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Hansen's disease (leprosy) in Japan, 1947–2020: an epidemiologic study during the declining phase to elimination

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Abstract

Objectives: Leprosy, or Hansen's disease was a major public health problem in Japan in the early 20th century. Today, the number of new cases has decreased significantly. We aimed to investigate the trends of leprosy in Japan over the past 73 years and the challenges faced in recent years.

Methods: We assessed the data on newly registered cases of leprosy from 1947 to 2020.

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Author contributions

RRY, MO, and NI contributed to the study conception and design. RRY, YM, SM, MA, MSM, SY, MY, MO, and NI contributed to the acquisition of data. RRY, MO, and NI contributed to the analysis and interpretation of the data. RRY did the literature search and contributed to the drafting of the manuscript. MA, MO, and NI critically appraised the manuscript for important intellectual content. All authors had full access to deidentified data. RRY, MO, and NI had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of data analysis.

Declaration of competing interest

All authors have no competing interests to declare.

Ethical considerations

Ethical approval was obtained from the ethical committees of the National Institute of Infectious Diseases (No.880), School of Tropical Medicine and Global Health of Nagasaki University (NU_TMGH_2020_110_1), National Sanatorium Tamazenshoen (01–01), and the University of the Ryukyus (No. 1680).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi: 10.1016/j.ijid.2022.10.027.

Results: A total of 10,796 newly registered cases of leprosy were reported during the study period, of which 7573 were registered in mainland Japan, 2962 in Okinawa, and 250 were of foreign origin. Most autochthonous cases were born before 1950 in mainland Japan and before 1975 in Okinawa. The number of nonautochthonous cases surpassed that of autochthonous cases in 1992. Nonautochthonous cases originated from 26 countries, particularly Brazil and the Philippines. Three cases of antimicrobial resistance have been detected among nonautochthonous cases since 2004.

Conclusion: Our data suggest that ongoing transmission of leprosy likely ceased in the 1940s in mainland Japan and in the 1970s in Okinawa. With the recent rise of nonautochthonous cases with globalization, continuous surveillance and efforts to maintain leprosy services within the country are necessary even after reaching the state of elimination.

Keywords

Birth year; Epidemiology; Hansen's disease; Japan; Leprosy

Introduction

Leprosy, also known as Hansen's disease, is a disease of the skin and peripheral nerves caused by *Mycobacterium leprae*, which can lead to life-long disfigurements if not treated early. It is classified as a neglected tropical disease by the World Health Organization (WHO) because it presents a largely hidden burden among poor communities with inadequate housing and sanitation, overcrowding, and limited access to basic health care. Worldwide, 200,000–250,000 new cases of leprosy are reported annually to the WHO, over 95% of which are from 23 global priority countries (World Health Organization [WHO], 2021a).

In many developed countries, leprosy has been considered eliminated. However, the issue remains, particularly due to migration related to globalization. In Japan, a few new cases of leprosy are recorded each year, most of which are imported or 'nonautochthonous' cases (Ishii *et al.*, 2000; Koba *et al.*, 2009). Recognizing this worldwide trend, the WHO began including data on nonautochthonous cases in its reporting in 2016 (World Health Organization, 2017).

Leprosy was a major public health concern in Japan in the early 20th century, with a prevalence of approximately 70 per 100,000 individuals in 1990 (Saikawa, 1981). The Government of Japan enacted the 'Act of Leprosy Prevention' in 1907, and hospitalization of patients at public sanatoriums was its main control strategy (Sato and Narita, 2003). After World War II, the country underwent exceptionally rapid economic growth, and the number of new cases decreased substantially (Ishii *et al.*, 2000; Koba *et al.*, 2009).

In this report, we present the patterns of newly diagnosed cases (both autochthonous and nonautochthonous) of leprosy in Japan, over a 73-year period. In the recent roadmap for neglected tropical diseases, the target for leprosy control changed from 'elimination of leprosy as a public health problem' to 'elimination (interruption of transmission)' (World Health Organization 2020). A collection of countries' experiences, including ours, may

provide the evidence to support in making important decisions to reflect this change. Further, we hope that the experiences and lessons of Japan can help devise policies for other countries with existing cases of leprosy and for those that have largely eliminated the disease but are faced with similar challenges as Japan.

Methods

Data source

Data on new leprosy cases were obtained from three sources: (i) the Ministry of Health and Welfare of Japan (1947–1973) (Ministry of Health and Welfare of Japan, 1975), (ii) the Okinawa Leprosy Prevention Association (1900–1998) (Saikawa, 1999), and (iii) an expert group (1964–1992, led by MO; 1993–2020, led by NI). Dermatologists and researchers from the Leprosy Research Center, a branch of the National Institute of Infectious Diseases, form the expert group on leprosy in Japan. Since 1964, this group has collected data through reporting from hospitals, clinics, and sanatoriums in Japan using a questionnaire. Okinawa was included in this dataset in 1974 after being ruled by the United States until 1972. For this study, we selected datasets for mainland Japan and Okinawa (Figure 1), depending on the availability and reliability of data. The data by the expert group were collected prospectively, with interactions with reporting physicians at times of ambiguity or missing data, and we regarded this dataset to be superior in quality over the other two datasets. For the overlapping years, the median differences between the datasets during the periods of 1964–1973 for mainland Japan and 1974–1998 for Okinawa were 15 (interquartile range [IQR] 25–75%, 13.25–38.25) cases and 1 (IQR 25–75%, 0.5–3) case, respectively. The population of Japan was obtained from a dataset issued by the Government of Japan (Statistics Bureau of Japan, 2022).

Our dataset included the location (prefecture) of diagnosis and year of diagnosis (1947–2020); birth year, age at diagnosis, sex, and country of origin (1964–2020); and location of birth, prefecture of residence, characteristics of skin lesions, peripheral nerve damage, grade II disabilities, duration between onset and first consultation, family history of leprosy, laboratory test results (polymerase chain reaction [PCR], skin slit smear [SSS], histopathology, and antiphenolic glycolipid-I [PGL-I] antibody test), Ridley-Jopling and WHO classifications, treatment, and leprosy reactions (1993–2020). Antimicrobial resistance testing for multidrug therapy (MDT) has been performed at the National Institute of Infectious Diseases since 2004, wherein the data are also provided here. This protocol has been described previously (Mori *et al.*, 2012).

