scientific reports

Check for updates

OPEN

High sodium intake increases interstitial lung disease and pulmonary sarcoidosis based on the Global Burden of Disease study 1999–2019

Zhigang Hu[1,2,3,4,6]✉, Yufeng Tian[5], Ailan Yang[4] & Xinyu Song[1,2,3,6]✉

This study investigated the relationships between dietary sodium intake and the incidence and prevalence of interstitial lung disease (ILD) and pulmonary sarcoidosis using data from the Global Burden of Diseases, Injuries, and Risk Factors Study 2019. This study assessed the strength of the abovementioned relationships via LASSO analysis and a generalized additive model with Poisson regression and determined the nonlinear and lagged effects via a distributed lag nonlinear model (DLNM). In the past three decades, global dietary sodium intake has decreased gradually. Two LASSO and generalized additive analyses both suggested that dietary sodium intake is obviously correlated with the incidence and prevalence of ILD and pulmonary sarcoidosis. The overall exposure–response curve revealed a dose–effect relationship between dietary sodium intake and the incidence and prevalence of ILD and pulmonary sarcoidosis. The maximum lag-specific RR of extremely high dietary sodium intake was 1.75 (95% CI: 1.61–1.91, lag 0 year) for incidence and 3.19 (95% CI: 2.24–4.53, lag 0 year) for prevalence relative to the reference. Our study suggests that dietary sodium intake is positively associated with the incidence and prevalence of ILD and pulmonary sarcoidosis. These findings may have important policy implications for dietary sodium intake-reduction strategies to decrease the burden of respiratory diseases and promote public health.

Keywords Interstitial lung disease, Pulmonary sarcoidosis, Incidence, Sodium, Prevalence

Interstitial lung disease (ILD) is defined as inflammation or fibrosis within the pulmonary interstitium and includes approximately 200 heterogeneous groups of disorders with overlapping clinical, radiological, physiological, and pathological features[1]. ILD may be divided into the following subgroups: idiopathic interstitial pneumonias, autoimmune-related ILD, hypersensitivity pneumonitis, sarcoidosis, and other types of ILD[2]. A study based on the Global Burden of Disease (GBD) 2019 dataset reported that the global incidence of ILD and pulmonary sarcoidosis increased by 118.6% from 1990 to 2019 and may have accounted for 31.2% of the total incidence among all chronic respiratory diseases in 2019[3]. Although the global burden of ILD is gradually increasing, therapeutic options for ILD are still limited, resulting in a poor median survival and various complications, especially idiopathic pulmonary fibrosis (IPF)[3]. Clinical features secondary to ILD are usually intractable and require readmission, which may decrease the quality of life and increase the economic and mental burdens of patients with ILD[4]. Therefore, the prevention and intervention of potential risk factors are highly important for reducing the global disease burden of ILD and pulmonary sarcoidosis.

Good dietary habits can provide a great opportunity for improving public health. Moreover, poor dietary practices lead to the occurrence and development of numerous diseases, such as obesity, hypertension, chronic

[1]Department of Respiratory and Critical Care Medicine, The First College of Clinical Medicine Science, China Three Gorges University, Yichang 443003, People's Republic of China. [2]Department of Respiratory and Critical Care Medicine, Yichang Central People's Hospital, Yichang 443003, People's Republic of China. [3]Clinical Medical Research Center for Precision Diagnosis and Treatment of Lung Cancer and Management of Advance Cancer Pain of Hubei Province, Zhijiang, People's Republic of China. [4]Department of Respiratory and Critical Care Medicine, Yichang Central People's Hospital at Zhijiang, Zhijiang 443200, People's Republic of China. [5]Department of Teaching Office, Three Gorges University, Yichang 443003, People's Republic of China. [6]Zhigang Hu and Xinyu Song contributed equally to this work. ✉email: hxq910813@163.com; sxy1421@163.com

obstructive pulmonary disease, cardiovascular disease, diabetes, and lung cancer[5–7]. Current studies on the associations between sodium intake and public health have focused mainly on hypertension and cardiovascular diseases[7]. High dietary sodium intake can induce deleterious vascular effects by impairing nitric oxide-mediated endothelial function, which increases cardiovascular morbidity and mortality independent of its effects on hypertension[8]. In addition, high dietary sodium intake may lead to alterations in the sympathetic nervous system and increased inflammatory levels by inhibiting anti-inflammatory regulatory T cells, increasing the number of proinflammatory Th17 T cells, and increasing the production of inflammatory cytokines[9,10]. A study by Chen et al. indicated that low dietary sodium intake possibly attenuates pulmonary fibrosis; in contrast, high dietary sodium intake increases fibrocytes. Lung inflammatory responses and pulmonary fibrosis caused by high sodium intake are very likely to be involved in the occurrence and development of ILD. However, few published studies have assessed the associations between dietary sodium intake and the incidence and prevalence of ILD.

In this study, we first determined whether dietary sodium intake is correlated with the incidence and prevalence of ILD and pulmonary sarcoidosis via least absolute shrinkage and selection operator (LASSO) regression analysis on the basis of the GBD Study 2019. A generalized additive model with Poisson regression was subsequently used to assess the strength of the two abovementioned associations with the adjustment of potentially confounding factors screened via the LASSO analysis. Finally, we investigated the lag effects of high dietary sodium intake on the incidence and prevalence of ILD and pulmonary sarcoidosis through two distributed lag nonlinear models.

Methods

Data source

The GBD Study is the single largest and most detailed scientific effort ever conducted to quantify levels and trends in global public health. Over 12,000 researchers from more than 160 countries and territories have participated in producing the most accurate, up-to-date, and comparable estimates of burden worldwide. The GBD Study provides a unique platform to compare the magnitude of diseases, injuries, and risk factors across age groups, sexes, countries, regions, and time. We obtained all original data from the GBD Study 2019 via the Global Health Data Exchange. The Global Health Data Exchange was constructed and is supported by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington. The IHME provides a rigorous and comparable measurement for quantifying morbidity and mortality for 369 health problems; moreover, the IHME also collects data on air quality, smoking and dietary intake to estimate the effects of these risk factors on public health. Researchers can use these freely available data to discuss and evaluate equitable strategies to best improve public health. Detailed descriptions and complete protocols of the GBD Study and the Global Health Data Exchange are available online (https://ghdx.healthdata.org/about-ghdx).

