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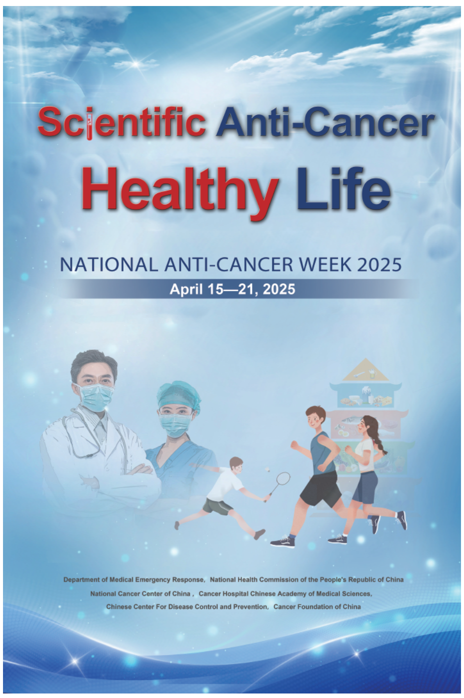

Preplanned Studies

Vital Surveillances

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Preplanned Studies

Temporal Trends and Sex Differences in the Incidence of Esophageal Squamous Cell Carcinoma and Adenocarcinoma from CI5 VIII–XII Data — Global, 1993–2017

Jiayue Li[1]; Kexin Sun[1]; Qian Zhu[1]; Xiaolan Wen[1]; Xinmei Lin[1]; Li Li[1]; Ru Chen[1]; Rongshou Zheng[1]; Wenqiang Wei[1]; Shaoming Wang[1,#]

Summary

What is already known about this topic?

Esophageal cancer (EC) consists of two main histological subtypes: esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC), each with distinct epidemiological patterns. Historically, ESCC has been the dominant subtype worldwide, especially in Asian countries. However, in recent decades, the incidence of EAC has been rising rapidly, particularly in European and American countries, reflecting significant shifts in global EC epidemiology.

What is added by this report?

This study presents a comprehensive analysis of 25 years of high-quality continuous data on ESCC and EAC incidence trends across 25 countries. It highlights declining ESCC rates in most regions, rising EAC rates in Western nations, pronounced sex differences, and narrowing ESCC-to-EAC ratios. These diverse trends reveal the need to investigate region-specific risk factors and their contributions to the shifting burden of EC globally.

What are the implications for public health practice?

The distinct trends of ESCC and EAC call for tailored public health strategies based on regional and histological patterns. Countries experiencing a rising burden of EAC or ESCC can implement targeted risk factor prevention and control measures to address the increasing trends. In clinical practice, a stronger focus on EAC in high-income countries and ESCC in regions, where it remains dominant, can improve early detection and treatment outcomes. Understanding these evolving patterns will aid in designing evidence-based interventions and optimizing resource allocation to reduce the global esophageal cancer burden effectively.

ABSTRACT

Introduction: Esophageal squamous cell carcinoma (ESCC) and adenocarcinoma (EAC) are the two primary subtypes of esophageal cancer. Historically, ESCC incidence has exceeded EAC, particularly in East Asia, Southern Africa, and parts of South America. However, in recent decades, EAC incidence has risen markedly in high-income countries due to lifestyle changes. Using the latest Cancer Incidence in Five Continents (CI5) data, we aimed to analyze global temporal trends and sex differences in the burden of ESCC and EAC.

Methods: We extracted ESCC and EAC incidence data from 25 countries in CI5 Volumes VIII-XII (1993–2017) for trend analysis. Age-standardized incidence rates (ASIRs) and ESCC-to-EAC ASIR ratios were calculated using Segi's World Standard Population, and annual percentage changes were estimated using Joinpoint regression. Additionally, we evaluated male-to-female ASIR ratios using data from 53 countries in CI5 Volume XII (2013–2017).

Results: Between 1993–2017, ESCC ASIRs declined in 19 countries but increased in Japan, the Czech Republic, Latvia, Denmark, and Lithuania. Conversely, EAC ASIRs increased in 17 countries, with the Republic of Korea being the only country reporting a decline. ESCC-to-EAC ASIR ratios narrowed in most countries, with EAC surpassing ESCC among males in 10 countries, including the United States, and among females only in the Philippines. From 2013–2017, males exhibited consistently higher ASIRs than females for both subtypes, with more pronounced sex differences observed for EAC.

Conclusions: This study highlights the changing epidemiology of ESCC and EAC globally and provides important scientific evidence for tailoring prevention and control strategies based on regional and histological-specific trends.

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Esophageal cancer (EC) is among the top ten causes of cancer-related mortality worldwide, with notable geographical and histological variation. The two primary subtypes, esophageal squamous cell carcinoma (ESCC) and adenocarcinoma (EAC) (*1*), differ significantly in risk factors, incidence trends, and regional distribution. Historically, ESCC has been the predominant subtype globally, particularly in the East Asia, Southern Africa, and parts of South America. In contrast, EAC incidence has risen markedly in high-income countries over recent decades (*2*), driven by lifestyle changes and raising public health concerns. Using data from Cancer Incidence in Five Continents (CI5) Volumes VIII–XII (1993–2017), this study provides a detailed analysis of ESCC and EAC trends across 25 countries, focusing on age-standardized incidence rates (ASIRs), sex differences, and the evolution of ESCC-to-EAC ASIR ratios. Between 1993 and 2017, ESCC ASIRs declined in 19 countries but increased in others, including Japan, the Czech Republic, Latvia, Denmark, and Lithuania. Conversely, EAC ASIRs increased in 17 countries, with the Republic of Korea being the only country to report a decline. Narrowing ESCC-to-EAC ASIR ratios were observed in most countries, with EAC surpassing ESCC among males in 10 countries, including the United States, the United Kingdom, and Germany, and among females only in the Philippines. From 2013 to 2017, males consistently exhibited higher ASIRs than females for both subtypes, with more pronounced sex differences in EAC. These findings highlight the evolving epidemiology of EC subtypes and offer valuable insights for tailoring prevention and control strategies to regional and histological-specific trends.

We extracted data on the incidence of ESCC and EAC by year of diagnosis, sex, and 5-year age group from national and regional population-based cancer registries included in CI5 VIII to XII (*3*). From 103 cancer registries across 39 countries reporting 25 consecutive years of data (1993–2017), we excluded registries with fewer than five ESCC/EAC cases (*n*=50), populations below 500,000 (*n*=0), or over 75% of EC cases are classified as unspecified (*n*=0) in each volume (Supplementary Figure S1, available athttps://weekly.chinacdc.cn/). When national data were unavailable, we aggregated regional registries. In total, 53 registries from 25 countries were included in trend analysis from 1993 to 2017. Additionally, we analyzed 248 registries from 53 countries in CI5 Volume XII (2013–2017) to evaluate sex differences at the country level. ASIRs were calculated using Segi's World Standard Population, and annual percentage changes (APCs) were estimated using Joinpoint regression. Statistical analyses were performed using R, version 4.2.3 (R Foundation for Statistical Computing, Vienna, Austria) and the Joinpoint Regression Program, version 5.2.0.0 (Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute).

From 1993 to 2017, the ASIRs for ESCC declined significantly in 19 countries, with the most substantial decline observed in the Philippines [APC −6.71%, 95% confidence interval (*CI*): −10.42% to −3.53%]. However, significant increasing trends were identified in five countries, with Latvia showing the highest increase (APC 4.92%, 95% *CI*: 2.11% to 8.60%) (Table 1). For EAC, ASIRs increased significantly in 17 countries, with the Czech Republic experiencing the most dramatic rise (APC 6.27%, 95% *CI*: 4.86% to 8.19%). In contrast, the Republic of Korea was the only country to report a significant decline in EAC incidence (APC −3.84%, 95% *CI*: −4.86% to −2.77%). Among males, notable reductions in ESCC ASIRs were observed in Italy (APC −4.83%, 95% *CI*: −5.31% to −4.34%), while the most pronounced increase in EAC ASIRs was reported in Norway (APC 5.18%, 95% *CI*: 4.28% to 6.37%). Similarly, females in the Philippines demonstrated the most significant reduction in ESCC ASIRs, whereas females in the Czech Republic exhibited the largest rise in EAC ASIRs (Table 1).

Although ASIRs for ESCC have historically been higher than those for EAC, the ESCC-to-EAC ASIR ratios gradually and significantly narrowed in most countries from 1993 to 2017, driven by declining ASIRs for ESCC and rising ASIRs for EAC. Exceptions to this trend were observed in Lithuania, where the ratio increased from 6.07 to 10.22, and in the Republic of Korea, where it rose substantially from 15.87 to 39.25. By 2017, EAC ASIRs surpassed ESCC ASIRs among males in 10 countries, including Australia, Canada, Denmark, Germany, Ireland, Israel, Norway, the Netherlands, the United Kingdom, and the United States. Among females, this transition occurred only in the Philippines. In contrast, Asian countries such as India, Japan, and the Republic of Korea continued to report ESCC ASIRs more than ten times higher than those for EAC (Figure 1).

Sex-specific analyses showed that males consistently

TABLE 1. The trends in age-standardized incidence rates of esophageal squamous cell carcinoma and esophageal adenocarcinoma by sex and country from 1993 to 2017.

Country	APC, % (95% *CI*)					
	ESCC			EAC		
	Both	Males	Females	Both	Males	Females
Australia	−1.83 (−2.44, −1.22)*	−1.68 (−2.65, −0.66)*	−2.03 (−3.14, −0.91)*	1.81 (0.62, 3.26)†	1.77 (0.49, 3.32)†	1.29 (−0.04, 2.82)
Canada	−2.53 (−4.06, −1.01)*	−2.61 (−4.67, −0.53)*	−2.35 (−4.19, −0.55)*	2.54 (1.77, 3.50)†	2.29 (1.17, 3.68)†	3.43 (1.85, 5.52)†
Colombia	−4.90 (−10.25, 0.35)	−4.25 (−7.51, −1.20)*	−5.37 (−10.23, −0.62)*	−1.85 (−5.21, 1.91)	−1.42 (−5.01, 2.79)	−1.63 (−8.10, 6.31)
Croatia	−1.77 (−2.75, −0.88)*	−2.00 (−3.27, −0.82)*	−1.20 (−6.20, 3.53)	3.59 (1.54, 6.00)†	3.99 (1.18, 7.55)†	0.21 (−4.27, 4.88)
Czech Republic	1.38 (0.96, 1.84)†	0.73 (0.56, 0.91)†	4.91 (2.25, 8.38)†	5.07 (3.17, 7.62)†	4.67 (2.95, 7.00)†	6.27 (4.86, 8.19)†
Denmark	0.73 (−0.41, 2.00)	0.72 (−0.98, 2.64)	0.65 (0.39, 0.95)†	2.28 (1.56, 3.13)†	1.90 (1.43, 2.47)†	3.26 (2.34, 4.38)†
France	−3.37 (−4.28, −2.55)*	−4.20 (−4.90, −3.57)*	0.55 (−0.54, 1.75)	1.75 (1.11, 2.44)†	1.75 (1.33, 2.22)†	0.56 (−2.98, 4.60)
Germany	−2.85 (−3.95, −1.85)*	−3.46 (−4.36, −2.59)*	−0.83 (−3.67, 1.84)	4.99 (1.41, 9.50)†	4.76 (−0.79, 11.74)	4.72 (0.58, 9.96)†
India	−3.65 (−4.41, −2.94)*	−3.71 (−6.59, −1.02)*	−3.51 (−4.42, −2.62)*	−2.26 (−10.79, 6.30)	−1.17 (−12.14, 10.76)	−4.63 (−14.13, 4.74)
Ireland	−1.16 (−1.85, −0.38)*	−1.16 (−2.43, 0.25)	−1.14 (−1.68, −0.56)*	1.36 (0.39, 2.51)†	1.39 (0.16, 2.90)†	0.49 (−1.16, 2.43)
Israel	−1.80 (−3.36, −0.24)*	−2.66 (−3.70, −1.65)*	−0.89 (−2.64, 0.91)	−0.93 (−1.95, 0.14)	−1.24 (−2.82, 0.41)	−0.24 (−2.24, 1.92)
Italy	−4.02 (−4.33, −3.69)*	−4.83 (−5.31, −4.34)*	−1.35 (−3.16, 0.96)	1.64 (1.01, 2.48)†	1.50 (0.62, 2.63)†	−0.04 (−2.69, 3.95)
Japan	2.50 (1.62, 3.48)†	2.23 (1.40, 3.15)†	3.49 (2.10, 5.05)†	4.46 (2.16, 7.15)†	4.46 (2.59, 6.65)†	3.15 (0.99, 5.63)†
Latvia	1.90 (0.25, 3.54)†	1.52 (−0.64, 3.64)	4.92 (2.11, 8.60)†	3.97 (−0.13, 8.60)	4.36 (2.83, 6.23)†	2.11 (−7.25, 11.66)
Lithuania	2.65 (−0.67, 6.40)	2.46 (−0.46, 5.79)	4.06 (2.63, 5.65)†	0.51 (−6.22, 7.50)	0.68 (−4.46, 5.89)	−0.39 (−4.78, 3.89)
New Zealand	−1.52 (−1.85, −1.18)*	−2.46 (−3.21, −1.73)*	−0.50 (−2.36, 1.53)	1.53 (−0.23, 3.62)	1.29 (−1.17, 4.26)	2.42 (1.64, 3.28)†
Norway	−1.50 (−2.20, −0.79)*	−2.16 (−2.79, −1.55)*	−0.20 (−1.25, 0.91)	5.37 (3.82, 7.58)†	5.18 (4.28, 6.37)†	4.96 (0.49, 11.10)†
Philippines	−4.52 (−7.34, −1.94)*	−3.68 (−7.28, −0.29)*	−6.71 (−10.42, −3.53)*	−0.28 (−3.59, 3.71)	−0.76 (−5.09, 4.19)	0.79 (−4.21, 7.60)
Slovenia	−2.13 (−3.17, −1.13)*	−2.83 (−3.82, −1.91)*	0.70 (−2.51, 4.09)	2.90 (−0.82, 7.32)	3.26 (1.08, 6.04)†	−1.40 (−12.64, 9.02)
Republic of Korea	0.10 (−0.63, 1.02)	−0.29 (−1.35, 1.00)	0.20 (−2.11, 3.13)	−3.84 (−4.86, −2.77)*	−4.05 (−7.71, 0.11)	−4.47 (−9.72, 0.52)
Spain	−2.81 (−4.84, −0.98)*	−3.18 (−5.28, −1.34)*	1.56 (−4.02, 7.51)	3.48 (0.80, 6.56)†	3.52 (0.77, 6.83)†	0.80 (−1.61, 3.27)
Switzerland	−2.55 (−3.30, −1.84)*	−3.05 (−3.16, −2.95)*	−1.45 (−4.28, 1.39)	1.58 (−0.03, 3.40)	1.44 (−0.82, 4.07)	0.63 (−0.19, 1.50)
The Netherlands	−0.34 (−1.27, 0.69)	−0.96 (−1.68, −0.19)*	0.52 (−0.08, 1.19)	4.57 (2.84, 6.97)†	4.39 (1.92, 7.82)†	4.28 (3.51, 5.24)†
United Kingdom	−1.41 (−1.75, −1.08)*	−1.57 (−2.07, −1.09)*	−1.30 (−2.06, −0.56)*	1.32 (0.98, 1.69)†	1.41 (0.99, 1.85)†	0.38 (0.06, 0.70)†
United States	−3.47 (−3.94, −3.06)*	−3.73 (−3.97, −3.52)*	−3.09 (−4.21, −2.04)*	1.42 (−0.33, 3.44)	1.27 (−0.47, 3.29)	1.55 (−0.57, 3.99)

Abbreviation: APC=annual percentage change; ESCC=esophageal squamous cell carcinoma; EAC=esophageal adenocarcinoma; *CI*=confidence interval.

* indicates significant decreasing trends.

† indicates significant increasing trends.

had higher ASIRs for both ESCC and EAC compared to females across most countries, with more pronounced sex differences observed for EAC, as shown in Figure 2. Particularly striking disparities were observed in countries such as Ukraine, Spain, Poland, Lithuania, Latvia, and France, where male-to-female ASIR ratios exceeded 10.0∶1. However, even greater sex disparities were noted in specific countries for ESCC, including Ukraine, the Republic of Korea, and Belarus, with male-to-female ASIR ratios of 16.67∶1, 13.37∶1, and 15.58∶1, respectively.

