

Leprosy Control

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Prevention

The basic intervention strategy in leprosy control is multidrug therapy (MDT; see Chapter 2.6), given to newly found leprosy cases. Preventive interventions, other than awareness raising and health education activities, are not routinely available. Yet it has long been argued that the elimination of leprosy cannot be achieved by a strategy based on MDT alone and that new tools and technologies are needed to attain this goal (1). Intensified, population-based approaches to case detection are no longer cost-effective, and a new approach is indicated that is appropriate to the current epidemiological situation. New cases are relatively rare even in endemic countries; health care resources are scarce with many competing demands; and leprosy control activities are difficult to sustain within integrated programs. The main risk of exposure to leprosy is close contact with new, untreated cases. As the risk of exposure to leprosy in the general community is very low, an increasing proportion of new cases will be from household contacts (2). Over the past few years, progress has been made in the areas of chemoprophylaxis and immunoprophylaxis to prevent leprosy, and these interventions have focused primarily on contacts of leprosy patients.

IMMUNOPROPHYLAXIS

BCG and leprosy vaccines

The Bacillus Calmette-Guérin (BCG) vaccination was originally developed as a vaccine against tuberculosis (TB; see Chapter 6.3), and it has been used extensively all over the world for decades for this purpose. At an early stage, it was recognized that BCG could possibly also protect against leprosy and several vaccine trials followed using BCG, often in combination with *M. leprae* or related mycobacterium vaccines. Convit et al. conducted a trial in Venezuela in the 1980s using a combination of live BCG plus heat-killed *M. leprae* (3). In the same time period, a trial was conducted in Malawi comparing different regimens of the BCG vaccination, including the combination of BCG with heat-killed *M. leprae* (4). Both trials showed that BCG was effective, that repeated doses of BCG gave additional protection, and that the addition of heat-killed *M. leprae* did not offer more protection than the BCG alone. In the early 1990s, a large trial was conducted in South India (5) of four different vaccines: BCG; BCG plus heat-killed *M. leprae*; the ICRC vaccine, made from cultivable leprosy-derived mycobacteria, probably belonging to the *M. avium intracellulare* complex prepared at the Indian Cancer Research Center (6); and “*Mycobacterium w (Mw)*”, a vaccine from India prepared from *Mycobacterium welchii* (7). In this study, the BCG plus the heat-killed *M. leprae* provided 64% protection; ICRC provided 65.5% protection; *Mw* provided 25.7% protection; and BCG alone provided 34.1% protection. Another trial in India in the 1990s among household contacts of leprosy patients used the *Mw* vaccine (8). For these contacts, the *Mw* vaccine showed a protective efficacy of 68.6% at 3 years, 59% at 6 years, and 39.3% at 9 years follow-up, indicating the need for a booster vaccination after 7–8 years. Finally, in Vietnam in the 1990s, three vaccines, BCG alone, BCG plus 10^7 killed *Mycobacterium vaccae*, and 10^8 killed *M. vaccae* alone, were studied in children living in close contact with leprosy (9). For all three vaccines, there was 52.5% protection for the first 4 years and 80.5% for the second 4 years. There were no significant differences in protection afforded by each of the vaccines, but the authors viewed the success of the killed preparation of *M. vaccae* to be an important finding (see Chapter 5.1).

Protective effect of BCG against leprosy

Meta-analyses have supported the protective effect of BCG against leprosy (10, 11, 12). In the most recent review, Merle et al. described the variable protection, ranging from 20 to 90%, of the BCG vaccination against leprosy in different study sites. They found that there is evidence of protection when the vaccine is given at a young age, but that there are inconsistent results when it is given at an older age. There is also some evidence, although inconsistent, regarding the benefit of revaccination. The BCG efficacy was found to be larger in observational studies than in trials: 60% versus 41%. The only variable that significantly explained the heterogeneity of the results after adjustment was the target population of the study, specifically, whether it consisted of contacts of leprosy cases or the general population. BCG efficacy appeared to be significantly higher among contacts of leprosy patients than among the general population: 68% versus 53% (12) (see Chapter 6.3).

It can be concluded that, to date, BCG is the best available vaccine for the prevention of leprosy. In Brazil, in addition to routine BCG vaccinations given at birth for TB, BCG has been officially recommended for household contacts of leprosy cases since the early 1970s. Since 1991, the Brazilian Ministry of Health also has advised that two doses of BCG be administered to both current household contacts and contacts whose index (original) cases were diagnosed within the previous 5 years. The vaccine is administered irrespective of TB or leprosy skin test results. If the contact never received BCG, or if this information is unknown, the contact receives two BCG doses at a 6-month interval. If the contact has already received one dose of BCG, a single dose is given (13). This policy was assessed in a cohort study of 3,536 contacts of 1,161 leprosy patients in Brazil, which showed that a booster BCG vaccination conferred 56% protective efficacy and that that percentage was not substantially affected by previous BCG vaccination (13). During 18 years of contact follow-up, it was observed that among the 122 new cases detected, leprosy was diagnosed in 28 (23%) relatively soon after vaccination (2–10 months). This observation raises the question of whether the BCG vaccination actually induces symptoms of leprosy in people already incubating the disease. An ongoing randomized, controlled trial in Bangladesh is studying the effectiveness of the BCG vaccine versus the BCG in combination with a single dose of rifampin (SDR) given 2 to 3 months later in the prevention of leprosy among contacts of newly diagnosed leprosy patients (14). In this study, 21 contacts of the 5,196 vaccinated contacts (0.40%) developed leprosy within 12 weeks after the BCG vaccination. All 21 cases presented with paucibacillary (PB) leprosy, including children and adults (15). About half of these cases had previously received the BCG vaccination, as indicated by the presence of a BCG scar; 43% presented with signs of nerve function impairment and/or Type 1 (reversal) reaction; and 56% of the index patients had multibacillary (MB) leprosy. The question is whether the BCG vaccination of contacts merely altered the incubation period or actually changed the course of the infection from self-limiting, subclinical infection to manifest leprosy disease. Further studies are ongoing in Bangladesh to elicit the underlying immunological mechanisms.

