

**Tuberculosis Control Program for Central Asia Region**

**Drug Resistance Survey (DRS) in Almaty Oblast – Kazakhstan**

**– Final report –**

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**Project HOPE**

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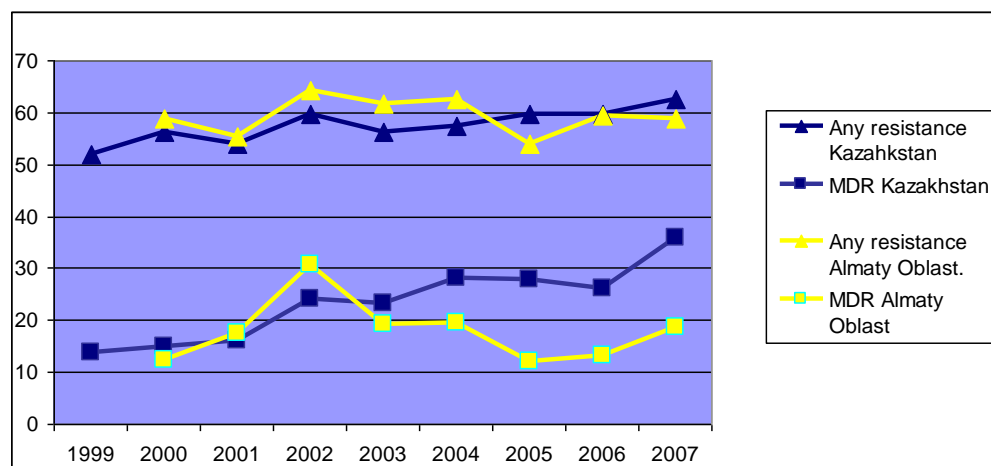
## Background

Anti TB drug resistance is significant health problem in Republic of Kazakhstan, identifying the country as one of the globally recognized hot spots for MDR TB. However, the real magnitude of the problem is still not known, since Kazakhstan's established drug resistance surveillance system is based on the information generated from laboratory registers. Laboratory reports on drug resistance are available since 1999, presenting high resistance and MDR TB rates and identifying drug resistance as a main reason for high treatment failure rates in TB patients.

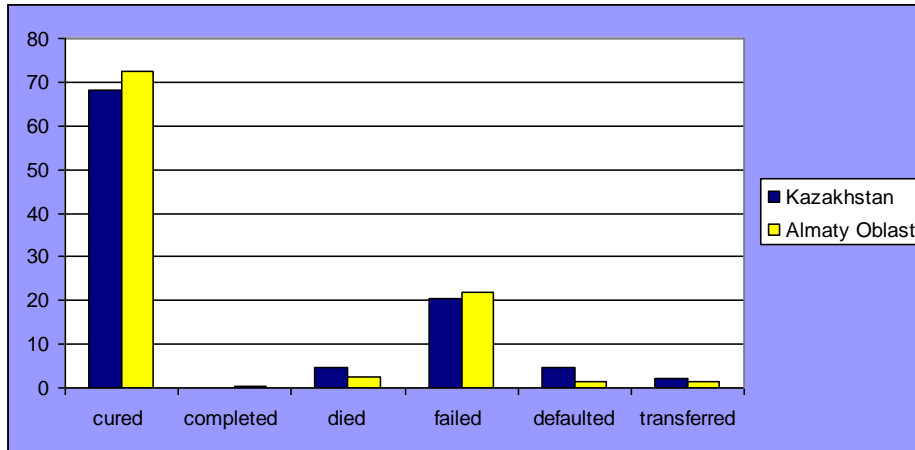
Laboratory assessment conducted by Project HOPE in 2004 in Almaty Oblast, found over reporting of drug resistance due to duplications of tests, as well as incorrect registration of patient category in lab registers. Although this problem was partly solved and the number of registration errors reduced after 2004, still the information based on lab registers can not provide accurate data on drug resistance.

In order to collect reliable data on drug resistance in Almaty Oblast, Project HOPE together with NRL and Almaty Oblast TB Dispensary conducted DRS in 2007-2008 with the following objectives:

- Determine the prevalence of drug resistance and multi-drug resistance in Almaty Oblast
- Identify the most common resistance patterns of M tuberculosis
- To evaluate the reliability of routinely reported drug resistance rates, provided by lab service
- Train the local TB staff and increase their capacity for conducting DRS



**Graph # 1 Drug resistance rates reported by TB laboratory service 1999 – 2007**



**Graph # 2 Treatment outcome for Kazakhstan and Almaty Oblast, 2007 cohort**

### Preparatory activities

Preparatory activities started in 2007 with identification of the survey area, protocol development and workshop for the local staff involved in implementation.

