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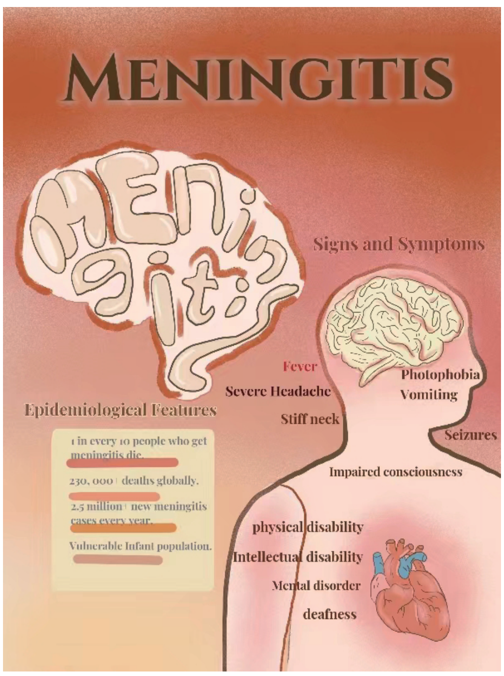




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Cover Image: designed by Yu Wu, the first author of the article on Page 745.

Preplanned Studies

# Long-Term Patterns of Meningitis Mortality: A Continual Downward Trend and a Vulnerable Infant Population — China, 1987–2021

Yu Wu[1,&]; Huiyun Fan[2,3,&]; Binbin Su[1]; Chao Guo[2,3,#]; Luzhao Feng[4,#]

**Summary**

**What is already known about this topic?**

Meningitis, a life-threatening disease, presents a significant public health challenge. Its rate of progress in burden reduction notably lags behind other diseases that can be prevented through vaccination.

**What is added by this report?**

This research explored the changes in the mortality rate of meningitis in China over a span of 35 years. The study further identified the effects of age, period, and cohort on the mortality trends.

**What are the implications for public health practice?**

In the context of minimal disparities between urban and rural settings, it is crucial to focus on and implement targeted prevention programs for meningitis within the infant population.

Meningitis, a critical infection that impacts the meninges — protective membranes surrounding the brain and spinal cord — presents a significant public health challenge due to its life-threatening nature (*1*). Insights from the Global Burden of Disease (GBD) study exposed an increase of 320,000 worldwide meningitis cases between 1990 and 2016 (*1*). Given its extensive population, China ranks among the top 10 nations globally for meningitis-associated mortalities. Despite prior research investigating worldwide trends in meningitis mortality, there remains a paucity of understanding regarding national trends and the discrepancies between urban and rural areas. The current study dissected changing patterns in China's meningitis mortality rate from 1987 to 2021 and spotlighted age-period-cohort effects influencing mortality changes. These revelations will equip the government with valuable insights into long-term trends and guide the development of targeted prevention strategies.

The mortality rates related to meningitis were extracted from the death registration system managed by the National Health Commission in China (*2*). This registry amalgamates several sources of data, including 1) death certificates and population demographics from the Department of Health, 2) changes in registered residences from the Department of Public Security, 3) cremation data from the Department of Civil Affairs, and 4) termination of social security information from the Department of Social Security. Age-standardized mortality rates (ASMR) were tabulated employing the direct method and the World Standard Population as a frame of reference (*3*). A joinpoint regression analysis was performed to detect fluctuations in meningitis mortality over time (*4*). Furthermore, an age-period-cohort model was used to ascertain the independent influence of age, period, and birth cohort on meningitis mortality rates in China (*5*). This research disclosed a steady decrease in meningitis mortality rates throughout urban and rural China over the past thirty years. Importantly, children, specifically those aged 0–4, present the highest risk of meningitis. These results effectively demonstrate the evolving trends of meningitis mortality and underscore the critical demographics for prevention strategies in China, offering valuable insights for future preventative measures against meningitis.

Figure 1 depicts the longitudinal trends in crude mortality rates and ASMR for meningitis among urban and rural populations in China, stratified by sex, from 1987–2021. Both crude mortality rates and ASMR saw a significant decrease from 1987 to 2002, and largely remained stable after 2002, despite some fluctuations observed between 2010 and 2013. Throughout the study period, higher ASMRs were typically seen in males and rural residents when compared to females and urban dwellers, respectively.

Table 1 details the results of the joinpoint regression analysis. The ASMR displayed a general decreasing trend in both urban and rural areas, although the substage trends were not consistent. The decline in urban ASMR was marginally steeper compared to the rural regions. In urban settings, ASMR experienced a

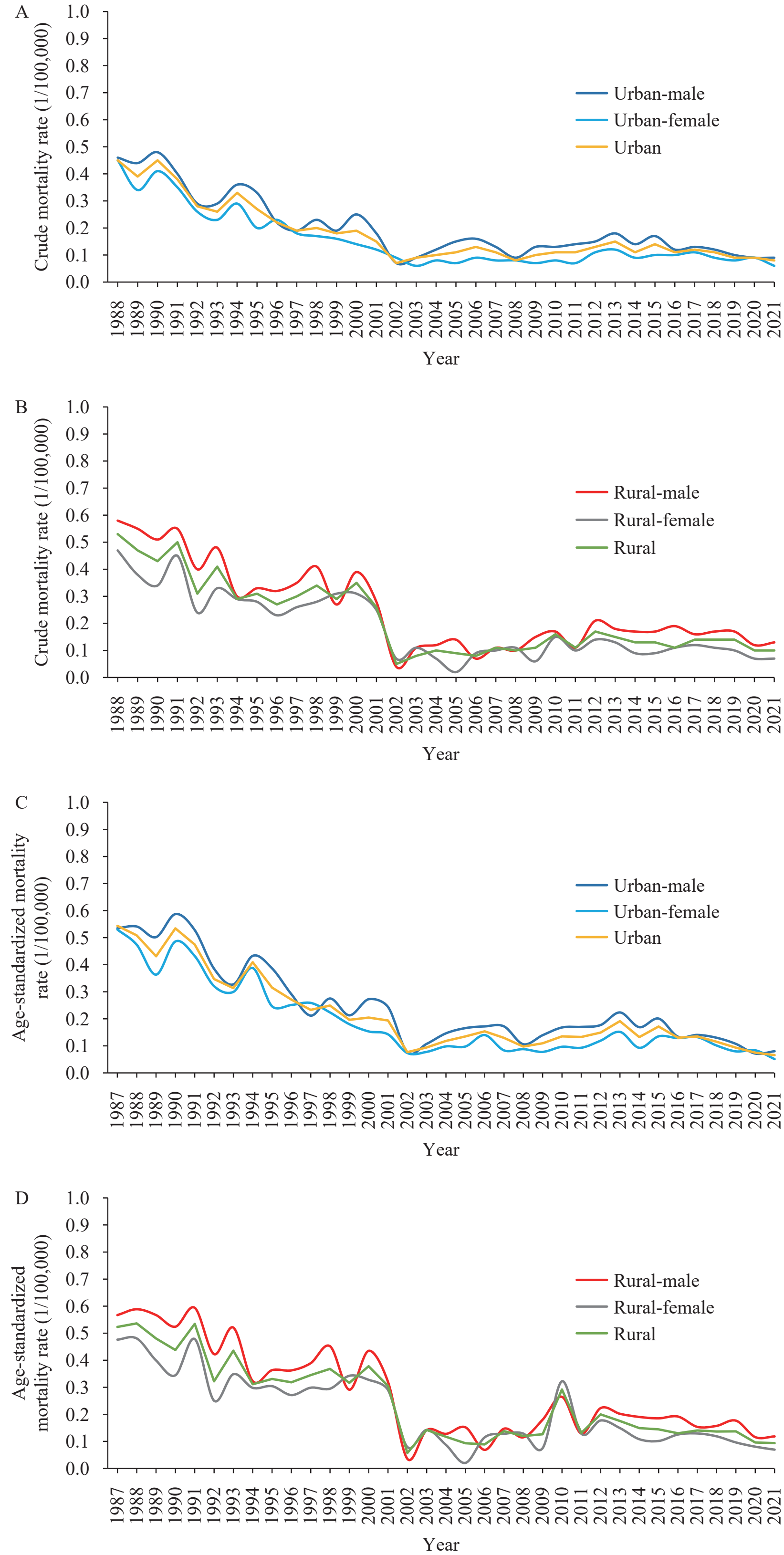


FIGURE 1. Trends in the crude and age-standardized mortality rates from meningitis in urban and rural areas of China, by sex, 1987–2021. (A) Crude mortality rates in urban areas. (B) Crude mortality rates in rural areas. (C) Age-standardized mortality rates in urban areas. (D) Age-standardized mortality rates in rural areas.

rapid decrease from 1987–2003, followed by a gradual rebound from 2003–2016, and a stark decline again from 2016–2021. Conversely, in rural areas, ASMR showed a slow reduction from 1987–1999, a rapid decline from 1999–2002, and a flat rebound from 2002–2021. Notably, a slight disparity was observed between sexes in meningitis mortality in urban and rural areas.

Figure 2 illustrates the net and local drifts of mortality rates due to meningitis. The net drift indicates the yearly percentage fluctuation in the predicted age-standardized mortality, as the local drift signifies the similar change over time. This pattern was consistently seen in both urban and rural areas of China. Throughout the study period, there was a substantial reduction in mortality resulting from meningitis (urban: −5.22%, 95% *CI*: −5.66% to −4.78%; rural: −4.51%, 95% *CI*: −5.04% to −3.98%). However, slight variances were observed in the annual changes between both genders. The decline in overall meningitis mortality was noticeably sharper in females compared to males in both urban (−5.49% *vs.* −4.83%) and rural areas (−5.25% *vs.* −3.88%). Also, the local drift curves for rural and urban locales displayed a predominantly positive U-shape. The decline was steepest for the 20–29 age group and routinely decreased with age in the 0–19 and 20–89 age groups. The curves demonstrated relative consistency between urban and rural areas, with the exception of the advanced age group.

