB** | | **TOTAL** | | |
| Children (0-14) | 2 | | 0 | | 2 | *5%* | |
| Adult | 9 | | 33 | | 42 | *95%* | |
| TOTAL | 11 | *25%* | 33 | *75%* | 44 | *100%* | |
| **Annual number of wound dressings** | | | | | | | |
| TOTAL | 5938 | *100%* | | | | | |
| Men | 3741 | *63%* | | | | | |
| Women | 1093 | *18%* | | | | | |
| **Annual number of nutritional assistance for leprosy and TB patients** | | | | | | | |
| Grand total of persons receiving nutritional assistance | | | | | | | |
| TOTAL | 140 | *100%* | | | | | |
| Men | 89 | *64%* | | | | | |
| Women | 51 | *36%* | | | | | |
| 10 kg Rice per month for persons affected by leprosy | | | | | | | |
| TOTAL | 55 | *39%* | | | | | |
| Men | 27 | *19%* | | | | | |
| Women | 28 | *20%* | | | | | |
| 10 kg Rice and 2 kg Health Mix per month for persons affected by tuberculosis | | | | | | | |
| TOTAL | 85 | *61%* | | | | | |
| Men | 62 | *44%* | | | | | |
| Women | 23 | *16%* | | | | | |

*DTMC – Doctor Typhagne Memorial Charitable Trust; TB – Tuberculosis; PB – paucibacillary; MB – multibacillary*

*Source: DTMC Trust*

## Geographical Features of Salem, Tamil Nadu

Tamil Nadu is the most South-Eastern province of India, with a population of 7.2 million and its capital in Chennai. The Salem district contains close to 3.5 million people, which are divided into 54% living in rural areas, 19% as part of the scheduled tribe and scheduled caste, and an overall literacy of 74%. Namakkal District, neighbouring in the south-west has a population of close to 1.5 million.(18)

Salem City is located in the centre of Salem District. About 830 000 inhabitants are registered here, whereas the city sees a lot of commuting from neighbouring villages and towns. The city finds itself surrounded by dotted hills and plains, 280 metres above sea levels. Temperature highs range from 30 to 40°C all year round and lows not below 20°C. Precipitation is highest during the months of October to December, when the Eastern Monsoon arrives, however rainfall quantities have decreased over the last years. The area is mainly known for the Salem Steel plant, which uses local iron-ore to produce steel. Additionally, agricultural products of the region, foremost Mango, Tapioca, Sago and Coffee are trademarks. Furthermore, the region imposes with mineral reservoirs as well as Sandal wood, dairy productions as well as cottage industries. Tourism mainly takes place in the surrounding hill stations of Yercaud and Kolli Hills.(18)

*Figure 3 – Salem District in Tamil Nadu, India*

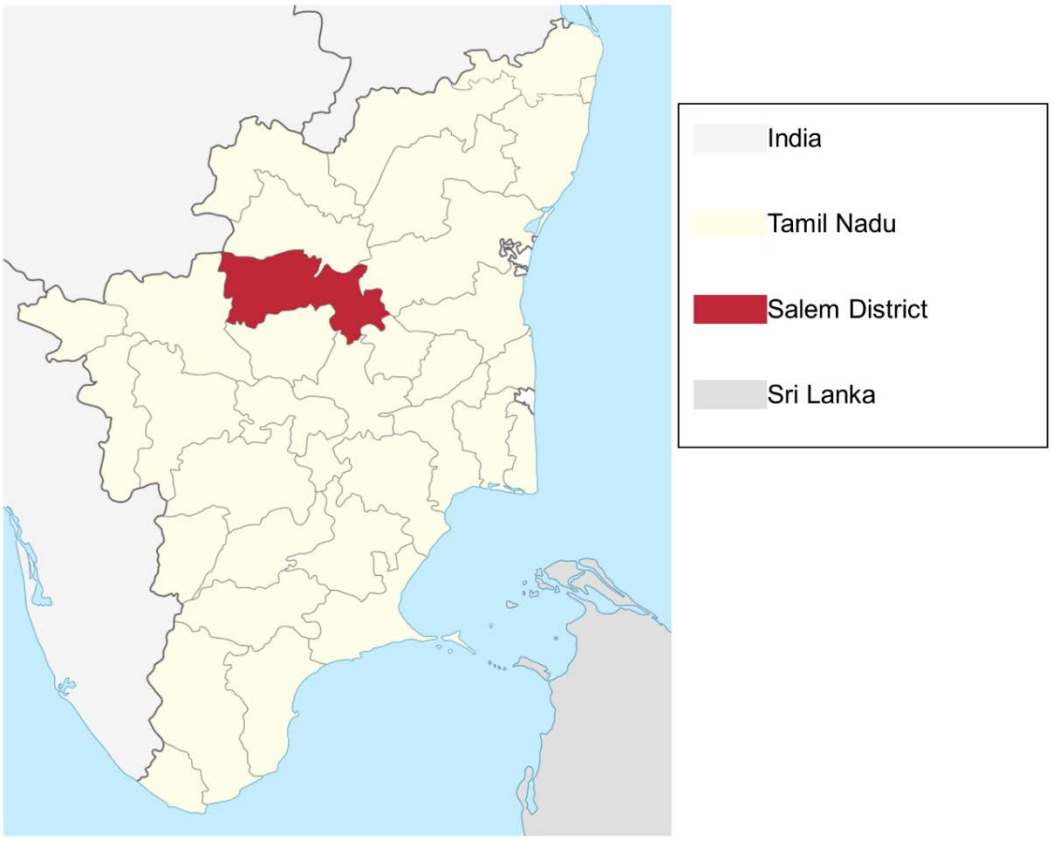



Figure adapted according to (19)

## Leprosy

In 1873 Gerhard Henrik Armauer Hansen[1] identified *Mycobacterium (M.) leprae*. As part of the *Mycobacterium* genus, which are gram positive bacteria and comprise more than 70 species, it shows a lipid-rich cell wall responsible for its acid-fast character, which however shows no methoxy-mycolates due to evolutionary gene losses.(20) *M. leprae* shows a doubling time of approximately 14 days, the longest of any known bacteria.(21) The complete genome of *M. leprae* was identified in 2001 and showed 3.27 Megabases (Mb).(22) In comparison, its close relative *M. tuberculosis* shows 4.41 Mb. Over half of *M. leprae's* genome contains non-coding genes or pseudogenes.

[1] The disease has previously also been named Hansen's disease.

Of the 1604 remaining potentially active genes 1439 are similar to genes found in *M. tuberculosis*. The evolutionary degradation of the *M. leprae* genome mainly accounted for a lack of metabolic capacities, which may explain the long doubling-time.(22)

The origin of leprosy based on the analysis of single-nucleotide polymorphisms (SNPs) showed four distinct subtypes. The origin of *M. leprae* is thought to have occurred 100 000 years ago either in Eastern Africa/Central Asia (SNP Type 2), spreading eastwards into Asia and Oceania (SNP Type 1) during migratory movements around 60 000 years ago. The original strand moved northward into Europe about 40 000 years ago and from there westwards to the Americas and to Western Africa (SNP Type 3) during colonisation. From Western Africa it may have spread to the Caribbean and South America during slave trade (SNP Type 4). The second option shows the origin of leprosy in Asia (SNP Type 1), moving to Eastern Africa/Central Asia (SNP Type 2) and thereafter continuing its spread as outlined above.(23)

*M. leprae* is not highly infectious and has an incubation period of 5 years on average. Reports exist however, describing the appearance of symptoms only after 20 years.(2) Transmission is thought to mainly result out of close and frequent contact with untreated, lepromatous cases.(2) Recent reports suggest that environmental factors may also play a role in the geographically distinct pattern of leprosy and its transmission.(24,25) Until the detection of Armadillos being infected, *M. leprae* was thought to be a human-only pathogen.(26,27) And it was only through the use of nine-banded Armadillos as a surrogate host, that sufficient quantities of leprosy DNA could be obtained for sequencing.(20,22) Today, the role of leprosy as a zoonotic disease is still not thoroughly established.(28,29) Most recent research found leprosy in squirrels (*Sciurus vulgaris*) on the British Isles.(30) Yet undiscovered host-diversity will therefore be an important consideration for future disease control measures.(31)

What is unique in leprosy is its susceptibility-pattern in the classical triad of host, pathogen and environment. It is estimated, that 95% of the world's population are genetically not susceptible to the disease.(2) At the same time, only minor pathogen and virulence variability is known.(32–34) Therefore, most clinical phenotypes might be

due to different genetic variability modulating the host's innate and adaptive immune response to *M. leprae*.(35–37)

Leprosy can occur at all ages, yet shows a peak in persons aged between 10 and 20 years and is very rare in very young, due to the long incubation period.(38) After puberty, males are twice as much affected as females. Furthermore, men show a higher prevalence of MB infections in all populations, suggesting different immune responses.(39,40)

Leprosy is curable through Multidrug therapy (MDT) consisting of dapsone, rifampicin and clofazimine, which has been recommended by the WHO study group since 1981.(41) Leprosy reactions, which are immunological reaction that can occur any time before, during or after MDT treatment and are described in more detail below are primarily treated with corticosteroids and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) to control the immunological reactions and pain.(39) Preventive measures, like the provision of single-dose rifampicin for contacts of newly detected cases are effective in the short-term,(40) however long-term preventive measures are not yet discovered. It has to be noted however, that a decent portion of the global decline in cases since the 1980's has been attributed to the worldwide coverage with BCG-vaccines besides the introduction of MDT, active case finding and improved socioeconomic conditions.(39,42)

## Global Epidemiology

In the 19$^{th}$ century leprosy was prevalent as far north as the Arctic Circle, showing the possibility of the Mycobacterium to withstand even cold climates. The geographical distribution today and the vanished occurrence in higher latitudes, is mainly thought to correlate with socioeconomic factors.(39)

The WHO's goal of a Prevalence Rate (PR) of less than 1 per 10 000 persons affected by leprosy, and therefore the elimination of leprosy on a public health level, was achieved globally in 2000 (2) and in India on a national level in 2005.(43) Since then

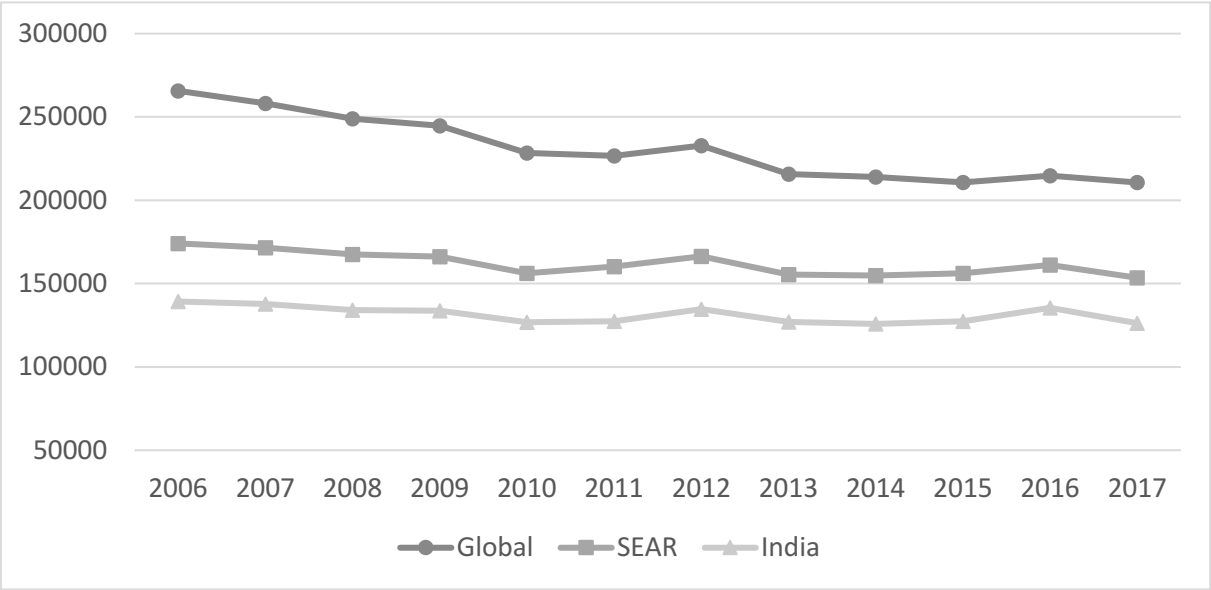
the global PR continued to be within the aspired range for 17 years and was set at 0.25 as a point-prevalence in 2017.(44)

In 2017, 22 global priority countries, as defined by the WHO contributed over 95% of new leprosy cases. India, Brazil and Indonesia were the top contributors and together account for almost 80% of the global new case load.(44) A geographical trend is therefore striking, even within countries like India, where 11 out of 35 States (resulting in about 65% of the country's population) accounted for over 90% of the national leprosy cases.(45)

Globally, 210 671 new cases were detected in 2017. The majority (59.80%) were MB cases. Women made up just over one third of the new cases, with 82 922 (39.36%) cases detected in females. 16 979 cases (8.06%) were found in children.(44)

