CHART AUDIT
of cases with TB/HIV co-infection in Moldova

Chisinau 2014

CONTRIBUTIONS

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ACRONYMS

ARVT	- Anti Retroviral Treatment
AST	- Antimicrobial Susceptibility Testing
CDC	- Center for Disease Control
DCDH	- Dermatology and Communicable Diseases Hospital
DOTS PLUS	- Directly Observed Treatment
INH	- Isoniazid
NCHM	- National Centre for Health Management
NPI	- National Phtysiopneumology Institute
OST	- Opioid Substitution Treatment
PAS Centre	- Centre for Health Policies and Studies
PCP	- Pneumocystis Carinii Pneumonia
PLHIV	- People Living with HIV
PWID	- People Who Inject Drugs
SD	- Standart Deviation
SYME-HIV	- HIV Monitoring & Evaluation Informational System
SYME-TB	- TB Monitoring & Evaluation Informational System
TB	- Tuberculosis
MDR-TB	- Multi-Drug Resistant TB
XDR-TB	- Extensively Drug-Resistant TB
TPT	- TB Preventive Treatment
TST	- Tuberculin Skin Test

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SUMMARY FINDINGS

From the TB/HIV cases identified in the SYME-TB for 2007 – 2011, a total of 750 people representing 921 cases met the chart audit criteria, some patients having registered more than one TB case during that period of time.

Three quarters of cases were male (74.4%), with a mean age of 34.9 years and more than half were from Balti and Chisinau municipalities (59.9%). The cases had a social vulnerability background, as 80.8% were unemployed and other economically inactive categories, 91.3% had a history of drug use and 39.3% had a history of imprisonment. More than half of cases had other associated TB and HIV comorbidity; such as Hepatitis C (37.4%), Hepatitis B (15.3%), mental health issues (3.4%) and other conditions (28.5%). There was a bias towards recording in the SYME-TB the use of injecting drugs as a mode of transmission, as almost no sexual mode of transmission was recorded and a large proportion remained with undocumented mode of transmission.

One in four cases (27% or 245 cases) has not been seen by the infectious diseases specialist at DCDH at all and a clinical record was missing at the clinic responsible[1] for the follow up of all people registered with HIV. Only 24.4% of the cases were seen by an infectious disease specialist for the first time before 2007, while majority of the cases were seen after 2007.

TB was diagnosed before or at the same time with HIV in 33.9% of cases, for another 24.7% TB was diagnosed within the first year after first visit to HIV specialist and for another fifth (20.7%) TB was diagnosed within 1-3 years after first visit to HIV specialist, and only for 20.7% TB occurred after 3-10 years after first visit. Therefore, the group of TB/HIV cases was in general late presenters, as 40.0% were in stage C of HIV disease according to CDC classification, while 31.5% were not clinically evaluated. Among those who had lab exams performed, 46.1% had CD4 counts < 200 cells/mm^3, and another 35.4% had CD4 counts between 201 and 499 cells/mm^3.

A quality of care indicator is the timing of starting ARV treatment in TB/HIV cases with CD4< 350 cells/mm3. In this subsample of TB/HIV patients with CD4 counts less than 350 cells/mm3 (n=444), 42.6% were already on ARV, while only additional 14.0% have received ARV within the first 8 weeks after initiation of TB treatment. Of note is that 132 patients (29.7% of them) did not receive ARV treatment at all and have died.

TB screening in known HIV patients was not working properly, as only 10.5% of TB/HIV cases had records of having been screened for TB in the 12 months preceding TB diagnosis, 30.0% had not been screened for TB, and for 59.5% there was no record. Most patients have been screened with X-ray (10.1% of the total sample, n=95). Only one case in the five-year period had records of being screened for TB using smear microscopy in the 12 months preceding TB diagnosis at the DCDH. Of 79 cases screened for TB with X-rays with valid records, 41.8% had a positive TB result and

1 During 2003-2007 it was the Republican Dermatovenerological Dispensary, during 2007-2010 the Republican Hospital for Infectious Diseases "Toma Ciorba" and since 2011 it has been the Dermatology and Communicable Diseases Hospital.

49.4% had a negative TB result while 8.9% had no result recorded. In prison sector, TB screening in known TB/HIV cases was even less frequent, as only 7.9% had record of having been screened for TB. None of PLHIV has received preventive therapy with Isoniazid.

Among TB/HIV co-infection cases, 61.3% were new cases, 18.0% were relapse, 9.2% treatment after default, 9.8% treatment after failure and 1.6% were classified as chronic TB. The share of new cases has increased from 52.3% in 2007 to 69.2% in 2011. Of all cases, 65.0% were symptomatic, 19.1% were detected based on screening results and 15.9% had no record. The most prevalent diagnosed location was pulmonary TB in 91.0% of cases, in 5.9% cases it was extra-pulmonary location and in 3.1% it was an extra-respiratory location. The most frequent form was pulmonary infiltrative form (65.6%), followed by pulmonary disseminated form (16.3%).

Almost all cases (99.3%) had TB diagnosis supported by microbiologic evidence. Microscopy result was positive for only 45.3% of cases, with a decreasing trend from 2007, when 51.6% were positive, to 37.9% in 2011. In 2.6% of cases a biopsy result was available. Culture was examined for 94.2% of cases and 51.1% had a positive culture result. Some 60.5% of cases had been performed an antimicrobial susceptibility test (AST). Of those who had resistance result to AST (n=315), three quarters (76.5%) had multi-drug resistant TB (MDR-TB), 11.7% had mono-resistant strain, 10.2% had poli-resistant strain and one person has been registered with extensively drug-resistant TB (XDR TB). HIV testing and counselling has good coverage in TB facilities, as almost all cases with unknown HIV status were tested for HIV at the time of TB diagnosis, only 28 cases records did not contain information if the HIV testing was done.

From the total of 921 reviewed cases, 911 have received TB treatment and 9 cases have refused the treatment. Three quarters (76.7%) were registered as being treated in public TB hospitals and 16.4% were treated in penitentiary hospitals, while 6.9% of cases were treated in outpatient settings only. The biggest number of cases initiated the inpatient intensive treatment at Phtysiopneumology Department of Balti Clinical Municipal Hospital, where a total 348 cases or 37.7% were hospitalised. The two facilities in Chisinau - Chisinau Clinical Municipal Phtysiopneumology Hospital and Phtysiopneumology Institute "Chiril Draganiuc" - hospitalised 323 cases or 35.3%. Only half of TB/HIV cases (53.3%) received infectious diseases specialist consultation for their HIV after TB diagnosis.

Almost all cases (94.8%) have received standard regimens and 5.2% have received individualized regimen. Only 2.2% or 20 cases have received DOTS plus regimen, 68.8% have received treatment regimen I, indicated for new smear-positive cases, 25.5% have received treatment regimen II, for relapse treatment. Given that 241 patients have been diagnosed with MDR-TB, there is a discrepancy between TB resistant forms diagnosed and treatment regimen received. According to follow-up discussions with service providers, causes included delay between the time of TB treatment initiation availability of sensitivity test results and patients refusing to change the regimen, but there is no written evidence of these two reasons. Another recommendation according to the national protocol is Pneumocystis Carinii Pneumonia (PCP) prevention during

TB treatment. Only every fourth case (25.3%) had records of prescription of co-trimoxazol, of which it was prescribed by infectious diseases specialist (15.6%) or TB specialist (9.7%). The rest three quarters have not received co-trimoxazole (58.5%) or had no records about it (16.2%).

Some 447 cases or 48.5% have had an outpatient continuation stage of TB treatment, as some cases have either completed treatment in inpatient conditions, i.e. patients in prisons, others defaulted from treatment during intensive stage and others have deceased in inpatient stage. Family doctors supervised treatment for 42.1% of cases, city TB specialist for 42.8% of cases and in 11.9% of cases it was the District TB specialist and 3.3% it was another medical provider. About 64.4% have been documented as good treatment adherers and 31.8% were recorded as taking their drugs irregularly and no records 3.8% of the sample. Of note is an increasing trend in good adherence to treatment by years, from 60.0% in 2007 to 69.2% in 2011.

The treatment outcomes reflect the different bottlenecks in timeliness of care. Only one third of cases had treatment success (of them 14.8% with cure and 20.7% with a completed treatment outcome), 16.4% were registered as defaulters, and 10.8% with treatment failure. One third of patients have deceased, either because of TB progression (20.1% or 184 cases) or for other causes (12.0% or 110 cases).

The cross-check with the national mortality database has shown a higher number of deceased TB/HIV patients recorded in the national mortality database, 336 cases compared to 294 reported as deceased in treatment outcome in SYME-TB. According to ICD-10 classification, the diagnosis at death was established as TB/HIV co-infection (code B200) for 52.7% of cases, another 29.2% had mentioned only TB and 7.4% HIV-related cause. Thus, a total 81.8% have mentioned TB as the primary cause of death compared to 62.6% in SYME TB. Other significant causes of death related to HIV (7.4%), liver cirrhosis (3.0%) and injury and poisoning (2.4%), while the rest of causes were distributed in less than 5%.

The missed opportunities in quality clinical care had to do with delays in timely clinical follow up by infectious diseases specialists for at least 27% of cases, but also insufficient efforts to detect TB early, as well as losing precious time between TB suspicion and final confirmation of TB. On average, 23 days standart deviation (SD 75 days) elapsed since the first TB suspicion until confirmed TB diagnosis and 28 days (SD 94 days) since the first TB suspicion until the initiation of TB inpatient treatment. Another bottleneck is the transition between the inpatient treatment stage and initiation of outpatient treatment stage. On average, there is a delay of 11 days between the two with a large range (SD 47 days).

OPPORTUNITIES FOR INTERVENTIONS

For HIV service component

Identified bottlenecks: late HIV diagnosis; reduced ARVT coverage; high mortality rate.

1. Ensure earlier HIV diagnosis and ARV treatment
   a. The key affected populations shall have access to HIV counselling and testing facilities, including rapid diagnostic techniques. People with confirmed HIV diagnosis shall be assessed for HIV stage, including viral load and CD4 counts.
   b. ART should be initiated in all individuals with HIV with CD4 count ≤ 500 cells/mm3 regardless of WHO clinical stage.

