

"Multidrug-Resistant strains of M. tuberculosis circulating in Kyrgyz Republic"

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September 2015

Annecy



Kyrgyz Republic

Total area: 199,951 km²

Population - 2015 estimate

5,895,100



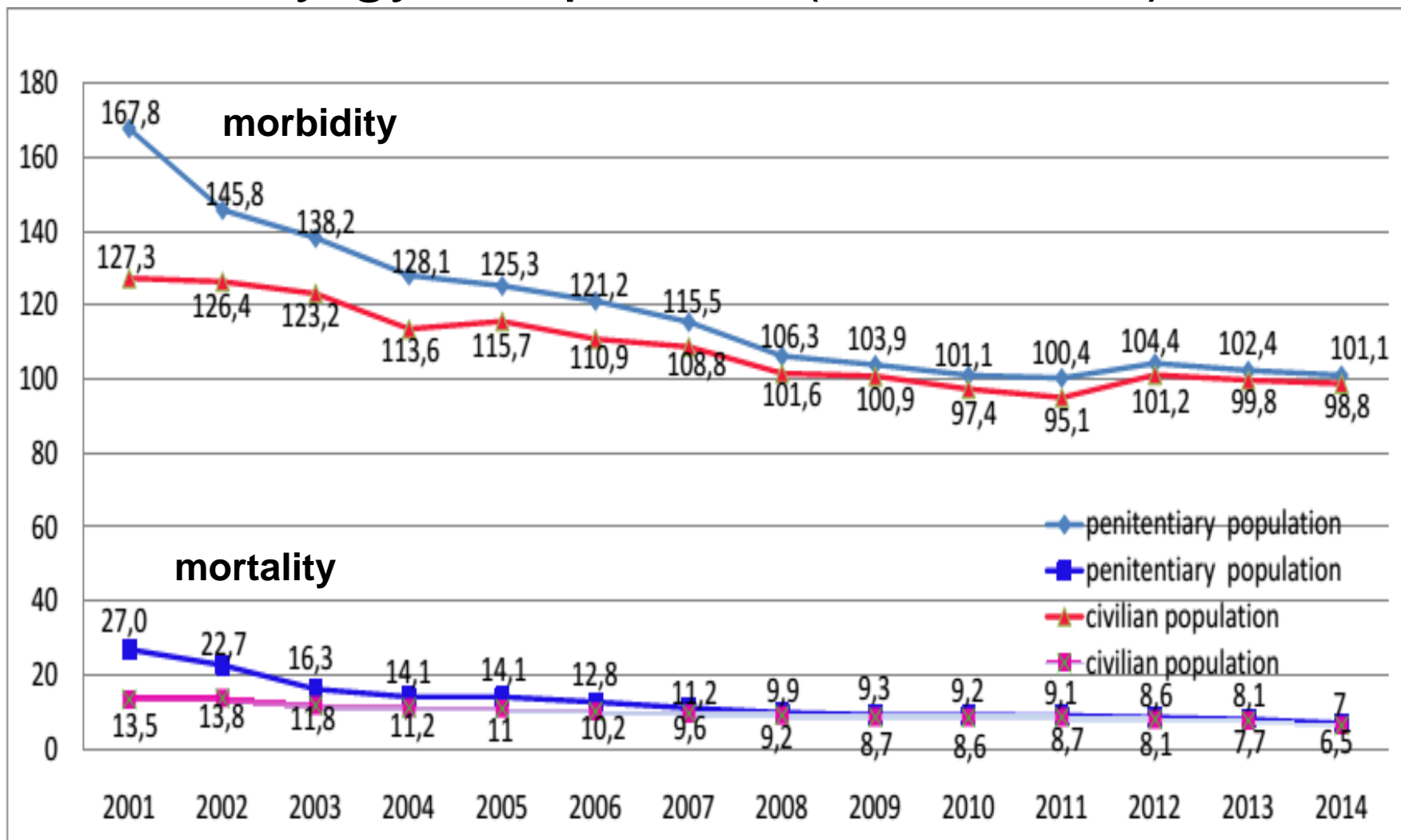
*National Statistical committee Kyrgyzstan. <http://www.stat.kg/>