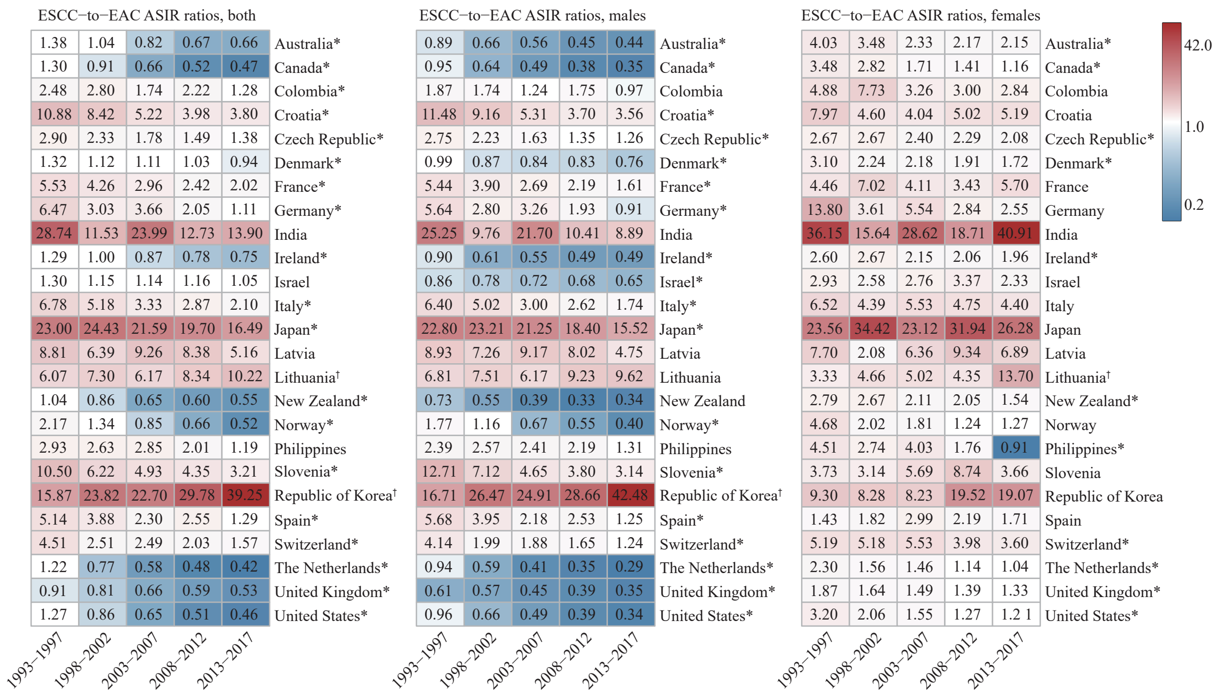

FIGURE 1. The ratios of age-standardized incidence rates for esophageal squamous cell carcinoma and esophageal adenocarcinoma by sex and country from 1993 to 2017.
Note: Blue represents ESCC<EAC, and red represents ESCC>EAC.
Abbreviation: ASIR=age-standardized incidence rates; ESCC=esophageal squamous cell carcinoma; EAC=esophageal adenocarcinoma.
* indicates significant decreasing trends.
† indicates significant increasing trends.

DISCUSSION

Our study highlights the contrasting trajectories of ESCC and EAC incidence globally. The declining ASIRs for ESCC in many countries reflect shifts in the prevalence of underlying risk factors, including reduced tobacco and alcohol consumption and improved dietary practices. In contrast, the rising ASIRs for EAC in high-income countries, consistent with prior studies (*2*), are linked to increasing rates of obesity (*4*), gastroesophageal reflux disease (GERD), and Barrett's esophagus, emphasizing the impact of lifestyle changes on these trends. The significant narrowing of ESCC-to-EAC ratios, coupled with pronounced sex differences, underscores the growing public health burden of EAC in high-income settings and highlights the need for tailored prevention strategies that address regional and sex-specific risk factors to reduce the global burden of esophageal cancer.

The persistent dominance of ESCC in Asia, compared to the rising burden of EAC in Western countries, reflects significant regional differences in risk factors. In Asia, high rates of tobacco smoking (*5*), heavy alcohol consumption, and diets rich in salted and pickled foods are major drivers of ESCC. Additionally, the interplay of *Helicobacter pylori* (*H. pylori*) infection and low body mass index (BMI) contributes to the high ESCC burden. In contrast, European and American countries have experienced a sharp rise in EAC incidence, driven by increasing obesity rates, GERD (*6*), and Barrett's esophagus. The lower prevalence of *H. pylori* infection in Western nations, due to improved sanitation and antibiotic use, may paradoxically offer less protection against EAC.

The contrasting trends in ESCC and EAC across countries provide valuable insights into esophageal cancer epidemiology. In Japan, the rising incidence of both ESCC and EAC reflects persistent risk factor prevalence and the impact of an aging population. Conversely, the Republic of Korea demonstrates stable ESCC trends and declining EAC incidence, likely attributable to effective smoking cessation programs, public health initiatives reducing alcohol consumption, improved dietary patterns, and lower rates of obesity and GERD. National screening programs for upper gastrointestinal cancers in both countries have further

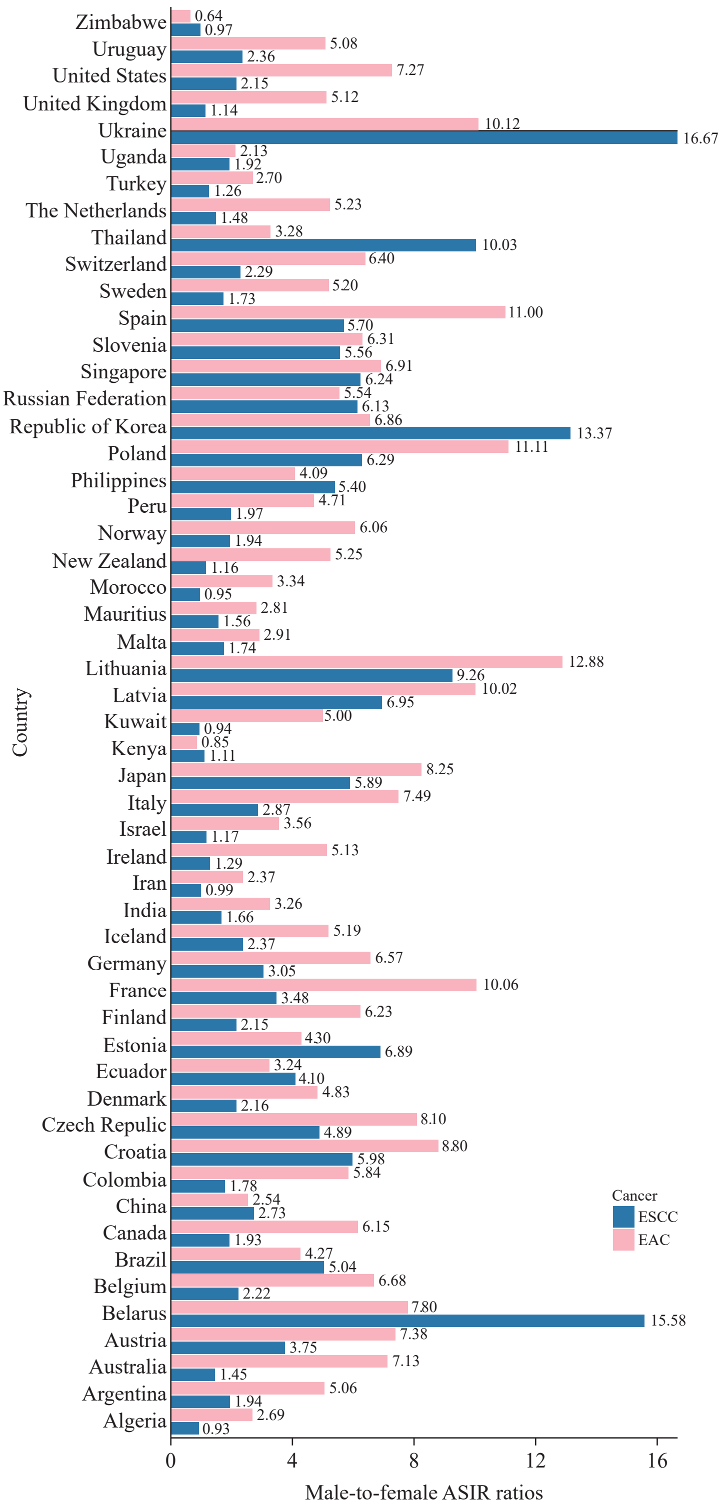

FIGURE 2. The male-to-female age-standardized incidence rate ratios for esophageal squamous cell carcinoma and esophageal adenocarcinoma by country from 2013 to 2017.
Abbreviation: ASIR=age-standardized incidence rate; ESCC=esophageal squamous cell carcinoma; EAC=esophageal adenocarcinoma.

influenced these trends by enabling early detection and timely interventions, particularly among high-risk populations such as smokers and heavy drinkers.

The persistent male predominance in both ESCC and EAC underscores the significant influence of sex-specific factors, including hormonal differences and lifestyle behaviors such as smoking and alcohol consumption (*7–10*). The pronounced male-to-female disparity in EAC, along with exceptionally high male-to-female ratios of ESCC in countries like Ukraine, Republic of Korea, Lithuania, and Belarus, warrants further investigation into underlying biological mechanisms and environmental determinants.

Our study has several limitations. Although this analysis relied on high-quality cancer registry data from CI5, it may have limitations in histological classification accuracy and population coverage. Regional data may not fully reflect national trends, especially in low- and middle-income countries. Furthermore, the lack of continuous histological data excluded several populous nations, including China, which bears the highest global burden of ESCC. This omission limits comprehensive assessment of global trends and the impact of histological transitions in esophageal cancer. Additionally, the ecological design precludes individual-level analysis of risk factors.

In conclusion, this comprehensive analysis of ESCC and EAC incidence trends highlights the shifting global burden of esophageal cancer. The findings reveal declining ESCC incidence in most countries, rising EAC incidence in high-income countries, and pronounced male predominance in both subtypes. Tailored prevention strategies that address regional and sex-specific risk factors are essential for reducing the global burden of esophageal cancer.

Conflicts of interest: No conflicts of interest.

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Ethical statement: Ethical approval is not applicable to our study.

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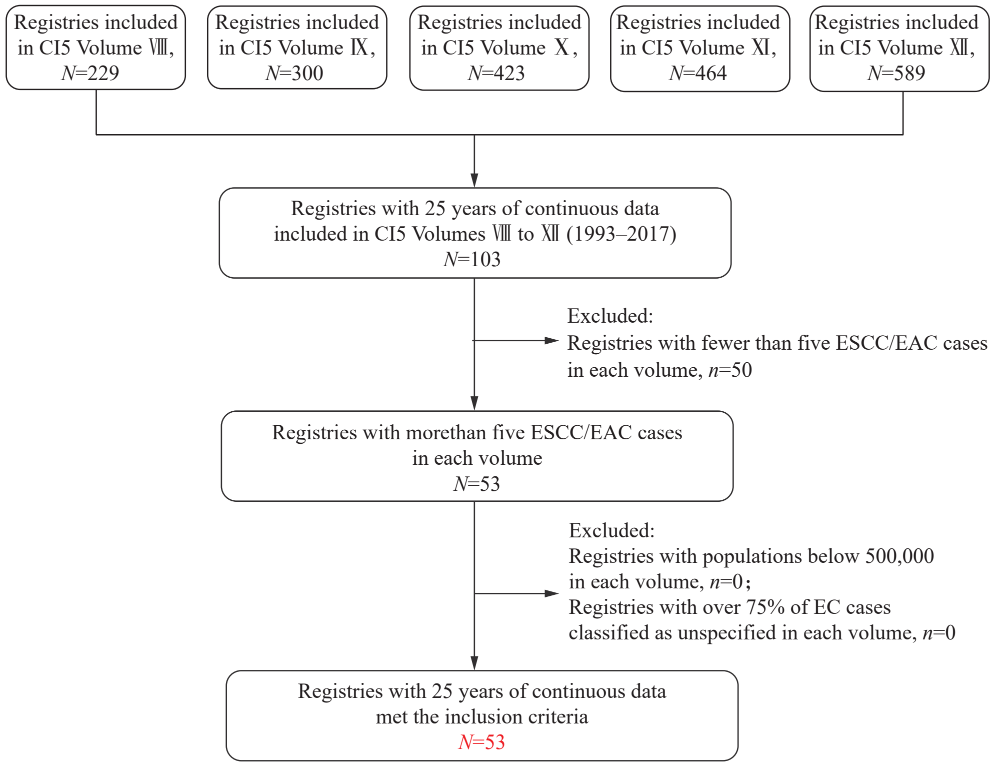
SUPPLEMENTARY MATERIAL



SUPPLEMENTARY FIGURE S1. Flowchart illustrating the selection process for ESCC and EAC data, including registry inclusion and exclusion criteria.
Note: Red indicates the number of registries ultimately included in the analysis.
Abbreviation: ESCC=esophageal squamous cell carcinoma; EAC=esophageal adenocarcinoma.

Preplanned Studies

Decomposition Analysis of Urban-Rural Disparities in Healthy Life Expectancy Among Older Adults — China, 2010–2020

Shuai Guo[1,&]; Jiatong Gao[2,&]; Yuling Li[2]; Zuliyaer Talifu[2]; Xu Wen[3,#]; Xiaoying Zheng[1,#]

Summary

What is already known about this topic?

As China's population ages rapidly, there is growing concern about whether increases in life expectancy are accompanied by improvements in healthy longevity for older adults.

What is added by this report?

From 2010 to 2020, healthy life expectancy expanded across different subgroups of the older population. Although urban-rural disparities in healthy life expectancy narrowed, morbidity has emerged as the primary contributor to these gaps, with the age groups driving these differences shifting toward older ages.

What are the implications for public health practice?

As longevity increases, health inequalities are transitioning from mortality-focused to morbidity-driven. This trend underscores the need for healthcare and elder care systems to address non-fatal health conditions affecting quality of life, particularly for women and the oldest-old.

ABSTRACT

Introduction: As China's population rapidly ages, concerns have emerged about whether increased longevity among older adults is accompanied by improvements in health status.

Methods: This study analyzed data from the 2010 and 2020 Chinese censuses to estimate healthy life expectancy (HLE) at age 60 and examined changes in urban-rural disparities and their driving factors. We applied the Sullivan method to estimate gender- and residence-specific HLE, while using the continuous change decomposition method to analyze how mortality and health status contributed to urban-rural differences.

Results: Between 2010 and 2020, both the absolute years of HLE and its proportion of total life expectancy increased, with the urban-rural gap narrowing over time. However, the primary driver of urban-rural HLE disparities has shifted from mortality levels to health status, a pattern more pronounced among men. Decomposition analysis further reveals that compared to 2010, the key age groups contributing to urban-rural HLE disparities in 2020 have shifted to older ages, reflecting a transition in health inequalities as the population ages. These findings suggest that while HLE among China's older population has improved, the nature of health inequalities is evolving.

Conclusions: Future public health policies should place greater emphasis on addressing non-fatal health conditions, particularly in rural areas and among the oldest-old, by improving the accessibility and quality of health services to promote healthy aging and reduce urban-rural health disparities.

In 2023, China's average life expectancy (LE) reached 78.6 years, nearing the 2030 target of 79.0 years set by Healthy China 2030, signaling continuous improvements in longevity (*1*). While mortality provides insight into population health, population aging coupled with epidemiologic transition may cause divergence between mortality and morbidity. Specifically, increases in LE are often accompanied by more years lived in poor health. As such, public health focus should shift toward achieving "healthy longevity," with healthy life expectancy (HLE) serving as a critical indicator that reflects both quality and length of life (*2*). Moreover, considering that LE at birth is less sensitive to mortality changes in older adults, LE and HLE of the older population have become more suitable measures for evaluating population health in aging societies. Previous research has examined trends in HLE and its disparities among China's older population (*3*–*4*). However, the distinct contributions of mortality and morbidity, as well as the specific age groups contributing to these differences, remain underexplored. This study, using mortality and self-rated health data from the 2010 and 2020

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censuses, applied the Sullivan method to estimate LE and HLE at age 60 by urban-rural residence. Additionally, we conducted continuous change decomposition analysis to assess the age-specific contributions of mortality and morbidity to the urban-rural HLE gap. Our findings reveal that older adults have become "longer-lived and healthier" between 2010 and 2020. The narrowing of urban-rural differences in HLE was the main driver behind the reduction in LE gaps. However, morbidity's contribution to urban-rural HLE gaps is increasing, particularly among older men, where the main contribution has shifted from mortality to morbidity. Furthermore, the age groups driving these differences are themselves aging over time. While China's older population demonstrates a clear trend toward the compression of morbidity, non-fatal health outcomes continue to significantly impact health disparities between population groups. This suggests that as longevity continues to improve, it is essential to not only ensure that additional years are spent in good health but also to pay closer attention to non-fatal health conditions and quality of life among rural populations and the oldest old.

Age-specific mortality and morbidity rates by gender and residence for 2010 and 2020 were derived from the sixth and seventh National Population Censuses. To obtain more accurate estimates of old-age mortality, we smoothed observed single age-specific mortality rates by fitting the Kannisto model for adults aged 80 and older, stratified by gender, residence, and time period (*5*). In this study, morbidity was measured using self-rated health (SRH). Health data for individuals aged 60 and above were collected through the question, "Your health status is ____?" Responses of "healthy" and "mostly healthy" were categorized as good SRH, while responses of "unhealthy but able to take care of yourself" and "disabled" were classified as poor SRH (*6*).