Recent developments in leprosy vaccines

Duthie et al. state that the ideal vaccine against leprosy would induce strong, long-lasting T-cell responses directed against *M. leprae* that would both prevent disease and reduce bacterial transmission (16). An effective sub-unit vaccine has not yet been found (although it is currently under development). The selection and production of recombinant antigens has been simplified by the completion and publication of the *M. leprae* genome in 2001 (17). Antigens have been identified (see Chapter 7.1; Chapter 6.3) that also are recognized by PB patients and stimulate IFN- γ secretion (18, 19, 20). The Infectious Disease Research Institute (IDRI), supported by the American Leprosy Missions (ALM), is currently assessing the vaccine potential of several of these antigens by experimental vaccination and infection in mice (16, 19). IDRI envisions leprosy vaccines to be used in interventions targeted at specific risk groups, such as household contacts (not whole populations), and possibly also as therapeutic vaccines (or immune therapy) for patients in conjunction with chemotherapy (16) (see Chapter 6.3).

CHEMOPROPHYLAXIS

Dapsone and Acedapsonone

The idea of chemoprophylaxis in leprosy is not new. In the 1960s and 1970s, trials were carried out in Uganda employing dapsone as chemoprophylaxis among school children (21), and in India employing dapsone among whole populations of endemic villages (22) and child contacts of non-lepromatous and lepromatous leprosy patients (22, 23, 24, 25, 26). Dapsone was given regularly, usually in a weekly dose, for 2 or 3 years. These studies were followed by trials with acedapsonone, which was given less often and for a shorter duration (every 10 weeks over 7 months) (27, 28). A meta-analysis of three eligible studies using dapsone (22, 23, 26) significantly favored dapsone to the placebo (4,337 participants, RR 0.60, 95% CI 0.48–0.76; indicating an overall reduction of leprosy among contacts of 40%). Similarly, a meta-analysis of two eligible studies using acedapsonone (27, 28) significantly favored acedapsonone to the placebo (1,259 participants, RR 0.49, 95% CI 0.33–0.72; indicating an overall reduction of leprosy among contacts of 51%) (29).

Rifampin

In 1988, a chemoprophylaxis study employing a single 25 mg/kg dose of rifampin was conducted in the Southern Marquesas Islands (30, 31, 32). This non-controlled trial treated 2,751 of the 2,786 (98.7%) inhabitants of the islands. In addition, 3,144 South Marquesans living elsewhere in French Polynesia were given the same chemoprophylaxis. Over the following 10 years, five cases were detected in the treated population, a number significantly smaller than the 17 cases that were predicted, based on the assumption that the case detection would have remained stable over the years without chemoprophylaxis. This finding suggested that the intervention was 70% effective. However, over the 10 years following the implementation of the chemoprophylaxis program, the detection rate in the Polynesian population that was not given the intervention declined by about 50%, suggesting an effectiveness of the chemoprophylaxis of only 35–40%.

Because of the high leprosy incidence rate in the Pacific islands, it was decided in the mid-1990s to carry out programs of chemoprophylaxis in the Federated States of Micronesia, Kiribati, and the Republic of the Marshall Islands (33). Around 70% of the population of the countries was screened for leprosy twice within a one-year interval, and chemoprophylaxis was administered to all healthy individuals once during each round. The combination of rifampin-ofloxacin-minocycline (ROM) was given to adults and rifampin only to children under 15 years of age (34). By 1999, a substantial reduction in case detection was observed, but it could not be established whether transmission of *M. leprae* in the population had been interrupted by the intervention (33). Recent prevalence and new case detection figures indicate that the intervention did not interrupt transmission. The Federated States of Micronesia and the Marshall Islands never reached the WHO leprosy elimination target, while Kiribati failed to maintain the elimination threshold (35). In 1999, a workshop was convened in Pohnpei (Federated States of Micronesia) to discuss the results of the chemoprophylaxis trials in the Western Pacific region and the prevention of leprosy in

general (36). At this workshop, Smith and Smith described the needs, opportunities, and feasibility of the preventive treatment of leprosy, including chemoprophylaxis and immunoprophylaxis (37). An important conclusion of the workshop was that further evidence of the effectiveness of these preventive interventions was required (36).

In 2000, a chemoprophylaxis intervention study with rifampin was started on five Indonesian islands highly endemic for leprosy (38). The intervention consisted of two doses of 600 mg of rifampin for adults and 300 mg for children (6–14 years old), with approximately 3.5 months between doses. To form similarly sized intervention groups, three islands were combined into one intervention group. Two types of chemoprophylactic intervention strategies were compared with a control group. The blanket (complete population) group included three islands on which prophylaxis was given to all eligible persons. The contact group included an island on which prophylaxis was given to all eligible contacts of all known and newly found leprosy patients. The control group was the population of an island on which no chemoprophylaxis was given. The population was actively screened before the intervention and subsequently once a year for three years. The cohort consisted of 3,965 persons. The yearly incidence rate in the control group was 39/10,000; the cumulative incidence after three years was significantly lower in the blanket group. No difference was found between the contact and control groups. This study showed that population-based prophylaxis was associated with a reduced leprosy incidence in the first three years after implementation. The study also showed that in this area of high endemicity, rifampin prophylaxis for spatially defined contacts only (e.g., household members and neighbors) did not appear to influence leprosy incidence and that further studies, including social contacts, are needed to establish the effect of prophylaxis given to contacts in areas of lower endemicity. The results of this study were promising but inconclusive, due to limitations in design and sample size.

