REGIONAL DIFFERENCES IN THE BURDEN OF MDR-TB AND XDR-TB IN KAZAKHSTAN BETWEEN 2013 AND 2022

Supplementary file

Supplementary Table S1. Age-standardized DALY rate of DR-TB (MDR+XDR) per 100,000 by region and year, administrative units of each year.

• The DALY rate decreased in all regions; national rate fell from 97.0 to 27.8 per 100 000 (−71%)
• Highest in 2013: Atyrau (219.3), Mangystau (136.1), North Kazakhstan (121.2). Highest in 2022: West Kazakhstan (69.5), Kyzylorda (62.5), North Kazakhstan (43.9).
• Trajectories were not monotonic (e.g., Zhambyl and Kyzylorda in 2019–2020, West Kazakhstan in 2022).

Darker colour = higher burden.

Region	2013*	2014*	2015*	2016*	2017*	2018	2019	2020	2021	2022	Change 2013–2022, %
Akmola	76.4	64.0	46.4	61.7	32.2	50.2	35.5	74.0	50.9	33.3	−56
Aktobe	110.4	131.4	74.3	88.3	57.1	41.0	57.1	36.2	33.8	13.1	−88
Almaty region	75.7	60.8	68.0	62.5	41.7	43.2	31.8	32.4	26.7	17.9	*see S2*
Atyrau	219.3	163.6	151.9	147.8	66.5	43.6	64.9	71.0	62.9	37.6	−83
East Kazakhstan	106.7	90.6	89.0	81.7	68.7	40.3	43.7	55.6	41.9	37.4	*see S2*
Almaty city	67.7	59.7	57.5	43.1	33.7	33.9	24.2	19.1	24.0	16.9	−75
Astana city	80.5	68.6	77.9	54.8	25.3	64.3	30.5	34.6	43.5	25.6	−68
Zhambyl	96.0	100.7	63.7	60.9	38.9	34.1	59.3	78.0	23.5	30.8	−68
West Kazakhstan	110.5	118.2	95.6	66.6	63.8	30.4	30.3	25.3	30.4	69.5	−37
Karaganda	92.0	83.4	64.2	44.5	28.9	34.1	34.5	39.7	19.0	26.2	*see S2*
Kostanay	99.0	101.0	106.4	90.5	52.6	65.8	56.2	47.5	49.6	41.2	−58
Kyzylorda	107.7	99.7	84.0	97.0	56.3	46.0	80.7	84.2	52.7	62.5	−42
Mangystau	136.1	84.7	80.6	68.1	53.3	56.3	41.7	43.6	25.1	29.1	−79
Pavlodar	117.0	117.7	97.5	87.4	71.6	24.8	36.4	25.9	31.4	21.3	−82
North Kazakhstan	121.2	137.4	62.1	116.7	55.9	40.1	45.5	53.6	36.0	43.9	−64
South Kazakhstan	85.2	45.1	61.3	47.8	33.8	–	–	–	–	–	–
Turkistan	–	–	–	–	–	31.5	18.7	27.3	27.7	16.9	–
Shymkent city	–	–	–	–	–	30.2	24.0	24.8	28.9	23.2	–
Abai	–	–	–	–	–	–	–	–	–	20.0	–
Zhetysu	–	–	–	–	–	–	–	–	–	11.2	–
Ulytau	–	–	–	–	–	–	–	–	–	9.5	–
Kazakhstan	**97.0**	**83.1**	**74.1**	**67.5**	**44.9**	**41.1**	**40.7**	**42.5**	**32.8**	**27.8**	**−71**

** TB deaths estimated for 2013–2017; 2016 corrected to full year. South Kazakhstan (incl. Shymkent) 2013–2017; Turkistan and Shymkent from 2018; Abai, Zhetysu, Ulytau in 2022 (East Kazakhstan, Almaty region and Karaganda include them until 2021). "–" unit did not exist.*

Supplementary Table S2. Age-standardized DALY, YLL and YLD rates of DR-TB per 100,000 by region and year, constant 2013 boundaries (16 regions).

• Comparable series for all 10 years: South Kazakhstan = Turkistan + Shymkent; East Kazakhstan incl. Abai; Almaty region incl. Zhetysu; Karaganda incl. Ulytau.
• DALY decreased in all 16 regions, from −37% (West Kazakhstan) and −42% (Kyzylorda) to −83% (Atyrau) and −88% (Aktobe); the decline was driven by YLL.
• YLD decreased more uniformly (−17% Kyzylorda to −65% North Kazakhstan).