Figures 3, 4, and 5 delineate estimates of age, period, and cohort effects on the mortality rates due to meningitis. The impact of age on mortality remained consistent across both genders and geographical locations, viz., urban and rural regions. Mortality rates due to meningitis were observed to peak during the 0–4 age range, after which they noticeably plummeted in the 5–9 age range. Post this decrease, the rates were largely stable, maintaining a minimal level across the 10–89 age brackets. Period effects demonstrated a similar consistently diminishing trend from 1987 to 2006 before entering a period of stability post-2007, irrespective of gender and location. Despite this, variations were noted in the period effects of urban and rural mortality rates due to meningitis, with the disparity between genders being less pronounced in urban areas in comparison to rural areas. Furthermore, cohort rate ratios exhibited a similar downward trend across genders and geographical locations. For cohorts born post-1952, the mortality rates due to meningitis have maintained a uniformly low level.

TABLE 1. Joinpoint analysis of age-standardized mortality rates due to meningitis in urban and rural areas.

| Residence | Mortality rate† (per 100,000) | | Entire range§ | | Segment 1 | | | Segment 2 | | | Segment 3 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1987 | 2021 | AAPC (%) | 95% *CI* | Period | APC (%) | 95% *CI* | Period | APC (%) | 95% *CI* | Period | APC (%) | 95% *CI* |
| Urban | | | | | | | | | | | | | |
| Total | 0.53 | 0.07 | −6.5* | (−8.6, −4.3) | 1987–2003 | −10.0* | (−11.8, −8.1) | 2003–2016 | 1.9 | (−1.4, 5.2) | 2016–2021 | −15.4* | (−25.2, −4.4) |
| Male | 0.53 | 0.08 | −6.3* | (−8.8, −3.7) | 1987–2003 | −9.4* | (−11.7, −7.0) | 2003–2015 | 2.4 | (−2.1, 7.2) | 2015–2021 | −14.3* | (−23.5, −4.0) |
| Female | 0.53 | 0.05 | −6.7* | (−9.3, −4.1) | 1987–2004 | −10.5* | (−12.4, −8.6) | 2004–2017 | 2.5 | (−1.2, 6.2) | 2017–2021 | −18.0* | (−32.5, −0.5) |
| Rural | | | | | | | | | | | | | |
| Total | 0.52 | 0.09 | −3.7* | (−9.6, 2.6) | 1987–1999 | −2.9 | (−6.9, 1.3) | 1999–2002 | −28.4 | (−65.0, 46.4) | 2002–2021 | 0.4 | (−1.7, 2.6) |
| Male | 0.57 | 0.12 | −3.3 | (−9.5, 3.3) | 1987–1999 | −3.2 | (−7.4, 1.2) | 1999–2002 | −32.1 | (−68.0, 44.0) | 2002–2021 | 2.2 | (−0.1, 4.5) |
| Female | 0.48 | 0.07 | −3.7* | (−13.9, 7.7) | 1987–2000 | −3.0 | (−9.3, 3.7) | 2000–2003 | −29.6 | (−80.3, 151.4) | 2003–2021 | 0.9 | (−3.2, 5.1) |

Abbreviation: APC=annual percent change; AAPC=average annual percent change; *CI*=confidence interval.

* Significant difference from zero ($P<0.05$).

† Standardization employed is based on the world standard population from the World Health Organization.

§ The time frame considered ranges from 1987 to 2021.

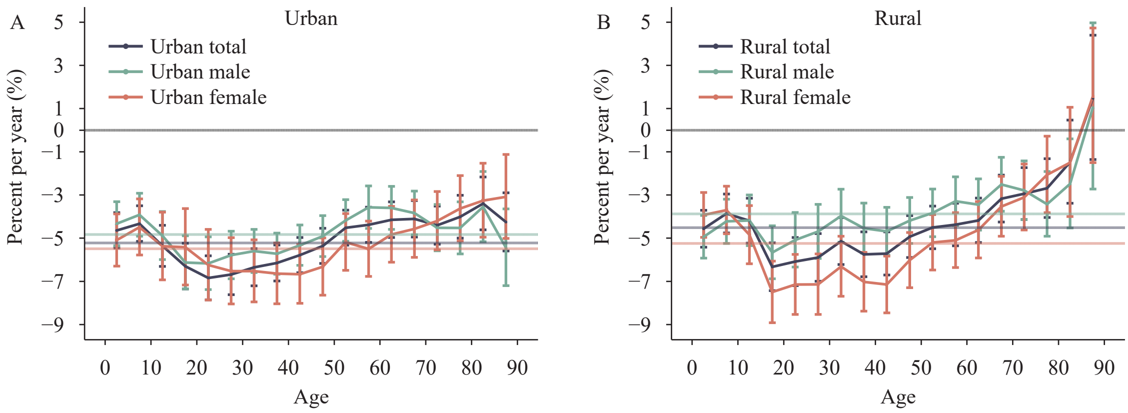


FIGURE 2. Net and local changes in mortality rates from meningitis and the associated gender disparities observed across different regions in China, 1987–2021. (A) Net and local drifts in urban areas. (B) Net and local drifts in rural areas.

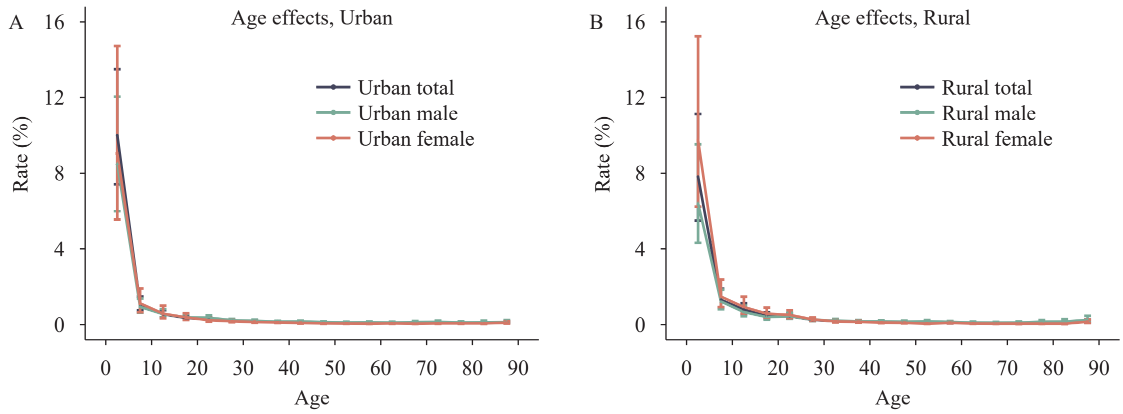


FIGURE 3. Parameter estimates of the effect of age on mortality rates due to meningitis in China from 1987 to 2021. (A) Age effects in urban areas. (B) Age effects in rural areas.

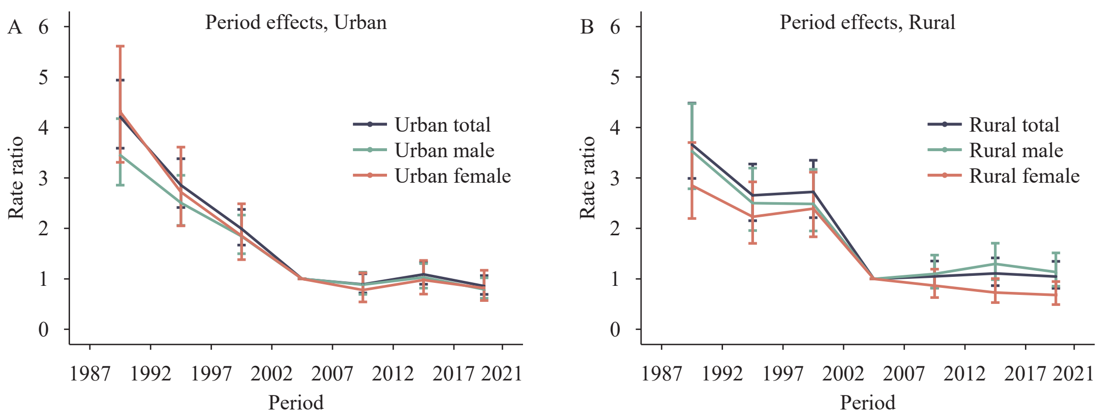


FIGURE 4. Estimates of the period effect on meningitis mortality rates in China from 1987 to 2021. (A) Period effects in urban areas. (B) Period effects in rural areas.

## DISCUSSION

The present investigation offers the first exhaustive review of longitudinal trends associated with meningitis mortality rates in China from 1987 to 2021, emphasizing the unique trends and age-period-cohort effects among rural and urban regions. The outcomes underscore a consistent decrease in the meningitis mortality rates within China, thus proving the efficacy of the preventive strategies related to

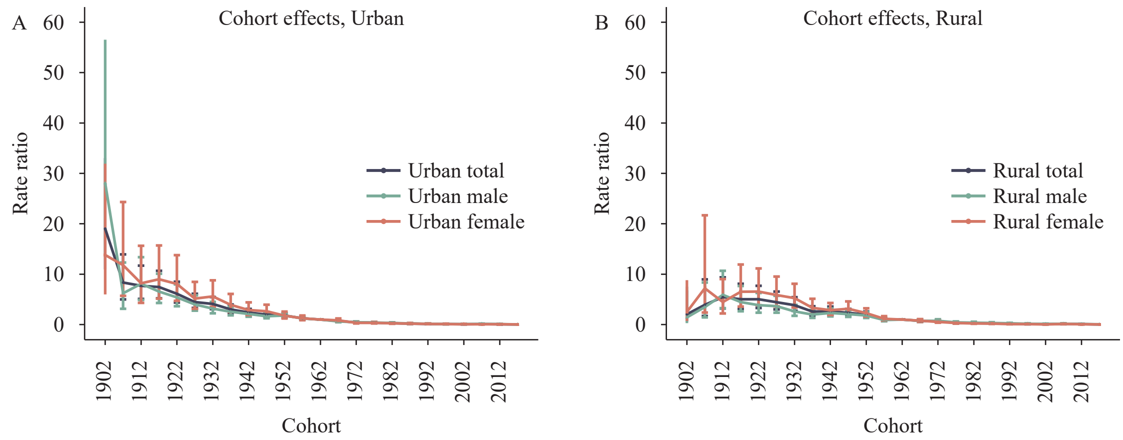


FIGURE 5. Estimated parameters of the cohort effect on the mortality rate from meningitis in China, 1987–2021. (A) Cohort effects in urban areas. (B) Cohort effects in rural areas.

meningitis implemented during the preceding three decades. Notable divergences were found among variables such as age, sex, and regional disparities in several patterns pertaining to meningitis mortality rates. Infants within the age bracket of 0–4 years are at the highest risk of acquiring meningitis. Negligible sex-based discrepancies were noted among age, period, and cohort effects associated with meningitis mortality, with the main rural-urban disparity being evident in the period effects. The identified high-risk groups necessitate immediate consideration and specialized preventative measures against meningitis.