The problem of tuberculosis in Kyrgyz Republic

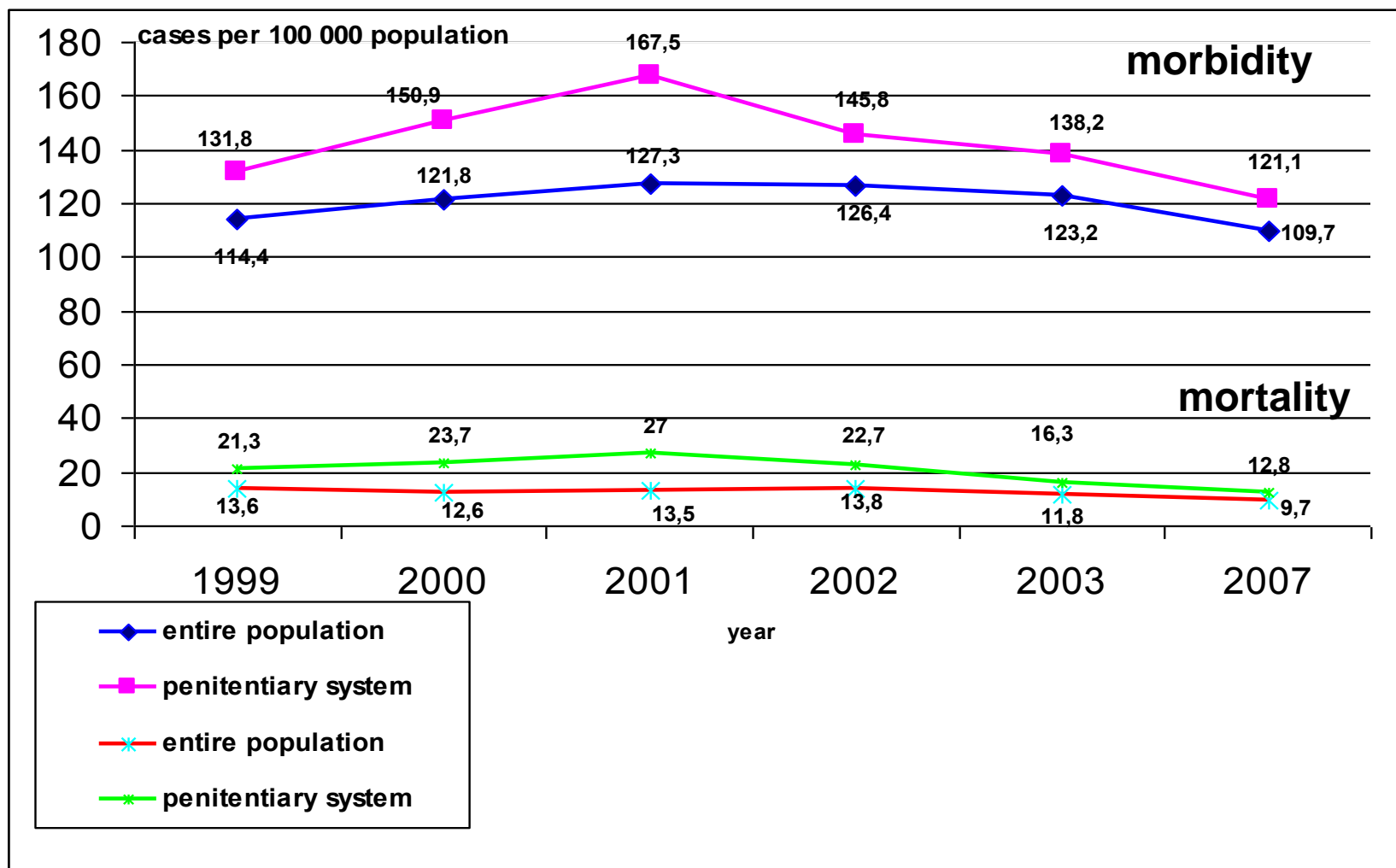
- Deterioration of public health infrastructure of KR after collapse of the Soviet Union in 1991.
- Decreased funding for programs designed to screen, diagnose and treat tuberculosis facilitated the spread of Tb.
- Poor socioeconomic situation, displacement of populations to urban areas unemployment and poverty.

- Poor or non-compliance with medication. Patients with untreated, active MDR-TB continue to spread their disease within their own families and communities.
- Increase in the population of Tb patients in penitentiary system is caused by overcrowdness in these facilities and lack of proper medical care.

Dynamics of TB morbidity and mortality in Kyrgyz Republic (2001-2014)



Problem of tuberculosis in penitentiary system



MDR and XDR TB is a major problem in Kyrgyz Republic both for civilians and penitentiary system.

Decades of treatment failures in Kyrgyz Republic led to development MDR and XDR TB resistant tuberculosis. According to WHO data, in 2013 in Kyrgyz Republic the prevalence of MDR-TB among new and previously treated patients was 26% and 56%, respectively. XDR tuberculosis cases represent about 10% of MDR cases in Kyrgyz Republic.

