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Research paper

Global burden of upper respiratory infections in 204 countries and territories, from 1990 to 2019

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A B S T R A C T

Background: Upper respiratory infections (URIs) are among the most common diseases. However, the related burden has not been comprehensively evaluated. Thus, we designed the present study to describe the global and regional burden of URIs from 1990 to 2019.
Methods: A secondary analysis was performed on the incidence, mortality, and disability-adjusted life years (DALYs) of URIs in different sex and age groups, from 21 geographic regions, 204 countries and territories, between 1990 and 2019, using the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019. Countries and territories were categorized according to Socio-demographic Index (SDI) quintiles.
Findings: Globally, the incident cases of URIs reached 17·2 (95% uncertainty interval: 15·4 to 19·3) billion in 2019, which accounted for 42·83% (40·01% to 45·77%) cases from all causes in the GBD 2019 study. The age-standardized incidence rate remained stable from 1990 to 2019, while significant decreases were found in the mortality and DALY rate. The highest age-standardized incidence rates from 1990 to 2019 and the highest age-standardized DALY rates after 2011 were observed in high SDI regions. Among all the age groups, children under five years old suffered from the highest incidence and DALY rates, both of which were decreased with increasing age. Fatal consequences of URIs occurred mostly in the elderly and children under five years old.
Interpretation: The present study provided comprehensive estimates of URIs burden for the first time. Our findings, highlighting the substantial incidence and considerable DALYs due to URIs, are expected to attract more attention to URIs and provide future explorations in the prevention and treatment with epidemiological evidence.
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1. Introduction

Infections of the upper respiratory tract, such as laryngitis, pharyngitis, nasopharyngitis, and rhinitis, are among the most common diseases in primary medical care [1,2]. The most common symptoms of upper respiratory infections (URIs) include coughing, a sore throat, nasal obstruction, and headache [1,3]. Although those conditions are often self-limited and non-fatal, the symptoms can significantly impair life quality and productivity [1]. In some cases, URIs even induce severe complications, such as pneumonia, otitis media, glomerulonephritis, and myocarditis, thus further adding to the costs of healthcare resources, resulting in a substantial financial burden for the society [4–6].

URIs are mainly caused by viruses, including rhinovirus, coronavirus, respiratory syncytial virus and so on [7–9]. Following virus infections, bacterial colonization may occur in some cases, which aggravates the disease and leads to prolonged recovery [9,10]. The recent pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) further exposed the potential threats of respiratory viruses [11]. URIs are important presentations for the reproduction and circulation of respiratory viruses [9]; however, comprehensive estimations of the incidence rates and the subsequent effects of URIs are still scarce, leaving a gap for the policymakers and services devoted to decrease the burden of those diseases. Therefore, in this study, we aimed to describe the incidence, mortality and disability-adjusted life years (DALYs) due to URIs in different sexes and age groups, at global and regional levels, during 1990 to 2019, using data from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019 [12].

2. Methods

2.1. Overview

The GBD 2019 study provided a comprehensive and up-to-date estimation of the epidemiology of diseases and injuries in different sexes and age groups, for 204 countries and territories, 21 regions,

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Research in context

Evidence before this study

We searched PubMed, Scopus, and Medline for articles published until December 22, 2020 focusing on the incidence, mortality, and overall burden of upper respiratory infections (URIs), using the MeSH terms including "global burden of disease", "incidence", "epidemiology", "respiratory tract infections", "common cold", "pharyngitis", "nasopharyngitis", "tonsillitis", "rhinitis", "sinusitis", "supraglottitis", and "epiglottitis", with no language restrictions. Although previous studies have regarded URIs as common diseases, the incidence of URIs has never been evaluated globally. The burden of URIs, in term of mortality or disability-adjusted life years (DALYs), has never been reported either.

Added value of this study

This study, for the first time, provided a comprehensive assessment on the burden of URIs, which presented 17·2 billion incident cases in 2019 globally. The age-standardized incidence rates remained stable from 1990 to 2019, while significant decreases were found in the mortality and DALY rates. Across Socio-demographic Index (SDI) quintiles, high SDI region had the highest age-standardized incidence rates from 1990 to 2019, and the highest age-standardized DALY rates after 2011. The incidence and DALY rates of URIs showed descending trends with increasing age, while fatal consequences occurred mostly in the elderly and children under five years old.

Implications of all the available evidence

The substantial incidence and considerable DALYs highlighted the overlooked burden of URIs, suggesting that more efforts are needed for the prevention and treatment of URIs. The age-specific estimations implied that children and old people may benefit most from intervention strategies targeted URIs.

from 1990 to 2019 [12]. Details about the study design and methods of GBD studies have been extensively described in existing GBD literature [12–18]. Data of GBD studies are publicly available online, and can be extracted by Global Health Data Exchange query tool (http://ghdx.healthdata.org/gbd-results-tool). In GBD 2019, URIs were defined as the infections of upper respiratory airways [12]. Detailed information about the International Classification of Disease (ICD) codes is provided in Supplementary Table 1. This study is not a part of the GBD Institute for Health Metrics and Evaluation Commission. We extracted data on the incidence, deaths, DALYs, and their age-standardized rates (ASRs, per 100,000 people) due to URIs, and performed a secondary analysis of GBD 2019. The detailed analysis plan is provided in our study protocol (Supplementary Material, pages 1 to 4). This study does not contain personal or medical information about an identifiable living individual, and animal subjects were not involved. The study adheres to the REporting of studies Conducted using Observational Routinely collected health Data (RECORD) guidelines.

