

Strengthening and aligning diagnosis and treatment of drug-resistant TB in Russian Federation

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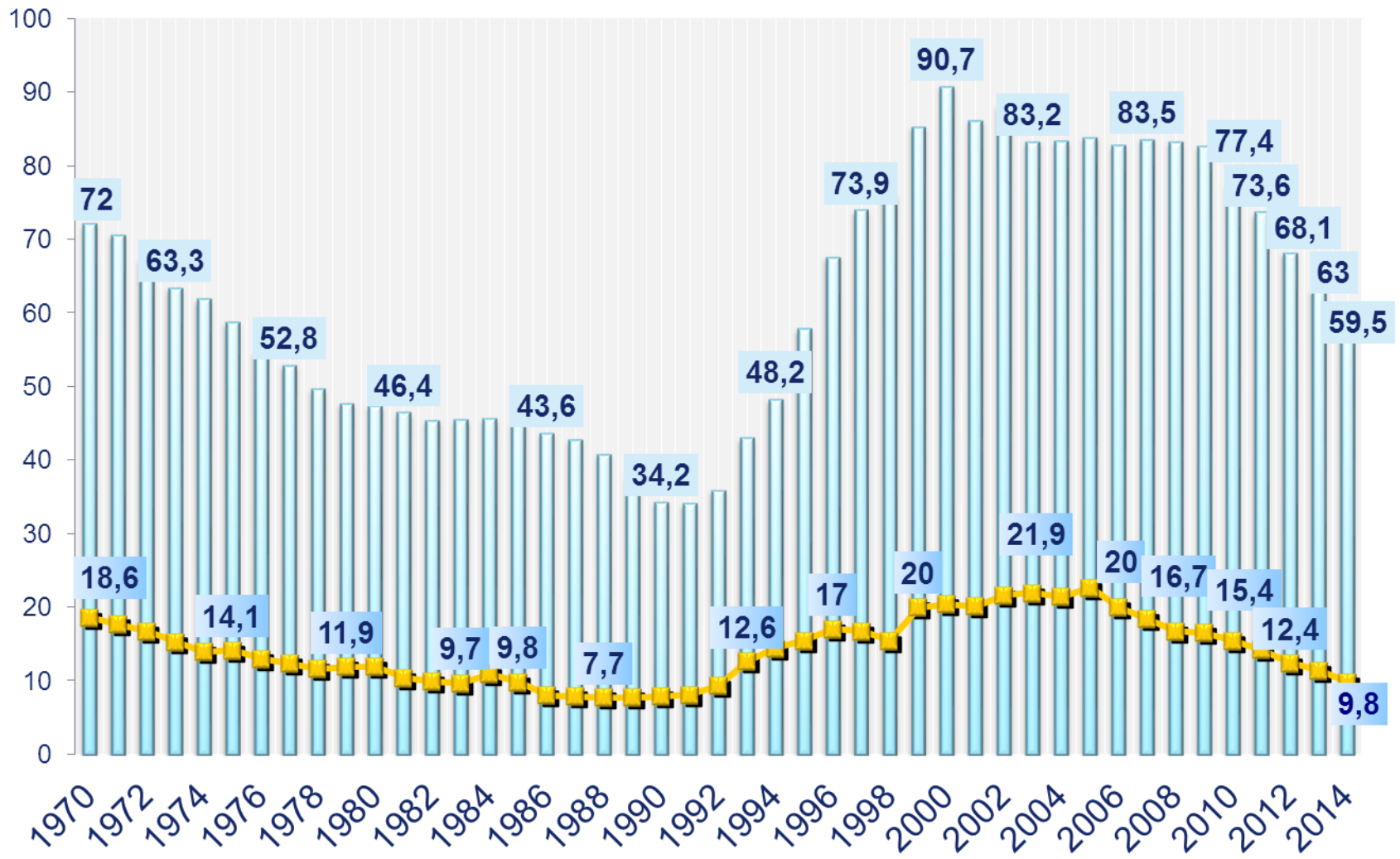
67th World Health Assembly



POST-2015 GLOBAL TUBERCULOSIS STRATEGY FRAMEWORK

VISION	A world free of tuberculosis – zero deaths, disease and suffering due to tuberculosis
GOAL	End the global tuberculosis epidemic
MILESTONES for 2025	<ul style="list-style-type: none">• – 75% reduction in tuberculosis deaths (compared with 2015);• – 50% reduction in tuberculosis incidence rate (compared with 2015) (less than 55 tuberculosis cases per 100 000 population)• – No affected families facing catastrophic costs due to tuberculosis
TARGETS for 2035	<ul style="list-style-type: none">• – 95% reduction in tuberculosis deaths (compared with 2015)• – 90% reduction in tuberculosis incidence rate (compared with 2015) (less than 10 tuberculosis cases per 100 000 population)• – No affected families facing catastrophic costs due to tuberculosis

TB Incidence and Mortality Rates in the Russian Federation, 2014 (per 100 000 population)

