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# Predictive factors associated to low tuberculosis treatment outcome: cross sectional study

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**Abstract**

**Background:** The standard treatment for new case of drug-susceptible tuberculosis according to WHO recommendations in the Republic of Moldova has been performed since 2000 and must achieve a treatment success rate of at least 85%. Actually the treatment success rate has increased due to excluding of MDR-TB patients from the general cohort. The major rate of patients with low outcome is represented by died and lost to follow-up cases (drop out).
**Material and methods:** A retrospective selective, descriptive study targeting social, demographic, economic and epidemiological peculiarities, case-management, radiological aspects diagnosis and microbiological characteristics of 154 patients with pulmonary tuberculosis was performed.
**Results:** It was established that the major risk factors for loss of follow-up were: low educational level, homelessness, history of detention, migration and delayed patient's direct addressing the specialized hospital services. The major risk factors for death were: low educational level, homelessness and other ways of detection (detection by civic organizations, during specialized consultations in other somatic hospitals) as a result of the unemployment and lack of health insurance.
**Conclusions:** Raising awareness among high risk patients and their families about tuberculosis, emphasizing that the diagnosis and treatment are free of charge and independent regarding their social and economical status will improve disease outcome.

**Key words**: tuberculosis, risk factors.

## Introduction

Tuberculosis represents a major global health problem, well recognized in the Republic of Moldova [1]. According to the WHO report in 2015, 10.4 million new cases were reported worldwide, of which 5,9 million (56%) were among men, 5.5 million (34%) among women and 1.0 million (10%) among children. From all new tuberculosis cases 1.2 million (11%) were people living with HIV. Two thirds of all cases were living in 6 countries: India, Indonesia, China, Nigeria, Pakistan and South Africa [2,3,4]. In the Republic of Moldova 4.211 cases were notified in 2015, 3.608 were new cases, 85% of them were tested by rapid diagnostic methods, 95% had HIV status, 90% had pulmonary tuberculosis and 64% were bacteriologically confirmed [1].

The standard treatment for new drug-susceptible tuberculosis according to WHO recommendations in the Republic of Moldova has been used since 2000 and lasts 6 months. It consists in a two phase regimen with four first-line drugs: isoniazid (H), rifampicine (R), ethambutol (E) and pyrazinamide (Z) in the intensive phase and two first-line drugs: isoniazid and rifampicine in the continuation phase [5]. It costs in average US$40 per person and must achieve at least 85% treatment success rate. In the top of causes of death worldwide tuberculosis was placed on the 5$^{th}$ place in lower-middle income countries in 2015 [6]. According to the WHO published data in 2014 in the Republic of Moldova the drug-susceptible treatment success rate in HIV-negative patients constituted 79%, in HIV-positive cohort 47% and in multidrug resistant tuberculosis (MDR-TB) cohort 53% [4]. The quality of TB control activities is demonstrated by the rate of MDR-TB cases at the regional level. Globally in 2015 there were estimated 580.000 new MDR-TB cases, but only 125.000 received DOTS-Plus regimen [4]. In 2015 in the Republic of Moldova 32 % (29%–34%) of new cases were MDR-TB and 69% (66%–72%) of retreated cases were MDR-TB [1].

The major determinants of tuberculosis treatment outcomes are socioeconomic inequalities in health [7]. Public health barriers which decrease treatment outcome are: geographic (long distance, natural barriers), economic (lack of social protection and medical insurance) and cultural barriers to health care access (stigma, poor housing and environmental conditions), malnutrition, harmful habits and substances abuse (tobacco smoking, alcohol abuse, illicit drug use), ethnic group affiliation and continuous contact with an infectious source [8,9]. In consequence, the distribution of low tuberculosis outcomes reflects the social determinants with impact on late disease diagnosis and treatment onset, poor treatment adherence and high rate of side effects [9, 10]. In comorbid groups the disease progression and low treatment outcome were determined by immune suppressive conditions: HIV-positive status [11,12,13,14], diabetes [15,16], cancer [17,18], silicosis [19], chronic respiratory diseases [20], gastrointestinal diseases, malnutrition [21], other immune suppressive causes (immune modulating drugs, immune suppressive therapy, antineoplastic drugs) [22,23,24,25]. The most relevant actions for improving the outcome in those patients must be performed in the frame of general medicine network, through the active screening and close follow-up of high risk groups [26,27]. In that subgroups the tight network between primary health care, tuberculosis specialized institutions and social services will ensure the highest treatment effectiveness [28].