Ethics statement

Ethical approval and informed consent were waived, considering the GBD is a publicly available database. No identifiable information was contained.

The incidence and prevalence of ILD

In the GBD Study 2019, ILD mainly includes ILD and pulmonary sarcoidosis but not drug-induced interstitial lung disorders[3]. The IHME derived primarily the incidence and prevalence data for ILD and pulmonary sarcoidosis from hospital inpatients and insurance claims data[3,11]. In a previous study based on the GBD Study 2019, the incidence of ILD and pulmonary sarcoidosis was found to be weakly positively associated with the sociodemographic index in 2019. Here, we analyzed the population-level incidence and prevalence of ILD and pulmonary sarcoidosis in adults aged 20 years or older by sex across the five SDI groups from 1990 to 2019. The three elements of population granularity were sex, SDI and year. The SDI represents an integrated indicator of income per average educational attainment and the total fertility rates[3]. In the GBD Study, the SDI was divided into five groups as follows: low, low-middle, middle, high-middle, or high.

Risk factors

Because we assessed the burden of ILD and pulmonary sarcoidosis in the past three decades, in this study, all included variables must include 30 years of data. The risk factors for poor air quality mainly include ambient particulate matter, ozone and household air pollution. Many values of ambient particulate matter were missing from 1990 to 2009. Smoking status had no data to match the data grouped by the SDI, sex or year. Therefore, ambient particulate matter and smoking were excluded from this study. We finally included the following variables as potential risk factors: sex, age, year, SDI, ozone, household air pollution, whole grains, vegetables, sugar- sweetened beverages (SSBs), transfats, sodium, fiber, processed meat, red meat, omegas, fruits, milk nuts, legumes, and calcium.

Statistical analysis

The statistical analysis of our study involved four main components. First, we performed descriptive statistics for all included variables globally from 1990 to 2019 via Stata 15. The Mann–Whitney U test was used to compare the differences in dietary sodium intake among groups by sex, SDI, year, and age. Generalized additive analyses (GAMs) with Gaussian regression were performed to explore the primary associations between sodium intake and the incidence and prevalence of ILD and pulmonary sarcoidosis. Second, LASSO analyses with a Poisson model were used to screen for potential risk factors for the incidence and prevalence of ILD and pulmonary sarcoidosis, which might allow us to evaluate the correlation between sodium intake and ILD. Tuning parameter (lambda) selection in our LASSO analysis was performed via 10-fold cross-validation. Compared with conventional regression analyses, LASSO analyses can address collinear covariates differently[12] and

eliminate exposures that are unrelated to the outcome[13]. Third, we performed a smoothing function to estimate the dose-dependent effects of dietary sodium intake on the incidence and prevalence of ILD and pulmonary sarcoidosis by using a GAM with Poisson regression. GAM analysis simultaneously adjusted for the effects of the confounding risk factors screened by LASSO analysis. The second and third parts of the statistical analyses were performed via Empower (R) (www.empowerstats. com; X&Y solutions, Inc., Boston, MA) and R software. Finally, two distributed lag nonlinear models (DLNMs) with quasi-Poisson models were employed to assess the lag-exposure-response relationships between dietary sodium intake and the incidence and prevalence of ILD and pulmonary sarcoidosis[14–16]. The statistical descriptions of the lag-exposure-response analysis are provided in the Supplementary section. We completed the fourth part of our analyses through the "DLNM" and "splines" packages of R software (version 4.1.0). The relative risk (RR) and 95% confidence interval (CI) represent the strength of all relationships with statistical significance defined by a two-sided P value < 0.05.

Results

Study population characteristics

Descriptive statistics for all included variables worldwide are shown in Table 1. The incidence of ILD and pulmonary sarcoidosis rapidly increased beginning in 1995, whereas the rapidly increasing prevalence of ILD and pulmonary sarcoidosis started in 2005. The incidence of ILD and pulmonary sarcoidosis increased from 118.669 ± 130.269 per 100,000 in 1990–1999 to 136.807 ± 166.649 per 100,000 in 2010–2019, meanwhile the prevalence increased from 567.770 ± 471.780 per 100,000 to 679.335 ± 607.571 per 100,000. Over time, the significantly increasing intake was found in the following foods, mainly including vegatables, sugar-sweetened beverages, fiber, omega, fruit, nuts and calcium (see Table S1). Age and male sex were positively associated with the incidence and prevalence of ILD and pulmonary sarcoidosis. Here, we describe dietary sodium intake in particular. In the past three decades, the mean value of global dietary sodium intake gradually declined from 3.56 ± 0.49 g/d in 1990 to 3.35 ± 0.43 g/d in 2019. Compared with females, males (3.73 ± 0.46 g/d) presented greater dietary sodium intake (3.14 ± 0.21 g/d). Compared with the four other SDI groups, the low-SDI group (2.82 ± 0.06 g/d) had significantly lower dietary sodium intake. GAM with Gaussian regression demonstrated that the incidence and prevalence of ILD/sarcoidosis were 26.8 per 100,000 (95% CI: 16.7 to 36.9 per 100,000, $P < 0.01$) and 39.5 per 100,000 (95% CI: 3.7 to 75.3 per 100,000, $P < 0.05$), respectively, for every 1-gram increase in dietary sodium intake.

LASSO and dose-dependent analyses

In terms of incidence, LASSO analysis revealed six risk factors associated with ILD and pulmonary sarcoidosis (see Figure S1): sex, age, year, SDI, omega and sodium intake. Increased dietary sodium intake was associated with an increased incidence of ILD and pulmonary sarcoidosis ($\beta = 0.203$). Smooth function still demonstrated that the incidence of ILD and pulmonary sarcoidosis increased with increasing dietary sodium intake (see Fig. 1A) after adjusting for the five other risk factors (adjusted RR = 1.28, 95% CI: 1.25–1.30, $P < 0.01$).

Another LASSO analysis (see Figure S1) suggested that the prevalence of ILD was correlated with ten risk factors: sex, age, year, SDI, ozone, SSB intake, transfat intake, fiber intake, legume intake, and sodium intake. Dietary sodium intake was positively associated with the incidence of ILD and pulmonary sarcoidosis ($\beta = 0.331$). Smooth function revealed that dietary sodium intake still had a dose-dependent effect on the prevalence of ILD and pulmonary sarcoidosis (see Fig. 1B) after adjusting for the nine other risk factors (adjusted RR = 1.43, 95% CI: 1.41–1.44, $P < 0.01$).

