

Cancer trends in Central Asia from 1990 to 2021: Analysis of the global burden of disease study

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ABSTRACT

Background: Central Asia is known to face various ecological challenges that constitute major risk factors for cancer. This study explored the cancer burden in Central Asia, where the estimates are among the highest worldwide.

Methods: Extracting data from the latest global burden of disease study (GBD 2021), the authors investigated the disability-adjusted life years (DALYs), deaths, and incidence of various cancer groups in Central Asian countries from 1990-2021. We conducted descriptive analyses of cancer statistics and calculated the average annual percent change (AAPC) to analyze the temporal patterns for individual country estimates.

Results: Over the study period, DALYs decreased and were primarily driven by premature deaths, with pronounced estimates in male subjects. While DALYs, deaths, and incidence figures were somewhat comparable for most countries, Kazakhstan had exceptionally high estimates during the 1990s. However, over the following decades, the country revealed the highest decrease for all the metrics, measured by the AAPCs for incidence -1.32% (95% uncertainty interval [UI]: -1.44% to -1.19%); deaths -2.28% (95% UI: -2.51% to -2.05%); DALYs -2.50% (95% UI: -2.74% to -2.24%). Across the region, the leading cancer sites were tracheal, bronchus, and lung, stomach, colon and rectum and esophageal cancers, in both sexes combined. Sex-specific cancer estimates showed slight variations, with a notable burden observed in females.

Conclusion: This study revealed an overall decrease in the cancer burden between 1990 and 2021. However, the temporal patterns of the risk factors remain a concern. Our findings highlight the importance of preventive measures and early diagnosis. Additionally, when interpreting GBD 2021 findings, future studies should consider the potential impact of salmon bias, where selective migration affects the modelled estimates.

Keywords: cancer, disability-adjusted life years, incidence, mortality, deaths, DALY, Central Asia, GBD 2021

INTRODUCTION

Cancer remains among the leading causes of mortality, with a substantially heterogeneous distribution of associated costs worldwide [1, 2]. The existing literature suggests that global estimates are projected to increase to 35 million cancer cases by 2050 [1], which is primarily attributed to global demographic changes. This implies that the contribution of cancer to global mortality indices may outweigh the current dominance of cardiovascular diseases in the future [3]. Such an increase will presumably bring socioeconomic challenges [2], requiring further improvements in prevention and control [4].

Historically, Asia has been associated with the highest burden of cancer [5], accounting for half of global estimates [1]. A recent study in [6] revealed that the number of newly identified cases in the region has doubled over the past three decades. This increase is also relevant for both cancer-related deaths and disability-adjusted life years (DALYs) and is common in most Asian countries [6]. Rather interesting, unlike

these temporal patterns for burden metrics, the distribution of cancer types and underlying risk factors varied across the region. This suggests that a country-specific population, environmental characteristics, dietary habits, and lifestyle are an explanation for the geographical variations in cancer profiles [5].

Central Asia consists of five countries that were once part of the Soviet Union (SU) [7]. These countries shared a common culture, lifestyle, and healthcare system for a long time. However, since SU collapsed in 1991, their socioeconomic systems have undergone significant changes [8]. The region itself is associated with enormous environmental challenges related to nuclear weapons testing and spacecraft launch site activities, as well as ecological issues related to drying of the Aral Sea, land degradation, and chronic pesticide exposure, have all associated with the cancer risk factors [9-12]. Taken together, these findings make Central Asia a subject of particular interest that underscores the need for further epidemiological research in this region.