Analysis

The data for mainland Japan and Okinawa were analyzed separately due to different endemicity trends. Okinawa, the southernmost part of Japan, consisting of over 40 inhabited and 110 uninhabited islands, was the last pocket of leprosy in the country. It constitutes approximately 1% of the total population. Based on the availability of data and to facilitate comparison, the study time-frame was divided into (i) 5-year blocks (for 1947–1950, 3 years) for comparison of newly registered cases, child and female cases, and incidence rates between 1947–2020; (ii) two periods (1964–1990 and 1991–2020) for comparison of the

countries of origin of nonautochthonous cases; and (iii) 10-year blocks (for 1993–2000, 7 years) for the comparison of clinical presentations in newly registered cases between 1993–2020.

The mean incidence for a given time is the sum of the newly registered annual cases of leprosy divided by the sum of the yearly population for that time, presented as the number of cases per 100,000 individuals. Temporal changes in incidence were evaluated using univariate linear regression and the slope of the regression line (β) was tested for significance. The chi-square test and Z-test of proportions were used, as applicable. Statistical significance was set at $P<0.05$. All analyses were performed using JMP version 14SW (JMP, Cary, NC, USA). Patients aged <15 years were classified as child cases. An Okinawa or nonautochthonous case was defined as that involving an individual born in Okinawa or outside Japan, respectively. Newly registered cases were mapped by prefecture of residence from 1993 to 2020 using QGIS 3.16 software (Open Source Geospatial Foundation Project; http://qgis.osgeo.org).

Results

Between 1947 and 2020, a total of 10,796 newly registered cases of leprosy were reported in Japan, of which 7573 were registered in mainland Japan and 2962 in Okinawa, and 261 were of foreign origin (Table 1). Figure 2 shows the trend of these new cases. The total number of new cases peaked in 1949 (924 cases). In mainland Japan, the number of leprosy cases declined from over 500 annually during the post-World War II period (1947–1950) to under 100 annually by the mid-1960s. Okinawa reported over 100 new cases annually until the late 1960s and more cases than mainland Japan until the late 1990s. The decrease in the incidence of new cases was significant in both mainland Japan (β −6.294; $P<0.001$) and Okinawa (β −1.645; $P<0.001$). The last autochthonous child case was reported in 1990 in both mainland Japan (family history of lepromatous [LL] case) and Okinawa. Thereafter, there have only been reports of sporadic cases (one or two autochthonous cases) from mainland Japan and Okinawa since 2003 and 2002, respectively. The number of nonautochthonous cases surpassed that of the autochthonous cases in 1992. The dataset for each year is provided in Supplementary File 1.

A total of 261 nonautochthonous leprosy cases were registered between 1964 and 2020. The annual median number of cases was 3 (IQR 25–75%, 2–7). Brazil, the Philippines, and South Korea were the top three countries of origin, but the trends differed between the two periods (1964–1990 and 1991–2020) (Table 2).

From 1993 to 2020, 260 new cases of leprosy were reported from 132 facilities (Table 3): 222 (85.4%) from 118 hospitals, 32 (12.3%) from eight sanatoriums, and six (2.3%) from private clinics. Among them, 220 (84.6%) were reported by dermatologists, 32 (12.3%) by doctors working in sanatoriums, and eight (3.1%) by other physicians. A total of 36 cases (13.8%) were from mainland Japan, 49 (18.9%) from Okinawa, and 175 (67.3%) were of foreign origin. There were no child cases among the three groups, except for a female aged 10 years from Madagascar, recorded in 1999. The median age of patients diagnosed from mainland Japan was >70 years, whereas for Okinawa, it gradually increased to 81

years (IQR 25–75%, 74–83) in the past decade. Two patients were in their 90s, with onsets between 1 year and 5 years before diagnosis. During the past three decades, the mean age for nonautochthonous cases was early 30s. Comparisons of the ages among the three groups are presented in Figure 3. More multibacillary (MB) than paucibacillary (PB) types were seen in all groups, with a statistical significance in the nonautochthonous group (chi-square test, *P*-value = 0.0085). Two (0.8%) patients had pure neuritic leprosy. Grade II disability was observed in 7.3% among the cases diagnosed between 2001 and 2020.

Figure 4 presents birth years of newly diagnosed cases of leprosy between 1993 and 2020. All cases from mainland Japan were born before 1942, except for three cases. The detailed descriptions of these cases are provided in Supplementary File 2. For Okinawa, all cases were born before 1975.

Figure 5 shows the geographical distributions of all cases by the prefecture of residence and autochthonous cases by the prefecture of birth, during the period between 1993 and 2020. For those with missing residences (16 cases, 6.2%), the institutional address where they were diagnosed was used. Cases were concentrated in Okinawa (52 cases, 20.0 %), with one case of foreign origin. The major industrial zones of Japan include prefectures of Tokyo (capital city), Kanagawa, Saitama, and Chiba in the Kanto region and Aichi, Mie, Osaka, and Hyogo. Prefectures from these zones, together with Shizuoka, where there are large Brazilian migrant communities, reported 114 (43.8%) cumulative cases, among which, 102 (89.5%) cases were of foreign origin. When autochthonous cases were mapped out by their prefecture of birth, the concentration of cases was seen in Kagoshima prefecture (six cases as opposed to one case by the prefecture of residence), besides Okinawa. The prefecture includes Amami-oshima, which is a string of islands geographically a part of the Okinawa archipelago but historically belongs to Kagoshima prefecture, and was also the last endemic site for leprosy in Japan. No case was reported from the northern part of the country for both autochthonous and nonautochthonous cases.

A total of 86 of 96 (88.7%) MB cases were PCR-positive, as were 26 (59.1%) of the PB cases (chi-square test, $P<0.0001$). The sensitivity of PCR was compared against SSS and histopathology and was found to be significantly greater than the two tests (Z-test of proportion, $P<0.0001$) in PB but not in MB type. In terms of disease spectrum, PCR was positive in all spectra, with the highest observed for borderline (100%), followed by LL (96.9%), and the least (55.6%) for tuberculoid subgroups (Table 4). The sensitivity for both SSS and acid-fast bacilli in histopathology increased consistently as the spectrum moved from indeterminate to LL subgroups. Anti-PGL-I antibody was positive in 40.1% of the cases, with a higher positive proportion seen in borderline lepromatous and LL subgroups.

Table 5 presents the different regimens of drugs used in treating leprosy in Japan. A total of 150 (69.4%) cases received MDT. Resistance testing against MDT (rifampicin, dapsone, and quinolone) was performed for 56 PCR-positive cases diagnosed between 2004 and 2020 (Table 6). All drug-resistant cases were nonautochthonous, MB type, with one case each coming from Brazil, South Korea, and the Philippines. They were registered as all newly diagnosed cases without previous family history and treatment for leprosy (Supplementary File 3).