The absolute numbers of newly detected cases have declined from 2007 until 2015. In 2016 an increase of newly detected cases was reported on all levels of analysis as depicted in Figure 4.(46) This increase can mainly be attributed to innovative and specified case-detection campaigns in micro-areas known to be endemic pockets of leprosy, like the NLEPs "Leprosy Case Detection Campaigns" (LCDC),(47) but also reflect the continuing spread and contagion of *M. leprae* in these regions. In its most recent efforts of LCDCs, the NLEP involved 163 districts of 20 States and Union Territories, including Tamil Nadu, encompassing a total population of 400 million from September to October 2016. House to house searches were carried out and every person physically examined in regard to leprosy suspicious lesions, that were thereafter tested via skin-smear in registered centers.(47) Excerpts of an interview conducted with the deputy director-general of the NLEP by the newspaper *The Indian Express*, suggested that at least 20 000 new cases were detected just in this period.(48,49) In 2017 the ANCD declined again, to values similar to the period from 2013 to 2015.(44)

*Figure 4 – Timeline of annually newly detected leprosy cases (ANCD) globally, in WHO's South-East Asia Region (SEAR) and India, from 2006 to 2017*




Sources: (44,50)

The WHO's South-East Asian Region (SEAR) accounts for 73% of the global new case load, and India for 82% of the newly detected cases in SEAR and almost 60% of the global new cases.(44)

The interpretation of global data ought to be made cautiously, as certain low-income countries, constituting a population of 530 million persons currently show no reporting on their national leprosy case load.(51) Furthermore, poor data collection and surveillance has been noted in some countries.(52) Therefore, various explanations concerning the decline in global leprosy numbers exist. Smith et al. conclude, that the most probable explanation for the decline in newly detected cases are due to less leprosy activities after the global and national elimination of leprosy as a public health problem.(53) The actual case-load could be up to eight-fold the currently reported numbers of the WHO.(51)

## Epidemiology of Disabilities due to Leprosy

Disabilities in leprosy are graded by WHO's leprosy disability grading system in grade zero, one and two, for each eye, hand and foot, as depicted in Table 2.(54)

*Table 2 – Grading of disabilities in Leprosy*

| | Eyes | Hands & Feet |
|---|---|---|
| **0** | No eye impairment due to leprosy; no evidence of visual loss | No sensory impairment, no visible impairment |
| **1** | Eye problems due to leprosy present (irregular blink), but no vision impaired (can read fingers at 6 metres distance) | Anesthesia present, but no visible deformity or damage; including muscle weakness without clawing |
| **2** | Severe visual impairments (cannot read fingers at 6 metres distance), Lagophthalmos, Uveitis, Corneal opacities | Visible impairments present; including ulcers and atrophy |

Three-Grade disability grading system for persons affected by leprosy adapted after Brandsma et al. (54) The sum of disabilities for each eye, hand and foot results in the Eyes-Hands-Feet (EHF) Score ranging from zero to 12.

Source: (1)

After the official elimination of the disease, the focus in terms of public health goals was set on reducing the disease-burden due to leprosy. Therefore, the WHO's Expert Committee on Leprosy in its eighth report defined and gathered monitoring indicators in three categories concerning leprosy:

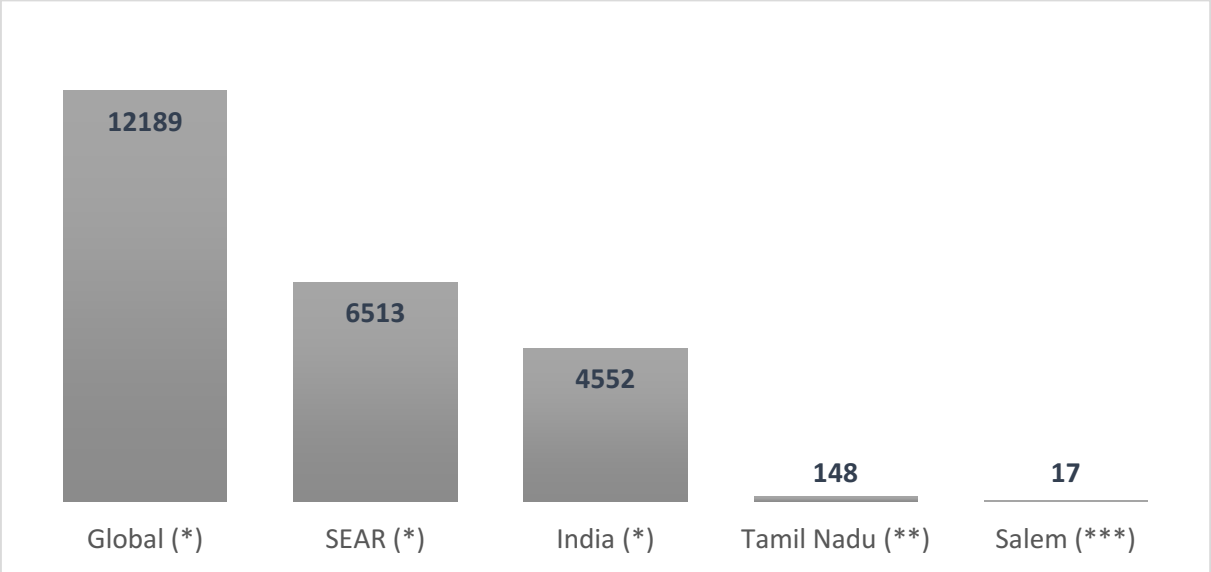
- Main indicators were defined as the ANCD Rate per 100 000 persons, G2D per 1 million persons, the treatment completion as well as the cure rates for MB and PB cases.
- Other indicators for monitoring purposes include amongst others the proportion of G2D as well as the rate of MB cases amongst new cases.
- Indicators for the evaluation of quality in existing services are defined as the prevalence of grade-2 disabilities in those who develop them throughout the course of MDT, the proportion of new cases diagnosed correctly, the prevalence-detection-ratio, the number of persons assessed at completion of treatment, and the number of relapses amongst those who completed MDT.(39)

Concerning the global burden of disabilities due to leprosy rough estimates suggest numbers as high as three million affected people.(55) The global number of grade-2

disabilities at diagnosis (G2D) in 2017 was 12 189, or 5.8% of all newly detected cases. This translates to an incidence rate of grade-2 disabilities of 1.6 per 1 million persons. Of these, 238 (1.95%) occurred in children. The SEAR accounts for 53.4% of all G2D cases globally. India contributing 4552 cases (69.89%) resulting in a national rate of 3.34 G2D per million.(44,45) (see Figure 5 and Figure 6)

The WHO's new target in terms of disabilities is defined as the reduction of the annual G2D-rate to less than 1 per 1 Million persons.(39,56)

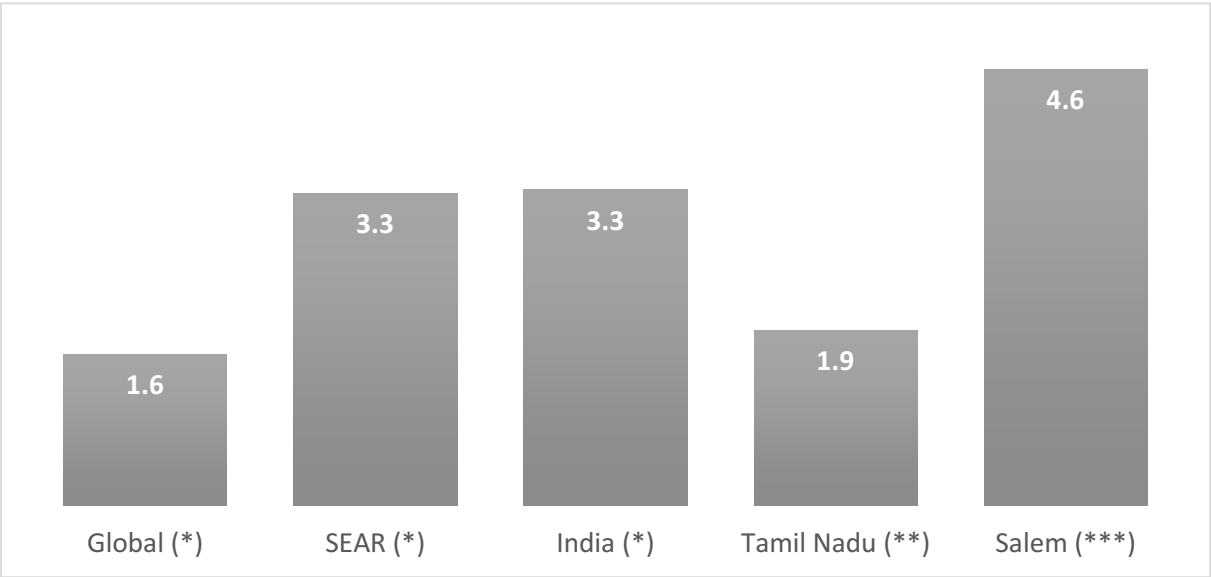
*Figure 5 – Absolute numbers of grade-2 disabilities amongst newly detected leprosy cases globally, in WHO's South-East Asia Region (SEAR), India, Tamil Nadu and Salem district*




*Data presented as per 31.12.2017; **Data presented as per 31.03.2018; *** Data presented as per 31.03.2016

Sources: (44,45,57)

*Figure 6 – Rate of grade-2 disabilities amongst newly detected leprosy cases (G2D-rate) per one Million inhabitants globally, in WHO's South-East Asia Region (SEAR), India, Tamil Nadu and Salem district*

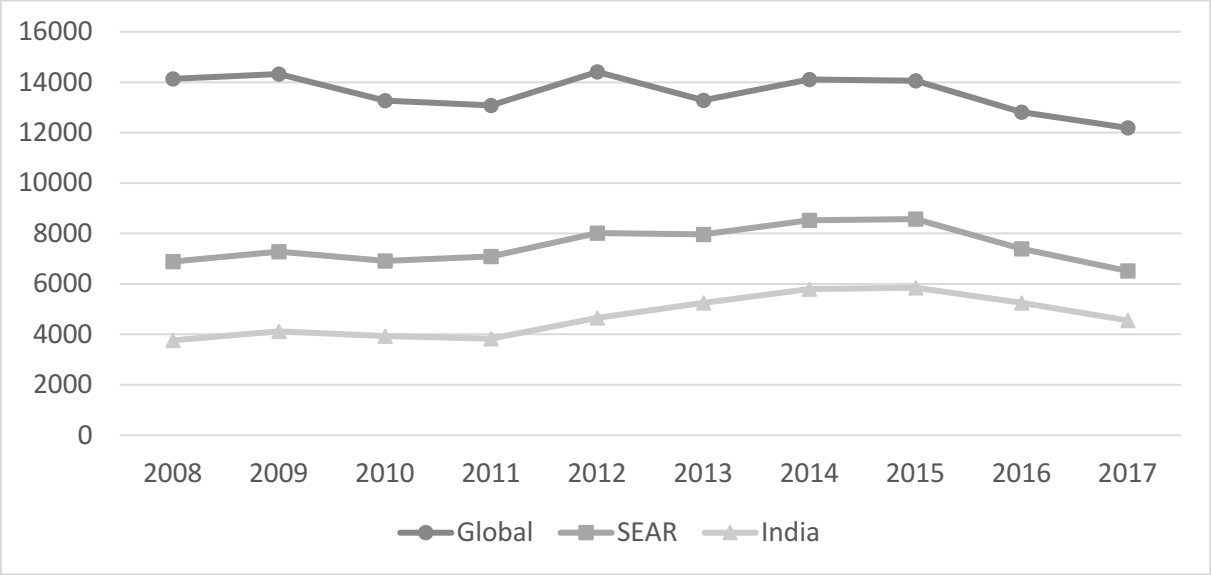



*Data presented as per 31.12.2017; **Data presented as per 31.03.2018; *** Data presented as per 31.03.2016

Sources: (44,45,57)

The annual new cases with grade-2 disabilities have decreased globally from 14 140 cases in 2008 to 12 189 in 2017 as depicted in Figure 7. In the SEAR as well as on a national level in India, the new caseload remained stagnant from 2008 to 2011, when an increase of new cases occurred annually until 2015, peaking in 8572 in the SEAR and 5851 cases in India respectively. The past two years saw a decrease of new G2D-cases on both levels of analysis.

