

DRUG-RESISTANT TB

SURVEILLANCE & RESPONSE



World Health
Organization

SUPPLEMENT: GLOBAL TUBERCULOSIS REPORT 2014

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***SUPPLEMENT
GLOBAL TUBERCULOSIS REPORT
2014***



**World Health
Organization**

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DRUG-RESISTANT TUBERCULOSIS

SURVEILLANCE & RESPONSE

TUBERCULOSIS (TB) DRUG RESISTANCE SURVEILLANCE HAS BEEN A **PATHFINDER** IN GLOBAL EFFORTS AGAINST **ANTIMICROBIAL RESISTANCE (AMR)**

20 YEARS: IT IS THE **OLDEST AND LARGEST AMR SURVEILLANCE PROJECT** IN THE WORLD

GLOBALLY, THE PROPORTION OF NEW CASES WITH MULTIDRUG-RESISTANT TB (MDR-TB)* HAS NOT CHANGED IN RECENT YEARS. HOWEVER, ALMOST HALF A MILLION NEW CASES CONTINUE TO EMERGE EACH YEAR AND SERIOUS EPIDEMICS IN SOME COUNTRIES JEOPARDIZE PROGRESS

THERE IS PROGRESS IN THE MDR-TB RESPONSE: 136 000 CASES ELIGIBLE FOR MDR-TB TREATMENT WERE DETECTED IN 2013, UP FROM 52 825 CASES DETECTED IN 2009. THE NUMBER OF MDR-TB CASES ENROLLED ON TREATMENT WENT UP FROM 30 500 IN 2009 TO 97 000 IN 2013

KEY CHALLENGES IN THE MDR-TB RESPONSE INCLUDE: GROWING GAPS BETWEEN NUMBERS DETECTED AND NUMBERS STARTED ON TREATMENT, POOR TREATMENT OUTCOMES DUE TO HEALTH SYSTEM WEAKNESSES AND INADEQUATE DRUG REGIMENS, AND INSUFFICIENT FUNDING INCLUDING FOR RESEARCH

5 PRIORITY ACTIONS ARE URGENTLY NEEDED TO ADDRESS THE GLOBAL MDR-TB CRISIS

* MDR-TB is defined as resistance to at least isoniazid and rifampicin, the two most powerful anti-TB drugs.



CONTENT HIGHLIGHTS

MARKING 20 YEARS OF ANTI-TB DRUG RESISTANCE SURVEILLANCE

1. The oldest and largest anti-microbial drug resistance (AMR) surveillance project in the world
2. Strong network of supranational TB reference laboratories fundamental to progress
3. Impressive progress in surveillance coverage
4. The burden of MDR-TB is low globally and in many countries
5. However, some countries have serious MDR-TB epidemics
6. More than half of the global burden of MDR-TB is in three countries: India, China and the Russian Federation
7. Global MDR-TB trend analysis available for the first time
8. Many more countries need to build capacity for continuous surveillance
9. Rapid molecular tests have a growing role in surveillance
10. Surveillance now expanding to cover more drugs

DRUG RESISTANCE SURVEILLANCE DRIVES POLICY AND RESPONSE

11. MDR-TB response is guided by evidence-based policies
12. The status of the MDR-TB response
13. Five priority actions to address the global MDR-TB crisis
 14. (1) Prevent the development of drug resistance through quality treatment of drug-susceptible TB
 15. (2) Expand rapid testing and detection of cases
 16. (3) Provide immediate access to effective treatment and proper care
 17. (4) Prevent transmission through infection control
 18. (5) Increase political commitment and financing
19. New drugs provide new hope
20. Financing for TB and MDR-TB



FOREWORD

Antimicrobial resistance (AMR) represents a growing threat to global public health and security. New resistance mechanisms continue to emerge and spread, undermining the world's ability to treat common infectious diseases. Surveillance to monitor the emergence and spread of drug resistance is a crucial component of the global strategy to combat AMR.

This special supplement to the *Global Tuberculosis Report 2014* marks the 20th anniversary of the *Global Project on Anti-Tuberculosis Drug Resistance Surveillance* and its TB Supranational Reference Laboratory Network. It remains the oldest and largest project on AMR surveillance in the world and guides the response to the epidemic of multidrug-resistant tuberculosis (MDR-TB) at national and global levels.

The first half of the document highlights the progress made in surveillance of anti-TB drug resistance between 1994 and 2013 as well as recent innovations. The second half of the document profiles the global status of the response to the MDR-TB epidemic, which remains a mix of success and failure. Following WHO's pronouncement in 2013 that MDR-TB represented a public health crisis, five priority areas for action, from prevention to cure, are defined.

As a pathfinder with two decades of experience to draw upon, the *Global Project on Anti-Tuberculosis Drug Resistance Surveillance* has not only facilitated the response to MDR-TB but can also be considered as a model for scaling up AMR surveillance for other infectious diseases.



Dr Mario Raviglione

Director, Global TB Programme
World Health Organization

MARKING 20 YEARS OF ANTI-TB

1

THE OLDEST AND LARGEST ANTIMICROBIAL DRUG RESISTANCE SURVEILLANCE PROJECT IN THE WORLD

The *Global Project on anti-TB drug resistance surveillance* (DRS), supported by the TB Supranational Reference Laboratory Network (SRLN), was established in June 1994 in Mainz, Germany by WHO and the Union.* It remains the oldest and largest project on surveillance of anti-microbial drug resistance (AMR) worldwide.

Since 1994, WHO has issued five guidelines on DRS and published key findings in a series of global reports.

* Formerly known as the International Union against TB and Lung Disease.

KEY WHO PUBLICATIONS ON DRUG RESISTANCE SURVEILLANCE (DRS), 1994–2014



The Global Project on anti-TB drug resistance surveillance is hosted by WHO. Key technical partners include KNCV Tuberculosis Foundation, the US Centers for Disease Prevention and Control (CDC), The Union and the Research Institute for Tuberculosis, Japan. Financing is provided mainly by the United States Agency for International Development (USAID), The Global Fund and The Union. Other financial partners include the Bill & Melinda Gates Foundation and the US President's Emergency Plan for AIDS relief (PEPFAR).