Lag-exposure–response analysis

The three-dimensional plot in Fig. 2 shows the exposure-response associations between dietary sodium intake and the incidence and prevalence of ILD and pulmonary sarcoidosis across various lag years. The estimated effects of dietary sodium intake on the incidence and prevalence of ILD and pulmonary sarcoidosis were dose-dependent and delayed. At 0 lag years, dietary sodium intake had the greatest effect on the incidence and prevalence of ILD and pulmonary sarcoidosis (see Fig. 2).

Furthermore, Fig. 3 and Table S2 further showed the cumulative exposure-response curve of dietary sodium intake on the incidence and prevalence of ILD and pulmonary sarcoidosis at 0–1 lag years, 0–3 lag years, and 0–7 lag years. The largest cumulative RR of dietary sodium intake was 4.43 (95% CI: 2.75–7.15 at 0–7 lag years) for the incidence of ILD and pulmonary sarcoidosis, whereas the largest cumulative RR was 5.73 (95% CI: 1.95–16.81 at 0–7 lag years) for prevalence.

The relationships between dietary sodium intake and the incidence and prevalence of ILD and pulmonary sarcoidosis at specific lag years were shown in Figs. S2 and S3. The associations between dietary sodium intake and the incidence of ILD and pulmonary sarcoidosis became insignificant after 5 lag years, whereas dietary sodium intake seemingly had no significant effect on the prevalence of ILD and pulmonary sarcoidosis after 2 lag years.

In our study, the lowest value of dietary sodium intake was used for the reference group. Figure 4; Table 2 present the lag-exposure-response relationships between dietary sodium intake and the incidence and prevalence of ILD and pulmonary sarcoidosis at the 50th (middle), 75th (high) and 95th percentiles (extremely high). In the pooled analysis, the higher the dietary sodium intake was, the greater the incidence and prevalence of ILD and pulmonary sarcoidosis. The maximal lag-specific RR of extremely high dietary sodium intake was 1.75 (95% CI: 1.61–1.91, lag 0 year) for incidence and 3.19 (95% CI: 2.24–4.53, lag 0 year) for prevalence compared with the reference.

	Mean	Min	P25	P50	P75	Max	IQR
Prevalence (per 100,000)							
Sex							
Male	618.305	31.420	150.168	419.214	974.764	2775.779	824.596
Female	600.309	32.575	165.175	478.798	931.503	2210.282	766.328
Age							
< 60	272.465	31.420	81.433	195.198	402.112	1150.419	320.678
> 60	1148.254	377.483	825.120	1066.365	1346.331	2775.779	521.211
Year							
1990 to 1999	567.770	31.420	150.510	445.136	882.603	1929.701	732.093
2000 to 2009	580.816	34.864	149.432	441.766	916.681	2363.037	767.249
2010 to 2019	679.335	35.258	159.319	496.025	1106.019	2775.779	946.700
SDI							
High SDI	693.860	42.912	185.395	518.103	1000.105	2775.779	814.711
High-mid SDI	446.282	37.618	165.552	406.593	684.800	1312.465	519.248
Mid SDI	503.244	31.420	117.196	403.565	856.103	1452.506	738.907
Low-mid SDI	834.974	42.099	177.593	641.232	1527.528	2086.700	1349.935
Low SDI	568.176	46.669	153.312	489.985	983.424	1475.115	830.113
Incidence (per 100,000)							
Sex							
Male	131.384	5.050	25.282	79.136	174.750	960.256	149.468
Female	122.969	4.669	25.525	89.654	175.336	691.735	149.811
Age							
< 60	47.188	4.669	13.496	30.961	67.757	223.822	54.261
> 60	255.157	101.268	150.732	192.645	283.323	960.256	132.591
Year							
1990 to 1999	118.669	4.669	25.365	84.964	163.990	782.563	138.626
2000 to 2009	126.053	4.921	25.178	81.634	172.203	907.377	147.025
2010 to 2019	136.807	4.900	26.336	82.735	193.695	960.256	167.358
SDI							
High SDI	252.453	7.612	44.879	137.316	432.658	960.256	387.779
High-mid SDI	99.737	5.316	27.523	81.520	162.095	328.844	134.573
Mid SDI	79.731	4.669	18.894	61.857	130.049	257.034	111.156
Low-mid SDI	122.079	5.890	25.208	92.520	217.071	332.525	191.863
Low SDI	81.883	7.136	23.484	66.667	137.653	217.802	114.170
Ambient ozone pollution (microg/m^3)	46.283	39.653	44.411	45.945	47.743	56.133	3.332
Household air pollution (ppp)	0.480	0.007	0.182	0.462	0.827	0.945	0.645
Whole grains (g/day)	25.876	9.741	24.297	27.117	30.869	38.942	6.571
Vegatables (g/day)	148.252	38.335	74.216	170.196	212.504	281.640	138.288
Sugar-sweetened beverages (g/day)	58.017	14.348	20.661	46.942	95.921	132.893	75.260
Transfat (% energy/day)	0.522	0.310	0.361	0.543	0.656	0.842	0.295
Sodium (g/day)	3.435	2.754	3.077	3.358	3.888	4.355	0.811
Fiber (g/day)	14.948	11.236	13.611	14.437	16.554	18.615	2.944
Provmeat (g/day)	13.081	4.075	6.756	8.085	17.635	34.826	10.879
Redmeat (g/day)	28.051	11.973	13.364	21.092	40	55.885	26.636
Omega (g/day)	0.032	0.009	0.014	0.029	0.050	0.069	0.036
Fruit (g/day)	125.350	70.468	88.410	130.962	155.906	199.153	67.496
Milk (g/day)	98.696	27.959	33.476	67.836	179.247	190.928	145.771
Nuts (g/day)	7.276	3.639	6.524	7.480	8.239	9.797	1.715
Legumes (g/day)	33.626	21.693	27.249	32.656	39.458	47.633	12.209
Calcium (g/day)	0.469	0.204	0.255	0.385	0.699	0.866	0.444

Table 1. Descriptive statistics for all included variables in the Global Burden of Disease Study 1990–2019. The values in Table represented the mean value, minimum value, the first quartile (P25), medium value (P50), the third quartile (P75), maximal value, interquartile range of the Prevalence and Incidence rows. Table showed the worldwide prevalence and incidence of ILD and pulmonary sarcoidosis in different sex, year and age, meanwhile Table showed the regional prevalence and incidence of ILD and pulmonary sarcoidosis in five SDI group.