The need for a more rigorous trial to determine the preventive effect of rifampin was met by the COLEP study conducted in Bangladesh (39). The objectives of this study were to determine empirically the effectiveness of chemoprophylaxis with a single dose of rifampin (SDR) in the prevention of leprosy among close contacts of leprosy patients, and to find the characteristics of the contact groups most at risk of developing clinical leprosy. COLEP was a single-center, double-blind, cluster-randomized, placebo-controlled trial, using the total contact group of a patient to determine the factors characterizing the sub-groups most at risk. In addition, a reference group was formed from the general population to determine the prevalence and incidence of leprosy in the total population of the study area (39). In total, 28,092 close contacts of 1,037 patients with newly diagnosed leprosy were included in the trial, of which 21,711 contacts fulfilled the study requirements. Of the 21,711 contacts, 18,869 (86.9%) were followed up at two and four years. Ninety-one of 9,452 contacts in the placebo group and 59 of 9,417 in the rifampin group had developed leprosy at four years. The overall reduction in the incidence of leprosy using SDR in the first two years was 57% (95% CI: 33–72%) (40). The groups did not differ between two and four years (40), or in a follow-up study at six years (41). The overall number needed to treat (NNT) to prevent a single case of leprosy among contacts was 297 (95% CI: 176–537). The trial showed that SDR given to contacts of patients with newly diagnosed leprosy is effective at preventing the development of clinical leprosy at two years. The initial protective effect was maintained, but no

difference in incidence was seen between the placebo and rifampin groups beyond two years (40, 41).

The COLEP study made clear distinctions in the characteristics of contacts with regard to genetic and physical distance to the original leprosy patient (index). Further interesting findings concerned the effect of SDR in relation to contact level. Firstly, the effect of the SDR depended on the contact level (40). The effect was larger if the contact was not blood-related to the index patient, if the index patient had PB leprosy, and if the contact was a social contact rather than a household contact or neighbor. In other words, the effect of SDR is highest in those contact groups with the lowest *a priori* risk for leprosy (i.e., those who are probably genetically less susceptible and those who are further removed from the index patient and therefore less exposed). Secondly, the effect of the SDR depended on the BCG status of the contact (42). If the contact had received a BCG vaccination as part of a childhood vaccination program (as established by the presence of a BCG scar), the protective effect of SDR was 80% (Table 1). Both childhood BCG vaccination and SDR have a protective effect for leprosy in contacts (each conveyed through different biological mechanisms) of nearly 60%, but if a contact who had previously received a BCG vaccination also received SDR, the protective effect appears to be additive to the effect of BCG.

TABLE 1 Protective effect of BCG and rifampin (SDR) on the incidence of leprosy among contacts after 2 years of follow-up, by intervention

Intervention	Leprosy	No Leprosy	Multivariate*		Protective effect
			OR	95% CI	
None	52	6418	1		
Rifampin only	22	6462	0.42	0.26–0.70	58%
BCG only	15	4291	0.43	0.25–0.76	57%
Rifampin and BCG	7	4259	0.20	0.08–0.50	80%

* Adjusted for age, sex, physical distance to, and classification of index patient

In 2014, an expert group reviewed the evidence for chemoprophylaxis in contacts and high-risk communities (43). The group also considered the definitions of ‘contact’ and ‘contact tracing’; discussed alternative prophylaxis regimens, the preliminary findings of operational pilot projects on post-exposure prophylaxis (PEP) in Indonesia, and the development of diagnostic tools; and identified the priority questions for operational research in leprosy transmission. A large, international program of pilot projects (the LPEP project) has been launched by the Novartis Foundation, in collaboration with several national leprosy programs and other partners of the International Federation of Leprosy Associations (ILEP), to assess the effect of chemoprophylaxis on the transmission of leprosy. The pilot projects are designed to demonstrate the feasibility, acceptability, cost-effectiveness, and real-world efficacy of contact tracing and PEP as a strategy for interrupting leprosy transmission. The projects are also intended to facilitate the integration of chemoprophylaxis experiences into national programs and guidelines, provide a toolkit for contact manage-

ment and PEP, create locally adaptable surveillance and response systems for PEP, and demonstrate the cost-effectiveness of chemoprophylaxis.

PREVENTIVE STRATEGIES AND THE ROLE OF CONTACTS

Contact management

With new leprosy cases becoming relatively rare in most endemic countries, it is not feasible any more to apply intensified, population-based approaches to case detection and target preventive interventions such as chemoprophylaxis and immunoprophylaxis to total populations groups, possibly with the exception of small, highly endemic pockets of leprosy. As the main risk of exposure to leprosy is faced by close contacts of new, untreated cases and the risk of exposure to leprosy in the general community is very low, an increasing proportion of new cases will be from household contacts. Thus contacts should be the main focus of a future leprosy control strategy. Such a strategy would have three basic pillars: (1) case detection, (2) case management, and (3) contact management. Case detection and case management have been the major components of past and present leprosy control strategies, including activities such as early case detection, appropriate treatment of leprosy disease and leprosy related complications, prevention of disability, and social action for stigma reduction (44). Contact management includes contact tracing and possibly the provision of preventive interventions aimed at contacts. Contact surveys have usually been recommended in national and international guidelines and were routinely performed in the past, but they have long been neglected in many countries due to lack of resources. It has now become clear that a strategy of early case detection and treatment with MDT is not sufficient to interrupt the transmission of *M. leprae* and reduce the incidence of leprosy significantly (45, 46). Well-developed contact management approaches will provide the opportunity to apply preventive measures and reduce transmission in endemic communities.