DRUG RESISTANCE SURVEILLANCE

2

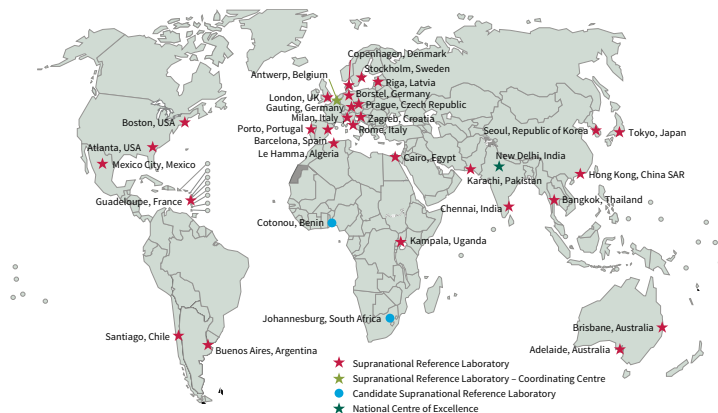
STRONG NETWORK OF TB SUPRANATIONAL REFERENCE LABORATORIES FUNDAMENTAL TO PROGRESS

The global TB Supranational Reference Laboratory Network (SRLN) included 14 laboratories in 1994. By 2014, the network included 33 laboratories covering all six WHO regions.

These laboratories conduct quality assurance, coordinate technical assistance to strengthen laboratory networks in all high TB and MDR-TB burden countries, and are the entry point for the introduction of new TB diagnostics.

Since 2013, the SRLN has expanded its membership to include Centres of Excellence. This is a new category of TB laboratory in large low- and middle-income countries that works specifically to build in-country laboratory capacity.

THE SUPRANATIONAL TB REFERENCE LABORATORY NETWORK (SRLN), 2014



Technical and financial partners: The SRLN is hosted and managed by WHO. The coordinating centre for the SRLN is the Prince Léopold Institute for Tropical Medicine in Antwerp, Belgium.

KEY RESULTS

IMPRESSIVE PROGRESS IN SURVEILLANCE COVERAGE

DATA ON LEVELS OF TB DRUG RESISTANCE AVAILABLE FOR COUNTRIES WITH 95% OF WORLD'S POPULATION AND TB CASES

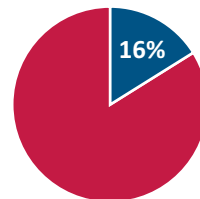
By 2014, data on drug resistance were available for 144 countries, which collectively have 95% of the world's population and TB cases. This shows impressive progress: in the period 1994–1999, data were available for only 35 countries with 20% of the world's population and 16% of the global TB burden.

Half of the 144 countries have continuous surveillance systems based on routine drug susceptibility testing of all TB patients. The remaining half relies on surveys of representative samples of patients.

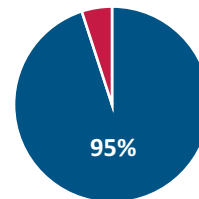
There are three main data gaps:

- Information is lacking from several countries in central and Francophone Africa.
- Data from three high TB burden countries (HBCs) – the Democratic Republic of the Congo, Kenya and Zimbabwe – are from the mid-1990s.
- Five HBCs – Afghanistan, Brazil, India, Indonesia and the Russian Federation – currently rely on sub-national data.

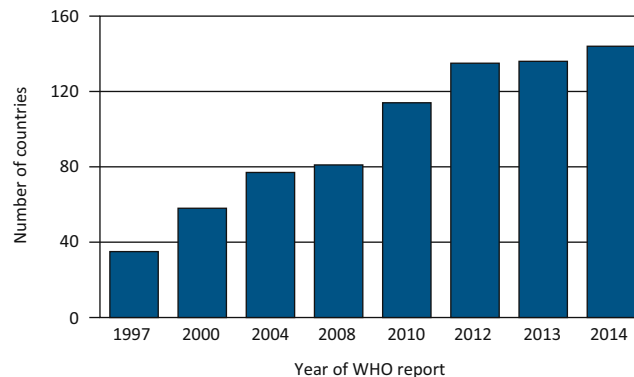
1997: DRS DATA AVAILABLE FOR COUNTRIES WITH 16% OF GLOBAL TB BURDEN



2014: DRS DATA AVAILABLE FOR COUNTRIES WITH 95% OF GLOBAL TB BURDEN



CUMULATIVE NUMBER OF COUNTRIES WITH DRS DATA AVAILABLE FOR PUBLICATION IN WHO REPORTS



THE BURDEN OF MDR-TB IS LOW GLOBALLY AND IN MANY COUNTRIES

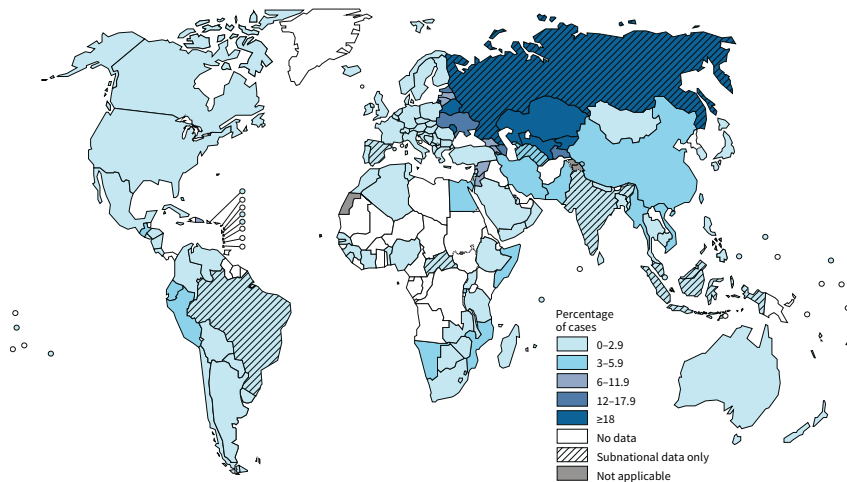
PREVIOUSLY TREATED TB PATIENTS HAVE A SIGNIFICANTLY HIGHER RISK OF MDR-TB COMPARED WITH NEW CASES

Globally, 5% of TB cases are estimated to have MDR-TB. Among new TB cases (that account for most of the global TB burden*), an estimated 3.5% have MDR-TB. The proportion is higher among people previously treated for TB, at 20.5%.

