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Research paper

Disease burden and attributable risk factors of respiratory infections in China from 1990 to 2019[☆]Zengliang Ruan^{a,1}, Jinlei Qi^{b,1}, Zhengmin (Min) Qian^c, Maigeng Zhou^b, Yin Yang^a, Shiyu Zhang^a, Michael G. Vaughn^d, Morgan H. LeBaige^c, Peng Yin^{b,*}, Hualiang Lin^{a,*}^a Department of Epidemiology, School of Public Health, Sun Yat-sen University, No. 74 Zhongshan Road 2, Guangzhou 510080, China^b National Centre for Chronic and Noncommunicable Disease Control and Prevention, Chinese Centre for Disease Control and Prevention, No. 27 Nanwei Road, Xicheng District, Beijing 100050, China^c Department of Epidemiology and Biostatistics, College for Public Health & Social Justice, Saint Louis University, Saint Louis, MO 63104, USA^d School of Social Work, College for Public Health & Social Justice, Saint Louis University, Saint Louis, MO 63103, USA

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ABSTRACT

Background: There was lack of data on the burdens and trends of upper and lower respiratory infections (URIs and LRIs) over the past three decades in China.**Methods:** We estimated the incidence, mortality, and disability-adjusted life years (DALYs) due to upper and lower respiratory infections (URIs and LRIs) and attributable risk factors in China by a systematic analysis of the Global Burden of Disease 2019 study. Incidence, mortality, and DALYs were stratified by sex, age, and province. Risk factors for respiratory infections were analyzed from exposure data.**Findings:** The age-standardized incidence rates of URIs and LRIs were 179,077 and 3926 per 100,000 persons in 2019, with a 7·52% and 35·07% decrease from 1990, respectively. Moreover, 2801 and 185,264 persons died of URIs and LRIs in 2019, respectively. DALYs for URIs and LRIs also decreased from 1,516,727 in 1990 to 928,617 in 2019 and from 38,278,504 in 1990 to 4,020,676 in 2019. The burden of URIs and LRIs were generally similar in males and females, but relatively higher in the new-borns and the elderly. Child malnutrition and low birth weight were the most important cause of age-standardized DALYs of LRIs and URIs, respectively.**Interpretation:** Future URI and LRI prevention strategies should focus on the maternal and child health, air pollution, and tobacco control, especially in young children and the elderly population.**Funding:** National Key R&D Program of China (2018YFA0606200); National Natural Science Foundation of China (82041021); Fundamental Research Funds for the Central Universities (20ykpy86) and Guangdong Basic and Applied Basic Research Foundation (2019A1515110003); Bill & Melinda Gates Foundation (No.: INV-006371).

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Research in context

Evidence before this study

We systematically searched the online databases Medline, Scopus, PsycINFO, ProQuest and Embase database for original research articles reporting the disease burden and attributable risk factors of respiratory infections using the search terms “respiratory infections”, “Global Burden of Disease”, “incidence”, “death”, “disability-adjusted life years” or “disease burden” with no restrictions on publishing date or languages. Previous studies reported that respiratory infection has become one of the major global health concerns and the leading causes of under-five mortality, but data on the burden and risk factors of upper and lower respiratory infections (URIs and LRIs) over the past 2 decades in China is currently lacking. Detailed estimates of URIs and LRIs burdens are crucial to provide information for prevention and resource allocation, and the methods and findings of Global Burden of Disease 2019 (GBD 2019) study enable us to conduct a comprehensive assessment of the burden of URIs and LRIs.

Added value of this study

Based on the methodology used in the GBD 2019, this study estimated the sex-, age-, and province-specific incidence, disability-adjusted life years (DALYs), and mortality of URIs and LRIs for 33 provinces in China from 1990 to 2019. We found that the total number of incident cases of URIs in China increased slightly from 2.29 billion in 1990 to 2.55 billion in 2019, while the number of incident cases of LRIs decreased from 71.56 million in 1990 to 55.84 million in 2019. By contrast, the age-standardized incidence rates of URIs and LRIs both decreased during that time. Specifically, a total number of 2801 and 185,264 persons died of URIs and LRIs in 2019, respectively, 81.41% and 65.94% reductions from 1990. URIs and LRIs resulted in 928,617 and 4,020,676 DALYs, which were 38.77% and 89.5% lower than that in 1990. In addition, our findings suggested that child malnutrition, air-borne particulate matter (PM), and second-hand smoke were the three major risk factors for age-standardized DALYs of LRIs, while low birth weight, short gestation, and air-borne PM were the largest contributors to age-standardized DALYs of URIs.

Implications of all the available evidence

Findings from this study suggested that respiratory infection is a heavy health burden and the leading causes of under-five mortality in China, and child malnutrition and low birth weight were the most important risk factors for age-standardized DALYs of LRIs and URIs, respectively.

1. Introduction

Respiratory infections (RIs) encompass a series of clinical conditions commonly caused by bacterial or viral infections [1,2]. The RIs can be divided into upper respiratory infections (URIs) and lower respiratory infections (LRIs) according to the infection site [3–5]. URIs usually include nasopharyngitis, rhinosinusitis, tonsillitis, laryngitis, and otitis media, but there are also severe and fatal URIs, such as croup and epiglottitis [1,6–9]. LRIs includes bronchitis and pneumonia, especially the bacterial causes of pneumonia which are associated with more severe clinical symptoms and complicates treatment due to increasing antibiotic resistance [1,6,7]. RIs are generally located in the upper respiratory airways (i.e., the mouth, nose, throat, larynx), but they may further

spread to the lower respiratory tract (i.e., the trachea, bronchi, and the respiratory structures within the lungs – the bronchioles and alveoli) and lead to severe problems, such as RSV bronchiolitis [4,10,11]. RIs have become one of the major global health concerns and the leading causes of under-five mortality [12–14].

Evidence-based planning of RI control and prevention requires an accurate assessment of the actual disease burden, such as DALYs. However, correctly designing and executing population-based epidemiological surveys over a long time period requires tremendous human, material, and financial resources. To date, no such study has been conducted in China for RIs.

To estimate disease burden and risk factors, the World Bank commissioned the Global Burden of Disease (GBD) study in 1992, which has continuously assessed the disease burden globally [15,16]. The latest GBD study 2019 reported on factors and burden for 369 diseases and injuries at global, national, and subnational levels [17]. This analysis was based on a wide range of sources, such as health administrative reports, disease surveillance, and vital registry information [18,19].

We thus conducted this study to provide a comprehensive assessment from 1990 to 2019. The results of this study will provide new estimations on the burden and trends of RIs and their risk factors at both national and subnational levels, which will help to facilitate development of government responses to improve respiratory health of Chinese population.

2. Methods

The details of the study design and the general methods were based on the GBD 2019 study and have been described previously [17,20]. Briefly, the GBD 2019 study is a systematic analysis that provides comprehensive estimations of sex-, age-, and subnational-specific incidence, prevalence, mortality, and DALYs of major medical conditions for 204 countries and territories from 1990 to 2019. This current study builds on the efforts of the GBD and focuses on trends of RIs in China. Data on sex-, age-, and province-specific disease burden for RIs from 33 province-level units in China, including 22 provinces, four cities, five autonomous regions, and two Special Administrative Regions (SAR), were analyzed from 1990 to 2019. These units are all referred to as provinces in our analyses. RI cases were defined in accordance with the World Health Organization disease definition and the 10th revision of the International Classification of Diseases (ICD-10) and were subdivided to URIs (J00–J06.9, J36–J36.0) and LRIs (A48.1, A70, B96.0–B96.1, B97.21, B97.4–B97.6, J09–J18.2, J18.8–J18.9, J19.6–J22.9, J85.1, J91.0, P23–P23.9, U04–U04.9, Z25.1).

Different types of input data were used for the estimation of RIs burden in the GBD 2019 study [17]. The first is the RIs incidence and prevalence data which were derived primarily from a systematic literature review, national population-representative surveys, the Chinese Center for Disease Control and Prevention cause-of-death reporting system, cancer registries, and hospital inpatient and outpatient data [20]. A Bayesian meta-regression tool (DisMod-MR 2.1), which included all the above-mentioned data and used different adjustment factors, was applied to derive the burden of RIs from 1990 to 2019 [17]. Moreover, all available data from censuses, surveys (including the One-per-Thousand Population Fertility Sample Survey, the Annual Survey on Population Change and the Intercensal Survey), surveillance systems (including the Disease Surveillance Point system, the Maternal and Child Health Surveillance system), vital registration systems (including the China Cancer Registry, and the Chinese Center for Disease Control and Prevention cause-of-death reporting system) and verbal autopsy were used to estimate the RIs mortality in the Cause of Death Ensemble model (CODEm) platform, which is a Bayesian,

hierarchical, ensemble model designed to estimate cause-specific mortality by year, area, sex and age [17,20,21]. The LRIs CODEm models was separately established with different covariates for under-5 years and 5–95+ years due to the different patterns, such as childhood stunting, childhood wasting, air pollution, second-hand smoking, zinc deficiency in under 5 years model, smoking prevalence, adult underweight, and education years per capita in 5–95+ years model [17]. Compared with the GBD 2017, all of the data sources were adjusted in GBD 2019 before modeling using a standardized approach. Our study followed the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) [22], and the data sources, code, and results are publicly available (please see the data sharing statement).