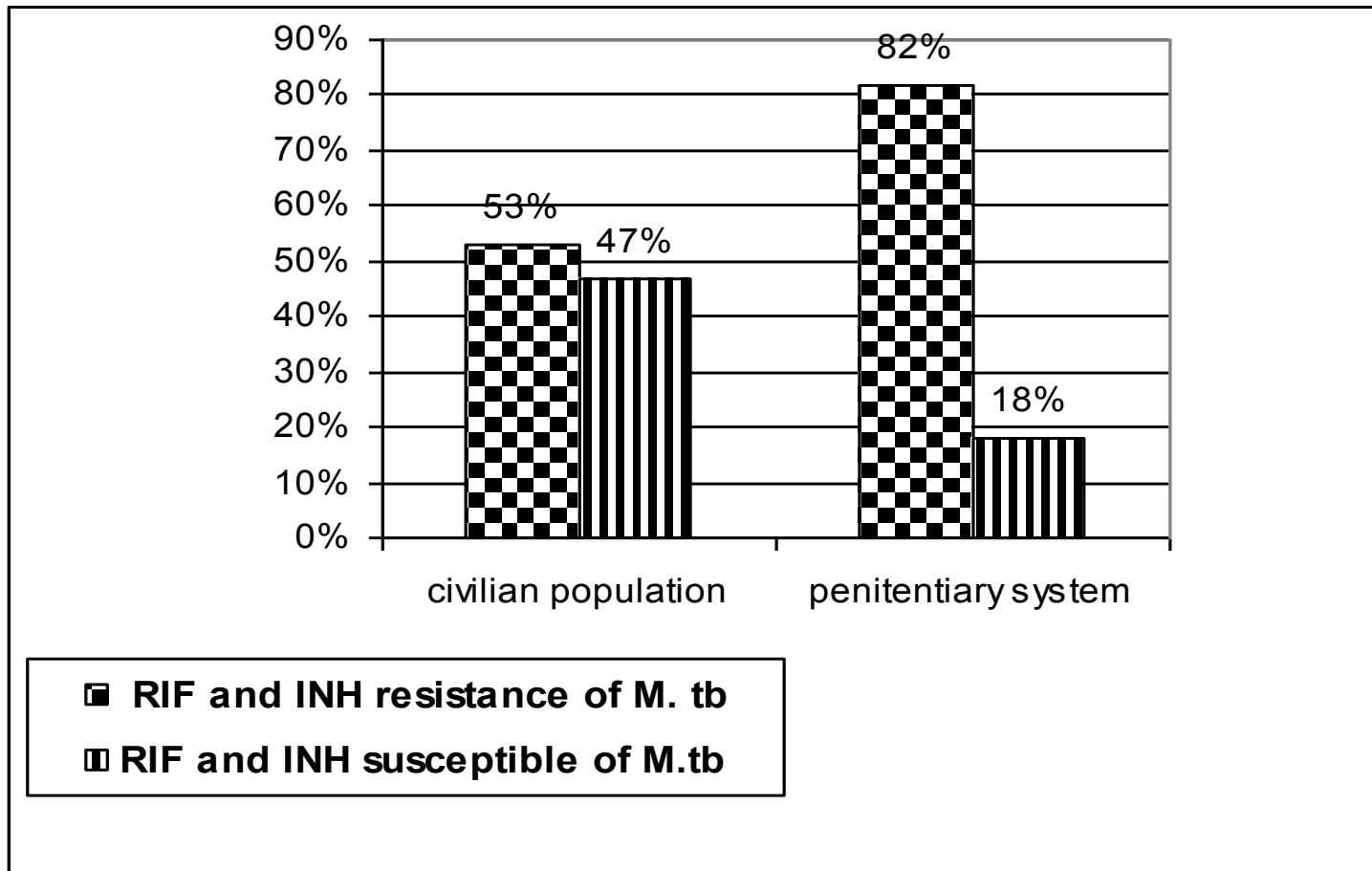
ISTC Project No #KR-851
ISTC Project No #KR-1596

Genetic markers of Multi-Drug and Extensive
Drug Resistant M. Tuberculosis in Kyrgyz
Republic