Levels of drug resistance among new cases are <3% in 108 (75%) of the 144 countries with drug resistance surveillance data. This includes almost all countries in the Region of the Americas, most countries in the African and South-East Asia regions, most countries in western Europe and several countries in the Western Pacific Region.

* In 2013, 5.4 million new TB cases and 0.7 million previously treated TB cases were reported to WHO.

PERCENTAGE OF NEW TB CASES WITH MDR-TB



HOWEVER, SOME COUNTRIES HAVE SERIOUS MDR-TB EPIDEMICS

IN ADDITION, EXTENSIVELY DRUG-RESISTANT TB (XDR-TB) HAS BEEN DETECTED IN 100 COUNTRIES

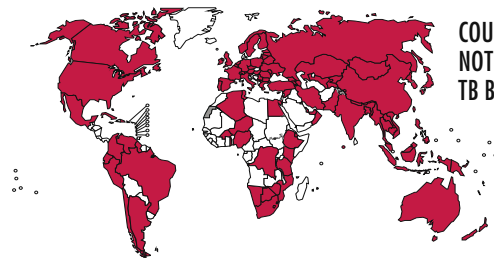
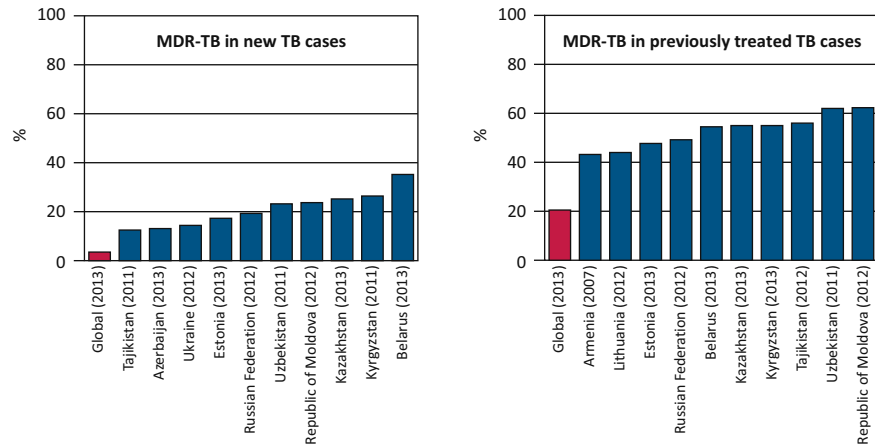
Eastern European and central Asian countries have the highest levels of MDR-TB, reaching 35% of new cases and 75% of previously treated cases in some settings.

In 2013, the average proportion of MDR-TB cases with XDR-TB* was 9.0%. The proportion of MDR-TB cases with XDR-TB was highest in Georgia (20.0%), Kazakhstan (22.7%), Latvia (21.7%), Lithuania (24.8%) and Tajikistan (Dushanbe city and Rudaki district: 21.0%).

By the end of 2013, 100 countries had notified at least one case of XDR-TB.

* XDR-TB is defined as MDR-TB plus resistance to at least one fluoroquinolone and a second-line injectable.

PROPORTIONS OF NEW AND PREVIOUSLY TREATED TB CASES WITH MDR-TB GLOBALLY AND IN THE TOP-TEN COUNTRIES



COUNTRIES (IN RED) THAT HAD NOTIFIED AT LEAST ONE CASE OF XDR-TB BY THE END OF 2013

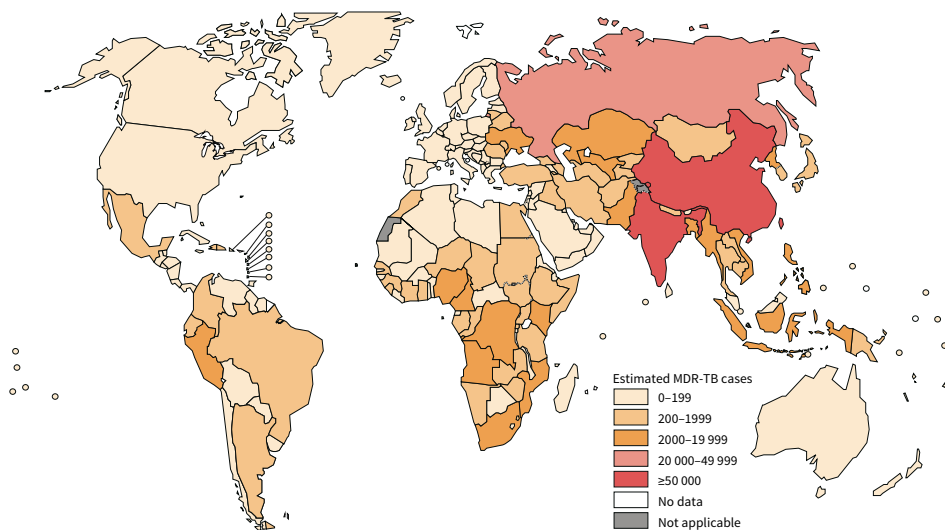
MORE THAN HALF OF THE GLOBAL BURDEN OF MDR-TB IS IN THREE COUNTRIES

THESE ARE INDIA, CHINA AND THE RUSSIAN FEDERATION

Drug resistance surveillance data indicate that in 2013, approximately 480 000 people developed MDR-TB worldwide.

Among TB patients reported by national TB programmes in 2013, there were an estimated 300 000 cases of MDR-TB. More than half of these cases were in India, China and the Russian Federation.