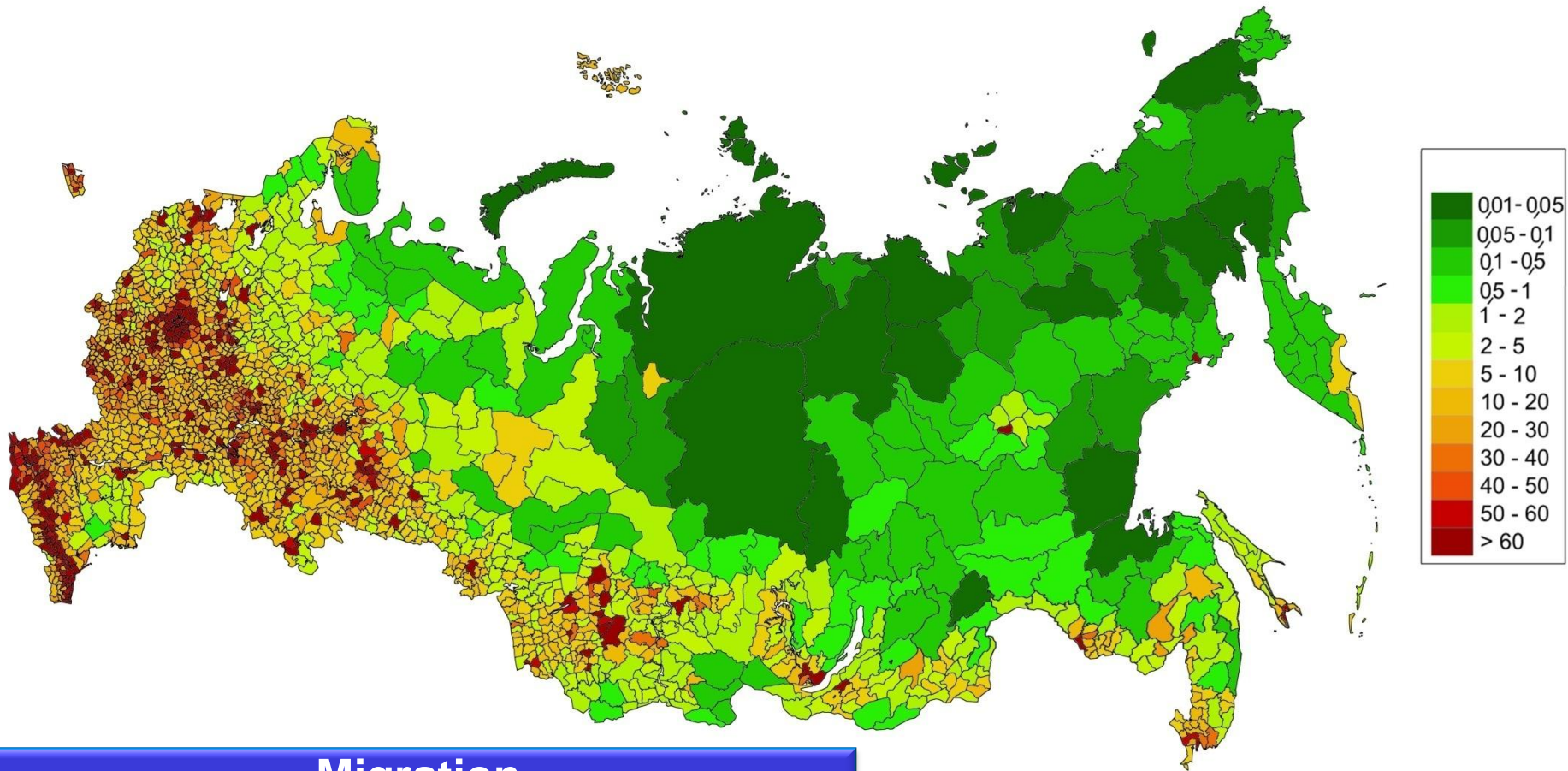


Incidence

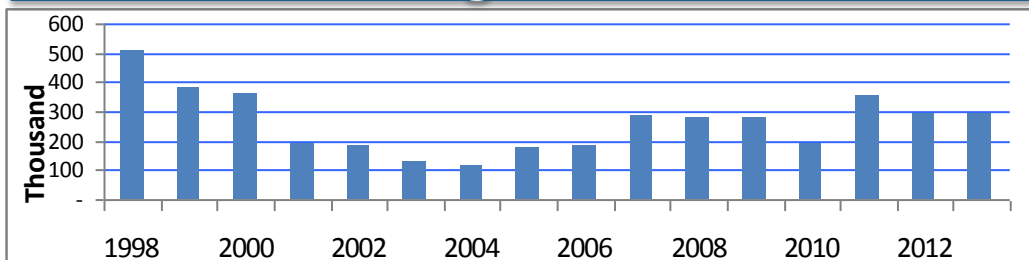
Mortality

Source: Form № 8, Rosstat

Population of the RF

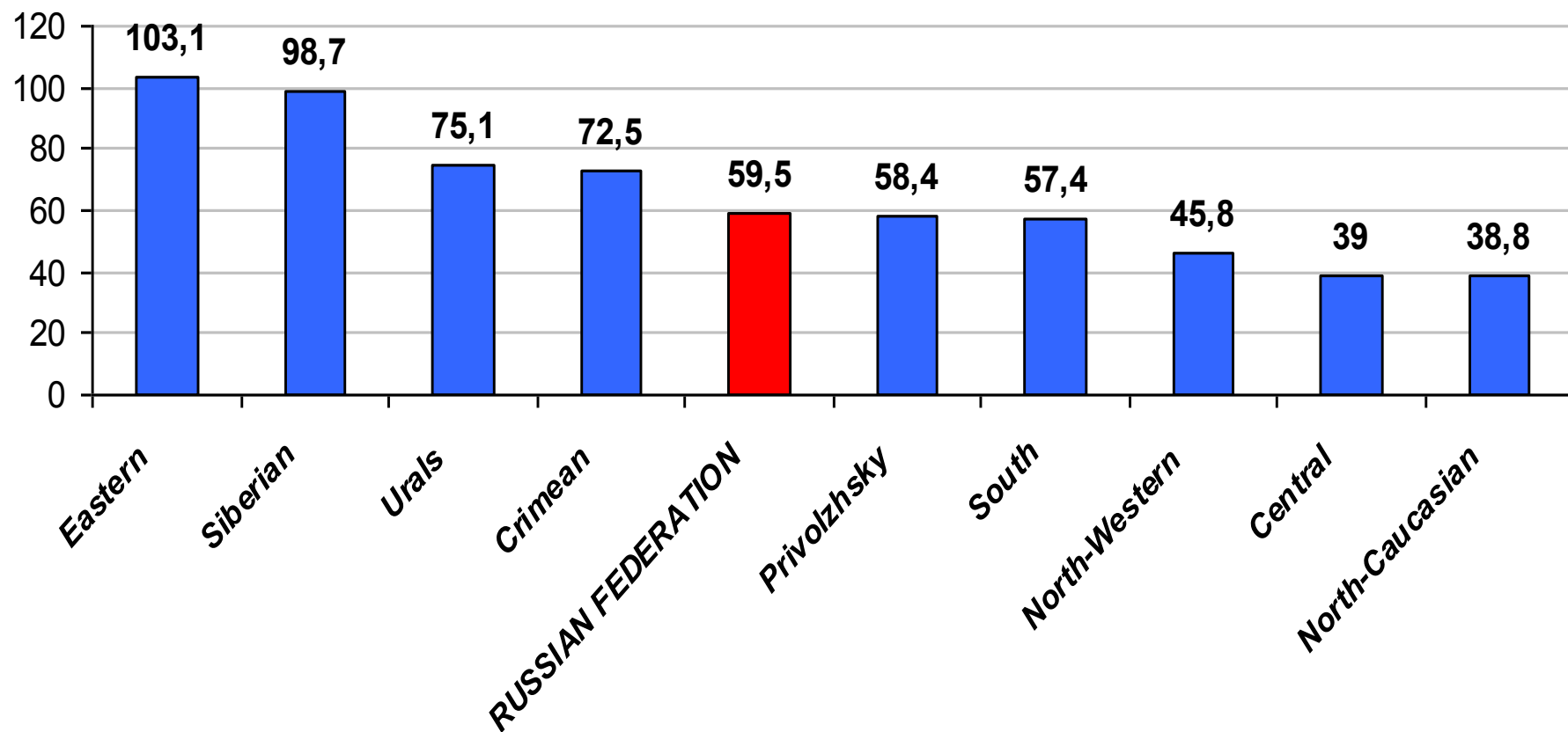


Migration

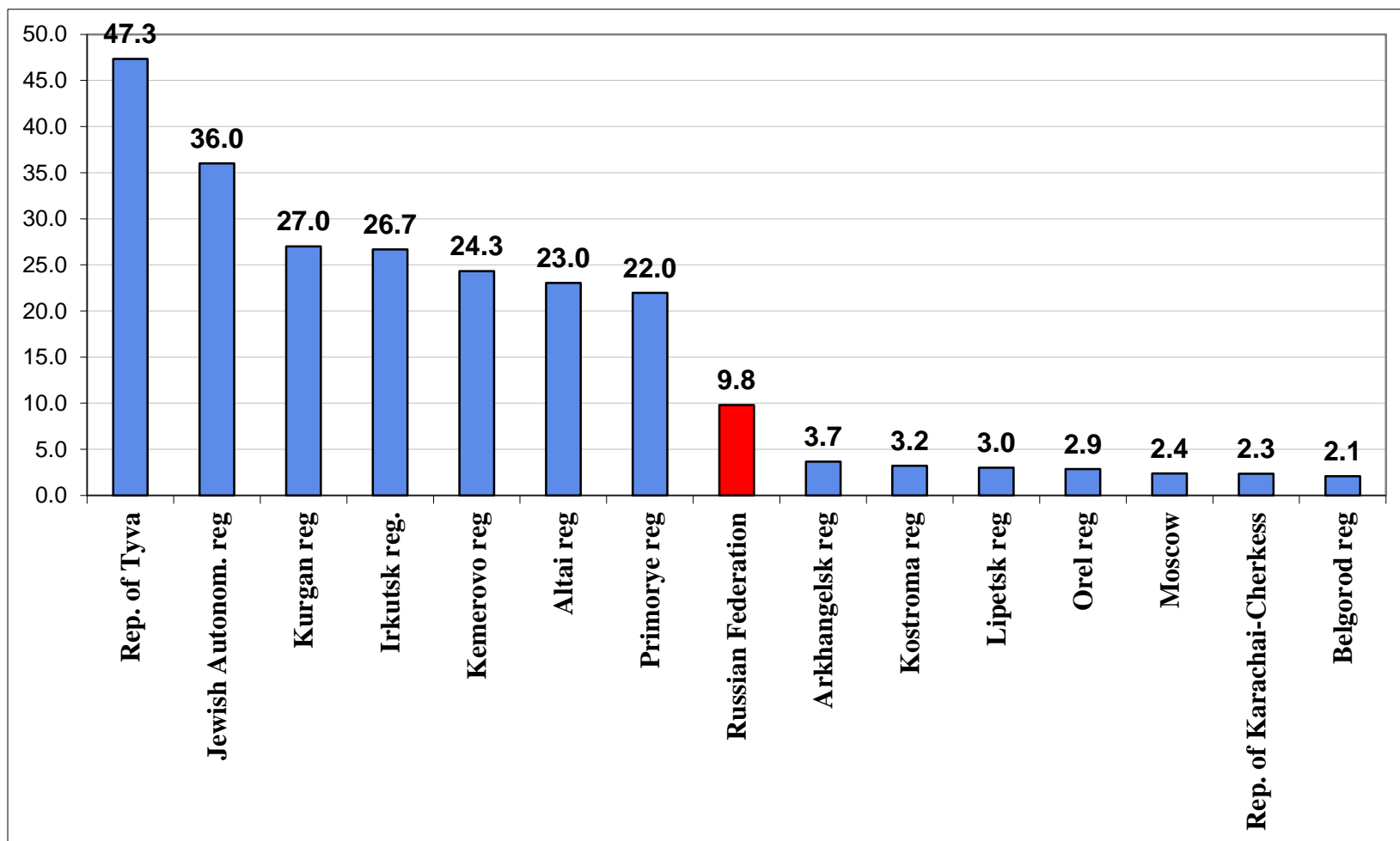


Total population in **2014** –
143666900

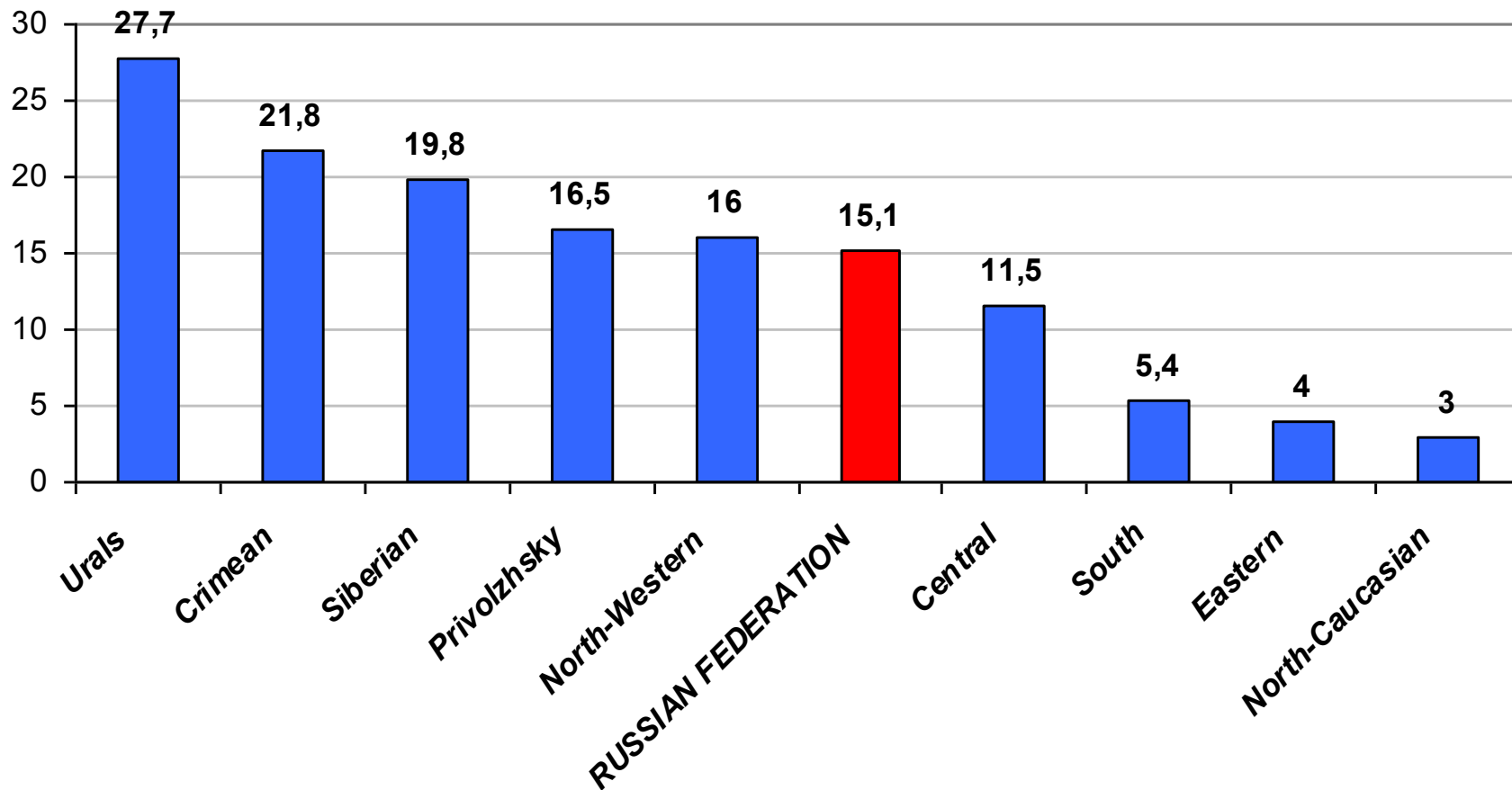