A. DALY, age-standardized per 100 000.

Region	2013*	2014*	2015*	2016*	2017*	2018	2019	2020	2021	2022	Change, %	Pattern
Akmola	76.4	64.0	46.4	61.7	32.2	50.2	35.5	74.0	50.9	33.3	−56	Fluctuating; temporary peak in 2020 (74.0)
Aktobe	110.4	131.4	74.3	88.3	57.1	41.0	57.1	36.2	33.8	13.1	−88	Steady decline after 2014; no TB deaths in 2022
Almaty region (2013 boundaries)	75.7	60.8	68.0	62.5	41.7	43.2	31.8	32.4	26.7	15.9	−79	Steady decline
Atyrau	219.3	163.6	151.9	147.8	66.5	43.6	64.9	71.0	62.9	37.6	−83	Highest in 2013; sharp fall 2016–2018; small rise 2019–2020
East Kazakhstan (2013 boundaries)	106.7	90.6	89.0	81.7	68.7	40.3	43.7	55.6	41.9	29.9	−72	Decline; small rise in 2020
Almaty city	67.7	59.7	57.5	43.1	33.7	33.9	24.2	19.1	24.0	16.9	−75	Steady decline
Astana city	80.5	68.6	77.9	54.8	25.3	64.3	30.5	34.6	43.5	25.6	−68	Fluctuating; peak in 2018 (64.3)
Zhambyl	96.0	100.7	63.7	60.9	38.9	34.1	59.3	78.0	23.5	30.8	−68	Temporary rise 2019–2020 (78.0), then decline
West Kazakhstan	110.5	118.2	95.6	66.6	63.8	30.4	30.3	25.3	30.4	69.5	−37	Low in 2018–2021; sharp rise in 2022 (YLL)
Karaganda (2013 boundaries)	92.0	83.4	64.2	44.5	28.9	34.1	34.5	39.7	19.0	23.6	−74	Steady decline
Kostanay	99.0	101.0	106.4	90.5	52.6	65.8	56.2	47.5	49.6	41.2	−58	Slow decline; above national level throughout
Kyzylorda	107.7	99.7	84.0	97.0	56.3	46.0	80.7	84.2	52.7	62.5	−42	Peak 2019–2020 (84.2); among highest in 2022
Mangystau	136.1	84.7	80.6	68.1	53.3	56.3	41.7	43.6	25.1	29.1	−79	Steady decline
Pavlodar	117.0	117.7	97.5	87.4	71.6	24.8	36.4	25.9	31.4	21.3	−82	Sharp fall in 2018; low thereafter
North Kazakhstan	121.2	137.4	62.1	116.7	55.9	40.1	45.5	53.6	36.0	43.9	−64	Fluctuating; above national level throughout
South Kazakhstan (2013 boundaries)	85.2	45.1	61.3	47.8	33.8	31.2	20.7	26.2	28.2	19.3	−77	Decline; below national level throughout
Kazakhstan	**97.0**	**83.1**	**74.1**	**67.5**	**44.9**	**41.1**	**40.7**	**42.5**	**32.8**	**27.8**	**−71**	**Decline −71%; small rise in 2020**

B. YLL, age-standardized per 100 000.

Region	2013*	2014*	2015*	2016*	2017*	2018	2019	2020	2021	2022	Change, %
Akmola	55.8	46.0	30.8	42.5	13.8	31.8	18.9	62.6	41.3	22.6	−59
Aktobe	85.3	109.0	50.5	64.1	36.0	21.3	38.4	26.7	21.3	0.0	−100
Almaty region (2013 boundaries)	60.7	45.4	52.4	46.7	28.4	30.4	20.6	24.0	18.0	7.7	−87
Atyrau	176.6	121.3	112.0	114.4	34.8	12.0	40.8	51.4	41.9	17.2	−90
East Kazakhstan (2013 boundaries)	87.0	72.2	70.5	65.2	50.7	24.0	28.2	45.3	29.7	17.9	−79
Almaty city	55.6	47.6	47.5	34.4	24.1	23.8	15.8	13.1	18.0	10.4	−81
Astana city	59.5	48.7	58.3	33.3	8.9	49.2	17.7	23.4	30.7	15.3	−74
Zhambyl	71.3	84.7	47.5	44.1	23.5	19.8	47.0	67.9	13.0	21.0	−71
West Kazakhstan	82.2	89.0	67.6	43.3	43.4	7.3	7.1	9.7	13.2	54.4	−34
Karaganda (2013 boundaries)	75.3	65.3	47.6	30.5	15.1	22.1	23.2	31.4	11.3	15.6	−79