Based on mortality data, we constructed abridged life tables (with an open age group set at 90 years and older) for 2010 and 2020 by gender and urban-rural residence. Using age-specific morbidity rates for the corresponding populations, we employed the Sullivan method (*7*) to estimate HLE and unhealthy life expectancy (UHLE) at age 60. To analyze urban-rural disparities in HLE, we applied the continuous change decomposition method (*8*), which allowed us to decompose the urban-rural gaps for both 2010 and 2020. This approach facilitated the estimation of overall and age-specific contributions of mortality and disability. Statistical analyses were conducted using *R* (version 4.3.2; the R Core Team, Vienna, Austria).

Between 2010 and 2020, HLE increased in both absolute terms (years) and relative terms (proportion of HLE to LE) for both men and women, while the urban-rural gap in LE narrowed. In 2010, urban men had an LE of 21.95 years, 3.04 years longer than rural men (18.91 years). By 2020, this gap had decreased to 1.83 years (23.27 *vs*. 21.44 years). This narrowing primarily resulted from faster improvements in rural men's LE, which increased by 2.53 years compared to a 1.32-year increase among urban men during this period. Similar patterns were observed among women — the urban-rural gap in LE decreased from 2.91 years (24.96 *vs*. 22.05 years) to 2.03 years (26.72 *vs*. 24.69 years) between 2010 and 2020, driven by an increase of 2.64 years in rural women's LE compared to a 1.76-year increase in urban women's LE. However, the reduction in the urban-rural gap for women (0.88 years) was smaller than that for men (1.21 years) (Figure 1).

Decomposition results are presented in Table 1. In 2010, the urban-rural gap in HLE was larger for women than for men (4.04 *vs*. 3.78 years). Furthermore, the contributions of mortality and morbidity to this gap varied between genders. For men, 2.09 years (55.29%) of the gap was attributed to mortality, while 1.69 years (44.71%) were due to morbidity. In contrast, the gap among women was primarily driven by morbidity, accounting for 2.22 years (54.95%). By 2020, although the urban-rural gap in HLE remained larger for women than for men (3.18 *vs*. 2.78 years), morbidity became the dominant contributor to the gap for both genders (men: 1.43 years, 51.39%; women: 1.79 years, 56.29%).

Figure 2 further displays age-specific contributions of mortality and morbidity to the urban-rural gap by gender. In 2010, the largest contribution came from the 70–74 age group for both men (0.83 years, 22.06%) and women (0.89 years, 22.05%). By 2020, this shifted to the 75–79 age group, with contributions of 0.49 years (17.62%) for men and 0.64 years (20.12%) for women. In contrast to 2010, the contributions across the under-85 age groups in 2020 became more evenly distributed, with smaller differences in their respective values, particularly for men.

DISCUSSION

Based on the most recent census data from 2010 and

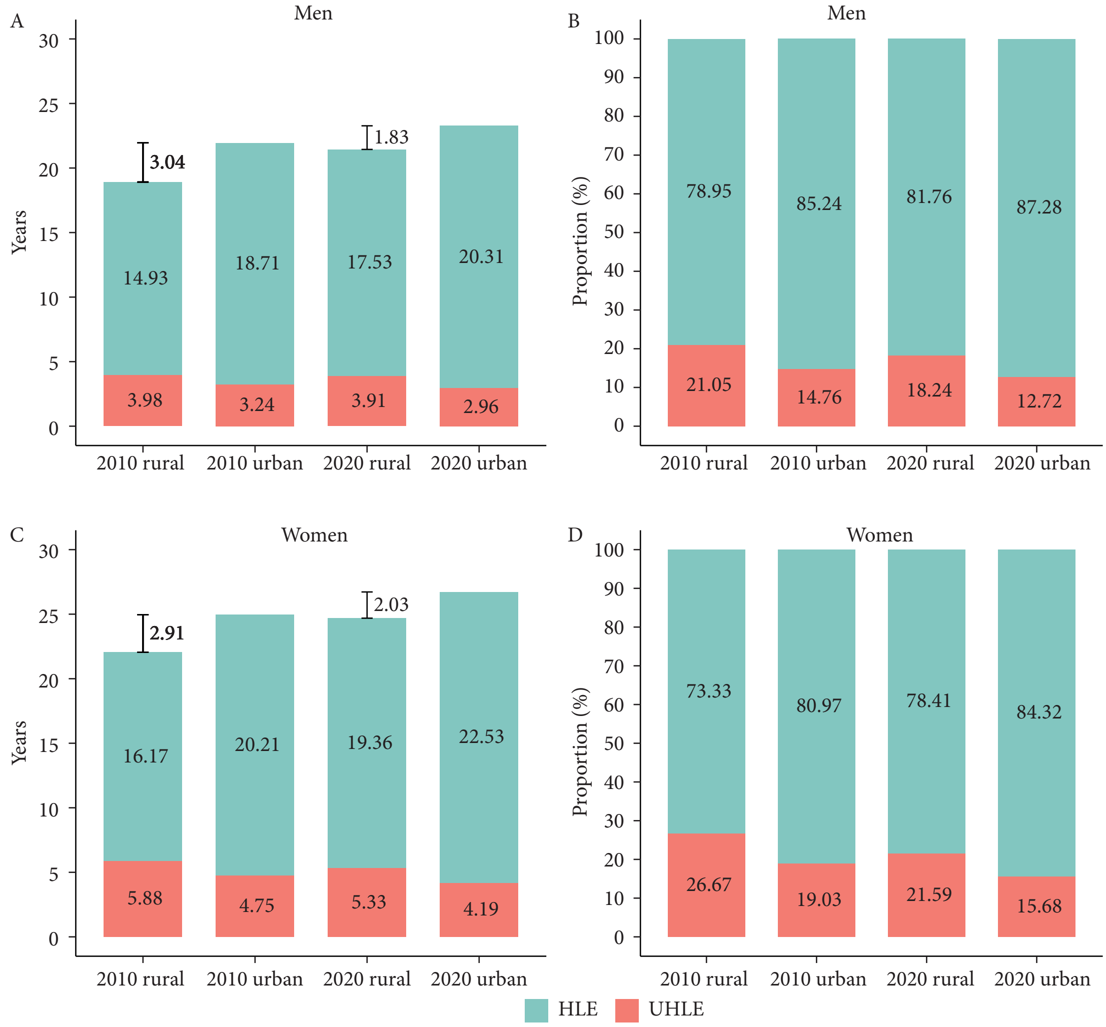

FIGURE 1. Healthy life expectancy and unhealthy life expectancy at age 60 by gender and residential area in 2010 and 2020. (A) HLE and UHLE in absolute terms among men; (B) HLE and UHLE in relative terms among men; (C) HLE and UHLE in absolute terms among women; (D) HLE and UHLE in relative terms among women.

Note: The vertical lines and numbers in the two charts on the left indicate the urban-rural disparities in life expectancy for each gender in 2010 and 2020.

Abbreviation: HLE=healthy life expectancy, UHLE=unhealthy life expectancy.

TABLE 1. Decomposition of the urban-rural gap in healthy life expectancy at age 60 by gender in 2010 and 2020.

Urban-rural HLE gap and its decomposition results	Men		Women	
	2010	2020	2010	2020
HLE, years				
(1) Urban	18.71	20.31	20.21	22.53
(2) Rural	14.93	17.53	16.17	19.35
(3) Difference	3.78	2.78	4.04	3.18
Contribution, years (%)				
(4) Mortality	2.09 (55.29)	1.35 (48.61)	1.82 (45.05)	1.39 (43.71)
(5) Morbidity	1.69 (44.71)	1.43 (51.39)	2.22 (54.95)	1.79 (56.29)

Note: The rows of the table have the following relationships: (3)=(1)−(2)=(4)+(5).

Abbreviation: HLE=healthy life expectancy.

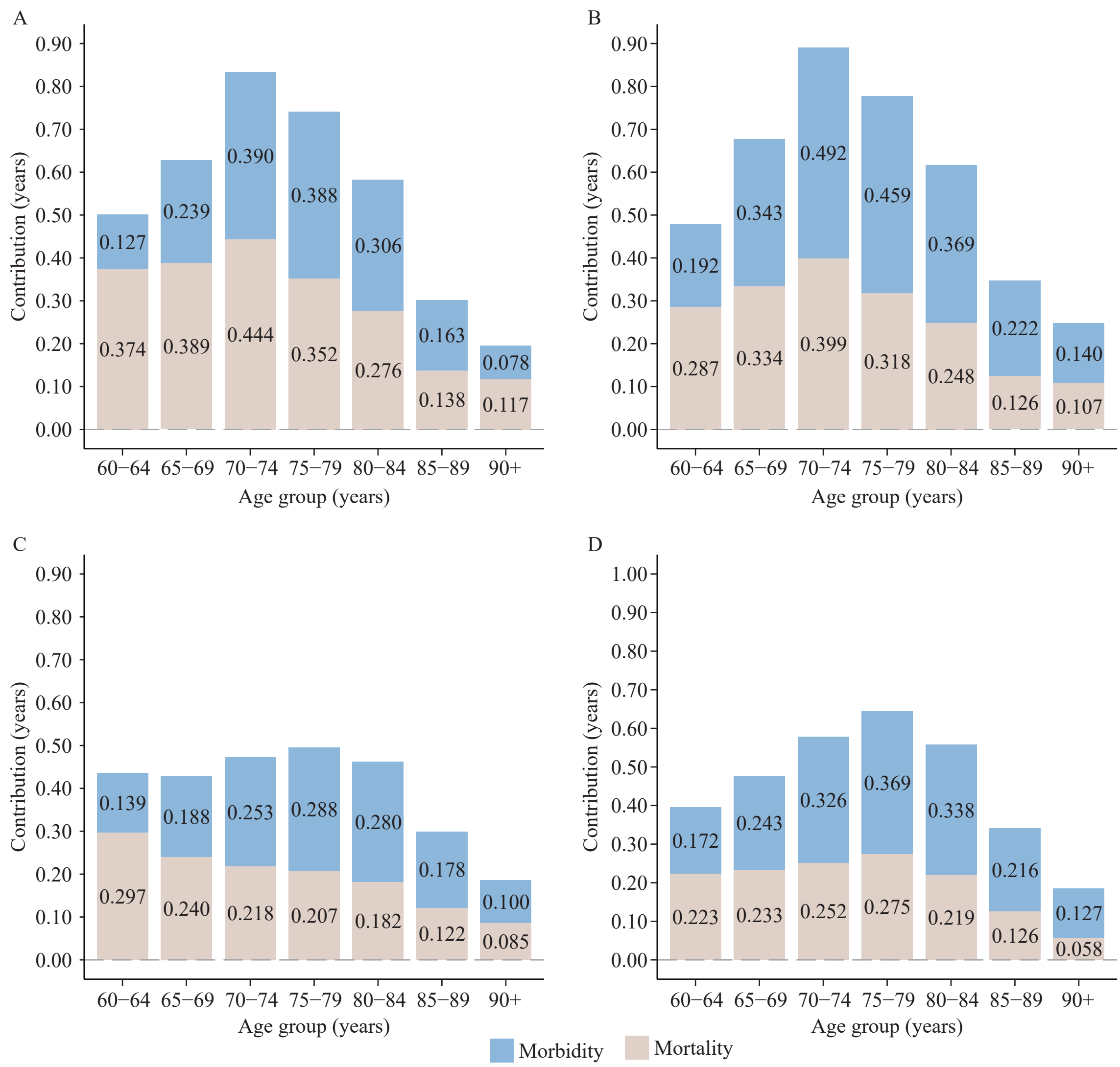

FIGURE 2. The contributions of mortality and morbidity to the urban-rural gap in healthy life expectancy by gender and 5-year age groups in 2010 and 2020. (A) Age-specific contributions among men in 2010; (B) Age-specific contributions among women in 2010; (C) Age-specific contributions among men in 2020; (D) Age-specific contributions among women in 2020.
Abbreviation: HLE=healthy life expectancy.

2020, we observed an upward trend in LE, HLE, and the ratio of HLE to LE among the older population, indicating a general expansion of healthy lifespan. Notably, the narrowing urban-rural gap in HLE suggests that older adults in rural areas have experienced greater health benefits from social development. However, the contribution of morbidity to the urban-rural disparity in HLE has become more pronounced, with older age groups increasingly contributing to this gap. These findings suggest that moving forward, non-fatal health conditions, including overall well-being, will play a greater role in shaping health disparities in aging populations, relative to mortality.

Our estimates of LE and HLE are consistent with previous studies using the same data source (*9*). Researchers have also found that the expansion of healthy lifespan was more pronounced in rural areas, with reductions in morbidity contributing more to HLE growth than declines in mortality. A possible explanation is that rural areas have experienced faster improvements in socioeconomic and healthcare conditions in recent years. Additionally, a selective effect may have led to a healthier profile among surviving older adults in rural areas at the time of the survey.

Previous studies on HLE decomposition often used counterfactual methods, which are best suited for comparing HLE at different time points within the same population. In contrast, this study applies a novel decomposition approach to estimate the contributions of mortality and morbidity to HLE differences between urban and rural populations at a single time point. We also broke these contributions down by age group, providing new insights to help policymakers better address the urban-rural HLE gap.

From a gender perspective, the male-female health-survival paradox (*10*) has consistently positioned morbidity as the primary driver of urban-rural HLE disparities among women. Over time, morbidity's contribution has increased significantly, and among men, it has surpassed mortality to become the dominant factor. Age-specific analysis revealed that the key age groups contributing to urban-rural disparities shifted to older cohorts in 2020 compared to 2010. Concurrently, the contributions from age groups under 85 have become more evenly distributed. These findings emphasize the importance of focusing on quality of life improvements for all older adults rather than merely extending lifespan. Targeted interventions should prioritize women and younger older adults to create a more comprehensive approach to healthy aging.

The transition from mortality-driven to morbidity-driven health disparities in aging populations necessitates a fundamental shift in public health and elder care policies. As older adults' health needs become increasingly influenced by chronic conditions and non-fatal health issues, implementing comprehensive health policies that prioritize long-term disease prevention, management, and overall well-being is critical, rather than solely focusing on extending life expectancy. For rural areas, where morbidity reduction has shown the most promise in improving health outcomes, policymakers should enhance access to quality healthcare services and improve health literacy. Furthermore, efforts should focus on improving quality of life for women and the oldest-old, as these groups experience higher morbidity rates that significantly affect their health outcomes.

A limitation of this study is that SRH may be influenced by various factors, including cultural norms, personal expectations, and understanding of health information (*11*). In rural areas, where healthcare quality and accessibility are generally lower, older adults may not fully recognize their health conditions, potentially leading to an overestimation of their SRH. Nevertheless, as the data were obtained from the Census, the potential selection effect is likely negligible, given the comprehensive coverage and representativeness of the dataset. Despite its subjectivity, SRH captures an individual's overall sense of well-being, offering a broader perspective compared to objective health measures.

In conclusion, our study provides a comprehensive and detailed analysis of urban-rural inequalities in healthy longevity among China's aging population, using a novel decomposition approach to distinguish between the impacts of mortality and morbidity on HLE. This framework addresses a significant gap in HLE research and can be applied to future studies.

Conflicts of interest: No conflicts of interest.

Ethical statement: The data used in this study were obtained from the Sixth and Seventh National Population Censuses. As these datasets contain aggregated information and do not include identifiable personal data, ethical approval and informed consent were not required.

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Preplanned Studies

The Cascade of Care for Diabetes and Risks of Functional Limitation — China, 2011–2020

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Summary

What is already known about this topic?

Uncontrolled diabetes can result in severe clinical complications, significantly increasing the risk of functional limitations in instrumental activities of daily living (IADL) and activities of daily living (ADL).

What is added by this report?

This study investigates the association between the Cascade of Care (CoC) for diabetes and functional limitations, providing evidence on the critical need for strengthening diabetes care to prevent functional limitations and improve quality of life.

What are the implications for public health practice?

The findings provide critical insights to guide public health strategies and interventions aimed at enhancing diabetes management across all stages of the CoC, with the goal of reducing functional limitations and their associated burden, ultimately improving long-term health outcomes for individuals with diabetes.

ABSTRACT

Introduction: Diabetes, if not treated well, can result in severe clinical complications and physical limitation. This study investigates gaps in the Cascade of Care (CoC) for diabetes among individuals aged 45 and older in China and its association with the risk of functional limitations.

Methods: Using data from the China Health and Retirement Longitudinal Study (CHARLS) from 2011 to 2020, the study analyzes the association between CoC and limitations in activities of daily living (ADL) and instrumental activities of daily living (IADL) through generalized estimating equations and Cox proportional hazards models. The CoC for diabetes consisted of five stages.

Results: The largest gap was found in the awareness stage (59.6%), while smaller gaps were observed in the transition from awareness to treatment (13.8%) and treatment-to-control (9.0%). Compared to individuals without diabetes, those in stages 1, 2, and 3 of the CoC had a significantly higher risk of ADL/IADL limitation, with stage 3 having the most pronounced impact.

Conclusions: The findings highlight poor diabetes management in China, especially in awareness and treatment stages, and show that low awareness, treatment, and glycemic control are linked to higher future risk of functional limitations. Early diagnosis and effective diabetes management are crucial to reducing these risks.

