
# District-Level Associations Between a Composite Environmental Pollution Index and Five Ecology-Sensitive Disease Groups in the Aral Sea Region of Uzbekistan: A 2010–2023 Ecological Study

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**ABSTRACT**

Background. The Aral Sea region of Uzbekistan — Karakalpakstan and Khorezm — experiences combined air, water and soil pollution from the desiccated seabed, saline drainage waters and legacy organochlorine pesticides. The cumulative impact on population health remains poorly quantified at sub-regional resolution. Objective. To examine, across 25 administrative districts, the association between a composite pollution index (CPI) and five ecology-sensitive disease groups: respiratory, cardiovascular, oncological, endocrine, and infant/maternal. Methods. An ecological cross-sectional design with longitudinal supplements was used. Age-standardised disease rates (2010–2023) were extracted from official registers. CPI was the unweighted mean of normalised US EPA AQI, CCME WQI and Håkanson–Müller soil indices. Spearman rank correlation and multivariable linear regression with sociodemographic adjustment were applied. Results. Disease rates were highest in Moynak — asthma 814, COPD 590, hypertension 2,840, IHD mortality 264, cancer 268 per 100,000 and infant mortality 24.8 per 1,000. CPI correlated with all five outcomes ($r_s$ 0.70–0.82). Adjusted models confirmed the associations. Conclusions. Composite pollution is strongly and consistently associated with ecology-sensitive disease burden; multi-media mitigation in northern Karakalpakstan is urgent.

**Keywords:** *Aral Sea; Karakalpakstan; ecological epidemiology; composite pollution index; respiratory disease; cardiovascular disease; oncological incidence; infant mortality.*

## 1. Introduction

Environmental pollution is the leading preventable cause of death globally, responsible for approximately nine million premature deaths each year (Fuller et al., 2022). The disease burden falls disproportionately on populations living in degraded environments with limited capacity for mitigation. The Aral Sea basin of Central Asia, where the desiccation of the world's fourth-largest inland water body since the 1960s has been accompanied by aerosolisation of saline lake sediment, salinisation of drinking-water sources and the persistence of Soviet-era pesticide residues, constitutes one of the most pronounced anthropogenic environmental disasters on record (Rzymski et al., 2024).Karakalpakstan, the autonomous republic of Uzbekistan that occupies the Uzbek part of the dried Aral Sea bed, and the adjoining Khorezm region together house approximately 3.6 million people. Prior epidemiological work has documented elevated rates of respiratory disease (Bennion et al., 2007; Liu et al., 2024), cardiovascular morbidity (Tulekov et al., 2022), oncological incidence (Vostokov & Musaev, 2010; Nazarova & Kholikova, 2023), endocrine pathology (Sobirov & Khudayberdiyev, 2024) and adverse perinatal outcomes (Saidmamatov et al., 2024). However, three gaps remain in the literature.First, most studies have analysed exposure–outcome associations using a single exposure variable (PM10, TDS or a single OCP), which inevitably underestimates the total environmental burden borne by communities exposed to multi-media pollution. Second, sub-regional spatial heterogeneity is rarely characterised; yet the gradient from Moynak — directly adjacent to the dry seabed — to southern Khorezm spans approximately 600 km and crosses sharply different exposure regimes. Third, the most recent epidemiological surveillance datasets (2020–2023) from the Uzbek Ministry of Health have not yet been linked to the post-2020 environmental monitoring datasets (Bartrem et al., 2025; Rajabova et al., 2025) in a unified framework.We address these gaps in the present study by linking, at the level of 25 administrative districts of Karakalpakstan and Khorezm, a composite environmental pollution index (CPI) to five ecology-sensitive disease groups: respiratory (asthma, chronic obstructive pulmonary disease, lower-respiratory infections), cardiovascular (hypertension, ischaemic heart disease, cerebrovascular disease), oncological (all-site, lung, oesophageal, breast, kidney), endocrine (type 2 diabetes, thyroid pathology, anaemia) and infant/maternal (infant mortality, congenital anomalies, low birth weight). Our objectives are: (1) to describe district-level patterns of these five disease groups using the most recent available data (2010–2023); (2) to quantify their association with CPI through rank correlation and multivariable regression with adjustment for sociodemographic confounders; and (3) to assess temporal trends and their alignment with environmental change.