ESTIMATED NUMBER OF MDR-TB CASES AMONG NOTIFIED TB PATIENTS, 2013



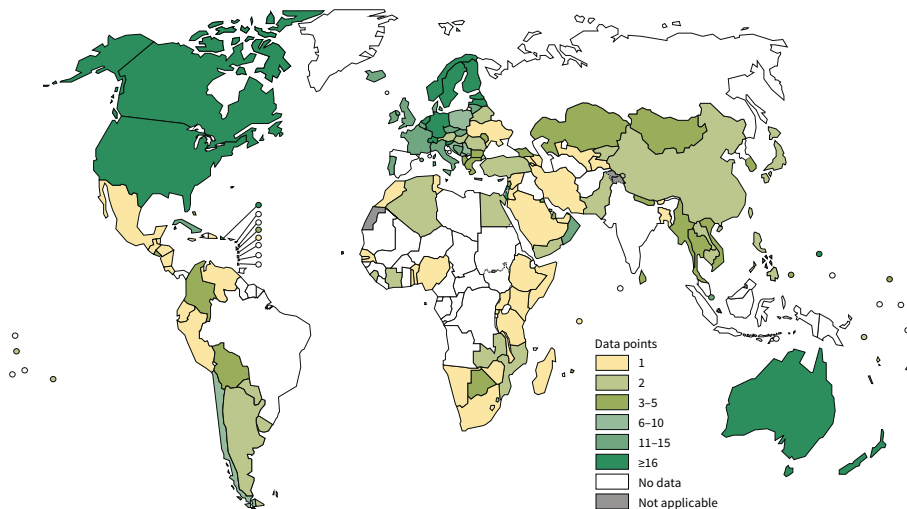
GLOBAL MDR-TB TREND ANALYSIS AVAILABLE FOR THE FIRST TIME

THE ESTIMATED PROPORTION OF NEW CASES WITH MDR-TB HAS NOT CHANGED IN RECENT YEARS

By 2013, data on trends in drug resistance were available for 96 countries: 66 based on continuous surveillance (i.e. routine testing for drug susceptibility among all TB patients) and 30 based on repeat surveys. Collectively, they accounted for 53% of the estimated burden of MDR-TB.

A first time analysis of trends focussed on the period 2008–2013 suggests that globally, the estimated proportion of new cases with MDR-TB has not changed and remains at about 3.5%.

NUMBER OF YEARS FOR WHICH NATIONAL MEASUREMENTS OF DRUG RESISTANCE WERE AVAILABLE AT THE END OF 2013^a



^a Data for China, Lao People's Democratic Republic and Pakistan include data from national prevalence surveys.

MANY MORE COUNTRIES NEED TO BUILD CAPACITY FOR CONTINUOUS SURVEILLANCE

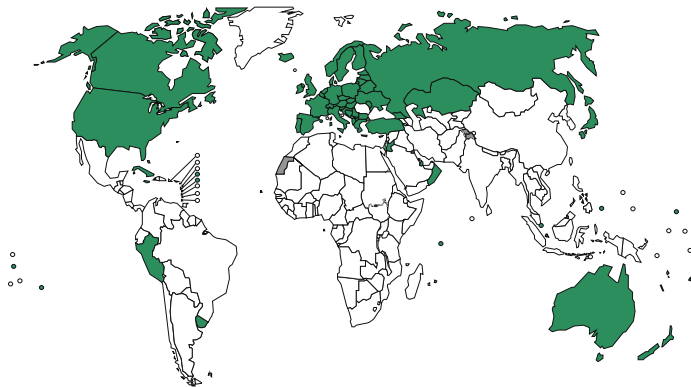
ROUTINE TESTING OF ALL TB PATIENTS ENABLES MUCH BETTER UNDERSTANDING OF TRENDS IN MDR-TB

Continuous surveillance systems (i.e. systems that meet pre-defined standards for data quality and coverage, and in which TB patients are routinely tested for drug resistance) are the best way to generate robust data on trends in drug resistance.

By the end of 2013, 72 countries had continuous surveillance systems. These included 10 high MDR-TB burden countries: Belarus, Bulgaria, Estonia, Georgia, Kazakhstan, Latvia, Lithuania, Republic of Moldova, the Russian Federation and Ukraine. A further seven high MDR-TB burden countries had trend data from special surveys of drug resistance and/or national TB prevalence surveys: China, Mozambique, Myanmar, Pakistan, the Philippines, Thailand and Viet Nam.

All countries need to build capacity for continuous surveillance. In the interim, repeat surveys should be implemented, particularly in high MDR-TB burden countries.

COUNTRIES (IN GREEN) WITH CONTINUOUS SURVEILLANCE SYSTEMS, 2013^a



^a Data from the Russian Federation are subnational only.

NEW TRENDS**RAPID MOLECULAR TESTS HAVE A GROWING ROLE IN SURVEILLANCE****THEY REDUCE LOGISTIC CHALLENGES AND DECREASE COSTS**

Rapid molecular tests such as the Xpert MTB/RIF assay are now being incorporated into drug resistance surveillance. They provide results much faster than conventional methods (culture and phenotypic DST), do not require sophisticated laboratory infrastructure, greatly reduce and simplify laboratory work and decrease costs.

Conventional methods require timely and refrigerated transportation of sputum samples with live bacteria, which are then grown in laboratories prior to testing. Samples also need to be decontaminated to isolate TB bacteria and prevent the growth of other organisms; in this process, there is a risk of killing TB bacilli (through too harsh decontamination) or contamination from other organisms. Molecular tests do not suffer from these limitations and as a result they may detect TB (including drug-resistant cases) that would have been missed by conventional methods.



FIND



FIND

SURVEILLANCE IS NOW EXPANDING TO COVER MORE DRUGS

REPRESENTATIVE DATA ARE REQUIRED ON RESISTANCE TO DRUGS THAT MAY BE PART OF NEW TB REGIMENS

To date, surveillance has focused primarily on resistance to rifampicin and isoniazid, the two most powerful first-line anti-TB drugs.

Fluoroquinolones (FQs) and pyrazinamide (Z) are key drugs being tested as part of new TB and MDR-TB regimens. Understanding the background prevalence of resistance to these drugs is essential.

In 2013, surveillance of resistance to FQs and Z was initiated in five countries: Azerbaijan, Bangladesh, Belarus, Pakistan and South Africa. Preliminary results show that resistance to rifampicin is often associated with resistance to Z. Resistance to ofloxacin (one of the FQs) is generally lower than rifampicin resistance, except in Asian countries where FQs are extensively used. Surveillance will expand to more countries in 2015.