Contact management first consists of a contact survey upon the identification of a new leprosy patient. It has been well established that close contacts of leprosy patients have an increased risk for leprosy. The COLEP study showed that the chance of finding a household contact with previously undiagnosed leprosy was ten-fold compared to the general population (see Table 2) (47, 48). The chance of finding leprosy among different categories of neighbors and social contacts was also higher than that of the general population (between three and five-fold; see Table 2).

The age of the contact, the disease classification (MB or PB) of the index patient, and the physical and genetic distance between them were independently associated with the risk of a contact acquiring leprosy. The conclusion of this study was that contact surveys for leprosy should not only focus on household contacts, but should also be extended, where possible, to neighbors and consanguineous relatives, especially when the patient has MB leprosy (47). A contact survey consists basically of either a home visit by (para) medical staff or an invitation to contacts of a

new patient to visit a clinic. The contacts are examined for the presence of leprosy symptoms and given health information about leprosy. New cases found during a contact survey are started on MDT. A contact survey is an effective intervention in itself and, when done consistently in a control area, will probably contribute considerably to reducing the transmission of *M. leprae* in the community (49).

TABLE 2 Prevalence of previously undiagnosed leprosy (PPUL) per 10,000 in the subgroups of the contact population of the COLEP study and in the general population sample

Leprosy contacts and general population	PPUL	95% CI*
Sharing kitchen and roof (“household”)	156	106–220
Sharing kitchen only	75	39–131
Sharing roof only & next-door neighbor, not sharing roof or kitchen	87	65–115
Neighbor of neighbor & social contact	49	38–63
General population sample	15	9–21

* 95% CI = 95% confidence interval for PPUL

At the time of the contact survey, it is possible to add preventive interventions targeted at contacts, such as chemoprophylaxis and immunoprophylaxis. Chemoprophylaxis provides a relatively short protective window (approximately 2 years). The studies on BCG protection in leprosy indicate an increased risk of tuberculoid leprosy in the first months after the BCG vaccination, but long-term protection afterwards. This finding suggests that a combined approach providing both chemoprophylaxis for immediate and short-term protection and immunoprophylaxis for long-term protection is an interesting option. However, Rifampin, a mycobactericidal drug, and BCG, containing live mycobacteria, cannot be given at the same time. In this case, two visits are necessary: immunization is provided during the first visit and chemoprophylaxis during a second visit after a number of weeks. A trial to assess the efficacy of a combined strategy is currently underway in Bangladesh (14). New generation sub-unit vaccines (see Chapter 6.3), which do not contain live bacteria, could solve this problem of separate applications of chemoprophylaxis and immunoprophylaxis (16).

Community mass prophylaxis

Trials of dapsone have indicated that mass chemoprophylaxis can be efficacious in preventing leprosy in high-risk populations. These studies are now only of historical interest, given that dapsone must be taken for a long time to achieve protection. Case studies from Micronesia, the Maldives, Indonesia, and French Polynesia have shown that blanket treatment of a population with rifampin or ROM is feasible and can achieve high coverage. These case studies showed that the number needed to treat (NNT) to prevent one case of leprosy depends on the protective effect of the prophylactic drug and the disease frequency, and that NNT is lower in high-endemicity areas. As a result, mass prophylaxis is most efficient in high-risk or high-endemicity populations (50).

Linking blanket prophylaxis for leprosy to mass drug administration programs for other neglected tropical diseases (NTDs) may provide logistical advantages. It remains unproven whether mass revaccination with BCG can provide additional protection to blanket chemoprophylaxis in populations at a high risk of leprosy. Mass treatment with antibiotic drugs needs to be considered very carefully with regard to unconstrained use and the threat of drug resistance.

Global Strategies

CONTROL, ELIMINATION, AND ERADICATION

Disease control is defined as the reduction of disease incidence, prevalence, intensity, morbidity, or mortality, or a combination of these, as a result of deliberate effort. Elimination, or the interruption of transmission, is the reduction to zero of the incidence of infection caused by a specific pathogen in a defined geographical area as a result of deliberate efforts. Eradication is the permanent reduction to zero of the worldwide incidence of infection caused by a specific pathogen as a result of deliberate efforts, with no risk of reintroduction (51). ‘Elimination as a public health problem’ is a separate concept from elimination and is based on the use of measurable targets for control set by the member states of the WHO.

The ‘elimination as a public health problem’ strategy was approved in 1991 by a resolution of the World Health Assembly (52). The strategy was based on early case detection and MDT treatment and used a registered prevalence of less than 1 in 10,000 as the measurable target. The use of prevalence rather than incidence of disease as a target differed from the standard elimination target of incidence. However the strategy created a political and financial commitment to leprosy and focused programs on case detection and treatment. The strategy simplified the diagnosis and treatment of leprosy, which facilitated implementation in areas with a weak health care infrastructure. Important simplifications included diagnostic methods without slit skin smears, classification based on number of skin lesions, and the delivery of MDT in PB and MB blister packs for both adults and children. The strategy resulted in a reduction in the registered prevalence of leprosy by over 90%; however, there was no similar change in new case detection trends. The prevalence of a disease is equal to its incidence multiplied by its duration. Therefore, the effect of the ‘elimination as a public health problem’ strategy on prevalence was almost entirely due to the reduction in treatment duration. Before MDT, dapsone treatment was continued for between 4–10 years and, in some cases, for life. MDT reduced the treatment duration to fixed periods of 6 months for PB and, initially, 24 months for MB, later shortened to 12 months. Since 2000, the prevalence of leprosy has leveled off because MDT coverage has reached 100%. After all patients were receiving fixed duration, short course MDT, there was no longer any potential to further reduce prevalence by reducing treatment duration.