Previous research has identified a variety of factors that contribute to meningitis, including infectious agents such as bacteria, mycobacteria, viruses, fungi, and parasites, as well as autoimmunity, cancer, and medicine reactions (*1*). Malnutrition, household overcrowding, HIV infection, lack of immunization, indoor air pollution, and sickle cell disease have been identified as risk factors that predispose individuals to meningitis and potential epidemics. In China, the decline in meningitis mortality rate surpasses the global average significantly (*1*). This decrease can be attributed to enhanced surveillance and diagnostic assessment, improved access to healthcare services, advancements in treatment and caregiving, and a reduction in individual treatment costs, particularly through the widespread administration of meningitis vaccinations for prevention (*1*,*6*–*7*). In 1984, China introduced a comprehensive prevention strategy primarily involving the widespread use of the group A meningococcal polysaccharide vaccine as a means to prevent epidemic cerebrospinal meningitis. This vaccination initiative was further expanded in 1985–1986, resulting in continued declines in incidence rates and the prevention of nationwide epidemics (*6*). In 2007, the national immunization program incorporated both the group A meningococcal polysaccharide vaccine and the group A and C meningococcal polysaccharide vaccine, with age-appropriate children receiving immunizations. Despite these advancements, China's absolute number of meningitis deaths remains comparable to nations like Nigeria and Ethiopia situated in the meningitis belt — positioning it amongst the highest globally (*1*). As such, there is an ongoing need for the persistent implementation of comprehensive meningitis prevention strategies.

Age is a critical demographic factor in the prevalence of meningitis, with existing research emphasizing a heightened incidence of the disease during the neonatal stage and the most elevated mortality rates in children below five years of age (*1*,*8*). This is attributed primarily to two factors: one, infants and children's immature immune system, which reduces their ability to battle infections, such as meningococcal and pneumococcal infections, which constitute significant causes of meningitis mortality (*1*). Second, the diagnosis of meningitis is particularly challenging in children and specifically, neonates (*9*). The symptoms of neonatal meningitis often mimic those encountered in neonates with sepsis or other infections, and their limited ability to verbally express their distress may lead to underreporting or a possible delay in the diagnosis. Vaccination has demonstrated effectiveness in preventing meningitis in infants (*1*,*10*). Thus, the creation and promotion of more specific vaccines are critical in the fight against this disease.

Previous research has illustrated high levels of meningitis in resource-limited environments due to a combination of factors inclining these regions to infection, epidemics, and poor health outcomes (*1*). The disparities between urban and rural areas were primarily observable in the overall reduction in meningitis mortality, the division of sub-stages, and variations in the effect of gender over time. The more rapid decline in urban regions can likely be credited to effective screening, diagnosis, and treatment of meningitis (*1*). The differing sub-stage trends we identified between rural and urban areas may be a result of China's urbanization process, which has seen a significant migration of rural inhabitants into cities, further intensifying healthcare disparities. Overall, the differences between urban and rural effects on meningitis mortality, regarding age, period, and cohort, were slight in China. This could be indicative of a narrowing gap over the past 30 years in terms of meningitis screening, diagnosis, and vaccine distribution between the two types of regions. However, considerable uncertainty surrounds the causal factors and risks associated with meningitis. Based on the unique urban-rural dynamic in China, it was crucial to implement active disease-specific meningitis surveillance, promote meningitis vaccines, and continually enhance diagnosis and treatment strategies to reduce the nation's meningitis mortality rate. Furthermore, gender disparities were apparent not only over time in urban and rural regions but also in the decreasing rates of meningitis mortality. Females exhibited a more rapid decline in mortality than males, potentially due to their higher propensity to seek medical attention and greater personal health standards, resulting in fewer infection opportunities and prompt care following infection. This gender gap seems to have grown more pronounced in rural regions in recent years, hence the observed gender disparities over time in urban and rural areas.

This study is subject to some limitations. First, the absence of detailed data on specific forms of meningitis, such as bacterial or viral meningitis, constrains the potential development of more targeted prevention strategies. Second, advances in the quality of meningitis mortality rate data might introduce a temporal bias into our analysis. Unfortunately, assessment reports on such improvements are absent, and noteworthy enhancements in data quality within extensive healthcare systems may require substantial time. As such, we presume that the mortality rate data utilized in this study holds consistent quality. Third, akin to other age-period-cohort analyses, a potential ecological fallacy could arise. Such a phenomenon implies that interpretations derived from population-level findings may not necessarily stand relevant at an individual level.

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Preplanned Studies

# A Cross-Sectional Survey of Iodized Salt Usage in Dining Establishments — 13 PLADs, China, 2021–2022

Ying Zhang[1,&]; Jichun Wang[2,&]; Xiuwei Li[1]; Wei Ma[1]; Jianqiang Wang[1]; Haiyan Wang[1]; Jing Xu[1,#]

**Summary**

**What is already known about this topic?**

The National Iodine Deficiency Disease Surveillance system is exclusively focused on monitoring cooking salt used within households. Currently, there is a lack of nationally representative data on the use of iodized salt in dining establishments.

**What is added by this report?**

This study evaluated 7,889 salt samples obtained from dining establishments located in 13 provincial-level administrative divisions across China. The findings indicated that coverage rate of iodized salt (CRIS) and the consumption rate of adequately iodized salt (CRAIS) were found to be 95.2% and 90.2%, respectively. Further, 880 samples were classified as iodized salt and 804 as adequately iodized salt. In coastal areas, the CRIS and CRAIS showed a significant decrease to 77.1% and 70.5%, respectively, when compared to the inland regions ($P$<0.01).

**What are the implications for public health practices?**

The data compiled could potentially fill the void in the national data concerning the use of iodized salt in dining establishments throughout China. It is of the utmost importance to increase the awareness of restaurant operators, particularly those located in coastal areas, about the benefits of iodine supplementation. Moreover, they should be encouraged to use adequately iodized salt.

Universal salt iodization has been established as a safe and effective method for the control of iodine deficiency disorders (IDDs) (*1–2*). Despite the annual National Iodine Deficiency Disease Surveillance, which began in 1995, only household cooking salt is analyzed. Yet, as the culture of eating out and ordering takeaway becomes more common, the contribution of household cooking salt to overall salt consumption has declined (*3*). Furthermore, current “Regulations on Salt Iodization to Mitigate the Risks of Iodine Deficiency” specify only that iodized salt is to be used in food products made and sold in deficient areas, leaving a gap in guidelines related to restaurant use. Hence, it is vital to scrutinize and assess the use of iodized salt (IS) and adequately IS (AIS) in dining establishments. At this stage, there remains a lack of nationwide, representative data on IS use in such settings. In response to this, the study in question employed a multiple-sampling technique to amass 7,889 salt samples from restaurants across 13 provincial-level administrative divisions (PLADs) in China, aiming to provide a nationally representative snapshot. Findings indicate that the coverage rate of IS (CRIS) and consumption rate of AIS (CRAIS) are 95.2% and 90.2%, respectively. However, when focused on coastal regions, the CRIS and CRAIS dropped to 77.1% and 70.5%, respectively, marking a significant difference from inland regions ($P$<0.01). This discrepancy suggests a need to enhance IDD awareness training for restaurant personnel in coastal areas to promote the procurement of IS.

This cross-sectional study was carried out from 2021 to 2022 across 13 PLADs of China, which were strategically divided into three regions: East, Central, and West. We executed a random selection of 4–5 PLADs from each region. Further, we subdivided each PLAD into five geographical divisions: east, west, south, north, and central. From each geographical division, two counties were randomly selected to serve as our sampling units. Each chosen county was then further dissected into five sampling areas, also based on geographical orientation. Subsequently, a town or sub-district with low water iodine levels was randomly picked from each particular sampling area. Within each chosen town or sub-district, we randomly selected two institutional canteens (either corporate or public) along with five medium-sized restaurants (MSRs) and five small restaurants (SRs). Ultimately, a total of 60 dining locations per county were selected, culminating in a comprehensive evaluation of 130 counties across China.

A 50-gram salt sample was meticulously extracted from the top, middle, and bottom sections of a salt package acquired from a selected dining establishment. The extraction process entailed using a moisture-free, airtight plastic bag. The salt iodine content (SIC) was then evaluated following the standards stipulated by the "General Test Method for Salt Industry Determination of Iodine" (GB/T 13025.7-2012). Salt that was iodized with $KIO_3$ was scrutinized utilizing direct titration, while salt iodized with KI or other compounds was analyzed via redox titration. Salt with an SIC less than 5 mg/kg was termed non-IS (NIS). AIS was characterized as SIC within an allowed fluctuation range, defined as a deviation of ±30% from the average iodine content level in edible salt (*4*). The term "CRIS" was used to denote the ratio of salt samples boasting an iodine content equal to or greater than 5 mg/kg to the total samples tested, while "CRAIS" denoted the ratio of AIS samples to the total number tested.