Taldy Kurgan City and Northern region of Almaty Oblast were selected, because of good infrastructure, well organized collaboration with rayons and confirmed quality of DST in Oblast TB laboratory in Taldy Kurgan.

The DRS protocol was developed by the Project HOPE regional laboratory specialist and Project HOPE Kazakhstan laboratory specialist, with close collaboration with the Head of Kazakhstan NRL and the head of Oblast TB laboratory. The protocol was presented and discussed with the NTP team and other organizations involved in TB control activities in Kazakhstan ( CDC; KNCV; Gorgas). The final version was approved by the Director of the National TB Centre and NTP manager.

The DRS protocol was based on WHO recommendations for conducting DRS<sup>1</sup>, defining the basic survey elements and principles:

**Survey area:** Northern region of Almaty oblast

**Sample size:** Separate sample sizes calculated for new cases and previously treated cases. 167 new TB cases and 80 previously treated. Calculation was based on available information on Rifampicin resistance and estimated number of culture positive cases.

**Enrollment criteria:** All culture positive TB cases registered from November 1, 2007 – October 31, 2008

**DST:** Performed by laboratory at Almaty Oblast TB Dispensary in Taldy Kurgan , by absolute concentration method for Isoniazid; Rifampicin; Ethambutol and Streptomycin. EQA provided by the NRL in Almaty (supported by SNL Borstel)

<sup>1</sup> Guidelines for surveillance of Drug Resistance in Tuberculosis. Second edition. WHO/CDS/TB/2003.320. World Health Organization, Geneva 2003

**Patient information:** Medical and demographic information collected from the patient's history and double-checked to reduce the possibility of misclassification of previously treated cases.

**Data entry and management:** WHO software, surveillance of drug resistance in tuberculosis (SDRTB 4.0).

A workshop for DRS in Almaty Oblast was conducted in October 2007, presenting to the local staff: patient enrolment procedures; DRS forms and registers and quality assurance procedures.

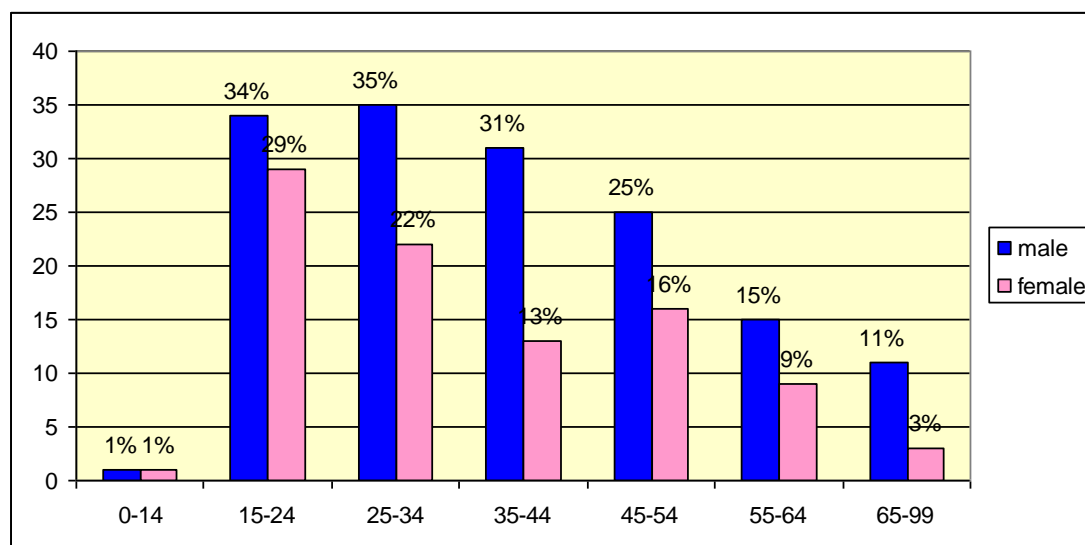
### DRS implementation process

Implementation started on November 1, 2007 with enrolment of all culture positive cases. As the national TB policy recommends culture test for every TB patient, selection of patients was done from Oblast culture register. Patient information was collected for each culture positive patient and double checked with the data available from the Oblast TB register (ESCM). DST results were collected only for the initial culture from diagnostic sputum specimen, collected before the start of TB treatment, or within the first month of treatment. Patient enrolment ended on October 31 and culture and DST results were completed by the end of 2008. All collected information was entered in WHO recommended SDRTB 4 database.

Results of this survey were shared with the NTP and presented at the IUATLD European Region Conference in Dubrovnik on May 26, 2009

### DRS results

A total number of 247 patients were enrolled in the DRS, 167 new TB cases and 80 previously treated. 154 patients were male, (100 new cases and 54 previously treated) and 93 female (68 new cases and 25 previously treated). Age distribution is presented in Graph # 3.