Following the success of the leprosy elimination strategy, there was interest in considering the potential of the eradication of leprosy. The criteria for eradication are scientific feasibility, epidemiological vulnerability, effective intervention, and the demonstration of elimination. Political will and popular support, economic factors, and synergy with other interventions are important (53). The case for the eradication of leprosy does not meet the criteria for eradication on a number of grounds, particularly the lack of an effective, safe, and affordable means of preventing transmission of disease and a measure of infection.

EARLY DETECTION AND TREATMENT

The approach to leprosy control since the advent of dapsone therapy in the 1950s has been that of secondary prevention, early case detection, and treatment. MDT was introduced in 1982 (54) in the face of growing concern about emerging dapsone resistance. The introduction of MDT did not change the basic strategy of case detection and treatment, but it did result in shorter treatments. The reduction in the duration of treatment led to a decrease in registered prevalence that in turn stimulated the concept of elimination as a public health problem strategy. Early detection is difficult to define whereas late detection, after nerve function impairment has happened, is more obvious. Early detection of leprosy based on the presence of a small number of ill-defined skin lesions can be difficult to diagnose and attempts to promote very early detection may be associated with over-diagnosis. Early diagnosis and treatment before nerve function impairment has occurred is deemed to be an effective means of preventing disability. It may also reduce the opportunity for exposure and transmission of the *M. leprae* infection. Modeling suggests that early detection and treatment can contribute to reducing transmission (55).

COMMUNITY AWARENESS AND ACCESS TO HEALTH CARE

A delay in the detection of leprosy can be considered as both patient-based and health system-based (56). Awareness of a possible diagnosis of leprosy in the community is important for promoting early and appropriate help-seeking behavior. Similarly, the awareness to suspect a diagnosis of leprosy is important within the health system, especially as health workers may see few new cases of leprosy.

Community awareness as well as the promotion of early case detection and self-referral also can increase the positive attitude of a community towards people affected by leprosy. Messages should be positive, stating that leprosy is curable, that drugs are free to those affected by leprosy, and that there is no place for stigma or discrimination (57). Surveys of community knowledge and attitudes toward leprosy can help inform the development of information, education, and communication (IEC) strategies (58).

Ensuring the availability of and access to health care and MDT drugs is very important (59). Particular attention needs to be paid to women, children, migrants, and ethnic minorities. A review of case detection data and audits of equity can be used to demonstrate equality of access to health care and to the diagnosis and treatment of leprosy.

TARGETS AND INDICATORS

The target set by the WHO for the elimination of leprosy as a public health strategy of less than 1 in 10,000 by the year 2000 proved to be effective and was attained at the global level at the end of 2000. However, the challenge in maintaining the momentum and sustainable leprosy programs came after achieving the target. The loss of momentum is clearly seen in the trends of new case detection over the years 2000 to 2006. Despite the benefits of the leprosy elimination target, the use of targets has been criticized (60).

The leprosy programs should be monitored by a range of indicators, as reliance on a single target can be misleading. The essential indicators (57) are as follows:

- Number and proportion of new cases with grade 2 disabilities
- Number and proportion of child cases among new cases
- Number and proportion of female cases among new cases
- Proportion of new cases correctly diagnosed
- Proportion of treatment defaulters
- Proportion of patients who develop new or additional disability during MDT
- Health systems and stakeholders

The elimination strategy was very focused on an elimination prevalence target by the year 2000, but had many unsustainable components. Components such as the Leprosy Elimination Campaigns and the Special Action Projects for the elimination of leprosy were resource-intensive activities. Therefore, the global strategy became more sustainable (61) and became integrated in all its aspects with existing general health services rather than remaining a vertical program (62). A number of health system approaches to sustainability have been developed in different settings, including linkages with tuberculosis programs, dermatology services, and, more recently, Neglected Tropical Diseases (NTDs) (51).

The primary responsibility for leprosy control lies with national governments, which may have a national program manager for leprosy or coordinate and supervise leprosy services within a department of disease control, communicable disease control, or NTDs. Governments are supported by a number of stakeholders such as the WHO, international non-governmental organizations (NGOs) such as ILEP, and local non-governmental organizations as well as organizations of people

affected by leprosy and professional associations such as the International Leprosy Association. Novartis and Novartis Foundation support programs and innovation as well as provide all MDT drugs free of cost.

FUTURE STRATEGIES

In 2011, the WHO introduced an enhanced global strategy to maintain the focus on sustainability and the reduction in the burden of leprosy (63). This strategy had a number of new components and focused on the reduction in grade 2 disability in new patients as an indicator of early detection. A target was set to reduce the rate per population of new cases with grade 2 disability by 35%. The purpose was to emphasize early new case detection, by increasing awareness and reducing delay in diagnoses; MDT; and the important issue of preventing disability. The WHO Expert Committee on Leprosy extended this strategy and set a new target of less than 1 in a million population of new patients with grade 2 disability by 2020 at a global level (64). Future strategies are likely to extend this target to reducing new child cases with grade 2 disability to zero by 2020. Future strategies also will address the issue of gender inequity in the diagnosis of leprosy, an issue highlighted by a recent ILEP report (65).

