

# ***Global, Regional, and National Burden of Urinary Tract Infections from 1990-2019: an Analysis of the Global Burden of Disease Study 2019***

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## **Research Article**

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# Abstract

## Objective

We aimed to estimate the burden of UTIs by age, sex, and socioeconomic status in 204 countries and territories from 1990–2019.

## Method

We used data from GBD 2019 to analyse the incidence, mortality, and disability-adjusted life-years (DALYs) due to UTIs at the global, regional, and national levels. Estimates are presented as numbers and age-standardised or age-specific rates per 100000 population, with 95% uncertainty intervals (UIs). We further explored the associations between the incidence, mortality, DALYs, and socio-demographic index (SDI) as a proxy for the development status of regions and countries.

## Results

In 2019, more than 404.6 million (95% UI 359.4-446.5) individuals had UTIs globally and nearly 236 786 people (198 433 – 259 034) died of UTIs, contributing to 5.2 million (4.5–5.7) DALYs. The age-standardised incidence rate increased from 4 715.0 (4 174.2-5 220.6) per 100 000 population in 1990 to 5 229.3 (4 645.3-5 771.2) per 100 000 population in 2019. At the GBD regional level, the highest age-standardised incidence rate in 2019 occurred in Tropical Latin America (13 852.9 [12 135.6–15 480.3] per 100 000 population). At the national level, Ecuador had the highest age-standardised incidence rate (15 511.3 [13 685.0–17 375.6] per 100 000 population). The age-standardised death rates were highest in Barbados (19.5 [13.7–23.5] per 100 000 population). In addition, age-standardised incidence, death, and DALY rates generally increased across the SDI.

## Conclusions

Our study results suggest a globally rising trend of UTI burden between 1990 and 2019. The results of this study could be useful in policy-making, priority setting, and resource allocation in UTI prevention and treatment.

## Introduction

Urinary tract infections (UTIs) refer to the presence of microbial pathogens within the urinary tract (urethra, bladder, ureters, or kidneys). The UTIs clinical armamentarium of UTIs can range from simple cases such as cystitis to severe cases such as uroseptic shock. UTIs may have different classifications. Clinically, UTIs are categorized as uncomplicated or complicated. Uncomplicated UTIs typically affect individuals who are otherwise healthy and have no structural or neurological urinary tract abnormalities,

whereas complicated UTIs are defined as UTIs associated with factors that compromise the urinary tract or host defence, including urinary obstruction, urinary retention caused by neurological disease, immunosuppression, renal failure, renal transplantation, pregnancy and the presence of foreign bodies such as calculi, indwelling catheters or other drainage devices.[1–3] UTIs can also be stratified as healthcare-associated urinary tract infections (HAUTIs) and community-associated urinary tract infections (CAUTIs).[4, 5] The location of the infection within the urinary tract is usually classified as cystitis, pyelonephritis and urosepsis. UTIs are caused by both gram-negative and gram-positive bacteria, as well as by certain fungi. *Escherichia coli* accounts for the majority of isolated pathogens in all clinical settings, but the local epidemiology of causative pathogens can vary considerably.[6, 7]

UTIs are among the most common bacterial diseases, affecting 150 million people worldwide annually, resulting in more than 6 billion dollars in direct health care expenditures.[8] In 2007 in the United States alone, there were 10.5 million ambulatory visits for UTIs, accounting for 0.9% of all ambulatory visits, and almost 2–3 million visits were to hospital emergency departments.[9] UTIs are also common among inpatients. In 2004, a study conducted in 49 Swiss hospitals showed that 1.5% of hospitalised patients developed symptomatic UTIs.[10] Approximately 50% of women will experience at least one UTIs during their lifetime, and, despite antibiotic intervention, 20 to 30% of women with an initial UTI will experience a recurrent UTIs within 3 to 4 months of the initial infection.[11] A previous study demonstrated that recurrent UTIs have a significant impact on health-related quality of life (QoL) and comprise a health and economic burden.[12] Furthermore, recurrent UTIs are also associated with a significant psychological burden, such as symptoms of anxiety and depression.[13]

However, the global burden of UTIs has not been described elsewhere and is an important estimate to report because it has implications for policy making and prevention efforts. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019 is an effort to measure the worldwide burden of 369 diseases and injuries in 204 countries from 1990 to 2019.[14] Using data from GBD 2019, this study provides estimates of the incidence, mortality, and disability-adjusted life-years (DALYs) of UTIs by sex and age at global, regional, and national levels across 204 countries and territories from 1990 to 2019.

## Methods

### Overview

The GBD 2019, conducted by the Institute of Health Metrics and Evaluation (IHME), used all the available up-to-date sources of epidemiological data and improved standardised methods to provide a comprehensive assessment of health loss across 369 diseases and injuries, for two sexes, and for 204 countries and territories.[14–16] The general methodology of GBD 2019, including its main changes compared with previous years, have been described in previous publications.[14] Methods were developed by and most analyses reported here were conducted at IHME. UTIs were identified based on the International Classification of Diseases and Injuries-10 diagnostic codes

(<http://ghdx.healthdata.org/record/ihme-data/gbd-2019-cause-icd-code-mappings>). The relevant indicators of UTIs were selected for the current analysis.