We calculated several metrics to represent the disease burden, including incidence, mortality, and DALYs, and the general methods to estimate these metrics have been described in previous reports [19,23]. Incidence was employed to represent the frequency of the disease, which was defined as the number of newly identified RI cases (incident cases) per 100,000 population, while mortality was defined as the actual number of RI-related death cases. DALYs and its two components (YLL and YLD) were used to represent the burden of RIs, which indicate the number of healthy years lost per year per 100,000 population. The DALYs is the sum of years of life lost (YLL) due to premature mortality and years lived with disability (YLDs) [24]. In addition, YLLs were calculated by multiplying the mortality count due to RIs by the standard life expectancy at age of death. YLDs were obtained by multiplying the number of newly identified RI cases by the disability weight and mean disability duration associated with RIs [25]. The point estimates of these measures were calculated from the mean of 1000 draw values of each model from the posterior distribution separately by year, province, cause of disease, sex, and age, and the 95% uncertainty intervals (95% UIs) were calculated with the 2.5th (the lower bound) and the 97.5th percentile (the upper bound) [26]. Moreover, we reported the estimations of burden of RIs and their trends by province, sex, and age group.

The GBD 2019 study used a comparative risk assessment (CRA) method to calculate the proportion of RIs attributable to a series of risk factors. This method has been employed in GBD studies since 2002 [27,28], and includes the following six steps: (1) inclusion of risk and outcome pairs; (2) evaluation of relative risk as a exposure function; (3) evaluation of exposures and distributions; (4) determination of the theoretical minimum risk exposure level (TMREL) and the counterfactual exposure; (5) estimation of attributable burden and population attributable fraction; and (6) estimation of the burden attributable to various combination of risk factors [28,29]. More specific methods can be found in previous reports [28]. In this study, we utilized the above methodology to present the proportion of DALYs due to URIs and LRIs that were attributable to different levels of risk factors.

This study was approved by the Ethical Review Committee of the National Center for Chronic and Non-communicable Disease Control and Prevention of the Chinese Center for Disease Control and Prevention. No individual identifiable information was used and thus informed consent was waived.

3. Role of the funding source

The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all data in the study and had the final responsibility for the decision to submit for publication.

4. Results

4.1. Trends of incidence of upper and lower respiratory infections in China from 1990 to 2019

Fig. 1 and Table 1 indicate a very slightly but steady increasing trend year by year in the number of cases of URIs from 1990 to 2019. In 2019, there was an estimated 2.55 (95% UI: 2.29–2.86) billion cases with URIs in China, 2.79% higher than that in 2010 [2.48 (95% UI: 2.21–2.80) billion], 4.87% higher than that in 2000 [2.43 (95% UI: 2.15–2.75) billion], and 11.13% higher than that in 1990 [2.29 (95% UI: 2.02–2.61) billion]. From 1990 to 2019, male and female cases with URIs increased by 9.16% (95% UI: 2.92–15.23%) and 13.37% (95% UI: 6.33–20.09%), respectively. Moreover, the number of incident cases with LRIs exhibited a decreasing trend from 1990 to 2010, but slightly went up again thereafter. Overall, an estimated number of 55.84 (95% UI: 51.69–60.03) million cases with LRIs were reported in 2019 in China, which was 7.66 higher than that in 2010 [51.86 (95% UI: 48.17–55.51) million], but 10.08% lower than that in 2000 [62.10 (95% UI: 57.86–66.94) million], and 21.98% lower than that in 1990 [71.56 (95% UI: 65.89–78.09) million]. LRI cases decreased significantly by 16.22% (95% UI: 11.36–21.54%) and 28.00% (95% UI: 23.67–32.25%) in males and females from 1990 to 2019. The national age-standardized incidence rate decreased significantly for both URIs and LRIs by 7.52% (95% UI: 2.19–12.95%) and 35.07% (95% UI: 31.47–39.07%) from 1990 to 2019, respectively. Furthermore, although URIs had higher all-age incidence and age-standardized incidence than LRIs, age-standardized incidence of LRIs decreased more than URIs from 1990 to 2019 (Fig. 1, Table 1).

The sex- and age-specific incidence of both URIs and LRIs appeared to have similar patterns from 1990 to 2019 (Fig. 2), and incidence rates for both were higher in the male population. For example, the age-standardized incidence rate of URIs was the largest in people younger than 1 years [2.75 (95% UI: 2.14–3.45) and 2.45 (95% UI: 1.91–3.08) for male and female per 100,000 in 1990; 2.74 (95% UI: 2.13–3.45) and 2.58 (95% UI: 2.01–3.27) for male and female per 100,000 in 2019], then subsequently decreased for the lowest estimates in people aged 85–89 years [1.09 (95% UI: 0.78–1.46) and 1.01 (95% UI: 0.72–1.35) for male and female per 100,000 in 1990; 1.09 (95% UI: 0.78–1.44) and 1.03 (95% UI: 0.73–1.38) for male and female per 100,000 in 2019]. These rates then increased slightly until the group of people aged 95 years and above. Moreover, a U-shaped curve was observed in the age-standardized incidence rates of LRIs with increases in age in 1990, which suggested that both new-borns [0.22 (95% UI: 0.19–0.27) and 0.25 (95% UI: 0.21–0.30) per 100,000 for male and female younger than one year] and the elderly [0.60 (95% UI: 0.51–0.71) and 0.72 (95% UI: 0.61–0.85) per 100,000 for male and female aged 95 years and above] had higher age-standardized incidence rates of LRIs in 1990. In 2019, although the age-standardized incidence rates of LRIs in older people [0.94 (95% UI: 0.79–1.09) and 0.49 (95% UI: 0.42–0.58) per 100,000 for male and female aged 95 years and above] were still high, incidence in new-borns have seen great decreases [0.05 (95% UI: 0.04–0.06) and 0.04 (95% UI: 0.03–0.06) per 100,000 for male and female younger than one year].

According to our province-specific results, all provinces showed decreasing trends in the age-standardized incidence rate of both URIs and LRIs from 1990 to 2019 (Fig. 3). Specifically, Heilongjiang province had the highest decrease rate of 0.12% (95% UI: 0.03–0.19%) for URIs, followed by Jilin Province [0.11% (95% UI: 0.03–0.18%)] and the Inner Mongolia Autonomous region [0.10% (95% UI: 0.02–0.18%)]. The Tibet Autonomous Region showed the least decrease in incidence rates [0.03% (95% UI: –0.03–0.09%)]. For LRIs, the Tibet Autonomous Region, Yunnan and Guizhou Provinces

Table 1
All-age incidence of upper and lower respiratory infections and the percentage changes by sex, 1990–2019.

Subcategories	All-age incidence (95% UI), No. × 10 ⁶			Age-standardized incidence rate (95% UI), per 100,000		
	1990	2019	Change (%)	1990	2019	Change (%)
Upper respiratory infections						
Male	1222·31 (1077·35–1391·08)	1334·33 (1199·22–1500·80)	9·16 (2·92–15·23)	200317·37 (176560·54–227976·33)	184090·64 (165449·92–207057·99)	–8·10 (–13·36––3·00)
Female	1069·78 (943·73–1222·36)	1212·78 (1089·77–1360·08)	13·37 (6·33–20·09)	186536·25 (164558·50–213142·04)	173867·76 (156232·80–194985·28)	–6·79 (–12·58––1·26)
Total	2292·09 (2022·85–2610·71)	2547·11 (2288·74–2856·37)	11·13 (4·60–17·54)	193640·40 (170894·71–220558·42)	179077·28 (160912·73–200820·31)	–7·52 (–12·95––2·19)
Lower respiratory infections						
Male	36·59 (33·72–39·99)	30·66 (28·35–33·02)	–16·22 (–21·54––11·36)	5997·18 (5526·24–6554·46)	4229·80 (3911·39–4555·22)	–29·47 (–33·95––25·38)
Female	34·97 (32·27–38·04)	25·18 (23·19–27·23)	–28·00 (–32·25––23·67)	6097·35 (5626·85–6633·14)	3609·51 (3325·27–3903·57)	–40·80 (–44·30––37·24)
Total	71·56 (65·89–78·09)	55·84 (51·69–60·03)	–21·98 (–26·78––17·66)	6045·71 (5566·70–6597·52)	3925·61 (3634·41–4220·31)	–35·07 (–39·07––31·47)