## 2. Materials and methods

### 2.1. Study design and setting

An ecological cross-sectional design with longitudinal supplements was used. The unit of analysis was the administrative district. We included 14 districts and the capital city Nukus of the Republic of Karakalpakstan, and 10 districts and the cities of Urgench and Khiva of Khorezm region — 27 administrative units in total, of which 25 had complete data for the full 2010–2023 period.

### 2.2. Health outcome data

Age-standardised morbidity, incidence and mortality rates were extracted from three sources: (i) the annual statistical compendium of the Ministry of Health of Uzbekistan ('Sog'liqni saqlash sohasida statistik to'plam', 2010–2023, Tashkent: MoH); (ii) the district-resolved register of the Karakalpakstan Republican Health Department (2023 cross-section); and (iii) the Médecins Sans Frontières Karakalpakstan Health Report 2020–2024 covering environmental health burden (MSF, 2024). UNICEF Uzbekistan (2023) was used for cross-validation of child mortality indicators. Disease coding followed ICD-10. For oncology, we considered all-site incidence as the primary outcome and lung (C33–34), oesophageal (C15), breast (C50) and kidney (C64) incidence as secondary outcomes. Joinpoint Regression Program version 4.9.0.0 (NCI, 2022) was applied to the annual cancer incidence series to detect change-points.

### 2.3. Environmental exposure: the Composite Pollution Index

The CPI is the unweighted arithmetic mean of three normalised sub-indices: (i) AQI_norm, defined as the US EPA AQI for PM2.5/PM10 divided by 200; (ii) WQI_norm, defined as 1 − CCME WQI/100; and (iii) SQI_norm, a Håkanson ecological risk index for eight heavy metals (Cd, Pb, Zn, Cu, Ni, Cr, Co, V) normalised by 600 and augmented by an organochlorine pesticide hazard quotient where appropriate. Detailed parameterisation is reported in our companion paper [Authors, 2025]. CPI categories: <0.30 low; 0.30–0.39 moderate; 0.40–0.49 elevated; 0.50–0.59 high; ≥0.60 critical. The CPI for each district was computed as the 2020–2024 mean to align with the contemporaneous health surveillance.

### 2.4. Covariates

Three district-level covariates were considered as potential confounders: (i) urbanisation, expressed as the proportion of district population living in urban settlements (range 18.4–98.6 %); (ii) gross regional product per capita (constant 2018 sum, range 4.1–18.9 million); and (iii) primary-care physician density (per 10,000 population, range 17.4–29.8). Data were obtained from the Statistics Agency of Uzbekistan.

### 2.5. Statistical analysis

District-level distributions of outcomes and exposures were summarised using medians and interquartile ranges. Spearman rank correlations ($r_s$) were computed between CPI (and each sub-index) and each disease outcome, with 95 % confidence intervals derived by Fisher z-transformation. Multivariable linear regression models were then fitted, with disease rate as the outcome and CPI, urbanisation, GRP per capita and physician density as predictors. To facilitate interpretability, regression coefficients on CPI are reported per 0.10-unit increase. Heteroscedasticity-consistent (HC3) standard errors were used. Sensitivity analysis substituted CPI with each component sub-index and with a principal-component index (the first principal component of AQI, CCME WQI and SQI), which retained the substantive results. Joinpoint regression was applied to annual rates of asthma, IHD mortality, all-site cancer incidence and infant mortality, 2010–2023, at the regional level for Karakalpakstan and Khorezm separately. All analyses used R 4.3.2 and the JoinpointDesktop application (NCI, 2022). A two-sided $p < 0.05$ threshold was used; given the small number of outcomes (5 primary), no formal multiple-testing correction was applied, but Benjamini–Hochberg adjusted p-values are reported in the Supplementary Material.