*Figure 7 – Timeline of annual cases with grade-2 disabilities amongst newly detected leprosy cases globally, in WHO's South-East Asia Region (SEAR), and India, from 2008 to 2017*




Sources: (44,50)

## Epidemiological Features in India, Tamil Nadu and Salem District

As stated above, India globally accounts for almost 60% of newly diagnosed leprosy cases, and over four-fifths of WHO's SEAR new diagnoses.(44)

In the reporting period 2017/18 126 164 new cases were reported.(44) A minus of 9321 cases compared to 135 485 new cases in the reporting period 2016/17. In this period almost half of the cases (49.57%) were MB cases. Women accounted for 39.17% of new cases, and children for 8.7%.(58) In 2016 over one-third of India's newly detected cases were attributed to persons who were members of the scheduled tribe and scheduled caste.(59)

In order to be able to put India's leprosy situation since the introduction of MDT in perspective, a comparison of data from 1981 and data from 2016 is depicted in Table 3.(58,60)

*Table 3 – Comparison of leprosy Indicators in India and Tamil Nadu in 1981 and 2016*

| | Estimated number of leprosy patients in India | Estimated prevalence Rate per 10.000 in India | Estimated number of leprosy patients in Tamil Nadu | Estimated prevalence Rate per 10.000 in Tamil Nadu |
|---|---|---|---|---|
| **1981** | 3 919 337 | 57.2 | 733 000 | 151.4 |
| | **Number of leprosy patients in India** | **Prevalence rate per 10.000 in India** | **Number of leprosy patients in Tamil Nadu** | **Prevalence rate per 10.000 in Tamil Nadu** |
| **2016** | 90 709 | 0.67 | 3077 | 0.39 |

Sources: (45,60)

In the reporting period 2017/18 Tamil Nadu, the state in which the presented study was conducted, showed a PR of 0.39 per 10 000 and an ANCD rate of 5.36 per 100 000.(45)

Salem, the district in which the presented study was conducted, showed a PR of 0.32 per 10 000 as of March 2015, and an ANCD of 4.80 per 100 000 in the reporting period 2014/15.(61)

Disability-wise, India contributed 4552 G2D-cases in 2017, 69.89% of the SEARs case load (see Figure 5 & Figure 7). The national rate of 3.34 G2D per million (44) is over three-fold to the goal of less than 1 per 1 million as defined in WHO's 2016 strategy.(56) Tamil Nadu registered 148 new G2D-cases in 2016, showing a G2D-rate of 1.85 per million.(58) Salem, the district presented in this analysis, had 17 G2D-cases in 2015 and therefore a rate of 4.6 per million, which constitutes the highest G2D-rate out of all levels of analysis (see Figure 6).(57)

## Pathophysiological Processes

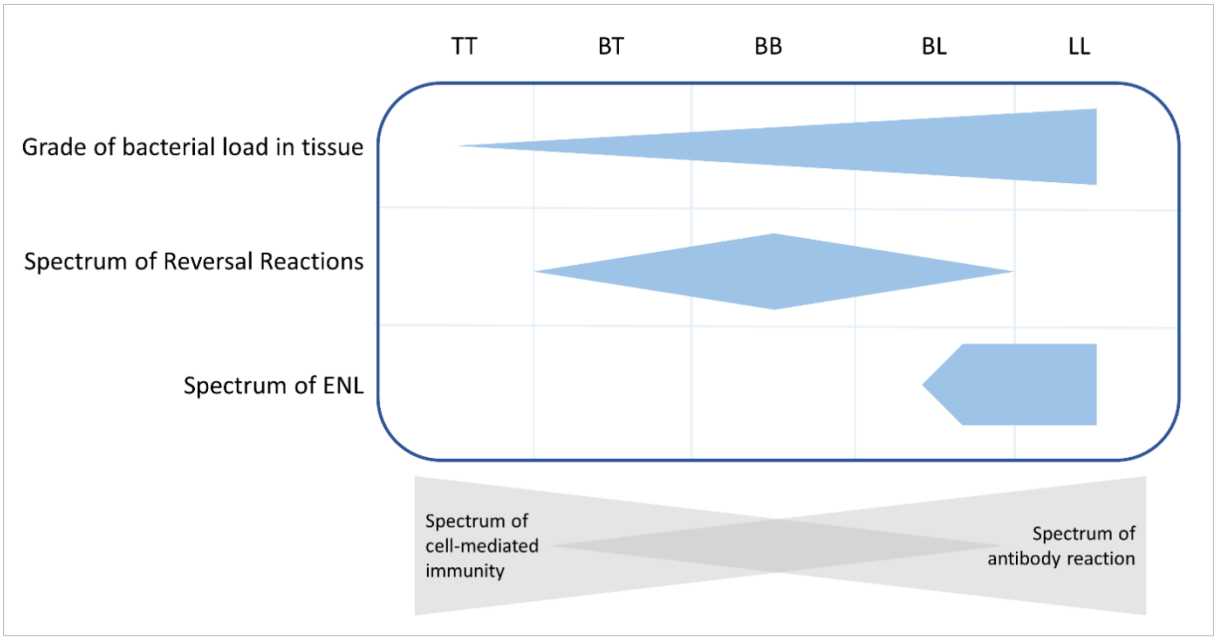
*M. leprae* is an obligate intracellular pathogen, which affects macrophages.(20) It differs from other *Mycobacteria* in its neurotropism, affecting Schwann cells in peripheral

nerves,(62) which in turn leads to their dedifferentiation into immature cells (63) and furthermore, to axonal dysfunction and demyelination causing sensory impairment, which is a key disease characteristic.(62,64) Keratinocytes, macrophages and histiocytes are the cell types affected in the skin accounting for the dermatological manifestation.(36,65)

Complications of leprosy include bacillary infiltration and spreading, nerve damage, and immunological reactions followed by disabilities and deformities.(66)

Nerve Functioning Impairment (NFI) generally results from the primary infection with *M. leprae*. NFI are aggravated by leprosy reactions, which are host-mediated immunological reactions to leprosy antigens, that can occur any time before, during or after the initiation of MDT treatment and affect about 30-50% of MB patients.(66–68) Leprosy reactions can be divided in Type 1 and Type 2 reactions and are the main determinant of leprosy-associated morbidity.(69,70) The affected nerves are mainly peripheral nerves. Exacerbations of these complications include recurrent reactions, which can be defined as chronic reactions if they occur at least three times within 12 months.(71,72) Immunological susceptibility according to Ridley-Jopling's classification of leprosy is depicted in Figure 8.

*Figure 8 - Spectrum of leprosy reactions in correlation to the classification of Ridley and Jopling.*




*TT – Tuberculoid leprosy; BT – Borderline tuberculoid leprosy; BB – Borderline leprosy; BL – Borderline lepromatous leprosy; LL – Lepromatous leprosy; ENL – Erythema Nodosum Leprosum*

Source: (68)

Borderline types of leprosy are the most prone to reactions, as their status can be described as immunologically unstable. “Upgrading” or Type 1 reactions thereby refer to an increase in cell-mediated immunity and a move towards the tuberculoid spectrum of the infection, whilst “downgrading” or Type 2 reactions comprise a loss of cell-mediated immunocompetence and increase in antibody response.(64)

Type 1 reactions (also called Reversal Reactions) occur in persons with borderline forms of leprosy (as seen in Figure 8) and present themselves with erythema and edema of the skin, tender and painful peripheral nerves and nerve function losses.(69) In the majority of cases these reactions occur in the first two months after the initiation of MDT treatment, when an intensification of cell-mediated immune response to *M. leprae* occurs. However, they can affect patients with all types of leprosy during all periods of the disease.(39,66,69,73,74) Around 30% of individuals with borderline infections are at risk for such reactions.(67,69) Type 1 reactions are understood to be “upgrading” immune responses to *M. leprae*.(39,66,69,73,74)

Type 2 reactions (also called Erythema Nodosum Leprosum - ENL) occur in persons with lepromatous (BL or LL) leprosy and can affect all tissues and organs other than the central nervous system.(70) ENL is thought to be caused by a deposition of immune complexes, clinically presenting with general symptoms like fever, malaise, lymphadenitis, uveitis, arthritis, dactylitis and/or orchitis.(66,68) Skin manifestations can range from painful and tender papules or nodules occurring in crops, to bullous ENL, showing lesions that can ulcerate. Nerves can be affected just as in Type 1 reactions. Joint tethering and fixation may occur through subcutaneous tissue involvement and affection of the autonomous nervous system.(68) Increased risk for type 2 reactions was found in persons with the lepromatous form of leprosy and a high bacterial index (≥3). Furthermore, women were more at risk, especially during hormonal changes (puberty, pregnancy, lactation). Also emotional and psychological stress possibly increases the risk.(71,72) Reduced risk was found in persons older than 40 years.(75) The onset of type 2 reactions is mainly acute, however especially type 2 reactions tend to become chronic reactions.(71,72) Borderline and Lepromatous cases are in 19% affected by this type of reaction.(75) Type 2 reactions are understood as "downgrading" reactions, as cell-mediated immunity decreases whilst antibody response increases.(64)

## Diagnosis of leprosy

The primary diagnosis of leprosy is based on the clinical assessment of suspicious skin lesions. Persons in endemic areas tend to know about the primary signs, complications and treatment of leprosy,(76,77) however, through stigmatization and discrimination of the affected persons, delayed diagnostic processes are common.(60,78) Most commonly, diagnosis is confirmed and classified according to the WHO’s classification (as shown in Table 4) as pauci- (PB) or multibacillary (MB) leprosy via slit-skin smear testing.(41)

*Table 4 – Comparison of WHO's and Ridley-Jopling's classification for the diagnosis of leprosy*

| **WHO** | **PB** | | **MB** | | |
|---|---|---|---|---|---|
| Dermatological Parameters | up to 5 hypopigmented/reddish skin patches with impaired sensibility | | more than 5 hypopigmented/reddish skin patches with impaired sensibility | | |
| Histological Parameters | no acid-fast bacilli | | acid-fast bacilli present | | |
| **Ridley Jopling** | **TT** | **BT** | **BB** | **BL** | **LL** |
| Clinical Parameters | localized disease with a singular hypopigmented and/or reddish skin patch with impaired sensibility | Numerous small skin lesions with deformities | Numerous skin lesions of various size and forms (maculae, papulae, plaques) | Large number of florid, asymmetric-al skin lesions | Generalized disease with various phenotypes, including: saddle-nose, loss of lateral aspects of eye-brows, gynaecomastia, testicular atrophy |
| Immunological Parameters | strongest immune response | | Immunologically unstable | | weakest immune response |
| Bacterial Index | 0 | 0 – 2+ | 2 – 5+ | 4 – 5+ | 5 – 6+ |
| **Disease Spectrum** | least severe form of disease | | | | most severe form of disease |

TT – Tuberculoid leprosy; BT – Borderline tuberculoid leprosy; BB – Borderline leprosy; BL – Borderline lepromatous leprosy; LL – Lepromatous leprosy

Sources: (41,79,80)

Paucibacillary leprosy shows up to 5 susceptible skin patches and no apparent acid-fast bacilli, whilst MB leprosy has more than 5 susceptible skin patches and/or the presence of acid-fast bacilli.(39) Current therapeutical guidelines are based on the WHO's scheme, which shows the advantage in its simple usability also in limited settings. However, this approach can both result in over- and under-diagnosis and therefore under- and over-treatment of leprosy.(81,82) Especially under-treatment could account for a number of relapses. A more accurate distinction, based on the

host's immune competency, can be made with Ridley-Joplings criteria, which can be established according to the clinical signs, histopathological features as well as the bacterial index.(79,80) It offers an estimate of the immune-competency and therefore the risk of leprosy reactions for each patient,(68) a distinction, which cannot very accurately be done with the WHO's scheme.(67,83) The Ridley-Joplings criteria classifies leprosy in five categories according to the immune response, or the least to the most severe disease form: Tuberculoid leprosy (TT), three Borderline forms and Lepromatous leprosy (LL) as depicted in Table 4.(79,80)

Besides these forms of leprosy, others exist outside this immunological spectrum. In "pure neuritic leprosy" (PNL) nerve trunks are affected but persons show no skin manifestations. "Indeterminate leprosy" (IND) shows hypopigmented maculae without clearly defined borders and only in some cases hyposensitivity. Especially for these cases, as well as for the differentiation between latent disease and active infection and also for case-confirmation in PB patients as well as for household-contact surveillance further diagnostic tools were developed.

Through the availability of comparative genomic analysis, the identification of *M. leprae*-specific genes, posing potential diagnostic tools such as serological tests on the peptide/protein level were identified and tested.(84,85) Limitations mainly arose out of the broad spectrum of inter-individual immune-response, with PB cases as well as cases with low/no bacterial count not being detected.(86) Nonetheless, rapid serologic tests for *M. leprae* antigens were developed and tested. A recent study comparing two serological tests using (i) antibodies against phenolic glycolipid-1 (PGL-1) and (ii) natural disaccharide octyl-leprosy IDRI diagnostic-1 (NDO-LID) however showed there limited capability in the diagnosis of especially PB leprosy cases as depicted in Table 5.(87)

*Table 5 – Diagnostic test values of PGL-1 and NDO-LID rapid serological tests for the diagnosis of leprosy*

| | | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|
| **PGL-1** | **PB** | 32.0% | 75.9% | 11.1% | 92.9% |
| | **MB** | 81.0% | 75.9% | 43.4% | 94.6% |
| **NDO-LID** | **PB** | 34.0% | 81.7% | 14.9% | 92.9% |
| | **MB** | 73.6% | 81.7% | 47.9% | 93.1% |

PGL-1 – phenolic glycolipid-1; NDO-LID – natural disaccharide octyl-leprosy IDRI diagnostic-1; PB – paucibacillary; MB – multibacillary; PPV – positive predictive value; NPV – negative predictive value

Table adapted according to (87)

Therefore, diagnostic approaches using Polymerase chain reaction (PCR) were established and their sensitivity and specificity enhanced by the introduction of real-time PCR. PCR analysis could be undertaken using various specimens and was found to be helpful in the diagnosis of cases with low bacterial load. Furthermore, PCR-based diagnosis proved helpful in the diagnosis of the “atypical” disease forms PNL and IND as mentioned above, with a sensitivity for disease forms with low bacterial loads of ~50-70%.(86,88,89) In a recent study using multiplex PCR compared to real-time PCR using *M. leprae*-specific DNA sequences the authors could show, that multiplex PCR showed significantly better results for detecting leprosy in multiple subgroups, including patients with IND and BT forms of the disease as well as persons with a negative bacterial index as depicted in Table 6.(90)