2.2. Data sources

The GBD 2019 study generated and provided estimates on the burden of 369 diseases and injuries, for both sexes, in 204 countries and territories, and from 1990 to 2019 [12,13]. For estimates of the non-fatal burden due to URIs, the GBD 2019 study extracted data from literature reviews and national surveys. Then, DisMod-MR 2.1 model, which was a Bayesian meta-regression modeling tool, was used to estimate the incidence and prevalence of URIs by location, year, age, and sex, based on all available data. Furthermore, the severity of URIs was split into mild and moderate/severe with different disability weights (DW). Mild URIs (DW, 95% CI: 0·006, 0·002–0·012) were characterized by mild discomfort, but no difficulty with daily activities. Moderate/severe URIs (DW, 95% CI: 0·051, 0·032–0·074) involved fever, aches, and malaise, causing some difficulty with daily activities. The years of disability (YLDs) were calculated by multiplying prevalence by DW.

Fatal burden attributed to URIs was analyzed using vital registration and surveillance data from the cause of death database. The deaths were distributed to different causes according to the ICD code mapping. Then, a generic Cause of Death Ensemble modeling (CODEm) approach was used to estimate the mortality due to URIs by age, sex, location, and year. The years of life lost (YLLs) for URIs were computed by multiplying the number of estimated deaths by the years of life remaining up to the standard life expectancy at the age of death [12,19]. The DALYs, which represented the total number of years lost to illness, disability, or premature death, were calculated as the sum of YLLs and YLDs [12,19,20].

The attributable mortality, YLLs, YLDs, and DALYs for 87 risk factors and combinations of risk factors were estimated in GBD 2019 [13]. The estimations of attributable burdens followed the general framework established for comparative risk assessment, which had been described in previous study [13]. The risk factors for URIs, including low birth weight, short gestation, household air pollution from solid fuels and ambient particulate matter pollution, as well as their attributable mortality and DALYs were extracted from GBD 2019. For every metric, 95% uncertainty intervals were presented based on the 25th and 975th ordered values of 1000 draws.

2.3. Socio-demographic index and geographic regions

Socio-demographic Index (SDI), ranging from 0 (worst) to 100 (best), was calculated from the indices of total fertility rate for women younger than 25 years old, average years of schooling for those 15 years old and older, and lag-distributed income per capita. SDI is regarded as a composite indicator of background social and economic conditions that influence health outcomes in each location, and a higher SDI indicates a better socioeconomic condition. Countries and territories were further categorized into high, high-middle, middle, low-middle, or low SDI regions according to the quintiles of SDI for the year 2019 [12]. GBD 2019 also categorized 204 countries and territories into 21 geographic regions. The included countries and territories for each geographical region were listed in Supplementary Table 2.

2.4. Statistical analyses

We analyzed the incidence, mortality and DALYs in 1990 and 2019, globally and regionally, to gain an overall impression of the URIs burden. Then, we used the ASRs of incidence, mortality and DALYs for comparisons between different groups by sex, age, year, and location. The comparisons were performed in different SDI regions, in 21 geographic regions, as well as in 204 countries and territories.

The percentage of changes in the numbers and ASRs of incidence, mortality, and DALYs were calculated between 1990 and 2019. To further quantify the dynamic changes over time from 1990 to 2019, the estimated annual percentage changes (EAPC) from 1990 to 2019 in ASRs were calculated [21,22]. It is assumed that the natural logarithm of ASR is linear along with time. Thus, the calculation of EAPC was based on the following formula:

$$Y = \alpha + \beta X + \varepsilon$$

Table 1
Age-standardized rates of incidence and DALY due to upper respiratory infections in global and different regions, in 1990 and 2019, and their percentage changes from 1990 to 2019.