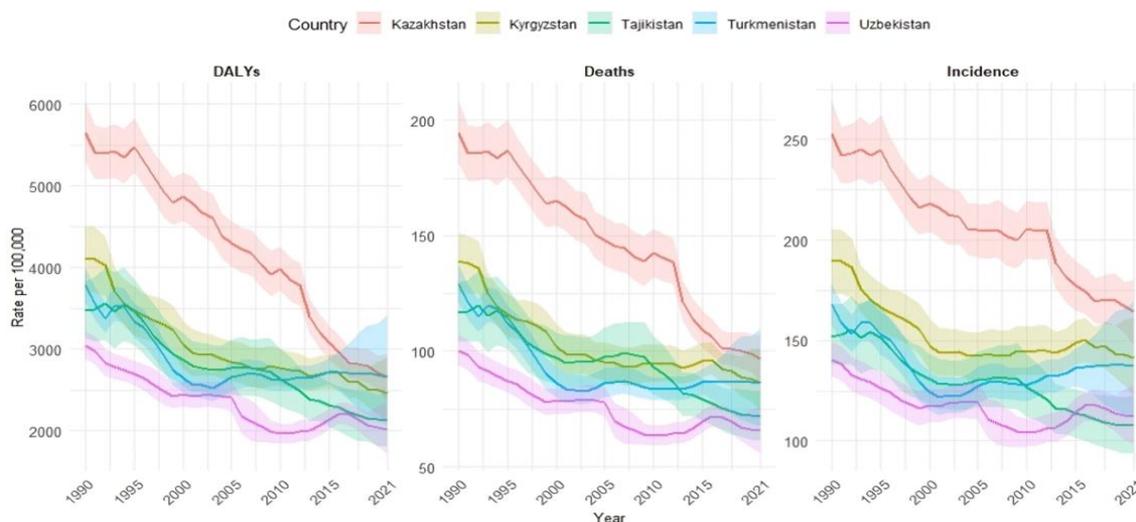


Figure 1. Overall trends in DALYs, deaths, and mortality rates for total cancers in Central Asia, 1990-2021 (Source: Authors' own elaboration)

The global burden of disease study (GBD 2021) [13] reported on the estimates of overall cancer burden on the global scale. Another study of both total cancer and 29 group of cancers in Asia [6] relied on the second last GBD 2021 iteration. However, analytic decisions in GBD 2021 studies improve with each iteration, requiring continuous updates to health metrics. For instance, in GBD 2021, a new redistribution approach for garbage codes and alternative strategies for sparse or unusual data were implemented. Additionally, the number of country-years for data types increased, improving inferences at the national level. Hence, departing from the latest iteration of the GBD 2021 study [13], we began by analyzing the total cancer burden in Central Asia. We then explored country-, sex-, and cancer-specific estimates of 33 cancer groups in five Central Asian countries from 1990 to 2021.

MATERIALS AND METHODS

Overview and Definitions

According to the United Nations, Central Asia comprises of following countries: Kazakhstan, Kyrgyzstan, Turkmenistan, Uzbekistan, and Tajikistan [7]. The GBD 2021 provides the comprehensive approach for analyzing the health-related metrics, disease burden and their risk factors in 204 nations and territories. It employs a consistent and continuously improved methodology. Taking advantage of the data available from GBD 2021 study [13], we analyzed the cancer burden in Central Asia, with a specific focus on the list of five countries. The general information on the data collection, aggregation and redistribution is available elsewhere [13]. Cancer cases were defined using the international classification of diseases (ICD), 9th and 10th revisions. These cancer-specific ICD codes that were in use are available in the **Table S1 in Supplementary Material**.

Data Sources and Measures

The data were from vital registration, surveillance, and verbal autopsy sources [13]. Country-specific age-standardized rates (ASR) for incidence, death, and DALYs were directly extracted from the GBD 2021. We report the ASR per 100,000 population, calculated using the GBD 2021 standard

population structure. The 2.5th and 97.5th percentiles of a set of 1,000 random draws were used to calculate the 95% uncertainty interval (UI) of the estimates. Incidence estimations incorporated a Bayesian meta-regression tool to provide values by location and year. The causes of death were modelled via multiple causes of death to redistribute the country- and cancer-specific garbage codes [13]. Finally, DALYs represent a combination of two metrics: years lived with disability (YLD) and years of life lost (YLL). Specifically, YLD is calculated by multiplying the disability weights by the corresponding cancer type. YLL, in turn, is a product of the death counts in each age category and its remaining life expectancy. Age-standardized populations were calculated using the GBD 2021 standard life table.