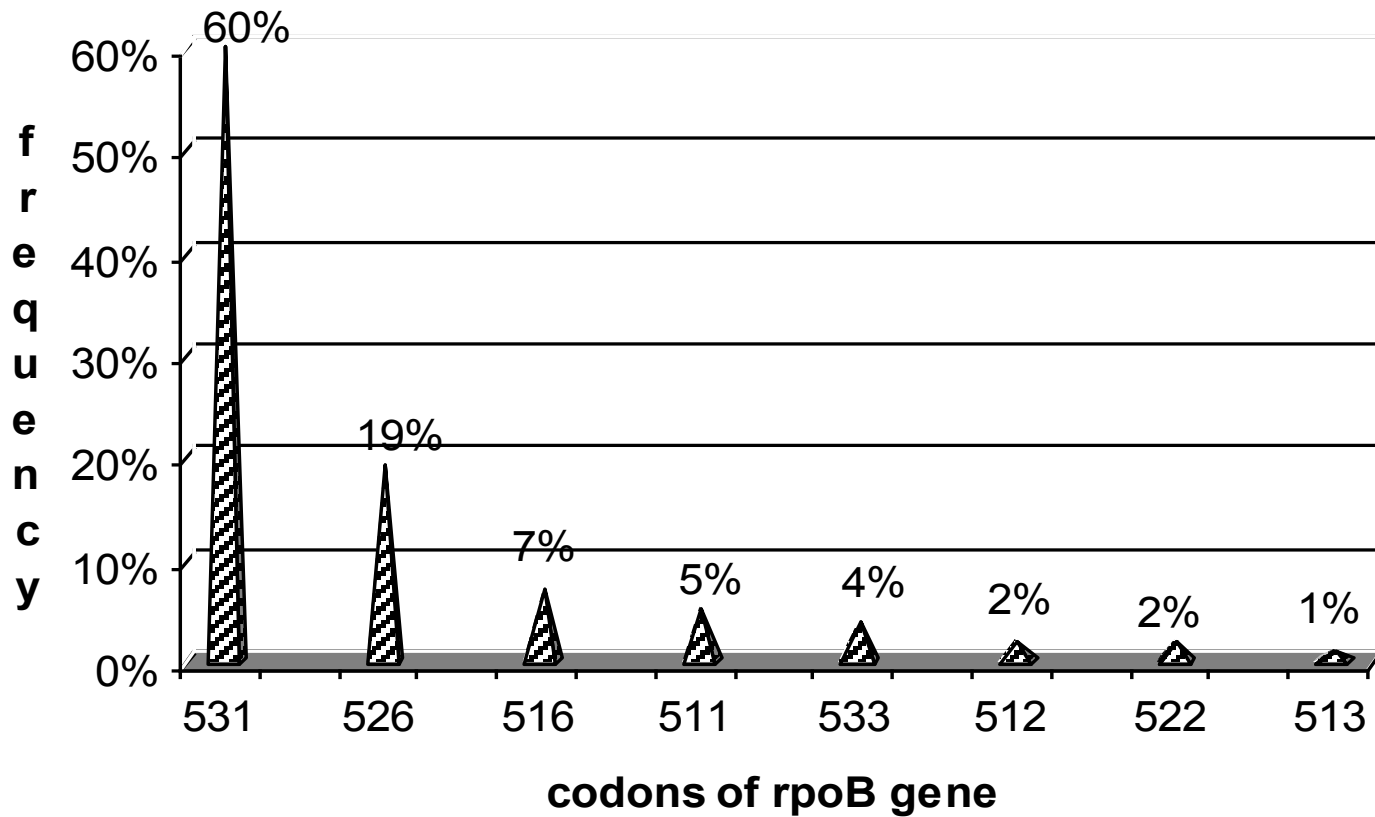
The aim of our study was to analysis of mutations in MDR and XDR resistant M. tuberculosis strains isolated in Kyrgyz Republic.

Total 1542 specimens obtained from patients with pulmonary tuberculosis were analyzed by Tb-biochip and bacteriological method. Mutations of rpoB, inhA, katG, ahpC and gyrA genes associated with rifampicin, isoniazid and fluoroquinolone were analyzed.