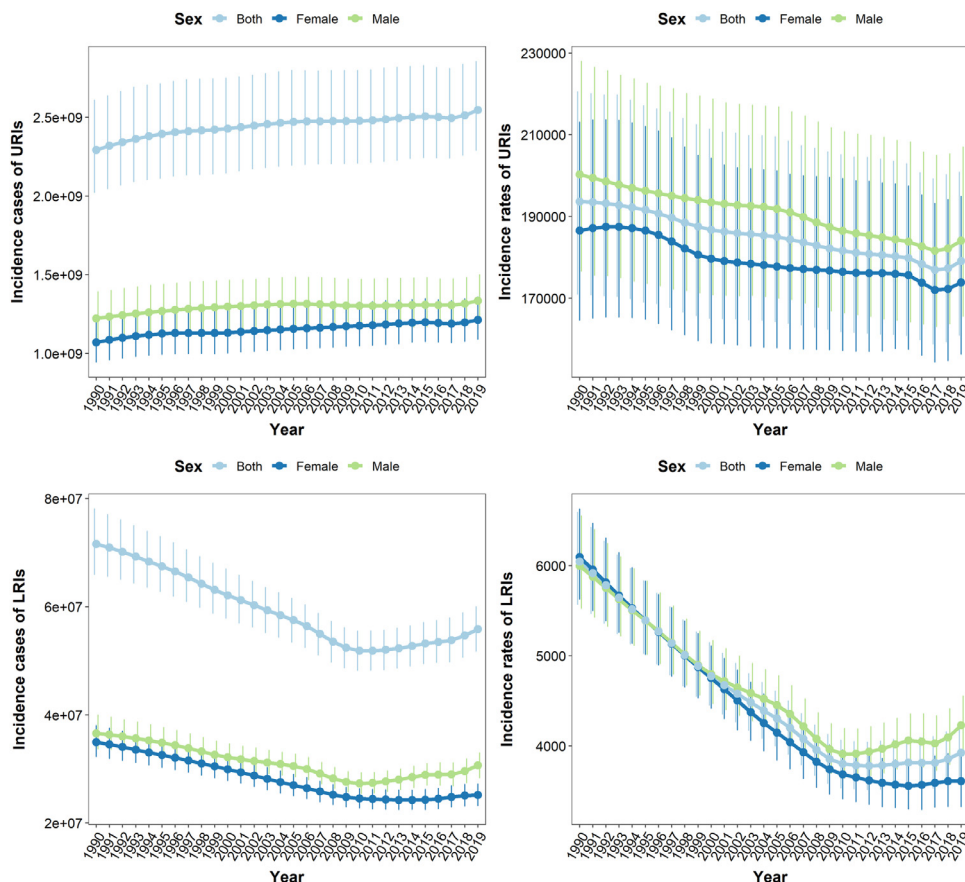


Fig. 1. Trends of incidence of upper and lower respiratory infections in China from 1990 to 2019.

exhibited the greatest decreases in rates of 0.55% (95% UI: 0.51–0.58%), 0.48% (95% UI: 0.43–0.52%) and 0.47% (95% UI: 0.42–0.51%), respectively. By contrast, Hong Kong showed a slight increase of 0.19% (95% UI: 0.11–0.29%) in age-standardized incidence.

4.2. Trends of death numbers attributable to upper and lower respiratory infections and the mortality rate in China from 1990 to 2019

The estimated number of all-age deaths due to URIs decreased from 15068.60 (95% UI: 3941.3–26195.89) in 1990 to 10,203.71 (95% UI: 4379.47–16027.95) in 2000, 3223.17 (95% UI: 1327.66–5118.68) in 2010 and 2801.30 (95% UI: -226.86–5829.47) in 2019, with 32.28%, 78.61% and 81.41% decreases, respectively. Mortality rates in males and females decreased by 79.72% (95% UI: -111.66–92.53%) and 82.94% (95% UI: -154.73–94.82%), respectively (Fig. 4 and Table 2). The overall number of deaths due to LRIs decreased from 543900.99 (95% UI: 476789.88–611012.10) in 1990 to 303377.64 (95% UI: 280654.47–326100.81) in 2000, 186498.95 (95% UI: 168411.08–204586.82) in 2010, and 185264.33 (95% UI: 157651.46–212877.21) in 2019, with 44.22%, 65.71% and 65.94% decreases, respectively. The number of deaths due to LRIs among male and female populations decreased by 63.21% (95% UI: 49.50–69.89%) and 68.81% (95% UI: 57.16–75.01%) from 1990 to 2019, respectively. Similarly, the national age-standardized mortality rate shrunk by 84.53% (95% UI: -92.24–94.61%) and 71.65% (95% UI: 62.72–76.13%) for URIs and LRIs from 1990 to 2019 (Fig. 4, Table 2).

The age-specific mortality rate of both URIs and LRIs generally showed U-shaped trends from 1990 to 2019 (Fig. 5), indicating that

both the children and old people were more vulnerable to these two types of diseases than young adults. The elderly aged 95 years and above had the highest age-standardized mortality rates [URIs: 169.35 (95% UI: 47.27–291.43) and 213.98 (95% UI: 41.63–386.33) for male and female in 1990 and 23.97 (95% UI: -1.92–49.86) and 25.88 (95% UI: -8.06–59.83) for male and female in 2019; LRIs: 2850.45 (95% UI: 2364.62–3336.29) and 2382.67 (95% UI: 1966.51–2798.83) for male and female in 1990 and 2509.95 (95% UI: 2006.20–3013.69) and 1395.85 (95% UI: 1060.06–1731.64) for male and female in 2019].

In the province-specific analyses (Fig. 6), all provinces showed decreasing trends in the age-standardized mortality of URIs from 1990 to 2019. For example, Ningxia and Hainan Province had the highest decreases of 0.91% (95% UI: -0.70–0.97%) and 0.91% (95% UI: -0.79–0.96%), while Hong Kong, Macao and Shanghai had the least decrease in rates of 0.27% (95% UI: -2.74–0.74%), 0.39% (95% UI: -0.71–0.76%), 0.69% (95% UI: -0.57–0.95%), respectively. For LRIs, Shaanxi Province had the highest decrease in mortality rates [0.86% (95% UI: 0.74–0.90%)], followed by Ningxia Province [0.85% (95% UI: 0.79–0.89%)] and Henan Province [0.84% (95% UI: 0.66–0.89%)], but the age-standardized mortality rate of LRIs from 1990 to 2019 in Hong Kong SAR increased by 1.35% (95% UI: 0.80–1.97%).

4.3. Trends of disability-adjusted life years of upper and lower respiratory infections in China from 1990 to 2019

We also observed substantial reductions in the absolute burdens of both upper and lower RIs from 1990 to 2019 (Fig. 7, Table 3). For example, the all-age DALYs attributable to URIs dropped from 1516.73 (95% UI: 731.73–2252.32) thousand years

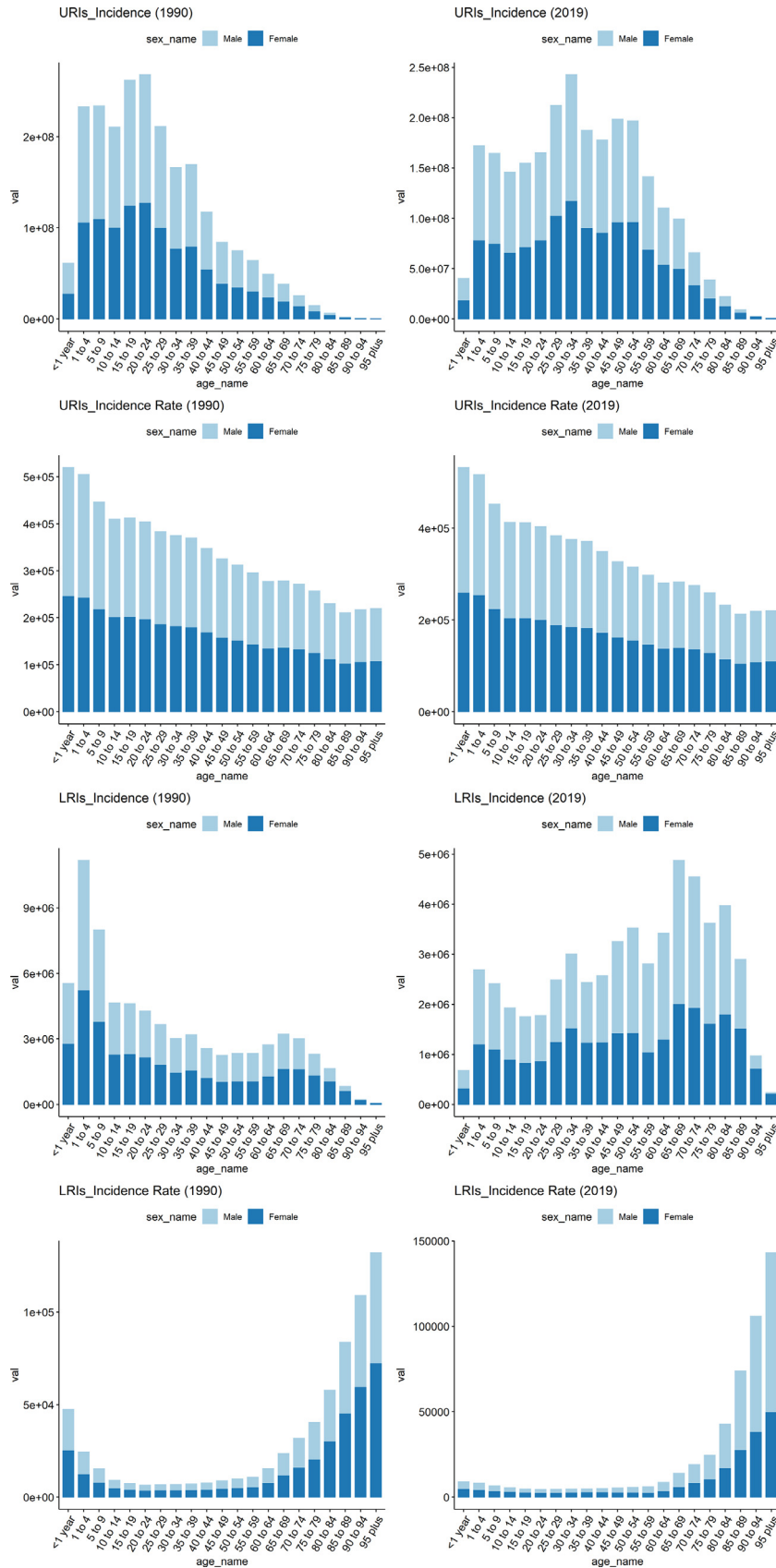


Fig. 2. The age-specific incidence of upper and lower respiratory infections in 1990 and 2019.