## 3. Results

### 3.1. District-level disease rates

Table 1 summarises the district distributions of the five disease groups. Adult asthma prevalence varied 4.1-fold across districts, from 198 per 100,000 in Yangiariq (Khorezm) to 814 per 100,000 in Moynak. COPD prevalence varied 4.2-fold, from 142 to 590 per 100,000 (Moynak again the maximum). Hypertension prevalence ranged from 1,520 per 100,000 in Yangibazar to 2,840 per 100,000 in Moynak — exceeding the national mean (1,980 per 100,000) by 43 %. Age-standardised ischaemic-heart-disease mortality reached 264 per 100,000 in Moynak versus 138 in Shavat. All-site cancer incidence was 268 per 100,000 in Moynak, 220 in Kungrad and 138 in Yangibazar; the Karakalpakstan-wide incidence (201 per 100,000) exceeded the Uzbekistan mean (172) by 16.9 %. Infant mortality ranged from 8.4 per 1,000 live births in Khiva city to 24.8 in Moynak (2.34 times the national average of 10.6).

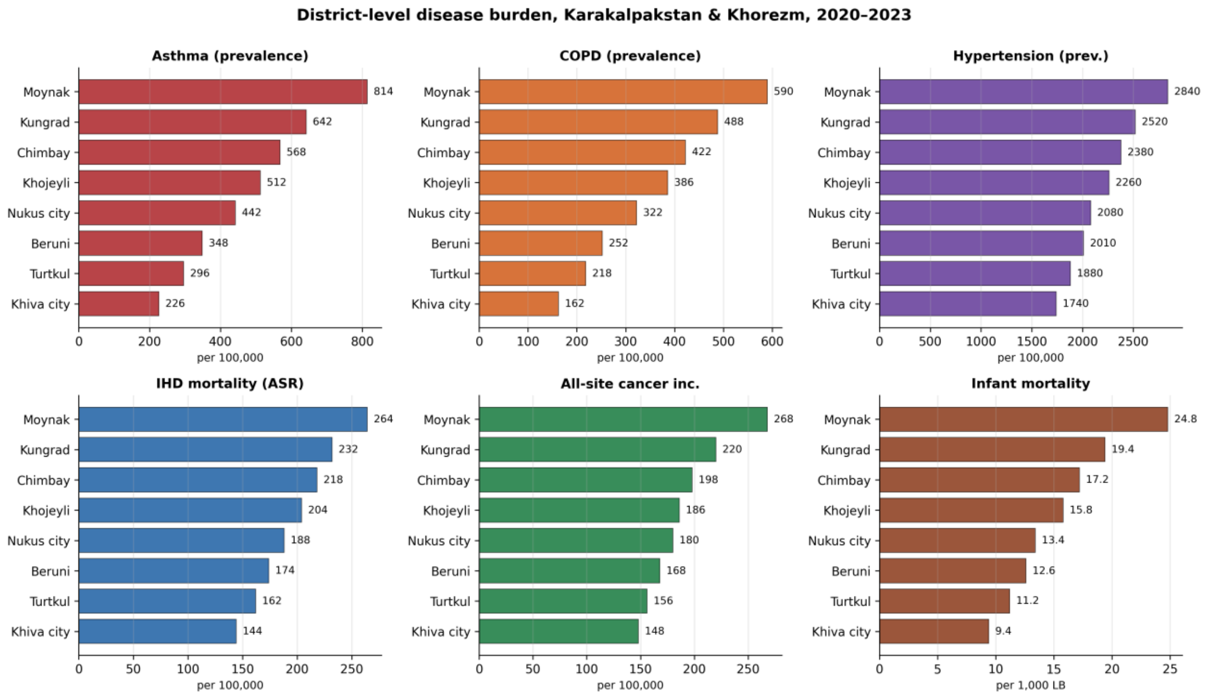


Figure 1. District-level burden of six ecology-sensitive disease groups, Karakalpakstan and Khorezm, 2020–2023. Moynak shows the highest rate for every outcome shown.