*Table 6 – Diagnostic test values of Real-time PCR and multiplex PCR for the diagnosis of certain leprosy subgroups*

| Leprosy subgroup | Diagnostic method | Positive | Negative | *p* |
|---|---|---|---|---|
| **IND** | RT-PCR | 58.5% | 41.4% | <0.05 |
| | Multiplex PCR | 75.6% | 24.3% | |
| **BT** | RT-PCR | 54.7% | 45.2% | <0.05 |
| | Multiplex PCR | 95.2% | 4.7% | |
| **BI = 0** | RT-PCR | 53.0% | 46.9% | <0.05 |
| | Multiplex PCR | 87.7% | 12.2% | |

IND – indeterminate leprosy; BT – Borderline tuberculoid leprosy; BI – bacterial index; rt-PCR – real time polymerase chain reaction

Table adapted according to (90)

Whilst the diagnosis of reactions due to leprosy is mainly based on clinical findings as mentioned above, the use of predictive biomarkers for reactions has been proposed and is currently being investigated. Studies hereby have shown, that RR and ENL showed differences in terms of their Interferon transcripts (91) as well as in their gene expression, suggesting innate factors regulating the immune-reaction to *M. leprae* antigens.(92) Interestingly, further studies elucidated CXCL10 as a potential biomarker for RR, and the nucleotide-binding oligomerization domain (NOD)-like receptor signaling pathway as a potential biomarker for ENL.(93) Furthermore, the complement and coagulation pathway was found to be enriched, with the increased deposition of C1q in skin lesions suggesting, that complement deposition may play an important role in leprosy reactions.(93) Based on these findings, decreased C4 levels as well as an increase in anti-LID-NDO antibodies at diagnosis were shown to be potential predictive markers of leprosy reactions.(94)

## Disabilities due to Leprosy

Complications of leprosy pose significant causes of disability and deformity, and therefore visibility of the disease, which creates branding and stigma, higher vulnerability for further complications associated with it and obligatory life-long care, which patients, as well as caregivers, have to approach comprehensively.(78,95,96)

As mentioned earlier, disabilities in leprosy are graded by WHO's leprosy disability grading system in grade zero, one and two, for each eye, hand and foot (see Table 2).(54) Generally, the WHO's maximum grading (which classifies the disability status of a person via their maximum scoring on any of the three testing sites), prevails in public health terms. However, the score of each site investigated, which results in an Eyes-Hands-Feet (EHF) score ranging from 0 to 12 points, is a potentially more sensitive tool to monitor disability-changes and hidden disabilities compared to the WHO's maximum grading.(97,98)

Epidemiological features of grade-2 disabilities at diagnosis were presented above. Global data regarding the rate of grade-1 disabilities at diagnosis (G1D) in leprosy, and the development of impairments is not available and only very limited information exists concerning the development of EHF-Scores during the lifespan of affected persons.(1) Saunderson *et al.* showed a correlation between episodes of neuropathy after diagnosis as well as a deterioration of disabilities and an increase of individual EHF scores in studies of the AMFES cohort, with a maximum follow-up period of 10 years.(99) The impairment status at MDT initiation was found to be the most important determinant for future impairment, and impairment dynamics were less favourable after release from treatment (RFT).(100) The Bangladesh Acute Nerve Damage Study showed, that the prevalence of nerve function impairments (NFI), defined as "clinically detectable impairment of motor, sensory or autonomic nerve function",(101) lies at 4.4% within PB patients, and 36% for MB cases in a time-period from registration up to two years after RFT. Two-thirds of acute NFI occurred after registration.(102) De Oliveira *et al.* showed that amongst patients without impairments at diagnosis, 5% of paucibacillary (PB) and 20% of multibacillary (MB) cases developed disabilities throughout the course of treatment. Within those showing grade-1 disabilities at diagnosis, 6% of PB cases, and 12% of MB cases deteriorated to grade-2 disabilities during treatment. The majority of both PB and MB cases remained on their respective disability grading from diagnosis until RFT.(83)

Measures to prevent injuries in anaesthetic limbs include wearing of proper shoes, with a hard and impenetrable sole and a soft foot-bed (e.g. Micro-cellular rubber). At the same time, they should be in line with local fashion trends, in order to reduce stigma, discrimination and increase the person's compliance in wearing them. Today, persons who are disabled through leprosy are taught to daily inspect all affected extremities, soak them in salt-water, scrap the callus, oil all affected extremities and dress wounds and ulcers. Additionally, affected persons are instructed to cook and drink with sheets covering hot surfaces and in case of lagophthalmos cover their eyes with sunglasses during the day and a wet towel at night.(103) Disregarding the importance of these preventive measures, affected persons state, that these instructions are highly unpractical, and pose a possibly distinguishable feature, which may lead to stigmatization.(104)

Reconstructive surgery poses the ultima ration for deformed extremities, which should include physiotherapy prior and after the intervention, as well as proper post-surgical management.(103)

## Social Determinants of Health

Generally, social determinants of health (SDH) are comprised of conditions of daily living and structural determinants of health. These encompass the conditions of work, leisure, homes and living spaces as well as the access to health care and education.(105) In other words SDH are all factors of health other than medical care[2].(106) Therefore, the WHO Commission on Social Determinants of Health (CSDH) defines SDH as "… the conditions in which people are born, grow, live, work, and age. … [These] are the consequences of … social policies and programmes, … economic arrangements, and … politics. Action on the social determinants of health must involve the whole of government, civil society and local communities, business, global fora, and international agencies. Policies and programmes must embrace all the

[2] In contrast to 'health care', the term 'medical care' is used in this context to refer to clinical services with appropriate structural and human resources.(106)

key sectors of society not just the health sector."(105) The goal of defining and working with the concept of SDH is to decrease health inequity,(9,105) which is "… caused by the unequal distribution of power, income, goods and services."(105)

In the conceptual framework of SDH, the CSDH includes a sequential approach to the development of health inequities, which categorizes:

- contextual factors, which include the sociopolitical context (e.g., the welfare state, public policies and programs, political institutions, educational opportunities and the labor market);
- structural mechanisms (e.g., rigid social hierarchies and social class division, that include hierarchies of power and access to resources), whereas the most important structural stratifiers are supposedly: Income, Education, Occupation, Social Class, Gender and Race/Ethnicity;
- and the individual's socioeconomic position, which is a resultant of the above two,
- and through intermediary determinants, such as the material resources (e.g., living and working conditions, food and nutrition, hygiene, etc.), behavior, biopsychosocial factors as well as the health system per se
- results in inequities in health and well-being. (see also Figure 9)

*Figure 9 – Adapted conceptual framework of inequities in health and well-being through social determinants of health*

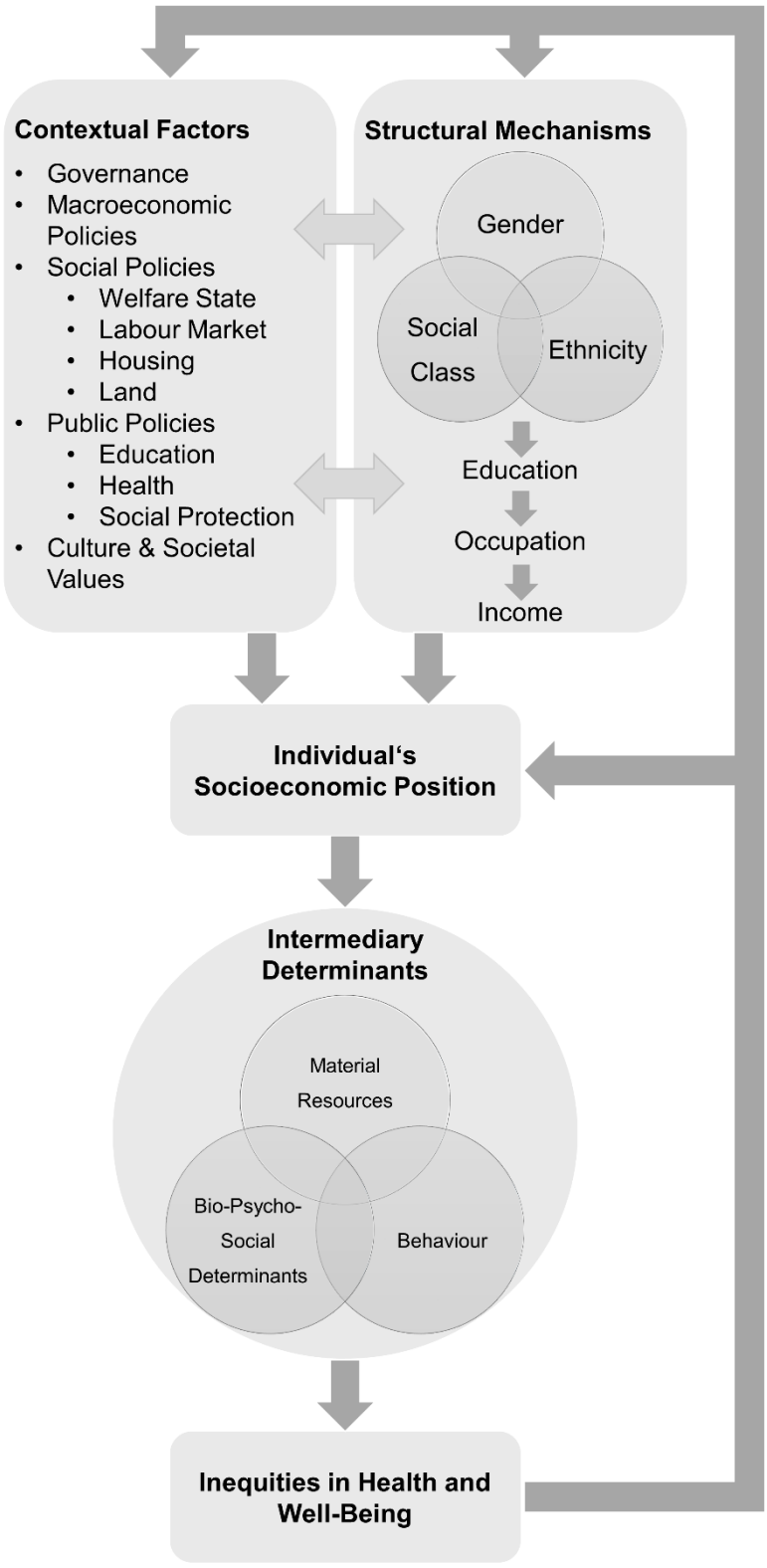



Figure adapted according to (9)

When elaborating the influence of SDH on the individual level the “model of the social production of disease” by Diderichsen et al. seems to be especially noteworthy. In this model, an individual is part of a society with one’s social position. The social position is the centerpiece for the production of health inequities. It leads to social stratification, which in turn leads to (i) differential exposure to health-damaging conditions, (ii) differential vulnerability concerning health condition and material resources, and (iii) determines differential consequences of disease and illness based on the individual’s position. The latter lead to differential health outcomes as well as economic and social consequences, which influences society and social policies.(107)

Engel’s biopsychosocial model furthermore incorporates the biological disease as well as psychological illness and influences on the social level into pathophysiological, diagnostic as well as therapeutic reflections.(108)

## History of Leprosy in India

Leprosy is one of the oldest diseases known to mankind with recordings available from ancient civilisations in Egypt, China and India. The oldest Hindu as well as Ayurvedic texts from 6 before Christ (BC) as well as the Bible refers to it. For as long as the disease has been known, discrimination accompanied it, which makes leprosy together with the HIV the “most stigmatised disease of all”.(2,60) Since the so called “lepers” (a discriminating term per se) were seen by society as contagious, in the course of the disease disfigured and therefore visible as well as distinguishable, and with traditional medicines incurable they were stripped of their rights and freedoms, dispelled from their respective homes, families and societies and branded as people afflicted. The disease was seen as a curse and divine punishment for past sins.(60,109)

Asvhatthaman: Legend of a Cursed Hero

By the middle of the first millennium BC the *Brahmins*, the most superior group of priests and scholars, controlled the northern part of the Indian subcontinent. The Vedas, as their oldest testament, where thereafter put into coexistence with the *Mahabharata*, supposedly being the greatest Indian epic, containing the Bhagavad-Gita and therefore the foundation of India's national religion – Hinduism. It came about in a time, in which new world-views gained momentum, and was extraordinarily not directed towards the *Brahmins* but rather for *Ksatriyas*, which were warriors and rulers, addressing ethical queries within the scope of violence, killing and *karma*. The *Mahabharata* can be said to be a standard scripture for Hindus and Indians alike, who will generally be able to outline the most central parts especially since Doordarshan, the Indian state television screened a 94-episode series of the tale in the 1980s.(110)

The story in brief, consists of a war between two lines of cousins, who rage over power and succession with several Hindu deities supporting either one or the other side of warriors. In the end both sides are exterminated and encounter each other in heaven.(110–112) In concern of the stigmatization of persons affected by leprosy one hero and villain of the *Mahabharata* is of interest. *Asvhatthaman*, a warrior of the *Kauravas* family-line, with a powerful jewel on his forehead is one of only three warriors of his family still alive after an 18-day war. Through the help of the god *Shiva*, he enters the camp of the *Pandavas*, the concurring cousin-line one night and kills every present soldier. As he is pursued by the remaining *Pandavas* after the massacre he releases a weapon out of this jewel, which devastates all wombs of *Pandava* women. For these two impious acts *Asvhatthaman* has to cut out his gem and is cursed by Lord *Krsna* himself.(110–112) "You shall wander this earth for 3000 years, … without companions, … for you shall have no place in human society, you vile and wicked man. Stinking of pus and blood, … you shall live … plagued by every disease."(110) In general perception, *Asvhatthaman* especially contracts leprosy, forming sores and ulcers that will never heal.(113) Even today, Indians connect *Asvhatthaman* with leprosy.