Recent studies estimate that approximately 12.4% of Chinese adults have diabetes (*1*), exceeding the global average of 1 in 9 (*2*), which poses a significant public health burden. Poorly managed diabetes can lead to severe complications and physical limitations. The Cascade of Care (CoC) model outlines the stages of long-term care (prevalence, screening, diagnosis, treatment, follow-up, and control), providing a framework for improving disease outcomes by identifying care gaps (*3*). Addressing these gaps is critical for improving health outcomes. However, the association between CoC for diabetes and associated health losses, such as functional limitations, remains underexplored. Gaining insights into this association could be key to enhancing diabetes management and reducing the risk of functional limitation.

This study used data from the China Health and Retirement Longitudinal Study (CHARLS), a nationally representative cohort of Chinese adults aged 45 and older. The survey, initiated in 2011, employed a multistage stratified probability proportional to size (PPS) sampling method, covering 17,708 participants from 10,257 households across 28 provincial-level administrative divisions (PLADs). Follow-up interviews were conducted in 2013, 2015, 2018, and

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2020 (*4*). After excluding cases with missing data at baseline, 10,945 individuals were included in the analysis. A care cascade framework for diabetes was used to evaluate management conditions, including diagnosis/awareness (self-reported diagnosis or high fasting blood glucose), treatment (receiving any treatment), and control (blood glucose or HbA1c within target levels). The CoC was divided into five stages: without diabetes (Stage 0), unaware (Stage 1), aware but untreated (Stage 2), treated but uncontrolled (Stage 3), and awareness-treated-controlled (stage 4). Functional limitations were defined as difficulty in any activities of IADL and activities of ADL and assessed using two variables: number of limitations (0 to 6) with a Generalized Estimating Equation (GEE) model and presence of any limitation using the Cox proportional hazards model.

The GEE model and Cox proportional hazards model were used to assess the association between CoC and ADL/IADL limitations, as well as specific functional domains. The GEE model utilized observations with repeated measurements from 2011 to 2020, applying Poisson distribution for the multi-categorical ADL/IADL limitations and logistic distribution for the dichotomous ADL/IADL items. In the Cox model, participants with baseline ADL/IADL limitations were excluded to examine the risk of new functional limitations. All models adjusted for age, gender, marital status, educational attainment, working status, total household consumption, smoking status, drinking status, Body Mass Index (BMI) and hypertension (HBP). Statistical analysis was conducted using STATA 17.0 (StataCorp LLC, College Station, TX, USA), with a significance level set at *P*<0.05.

In 2011, 15.8% of individuals were identified as having diabetes. Among these individuals, 40.4% were aware of their condition, 26.6% received treatment, and only 17.6% successfully achieved glycemic control. The largest gap in the CoC occurred at the awareness stage, with 59.6% of diabetics unaware of their condition, followed by a 13.8% drop between awareness and treatment, and a smaller gap (9.0%) between treatment and control. These findings highlight critical shortcomings in diabetes care management in China. In 2011, 17.2% of respondents experienced limitations in ADL and 21.6% experienced limitations in IADL, with the prevalence of these limitations increasing over time. Table 1 andSupplemental Table S1 (available at https://weekly.chinacdc.cn/) illustrate the prevalence of ADL and IADL limitations over time and across different stages of the CoC. The prevalence of these limitations increased over time at all stages, with higher rates observed among those with poorer diabetes management. Notably, the prevalence significantly decreased as diabetes was better managed along the care cascade.

The GEE model examined the association between CoC and ADL/IADL limitations across 47,920 observations from 2011 to 2020 (Table 2 and

TABLE 1. Prevalence of ADL/IADL limitations over time at different stages of the diabetes care cascade.

Subgroup	Total	Year					*P*
		2011	2013	2015	2018	2020	
ADL limitation							
CoC Stage 0	21.1	16.4	18.3	22.9	22.7	26.8	<0.001
CoC Stage 1	24.8	20.7	22.0	26.3	26.8	30.1	<0.001
CoC Stage 2	26.8	17.4	22.5	30.8	29.6	37.0	<0.001
CoC Stage 3	32.8	27.6	29.4	35.2	32.9	42.5	0.001
CoC Stage 4	29.4	24.8	27.9	29.4	31.2	36.0	0.072
IADL limitation							
CoC Stage 0	26.3	20.8	25.3	28.0	29.1	29.7	<0.001
CoC Stage 1	28.8	23.1	27.6	30.2	32.6	32.1	<0.001
CoC Stage 2	30.8	23.3	26.9	32.5	39.9	34.0	<0.001
CoC Stage 3	34.1	32.0	24.9	34.0	38.9	45.2	<0.001
CoC Stage 4	30.9	33.3	23.4	30.3	30.1	38.2	0.320

Note: CoC Stage 0=without diabetes; CoC Stage 1=unaware; CoC Stage 2=aware but untreated; CoC Stage 3=treated but uncontrolled; CoC Stage 4=awareness-treated-controlled.

Abbreviation: ADL=activities of daily living; IADL=instrumental activities of daily living.

Supplemental Table S2, available at https://weekly.chinacdc.cn/). Stage 3 (treated but uncontrolled) was significantly associated with a 59.6% increased risk of ADL limitations compared to those without diabetes, affecting all ADL items (59.5%–119.3%). Stage 1 (unaware) raised risks for bathing (19.6%) and eating (35.6%), while stage 4 (awareness-treated-controlled) increased risks for bathing (60.4%) and controlling urination/defecation (125.0%). For IADL, stage 3 was associated with a 42.5% increased risk overall and elevated risks for housework (96.9%), meal preparation (99.1%), shopping (61.1%), and money management (43.9%). Stage 1 was linked to a 17.9% higher risk in shopping, while stages 2 and 4 showed no significant associations.

The Cox proportional hazards model analyzed the impact of CoC on new-onset functional limitations in 7,873 individuals without baseline ADL/IADL limitations (Table 3 and Supplemental Table S3, available at https://weekly.chinacdc.cn/). For ADL limitations, compared to those without diabetes, the risk increased by 32.3% in Stage 2 and 67.9% in Stage 3, with no significant associations observed in stages 1 and 4. Stage 1 was associated with increased risks ranging from 34.1% to 52.2% for specific activities including dressing, bathing, eating, and getting in/out of bed, while Stage 3 showed elevated risks of 47.8% to 109.7% across all ADL domains except eating. For

TABLE 2. Association between cascade of diabetes care and limitation in ADL/IADL using generalized estimating equation model.

Subgroup	IRR (95% *CI*)
ADL	
With diabetes but unaware	1.094 (0.985, 1.215)
Being awareness but not treated	1.127 (0.933, 1.362)
Treated but uncontrolled	1.596 (1.361, 1.871)*
Awareness, treated and controlled	1.314 (0.993, 1.741)
IADL	
With diabetes but unaware	1.060 (0.966, 1.163)
Being awareness but not treated	1.079 (0.908, 1.282)
Treated but uncontrolled	1.425 (1.226, 1.656)*
Awareness, treated and controlled	1.143 (0.872, 1.499)

Note: All models were adjusted for age, gender, marital status, educational attainment, working status, total household consumption, smoking status, drinking status, body mass index, and hypertension.
Abbreviation: ADL=activities of daily living; IADL=instrumental activities of daily living; IRR=incidence rate ratio; *CI*=confidence interval.
* *P*<0.05.

TABLE 3. Association between cascade of diabetes care and new limitation in ADL/IADL using Cox proportional hazards model.

Subgroup	*HR* (95% *CI*)
ADL	
With diabetes but unaware	1.131 (0.976, 1.312)
Being awareness but not treated	1.323 (1.032, 1.694)*
Treated but uncontrolled	1.679 (1.302, 2.164)*
Awareness, treated and controlled	1.302 (0.853, 1.987)
IADL	
With diabetes but unaware	1.120 (0.980, 1.280)
Being awareness but not treated	1.050 (0.815, 1.353)
Treated but uncontrolled	1.307 (1.014, 1.685)*
Awareness, treated and controlled	1.045 (0.685, 1.594)

Note: All models were adjusted for age, gender, marital status, educational attainment, working status, total household consumption, smoking status, drinking status, Body Mass Index and hypertension.
Abbreviation: ADL=activities of daily living; IADL=instrumental activities of daily living; *HR*=hazard ratio; *CI*=confidence interval.
* *P*<0.05.

IADL limitations, Stage 3 was the only stage significantly associated with an increased risk, showing a 1.307-fold increase. Stage 1 increased the risk for meal preparation and shopping by 26.5% and 33.3%, respectively, and Stage 2 elevated the risk in medication management by 58.0%. No significant associations were found for managing money across any stage. All models were tested for proportional-hazards assumption (*P*>0.05, Supplemental Table S4, available at https://weekly.chinacdc.cn/).

DISCUSSION

This study revealed significant gaps in diabetes care cascade performance across China, reflecting poor nationwide diabetes control. Individuals at stages 1, 2, and 3 of the CoC, representing progressively poorer diabetes management, demonstrated higher rates of ADL and IADL limitations, with Stage 3 showing the strongest associations. Additionally, new-onset functional impairments were more likely to develop in stages 2 and 3, underscoring the critical need for improved diabetes care.

Our results reemphasized the substantial gaps in diabetes management among Chinese adults aged 45 and older. Of the 15.8% with diabetes, only 40.4% were aware of their condition, 26.6% received treatment, and merely 17.6% achieved glycemic control. Similarly, another national study reported comparably low rates of awareness (41.0%), treatment (32.7%), and control (6.2%) (*5*). These rates were notably lower than those in countries like the Republic of Korea, where the corresponding figures were 69.2%, 63.5%, and 28.0% in 2016–2017 (*6*). While differences in diabetes definitions, study populations, and data collection methods may partially explain these disparities, strengthening awareness, treatment, and control remains critical to preventing complications and improving health outcomes in China.

Our findings provide new insights into the association between CoC and ADL/IADL limitations. Notably, treated but uncontrolled diabetes (Stage 3) increased the probability of limitations across most functional domains. Poor glycemic management raises the likelihood of complications such as cardiovascular disease (*7*) and muscle strength decline (*8*), which can significantly restrict physical function. Being unaware of diabetes (stage 1) was also associated with a higher risk of limitations in most items, despite not being directly linked to overall ADL/IADL limitations. This may be attributed to prolonged disease duration before diagnosis, as longer diabetes duration has been linked to poor glycemic control (*9*). Previous studies have suggested that functional limitations increase with the duration of diabetes (*10*). Although our study could not directly examine the specific impact of diabetes duration on limitation risk, the results support these conclusions indirectly.

To our knowledge, this is the first nationally representative study to comprehensively examine the association between the CoC and risk of functional limitations in China. Our study has several strengths. First, it utilizes data from a longitudinal, nationally representative survey, ensuring generalizability to Chinese adults aged 45 and older. Second, the prospective Cox proportional hazards model enables evaluation of the temporal association between CoC and the incidence of functional limitations. Third, the study employs a robust definition of diabetes that includes self-reported cases, HbA1c values, and diabetes medication use.

These findings highlight the crucial link between effective diabetes management and the prevention of functional limitations, emphasizing the need for improved CoC within the healthcare system. Our results can guide policymakers in prioritizing improvements to the diabetes care pathway, reducing the burden of limitations among older adults and promoting healthy aging. Identifying CoC gaps and their association with functional limitations can help design targeted educational programs for healthcare providers and patients, thereby improving health outcomes and quality of life for individuals with diabetes.

Interpreting these data involves several limitations. First, as nutrition is a major risk factor for diabetes, the lack of dietary assessments may restrict our understanding of CoC and limitation risk. However, we adjusted for other socioeconomic and behavioral factors, which helps mitigate some of this bias. Second, this study did not account for the co-existence of other conditions, which may overestimate the CoC level and underestimate the association between CoC loss and functional limitations because multimorbidity is more likely to contribute to adverse health outcomes. Nevertheless, the incidence of other conditions like stroke in this study is relatively low (5%), potentially reducing their impact on the results. Third, the study population consists of middle-aged and elderly individuals, which may limit the generalizability of our findings to the broader population, and caution is needed when extrapolating these results. Further research is needed to fully understand the relationship between CoC and limitation risk, particularly regarding diabetes duration.

In conclusion, this study revealed inadequate diabetes management along the CoC for Chinese adults aged 45 and older, indicating a significant unmet demand for diabetes care and challenges in achieving universal health coverage. Low awareness, treatment, and control significantly increase the risk of functional limitations, especially when diabetes is unrecognized or poorly managed. This emphasizes the urgent need to enhance the CoC to mitigate functional decline in the aging population. Raising early awareness and ensuring timely treatment are crucial for reducing limitations among individuals with diabetes. The findings also provide valuable insights for policymakers and service providers to identify diabetes care priorities.

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SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. Prevalence of ADL and IADL limitations over time.

Subgroup	Total	Year					*P*
		2011	2013	2015	2018	2020	
ADL limitation	22.0	17.2	19.1	23.8	23.5	27.7	<0.001
IADL limitation	26.9	21.6	25.6	28.5	29.9	30.4	<0.001

Abbreviation: ADL=activities of daily living; IADL=instrumental activities of daily living.

SUPPLEMENTARY TABLE S2. Association between cascade of diabetes care and limitation in the domains of ADL/IADL using generalized estimating equation model.

Subgroup	*OR* (95% *CI*)	Subgroup	*OR* (95% *CI*)
Dressing		Doing housework	
With diabetes but unaware	1.110 (0.922, 1.337)	With diabetes but unaware	1.049 (0.908, 1.213)
Being awareness but not treated	1.271 (0.908, 1.761)	Being awareness but not treated	1.093 (0.841, 1.421)
Treated but uncontrolled	1.742 (1.307, 2.321)*	Treated but uncontrolled	1.969 (1.583, 2.450)*
Awareness, treated and controlled	1.383 (0.840, 2.279)	Awareness, treated and controlled	1.207 (0.809, 1.801)
Bathing		Preparing hot meals	
With diabetes but unaware	1.196 (1.008, 1.420)*	With diabetes but unaware	1.098 (0.937, 1.288)
Being awareness but not treated	1.130 (0.821, 1.554)	Being awareness but not treated	1.101 (0.822, 1.475)
Treated but uncontrolled	2.193 (1.704, 2.822)*	Treated but uncontrolled	1.991 (1.569, 2.526)*
Awareness, treated and controlled	1.604 (1.030, 2.498)*	Awareness, treated and controlled	1.227 (0.791, 1.904)
Eating		Shopping	
With diabetes but unaware	1.356 (1.070, 1.720)*	With diabetes but unaware	1.179 (1.008, 1.381)*
Being awareness but not treated	0.921 (0.544, 1.557)	Being awareness but not treated	0.986 (0.725, 1.341)
Treated but uncontrolled	1.753 (1.181, 2.603)*	Treated but uncontrolled	1.611 (1.246, 2.083)*
Awareness, treated and controlled	1.237 (0.587, 2.604)	Awareness, treated and controlled	1.026 (0.635, 1.657)
Getting in/out of bed		Taking medications	
With diabetes but unaware	1.071 (0.896, 1.280)	With diabetes but unaware	1.057 (0.880, 1.271)
Being awareness but not treated	1.126 (0.817, 1.551)	Being awareness but not treated	1.222 (0.887, 1.683)
Treated but uncontrolled	1.610 (1.217, 2.130)*	Treated but uncontrolled	1.249 (0.913, 1.710)
Awareness, treated and controlled	1.432 (0.898, 2.285)	Awareness, treated and controlled	1.249 (0.751, 2.072)
Using the toilet		Managing money	
With diabetes but unaware	1.079 (0.936, 1.243)	With diabetes but unaware	1.098 (0.953, 1.266)
Being awareness but not treated	1.049 (0.809, 1.360)	Being awareness but not treated	1.108 (0.854, 1.439)
Treated but uncontrolled	1.595 (1.271, 2.003)*	Treated but uncontrolled	1.439 (1.135, 1.824)*
Awareness, treated and controlled	1.399 (0.956, 2.047)	Awareness, treated and controlled	0.885 (0.562, 1.394)
Controlling urination and defecation			
With diabetes but unaware	1.105 (0.902, 1.352)		
Being awareness but not treated	1.388 (0.983, 1.961)		
Treated but uncontrolled	1.961 (1.451, 2.650)*		
Awareness, treated and controlled	2.250 (1.418, 3.571)*		

Note: All models were adjusted for age, gender, marital status, educational attainment, working status, total household consumption, smoking status, drinking status, Body Mass Index and hypertension.
Abbreviation: ADL=activities of daily living; IADL=instrumental activities of daily living; *OR*=odds ratio; *CI*=confidence interval.
* $P<0.05$.

SUPPLEMENTARY TABLE S3. Association between cascade of diabetes care and new limitation in the domains of ADL/IADL using Cox proportional hazards model.