	Age-standardized incidence rate per 100,000 people (95% UI)		Percentage change,% (95% UI)	Age-standardized DALY rate per 100,000 people (95% UI)		Percentage change,% (95% UI)
	1990	2019		1990	2019	
Global	228,685·1 (204,234·0 to 256,840·9)	225,505·7 (201,156·4 to 253,739·5)	−1·39 (−1·86 to −0·88)	115·0 (64·9 to 179·6)	84·4 (52·0 to 128·2)	−26·66 (−48·27 to −5·26)
SDI groups						
High SDI	289,513·8 (257,792·1 to 327,631·1)	289,895·3 (258,319·8 to 327,787·7)	0·13 (−0·54 to 0·83)	104·5 (64·8 to 161·0)	100·5 (60·7 to 156·5)	−3·79 (−6·49 to −2·13)
High-middle SDI	224,834·6 (200,103·6 to 252,981·9)	224,127·8 (199,771·6 to 252,258·8)	−0·31 (−1·13 to 0·49)	100·6 (65·8 to 147·4)	79·9 (48·5 to 125·1)	−20·58 (−35·19 to −5·22)
Middle SDI	222,861·6 (198,846·9 to 250,337·5)	216,855·0 (193,044·0 to 244,451·5)	−2·70 (−3·45 to −1·92)	114·8 (69·3 to 165·0)	80·3 (49·6 to 123·4)	−30·03 (−47·93 to −6·22)
Low-middle SDI	212,208·2 (189,142·2 to 238,537·2)	212,159·3 (189,199·0 to 238,387·7)	−0·02 (−0·89 to 0·78)	106·5 (56·5 to 169·3)	78·9 (49·3 to 121·3)	−25·98 (−52·71 to 0·33)
Low SDI	203,406·3 (181,509·5 to 227,726·0)	193,290·3 (171,499·8 to 217,738·4)	−4·97 (−6·20 to −3·84)	149·7 (51·8 to 321·7)	88·1 (50·3 to 136·5)	−41·14 (−67·16 to 2·25)
Geographic regions						
East Asia	189,333·4 (167,860·8 to 213,966·9)	190,698·6 (168,867·9 to 215,213·0)	0·72 (−0·18 to 1·55)	136·6 (64·2 to 202·1)	70·3 (43·3 to 110·1)	−48·53 (−69·03 to −0·49)
Southeast Asia	267,887·2 (239,644·4 to 301,538·3)	261,531·7 (233,171·2 to 295,836·2)	−2·37 (−3·89 to −0·91)	98·5 (60·8 to 150·6)	91·4 (55·7 to 142·3)	−7·26 (−15·07 to −1·24)
Oceania	205,910·6 (181,518·1 to 231,345·8)	205,878·5 (182,503·1 to 232,271·4)	−0·02 (−3·12 to 3·30)	73·0 (44·0 to 114·0)	71·9 (43·2 to 113·0)	−1·53 (−6·36 to 3·14)
Central Asia	148,710·8 (132,780·9 to 168,992·4)	142,938·2 (127,920·2 to 161,630·6)	−3·88 (−5·49 to −1·97)	119·2 (81·3 to 159·8)	69·9 (48·5 to 98·5)	−41·38 (−55·26 to −17·88)
Central Europe	198,716·3 (176,485·7 to 224,275·2)	198,152·8 (176,012·0 to 222,748·8)	−0·28 (−1·44 to 0·72)	75·4 (48·3 to 113·6)	69·0 (41·8 to 108·4)	−8·49 (−14·36 to −4·79)
Eastern Europe	221,275·1 (197,057·6 to 249,158·2)	221,389·6 (196,813·6 to 249,489·3)	0·05 (−1·01 to 1·09)	104·5 (74·0 to 146·8)	82·0 (51·8 to 124·6)	−21·58 (−31·05 to −14·08)
High-income Asia Pacific	297,108·5 (264,402·9 to 335,724·1)	296,308·6 (263,732·5 to 335,569·8)	−0·27 (−1·58 to 1·09)	110·2 (69·4 to 169·0)	102·9 (62·1 to 161·6)	−6·63 (−11·26 to −3·58)
Australasia	286,094·2 (253,677·1 to 325,510·1)	286,773·8 (252,857·4 to 323,763·7)	0·24 (−3·46 to 4·16)	101·3 (62·3 to 156·1)	98·9 (60·0 to 154·1)	−2·45 (−6·66 to 1·82)
Western Europe	274,344·5 (243,081·4 to 311,554·0)	274,078·1 (243,453·0 to 310,107·9)	−0·10 (−1·22 to 0·97)	99·2 (61·6 to 153·5)	95·1 (57·4 to 149·4)	−4·07 (−6·88 to −2·00)
Southern Latin America	283,763·7 (251,711·0 to 320,315·6)	283,797·1 (251,912·0 to 321,501·1)	0·01 (−2·92 to 3·43)	100·2 (61·6 to 154·6)	98·1 (58·9 to 154·4)	−2·15 (−5·92 to 1·59)
High-income North America	329,983·2 (293,020·8 to 372,241·8)	329,985·1 (293,532·4 to 371,758·3)	0·00 (−0·87 to 0·87)	116·3 (71·0 to 177·9)	114·0 (69·2 to 176·3)	−1·91 (−3·39 to −0·77)
Caribbean	239,260·0 (213,528·7 to 268,128·5)	238,699·4 (212,367·9 to 269,468·6)	−0·23 (−2·94 to 2·02)	98·2 (58·4 to 151·5)	87·7 (53·6 to 135·1)	−10·75 (−29·38 to −0·39)
Andean Latin America	258,266·9 (229,700·2 to 291,266·1)	257,441·1 (228,132·4 to 290,448·1)	−0·32 (−3·39 to 2·85)	117·1 (69·4 to 177·3)	92·8 (57·2 to 141·9)	−20·80 (−44·04 to 1·29)
Central Latin America	256,920·1 (229,163·1 to 288,020·1)	254,828·1 (226,222·8 to 287,514·9)	−0·81 (−2·38 to 0·98)	130·0 (93·8 to 182·7)	92·0 (56·8 to 141·6)	−29·24 (−40·86 to −20·14)
Tropical Latin America	324,986·0 (289,650·9 to 367,503·5)	316,173·7 (280,772·6 to 357,232·4)	−2·71 (−4·67 to −0·81)	122·0 (78·0 to 184·9)	111·1 (67·7 to 172·5)	−8·93 (−13·42 to −5·82)
North Africa and Middle East	244,702·0 (219,422·8 to 273,649·5)	238,138·2 (212,420·9 to 268,000·1)	−2·68 (−4·10 to −1·34)	86·0 (53·2 to 134·1)	82·1 (49·8 to 128·4)	−4·57 (−9·17 to −1·57)
South Asia	197,011·2 (175,267·5 to 221,831·3)	198,648·4 (176,430·0 to 223,879·3)	0·83 (−0·20 to 1·81)	92·3 (48·0 to 150·8)	71·7 (44·4 to 110·4)	−22·32 (−49·47 to 2·04)
Central Sub-Saharan Africa	255,561·2 (227,831·3 to 286,893·3)	255,365·8 (227,058·5 to 288,486·3)	−0·08 (−2·86 to 2·64)	184·7 (66·9 to 420·0)	104·6 (61·8 to 162·6)	−43·35 (−71·72 to 2·29)
Eastern Sub-Saharan Africa	215,341·7 (192,298·8 to 241,235·6)	214,881·3 (191,322·8 to 241,732·2)	−0·21 (−1·88 to 1·44)	237·9 (59·4 to 608·0)	109·8 (56·2 to 182·8)	−53·86 (−76·07 to 3·07)
Southern Sub-Saharan Africa	217,047·6 (192,260·3 to 244,426·1)	215,089·1 (190,638·8 to 242,314·3)	−0·90 (−2·28 to 0·38)	110·5 (75·0 to 158·1)	89·1 (58·6 to 133·4)	−19·34 (−36·01 to −0·89)
Western Sub-Saharan Africa	195,383·6 (173,327·2 to 219,795·9)	192,479·2 (170,322·4 to 217,287·0)	−1·49 (−2·62 to −0·56)	80·1 (46·7 to 122·6)	72·3 (44·5 to 109·8)	−9·66 (−26·93 to 0·44)