Identified bottlenecks: poor TB screening; inadequate clinical follow-up; inappropriate level of TB preventive treatment.

2. Intensify TB case-finding
   a. PLHIV should be regularly screened for TB with a clinical algorithm. Those with no obvious risk for TB should perform tuberculin skin test (TST); positive TST is a condition to initiation of TB preventive treatment (TPT). Those who report respiratory systems or history of TB exposure shall be assessed for active TB disease (including clinical examination, bacteriological investigation and X-ray).

Identified bottlenecks: excessive time to diagnose TB in HIV-infected patients; late ART initiation; high mortality rate.

3. Ensure timely TB and ARV treatment
   a. TB treatment in HIV-infected patients is a priority and should be initiated as soon as active TB has been diagnosed. The time between the first TB suspicion and initiation of TB inpatient treatment shall be reduced through TB/HIV collaborative measures.
   b. ART should be initiated in all TB patients living with HIV irrespective of their CD4 counts. TB treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment. Those with profound immunosuppression should receive ART immediately within the first 2 weeks of initiating TB treatment. Efavirenz should be used as the preferred non-nucleoside reverse transcriptase inhibitor in patients starting ART while on TB treatment.

For TB service component

Identified bottlenecks: reduced rate of ambulatory treatment, large transition lag between in-patient and out-patient treatment.

1. Ensure high-quality TB treatment
    a. Encourage initiation of TB treatment in outpatient settings, limiting hospital admissions to only severe cases. TB patients with known positive HIV status should receive TB treatment based on WHO recommended regimens.
    b. The optimal dosing frequency is daily during the intensive and continuation stages. The transition time lag from in-patient to out-patient treatment shall be reduced through enhanced case-management.

Identified bottlenecks: long time between TB suspicion and results of AST; inadequate treatment of MDR-TB patients with HIV including delay in treatment initiation.

2. Improve timely TB diagnosis based on rapid techniques
    a. The TB diagnosis is based on bacteriological methods. In HIV-infected TB suspects, there is a need to expand testing with Xpert MTB/RIF method as the initial diagnostic method, followed by determining full resistance profile using rapid techniques in TB cases and timely initiation of anti-tuberculosis treatment based on obtained resistance pattern.

Identified bottlenecks: inadequate follow-up by infectious diseases specialists; unsatisfactory preventive treatment with co-trimoxazole.

3. Ensure appropriate TB/HIV clinical management
    a. Routine HIV testing is offered to majority of TB patients. However, there is a need to improve links with the HIV service and have routine consultations of TB/HIV patients by the infectious diseases specialist.
    b. Routine co-trimoxazole preventive therapy should be administered in all HIV-infected patients with active TB disease regardless of CD4 counts.

For both HIV and TB services

Identified bottlenecks: unsatisfactory patient follow-up, poor case management; deficient recording and reporting system.

1. Improve collaborative measures
    a. All people living with HIV who are diagnosed with TB should receive integrated services for prevention, diagnosis, treatment and care of TB and HIV.
    b. HIV programs and TB-control programs should ensure access to a continuum of comprehensive and integrated prevention, care and treatment for people living with HIV who are receiving or who have completed their antituberculosis treatment.
    c. The recording and reporting system shall be improved, including quality control of medical records. The reporting systems need to be integrated, including with national vital statistics databases.

Identified bottlenecks: unsatisfactory patient follow-up; poor case management.

2. Involve community-based organizations and NGOs in TB/HIV control
   a. Community-based organizations and NGOs active in HIV prevention field should support medical service providers in identifying sceptical HIV patients and motivate them to seek health care and follow up with infectious diseases specialists.
   b. Harm reduction NGOs should integrate TB screening questionnaire to all their clients through outreach and fixed work.
   c. NGOs should focus on providing case-management services for patient navigation among the two systems.
   d. Community-based organizations should be on the alert for symptoms of TB among their target group and refer to TB services.
   e. Community-based organizations and NGOs active in HIV prevention should educate their target group about TB symptoms: cough lasting for two to three weeks or longer or a current cough (of any duration), fever, weight loss and night sweats.

BACKGROUND

In Moldova, tuberculosis (TB) continues to be the top cause of mortality among the PLHIV. According to national data provided by the National Phtysiopneumology Institute, in 2012, 5% of the 3,800 newly registered TB cases were TB/HIV co-infection cases. Of the total number of 588 TB patients, who died in 2012, 13% had the TB/HIV co-infection. Of the deceased persons who had the TB/HIV co-infection 30.3% had MDR TB.[2] During 1987-2007, there were 528 AIDS cases (12.7% of all HIV positive persons) in Moldova, 255 of them (48.3%) being associated with TB. Most cases were concentrated in the two main cities: Chisinau and Balti.[3]

At the same time, the routine statistics do not provide accurate information on the number of TB/HIV co-infection cases and on treatment outcomes, including on deaths. A special study conducted for a cohort of 92 patients with TB/HIV co-infection showed that two thirds of them were from key affected populations, former prisoners or people who injected drugs (PWID). During the first year of research, over two thirds of the patients who had been receiving treatment died.[4]

While there are written algorithms of coordination of care between TB and HIV specialists, it is not clear how they work in practice and the quality and coordination of care between the two vertical systems have not been assessed thus far. Therefore, a need to assess the quality of care for such patients has emerged.

This operational research has been planned to monitor and evaluate the National Programme for Prevention and Control of Tuberculosis and the National Programme of Prevention and Control of HIV/AIDS and STIs, the TB/HIV component of collaborative actions. This research is part of the implementation plan of the Global Fund HIV Grant in Moldova. The research results will be used to evaluate both national programmes.

The timing of the first clinical chart audit is also taking into account a new development: initiation, in 2013, of the GeneXpert technology that allows identifying TB much earlier than in the previous period. It was introduced throughout the country in many TB settings and has been installed at Dermatology and Communicable Diseases Hospital (DCDH), the entity responsible for all HIV clinical care in the country since 2003. We hope that it will significantly change the landscape and the clinical outcomes for the patients with TB/HIV co-infection.

The study team has used a new method for Moldova, a clinical chart audit of TB and HIV cases, developing a new know-how in this area that could be useful for other countries around the world. The Centre for Health Policies and Studies (PAS Centre) staff designed and developed the study method, by applying the chart audit method to patients with TB/HIV co-infection. UNAIDS RCA has provided technical assistance to finalise the study protocol, the data collection and to oversee parts of data collection.

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2 Domente L. TB/HIV co-infection: goals and challenges. Presented on April 4 2013.

3 MoH, UNAIDS (2010). National HIV/AIDS Response Analysis Republic of Moldova 2010. http://aids.md/aids/files/871/Moldova_AIDS_National%20AIDS%20Responce%20Analyses%202010.pdf

4 National Coordination Council, UNAIDS Moldova. Midterm Review of the National Programme on Prevention and Control of HIV/AIDS/STIs 2006-2010, March 2009. Unpublished work.

METHODS

Goal of the study

Produce strategic information on the quality of the clinical management of TB/HIV co-infection cases to be used in the decision-making on increasing life expectancy and improving the quality of life of PLHIV.

Objectives

- Conduct a quantitative assessment of the quality of health care services provided to cases of TB/HIV co-infection
- Identify the risk factors associated with the mortality among the TB/HIV cases
- Identify and systematise the potential shortcomings in the management of the TB/HIV co-infection cases
- Assess the causes of death of PLHIV
- Make recommendations for further improvement of the clinical management of the TB/HIV co-infection cases

Quality assessment of the clinical management of the TB/HIV co-infection cases

- The research is an exhaustive retrospective analysis of the cohort based on a structured questionnaire.

Inclusion criteria:

- TB cases notified during 1 January 2007 – 31 December 2011
- People with HIV-positive status registered by the National Centre for Health Management (NCHM) in the SYME-TB
- People aged 18 years and older at the time of diagnosis/notification
- TB treatment results registered in the SYME-TB during data collection

The residents of the Transnistrian region, on the left bank of the Nistru River, as well as those who received medical treatment in the Transnistrian region, were not included in the study.

The quality of health care services provided to the HIV/TB co-infection cases is measured under the applicable national clinical guidelines and protocols and according to the following criteria:

a. The person living with HIV is taken under medical follow up and undertakes annual medical checkups for early diagnosing of TB through chest X rays every 6 months or the Mantoux probe;
b. The optimal period of time when the suspected TB status is established and until the confirmation of the TB diagnosis;
c. The TB/HIV patient is enrolled in the TB treatment under the standard regimens upon the confirmation of the TB diagnosis;

d. The TB/HIV patient enrolled in TB treatment receives co-trimoxazole according to the national standards;

e. The TB/HIV patient with CD4 count less than 350 cell/mm^3 at an advanced HIV stage is enrolled in ARV treatment upon the confirmation of the TB diagnosis or no later than 2 to 8 weeks after the initiation of the TB treatment;

f. The TB/HIV patient adheres/adhered to ARV and TB treatments, the adherence being measured by the regular administration of drugs according to the national protocols throughout the entire TB treatment.

g. ARV treatment is efficient, the efficiency being measured by the increase in the CD4 count and Viral Load undetermined after 6 months from the initiation of the ARV treatment;

h. TB treatment is efficient, the efficiency being measured by the results of the TB treatment – cured or treatment completed.

The following sources were used for data collection:

a. The SYME TB managed by the NCHM and the Phthisiopneumology Institute "Chiril Draganiuc";

b. Patients' charts from the in-patient health facilities involved in TB treatment at national, regional and municipal level;

c. The SYME HIV managed by the Dermatology and Communicable Diseases Hospital;

d. Charts of patients living with HIV from the outpatient DCDH facility;

e. The national mortality database managed by the NCHM.

If a person living with HIV notified/was diagnosed with several TB cases during the period of the research (2007-2011), then every case was assessed for both TB and HIV.

Firstly, the cases that met the inclusion criteria were extracted from the NCHM-managed database of TB cases to which the Phthisiopneumology Institute "Chiril Draganiuc" has unlimited access. The HIV/TB cases with unknown HIV status in the TB data base were not checked against the HIV data base if they were or if they were not under the HIV medical follow up.