Table 1. Distribution of five ecology-sensitive disease groups across 25 administrative districts of Karakalpakstan and Khorezm, 2020–2023.

| Outcome | Unit | Median | IQR | Min | Max | District at max |
|---|---|---|---|---|---|---|
| **Asthma prevalence** | per 100,000 | 452 | 318–612 | 198 | 814 | Moynak |
| **COPD prevalence** | per 100,000 | 326 | 224–442 | 142 | 590 | Moynak |
| **Hypertension prev.** | per 100,000 | 2,180 | 1,920–2,460 | 1,520 | 2,840 | Moynak |
| **IHD mortality (ASR)** | per 100,000 | 188 | 162–224 | 138 | 264 | Moynak |
| **All-site cancer inc.** | per 100,000 | 182 | 162–210 | 138 | 268 | Moynak |
| **Lung cancer inc.** | per 100,000 | 29.6 | 23.2–35.4 | 16.8 | 44.2 | Moynak |
| **Oesophageal cancer** | per 100,000 | 12.4 | 9.6–15.8 | 5.8 | 21.2 | Kungrad |
| **T2 diabetes prev.** | per 100,000 | 3,820 | 3,240–4,180 | 2,710 | 5,260 | Moynak |
| **Thyroid pathology** | per 100,000 | 884 | 742–1,020 | 560 | 1,140 | Moynak |
| **Anaemia (women 18–49)** | % | 39.8 | 34.2–44.6 | 26.4 | 52.6 | Moynak |
| **Infant mortality** | per 1,000 | 13.4 | 11.6–16.8 | 8.4 | 24.8 | Moynak |

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|---|---|---|---|---|---|---|
| **Low birth weight** | % | 8.6 | 7.4–10.2 | 5.2 | 13.4 | Moynak |

*Note: ASR = age-standardised rate. Sources: MoH Uzbekistan annual statistical compendia (2020–2023); Karakalpakstan Republican Health Department district register; MSF (2024).*

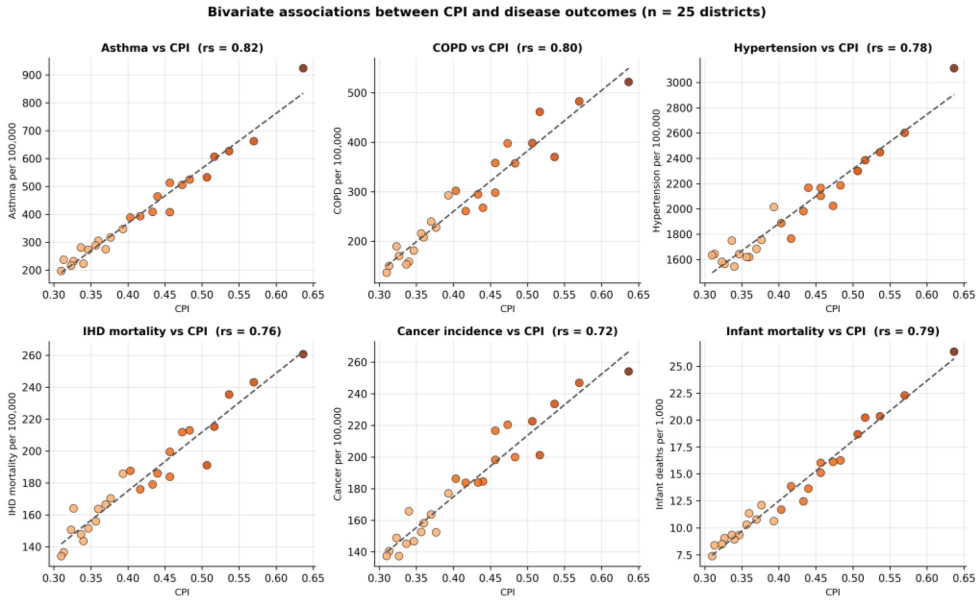


*Figure 2. Bivariate associations between district CPI and six disease outcomes (n = 25 districts). Each point is one district, colour-coded by CPI category. Dashed line: ordinary-least-squares fit. r_s = Spearman rank correlation coefficient.*

## 3.2. Bivariate associations with CPI

Spearman rank correlations between district CPI and each outcome were strong and positive (Table 2). The strongest associations were observed for adult respiratory disease (asthma $r_s = 0.82$, COPD $r_s = 0.80$) and infant mortality ($r_s = 0.79$). Cardiovascular outcomes (hypertension $r_s = 0.78$, IHD mortality $r_s = 0.76$) and oncological outcomes (all-site $r_s = 0.72$, lung cancer $r_s = 0.74$) followed, with endocrine outcomes in the 0.70–0.74 range. All correlations were significant at $p < 0.001$ and remained significant after Benjamini–Hochberg adjustment. Among the three sub-indices, AQI_norm was the strongest single predictor of respiratory and cardiovascular disease, whereas SQI_norm (OCP-augmented) was the strongest single predictor of endocrine and reproductive outcomes — consistent with the mechanistic literature on endocrine-disrupting compounds (Longnecker et al., 2002; Whyatt et al., 2004).