DALYs, disability adjusted life years; UI, uncertainty interval; SDI, Socio-demographic Index.

where Y refers to ln (ASR), X refers to calendar year, α refers to the intercept, β represents the annual change in ln (ASR), and ε represents the error term. Furthermore, EAPC was calculated as EAPC = $100 \times (e^{\beta} - 1)$. In addition, 95% confidence intervals were obtained from the linear model. The positive EAPC indicated an upward trend, whereas the negative one represented a descending trend.

The correlations between SDI level and age-standardized incidence, mortality and DALY rates were measured by Spearman's rank sum correlation tests, and visualized by Locally Weighted Scatterplot Smoothing curves. All statistical analyses were performed using the R program (version 4.0.3). A P value of less than 0·05 was regarded as statistically significant.

2.5. Role of the funding source

The study was funded by the National Natural Science Foundation of China (81770057). The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data in the study and accepted responsibility to submit for publication.

3. Results

3.1. Incident cases of URIs increased from 1990 to 2019 in global

Globally, the incident cases of URIs reached 17·2 (15·4 to 19·3) billion in 2019, accounting for 42·82% (40·01% to 45·77%) cases from all the diseases and injuries in the GBD 2019 study (Supplementary Table 3). The age-standardized incidence rate decreased by 1·39% (−1·86% to −0·88%) with an EAPC of −0·08% (−0·09% to −0·06%) from 1990 to 2019, whereas the incident cases of URIs increased by 37·07% (34·12% to 40·05%) between 1990 and 2019 (Table 1, Supplementary Fig. 1, and Supplementary Table 4). Among all SDI quintiles, high SDI regions presented the highest age-standardized incidence rates from 1990 to 2019 (Fig. 1A), and the highest incidence rates in all age groups in 2019 (Supplementary Fig. 2A). However, high SDI regions presented a decreasing trend in age-standardized incidence rate (EAPC: −0·11%, −0·15% to −0·07%), whereas middle SDI regions showed an increasing trend (EAPC: 0·06%, 0·02% to 0·11%). Among 21 geographical regions, the high-income North America presented the highest age-standardized incidence rate in 2019 (329,985·1 per 100,000 people, 293,532·4 to 371,758·3), but also the most significant decreasing trend (EAPC: −0·26%, −0·35% to −0·17%) among geographic regions. In addition, among 204 countries or territories, Thailand (344,287·9 per 100,000 people, 305,038·3 to 389,666·8), the United States of America (331,560·4 per 100,000 people, 294,985·4 to 373,552·9), and Brazil (316,667·6 per 100,000 people, 281,156·0 to 358,064·7) presented the highest age-standardized incidence rates (Supplementary Table 5).

3.2. Low SDI regions presented highest mortality rate due to URIs

Globally, the estimated deaths due to URIs decreased from 34,403·5 (7,130·0 to 68,309·4) cases in 1990 to 9,464·1 (5,536·7 to 14,913·7) cases in 2019. Meanwhile, the age-standardized mortality rate also decreased from 1990 (0·7 per 100,000 people, 0·2 to 1·3) to 2019 (0·1 per 100,000 people, 0·1 to 0·2), with an EAPC of −6·30% (−6·53% to −6·08%) (Supplementary Tables 4 and 6). Among SDI quintiles, high SDI regions had the lowest age-standardized mortality rate from 1990 to 2019. Additionally, the highest age-standardized mortality rate was presented in middle SDI regions before 1998, and in low SDI regions from 1998 to 2019 (Fig. 1B). Descending trends of ASRs were observed in all the SDI groups. Detailed mortality and age-standardized mortality rates related to URIs in different regions, in 1990 and 2019, and their EAPCs from 1990 to 2019 are presented in Supplementary Tables 4 and 6.