Subgroup	*HR* (95% *CI*)	Subgroup	*HR* (95% *CI*)
Dressing		Doing housework	
With diabetes but unaware	1.341 (1.060, 1.697)*	With diabetes but unaware	1.108 (0.927, 1.326)
Being awareness but not treated	1.600 (1.080, 2.369)*	Being awareness but not treated	1.291 (0.954, 1.747)
Treated but uncontrolled	1.906 (1.267, 2.868)*	Treated but uncontrolled	1.812 (1.356, 2.417)*
Awareness, treated and controlled	0.730 (0.272, 1.958)	Awareness, treated and controlled	0.853 (0.457, 1.594)
Bathing		Preparing hot meals	
With diabetes but unaware	1.363 (1.090, 1.704)*	With diabetes but unaware	1.265 (1.037, 1.542)*
Being awareness but not treated	1.404 (0.961, 2.051)	Being awareness but not treated	1.235 (0.863, 1.766)
Treated but uncontrolled	2.097 (1.452, 3.028)*	Treated but uncontrolled	2.050 (1.489, 2.822)*
Awareness, treated and controlled	1.147 (0.543, 2.425)	Awareness, treated and controlled	1.040 (0.537, 2.012)
Eating		Shopping	
With diabetes but unaware	1.522 (1.082, 2.139)*	With diabetes but unaware	1.333 (1.085, 1.638)*
Being awareness but not treated	1.635 (0.905, 2.952)	Being awareness but not treated	1.358 (0.937, 1.966)
Treated but uncontrolled	1.731 (0.880, 3.404)	Treated but uncontrolled	1.912 (1.332, 2.743)*
Awareness, treated and controlled	0.943 (0.233, 3.815)	Awareness, treated and controlled	1.158 (0.575, 2.331)
Getting in/out of bed		Taking medications	
With diabetes but unaware	1.263 (1.007, 1.584)*	With diabetes but unaware	1.173 (0.907, 1.517)
Being awareness but not treated	1.634 (1.144, 2.334)*	Being awareness but not treated	1.580 (1.058, 2.360)*
Treated but uncontrolled	1.603 (1.059, 2.425)*	Treated but uncontrolled	1.373 (0.841, 2.240)
Awareness, treated and controlled	1.414 (0.730, 2.739)	Awareness, treated and controlled	1.806 (0.930, 3.506)
Using the toilet		Managing money	
With diabetes but unaware	1.133 (0.949, 1.352)	With diabetes but unaware	1.092 (0.901, 1.324)
Being awareness but not treated	1.233 (0.914, 1.662)	Being awareness but not treated	1.302 (0.938, 1.806)
Treated but uncontrolled	1.478 (1.081, 2.022)*	Treated but uncontrolled	1.367 (0.957, 1.952)
Awareness, treated and controlled	1.516 (0.948, 2.423)	Awareness, treated and controlled	0.797 (0.396, 1.601)
Controlling urination and defecation			
With diabetes but unaware	1.271 (0.971, 1.663)		
Being awareness but not treated	1.336 (0.846, 2.108)		
Treated but uncontrolled	1.967 (1.271, 3.046)*		
Awareness, treated and controlled	1.177 (0.485, 2.856)		

Note: All models adjusted for age, gender, marital status, educational attainment, working status, total household consumption, smoking status, drinking status, Body Mass Index and hypertension.
Abbreviation: ADL=activities of daily living; IADL=instrumental activities of daily living; *HR*=hazard ratio; *CI*=confidence interval.
* P<0.05.

SUPPLEMENTARY TABLE S4. Results of test for proportional-hazards assumption.

Subgroup	*P*	Subgroup	*P*
ADL	0.61	IADL	0.18
Dressing	0.28	Doing housework	0.07
Bathing	0.06	Preparing hot meals	0.10
Eating	0.13	Shopping	0.64
Getting in/out of bed	0.43	Taking medications	0.72
Using the toilet	0.66	Managing money	0.37
Controlling urination and defecation	0.47		

Abbreviation: ADL=activities of daily living; IADL=instrumental activities of daily living.

Preplanned Studies

Epidemiological Analysis of the Decline of Myocarditis Burden — China, 1992–2021

Shengnan Wang[1]; Xiangfeng Zhu[1]; Yanwu Nie[1]; Zeyu Xiao[1]; Mingzhu Huang[1]; Zhimin Yao[2,#]; Lei Wu[1,#]

Summary

What is already known about this topic?

Myocarditis is a prevalent cardiovascular condition that can lead to severe complications. The number of patients with myocarditis, new cases, and deaths in China has been on an upward trend over the years, causing a certain disease burden.

What is added by this report?

The overall burden of myocarditis in China is on a downward trend; however, the age-standardized mortality rate (ASMR) and age-standardized disability-adjusted life years (DALYs) rate remain higher than the global average. The age-standardized incidence rate (ASIR), ASMR and age-standardized DALYs rate were higher in men than in women. Individuals younger than 5 years or older than 70 years, the period from 2002–2016, and birth cohort earlier than 1957 were identified as risk factors for myocarditis-related mortality.

What are the implications for public health practices?

We should still prioritize the prevention and treatment of myocarditis. It is recommended that primary and secondary prevention efforts focus on individuals younger than 5 years, older than 70 years, and males, with an emphasis on proactive health education and management.

ABSTRACT

Introduction: Myocarditis is a common cardiovascular disease that can lead to severe complications. This study investigates the epidemiological characteristics of myocarditis in China by analyzing incidence, mortality, and disability-adjusted life years (DALYs) trends from 1992 to 2021.

Methods: Using the Global Burden of Disease Study（GBD 2021）database, this study analyzed myocarditis incidence, mortality, DALYs, age-standardized rates, and average annual percent change (AAPC) from 1992 to 2021. An average percent change (APC) model was applied to assess the impact of age, period, and birth cohort on myocarditis mortality risk. Disease burden comparisons were made across different age and gender groups in China.

Results: Compared to 1992, China saw a decline in age-standardized incidence, mortality, and DALYs rates of myocarditis in 2021. From 1992 to 2021, the AAPC in the standardized incidence rate, mortality rate, and DALYs rate of myocarditis in China were −0.223 (95% *CI*: −0.234 to −0.212), −0.525 (95% *CI*: −0.861 to −0.187), and −1.958 (95% *CI*: −2.219 to −1.696), respectively. Males had higher rates than females, with faster declines observed in females. Risk factors for myocarditis mortality included being under 5 or over 70 years old, living in 2002–2016, and belonging to birth cohorts before 1957. APC model results were similar for males and females.

Conclusions: Although China's myocarditis disease burden is decreasing,its age-standardized mortality and DALYs rates remain above global levels. Continued vigilance in prevention and control is essential. Priority should be given to primary and secondary prevention for individuals under 5, over 70, and males, with a focus on health education and management.

Myocarditis is an inflammatory lesion of the myocardium, which is a common one in cardiovascular diseases. It is characterized by inflammatory infiltration in the myocardium and degeneration and necrosis of non-ischemic cardiomyocytes (*1*). Meanwhile, myocarditis is also an important cause of sudden cardiac death, acute heart failure, and chronic dilated cardiomyopathy (*2*). Data from Global Burden of Diseases (GBD) 2019 reported that the number of patients, new cases, and deaths of myocarditis in China increased by 85.62%, 47.51%, and 50.22%, respectively, in 2019 compared with 1990. Before the

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coronavirus disease 2019 (COVID-19) pandemic, the global incidence of viral myocarditis was about 1 to 10 cases per 100,000 people per year (*3*). After the outbreak of COVID-19, it found that in patients hospitalized for COVID-19 the incidence of acute myocarditis is 2.4 to 4.1 cases per 1000 people (*4*). This study used GBD 2021 data and an age-period-cohort model to analyze the trend of the burden of myocarditis in China, and found that the burden of myocarditis in China has generally decreased from 1992 to 2021. However, the number of morbidity and mortality continue to rise, and both the ASMR and age-standardized disability-adjusted life-years (DALYs) rate remain above the global average the overall burden of myocarditis in China is showing a downward trend. The findings may assist policymakers in making more informed decisions, improving resource allocation, and optimize healthcare resources.

The data source is the Global Burden of Disease Research 2021 (GBD 2021) database.It documents the incidence, prevalence, mortality, years of life lost (YLLs), years lived with disability (YLDs), and DALYs due to 371 diseases and injuries in 204 countries or regions around the world (*5*). The IE algorithm of the age-period-cohort model was applied in this study. This algorithm integrates the three variables of age, period, and cohort into a single variable through a series of linear algebraic transformations, making the model estimable. This study selected three indicators: incidence, mortality and DALYs. Based on the globally age-standardized population figures provided by GBD 2021 (*6*), we conducted age-standardization for these indicators to investigate the epidemiological characteristics of myocarditis in the overall Chinese population and in male and female populations from 1992 to 2021.

Compared with 1992, the number of cases and deaths of myocarditis in China increased, and DALY decreased in 2021. Meanwhile, the age-standardized incidence rate, mortality rate and DALYs rate all decreased. The changes of disease burden of myocarditis in the world were consistent with those in China. Among them, the age-standardized incidence rate and DALYs rate changed more than the world, while the age-standardized mortality rate showed the opposite characteristics (Table 1).

The ASIR of myocarditis in China is consistent with the global rates (Figure 1A), indicating similar trends and incidence levels. The ASMR and age-standardized DALYs rate initially increased and then decreased. However, the burden of disease in China was high, with a larger fluctuation range of ASMR and DALYs rates compared to the global average (Figure 1B, 1C). From 1992 to 2021, the ASIR, ASMR, and age-standardized DALYs rate of myocarditis exhibited similar characteristics among Chinese men and women when considering the entire population. The ASIR, ASMR, and age-standardized DALYs rate for myocarditis were higher in men than women; however, there is an overlap between their uncertainty intervals.

The ASMR and age-standardized DALYs rate first increased and then decreased, and the turning points from increasing to decreasing were 2001 and 1999, respectively (Supplementary Table S1, available at https://weekly.chinacdc.cn/). In general, the age-standardized incidence rate, mortality rate and DALYs rate of myocarditis in China showed a downward trend from 1992 to 2021, and the AAPC was −0.223 (95% *CI*: −0.234 to −0.212), −0.525 (95% *CI*: −0.861 to −0.187) and −1.958 (95% *CI*: −2.219 to −1.696), respectively. Meanwhile, the ASIR, ASMR, and age-standardized DALYs rate of myocarditis in Chinese

TABLE 1. The analysis of incidence, death and DALYs of myocarditis in China and the world in 1992 and 2021.

Area		Incidence		Death		DALYs	
		Number (10,000)	P’	Number (10,000)	P’	Number (10,000)	P’
Global	1992	82.13	16.87	2.26	0.56	104.25	19.78
	2021	131.97	16.16	3.18	0.40	96.31	12.41
	2021 *vs*. 1992 (%)*	60.69	−4.20	40.43	−28.53	−7.61	−37.28
China	1992	18.64	17.41	0.84	1.08	46.07	44.59
	2021	26.93	16.33	1.42	0.92	34.35	25.26
	2021 *vs*.1992 (%)*	44.47	−6.20	69.03	−14.41	−25.43	−43.36

Note: P’ was Age-standardized rate, expressed as 1/100,000.
* Percentage change (%) was calculated as the difference between 2021 and 1992 divided by the amount in 1992.
Abbreviations: DALYs=disability-adjusted life years.

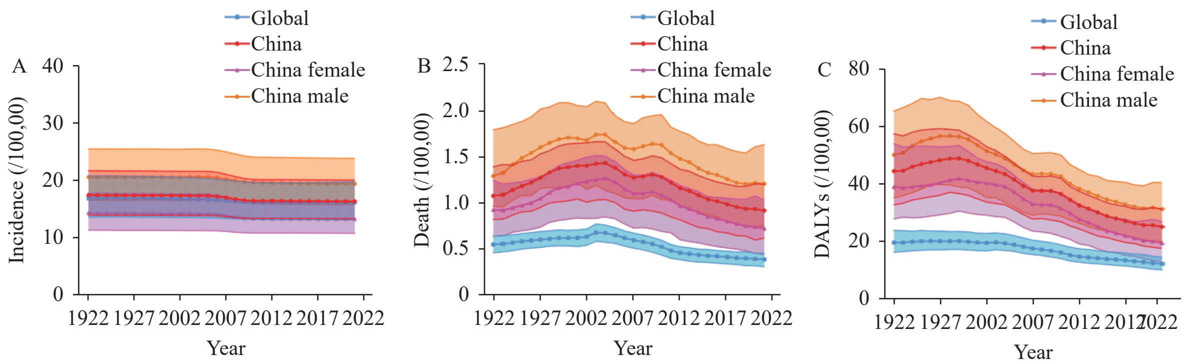

FIGURE 1. Disease burden of myocarditis in China and the world from 1992 to 2021. (A) ASIR; (B) ASMR; (C) Age-standardized DALYs rate.

Note: Shaded sections indicate 95% uncertainty intervals.

Abbreviations: ASIR=age-standardized incidence rate; ASMR=age-standardized mortality rate; DALYs=disability-adjusted life years

men and women displayed a declining trend from 1992 to 2021, with a more rapid decrease observed in women. The AAPC of the disease burden of myocarditis in both genders was less than 0. Except for the AAPC of male ASMR, the AAPC of other disease characteristics were statistically significant (Table 2).

The age-period-cohort model revealed that age significantly influences myocarditis mortality, with initial risk decline, subsequent stabilization, and later escalation (Figure 2). The highest risks were in those under 5 and over 95 years, with the latter 177.6 times more likely to die than the 25–29 age group. Age acted as a protective factor for 5–69-year-olds but a risk factor for younger and older ages. Period effects showed the lowest mortality risk in 1992–1996, peaking in 2007–2011, with a 1.41-fold increased risk compared to the earlier period. Cohort analysis indicated the highest death risk in those born 1912–1916 and the lowest during 2017–2021, with a 14.5-fold increased risk for the former. Meanwhile, the mortality risk of men and women was affected by age, period and birth cohort, which was basically consistent with the characteristics of the whole population (Figure 2). Under the age of five and over 95 years old for male and female two peak death risk, while both the lowest risk of death ages at 10–14 and 45–49 years old, respectively, where the highest risk of death is 163.52 and 239.71 times higher, respectively, than the lowest risk. Overall, both genders reflected the same results, with the age effect having the greatest impact on the risk of death, followed by the cohort effect, and finally the period effect having the least impact.

DISCUSSION

In this article, Myocarditis estimated disease burden and its changes in China were analyzed in detail. The findings indicate that the ASIR, ASMR, and DALYs rate for myocarditis in China in 2021 were lower than those in 1992. Conversely, the incidence and mortality of myocarditis globally and within China in 2021 showed a marked increase from 1992, while DALY has decreased both globally and in China. This could stem from advancements in medical technology that allow more effective treatments, shortening recovery times and thus minimizing disability from the illness. Furthermore, an increase in the proportion of the older adult population might result in more deaths, yet potentially lower long-term disability impacts, thereby possibly reducing the overall DALYs. We found that the ASMR and age-standardized DALYs rates were higher than the global averages. This may be due to the uneven distribution of medical resources in China, lifestyle and environmental factors related to the progression of myocarditis. Nevertheless, given the significant rise in myocarditis cases and fatalities, a comprehensive understanding of myocarditis is essential, along with heightened focus on its prevention and treatment. Meanwhile, the AAPC of the burden of myocarditis was less than 0 in both men and women from 1992 to 2021, and it was lower in women than in men. This suggests that we should strengthen health management and health promotion for the male population. This phenomenon may be related to the differences in physiological structure and immune system between men and women. Some studies have

TABLE 2. Changes in AAPC for each indicator of myocarditis disease burden in China, 1992−2021.

Measure	Sex	AAPC	95% *CI*	t	*P*
Age-standardized incidence rate	Both	−0.223	−0.234, −0.212	−39.738	<0.001
	Female	−0.270	−0.285, −0.256	−35.934	<0.001
	Male	−0.200	−0.216, −0.185	−24.724	<0.001
Age-standardized mortality rate	Both	−0.525	−0.861, −0.187	−3.045	0.002
	Female	−0.764	−0.963, −0.565	−7.5	<0.001
	Male	−0.23	−0.612, 0.154	−1.173	0.241
Age-standardized DALYs rate	Both	−1.958	−2.219, −1.696	−14.547	<0.001
	Female	−2.329	−2.645, −2.012	−14.251	<0.001
	Male	−1.610	−1.91, −1.309	−10.416	<0.001

Abbreviation: AAPC=average annual percent change; *CI*=Confidence Interval; DALYs=disability-adjusted life years.