There is a strong relationship between the investments in

activities for strengthening tuberculosis control programs, diagnostics, treatment and effectiveness of tuberculosis national policy. World Health Organization, International Union against Tuberculosis and Lung Diseases, and UNDP emphasized that interventions from outside the health sector, social protection and urban planning have the biggest potential to increase tuberculosis control. Those organizations recommend to pay attention and to solve social issues of tuberculosis patients [5]. Higher rate of low tuberculosis outcomes in disadvantaged groups such as in poor, comorbid, addictive groups and ethnic minorities demonstrated that inter-sector collaboration is underestimated and the community participation is unsatisfactory [29].

In the frame of supportive actions, there were established duties of the social worker to be performed within the National Tuberculosis Control Programme for assistance of tuberculosis patients, their families and other categories of population with risks: identifying their social rights, type of social assistance and services for promoting social support [30, 31]. Starting with obtaining and assistance in identifying documents for the local governmental social services, the patients will be assisted in registering in the list of the general practitioner, in establishing and maintaining a favorable partnership with authorities, municipality and non-governmental organizations. In association to the social security options, the psychosocial counseling and opportunities to get a free medical examination for tuberculosis and associated diseases must be provided [32].

According to the economical status of tuberculosis patients there are different possibilities for each patient to ensure a high quality adherence to tuberculosis treatment, that are more or less satisfied by the local municipality: financial assistance – food parcels, travel vouchers, financial support [33]. It was well recognized that only governmental-public organizations have no sufficient impact on the quality of care of tuberculosis patients and treatment outcome. So, all stakeholders must agree a strong partnership for improving disease control including health focused NGOs and other organizations oriented for serving poor communities, vulnerable subpopulations, ethnic minorities, migrant workers, etc. [32,34]. However, academic institutions, medical and public health schools, throughout the scientific programmes must provide technical support for analysis of health determinants, epidemiology and monitoring of high risk patients for establishing community-based health projects and improving tuberculosis treatment outcome.

So, the aim of the study was to assess the major determinants of low tuberculosis treatment outcome: death and loss to follow-up in the period 2014-2016. Objectives were: 1. Assessment of tuberculosis treatment outcome dynamics in pulmonary tuberculosis cases registered in Chisinau during 2011-2015. 2. Assessment of general, socio-economic and epidemiological risk factors of pulmonary tuberculosis patients with low treatment outcome (death and loss to follow-up). 3. Evaluation of case-management, diagnosis, radiological aspects and microbiological characteristics of patients with low tuberculosis treatment outcome (death and loss to follow-up). 4. Establishment of a method for the comprehensive evaluation of risk factors for low treatment outcome (death and loss to follow-up).

## Material and methods

It was performed a retrospective selective, descriptive study targeting social, demographic, economic and epidemiological peculiarities, case-management, diagnosis radiological aspects and microbiological characteristics of 154 patients with pulmonary tuberculosis registered in Chisinau city. The electronic system for monitoring and follow-up of tuberculosis cases (SIME TB) was used for the patients' selection. Data were extracted from the statistic templates F089/1-e "Declaration about patient's established diagnosis of new case/relapse of active tuberculosis and restart of the treatment and its outcomes". Inclusion criteria were: age > 18 years old, new case of pulmonary tuberculosis, signed informed consent. New case is the patient never treated for TB or has taken anti-TB drugs less than one month. The investigational schedule included demographic, social and epidemiological data: sex (male/female ratio), age (distribution in age groups), demographic characteristics (urban/rural residence), educational level, socio-economic status (employed, unemployed, retired, disabled, student), health insurance status (lack or presence of insurance), migration and detention history, presence of high risks (close contact with an infectious source, comorbidities: HIV-infection, diabetes, psychiatric diseases, immune suppressive treatment), type of infectious cluster, health care seeking behavior, way of the patient's detection. All selected patients were diagnosed and managed according to the National Clinical Protocol 123 "Tuberculosis in adults". Enrolled patients were distributed in three groups: the 1st group – control group (1) was constituted of 57 patients successfully treated (cured) in the period 01.01.2016-31.12.2016, the 2nd group – study group (2) was constituted of 22 patients lost to follow-up in the period of 01.01.2013-31.1201.2016, the 3rd group – study group (3) was constituted of 75 patients died during the treatment in the period of 01.01.2014-31.12.2016. Statistic analysis was carried out using the quantitative and qualitative research methods. Statistical survey was performed using Microsoft Excel XP soft.

