

# **Stop TB Japan Action Plan**

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Ministry of Foreign Affairs

Ministry of Health, Labour and Welfare

Japan International Cooperation Agency

Japan Anti-Tuberculosis Association

Stop TB Partnership Japan

The Stop TB Japan Action Plan was formulated in response to “The Global Plan to Stop TB 2006 – 2015” of WHO. WHO recently adopted a new global plan, “Global Strategy and Targets for Tuberculosis Prevention, Care and Control after 2015”. We revised the plan with the aim of achieving a state of low tuberculosis (TB) prevalence as early as possible, as well as contributing to the goal of ending the global TB epidemic. Although the timeline of the revised Action Plan goes to the end of 2020, reconsideration will be made as necessary, in accordance with the revisions of WHO strategy.

## **I. BACKGROUND OF FORMULATION OF THE STOP TB JAPAN ACTION PLAN**

1. TB is a chronic infectious disease such that once infected with its bacilli, the person carries a life-long risk of disease development. The spread of the disease respects no borders, and untiring efforts under international cooperation and partnerships are indispensable for its elimination. Thus, the Ministry of Foreign Affairs (MOFA), Ministry of Health, Labour and Welfare (MHLW), Japan International Cooperation Agency (JICA), Japan Anti-Tuberculosis Association (JATA), and Stop TB Partnership Japan (STBJ) jointly announced the "Stop TB Japan Action Plan" on July 24, 2008, with the determination that the Japanese public and private sectors would actively engage in international efforts for TB control, calling for strengthening of international cooperation and partnership.

2. The Action Plan was developed in 2008 with the objective of reducing TB deaths by 10% worldwide, especially in Asia and Africa, through cooperation among Japan's public and private sectors. It was based on the concept of “human security” that seeks to protect individuals exposed

to a threat and to empowering individuals to make their own decisions and take action against the threat. The Plan referred to the need for strengthening TB control in each country through bilateral cooperation by JICA, for strengthening financial support to international organizations (e.g., the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM)), and involving Japanese NGOs in these activities. Moreover, it clearly stated the importance of enhancing infrastructures for cultivating human resources for the national control program and for encouraging research activities in those countries.

3. Since the start of the Plan, biannual meetings have been held to monitor implementation of the Action Plan by each party, with discussions and information-sharing regarding such matters as national budgets and TB control program activities. The meetings have contributed to ensuring TB-related funding, including contributions to international organizations, and to implementing bilateral cooperation projects by JICA and NGOs. These discussions also help deepen the parties' understanding of the GFATM mechanism and involvement in it. Since the establishment of the Action Plan, great progress in research and development of new anti-TB drugs, diagnostics, and vaccines has been made. (For details of the background and progress, see Attachment 1.)

## II. TB SITUATION IN THE WORLD AND IN JAPAN

### 1. Global TB Situation

The global target to halt and begin to reverse the incidence of TB by 2015 has been attained. Also, the target to reduce the mortality rate by 50% by 2015 compared with a baseline of 1990 is expected to be accomplished. However, achieving the target of halving the prevalence rate of TB is more difficult.

WHO estimates that 8.6 million people developed TB and 1.3 million people died from the disease in 2012. In addition, an estimated 450,000 people developed multidrug-resistant (MDR)-TB, and 170,000 people died from MDR-TB.

Furthermore, one third of newly occurring TB cases remain undiagnosed, and it is an urgent problem that 3 million TB patients are not properly diagnosed or treated every year. In addition to existing problems such as TB co-infected with HIV, new challenges include TB control in children, reactivation and relapse of TB due to the aging population, and complications with diabetes and cancer.

## 2. TB Situation in Japan

As of 2012, more 21,000 new TB patients are registered each year, making it a major infectious disease domestically. The TB incidence rate in Japan (16.7 per 100,000 population in 2012) is four to five times higher than that of western European countries, and Japan is still categorized as a country with an intermediate burden of TB.

The majority of incident cases involve those with high risk, such as the elderly (more than half of newly registered patients are 70 years or older), socioeconomically vulnerable people, and those with medical risk due to an underlying disease. In general, the incidence rate in western Japan is higher than in eastern Japan; however, the fact that major large cities have a higher incidence than surrounding areas reflects the socioeconomic risk of TB in urban areas. Although the influence of immigrants from high TB burden countries is smaller than that of western European countries, it is increasing remarkably among young people and in some specific areas.