Type 1 leprosy reactions were reported in 30 (11.5%) cases, and type 2 reactions or erythema nodosum leprosum were reported in 24 (9.2%) cases. A total of 12 (4.6%) patients presented with symptoms compatible with reactions but were not classified. Six patients received thalidomide for erythema nodosum leprosum treatment.

Discussion

Our dataset is one of the most detailed longitudinal nationwide datasets for new cases of leprosy in recent years, and we observed a steep decline in cases in Japan over the 73-year study period. Japan has reached elimination status for leprosy, as currently defined by less than one case per 100,000 population sometime in the first half of the 20th century in mainland Japan and in the early 1990s in Okinawa. However, we are still experiencing cases due to globalization and intercontinental migration, which are bringing in new challenges. This is a challenge to the country and to the affected individuals because diagnosis tend to get delayed owing to the physicians' limited awareness and knowledge of the disease. In the long run, nonautochthonous cases may potentially pose a challenge for transmission of leprosy within Japan unless we maintain some form of surveillance system in place.

It was exceptionally interesting to observe the continuous steep decline of number of new leprosy cases in Japan over this study period as the country has undergone a very rapid development from the 1950s to 1970s. During this time, the gross domestic product of Japan grew almost by 30 folds, which is currently the third largest in the world (National Economic Indicators, 2021). Leprosy is commonly known to be related to poor hygiene and nutrition as well as socioeconomic conditions (Dwivedi *et al*, 2019; Pescarini *et al.,* 2018; Saikawa, 1981). Multiple factors contribute to this decline, and it is almost impossible to identify specific causal factors. Besides improvements in living conditions, it is possible that the strict segregation mandated by the government contributed, to some extent, to reducing disease transmission among the general public before effective microbial treatment became readily available (Saikawa, 1981). In contrast with mainland Japan, Okinawa experienced a delay in case decline, most likely due to a lag in leprosy control measures, geographic characteristics (many islands), strong stigma against patients with leprosy, and slow improvement of water and sewage systems (Koba *et al.,* 2009).

Because infection by *M. leprae* is known to happen at a very early stage of life, birth years of cases of leprosy may potentially provide evidence for continued infection transmission as well as an estimation for when transmission cessation occurred (Feldman and Sturdivant, 1975; Koba *et al.,* 2009). We found that most autochthonous cases in mainland Japan were born before the 1940s. and estimate that the ongoing transmission ceased in mainland Japan sometime during the 1940s. We define cessation of ongoing transmission as the absence of new cases by birth year for a period of at least 5 years. Of the three sporadic cases born after 1950, two cases were individuals living in proximity to Okinawa (Kagoshima and Nagasaki prefectures), and they may have exhibited the Okinawa pattern more. The third case was a Japanese-Brazilian who was the first generation born in Japan with a family history of leprosy. In Okinawa, no cases have been reported in patients born after 1975, and thus, the ongoing transmission highly likely ceased in the 1970s. Interestingly, a report by Nagao in 1985 analyzed new cases of leprosy against their birth years by different locations

in the Miyako Islands of Okinawa and found that all cases reported in 1975–1984 were born before the 1970s (Nagao, 1985). Moreover, a study in the United States showed a decrease in overall incidence rates by successive birth cohorts between 1855–1970 (Feldman and Sturdivant, 1975). Notably, there is a lack of epidemiological reports, which include birth years in the reporting of leprosy in recent years. Because it provides valuable insights into the status of transmission of leprosy within a defined area, we suggest that this needs to be revisited as one indicator to assess transmission in the current epidemiological data collection for leprosy.

Japan, as an archipelago, is an interesting country to investigate the transmission as well as the incubation period of leprosy. The genomic analysis of *M. leprae* in our cases has proven the circulation of leprosy in Japan has been through in-country infections (Benjak *et al.,* 2018). The median incubation period of leprosy is estimated at 2–5 and 8–12 years for PB and MB types, respectively, but can be longer than 20 years in some patients (Fine, 1982; Diniz and Maciel, 2018; Taggart *et al.*, 2022). The cases in our older adult population, some aged over 90 years, is surprising because this indicates that the incubation period can be longer than previously known.

In our study, data on family history were missing in several cases (24.6%). Moreover, we are unsure of the credibility of these data because patients and their families tend to hide their history of the disease due to fear of stigma. The higher rate of missing data for Okinawa, where stigma is more apparent, demonstrates this tendency. However, assuming the data are accurate, there was no family history of leprosy in the two oldest cases, as also most of the older cases were diagnosed in 1993–2020. This shows that when the duration from infection to onset is long, it becomes more challenging to trace the point or source of transmission. This is corroborated by recent reports of autochthonous cases in Europe and the Americas (Beauvillain *et al.,* 2021; Naidu *et al.,* 2021; Rendini and Levis, 2017). In contrast, earlier studies report that being a family contact of a patient plays an increasingly important role in disease transmission when closer to elimination (Koba *et al.,* 2009). Our sporadic cases indeed tended to have a family history of leprosy. Furthermore, the scenario of our Japanese-Brazilian case born in Japan raised a question of how to better define an ‘autochthonous’ case. The working definition we used in our study for ‘autochthonous’ was being born in Japan. However, with globalization, the place of birth less frequently reflects race or origin, and the differentiation between autochthonous and nonautochthonous is becoming more obscure, thus making the task complex. In addition, studies have highlighted the possibility of international migration as a source of transmission (Rendini and Levis, 2017). We have not yet seen a case in Japan in which we suspect infection happened from a nonautochthonous case outside of the same household, but caution is needed as the country continues to experience import of new cases from abroad.

Two factors seemingly affect the number of nonautochthonous cases diagnosed in Japan: the size of the migratory population and the endemicity of leprosy in the country of origin. From 1964 to 1990, cases of leprosy from South Korea were the highest, which probably reflected both the number of the South Koreans in Japan and the endemicity of the disease in South Korea during that period. Leprosy was endemic in South Korea until the late 1970s to the 1980s (Chae, 2020). To date, following India, Brazil has been the second most

endemic country with leprosy (World Health Organization [WHO], 2021a). Notably, cases from Brazil during 1991–2020 accounted for 43.6% of the total new registered cases of leprosy among patients of foreign origin during that period. The number of residents from Brazil in Japan started to increase in the 1980s and declined during the financial crisis in 2007–2008 (Immigration Services Agency of Japan, 2021); new cases of leprosy from Brazil also declined considerably since 2007. The population of Filipinos surpassed Brazilians in 2012 (Immigration Services Agency of Japan, 2021), and we are currently seeing more cases in this population. Demographically, most nonautochthonous cases were of working age at the time of diagnosis. This is also reflected in the geographical distribution of the cases, as demonstrated by the increased concentration of cases around Japan's industrial zones. Similar geographical patterns of leprosy distribution within countries have been previously reported (Suárez-García *et al.,* 2020; Souza *et al.*, 2019).