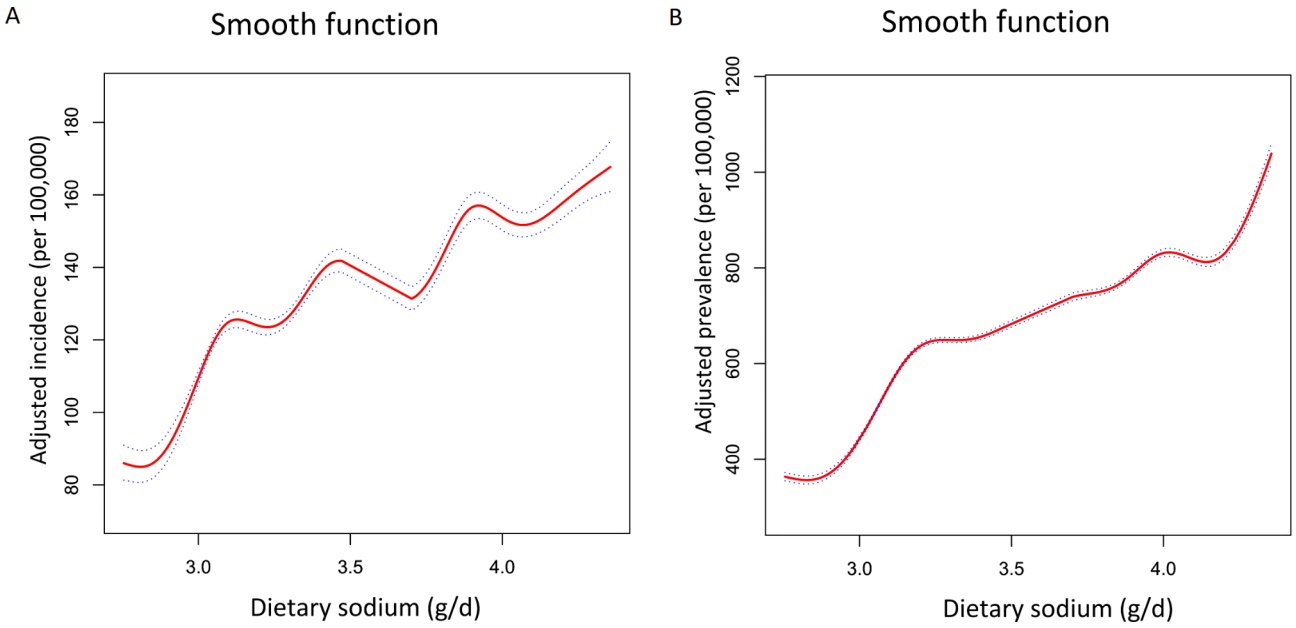

Fig. 1. Smooth function of dietary sodium intake on the incidence and prevalence of interstitial lung disease and pulmonary sarcoidosis. (**A**) the incidence; (**B**) the prevalence.

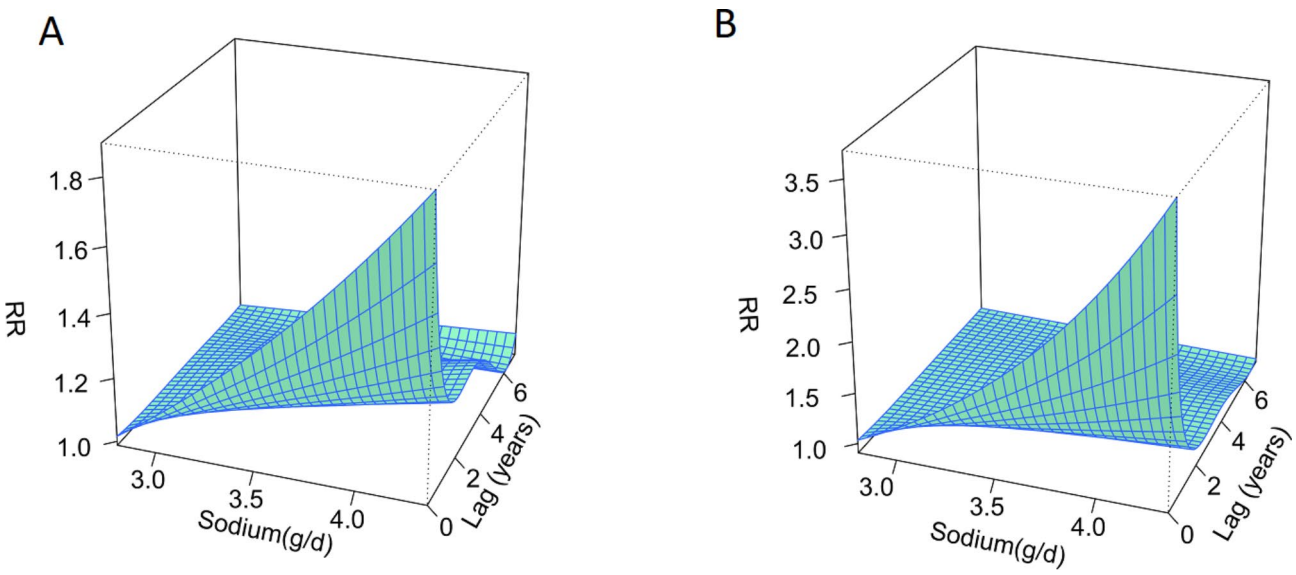

Fig. 2. 3D plots of dietary sodium intake on the incidence and prevalence of interstitial lung disease and pulmonary sarcoidosis at lag 0–7 years. The lowest value was reference: (**A**) the incidence; (**B**) the prevalence.