While both TB epidemiology and the circumstances for TB control are changing, it is of major concern that citizens are generally losing interest in TB and that the provision of medical services may be degraded due to doctors' lack of experience with TB. (For details of the TB situation throughout the world and in Japan, see Attachment 2.)

## III. SUMMARY OF WHO'S NEW GLOBAL STRATEGY

The new global strategy declared by WHO in May 2014 is summarized as follows.

1. Vision and Goal: With the vision of the world free of TB, the following targets are set to end the global TB epidemic.

Milestone for 2025: 75% reduction in TB death (compared with 2015)

50% reduction in incidence rate (compared with 2015; below 55 TB cases per 100,000 population)

Target for 2035: 95% reduction in TB deaths (compared with 2015)

90% reduction in TB incidence rate (compared to 2015, i.e., below 10 TB cases per 100,000 population)

2. Three pillars and components of bold, innovative New Strategy

WHO proposes to implement the works in the strategy under following three pillars.

① Integrated, patient-centered care and prevention

- Early diagnosis of TB including universal drug-susceptibility testing, and systematic screening of contacts and high-risk groups
- Treatment of all people with TB including drug-resistant TB, and patient support
- Collaborative TB/HIV activities, and management of co-morbidities
- Preventive treatment of persons at high risk, and vaccinations against TB

② Bold policies and supportive systems

- Political commitment with adequate resources for TB care and prevention
- Engagement of communities, civil society organizations, and public and private care providers
- Universal health coverage policy, and regulatory frameworks for case notification, vital registration, quality and rational use of medicines, and infection control
- Social protection, poverty alleviation and actions on other determinants of TB

③ Intensified research and innovation

- Discovery, development and rapid uptake of new tools, interventions and strategies
- Research to optimize implementation and impact, and promote innovations

#### IV. CONTRIBUTIONS OF JAPAN TO ATTAINING GLOBAL TARGETS

In an effort to achieve WHO's goal of ending the global TB epidemic, both the public and the private sectors of Japan contribute to the world by mobilizing their wisdom and technology, in accordance with the concept of human security.

##### 1. Goal

With a target of 10% reduction in TB deaths, public and private sectors work together to reduce the TB mortality rate worldwide, especially in Asia and Africa.

##### 2. Support for High Burden Countries through GFATM, WHO, and Bilateral Cooperation

The Government continues to contribute as a major donor to GFATM, in whose establishment Japan played an important role.

The Government shall maintain commitment to TB control in high-burden countries through WHO and JICA, and further expand and strengthen it. JICA shall continue its cooperation in TB high-burden countries and international training programs in Japan as well as in

third countries with the goal of TB control in high-burden countries, in accordance with the Government's policies such as Country Assistance Policies.

To implement the Government's bilateral cooperation, JATA shall collaborate with JICA in JICA's TB-related cooperation, including projects in trust, dispatch of experts, and training courses. The Government, JICA, and JATA shall promote and strengthen operational research necessary for more effective implementation of TB control, as well as research and development such as the ongoing joint research program of Thailand and Japan.

Furthermore, JATA shall reinforce its current TB experts' network with over 2200 alumni, mostly from developing countries, who have attended international TB training courses in Japan. STBJ shall play a leading role in the global Stop TB Partnership movement, in liaison with the Stop TB Partnership based in Geneva and individual countries' Partnerships.

### 3. Helping the World Attain Universal Health Coverage through TB Control

In order to realize universal health coverage (UHC), it is necessary to enhance accessibility to such basic health services as mother-and-child health, lifestyle-related disease control, and TB services. Also, UHC and TB control should be complementary, as improvement in geographic and economic access to medical services in UHC will also benefit TB control.

The Government, JICA, and JATA shall consider the possibility of providing international cooperation and technical support toward the promotion of UHC, adapting to each country's actual situation, so that the TB control program and promotion of UHC generate synergistic effects. Especially in Asian countries, it is highly possible that approaches based on Japan's experience may be applied in such areas as developing patient support for medical fee payments and living (i.e., public insurance system and public support for fees), installment and maintenance of hardware infrastructures, and establishment of laboratory network and medical information systems.

### 4. Forging Breakthroughs in Innovative Technology

In order to attain WHO's global target for 2035, innovative technological breakthroughs in various fields (e.g., prevention, diagnosis, and treatment of TB) are needed. Japan has been leading the world in studies on immunology, genetic engineering, biotechnology, drug-development technology, and TB research. With its high-capacity TB research and its scientific and technological potential, Japan will be able to contribute to a new series of breakthroughs in the field of TB.