## Data sources

Data on UTI burden in 204 countries and territories from 1990 to 2019 were obtained from the Global Health Data Exchange GBD Results Tool (<http://ghdx.healthdata.org/gbd-results-tool>) (date of data extraction, 10 April 2021). GBD 2019 data were extracted from censuses, household surveys, civil registration and vital statistics, disease registries, health service use, air pollution monitors, satellite imaging, disease notifications, and other sources. Cause-specific death rates and cause fractions were calculated using the cause of death ensemble model and spatiotemporal Gaussian process regression. Cause-specific deaths were adjusted to match the total all-cause deaths calculated as part of the GBD population, fertility, and mortality estimates. A Bayesian meta-regression modelling tool, DisMod-MR 2.1, was used to ensure consistency between incidence, prevalence, remission, excess mortality, and cause-specific mortality for most causes.[14] The rates were standardised according to the GBD world population and were reported per 100 000 person-years. The GBD 2019 uses various interrelated metrics to measure population health loss, including number of deaths and mortality, number of cases and prevalence, years of life lost (YLL) due to premature death, years lived with disability (YLD), and DALYs. For this report, we used the GBD Results Tool to extract estimates and their 95% uncertainty intervals (UIs) for deaths, incidence of cases, and DALYs as measures of UTI burden from 1990 to 2019 by region and country.

The socio-demographic index (SDI) is a composite indicator of a geographical location's development status. In GBD 2019, the SDI was calculated based on the total fertility rate among females younger than 25 years, educational attainment for those aged 15 years or older, and lag distributed income per capita. The SDI ranged from 0 to 1, where 0 represents the fewest years of schooling, lowest income per capita, and highest fertility, and 1 represents most years of schooling, highest income per capita, and lowest fertility.

## Data analysis

To characterize the UTI burden by age, sex, year, and location, a descriptive analysis was conducted. The number of cases and deaths as well as age-standardised incidence, age-adjusted mortality, and age-standardised DALYs per 100 000 population for both sexes combined were calculated and compared at the global, regional, and country levels. UIs were calculated from 1000 draw-level estimates for each parameter, and 95% UIs were defined by the 25th and 975th values of the ordered 1 000 estimates; a 95% UI excluding 0 was considered to be statistically significant. Finally, we examined the shape of the association of UTIs in terms of age-standardised incidence, death, and DALYs-with the SDI using fit spline models. The maps were made using ECharts software. All statistical analyses were performed using GraphPad Prism 8 software.

## Results

In 2019, more than 404.6 million (95% UI 359.4-446.5) incident cases of UTIs occurred worldwide, and nearly 236 786 people (198 433-259 034) died of UTIs (Supplement Table 1). The age-standardised incidence rate of UTIs was 5 229 (4 645-5 771) per 100 000 population, with an age-standardised death rate of 3.1 per 100 000 population (2.6-3.3). UTIs contributed to 5.2 million (4.5-5.7) DALYs worldwide with an age-standardised DALY rate of 67.2 (57.6-73.7) per 100 000 population in 2019.

The world map of age-standardised incidence, death, and DALY rates of UTIs in 2019 is shown in Figure 1. At the national level, India had the highest number of incident cases (100.8 million [88.1-112.6]), deaths (55 558 [42 788-66 161]), and DALYs (1.59 million [1.25-1.85]) in 2019, comprising nearly one fourth of new cases, deaths, and DALYs globally that year. Ecuador had the highest age-standardised incidence rate (15 511.3 [13 685.0-17 375.6] per 100 000 population), followed by Brazil (13 858.6 [12 152.9-15 487.4] per 100 000 population) and Paraguay (13 675.8 [11 490.6-15 815.8] per 100 000 population). In 2019, the age-standardised death rates were highest in Barbados (19.5 [13.7-23.5] per 100 000 population), Uruguay (15.9 [8.3-18.6] per 100 000 population), and Portugal (15.5 [5.7-18.5] per 100 000 population). The highest age-standardised DALY rates were seen in Barbados (327.0 [233.0-401.6] per 100 000 population), Armenia (249.2 [112.0-327.6] per 100 000 population), and Seychelles (209.7 [119.2-249.2] per 100 000 population) (Supplement Table 2).

At the regional level, Tropical Latin America (13 852.9 [12 135.6-15 480.3] per 100 000 population), Andean Latin America (13 216.7 [11 575.1-14 868.5] per 100 000 population), and Australasia (10 187.5 [8 884.9-11 387.3] per 100 000 population) had the highest age-standardised incidence rates in 2019. In contrast, East Asia (1 575.5 [1 371.2-1 784.8] per 100 000 population), Oceania (1 587.5 [1 361.1-1 816.3] per 100 000 population), and Southeast Asia (2 494.5 [2 161.4-2 805.4] per 100 000 population) had the lowest age-standardised incidence rates in 2019. In all regions, the age-standardised incidence rate was significantly higher among females than males in 2019 (Figure 2A and Supplement Table 3). The age-standardised death rates in 2019 were highest in Southern Latin America (10.0 [6.1-11.2] per 100 000 population), Tropical Latin America (9.4 [5.8-10.5] per 100 000 population), and Western Europe (7.7 [5.5-8.6] per 100 000 population). In contrast, North Africa and the Middle East (0.6 [0.5-0.8] per 100 000 population), East Asia (0.7 [0.6-0.9] per 100 000 population), and Southern Sub-Saharan Africa (0.8 [0.7-1.0] per 100 000 population) had the lowest age-standardised death rates in 2019 (Figure 2B and Supplement Table 3). The regions with the most DALYs in 2019 were Tropical Latin America (171.3 [117.0-187.9] per 100 000 population), Southern Latin America (143.5 [91.7-159.1] per 100 000 population), and Central Asia (127.9 [107.8-144.9] per 100 000 population). The lowest DALY rates were seen in East Asia (15.2 [13.0-18.8] per 100 000 population), North Africa and the Middle East (15.7 [13.6-18.5] per 100 000 population), and Southern Sub-Saharan Africa (26.6 [21.0-32.6] per 100 000 population) (Figure 2C and Supplement Table 3).