National Leprosy Programs

The approach of the Indian people as well as the Indian government towards persons affected by leprosy over the decades was by Navin Chawla[3] described as “benign neglect”.(60) The affected persons were physically as well as psychologically outcasted and discriminated, the only one taking care of them being voluntary institutions, which created colonies were thousands of ill were living together. Having the status of a divine punishment, it was Christian missionaries who initiated efforts in the caretaking of leprosy patients. In 1874 “The Leprosy Mission Trust India” (TLMTI) was founded, and “The Mission to Lepers”, a descending institution is still amongst the leading institutions in actions against leprosy today.(114) In the 20th century, multiple grand-scale non-governmental leprosy relief institutions were created in India. One being the “Gandhi Memorial Leprosy Foundation” (GMLF), which based its work on their namesake’s idea of eliminating leprosy as one item of his 18 Point Constructive Programmes (see Photograph 1).(115) In 1925 the “Indian Council of the British Empire Leprosy Relief Association”, which was later renamed to “Hindu Kusht Nivaran Sangh” was formed.(116) These and numerous other NGOs lay the foundation of government initiatives, which started by the appointment of an expert committee to evaluate the national situation in 1941. The GMLF’s method of Survey, Education and Treatment was adopted by the installed committee and in 1954 integrated into the newly created “National Leprosy Control Programme” (NLCP). Already prior to it, the First Leprosy Plan was put in action, through which 17.000 cases were detected from 1951 to 1956. It was the start of a number of national and international plans, which continue to tackle the spread of the disease up to today.(60,117)

[3] Nawin B. Chawla was a civil servant of the Indian Administrative Service and former Chief Election Commissioner. He was the founder of “The Lepra India Trust”. In 1986 he published the monograph entitled “The Vocational Rehabilitation and Social Reintegration of the Leprosy Affected in India”.

*Photograph 1 – Mahatma Gandhi's 18 Point Constructive Programmes as exhibited at the Gandhi Memorial Museum in Madurai, Tamil Nadu, India*


*Photographed by the author*

The medical regimen available at that time, which was introduced in the 1940s was based on dapsone, a sulfone active agent, which had to be taken over many years, sometimes up to a lifetime and to which *M. leprae* started to create resistance in single-use therapeutic regimens.(41) As mentioned earlier, current treatment is based on dapsone, rifampicin and clofazimine, the two latter drugs only being discovered in the early 1960s.(39,41)

In accordance to these developments the Indian government consecutively established a high-power committee to deal with the problem of leprosy in 1981 and in 1983 launched the National Leprosy Elimination Programme (NLEP) being the continuation of the NLCP as a centrally sponsored National Health Programme. The features of the latter were a decentralized functioning, being funded through state health societies but functioning under the National Rural Health Mission (NRHM).(60,117) The main focus

was set on highly qualitative and sustainable actions, prioritizing disability prevention and medical rehabilitation. The removal of stigma and discrimination was also included. Five basic activities were scheduled, being:

- Surveys and Case Detection
- Case Registration for Treatment
- Treatment Provision
- Patient, Family and Society Education regarding Leprosy
- Deformity-Correction through Care-after-Cure Programs

The inclusion of districts happened in a phased manner, with full-country coverage being achieved by the year 1996.(60,109)

It was the 44th World Health Assembly in 1991, which launched the biggest to that time, international initiative to eliminate leprosy at a global level by the year 2000 and defined elimination arbitrarily as a prevalence of one case per 10 000 persons.(118) To enhance this goal, the first phase of World Bank support to the NLEPs campaigns ran from 1993 to 2000 and made MDT available free-of-cost to all registered cases, with the support of the Nippon Foundation.(109) From 1998 to 2004 the NLEP introduced its modified leprosy elimination campaigns, which were held five times in that period. This was accompanied by the 2nd World Bank support from 2000 to 2004, during which the NLEPs activities were further decentralized and put under responsibility of the respective States and Union Territories. Additionally, leprosy services were integrated into the public health care system, ending the vertical approach. In December 2005 leprosy was declared eliminated as a public health problem on a national level in India.(60,109)

While the Government of India introduced its plan of elimination in 2005 and the NLEPs 11th Plan from 2007 to 2012, the WHO launched its “Global Strategy for Further Reducing the Leprosy Burden and Sustaining Leprosy Control Activities 2006-2010”. The goals within the latter were set to sustain services for leprosy patients even in the official state of elimination of the disease in public health terms and therefore in

monetary scarcity. The services were to be continuously integrated into the general health care systems, whilst sustaining quality of services. Underserved communities were to be reached and partnerships were to ensure the further reduction of the disease burden.(60,103,109,119) However, international as well as national focus shifted away from leprosy and new cases occurred. Incidence numbers even increased in the post-elimination era in so called “pockets” – hyperendemic areas, which led to an overall stagnation of the leprosy situation. To stop the complacency and increase political commitment the WHO together with the Nippon Foundation organized the International Leprosy Summit, in which representatives of 17 high-burden leprosy countries, amongst them India reaffirmed their commitment to eliminating leprosy by signing the Bangkok Declaration to achieve a leprosy-free-world.(120) The foundation of the declaration as well as the continuation of WHO’s programs, namely the “Enhanced Global Strategy to Further Reducing the Disease Burden Due to Leprosy 2011-2015” were mainly based on the concept created in the Eighth Report of the WHO Expert Committee on Leprosy, which was created in 2012.(39)

In 2016 the WHO launched its newest “Global Leprosy Strategy 2016-2020 – Accelerating towards a Leprosy-Free World”, which envisions a leprosy-free world and targets on (i) zero grade-2-Disabilities in pediatric patients, (ii) reduction of new leprosy patients with grade-2-disabilities to less than one case per one million persons and (iii) zero countries with legislations allowing discrimination against people affected by leprosy by 2020. The strategy is based on early detection, prompt treatment, social inclusion of affected persons, research enhancement, and extension of partnerships.(56)

## Stigmatization and Discrimination of Persons Affected by Leprosy

Stigma can be differentiated into public stigma, which is defined as a general or group-specific, negatively rated characteristic that in turn leads to social defamation and disadvantage. And on the other hand, self-stigma concerning the internalization of the social aspect.(121) Discrimination is defined as prejudice towards a group with certain characteristics, whereas these characteristics in turn become triggers of the

discriminatory process and can be described as enacted stigma, which restricts access to social structures and resources.(122)

Leprosy as a disease itself is stigmatizing through visible skin lesions, which can also be the source of discrimination. As stated above, complications make leprosy one of the most stigmatized diseases, leaving affected persons marked for life, oftentimes unable to work and therefore an outcast of society.(78) Furthermore, as complications may occur after completion of treatment and the assumed cure of the disease, patients are found to be confused concerning the definition of “cure”, and reluctant to seek medical care again.(64,68)

Today, leprosy is still seen as a curse and divine punishment as mentioned above. This results in a paradoxical utilisation of health services, which are not consulted at first signs of the disease because of the generally prevailing internalized stigma.(60,78,109) Factors contributing to higher perceived stigma amongst leprosy affected persons were found to be illiteracy, perceived economical inadequacy, change of occupation due to the disease, and lack of knowledge about leprosy and its treatment.(96)

Two population-groups rank amongst the most vulnerable of the affected persons: women and children.(123) Poverty, poor education, discriminatory laws and policies – in short their marginalised position, are the reason for their respective vulnerability. Two-thirds of the world’s illiterate are women,(124) who also make up the majority of poor and landless persons as well as the largest number of globally poor living on less than one US-Dollar a day.(125) Women with leprosy therefore experience discrimination because of their gender as well as their disabilities. A survey in Kolkata found that women delayed visiting medical care centers for diagnosis and/or follow-up, until their guardian/spouse felt it was necessary and possible besides their household-duties, which easily led to conflicts and demotivated them from seeking medical help. Furthermore, in the same study, the authors could show, that medical advice as not to walk long distances and not to work with hot utensils were perceived as not practical.(104)

## India's Legal Situation

Contrary to general conception of Indian laws, and also contrary to India signing the UN Resolution to End Discrimination Against People Affected by Leprosy,(126) laws discriminating persons affected by leprosy still partly exist on the statute books of India.(117,127) The far-reaching consequences of such laws directly and indirectly influence a country and its people. Persons affected by leprosy are officially, historically and culturally as well as out of knowledge-gaps, misunderstandings and partly irrational social dynamics discriminated, which contributes to the social stigma associated with the disease.(60) The National Law Commission of India in its 256th report in April 2015 denunciated Indian legislation and called for a remake of several laws,(117) which was partly enacted by the 2016 Repealing and Amending Act by the Indian Ministry of Law and Justice.(127)

The official legal perspective was originally represented in the installation of the Lepers Act of 1898. This law was based on the premise that people affected by leprosy would remain so for their entire life, which was true at that time due to a lack of medication. The act largely employs for:

- segregating beggars suffering from leprosy from unaffected persons
- disallowing leprosy patients from preparation, handling or selling of eatables, drinks, drugs and/or clothing
- forbidding leprosy patients from using public wells, tanks, taps, etc. for the purpose of bathing or washing
- restricting leprosy patients from working as barbers, cooks and domestic servants
- disallowing leprosy patients from using public vehicles and public transport
- debarring leprosy patients from inheriting ancestral properties.(128)

Further national Indian laws addressing the incurable lepers, discriminating them directly as well as indirectly and making social stigma and inclusion acceptable from a legislative to a societal point of view, were the Indian Divorce Act 1869, the Indian

Christian Marriage Act 1872, the Dissolution of Muslim Marriage Act 1939, the Special Marriage Act 1954, the Hindu Marriage Act 1955 and the Hindu Maintenance and Adoption Act 1956. Also, in 1956 the Life Insurance Cooperation Act was passed, which permits higher rates to be charged for persons affected by leprosy due to their supposedly higher mortality risk. More recent legislature includes the State Beggary Act, in which persons affected by leprosy are categorized together with lunatics. The Motor Vehicles Act 1988 and the Railways Act 1989, which deny people affected by leprosy the right to obtain a driving licence or to travel by railway.(117)

The Lepers Act, was repealed by the States of Gujarat, Assam, Nagaland, Meghalaya, West Bengal, Tamil Nadu, Tripura, Punjab, Karnataka, Orissa, Himachal Pradesh, and Maharashtra, and the Union Territories of Delhi, Andaman and Nicobar Islands, Lakshadweep, Dadra and Nagar Haveli and Chandigarh, but existed on the statute books of the nation until 2016, when it was fully repealed by the Indian Ministry of Law and Justice in May 2016.(117,127)

In the draft of a Sikh Marriage Act 2016 by MP Dr. Dharam Vira Gandhi every Sikh marriage should have the opportunity to be dissolved, when a spouse “has been suffering from a virulent and incurable form of leprosy”.(129)

India has signed the UN Resolution to End Discrimination Against People Affected by Leprosy, so “that persons affected by leprosy and their family members should be treated as individuals with dignity and are entitled to all basic human rights and fundamental freedoms under customary international law, relevant conventions and national constitutions and laws;” calling for governments to “take effective measures to eliminate any type of discrimination against persons affected by leprosy and their family members”.(126) However, drafts as the like of MP Dr. Dharam Vira Gandhi showcase the continuing gap in knowledge and the resulting discrimination persons affected by leprosy still face today. Besides the correction of official laws and regulations, awareness-campaigns disseminating knowledge regarding these changes and the up-to-date knowledge about leprosy have to continuously be carried out.

## India's Social Structure

In India the social structure divides society into classes. Backward classes comprise of Scheduled Tribes (ST), Scheduled Castes (SC), and Other Backward Classes (OBC). Backwardness is thereby defined by a lack of adequate opportunities for individual social, economic, and/or educational development.(130,131) Therefore, persons falling in these social categories can be defined as marginalized and disadvantaged.(130) The status of STs and SCs is constitutionally defined as communities that are scheduled according to Articles 341 and 342 of India's Constitution, respectively.(132–134) Articles 341 and 342 state that the president can, by public notification, specify the communities that are deemed as STs or SCs.(132) In contrast, it is the National Commission for Backward Classes Act, that governs OBCs, which are defined as any other backward class, other than ST and SC.(135) On a state-level in Tamil Nadu, OBCs are further divided into Backward Classes (BC) and Most Backward Classes (MBC).(136)

In 2016 the NLEP reported, that over one-third of India's newly detected cases were made-up of members of a ST or SC.(59) While OBCs and other lower parts of India's society were not explicitly depicted in the report, the correlation between social status, the pattern of transmission and infection, as well as the probability of successful treatment, is also in this case an important consideration.(1,4,137,138)

Noteworthy in this regard and demonstrating the strong social effects of leprosy are the attitudes of persons affected, as well as of the general public towards the disease. Whilst the aspects of stigmatization and discrimination of affected persons and recent regulatory approaches in India have been described above, it is their influence on the structural mechanism of health, which exhibits the practical implications of day-to-day living with the disease. Using standardized interviews, the authors of a study conducted in rural Tamil Nadu could show, that the mode of spread of leprosy was known by 91% of affected persons and 84% knew, that the condition is curable.(77) Of the family members of affected persons, 82% knew the mode of spread but only 64% thought that leprosy was curable. Moreover, 91% of patients stated, that they did not inform their

families straight after they received the diagnosis. Ninety-one percent of family members stated, that they would not eat food cooked by a person cured from leprosy and 73% said they would not share articles with the person affected. Whether persons affected by leprosy should be able to marry remained a controversial point also in this study, with 55% of interviewed family members stating they would not support it. Eighteen percent of family members openly stated, that persons affected by leprosy should not stay within the family.(77) A situation we found repeatedly during our field visits as depicted in Photograph 2.