## Results and discussion

According to the published data by the Moldovan National Centre for Management in Health during the period 2011-2015 it was registered an important mortality decline (with 12,3/100.000) in Chisinau: 2011 – 19,2/100.000, 2012 – 15,4/100.000, 2013 – 10,8/100.000, 2014 – 10 /100.000, 2015 – 6,9 /100.000 population. Due to the improving of the treatment quality, the rate of died MDR-TB patients is continuously decreasing: 2011 – 51.7%, 2012 – 47.2%, 2013 – 46%, 2014 – 34.6%, and 2015 – 23.2%. The treatment success rate increased (+33.7%) from 2010 to 2014 in the positive acid fast bacilli patients: 2010 – 45%, 2011 – 56.7%, 2012 – 57.5%, and in bacteriologically confirmed cases 2013 – 70.3%, 2014 – 78.7%. The treatment failure rate showed a sharp decrease

from 2010 to 2015 due to definition changes: 2010 – 26.9%, 2011 – 23.6% and 2012 – 18.2%. During this period of time all cases identified with MDR-TB and performing drug-susceptible treatment were considered therapeutic failure. Starting from 2013 patients with treatment failure were considered only patients with microbiological smear positive after 5 months of treatment. Actually the rate of treatment failure is very low: 2013 – 6% and 2014 – 2.8%. The rate of patients lost to follow-up decreased evidently: 2010 – 15.8%, 2011 – 16%, 2012 – 13.7%, 2013 – 9.3% and 2014 – 11.2%.

Clinical study established a similar sex distribution in the cured (the 1st group) and lost to follow-up group (the 2nd group), with male/female ratio=1,43/1 in the 1st group and 1/1 in the 2nd group. Comparing control group of cured patients (the 1st group) and died patients (the 3rd group) it was established a predominance of men in the 3rd group: 62 (82.6%) *vs.* 33 (58.9%) women, with male/female ratio=2,69/1. Repartition of the patients into three age groups, identified that the largest represented were 18-44 years old in all three groups. Comparing the groups it was established that the rate of young (18-44 years) patients, economical and reproductive active people predominated in the 2nd group: 19 (86.3%) *vs.* control group 32 (57.1%). Patients from the age groups >45years predominated in the 3rd group without achieving the statistical threshold. So, while distributing patients according to the biological characteristics it was argued that men and women had the same probability to be cured or to default the treatment, but men more frequently die due to tuberculosis.

Demographic distribution identified that all the enrolled patients were from the Republic of Moldova and in all groups there was a similar proportion of individuals from the urban and rural areas.

**Table 1**

**Distribution of patients by demographic data**

| Indices | Sex Age Residence | CG (1) N=56 (P %) | LFUG (2) N=22 (P %) | DG (3) N=75 (P %) |
|---|---|---|---|---|
| Sex | Men | 33 (58,9) | 11 (50,0) | 62 (82,6) ## ••• |
| | Women | 23 (41,1) | 11 (50,0) | 13 (17,3) ## ••• |
| Age groups | 18-44 years | 32 (57,1) | 19 (86,3) ** | 37 (49,3)••• |
| | 45-64 years | 13 (32,2) | 2 (9,1) | 29 (38,6) ••• |
| | > 65 years | 11 (19,6) | 1 (4,5) * | 9 (12,0) |
| Residence | urban | 35 (62,5) | 17 (77,3) | 50 (66,7) |
| | rural | 21 (37,5) | 5 (22,7) | 25 (33,3) |

**Note:** Applied statistical test: paired simple T-test, P – probability; Statistically significant differences between: LFUG (2) compared to the control group (CG) (1) * – p<0.05; ** – p<0.01; *** – p<0.001; DG (3) compared to the control group (CG) (1) # – p<0.05; ## – p<0.01; – p<0.001; LFUG (2) compared to the died group (DG) (3) •• – p<0.05; •• – p<0.01; •••– p<0.001.