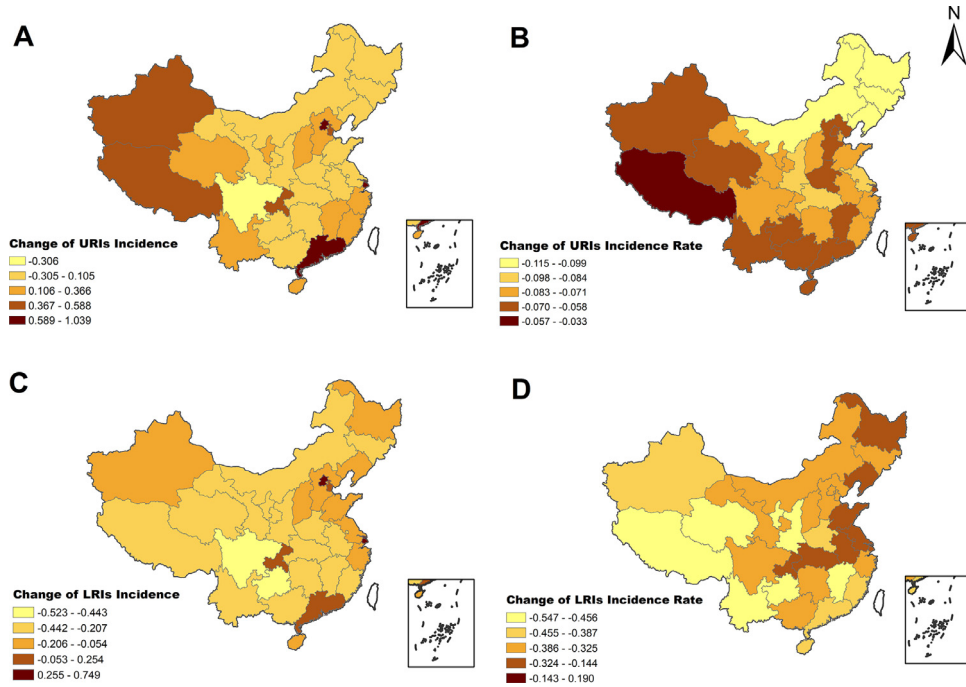


Fig. 3. The change of province-specific incidence of upper and lower respiratory infections from 1990 to 2019.

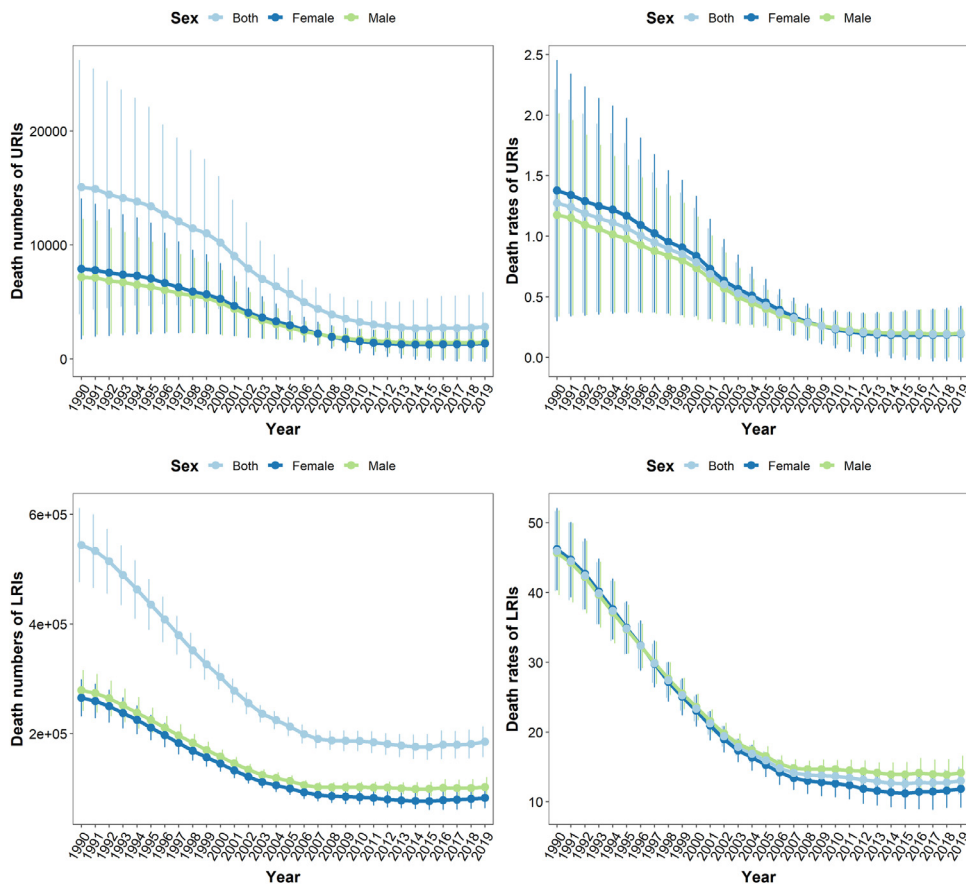


Fig. 4. Trends of death numbers attributable to upper and lower respiratory infections and the mortality rate in China from 1990 to 2019.

Table 2
All-age death numbers and age-standardized mortality rate of upper and lower respiratory infections and the percentage changes by sex, 1990–2019.

Subcategories	All-age deaths, (95% UI)			Age-standardized mortality rate (95% UI), per 100,000		
	1990	2019	Change (%)	1990	2019	Change (%)
Upper respiratory infections						
Male	7172.88 (2070.46–12275.30)	1454.53 (5.05–2904.00)	–79.72 (–92.53–111.66)	1.18 (0.34–2.01)	0.20 (0.01–0.40)	–82.93 (–93.71–78.18)
Female	7895.72 (1727.56–14063.87)	1346.78 (–248.41–2941.96)	–82.94 (–94.82–154.73)	1.38 (0.30–2.45)	0.19 (–0.04–0.42)	–85.98 (–95.74–109.44)
Total	15068.60 (3941.30–26195.89)	2801.30 (–226.86–5829.47)	–81.41 (–93.53–131.00)	1.27 (0.33–2.21)	0.20 (–0.02–0.41)	–84.53 (–94.61–92.24)
Lower respiratory infections						
Male	278796.68 (242116.82–315476.55)	102570.35 (84930.16–120210.54)	–63.21 (–69.89–49.50)	45.69 (39.68–51.70)	14.15 (11.72–16.58)	–69.03 (–74.65–57.49)
Female	265104.31 (231555.04–298653.59)	82693.98 (64032.15–101355.81)	–68.81 (–75.01–57.16)	46.23 (40.38–52.08)	11.86 (9.18–14.53)	–74.35 (–79.45–64.78)
Total	543900.99 (476789.88–611012.10)	185264.33 (157651.46–212877.21)	–65.94 (–71.32–55.20)	45.95 (40.28–51.62)	13.03 (11.08–14.97)	–71.65 (–76.13–62.72)