TB Incidence by the Federal Districts of the RF in 2014 (per 100 000 population)



TB Mortality Rates by the Federal Entities of the RF in 2014 (per 100 000 population)



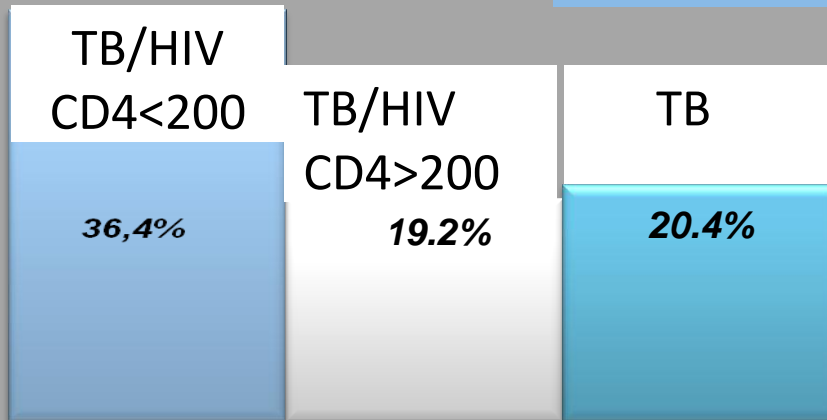
Proportion of New HIV/TB Cases Among All New Notified TB Cases by the Federal Districts, 2014