Discussion

On the basis of global time series data, this study explored the associations between dietary sodium intake and the incidence and prevalence of ILD and pulmonary sarcoidosis via multiple statistical analyses. Our study provides novel knowledge on dietary sodium intake and the burden of ILD and pulmonary sarcoidosis from the perspective of several important aspects. Our findings suggest that dietary sodium intake is positively correlated with the incidence and prevalence of ILD and pulmonary sarcoidosis. In addition, our study reveal that dietary sodium intake still contributes to a significant lag-exposure-response effect on the incidence at 0–5 lag years and the prevalence at 0–2 lag years. The maximal lag-specific effect was found in 0 lag years among the single lag years. The largest cumulative RR of dietary sodium intake for the incidence and prevalence of ILD and pulmonary sarcoidosis were 4.43 (95% CI: 2.75–7.15) and 5.73 (95% CI: 1.95–16.81), respectively. These findings indicate that dietary sodium intake restriction potentially provides a protective effect on public health, even with prolonged clinical benefits in terms of the risk of ILD and pulmonary sarcoidosis.

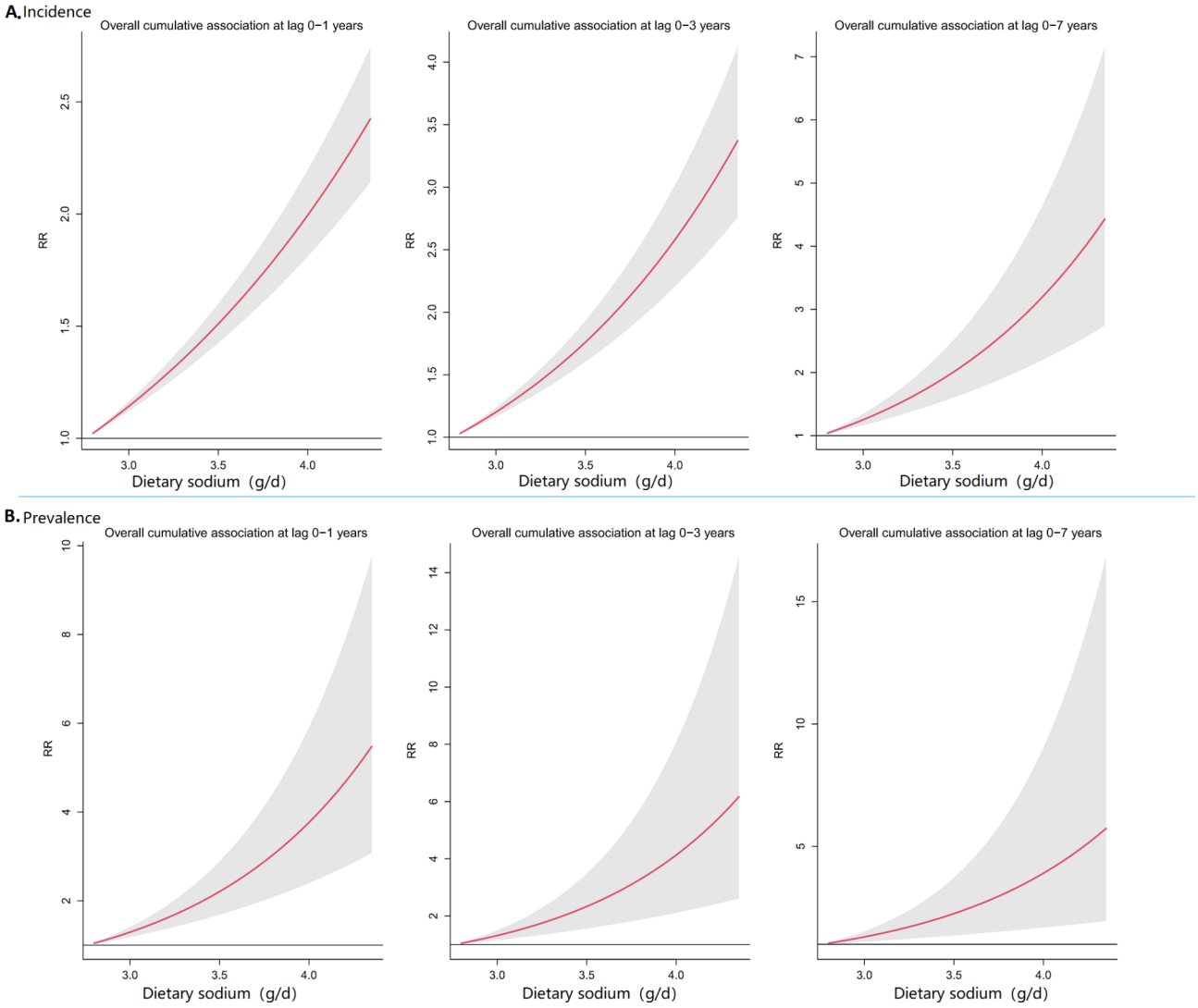

Fig. 3. : The cumulative exposure–response curve of dietary sodium intake on the incidence and prevalence of interstitial lung disease and pulmonary sarcoidosis at lag 0–1 years, lag 0–3 years, and lag 0–7 years. The lowest value was reference: (**A**) the incidence at lag 0–1 years, lag 0–3 years, and lag 0–7 years; (**B**) the prevalence at lag 0–1 years, lag 0–3 years, and lag 0–7 years.

Unfortunately, no studies have investigated the effect of dietary sodium intake on the burden of ILD in the human population. As mentioned above, ILD is characterized by inflammation or fibrosis within the pulmonary interstitium.

We may deduce the potential mechanisms linking dietary sodium intake with the occurrence of ILD on the basis of the results from animal studies, as follows.

First, Zhang et al. suggested that high sodium levels can aggravate pulmonary inflammation and edema by increasing monocyte recruitment in the pulmonary interstitium and induce the proinflammatory profile of pulmonary macrophages through the p38/cFos/AP1 and Erk1/2/cFos/AP1 pathways[10]. Proinflammatory cytokines and/or chemokines secreted by monocytes and macrophages may exacerbate pulmonary injuries. Recruited monocytes and macrophages play important roles in pulmonary inflammation and fibrosis[18]. Another study showed that high dietary sodium intake might result in a significant increase in the number of lung macrophages and/or dendritic cell phenotypes after bleomycin treatment[9]. Moreover, high dietary sodium intake substantially increased the number of lung fibrocytes compared with low sodium intake in bleomycin-induced and control mice[9]. Taken together, high dietary sodium intake may induce lung proinflammatory cytokine secretion and drive the shift of multiple types of lung cells toward fibrocyte differentiation to promote and maintain pulmonary inflammation and the profibrotic response[9].