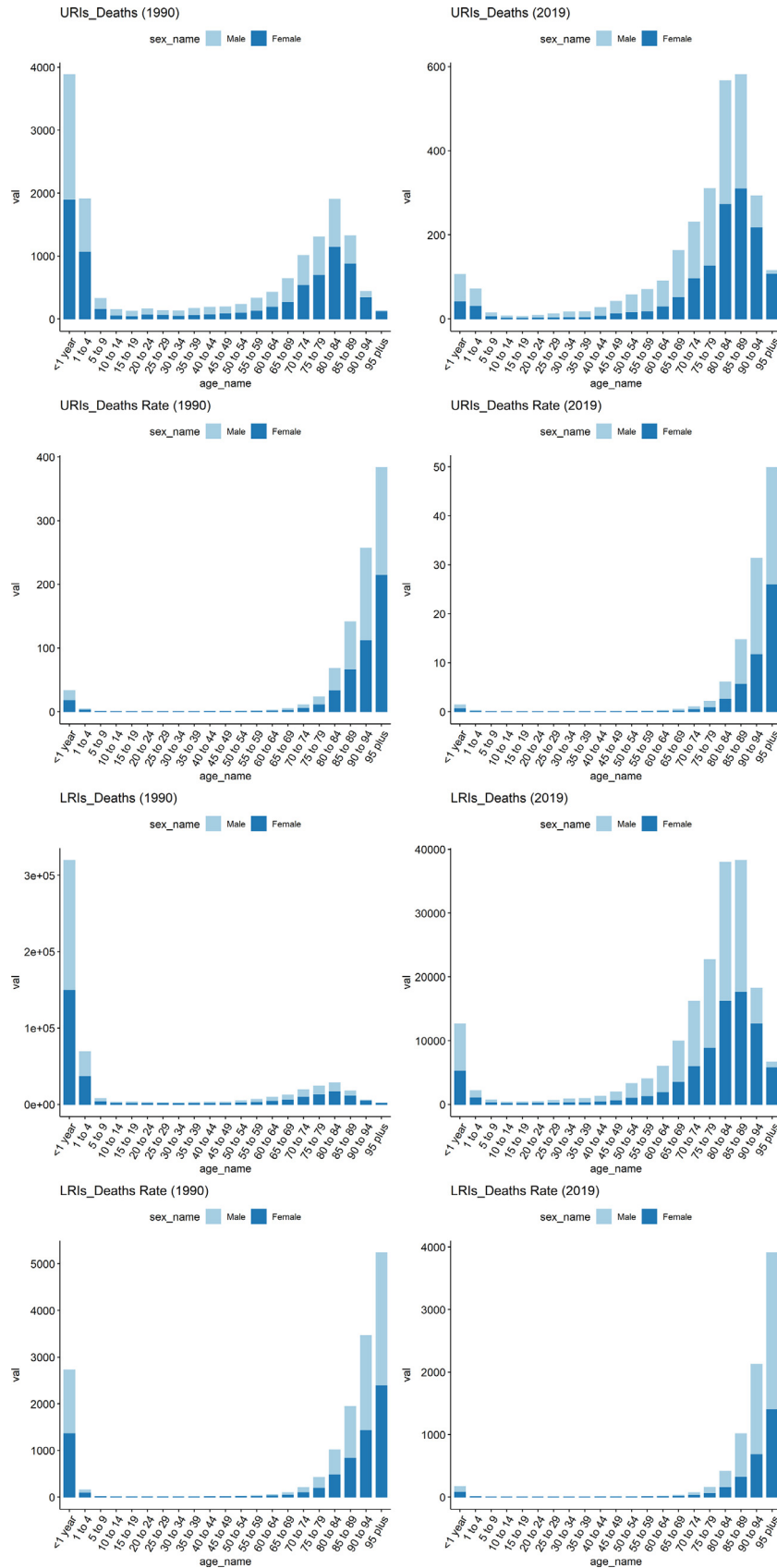


Fig. 5. The age-specific death numbers and mortality rates of upper and lower respiratory infections in 1990 and 2019.

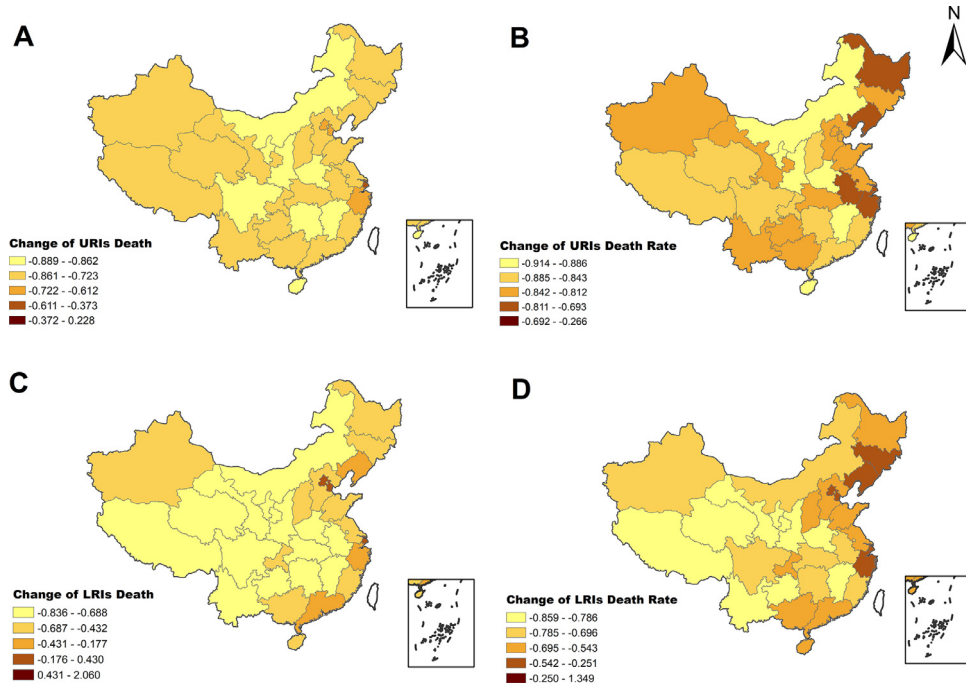


Fig. 6. The change of province-specific death numbers and mortality rates of upper and lower respiratory infections from 1990 to 2019.

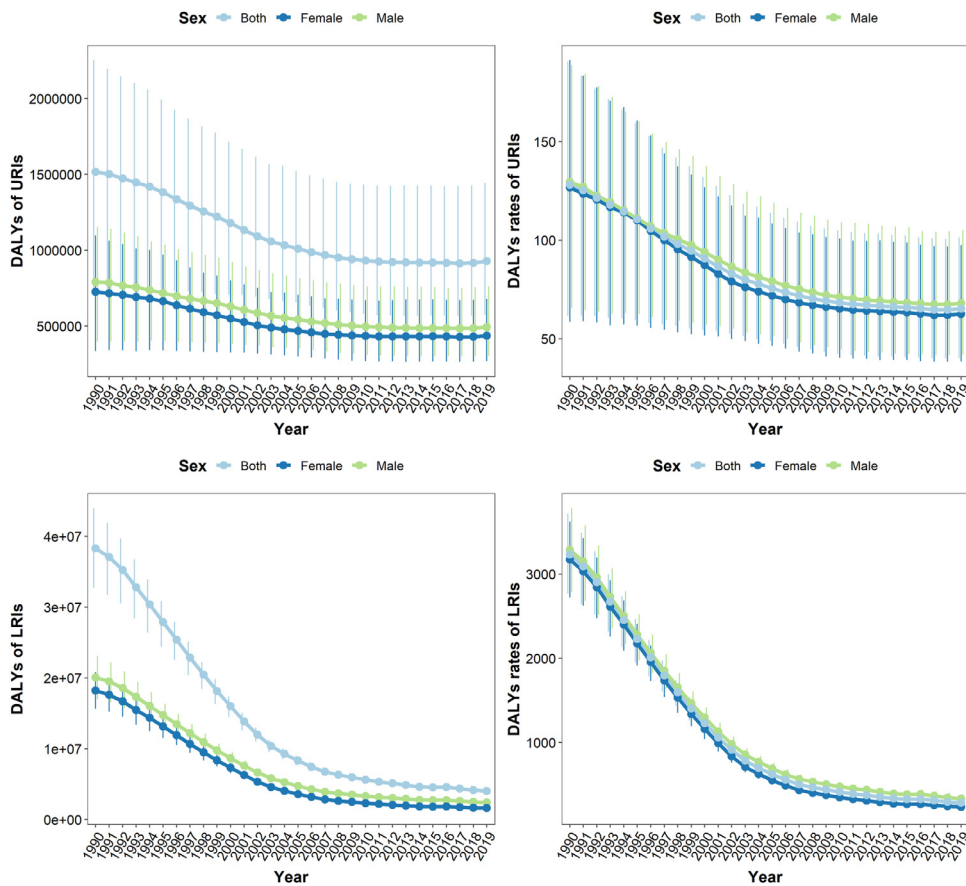


Fig. 7. Trends of disability-adjusted life years of upper and lower respiratory infections in China from 1990 to 2019.

Table 3
All-age disability-adjusted life-years (DALYs) of upper and lower respiratory infections and the percentage changes by sex, 1990–2019.