Source: Form № 33

MDR-TB and HIV-Infection

Data from Moscow (n=226)



Zimina V., Vasilyeva I., 2012

MDR TB among new TB cases:

Data from Kemerovo (n=6131)

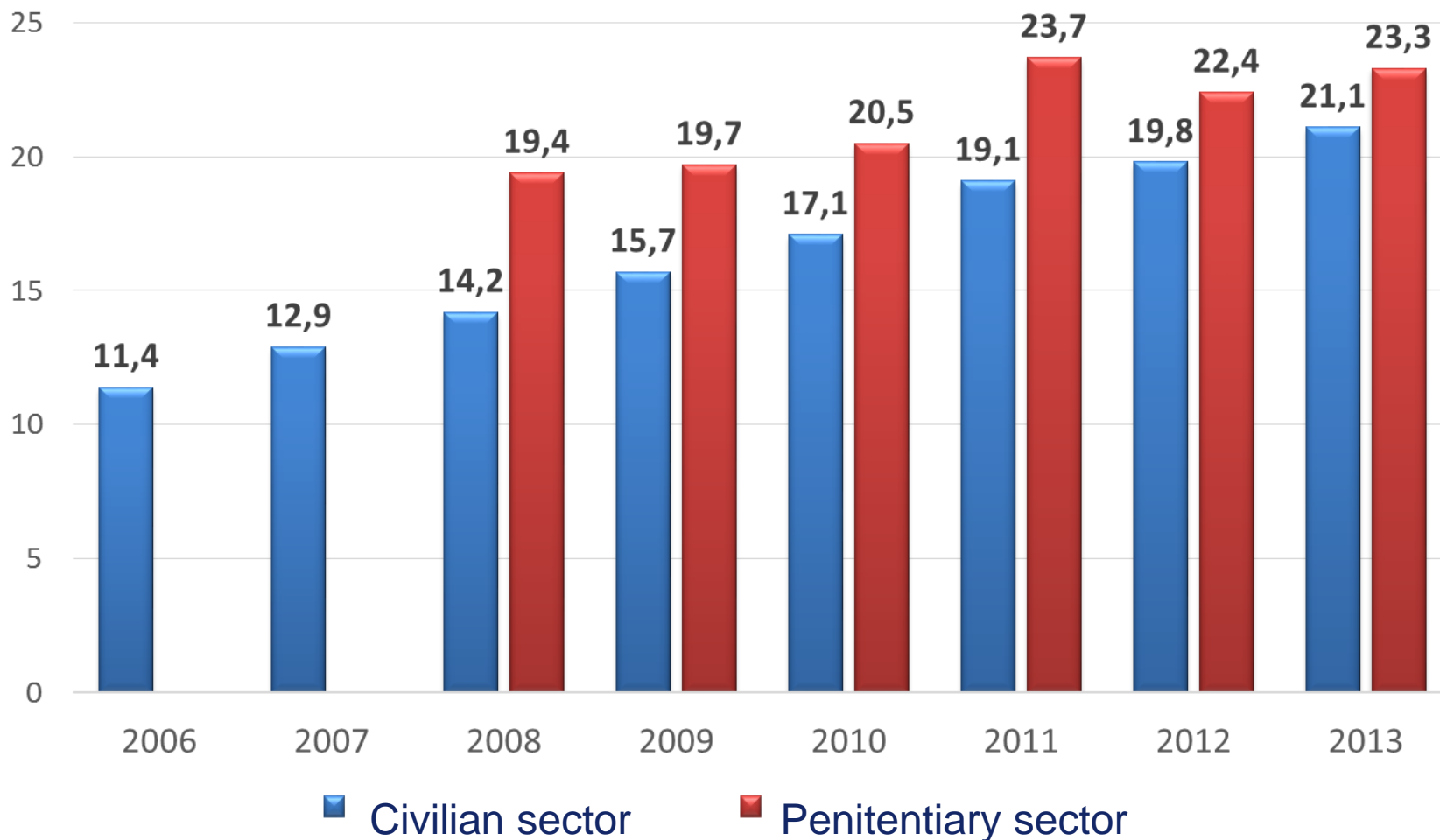
TB - 28 %
TB/HIV - 41,2%

MDR TB among relapses:

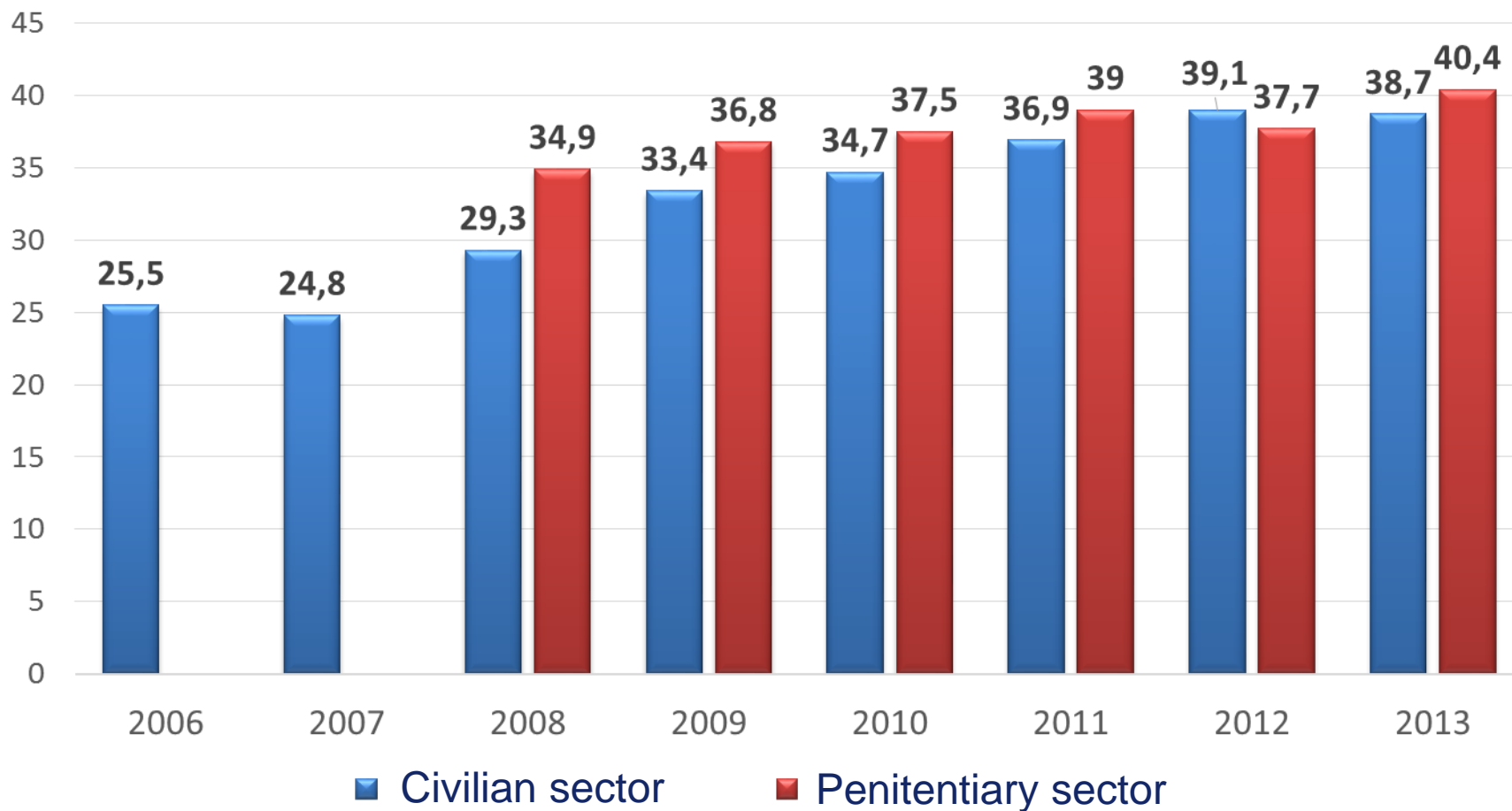
TB - 48,5%
TB/HIV - 54,7%

Piyanzova T. 2014

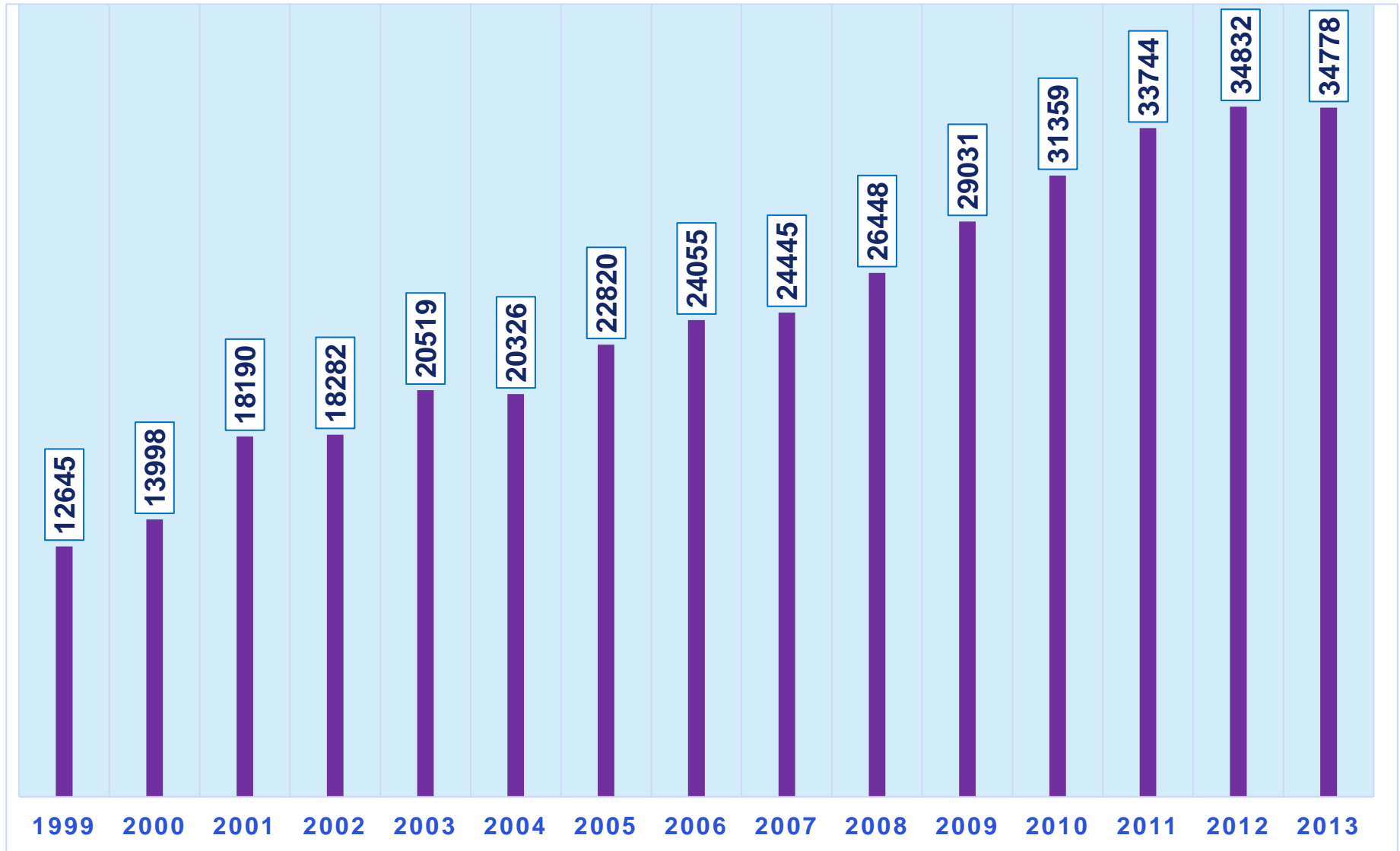
Proportion of New Pulmonary MDR-TB cases in RF, 2006-2013