The male-to-female ratio during the period of decreasing leprosy incidence differs largely across countries (Chen *et al.,* 2007; Feldman and Sturdivant, 1975; Hambridge *et al.,* 2021; Irgens and Skjaerven, 1985; Irgens *et al.,* 1990). In our recent autochthonous cases, we observed more female patients, especially those from Okinawa, which we believe is attributed to higher life expectancy in women (87.74 years) than in men (81.64 years) in Japan (Ministry of Health, 2022). The male-to-female ratio was high among our nonautochthonous cases, which reflects the migratory population of the young male workforce in Japan.

An increasing proportion of MB types have been described in other populations with declining leprosy incidence (Chen *et al.,* 2007; Feldman and Sturdivant, 1975; Hambridge *et al.,* 2021; Irgens *et al.,* 1990; Irgens and Skjaerven, 1985); this pattern was also observed in our autochthonous cases, both from mainland Japan and Okinawa.

We observed that PCR was superior to other methods for diagnosis confirmation. However, no differences were observed in the diagnosis of MB types between SSS, histopathology, and PCR. Because PCR is not always available in resource-limited settings where leprosy is endemic, SSS should be the mainstay of diagnostics for MB type leprosy (Banerjee *et al.,* 2011). For the PB type of leprosy, our results for SSS were not surprising because this is the characteristic of the PB type but, again, emphasized the importance of other methods in its diagnosis. The use of PCR where available and the development of novel field-friendly diagnostic tools, especially for diagnosing the PB type of leprosy, should be encouraged. The effectiveness of the sole use of the anti-PGL-I antibody test was not observed, supporting previous studies (Richardus *et al.,* 2017).

Unfortunately, treatment duration and outcomes of the cases were not collected; however, patients with severe disease (*e.g.,* high bacterial index and numerous skin lesions) were treated for up to 3 years. In Japan, we have our own guidelines for managing leprosy, wherein it is recommended that patients are treated until their bacterial index turns negative or until their active skin lesions disappear (Goto *et al.*, 2013). It also lists alternative treatments when there are contraindications to using the standard MDT, and therefore, we observed some extent of heterogeneity in the types of treatment used. Worldwide, MDT has been used to treat *M. leprae* infection, with no change in its regimen for decades

since 1981 (Smith *et al.*, 2017). There is an ongoing discussion regarding the need for MDT alternatives for cases with adverse events or antimicrobial resistance (World Health Organization [WHO], 2021b). Some antimicrobials listed in this report may support the selection of the candidates.

Monitoring for antimicrobial resistance at our reference center is ongoing as well as in other reference centers in different regions. Although these cases were registered as new, we are uncertain if they were primary or secondary resistance because most often, patients tend to hide their disease status back in their home country. Dapsone resistance has been previously reported from untreated and/or relapse cases of leprosy in Brazil and in South Korea, with varying rates of 1.2–12.7% and 19.2–34%, respectively (Cambau *et al.,* 2018; Andrade *et al.,* 2022; You *et al.,* 2005; Lee *et al.,* 2001; Wu *et al.,* 2022). In contrast, although some efforts have been made for antimicrobial resistance surveillance in the Philippines, as far as the studies show, quinolone resistance has never been reported from the country previously (Cambau *et al.,* 2018; Matsuoka *et al.,* 2007). This is alarming and highlights the importance of continued monitoring of antimicrobial-resistant cases worldwide.

Our study has a few limitations. First, our dataset was obtained from three sources with differences in data collection, which may introduce bias. However, it was important that we integrated these datasets to observe the trend over a longer period. Although we did select one dataset over another, the discrepancies between the overlapping years were not substantial as was described. Second, the efforts to collect data on newly diagnosed leprosy cases have been led by our expert group throughout the years; however, not all physicians in the country are aware of this reporting system. Although the surveillance covers the whole country, we cannot rule out the possibility of unreported cases because leprosy is not on the list of mandatory infectious diseases to be reported to the Government of Japan.

Conclusion

As demonstrated in this study, we no longer have any ongoing transmission of leprosy in Japan; however, we are still challenged with new cases as we embrace globalization. It is necessary that even after reaching the state of elimination, countries maintain diligence in understanding the status of leprosy within the country. Raising awareness and education about the disease, including reporting, to physicians must be continued to retain and build the capacity for continued leprosy services. This also includes the laboratory capacity to diagnose the disease. It is only when efforts from countries with all stages of leprosy endemicity are made that we can further leprosy control and reach our target of zero leprosy worldwide.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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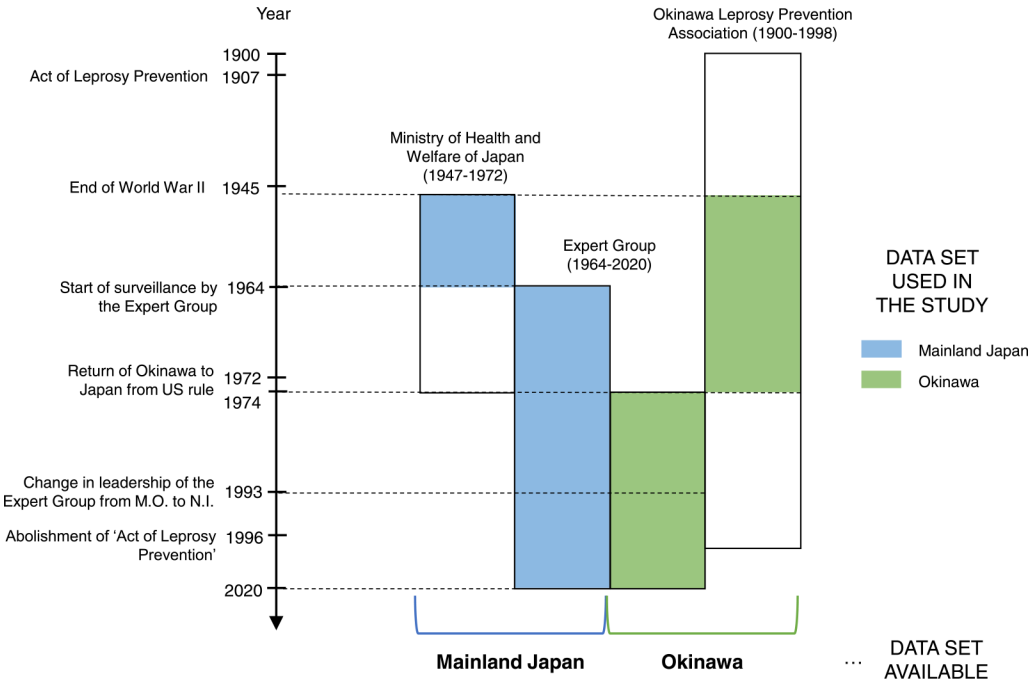

Figure 1.
Data sources in the study.