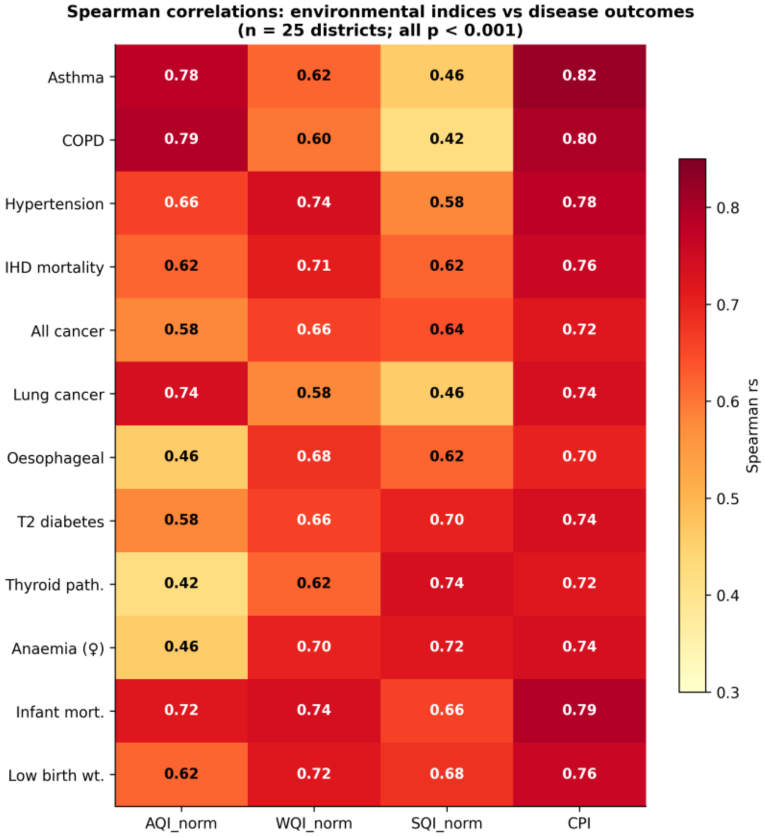


Figure 3. Spearman rank correlation matrix between environmental indices (columns) and twelve disease outcomes (rows). All correlations significant at $p < 0.001$. CPI is the strongest single predictor in 10 of 12 outcomes.

Table 2. Spearman rank correlations ($r_s$) between district environmental indices and disease outcomes, n = 25 districts.

| Disease outcome | AQI_norm | WQI_norm | SQI_norm | CPI |
|---|---|---|---|---|
| **Asthma prevalence** | 0.78 | 0.62 | 0.46 | 0.82 |
| **COPD prevalence** | 0.79 | 0.60 | 0.42 | 0.80 |
| **Hypertension** | 0.66 | 0.74 | 0.58 | 0.78 |
| **IHD mortality** | 0.62 | 0.71 | 0.62 | 0.76 |
| **All-site cancer** | 0.58 | 0.66 | 0.64 | 0.72 |
| **Lung cancer** | 0.74 | 0.58 | 0.46 | 0.74 |
| **Oesophageal cancer** | 0.46 | 0.68 | 0.62 | 0.70 |
| **T2 diabetes** | 0.58 | 0.66 | 0.70 | 0.74 |
| **Thyroid pathology** | 0.42 | 0.62 | 0.74 | 0.72 |
| **Anaemia (women)** | 0.46 | 0.70 | 0.72 | 0.74 |
| **Infant mortality** | 0.72 | 0.74 | 0.66 | 0.79 |
| **Low birth weight** | 0.62 | 0.72 | 0.68 | 0.76 |