Proportion of Pulmonary MDR-TB Cases of all Relapse Cases, 2006-2013

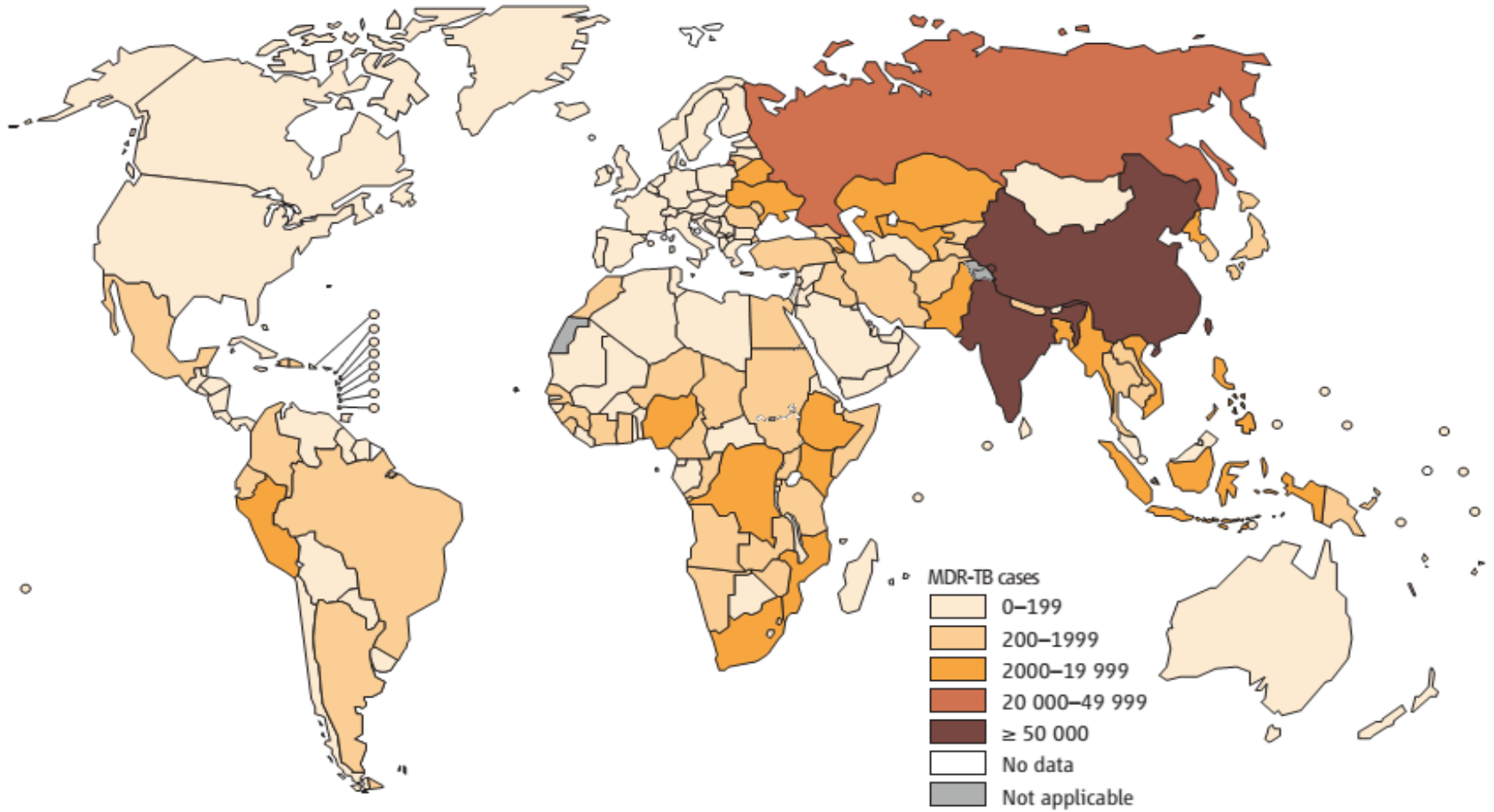


Number of MDR-TB patients in the Russian Federation in 1999–2013



DST in RF

DST coverage in RF
94,9%

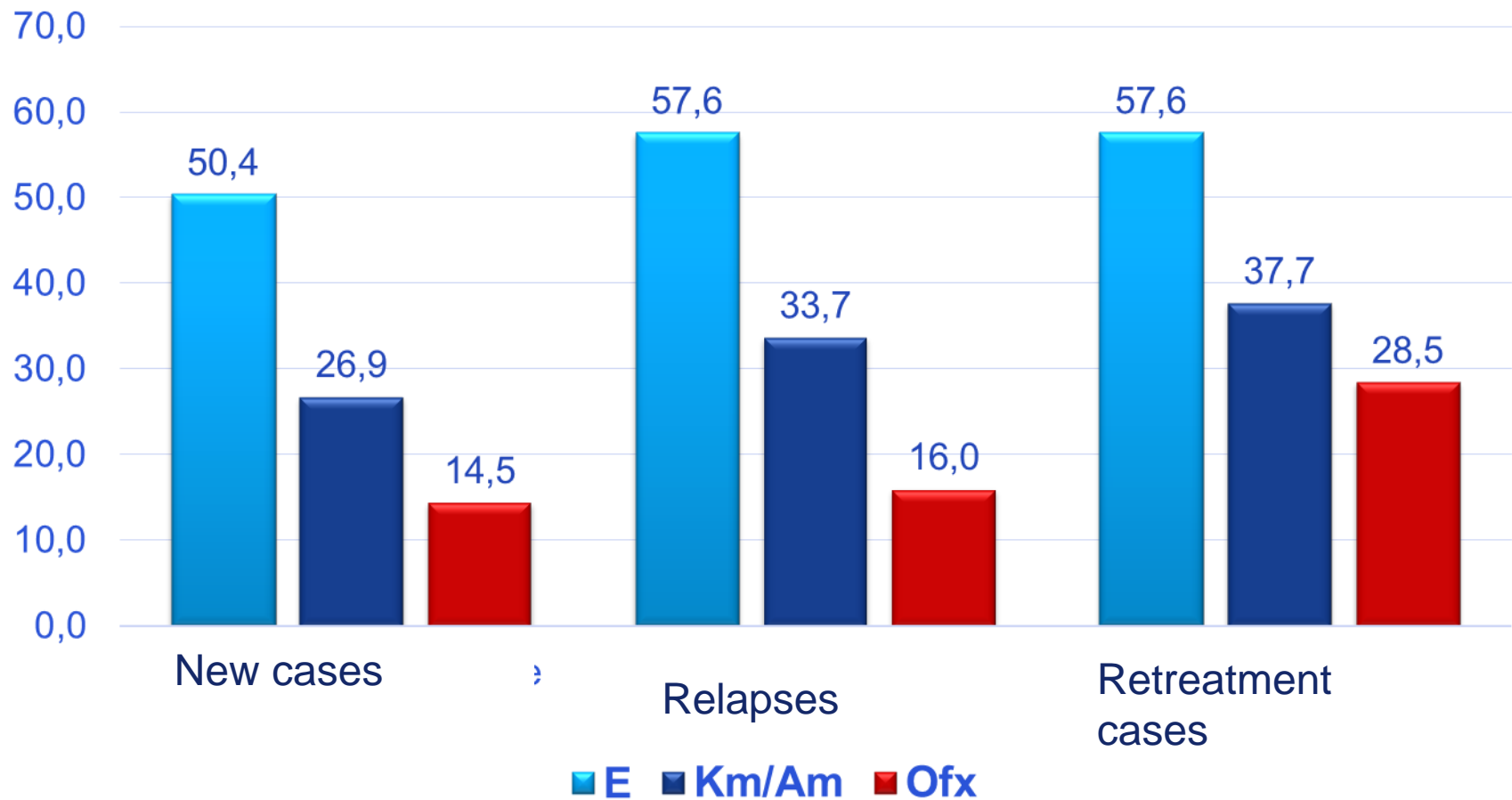


XDR-TB in 13 regions of RF, 2013

- ❖ Among new cases– 2.7% (0 – 5.9%)
- ❖ Among relapses – 6.7% (0 – 15.6%)
- ❖ Among other retreatment cases – 7.8% (0 – 24.2%)

*Circular
“TB situation in the areas of CTRI supervision,
2010-2013”.
Moscow, 2014*

Additional DR in MDR-TB patients (%) in 11 regions of the RF, 2013 n=1905



Priority activities of the RF MoH on TB/MDR-TB

Quality detection and control of drug resistance transmission

- ❖ Full coverage of the bacteriological laboratories by the National System of Quality Assurance;
- ❖ Broad introduction of new methods of rapid DR detection;
- ❖ Establishment of the network of Reference laboratories.

Priorities of the diagnostics

- ❖ DR TB testing of all patients: new cases and previously treated
- ❖ TB case detection with the use of molecular-genetic methods (MGM) and cultures on liquid media.
- ❖ Access to MGM examination for *patients with high risk of MDR-TB and HIV* irrespective of geographical conditions of their place of residence or social status.

Implementation of rapid DST

- TB- Biochip (RF)
- Multiplex PCR (RF)
- Gene Xpert MTB/RIF
- DNA – strip Hain Lifescience



Comprehensive treatment of TB patients

- Introduction of clinical recommendations (protocols) for treatment of TB with due consideration of drug resistance of an agent; annual revision of recommendations (protocols)
- Monitoring of TB treatment quality in the regions of Russia performed by the TB institutes
- Application of surgical methods of treatment

Funds for procurement of the reserve drugs are being allocated from the Federal budgets

Russian Society of Phthisiologists (RSP) developed *Federal Clinical Recommendations (protocols)*

- ❖ **Diagnostics and treatment of pulmonary TB**
- ❖ **Diagnostics and treatment of M/XDR-TB**
- ❖ **Diagnostics and treatment of patients with TB-HIV co-infection**
- ❖ **Microbiological and molecular-genetic diagnostics of TB**

Novelties in chemotherapy:

- Chemotherapy algorithms are based on molecular-genetic DST
- Principal regimen design is based on the DST results
- Treatment regimen for XDR-TB