PROGRESS IN DRUG-RESISTANT TB SURVEILLANCE AND RESPONSE IN THE 10

| | BEST ESTIMATE OF NUMBER OF MDR-TB CASES AMONG NOTIFIED PULMONARY TB PATIENTS | LATEST YEAR OF SURVEY ^a OR SURVEILLANCE | NUMBER OF COMPLETED NATIONAL SURVEYS OR SURVEILLANCE | SURVEY OR SURVEILLANCE | COVERAGE OF COMPLETED SURVEY OR SURVEILLANCE (NATIONAL OR SUBNATIONAL) |
|--------------------|--|--|--|------------------------------|--|
| | | 2010–2014 | 2 or more | surveillance | national |
| | | 2005–2009 | 1 | survey | |
| | | ≤2004 | 0 | | subnational |
| India | 62 000 | 2014 | 0 | survey | subnational |
| China | 54 000 | 2014 | 1 | survey | national |
| Russian Federation | 41 000 | 2012 | 0 | surveillance | subnational |
| Pakistan | 13 000 | 2013 | 1 | survey | national |
| Ukraine | 9 400 | 2014 | 1 | surveillance | national |
| Myanmar | 9 300 | 2013 | 3 | survey | national |
| Philippines | 8 500 | 2012 | 2 | survey | national |
| Uzbekistan | 7 900 | 2011 | 1 | survey | national |
| South Africa | 6 900 | 2014 | 1 | survey | national |
| Indonesia | 6 800 | 2010 | 0 | survey | subnational |
| Global | 300 000 | 52% ^c | 46% ^d | 37% ^e | 69% ^f |

— indicates that data are not available

^a Including ongoing surveys.

^b Number of notified cases includes multidrug-resistant (MDR-TB) and rifampicin-resistant (RR-TB) cases.

^c Proportion of countries with survey or continuous surveillance data from 2009–2014 (global value “green” indicates that >50% of countries have such data).

^d Proportion of countries with 2 or more completed national surveys or years of continuous surveillance (global value “red” indicates <50% of countries have such data).

^e Proportion of countries with continuous surveillance (global value “red” indicates <50% of countries have such data).

^f Proportion of countries with national coverage of surveys or continuous surveillance (global value “green” indicates that >50% of countries have such data).

COUNTRIES WITH THE HIGHEST BURDEN OF MDR-TB AND GLOBALLY

| NEW BACTERIOLOGICALLY- CONFIRMED CASES TESTED FOR MDR/RR-TB, 2013 (%) | RETREATMENT CASES TESTED FOR MDR/RR-TB, 2013 (%) | NOTIFIED ^b / ESTIMATED MDR-TB CASES, 2013 (%) | CASES ENROLLED ON MDR-TB TREATMENT / NOTIFIED MDR/RR-TB CASES, 2013 (%) | MDR-TB PATIENTS SUCCESSFULLY TREATED, 2011 COHORT (%) |
|---|--|--|---|---|
| ≥75% | ≥75% | ≥50% | 100% | ≥75% |
| ≥ 50% but <75% | ≥ 50% but <75% | ≥ 20% but <50% | ≥ 80% but <100% | ≥ 50% but <75% |
| <50% | <50% | <20% | <80% | <50% |
| — | — | 57% | 59% | 50% |
| 11% | 32% | 8% | 52% | 50% |
| 84% | 23% | 33% | >100% | 37% |
| 5% | 22% | 20% | 58% | 70% |
| 81% | 52% | >100% | 85% | 34% |
| 13% | 70% | 21% | 34% | 71% |
| 3% | 70% | 47% | 57% | 41% |
| 99% | 45% | 73% | 46% | 53% |
| — | — | >100% | 41% | 45% |
| 0% | 39% | 13% | 89% | 60% |
| 9% | 17% | 46% | 71% | 48% |

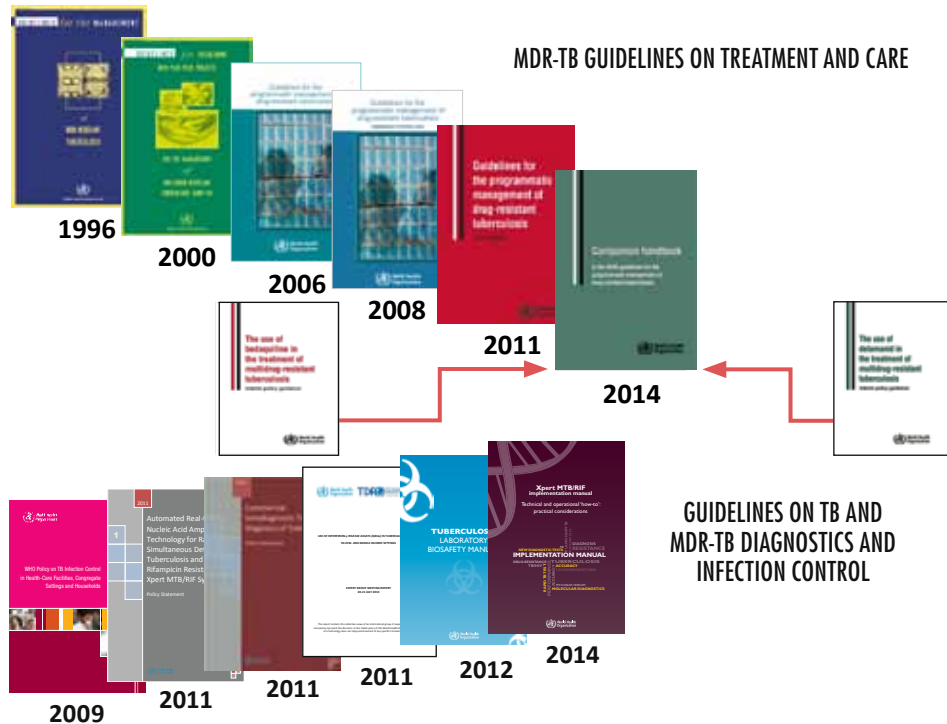
DRUG RESISTANCE SURVEILLANCE

11

MDR-TB RESPONSE IS GUIDED BY EVIDENCE-BASED POLICIES

WHO GUIDANCE FOR DIAGNOSIS AND CARE OF DRUG-RESISTANT TB HAS BEEN AVAILABLE SINCE 1996

Surveillance data compiled since 1994 have been essential to inform and guide the response to MDR-TB. The first guidance on MDR-TB treatment and care was issued in 1996. Since then updated guidance has been issued, including guidelines on laboratories, diagnostics and infection control.