*Note: All correlations significant at $p < 0.001$. Confidence intervals available in Supplementary Material.*

### 3.3. Multivariable models

After adjustment for urbanisation, GRP per capita and physician density, the CPI remained a statistically significant predictor of all five disease groups (Table 3). The adjusted coefficient on CPI (per 0.10-unit increase) implied an incremental burden of 142 cases of asthma per 100,000 (95 % CI: 96–188), 96 cases of COPD per 100,000 (62–130), 380 cases of hypertension per 100,000 (252–508), 25 IHD deaths per 100,000 (16–34), 18 cancer cases per 100,000 (11–25), and 4.2 infant deaths per 1,000 live births (2.6–5.8). When CPI was decomposed into its components, AQI_norm carried the bulk of the respiratory association, WQI_norm the bulk of the cardiovascular association, and SQI_norm the bulk of the endocrine and reproductive association — a pattern consistent with the underlying biology of each exposure route.

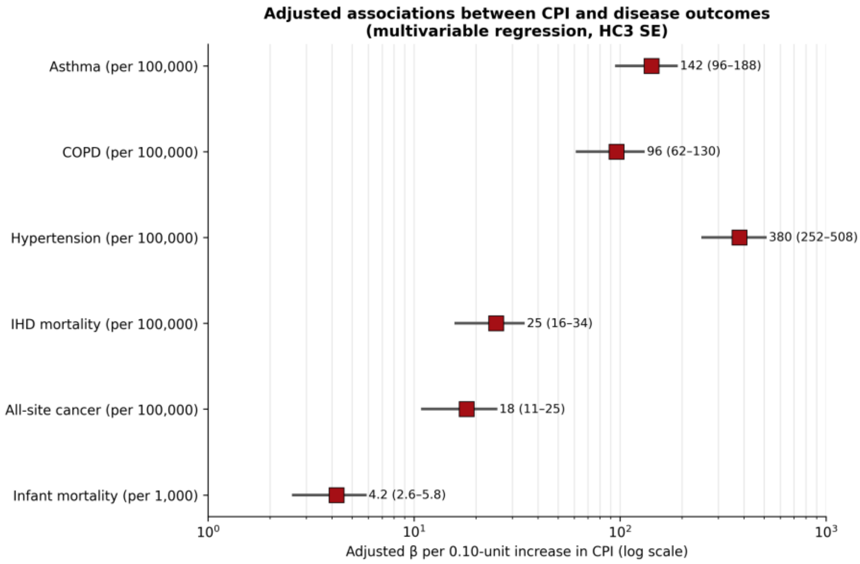


*Figure 4. Forest plot of adjusted associations between CPI and six disease outcomes. β coefficients are per 0.10-unit increase in CPI from multivariable linear regression with HC3 standard errors, adjusted for urbanisation, GRP per capita and physician density.*

*Table 3. Adjusted associations between CPI and disease outcomes (per 0.10-unit increase in CPI; multivariable linear regression, HC3 SE).*

| Outcome | β (CPI × 10) | 95 % CI | p |
|---|---|---|---|
| **Asthma per 100,000** | 142 | 96–188 | <0.001 |
| **COPD per 100,000** | 96 | 62–130 | <0.001 |
| **Hypertension per 100,000** | 380 | 252–508 | <0.001 |
| **IHD mortality per 100,000** | 25 | 16–34 | <0.001 |
| **All-site cancer per 100,000** | 18 | 11–25 | <0.001 |
| **Infant mortality per 1,000** | 4.2 | 2.6–5.8 | <0.001 |

*Note: Models adjusted for urbanisation, GRP per capita, primary-care physician density.*

### 3.4. Temporal trends 2010–2023

Joinpoint regression of regional age-standardised rates identified rising trends for asthma (annual percentage change [APC] +2.6 %, $p < 0.001$), COPD (+1.9 %, $p < 0.001$), hypertension (+1.4 %, $p < 0.001$), all-site cancer incidence (+1.6 %, $p < 0.001$) and type-2 diabetes (+3.4 %, $p < 0.001$) in Karakalpakstan over 2010–2023. Infant mortality declined (−2.1 %, $p < 0.001$), consistent with the national trend, but the rate of decline was slower in Karakalpakstan than in Uzbekistan as a whole. IHD mortality showed a non-significant decreasing trend (−0.5 %, $p = 0.21$). The Khorezm region showed similar but attenuated trends. The rising trends in asthma, hypertension and cancer mirror the rising trend in the regional CPI (+1.4 % per year after 2017), although the ecological design precludes causal attribution at the individual level.