The data for this study were inputted into Microsoft Excel 2016 (Microsoft Corporation, Redmond, Washington, USA) and subsequently transferred to SAS 9.4 for Windows (SAS Institute, Cary, NC, USA) to facilitate analysis. A test to verify a normal distribution was carried out on continuous data; data that were skewed were represented via median (quartile range). To compare groups with skewed data, nonparametric tests (including the Wilcoxon and Kruskal-Wallis tests) were utilized. Count and percentage, used to express qualitative data, were tested for proportional differences using the Chi-squared test. All of the statistical tests used were two-tailed, with $P<0.05$ being indicative of a statistically significant difference.

This study evaluated 131 counties across 13 PLADs in China, encompassing a population of 75,374,000 individuals with a per capita income of 35,508 Chinese Yuan (CNY). Among these counties, 19 (14.5%) are located along the coast in the PLADs of Liaoning, Fujian, Shandong, and Jiangsu. The details of the sample size are presented in Table 1.

Among the 7,882 salt samples gathered, 95.2% were iodized, with notable variation across PLADs ($\chi^2$=1592.59, $P<0.01$). Of the 376 identified NIS, 58.5% were found in Shandong Province, 16.5% in Hebei Province, and 10.4% in Liaoning Province. A total of 7,107 AIS were discovered, with a consumption rate of 90.2% also showing significant provincial variation ($\chi^2$=983.73, $P<0.01$). The median iodine content of IS was 25.3 mg/kg, presenting significant provincial variation as well ($\chi^2$=1903.81, $P<0.01$; Table 2).

The coastal regions' CRIS and CRAIS were observed to be less than 80%, significantly lower compared to those of inland regions ($P<0.01$; Table 3). There was a slightly lower CRIS found in MSRs in comparison to canteens and SRs, although the difference was not statistically significant ($P$=0.30). In canteens, SRs, and MSRs, the CRAIS exceeded 90% with no significant

TABLE 1. Characteristics of the surveyed areas and dining establishments.

| PLADs | Counties (*N*) | | | Residents (million) | Per capita income (thousand CNY/year) | Number of dine-out places | Types of dine-out places | | | Service type | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Total | Coastal | Inland | | | | Canteen | MSR | SR | Table meal | Fast food |
| Anhui | 10 | 0 | 10 | 8.4 | 29.6 | 610 | 110 | 250 | 250 | 532 | 78 |
| Fujian | 10 | 3 | 7 | 5.1 | 36.6 | 600 | 100 | 250 | 250 | 394 | 206 |
| Gansu | 10 | 0 | 10 | 3.4 | 24.7 | 600 | 102 | 198 | 300 | 488 | 112 |
| Hebei | 10 | 0 | 10 | 5.0 | 30.8 | 600 | 100 | 250 | 250 | 420 | 180 |
| Henan | 10 | 0 | 10 | 9.0 | 26.4 | 601 | 100 | 249 | 252 | 461 | 140 |
| Inner Mongolia | 10 | 0 | 10 | 3.2 | 40.1 | 600 | 100 | 242 | 258 | 496 | 104 |
| Jiangsu | 10 | 4 | 6 | 9.9 | 56.8 | 600 | 100 | 250 | 250 | 507 | 93 |
| Liaoning | 10 | 2 | 8 | 4.5 | 37.8 | 601 | 100 | 250 | 251 | 500 | 101 |
| Shandong | 10 | 10 | 0 | 6.7 | 56.2 | 601 | 101 | 253 | 247 | 466 | 135 |
| Shanxi | 11 | 0 | 11 | 5.3 | 28.6 | 660 | 112 | 261 | 287 | 584 | 76 |
| Sichuan | 10 | 0 | 10 | 4.6 | 29.6 | 600 | 100 | 250 | 250 | 576 | 24 |
| Xinjiang | 10 | 0 | 10 | 3.7 | 27.9 | 603 | 104 | 237 | 262 | 390 | 213 |
| Yunnan | 10 | 0 | 10 | 6.5 | 37.1 | 606 | 103 | 223 | 280 | 495 | 111 |
| Total | 131 | 19 | 112 | 75.4 | 35.5 | 7,882 | 1,332 | 3,163 | 3,387 | 6,309 | 1,573 |

Abbreviation: PLADs=provincial-level administrative divisions; MSR=medium-sized restaurant; SR=small restaurant; CNY=Chinese Yuan.

TABLE 2. Coverage rates for IS and AIS and iodine content at dining establishments by PLAD.

| PLADs | IS | | | AIS | |
|---|---|---|---|---|---|
| | *N* | CR (%) | Median (P25, P75) (mg/kg) | *N* | CR (%) |
| Anhui | 604 | 99.0 | 21.7 (20.1, 23.3) | 572 | 93.8 |
| Fujian | 589 | 98.2 | 24.2 (23.0, 25.4) | 575 | 95.8 |
| Gansu | 600 | 100.0 | 26.6 (24.1, 29.6) | 562 | 93.7 |
| Hebei | 538 | 89.7 | 24.3 (21.9, 26.4) | 511 | 85.2 |
| Henan | 592 | 98.5 | 25.0 (22.8, 27.7) | 555 | 92.4 |
| Jiangsu | 595 | 99.2 | 24.5 (21.8, 26.9) | 566 | 94.3 |
| Liaoning | 561 | 93.5 | 24.5 (21.9, 26.9) | 523 | 87.2 |
| Inner Mongolia | 587 | 97.7 | 25.2 (23.3, 27.2) | 561 | 93.3 |
| Shandong | 381 | 63.4 | 23.4 (20.6, 26.0) | 334 | 55.6 |
| Shanxi | 656 | 99.4 | 27.7 (25.4, 29.8) | 599 | 90.8 |
| Sichuan | 597 | 99.5 | 26.9 (24.9, 28.8) | 583 | 97.2 |
| Xinjiang | 602 | 99.8 | 28.1 (25.2, 31.1) | 575 | 95.4 |
| Yunnan | 604 | 99.7 | 25.8 (24.1, 27.6) | 591 | 97.5 |
| Total | 7,506 | 95.2 | 25.3 (22.8, 27.7) | 7,107 | 90.2 |

Abbreviation: PLADs=provincial-level administrative divisions; IS=iodized salt; AIS=adequately iodized salt; CR=coverage rate.

TABLE 3. Coverage rates of IS and AIS based on location, types of dining establishments, and types of services.

| Variable | IS | | | | AIS | | | | Total salt sample | |
|---|---|---|---|---|---|---|---|---|---|---|
| | *N* | CR (%) | $\chi^2$ | *P* | *N* | CR (%) | $\chi^2$ | *P* | *N* | % |
| Coastal or inland areas | | | 962.6 | <0.001 | | | 584.2 | <0.001 | | |
| Coastal | 880 | 77.1 | | | 804 | 70.5 | | | 1,141 | 14.5 |
| Inland | 6,626 | 98.3 | | | 6,303 | 93.5 | | | 6,741 | 85.5 |
| Types of dine-out places | | | 2.4 | 0.30 | | | 0.2 | 0.93 | | |
| Canteen | 1,268 | 95.2 | | | 1,202 | 90.2 | | | 1,332 | 16.9 |
| MSR | 2,999 | 94.8 | | | 2,847 | 90.0 | | | 3,163 | 40.1 |
| SR | 3,239 | 95.6 | | | 3,058 | 90.3 | | | 3,387 | 43.0 |
| Service types | | | 3.0 | 0.08 | | | 0.2 | 0.66 | | |
| Table meal | 5,995 | 95.0 | | | 5,684 | 90.1 | | | 6,309 | 80.0 |
| Fast food | 1,511 | 96.1 | | | 1,423 | 90.5 | | | 1,573 | 20.0 |

Abbreviation: MSR=medium-sized restaurant; SR=small restaurant; IS=iodized salt; AIS=adequately iodized salt; CR=coverage rate.

differences observed ($P$=0.93). The CRIS and CRAIS in fast food-serving establishments were marginally higher than those providing table meal service, even though the difference was not statistically meaningful ($P$>0.05).

## DISCUSSION

The findings of this study indicated that the CRIS and CRAIS in dining-out venues were 95.2% and 90.2%, respectively. It was observed that these measurements were notably lower in coastal regions as compared to inland areas. However, no significant variance in CRIS and CRAIS was discovered among canteens, MSRs, and SRs. Furthermore, there was no statistically significant distinction in CRIS and CRAIS between establishments offering table meals and those providing fast food.

According to China's "Criteria for Elimination of Iodine Deficiency Disorders (GB16006-2008)" introduced in 2008, a household CRIS of ≥95% and a CRAIS >90% are requisite for IDD elimination. Hence, the values for household CRIS, CRAIS, and SIC have been incorporated into the national IDD control project as critical indicators for monitoring and evaluating iodine nutrition. However, due to rapid economic progress and increased speed of contemporary life, eating out, buying takeout, and consuming packaged foods are becoming the norm in China. Interestingly, in certain economically advanced areas of the country, household cooking salt no longer significantly influences the population's iodine status (*5–7*). Two surveys conducted in Shanghai illuminated that household salt iodine intake failed to impact the iodine status of pregnant women (*5*) and children (*6*). Further, a monitoring study in Tianjin from 2016 to 2020 unveiled no correlation between the CRIS, CRAIS, and SIC of household cooking salt and iodine status indices within the population (specifically urinary iodine concentration and thyroid volume) once confounding factors were adjusted for (*7*). The said study's authors proposed that the IDD control project's household salt-related indicators should be amended to accommodate other indicators, such as SIC in school canteens (*7*). This current study involves an assessment of 7,889 salt samples taken from restaurants nationwide and effectively addresses the deficiency of IS monitoring data on such establishments. Furthermore, this study lays the groundwork for subsequent adjustments of IS monitoring indicators by providing essential data.

Multiple studies (*8–9*) investigating household salt usage have discovered that the CRIS and the CRAIS in coastal regions were noticeably lower than those in inland areas. A research project in Qingdao City found that household CRIS and CRAIS stood at 88.2% and 86.2%, respectively, failing to meet the elimination criteria for IDD (*8*). A similar study in Guangxi Zhuang Autonomous Region indicated significantly lower CRIS and CRAIS (75.59% and 63.25%) in coastal households than in their inland counterparts (*9*).