Statistical Analysis

This study presents descriptive and exploratory analyses and does not aim to draw causal inferences. The authors disaggregated data by country, year, sex and cancer-type. We present the average annual percent change (AAPC) over a specified period (1990-2021). Regression models were fitted to identify significant changes in the AAPC of the temporal patterns of total cancers. A model fit was evaluated with Bayesian information criterion and confirmed that a model with zero joinpoints was appropriate based on the observed data patterns. The AAPC models were fitted as log-linear models, assuming uncorrelated errors. All data analyses and visualizations were performed using the R software (version 4.3.2) and joinpoint trend analysis software (V5.2.0).

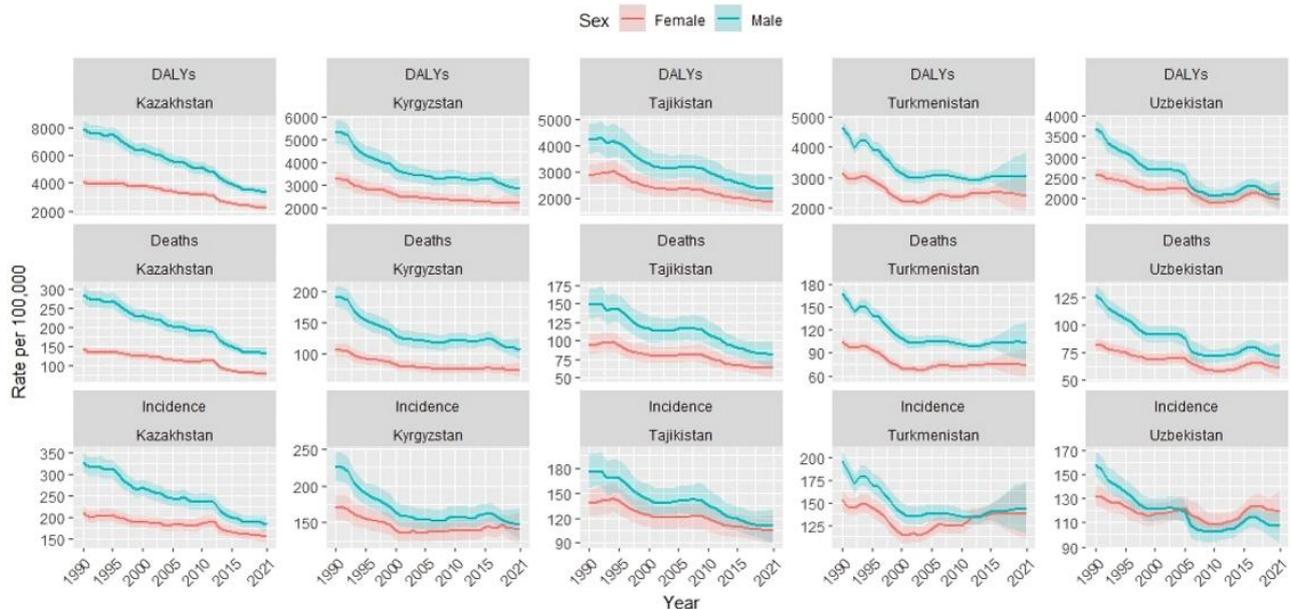
RESULTS

The total cancer-related burden metrics were somewhat heterogeneous in 1990 but by 2021, the estimates were mostly comparable. Overall, across all metrics, the highest and lowest estimates were observed for Kazakhstan and Uzbekistan, respectively. The remaining three countries (Kyrgyzstan, Tajikistan, and Turkmenistan) revealed highly overlapping estimates during 1990-2021 (**Figure 1** and **Table 1**).

Table 1. Age-standardized estimates for total cancer incidence, deaths, and DALYs for both sexes in 1990 and 2021 and the percentage change during 1990-2021 in Central Asian countries