Between 1990 and 2019, the global number of individuals with UTIs increased from approximately 252.2 million (223.3-279.3) to more than 404.6 million (359.4-446.5) (Supplement Table 1), an increase of approximately 152.4 million cases. The age-standardised incidence rate at the global level increased from 4 715.0 (4 174.2 -5 220.6) per 100 000 population in 1990 to 5 229.3 (4 645.3-5 771.2) per 100 000

population in 2019. Both the number of incident cases and age-standardised incidence rate were significantly higher in females than males in all years from 1990 to 2019 (Figure 3A). The number of deaths increased from approximately 99 000 to 237 000—an increase of approximately 130 000 deaths. The age-standardised death rate at the global level increased from 1.8 (1.7-2.0) per 100 000 population in 1990 to 3.1 (2.6-3.3) per 100 000 population in 2019 (Figure 3B Supplement Table 1). UTIs led to nearly 5.2 million (4.5-5.7) DALYs in 2019, which was an increase from approximately 3.1 million (2.7-3.4) in 1990. The age-standardised rate of DALYs increased from 57.6 (49.6-63.2) per 100 000 population in 1990 to 67.2 (57.6-73.7) per 100 000 population in 2019 (Figure 3C and Supplement Table 1).

In 2019, the number of incident cases increased with age and peaked in the 30-34 year age group for both females and males, and then decreasing trends for the number of incident cases were seen up to the 75-79 year age group (Figure 4A and Supplement Table 5). The global incidence rate reached the highest level within the 30-34 and >80 year age categories for females and males, respectively. In addition, the number of deaths was higher in females and increased with age except for the <1 year old group, peaking in the >80 year old age group for both females and males. However, the global death rate was higher among males and increased with age in 2019 (Figure 4B). In 2019, the number of DALYs was higher in females except for the <1 and 45-49 year age groups, and the highest number of DALYs occurred in the group aged >80 years for both females and males. The global DALY rate peaked in the >80 year old age for females and males (Figure 4C).

Figure 5 presents the global and regional-level observed UTI burden from 1990 to 2019 versus the expected level based only on the SDI values of the global regions. Between 1990 and 2019, the age-standardised incidence rate increased in all regions except Western Europe (Figure 5A). The observed trend in Western Europe was a decrease in the age-standardised incidence rate from 1990 to 2010 and then a slight increase until 2019 (Figure 5A and Supplement Table 6). In addition, a positive association was found between the age-standardised death rate and SDI at the global level and for all GBD regions. However, there were large regional differences. Southern Latin America, Tropical Latin America, and Western Europe showed the largest increases in observed age-standardised death rates with increases in SDI, whereas Western Sub-Saharan Africa, Eastern Sub-Saharan Africa, and central Sub-Saharan Africa showed decreases in observed age-standardised death rates with increasing SDI value (Figure 5B and Supplement Table 6). A relatively similar pattern was also observed for DALY rates and SDI value. A higher SDI was associated with higher age-standardised DALY rates of UTIs globally and in all regions (Figure 5C).

Figure 6 shows the national-level observed age-standardised incidence, death, and DALY rates and their association with the SDI index in 2019. A positive association of age-standardised incidence, death rate of UTIs and SDI for 204 countries and territories in 2019 was noted (Figure 6A and 6B). Across countries, as SDI increases, age-standardized DALY rate increases until SDI is approximately 0.75, but then decreases with higher SDI. The age-standardised DALY rate was higher than the expected level for a number of countries/territories, including Armenia, Seychelles, Turkmenistan, and Tajikistan (Figure 6C).

## Discussion

In this paper, we presented the first thorough and comprehensive analysis of the burden UTIs from the GBD 2019 study between 1990 and 2019 at the global, regional and national levels. We estimated that more than 404.6 million (359.4-446.5) incident cases of UTIs occurred worldwide, and nearly 236 786 people (198 433 – 259 034) died of UTIs in 2019. Consistent with a previous report, UTIs are one of the most common health problems and entail a high consumption of health system resources.[17]

From 1990 to 2019, the total numbers of incident cases, deaths, and DALYs of UTIs increased markedly worldwide. The striking increase in numbers was primarily driven by population growth worldwide, specifically in low-income and middle-income countries.[15] For example, in India, the number of incident cases more than doubled between 1990 and 2019, the largest increase worldwide. Such infections therefore represent a great health care burden and, as such, demand further research to advance treatment options and improve patient care. We also showed the age-standardised incidence, death, and DALY rates all increase from 1990 to 2019. One potential explanation for this global increase in age-standardised incidence is global ageing. The risk of UTIs increases with age. Indeed, after 65 years of age in noninstitutionalized people, the rate of UTIs was 10.9% for men and 14% for women.[18] In a cross-sectional, population-based study in Sweden and Finland, among women after the age of 85, one-third were diagnosed with UTI within a 1-year period and two-thirds in a 5-year period.[19] Moreover, lengthening life spans correlate with increased time in hospitals or long-term care facilities and exposure to drug-resistant pathogens. With the ageing of the global population, UTIs in the elderly pose a unique clinical challenge in terms of healthcare burden.

Patients with type 2 diabetes mellitus are at increased risk of infections, with the urinary tract being the most frequent infection site.[20, 21] Alterations in the immune system, in addition to poor metabolic control of diabetes, and incomplete bladder emptying due to autonomic neuropathy, may all contribute to the pathogenesis of UTIs in diabetic patients.[20, 22]. An observational study of all patients with type 2 diabetes based on the UK General Practice Research Database (GPRD) found that the incidence rate of UTIs was 46.9 per 1 000 person-years among diabetic patients and 29.9 per 1 000 person-years among patients without diabetes.[23] Similarly, another American database study found that UTI diagnosis was more common in subjects with diabetes than in those without diabetes (9.4% vs 5.7%) among 89 790 matched pairs of patients with and without type 2 diabetes mellitus during 12-month follow-up.[24] Moreover, patients with diabetes have worse outcomes of UTIs than those without diabetes. Diabetes was identified as to be an important risk factor for poor clinical response after 72 h of antibiotic treatment in patients with acute pyelonephritis.[25] A previous study also showed acute pyelonephritis in elderly people with DM is associated with risk of bacteraemia, long hospitalization, and mortality.[26] According to the GBD 2017 study estimation, the incidence of diabetes increased from 11.3 million in 1990 to 22.9 million in 2017 worldwide, with a more than 100% increase.[27] The increased risk of UTIs among diabetic patients, coupled with the increase in the prevalence of diabetes mellitus worldwide may impose a substantial healthcare burden.