Subcategories	All-age DALYs (95% UI), no. in thousands			Age-standardized DALY rate (95% UI), per 100,000		
	1990	2019	Change (%)	1990	2019	Change (%)
Upper respiratory infections						
Male	790•40 (401•20–1150•60)	492•72 (304•89–760•55)	–37•66 (–60•11–11•32)	129•53 (65•75–188•56)	67•98 (42•06–104•93)	–47•52 (–66•42–6•29)
Female	726•33 (336•70–1096•26)	435•90 (269•62–679•08)	–39•99 (–63•95–16•14)	126•65 (58•71–191•15)	62•49 (38•65–97•36)	–50•66 (–70•36–4•51)
Total	1516•73 (731•73–2252•32)	928•62 (573•83–1440•47)	–38•77 (–62•03–13•18)	128•14 (61•82–190•28)	65•29 (40•34–101•27)	–49•05 (–68•40–5•81)
Lower respiratory infections						
Male	20069•10 (17034•10–23092•18)	2404•38 (2083•38–2767•03)	–88•02 (–90•31–84•05)	3289•01 (2791•62–3784•44)	331•72 (287•43–381•75)	–89•91 (–91•84–86•58)
Female	18209•40 (15640•88–20775•64)	1616•29 (1399•08–1923•35)	–91•12 (–92•84–88•34)	3175•16 (2727•29–3622•64)	231•72 (200•58–275•74)	–92•70 (–94•11–90•41)
Total	38278•50 (32813•98–43962•34)	4020•68 (3555•79–4589•77)	–89•50 (–91•31–86•38)	3233•85 (2772•20–3714•03)	282•68 (249•99–322•69)	–91•26 (–92•77–88•67)

in 1990 to 1179·75 (95% UI: 709·83–1713·64) thousand years in 2000, 931·39 (95% UI: 582·19–1431·48) thousand years in 2010 and 928·62 (95% UI: 573·83–1440·47) thousand years in 2019, with decreases of 22·22%, 38·59% and 38·77%, respectively. Moreover, in comparing with reductions of 37·66% (95% UI: –11·32–60·11%) and 39·99% (95% UI: –16·14–63·95%) were observed in male and female populations from 1990 to 2019, respectively. Meanwhile, in comparing with the total DALYs from LRIs of 38287·50 (95% UI: 32813·98–43962·34) thousand years in 1990, and we observed greater reductions of 58·21% in 2000 [15995·1 (95% UI: 14538·95–17366·2) thousand years], 85·35% in 2010 [5605·95 (95% UI: 5244·93–6055·58) thousand years], and 89·50% in 2019 [4020·68 (95% UI: 3555·79–4589·77) thousand years]. Furthermore, the total DALYs from LRIs had notable decreases of 88·02% (95% UI: 84·05–90·31%) and 91·12% (95% UI: 88·34–92·84%) for male and female populations, respectively. In addition, declines in the age-standardized DALY rates from 1990 to 2019 were also observed, which were 49·05% (95% UI: 5·81–68·40%) for URIs and 91·26% (95% UI: 88·67–92·77%) for LRIs. These results generally remained similar when we divided the all-age DALYs into YLDs and YLLs, except that the YLDs from URIs were much less than that from LRIs, but YLLs from URIs and LRIs were roughly equal (Supplementary Figs. 1 and 2, Supplementary Tables 1 and 2).

The age-specific DALYs rate is similar to the mortality rate, which displayed U-shaped trends for both URIs and LRIs with increases in age in both 1990 and 2019 (Fig. 8). Children younger than 1 year had the highest estimate of age-standardized DALYs rates [URIs: 1508·45 (95% UI: 210·19–2685·60) and 1595·60 (95% UI: 188·27–2977·81) for male and female in 1990; 162·93 (95% UI: 97·92–290·78) and 139·72 (95% UI: 80·73–259·25) for male and female in 2019; LRIs: 1·21 (95% UI: 1·02–1·41) and 1·20 (95% UI: 1·02–1·38) per 100,000 for male and female in 1990, 0·08 (95% UI: 0·07–0·10) and 0·07 (95% UI: 0·06–0·08) per 100,000 for male and female in 2019], then the estimates decreased sharply, and gradually increased in the elderly population. Similar patterns can be found in the age-specific YLDs and YLLs rates (Supplementary Figs. 3 and 4).

Most provinces were found to have decreasing trends in the age-standardized DALY rate of both URIs and LRIs from 1990 to 2019 (Fig. 9, Supplementary Figs. 5 and 6). For URIs, the Tibet Autonomous Region had the highest decrease in age-standardized DALY rate [0·69% (95% UI: 0·02–0·88%)], Heilongjiang Province had the highest decrease for age-standardized YLD rate [0·13% (95% UI: 0·04–0·21%)], and the Ningxia province had the highest decrease for age-standardized YLL rate [0·97% (95% UI: 0·06–0·99%)], while the Shanghai Municipality, Tibet Autonomous Region and Macao SAR had the lowest decrease rates for age-standardized DALYs [0·15% (95% UI: 0·05–0·23%)], YLDs [0·03% (95% UI: –0·04–0·10%)] and YLLs [0·68% (95% UI: 0·03–0·87%)] rates, respectively. For LRIs, the Shaanxi Province had the highest decrease rates for age-standardized DALY and YLL rates [both of them are 0·96% (95% UI: 0·93–0·97%)], and Tibet Autonomous Region had the highest decrease in age-standardized YLD rate [0·56% (95% UI: 0·51–0·62%)], while Hong Kong SAR had slight increase rates for age-standardized DALY, YLD, and YLL rates [0·19% (95% UI: –0·53–0·14%), 0·15% (95% UI: 0·03–0·28%) and 0·19% (95% UI: –0·53–0·14%), respectively].

4.4. Risk factors attributable to disability-adjusted life years due to upper and lower respiratory infections in China, 2019

As revealed in Table 4, all risk factors considered in the GBD 2019 study for both sexes account for 0·15% (95% UI: 0·08%, 0·36%) and 72·50% (95% UI: 67·45%, 77·23%) of the total age-standardized DALYs due to URIs and LRIs, respectively. Of all risk factors, 0·05% (95% UI: 0·03%, 0·10%) and 0·12% (95% UI: 0·05%, 0·31%) of

the URIs DALYs could be attributed to environmental/occupational and behavioral risks, while 38·74% (95% UI: 31·32%, 46·34%) and 55·52% (95% UI: 49·33%, 60·96%) of the LRI DALYs were caused by these two major groups of risks. The three leading risk factors in 2019 for age-standardized DALYs of LRIs included child malnutrition (21·62%, 95% UI: 11·83–28·47%), ambient PM pollution (19·66%, 95% UI: 13·79–26·24%), and second-hand smoke (16·48%, 95% UI: 10·78–22·21%). The three largest contributors to age-standardized DALYs of URIs were low birth weight (0·10%, 95% UI: 0·04–0·26%), short gestation (0·08%, 95% UI: 0·03–0·20%), and ambient particulate matter pollution (0·04%, 95% UI: 0·02–0·08%). In addition, the risk factors attributable to DALYs due to URIs and LRIs were similar in different sex groups, except for the smoking and alcohol use, which were associated with greater DALYs in the male population (Table 4).

5. Discussion

We presented an up-to-date overview of the spatial and temporal distribution of disease burden of URIs and LRIs in China based on GBD 2019. The results indicated that, although the disease burden in both the young children and the elderly remained high in 2019, substantial progress has been made in China during the past decades, especially for the LRIs, which dropped from being the top cause of DALYs in 1990 to the 24th highest cause in 2019 [17]. However, such declines did not occur equally in different provinces, and incident cases and the total YLDs for URIs remained high in 2019.

Our results suggest that the disease burden of URIs and LRIs generally decreased year by year from 1990 to 2019. These findings can be partially explained by the rapid and sustained socio-economic development in China, which ushered in a series of government policies to improve healthcare, medical treatment, nutrition, educational attainment, and the observable reductions in disease burden [30,31]. For example, the Chinese government released the Healthy China 2030 blueprint to promote population health via the adoption of the most pertinent strategies such as reducing risk factors, improving nutrition and encouraging healthier lifestyles [32]. Such interventions aimed at improving childhood nutrition were reported to be effective in protecting children from dying from respiratory infections [33]. Moreover, an essential goal of the integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhea (GAPPD) was to provide universal access to disease management for RI patients [34]. Furthermore, the decrease in RIs might also attribute to the so-called nutritional transition, i.e., the shift in dietary consumption from traditional diets rich in fiber to Western diets rich in sugars and fat that corresponds with demographic and economic changes [35]. Unfortunately, the current study did not include detailed dietary information. In addition, government-sponsored health-care reform in rural regions, early detection of RIs, and programs to reduce air pollution were also the potential drivers of this reduction [36,37]. Another possible explanation is the optimized use of antibiotics, which has already been found to be an efficient intervention in patients with RIs [38]; however, the universal use of antibiotics for treating RIs is a double-edged sword because of the increased possibility of antimicrobial resistance [39].