Country	Incidence (95% UI)			Deaths (95% UI)			DALYs (95% UI)		
	ASR (per 100,000) 1990	ASR (per 100,000) 2021	AAPC, 1990-2021	ASR (per 100,000) 1990	ASR (per 100,000) 2021	AAPC, 1990-2021	ASR (per 100,000) 1990	ASR (per 100,000) 2021	AAPC, 1990-2021
Kazakhstan	252.70 (236.44 to 269.47)	164.35 (147.45 to 180.61)	-1.32** (-1.44 to -1.19)	194.23 (181.13 to 208.55)	96.61 (85.54 to 107.32)	-2.28** (-2.51 to -2.05)	5,641.34 (5,293.74 to 6,044.59)	2,661.02 (2,358.67 to 2,944.37)	-2.50** (-2.74 to -2.24)
Uzbekistan	140.43 (132.0 to 149.19)	112.28 (98.25 to 127.75)	-0.62** (-0.91 to -0.31)	100.29 (94.21 to 107.01)	65.63 (55.79 to 76.14)	-1.27** (-1.57 to -0.96)	3043.03 (2,883.16 to 3,215.42)	2,023.89 (1,725.37 to 2,347.53)	-1.25** (-1.51 to -0.99)
Kyrgyzstan	189.33 (172.72 to 204.91)	141.34 (122.16 to 161.56)	-0.74** (-1.03 to -0.43)	138.82 (125.67 to 151.21)	86.43 (73.36 to 101.50)	-1.26** (-1.58 to -0.93)	4119.77 (3,714.36 to 4,498.60)	2,461.86 (2,096.45 to 2,901.72)	-1.46** (-1.69 to -1.21)
Tajikistan	152.01 (138.20 to 167.72)	107.76 (94.19 to 122.83)	-1.18** (-1.32 to -1.02)	116.92 (104.75 to 130.06)	72.03 (61.26 to 82.87)	-1.60** (-1.79 to -1.40)	3471.33 (3,139.18 to 3,829.75)	2,130.35 (1,811.74 to 2,469.26)	-1.69** (-1.84 to -1.53)
Turkmenistan	168.01 (158.00 to 178.05)	137.21 (111.96 to 169.48)	-0.44* (-0.80 to -0.07)	129.15 (121.21 to 137.07)	86.05 (67.48 to 109.77)	-1.11** (-1.55 to -0.64)	3778.97 (3,575.47 to 3,994.26)	2,664.26 (2,085.31 to 3,427.03)	-0.89** (-1.27 to -0.51)

Note: *p < 0.050 & **p < 0.001

**Figure 2.** Sex-specific trends in DALYs, deaths, and mortality rates for total cancers in Central Asia, 1990-2021 (Source: Authors' own elaboration)

Although the AAPC analysis found downward patterns for all locations, its estimates varied from country to country. Kazakhstan was associated with the steepest decrease in DALYs, deaths, and incidence, followed by Tajikistan, Kyrgyzstan, Uzbekistan, and Turkmenistan (Table 1 and Figure S1, Figure S4, and Figure S7 in Supplementary Material).

The total cancer burden was more pronounced in male subjects (Figure 2), and this predominance was common among all countries. Similar to the aggregated AAPC estimates, the sex-specific trend analyses showed a consistent order of countries, where Kazakhstan and Turkmenistan had the highest and lowest AAPC slopes for all metrics in the region, respectively (Figure S2, Figure S3, Figure S5, Figure S6, Figure S8, and Figure S9 and Table S2 and Table S3 in Supplementary Material).

In terms of country-and-cancer-specific estimates for both sexes combined, all countries shared comparable patterns

over time (Figure S10-Figure S24 in Supplementary Material). For DALYs, the five leading cancer sites were tracheal, bronchus, and lung (TBL), followed by stomach, colon and rectum, breast and esophageal cancers. This was also the case for death causes and incidence, where the cancer types and their order remained mostly unchanged. In contrast, disaggregation by sex, country, and cancer type revealed slightly diverse patterns (Figure S25-Figure S54 and Table S4-Table S8 in Supplementary Material). Specifically, among the countries, cancer groups were comparable for DALYs and deaths, although they were slightly different in terms of incidence. As such, in male subjects, the leading cancers were mostly TBL, stomach, colon and rectum, esophageal and liver cancers. In females, these were the breast, stomach, cervical, colon and rectum, and TBL. For incidence, however, non-melanoma skin cancers ranked high in all countries, particularly in Uzbekistan and Turkmenistan.

DISCUSSION

The total cancer burden, measured by DALYs, deaths, and incidence for both aggregated and sex-specific estimates, decreased in AAPCs during 1990-2021 for all Central Asian countries, with Kazakhstan having the most pronounced decline. Drawing upon the contribution to DALYs and deaths, the top-ranked list of cancer types mostly remained the same. For instance, however, they experienced slight changes. This implies that the cancer burden is primarily due to premature deaths. Despite improvements in health metrics, cancer remains a public health concern in the region due to its contribution to both observed and projected burden estimates.