The increase in UTI burden might be linked to the seasonality and climate factors. An observational study in South Korea from 1997 to 1999 found that the incidence of UTIs was higher in the summer season.[28] A recent study indicated that higher temperature, more monthly sunshine hours, higher humidity, more rain days and more rainfall are associated with an increase in female acute pyelonephritis incidence in Taiwan (Province of China).[29] In our study, some countries in Tropical Latin America and Southern Latin America had high age-standardised incidence, mortality, and DALY rates over the study period, these findings are consistent with previous literature. Increased temperature enhances perspiration, causes body water loss and relative dehydration and leads to more concentrated urine and less frequent voiding.[30] Hot weather and more monthly sunshine-hours may also cause more sweating and more moisture over the perineal area which may lead to the transfer of bacteria from the rectum to the urethra in females. Moreover, the longer water residence times and increased rainfall extend the disease in wet regions due to a dilution effect causing bacteria to invade the urethra or colonize more easily, eventually causing UTIs. Seasonality and climate factors should be taken into consideration when interpreting surveillance reports and the results of interventions against UTIs.

The age-standardised incidence rates were universally higher in females than in males from 1990 to 2019. UTIs occur more frequently in women than in men, which may be due to a variety of factors, including the shorter distance between the anus (the usual source of uropathogens), the shorter length of the female urethra, the wetter environment surrounding the female urethra, and the antibacterial activity of prostate secretions.[31] However, other reasons besides anatomical differences that make women more susceptible are not clear. Previous reports indicate that the risk factors for UTIs are different in males and females, and this difference should be considered in national policy makers' prevention programmes. Risk factors for UTIs in men may include sexual transmission by an infected female partner, anal intercourse, preputial obliteration, prostate enlargement and urological interventions, such as transrectal prostate biopsy.[32, 33] In contrast, being postmenopausal, urinary incontinence, prior history of symptomatic UTIs, and sexual activity were found to have considerable attributable burden in females.[34] Mortality rates are reported to be higher in females than in males due to the development of pyelonephritis.[35] Similar to the report, in our analyses, we observed that the age-standardised death and DALY rates were higher in females than in males from 1990 to 2019. This trend could be driven by various factors, including a higher prevalence of recurrent UTIs,[36] infection in pregnant women,[37] and infection in elder women.[38]

Our results showed that the number and rate of UTI incidence peaked in the 30–34 year age group in women in 2019. Similar results were also reported in previous studies.[11, 39] UTIs are common among young healthy women even though they generally have anatomically and physiologically normal urinary tracts. For men, the incidence of UTIs also peaked in the 30–34 year age group; however, rates increased steadily with increasing age. One potential explanation for this trend is the high prevalence of prostate enlargement in elderly men, which is an important risk factor for UTIs.[33] We also noticed that the global death and DALY rates due to UTIs increase steadily with increased age, peaking at the oldest age group for both women and men in 2019. More attention should be given to the prevention and management of UTIs in young women and older people.



A positive association was found between UTI burden and the development level of GBD regions and countries which has not been previously reported. The differences in UTI burden among SDI levels could be expected due to epidemiological characteristics of UTI-related risk factors in regions and countries with different SDI levels. According to the GBD 2017 study, high-SDI regions and countries had a higher prevalence of diabetes than low-SDI regions and countries.[27] In addition, the high-SDI regions also had a higher life expectancy than the low SDI regions.[15] Therefore, more effective interventions, such as comprehensive control of diabetes should be carried out to reverse this trend, especially in high-SDI countries.

There were several limitations of this study. First, the accuracy and robustness of GBD estimates depend to a large extent on the quality and quantity of surveillance data used in the modelling. Existing positive surveillance systems are not sensitive, and mild UTIs due to asymptomatic bacteriuria are less likely to be diagnosed and reported. Antibiotics for the treatment of UTIs seem to be a relatively easy treatment, and antibiotic self medication is highly prevalent in the developing countries due to wild availability and poor regulatory controls for selling these drugs.[40] In addition, high-quality epidemiological studies (especially on incidence and disease severity) are still rare for large portions of the world, especially in low-income regions. Thus, there might be substantial underreporting of UTIs cases in many countries. Second, the roles of specific risk factors for UTIs were not estimated, and such information could help to explain geographic and temporal patterns in the disease burden. Another limitation of our study was the inability to distinguish uncomplicated and complicated UTIs, CAUTIs and HAUTIs, which may have different outcomes.

## **Conclusion**

Despite its limitations, the present study provides the most comprehensive review of UTI burden at the global, regional and national levels. The study results suggest a globally rising trend of UTI burden between 1990 and 2019. We highlight global and regional trends that can help to inform global and local interventions to lower UTI burden and curtail the increasing number of incident cases, especially in females and high-SDI countries.

## **Declarations**

### **Ethical Approval and Consent to participate**

Not applicable.

### **Consent for publication**

Not applicable.

### **Availability of data and materials**

Not applicable.

## Competing interests

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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## Author contributions

ZLZ and JZ contributed equally to this paper. JZ and HLC designed the study, had full access to all data in the study, and take responsibility for the integrity and accuracy of the data analysis. KMZ and JZ contributed to data collection, data analysis, data interpretation, and the literature search. ZLZ and HLC drafted the manuscript. SC final revised the manuscript. All authors contributed to data acquisition, data analysis, or data interpretation, and all reviewed and approved the final version of the manuscript.