Given this data, it was important to examine if a substantial difference existed in IS usage between inland and coastal restaurant settings. This study found that the CRIS and CRAIS in coastal restaurants were merely 77.1% and 70.5%, respectively, a marked difference to the 98.3% and 93.5% in inland establishments.

Interviews suggested that missing or inaccurate information may be contributing to this discrepancy, with one such misconception being the unnecessary consumption of iodized salt due to the regular intake of seafood in coastal areas. It should be noted that while coastal residents generally consume more seafood, the iodine content in seafood is only marginally higher than that in land-based animal foods (*10*). Thus, the iodine intake tends to be lower in coastal regions.

The highest quantities of iodine in seafood are generally found in specific types of seaweed, but consumption of seaweed is quite minimal. Furthermore, the presence of private salt farms in some coastal regions encourages the use of non-iodized coarse sea salt, resulting in a reduced CRIS.

A study by Mao et al. (*11*) found that the urinary iodine concentration in pregnant women living in Zhejiang Province's coastal areas was 107.54 μg/L, significantly lower than that of pregnant women in inland areas (152.54 μg/L). It was speculated that this iodine deficiency was linked to the low local CRIS. Similar research by Chen et al. pointed out that the median urinary iodine of pregnant women in rural coastal areas of Fujian (134.9 μg/L) fell short of the World Health Organization's recommendation (*12*).

To decrease the risk of iodine deficiency among residents of coastal areas, notably pregnant women and lactating mothers, it is crucial to raise not only household CRIS rates but also restaurant operators' awareness of iodine supplementation. Encouraging restaurant operators to purposely purchase and utilize AIS can be a significant step in this direction.

A prior study indicated a higher incidence of CRAIS in large or MSRs compared to SRs (*13*). This was initially attributed to the deficient regulatory mechanisms within SRs, insufficient food safety awareness and improper management. However, the current study reveals no significant variance in CRIS and CRAIS distribution across diverse dining establishments. This can be reasoned through several factors. First, the recent years have seen an increase in coverage of food safety awareness and educational programs, thus augmenting the health consciousness of individuals responsible for SRs or those involved in procurement. Second, the introduction of efficient regulatory mechanisms has significantly mitigated the circulation of substandard IS in the marketplace.

This study possesses certain limitations. Due to its cross-sectional design, evaluating the temporal relationship between various factors was unattainable, thereby complicating the inference of causation. Additionally, a number of elements influencing the concentration of IS, inclusive of storage methods, purchase dates, and individual health consciousness, were not incorporated in the survey.

To our understanding, this constitutes the first substantial study examining the utilization of IS in dining establishments, thus yielding national-level representative data. This research scrutinized the usage of IS in 7,882 dining venues across 13 PLADs in China, thereby filling an existing void regarding IS data in such establishments within the country. The employment of IS in China's dining places was deemed satisfactory. Moreover, CRIS and CRAIS in Canteens, MSRs, and SRs matched the criteria set for IDD eradication. Notwithstanding, the CRIS and CRAIS in coastal regions were significantly inferior to those in inland areas. Consequently, augmenting IDD knowledge among restaurant personnel in coastal areas is vital, enhancing their consciousness about purchasing IS. Similarly, it is crucial to bolster local supervision and surveillance mechanisms to suppress the distribution of non-compliant IS in the market.

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Vital Surveillances

# Patterns in the Incidence of Scarlet Fever Among Children Aged 0–9 Years — China, 2010–2019

Jinyu Cui[1]; Yewu Zhang[1]; Hui Ge[1]; Yu Cao[1]; Xuemei Su[1,#]

## ABSTRACT

**Introduction**: This study investigates the patterns of scarlet fever among Chinese children aged 0–9 years from 2010 to 2019. The objective is to provide insights that may inform potential adjustments to China's current prevention and control tactics for this illness.

**Methods**: The present study utilized data on the occurrence of scarlet fever in children from 2010 to 2019, sourced from the National Notifiable Disease Reporting System database, managed by the Chinese Center for Disease Control and Prevention. This research implemented SAS9.4 software to construct trajectory models representing the temporal incidence of scarlet fever, accounting for key variables such as sex, geographic region, urban versus rural dwellings, and various age brackets.

**Results**: From 2010 to 2019, a total of 554,695 scarlet fever cases were reported among children aged 0–9 years in the 31 mainland Chinese provincial-level administrative divisions, signifying a rate of 35.36 per 100,000 individuals. An inconsistent yet generally rising trend was observed, evidenced by a 3.17-fold increase in reported cases and a 3.02-fold escalation in incidence rate over this period. Examination of these trends revealed three distinctive developmental patterns for both males and females, with the lowest prevalence in the first trajectory and the highest in the third. The incidence was consistently higher among males than females in all trajectories. The urban and northern regions displayed equal or greater trajectory rates than their rural and southern counterparts, respectively. In terms of age groups, the lowest incidence was observed in the 0–1-year age group, while the highest was recorded in the 4–5 and 6–7-year age groups.

**Conclusions**: Between 2010 and 2019, there was a marked increase in the incidence of scarlet fever among children in China. The disease predominantly impacts urban-dwelling children, ranging from 4 to 7 years old, in the northern regions of the country. The incidence is reported to be higher among boys compared to girls.

Scarlet fever is an acute respiratory disease caused by *Streptococcus* pyogenes (Group A *Streptococcus*, GAS) infection (*1*), and is classified as a Class B infectious disease in China. The principal sources of infection are individuals afflicted with scarlet fever and GAS carriers. The disease is primarily characterized by fever, sore throat, diffuse rash, and a "strawberry tongue". Transmission primarily occurs through respiratory droplets (*2*), but can also result from direct contact with an infected person's skin or bodily fluids (*3*). Though it is possible for people of any age to contract GAS, it predominantly affects children under the age of 10 (*4*). Once considered a fatal disease for children in the 19th century, both morbidity and mortality of scarlet fever drastically decreased worldwide with the widespread use of antimicrobial drugs. In the early 21st century, China's average annual incidence rate of scarlet fever was relatively low, at 1.46 per 100,000 individuals. Nonetheless, this rate has been on the rise since 2011, surpassing 4.00 per 100,000 individuals annually (*5*–*6*). Increased rates of scarlet fever have also been reported concurrently in England, the Republic of Korea, and other countries (*7*–*8*). The current literature on scarlet fever in China mostly focuses on specific provinces rather than on the country as a whole. This study utilized data from reported cases of scarlet fever amongst children aged 0–9 years in China from 2010 to 2019, applying trajectory model analysis to probe the disease's incidence patterns and attributes by age, gender, urban-rural location, and region over this period. The objective was to discern the long-term trend of scarlet fever incidence in China and offer insights to inform modifications to the country's prevention and control strategies for the disease.

## METHODS

### Source of Data

This study focuses on scarlet fever, a condition primarily impacting children under ten years of age. Data were collected on reported instances of this disease within this demographic, from January 1, 2010 to December 31, 2019, spanning all 31 provincial-level administrative divisions (PLADs) in China. Case information was sourced from the National Notifiable Disease Reporting System (NNDRS), a division of the Chinese Center for Disease Control and Prevention. Each case was classified into one of numerous subgroups, established through various combinations of categories such as gender (i.e., male or female), region (divided into North, Northeast, East, Central, South, Southwest, or Northwest China) (Table 1), type of area (i.e., urban or rural), and age groupings (i.e., 0–1, 2–3, 4–5, 6–7, 8–9 years). This categorization resulted in 70 distinct groups for each, male and female.

## Statistical Analysis

The latent class growth model (LCGM), also known as the trajectory model, is a semi-parametric statistical modeling technique. This model seeks to classify subgroups within an analysis based on distinctive developmental trajectory trends. It determines the quantity and configuration of the trajectories, describing and fitting each developmental trajectory set. The trajectory model is tailored according to different data distributions. This study examined data pertaining to the incidence of scarlet fever, which presents as continuous data within a designated range. Consequently, a censored normal distribution model was employed to fit the trajectory of annual changes in the incidence of scarlet fever. In this censored normal distribution model, the latent variable $y_{it}^*$ is utilized to represent the predicted value of the dependent variable Y, as illustrated below:

$$y_{it}^* = \beta_0^j + \beta_1^j X_{it} + \beta_2^j X_{it}^2 + \beta_3^j X_{it}^3 + \varepsilon_{it}$$

Here, $X_{it}$, $X_{it}^2$, and $X_{it}^3$ represent the independent variables of the primary, secondary, and tertiary terms. The $\varepsilon_{it}$ represents the residuals assuming a normal distribution. The $\beta_0^j$ represents the intercept. The $\beta_1^j$, $\beta_2^j$, and $\beta_3^j$ represent the slopes. Three metrics were used to evaluate the effectiveness of the trajectory model 1) Bayesian Information Criterion (BIC), in which lower absolute values indicate a better fit. 2) Log Bayes Factor: approximately equal to two times the difference in the BIC values for the two models being compared. Values greater than 6 indicate that a more complex model is acceptable. 3) Average Posterior Probability (AvePP), in which group averages of >0.7, the fitting effect is better (*9*).

In this study, the Proc traj procedure was employed using the SAS software (version 9.4, SAS Institute Inc., Cary, USA). The independent variable identified was the year, and the dependent variable was the incidence rate for each subgroup. We applied a censored normal distribution model to accurately fit the incidence rate trajectory for each respective subgroup.