Prevalence of multi-drug resistant tuberculosis among primary TB patients in common population (n=593) and in penitentiary system (n=268)



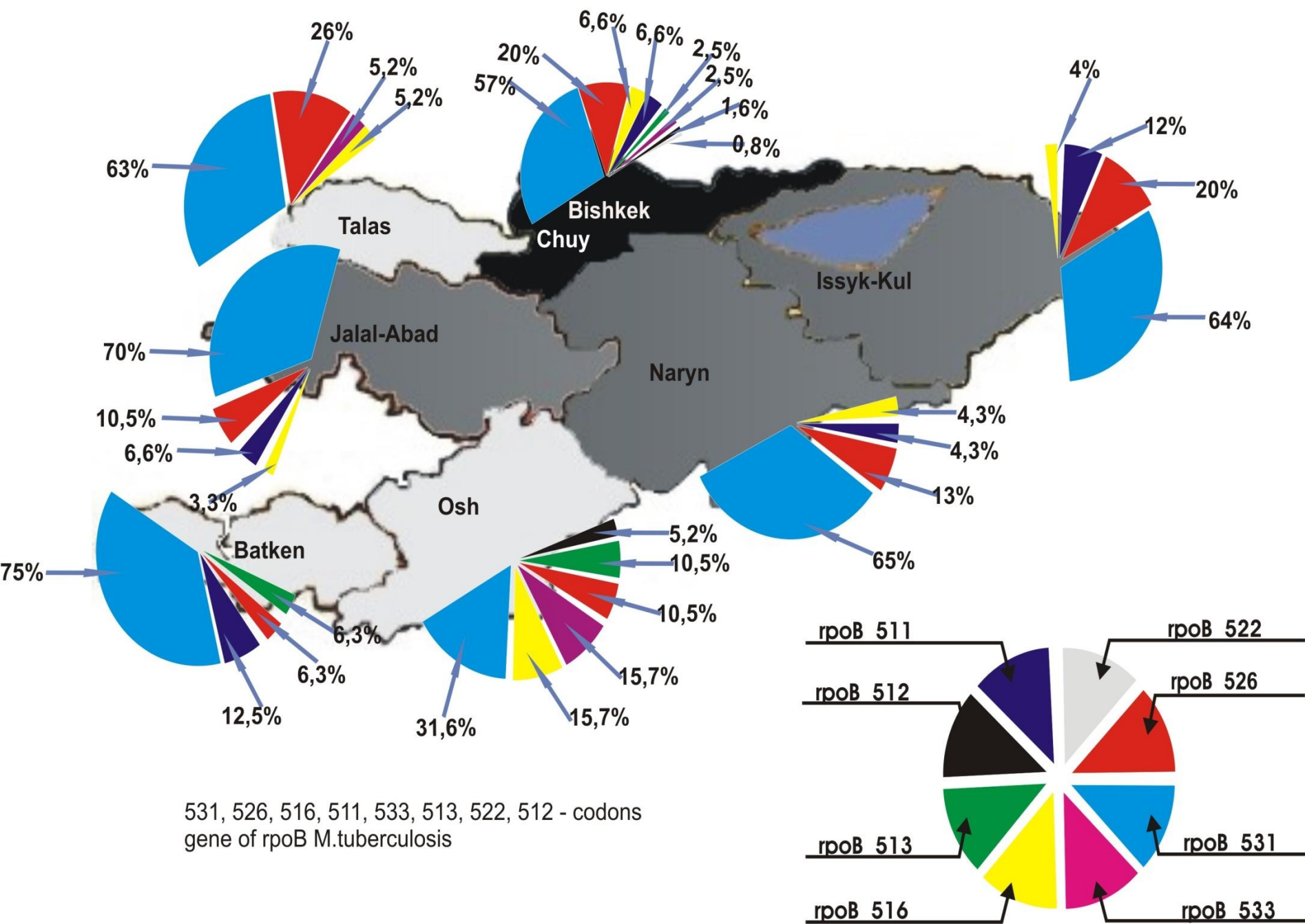
Frequencies of the *rpoB* mutations associated with rifampicin-resistant *M. tuberculosis* strains from Kyrgyz Republic