Integration with other NTDs is an important opportunity for leprosy control. Leprosy shares many cross-cutting issues with other NTDs such as poverty, drug administration, community awareness, stigma, and discrimination, which will provide synergy, financial support, and political momentum for leprosy control (51).

Case Studies

NATIONAL LEPROSY ELIMINATION PROGRAM IN BANGLADESH

The National Leprosy Elimination Program (NLEP) in Bangladesh achieved elimination of leprosy as a public health problem based on a registered prevalence of less than 1 in 10,000 at the end of 1998, and now aims to achieve this goal at a sub-national (district) level by 2015. The 'Post Elimination National Leprosy Control Strategy 2011 – 2015' has been formulated to sustain the achievements and improve the quality of clinical services (66).

The objectives of the NLEP are to provide MDT services in all health complexes at the upazila (sub-district) level and below, to provide MDT to all people with leprosy, and to achieve at least an 85% treatment completion rate (cure rate) among patients who were put on MDT. NLEP also aims to reduce the grade 2 disability rate among newly detected cases to less than 5%, and to

implement information, education, and communication activities to increase community awareness about leprosy, promote voluntary case reporting, and minimize social stigma. NLEP also will establish a simple and effective recording and reporting system to monitor progress.

Collective efforts have been made to promote awareness for reducing stigma and discrimination against people affected by leprosy, sustaining the interest of policy makers, and encouraging the involvement of general health services and other stakeholders, such as NGOs, in leprosy control. The leprosy elimination activities are integrated into the general health services, and specialized leprosy staff are retained at certain levels to ensure technical support and guidance. General medical practitioners and medical, nursing, and paramedical institutions are involved through training and leprosy orientation activities.

For over 15 years, leprosy services in Bangladesh have been delivered through a partnership of government health care services and a variety of NGOs involved in leprosy. This collaboration is organized through the National Leprosy and Tuberculosis Coordinating Committee (LTCC). NGOs have been assigned certain geographic areas to implement leprosy control according to the NLEP guidelines. NGOs provide manpower, training, and technical resources, with assistance from the governmental health services at the national and local levels in terms of clinic facilities, drug distribution, central coordination, supervision, and monitoring. The NLEP has been developed in consultation with all leprosy NGOs and other national and international organizations to achieve a “leprosy-free Bangladesh”.

Both the incidence and prevalence of leprosy in Bangladesh have shown a decreasing trend over the past 15 years, but the number of newly detected cases increased in 2014 to 3621, compared to 3141 in 2013 (67). The number of endemic areas was 15 (13 districts and 2 city corporations) in 1998, but was reduced to only one district (Nilphamari) by the end of 2014. Of all 3621 newly detected cases in 2014, 46% were MB, 38% female, 5.4% children, and 14% had grade 2 disabilities (68). The estimated prevalence rate in 2014 was 0.23/10,000 population.

The NLEP is gradually losing attention on the public health agenda due to reduced funding. MDT is still available free of cost, but the supply of other medicines, the logistics for the management of complications and treatment of leprosy, and the services for the prevention of disability are inadequate. Expertise is difficult to sustain because of a lack of training and capacity building in combination with the gradual retirement of senior staff.

NATIONAL LEPROSY CONTROL STRATEGY IN BENIN

Benin is in the West African subregion. In 2014, the population was estimated at 10.6 million (69), spread over 12 departments. The national leprosy control program, one of the key control programs of the ministry of health, is run at the central level by a national coordination office with focal points in each department. The leprosy supervisors ensure the identification of patients, the clinical management of patients, and the reporting of leprosy control activities in the 77 districts of the country. The data related to the leprosy control activities are collected during quarterly

monitoring visits organized by the national coordination office. Health workers, assisted by community intermediaries, are responsible for data collection. Leprosy statistics report sheets are used for case-recording and the data are computerized using Excel 2007 software prior to map conversion using Arc View GIS 3.2 software.

LEPROSY INDICATORS TRENDS IN BENIN: 1995–2014

Table 3 summarizes the main leprosy control indicators for the period analyzed. From 1995 to 2014, 8460 leprosy cases were detected in Benin (70). The 20-year follow-up enabled the assessment of the prevalence of leprosy and its distribution at the district and departmental levels. The follow-up also helped in evaluating the work of the Benin National Leprosy Control Program during this period. The highest prevalence rate was recorded in 1997 (1.10 per 10 000 inhabitants). The lowest was recorded in 2014 (0.21 per 10 000 inhabitants). Data analysis by department shows that the Plateau department was the most endemic throughout the period. In 1995, 31 districts had prevalence rates above the WHO elimination target. These districts were concentrated in the departments of Zou/Collines and Atacora/Donga (see Figure 1). In 2014, there were only five endemic districts (prevalence greater than 1 in 10,000) located in Atacora (2 districts), Mono (1 district), Zou (1 district), and Plateau (1 district), respectively (see Figure 1).

The improved endemic situation observed in 2014 was achieved thanks to the efforts of the National Leprosy Control Program with the support of the Foundation Raoul Follereau, which organizes detection and treatment using the WHO MDT. Despite the improvement in these indicators at the national level, the new case incidence continued in some departments such as Plateau and Zou. Untreated MB leprosy patients are seen as the principal reservoir of *M. leprae*. At the start of MDT in 1995, the Plateau department already had the highest prevalence rate (1.04 cases per 10,000 inhabitants), which could explain the persistence of the disease in this district. The analysis also showed a reduction in new cases detected, along with an increasing proportion with grade 2 disability and MB, reflecting a delay in the detection of cases. It is important to implement an appropriate strategy for early detection, such as the MB contact examination.