DRIVES POLICY AND RESPONSE

12

THE STATUS OF THE MDR-TB RESPONSE

THERE IS SIGNIFICANT PROGRESS IN MDR-TB DETECTION BUT TREATMENT CHALLENGES COMPROMISE GAINS

Drug resistance surveillance data indicate that in 2013, approximately 480 000 people developed MDR-TB worldwide. If all notified TB patients (6.1 million, new and previously treated) had been tested for drug resistance in 2013, an estimated 300 000 cases of MDR-TB would have been detected.

In 2013, 136 000 of the estimated 300 000 MDR-TB patients who could have been detected were diagnosed and notified. This represents a tripling in MDR-TB detection compared with 2009.

Also in 2013, 97 000 MDR-TB patients were started on treatment, a three-fold increase compared with 2009. However, 39 000 patients diagnosed with MDR-TB (plus an unknown number detected in previous years) were on waiting lists for treatment.

Globally, only 48% of the MDR-TB patients in the 2011 cohort of detected cases were successfully treated. 16% died, 24% did not have their treatment outcome documented or interrupted treatment, and 12% were not cured despite receiving treatment. The treatment success rate for XDR-TB patients in the 2011 cohort was only 22%.

300 000



cases of MDR-TB estimated among TB patients reported by national TB programmes in 2013

136 000



patients with MDR-TB

(136 000 out of 300 000) were detected and reported in 2013

97 000



people with TB were started on second-line treatment for MDR-TB in 2013, leaving many patients on waiting lists for treatment

48%



of MDR-TB patients globally had a successful treatment outcome

Five out of the 27 high MDR-TB countries achieved a treatment success rate of $\geq 70\%$

FIVE PRIORITY ACTIONS TO ADDRESS THE GLOBAL MDR-TB CRISIS

ACTIONS NEEDED ON ALL FRONTS FROM PREVENTION TO CURE

MDR-TB is a global health security risk and carries grave consequences for those affected. WHO therefore called for MDR-TB to be addressed as a public health crisis in 2013.

Five priority actions are crucial to accelerate the response against the MDR-TB epidemic:

- Prevent MDR-TB as a first priority.
- Scale up rapid testing and detection of all MDR-TB cases.
- Ensure prompt access to appropriate MDR-TB care, including adequate supplies of quality drugs and scaled-up country capacity to deliver services.
- Prevent transmission of MDR-TB through appropriate infection control.
- Underpin and sustain the MDR-TB response through high level political commitment, strong leadership across multiple governmental sectors, ever-broadening partnerships, and financing for care and research.



Prevent the development of drug resistance through high quality treatment of drug-susceptible TB



Expand rapid testing and detection of drug-resistant TB cases



Provide immediate access to effective treatment and proper care



Prevent transmission through infection control



Increase political commitment with financing

PREVENT THE DEVELOPMENT OF DRUG RESISTANCE THROUGH HIGH QUALITY TREATMENT OF DRUG-SUSCEPTIBLE TB

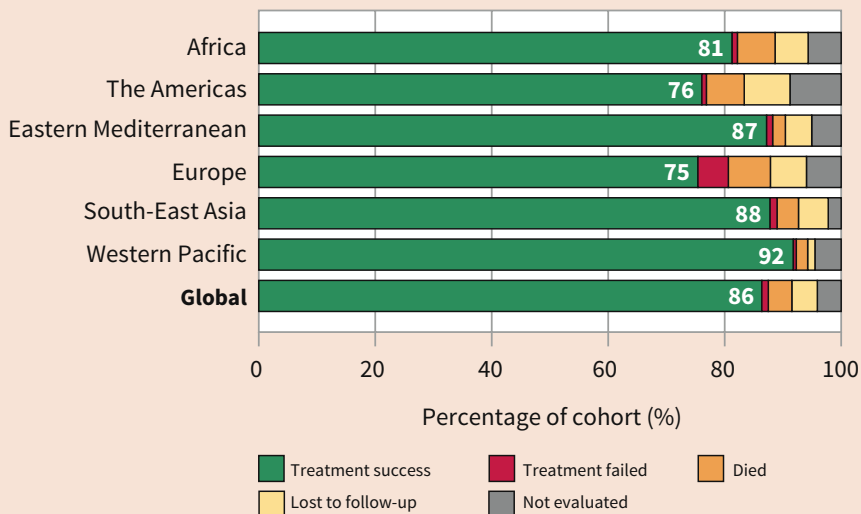
THE BEST PREVENTION AGAINST MDR-TB IS QUALITY TREATMENT OF DRUG-SUSCEPTIBLE TB

Adequate treatment of drug-susceptible TB remains the cornerstone of efforts to prevent the emergence and spread of drug-resistant TB.

Globally, more than 95% of people who develop TB for the first time do not have rifampicin resistance or MDR-TB and can thus be treated successfully using a standard, inexpensive, 6-month course of treatment.

Globally in 2012, the treatment success rate for drug-susceptible TB was 86%, a level that has been maintained for several years.