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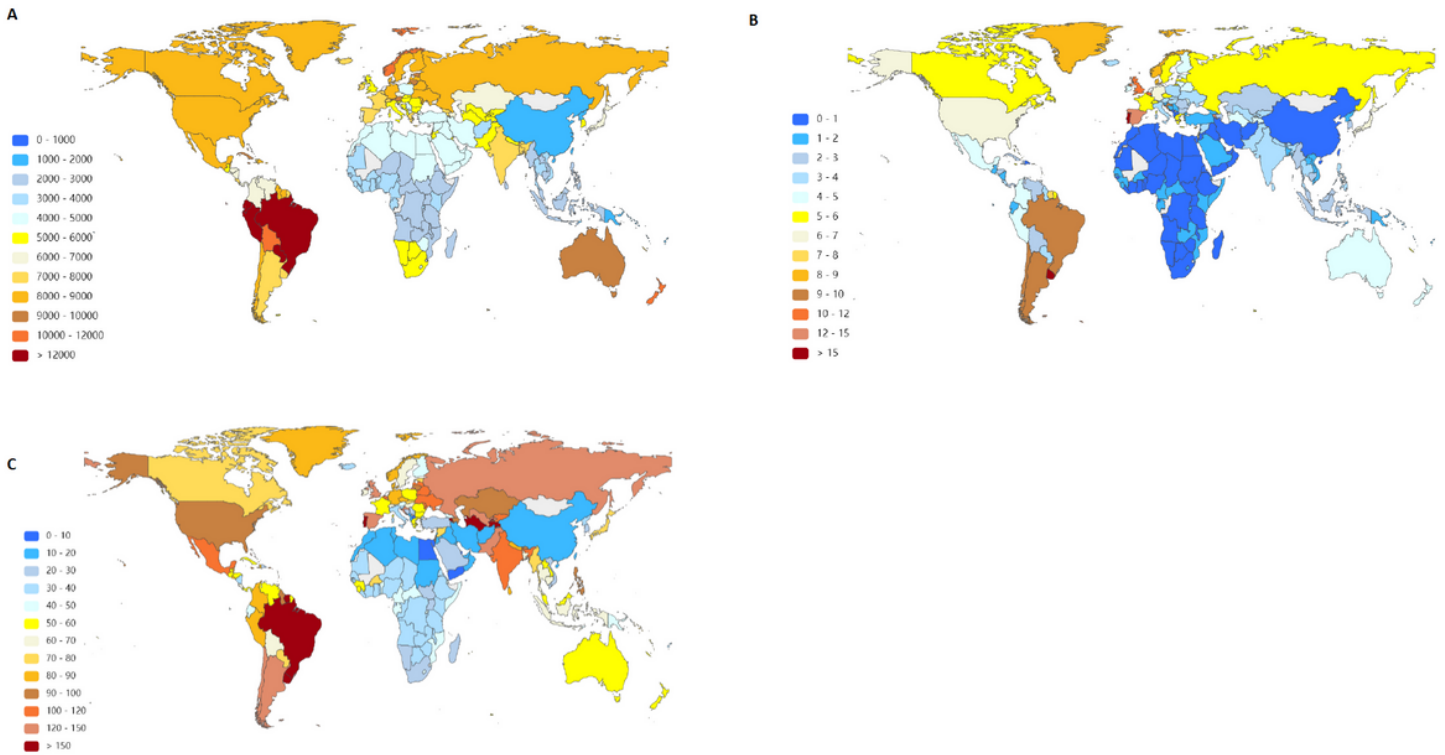
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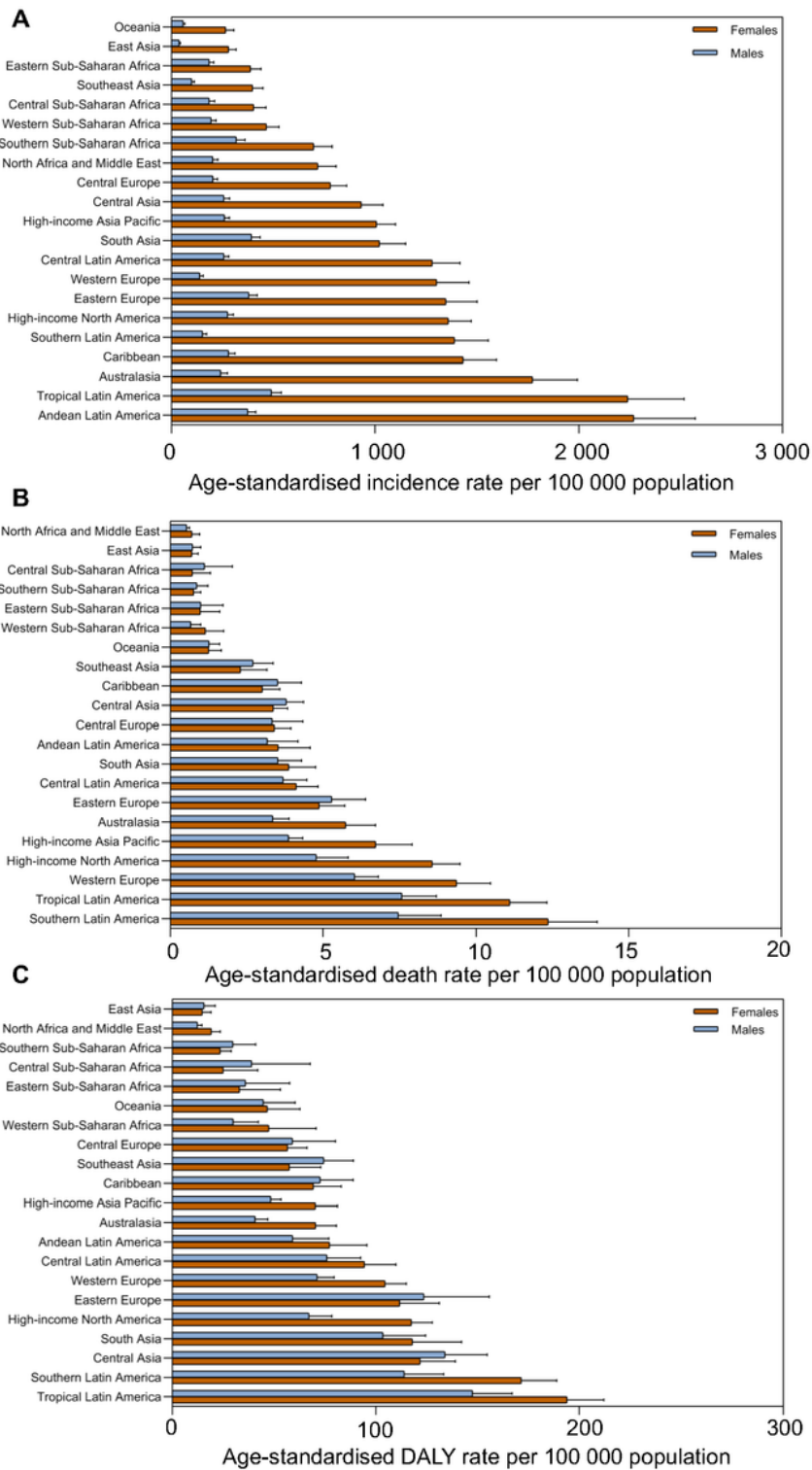
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## Figures