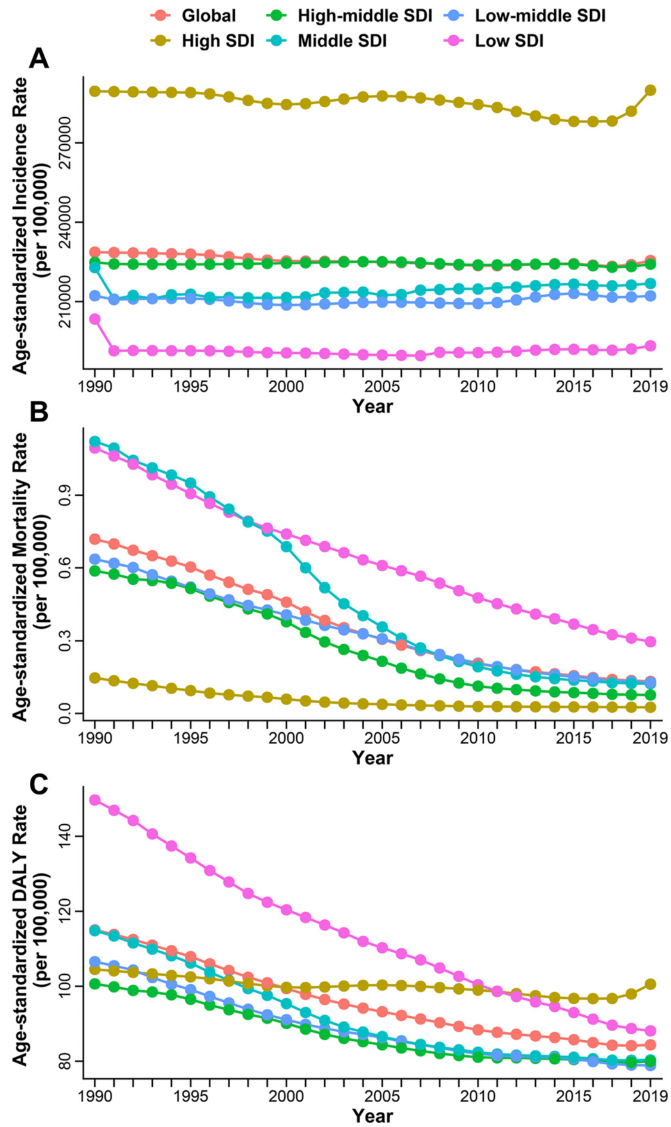

Fig. 1. Upper respiratory infections related burden from 1990 to 2019 across SDI quintiles.

Age-standardized incidence (A), mortality (B) and DALY (C) rates of upper respiratory infections.

DALY, disability-adjusted life year; SDI, Socio-demographic Index.

3.3. Decrease in age-standardized DALY rate stagnated in high SDI regions

Globally, the number of URIs-related DALYs was almost constant over the past 30 years. However, the age-standardized DALY rate decreased from 115·0 per 100,000 people (64·9 to 179·6) in 1990 to 84·4 per 100,000 people (52·0 to 128·2) in 2019, with an EAPC of −1·14% (−1·21% to −1·06%) (Table 1, Supplementary Fig. 1, and Supplementary Table 4). Low SDI regions showed the steepest decline in age-standardized DALY rate from 1990 to 2019 (EAPC: −1·83%, −1·88% to −1·78%). In contrast, in high SDI regions, the decrease of age-standardized DALY rate stagnated, and a rising trend has been observed in recent years. Thus, the highest age-standardized DALY rate was shown in low SDI regions from 1990 to 2011, but after 2011, high SDI regions took over (Fig. 1C). Moreover, in 2019, among the 21 geographical regions, the highest age-standardized DALY rate was found in high-income North America (114·0 per 100,000 people, 69·2 to 176·3) (Table 1). The DALYs and age-standardized DALY rate due