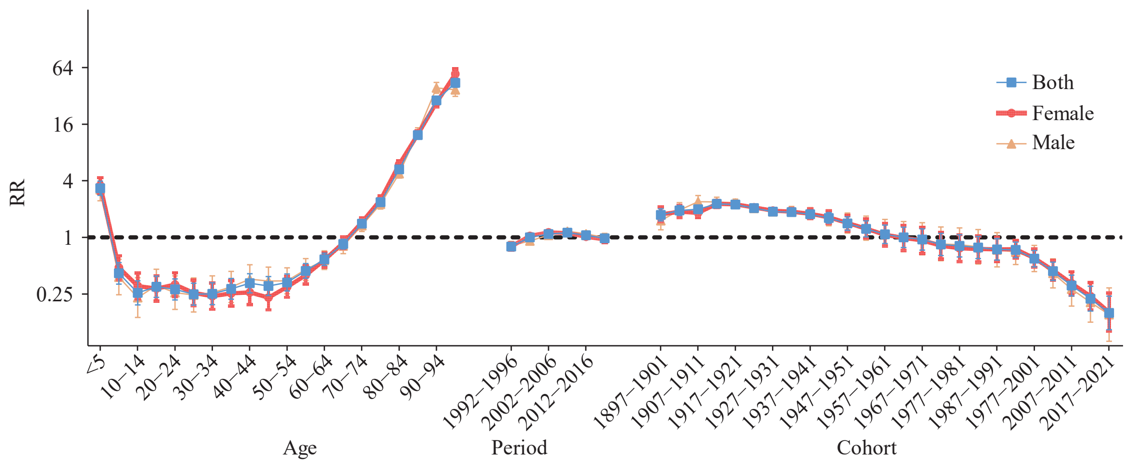

FIGURE 2. Age-period-cohort modeling to analyze the risk and 95% *CI* of death from myocarditis in China.
Abbreviation: RR= relative risk; *CI*=confidence interval.

shown that there is a significant gender difference between cardiomyocytes and fibroblasts, which affects the size of the heart; moreover, about 30% of men have larger hearts than women do (*7*). Furthermore, women have smaller coronary vessels than men do, premenopausal women have lower blood pressure, and the percentage of LVEF is higher in women than in men (*8*). In addition to the variations in cardiac physiological functions attributable to gender, differences in sex hormones may significantly contribute to the heightened incidence observed in males. Sex hormones seem to modulate the acute cardiac response to inflammation, potentially influencing the risk of progressing to chronic dilated cardiomyopathy (*9*). Conversely, testosterone promotes immune dysfunction by inhibiting anti-inflammatory cells and activating Th1-type immune responses, thus facilitating the development of myocarditis through abnormal immune-mediated mechanisms (*10*).

In this study, being under 5 years or over 70 years of age, during the period 2002–2016, and belonging to a birth cohort prior to 1957 were identified as risk factors for mortality from myocarditis. This indicates that prevention and treatment efforts for myocarditis should particularly target children under 5 years of age and older adult individuals over 70. Pediatric myocarditis is a condition that can develop rapidly, leading to severe complications such as acute heart failure, cardiogenic shock and fatal arrhythmias. Fulminant myocarditis, a particularly severe form of myocarditis, has a sudden onset and rapid progression, causing hemodynamic changes that typically result in heart failure and life-threatening arrhythmias as well as cardiogenic shock within 2 to 3 days. This form of myocarditis is more common in children and has a high mortality rate, with serious arrhythmias being a common cause of sudden death in children. Myocarditis has been identified as an important cause of sudden cardiac death in young children (*11*). The challenge of diagnosing myocarditis in this group, coupled with the disease's swift progression, leads to a high mortality rate among affected children. Additionally, children's immune systems may overreact to pathogens, exacerbating myocardial damage. Thus, the swift progression of myocarditis and the potential for severe cardiac complications, along with an overactive immune response, contribute to the high mortality rate in children with the disease. Therefore,early identification and provision of appropriate testing and supportive care for affected children are essential to mitigate mortality rates. Additionally, the increased mortality observed in older adult may stem from diminished immune function associated with aging, which impairs the immune system's adaptability to infections and reduces the influx of T cells from the thymus into the periphery. Concurrently, chronic immune activation and memory cell expansion may also contribute, ultimately leading to immune cell senescence and disorders within the immune system, diminishing the capacity to respond to new antigens (*12*). Furthermore, the comparative analysis of age-period-cohort model results between male and female populations revealed no significant disparity in mortality risk across genders. This indicates that age, period, and birth cohort are not significant determinants of mortality differences between men and women.

Nevertheless, this study was subject to at least two limitations. Primarily, it relies on GBD 2021 data analysis, yet the database does not specify myocarditis incidence and prevalence across different provincial-level administrative divisions, regions, and seasons. Secondly, GBD data is mainly estimated by combining statistical models and system dynamics models, and there may be some differences between the data and the actual situation.

This research found that the disease burden of myocarditis in China has decreased in the past 30 years. However, the incidence and mortality rates continue to rise, and the ASMR and the ratio of DALYs remain higher than the global average. Although there is a significant downward trend in mortality and DALYs rates among children under 5, both the under-5 and over-70 age groups are still identified as risk factors for myocarditis mortality. The probability of myocarditis occurrence in men is higher than in women in China, with the AAPC of myocarditis burden being negative for both genders, and lower in women than in men. Therefore, we should focus on the myocarditis burden in men, young children, and the elderly, and relevant departments should adopt more proactive measures to mitigate this burden, including enhancing health education and advancing medical diagnosis and treatment levels.

Conflicts of interest: No conflicts of interest reported.

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SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. Joinpoint regression analysis: trends in indicators of myocarditis disease burden in China from 1992 to 2021.

Measure	Trend	APC	95% *CI*	t	*P*
Age-standardized incidence rate	1992−2003	−0.033	−0.039 to −0.028	−13.259	<0.001
	2003−2006	−0.195	−0.273 to −0.117	−5.214	<0.001
	2006−2009	−1.573	−1.65 to −1.496	−42.431	<0.001
	2009−2021	−0.064	−0.069 to −0.06	−29.156	<0.001
Age-standardized death rate	1992−2001	3.340	2.882 to 3.801	15.47	<0.001
	2001−2010	−1.469	−1.991 to −0.944	−5.828	<0.001
	2010−2017	−3.583	−4.374 to −2.787	−9.279	<0.001
	2017−2021	−1.483	−2.988 to 0.046	−2.03	0.057
Age-standardized DALYs rate	1992−1999	1.548	1.031 to 2.068	6.294	<0.001
	1999−2010	−2.899	−3.187 to −2.609	−20.686	<0.001
	2010−2016	−4.177	−4.993 to −3.355	−10.447	<0.001
	2016−2021	−2.008	−2.842 to −1.167	−4.966	<0.001

Abbreviation: APC=annual percent change; *CI*=confidence interval; DALYs=disability-adjusted life years.

Vital Surveillances

Burden of Musculoskeletal Disorders — Global and BRICS+ Nations, 1990–2021

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ABSTRACT

Introduction: Musculoskeletal (MSK) disorders are escalating in the BRICS+ nations. The BRICS+ countries include five primary members of Brazil, Russia, India, China, and South Africa, and five new members of Saudi Arabia, Egypt, the United Arab Emirates (UAE), Iran, and Ethiopia by January 1st, 2024.

Methods: Utilizing the Global Burden of Disease (GBD) 2021 database, the study measured MSK disorders burden through incidence, prevalence, and disability-adjusted life years (DALYs), segmented by location, sex, and disease type. The average annual percentage change (AAPC) from 1990 to 2021 was evaluated to track the burden changes.

Results: In 2021, among BRICS+ nations, Brazil (2,267) and China (1,616) presented the highest and lowest age-standardized DALYs of MSK disorders per 100,000, respectively. Females had higher DALYs than males. The largest decrease and increase in age-standardized DALYs from 1990 to 2021 occurred in China (−2.35%) and Saudi Arabia (10.74%), respectively. Among all MSK disorders in 2021, low back pain (LBP) was the leading cause of the DALYs, while gout was the least contributor in BRICS+ nations. For males, the DALYs due to LBP, rheumatoid arthritis (RA), osteoarthritis (OA), neck pain (NP), and other MSK disorders except gout were lower than those for females. From 1990 to 2021, age-standardized DALYs of MSK disorders exhibited a significant decreasing trend in China [AAPC=−0.34; 95% confidence interval (*CI*): −0.38, −0.30], no significant change in Brazil and South Africa, and a growth trend in other nations, with the largest increasing trend detected in Saudi Arabia (AAPC=0.33; 95% *CI*: 0.31, 0.34).

Conclusions: MSK disorders imposed a substantial burden on BRICS+ countries, particularly in Brazil and Iran, with distinct patterns requiring tailored healthcare policies and resource distribution.

Musculoskeletal (MSK) disorders encompass any form of discomfort or permanent and disabling injury affecting the motor organs, including muscles, tendons, bones, cartilage, ligaments, and nerves (*1*). MSK health is fundamental to quality of life across all age groups. Research has demonstrated that individuals with MSK disorders face twice the risk of developing other chronic systemic diseases compared to those without such disorders (*2*). As a major contributor to global disability, MSK disorders pose significant and increasing threats to public health worldwide.

The BRICS group originally comprised Brazil, Russia, India, China, and South Africa, with five additional members — Saudi Arabia, Egypt, the United Arab Emirates (UAE), Iran, and Ethiopia — officially joining on January 1st, 2024, forming "BRICS+". As of 2022, BRICS+ nations represented 45.5% of the global population and approximately 37% of global GDP by 2023 (*3–4*), establishing them as increasingly influential contributors to global health and development initiatives. Despite their significance, a comprehensive assessment of MSK disorder burden across these countries remains lacking. This cross-country study utilizes data from the Global Burden of Disease (GBD) 2021 database to examine the disease burden and temporal trends of MSK disorders in BRICS+ nations from 1990 to 2021. The findings will enhance understanding of MSK disorder burden patterns and support the development of effective intervention strategies.

METHODS

The GBD 2021 database, developed by the Institute for Health Metrics and Evaluation (IHME) at University of Washington (*5*), provides a systematic scientific assessment of disease and injury incidence, prevalence, and mortality across 204 countries and territories for 371 diseases and injuries. The GBD

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database has standardized crude rates of incidence, prevalence, DALYs, and other metrics by age with reference to the world population.

According to the International Classification of Diseases, 10th Version (ICD-10), GBD 2021 categorizes MSK disorders into 6 major groups: rheumatoid arthritis (RA), osteoarthritis (OA), low back pain (LBP), neck pain (NP), gout, and other MSK diseases (*6*). Since MSK disorders are age-dependent, we primarily used age-standardized indicators, including rates and uncertainty intervals (UI) of incidence, prevalence, and DALYs in this study.

In the GBD study, countries are categorized into four income groups — low, lower-middle, upper-middle, and high — based on their Gross National Income (GNI) per capita, following the World Bank's classification system.

We used the Joinpoint regression program (version 5.0.2, National Cancer Institute, Bethesda, United States) for analysis. The average annual percentage change (AAPC) and its 95% confidence interval (*CI*) from 1990 to 2021 were calculated to determine both the direction and magnitude of the overall trends in disease burden. The significance level was set at α of 0.05.

RESULTS

Globally, the age-standardized incidence rate of MSK disorders decreased from 4.64% in 1990 to 4.35% in 2021. Females consistently exhibited higher age-standardized incidence rates than males. For males, the rate decreased from 3.78% in 1990 to 3.51% in 2021, while for females, it declined from 5.47% to 5.17%. Among BRICS+ nations, Russia reported the highest age-standardized incidence rates in both 1990 (5.93%) and 2021 (5.83%), while China had the lowest rates at 4.04% in 1990 and 3.63% in 2021 (Table 1).

Between 1990 and 2021, Saudi Arabia, UAE, Brazil, and Egypt experienced increases in age-standardized incidence of MSK disorders, led by Saudi Arabia with a 3.55% increase. Conversely, other BRICS+ countries exhibited decreases, with China demonstrating the most substantial decline (−11.28%) (Supplementary Figure S1A, available at https://weekly.chinacdc.cn/). In 2021, sex disparities in age-standardized incidence were most pronounced in India and Iran (Table 1).

The global age-standardized prevalence rate of MSK disorders increased from 19.18% in 1990 to 19.83% in 2021. Among BRICS+ nations, Brazil reported the highest age-standardized prevalence rates in both 1990 (22.39%) and 2021 (22.66%), while Ethiopia had the lowest rates at 16.40% in 1990 and 17.24% in 2021. Saudi Arabia demonstrated the largest increase in prevalence rate (11.19%) from 1990 to 2021.

The global age-standardized DALYs per 100,000 population for MSK disorders increased from 1,886 in 1990 to 1,909 in 2021, with consistently higher rates in females than males. Among BRICS+ nations, Brazil had the highest age-standardized DALYs in both 1990 and 2021, while Ethiopia had the lowest in 1990 and China in 2021. From 1990 to 2021, China exhibited a slight decline with fluctuations in age-standardized DALYs (−2.35%), South Africa showed relatively stable trends, and other BRICS+ countries experienced increases, with Saudi Arabia reporting the largest increase (10.74%) (Supplementary Figure S1). Notably, DALYs were consistently lower in males than females across all global regions and BRICS+ nations in both 1990 and 2021 (Table 1).

Regarding specific disease types, LBP was the leading cause of MSK disorder DALYs globally, decreasing from 937 per 100,000 in 1990 to 832 in 2021, while gout and RA contributed relatively low DALYs (Table 2). Gout DALYs increased slightly from 17 in 1990 to 20 in 2021. Russia exhibited the highest LBP DALYs were at 1,255 per 100,000 in 1990, while India reported the lowest (575) in 2021. Globally, LBP DALYs declined from 1990 to 2021, while RA, OA, NP, and gout remained relatively stable, and other MSK disorders increased. Except for gout, all MSK disorders caused higher DALYs in females than males, a pattern consistent across BRICS+ nations. In 2021, high-income countries had the highest average NP DALYs (309/100,000), upper-middle-income countries had the highest LBP DALYs (900/100,000), and lower-middle-income countries had the highest DALYs for other MSK disorders (582/100,000). Males in high and upper-middle-income countries experienced higher MSK disorder burdens, with high-income countries reporting the highest LBP and gout DALYs. Females in lower-middle-income countries had the highest LBP DALYs, and DALYs for other MSK disorders increased with national income levels (Figure 1).

Table 3 and Supplementary Table S1 (available at https://weekly.chinacdc.cn/) present the joinpoint regression analysis for age-standardized MSK disorder indicators from 1990 to 2021. Globally, MSK incidence rates declined significantly, with an AAPC of

TABLE 1. Age-standardized incidence, prevalence, and DALYs rates of MSK disorders in 1990 and 2021 in BRICS+ nations.