While distributing patients according to the economic status, it was established that employed persons, that are contributing to the health budget by paying taxes, health insurance policy and social taxes predominated in the 1st group (control) comparing with the study groups. Disabled patients in all three groups demonstrated that most of them had no social protection and financial income. Low rate of retired patients was due to the young age of selected patients. Students were in a very limited number. Unemployed patients were the majority of all three groups, but statistically predominated in the 3rd group. Health insurance represents the major condition for accessing health care in the Republic of Moldova. Patients without insurance predominated in all study groups comparing with the control one.

**Table 2**

**Socio-economic status of patients with pulmonary tuberculosis**

| Economic indices | State | CG (1) N=56 *(P%)* | LFUG (2) N=22 *(P%)* | DG (3) N=75 *(P%)* |
|---|---|---|---|---|
| Stable | Employed | 9 (16,1) | 1 (1,3) ** | 3 (4,0) # |
| | Disabled | 1 (1,7) | 1 (1,3) | 3 (4,0) |
| | Retired | 7 (12,5) | 3 (4,0) | 6 (8,0) |
| | Student | 2 (3,6) | 1 (1,3) | 0 |
| Vulnerable | Unemployed | 37 (66,1) | 16 (72,7) | 63 (84,0) # |
| | Lack of insurance | 35 (62,5) | 19 (86,4) *** | 61 (81,3) # |

**Note:** Applied statistical test: paired simple T-test, P – probability, Statistically significant differences between: LFUG (2) compared to the control group (CG) (1) * – p<0.05; ** – p<0.01; *** – p<0.001; DG (3) compared to the control group (CG) (1) # – p<0.05; ## – p<0.01; ### – p<0.001.

Considering these results, *mass media* must inform general population about full accessibility to all related diagnostic tools and specific treatment for tuberculosis is free of charge for all Moldovan citizens regardless of their health insurance and economic status.

**Table 3**

**Distribution of patients according to the last graduate level**

| Educational level | Educational status | CG (1) N=56 *(P %)* | LFUG (2) N=22 *(P %)* | DG (3) N=75 *(P %)* |
|---|---|---|---|---|
| Illiteracy | No school attendance | 0 | 5 (22,7) ** | 4 (5,3) |
| Primary level | Primary & general incomplete school | 25 (44,6) | 7 (31,9) | 33 (44,0) |
| Secondary level | Completed general school | 11 (19,6) | 4 (18,2) | 27 (36,0)## |
| | Professional school | 15 (26,9) | 6 (27,3) | 8 (10,7) ## |
| Higher education | Superior studies | 5 (8,9) | 0 | 3 (4,0) |

**Note:** Applied statistical test: paired simple T-test, P – probability; Statistically significant differences between: LFUG (2) compared to the control group (CG) (1) * – p<0.05; ** – p<0.01; *** – p<0.001; DG (3) compared to the control group (CG) (1) # – p<0.05; ## – p<0.01; ### – p<0.001.

Assessing the educational level it was established that most of the patients from all three groups graduated primary and general incomplete school. However, the completed general studies were more frequently identified in the patients from the 3rd group comparing with the control group and gradu-

ated professional school more frequently patients from the control group comparing with the 3rd group. Higher education was established in a limited number of cases. So, awareness and information about disease signs as well as education for risk reduction of persons with low degree of education are the most important tools that must be performed by the civil society organizations. Exposed data are revealed in the table 4.