Kostanay	74.3	78.2	84.3	70.1	33.0	48.7	38.4	35.2	34.9	27.2	−63
Kyzylorda	78.7	67.2	57.1	71.3	29.6	20.0	53.5	66.2	34.2	38.3	−51
Mangystau	111.1	57.3	55.5	46.7	32.3	36.9	25.7	27.9	11.2	17.0	−85
Pavlodar	94.1	97.7	76.5	66.9	52.7	9.1	21.4	12.5	18.8	8.2	−91
North Kazakhstan	97.7	116.9	40.8	97.2	38.4	23.7	30.8	43.9	27.6	35.7	−63
South Kazakhstan (2013 boundaries)	72.4	32.4	48.7	36.4	23.3	19.6	8.6	17.6	19.9	10.8	−85
Kazakhstan	**77.2**	**64.0**	**55.9**	**50.3**	**28.8**	**25.6**	**26.1**	**32.0**	**22.1**	**17.0**	**−78**

C. YLD, age-standardized per 100 000.

Region	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	Change, %
Akmola	20.6	18.0	15.6	19.2	18.4	18.4	16.6	11.4	9.6	10.7	−48
Aktobe	25.1	22.4	23.8	24.2	21.1	19.7	18.8	9.5	12.5	13.1	−48
Almaty region (2013 boundaries)	15.0	15.4	15.7	15.8	13.4	12.8	11.1	8.4	8.7	8.2	−45
Atyrau	42.7	42.4	39.9	33.4	31.7	31.6	24.1	19.6	21.0	20.4	−52
East Kazakhstan (2013 boundaries)	19.6	18.4	18.5	16.4	18.0	16.3	15.6	10.3	12.2	12.0	−39
Almaty city	12.1	12.1	10.0	8.7	9.5	10.1	8.4	6.0	6.0	6.5	−46
Astana city	21.0	19.9	19.6	21.4	16.4	15.1	12.8	11.2	12.8	10.3	−51
Zhambyl	24.7	16.0	16.2	16.8	15.5	14.3	12.3	10.1	10.5	9.8	−60
West Kazakhstan	28.3	29.2	28.1	23.3	20.5	23.1	23.3	15.6	17.2	15.1	−47
Karaganda (2013 boundaries)	16.8	18.2	16.6	14.0	13.8	12.1	11.3	8.3	7.7	8.0	−52
Kostanay	24.6	22.8	22.1	20.4	19.6	17.1	17.8	12.2	14.7	14.1	−43
Kyzylorda	29.0	32.5	26.9	25.7	26.7	26.0	27.2	18.0	18.4	24.2	−17
Mangystau	24.9	27.3	25.1	21.4	21.0	19.4	16.0	15.7	14.0	12.1	−52
Pavlodar	22.9	20.1	21.0	20.6	18.8	15.7	15.1	13.4	12.6	13.1	−43
North Kazakhstan	23.5	20.4	21.2	19.6	17.6	16.4	14.7	9.8	8.3	8.2	−65
South Kazakhstan (2013 boundaries)	12.7	12.7	12.6	11.3	10.5	11.6	12.1	8.6	8.3	8.4	−34
Kazakhstan	**19.9**	**19.0**	**18.2**	**17.1**	**16.1**	**15.5**	**14.6**	**10.5**	**10.7**	**10.8**	**−45**

** TB deaths estimated for 2013–2017; 2016 corrected to full year.*

Supplementary Table S3. DR-TB burden by HIV status, Kazakhstan, 2013–2022.

• The share of HIV-positive patients increased from 4.2% (2013) to 6.1% (2022).
• HIV-positive patients accounted for a larger share of TB deaths (6.3–22.0%) and DALYs (6.6–19.1%) than of cases.

Year	HIV+ cases	% of all cases	HIV+ TB deaths	% of TB deaths	HIV+ DALY	% of DALY
2013*	304	4.2	41.1	13.8	2,448	13.3
2014*	306	4.4	33.0	12.9	1,929	12.1
2015*	277	4.1	33.6	14.6	1,976	13.8
2016*	299	4.7	35.7	16.8	2,051	15.4
2017*	332	5.6	27.9	22.0	1,685	19.1
2018	276	4.9	7.0	6.3	523	6.6
2019	329	5.9	8.0	6.6	647	8.1
2020	248	6.2	13.0	8.7	773	8.9
2021	252	6.0	11.0	9.6	661	9.8
2022	268	6.1	10.0	11.9	692	12.0

** TB deaths estimated for 2013–2017. HIV-positive: HIV risk factor, positive HIV test (code 113) or ART recorded; patients without a test result classified as HIV-negative.*

Supplementary Table S4. Socio-economic and health-system indicators by region (Bureau of National Statistics), 2013 and 2022.