After cases were extracted, an anonymous unique identifier was created for each case without using any criteria that would allow for the direct or indirect identification of the person. Once extracted from the data base, each TB case with HIV-positive status was attributed a unique anonymous identifier that was password-protected (a separate access password was provided to each assessment officer) and made available to the data collection coordinators. Data coordinators were selected from among the senior medical staff are entitled to access the patients' data. The password was provided verbally without any electronic or hard copy records.

For each TB case a questionnaire consisting of three components on HIV, TB and mortality was filled out. The TB component was filled out first and then the anonymously codified questionnaire was passed to the assessor of the HIV component. To complete the TB part, field trips were made.

The assessor of the mortality component worked independently and extracted the TB cases identified by the NCHM in the national mortality database and filled out the questionnaire with the mortality indicators. The corresponding parts of the questionnaire were submitted to the other two assessors. All fields that may directly or indirectly identify the deceased persons were excluded from the copy of the file with the extracted data. This anonymous ID file was imported into the database of the study to avoid data entry.

Each questionnaire was discussed by the assessor of the HIV component and by the assessor of the TB component to validate the data collected by all three reviewers. The assessor of the mortality component intervened only upon request. Anonymously codified questionnaires were centralised at the PAS Centre. The codified questionnaires were checked by editors at the national level. The assessors of the HIV and TB components were responsible for entering the data into the database.

The database was checked in terms of completeness and consistency of the data entered.

Data analysis

Data analysis of both components was performed using the SPSS version 17 that generated frequency and bivariate reports, the descriptive analysis of data and relevant statistical tests.

Limitations

1. **Data quality issues:** given the retrospective nature of data collection and the fact that it was based on the clinical chart audit, the use of a standardised questionnaire has revealed a large amount of missing data and low accuracy of data in the clinical charts. To avoid misinterpretation of the missing data, the results are presented with missing data as a separate category where possible and where not possible, indicating the sample size.
2. **Discrepancies between the clinical records and database records:** During the collection of data, some discrepancies were noted between the records in the TB charts, the records in the HIV charts and what had been reported in the SYME-TB. The table below captures the number of cases where such discrepancies were noted. The discrepancies included: different treatment results reported in the SYME-TB compared to the clinical chart; dates of various clinical milestones were 2-3 days different in the SYME-TB compared to the clinical chart; the type of cases identified – more patients were reported in the SYME-TB as preventive cases, whereas, in fact, they were symptomatic cases. In all those cases the clinical chart was used as the basis for data. The highest number of discrepancies was noted between the SYME TBC and SYME HIV, where 112 cases were missing in the DCDH data. Those patients were presented as the ones that have the information on the HIV-related aspects missing.

TABLE 1: Discrepancies between the records of different recording systems

	n	Percent
Inpatient and outpatient TB chart	10	1.1
Inpatient TB chart and SYME-TB	80	8.7
Outpatient TB chart and SYME-TB	75	8.1
TB charts and DCDH's chart	112	12.2

3. Discrepancies between the cases registered in the SYME-TB and in the National Mortality Database

The analysis of the deceased cases extracted from the National Mortality Database administered by the NCHM has highlighted a number of discrepancies in relation to the deceased cases registered in the SYME-TB. There were a total of 326 cases registered in the SYME-TB compared to 336 cases in the National Mortality Database. After the manual cross-checked of the data by the data coordinators, a total of 20 cases were identified as missing in the SYME-TB as mortality cases and had been entered as cases with completed treatment (14 cases), cure (3), default and permanent migration (2) and clinical failure(1). On the other hand, 10 deceased cases that are found in the SYME-TB were missing in the National Mortality Database. Those could be the persons whose relatives have not claimed their death certificates.

RESULTS

Socio-demographic characteristics of the sample

The sample covered 750 patients registered as TB/HIV cases in the SYME-TB during 2007-2011. Since the analysis is based on the number of cases, some patients have had more than one TB case registered during the five-year period (for example, a patient had a primary TB that ended with a default, then retreatment after default), with a total of 921 cases. Further, we present the data based on the registered cases.

Of the total number of 921 cases, 74.4% were males and 25.6% were females. At the time of the TB notification the age ranged between 18 and 75 years, with a mean age of 34.91 years and a standard deviation of 8.1 years. More than half of cases (59.9%) came from Chisinau and Balti municipalities, 22.5% from rural areas, 13.2% from district centres, and 3.9% were homeless.

During the five-year period, the share of cases coming from Chisinau and Balti dropped from 75.8% in 2007 to 47.2% in 2011, and the share of rural cases increased from 12.4% in 2007 to 30.3% in 2011, accordingly. The share of homeless TB/HIV patients also increased from 2.6% in 2007 to 6.7% in 2011. This is likely associated with the national trend of HIV epidemic, which originally was focused in Chisinau and Balti in late 1990s, expanding to the district centers and rural areas in 2000s.

The sample covered mostly unemployed persons (80.8%) and other groups of economically inactive population (persons with disabilities - 9.0%, retired persons - 0.9%, students - 0.5%) and only 8.6% of audit subjects were employed, which revealed a more vulnerable part of the HIV population that had been affected by the TB co-infection (Table 2).

TABLE 2: Socio-demographic characteristics of the sample, by years

	2007	2008	2009	2010	2011	Total
Sex						
Male	75.3	78.7	74.6	70.1	73.3	74.4
Female	24.7	21.3	25.4	29.9	26.7	25.6
Age, years						
18-24	8.4	6.9	7.1	6.0	3.6	6.3
25-29	27.3	18.8	24.3	17.9	19.0	21.1
30-39	46.8	49.0	52.1	47.3	50.8	49.2
40-49	11.7	17.8	14.2	21.4	21.0	17.6
50-59	4.5	5.9	2.4	6.0	5.1	4.9
60+	1.3	1.5	0	1.5	5	1.0
Area						
Chisinau and Balti	76.0	68.8	59.2	51.7	47.2	59.9
District center	9.1	10.9	11.8	18.4	14.9	13.2
Rural	12.3	17.8	24.9	25.4	30.3	22.5
Homeless	2.6	2.5	3.0	4.5	6.7	3.9
No record	0	0	1.2	0	1.0	4
Occupation						
Unemployed	79.2	83.7	80.5	79.6	80.5	80.8
Employed	10.4	8.4	7.7	8.0	8.7	8.6
Disabled	9.1	5.9	11.2	10.0	9.2	9.0
Retired	6	1.0	0	2.0	5	9
Students	6	1.0	6	5	0	5
Other	0	0	0	0	5	1
No record	0	0	0	0	5	1
Count	**154**	**202**	**169**	**201**	**195**	**921**
Total %	**16.7**	**21.9**	**18.3**	**21.8**	**21.2**	**100.0**

Risk factors

Higher vulnerability of TB/HIV patients is confirmed by the prevalence of risk factors. A total of 91.3% of cases were using drugs at the time of TB notification or had a history of drug use. 27.5% of cases had a history of drinking and 39.3% of cases had a history of imprisonment. Of note is that more than half of the reviewed clinical charts (53.5%) had no records of evaluation of drinking habits, and most cases had no records

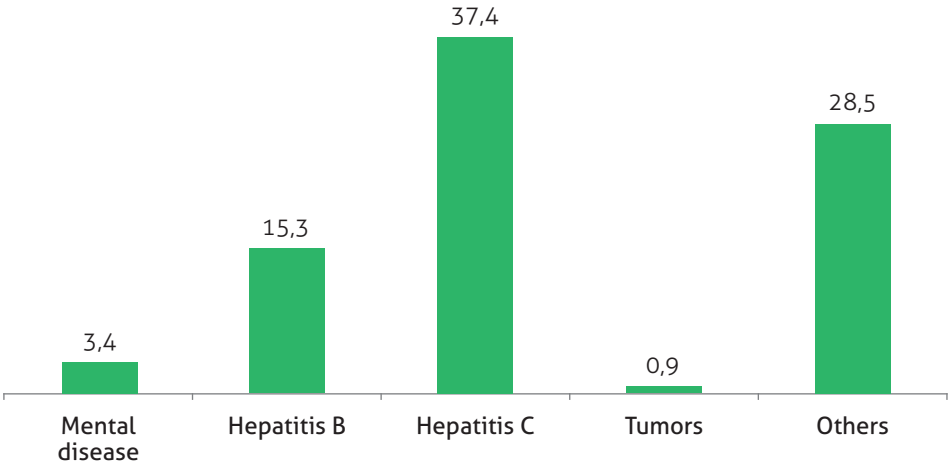
of evaluation if the patient was on opioid substitution treatment (OST) (Table 3). Of note is another trend of a decreasing share of people who used drugs from among the TB/HIV cases – from 80.5% in 2007 to 43.6% in 2011. Very few (2.6% or 16 cases) were found to be on OST at the time of TB treatment, revealing a missed opportunity of proper managing the TB/HIV co-infection. TB/HIV cases were also a relatively stable population, as 78.1% did not have a history of migration, 20.1% were migrants before the notification of the TB case and only 0.4% had migrated after TB case notification.