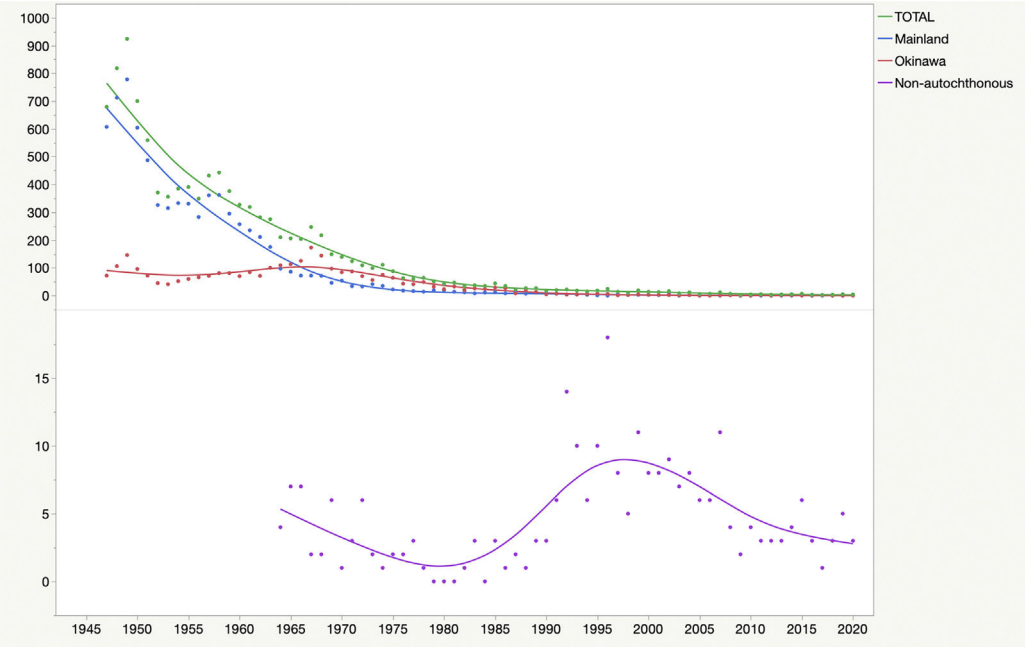

Figure 2.
Trends of newly registered cases of leprosy in Japan, 1947–2020.

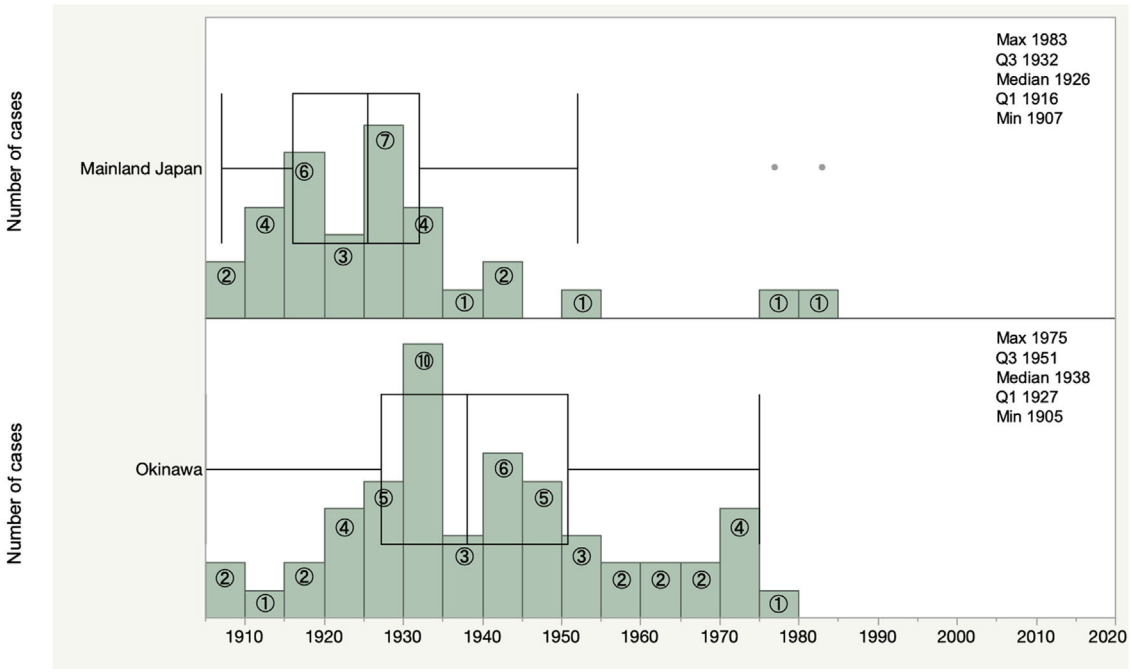

Figure 3.
Years of birth of newly registered autochthonous cases of leprosy in Japan, 1993–2020.