*Photograph 2 – Separate housing of the leprosy affected person on the left (no electricity, open space, thatched roofing) and family members on the right (including electricity, brick wall and iron sheet roof)*

*Photographed by the author*

## Poverty in India

As defined by the World Bank Group, those who live in extreme poverty include people living on less than US$1.90 (€1.71 or 124.67INR) per day.(139,140) The Reserve Bank of India declared that 21.9% of Indian nationals lived below the poverty line in 2011-12.

This rate showed differences between the urban population (13.7%) and the rural population (25.7%) living in poverty.(141) The global multidimensional poverty index (MPI) is an index of poverty, using public national information to evaluate 10 indicators in the dimensions of (i) Health, (ii) Education, and (iii) Living standards. A person is considered to be poor if they are disadvantaged in at least one-third of the indicators. The report for India in 2018 shows that 27.5% of persons living in India are poor, and 8.6% are severely poor.(142) The four main contributing factors of poverty in India and their definitions are:

(i) **Cooking fuel** (25.8%)
"A household cooks with dung, agricultural crop, shrubs, wood, char-coal or coal."

(ii) **Sanitation** (24.2%)
"The household's sanitation facility is not improved (according to SDG guidelines) or it is improved but shared with other households. A household is considered to have access to improved sanitation if it has some type of flush toilet or latrine, or ventilated improved pit or composting toilet, provided that they are not shared. If country survey report uses other definitions of 'adequate' sanitation, we follow the survey report."

(iii) **Housing** (23.3%)
„The household has inadequate housing: the floor is of natural materials or the roof or walls are of natural or rudimentary material."

(iv) **Nutrition** (20.5%)
"Any person under 70 years of age for whom there is nutritional information is undernourished." (142)

In Tamil Nadu 11.28% of persons lived below the poverty line, according to the Reserve Bank of India. Again, differences were reported between the urban population (6.5%) and the rural population (15.8%) living in poverty.(141) The MPI report for India showed, that in Tamil Nadu 7.4% are poor, and 0.6% severely poor. The four main contributing factors to poverty in Tamil Nadu are (i) Nutrition, (ii) Years of schooling[4], (iii) Cooking fuel, and (iv) Housing.(142)

[4] "No household member aged 10 years or older has completed six years of schooling."(142)

The World Bank reported in 2012, that 43% of Scheduled Tribes live below the poverty line. Furthermore, 29% of Scheduled Castes and 21% of Other Backward Castes do so, whilst only 12% of persons in other classes are poor.(143)

## Structural Mechanisms as Risk Factors for Leprosy

Leprosy, as a neglected tropical disease (NTD) has been shown, to be a disease in which contextual factors, structural mechanisms and the individual's socioeconomic position correlates with the risk of transmission, infection as well as the probability to proceed to a successful cure.(3–8,10) As with other NTDs, leprosy therefore exhibits the interconnection between poverty, neglected populations and pathologies, and reflects health inequities within a population.(9,144)

A recent meta-analysis of contextual, structural and socioeconomic risk-markers for leprosy in high burden countries such as India found household contacts of leprosy patients, ≥5 persons residing in one household, male persons, persons who ever experienced food shortage in the past as well as persons performing manual labor at an increased risk of contracting leprosy, as depicted in Table 7.

*Table 7 – Structural mechanisms of social determinants of health associated with a higher risk of a leprosy infection in high-burden countries*

| Risk-Factor | RR | 95% CI |
|---|---|---|
| Household Contact with Leprosy Patient | 3.40 | 2.24 – 5.18 |
| Manual labor | 2.15 | 0.97 – 4.74 |
| Ever Food Shortage | 1.39 | 1.05 – 1.85 |
| ≥5 Residents in the Household | 1.38 | 1.14 – 1.67 |
| Male Sex | 1.33 | 1.06 – 1.67 |

RR – Relative Risk; CI – Confidence Interval

Table adapted according to (8)

Altogether marginalized persons can be defined as a focus group for the achievement of public health targets for leprosy, as it is their living conditions, motivation, and understanding that determine early reporting, treatment compliance, and the actions of

lifelong care.(1,137,138) With aspects of contextual factors concerning India's regulations towards persons affected by leprosy and structural mechanisms associated with a higher risk of a leprosy infection as presented it becomes obvious, that social determinants of health play a key role in the strive to eliminate leprosy. What however remains unclear is whether contextual factors, structural mechanisms, and/or the individual's socioeconomic position contribute most to the risk of infection with leprosy. Furthermore, persons with disabilities were generally shown to experience social and health-status disparities.(11–15) However, it remains unclear, whether a relationship between disabilities due to leprosy and social determinants of health exists.(1)

The objective of this study was to determine whether unequal structural mechanisms, a lower socioeconomic status and therefore inequities in social determinants of health correlate with higher severity of disabilities in persons affected by leprosy.(1)

# Patients and Methods

Both methods and results of the presented work have partially been published in (1), which has hereby been noted. Therefore, similarities to these works may occur both in form and content throughout preceding as well as subsequent parts of this work.

## Study Area

The present study was performed in Salem district, Tamil Nadu, India. The work was based on a long-lasting cooperation between the Doctor Typhagne Memorial Charitable (DTMC) Trust, Salem, Tamil Nadu, India and the Medical University of Graz, Austria.(1)

## Study Population

The inclusion criteria comprised of leprosy-affected persons from Salem district who were part of the DTMC Trust lifelong-care program. A completed leprosy multidrug-therapy (MDT) treatment regimen or a negative slit-skin smear result in those with dapsone-only treatment before the introduction of MDT was necessary. Additionally, disabilities due to leprosy of grade-1 or higher had to be present on eyes, hands and/or the feet in order to be recorded. Participants were required to be aged 18 years or older, and geographical reachability as well as personal presence given.(1)

## Data Collection

An extension of the local register regarding lifelong-care for disabled persons due to leprosy was conducted in October and November 2016, in Salem, Tamil Nadu, India. This enhanced the range of structural mechanisms and the individual's socioeconomic status among participants. From November 1$^{st}$ 2016 to October 31$^{st}$ 2017, persons meeting all inclusion criteria were added to the updated register during routinely conducted annual follow-up visits through medical staff of the DTMC Trust. The survey for each patient consisted of demographic, economic, household and disability

parameters. Participants were categorized by social class as per national and state-wise classifications.(145–147) Furthermore, the participant's status regarding a monthly Deformity Pension (DP) through the Indian National Government comprising 1000 INR (15.24 USD or 13.71€) per month was followed-up. Status of the household was also included, which consisted of ownership status, the number of persons living together, and the size of their respective living spaces. Deformity history was obtained and disabilities evaluated according to Brandsma's Operational Guidelines of WHO's disabilities grading for eyes, hands and feet, as presented in Table 2.(54) Participants were inspected and tested, which included eye-lid strength testing and vision testing at a distance of six-meters. Sensory impairment of the acre was tested with a ballpoint-pen. The following testing sites were used for the hands: distal pulp of digit V and hypothenar eminence, distal pulp of digits I and II, as well as thenar eminence. Testing sites of the feet included: digit I, 1$^{st}$ and 5$^{th}$ metatarsal head and the mid-lateral border of the foot. The Eyes-Hands-Feet (EHF) sum-score was then calculated for the individual impairment for each eye, hand and foot (each of the six features received a grading from between zero and two, resulting in a maximum grade of 12 points).(1)

## Data Analysis

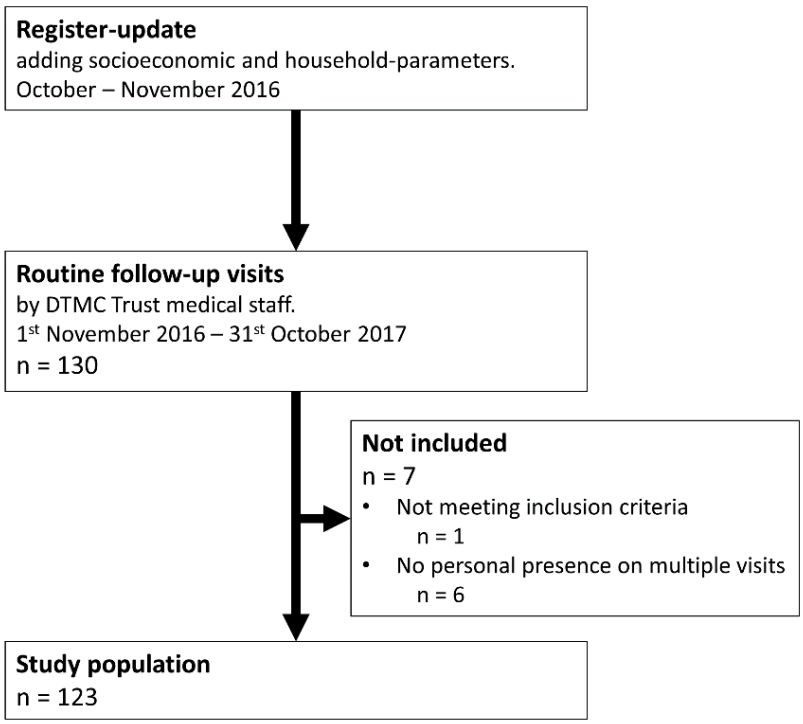
Normal distribution of the data was verified with the Kolmogorov–Smirnov test. Patient characteristics of the study population are presented as descriptive statistics. Significant predictors were determined via stepwise multiple linear regression analysis, with the EHF score as the dependent variable, and the following as explanatory variables: Gender, age, time after release from treatment, monthly income, and living space. Analysis of variance (ANOVA) was used to determine the statistical significance of F values. The level of significance was set at an alpha value of $p = 0.05$. The software package used was IBM® SPSS® Statistics V25.0 (New York, NY, USA).(1)

The currency exchange conversions used in this study were taken from the International Monetary Fund's Online Exchange Rate Wizard, and represent average exchange rates from November 1$^{st}$ 2016 to 31$^{st}$ October 2017.(1)

## Ethical Considerations

Approval for the study and the presented methodology was granted by the ethical review committee of the Medical University of Graz, Austria (29–578 ex 16/17). Informed consent was obtained from all study participants in written form if they were literate, otherwise orally after direct translation to the local language and documentation of their approval via fingerprint. All study participants were reassured that nonparticipation would not affect their care.(1)

*Figure 10 - Flow diagram of study conduction and included leprosy affected persons from the updated register of the DTMC Trust.*




Source: (1)

Further information is available in Supplementary Table 1.

## Funding

This research received no external funding.

# Results

## Demographical Data

A total of 123 patients were included into the study, with 41/123 (33.33%) women and 82/123 (66.67%) men. The age ranged from 27 to 95 years, with a mean of 65 years.(1) Table 8 summarizes the demographical information.

*Table 8 – Demographical information of study participants in Salem district, Tamil Nadu, India*

| | | Female | | Male | | Total | |
|---|---|---|---|---|---|---|---|
| **Study participants** | | 41 | *33.33%* | 82 | *66.67%* | 123 | *100.00%* |
| **Mean Age** | years | 63 | | 66 | | 65 | |
| **Social Class** | | | | | | | |
| Scheduled Tribe | | 2 | *4.88%* | 8 | *9.76%* | 10 | *8.13%* |
| Scheduled Caste | | 13 | *31.71%* | 25 | *30.49%* | 38 | *30.89%* |
| Most Backward Caste | | 20 | *48.78%* | 32 | *39.02%* | 52 | *42.28%* |
| Backward Caste | | 6 | *14.63%* | 17 | *20.73%* | 23 | *18.70%* |
| Forward Caste | | 0 | *0.00%* | 0 | *0.00%* | 0 | *0.00%* |
| **Literacy** | | | | | | | |
| Literate | | 4 | *9.76%* | 19 | *23.17%* | 23 | *18.70%* |
| Illiterate | | 37 | *90.24%* | 63 | *76.83%* | 100 | *81.30%* |

Source: (1)

The number of persons stating to be married was 85/123 (69.11%). However, one-fifth of the latter, or 17/123 (13.82%) were found to be living by themselves − only 55.28% of participants (n=68) shared a home with their spouse. Of the remaining participants, 19/123 (15.45%) declared themselves unmarried, and 19/123 (15.45%) were widowed.(1)

## Economic Situation

The average monthly income of the total study population was 1252 INR, which is equivalent to 17.16 Euro (€) or 19.08 US dollar (USD) as depicted in Table 9. For the 68 participants living with their spouses, the average income was 1434 INR per month. Their partners had an average income of 740 INR over the same period, resulting in a monthly household total of 2174 INR. The participants' average monthly income was enabled mainly through the provision of the Deformity Pension through the Indian National Government, comprising 1000 INR (13.71€ or 15.24 USD) per month, which 81.30% (100/123) of the participants received. 92/123 participants (74.80%), and 29/47 (61.70%) below the age of 65 years indicated that they were unemployed. Of the participants who were employed, 18/31 (58.06%) depended on seasonal day-work, 11/31 (35.48%) were self-employed, whilst 2/31 (6.45%) had a permanent position. The average monthly income for employed study-participants was 1782 INR (24.43€ or 27.16 US$).(1)