Hierarchy of risk groups according to the widest rate of patients identified that the biggest impact on the developing of active pulmonary tuberculosis in all three groups determined the patient's vulnerable economic status and living in poor conditions. Extreme poverty (homeless individuals) was identified only in the study groups. History of migration during last year and history of imprisonment statistically predominated in the 2nd group. Low rate of family TB clusters affiliated to each investigated patient in all groups was due to the low quality of epidemiological cross-examination, rather than to the lack of closed (family) contacts. Patients with associated diseases were one third of the 2nd group and one half of the 3rd group. Comorbid patients statistically predominated in the 3rd group comparing with the 2nd group and control group. Among associated diseases, HIV infection was established in 3 (5.4%) cases of the 1st group, 4 (18.2%) cases in the 2nd group and 13 (17.3%) cases in the 3rd group. Diabetes was diagnosed only in 1 (1.7%) case of the 1st group. Chronic alcoholism was diagnosed in 1 case (1.7%) in the 1st group, 4 (18.2%) cases in the 2nd group and 16 cases (21.3%) in the 3rd group. Neoplasm was diagnosed only in1 (1.3%) case in the 3rd group.

So, the distribution of patients with pulmonary tuberculosis with different low outcomes established the primary target groups in frame of which must be performed awareness, education, and improvement of health behavior of social and economically vulnerable groups, comorbid groups, migrants and homeless people.

**Table 4**

**Rate of high risk groups**

| | Risk groups | CG (1) | LFUG (2) | DG (3) |
|---|---|---|---|---|
| | | N=56 *(P %)* | N=22 *(P %)* | N=75 *(P %)* |
| Social groups | Poor living conditions | 32 (57,1) | 15 (68,1) | 52 (69,2) |
| | Homelessness | 0 | 3 (13,6) * | 16 (21,3) ### |
| | Migration | 5 (8,9) | 7 (31,8) * | 3 (4,0) ••• |
| | History of detention | 0 | 3 (13,6) * | 1 (1,3) |
| EG | Closed contact | 11 (19,6) | 1 (4,5) * | 3 (4,0) |
| MBG | Associated diseases | 8 (14,3) | 6 (27,3) | 34 (45,3) ### •• |

**Note:** SG – social group, EG-epidemiological group, MBG-medico-biological group.
Applied statistical test: paired simple T-test, P – probability;
Statistically significant differences between: LFUG (2) compared to the control group (CG) (1) * – p<0.05; ** – p<0.01; *** – p<0.001; DG (3) compared to the control group (CG) (1) # – p<0.05; ## – p<0.01; ### – p<0.001; LFUG (2) compared to the died group (DG) (3) • – p<0.05; •• – p<0.01; ••• – p<0.001.

Studying case-management it was identified that general medical staff was involved in the detection of one half of the control group and lower rate in study groups. The rate of patients detected by the passive way based on the microscopic examination of the symptomatic cases was statistically higher in control than in study groups. The rate of high risk groups investigated through active screening was low in all three groups that demonstrated low disease control in vulnerable populations. Specialized medical staff diagnosed more frequently patients from the 3rd group comparing with the 2nd during interdisciplinary consultations. Direct addressing to the hospital specialized services was used more frequently by the patients from the 2nd group comparing with control and the 3rd groups, due to the lack of health insurance and lack of direct addressing to the primary health care sector. Other ways of detection predominated in the 3rd group comparing with the control one. It was used for diagnosis of patients hospitalized in somatic clinical hospitals and for detection of high risk individuals performed by the civic organizations.

**Table 5**

**Case-management characteristics**

| Health level | Detection ways | CG (1) | LFUG (2) | DG (3) |
|---|---|---|---|---|
| | | N=56 *(P %)* | N=22 *(P %)* | N=75 *(P %)* |
| PHC | Detected by GPs-symptomatic way | 21 (37,5) | 1 (4,5) *** | 14 (18,7)# |
| | Detected by GPs -screening of HRG | 7 (12,5) | 4 (18,2) | 2 (2,7) |
| Ambulatory specialized level | Detected by SP- symptomatic way | 12 (21,5) | 2 (9,1) | 22 (29,3) •• |
| | Detected by SP-screening of HRG | 1 (1,7) | 1 (4,5) | 1 (1,3) |
| Hospital level | Direct addressing | 9 (16,1) | 11 (50,0) ### | 16 (21,3) ••• |
| Other | Other ways | 0 | 3 (13,6) | 20 (26,7) ### |

**Note:** Applied statistical test: paired simple T-test, P – probability;
PHC-primary health care, GPs-general practitioners, SP-specialist pneumophtysiologist.
Statistically significant differences between: LFUG (2) compared to the control group (CG) (1) * – p<0.05; ** – p<0.01; *** – p<0.001; DG (3) compared to the control group (CG) (1) # – p<0.05; ## – p<0.01; ### – p<0.001; LFUG (2) compared to the died group (DG) (3) • – p<0.05; •• – p<0.01; ••• – p<0.001.