# RESULTS

**Patterns in scarlet fever incidence among children aged 0–9 years in China from 2010 to 2019.** From 2010 to 2019, a total of 554,695 cases of scarlet fever were reported in children aged 0–9 years across all 31 PLADs in China. This figure results in an average annual incidence rate of 35.36 per 100,000 individuals. Despite variations, all PLADs reported instances of the disease. The year 2010 recorded the lowest incidence rate with 18,751 cases, translating to a rate of 12.09 per 100,000. However, there was a significant increase in 2011 to 59,793 cases, escalating the incidence rate to 41.57 per 100,000. Subsequently, the incidence rates of scarlet fever presented an irregular yet increasing trend, recurring approximately

TABLE 1. PLADs included in each region of China.

| Region | North China | Northeast China | East China | Central China | South China | Southwest China | Northwest China |
|---|---|---|---|---|---|---|---|
| PLADs | Beijing | Liaoning | Shanghai | Henan | Guangdong | Chongqing | Shaanxi |
| | Tianjin | Jilin | Jiangsu | Hubei | Guangxi | Sichuan | Gansu |
| | Hebei | Heilongjiang | Zhejiang | Hunan | Hainan | Guizhou | Qinghai |
| | Shanxi | – | Anhui | – | – | Yunnan | Ningxia |
| | Inner Mongolia | – | Fujian | – | – | Tibet | Xinjiang |
| | – | – | Jiangxi | – | – | – | – |
| | – | – | Shandong | – | – | – | – |

Note: −, not applicable.
Abbreviation: PLADs=provincial-level administrative divisions.

every 3–4 years, with a peak in 2019 reporting 78,242 cases and an incidence rate of 48.56 per 100,000. Over this decade, the number of reported scarlet fever cases among children in China multiplied by 3.17 times, with the incidence rate intensifying by 3.02 times (Figure 1).

**Identification of heterogeneity in the incidence trends of scarlet fever among boys and girls by region, urban and rural areas, and age groups.** Line graphs were utilized to separately chart the trajectories of scarlet fever incidence rates over time for specific subpopulations (7/70) of boys and girls in China. Analysis revealed obvious heterogeneity in the incidence rate trends across the years for different regions, contrasting urban and rural areas, and between age groups for boys and girls. This justified employing the trajectory model to discern distinct patterns of scarlet fever incidence over time. Notably, incidence rates for girls were considerably lower than for boys; consequently, the trajectories for male and female children were modeled distinctly to more effectively investigate the epidemiological trends of scarlet fever in Chinese children aged 0–9 years (Figure 2).

**Modeling scarlet fever incidence trajectories across regions, urban/rural locations, and age groups** The model achieved optimal performance for both sexes when implemented with three developmental trajectories. These trajectories respectively conformed to the 1st, 5th, and 5th order development trends. The first trajectory evidenced the least incidence rate, showing a slight positive linear progression. The second and third trajectories demonstrated an "up-down-up-down-up" curve, indicative of an overall oscillating upward trend. Nevertheless, the third trajectory was associated with the highest incidence rate and the most pronounced overall increase (Table 2).

The boys' trajectory model interpretation divulges that trajectory group 3 is solely composed of urban residents aged 4–7 years from Northeastern, Northern, and Northwestern China, alongside rural populations aged 4–5 years from Northeastern China. Compared to other groups, this assemblage demonstrated a notable surge in incidence rates, frequent variations, and a significant aggregate escalation. Conversely, in Eastern, Southern, Central, and Southwestern China, the trajectory of the incidence rate within each subgroup demonstrated relative uniformity, primarily aligning within trajectory group 1. This category exhibited a less pronounced incidence rate, minimal fluctuations, and a more stable overall progression.

Our examination of the various groups revealed that the incidence rate trajectories of all urban subgroups were either higher or equal to their rural counterparts. Similarly, the incidence rate trajectories of subgroups in northern areas matched or exceeded those in central and southern regions. As for age, the incidence rate trajectory for the group aged 0–1 year was the lowest amongst all groups in each region. However, as age increased, the incidence rate trajectory also increased, revealing the highest rates in the 4–5 and 6–7-year age groups (Figure 3).

The evaluation of fit results from the trajectory model for girls indicated that the variations in developmental trends across each trajectory group and its constituent subgroups closely mirrored those observed in boys (Figure 4). However, both the incidence rates for each trajectory group and the increments in these rates were relatively lower than those found in boys, suggesting a higher incidence rate among the male cohort.

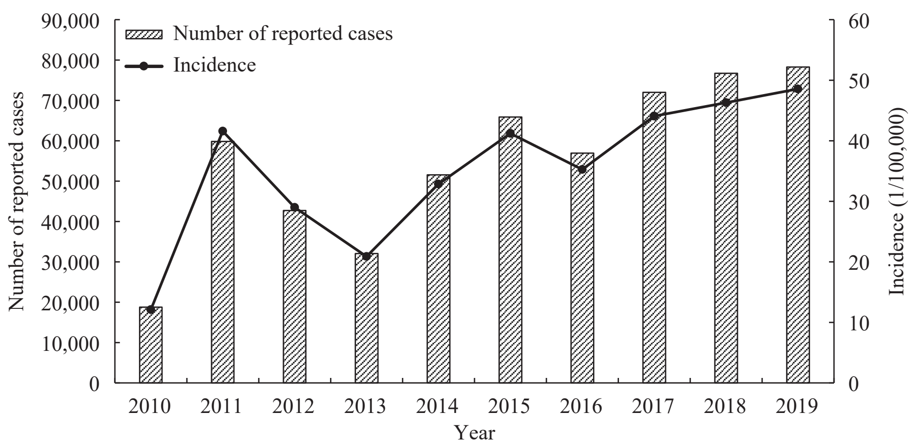
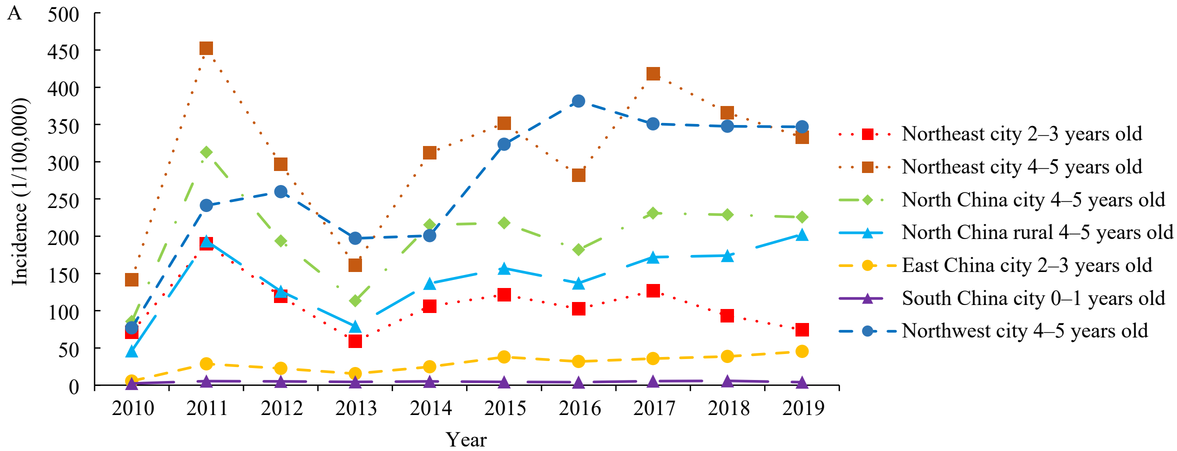



FIGURE 1. Reported cases and incidence rate of scarlet fever in children aged 0–9 years in China, 2010–2019.

TABLE 2. Estimated parameters for fitting three trajectory groups for boys and girls.

| Trajectory | Boys | | | | | | | | Girls | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Intercept | Parameter estimation | | | | | *P*-value | AvePP | Intercept | Parameter estimation | | | | | *P*-value | AvePP |
| | | 1 | 2 | 3 | 4 | 5 | | | | 1 | 2 | 3 | 4 | 5 | | |
| 1 | 18.02 | 1.78 | − | − | − | − | <0.01 | ≥0.85 | 12.00 | 1.62 | − | − | − | − | <0.01 | ≥0.84 |
| 2 | 37.68 | 484.13 | −227.75 | 46.65 | −4.3 | 0.15 | <0.01 | ≥0.82 | 26.25 | 326.87 | −153.35 | 31.48 | −2.92 | 0.10 | <0.01 | ≥0.93 |
| 3 | 96.52 | 1243.22 | −581.39 | 118.53 | −10.89 | 0.37 | <0.01 | ≥0.99 | 65.11 | 769.04 | −354.63 | 71.68 | −6.54 | 0.22 | <0.01 | ≥0.99 |

Note: −, not applicable.
Abbreviation: AvePP=average posterior probability.



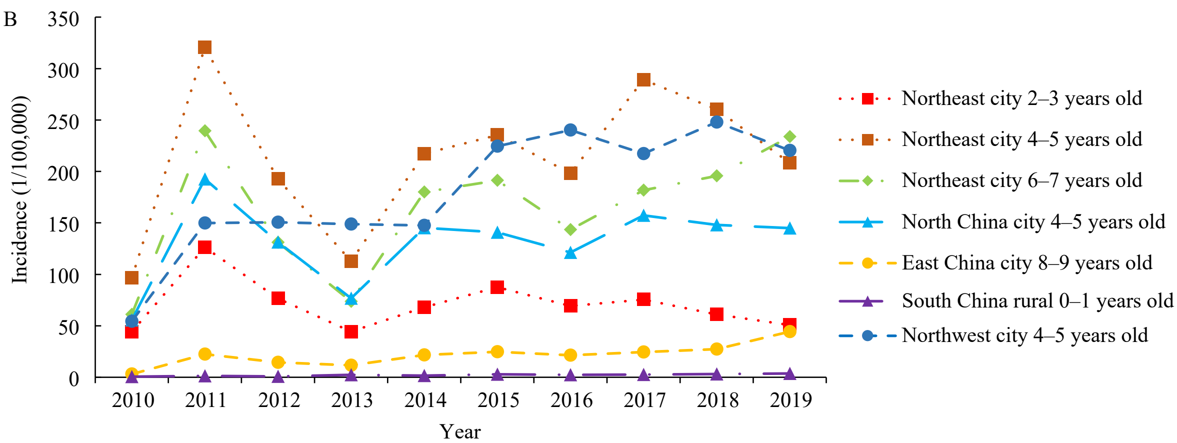




FIGURE 2. Trends in scarlet fever incidence among boys and girls aged 0–9 years in China from 2010 to 2019. (A) Incidence rate patterns for boys. (B) Incidence rate patterns for girls.