• Per capita income varied about 3-fold between regions (highest in Atyrau); the number of social assistance recipients increased sharply after the 2018 reform of the programme; physician density differed up to 3.7-fold.

Region (2013 boundaries)	Income per capita, thousand KZT (2013)	Income per capita, thousand KZT (2022)	Social assistance recipients per 1 000 (2013)	Social assistance recipients per 1 000 (2022)	Physicians per 10 000 (2013)	Physicians per 10 000 (2022)
Akmola	47.3	151.3	2.0	16.4	30.7	24.0
Aktobe	55.1	142.5	0.4	32.6	47.1	49.4
Almaty region	43.4	121.5	2.6	48.8	22.7	24.4
Atyrau	110.2	291.9	5.1	10.4	33.5	30.1
East Kazakhstan	49.8	163.5	6.5	36.1	41.6	43.4
Almaty city	95.1	238.5	0.6	12.9	71.3	65.9
Astana city	92.6	238.7	1.2	16.4	84.7	76.7
Zhambyl	36.5	113.0	6.6	41.9	30.5	29.0
West Kazakhstan	57.0	151.9	7.1	25.4	35.6	32.8
Karaganda	59.3	177.7	4.7	11.9	40.1	46.4
Kostanay	48.0	156.1	4.9	26.0	26.1	29.4
Kyzylorda	46.5	120.9	2.9	84.6	36.2	35.1
Mangystau	86.3	200.2	6.0	30.1	33.2	33.0
Pavlodar	59.0	181.4	1.9	29.5	41.5	39.7
North Kazakhstan	47.3	156.4	5.4	17.6	29.8	31.7
South Kazakhstan	33.8	94.6	2.9	90.1	31.0	35.2

Income: per capita nominal money income (BNS 641101); social assistance: recipients of targeted social assistance (BNS 663101) per 1 000 population; physicians: physicians of all specialties at year end (BNS 631501) per 10 000 population. All 10 years were used in the analysis. Values for merged units are population-weighted (income) or summed (counts).

Supplementary Table S5. Spearman rank correlation between regional DR-TB burden (age-standardized rates) and indicators, 2013–2022.

• Social assistance was positively correlated with prevalence (ρ = 0.28, p < 0.001); physician density was negatively correlated with DALY (ρ = −0.25, p = 0.002) and TB mortality; both associations persisted for the actual administrative units.

A. Main analysis: 16 regions in constant 2013 boundaries, ranks within year pooled over 2013–2022 (n = 160).

Outcome	Income ρ	p	Social assistance ρ	p	Physicians ρ	p
DALY	0.06	0.449	0.19	0.017	−0.25	0.002
YLL	0.03	0.668	0.13	0.105	−0.20	0.010
YLD	0.21	0.009	0.27	<0.001	−0.16	0.047
Prevalence	0.20	0.011	0.28	<0.001	−0.17	0.035
TB mortality	−0.01	0.935	0.13	0.103	−0.20	0.010

B. Sensitivity analysis: actual administrative units of each year, percentile ranks within year (n = 168).

Outcome	Income ρ	p	Social assistance ρ	p	Physicians ρ	p
DALY	0.12	0.109	0.13	0.102	−0.19	0.014
YLL	0.09	0.262	0.08	0.314	−0.15	0.055
YLD	0.25	0.001	0.21	0.008	−0.12	0.115
Prevalence	0.24	0.002	0.22	0.004	−0.14	0.069
TB mortality	0.04	0.569	0.09	0.264	−0.16	0.036

C. Correlation with the DALY rate in each year, 16 regions (n = 16).

Year	Income ρ	p	Social assistance ρ	p	Physicians ρ	p
2013	0.27	0.311	0.45	0.078	−0.03	0.914
2014	0.17	0.520	0.40	0.128	−0.22	0.412
2015	0.27	0.305	0.41	0.116	−0.16	0.557
2016	0.01	0.966	0.42	0.107	−0.45	0.083
2017	0.10	0.721	0.31	0.240	−0.13	0.625
2018	0.14	0.602	−0.14	0.594	−0.21	0.444
2019	−0.17	0.535	0.22	0.418	−0.23	0.387
2020	−0.25	0.350	0.09	0.729	−0.39	0.137
2021	0.07	0.787	−0.13	0.633	−0.19	0.471
2022	−0.02	0.940	−0.14	0.594	−0.45	0.083

Supplementary Table S6. Linear mixed models: % change in age-standardized rate per 1 SD increase in each indicator (95% CI).