Our findings on downward temporal patterns for the metrics (e.g., DALYs, deaths, and incidence) returned consistent with those from preceding studies [5, 6, 13, 14]. Given that cancer has historically posed a public health concern in the region, all countries have adopted national strategies, often assisted by international agencies, resulting in improvements in cancer metrics over the last decades [8, 15, 16].

Kazakhstan had notably high burden metrics in the early 1990s. Thereafter, however, the patterns for all measures saw a decline over the following decades and finally ended up with estimates that were similar to other countries in the region by 2021. Although newly emerging socioeconomic challenges run all countries in Central Asia into transforming healthcare systems [8, 17], Kazakhstan was the country that actively implemented approaches from international development organizations [8]. Shortly after the dissolution of SU, it became a member of the World Health Organization to facilitate its activities in the country, following common health indicators and improving reporting practices [18-20]. These activities may have contributed to the observed improvement in cancer statistics. Hence, current evidence suggests that Kazakhstan has made exceptional progress in reducing the burden of non-communicable diseases, including cancer compared to other countries in the region [14].

The TBL was one of the leading causes of cancer burden across all countries in Central Asia. Smoking remains among the most influential risk factors; therefore, tobacco control remains a priority policy target in the region, acknowledging its effectiveness in reducing tobacco-related cancers [6, 21]. Historically, TBL has been the primary cause of cancer mortality in the region due to the high prevalence of smoking and air pollution [11, 22]. However, the existing evidence suggests things are not getting any better [23]: smoking prevalence remains stable in the region, and its rate of change is diverse among countries. Specifically, despite the pronounced decline in cancer estimates for Kazakhstan, the country was not associated with any significant changes in smoking prevalence [23]. Thus, policymaking in both the country and the region should focus on efforts to control tobacco consumption to reduce the cancer burden on the population [5].

Other than TBL, the cancer burden was largely attributed to stomach cancer, colon and rectum cancers, and esophageal cancer in both sexes, particularly among males. In females, those were the breast, stomach, cervical, colon and rectum, and TBL. The contribution of gastrointestinal cancers to the overall burden estimates was pronounced, irrespective of

location or sex. For the majority of these cancers, smoking, alcohol consumption, obesity, physical inactivity, and infections remain the major risk factors [24]. Furthermore, current evidence suggests that improved access to clean drinking water and sanitation can potentially reduce the transmission of *Helicobacter pylori*, which is associated with a reduction in the risk of stomach cancer [6, 25]. Survival in patients with colon and rectum and esophageal cancers relies on the stage at diagnosis and the availability of subsequent treatment [6, 24, 26]. This requires improved access to screening services for the early detection [27]. Acknowledging the impact of premature deaths on DALYs, policies in the region should prioritize efforts targeting modifiable risk factors, along with strengthening early diagnosis and improving access to treatment, to effectively grapple with the burden caused by these cancer groups.

Across locations, sex-specific cancers had a limited impact on male participants, whereas in females, they were the primary contributors to the burden. Despite a notable reduction in the estimates for breast and cervical cancer over time, they have consistently ranked among the top causes. These cancer types remain preventable, and strategies consist of primary prevention measures, improvement, reduction of common risk factors exposure, cancer awareness, and vaccination [6, 28]. The observed estimates highlight the importance of these measures in reducing the burden of breast and cervical cancers [5].

When analyzing the burden attributable to common risk factors, such as tobacco use, alcohol use, air pollution, unhealthy diet, and low physical activity [14], the distribution of DALYs attributable to these risk factors was roughly stable across countries during 1990-2021 (**Figure S55-Figure S59** in **Supplementary Material**). On the one hand, the observed decrease in burden estimates might converge with the global average [13], where the reduction likely reflects a broader secular trend in cancer control efforts rather than effects unique to the national context. Furthermore, a recently revealed worldwide reduction in cancer severity [29] over the last three decades might be a plausible explanation for the burden decrease. This might be due to advancements in cancer treatment and management, which became possible by the implementation of screening programs, improvements in medical imaging and related technologies, as well as an overall increase in cancer prevention awareness worldwide.