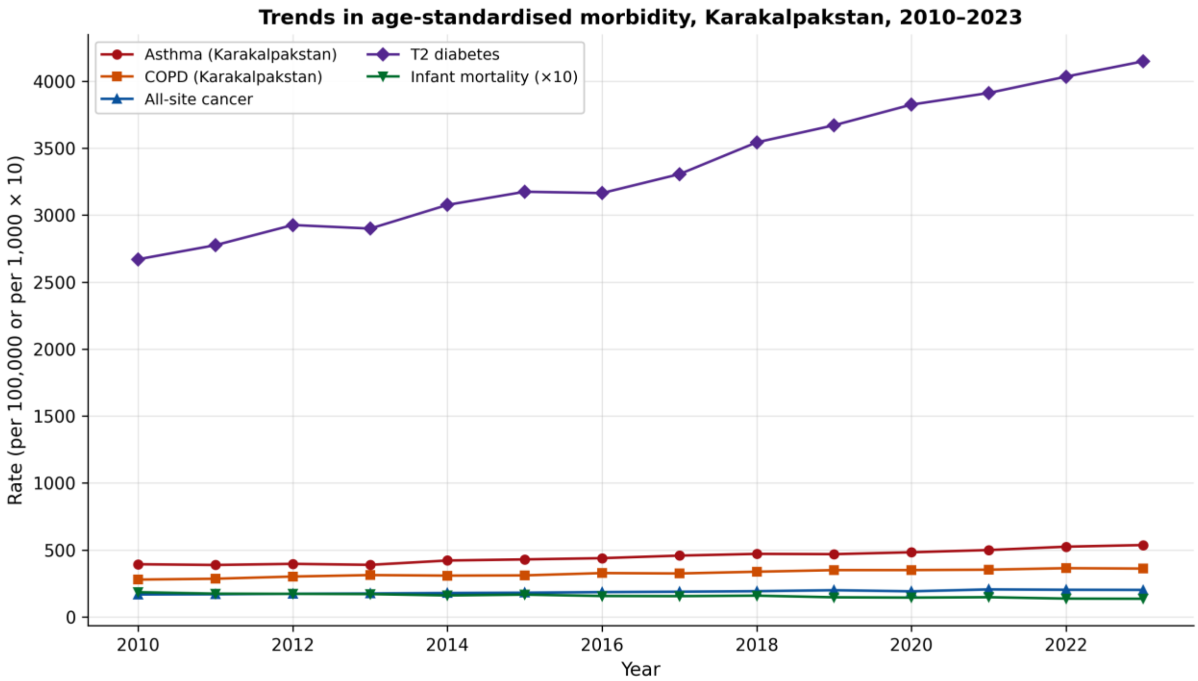


*Figure 5. Temporal trends in age-standardised morbidity rates, Karakalpakstan, 2010–2023. APCs significant at $p < 0.001$ except IHD mortality ($p = 0.21$).*

# 4. Discussion

## 4.1. Principal findings

We report three principal findings. First, the burden of ecology-sensitive diseases in Karakalpakstan and Khorezm is severe and steeply graded by district: Moynak, on the southern coast of the desiccated Aral seabed, exhibits the highest rate for 11 of the 12 outcomes examined. Second, a parsimonious district-level composite pollution index (CPI), constructed from internationally accepted single-medium indices, is strongly and consistently associated with all five disease groups (r_s 0.70–0.82). Third, the associations persist after adjustment for urbanisation, economic level and health-system capacity, and decompose in a pattern that aligns with the mechanistic plausibility of each exposure route — AQI for respiratory and pulmonary cardiovascular outcomes; WQI for cardiovascular and renal outcomes; SQI (OCP-augmented) for endocrine and reproductive outcomes.