*Table 9 – Economic information of study participants in Salem district, Tamil Nadu, India*

| | | Female | | Male | | Total | |
|---|---|---|---|---|---|---|---|
| **Average monthly income** | INR | 1444.88 | *[0 - 15000]* | 1156.10 | *[0 - 6800]* | 1252.36 | *[0 - 15000]* |
| <1000 INR | | 3 | *7.32%* | 8 | *9.76%* | 11 | *8.94%* |
| 1000 INR | | 31 | *75.61%* | 61 | *74.39%* | 92 | *74.80%* |
| >1000 INR | | 7 | *17.07%* | 13 | *15.85%* | 20 | *16.26%* |
| **Employment Status** | | | | | | | |
| Unemployed | | 29 | *70.73%* | 63 | *76.83%* | 92 | *74.80%* |
| Working | | 12 | *29.27%* | 19 | *23.17%* | 31 | *25.20%* |

Source: (1)

## Household Situation

Most participants (74.80%) were living in their own house, while 3/123 (2.44%) were homeless as shown in Table 10. Living spaces were 28.68m$^2$ on average and ranged from 4 to 140m$^2$ (excluding homeless participants). The number of people per

household ranged from between one and nine persons, resulting in an average living space of 12.2m$^2$ per person.(1)

*Table 10 – Household information of study participants in Salem district, Tamil Nadu, India*

| | Female | | Male | | Total | |
|---|---|---|---|---|---|---|
| **n** | **41** | | **82** | | **123** | |
| **Household Ownership Situation** | | | | | | |
| Own House | 29 | 70.73% | 63 | 76.83% | 92 | 74.80% |
| With Family Members | 2 | 4.88% | 8 | 9.76% | 10 | 8.13% |
| Renting | 4 | 9.76% | 3 | 3.66% | 7 | 5.69% |
| Government Leprosy Home | 6 | 14.63% | 5 | 6.10% | 11 | 8.94% |
| Homeless | 0 | 0.00% | 3 | 3.66% | 3 | 2.44% |
| **Roof Type*** | | | | | | |
| Concrete | 4 | 9.76% | 12 | 15.19% | 16 | 13.33% |
| Corrugated Sheet | 7 | 17.07% | 14 | 17.72% | 21 | 17.50% |
| Thatched | 10 | 24.39% | 23 | 29.11% | 33 | 27.50% |
| Tiled | 20 | 48.78% | 30 | 37.97% | 50 | 41.67% |

* Excluding homeless persons (n = 120)
Source: (1)

One-hundred and twenty out of one-hundred and twenty-three (97.56%) participants had no water source inside their house. The average distance to the next water source was 25.09m as depicted in Table 11. There were 91/123 (73.98%) regularly defecating in the open, with the average distance to these locations being 121.55m. Cooking was carried out by 62/123 (50.41%) over open fire, 51/123 (41.46%) were using gas stoves, and 2/123 (1.63%) persons had electric stoves. 8/123 (6.50%) persons did not cook themselves but had access to a central food dispensary. The average distance to kitchens and food dispensaries was 19.04m, whilst distances to work or social activities added up to 343.08m on average.(1)

*Table 11 – Average walking distance to places of daily interest presented based on an EHF score threshold at 7 points*

| EHF Score | | <7 | | ≥7 | | Total | |
|---|---|---|---|---|---|---|---|
| | n | 47 | 38.21% | 76 | 61.79% | 123 | 100% |
| **Average walking distance to** | | | | | | | |
| Water source | m | 37.57 | | 17.37 | | 25.09 | |
| Toilet | m | 116.06 | | 124.95 | | 121.55 | |
| Kitchen or Food Dispensary | m | 4.17 | | 28.24 | | 19.04 | |
| Work or Social Activities | m | 399.45 | | 308.22 | | 343.08 | |

EHF Score – Eyes-Hands-Feet Score; m - metres
Source: (1)

## Disabilities

Disability-scores of the study population based on WHO's maximum grading are presented in Table 12. Forty of one-hundred and twenty-three (32.53%) participants currently had at least one ulcer, automatically resulting in a grade-2 disability on the respective hand or foot.(1)

*Table 12 – Disability information of study participants in Salem district, Tamil Nadu, India*

| | Female | | Male | | Total | |
|---|---|---|---|---|---|---|
| **Disabilities Eyes** | | | | | | |
| Grade-0 | 35 | *85.37%* | 60 | *73.17%* | 100 | *81.30%* |
| Grade-1 | 0 | *0.00%* | 0 | *0.00%* | 0 | *0.00%* |
| Grade-2 | 6 | *14.63%* | 17 | *20.73%* | 23 | *18.70%* |
| **Disabilities Hands** | | | | | | |
| Grade-0 | 3 | *7.32%* | 7 | *8.54%* | 10 | *8.13%* |
| Grade-1 | 0 | *0.00%* | 7 | *8.54%* | 7 | *5.69%* |
| Grade-2 | 38 | *92.68%* | 68 | *82.93%* | 106 | *86.18%* |
| **Disabilities Feet** | | | | | | |
| Grade-0 | 0 | *0.00%* | 2 | *2.44%* | 2 | *1.63%* |
| Grade-1 | 11 | *26.83%* | 11 | *13.41%* | 22 | *17.89%* |
| Grade-2 | 30 | *73.17%* | 69 | *84.15%* | 99 | *80.49%* |

Source: (1)

Furthermore, site-specific grading showed that the majority had grade-2 disabilities on both hands or both feet, and that 51.22% had grade-2 disabilities on both hands and both feet as depicted in Table 13.(1)

*Table 13 – Detailed disability information of study participants affected by leprosy presented based on an income threshold at 1000 INR per month*

| | | ≤1000 INR/M | | >1000 INR/M | | Total | |
|---|---|---|---|---|---|---|---|
| **n** | | 103 | *83.74%* | 20 | *16.26%* | 123 | *100.00%* |
| **Disabilities Eyes** | Grade-2 both sides | 10 | *9.71%* | 0 | *0.00%* | 10 | *8.13%* |
| **Disabilities Hands** | Grade-2 both sides | 71 | *68.93%* | 8 | *40.00%* | 79 | *64.23%* |
| **Disabilities Feet** | Grade-2 both sides | 69 | *66.99%* | 7 | *35.00%* | 76 | *61.79%* |
| **Combined Disabilities** | | | | | | | |
| Grade-2 on both Eyes & Hands | | 8 | *7.77%* | 0 | *0.00%* | 8 | *6.50%* |
| Grade-2 on both Eyes & Feet | | 9 | *8.74%* | 0 | *0.00%* | 9 | *7.32%* |
| Grade-2 on both Hands & Feet | | 59 | *57.28%* | 4 | *20.00%* | 63 | *51.22%* |
| Grade-2 on both Eyes, Hands & Feet | | 8 | *7.77%* | 0 | *0.00%* | 8 | *6.50%* |
| **Average EHF Score** (95% CI) | | 7.398 (6.984 – 7.813) | | 5.050 (3.840 – 6.260) | | 7.016 (6.595 – 7,437) | |
| **EHF Score** | <7 | 33 | *32.04%* | 14 | *70.00%* | 47 | *38.21%* |
| | ≥7 | 70 | *67.96%* | 6 | *30.00%* | 76 | *61.79%* |

Detailed disability grading of study participants stratified according to income. Relative Ratios are related to the respective subgroup including a detailed view on the disabilities of each pair of interest - eyes, hands and feet and quantities of combined grade-2 disabilities. EHF score averages as well as stratification with a cut-off at 7 included. INR/M – Indian rupee per month; EHF score – Eyes-Hands-Feet score; CI – Confidence Interval

Source: (1)

## Regression Analysis

Stepwise multiple linear regression analysis built a significant model, where $F(2, 120) = 13.960$, $p \leq 0.001$, effect size (Cohen's f2) = 0.81, explaining 18.9% of the variance in EHF scores ($R2 = 0.189$). The adjusted R2 was found to be equal to 0.175.

Analysis of variance inflation factors (VIFs) did not demonstrate multicollinearity between factors, as depicted in Table 14. No violations of linearity were detected.(1)

*Table 14 – Independent variables of regression analysis with Eyes-Hands-Feet (EHF) score as dependent variable in study participants disabled through leprosy*

| Dependent Variable | Independent variables | | Collinearity | |
|---|---|---|---|---|
| | beta | P | VIF | Tolerance |
| Gender (0 female, 1 male) | -0.009 | 0.912 | 1.033 | 0.968 |
| Age | 0.340 | <0.001 | 1.000 | 1.000 |
| Time after RFT (years) | 0.118 | 0.174 | 1.109 | 0.902 |
| Income (INR/M) | -0.078 | 0.360 | 1.060 | 0.944 |
| Living space ($qm^2$) | -0.276 | 0.001 | 1.000 | 1.000 |

VIF – Variance inflation factors; RFT – release from treatment; INR/M – Indian rupee per month

Source: (1)

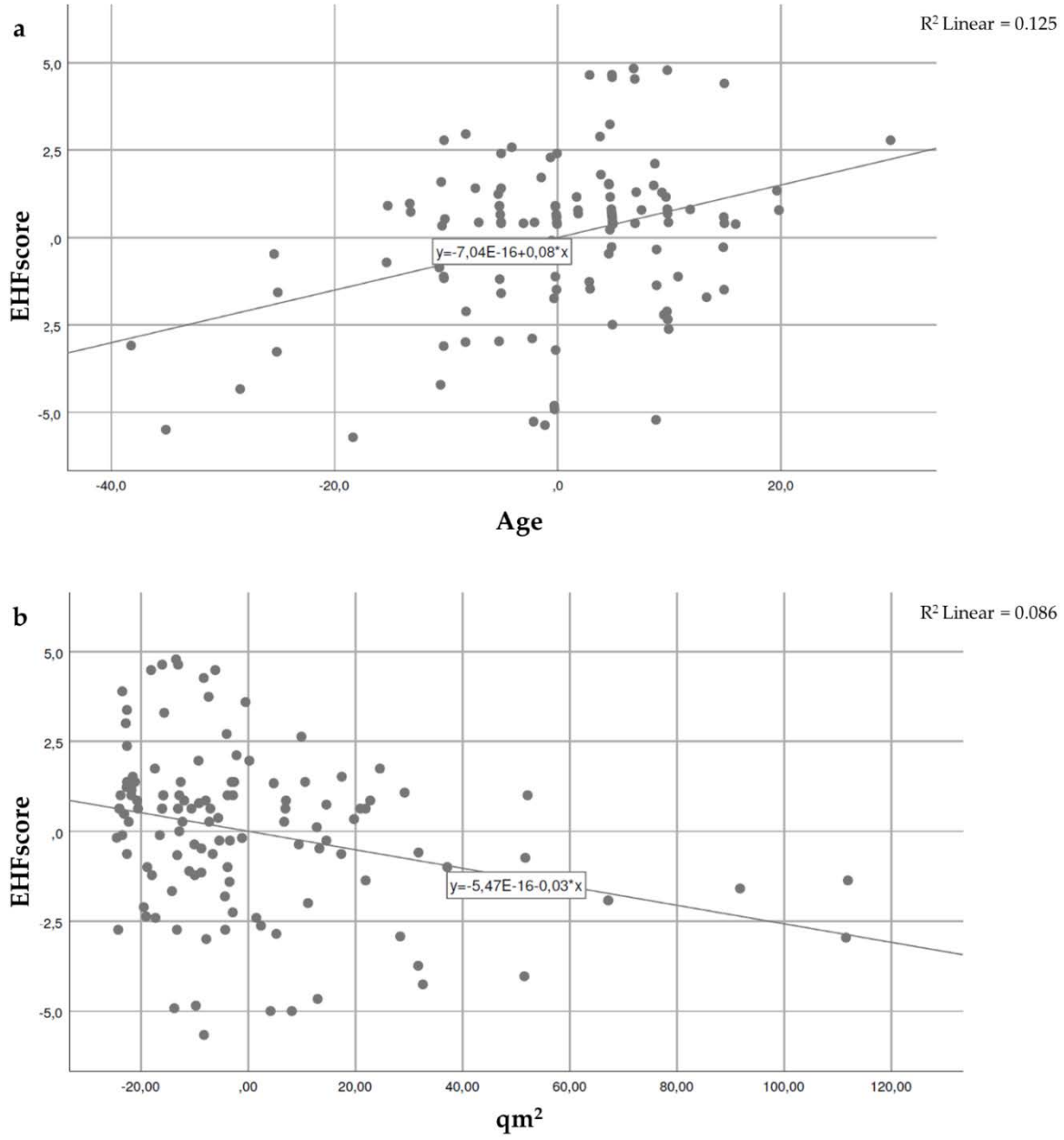
Significant predictors of a higher EHF score in persons affected by leprosy were found to be higher age (Figure 11a) as well as less living space (Figure 11b), as shown in Table 15.(1)

*Table 15* – Multiple linear regression analysis of factors significantly associated with EHF scores in leprosy-affected study participants

| Significant predictors | Standardized Beta | 95% CI | | *P* |
|---|---|---|---|---|
| | | Lower | Upper | |
| Age | 0.340 | 0.039 | 0.111 | <0.001 |
| Living space | –0.276 | –0.041 | –0.011 | 0.001 |

Source: (1)

*Figure 11 – Linear regression plots to depict the relationship between the EHF score, a) age, and b) living space in leprosy affected study participants*




EHFscore – Eyes-Hands-Feet Score; $qm^2$ – square metres

Source: (1)

Generally, women (6.976, 95% CI, 6.396 to 7.555) had a slightly lower average EHF score than men (7.073, 95% CI, 6.468 to 7.605); however, gender was excluded as a non-significant predictive variable for the EHF score (beta = 0.009; p = 0.912).