TABLE 3: Prevalence of risk factors among patients with TB/HIV co-infection, by year

	2007	2008	2009	2010	2011	Total
History of alcohol misuse						
Yes	26.6	25.7	25.4	30.3	28.7	27.5
No	16.9	16.3	18.3	24.4	19.0	19.1
No records	56.5	57.9	56.2	45.3	52.3	53.4
History of drug use						
Yes, currently	80.5	72.8	64.5	57.2	43.6	63.0
Yes, in the past	13.0	19.3	29.0	36.8	40.5	28.3
No records	6.5	7.9	6.5	6.0	15.9	8.7
Patient on OST						
Yes, during the TB treatment	3.1	3.3	0.9	1.7	4.1	2.6
Yes, in the past	0.0	1.3	0.0	0.0	2.1	0.7
No	26.8	20.3	5.3	7.0	2.1	13.4
No records	70.1	75.2	93.8	91.3	91.8	83.3
Prison history						
No	55.8	55.4	56.2	59.2	62.6	58.0
Less than 1 year before TB	1.3	2.5	1.2	1.5	2.6	1.8
1-3 years before TB	7.1	5.9	5.9	6.5	9.2	6.9
Over 3 years, before TB	10.4	17.8	13.6	19.9	11.3	14.9
During the TB case	22.7	16.3	17.8	10.4	13.3	15.7
No record	2.6	2.0	5.3	2.5	1.0	2.6
Migration history						
Yes, 1 year before TB	15.6	21.3	18.3	19.9	24.1	20.1
Yes, after TB	0.0	0.0	0.6	0.5	1.0	0.4
No	83.1	77.2	81.1	78.6	71.8	78.1
No record	1.3	1.5	0	1.0	3.1	1.4
Count	**154**	**202**	**169**	**201**	**195**	**921**
% of Total	**16.7**	**21.9**	**18.3**	**21.8**	**21.2**	**100.0**

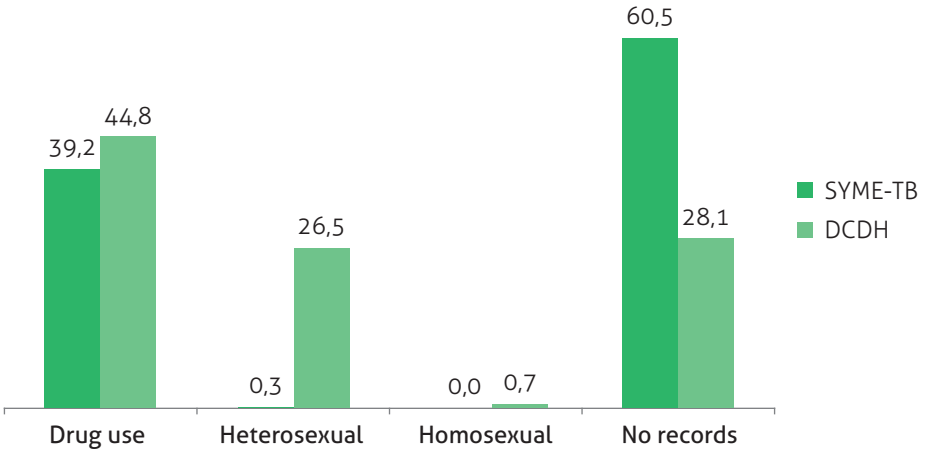
Of all cases 61.6% had at least one co-infection. The most frequent was Hepatitis C, as 37.4% had records of it, and 15.3% had registered Hepatitis B, 3.4% had a recorded mental health issue, and 28.5% had other co- infections (Figure 1). In addition, in 210 female cases with TB/HIV co-infection, 8 women or 3.8% had also documented pregnancy at the time of TB case notification.

FIGURE 1: Prevalence of co-morbidities among patients with TB/HIV co-infection, in the total sample (in %)



Discrepancies in documenting the way of HIV transmission in the SYME-TB and DCDH recording systems has been noted and the SYME-TB had not documented the mode of HIV transmission in 60.5% of cases, with a selective bias towards documenting HIV transmission associated to drug use. Yet, even in the DCDH's systems, the mode of HIV transmission was not documented in 28.1% of cases (Figure 2).

FIGURE 2: Mode of HIV transmission, as recorded in the SYME-TB and DCDH's systems (in %)



Timing of TB and HIV diagnosis

In more than two thirds of cases (69.1%) TB was diagnosed in people with an already known HIV status, in 12.5% of cases TB was diagnosed first and then HIV was diagnosed, and in 17.4% of cases TB and HIV were diagnosed simultaneously (in 1.1% of cases records were missing).

TABLE 4: Timing of TB and HIV diagnosis, by year and by type of setting

	Year					Setting			Total	
	2007	2008	2009	2010	2011	Public hospital	Prison hospital	Outpatient setting	count	%
TB diagnosed in a known HIV patient	74.5	67.8	70.4	64.7	69.2	67.4	82.1	56.3	636	69.1
HIV diagnosed in a TB patient	13.1	11.4	10.7	12.9	14.4	13.2	4.0	25.0	115	12.5
TB and HIV diagnosed at the same time	9.2	20.3	18.3	21.4	15.9	18.3	13.9	15.6	160	17.4
No record	3.3	5	6	1.0	5	1.1	0	3.1	10	1.1
Count	**153**	**202**	**169**	**201**	**195**	**706**	**151**	**64**	**N/A**	**921**
% of Total	**16.6**	**22.0**	**18.4**	**21.8**	**21.2**	**76.7**	**16.4**	**6.9**	**921**	**100.0**

Quality of HIV follow-up and care

A significant number of TB/HIV co-infection cases registered in the SYME-TB during 2007-2011 were missing in the SYME-HIV and many of them had not been seen by an infectious diseases specialist of the DCDH. A total of 43 cases (5%) were not registered in the SYME-HIV with a date of HIV diagnosis and 245 cases (27%) of TB/HIV cases have not been seen by the infectious diseases specialist of the DCDH at all.

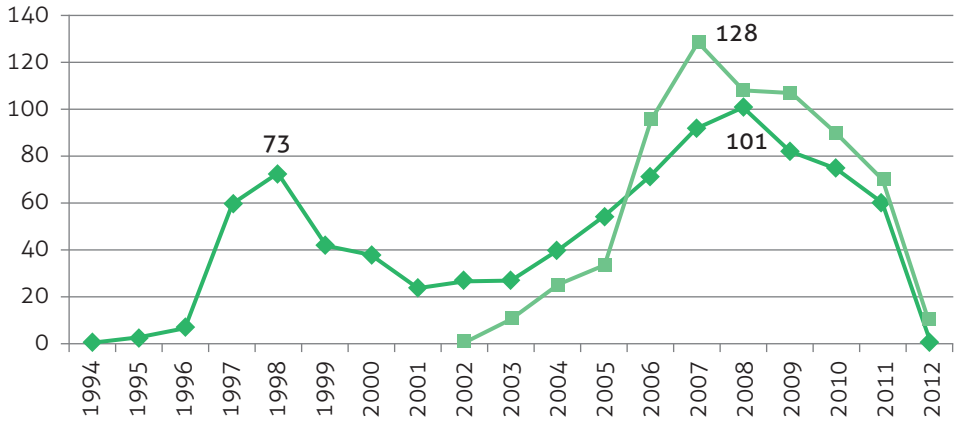
TABLE 5: TB/HIV cases missing in the SYME-HIV and DCDH database

	HIV diagnosis		1st visit to DCDH	
	n	%	n	%
Valid	878	95	676	73
Missing	43	5	245	27

Of cases who had HIV diagnosis established (n=676), over half (52.3%) were PLHIV who had been diagnosed with TB during the five-year period (2007-2011) have received their HIV diagnosis during 2006-2012, (as some received a final diagnosis of HIV after

TB), a bit over fifth (22.8%) had their HIV established between 2000-2005, another fifth (20.1%) had their HIV established before 2000. If to look at the trend of the first visit to an infectious diseases specialist of the DCDH, only 165 of cases (24.4%) have been seen by the DCDH before 2007, while most cases were in the DCDH registry starting 2007.

FIGURE 3: Time of HIV diagnostic and the first visit to the infectious diseases specialist of the DCDH



The HIV disease stage at first visit was advanced for this cohort, as confirmed by the clinical diagnosis. Some 40.0% of TB/HIV cases were diagnosed in C clinical stage according to the CDC HIV disease classification, with manifestation of AIDS-indicator conditions and less than one third (27.8%) were in A or B clinical stages. No clinical staging was done for 31.5% of TB/HIV cases, but given that HIV was established simultaneously or after TB, they were most likely in advanced HIV disease stage as well.

TABLE 6: Clinical staging of HIV at the first visit to the infectious diseases specialist

Stage		n	Percent
Asymptomatic or acute HIV	A1	84	9.1
	A2	61	6.6
	A3	3	0.3
Symptomatic, non A non C	B2	76	8.3
	B3	32	3.5
AIDS-indicator conditions	C1	33	3.6
	C2	58	6.3
	C3	284	30.8
No record		**290**	**31.5**
Total		**921**	**100**

The laboratory results confirm the advanced stage of HIV at the first visit to the infectious diseases specialist and before the TB diagnosis. Of patients seen by the infectious diseases specialist, 98.2% had a record of CD4 count result and 59.9% had a

viral load result. The first CD4 count was on average 302 cells/mm^3, with a range from 1 to 1627 cells/mm^3. Of patients who had a CD4 count checked (n=664), 46.1% had a CD4 count <200 cells/mm^3, 35.4% had a CD4 count between 201 and 499 cells/mm^3 and only 18.5% had a CD4 count over 500 cells/mm^3. Among the patients who underwent a PCR test (n=405), the average viral load was 481,948 copies per ml, with 47.7% having a viral load < 100,000 copies/ml, 39.8% having a viral load between 100,001 and 1,000,000 copies/ml and 12.6% having a viral load over 1,000,001 copies/ml.

TABLE 7: The first and last laboratory results at the first visit to the infectious diseases specialist and before the TB diagnosis

	n	Minimum	Maximum	Mean	Std. Deviation
First CD4 count	664	1	1627	302	279
First RNA count	405	8	9,500,000	481,948	1,080,095
Last CD4 count before TB	427	1	1566	271	255
Last viral load count before TB	289	25	9,500,000	397,234	940,179

The last lab monitoring of HIV before the TB diagnosis has worse results, an average 271 cells/mm3 (46.4% of cases with a CD4 count) and 397,234 RNA copies (31.4% of cases with viral load result).

Despite the advanced HIV status and low immune status, only one third (33.4%) of HIV cases were on ARV at the time of TB diagnosis, with somewhat higher share in prisons (39.1%) compared to those that were managed in public hospitals (32.6%) and those treated in outpatient settings (29.7%). If to measure the share of those on ART in the subsample of those seen by an infectious diseases specialist (n=676), then 45.5% would be on ART at the time of TB diagnosis.