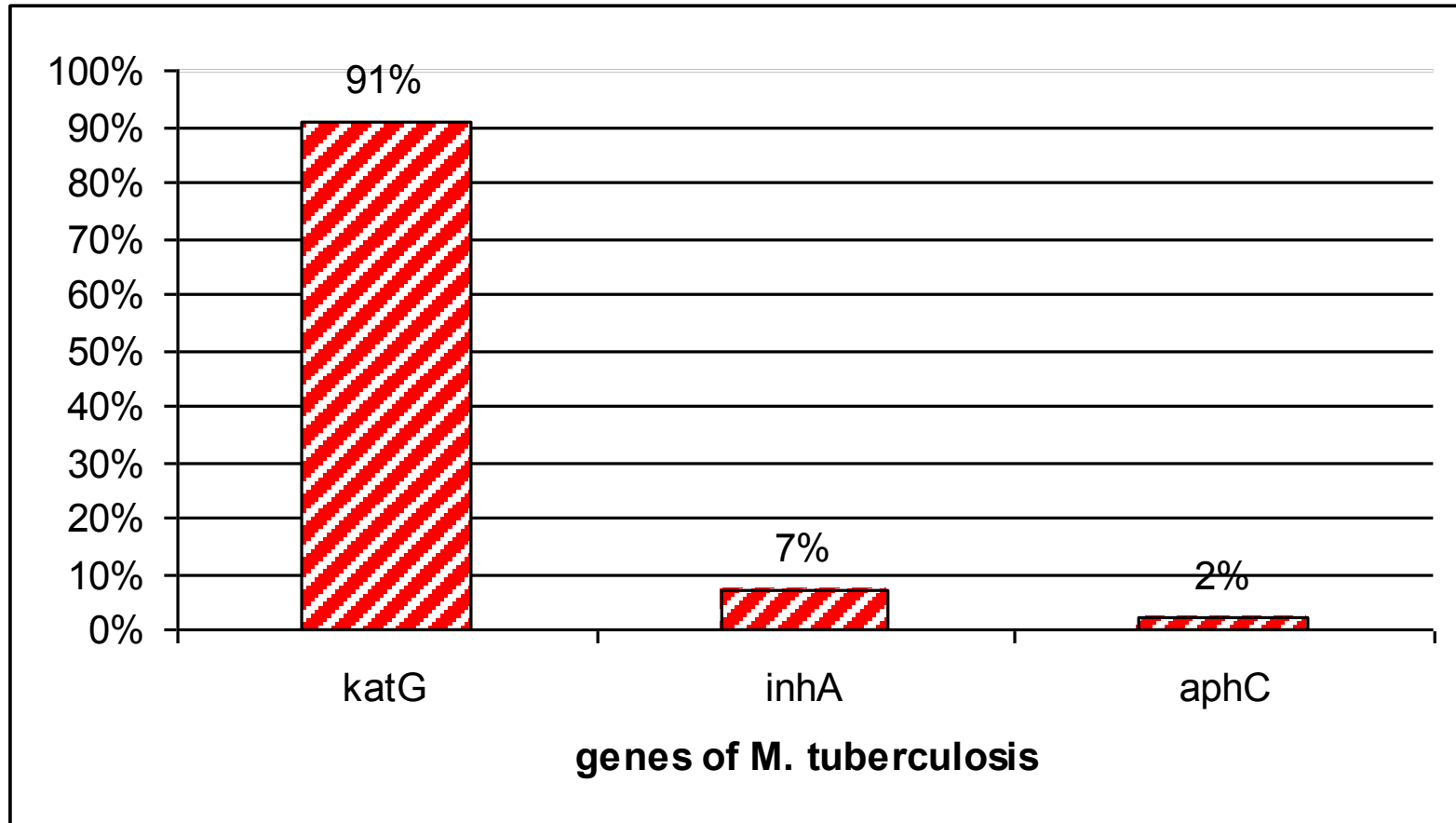
Type of the rpoB mutations associated with rifampicin-resistancy of *M. tuberculosis*

Codons	Amino-acid change	Nucleotide change	Cases (%)
533	Leu→Pro	CTG→CCG	8 (5,1%)
531	Ser→Leu	TCG→TTG	91 (58,4%)
531	Ser→Trp	TCG→TGG	2 (1,3%)
526	His→Asp	CAC→GAC	11(7%)
526	His→Tyr	CAC→TAC	10 (6,4%)
526	His→Pro	CAC→CCC	4 (2,5%)
526	His→Leu	CAC→CTC	5 (3,2%)
516	Asp→Tyr	GAC→TAC	8 (5,1%)
516	Asp→Val	GAC→GTC	3 (2%)
513	Gln→Gly	CAA→GGC	2 (1,3%)
512	Ser→Thr	AGC→ACC	2 (1,3%)
522	Ser→Leu	TCG → TTG	2 (1,3%)
511	Leu→Pro	CTG→CCG	8 (5,1%)
			156 (100%)

The distribution rifampicin-resistant *M. Tuberculosis* strains with mutations in different Republic regions