In order to bring together the powers of Japan's science and technology, MHLW shall scale up comprehensive research and development for TB control, including new TB vaccines, new anti-TB drugs against MDR-TB, and new diagnostics, in line with discussions of the Panels of Research and Development, Production, and Distribution of Section of Vaccination, Council for Health and Welfare Science, and in Joint Meeting on Emerging and Re-emerging Infectious Disease Control Promotion Project." Also, when TB studies are adopted in the Plan of Medical Research Promotion stipulated by the Headquarters of Promotion of Health and Medical Care Strategy, MHLW shall ensure necessary funding through the Japan Medical Research Development Organization (planned to be established on April 1, 2015). Moreover, considering collaboration with the Innovation Network Corporation of Japan (INCJ) and the Global Health Innovative Technology (GHIT) Fund, it shall support further TB research and development.

Any promising innovative technology from the following specific areas of research and development should be supported with priority for its earliest practical application.

- New TB vaccine
- Innovative medicine for short-term, effective treatment of MDR-TB
- Simple, rapid, and accurate diagnostics of TB for point of care use
- Research for diagnosis and treatment of latent TB infection (LTBI)
- Establishment of biomarkers for innovative diagnostics and clinical trials

STBJ shall ensure that these technologies can be put practical use as quickly as possible.

##### 5. Globalization of Japan's Technology and Leadership

Japan will lead in and contribute to attaining the goal of the global TB strategy by joint public and private efforts for global expansion of new anti-TB drugs, new TB vaccines, and new diagnostic technologies developed in Japan, as well as digital X-ray technology. In such efforts, the Government actively supports the global expansion of new technologies of Japanese origin. For this purpose, INCJ is expected to accelerate and expand its use in practice, as its mission is to discover Japan's superb technologies and ideas and to introduce them to the world.

For TB, WHO requires an innovative system, due to limitations of the conventional method based on sputum smear microscopy for symptomatic patients. In order to meet this need, public and private sectors should work together to introduce and expand the chest X-ray screening

system that has been widely applied in Japan and has proven so useful, as well as simple TB diagnostics such as the LAMP method developed in Japan. For X-ray examinations, expansion and quality control of computerized radiography are important, due to its advantages of high-quality images with low radiation dose exposure, low operating cost, and elimination of waste fluid disposal causing environmental pollution. Furthermore, use of Japan's experience in quality control of TB diagnosis and treatment by the TB Expert Committee of public health centers would be utilized.

In order for innovations and technologies developed in Japan to be introduced and used widely in developing countries, it is necessary to build a system appropriate to each country. To build an appropriate system, for example, operational research on their technical transfer or practical use may be included in the international training courses conducted by JICA and JATA.

#### 6. Forging GHIT and Other Creative and International Public-Private Partnerships

The GHIT Fund is a creative framework to maximize the use of knowledge on drug development accumulated in Japan, through international public-private partnerships so that people in developing countries can overcome hardships caused by infectious diseases such as TB. MOFA, MHLW, JATA, and STBJ shall cooperate with GHIT with the necessary support so that it can achieve success as early as possible.

#### 7. Roles of TB-related NGOs

NGOs (e.g., JATA, STBJ, AMDA, SHARE, and RESULTS JAPAN), in cooperation with the Government, shall actively extend advocacy activities on the importance of worldwide TB control towards achieving the global target. Also, they should endeavor to eliminate TB by engaging in actions against TB. The Government should cooperate closely with NGOs and support their activities.

### V. OVERCOMING TB IN JAPAN WHILE CONTRIBUTING TO WORLD CONTROL

#### Working to become a low-burden country by 2020

While pursuing the global target and contributing to worldwide TB control, Japan aims to become a low TB burden country (i.e., a country with an incidence rate of less than 10 per 100,000 population) by the 2020 Tokyo Olympics.

For this purpose, MHLW will implement thorough measures against TB by ensuring the necessary budget and personnel and by revising "Prevention Guidelines of Control of TB as a Designated Infectious Disease", and Japan's determination to achieve low prevalence by 2020 should be publicly announced.

The JATA/Research Institute of Tuberculosis (RIT), Anti-Tuberculosis Women's Society, and other organizations related to TB control should make maximum efforts towards the target of realizing a low TB burden state. Playing a leading role in these actions, RIT should provide technical guidance and support for the Government, local governments, and public health centers so that their fight against TB will be most effective.

STBJ should support the activities of TB-related organizations through enhancing public awareness of TB and advocacy.

Priority should be given to the following issues in Japan.