**Graph # 3** Age and sex distribution of TB patients enrolled in DRS survey

Any resistance was found in 30,5% of new TB cases and 50% of previously treated cases. MDR rates were 11,4% and 30,2% respectively. The summary of DSR results and resistance patterns found are presented in the Table # 1.

**Table # 1. Drug resistance summary**

	New cases		Previously treated	
<b>total</b>	<b>167</b>	<b>100%</b>	<b>80</b>	<b>100%</b>
sensitive	116	69,5%	40	50,0%
any resistance	51	30,5%	40	50,0%
<b>mono resistance</b>				
H	5	3,0%	2	2,5%
R	0	0,0%	1	1,3%
E	2	1,2%	0	0,0%
S	10	6,0%	2	2,5%
<b>H+R</b>				
HR	0	0,0%	1	1,3%
HRE	1	0,6%	0	0,0%
HRS	7	4,2%	12	15,0%
HRES	11	6,6%	11	13,8%
<b>Other H resistance</b>				
HE	0	0,0%	1	1,3%
HS	5	3,0%	4	5,0%
HES	5	3,0%	1	1,3%
<b>Other R resistance</b>				
RE	0	0,0%	0	0,0%
RS	2	1,2%	2	2,5%
RES	2	1,2%	0	0,0%
<b>Other poly resistance</b>				
ES	1	0,6%	3	3,8%
<b>Any H resistance</b>	<b>35</b>	<b>20,4%</b>	<b>32</b>	<b>40,5%</b>
<b>Any R resistance</b>	<b>24</b>	<b>13,8%</b>	<b>27</b>	<b>33,8%</b>

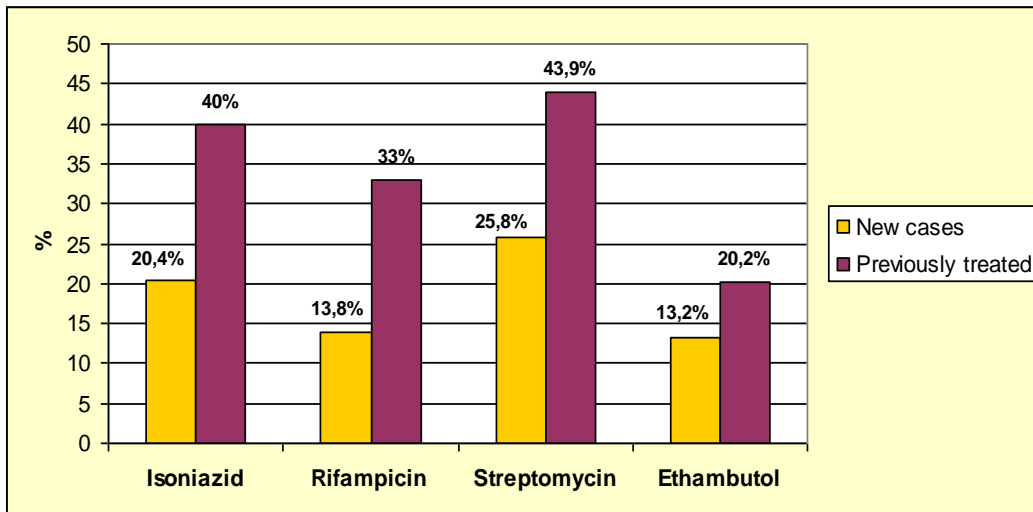
The highest resistance rates were found for MDR patterns and the most common resistance patterns in both groups were resistance to four (HRES) and three drugs (HRS). This may be result of late diagnosis of MDR and delay in the start of MDR TB treatment, which cause amplification of drug resistance and rapid development of resistance to drugs that have not been used previously.

Out of 19 new MDR cases, two had other chronic disease (diabetes mellitus and peptic ulcer) and two were jobless. No one reported alcohol or drug abuse and contact with TB. As the information was based on patient's statement, it is likely that such information was not provided due to stigma.

High MDR TB rates in new cases, found in this survey were expected, taking into account the treatment failure rate of 21,9%, reported for Almaty Oblast. Out of 24

previously treated patients, 10 were treatment failure and 14 relapses. Resistance rates to individual drugs are presented in Graph # 4. The highest rate, as expected in both groups was for Streptomycin.