MULTIBACILLARY CONTACTS SURVEY

The MB contact examination was designed to investigate the contacts of MB leprosy cases in order to detect new cases of leprosy and to inform and educate those around the index cases on the early signs of leprosy. A list of MB patients was established for the period from January 2012 to June 2014. A total of 294 index cases were identified for home visits and contact examination. Each index case was informed of the day the team would visit, 3054 contacts were examined, and a total of 49 new cases of leprosy were detected.

The Benin program is using computerised information on the geographical distribution of and trends in leprosy to develop focused approaches to case detection in endemic areas and districts

with persistent new case detection rates. This approach is enhanced by contact surveys of MB patients.

TABLE 3 Leprosy main indicators from 1995–2014

Year	Detection (rate/10000)	Prevalence (Rate/10000)	Children (%)	Grade 2D (%)	MB (%)	Women (%)
1995	763 (1.41)	560 (1.04)	71 (9)	95 (12)	404 (53)	404 (53)
1996	592 (1.05)	492 (0.88)	68 (11)	74 (12)	278 (47)	276 (47)
1997	663 (1.15)	637 (1.10)	66 (10)	85 (13)	311 (47)	313 (47)
1998	711 (1.19)	529 (0.86)	64 (9)	106 (15)	368 (52)	342 (53)
1999	619 (1.01)	480 (0.78)	51 (8)	109 (18)	381 (61)	275(44)
2000	645 (1.02)	489 (0.77)	40 (6)	97 (15)	414 (64)	287 (45)
2001	391 (0.60)	278 (0.43)	56 (14)	70 (18)	345 (88)	165 (42)
2002	392 (0.58)	294 (0.44)	33 (8)	85 (22)	253 (64)	184 (47)
2003	377 (0.54)	297 (0.43)	48 (13)	79 (21)	240 (64)	175 (46)
2004	453 (0.63)	333 (0.46)	44 (10)	84 (19)	304 (67)	218 (48)
2005	397 (0.53)	306 (0.41)	43 (11)	86 (22)	238 (60)	173 (44)
2006	404 (0.52)	322 (0.41)	35 (9)	90 (22)	290 (72)	188 (47)
2007	345 (0.42)	284 (0.35)	41 (12)	80 (23)	212 (61)	168 (49)
2008	298 (0.36)	217 (0.26)	30 (10)	75 (25)	196 (66)	122 (41)
2009	248 (0.29)	185 (0.22)	16 (6)	47 (19)	170 (68)	127 (51)
2010	227 (0.26)	180 (0.21)	14(6)	45 (20)	170 (75)	101 (44)
2011	246 (0.27)	192 (0.21)	13 (5)	41 (17)	193 (78)	118 (48)
2012	243 (0.26)	185 (0.22)	18 (7)	50 (21)	193 (79)	106 (44)
2013	254 (0.27)	227 (0.24)	19 (7)	47 (18)	170 (67)	105 (41)
2014	192 (0.18)	227 (0.21)	22 (11)	45 (23)	142 (74)	92 (48)