Nevertheless, more men showed an EHF score above nine (14.63%) than women (7.32%).(1)

Monthly income showed significant negative correlation in Pearson's correlation (-0.076, p = 0.026). However, it was excluded as a non-significant predictive variable (beta = -0.078; p = 0.360).(1)

Data stratification according to the time since RFT saw limitations due to a lack in exact monitoring prior to MDT regimens. Therefore, patients with no record (n = 27) were included with 1988 as the completion year. This assumption was made based on the introduction of MDTs in 1986 in Tamil Nadu, with the longest regular therapeutic regimen taking one year. When MDT was introduced, all of these patients had to either provide a negative slit-skin smear or were provided with a 12-month course of MDT before RFT. Time since RFT showed a significant positive correlation in Pearson's correlation (0.199; p = 0.014). However, it was excluded as a non-significant predictive variable for the EHF score (beta = 0.118; p = 0.174).(1)

# Discussion

Leprosy can be considered a disease, in which social determinants of health determine the risk of transmission and infection, as well as the probability of proceeding to a successful cure.(3,5,6,8,60,137,138) Belonging to the NTDs it is therefore consistent in terms of the interconnectivity of poverty and neglected populations as the most vulnerable for NTDs.(144) In this cross-sectional study, which included persons affected by leprosy who were RFT, showed disabilities due to *M. leprae* and were part of a lifelong care program of a nongovernmental institution in the district of Salem, Tamil Nadu, we undertook descriptive as well as multiple stepwise linear regression analyses to provide information about the socioeconomic status, structural characteristics, and the disability status of the affected persons.(1)

We included one-third female and two-thirds male study participants, which is coherent with the commonly reported gender distribution of leprosy.(148) The demographical information of our study population furthermore shows mainly illiterate and therefore poorly educated affected persons, a common result in study populations concerning leprosy.(8) The high rate of illiterate participants stresses the demand for increased visual information rather than written guidance.(1) Moreover, social class distribution seems especially noteworthy, as all study participants belonged either to SCs, STs, or OBCs, constituting the lowest parts of India's social hierarchy, and none was a member of the forward classes.(1) In its annual reports the NLEP highlights new cases in persons belonging to the SCs and STs. In the reporting period of 2015-2016, these two classes made up more than one-third (37.36%) of the national annual new caseload. In Tamil Nadu 21.99% of new cases were found in persons from SCs and STs.(59) Therefore, these persons, together with those belonging to OBCs, which were not explicitly reported, can be prioritized as those who require particular focus concerning the risk of transmission and infection, therapeutic compliance and disability prevention as well as care. The social status of persons affected by leprosy is represented in our results on the marriage status of the study participants. Just over half of the participants were married and living with their spouse, whilst around one-third either declared

themselves married, however lived by themselves, or were unmarried. In a society in which marriage possesses a high relevance, it demonstrates the ambivalent social acceptance of persons affected by leprosy, as reported by Stephen et al.(77)

Our study population lived well below the line of extreme poverty as defined by the World Bank as being less than US$1.90 (€1.71 or 124,67INR) per day.(139,140) Of the surveyed persons, the average lived with US$0.63 (€0.56), and employed study participants with US$0.89 (€0.80) per day.(1) It has to be noted, that the employed study participants majorly depended on external factors as adequate climate conditions, e.g., for agricultural work, and employer goodwill or nescience regarding their health status, as only two participants had a permanent position.(1) In terms of the MPI criteria for poverty, our population generally showed disadvantages in all three dimensions. Especially in terms of living standards, our study population showed deprivation in the means of (i) Cooking fuel, (ii) Sanitation, and (iii) Housing. This displays the deprived economic situation, and the extreme poverty in which persons affected by leprosy and especially those unemployed live in today. Governmental support is present, showcased in the high number of deformity-pension recipients.(1) However, it was found, that out-of-pocket health expenditure was increased in disabled persons with low income.(149) Furthermore, leprosy affected person's spending in primary care services was linked to the strength of public health services by Tiwari et al. recently.(150) Even though our results showed a monthly income that was excluded as a non-significant predictive variable for higher disabilities, the above-mentioned results stress the need for a continued comprehensive approach to enhance the structural, financial, and more generally socioeconomic position of persons affected by leprosy, as for example with social and work reintegration measures.(1)

The household situation in our study population showed low housing standard, yet generally a high ratio of persons owning their property and having a durable roof, with 55% having either a tiled or cement roof.(1) However, when taking into account the U.S. Department of Housing and Urban Development's proposal of an overcrowding cut-off at 165 square feet (equaling 15.33 $m^2$) average living space per person (151),

91/123 (73.98%) of our study participants lived below that, showcased in the average living space of 12.2m$^2$ within the total study population. Furthermore, the vast majority of study participants had no water source inside their home, with an average walking distance of more than 50 metres for each time fetching water. More than two-thirds of study participants were defecating in the open, with an average distance of over 120 metres to the respective location.(1) Open defecation is a culturally deeply-rooted habit within Indian people's habits, which poses hygienic issues.(152) Furthermore, in a population with potentially anaesthetic and/or ulcers on their feet due to leprosy, further problems of injury and wound infection occur. These considerations are also valid in persons cooking over open fire, as over half of our study participants do. Wood is collected mainly with bare hands, which in persons affected by leprosy may be anaesthetic and/or show ulcers. The longest distances were covered by persons affected by leprosy to participate in work and/or social activities.(1) However, it remains unclear, whether the correct strategy in preventing wounds in persons affected by leprosy comprises of (i) minimizing these activities, which would mean isolation and an even more difficult social reintegration; or (ii) protection as for example through Micro-Cellular Rubber shoes, which protect the feet and offer an adaptive anatomical insole, yet may function as an obvious sign of leprosy which might provoke discrimination and stigmatization; or (iii) no special measures at all.(153,154)

Our study population showed advanced disabilities and disfigurements due to leprosy, especially on their hands and feet. The average EHF score of 7.016 in the higher half of the scoring system, and 12.20% showed an EHF score over nine. More than half showed grade-2 disabilities on both hands and feet. The rate of disabilities on the eyes was much lower, however this can be explained with a much more delicate disability classification in a population with generally poor eyesight analysis and vision adjustment.(1) These results are generally in accordance with earlier reports of the Salem region.(155) In accordance with these results the current rate of G2D especially in Salem, showing the highest rate of all levels analysed (see Figure 6) urges further measures to reduce these incurable conditions.(1,44,45,57)

In our regression analysis we could identify two significant predictors of higher EHF scores in our study population of persons affected by leprosy, namely (i) higher age and (Figure 11a) (ii) less living space (Figure 11b). In our exploratory study, these variables built a highly-significant linear regression model, showing an acceptable yet rather weak effect size ($R^2$ = 0.189 and $R^2$ adjusted = 0.175) without multicollinearity (Table 14).(1) Whether disabilities and EHF scores due to leprosy are progressing throughout the life of an affected person has not been thoroughly investigated as presented in the introduction. In order to control for effects of disability dynamics we included time after RFT as a second variable besides the significant predictor of higher age (Figure 11a). As disease and disability-development prior to the introduction to MDT remains unclear, the presented grouping with its limitations as presented above was chosen. However, no significant correlation to higher EHF scores could be found with a longer period since RFT as depicted in Table 14. Income as well as gender were both excluded as significant predictors of higher EHF scores in our analysis.(1)

In accordance with the presented *Adapted conceptual framework of inequities in health and well-being through social determinants of health* (Figure 9), Diderichsen's model of the social production of disease as well as Engel's biopsychosocial approach to medicine, a comprehensive approach is needed to address present challenges of contextual factors, structural mechanisms, the individual's socioeconomic position as well as intermediary determinants, in order to minimize inequities in health and well-being.(1,9,107,108,156) In India these approaches ought to consider the rich historical background, the legal situation, as well as India's social structure, all strongly influencing the social determinants of health.(1) The triple jeopardy of women, leprosy and discrimination needs special addressing and is based mainly on the general reduction of gender-based inequalities. The second pillar of the WHO's Leprosy Strategy 2016-2020 aims to reduce G2D, emphasizing the need to protect affected persons from incurable, disfiguring and stigmatising conditions due to a curable disease.(56) Trends since 2015 are promising (Figure 7), yet have been based mainly on case-detection campaigns, posing a laborious and vertical approach, rather than an integrated approach through primary care. Furthermore, G2D-rates in more defined

geographical as Salem (Figure 6) show, that patients are still reporting late and/or are diagnosed at a late stage in the disease.(1) Furthermore, already disabled persons as well as those developing disabilities throughout the course of their life ought not to be forgotten in integrative care approaches. It is in part also their status, which leads to the stigma of the disease, which in return might produce G2D due to neglected paresthesia, ulcers and disfigurements.(1)

### Study Limitations

Our study is limited to the presented number of participants and cannot be seen as a long-term evaluation of the functioning care by the Indian Health Authorities. The DTMC Trust as a nongovernmental charitable care-provider poses a possible selection-bias per se. The limitations of a convenience-sampling technique apply, and the parameters were limited to the extended register of the DTMC Trust. Limitations regarding time since RFT are presented with the results.(1)

## Conclusion

This study determined the correlation of social determinants of health and disability scores in persons affected by leprosy. In a sampled population we could show, that persons disabled through leprosy generally live in poor living standards and low socioeconomic situations. Inequalities in social determinants of health were shown to correlate with higher disabilities due to leprosy. As social determinants are therefore critical not only concerning the risk of transmission and infection, the probability of a successful cure but also concerning the disability status of affected persons, there integrative improvement will be essential to tackle leprosy and its consequences. Our results suggest that especially age and less living space are predictors of higher disabilities due to leprosy. Further research is needed to dissect the exact development of impairments after RFT in order to take targeted actions against disability deterioration. These investigations should ideally be prospective trials with an adequate follow-up period.

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# Appendix

*Supplementary Table 1 – STROBE Statement adapted according to* (1)

*Checklist of items that should be included in reports of cohort studies*

| | Item No | Recommendation |
|---|---|---|
| **Title and abstract** | 1 | (a) Indicate the study's design with a commonly used term in the title or the abstract<br>**Manuscript, Title, Abstract** |
| | | (b) Provide in the abstract an informative and balanced summary of what was done and what was found<br>**Manuscript, Abstract** |
| **Introduction** | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported<br>**Manuscript, Introduction** |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses<br>**Manuscript, Introduction** |
| **Methods** | | |
| Study design | 4 | Present key elements of the study design early in the paper<br>**Manuscript, Materials and Methods, Data Collection & Data Analysis** |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection<br>**Manuscript, Materials and Methods, Study Area & Study Population & Data Collection** |
| Participants | 6 | (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>**Manuscript, Materials and Methods, Study Population** |
| | | (b) For matched studies, give matching criteria and number of exposed and unexposed<br>No matching was undertaken |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable<br>**Manuscript, Materials and Methods, Data Collection & Data analysis** |

| | | |
|---|---|---|
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group<br>**Manuscript, Materials and Methods, Study Population & Data Collection** |
| Bias | 9 | Describe any efforts to address potential sources of bias<br>Not applicable |
| Study size | 10 | Explain how the study size was arrived at<br>**Manuscript, Materials and Methods, Data Collection** |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why<br>**Manuscript, Materials and Methods, Data Analysis** |
| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding<br>**Manuscript, Materials and Methods, Data Analysis** |
| | | (b) Describe any methods used to examine subgroups and interactions<br>**Manuscript, Materials and Methods, Data Analysis** |
| | | (c) Explain how missing data were addressed<br>**Manuscript, Results, Regression Analysis** |
| | | (d) If applicable, explain how loss to follow-up was addressed<br>Not applicable |
| | | (e) Describe any sensitivity analysis<br>**Manuscript, Materials and Methods, Data Analysis** |
| **Results** | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed<br>**Manuscript, Results, Demographical Data** |
| | | (b) Give reasons for non-participation at each stage<br>**Manuscript, Materials and Methods** |
| | | (c) Consider using a flow diagram<br>**Manuscript, Materials and Methods** |
| Descriptive data | 14* | (a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders<br>**Manuscript, Results, Demographical Data** |
| | | (b) Indicate number of participants with missing data for each variable of interest<br>**Manuscript, Results, Regression Analysis** |
| | | (c) Summarise follow-up time (eg, average and total amount)<br>Not applicable |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time<br>Not applicable |

| | | |
|---|---|---|
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included<br>**Manuscript, Results, Regression Analysis** |
| | | (b) Report category boundaries when continuous variables were categorized<br>**Manuscript, Results** |
| | | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period<br>Not applicable |
| Other analyses | 17 | Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses<br>Not applicable |
| **Discussion** | | |
| Key results | 18 | Summarise key results with reference to study objectives<br>**Manuscript, Results** |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias<br>**Manuscript, Discussion, Regression Analysis & Study Limitations** |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence<br>**Manuscript, Discussion** |
| Generalisability | 21 | Discussion the generalisability (external validity) of study results<br>**Manuscript, Discussion & Conclusion** |
| **Other information** | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based<br>**Manuscript, Materials and Methods, Funding** |

*Give information separately for exposed and unexposed groups.