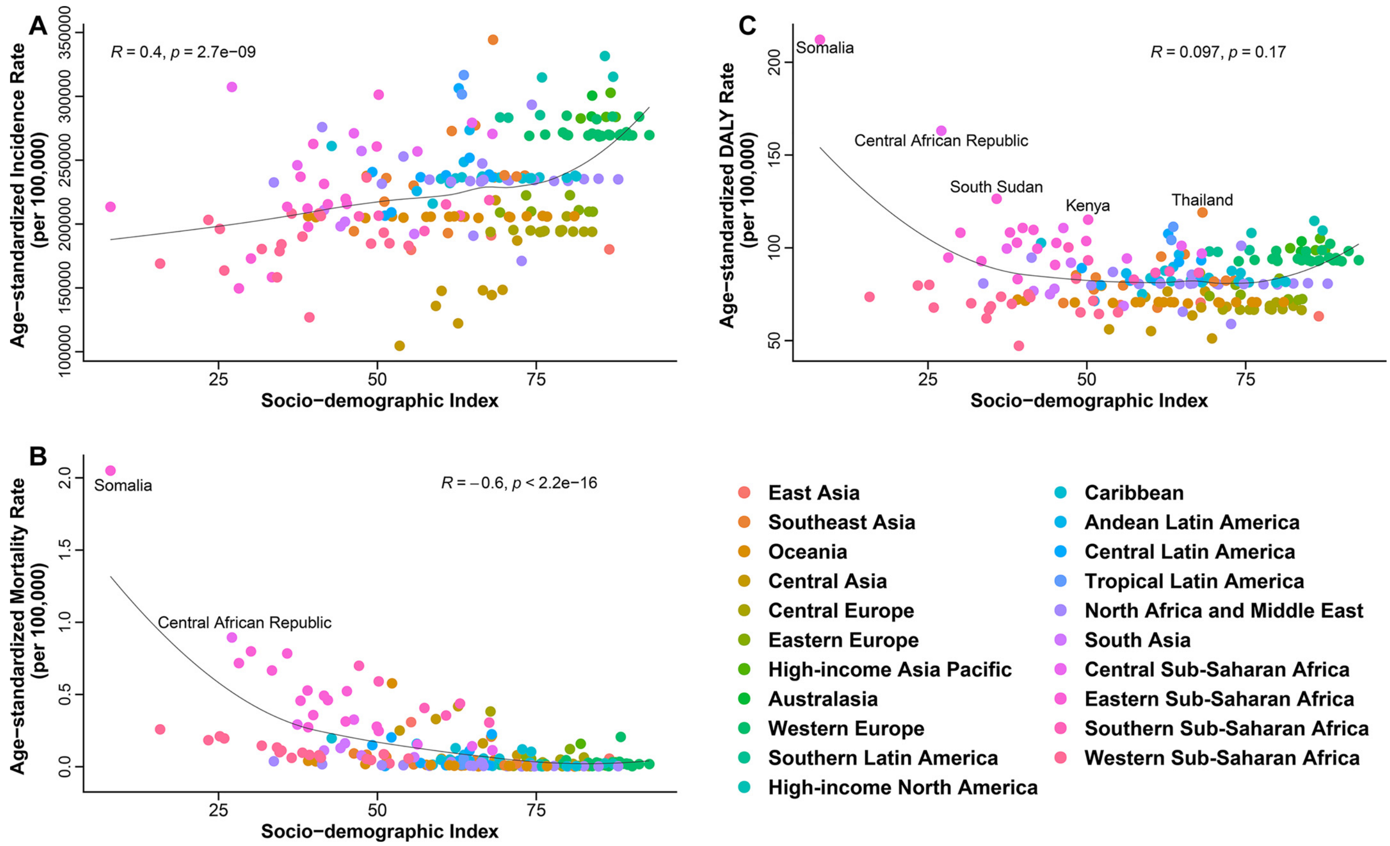

Fig. 2. Upper respiratory infections related burden in countries with different SDI levels in 2019.

Age-standardized incidence (A), mortality (B) and DALY (C) rate of upper respiratory infections. Every dot represented a country or territory and its color implied the region that the country or territory located.

DALY, disability-adjusted life year; SDI, Socio-demographic Index.

to URIs in 204 countries and territories, in 1990 and 2019, are presented in Supplementary Tables 3 and 5.

3.4. Correlations between SDI and the burden of URIs

A moderate positive correlation was found between the age-standardized incidence rate of URIs and SDI (R = 0·4, P < 0·05) in 2019, but the age-standardized mortality rate was negatively correlated with SDI (R = −0·6, P < 0·05). Whereas the age-standardized DALY rate did not show significant correlation with SDI level (R = 0·097, P = 0·17) (Fig. 2A–C). The percentage change from 1990 to 2019 in age-standardized incidence rate was less than 5% in most countries and territories, except in Pakistan, which showed an increase of 8·59% (4·94% to 12·13%). Most countries and territories showed decreases in age-standardized mortality rates, except for Panama, Costa Rica, Singapore, Kuwait, Ghana and Ukraine. The age-standardized DALY rate in Panama slightly increased from 1990 to 2019, whereas other countries or territories showed decreases or insignificant changes. Noticeably, the decreases were more remarkable in countries or territories with a lower SDI level (Supplementary Fig. 3A–C).

3.5. Burden of URIs in different sexes and age groups

Similar as observed in overall population, the ASRs of mortality (EAPC: −6·81%, −7·05% to −6·57% in females; −5·88%, −6·10% to −5·66% in males) and DALYs (EAPC: −1·19%, −1·28% to −1·11% in females; −1·09%, −1·15% to −1·02% in males) in males and females both decreased from 1990 to 2019. However, in both sexes, the age-standardized incidence rates were decreasing but also fluctuating, and an increasing trend was observed in recent years (Supplementary Figs. 4A–C). Moreover, in all metrics, the burden of URIs was higher in males than in females.

The incidence rate of URIs decreased with increasing age, and the highest incidence rate was observed in the group under five years old (300,532·1 per 100,000 people, 233,076·1 to 379,041·9) (Supplementary Table 7). Deaths related to URIs mostly occurred in the elders and the children under five years old (Fig. 3A–B). Low SDI regions had the highest mortality rate in children under five years old, whereas other SDI-based groups, especially the middle SDI regions, showed the highest mortality rates in the oldest age group (>80 years old) (Supplementary Fig. 2B). Among all the age groups, the highest DALY rate was observed in the group under five years of age (Fig. 3C), especially in the low SDI regions (Supplementary Fig. 2C).

3.6. Risk factors

GBD 2019 assessed the contributions of four risk factors for URIs-related mortality and DALYs. Among those risk factors, the leading one was low birth weight, the second was short gestation, and others included household air pollution from solid fuels and ambient particulate matter pollution. Totally, 0·89% of deaths and 0·14% of DALYs related to URIs were attributed to those four risk factors. The age-standardized mortality and DALY rates attributable to low birth weight or short gestation were the highest in low SDI regions. The attribution of household air pollution increased with decreasing SDI quintiles, and the contribution of ambient particulate matter pollution peaked in middle SDI regions (Fig. 4A–B). From 1990 to 2019, the attribution of all the four risk factors to URIs-related mortality and DALYs decreased in both sexes (Supplementary Figs. 5A–B).