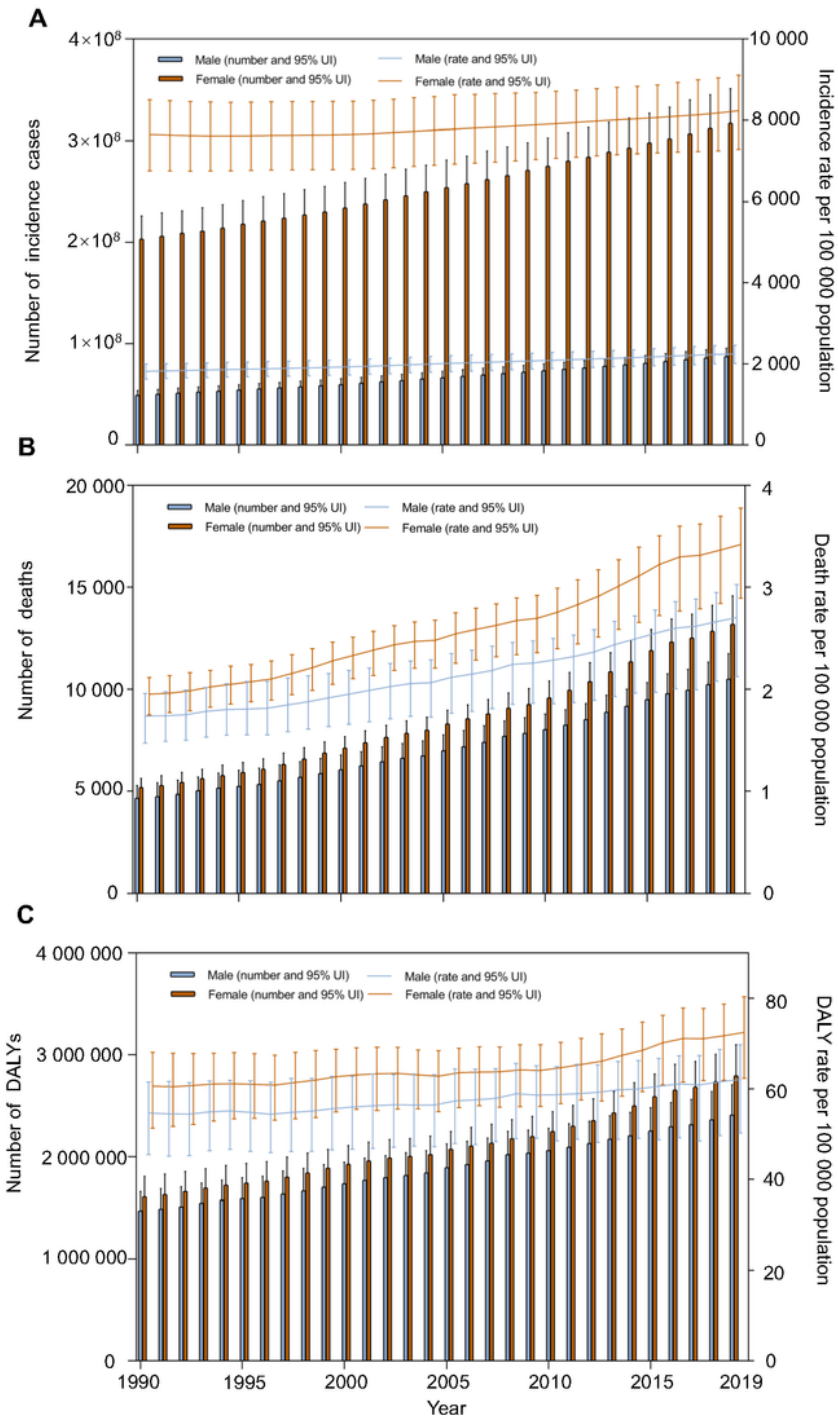
**Figure 1**

A. Global age-standardised incidence rates of UTIs in 2019 B. Global age-standardised death rates of UTIs in 2019 C. Global age-standardised DALY rates of UTIs in 2019