On the other hand, the decrease in burden metrics might be an artifact of massive migration following SU collapse (**Figure S60** in **Supplementary Material**), further suspecting a salmon bias effect (remigration due to poor health) [30]. In the 20th century, there were large-scale deportations in SU, where different ethnic groups were forcibly relocated to and within Central Asia. Thus, upon dissolution of SU, the 1990s witnessed waves of repatriation among these ethnic groups. For instance, Germany was among the most popular locations for migrants from SU during 1990-2000, particularly for ethnic Germans [31]. The study in [32] performed in Germany on those who returned from SU revealed increased all-cause mortality risks for immigrants, especially for those who returned in 1996 and after. This implies that despite the fact that these individuals lived most of their lives in a Central Asian country, contributing to disease burden, their deaths may not have been recorded in that (Central Asian) country's mortality statistics, further decreasing their burden. In addition, the incidence estimates decline slowed in 2000, and thereafter saw slight fluctuations

in most countries, which might also imply that people who left a country in the 1990s might return as they were diagnosed with cancer. Notably, the existing literature on the effect of salmon bias on population metrics has yet to be clarified. Previous studies have identified its effect on decreasing mortality patterns [33, 34]. However, another study in [35] revealed that immigrants with poor health are less likely to return to their country of origin. This phenomenon has rarely been discussed in literature when interpreting aggregated population metrics. Although we have no supportive data for this bias, we speculate that it may have partially affected the estimates in our study. Hence, it may require further attention in future studies, especially those departing from the GBD 2021.

Limitations

Our study had several limitations. The study sourced data from the latest GBD 2021 iteration, which reports aggregated, standardized, and extrapolated estimates at different population levels. Hence, when it comes to specific locations, GBD 2021 presents modelled estimates rather than observations for the locations. These factors may potentially result in distortions of the burden estimates, particularly in regions where data are sparse. Furthermore, cause-of-death misclassification remains a concern. For instance, a recent study in [36] analyzing over a million death certificates revealed several issues with cause of death coding. The authors suggested that improving coding practices can potentially affect epidemiological parameters. Furthermore, recent studies comparing GBD 2021 estimates with those from GLOBOCAN revealed systematic differences across metrics between institutions, highlighting the need for further validation studies, with a particular focus on countries with a high disease burden [37, 38]. Similarly, studies comparing national data with GBD 2021 data have also revealed substantial discrepancies [39, 40]. Therefore, our findings should be interpreted with caution. Historically, human migration has been a common reaction to challenges related to unemployment, poverty, or even war in Central Asia [41]. Therefore, it is plausible that some cases were missing or left the country, especially during the early post-SU period when living conditions were poor. Finally, the burden of cancer increases with age and becomes more pronounced in older age groups. Between 1990 and 2021, Kazakhstan experienced the lowest population growth of 15%, while other Central Asian countries, on average, had a 40% increase. Such a demographic transition toward a younger population may have affected cancer epidemiology.

CONCLUSION

Despite some encouraging findings in this study, both regional and national cancer burden remains a public health issue in Central Asia, with notably high estimates in male subjects. The leading cancer groups and distribution of risk factors were somewhat similar across countries; however, the burden of sex-specific cancers was more pronounced in females. Considering that a large proportion of cancers are avoidable, preventive measures remain the most important tools for controlling the burden. Future studies should focus on the impact of risk factors distributions on health metrics, as well as the possible systematic errors when interpreting estimates from the GBD 2021.

Author contributions: **ZB, AM, & ZK:** data curation, formal analysis, and writing—original draft; **ZB & AM:** funding acquisition; **RA & AG:** conceptualization and supervision; & **DZ, SS, & AK:** writing—review & editing. All authors have agreed with the results and conclusions.

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Ethical statement: The authors stated that the study does not require any ethical approval since the study used publicly available, aggregated data from IHME without any personally identifiable information.

AI statement: The authors stated that no AI tools were used for data analysis, statistical processing, figure generation, or interpretation of results. The authors retain full responsibility for the integrity, originality, and scientific accuracy of the work.

Declaration of interest: No conflict of interest is declared by the authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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