Identifying the clinical radiological forms of pulmonary tuberculosis it was established that infiltrative opacities prevailed in the control group comparing with study groups. Appreciating clinical radiological forms it was established that the majority of cases had pulmonary infiltrative tuberculosis. Other radiological forms: disseminated tuberculosis prevailed in the 3rd group comparing with the 1st group and fibro-cavernous tuberculosis in the 2nd group comparing with the 1st group. Distributing patients according to the number of the affected lungs it was established that one lung was in-

volved in two thirds of the 1st and the 2nd group and both lungs were affected in two thirds of the 3rd group. Destructive forms of pulmonary tuberculosis were identified more frequently in the 3rd group comparing with the 2nd group. Extensive forms of pulmonary tuberculosis affecting 3 and more lung segments predominated in the 3rd group comparing with the 1st and with the 2nd group.

**Table 6**

**Radiological characteristics**

| Parameters | Detection ways | CG (1) N=56 (P %) | LFUG (2) N=22 (P %) | DG (3) N=75 (P %) |
|---|---|---|---|---|
| Forms of TB | PIT | 54 (96,4) | 17 (77,3) * | 57 (76,0) ## |
| | PDT | 2 (3,6) | 2 (9,1) | 13 (17,3) •• |
| | FCVT | 0 | 3 (13,6) * | 5 (6,7) |
| Localization | 1 lung | 38 (67,8) | 16 (72,7) | 19 (25,3) ) ### ••• |
| | Both lungs | 18 (32,2) | 6 (27,3) | 56 (74,7) ••• |
| Features | Lung destruction | 19 (33,9) | 5 (22,7) | 35 (46,7) • |
| | Extensive forms | 5 (22,7) | 6 (27,3) | 45 (60,1) ### ••• |

**Note:** PIT- pulmonary infiltrative tuberculosis, PDT- pulmonary disseminated tuberculosis;
FCVT- pulmonary fibro-cavernous tuberculosis;
Statistically significant differences between: LFUG (2) compared to the control group (CG) (1) * – p<0.05; ** – p<0.01; *** – p<0.001; DG (3) compared to the control group (CG) (1) # – p<0.05; ## – p<0.01; ### – p<0.001; LFUG (2) compared to the died group (DG) (3) • – p<0.05; •• – p<0.01; ••• – p<0.001.

**Table 7**

**Microbiological features**

| Characteristics | | CG (1) N=56 (P %) | LFUG (2) N=22 (P %) | DG (3) N=75 (P %) |
|---|---|---|---|---|
| Microbiological | Microscopic positive | 28 (50,0) | 5 (22,7) *** | 20 (26,7) ### ••• |
| | Culture positive | 35 (62%) | 6 (27,3) *** | 16 (21,3) ### ••• |
| | GeneXpert MTB/Rif positive | 43 (76%) | 12 (54,5) *** | 34 (45,3) ### ••• |
| GeneXpert MTB/Rif | Sensible | 43 (100%) | 8 (66,7) | 26 (76,5) |
| | Resistant | 0 | 4 (33,7) | 8 (33,5) |

**Note:** Applied statistical test: paired simple T-test, P – probability;
Statistically significant differences between: LFUG (2) compared to the control group (CG) (1) * – p<0.05;
** – p<0.01; *** – p<0.001; DG (3) compared to the control group (CG) (1) # – p<0.05; ## – p<0.01; ### – p<0.001; LFUG (2) compared to the died group (DG) (3) • – p<0.05; •• – p<0.01; ••• – p<0.001.