TREATMENT OUTCOMES FOR NEW AND RELAPSE CASES, 2012, GLOBALLY AND FOR THE SIX WHO REGIONS



EXPAND RAPID TESTING AND DETECTION OF CASES

PROGRESS IN MDR-TB DIAGNOSIS ESSENTIAL TO FIND AND TREAT MORE PEOPLE WITH MDR-TB

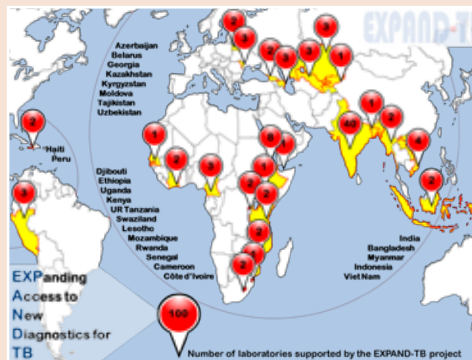
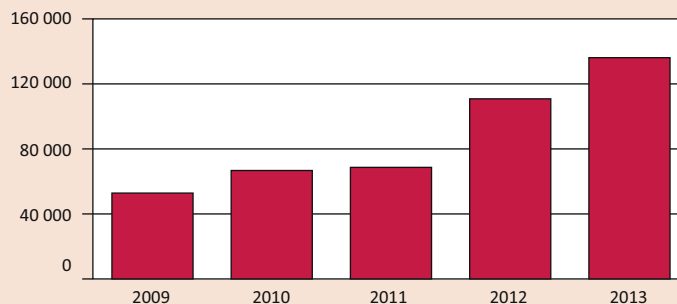
The tripling of MDR-TB detection between 2009 and 2013 follows concerted efforts to strengthen laboratories and roll out rapid tests.

EXPAND-TB, the largest global project focused on accelerating access to modern diagnostics for TB and MDR-TB, is supporting 27 low- and middle-income countries. Between the start of the project in 2009 and the end of June 2014, 89 261 people with MDR-TB were detected in the 97 state-of-the-art laboratories supported by EXPAND-TB partners.

Since 2010, when WHO approved the Xpert MTB/RIF assay (for the simultaneous detection of TB and rifampicin resistance), global roll out of the technology has been impressive. By June 2014, a total of 3269 GeneXpert machines had been procured in the public sector in 108 countries eligible for concessional pricing, and over 1 million cartridges were being procured each quarter.



RIFAMPICIN-RESISTANT AND MULTIDRUG-RESISTANT TB (RR-/MDR-TB)
CASES DETECTED GLOBALLY, 2009–2013



EXPAND-TB IS A MULTI-PARTNER COLLABORATIVE EFFORT. A FULL LIST OF PROJECT PARTNERS IS PROVIDED IN CHAPTER 6 OF THE 2014 GLOBAL TB REPORT.

PROVIDE IMMEDIATE ACCESS TO EFFECTIVE TREATMENT AND PROPER CARE

PROGRESS EVIDENT BUT HEALTH SYSTEM CHALLENGES STILL BLOCK UNIVERSAL ACCESS

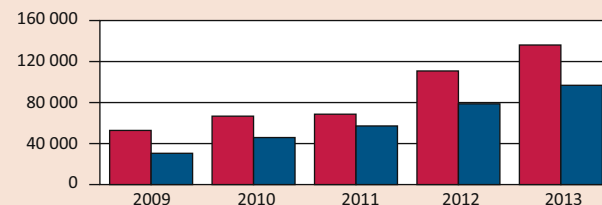
The Global Drug Facility (GDF) of the Stop TB Partnership increased its supplier base for second-line anti-TB drugs from 10 to 19 between 2009 and 2014, resulting in an increase in the available number of second-line drugs (12 to 23) and price reductions.

Country progress to improve delivery of MDR-TB treatment through new approaches is also evident. For example, a shift away from hospitalization to ambulatory care is happening, especially in central Asian countries; treatment of XDR-TB patients is expanding worldwide; and several countries are pioneering shorter regimens for MDR-TB under operational research conditions.

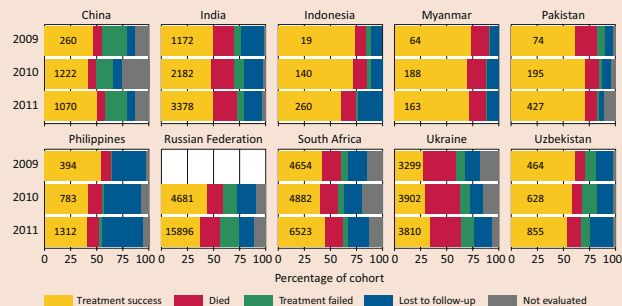
Nonetheless, health service capacity to treat patients has not kept up with the pace of diagnosis, creating growing “waiting lists” for MDR-TB treatment in several countries. In addition, lack of patient follow-up remains a major health service constraint. Patient-centred care (including enablers and social support) is important to improve treatment outcomes.



RIFAMPICIN-RESISTANT AND MULTIDRUG-RESISTANT TB (RR-/MDR-TB) CASES DETECTED (RED) AND TB CASES ENROLLED ON MDR-TB TREATMENT (BLUE) GLOBALLY, 2009–2013



TREATMENT OUTCOMES FOR PATIENTS DIAGNOSED WITH MDR-TB, TOP 10 COUNTRIES, 2009–2011 COHORTS. THE TOTAL NUMBER OF CASES WITH OUTCOME DATA IS SHOWN BESIDE EACH BAR



PREVENT TRANSMISSION THROUGH INFECTION CONTROL



A VITAL INTERVENTION THAT REMAINS NEGLECTED

TB infection control is essential to minimize the risk of disease transmission but remains one of the most neglected components of TB prevention and care.

In 2013, more than 50% of new cases of MDR-TB were among people never before treated for TB, highlighting the importance of transmission and the lack of appropriate infection control measures, particularly at community level.

MDR-TB transmission in health care facilities and in congregate settings such as prisons is a well-known public health threat. This can be effectively addressed by appropriate infection control measures (a mix of environmental, personal protection and administrative measures), rapid identification of drug resistance, and prompt, appropriate treatment of MDR-TB patients.



INCREASE POLITICAL COMMITMENT WITH FINANCING

FUNDING AND BROAD COLLABORATION ARE ESSENTIAL FOR IMPLEMENTATION OF CURRENT INTERVENTIONS AND RESEARCH FOR NEW TOOLS

Without intensified political commitment, financing and coordinated action by many stakeholders, the MDR-TB crisis cannot be effectively addressed.

The World Health Assembly (WHA) resolution on M/XDR-TB in 2009 called for universal access to diagnosis and care. In 2014, three further resolutions with important implications for the MDR-TB response were issued. The topics of these resolutions were (1) the post-2015 global TB strategy; (2) antimicrobial resistance; and (3) palliative care.

The increased commitment of Member States reflected in these resolutions now needs to be translated into well-defined actions. The MDR-TB response needs to be multisectoral and fully financed for current interventions and research for new tools. It needs to encompass a broad range of stakeholders from both the public and private sectors.