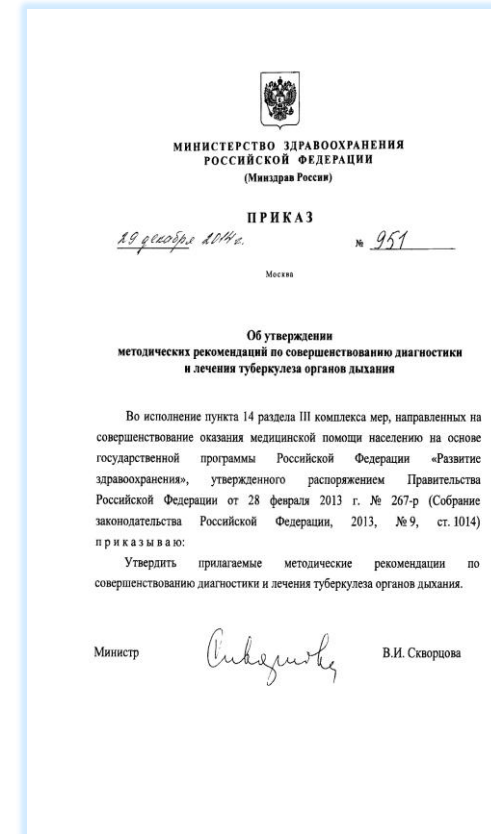
Clinical recommendations on M/XDR-TB approved by the WHO EURO



Executive Order of Ministry of Health on Improvement of TB Diagnostics and Treatment, 2014

December 2014

Order was prepared
within the complex of
measures of the
State Program of the
Government of RF
"Development of Health»



TB chemotherapy based on molecular DST



1. On the basis of individual DST results received with molecular-genetic techniques

Sensitivity to **HR** - **I regimen**

Resistance to :

R/ HR - **IV regimen (for MDR TB)**

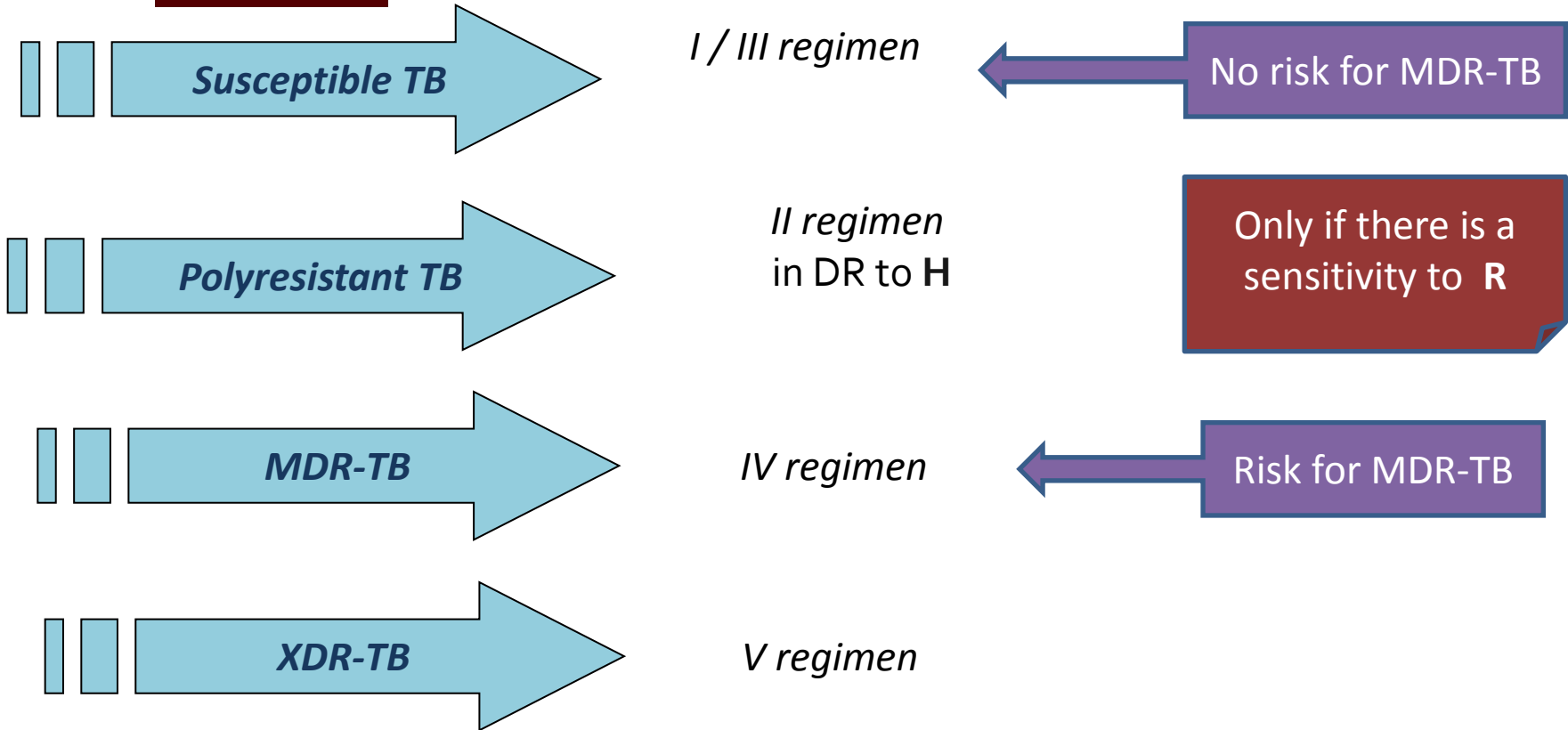
R/HR Fq - **V regimen (for XDR TB)**

2. On the basis of DST results to 1st and 2nd lines drugs using liquid or solid media techniques.



*Main factor to choose regimen—
DST result*

Regimens of chemotherapy



*Regimens without DST results should be exception but
not a rule*

FEDERAL CLINICAL RECOMMENDATIONS OF RUSSIAN PHTHIATRISTS' SOCIETY

Prescription of Regimen with Bedaquiline

- Within MDR TB chemotherapy regimen (IV) bedaquiline is prescribed :
 - ❖ When it is impossible to provide the regimen of 5 first and second line drugs provided that the patient is sensitive to 3 and more TB drugs
 - ❖ As the 6th drug to basic chemotherapy regimen IV
- For XDR TB chemotherapy regimen (V) bedaquiline is prescribed: if there is sensitivity to 3 and more TB drugs out of the prescribed combination
- Bedaquiline is not to be used along with moxifloxacin; levofloxacin in the dose of 1.0 is to be prescribed to the patient.
- Under any other conditions prescription of bedaquiline is not allowed.
- It is prohibited to add bedaquiline to ineffective chemotherapy regimen.

Pharmacovigilance for Bedaquilin

Preventing development of drug resistance:

- Appointment of Bedaquiline strictly on the evidence in accordance with the Order of MOH
- Use of the drug under certain conditions in accordance with the recommendations of the RSP (qualitative DST first and second line drugs, high adherence to treatment).

Prevention of adverse effects:

- Selection of patients for bedaquiline appointment (excluded children, PLHIV receiving antiretroviral therapy, persons with cardiovascular disease).
- Exception of joint use of drugs prolonging the QT interval (including moxifloxacin).
- Systematic monitoring of adverse effects (laboratory and instrumental monitoring of the of a heart, liver, kidneys function).

Surveillance of adverse effects occurred:

- System spontaneous messages of Roszdravnadzor.
- Cohort monitoring of adverse effects.