When assessing the laboratory features of the enrolled cured new pulmonary tuberculosis cases, it was identified that one half of patients were microscopic positive for acid-fast-bacilli, 35 (62%) were identified to have positive bacteriological results (culture on solid Lowenstein-Jensen ether liquid MGIT BACTEC). The sensibility to the rifampicine through GeneXpert MTB/Rif assay was established positive in the entire control group. Drug sensitivity testing identified mono-resistance to isoniazid in 1 patient, poli-resistance to isoniazid and streptomycine in 3 cases and monoresistance to streptomycine in 1 case. In the 2nd and the 3rd group only every fifth patient was microbiological positive, due to the short duration of hospitalization. In the 2nd group were identified 4 patients with MDR-TB and there were no patients with mono- and poliresistance. In the 3rd group were identified 2 patients with MDR-TB and there were no patients with mono- and poliresistance.

An important research outcome represents the relative risk (RR), odds ratio (OR) and attributable risk (AR) indices for identifying the priority interventions in the frame of specific subgroups for low outcome. In the table 8 were represented only risk factors and features which predominated and exposed statistical difference between lost to follow-up and control groups. It was established that major risk factors for loss to follow-up were: low level of education, patient's homeless state and history of detention, followed by the migration and direct addressing to the specialized hospital services due to the lack of referral general practitioner and other socio-economical vulnerable characteristics.

**Table 8**

**Risk factors for loss to follow-up**

| Factors | | Statistical indices RR | OR | AR% |
|---|---|---|---|---|
| Age | 18-44 years | 1,13-10,72 | 1,31-18,62 | **33%** |
| Social economical features | Lack of insurance | 1,08-1,82 | 1,05-15,04 | **27%** |
| | Low educational level | 2,83-6,51 | N/A | **100%** |
| | Homelessness | 2,67-5,82 | N/A | **100%** |
| | Migration | 1,35-5,01 | 1,34-17,51 | **72%** |
| | History of detention | 2,71-5,91 | N/A | **100%** |
| Case-management | Direct addressing to the hospital | 1,51-5,73 | 1,79-15,99 | **68%** |

**Note:** RR-relative risk, OR-odds ratio; AR-attributable risk, N/A-non available.

**Table 9**

**Risk factors for death due to the tuberculosis progression**

| Factors | | Statistical indices RR | OR | AR% |
|---|---|---|---|---|
| Demographics | Men | 1,81 (1,14-2,86) | 3,32 (1,49-7,41) | **29%** |
| Social economical | Unemployment | 1,68 (1,05-2,69) | 2,83 (1,25-6,46) | **21%** |
| | Lack of insurance | 1,58 (1,03-2,45) | 2,61 (1,18-5,78) | **23%** |
| | Low educational level | 1,81 (1,54-2,11) | N/A | **100%** |
| | Homelessness | 1,96 (1,64-2,35) | N/A | **100%** |
| Case-management | Associated diseases | 1,75 (1,34-2,29) | 4,97 (2,07-11,94) | **69%** |
| | Other way of detection | 2,02 (1,67-2,43) | N/A | **100%** |

**Note:** RR-relative risk, OR-odds ratio, AR-attributable risk, N/A-non available.

The next table reflects data assessing risk factors and features which statistically predominated in the group of died patients comparing with the control group. It was established that major risk factors for death were similar as with those that determined the drop up: low level of education, homelessness and ways of detection other than passive and active way according to the national policy, and unemployment that was associated to the social vulnerability.

## Conclusions

The standard treatment for new case of drug-susceptible tuberculosis according to WHO recommendations in the Republic of Moldova has been performed since 2000, lasts 6 months, consists in a two phase regimen and must achieve a treatment success rate of at least 85%.

The treatment success rate increased in last 5 years due to excluding of MDR-TB cohort from the assessed cohort.

Actually, the major rate of patients with low outcome is represented by died and lost to follow-up cases.

Comparing the control group consisting of cured patients and the study group that dropped out it was identified that major risk factors for loss to follow up were: low educational level, homelessness and history of detention, migration and direct addressing to the specialized hospital services.

Comparing the control group consisting of cured patients and the study group of died patients it was identified that major risk factors for death were: low educational level, homelessness and other ways of detection (detection by NGOs, specialized consultations in other somatic hospitals) as a result of the unemployment and lack of health insurance.

Raising awareness among socially vulnerable groups and their families about tuberculosis, emphasizing that the diagnosis and treatment are free of charge and independent regarding their social status will improve treatment outcome and disease control at the local level.

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