Previous studies have also suggested that high dietary sodium intake is an environmental risk factor for the occurrence and development of autoimmune diseases by promoting a shift in T-helper (Th)-1 and Th17 proinflammatory phenotypes[19,20]. Autoimmune diseases, such as rheumatoid arthritis and multiple sclerosis, are widely known as important risk factors for the occurrence and development of ILD[21,22]. Approximately

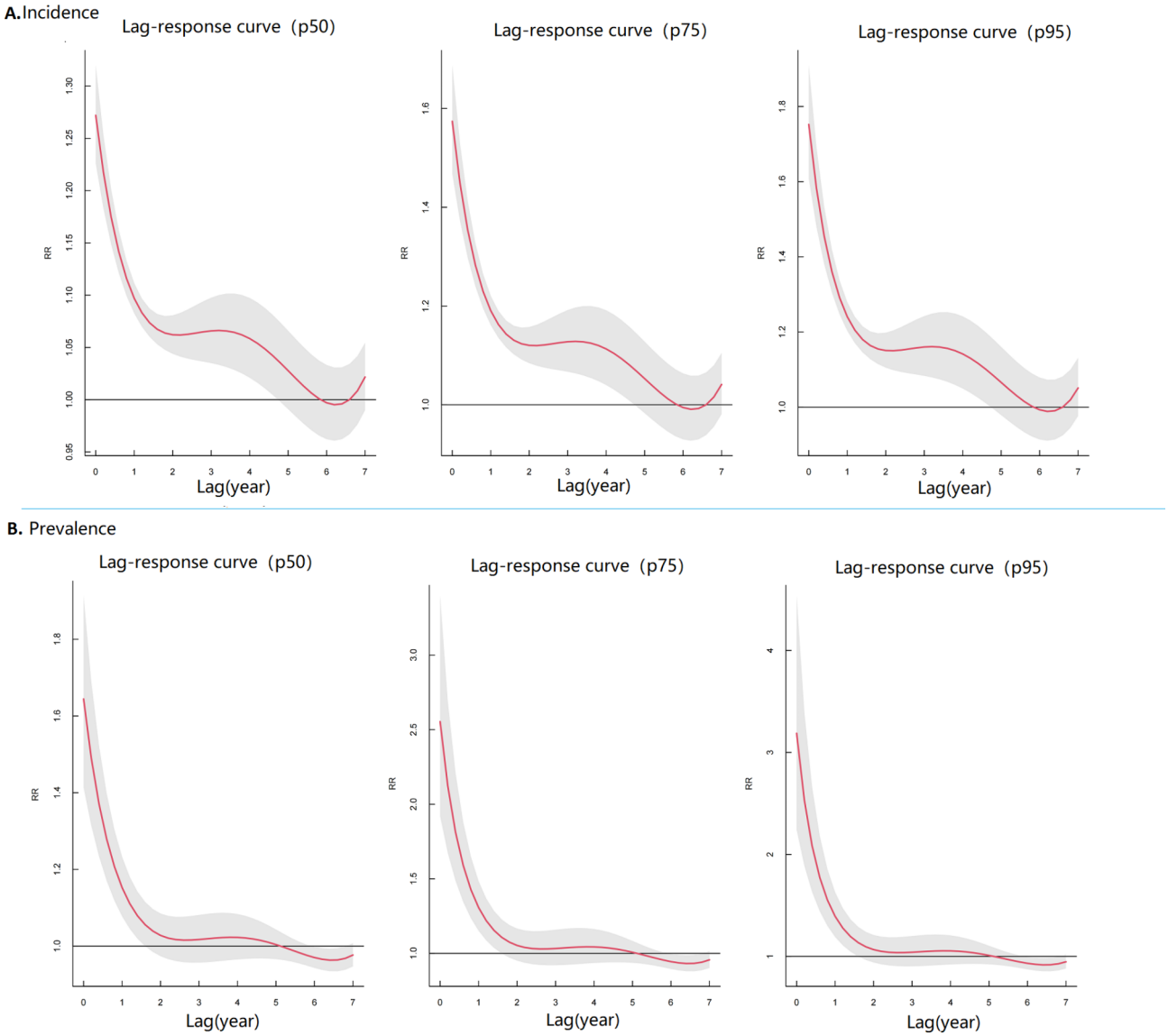

Fig. 4. The lag–exposure–response relationships between dietary sodium intake on the incidence and prevalence of interstitial lung disease and pulmonary sarcoidosis at the 50th percentile (middle, p50), 75th percentile (high, p75) and 95th percentile (extremely high, p95).The lowest value was reference: (**A**) the incidence at p50, p75 and p95 of dietary sodium intake; (**B**) the prevalence at p50, p75 and p95 of dietary sodium intake.

20% of ILD may be attributed to autoimmune diseases[21,22]. Furthermore, increases in Th17 cells and IL-17 itself secondary to high sodium levels were found to promote pulmonary inflammation and fibrosis processes by promoting cytokine production and fibroblast proliferation[23]. The molecular pathways by which IL-17 affects the development of pulmonary fibrosis also include increasing the epithelial-mesenchymal transition and alveolar apoptosis, the accumulation of myofibroblasts, and impairment of the fibrinolytic system[24].

In addition, the results of the present study suggest that remodeling of the pulmonary microvasculature potentially participates in the development of ILD and pulmonary fibrosis by injuring endothelial cells, increasing the endothelial- mesenchymal transition, and altering the perivascular mesenchyme[25,26]. An animal study suggested that high dietary sodium intake is likely to result in remodeling of the pulmonary microvasculature via the proliferation and hypertrophy of pulmonary arterial cells[27]. High dietary sodium intake could impair the barrier function of the vascular endothelium and promote sodium entry into the interstitium by increasing the activity of endothelial sodium channels[28]. The decreased function of the vascular endothelium might contribute to leukocyte adhesion to the endothelium mediated by reactive oxygen species and eNOS, which potentially increases the level of inflammation in the pulmonary interstitium[28]. Taken together, high dietary sodium intake may affect the development of ILD by inducing remodeling of the pulmonary microvasculature and damaging the function of the vascular endothelium.