**Figure 2**

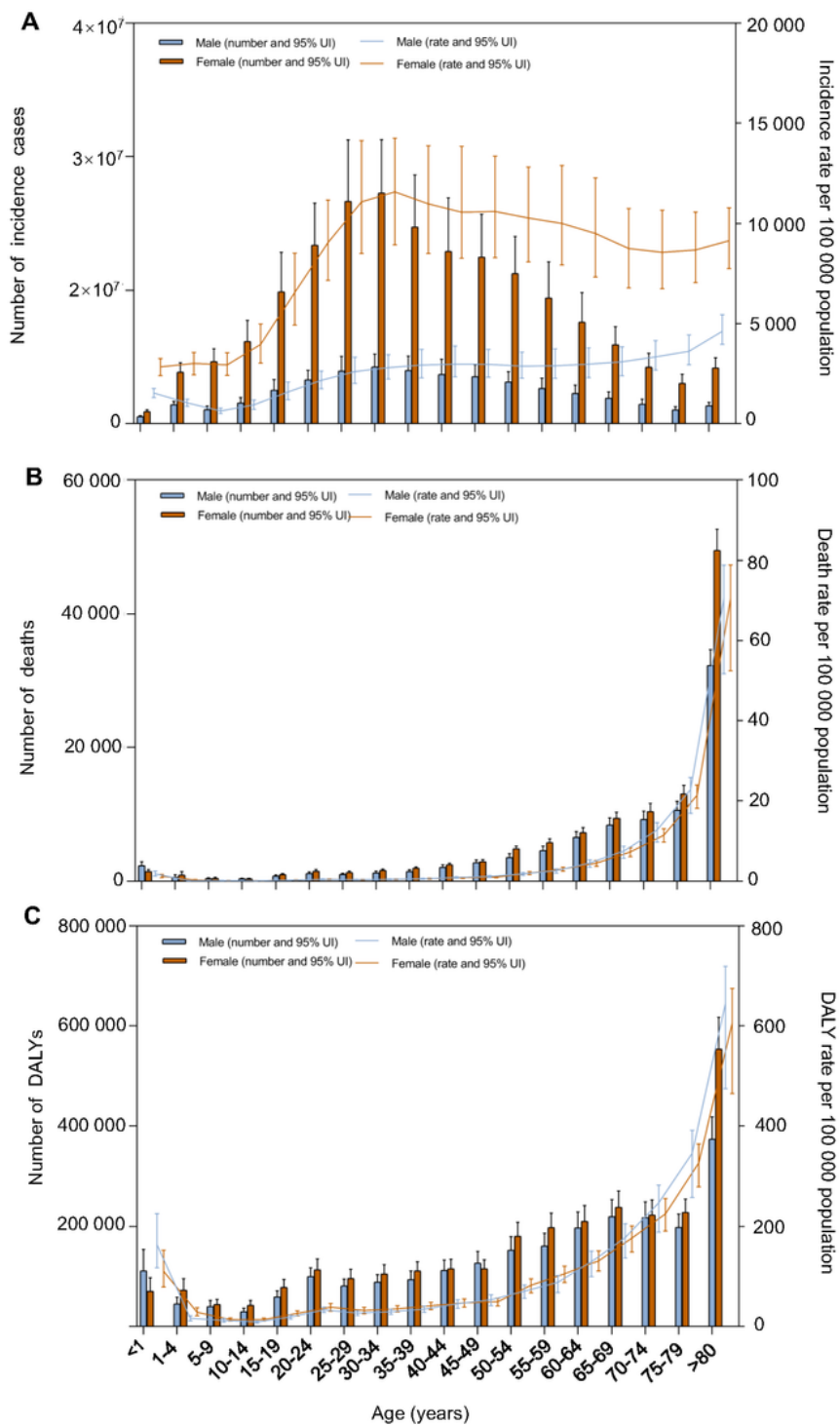
The age-standardised incidence (A), death (B) and DALY rates of UTIs in 2019 for 21 GBD regions, by sex



**Figure 3**

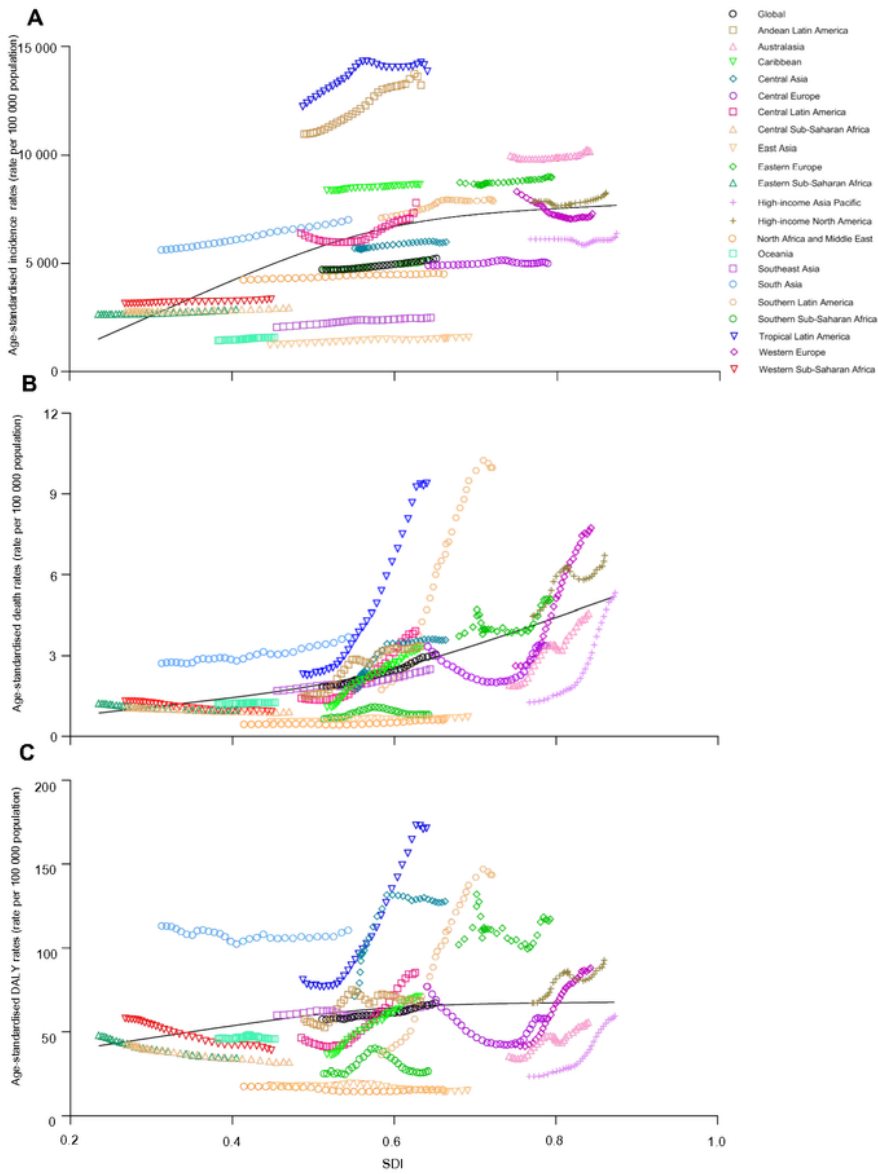
Trends from 1990 to 2019 in number and age-standardised rates of incidence (A), death (B), and DALY (C) of UTIs at the global level, by sex