• Main analysis: social assistance was associated with higher prevalence (5.7 (2.9; 8.7)%) and YLD; physician density with lower DALY (−11.6 (−20.8; −1.4)%), YLL and TB mortality; income with none of the outcomes.

• Actual administrative units: the association of social assistance with prevalence persisted (5.0 (1.6; 8.5)%); the association of physician density with DALY was in the same direction but not significant (−5.7 (−17.3; 7.6)%).

• Model: ln(rate + 1) = income + social assistance + physicians (z-scores, entered together) + year fixed effects + random intercept for region.

A. Main analysis: 16 regions in constant 2013 boundaries (160 region-years).

Outcome	Income: % (95% CI)	p	Social assistance: % (95% CI)	p	Physicians: % (95% CI)	p
DALY	6.1 (−9.0; 23.7)	0.447	3.2 (−4.4; 11.4)	0.420	−11.6 (−20.8; −1.4)	0.027
YLL	10.8 (−6.7; 31.5)	0.241	−0.1 (−12.1; 13.5)	0.985	−13.7 (−23.3; −2.8)	0.015
YLD	−3.1 (−9.8; 4.1)	0.391	5.4 (2.6; 8.3)	<0.001	−5.5 (−12.4; 1.9)	0.139
Prevalence	−3.0 (−9.8; 4.4)	0.421	5.7 (2.9; 8.7)	<0.001	−6.5 (−13.5; 1.0)	0.087
TB mortality	3.2 (−4.5; 11.6)	0.429	0.4 (−3.9; 5.0)	0.848	−5.6 (−10.2; −0.6)	0.028

B. Sensitivity analysis: actual administrative units of each year (168 region-years).

Outcome	Income: % (95% CI)	p	Social assistance: % (95% CI)	p	Physicians: % (95% CI)	p
DALY	1.4 (−13.9; 19.3)	0.868	−0.1 (−8.6; 9.1)	0.975	−5.7 (−17.3; 7.6)	0.383
YLL	−1.9 (−23.7; 26.2)	0.882	−6.2 (−19.5; 9.4)	0.417	−4.2 (−20.9; 16.0)	0.659
YLD	0.2 (−6.6; 7.5)	0.955	4.7 (1.4; 8.2)	0.005	−4.5 (−11.2; 2.8)	0.223
Prevalence	0.5 (−6.5; 7.9)	0.895	5.0 (1.6; 8.5)	0.004	−5.5 (−12.3; 1.9)	0.143
TB mortality	2.0 (−5.4; 9.9)	0.603	−1.7 (−6.2; 3.0)	0.465	−4.2 (−9.0; 0.8)	0.098

SD (main analysis): income 47.9 thousand KZT; social assistance 40.0 recipients per 1 000; physicians 16.5 per 10 000. Year fixed effects account for income inflation and the 2018 reform of targeted social assistance (≈25-fold increase in recipients); the association of social assistance with prevalence was not statistically significant when 2013–2017 and 2018–2022 were analyzed separately.

Supplementary Table S7. Sensitivity analyses: national DALY and YLD of DR-TB, Kazakhstan.

- *The decline in DALYs between 2013 and 2022 was 65–76% across scenarios (main estimate 69%).*
- *Varying L (0.75–2.0 years) changed YLD levels but not the trend.*

A. Proportion of TB deaths for 2013–2017 (year-specific 2018–2022 proportions) and 2016 correction (min–max).

Year	DALY, main	DALY, minimum	DALY, maximum
2013	18,343	16,625	23,968
2014	15,889	14,477	20,345
2015	14,275	12,964	18,111
2016	13,288	11,881	17,455
2017	8,804	8,083	10,858
2018	7,952	7,952	7,952
2019	8,019	8,019	8,019
2020	8,689	8,689	8,689
2021	6,773	6,773	6,773
2022	5,775	5,775	5,775

2018–2022: observed TB deaths, no variation.

B. Duration of disease L.

Year	YLD, main (L = 1.5 MDR; 2.0 XDR)	YLD, L = 0.75	YLD, L = 2.0
2013	3,720	1,830	4,879
2014	3,597	1,766	4,710
2015	3,476	1,695	4,521
2016	3,294	1,599	4,264
2017	3,105	1,503	4,009
2018	3,003	1,434	3,824
2019	2,858	1,400	3,734
2020	2,051	1,010	2,693
2021	2,135	1,061	2,828
2022	2,213	1,106	2,949