Country	Sex	Age-standardized incidence (%)				Age-standardized prevalence (%)				Age-standardized DALYs (per 100,000)			
		1990		2021		1990		2021		1990		2021	
		Rate	95% *UI*	Rate	95% *UI*	Rate	95% *UI*	Rate	95% *UI*	Rate	95% *UI*	Rate	95% *UI*
Global	Both	4.64	4.20−5.10	4.35	3.96–4.76	19.18	18.08–20.28	19.83	18.81–20.94	1,886	1,380–2,523	1,909	1,395–2,548
	Male	3.78	3.42–4.14	3.51	3.20–3.84	16.06	15.11–17.04	16.72	15.81–17.70	1,493	1,083–1,995	1,518	1,104–2,029
	Female	5.47	4.94–6.03	5.17	4.69–5.67	22.16	20.94–23.39	22.85	21.69–24.07	2,261	1,667–3,015	2,286	1,675–3,051
High-income countries													
Saudi Arabia	Both	4.62	4.17–5.09	4.79	4.33–5.28	17.61	16.48–18.74	19.58	18.37–20.85	1,685	1,219–2,237	1,866	1,364–2,483
	Male	3.96	3.57–4.34	4.11	3.72–4.53	14.66	13.67–15.70	16.37	15.26–17.55	1,319	952–1,782	1,452	1,042–1,963
	Female	5.60	5.05–6.19	5.80	5.22–6.39	22.04	20.44–23.63	24.38	22.91–26.08	2,234	1,625–2,967	2,489	1,807–3,261
UAE	Both	4.32	3.91–4.72	4.47	4.06–4.89	17.54	16.49–18.59	19.19	18.14–20.34	1,668	1,204–2,219	1,813	1,310–2,433
	Male	3.78	3.39–4.12	3.96	3.57–4.34	15.26	14.28–16.25	17.15	16.14–18.22	1,378	988–1,860	1,551	1,115–2,071
	Female	5.45	4.94–5.98	5.69	5.12–6.24	22.45	21.02–23.96	24.66	23.26–26.19	2,282	1,665–3,019	2,542	1,870–3,357
Upper-middle-income countries													
Brazil	Both	5.00	4.51–5.54	5.15	4.65–5.68	22.39	21.1–23.72	22.66	21.37–24.02	2,251	1,664–2,995	2,267	1,670–3,018
	Male	4.07	3.67–4.48	4.20	3.80–4.62	19.19	17.97–20.44	19.44	18.25–20.69	1,824	1,330–2,427	1,837	1,341–2,456
	Female	5.87	5.27–6.53	6.03	5.42–6.67	25.38	23.94–26.78	25.60	24.17–27.13	2,648	1,978–3,513	2,658	1,977–3,518
Russia	Both	5.93	5.34–6.54	5.83	5.26–6.42	20.00	18.72–21.27	20.23	19.00–21.48	1,978	1,449–2,688	2,003	1,470–2,717
	Male	4.96	4.48–5.45	4.86	4.39–5.34	16.45	15.40–17.51	16.72	15.68–17.86	1,491	1,087–2,052	1,519	1,105–2,087
	Female	6.72	6.04–7.43	6.65	6.00–7.32	22.77	21.28–24.27	23.11	21.71–24.54	2,343	1,730–3,149	2,387	1,760–3,218
China	Both	4.04	3.65–4.44	3.63	3.31–3.95	16.97	15.95–17.98	17.40	16.41–18.41	1,616	1,170–2,151	1,578	1,140–2,129
	Male	3.30	2.99–3.60	3.08	2.82–3.37	14.40	13.51–15.33	15.20	14.28–16.19	1,306	944–1,739	1,318	946–1,774
	Female	4.79	4.30–5.29	4.18	3.80–4.55	19.56	18.37–20.70	19.59	18.37–20.70	1,930	1,400–2,580	1,839	1,333–2,484
South Africa	Both	4.26	3.86–4.65	4.12	3.74–4.51	17.70	16.67–18.72	18.35	17.32–19.37	1,707	1,255–2,256	1,713	1,262–2,267
	Male	3.52	3.19–3.84	3.51	3.20–3.83	15.31	14.41–16.22	16.30	15.44–17.21	1,359	990–1,831	1,428	1,043–1,920
	Female	4.91	4.44–5.39	4.66	4.22–5.14	19.77	18.58–20.97	20.18	18.99–21.36	2,003	1,476–2,654	1,962	1,447–2,591
Egypt	Both	4.80	4.33–5.31	4.95	4.48–5.46	18.62	17.51–19.85	20.48	19.26–21.76	1,836	1,339–2,445	2,018	1,473–2,678
	Male	4.00	3.61–4.43	4.14	3.75–4.56	15.25	14.23–16.33	17.06	16.05–18.22	1,421	1,025–1,912	1,589	1,154–2,131
	Female	5.63	5.10–6.22	5.83	5.25–6.45	22.15	20.74–23.73	24.24	22.77–25.79	2,269	1,651–2,997	2,489	1,818–3,266
Lower-middle-income countries													
India	Both	4.13	3.72–4.55	3.80	3.44–4.17	18.95	17.83–20.15	19.95	18.83–21.24	1,835	1,361–2,417	1,906	1,407–2,510
	Male	3.04	2.74–3.33	2.66	2.41–2.91	15.36	14.4–16.39	15.86	14.83–16.92	1,411	1,044–1,864	1,419	1,037–1,880
	Female	5.31	4.77–5.87	4.94	4.45–5.44	22.85	21.55–24.26	24.07	22.75–25.55	2,294	1,705–3,016	2,394	1,773–3,143
Iran	Both	5.65	5.08–6.23	5.40	4.88–5.94	19.99	18.63–21.34	21.02	19.74–22.35	2,036	1,489–2,707	2,112	1,540–2,812
	Male	4.76	4.29–5.23	4.35	3.92–4.76	16.35	15.22–17.47	17.07	16.02–18.22	1,581	1,152–2,127	1,612	1,167–2,172
	Female	6.59	5.94–7.29	6.49	5.86–7.16	23.82	22.2–25.38	25.06	23.5–26.62	2,515	1,840–3,324	2,621	1,910–3,479
Low-income countries													
Ethiopia	Both	4.47	4.02–4.92	4.32	3.91–4.75	16.40	15.34–17.44	17.24	16.20–18.29	1,581	1,166–2,105	1,613	1,171–2,156
	Male	3.82	3.44–4.20	3.71	3.35–4.06	14.28	13.35–15.23	15.25	14.28–16.22	1,325	975–1,775	1,372	990–1,851
	Female	5.12	4.61–5.66	4.94	4.45–5.45	18.53	17.32–19.67	19.25	18.05–20.44	1,841	1,354–2,444	1,855	1,359–2,479

Abbreviation: MSK=musculoskeletal; DALYs=disability-adjusted life years; *UI*=uncertainty interval.

TABLE 2. Age-standardized DALYs (95% *UI*) per 100,000 population for different MSK disorders in BRICS+ nations by sex in 1990 and 2021.

Country	Sex	RA		OA		LBP		NP		Gout		Other MSK disorders	
		1990	2021	1990	2021	1990	2021	1990	2021	1990	2021	1990	2021
Global	Both	36 (29–46)	36 (27–46)	223 (107–450)	245 (117–493)	937 (669–1,261)	832 (596–1,115)	242 (162–344)	242 (163–343)	17 (11–24)	20 (14–29)	431 (306–585)	534 (375–724)
	Male	22 (17–28)	22 (17–29)	182 (88–369)	201 (96–405)	721 (512–974)	635 (454–854)	203 (135–288)	199 (134–284)	26 (18–38)	32 (21–45)	338 (237–467)	429 (298–589)
	Female	50 (39–64)	49 (36–64)	258 (123–520)	284 (136–573)	1–142 (817–1,533)	1–022 (732–1,370)	280 (187–399)	285 (190–402)	8 (5–12)	10 (7–14)	523 (375–704)	637 (450–858)
High-income countries													
Saudi Arabia	Both	9 (6–12)	15 (10–21)	193 (93–389)	233 (112–468)	888 (629–1191)	907 (646–1,205)	331 (220–471)	331 (221–471)	15 (10–22)	20 (14–28)	249 (169–356)	361 (253–509)
	Male	4 (2–5)	7 (5–10)	173 (83–347)	207 (100–416)	753 (524–1013)	768 (548–1,021)	210 (137–297)	208 (136–297)	20 (13–30)	26 (18–38)	160 (96–246)	235 (156–352)
	Female	17 (11–23)	26 (18–38)	222 (107–444)	271 (130–541)	1–083 (774–1,443)	1–110 (783–1,481)	519 (346–747)	518 (346–749)	7 (5–11)	10 (6–14)	387 (279–532)	553 (400–757)
UAE	Both	14 (10–19)	16 (12–23)	201 (96–407)	221 (105–444)	803 (571–1,068)	824 (589–1,101)	302 (201–428)	287 (192–408)	18 (12–26)	24 (16–34)	331 (231–457)	442 (308–604)
	Male	8 (6–11)	8 (6–12)	181 (87–369)	207 (98–418)	693 (494–935)	724 (518–974)	210 (138–302)	210 (137–298)	23 (15–33)	27 (19–40)	262 (171–373)	374 (251–526)
	Female	26 (18–37)	41 (28–55)	234 (111–480)	268 (128–543)	1–016 (724–1,356)	1–059 (758–1,403)	520 (346–752)	517 (347–750)	8 (5–12)	10 (6–14)	478 (344–647)	647 (471–869)
Upper-middle-income countries													
Brazil	Both	29 (21–38)	28 (21–37)	228 (109–460)	260 (125–525)	1–002 (715–1,345)	1–034 (745–1,388)	276 (185–397)	276 (185–398)	6 (4–9)	8 (5–11)	709 (509–961)	660 (469–899)
	Male	17 (13–23)	16 (12–22)	206 (99–416)	229 (110–462)	767 (548–1,031)	793 (563–1,061)	246 (166–356)	247 (165–358)	9 (6–12)	11 (7–15)	578 (413–798)	541 (380–750)
	Female	39 (29–52)	39 (28–51)	247 (119–497)	286 (138–575)	1–222 (871–1,639)	1–254 (908–1,677)	304 (202–435)	304 (202–435)	4 (3–6)	6 (4–8)	832 (602–1,118)	770 (554–1,034)
Russia	Both	35 (28–44)	38 (29–49)	279 (133–566)	286 (137–579)	1–255 (899–1,690)	1–206 (867–1,623)	268 (180–384)	268 (180–384)	11 (8–16)	13 (9–19)	130 (92–179)	191 (139–263)
	Male	16 (13–21)	19 (15–24)	242 (116–493)	250 (120–506)	955 (683–1,293)	923 (657–1,241)	242 (162–349)	243 (163–350)	20 (14–29)	23 (15–32)	15 (12–22)	61 (41–93)
	Female	49 (38–61)	53 (40–69)	300 (142–601)	310 (147–623)	1–481 (1–065–1,985)	1–433 (1–032–1,926)	290 (192–417)	290 (192–416)	6 (4–9)	7 (5–11)	218 (155–305)	294 (212–400)
China	Both	42 (33–54)	42 (31–55)	211 (102–424)	245 (117–492)	749 (530–1,014)	603 (428–810)	248 (164–353)	255 (167–358)	20 (13–29)	25 (17–36)	346 (241–476)	408 (283–564)
	Male	28 (20–36)	31 (23–40)	169 (81–341)	197 (94–397)	572 (402–779)	488 (347–658)	214 (142–308)	216 (145–308)	30 (20–44)	39 (26–55)	293 (202–410)	347 (238–485)
	Female	58 (44–74)	54 (39–73)	251 (121–503)	290 (139–583)	926 (658–1,253)	716 (506–960)	284 (188–406)	294 (194–414)	10 (7–15)	12 (8–18)	402 (284–547)	472 (333–647)
South Africa	Both	73 (57–92)	56 (43–72)	242 (116–487)	260 (126–521)	759 (540–1,019)	693 (498–928)	293 (195–422)	289 (192–413)	16 (11–23)	17 (12–25)	324 (236–443)	397 (287–532)
	Male	59 (44–76)	44 (34–60)	234 (113–471)	250 (121–504)	574 (409–769)	557 (396–748)	227 (150–332)	226 (149–326)	27 (18–39)	29 (20–42)	239 (170–336)	322 (230–443)
	Female	85 (66–108)	66 (50–83)	247 (118–497)	266 (128–537)	913 (650–1,225)	812 (582–1,086)	353 (233–506)	348 (230–495)	8 (5–11)	9 (6–12)	397 (290–532)	462 (338–616)

Continued

Country	Sex	RA		OA		LBP		NP		Gout		Other MSK disorders	
		1990	2021	1990	2021	1990	2021	1990	2021	1990	2021	1990	2021
Egypt	Both	11 (8–16)	16 (11–22)	184 (89–376)	213 (103–441)	944 (670–1,267)	965 (698–1,290)	364 (240–521)	358 (238–510)	14 (9–20)	18 (12–26)	319 (213–447)	448 (310–610)
	Male	4 (3–6)	6 (4–9)	165 (79–329)	189 (90–397)	778 (546–1,052)	800 (567–1,081)	211 (136–303)	210 (138–303)	21 (14–30)	25 (16–36)	242 (159–347)	358 (245–508)
	Female	19 (13–26)	28 (19–38)	205 (98–421)	241 (116–493)	1–117 (801–1,508)	1–145 (826–1,520)	523 (345–757)	520 (343–755)	7 (5–11)	9 (6–13)	398 (274–552)	547 (382–743)
Lower-middle-income countries													
India	Both	35 (26–44)	41 (32–52)	185 (90–375)	221 (106–447)	824 (594–1,107)	714 (509–955)	157 (105–226)	159 (105–228)	12 (8–17)	13 (9–19)	621 (441–842)	758 (535–1,027)
	Male	21 (14–27)	24 (17–30)	144 (70–291)	168 (81–340)	556 (396–747)	445 (315–599)	138 (92–201)	139 (92–201)	17 (12–25)	19 (13–28)	535 (378–727)	625 (435–852)
	Female	49 (38–64)	57 (44–73)	229 (110–460)	272 (130–545)	1–114 (804–1,493)	984 (704–1,320)	179 (118–256)	179 (118–256)	6 (4–9)	7 (5–10)	717 (509–967)	896 (638–1,210)
Iran	Both	10 (7–14)	13 (9–19)	187 (89–377)	215 (103–433)	1–132 (811–1,523)	1–028 (740–1,370)	432 (287–618)	433 (289–618)	14 (9–20)	15 (10–22)	263 (178–371)	407 (284–560)
	Male	3 (2–5)	5 (3–7)	167 (80–337)	187 (90–380)	936 (667–1,256)	804 (573–1,074)	289 (192–417)	290 (192–415)	20 (13–29)	22 (15–32)	166 (104–246)	304 (209–433)
	Female	17 (12–23)	22 (15–30)	207 (99–419)	242 (115–484)	1–335 (962–1,788)	1–257 (909–1,674)	582 (385–830)	580 (384–825)	7 (5–10)	8 (5–12)	366 (254–503)	512 (361–698)
Low-income country													
Ethiopia	Both	12 (8–20)	11 (7–15)	174 (84–354)	221 (106–444)	884 (632–1,180)	822 (584–1,106)	236 (155–337)	237 (156–338)	13 (9–19)	14 (9–20)	262 (183–358)	307 (207–427)
	Male	10 (7–14)	9 (6–12)	155 (75–312)	198 (95–397)	720 (511–960)	673 (479–903)	208 (137–295)	209 (137–294)	19 (13–28)	21 (14–30)	214 (144–303)	263 (172–375)
	Female	14 (9–29)	13 (8–20)	195 (94–396)	245 (118–491)	1–052 (753–1,405)	973 (689–1,306)	264 (172–376)	266 (173–379)	7 (4–10)	7 (5–11)	310 (224–419)	352 (243–478)

Abbreviation: DALYs=disability adjusted life years; MSK=musculoskeletal; RA=rheumatoid arthritis; OA=osteoarthritis; LBP=low back pain; NP=neck pain; *UI*=uncertainty interval.

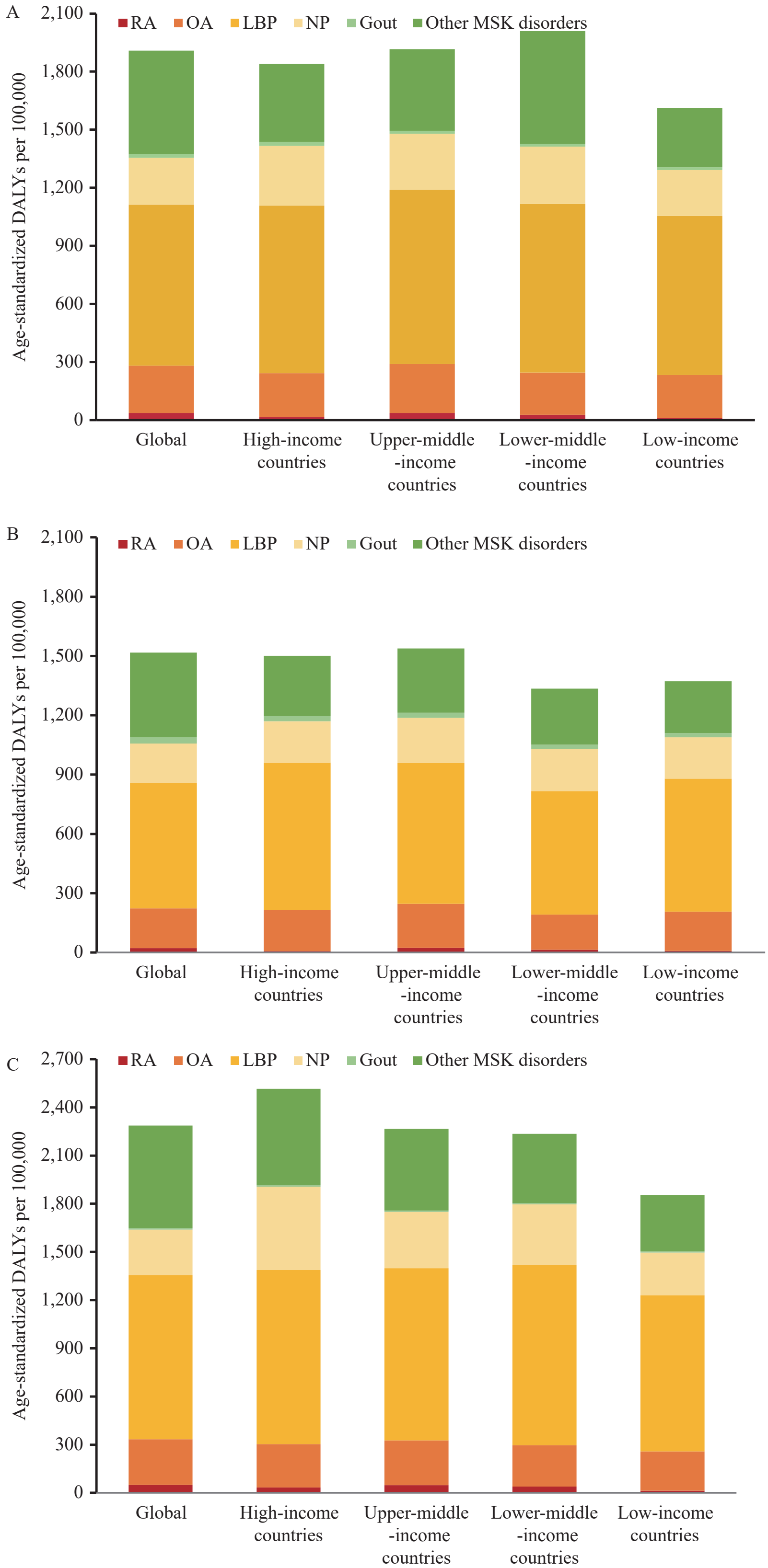

FIGURE 1. Age-standardized DALYs caused by different types of MSK disorders by sex in BRICS+ nations, 2021. (A) Both sexes; (B) Male; (C) Female.