1. Strengthen TB prevention for the elderly, high-risk groups, and danger groups\*
2. Intensify treatment of LTBI.
3. Restructure medical care provision systems appropriate to local needs.
4. Promote research on new tools for TB control.
5. Cultivate human resources and address technical support.
6. Reinforce TB control in mega cities.

\*People in specific occupations who are likely to spread infections once they develop the disease.

## VI. IMPLEMENTING THE ACTION PLAN

### 1. Follow-up Meeting

For each party to monitor the progress of implementing the Action Plan, MOFA, MHLW, JICA, JATA, and STBJ shall exchange views as necessary.

### 2. Cooperation with New Parties

Each of these five parties shall collaborate with other groups or organizations (e.g., Japan Medical Development Organization, INCJ, GHIT Fund, Product Development Partnerships\* (PDPs) such as Aeris, business corporations, and STB Kansai) in support of the Action Plan, according to party and partner standpoints.

\*Public-private partnerships for developing medicines in developing countries



### 3. Promoting the Action Plan

STBJ monitors the progress of the Action Plan. The five parties cooperatively work toward fully implementing the Plan, including funding issues.

## **Stop TB Japan Action Plan and TB Control**

### 1. History of formulating the Stop TB Japan Action Plan

In 2006, the WHO and Stop TB partnership in Geneva set a global target of reducing mortality and prevalence rates of TB by 50% by 2015, compared with the 1990 level in its Global Plan to Stop TB 2006-2015, which was later revised as 2011-2015.

In March 2007, Mr. Winston Zulu, a patient from Zambia with the dual burden of AIDS and TB, made a courtesy visit to Mr. Shinzo Abe, then Prime Minister of Japan (Abe's first cabinet) to discuss the current TB epidemic in Africa, the increasing need for TB control, and his expectation of support from the Japanese Government. In addition, in November 2007, STBJ was established, and in December the nonpartisan group "Stop TB Promotion Parliamentarian Union" was founded to support STBJ.

In the fourth Tokyo International Conference on African Development (TICAD-IV) of May 2008 and in the G8 summit in Toyako and Hokkaido of July 2008, it was stated that strengthening TB control and supporting WHO's global TB strategy were urgently needed in order to attain the MDGs for health in the Yokohama Action Plan and in the Toyako Framework for Action on Global Health - Conference Report of the health-advisory group.

On July 24, 2008, MOFA, MHLW, the Western Pacific Regional Office of WHO, JATA, and STBJ cosponsored the international TB symposium "Toward TB Elimination in the World - From Asia to Africa," where the "Stop TB Japan Action Plan" was announced by MOFA, MHLW, JICA, JATA, and STBJ.

### 2. Progress of TB Control since the Announcement of the Stop TB Japan Action Plan

#### - Securing funding of TB Control (e.g., GFATM and TB control in Japan)

The Japanese government, as a major donor country of the GFATM, had contributed USD \$2,155,880,000 to GFATM by March 2014. MHLW has secured the budget for TB control, including voluntary contributions to WHO, as well as for domestic TB control.

#### - Implementing bilateral cooperation

The Japanese government extended support to TB control in high TB burden countries,

mainly in Asia and Africa (e.g., Indonesia, Cambodia, Myanmar, Bangladesh, Afghanistan, Kenya, and Zambia) in the framework of bilateral technical cooperation and Grant Aid. Specifically, in Indonesia and Kenya, Japan has contributed to improving the quality of smear and culture examinations for TB by introducing and intensifying the external quality assurance system for the TB diagnostic centers, which is essential for TB diagnosis. In Zambia, Japan strengthened activities against TB/HIV co-infection and developed a simple and rapid TB diagnostic tool that could be used at low cost. In Myanmar, the assistance included the provision of anti-TB drugs, strengthening TB control in urban areas and technical assistance in conducting a national TB prevalence survey. In Cambodia, technical cooperation has been extended in three phases, lasting 13 years (1999 to 2013); this assistance, along with Grant Aid, has resulted in reducing TB prevalence by half, for which WHO highly recognized the contribution of the Japanese Government.

In Afghanistan, assistance is being provided for constructing a hospital for patients with TB and other infectious diseases, and for technical cooperation for the national TB control program. In areas of the Philippines that were seriously hit by Typhoon Yolanda in November 2013, a survey was conducted to determine its influence on the TB diagnosis capacity of health centers, and microscopes were provided based on the survey results.