We observed that the mortality from URIs and LRIs decreased faster than incidence over the study period, indicating an advancement in decreasing the risk of infection than in protecting against mortality, which is in accordance with the global estimates [36]. This may be attributable to improvements in health services that occurred in conjunction with the economic development during the past three decades. As such, those who had RIs could receive more effective clinical treatment and health care that lead to a better prognosis. Moreover, our analysis estimated that the deaths

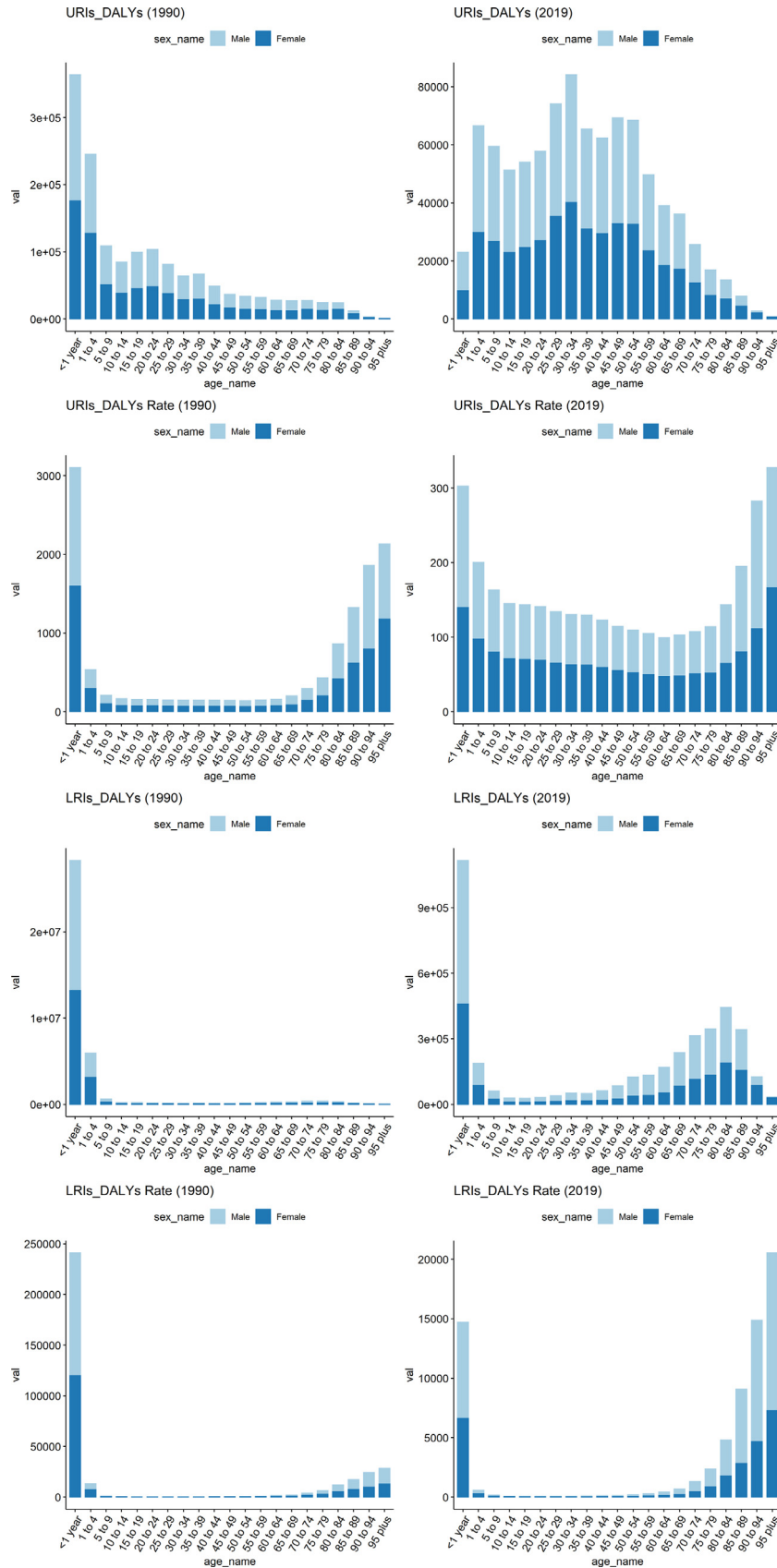


Fig. 8. The age-specific disability-adjusted life years of upper and lower respiratory infections in 1990 and 2019.

Table 4
Risk factors attributable to disability-adjusted life years due to upper and lower respiratory infections by sex in China, 2019.

Risk factors	Percentage (%) of disability-adjusted life years (95% UI)					
	Upper respiratory infections			Lower respiratory infections		
	Both sexes	Males	Females	Both sexes	Males	Females
All risk factors	0·15 (0·08, 0·36)	0·15 (0·08, 0·35)	0·15 (0·07, 0·37)	72·50 (67·45, 77·23)	73·75 (68·90, 78·38)	70·43 (64·74, 75·64)
Environmental/occupational risks	0·05 (0·03, 0·10)	0·05 (0·03, 0·10)	0·05 (0·03, 0·10)	38·74 (31·32, 46·34)	38·18 (30·79, 45·76)	39·07 (31·63, 46·63)
Unsafe water, sanitation, and handwashing	0 (0, 0)	0 (0, 0)	0 (0, 0)	4·10 (1·65, 6·69)	4·05 (1·63, 6·61)	4·12 (1·67, 6·69)
No access to handwashing facility	0 (0, 0)	0 (0, 0)	0 (0, 0)	4·10 (1·65, 6·69)	4·05 (1·63, 6·61)	4·12 (1·67, 6·69)
Air pollution	0·05 (0·03, 0·10)	0·05 (0·03, 0·10)	0·05 (0·03, 0·10)	26·55 (18·69, 35·20)	26 (18·30, 34·64)	26·96 (19·08, 35·73)
Particulate matter	0·05 (0·03, 0·10)	0·05 (0·03, 0·10)	0·05 (0·03, 0·10)	26·55 (18·69, 35·20)	26 (18·30, 34·64)	26·96 (19·08, 35·73)
Ambient particulate matter	0·04 (0·02, 0·08)	0·04 (0·02, 0·08)	0·04 (0·02, 0·08)	19·66 (13·79, 26·24)	19·88 (13·85, 26·62)	19·35 (13·63, 25·74)
Household pollution from solid fuels	0·01 (0·01, 0·03)	0·01 (0·01, 0·03)	0·01 (0·01, 0·03)	6·89 (3·15, 12·29)	6·12 (2·74, 11·06)	7·61 (3·57, 13·77)
Non-optimal temperature	0 (0, 0)	0 (0, 0)	0 (0, 0)	13·32 (8·76, 17·67)	13·24 (8·72, 17·62)	13·28 (8·70, 17·56)
High temperature	0 (0, 0)	0 (0, 0)	0 (0, 0)	0·67 (0·06, 1·19)	0·71 (0·07, 1·28)	0·66 (0·06, 1·17)
Low temperature	0 (0, 0)	0 (0, 0)	0 (0, 0)	12·69 (7·93, 16·99)	12·58 (7·90, 16·81)	12·66 (8·00, 16·87)
Behavioural risks	0·12 (0·05, 0·31)	0·12 (0·05, 0·31)	0·11 (0·04, 0·31)	55·52 (49·33, 60·96)	58·02 (52·16, 63·24)	51·93 (44·77, 58·03)
Child and maternal malnutrition	0·12 (0·05, 0·31)	0·12 (0·05, 0·31)	0·11 (0·04, 0·31)	34·58 (27·07, 40·71)	29·98 (23·30, 36·15)	38·73 (30·36, 45·68)
Suboptimal breastfeeding	0 (0, 0)	0 (0, 0)	0 (0, 0)	4·59 (3·12, 6·13)	4·00 (2·67, 5·38)	5·11 (3·44, 6·86)
Non-exclusive breastfeeding	0 (0, 0)	0 (0, 0)	0 (0, 0)	4·59 (3·12, 6·13)	4·00 (2·67, 5·38)	5·11 (3·44, 6·86)
Child growth failure	0 (0, 0)	0 (0, 0)	0 (0, 0)	23·56 (16·56, 29·20)	20·35 (13·96, 25·92)	26·53 (18·42, 32·83)
Child underweight	0 (0, 0)	0 (0, 0)	0 (0, 0)	1·62 (0·77, 3·57)	1·36 (0·65, 2·96)	1·88 (0·93, 3·99)
Child malnutrition	0 (0, 0)	0 (0, 0)	0 (0, 0)	21·62 (11·83, 28·47)	18·66 (10·01, 25·19)	24·37 (13·62, 31·99)
Child stunting	0 (0, 0)	0 (0, 0)	0 (0, 0)	3·02 (0·05, 9·79)	2·55 (0·04, 8·48)	3·51 (0·05, 11·19)
Low birth weight and short gestation	0·12 (0·05, 0·31)	0·12 (0·05, 0·31)	0·11 (0·04, 0·31)	9·43 (8·28, 10·54)	8·22 (6·86, 9·45)	10·49 (9·05, 11·88)
Short gestation	0·08 (0·03, 0·20)	0·08 (0·03, 0·19)	0·07 (0·03, 0·21)	6·05 (5·27, 6·79)	5·12 (4·27, 5·95)	7·01 (6·03, 7·97)
Low birth weight	0·10 (0·04, 0·26)	0·10 (0·04, 0·25)	0·10 (0·04, 0·28)	7·99 (7·00, 8·95)	6·87 (5·77, 7·91)	9·05 (7·84, 10·28)
Tobacco	0 (0, 0)	0 (0, 0)	0 (0, 0)	26·13 (20·44, 31·83)	31·11 (25·65, 36·60)	20·45 (14·18, 26·68)
Smoking	0 (0, 0)	0 (0, 0)	0 (0, 0)	10·73 (8·25, 13·44)	18·44 (14·50, 22·67)	2·14 (1·37, 3·10)
Second-hand smoke	0 (0, 0)	0 (0, 0)	0 (0, 0)	16·48 (10·78, 22·21)	14·41 (9·42, 19·55)	18·66 (12·28, 24·96)
Alcohol use	0 (0, 0)	0 (0, 0)	0 (0, 0)	2·81 (1·32, 4·19)	4·95 (2·44, 7·33)	0·49 (0·13, 0·92)

Abbreviation: UI, uncertainty interval.