## CONCLUSIONS

The incidence rate of scarlet fever among children from 0–9 years old in China displayed a volatile upward trend from 2010 to 2019, with a peak every 3–4 years. This pattern mirrored the incidence level in China from 1980–1994 and was significantly higher than the rate from 1995–2009 (*10*). Multiple factors may contribute to the escalating incidence of scarlet fever in China. First, the prevalent GAS genotypes in recent years in China predominantly were emm1 and emm12, diverging from the genotypes prevalent in the 1990s (*11*). Simultaneously, pathogenic surveillance of GAS in various provinces across China indicates that the proportions of each scarlet fever subtype are in constant flux (*12–13*), hindering the development of a formidable herd immunity. Secondly, at the dawn of the 21st century, scarlet fever sustained a low incidence rate for an extended time in China, leading to a relatively weak herd immunity and a considerable

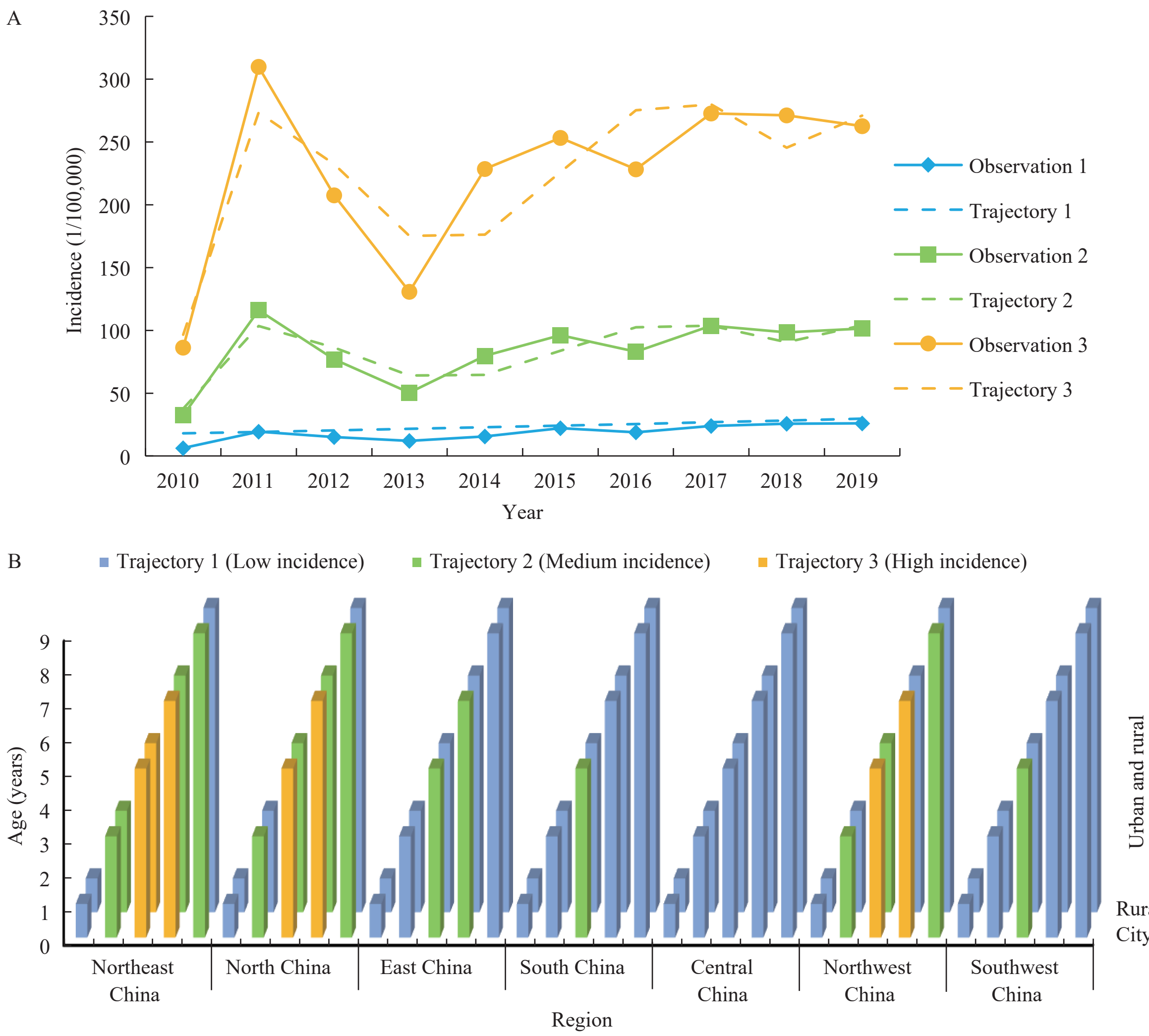



FIGURE 3. Depiction of fitted trajectory results for the incidence of scarlet fever in male children aged 0–9 years in China, 2010–2019. (A) Trend of trajectories for each group. (B) Subgroups represented within each group's trajectories.

build-up of susceptible individuals (*14*). This condition facilitates the dissemination of scarlet fever among the populace, subsequently enhancing the risk of infection.

The trajectory model analysis revealed disparities in the incidence of scarlet fever in China, based on gender and age of the population. The incidence was found to be higher in boys across all three developmental trajectories, supporting previous research (*15*). This could potentially be attributed to boys being more active, displaying less hygiene practice, and consequently being more exposed to pathogens, thus resulting in a higher incidence rate. The mean annual incidence of scarlet fever among children aged 0–9 years in China was demonstrably higher, specifically 35.36 per 100,000, significantly surpassing the rate observed in the general population (*5*). Additionally, the most substantial increase in incidence was observed among children aged 4–5 and 6–7 years — an element that significantly influenced the shift in the overall incidence of scarlet fever in China. This trend may be attributed to children and adolescents' underdeveloped immune systems, lower immunity levels, and increased time spent in enclosed, pathogen-prone spaces like schools. Furthermore, a lack of personal hygiene awareness and high concentration of children in school settings possibly contribute to the heightened risk of contracting scarlet fever.

The findings from our analysis revealed that urban locales within China demonstrated a more substantial incidence rate of scarlet fever compared to their rural counterparts, reinforcing the conclusions from previous studies conducted in this nation (*16*). A significant correlation between population density and the prevalence of scarlet fever was also unveiled in this study (*17*). The accelerating economic progression

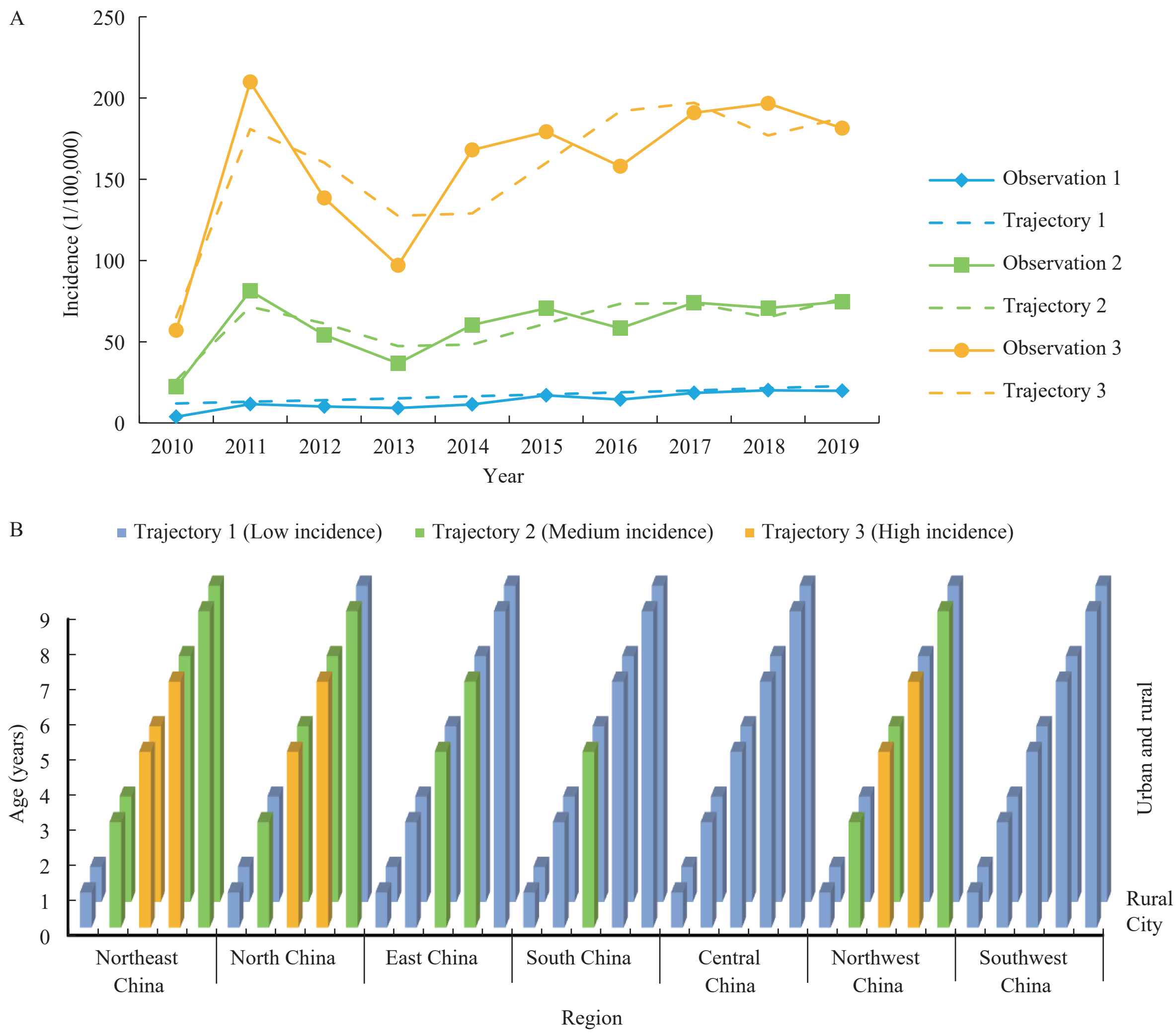



FIGURE 4. Illustrated fitted trajectory results for the incidence of scarlet fever among female children aged 0–9 years in China, 2010–2019. (A) Demonstration of the trend in trajectories for each group. (B) Identification of the subgroups incorporated in each group's trajectories.

occurring in urban spaces, along with the increase in the influx of transient population, could be associated with an elevated concentration of individuals susceptible to this disease within these regions. Contributing factors such as a denser presence of educational institutions and larger class populations synergistically amplify the propagation of scarlet fever, consequently causing an escalation in its incidence within urban environments.