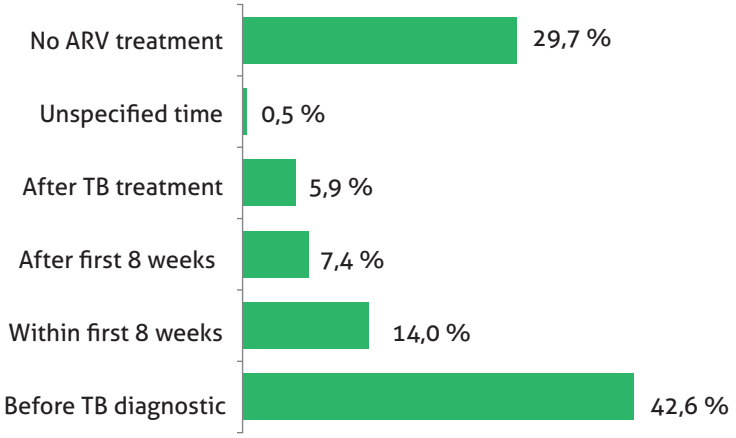
TABLE 8: Share of cases who were on ARV at the time of TB diagnosis, by type of settings (in %)

	Setting			Total	
	Public hospital	Prison hospital	Outpatient setting	count	%
Yes	32.6	39.1	29.7	308	33.4
No	44.8	53	45.3	425	46.1
No record	22.7	7.9	25	188	20.4
Count	**706**	**151**	**64**	**N/A**	**921**
% of Total	**76.7**	**16.4**	**6.9**	**921**	**100**

25.1% of HIV cases initiated the ART before the TB treatment, 0.3% during first 8 weeks of TB treatment, 4.9% after 8 weeks of TB treatment, 3.7% after the TB treatment was finished, while 56.8% did not receive ART or did not have records about receiving it.

An indicator for quality of care is the time of initiation of the ARV treatment in TB/HIV cases with CD4<350 cells/mm^3. In the subsample of TB/HIV patients with CD4 counts less than 350 cells/mm^3 (n=444), 42.6% were already on ARV, while only 14.0% received ARV within the first 8 weeks after the initiation of TB treatment. Of note is that 132 patients (29.7%) had not received the ARV treatment at all and died.

FIGURE 4: Timing of the ARV treatment in relation to the TB treatment



Only 20.4% of cases had records of good adherence to the ARV treatment before the TB treatment and 20.7% after the TB treatment, another 20% were recorded as not being adherent to the ART before and after the TB treatment, while for the rest of patients such records were missing in the patient charts. No adverse reactions to ART were recorded by the infectious diseases specialist during the TB treatment. For only 3 cases or 0.3% ART regimen was changed during the TB treatment.

Of the total TB/HIV cases, 486 did not have a previously known Hepatitis B or C infection and three quarters of them (75%) were screened for Hepatitis B or C, with higher shares in prisons (86-88%) compared to cases treated for TB in public hospitals or outpatient settings.

TABLE 9: Screening for Hepatitis B and C in HIV patients in follow-up by the DCDH

	Year					Setting			Total
	2007	2008	2009	2010	2011	Public hospital	Prison hospital	Outpatient settings	
Hep C	63.0	71.0	85.2	74.5	78.1	71.1	86.0	75.7	74.7
Hep B	62.5	71.0	83.9	77.3	78.1	70.7	88.8	75.0	75.0
Count	**81**	**93**	**88**	**110**	**114**	**342**	**107**	**37**	**486**
% of Total	**16.7**	**19.1**	**18.1**	**22.6**	**23.5**	**70.4**	**22.0**	**7.6**	**100.0**

TB screening in known HIV patients was not working properly in the DCDH. Only 10.5% of TB/HIV cases had records of having been screened for TB in the 12 months preceding the TB diagnosis, 30.0% had not been screened for TB, and for 59.5% there were no records. In prisons TB screening in known TB/HIV cases was even less frequent, as only 7.9% had record about having been screened for TB.

TABLE 10: Share of HIV cases which were screened for TB in 12 months preceding the TB diagnosis, by year and by type of setting

	Year					Setting			Total	
	2007	2008	2009	2010	2011	Public hospital	Prison hospital	Outpatient setting	count	%
Yes	9.2	6.9	10.1	11.9	14.4	10.5	7.9	17.2	97	10.5
No	28.1	23.3	23.7	35.8	37.9	30.5	27.8	29.7	276	30.0
No record	62.7	69.8	66.3	52.2	47.7	59.1	64.2	53.1	548	59.5
Count	**153**	**202**	**169**	**201**	**195**	**706**	**151**	**64**		**921**
% of Total	**16.6**	**22.0**	**18.4**	**21.8**	**21.2**	**76.7**	**16.4**	**6.9**	**921**	**100.0**

Of those screened, most patients have been screened with X-ray (10.1% of the total sample, n=95). Only one case during the five-year period had records of being screened for TB using smear microscopy in the 12 months preceding the TB diagnosis at the DCDH. Of 79 cases screened for TB with X-rays with valid records, 41.8% had a positive TB result and 49.4% had a negative TB result while 8.9% had no result registered. Given that all cases eventually developed TB, this fact points to ineffectiveness of X-ray as the only method for TB screening in detecting TB cases even in those cases that have been screened for TB.

Another national recommendation in preventing TB in HIV patients is the preventive therapy with isoniaside, but none of the HIV patients received it.

REVIEW OF TB CASE-MANAGEMENT AND FOLLOW-UP IN TB SETTINGS

Among the TB/HIV co-infection cases, 61.3% were new cases, while the others were retreatment cases: 18.0% were a relapse, 9.2% treatment after default, 9.8% treatment after failure and 1.6% were classified as chronic TB. The share of new cases increased from 52.3% in 2007 to 69.2% in 2011. In prison system, the number of new cases was lower than in the public system (41.7% new cases in prison system compared to 65.3% in public hospitals and 62.5% among the patients treated in outpatient settings only). In addition, a double share was defined as treatment after default (6.5% in 2007 and 12.3% in 2011).

TABLE 11: Type of TB cases, by year and by type of setting

	2007	2008	2009	2010	2011	Public hospital	Prison hospital	Outpatient setting	Total
new case	52.3	58.9	63.3	61.2	69.2	65.3	41.7	62.5	61.30
relapse	22.9	18.8	16.0	18.4	14.9	15.9	32.5	9.4	18.04
default	6.5	7.9	7.7	10.9	12.3	9.1	5.3	20.3	9.24
failure	15.0	12.9	10.0	8.5	3.6	8.2	17.9	7.8	9.78
chronic	3.3	1.5	3.0	1.0	0	1.6	2.6	0	1.63
Total count	**153**	**202**	**169**	**201**	**195**	**706**	**151**	**64**	**920**
Total %	**16.6**	**22.0**	**18.4**	**21.8**	**21.2**	**76.7**	**16.4**	**6.9**	**100.0**

A total 38.7% of cases had a documented history of TB and TB treatment in the past, less among cases treated in the public system (34.7%) compared to those treated in the prison system (58.3%). The share of new TB cases among the HIV patients increased during 2007-2011 from 51.6% to 69.2% (Table 12).

TABLE 12: History of TB at the time of case notification, by year and by type of setting

	2007	2008	2009	2010	2011	Public hospital	Prison hospital	Outpatient	Total
Yes	48.4	40.6	36.5	38.8	30.8	34.7	58.3	37.5	38.7
No	51.6	59.4	62.9	61.2	68.7	65.2	41.7	62.5	61.1
NR	0	0	6	0	5	1	0	0	2
Total count	**153**	**202**	**170**	**201**	**195**	**706**	**151**	**64**	**921**
Total %	**16.6**	**21.9**	**18.5**	**21.8**	**21.2**	**82.4**	**17.6**	**6.9**	**100.0**

Of all cases, 65.0% were symptomatic, 19.1% detected based on screening results and 15.9% had no record on the type of case.

Contrary to the trend in the general population, where TB is most often notified by the family doctor, the TB cases among HIV patients were notified at the outpatient specialised level, by specialists in prisons (25.3%), by the TB specialist (pulmonologist) (18.0%), by the DCDH (14.6%) and only in a quarter of cases by the family doctor (25.2%). However, the share of TB case notifications by family doctors had an increasing trend (19.0% in 2007 versus 27.2% in 2012), while the role of TB specialists and DCDH has been decreasing (TB specialists 26.8% in 2007 and 16.9% in 2011, DCDH 20.9% in 2007 and 13.3% in 2011).

TABLE 13: Type of medical facility/specialist who notified the TB case, by years

	2007	2008	2009	2010	2011	Total
Family doctor	19.0	26.9	23.5	26.4	28.7	25.2
TB specialist	26.8	19.4	12.4	15.9	16.9	18.0
Other specialist	18.3	26.9	30.6	22.9	27.2	25.3
TB hospital	2.0	1.0	0	1.5	1.5	1.2
DCDH	20.9	10.4	14.1	15.4	13.3	14.6
No record	**13.1**	**15.4**	**19.4**	**17.9**	**12.3**	**15.7**

TB DIAGNOSIS

The most prevalent diagnosed form of TB was pulmonary TB in 91.0% of cases, extrapulmonary TB in 5.9% of cases and extrarespiratory TB in 3.1% of cases. The most frequent form of TB was pulmonary infiltrative (65.6%), followed by pulmonary disseminated form (16.3%) (Table 14).

TABLE 14: TB diagnosis, location and form, at the time of case notification, total sample

Location	Form	Count	Percent
Pulmonary	Primary complex	5	5
	Disseminated	150	16,3
	Nodular	48	5,2
	Infiltrative	605	65,6
	Fibro-cavitary	23	2,5
	Tracheo-bronchial	8	9
	Total	**839**	**91**
Extrapulmonary	Pleurisy	44	4.8
	Lymph nodes	9	98
	Other forms	1	1
	Total	**54**	**5.9**
Extrarespiratory	Meningitis	8	9
	Bone and joint	1	1
	Uro-genital	2	2
	Peripheral adenopathy	17	1.8
	Intestinal	1	1
	Total	**29**	**3.1**
Total		**921**	**100**

More than half of cases (61.1%) did not have registered complications. Of those who had, the most frequent were pleurisy (14.2%), respiratory failure (8.5%), failure of other organs (2.9%), pulmonary heart failure (2.4%) and hemoptysis (2.3%), other complications being registered in less than 2% of cases.

TABLE 15: Frequency of complications, total sample

Complications	Count	Percent
Hemoptysis	21	2.28
Pulmonary hemorrhage	5	0.54
Pneumothorax	1	0.11
Respiratory failure	78	8.47
Pulmonary hear failure	22	2.39
Failure of affected organs	27	2.93
Meningitis	14	1.52
Pleurisy	131	14.22
Other	53	5.75
Bronchial	3	0.33
Laryngeal	2	0.22
Intestinal	2	0.22
No complications	562	61.02
Total	**921**	**100**

Almost all cases (99.3%) had TB diagnosis supported by microbiologic evidence. Microscopy result has been obtained in almost all cases in both public and prison systems. The result was positive for only 45.3% of cases with few differences between the two systems, but with a decreasing trend from 2007, with 51.6% positive results, to 37.9% in 2011 (Table 16). In 2.6% of cases a biopsy result was available.