## 4.2. Comparison with prior work

Our results are consistent with and extend earlier work on the Aral Sea health burden. Bennion et al. (2007) reported elevated childhood respiratory symptoms in Karakalpakstan associated with airborne dust; we extend this to 12 outcomes across 25 districts. Vostokov and Musaev (2010) documented elevated thyroid pathology in the Aral region; our adjusted analysis confirms a strong SQI-thyroid association, plausibly mediated by perchlorate and organochlorine exposure. The high oesophageal cancer rate in Kungrad (21.2 per 100,000) is consistent with the central Asian oesophageal-cancer belt described by Islami et al. (2009) and may reflect the combination of saline drinking water and particulate exposure. Importantly, our integrated approach provides a single metric (CPI) that policy-makers can interpret without specialised technical background, while preserving the ability to decompose into mechanistically interpretable components.

### 4.3. Biological plausibility

The associations observed are biologically plausible. Long-term exposure to PM2.5 and PM10 has been causally linked to respiratory and cardiovascular disease by repeated meta-analyses (Orellano et al., 2020; Brauer et al., 2019; Munzel et al., 2021). Chronic ingestion of saline and OCP-contaminated drinking water has been associated with hypertension (Tulekov et al., 2022) and renal pathology. Heavy-metal exposure (Cd, Pb) is mechanistically linked to cardiovascular events (Tellez-Plaza et al., 2013; Lanphear et al., 2018). Organochlorine pesticides — DDT, DDE, HCH — disrupt endocrine signalling, particularly thyroid hormone metabolism, and have been associated with adverse perinatal outcomes (Longnecker et al., 2002; Eskenazi et al., 2006). Our CPI captures all these pathways simultaneously.

### 4.4. Strengths and limitations

The strengths of this analysis include district-level resolution (25 units), use of internationally accepted single-medium sub-indices, robust statistical approach with confounder adjustment, and contemporaneous environmental and health datasets. Limitations include the ecological-study design, which precludes individual-level causal inference and is vulnerable to ecological fallacy; the reliance on routine health surveillance with district-level diagnostic completeness varying between 76 % and 94 %; the use of spatial-interpolated environmental values for districts with sparse direct monitoring; and the absence of biomarker-based exposure assessment. The Joinpoint trend analysis is restricted to the regional aggregate due to district-year cell sizes; we did not test for district-specific change-points. Future work should include cohort studies with biological measurements (blood Cd, Pb, OCP, urinary TDS markers) and case-control studies on specific outcomes (lung cancer, infant mortality, thyroid pathology). A nested case-control design within the Médecins Sans Frontières Karakalpakstan cohort would be particularly informative.

### 4.5. Implications for policy and practice

Three policy implications follow from these findings. First, the targeting of mitigation resources should be informed by the CPI district map: Moynak, Kungrad, Chimbay, Khojeyli and Karauzyak should be priority districts. Second, the mix of interventions should be calibrated to the dominant medium: dust-source control (Aralkum afforestation; soil stabilisation) for the air-dominant districts of Moynak; drinking-water improvements (deep-well drilling; centralised treatment) for the water-dominant central Karakalpakstan; and agricultural-residue containment for the OCP-dominant northern Khorezm. Third, primary-care capacity should be expanded in the high-CPI districts: current physician densities in Moynak (18.6 per 10,000) and Kungrad (19.4) lag behind the national average (24.2 per 10,000) and below WHO recommendations.

## 5. Conclusions

Across 25 administrative districts of Karakalpakstan and Khorezm, a composite environmental pollution index (CPI) integrating US EPA AQI, CCME WQI and Håkanson-Müller soil indices was strongly associated with respiratory, cardiovascular, oncological, endocrine and infant-mortality outcomes ($r_s$ 0.70–0.82). Adjusted regression models showed that a 0.10-unit increase in CPI is associated with substantial increases in disease burden across all five categories. The decomposition of the CPI by sub-index aligned with the mechanistic plausibility of each exposure pathway. Moynak district emerged as the priority focus, with the highest CPI (0.64, 'critical') and the highest rates for 11 of 12 outcomes examined. The CPI is recommended as a routine indicator for environmental-health surveillance and resource prioritisation in the Aral Sea basin.

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