	Min	Middle	High	Extremely high
Dietary sodium and the incidence				
Lag 0	Ref	1.2 7(1.23,1.32)	1.58 (1.47,1.69)	1.75 (1.61,1.91)
Lag 1	Ref	1.10 (1.08,1.11)	1.19 (1.16,1.33)	1.24 (1.20,1.28)
Lag 2	Ref	1.06 (1.04,1.08)	1.12 (1.08,1.16)	1.15 (1.10,1.20)
Lag 3	Ref	1.07 (1.03,1.10)	1.13 (1.07,1.19)	1.16 (1.08,1.24)
Lag 4	Ref	1.06 (1.02,1.10)	1.11 (1.04,1.19)	1.14 (1.05,1.24)
Lag 5	Ref	1.03 (0.99,1.07)	1.05 (0.98,1.13)	1.07 (0.98,1.16)
Lag 6	Ref	0.99 (0.96,1.03)	0.99 (0.93,1.06)	0.99 (0.91,1.08)
Lag 7	Ref	1.02 (0.99,1.05)	1.04 (0.98,1.10)	1.05 (0.98,1.13)
Dietary sodium and the prevalence				
Lag 0	Ref	1.64 (1.41,1.91)	2.55 (1.92,3.40)	3.19 (2.24,4.53)
Lag 1	Ref	1.15 (1.08,1.23)	1.31 (1.15,1.48)	1.39 (1.19,1.63)
Lag 2	Ref	1.03 (0.97,1.09)	1.05 (0.95,1.17)	1.07 (0.94,1.21)
Lag 3	Ref	1.02 (0.96,1.08)	1.03 (0.92,1.16)	1.04 (0.90,1.20)
Lag 4	Ref	1.02 (0.97,1.08)	1.04 (0.94,1.16)	1.05 (0.92,1.21)
Lag 5	Ref	1.00 (0.97,1.04)	1.00 (0.94,1.08)	1.01 (0.92,1.10)
Lag 6	Ref	0.97 (0.94,1.00)	0.94 (0.90,1.00)	0.93 (0.87,1.00)
Lag 7	Ref	0.98 (0.95,1.01)	0.96 (0.90,1.01)	0.95 (0.88,1.02)

Table 2. The lag-exposure-response relationships between dietary sodium intake on the incidence and prevalence of interstitial lung disease and pulmonary sarcoidosis. Dietary sodium intake was divided into four groups as follows: the lowest value(reference), 50th percentile (middle), 75th percentile (high) and 95th percentile (extremely high).

This study has several strengths. First, we provide important evidence for guiding public health strategies to prevent ILD and pulmonary sarcoidosis. This study indicated that the low dietary sodium intake levels recommended by dietary guidelines[29] may be beneficial in reducing the incidence and prevalence of ILD and pulmonary sarcoidosis in clinical practice. Second, our findings were based on 30-year time series data concerning dietary sodium intake and ILD and pulmonary sarcoidosis from the GBD Study 2019, which potentially reduced the selection bias caused by the small sample size and regional and racial limitations. Third, various statistical analyses, including LASSO, GAM and DLNM, were used to explore the correlation between dietary sodium intake and ILD, which made our results more convincing.

Some limitations of this study need to be acknowledged. Like other studies based on the GBD Study[30–32], our results were potentially influenced by statistical assumptions and data sources. The reported incidence and prevalence rates might not be 100% correct worldwide. Moreover, the diagnosis of ILD can only be accomplished through multidisciplinary collaboration. Therefore, the incidence and prevalence of ILD might be underestimated and underreported worldwide, especially in low SDI countries. The GBD aims to obtain new and better-quality data and produce more reliable estimates in the future[30]. Additionally, the absence of some important data (such as smoking, ambient particulate matter, personal lifestyle and comorbidity data, among others) potentially affected the results of our study despite the inclusion of 20 risk factors. Finally, the causal relationship between dietary sodium intake and the burden of ILD could not be confirmed even though we performed dose-dependent and lag-exposure-response analyses. More longitudinal cohort studies and randomized controlled trials involving personalized prevention and intervention methods are warranted to further estimate the effect of dietary sodium intake restriction in preventing and treating ILD and pulmonary sarcoidosis.

Conclusion

Our study introduced an effective strategy by which low dietary sodium intake can reduce the incidence and prevalence of ILD and pulmonary sarcoidosis in clinical practice. Additional research is needed to further explore and determine the reliability of the abovementioned relationship; moreover, the underlying mechanisms by which dietary sodium intake affects the occurrence and development of ILD and pulmonary sarcoidosis remain to be studied. Health professionals, in their practices, urgently need to develop effective programs to support the proposed strategy of low dietary sodium intake via updated dietary guidelines. Even though dietary sodium intake restriction has no significant effect on ILD or pulmonary sarcoidosis, it still has profound effects on various health outcomes and the well-being of the nation, supporting all individuals to live healthier lives[7]. Our findings provide new and significant implications for promoting public health via a dietary sodium intake reduction strategy. Moreover, such public health policies that target low dietary sodium intake levels are simple, inexpensive and can effectively decrease the global disease burden.

Data availability

Data sources and code used in the Global Burden of Disease Study 2019 are available on the internet. (http://ghdx.healthdata.org/gbd-results-tool). The lead author affirms that the manuscript is an honest, accurate, and

transparent account of the study being reported; that no important aspects of the study have been omitted; and that discrepancies from the study as planned have been explained.