The analysis revealed a notably higher incidence of scarlet fever in northern China compared to the southern and central regions — a finding supported by previous studies (*18*). Recent years have seen a significant rise in scarlet fever rates in the north, while its increase has been more gradual in both the central and southern areas. The elevated prevalence of this disease in the northern region has largely contributed to the rise in national incidence. Scarlet fever, an acute respiratory infection, is influenced by varying meteorological elements and atmospheric pollutants. Factors such as monthly average temperature, humidity, and rainfall have displayed an inverse correlation with the onset of scarlet fever (*19*–*20*), whereas atmospheric pollutant concentration showed a positive correlation (*21*–*22*). The humid climate and enhanced rainfall in the south promote bacterial adhesion to droplets, thereby lowering airborne pathogen concentration and potentially limiting scarlet fever transmission. Consequently, this results in a lower incidence rate. Conversely, the drier climate, reduced humidity, and severe air pollution found in high-altitude areas of northern China may exacerbate airborne pathogen concentration and thus increase the susceptibility of individuals to infection, accounting for the higher incidence rates in these regions.

This study is not without its limitations. The case data analyzed were drawn from the National Notifiable Disease Reporting System. Given that the reporting of scarlet fever is dependent on the quality of healthcare and diagnostic accuracy in each region, the potential for underdiagnosis and misdiagnosis cannot be discounted. However, the broad geographical coverage of the study and the extended duration of analysis lend considerable credibility to the findings.

Overall, the prevalence of scarlet fever in China has steadily increased in recent years. The rates are observed to be highest among urban populations, particularly those aged 4–7 years old in the Northeast, North, and Northwest China, as well as that in rural populations in the Northeast, particularly those aged 4–5 years old. It is crucial to enhance preventive and control measures targeting these high-prevalence populations and regions. Timely disinfection of densely populated areas, increased ventilation, and stringent maintenance of environmental hygiene are vital. Reinforcing scarlet fever surveillance and early warning systems will enable timely responses to potential outbreaks, limiting the spread of the disease, and thereby protecting public health.

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Perspectives

# Reviewing the Chinese-Specific Reference Amounts Study Conducted by Sun et al., 2022

W. Marty Blom[1,#]; Joost Westerhout[1]; Geert F. Houben[1]

The need for region-specific food intake values to accurately estimate food allergen risk is underscored by the recent Ad Hoc Joint Food and Agriculture Organization/World Health Organization (FAO/WHO) Expert Consultation on Risk Assessment of Food Allergens (*1*). A recent study published by Sun et al. in *China CDC Weekly* 2022, titled *A Chinese-Specific Reference Amounts Study with TNO Food Allergen Risk Assessment Models — China, 2022*, critically examines and applies a previously established sensitivity analysis aimed at deriving food intake values for food allergen risk assessment (RA) (*2*–*3*). In their examination of Chinese food consumption data, the authors find that "the 95th–99th percentiles of the food consumption distribution per eating occasion for condiments and chocolates are the optimal point estimates for use in deterministic allergen RA, aiming to protect 99% of allergic individuals from allergic reactions due to unintended peanut presence." This finding significantly deviates from those of Blom et al., which suggested that the 50th–75th percentiles of the food consumption distribution per eating occasion in various global contexts would suffice for achieving a similar safety objective aimed at protecting 95%–99% of allergic individuals from objective allergic reactions due to unintended allergen presence (*3*–*4*).

While a more cautious approach to consumption estimations may appear safe from a risk management perspective, such an approach could involve a degree of overprotection that may result in unwarranted restrictions for both the Chinese food-allergic population and the food industry. Achieving a balance between guaranteeing safety and implementing realistic, pragmatic protocols is vital (*1*). Thus, a risk assessment that incorporates unnecessary high-intake figures may not provide risk managers with the most effective information(*5*).

Hence, we evaluated the potential causes of the elevated *P*-values discovered in the study by Sun et al. (*2*). We focused on identifying elements that could significantly augment the sensitivity analysis, ultimately leading to the establishment of a more robust food intake estimation for China.

Several factors in the data utilized by Sun et al. (*2*) could be contributing to the observed elevated *P*-values (Table 1), thus likely resulting in an excessively conservative outcome, more so than what was projected when the sensitivity analysis method was initially applied. For instance, the food consumption distribution employed in the study lacks the necessary diversity in comparison to the food consumption distribution from other research, thereby contributing to a less refined point estimate (Table 2). A striking similarity can be seen between the consumption ranges of condiments in China and the Netherlands, hovering between 25 grams to approximately 250 grams within the 50th and 99th percentile of the intake distribution (Table 2).

According to the Dutch National Food Consumption Surveys (DNFCS) (https://www.rivm.nl/publicaties/diet-of-dutch-results-of-dutch-national-food-consumption-survey-2012-2016), individual food product consumption is measured per eating occasion at the gram level, which allows for a higher degree of differentiation within the food intake distribution (*4*). Conversely, the Chinese National Nutrition and Health Survey of 2002 utilizes a different measurement scale in *liang*, resulting in steps of 25 or 50 grams in quantifying food consumption in their survey (*2*, personal communication Prof. Wu). Consequently, the intake quantity for the P50 to P65 range in the food distribution is the same at 25 grams, with all *P*-values from P75–P90 measured at 50 grams.

This hinders the sensitivity analysis from effectively differentiating between the percentile ranges P50–P65 and P75–P90. Therefore, a food intake distribution with greater differentiation and detail in the consumed amounts might allow for a more highly tuned intake distribution for a food group. Consequently, it may lead to a different optimal point estimate than the one uncovered in Sun et al.'s study (*2*).

The implications of this research might be further explored through a comprehensive analysis of detailed food consumption data from China. In the absence of such records, comparable information from alternative

TABLE 1. Potential elements contributing to the higher percentiles of food consumption distribution in the sensitivity analysis of Sun et al.'s study (*2*) compared to Blom et al.'s studies (*3–4*).

| Element | Study by Sun et al. 2022 (*2*) | Recommended analyses |
|---|---|---|
| Characteristics of dietary consumption data | The 2002 food survey dataset, marked by limited differentiation in food consumption amounts (with intervals of 25 or 50 grams), stems from the use of Chinese measurement units known as *jin* and *liang*. | The data derived from the food consumption survey can be used to provide a higher degree of specificity, particularly relating to the amounts consumed. This includes detailed information regarding the weight in grams of the product consumed during each eating occasion. Further description of the survey is available in reference (*4*). In the absence of specific data, conduct a simulation study utilizing more detailed food consumption survey statistics from various countries. This would help to examine whether the incremental steps utilized in the data set of Sun et al. could have potentially resulted in the observed high *P*-values. |
| Chosen case study | The point estimate recommendation was derived from the analysis of two distinct food groups. | The analysis was conducted on all food groups identified in a food consumption survey, which typically encompasses between 50 to 60 food groups (*3–4*). |
| Threshold dataset | Peanut population ED value distribution of 2014 (*6*) | The model averaging method developed by (*7*) is utilized herein, applying ED-distributions to the extended threshold dose datasets for 14 allergenic foods, as discussed in the work of (*5*). |
| Safety objective | ED01 of the population distribution for peanut | To use a broader range of ED values (*5*), including the officially recommended ED05 (*8*). |

Abbreviation: ED=Effective Dose.

TABLE 2. Comparison of intake distribution between the limited differentiation in food consumption amounts from the Sun et al.'s study, and a comparable food group in the Dutch Food Consumption Survey (2007–2010).

| Intake distribution percentile | Intake distribution (grams) | |
|---|---|---|
| | Reported in Sun et al. (*2*) for condiments | The "Sauces and Condiments" food group, as reported in the Dutch National Food Consumption Survey 2007–2010 (DNFCS), demonstrated a high degree of differentiation (*4*) |
| P50 | 25 | 25.3 |
| P55 | 25 | 28.4 |
| P60 | 25 | 31.6 |
| P65 | 25 | 35.5 |
| P70 | 40 | 40.1 |
| P75 | 50 | 46.1 |
| P80 | 50 | 53.7 |
| P85 | 50 | 64.0 |
| P90 | 50 | 79.1 |
| P95 | 75 | 112.4 |
| P97.5 | 100 | 149.4 |
| P99 | 125 | 205.8 |
| P100 | 250 | 733.3 |

countries could be utilized in conjunction with simulation studies (Table 1).

The original study conducted a sensitivity analysis for the Effective Dose 01 (ED01) of the population ED-distribution; however, the recent FAO/WHO expert consultation advised the use of Reference Doses based on the ED05 of the population ED-distribution (*8*). In light of selecting a different ED value as the safety objective, sensitivity analysis should be utilized to ascertain the optimal point estimate for the corresponding safety level (*3*).

This brief review of the study conducted by Sun et al., 2022, aims to facilitate enhanced sensitivity analyses and foster collaborative efforts towards developing Chinese and globally harmonized recommendations for reference amounts for food allergen RA.

**Conflict of interest**: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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