**Figure 4**

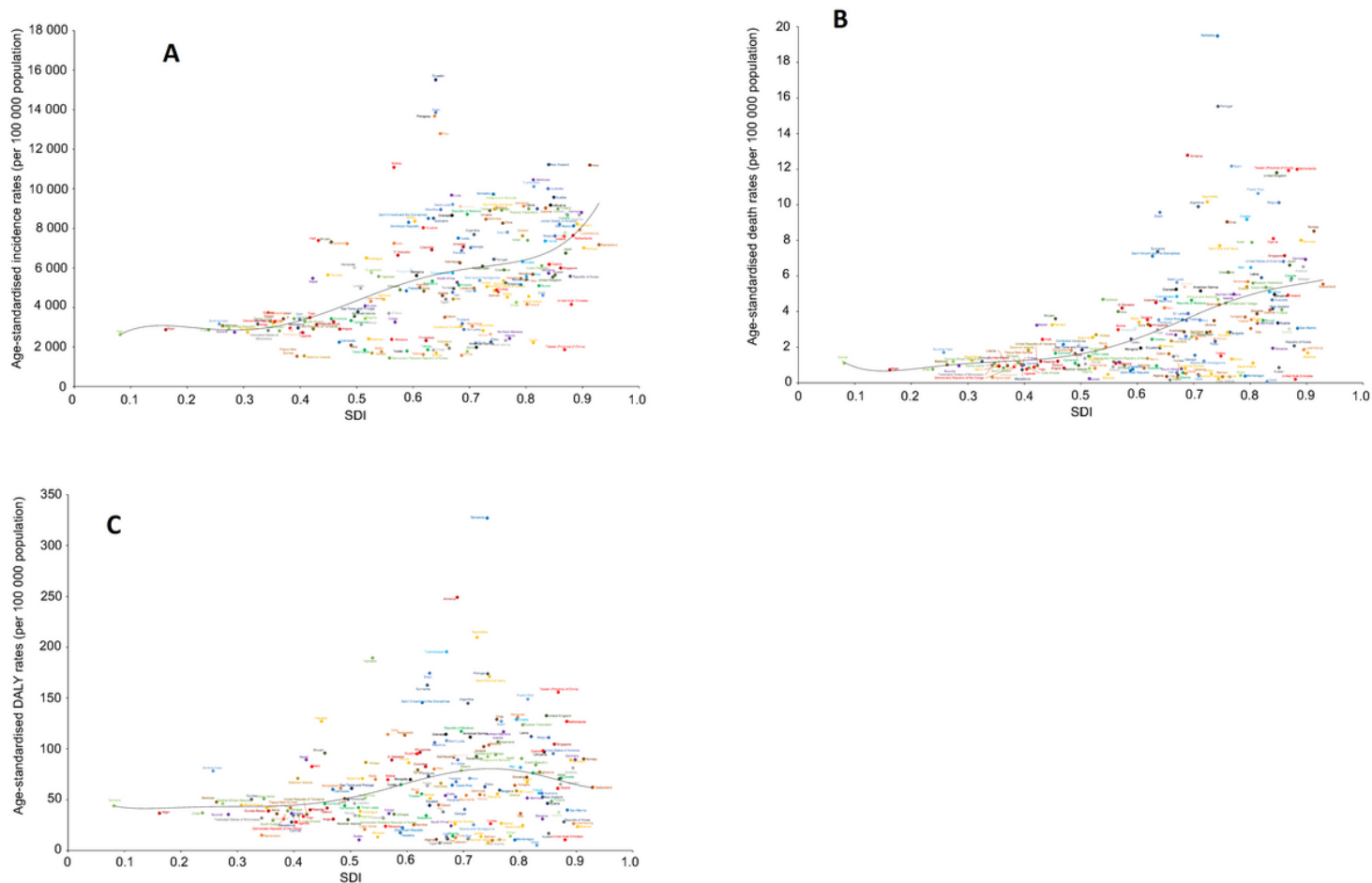
Global number and age-standardised rates of incidence (A), death (B) and DALY (C) of UTIs per 100 000 population by age and sex, 2019



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**Figure 5**

Global number and age-standardised rates of incidence (A), death (B) and DALY (C) of urinary tract infection per 100 000 population by SDI, 1999-2019



**Figure 6**

A. Age-standardised incidence rates of UTIs for 204 countries and territories by SDI 2019 B. Age-standardised death rates of UTIs for 204 countries and territories by SDI 2019 C. Age-standardised DALY rates of UTIs for 204 countries and territories by SDI 2019

## Supplementary Files

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