THE 2014 WORLD HEALTH ASSEMBLY



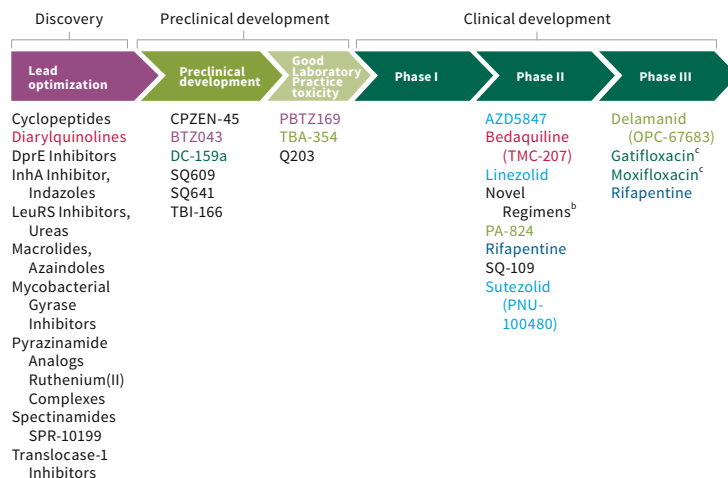
LOOKING AHEAD

NEW DRUGS PROVIDE NEW HOPE

RATIONAL USE IS PARAMOUNT TO PROTECT NEW DRUGS AND PREVENT RESISTANCE

Progress has been made in research and development of new drugs for TB over the last decade. Bedaquiline and delamanid are two new drugs for use in the treatment of MDR-TB which have emerged over 2013–14, and WHO has developed interim guidance on their use. Further, novel drug regimens for shortened treatment of drug-susceptible and/or drug-resistant TB, including new or re-purposed drugs, are under investigation.

WHO has produced a generic policy implementation package for the introduction of new TB drugs or combination of drugs, and is supporting, with other partners, uptake in several countries to inform scaled-up efforts. This policy implementation package includes: delivery model design, monitoring and evaluation, pharmacovigilance, financing, procurement and supply support, private sector engagement, technical assistance, and operational research.

THE DEVELOPMENT PIPELINE FOR NEW TB DRUGS, AUGUST 2014^a

Chemical classes: **fluoroquinolone**, **rifamycin**, **oxazolidinone**, **nitroimidazole**, **diarylquinoline**, **benzothiazinone**

^a Details for projects listed can be found at <http://www.newtbdrugs.org/pipeline.php> and ongoing projects without a lead compound series identified can be viewed at <http://www.newtbdrugs.org/pipeline-discovery.php>

^b Combination regimens: NC-001 -(J-M-Pa-Z), Phase IIa, NCT01215851; NC-002-(M-Pa-Z), Phase IIb, NCT01498419; NC-003-(C-J-Pa-Z), Phase IIa, NCT01691534; PanACEA-MAMS-TB-01-(H-R-Z-E-Q-M), Phase IIb, NCT01785186

^c These trials have been completed and results published.

LOOKING AHEAD

FINANCING FOR TB AND MDR-TB

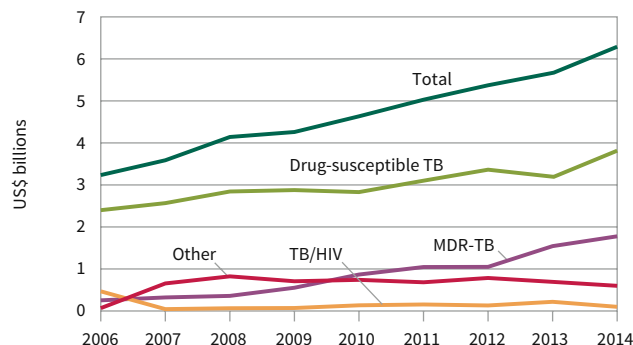
GLOBALLY, FUNDING GAP FOR TB AND MDR-TB PREVENTION, DIAGNOSIS AND TREATMENT ABOUT US\$ 2 BILLION PER YEAR

It is estimated that about US\$ 8 billion per year is required for a full response to the TB epidemic in low- and middle-income countries, of which about one fifth is for detection and treatment of MDR-TB. The amount excludes resources required for research and development for new TB diagnostics, drugs and vaccines, which is estimated at about US\$ 2 billion per year.

Based on reports to WHO from 122 countries with 95% of reported TB cases, funding reached US\$ 6.3 billion in 2014, leaving an annual gap of about US\$ 2 billion. The countries that reported the largest amounts of funding for MDR-TB were India, Kazakhstan, the Russian Federation, South Africa and Ukraine. More funding is needed from both domestic and international donor sources.

In the growing number of countries in which health insurance schemes are used to finance health care, it is essential that coverage of TB and MDR-TB patients is included to ensure that they can access care without incurring catastrophic costs.

FUNDING FOR TB PREVENTION, DIAGNOSIS AND TREATMENT BY INTERVENTION AREA, 2006–2014 (CONSTANT 2014 US\$ BILLIONS)





TAKE-AWAY MESSAGES

Surveillance of TB drug resistance over the last two decades has informed and guided the response to the MDR-TB epidemic, and recent innovations in molecular diagnostics allow a definitive shift to routine surveillance (rather than special surveys). As a pathfinder with two decades of experience to draw upon, the *Global Project on Anti-Tuberculosis Drug Resistance Surveillance* is a model for scaling up surveillance of antimicrobial resistance (AMR) to other infectious diseases.

Considerable progress in the global and national response to the MDR-TB epidemic is evident, particularly since 2009 when the World Health Assembly called for universal access to diagnosis and treatment of MDR-TB. However, it remains far from sufficient. While the percentage of new TB cases that have MDR-TB globally remains unchanged, some countries have severe epidemics and in many settings the treatment success rate is alarmingly low. Five priority actions, from prevention to cure, are required. Health system barriers, diagnostic and treatment challenges and inadequate funding for care and research must be urgently addressed.

The time to act is now.



8 YEAR OLD JEROME FROM MANILA WAS CURED OF MDR-TB IN 2013

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