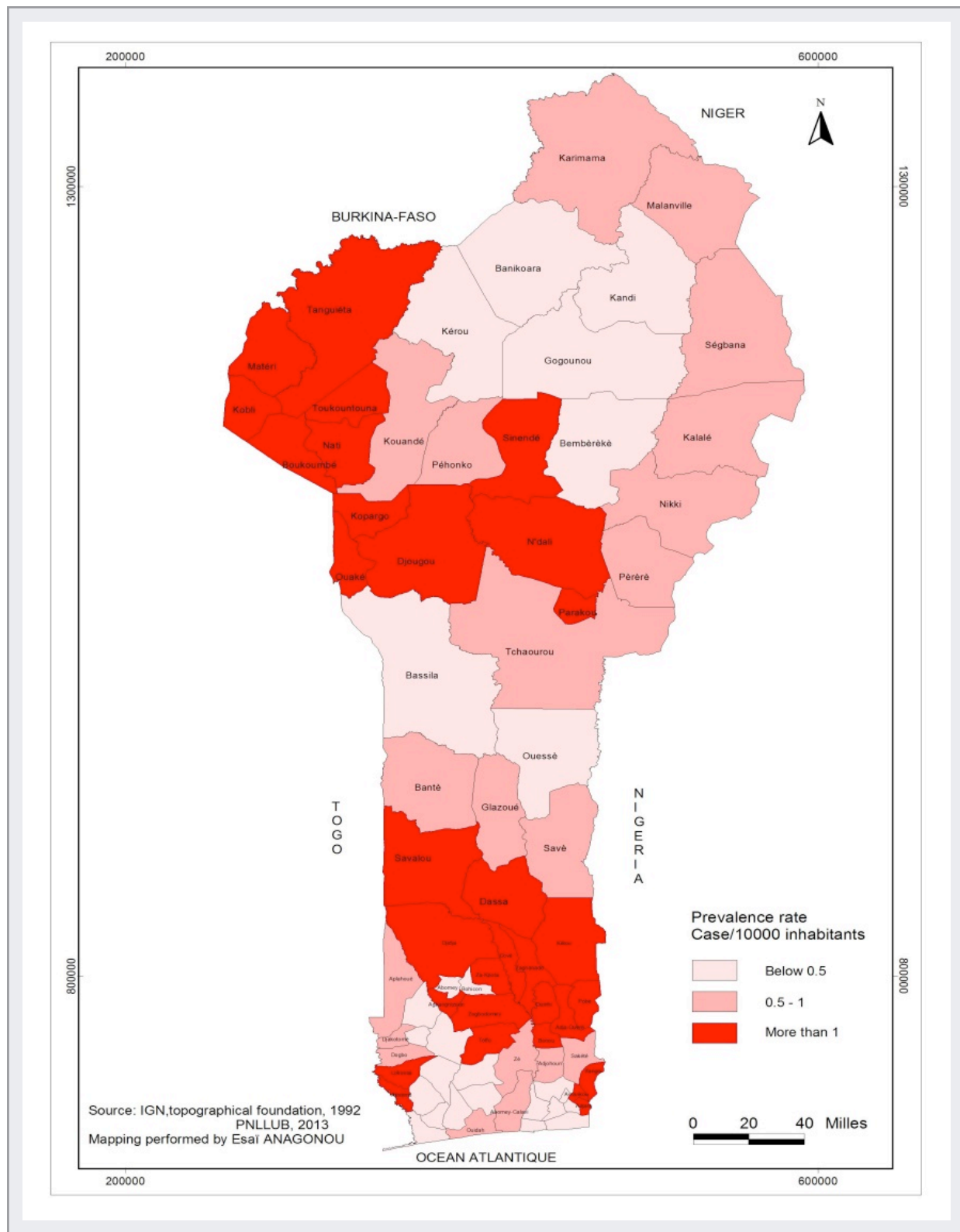


FIG 1 Map of the leprosy prevalence in Benin in 1995.

Control

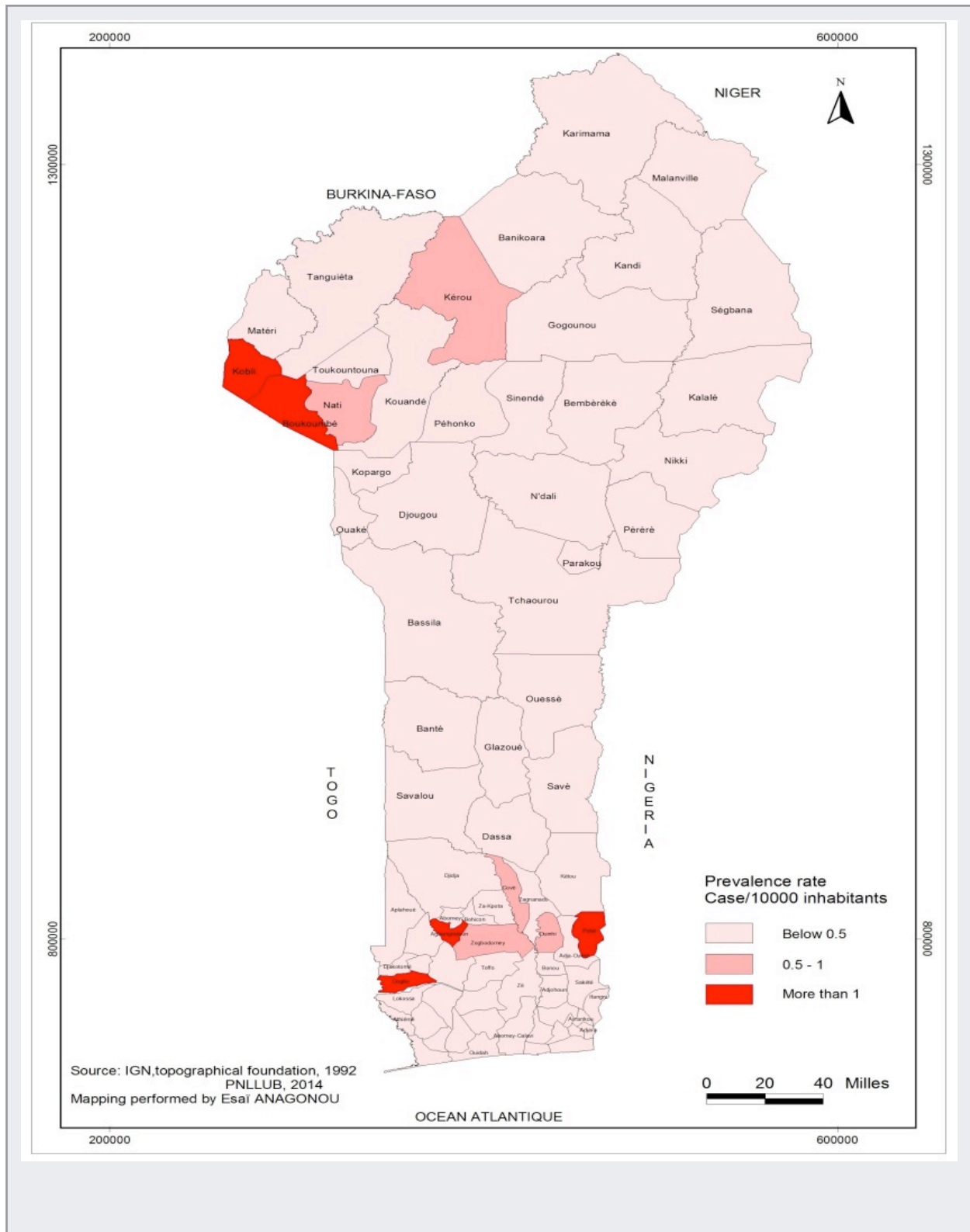


FIG 2 Map of the leprosy prevalence in Benin in 2014.

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