

Supplementary Table 1. Socio-demographic and clinical characteristic of multi- and extensively-drug resistant tuberculosis cases across all study sites#

Characteristics	Lithuania (N=318)			Latvia (N=223)			Romania* (N=143)			Estonia (N=61)			All sites (N=745)		
	n	Total	%	n	Total	%	n	Total	%	n	Total	%	n	Total	%
Demographic factors															
Age group (years)															
15<29	36	318	11%	32	223	14%	30	143	21%	12	61	20%	110	745	15%
30-39	70	318	22%	41	223	19%	28	143	20%	10	61	16%	149	745	20%
40-49	87	318	27%	57	223	26%	38	143	27%	13	61	21%	195	745	26%
50-59	84	318	27%	61	223	27%	35	143	24%	18	61	30%	198	745	27%
60+	41	318	13%	32	223	14%	12	143	8%	8	61	13%	93	745	12%
Gender															
Male	269	318	85%	168	223	75%	105	143	73%	46	61	75%	588	745	79%
Female	49	318	15%	55	223	25%	38	143	27%	15	61	25%	157	745	21%
Social status															
Living settings															
Urban	193	318	61%	118	223	53%	143	143	100%	49	61	80%	503	745	68%
Rural	125	318	39%	105	223	47%	0	143	0%	12	61	20%	242	745	32%
Employment															
Unemployed	278	318	87%	105	223	47%	74	142	52%	31	61	51%	488	744	65%
Retired	0	318	0%	48	223	22%	14	142	10%	10	61	16%	72	744	10%
Employed	40	318	13%	70	223	31%	54	142	38%	20	61	33%	184	744	25%
Homelessness															
Homeless	22	318	7%	24	223	11%	3	143	2%	7	61	11%	56	745	8%
Has home	296	318	93%	199	223	89%	140	143	98%	54	61	89%	689	745	92%
Substance abuse**															

Smoking															
Yes	254	318	80%	70	114	61%	108	133	81%	9	12	75%	441	577	76%
No	64	318	20%	44	114	39%	25	133	19%	3	12	25%	136	577	24%
Alcohol abuse															
Yes	289	318	91%	85	223	38%	27	137	20%	27	61	44%	428	739	58%
No	29	318	9%	138	223	62%	110	137	80%	34	61	56%	311	739	42%
Recreational drug use															
Yes	17	318	5%	13	223	6%	2	126	2%	5	60	8%	37	727	5%
No	301	318	95%	210	223	94%	124	126	98%	55	60	92%	690	727	95%
Co-morbidities															
HIV co-infection															
Yes	4	136	3%	12	195	6%	0	143	0%	4	61	7%	20	535	4%
No	132	136	97%	183	195	94%	143	143	100%	57	61	93%	515	535	96%
Hepatitis B															
Yes	1	1	100%	2	5	40%	1	15	7%	1	39	3%	5	60	8%
No	0	1	0%	3	5	60%	14	15	93%	38	39	97%	55	60	92%
Hepatitis C															
Yes	1	1	100%	12	12	100%	0	15	0%	1	39	3%	14	67	21%
No	0	1	0%	0	12	0%	15	15	100%	38	39	97%	53	67	79%
Diabetes mellitus															
Yes	4	318	1%	8	223	4%	8	143	6%	4	61	7%	24	745	3%
No	314	318	99%	215	223	96%	135	143	94%	57	61	93%	721	745	97%
Renal failure															
Yes	0	318	0%	1	223	0%	2	143	1%	0	61	0%	3	745	0%
No	318	318	100%	222	223	100%	141	143	99%	61	61	100%	742	745	100%
Chronic liver disease															
Yes	2	318	1%	5	223	2%	3	143	2%	3	61	5%	13	745	2%
No	316	318	99%	218	223	98%	140	143	98%	58	61	95%	732	745	98%

Immunocompromising condition															
Yes	0	318	0%	1	223	0%	2	143	1%	4	61	7%	7	745	1%
No	318	318	100%	222	223	100%	141	143	99%	57	61	93%	738	745	99%
Cancer															
Yes	6	318	2%	4	223	2%	2	143	1%	3	61	5%	15	745	2%
No	312	318	98%	219	223	98%	141	143	99%	58	61	95%	730	745	98%
Psychiatric illness															
Yes	3	318	1%	13	223	6%	5	143	3%	4	61	7%	25	745	3%
No	315	318	99%	210	223	94%	138	143	97%	57	61	93%	720	745	97%
Disease characteristics															
Treatment status															
New case	110	318	35%	122	223	55%	55	143	38%	52	61	85%	339	745	46%
Re-treatment case	208	318	65%	101	223	45%	88	143	62%	9	61	15%	406	745	54%
Localization															
Pulmonary	305	318	96%	212	223	95%	141	143	99%	55	61	90%	713	745	96%
Pulmonary with extrapulmonary involvement	13	318	4%	11	223	5%	2	143	1%	6	61	10%	32	745	4%
Drug resistance pattern															
MDR***	195	315	62%	97	223	43%	71	116	61%	38	58	66%	401	712	56%
MDR + FQres	22	315	7%	5	223	2%	5	116	4%	11	58	19%	43	712	6%
MDR + INJres	52	315	17%	95	223	43%	32	116	28%	8	58	14%	187	712	26%
XDR	46	315	15%	26	223	12%	8	116	7%	1	58	2%	81	712	11%
Presence of cavities															
Yes	172	318	54%	147	219	67%	105	142	74%	37	61	61%	461	740	62%
No	146	318	46%	72	219	33%	37	142	26%	24	61	39%	279	740	38%