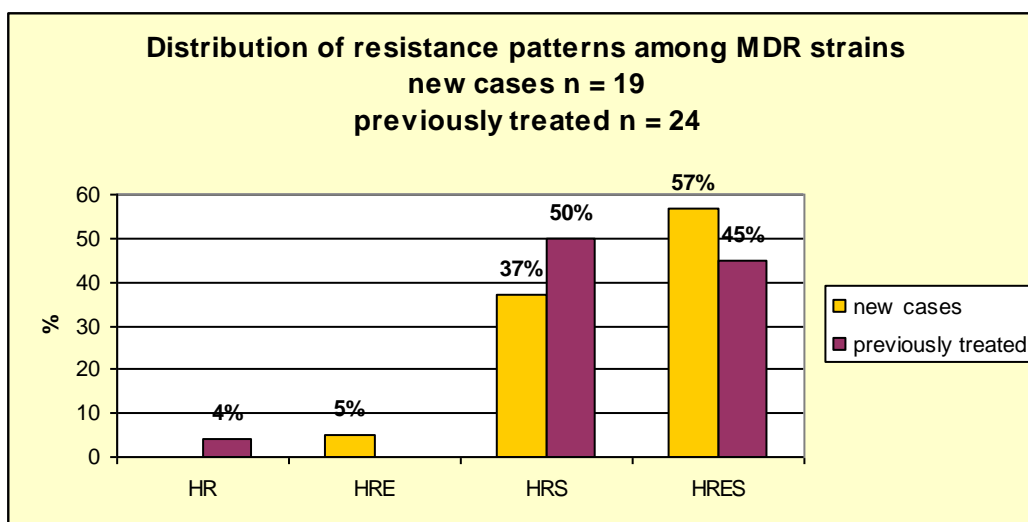
Mono resistance was found in 10,2% of new cases and 6,3% in previously treated cases. Only a few poly resistance patterns were found; two RS patterns in each group and two RES in new cases. Low rates of Rifampicin resistance in non MDR cases, supports the fact that resistance to Rifampicin could be used as a marker for MDR TB.



**Graph # 4 Resistance to individual drugs**

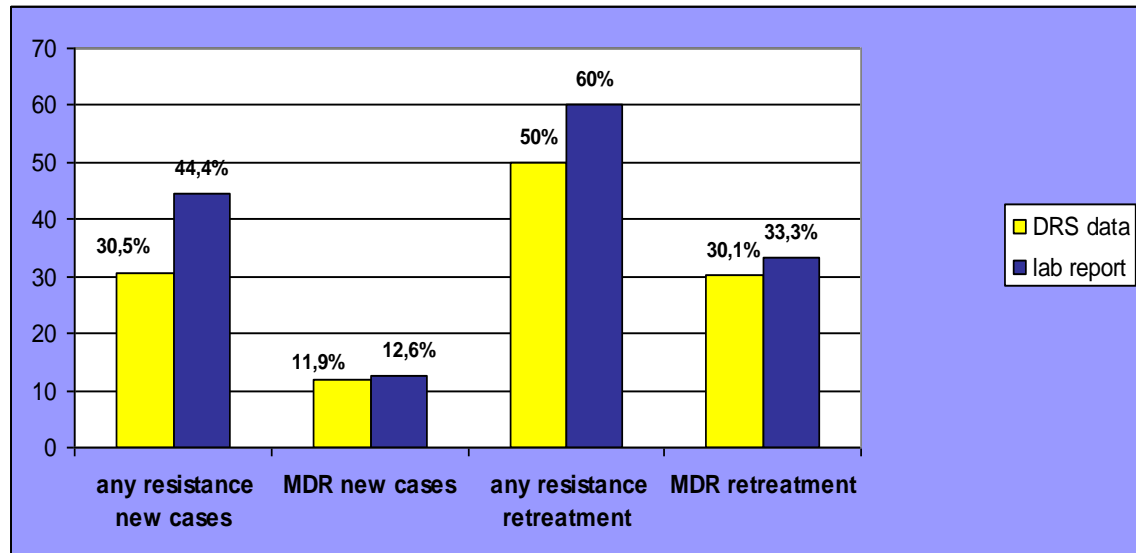
Six patients had a history of incarceration: two new cases, sensitive to all tested drugs and four previously treated, two of them with MDR TB.

HIV test results were available for 193 participants of the survey and among them no positive result was found



**Graph # 5 MDR resistance patterns**

One of the objectives of this DRS was compare drug resistance rates from this survey with drug resistance data reported by laboratory service. Resistance rates found in this survey were lower than national rates reported by the NTP, as well as Oblast rates. This finding supports the fact that the laboratory register is not always a reliable source for evaluation of the drug resistance problem



**Graph # 6 Comparisons of drug resistance rates: laboratory report and DRS report**

### Conclusions

- High rates of drug resistance and MDR in new and previously treated patients are a serious threat for the National TB program. Early diagnosis and treatment of MDR is the main priority for the NTP in order to reduce the high treatment failure rates
- The Surveillance system, based on routine lab registration, does not provide reliable information on drug resistance and needs improvement in terms of accurate registration on previous treatment
- Expansion of a well coordinated DRS countrywide could provide reliable information on the magnitude of the problem and identification of the most common causes of MDR TB