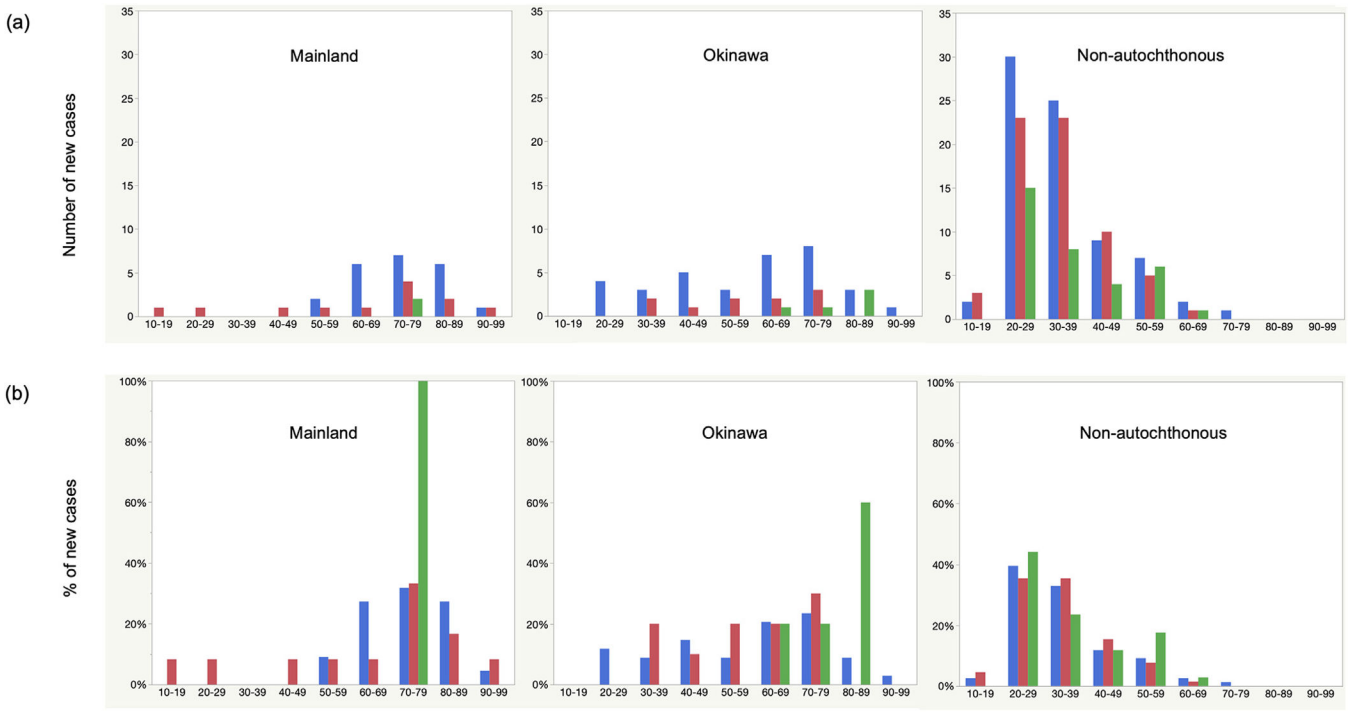

Figure 4.

Numbers (a) and percentages (b) of newly diagnosed leprosy cases by age groups in Japan, 1993–2020. In blue, 1993–2000; in red, 2001–2010; in green, 2011–2020.

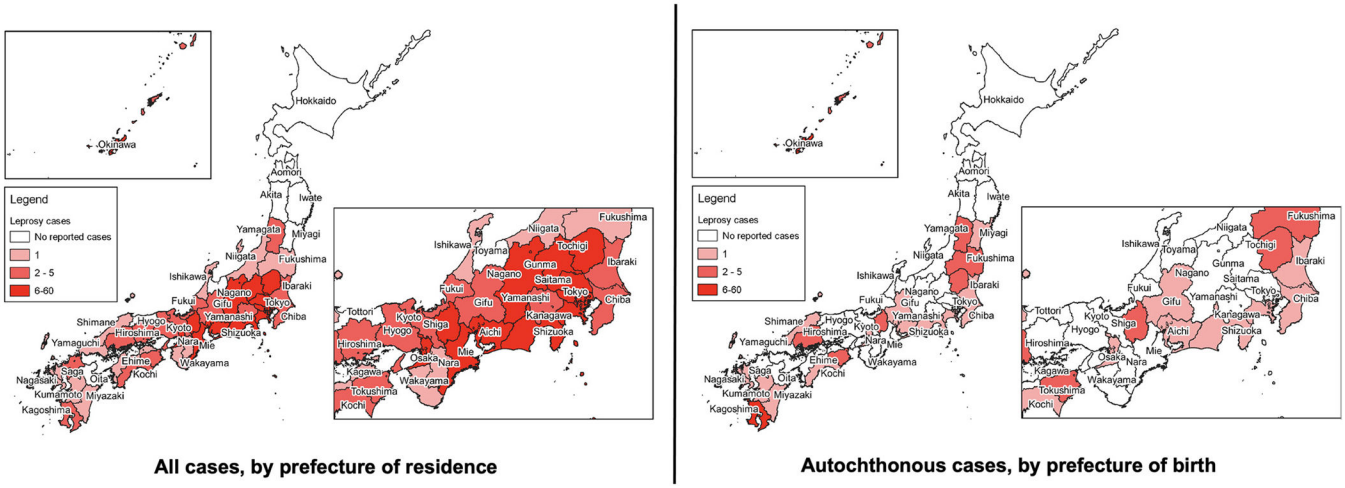

Figure 5.
Distribution of newly registered cases of leprosy in Japan, 1993–2020.

Table 1

Trends of Hansen's disease in Japan by 5-year periods between 1947 and 2020.

Period	Japan (ALL)	Mainland				Okinawa				Nonautochthonous
	New cases (a+b+c)	New cases (a)	Child (<15 years) %	Female%	Mean incidence rate (/100,000 population)	New cases (b)	Child (<15 years) %	Female%	Mean incidence rate (/100,000 population)	New cases (c)
1947–1950	3121	2701	NR	NR	0.8361	420	14%	35%	17.9327	NR
1951–1955	2062	1792	NR	NR	0.4133	270	19%	29%	6.3454[a]	NR
1956–1960	1927	1558	NR	NR	0.3398	369	17%	36%	8.6485	NR
1961–1965	1292	804	NR	NR	0.1680	477	21%	32%	10.3916	11[b]
1966–1970	956	315	6%	42%	0.0623	623	23%	40%	13.1216	18
1971–1975	531	165	13%	38%	0.0304	352	18%	41%	7.1183	14
1976–1980	280	86	17%	49%	0.0149	188	7%	43%	3.4856	6
1981–1985	196	57	12%	39%	0.0095	132	5%	41%	2.3023	7
1986–1990	129	48	4%	42%	0.0078	71	1%	31%	1.1815	10
1991–1995	93	19	0%	47%	0.0030	28	0%	46%	0.4475	46
1996–2000	81	14	0%	50%	0.0022	17	0%	35%	0.2619	50
2001–2005	55	9	0%	56%	0.0014	8	0%	25%	0.1194	38
2006–2010	32	3	0%	0%	0.0005	2	0%	50%	0.0291	27
2011–2015	24	1	0%	0%	0.0002	4	0%	50%	0.0567	19
2016–2020	17	1	0%	0%	0.0002	1	0%	100%	0.0139	15
Total	10,796	7573				2962				261

NR, no report.