Control of bedaquiline usage

Prescription of bedaquiline is controlled by experts of TB institutes and headquarters of regional TB services

DST to H, R, Km/Am, Cm and Ofx is compulsory

Less than 5% of defaults among new TB cases

Confirmed quality of the laboratory examinations

Training courses on diagnostics and treatment in accordance with the new clinical recommendations

Register of the patients using bedaquiline

Register of the patients using bedaquiline

- Use of the drug under control of the Central TB research Institute.
- Screening patients for the drug usage.
- Visits (1 per month at an intensive phase, 1 every 3 months at a continuation phase).
- Monitoring of treatment efficacy and adverse effects.
- Detailed information about any side effects, their severity, relation to bedaquiline usage and methods of relief.
- Analysis of the obtained data on efficacy and safety of bedaquiline.

Priority activities of the RF MoH on TB/MDR-TB

- **Improvement of TB patients' adherence to treatment, scale up of patient centered approach**
- **Enhancement of the work with the socially vulnerable groups as well as improvement of health education activities for the general public and patients**
- **Improvement of TB infection control in TB facilities, development of methods which replace in-patient treatment**
- **Epidemiological monitoring on the basis of the Federal registry**

Priority activities of the RF MoH on TB/MDR-TB

➤ Improvement of TB/HIV control:

Collaboration of TB service and AIDs centers

TB prevention among HIV-infected

Early TB case detection and rapid DST

HIV testing among all TB patients (*in 2013 96.3% of new TB patients was tested for HIV*)

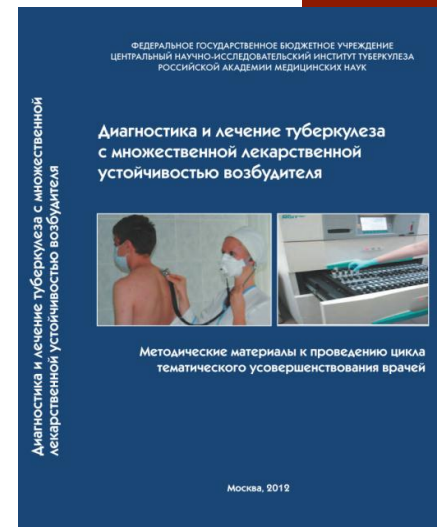
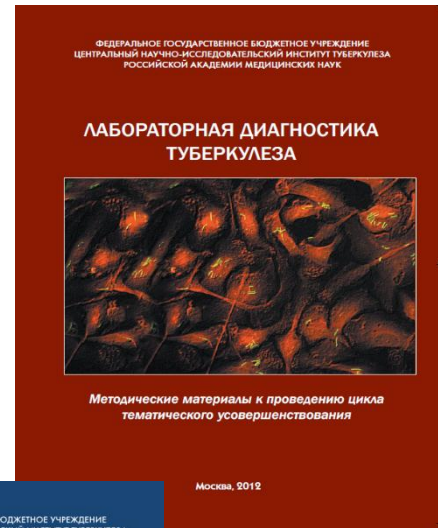
Multidisciplinary approach to TB/HIV treatment

Ambulatory treatment and follow-up surveillance

Priority activities of the RF MoH on TB/MDR-TB

➤ Improvement of educational programs

Educational programs on laboratory diagnostics and treatment of M/XDR-TB



Priority activities of the RF MoH on TB/MDR-TB

Scientific research

- ❖ development of new shorter regimens of chemotherapy for MDR/XDR-TB
- ❖ development of regimens for TB prevention in HIV-infected individuals

- ❖ search for new TB biomarkers
- ❖ search for new drug candidates
- ❖ study of TB immunopathogenesis
- ❖ development of new diagnostic tests
- ❖ search for the genes responsible for susceptibility to TB
- ❖ search for new vaccines

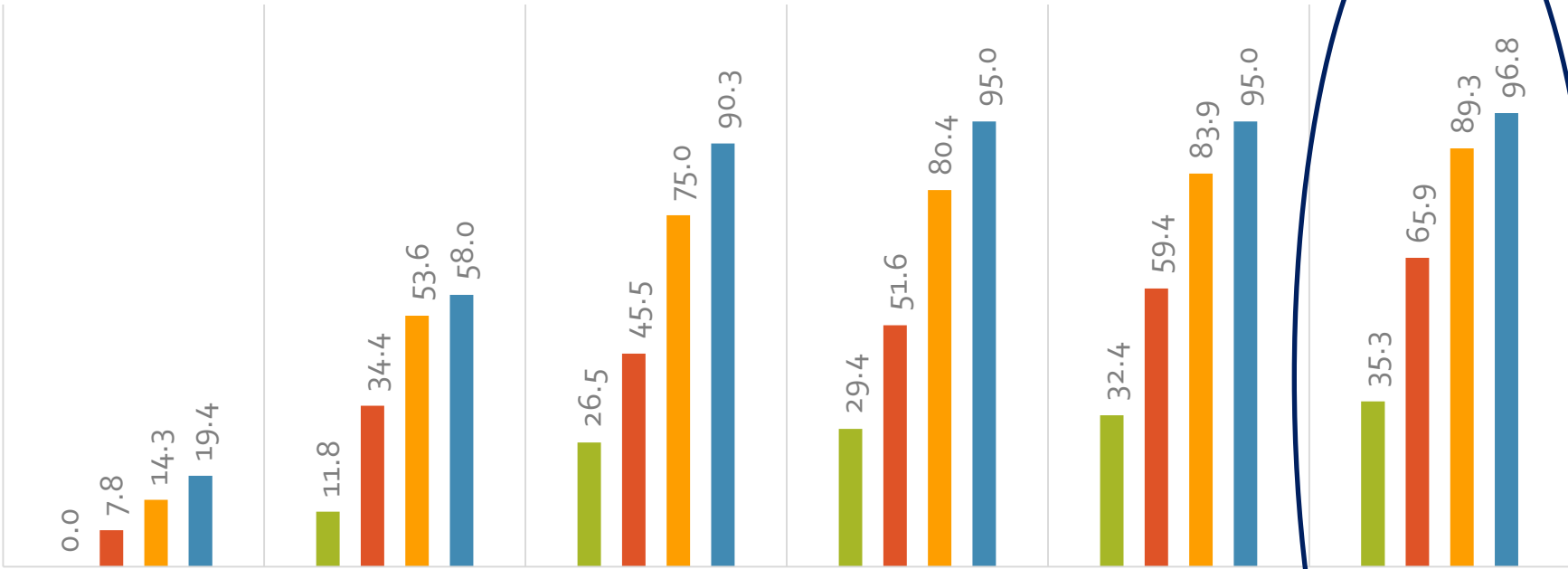
Factors increasing the treatment efficacy of XDR TB patients

Factors	N	Culture negative to 12 months of treatment	Culture positive to 12 months of treatment	OR	CI95%	p
Rapid detection of XDR	77	70	7	8,3	3,26 – 22,03	<0,05
Moxifloxacin	140	111	29	7,02	2,90-17,21	<0,05
Linezolid	76	69	7	8,03	3,16-21,30	<0,05
Bedaquilin+linezolid	31	30	1	15,74	2,20-318,75	<0,05

The inclusion of linezolid and bedaquiline in the treatment regimen

TREATMENT EFFICACY OF XDR TB PATIENTS BY CULTURE NEGATIVATION DEPENDING ON DRUG REGIMEN (N=185)

- 1st group (Ofx) n=34
- 2nd group (Mfx+Clr+Amx) n=64
- 3rd group (Mfx+Lzd) n=56
- 4th group (Lzd+Bq) n=31



P 1,4<0,05

P 1,2 1,3 1,4
2,4<0,05

P 1,3 1,4 2,3
2,4<0,05

P 1,3 1,4 2,3
2,4<0,05

P 1,2 1,3 1,4 2,3
2,4<0,05

P 1,2 1,3 1,4 2,3
2,4<0,05

Thank you for your attention!