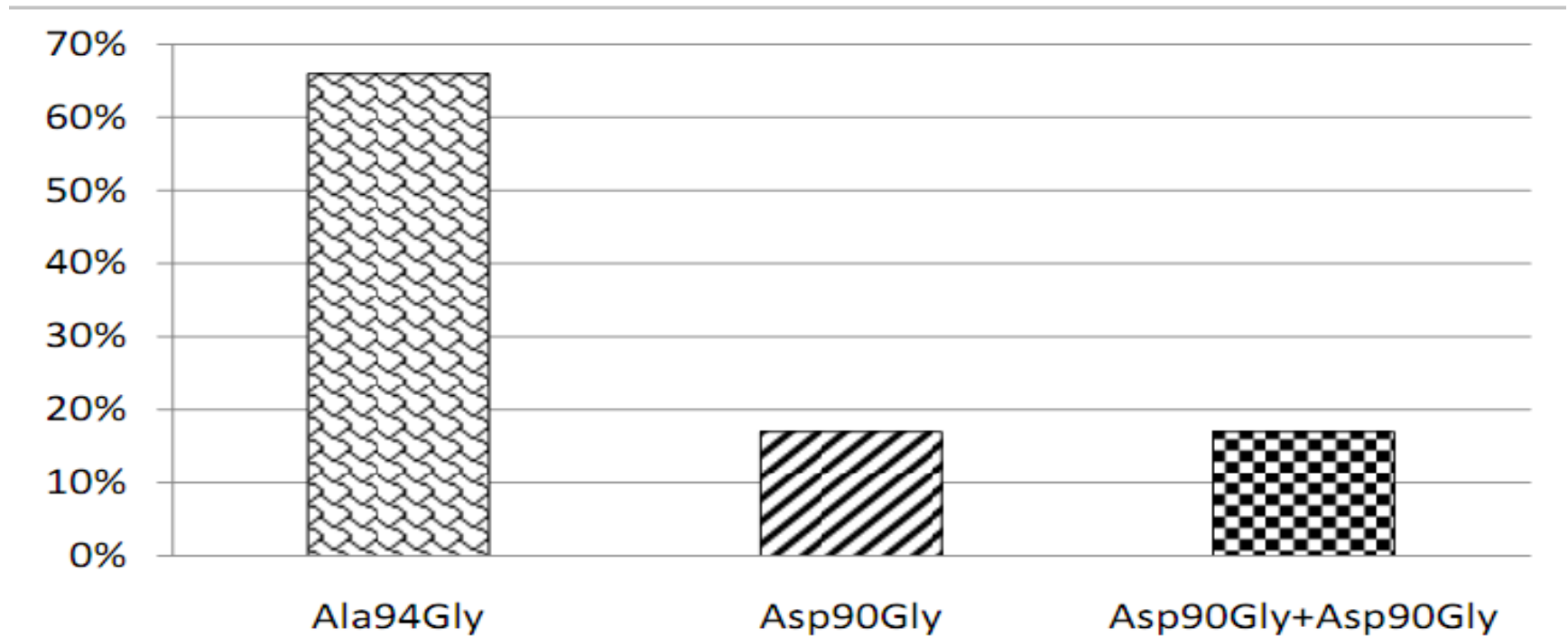
Frequencies of the katG, inhA and ahpC mutations associated with isoniazid-resistance of MTb