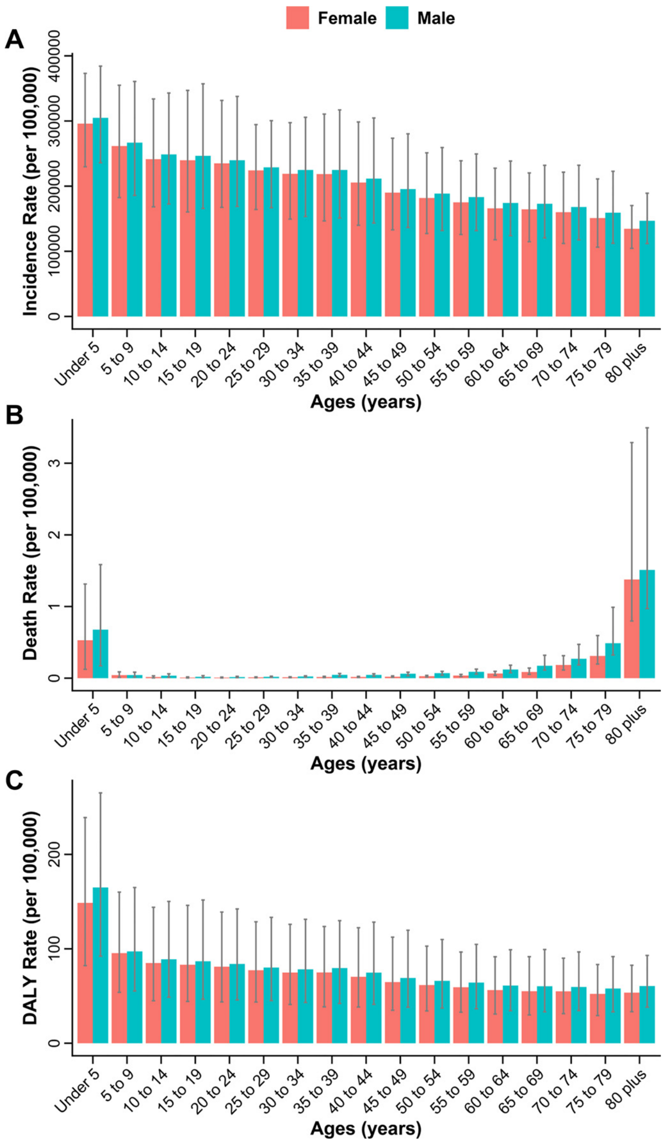

Fig. 3. Upper respiratory infections related burden in different age groups in 2019.
Incidence (A), mortality (B) and DALY (C) rates of upper respiratory infections.
DALY, disability-adjusted life year.

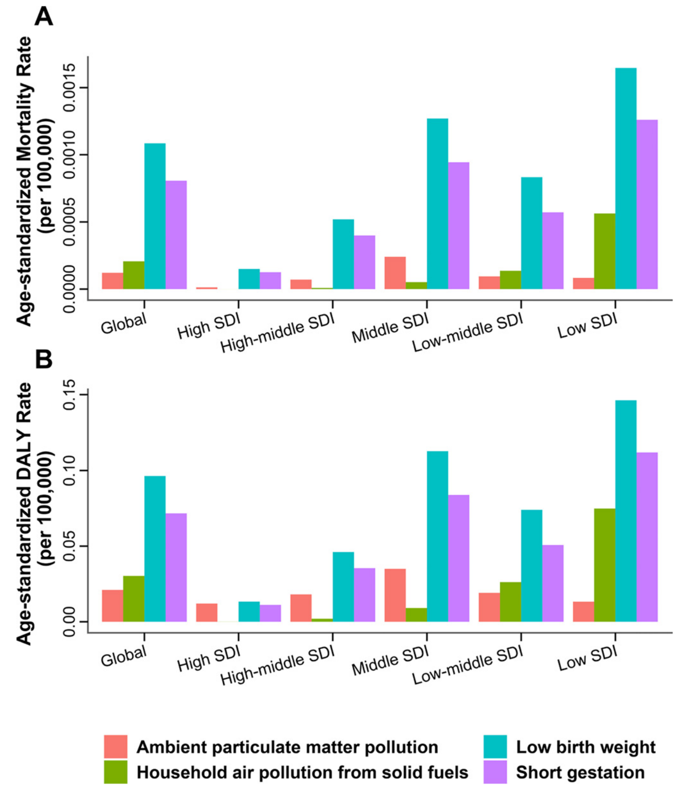

Fig. 4. The burden of upper respiratory infections attributable to risk factors across SDI quintiles in 2019.
Age-standardized mortality (A) and DALY (B) rates of upper respiratory infections.
DALY, disability-adjusted life year; SDI, Socio-demographic Index.

4. Discussion

Several studies have reported that URIs were among the most common diseases [2,3]. Our study, for the first time, comprehensively estimated the incidence of URIs in different sex and age groups, at global and regional levels in the past 30 years. In this study based on GBD 2019, we reported that the estimated incident cases of URIs reached more than 17 billion in 2019, accounting for about 43% cases of all the GBD diseases and injuries. As an important and common presentation for the reproduction and circulation of more than 200 known virus strains [23,24], the massive incidence of URIs may possess an unexpected threat to human health and should never be overlooked. The current pandemic of SARS-CoV-2, which presents mild URI syndromes in most of the patients, has led to severe diseases in some cases and caused more than three million deaths to date [25]. Vaccines for the prevention of URIs have been evaluated since 1970s [26]. However, the development and popularization of effective vaccines remains challenging in recent years [27]. Moreover, the high incidence of URIs also increases the latent risk of antibiotics resistance because of antibiotics misuse [28,29].

Our study found the highest age-standardized incidence rates from 1990 to 2019 in high SDI regions among SDI quintiles, and the age-standardized incidence rates were moderately correlated with SDI levels. Several potential reasons may explain this phenomenon. First, with a higher degree of urbanization, dense population in high SDI regions might prompt the spread of respiratory viruses, thus causing higher URIs incidence rate. Second, with sound medical systems and adequate medical resources, URIs patients are more likely to be treated and reported in high SDI regions. Whereas, in low SDI regions, medical resources are less accessible, so mild URIs may be undetected, which may incline high SDI regions toward a relatively higher incidence rate. Meanwhile, the overall burden of URIs may be much heavier than we estimated, considering that the data collection was restricted in regions with less developed medical systems.