TABLE 16: Microscopy result in TB/HIV cases, by year and by type of setting

	2007	2008	2009	2010	2011	Public hospital	Prison hospital	Outpatient	Total
Positive	51.6	50.0	47.6	40.8	37.9	45.4	47.0	39.1	45.28
Negative	44.4	44.6	47.6	53.2	55.4	48.2	53.0	53.1	49.40
Not done	3.3	3.5	2.4	4.0	3.6	4.0	0	4.7	3.37
No record	7	2.0	2.4	2.0	3.1	2.4	0	3.1	1.95
Total count	**153**	**202**	**170**	**201**	**195**	**707**	**151**	**64**	**921**
Total percent	**16.6**	**21.9**	**18.5**	**21.8**	**21.2**	**76.7**	**16.4**	**6.9**	**100.0**

The culture was examined for 94.2% of cases. 51.1% of cases had a positive culture result, 33.0% had a negative result, while for 4.1% of cases, the result remained unfinished or the test had not been performed (5.8%) or it was not included in the patient chart (6.0%).

TABLE 17: Culture result in TB/HIV cases, by year and by type of setting

	2007	2008	2009	2010	2011	Public hospital	Prison hospital	Outpatient	Total
Positive	47.7	51.0	46.5	56.7	52.3	52.1	52.3	37.5	51.1
Negative	30.1	31.2	38.2	31.3	34.4	32.5	35.8	32.8	33.0
Unfinished	7.2	6.4	1.8	5	5.1	3.7	7.9	0	4.1
Not performed	11.1	4.5	4.7	4.5	5.1	6.1	2.6	9.4	5.8
No record	3.9	6.9	8.8	7.0	3.1	5.7	1.3	20.3	6.0
Total count	**153**	**202**	**170**	**201**	**195**	**707**	**151**	**64**	**922**
Total %	**16.6**	**21.9**	**18.5**	**21.8**	**21.2**	**76.7**	**16.4**	**6.9**	**100.0**

A total 60.5% of cases underwent the sensitivity test, with a higher share among the patients treated in prison hospitals (70.5%) compared to those treated in public hospitals (58.9%) and the lowest among the patients treated in outpatient settings only (51.6%).

TABLE 18: Percent of cases that were tested for TB resistance, by year and by type of setting

	Year					Setting			Total
	2007	2008	2009	2010	2011	Public hospital	Prison hospital	Outpatient setting	
Yes	53.7	55.7	63.2	66.7	61.3	58.9	70.5	51.6	60.5
No	30.5	35.7	26.4	25.4	32.1	33.5	15.9	25.8	30.0
No records	15.9	8.7	10.3	7.9	6.6	7.6	13.6	22.6	9.5
Count	**82**	**115**	**87**	**126**	**106**	**397**	**88**	**31**	**516**
% of Total	**15.9**	**22.3**	**16.9**	**24.4**	**20.5**	**76.9**	**17.1**	**6.0**	**100.0**

Of persons who had positive result to resistance testing (n=315), three quarters (76.5%) had multi-drug resistant TB (MDR TB), 11.7% had mono-resistant strain, 10.2% had poli-resistant strain and one person was registered with extensively drug-resistant TB (XDR TB).

TABLE 19: Type of TB resistance among the people who tested positive, by year and by type of setting

Strain resistance	Year					Setting			Total	
	2007	2008	2009	2010	2011	Public hospital	Prison hospital	Outpatient	count	%
Mono	4.3	7.8	10.9	15.5	16.7	12.3	7.9	17.6	37	11.7
Poli	10.9	9.4	10.9	9.5	10.6	11.9	6.3	0.0	32	10.2
MDR	76.1	82.8	78.2	75.0	71.2	74.5	84.1	76.5	241	76.5
XDR	2.2	0	0	0	0	0.4	0	0	1	0.3
No record	6.5	0	0	0	1.5	0.9	1.6	5.9	4	1.3
Count	**46**	**64**	**55**	**84**	**66**	**235**	**63**	**17**	**N/A**	**315**
% of Total	**14.6**	**20.3**	**17.5**	**26.7**	**21.0**	**74.6**	**20.0**	**5.4**	**315**	**100.0**

HIV TESTING IN TB SETTINGS

The TB patients are a group of people who are recommended to be tested for HIV. The results show that HIV testing and counselling has good coverage in TB facilities, as almost all cases with unknown HIV status were tested for HIV at the time of the TB diagnosis, and for only 28 cases records did not contain information if the HIV testing was performed.

TABLE 20: HIV testing of TB patients in the past 12 months, by year and by type of setting

	Year					Setting			Total	
	2007	2008	2009	2010	2011	Public hospital	Prison hospital	Outpatient	count	%
Yes	18.3	17.4	15.3	20.5	19.2	20.7	5.3	25.0	136	18.2
No	8	0	0	0	0	2	0	0	10	1
Known HIV+ status	77.1	79.5	81.8	76.4	75.6	75.0	93.2	72.5	583	78.0
No record	3.8	3.1	2.9	3.1	5.1	4.2	1.5	2.5	27	3.6
Count	**131**	**161**	**137**	**161**	**156**	**575**	**132**	**40**		**747**
% of Total	**17.6**	**21.6**	**18.4**	**21.6**	**20.9**	**77.0**	**17.7**	**5.4**	**747**	**100.0**

The collaboration between the TB and HIV service was not effective. The results show that only half of the TB/HIV cases (53.3%) received the consultation of the infectious diseases specialist. The prison system had a much better indicator, as 93.4% of TB/HIV cases were seen by infectious diseases specialist as well compared to only 44.6% in the public TB hospitals.

TABLE 21: Percent of TB/HIV cases that had a recorded consultation by an infectious diseases specialist, by year and by type of setting

	Year					Setting			Total	
	2007	2008	2009	2010	2011	Public hospital	Prison hospital	Outpatient setting	count	%
Yes	55.6	48.5	50.9	51.2	61.0	44.6	93.4	54.7	491	53.3
No	34.6	42.1	34.9	39.8	27.2	43.3	5.3	26.6	331	35.9
No record	9.8	9.4	14.2	9.0	11.8	12.0	1.3	18.8	99	10.7
Count	**153**	**202**	**169**	**201**	**195**	**706**	**151**	**64**		**921**
% of Total	**16.6**	**22.0**	**18.4**	**21.8**	**21.2**	**76.7**	**16.4**	**6.9**	**921**	**100.0**

TB TREATMENT

Of the total number of 921 assessed cases, 911 persons followed the TB treatment and 9 persons refused the treatment from the very beginning after being TB diagnosed.

Of total cases, 76.7% were registered as having initiated the treatment in public hospitals and 16.4% were treated in prison hospitals, while 6.9% of cases received treatment in outpatient settings only, without being hospitalised. The biggest number of patients was treated in the units of the Phtysiopulmonology Department of Balti Clinical Municipal Hospital, where a total of 348 of patients or 37.7% of cases were hospitalised. The two facilities in Chisinau - Chisinau Clinical Municipal Phtysiopulmonology Hospital and Phtysiopneumology Institute "Chiril Draganiuc" hospitalised 323 of patients or 35.03% of cases.

TABLE 22: Distribution of TB/HIV cases by inpatient treatment facility where TB treatment was initiated

Inpatient facility	Frequency	Percent
Phtysiopneumology Institute "Chiril Draganiuc"	130	14.10
Chisinau Clinical Municipal Phtysiopulmonology Hospital	193	20.93
Vorniceni Hospital	18	1.95
Phtysiopneumology Department of Balti Clinical Municipal Hospital	348	37.74

Inpatient facility	Frequency	Percent
Phtysiopneumology Unit of Soroca Clinical Municipal Hospital	7	76
Phtysiopneumology Unit of Soroca Clinical Municipal Hospital	11	1.19
Prison no.16 Pruncul	135	14.64
Prison no. 13 Chisinau	14	1.52
Prison no. 11 Balti	2	22
Patients who received treatment in outpatient settings only	64	6.94
Total	**921**	**100**

As for the treatment regimen followed, a total of 94.8% of patients followed a standard treatment regimen and 5.2% of patients followed an individualised treatment regimen. By types of treatment, 68.8% of patients followed the treatment regimen of category I that is prescribed for new smear-positive patients; 25.5% of patients followed the treatment regimen of category II, for relapse treatment, and only 2.2% or 20 of cases followed the DOTS Plus treatment. Given that 241 patients were diagnosed with MDR-TB, there was a gap between the diagnosed TB resistant forms and the treatment regimen received. This was due among other reasons to the delay between the initiation of TB treatment and the receipt of results on resistance prevented the initiation of the MDR treatment regimens from the outset and after the receipt of results, or to the fact that the physicians did not change the treatment regimens for the patients, or the patients refused to follow the treatment, or they died.

TABLE 23: Treatment regimen prescribed at the time of treatment initiation, by year and by type of setting

	Year					Setting			Total	
	2007	2008	2009	2010	2011	Public hospital	Prison hospital	Outpatient setting	Count	%
Category I	52.6	58.9	64.1	59.8	68.8	65.1	41.3	62.3	557	61.0
Category II	36.2	37.1	32.3	32.7	25.5	28.5	51.3	36.1	299	32.7
Category IV	10.5	3.0	3.0	2.5	2.6	4.1	4.7	1.6	37	4.1
DOTS Plus	7	1.0	6	5.0	3.1	2.3	2.7	0	20	2.2
Count	**152**	**202**	**167**	**199**	**192**	**702**	**150**	**61**	**N/A**	**913**
% of Total	**16.7**	**22.1**	**18.3**	**21.8**	**21.1**	**76.9**	**16.4**	**6.7**	**913**	**100.0**

Good adherence to the inpatient treatment was documented in 71.9% of cases, while 24.2% of cases were documented as not taking their TB medicines regularly in the inpatient facilities, with lower adherence rate in the public hospitals compared to prison hospitals (67.9% versus 90.7%). In 3.9% of cases patients had no records of treatment adherence in their charts.