Abbreviations: DALYs=disability adjusted life years; MSK=musculoskeletal; RA=rheumatoid arthritis; OA=osteoarthritis; LBP=low back pain; NP=neck pain.

TABLE 3. The trend of age-standardized incidence, prevalence, and DALYs rates (per 100,000 population) for MSK disorders in BRICS+ nations from 1990 to 2021.

Country	Age-standardized incidence			Age-standardized prevalence			Age-standardized DALYs		
	AAPC	95% *CI*	*P*	AAPC	95% *CI*	*P*	AAPC	95% *CI*	*P*
Global	−0.21	−0.22, −0.20	<0.001	0.11	0.09, 0.13	<0.001	0.04	0.02, 0.06	<0.001
High-income countries									
Saudi Arabia	0.12	0.11, 0.12	<0.001	0.34	0.33, 0.35	<0.001	0.33	0.32, 0.34	<0.001
UAE	0.11	0.11, 0.12	<0.001	0.29	0.28, 0.30	<0.001	0.27	0.25, 0.29	<0.001
Upper-middle-income countries									
Brazil	0.10	0.08, 0.11	<0.001	0.04	0.03, 0.05	<0.001	0.02	−0.01, 0.04	0.066
Russia	−0.05	−0.06, −0.04	<0.001	0.04	0.03, 0.06	<0.001	0.04	0.01, 0.08	0.033
China	−0.34	−0.38, −0.30	<0.001	0.09	0.07, 0.11	<0.001	−0.06	−0.10, −0.02	0.005
South Africa	−0.11	−0.12, −0.10	<0.001	0.12	0.10, 0.13	<0.001	0.01	−0.01, 0.03	0.273
Egypt	0.10	0.09, 0.11	<0.001	0.31	0.30, 0.31	<0.001	0.30	0.29, 0.32	<0.001
Lower-middle-income countries									
India	−0.27	−0.33, −0.21	<0.001	0.16	0.10, 0.21	<0.001	0.12	0.06, 0.17	<0.001
Iran	−0.13	−0.15, −0.11	<0.001	0.17	0.15, 0.18	<0.001	0.12	0.10, 0.15	<0.001
Low-income country									
Ethiopia	−0.11	−0.11, −0.10	<0.001	0.16	0.15, 0.17	<0.001	0.07	0.06, 0.08	<0.001

Abbreviation: DALYs=disability-adjusted life years; MSK=musculoskeletal; *CI*=confidence interval; AAPC=average annual percentage change.

−0.21 [95% confidence interval (*CI*): −0.22, −0.20]. Among BRICS+ nations, Saudi Arabia, UAE, Brazil, and Egypt showed increasing trends, while others declined, with China experiencing the largest decrease [average annual percentage change (AAPC)=−0.34; 95% *CI*: −0.38, −0.30] and Saudi Arabia had the largest increase (AAPC=0.12; 95% *CI*: 0.11, 0.12). Age-standardized prevalence rates increased globally and across all BRICS+ nations, with Saudi Arabia showing the most substantial increase (AAPC=0.34; 95% *CI*: 0.33, 0.35). China's MSK DALYs demonstrated a significant decline, while other nations, except Brazil and South Africa, showed growth, with Saudi Arabia and UAE leading the increase. Globally, DALYs exhibited a fluctuating trend with an AAPC of 0.04% (95% *CI*: 0.02%, 0.06%). High-income countries like Saudi Arabia experienced a consistent increase in DALYs, while lower-middle-income countries like India and Iran showed M-shaped trends. Ethiopia, a low-income nation, experienced a down-up-down trend. Upper-middle-income countries displayed varied trends, with Egypt's DALYs increasing until 2019 before stabilizing. Russia, China, and South Africa initially showed declining DALYs, with China exhibiting a unique down-stable-up-stable-up pattern. Sex differences in DALY trends were complex and varied by country. The trend in DALYs among males in China was more complex compared to females, while the opposite was true in South Africa. Moreover, the AAPCs for males in both countries were positive, differing from those for females.

DISCUSSION

This study analyzed the disease burden, major types, and trends of MSK disorders in BRICS+ nations between 1990 and 2021 using the GBD 2021 database. The 10 countries are classified into different income levels, including high, upper-middle, lower-middle, and low-income countries. Overall, MSK disorders imposed a heavier disease burden on females than males across BRICS+ countries, with higher rates observed in lower-middle and upper-middle income countries.

From 1990 to 2021, Russia maintained the highest age-standardized incidence of MSK disorders, while China consistently reported the lowest. Among BRICS+ nations, Saudi Arabia showed the largest increase (3.55%) in age-standardized incidence, with Brazil and Egypt are also demonstrating upward trends. Conversely, China experienced the most substantial decline (−11.28%) in age-standardized incidence. Regarding age-standardized prevalence, MSK disorders were most common in Brazil, followed by Iran and Russia, and least common in Ethiopia and China. Saudi Arabia exhibited the largest increase in prevalence (11.19%) over the past three decades.

Brazil had the highest age-standardized DALYs per 100,000 population for MSK disorders among BRICS+ nations in both 1990 and 2021. Saudi Arabia, UAE, and Egypt showed consistent increasing trends in DALYs, with Saudi Arabia experiencing the largest increase (10.74%). YLDs caused by metabolic, behavioral, and environmental or occupational risk factors have been increasing across all age groups in Saudi Arabia, thereby exacerbating the burden of MSK disorders (*7*). China demonstrated the largest decrease in DALYs (−2.35%), primarily due to reductions in low back pain, related to improvements in sanitation and healthcare services. However, with rapid population aging, China will face immense challenges in managing the burden of MSK disorders in the future (*8*–*9*). The DALYs attributed to MSK disorders in Ethiopia remained relatively low, which may be related to poor documentation of the magnitude of NCDs at both national and subnational levels (*10*).

Sex disparities in MSK disorders are evident, with females experiencing a greater disease burden than males both globally and across BRICS+ nations. These differences likely stem from physiological factors such as ligament relaxation, hormonal influences (estrogen and progesterone), and behavioral factors, including exercise habits and work posture (*11*). Pregnancy and menopause significantly contribute to MSK disorders in females (*12*). Saudi Arabia exhibited the largest sex disparity in 2021, followed by Iran, which can be attributed to differences in life expectancy and cultural gender inequalities (*13*).

LBP was the predominant contributor to MSK-related DALYs in 2021, with Russia showing the highest burden, followed by Brazil and Iran. High body mass index (BMI), a significant risk factor for MSK disorders, may explain the elevated DALYs in these countries (*14*–*15*). Additionally, increased tobacco use in Iran potentially influences LBP prevalence (*15*). While gout had comparatively low DALYs globally and across BRICS+ nations, it imposed a greater burden on males, possibly due to unhealthy lifestyle behaviors such as smoking and alcohol consumption, as well as hormonal differences.

As life expectancy increases across BRICS+ nations, maintaining physical function and quality of life becomes increasingly challenging, particularly for females who generally live longer. MSK health is fundamental to quality of life across all age groups. Occupational risks, tobacco use, high BMI, and kidney dysfunction were the primary contributors to MSK disorder DALYs globally, accounting for over 20% of the global burden (*6*). BRICS+ countries could benefit from strengthened coordination in policy development and implementation to collectively advance global MSK health.

This study has several limitations. First, it relies on GBD modeling, which may not fully capture the actual situation, particularly in less developed countries. Second, some MSK disorders were grouped together without specific analysis. Finally, the study did not consider different age groups, which will be addressed in future research.

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SUPPLEMENTARY MATERIAL

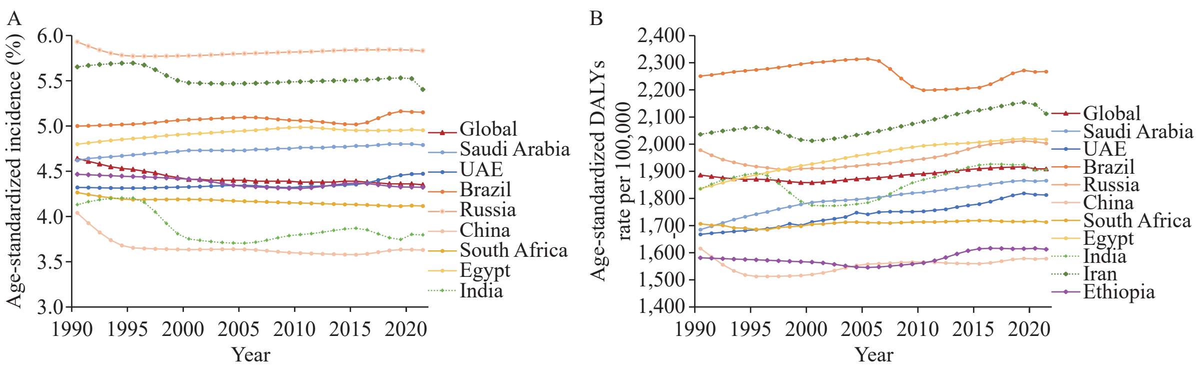
SUPPLEMENTARY TABLE S1. Log-transformed joinpoint trends of MSK disorders DALYs by sex in BRICS+ nations between 1990 and 2021.

Country	Sex	Trend 1		Trend 2		Trend 3		Trend 4		Trend 5		Trend 6		1990–2021 AAPC, (95% *CI*)
		Years	APC	Years	APC	Years	APC	Years	APC	Years	APC	Years	APC	
Global	Both	1990–1993	−0.25*	1993–1996	−0.05*	1996–2000	−0.16*	2000–2016	0.18*	2016–2019	0.06	2019–2021	−0.21*	0.04* (0.02–0.06)
	Male	1990–2003	−0.13*	1993–1996	0.01	1996–2000	−0.13*	2000–2018	0.18*	2018–2021	−0.24*	NA	NA	0.05* (0.03–0.08)
	Female	1990–1992	−0.34*	1992–2000	−0.15*	2000–2017	0.18*	2017–2021	−0.04	NA	NA	NA	NA	0.04* (0.02–0.05)
High-income countries														
Saudi Arabia	Both	1990–1994	0.70*	1994–2000	0.51*	2000–2004	0.13*	2004–2012	0.25*	2012–2018	0.28*	2018–2021	0.03*	0.33* (0.31–0.34)
	Male	1990–1994	0.81*	1994–2000	0.50*	2000–2004	−0.07*	2004–2010	0.09*	2010–2018	0.34*	2018–2021	0.10*	0.31* (0.29–0.32)
	Female	1990–1994	0.56*	1994–2000	0.34*	2000–2004	0.20*	2004–2010	0.52*	2010–2018	0.33*	2018–2021	−0.02	0.35* (0.33–0.36)
UAE	Both	1990–1997	0.22*	1997–2005	0.40*	2005–2011	0.07*	2011–2015	0.35*	2015–2019	0.55*	2019–2021	−0.21*	0.27* (0.25–0.29)
	Male	1990–2008	0.41*	2008–2015	0.27*	2015–2019	0.63*	2019–2021	−0.03	NA	NA	NA	NA	0.38* (0.37–0.39)
	Female	1990–2003	0.32*	2003–2008	0.50*	2008–2011	0.15	2011–2019	0.62*	2019–2021	−0.72*	NA	NA	0.34* (0.32–0.37)
Upper−middle-income countries														
Brazil	Both	1990–2003	0.21*	2003–2006	−0.02	2006–2009	−1.56*	2009–2015	0.01	2015–2019	0.77*	2019–2021	−0.18*	0.02 (–0.01–0.04)
	Male	1990–2005	0.29*	2005–2010	−1.50*	2010–2015	0.22*	2015–2019	0.72*	2019–2021	−0.06	NA	NA	0.02 (–0.00–0.04)
	Female	1990–2002	0.14*	2002–2006	0.00	2006–2009	−1.20*	2009–2015	−0.04*	2015–2019	0.76*	2019–2021	−0.23*	0.01 (–0.01–0.04)
Russia	Both	1990–1993	−0.79*	1993–1998	−0.29*	1998–2010	0.17*	2010–2016	0.50*	2016–2019	0.19	2019–2021	−0.22	0.04* (0.01–0.08)
	Male	1990–1992	−0.89*	1992–1997	−0.34*	1997–2007	0.17*	2007–2011	0.25*	2011–2016	0.55*	2016–2021	0.01	0.06* (0.04–0.09)
	Female	1990–1993	−0.73*	1993–1997	−0.32*	1997–2004	0.08*	2004–2010	0.24*	2010–2018	0.48*	2018–2021	−0.11	0.07* (0.04–0.09)
China	Both	1990–1994	−1.58*	1994–2000	0.06	2000–2004	0.60*	2004–2009	0.17*	2009–2014	−0.10	2014–2021	0.20*	−0.06* (−0.10–−0.02)
	Male	1990–1994	−0.78*	1994–2000	0.04	2000–2005	0.53*	2005–2015	−0.07*	2015–2018	0.60*	2018–2021	0.08	0.03* (0.01–0.06)
	Female	1990–1994	−2.13*	1994–2000	0.07	2000–2004	0.57*	2004–2010	0.23*	2010–2014	−0.20*	2014–2021	0.13*	−0.14* (−0.18–−0.11)
South Africa	Both	1990–1995	−0.26*	1995–2003	0.21*	2003–2007	−0.05	2007–2015	0.06*	2015–2021	−0.05*	NA	NA	0.01 (−0.01–0.03)
	Male	1990–1994	−0.09*	1994–1998	0.25*	1998–2005	0.14*	2005–2015	0.28*	2015–2021	0.08*	NA	NA	0.16* (0.14–0.17)
	Female	1990–1996	−0.40*	1996–2003	0.23*	2003–2007	−0.14	2007–2021	−0.04*	NA	NA	NA	NA	−0.06* (−0.08–−0.04)
Egypt	Both	1990–1993	0.60*	1993–1998	0.47*	1998–2009	0.36*	2009–2019	0.14*	2019–2021	−0.06	NA	NA	0.30* (0.29–0.32)
	Male	1990–1993	0.68*	1993–1999	0.53*	1999–2009	0.40*	2009–2015	0.17*	2015–2019	0.25*	2019–2021	−0.05	0.36* (0.34–0.38)
	Female	1990–1993	0.56*	1993–1997	0.45*	1997–2007	0.38*	2007–2010	0.33*	2010–2019	0.13*	2019–2021	−0.10*	0.30* (0.29–0.31)

Continued

Country	Sex	Trend 1		Trend 2		Trend 3		Trend 4		Trend 5		Trend 6		1990–2021 AAPC, (95% *CI*)
		Years	APC	Years	APC	Years	APC	Years	APC	Years	APC	Years	APC	
Lower−middle-income countries														
India	Both	1990–1995	0.69*	1995–2000	−1.43*	2000–2005	0.11	2005–2009	1.07*	2009–2016	0.57*	2016–2021	−0.29*	0.12* (0.06–0.17)
	Male	1990–1995	0.64*	1995–2000	−1.63*	2000–2005	0.15	2005–2010	1.02*	2010–2018	0.34*	2018–2021	−1.18*	−0.00 (−0.12–0.12)
	Female	1990–1995	0.68*	1995–2000	−1.38*	2000–2005	0.02	2005–2009	0.99*	2009–2015	0.63*	2015–2021	−0.04	0.13* (0.09–0.17)
Iran	Both	1990–1995	0.28*	1995–2000	−0.54*	2000–2003	0.26*	2003–2019	0.40*	2019–2021	−0.98*	NA	NA	0.12* (0.10–0.15)
	Male	1990–1995	0.32*	1995–2000	−0.96*	2000–2009	0.44*	2009–2015	0.69*	2015–2019	0.08	2019–2021	−1.34*	0.08* (0.06–0.10)
	Female	1990–1995	0.24*	1995–2000	−0.28*	2000–2015	0.23*	2015–2019	0.58*	2019–2021	−0.66*	NA	NA	0.13* (0.12–0.15)
Low-income country														
Ethiopia	Both	1990–2000	−0.10*	2000–2005	−0.28*	2005–2010	0.22*	2010–2015	0.69*	2015–2021	−0.03*	NA	NA	0.07* (0.06–0.08)
	Male	1990–2000	−0.01*	2000–2005	−0.15*	2005–2010	0.33*	2010–2015	0.74*	2015–2019	−0.33*	2019–2021	0.10*	0.11* (0.10–0.12)
	Female	1990–1999	−0.07*	1999–2005	−0.36*	2005–2010	0.08*	2010–2015	0.59*	2015–2019	0.16*	2019–2021	−0.22*	0.02* (0.01–0.04)

Abbreviation: DALYs=disability adjusted life years; MSK=musculoskeletal; *CI*=confidence interval; APC=annual percentage change; AAPC=average annual percentage change; NA=not applicable.
* *P*<0.05.



SUPPLEMENTARY FIGURE S1. Age-standardized rates of MSK disorders in BRICS+ nations, 1990–2021. (A) Age-standardized incidence (%); (B) Age-standardized DALYs rate (per 100,000).
Abbreviation: DALYs=disability adjusted life years; MSK=musculoskeletal.

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