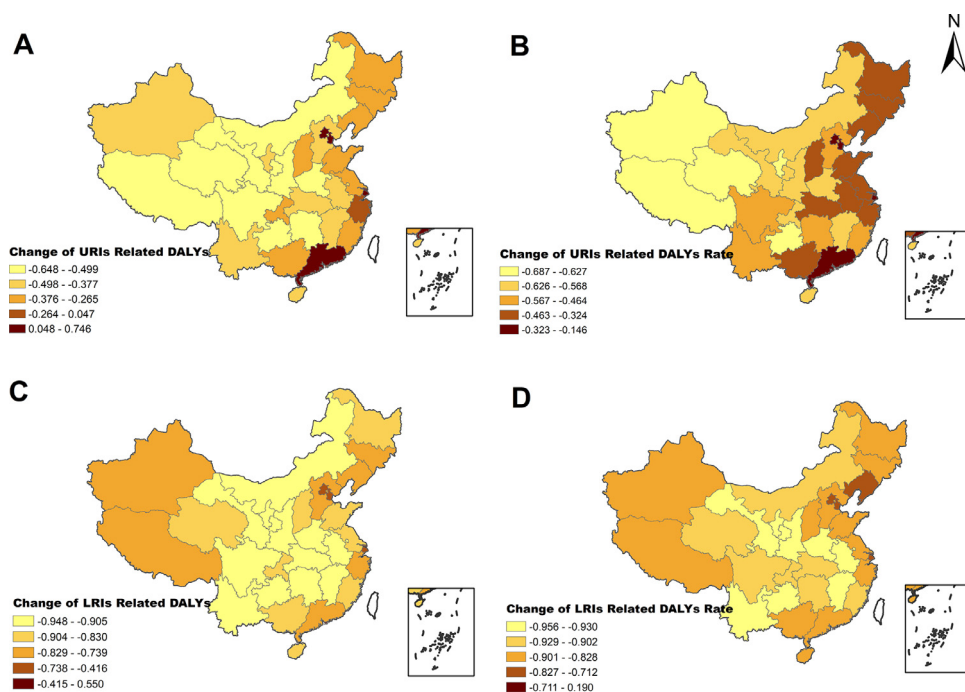


Fig. 9. The change of province-specific disability-adjusted life years of upper and lower respiratory infections from 1990 to 2019.

due to URI significantly decreased from 15,069 in 1990 to 2801 in 2019. Though significant progress has been made in the effective antibiotics, there were still some deaths due to URI, which might be attributable to severe and fatal URIs stemming from croup and epiglottitis [8,9]. This is particularly the case for vulnerable subpopulations, such as the elderly and the children, which was supported by our age-specific mortality (Fig. 5), showing that the deaths due to URIs in 2019 mainly occurred in these vulnerable subpopulations. Therefore, it is urgent that actions are taken to eliminate preventable deaths in these susceptible persons from RIs [40].

We observed no statistical changes or even slight increases in the age-standardized incidence, mortality rate, or DALY, YLD, and YLL rates of RIs in Hong Kong, which was different from other regions in China. This might be due to the fact that population health is closely tied to economic development. Since Hong Kong has reached a high level of economic prosperity in the 1990s, people in Hong Kong might have reached a ceiling effects whereby fewer relative gains in health status can be achieved. Other provinces in China lagged in their transition from poverty to prosperity, but have gained substantially over the last three decades as enhancements to medical care have gone hand-in-hand with a booming economy.

To the best of our knowledge, previous reports related to the disease burden of RIs mainly focused on the LRIs. The results suggest tremendous progress has been made in the control and prevention of LRIs during the past three decades. For example, the LRI death rates were much lower than global estimates in 2016 for all age groups combined (13.0 vs. 32.2 per 100,000 people), including children younger than 5 years (86.8 vs. 103.3 per 100,000 people) [21]. Moreover, we also observed that the rate of DALYs, YLDs and YLLs per 100,000 population in China was lower than that in the Eastern Mediterranean Region (282.7 vs. 1712, 5.1 vs. 9.7 and 277.6 vs. 1702, respectively) [41]. Despite these gains, there is still rooms for improvement as we can observe that the incidence of and mortality rates attributable to LRIs among children younger than 5 years is lower in North America and Western Europe [36]. Greater efforts are needed in coping with child malnu-

trition or childhood wasting, because these are leading risk factors for age-standardized DALYs of LRIs in both China and the world.

Another important finding from the present work is that the change patterns in incidence, mortality and DALYs in different provinces are not equal, and the great variations in degree of reduction in URIs and LRIs across different provinces in China remains a challenge. Although the policies to equalize inequalities in different areas has been a government priority in China for a long time, equity at the province level can only be accomplished when sufficient and detailed information is analyzed to guide investments [20]. However, previous reports have also pointed out a lack of such data, and province-specific strategy development and interventions are needed in some provinces to lessen major risk factors to improve health equity in the future [20]. While we did not examine the reasons for the difference in province-specific disease burden and these trends in China, our results can still provide important evidence on guiding the priority setting and resource allocation at the province level.

According to the present study, child malnutrition, PM, and second-hand smoke were the three leading risk factors for age-standardized DALYs of LRIs, while low birth weight, short gestation, and PM were the largest contributors to age-standardized DALYs of URIs. Thus, public health prevention strategies targeting maternal nutrition, air pollution, and tobacco control should be a top priority for the control of URIs and LRIs in China. Furthermore, measures that focus on the behavioral risk factors, such as diet and tobacco control, have been proven to be cost-effective [42–44]. Moreover, as a result of more environmentally-conscious construction in China, fundamental progress in air quality improvements has been achieved in recent years [45], which would further contribute to the reduction of URIs and LRIs in China. Previously, studies have reported on the interaction between economic development and air pollution, which often occurs in rapidly urbanizing countries, and further research on health impact of carbon-based energy production would be useful in guiding policies to reduce the use of fossil fuels [30,36,46].

Several limitations should be addressed in the GBD 2019 study pertaining to URIs and LRIs in China. First, there is a lack of studies

on the disease duration of both URIs and LRIs in China. Although GBD collaborators put great effort into the collection of all available data to estimate disease burden, the quality and quantity of data on URIs and LRIs are still limited. Moreover, the great methodological heterogeneity in previous published and unpublished studies might also affect the accuracy of the estimation. However, the short supply of data and heterogeneity in methodology can be evaluated and addressed by DisMod-MR 2.1, which had been validated in previous studies [19]. Moreover, this work only focused on the disparities of disease burden from URIs and LRIs by sex, age, and province; however, previous publications have also revealed that other common factors, such as living in urban or rural areas, might be associated with different type of RIs [47]. Furthermore, the uncertainty interval of DALYs in the GBD study might be underestimated because the independence of YLLs from YLDs was assumed. Additionally, there was a lack of robust mortality data from some remote and poorer regions in China, which may also affect the precision of our assessment. Therefore, further epidemiological surveys are needed to provide more detailed information on disease burden of URIs and LRIs.

In conclusion, this study demonstrates that URIs and LRIs still represent an immense health burden in China, although the incidence, mortality, and DALYs due for these two diseases have generally declined over the past three decades. This study includes burden estimates of URIs and LRIs for different age groups and 33 Chinese provinces, which can help health authorities monitor incidence trends as well as help determine appropriate priorities and goals in health policy. More importantly, this study highlights the need for developing more targeted strategies, especially for young children and the elderly in order to reduce the burden of URIs and LRIs throughout China. In addition, there is an opportunity for further epidemiological studies that include more detailed information on the burden of these two diseases and other possible risk factors, including dietary changes, as well as investigate the reasons behind the heterogeneity observed between different provinces in China in this study.

Author contributions

ZR, JQ, HL and PY conceived the study. ZR and JQ prepared the first draft and finalized the manuscript based on comments from all other authors. MZ and PY collected and analyzed the data. YY, SZ and JQ participated in the data preparation and verified the data. ZQ, MG and MHL provided important comments on the manuscript. All authors reviewed the drafted manuscript for critical content and approved the final version. HL and PY lead the research. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Declaration of Interests

We declare no competing interests.

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Data sharing statement

JQ, PY, and MZ have full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. The data used for the analyses are available by an email request to the corresponding author (PY). For more data sources, code, and results, please visit: <http://ghdx.healthdata.org>, <https://github.com/ihmeuw/ihme-modeling> and <https://vizhub.healthdata.org/gbd-compare>.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.lanwpc.2021.100153.

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