In addition to international training courses in Japan, the third country training programs were conducted in Egypt and Brazil to develop human resources for TB control. In Kenya, plans included sending a TB expert in July 2014 to improve the quality of recording and reporting laboratory work and to intensify external quality assurance of these services under the ongoing administrative devolution.

#### -NGOs' Project Operation in Communities of Developing Countries

After the serious earthquake in Haiti, STBJ investigated its influence on TB control using the grant scheme for NGOs by MOFA. In 2011 and 2012, based on the results of the investigation, JAPAN RESULTS implemented a project for strengthening TB laboratories in collaboration with the Haitian government, JATA, and STBJ and funded by the Japan platform's fund. In 2013, as a joint project under the "public-private partnership for accelerated economic growth" under MOFA, "Data Collection Survey for Public Private Partnership Program on the evaluation of LAMP method for diagnosis of tuberculosis" was conducted with the cooperation of JICA and Eiken Chemical Co., Ltd., in collaboration with Japan RESULTS and RIT/JATA.

In Zambia, JATA contributed to improving the TB diagnostic capacity at health centers and strengthening TB controls in the community using community volunteers as treatment supporters, through "Grant Assistance for Japanese NGO Projects" (2008 to 2012) and "JICA Grassroots Grant Aid Project" (2012 to 2015). In the Philippines, JATA also extended technical cooperation to improve TB control in urban pocket areas in Manila through "Grant Assistance for Japanese NGO Projects" (2008 to 2012) and "JICA Grassroots Grant Aid Project" (2012 to 2015). Its contribution was highly recognized by the Embassy of Japan in the Philippines.

Furthermore, STBJ raised public awareness of TB using Indonesian shadow puppets "Wayang Kulit" funded by MOFA's grant for the NGO project in Indonesia.

#### -Enhancing Commitment to GFATM Programs

In Afghanistan, the JICA office was appointed as the Principal Recipient. Sub-recipients were the Japan-Nepal Health and Tuberculosis Research Association (JANTRA) in Nepal, which was established with the support of JATA, and the Cambodia Anti-Tuberculosis Association, which was established with the support of JATA and the Women's Society for TB Prevention. These organizations contribute much to TB control by implementing GFATM programs in their countries.

#### -Progress in Developing New Anti-TB Drugs, Diagnostics, and Vaccines

Much progress has been made in research and development of anti-TB drugs, diagnostics, and vaccines. Delamanid, a new anti-TB drug developed after 40 years, was developed by Otsuka Pharmaceutical and was approved as a drug for MDR-TB by the Pharmaceutical Committee of European Commission in November 2013. In Japan, an application for manufacturing and marketing the drug was submitted in March 2013, and approval is expected in the near future. RIT/JATA has been involved in its pre-clinical drug evaluation study.

Eiken Chemical Co., Ltd., in collaboration with the Foundation for Innovative New Diagnostics (FIND) in Geneva, developed the LAMP-TB method for simple, rapid TB diagnostics, which is now being evaluated in 14 developing countries in order to receive endorsement from WHO. As part of this project, LAMP-TB was evaluated in the Haiti project under MOFA's public-private partnership for accelerated economic growth.

The National Institute of Biomedical Innovation, Create Vaccine Co., Ltd. (established jointly by Sumitomo Dainippon Pharma and Japan BCG Manufacturing Co. Ltd., and funded by

INCJ), and Aeras (an international NPO based in Washington DC, promoting research and development of new TB vaccines in cooperation with research institutions or corporations in various countries) agreed to work together to develop the first new TB vaccine in 90 years. This vaccine development is partially subsidized by the research fund of MHLW and by the GHIT Fund. STBJ has coordinated the facilitation of these three projects.

RIT/JATA is conducting chemical-substance screening for developing anti-TB drugs under concession from the Global Alliance for TB Drug Development (a New York based NGO that promotes anti-TB drug development in a coalition of public and private institutions, academia, and charities) and is funded by the GHIT Fund.

#### -New Framework Based on Public-Private Partnership

The GHIT Fund, a fund for the specific purpose of research and development of pharmaceutical drugs for developing countries, was established by contributions from MOFA, MHLW, UNDP, the Bill and Melinda Gates Foundation, and Japan's five major pharmaceutical companies. This fund aims to develop innovative medicines of Japanese origin through promoting research and development collaboration between Japan and overseas countries. It targets AIDS, TB, malaria, and other neglected tropical diseases. Great progress toward this target is highly expected so that new drugs against such diseases will become readily available for poor people in developing countries.