A total of 151 patients or 16.6% of cases changed the treatment regimen, and only 9 of them changed it due to adverse reactions. In general, only 24 patients or 2.6% of cases in the total sample had adverse reactions to the TB medicines.

A total of 447 of cases or 48.5% received TB treatment at continuation stage in outpatient settings, as most patients had either completed the treatment at the inpatient stage only or defaulted the treatment at the intensive stage while in inpatient settings or died in inpatient settings. The treatment at continuation stage was supervised by the family doctor in 42.1% of cases, by the city TB specialist in 42.8% of cases, by the district TB specialist in 11.9% of cases and by another medical worker in 3.3% of cases.

Of cases treated in outpatient settings, 64.4% had good treatment adherence and 31.8% were taking their drugs irregularly, while no records were available for 3.8% of the sample. Of note is also an increasing trend of higher adherence to treatment by years, from 60.0% in 2007 to 69.2% in 2011.

TABLE 24: Adherence to TB treatment at outpatient stage, by year and by type of setting

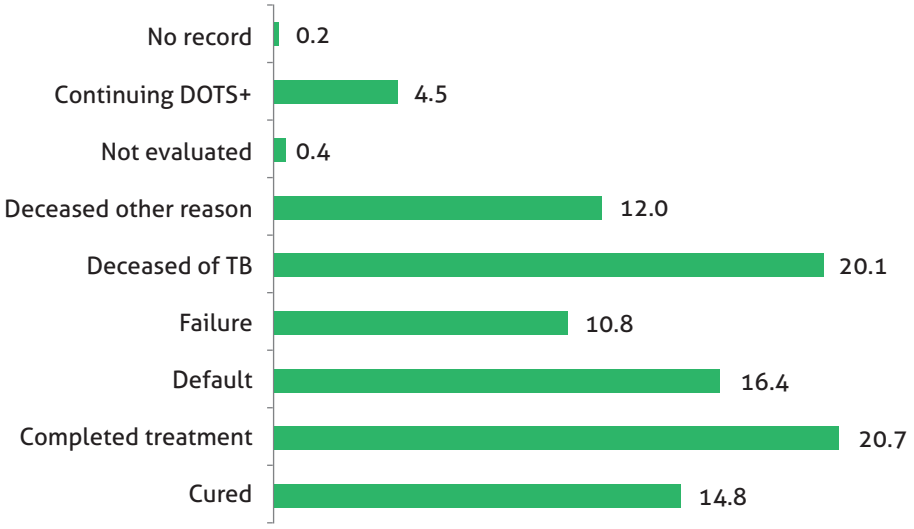
	Year					Setting			Total	
	2007	2008	2009	2010	2011	Public hospital	Prison hospital	Outpatient setting	count	%
Yes	60.0	58.6	69.4	63.8	69.2	64.0	33.3	70.0	288	64.4
No	29.2	39.4	29.4	28.7	30.8	32.5	0	28.0	142	31.8
NR	10.8	2.0	1.2	7.4	0	3.6	66.7	2.0	17	3.8
Count	**65**	**99**	**85**	**94**	**104**	**394**	**3**	**50**	**N/A**	**447**
% of Total	**14.5**	**22.1**	**19.0**	**21.0**	**23.3**	**88.1**	**7**	**11.2**	**447**	**100.0**

Another recommendation according to the national protocol is to prevent Pneumocystis Carinii Pneumonia (PCP) with co-trimoxazole during the TB treatment. Over half of cases (58.5%) did not receive it, in 16.2% of cases there were no records. In 15.6% of cases the preventive treatment was prescribed by the infectious diseases specialist and in 9.7% of cases by the TB specialist.

TREATMENT OUTCOMES

According to the results as recorded in the patient charts, only one third of cases had treatment success, of them 14.8% with cure and 20.7% with completed treatment. One in four cases ended the treatment with default or failure (16.4% default, 10.8% failure) and one third of patients died, either due to TB progression (20.1% or 184 cases) or to other causes (12.0% or 110 cases). For 0.6% of cases the treatment outcome was not recorded and 4.5% of cases continued the treatment at the time of the chart audit. There were no significant differences in treatment outcomes by year or by type of facilities where the treatment was initiated. In the subsample of cases with registered treatment default (n=141), only 38% or 48 of cases had a documented reason of the default.

FIGURE 5: TB treatment outcomes, total sample



Where possible, the data on deaths "due to other causes" were collected as recorded in the patient chart. In 16 cases, other causes were described, of them at least a part could be attributed to AIDS (bilateral pneumonia, generalized criptococcosis and generalised fungal infection, septicemia), others could be independent but could also be a consequence of TB and HIV (renal failure, cerebral oedema). Other causes of death could be attributed to hepatitis (cirrhosis) or be independent (pulmonary cancer, uterine cancer, overdose). But for 83 cases no other cause was indicated at all, meaning that it made it impossible to evaluate if they were related to HIV and TB or not.

There were no significant differences in treatment outcomes by years, but there were significant differences between the places where patients initiated the TB treatment. The worst results were registered in Chisinau and Balti TB hospitals, where the cure was the lowest - 14.4% and 17.4% with completed treatment (compared to 17.2% cured and 28.5% with completed treatment among the patients who initiated the treatment in prison hospitals and compared to 14.5% cured and 40.3% with completed treatment among the patients who were treated only in outpatient settings). The rate of deaths was also higher among the patients who initiated the TB treatment in Chisinau and Balti

TB hospitals (36.0% compared to 24.2% among those treated only in outpatient settings and 17.2% in prison hospitals). This could also be related to the different severity of cases admitted to hospitals compared to those treated only in outpatient settings.

TABLE 25: TB treatment outcomes, by year and by type of setting

	2007	2008	2009	2010	2011	Public hospital	Prison hospital	Outpatient setting	Total
Cured	22	33	30	23	28	101	26	9	136
	14.5	16.4	17.8	11.4	14.5	14.4	17.2	14.5	14.8
Completed treatment	30	34	36	51	39	122	43	25	190
	19.7	16.9	21.3	25.4	20.2	17.4	28.5	40.3	20.7
Default	21	34	34	36	24	121	19	9	149
	13.8	16.9	20.1	17.9	12.4	17.2	12.6	14.5	16.3
Failure	29	32	18	7	14	71	27	2	100
	19.1	15.9	10.7	3.5	7.3	10.1	17.9	3.2	10.9
Death due to TB progression	19	31	36	55	43	156	20	8	184
	12.5	15.4	21.3	27.4	22.3	22.2	13.2	12.9	20.1
Death due to other causes	31	35	11	16	17	97	6	7	110
	20.4	17.4	6.5	8.0	8.8	13.8	4.0	11.3	12.0
Not evaluated	0	0	0	0	4	2	2	0	4
	0	0	0	0	2.1	3	1.3	0	4
In treatment	0	2	4	13	22	33	6	2	41
	0	1.0	2.4	6.5	11.4	4.7	4.0	3.2	4.5
No record	0	0	0	0	2	0	2	0	2
	0	0	0	0	1.0	0	1.3	0	2
Count	**152**	**201**	**169**	**201**	**193**	**703**	**151**	**62**	**916**

TIME-RELATED BOTTLENECKS IN QUALITY OF CARE OF TB/HIV CASES

One of the first bottlenecks in the continuum of care for PLHIV that has long-term consequences on the timeliness of care relates to the time elapsed since the establishment of the HIV initial diagnosis until the visit to an infectious diseases specialist of the DCDH facility[5]. Only 0.7% of patients had their first visit to the infectious diseases specialist the same day with the HIV diagnosis, and a total 29.2% of patients had the HIV diagnosis established and saw a physician in the same year. However, a big part of patients had a time lag measured in years between the HIV diagnosis and the first visit to the infectious diseases specialist: 11.3% of cases between one and three years, 22.5% of cases between three and ten years, 7.1% of cases for more than ten years, while 27.9% of cases never made it to the infectious diseases specialist.

TABLE 26: Time difference between time of HIV diagnosis and first visit to the infectious diseases specialist

	Frequency	Percent
Infectious diseases specialist	6	7
Same day	13	1.4
1 day - 1 year	269	29.2
1-3 years	104	11.3
3-10 years	207	22.5
10+ years	65	7.1
Total	**664**	**72.1**
No records	**257**	**27.9**
Total	**921**	**100.0**

The situation of not being under HIV follow-up had repercussions on the timing of TB diagnosis and the clinical prognosis and treatment outcomes. In almost one fourth of cases the TB diagnosis preceded the first visit to the infectious diseases specialist (in 4.6% of cases after more than one year and in 19.3% of cases within one year after establishing the TB diagnosis). For quite a few patients the TB diagnosis was established in the same year of their first visit to the infectious diseases specialist. 18.1% of cases were late presenters, and another 15.2% of cases were seen by the infectious diseases specialist 1-3 years before the TB diagnosis. In 15.2% of cases the TB diagnosis was established 3-10 years after the establishment of the HIV treatment by an infectious diseases specialist. In 26.6% of cases patients were not seen by the infectious diseases specialist of the DCDH facility at all.

5 In Moldova, during 1987-2011 the AIDS Center was responsible for HIV diagnosis based on HIV blood test. Since 2003, the clinical HIV follow-up by an infectious disease specialist has been the responsibility of a different entity - the DCDH.

TABLE 27: Time difference between the first visit to the infectious diseases specialist and TB diagnosis

	Frequency	Percent
TB more than 1 year before HIV	42	5
TB 1 day to 1 year before HIV	178	19
TB and HIV same time	9	1
TB 1 day to 1 year after HIV	167	18
TB 1-3 years after HIV	140	15
TB 3-10 years after HIV	140	15
Total	**676**	**73**
No records	**245**	**27**
	921	**100**

If finally an HIV patient gets on the radar for TB symptoms based on screening performed by an infectious diseases specialist, precious time is lost since the first TB suspicion until confirming the TB diagnosis. On average, it took 23 days (SD 75 days) since the first TB suspicion until confirming the final TB diagnosis, and 28 days (SD 94 days) since the first TB suspicion until the initiation of the TB inpatient treatment.

The next bottleneck is the transition from the inpatient treatment stage and initiation of the outpatient treatment stage. On average, there was a delay of 11 days between the two stages with a wide range (SD 47 days).