[a] Calculated from population data of Okinawa from 1952–1955 due to unavailability of data for 1951.

[b] Sum of cases for 1964 and 1965.

Table 2

Country of origin of nonautochthonous cases of leprosy in Japan, 1964–2020.

1964–1990			1991–2020			ALL		
Country of origin	**Case no.**	**%**	**Country of origin**	**Case no.**	**%**	**Country of origin**	**Case no.**	**%**
South Korea	42	63.6%	Brazil	85	43.6%	Brazil	87	33.3%
Philippines	7	10.6%	Philippines	39	20.0%	Philippines	46	17.6%
Viet Nam	4	6.1%	Indonesia	15	7.7%	South Korea	45	17.2%
Taiwan R.O.C.	3	4.5%	Nepal	15	7.7%	Indonesia	16	6.1%
Brazil	2	3.0%	Bangladesh	8	4.1%	Nepal	15	5.7%
India	2	3.0%	Myanmar	6	3.1%	Bangladesh	9	3.4%
Indonesia	1	1.5%	Thailand	4	2.1%	Myanmar	6	2.3%
USA (Hawaii)	1	1.5%	Paraguay	3	1.5%	Viet Nam	5	1.9%
Comoros	1	1.5%	South Korea	3	1.5%	Thailand	4	1.5%
Bangladesh	1	1.5%	Sri Lanka	3	1.5%	India	4	1.5%
French Polynesia	1	1.5%	India	2	1.0%	Paraguay	3	1.1%
Kuwait	1	1.5%	Micronesia	2	1.0%	Sri Lanka	3	1.1%
			Timor-Leste	1	0.5%	Taiwan R.O.C.	3	1.1%
			Viet Nam	1	0.5%	Micronesia	2	0.8%
			Bolivia	1	0.5%	USA (Hawaii)	2	0.8%
			Cambodia	1	0.5%	Timor-Leste	1	0.4%
			China	1	0.5%	Bolivia	1	0.4%
			Madagascar	1	0.5%	Cambodia	1	0.4%
			Marshall Islands	1	0.5%	China	1	0.4%
			Palau	1	0.5%	Madagascar	1	0.4%
			USA (Hawaii)	1	0.5%	Marshal Island	1	0.4%
			Tanzania	1	0.5%	Palau	1	0.4%
Sub-Total	66		Sub-Total	195		Tanzania	1	0.4%
						Comoros	1	0.4%
						French Polynesia	1	0.4%
						Kuwait	1	0.4%
						Total	261	

Table 3

Clinical presentations of newly registered cases of leprosy in Japan, 1993–2020.

		Mainland			Okinawa			Nonautochthonous			Total
		1993–2000	2001–2010	2011–2020	1993–2000	2001–2010	2011–2020	1993–2000	2001–2010	2011–2020	1993–2020
Number of cases		21	11	2	35	11	5	76	65	34	260
Sex	Male	10	6	2	22	8	2	56	51	21	178
	Female	11	5	0	13	3	3	20	14	13	82
	Male/female ratio	0.9	1.2	0.0	1.7	2.7	0.7	2.8	3.6	1.6	2.2
Age	Median age (IQR 25%–75%)	77 (69–80)	73 (47–80)	76 (75–76)	61 (46–73.5)	64 (46.5–70.5)	81 (74–83)	32 (25.8–39.3)	31 (25–37)	33 (27–45)	36 (28–59.3)
	Children younger than 15 years	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1.3%)	0 (0%)	0 (0%)	1 (0.4%)
Ridley-Jopling classification	I	0 (0%)	1 (9.1%)	0 (0%)	2 (5.7%)	0 (0%)	0 (0%)	2 (2.6%)	2 (3.1%)	0 (0%)	7 (2.7%)
	TT	1 (4.8%)	0 (0%)	0 (0%)	4 (11.4%)	2 (18.2%)	0 (0%)	13 (17.1%)	2 (3.1%)	2 (5.9%)	24 (9.2%)
	BT	5 (23.8%)	1 (9.1%)	1 (50%)	15 (42.9%)	5 (45.5%)	1 (20.0%)	23 (30.3%)	16 (24.6%)	12 (35.3%)	79 (30.4%)
	BB	0 (0%)	1 (9.1%)	0 (0%)	5 (14.3%)	0 (0%)	0 (0%)	9 (11.8%)	3 (4.6%)	1 (2.9%)	19 (7.3%)
	BL	11 (52.4%)	4 (36.4%)	1 (50%)	4 (11.4%)	4 (36.4%)	3 (60.0%)	15 (19.7%)	26 (40.0%)	8 (23.5%)	76 (29.2%)
	LL	3 (14.3%)	4 (36.4%)	0 (0%)	5 (14.3%)	0 (0%)	1 (20.0%)	14 (18.4%)	16 (24.6%)	10 (29.4%)	53 (20.4%)
	PNL	1 (4.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2.9%)	2 (0.8%)
WHO classification	Multibacillary	16 (76.2%)	10 (90.9%)	2 (100%)	21 (60.0%)	5 (45.5%)	4 (80.0%)	44 (57.9%)	53 (81.5%)	21 (61.8%)	176 (67.7%)
	Paucibacillary	5 (23.8%)	1 (9.1%)	0 (0%)	14 (40.0%)	6 (54.5%)	1 (20.0%)	32 (42.1%)	12 (18.5%)	13 (38.2%)	84 (32.3%)
G2D	(+)	NA	4 (36.4%)	2 (100%)	NA	1 (9.1%)	0 (0%)	NA	6 (9.2%)	6 (17.6%)	19 (7.3%)
Duration between onset and the first consultation	≤1 year	6 (28.6%)	7 (63.6%)	1 (50.0%)	10 (28.6%)	5 (45.5%)	4 (80.0%)	20 (26.3%)	48 (73.8%)	20 (58.8%)	121 (46.5%)
	1–2 years	4 (19.0%)	0 (0%)	0 (0%)	9 (25.7%)	1 (9.1%)	0 (0%)	14 (18.4%)	1 (1.5%)	0 (0%)	29 (11.2%)
	2–4 years	2 (9.5%)	1 (9.1%)	0 (0%)	5 (14.3%)	2 (18.2%)	1 (20.0%)	17 (22.4%)	12 (18.5%)	6 (17.6%)	46 (17.7%)
	5–9 years	1 (4.8%)	2 (18.2%)	1 (50.0%)	3 (8.6%)	2 (18.2%)	0 (0%)	4 (5.3%)	2 (3.1%)	3 (8.8%)	18 (6.9%)
	≥10 years	5 (23.8%)	1 (9.1%)	0 (0%)	4 (11.4%)	1 (9.1%)	0 (0%)	5 (6.6%)	2 (3.1%)	4 (11.8%)	22 (8.5%)
	No data	3 (14.3%)	0 (0%)	0 (0%)	4 (11.4%)	0 (0%)	0 (0%)	16 (21.1%)	0 (0%)	1 (2.9%)	24 (9.2%)
Family history of leprosy	(+)	1 (4.8%)	1 (9.1%)	0 (0%)	4 (11.4%)	2 (18.2%)	1 (33.3%)	9 (15.8%)	12 (20.7%)	2 (6.9%)	32 (12.3%)
	No data	5 (23.8%)	1 (9.1%)	1 (50.0%)	19 (54.3%)	5 (45.5%)	2 (40.0%)	19 (25.0%)	7 (10.8%)	5 (14.7%)	64 (24.6%)