episode															
fully adherent	n.d.			44	175	25%	62	138	45%	42	51	82%	148	364	41%
short interruptions (1-6 days)	n.d.			67	175	38%	44	138	32%	1	51	2%	112	364	31%
long interruptions (7 days – 2 months)	n.d.			64	175	37%	32	138	23%	8	51	16%	104	364	29%
Presence of unsuccessful treatment outcomes at any treatment cycle															
Yes	181	318	57%	77	211	36%	64	138	46%	12	49	24%	334	716	47%
No	137	318	43%	134	211	64%	74	138	54%	37	49	76%	382	716	53%

#the detailed per-site analysis is provided for a total number of patients recruited into the study; however for 8 patients no confirmed survival data were available and therefor only 737 patients were included into survival analysis.

*Bukharest city only

**Alcohol excess and recreational drug use were determined by physicians and reported as stated in patients' case histories according to nationally accepted breakdown categorization

***MDR – multi-drug resistance, no additional resistance to fluoroquinolones or second-line injectable agents; XDR-extensive drug-resistance; INJres - resistance to second-line injectable agents; FQres – resistance to fluoroquinolones

n.d. – no data

Supplementary Table 2. Treatment received and mortality rates across the total sample (n=689)

		Total		Mortality				
		n	col.- %	Person-years	Deaths	rate	95% CI	
Anti-TB treatment								
Injectables	yes	514	70%	1427	118	8.27	6.90	9.90
	no	175	30%	490	75	15.29	12.19	19.18
Amikacin	yes	57	8%	166	14	8.43	4.99	14.23
	no	632	92%	1752	179	10.22	8.83	11.83
Kanamycin	yes	326	44%	921	68	7.39	5.82	9.37
	no	363	56%	997	125	12.53	10.52	14.94
Capreomycin	yes	228	31%	613	52	8.48	6.46	11.13
	no	461	69%	1305	141	10.81	9.16	12.75
Fluoroquinolones	yes	641	86%	1821	161	8.84	7.58	10.32
	no	48	14%	97	32	33.07#	23.39	46.77
Ofloxacin	yes	549	74%	398	62	8.62	7.26	10.23
	no	140	26%	1520	131	15.58	12.15	19.18
Moxifloxacin	yes	110	15%	344	24	6.99	4.68	10.42
	no	579	85%	1575	169	10.73	9.23	12.48
Levofloxacin	yes	9	1%	26	0	0.00	n.a.	n.a.
	no	680	99%	1892	193	10.20	8.86	11.75
Ciprofloxacin	yes	103	14%	303	28	9.24	6.38	13.38
	no	586	86%	1615	165	10.22	8.77	11.90
Prothionamid/ Ethionamid	yes	600	81%	1673	156	9.32	7.97	10.91
	no	89	19%	245	37	15.12	10.96	20.87
Cycloserine	yes	574	78%	1648	147	8.92	7.59	10.49
	no	115	22%	270	46	17.02	12.75	22.72
PAS	yes	396	54%	1113	102	9.17	7.55	11.13
	no	293	46%	805	91	11.30	9.20	13.88
Amoxicillin/clavulanate	yes	113	15%	331	29	8.76	6.09	12.61
	no	576	85%	1587	164	10.33	8.87	12.04
Linezolid	yes	8	1%	31	0	0.00	n.a.	n.a.
	no	681	99%	1887	193	10.23	8.88	11.78
	yes	18	2%	57	5	8.77	3.65	21.06
	no	671	98%	1861	531	10.10	8.76	11.66
Five most frequent combinations (all drugs, FQ and INJ grouped):								
INJ+FQ+Pt/Eth+PAS+CS		180	27%	502	44	8.76	6.52	11.77
INJ+FQ+Pt/Eth+CS		134	20%	351	25	7.12	4.81	10.53
INJ+FQ+Pt/Eth+PAS+ CS + AMOX		67	10%	188	16	8.51	5.21	13.89
FQ+Pt/Eth+ CS		55	8%	180	17	9.47	5.89	15.23
FQ+Pt/Eth+ PAS+ CS		33	5%	86	12	13.94	7.92	24.55

SLD-second-line drugs, INJ – second-line injectable agents; FQ – fluoroquinolones; PT/ETH - prothionamide/ethionamide, PAS - para-aminosalicylic acid, CS - cycloserine, AMOX – amoxicillin/clavulanate

highest mortality rates >20