TABLE 28: Average time necessary to evaluate and treat TB

	n	Months	Mean, days	Std. dev., days
Time between the first TB suspicion and the TB diagnosis	705	1	23	75
Time between the TB suspicion and the initiation of the TB treatment	633	1	28	94
Time between the end of the inpatient stage and the initiation of the outpatient stage	345	0	11	47
Average time of the inpatient treatment	784	4	115	120
Average time of the outpatient treatment	407	8	239	151
Average time between the initiation of the outpatient stage and the default treatment	49	6	175	171

THE ANALYSIS OF DIFFERENCES IN THE TREATMENT OUTCOMES AMONG THE GROUPS

The analysis of socio-demographic characteristics and risk factors for each group based on the TB treatment outcomes has revealed certain meaningful differences. There were more males among the default (80.7%) and deceased patients (78.6%) than among the patients with treatment success (67.5%). The average age was the highest among the patients with treatment success (44.9 years on average) compared to 36.6 years among the deceased patients. The default patients had the longest imprisonment history (51.4%), followed by the deceased patients (40.1%) and patients with treatment success (35.5%). The drug use history or the current drug use was high in all groups and seemed to not be a factor of the treatment outcome. A history of alcohol misuse was reported almost twice as often among the deceased patients (33.7%) than among the group with treatment success (18.1%).

TABLE 29: Socio-demographic characteristics and risk factors, by treatment outcomes

		Outcomes				Sig.
		Success (cure or completed treatment)	Default and failure	Death	TOTAL	
Sex	male	67.5	80.7	78.6	75.0	***
Age		45	37	37	37	
History of imprisonment		35.3	51.4	40.1	41.5	***
Alcohol misuse	Yes	18.1	32.5	33.7	27.5	***
	No	22.4	15.3	19.7	19.4	
	No record	59.5	52.2	46.6	53.0	
Drug misuse	Yes, now	58.6	65.9	66.7	63.4	***
	Yes, in the past	35.9	25.3	21.8	28.1	
	No record	5.5	8.8	11.6	8.5	

The most important HIV-related factors, for which the association with the treatment outcomes was noticed, were the value of the first CD4 count, the established HIV clinical staging and being on ARV treatment at the time of TB case notification. Among the deceased patients, who had been tested for CD4 counts (n=106), almost two thirds (64.2%) had CD4 counts below 200 cells/mm^3 compared to 41.0% among the patients with treatment success, and 39.9% among the cases with treatment default and failure. Almost half of those deceased (46.3%) did not have the clinical staging compared to those with treatment success (19.9%). Only one in five persons among the deceased patients (20.7%) had been on ARV treatment at the time of TB diagnosis compared to almost half of those who had a successful and completed treatment (47.9%).

TABLE 30: Key HIV factors related to the clinical outcomes

		Outcomes			Total	Sig.
		Treatment success or completed treatment	Treatment default and failure	Death		
First CD4 count	<200	41.0	39.9	64.2	46.9	***
	200-500	38.1	39.3	24.8	34.9	
	>500	20.9	20.8	10.9	18.2	
Clinical staging	C3	32.5	30.5	30.6	31.3	***
	Other	47.5	39.4	23.1	36.9	
	No record	19.9	30.1	46.3	31.8	
On ARV treatment at the time of diagnosis	Yes	47.9	27.7	20.7	32.9	***
	No	39.3	53.8	48.6	46.6	
	No record	12.9	18.5	30.6	20.5	

The analysis of socio-demographic characteristics and risk factors for each group based on the TB treatment outcomes has revealed certain meaningful differences. The share of males was higher among the default (80.7%) and deceased patients (78.6%) than among the patients with treatment success (67.5%). The average age was the highest among the patients with treatment success (44.9 years) compared to 36.6 years among the deceased patients. The default cases had the longest imprisonment history (51.4%), followed by the deceased patients (40.1%) and patients with treatment success (35.5%). The drug use history or the current drug use was high in all groups and seemed to not be a factor of the treatment outcomes. A history of alcohol misuse was reported almost twice as often among the deceased patients (33.7%) than among the group with treatment success (18.1%).

TABLE 31: Key TB-related factors of the clinical outcomes

		Outcomes			Total	Sig.
		Treatment success	Treatment default and failure	Death		
History of TB		26.4	45.4	43.2	37.5	***
Type	new case	73.6	55	56.5	62.5	***
	relapse	16.3	18.9	17.3	17.4	
	after default	3.7	12.4	11.2	8.7	
	after failure	6.1	12.9	11.2	9.8	
	chronic	3	8	3.7	1.6	
Resistance to TB drugs	Yes	41.1	60.4	71.3	57.7	***
	No	45.6	30.9	20.7	32.3	
	No record	13.3	8.7	7.9	10	
Inpatient adherence	Yes	87.1	51.8	72.6	71.7	***
	No	9.7	44.7	23.1	24.6	
	No record	3.2	3.5	4.3	3.7	
Outpatient adherence	Yes	78.6	35	54.7	63.4	
	No	17.7	61.5	37.7	32.5	***
	No record	3.6	3.4	7.5	4.1	

As far as the time criterion is concerned, the time elapsed between different milestones seems to have had a limited role in the treatment outcomes. The only statistically significant difference is the time elapsed since the first TB suspicion until the initiation of the TB treatment: on average 22 days for the group with treatment success compared to 31 days for deceased patients.

TABLE 32: Average time between key HIV and TB clinical events

Outcomes		Time between HIV diagnosis and initiation of ARVT	Time between TB suspicion and HIV diagnosis	Time between the first suspicion of TB and confirmation of the TB diagnosis	Time between the first TB suspicion and initiation of TB treatment	Time between the completion of the inpatient stage and initiation of the outpatient stage
Treatment success (cure or finished treatment)	N	270	238	280	237	191
	Mean	**1257**	**371**	**24**	**22**	**7**
	Std. Dev.	1437	776	62	60	32
Default and failure	N	189	135	185	171	89
	Mean	**1386**	**353**	**18**	**19**	**17**
	Std. Dev.	1,468	723	47	42	49
Death	N	162	115	207	196	40
	Mean	**1419**	**459**	**26**	**31**	**-4**
	Std. Dev.	1,548	659	109	117	68
Total	N	621	488	672	604	320
	Mean	**1338**	**386**	**23**	**24**	**8**
	Std. Dev.	1475	735	77	80	43
p		0.47	0.57	0.28	0.03	0.47

As for the deceased patients, on average 6.6 months elapsed since the first TB suspicion until the time of death, and 5.8 months or 178 days elapsed since the TB diagnosis and the initiation of the TB treatment until the time of death.

Of the deceased patients who had been followed-up by the DCDH's infectious diseases specialist (n=189), on average 757 days (2.07 years, median 589 days) elapsed since their first encounter with the infectious diseases specialist until the time of death. The difference between the time of TB diagnosis and the time of HIV diagnosis emphasises the missed opportunity to prevent the development of TB, which had fatal consequences, in HIV patients through proper screening and preventive treatment with INH.

For 322 cases the date of death was registered. Of all deceased patients (n=326), the autopsy was performed in 62.3% of cases; while in 12.9% of cases it was not performed (in 24.8% or 81 of cases there were no record whether the autopsy was carried out or not).

THE RESULTS OF THE ANALYSIS OF TB/HIV CASES OF DEATH EXTRACTED FROM THE NATIONAL MORTALITY DATABASE

A total of 336 cases were registered in the National Mortality Database (for explanations about the difference in the number of cases in the two databases, please check the Chapter on Limitations). Of the 336 cases, 75.3% were male and 24.7% were female. Most deaths occurred in hospitals (74.1%), one in five deaths happened at home (20.5%), and 5.4% of deaths occurred in other places. For the most part, the cases of death were reported as being caused by the disease (97.3%), an insignificant proportion of deaths was reported as being caused by accidents (0.9%) and for 1.8% of cases the cause was not established. In 64.3% of cases the cause of death was established by an autopsist, in 19.6% of cases by a forensic medicine specialist, in 12.5% of cases by the physician who treated the patient and in 3.6% of cases by the physician who registered the death. The cause of death was established based on autopsy in 75.6% or 254 of cases, in 15.5% of cases based on medical records, in 6.0% of cases based on earlier clinical follow-up and in 3.0% of cases based on external body examination.

According to the ICD-10 classification of diseases, it was established that the main disease which caused the death was the TB/HIV co-infection (B200) in 52.7% of cases, TB in 29.2% of cases, and HIV-related causes in 7.4% of cases. A few other cases were likely attributed to either TB or HIV, such as bacterial and unspecified pneumonia (3 cases) and encephalitis (1 case). Other death causes included liver cirrhosis (3.0%), cancer (1.5%), injuries and poisoning (8 cases), and alcohol and drug misuse (2 cases). Additional causes of death included pulmonary TB (5 cases), 10 cases of substance misuse, and injuries and causes related to psychoactive substance misuse (8 cases).

TABLE 33: Main causes of death according to the National Mortality Database managed by the NCHM

Main causes of death			
IDC-10 code	**Disease**	**count**	**%**
A10	TB	98	29.2
B200	HIV with TB	177	52.7
B20	HIV	25	7.4
C00-50	Cancer	5	1.5
E149	Diabetes	1	0.3
F102	Disorder related to the psychoactive substance misuse	1	0.3
G042	Encephalitis	1	0.3
G312	Degeneration of nervous system due to alcohol misuse	1	0.3
I10-80	Cardio-vascular and cerebro-vascular diseases	5	1.5
J 15-18	Bacterial and unspecified pneumonia	3	0.9
K746	Liver cirrhosis	10	3
R980	Unattended death	1	0.3
X 0-7 and Y 0-3	Injuries and poisoning	8	2.4
	Total	**336**	**100**
Additional causes of death			
A10	Pulmonary TB	5	
B153	Acute hepatitis	1	…
F10	Substance misuse	10	…
S 00-50, T00-60	Injuries and causes related to psychoactive substance misuse	8	…

Compared to the structure of causes of death in the National Mortality Database, where TB was considered as the primary cause of death in 81.8% of cases, either solely or combined with HIV, the SYME-TB attributed the death to TB progression in 62% of cases, while 37.4% of cases were registered as “due to other causes”.