I, indeterminate; TT, tuberculoid; BT, borderline tuberculoid; BB, borderline borderline; BL, borderline lepromatous; LL; lepromatous; PNL, pure neuritic leprosy; WHO, World Helath Organization; G2D, grade-II disabilities.

Table 4

Percentage positivity (sensitivity) of laboratory tests performed on cases of leprosy in Japan, 1993–2020.

(a)	Total	Multibacillary	*P*-value	Paucibacillary	*P*-value
Polymerase chain reaction (positive: negative) (n = 141)	112: 29 (79.4%)	86: 11 (88.7%)	-	26: 18 (59.1%)	-
AFB in slit-skin smear (positive: negative) (n = 211)	129: 82 (61.1%)	129: 21 (86.0%)	0.5433	0: 61 (0%)	< 0.0001
AFB in histopathology (positive: negative) (n = 230)	154: 76 (67.0%)	147: 15 (90.7%)	0.5896	7: 61 (10.3%)	< 0.0001
Anti-PGL-I antibody (n = 110)	45: 65 (40.1%)	41: 37 (52.6%)	<0.0001	4: 28 (12.5%)	< 0.0001
(b) Spectrum of leprosy	Polymerase chain reaction (positive: negative) (n = 141)	AFB in slit-skin smear (present: absent) (n = 211)	AFB in histopathology (present: absent) (n = 230)	Anti-PGL-I antibody (positive: negative) (n = 110)	
Indeterminate	3: 1 (75.0%)	0: 5 (0%)	0: 6 (0%)	0: 4 (0%)	
Tuberculoid	5: 3 (62.5%)	0: 14 (0%)	0: 13 (0%)	0: 5 (0%)	
Borderline tuberculoid	25: 16 (61.0%)	14: 48 (22.6%)	28: 46 (37.8%)	5: 28 (15.2%)	
Borderline borderline	6: 0 (100%)	10: 3 (76.9%)	13: 2 (86.7%)	0: 2 (0%)	
Borderline lepromatous	42: 7 (85.7%)	62: 8 (88.6%)	66: 6 (91.7%)	22: 18 (55.0%)	
Lepromatous	31: 1 (96.9%)	43: 2 (95.6%)	47: 2 (95.2%)	18: 7 (72.0%)	
Pure neuritic leprosy	0: 1 (0%)	0: 2 (0%)	0: 1 (0%)	0: 1 (0%)	

AFB, acid-fast bacilli; PGL-I, phenolic glycolipid-I.

Table 5

Treatment of leprosy cases in Japan, 1993–2020.

No. of drugs	Single drug	n	Two drugs	n	Three drugs	n	Four drugs	n	Five drugs	n
Regimen	DDS	5	DDS+RFP(MDT/PB)	34	DDS+RFP+CLF (MDT/MB)	116	MDT+OFLX	4	MDT+OFLX+CAM	1
	RFP	2	DDS+SPFX	1	DDS+RFP+OFLX	7	MDT+CAM	1		
	CLF	1	DDS+OFLX	1	DDS+RFP+LVFX	3	MDT+LVFX	14		
	SPFX	2	CLF+SPFX	1	DDS+CLF+SPFX	1	MDT+SPFX	2		
	OFLX	1	RFP+CLF	1	DDS+CLF+LVFX	1	MDT+MINO	2		
	LVFX	1	DDS+MINO	1	DDS+CLF+CAM	3	DDS+RFP+OFLX+SPFX	3		
			DDS+CLF	2	DDS+RFP+SPFX	2	DDS+CLF+SPFX+CAM	1		
					RFP+CLF+OFLX	1	DDS+RFP+OFLX+MINO	2		
							OFLX+MINO+CAM+LVFX	1		
Total number, by regimen (%)	12 (5.5%)		40 (18.4%)		134 (61.8%)		30 (13.9%)		1 (0.5%)	
							Total number (%)		216 (100%)	

CAM, clarithromycin; CLF, clofazimine; DDS, dapsone; LVFX, levofloxacin; MB, multibacillary; MDT, multidrug therapy; MINO, minocycline; OFLX; ofloxacin; PB, paucibacillary; RFP, rifampicin; SPFX, sparfloxacin.

Table 6

Resistance to multidrug therapy in cases of leprosy diagnosed in Japan, 2004–2020.

Country	No. of polymerase chain reaction (+) samples tested for mutation	Mutation			
		No mutation	*fol P* (dapsone)	*rpo B* (rifampicin)	*gyr A* (quinolones)
Bangladesh	1	1	0	0	0
Brazil	14	13	1	0	0
Cambodia	0	0	0	0	0
East Timor	1	1	0	0	0
Indonesia	7	7	0	0	0
Japan	7	7	0	0	0
South Korea	1	0	1	0	0
Myanmar	1	1	0	0	0
Nepal	10	10	0	0	0
Philippines	12	11	0	0	1
Sri Lanka	0	0	0	0	0
Tanzania	0	0	0	0	0
Thailand	1	1	0	0	0
Viet Nam	1	1	0	0	0
Total	56	53	2	0	1
%	100%	94.6%	3.6%	0.0%	1.8%