Compared with the high incidence rates, the estimated deaths due to URIs were quite small in our study. As a precursor of some severe complications, including pneumonia, glomerulonephritis, and myocarditis, URIs might not be diagnosed in a real clinical scenario if more severe relevant diseases exist [4–6]. Thus, fatal consequences of the complications might not be calculated into the death toll of URIs, leading to underestimated death burden in the GBD 2019 study. However, URIs still caused about 6·4 million DALYs in 2019 globally, as the symptoms significantly affect life quality and productivity, resulting in a considerable non-fatal burden [4,15]. The most severe fatal burden was observed in low SDI regions, whereas high SDI regions presented with the highest age-standardized DALY rates. The remarkable age-standardized incidence rate found in high SDI regions may account for its high DALY rate. Significant reductions in age-standardized mortality and DALY rates were observed across SDI quintiles as well as geographic regions. The general advancement of clinical care and the enrichment of medical resource in most regions may be the potential reasons.

Discrepancies in URIs burden were also found between different sexes and age groups. From 1990 to 2019, males had higher age-standardized incidence, DALY, and mortality rates due to URIs. Moreover, across all age groups, the incidence, DALY, and mortality rates were also higher in males. Sex-specific differences in the susceptibility to and severity of infectious diseases have been observed in various studies [30-32]. A greater fatality rate for males was also reported in the coronavirus disease 2019 pandemic [31]. Differences in the risk of being exposed to virus and immune responses between males and females may underlie this phenomenon, but the precise mechanism remains unclear [30,31].

Among all the age groups, children under five years old had the highest incidence and DALY rates of URIs, which is consistent with previous studies [33]. A previous review highlighted that adults had an average of two to four episodes of common cold annually, whereas children might have as many as six to eight episodes [33]. Our study indicated that, globally in 2019, averagely about 2·25 episodes happened per individual per year, while about three episodes happened for a child under five years old. We also found the highest URIs related mortality in the elders and in children under five years old, which was consistent with previous findings that URIs were associated with increased risk of lower respiratory complications and deaths in those age groups [9,34].

Risk factors contributing to the burden of URIs were also evaluated in the present study. Low birth weight and short gestation were the leading risk factors for mortality and DALYs due to URIs, especially in low SDI countries. Low birth weight and preterm infants are vulnerable to infectious diseases, and are at a higher risk of developing severe infections [35,36]. Investments in health services are needed to improve the medical care and to mitigate URIs related burden in low birth weight and preterm infants. Household air pollution from solid fuels and ambient particulate matter pollution were also recognized as risk factors. Air pollution is considered to be a contributor to respiratory infections [37]. The contribution of household air pollution from solid fuels decreased with increasing sociodemographic development. However, the contribution of ambient particulate matter pollution peaked in middle SDI regions, where adequate attention should be paid to the emissions from vehicles and industry. Whereas, only 0·89% and 0·14% of URIs related deaths and DALYs, respectively, were attributable to all the risk factors assessed in GBD 2019, and risk factors for the high incidence rates were not estimated. Previous studies had put forward several possible risk factors for the morbidity of URIs, such as inadequate sleep duration and psychological stress [38-41]. In the future, more extensive and comprehensive evaluations of risk factors are necessary to evaluate the URIs-related burden.

To the best of our knowledge, the present study is the first one to comprehensively describe the burden related to URIs in different sexes and age groups, at different geographical levels, from 1990 to 2019. However, there are several limitations in our study. First, as with all research based on GBD, limitations of the methods in GBD 2019 result in biases in the current study [12]. Changes in reporting system across geography and over time may impact the availability of primary records, and imperfections of the data quality and quantity, especially in less developed regions, would compromise the accuracy of comparison between countries and regions. However, robust statistical methods, such as DisMod-MR 2.1, were used to offset the disadvantages. Second, as noted earlier, the symptoms of URIs are mild and self-limited in most cases, thus patients who do not seek medical care may not be detected, which may render the burden of URIs underestimated. Third, the analyses of risk factors are limited in GBD 2019 as mentioned. Moreover, although data of etiologies were provided for lower respiratory infections in the GBD 2019 study [15], the URIs burden attributable to specific etiologies were not available. To further specify the burden of URIs, more health surveys with a wider coverage of possible risk factors and etiologies are needed in the future.

In conclusion, URIs possessed the most substantial incident cases in GBD 2019. Although fatal consequences were relatively rare, URIs still caused considerable DALYs. Across SDI quintiles, the highest age-standardized incidence rates from 1990 to 2019 and the highest age-standardized DALY rates after 2011 were observed in high SDI regions. Our study provided a comprehensive estimation on the burden of URIs for the first time, which supports future explorations in the prevention and treatment of URIs with more epidemiological evidence.

Declaration of Competing Interest

We declare that we have no conflicts of interest.

Contributors

XJ designed the study and drafted the manuscript. XJ and JR extracted, collected, and analyzed data. XJ and GW verified the underlying data. XJ, JR, JZ, YG, HZ, JL, RL, XW and GW reviewed the results and revised the manuscript. GW supervised the study. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Data sharing statement

Data sources and code used in the Global Burden of Diseases, Injuries, and Risk Factors Study 2019 are publicly available on the internet (http://ghdx.healthdata.org/gbd-results-tool).

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2021.100986.

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