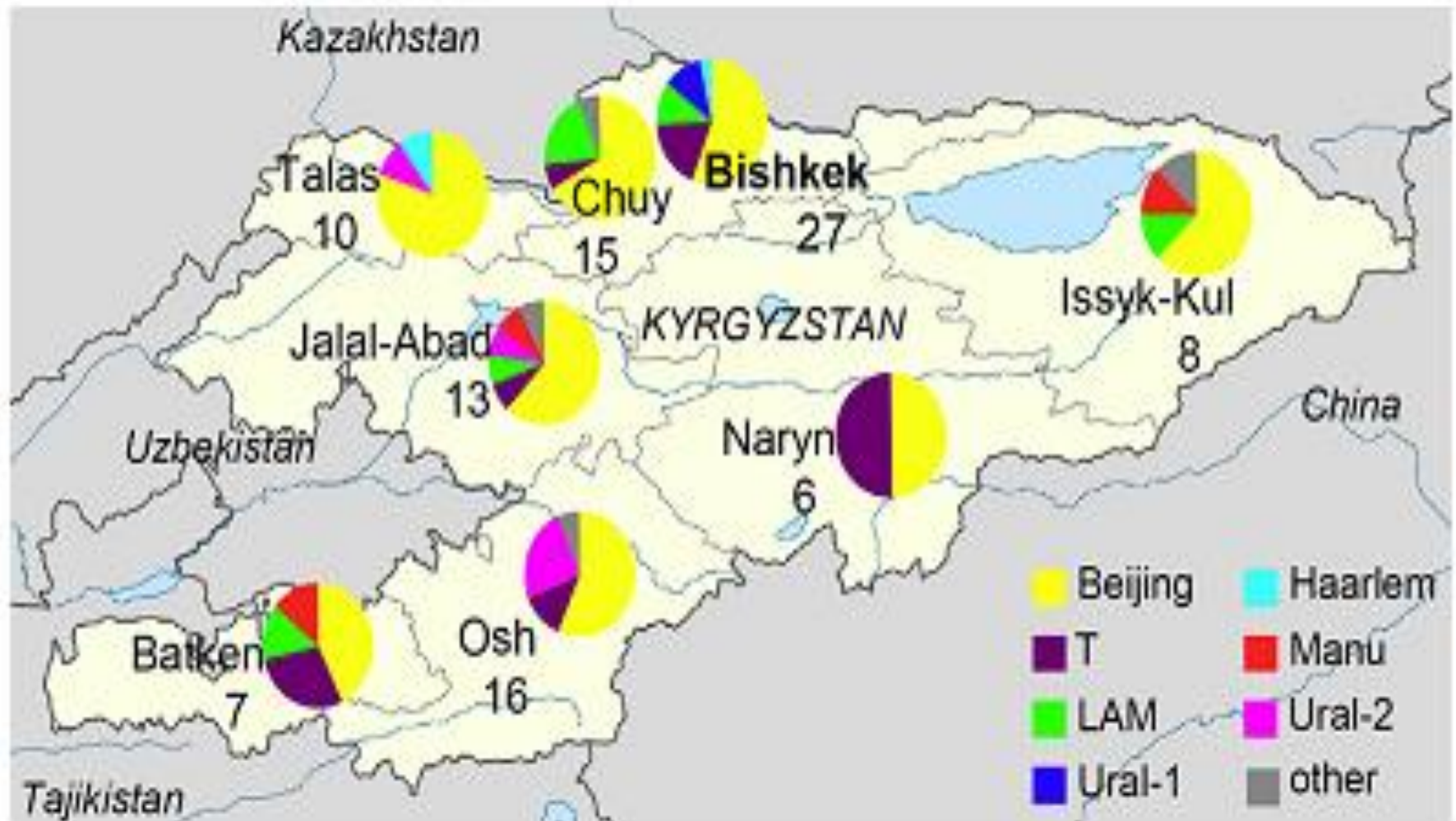
Type of mutations of katG, inhA and ahpC gene associated with isoniazid-resistancy of M. tuberculosis

gene of M. tb	Mutation	Nucleotide change	Cases (%)
katG	Ser315→Thr	AGC→ACC	182 (89%)
	Ser315→Asn	AGC→AAC	2 (1%)
	Ser315→Arg	AGC→AGA	2 (1%)
inhA	inhA_T15	C→T	15 (7%)
ahpC	ahpC_A9	G→A	4 (2%)

Fluoroquinolone-resistant strains of M.tb circulating in the Kyrgyz Republic



Regional distribution of the genetic families identified in 103 *M. tuberculosis* strains from Kyrgyzstan. Exact number of strains per location is shown under the city's name. (Tuberculosis 93 (2013))



Distribution of *rpoB*, *katG*, *inhA* alleles in different spoligotype-defined families

Genotype	<i>rpoB</i>			<i>katG</i> 315		<i>inhA</i> -15	MDR	Susceptible
	wt	531	526	wt	m			
Beijing (<i>n</i> = 62)	45	13	4	45	17	2 (1 [*])	14	31
Non-Beijing (<i>n</i> = 41)	38	1	2	33	8	4 (2 [*])	3	31
T (<i>n</i> = 14)	13	—	1	11	3	—	1	11
LAM (<i>n</i> = 9)	7	1	1	7	2	2 (1 [*])	2	6
Ural-1 (<i>n</i> = 3)	3	—	—	1	2	1 (1 [*])	—	1
Ural-2 (<i>n</i> = 6)	6	—	—	5	1	—	—	5
Other (<i>n</i> = 9)	9	—	—	9	—	1	—	8
TOTAL (<i>n</i> = 103)	83	14	6	78	25	6	17	61

* Simultaneous mutation in *inhA* -15 and *katG*315.

Conclusion

- In Kyrgyz Republic the main cases of M.Tb resistance to rifampicin is Ser531Leu mutation in rpoB gene,
- to isoniazid – Ser315Thr mutation of katG gene.
- The cause of resistance to fluoroquinolone are gyrA gene mutations Ala94Gly and Asp90Gly.
- The most common genetic family of MTb strain is Beijing (60%) associated with most of MDR cases.

THANK YOU