[Attachment 2]

**Global TB Situation, 2012**

	Global	HIV-positive TB	MDR-TB	Children (Age<15)
Incidence	8,600,000	1,100,000	450,000	530,000
Mortality	1,300,000	320,000	170,000	74,000

Number of HIV-positive TB, MDR-TB and Children are included in Global total.

**TB incidence and patient detections by WHO region, 2012**

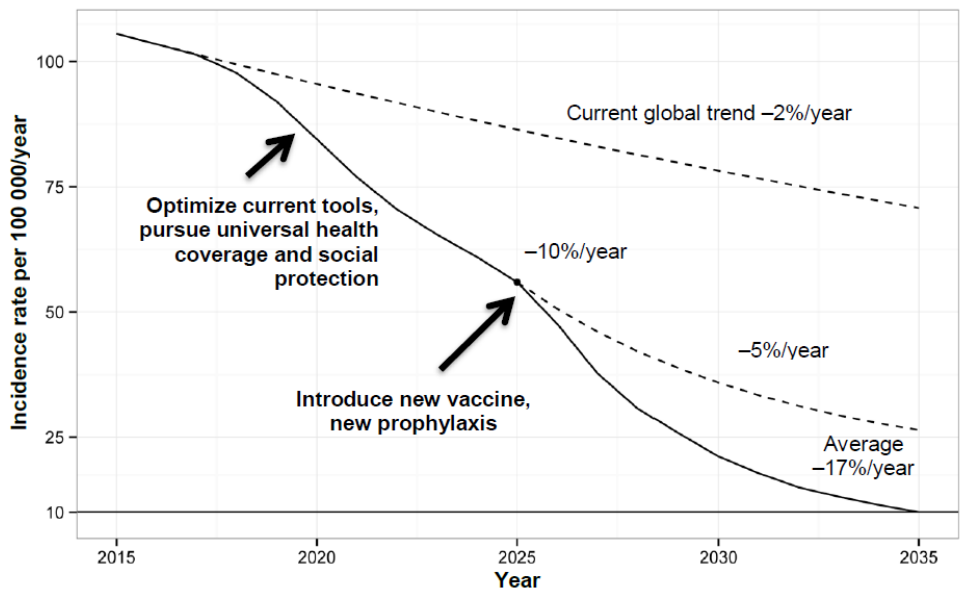
	Western Pacific	South-East Asia	Africa	Eastern Mediterranean	Europe	The Americas	Global
Mortality <sup>1)</sup>	115,000	501,000	480,000	104,000	40,000	25,000	1,260,000
Incidence	1,600,000	3,400,000	2,300,000	670,000	360,000	280,000	8,600,000
Total new cases	1,345,000	2,331,000	1,413,000	431,000	337,000	233,000	6,090,000
Undetected <sup>2)</sup>	16%	30%	39%	36%	6%	17%	29%

1) Mortality: Includes deaths among HIV-positive TB cases

2) Undetected: 1 – no. notified cases / estimated no. new cases

Reference: “WHO Global Tuberculosis Report 2013”

**Projected acceleration in the decline of global tuberculosis incidence rates to target levels**



Reference: “WHO Global strategy and targets for tuberculosis prevention, care and control after 2015”

**TB Situation in Japan, 2012**

No. of newly registered patients	21,283
Incidence rate (per 100,000 population)	16.7
No. of TB deaths	2,110

● No. of newly registered TB patients by age group ( ( ): Proportion in %)

	Age > 39	40-49	50-59	60- 69	70- 79	80+
No. of newly registered patients	3,044 (14.3%)	1,600 (7.5%)	1,795 (8.4%)	3,012 (14.2%)	4,595 (21.6%)	7,237 (34.0%)
Incidence rate (per 100,000 population)	5.6	9.1	11.5	16.3	33.7	81.0

● High-incidence areas

	Osaka City	Sakai City	Nagoya City	Kobe City	Special Wards of Tokyo Metropolis
Incidence rate (per 100,000 population)	42.7	27.9	25.4	24.4	24.3

●No. of newly registered patients with risk factor ( ( ): Proportion in % per total cases)

Diabetes mellitus	3,036	(14.3%)
Healthcare worker <sup>1)</sup>	636	(2.9%)
Unemployed / Day laborer <sup>2)</sup>	1,637	(26.4%)

1) Healthcare worker: Includes; clinical nurses, public health nurses, doctors, physical/occupational therapists, laboratory technicians, radiology technologists.

2) Unemployed/Day laborer: Excludes; entertainment workers, healthcare workers, other regular employees, self-employed workers, home workers, and students. Number refers only to those aged 20-59 years..