Received: 13 June 2024; Accepted: 25 October 2024
Published online: 29 October 2024

References

1. Wijsenbeek, M., Suzuki, A. & Maher, T. M. Interstitial lung diseases. *Lancet (London England)* **400**(10354), 769–786 (2022).
2. Cottin, V. et al. Presentation, diagnosis and clinical course of the spectrum of progressive-fibrosing interstitial lung diseases. *Eur. Respir. Rev.* **27**(150), 180076 (2018).
3. Ma, X. et al. Global and regional burden of interstitial lung disease and pulmonary sarcoidosis from 1990 to 2019: results from the Global Burden of Disease study 2019. *Thorax* **77**(6), 596–605 (2022).
4. Yuan, X. Y. et al. Evaluation of health-related quality of life and the related factors in a group of Chinese patients with interstitial lung diseases. *PLoS ONE* **15**(7), e0236346 (2020).
5. Berthon, B. S. & Wood, L. G. Nutrition and respiratory health–feature review. *Nutrients* **7**(3), 1618–1643 (2015).
6. Kaluza, J., Larsson, S. C., Orsini, N., Linden, A. & Wolk, A. Fruit and vegetable consumption and risk of COPD: a prospective cohort study of men. *Thorax* **72**(6), 500–509 (2017).
7. Mayne, S. T., McKinnon, R. A. & Woodcock, J. Reducing sodium intake in the US: Healthier lives. *Healthier Future JAMA* **326**(17), 1675–1676 (2021).
8. Patik, J. C., Lennon, S. L., Farquhar, W. B. & Edwards, D. G. Mechanisms of dietary sodium-induced impairments in endothelial function and potential countermeasures. *Nutrients* **13**(1), 270 (2021).
9. Chen, W., Pilling, D. & Gomer, R. H. Dietary NaCl affects bleomycin-induced lung fibrosis in mice. *Exp. Lung Res.* **43**(9–10), 395–406 (2017).
10. Zhang, W. C. et al. High salt primes a specific activation state of macrophages, M(Na). *Cell. Res.* **25**(8), 893–910 (2015).
11. GBD Chronic Respiratory Disease Collaborators. Prevalence and attributable health burden of chronic respiratory diseases, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Respir. Med.* **8**(6), 585–596 (2020).
12. Tetteh, J. et al. Marijuana use and suicidal behaviours among school-going adolescents in Africa: assessments of prevalence and risk factors from the Global School-Based Student Health Survey. *Gen. Psychiatry* **34**(4), e100558 (2021).
13. Hu, Z. et al. Delayed hospital admission and high-dose corticosteroids potentially prolong SARS-CoV-2 RNA detection duration of patients with COVID-19. *Eur. J. Clin. Microbiol. Infect. Dis.* **40**(4), 841–848 (2021).
14. Gasparrini, A., Armstrong, B. & Kenward, M. G. Distributed lag non-linear models. *Stat. Med.* **29**(21), 2224–2234 (2010).
15. Gasparrini, A. Distributed lag linear and non-linear models in R: The package dlnm. *J. Stat. Softw.* **43**(8), 1–20 (2011).
16. Gasparrini, A. Modelling Lagged associations in environmental time series data: a simulation study. *Epidemiology* **27**(6), 835–842 (2016).
17. Nguyen, V. T. et al. The protective effect of green space on heat-related respiratory hospitalization among children under 5 years of age in Hanoi. *Vietnam Environ. Sci. Pollut. Res. Int.* **29**(49), 74197–74207 (2022).
18. Hügle, T. Immunology of fibrotic lung disease: managing infections whilst preventing autoimmunity? *J. Inflamm. Res.* **4**, 21–27 (2011).
19. Kleinewietfeld, M. et al. Sodium chloride drives autoimmune disease by the induction of pathogenic TH17 cells. *Nature* **496**(7446), 518–522 (2013).
20. Sharif, K., Amital, H. & Shoenfeld, Y. The role of dietary sodium in autoimmune diseases: The salty truth. *Autoimmun. Rev.* **17**(11), 1069–1073 (2018).
21. Bosello, S. L. et al. Interstitial lung disease associated with autoimmune rheumatic diseases: checklists for clinical practice. *Front. Med.* **8**, 732761 (2021).
22. Nagy, A. et al. Autoimmune progressive fibrosing interstitial lung disease: predictors of fast decline. *Front. Pharmacol.* **12**, 778649 (2021).
23. Lei, L. et al. Th17 cells and IL-17 promote the skin and lung inflammation and fibrosis process in a bleomycin-induced murine model of systemic sclerosis. *Clin. Exp. Rheumatol.* **100**(5), 14–22 (2016).
24. Fathimath Muneesa, M., Shaikh, S. B., Jeena, T. M. & Bhandary, Y. P. Inflammatory mediators in various molecular pathways involved in the development of pulmonary fibrosis. *Int. Immunopharmacol.* **96**, 107608 (2021).
25. Farkas, L. & Kolb, M. Pulmonary microcirculation in interstitial lung disease. *Proc. Am. Thorac. Soc.* **8**(6), 516–521 (2011).
26. Karampitsakos, T. et al. Pulmonary hypertension in patients with interstitial lung disease. *Pulm. Pharmacol. Ther.* **50**, 38–46 (2018).
27. Xiang, R. P. et al. Sodium chloride-induced acute and chronic pulmonary hypertension syndrome in broiler chickens. *Poult. Sci.* **83**(5), 732–736 (2004).
28. Wenstedt, E. F. E., Olde Engberink, R. H. G. & Vogt, L. Sodium handling by the blood vessel wall: critical for hypertension development. *Hypertension* **71**(6), 990–996 (2018).
29. USDA and DHHS. *Dietary Guidelines for Americans, 2020–2025*. https://www.dietaryguidelines.gov/sites/default/files/2020-12/Dietary_Guidelines_for_Americans_2020–2025.pdf (Accessed 30 Sptember) (2021).
30. GBD 2019 Cancer Risk Factors Collaborators. The global burden of cancer attributable to risk factors, 2010-19: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet (London England)* **400**(10352), 563–591 (2022).
31. GBD 2019 Diabetes in the Americas Collaborators. Burden of diabetes and hyperglycaemia in adults in the Americas, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Diabetes Endocrinol.* **10**(9), 655–667 (2022).
32. GBD 2019 LRI Collaborators. Age-sex differences in the global burden of lower respiratory infections and risk factors, 1990–2019: results from the Global Burden of Disease Study 2019. *Lancet Infect. Dis.* **22**(11), 1626–1647 (2022).

Acknowledgements

The authors would like to thank all participants who participated in the study.

Author contributions

Z.H. and X.S. wrote the main manuscript text. A.Y and Y.T. prepared Figs. 1, 2, 3 and 4. All authors reviewed the manuscript.

Funding

This work was supported by the Natural Science Foundation of China (No. 82300039) and Hubei Provincial Natural Science Foundation of China (2022CFB696).

Declarations

Ethics approval and consent to participate

Ethics approval of this study was deemed exempt for review by the Institutional Review Board at China, Three Gorges University.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-024-77769-w.

Correspondence and requests for materials should be addressed to Z.H. or X.S.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.