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Post-pandemic epidemiological trends of respiratory infectious diseases in Taiwan: A retrospective analysis

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ABSTRACT

Background: This study analyzed the epidemiological trends of three significant respiratory infectious diseases in Taiwan: invasive pneumococcal disease (IPD), influenza with severe complications, and tuberculosis during post-COVID-19 pandemic period.

Methods: We utilized data from Taiwan's Centers for Disease Control and Prevention (CDC) website and classified the COVID-19 prevention policies into three phases for the year 2021, 2022, and 2023. We then performed a statistical analysis of reported case numbers for the three respiratory diseases during the 3-year period using the Kruskal–Wallis test, followed by joinpoint regression model for the identification of seasonal distribution and variation.

Results: An annual increase was observed in cases of IPD and influenza with severe complication, with influenza exhibiting a significant surge in 2023 ($p < 0.001$). IPD showed a non-significant upward trend ($p = 0.111$), while tuberculosis cases decreased annually ($p = 0.114$) with the gradual slowdown in the incidence rate reduction. Also, seasonal analysis revealed that IPD peaked in winter and spring, while influenza with severe complication peaked anomalously in the summer of 2023, suggestive of a prominent summer influenza. Finally, imported cases of influenza with severe complication, primarily from East and Southeast Asia, were noted only in 2023.

Conclusions: The relaxation of COVID-19 preventive measures in Taiwan led to a marked resurgence of respiratory infectious diseases, particularly influenza with severe complication, accompanied by anomalous seasonality in 2023. This study highlights the need for continued vigilance and appropriate public health strategies, including vaccination and non-pharmaceutical interventions, to manage respiratory infectious diseases in the post-pandemic era.

1. Introduction

Since the first case of coronavirus disease (COVID-19) was confirmed in Wuhan, China, at the end of 2019, the pandemic rapidly spread across the globe.[1] According to data from World Health Organization (WHO), as of June 03, 2024, the cumulative number of confirmed cases worldwide is 775,522,404.[2] During the COVID-19 pandemic, countries around the world adopted strict policies to prevent the spread of the virus, including border control, implementation of quarantine policies, regulations on wearing masks, and the administration of vaccines.[3–5] These strict preventive strategies against the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had collateral benefits as well; for instance, the incidence of several respiratory infectious diseases also decreased, including in Taiwan.[6–10]

However, COVID-19 had caused severe financial impacts on hospitals and healthcare facilities worldwide. The World Bank projects that the global economy will shrink by nearly 8 %, while the United Nations estimates that the pandemic will result in approximately 2 trillion dollars in economic losses.[11] Hence, as the pandemic gradually came under control, governments moved toward relaxing pandemic policies and

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reopening borders. On May 5, 2023, the WHO announced that the COVID-19 epidemic would no longer be listed as a public health emergency of international concern.[12]

With the gradual full-scale reopening, not only did confirmed COVID-19 cases grow exponentially, but the incidence of other respiratory infectious diseases also increased significantly, including influenza, respiratory syncytial virus, rhinovirus, adenovirus, and human metapneumovirus.[13–15] Additionally, some countries reported increased cases of invasive respiratory bacterial diseases by late 2021 as pandemic restrictions were lifted.[16] According to the study by Lee et al., which referred data from WHO, a significant increase in cases of influenza virus infection was observed in both the Northern and Southern hemispheres compared to 2021.[17] This phenomenon of increased influenza cases in the post-COVID-19 pandemic period reflects the changes in respiratory infectious diseases before and after the lifting of COVID-19 pandemic control policies, highlighting a significant epidemiological variation following the adjustment of public health interventions.

Beyond the global post-pandemic rebound of influenza, there was also a significant worldwide increase in invasive pneumococcal disease (IPD), including in Canada, Portugal, and Germany.[18–20] Moreover, following the complete relaxation of COVID-19 control policies in England in 2022, the incidence of IPD among children surpassed not only the pandemic-era rates but also pre-pandemic levels.[21]

Compared to other developed countries, Taiwan delayed the relaxation of its COVID-19 preventive measures. It remains unclear if Taiwan has the same epidemiological trends of respiratory infectious diseases in the post-pandemic era. To explore this, our study investigated the epidemiological trends of three significant notifiable respiratory diseases in Taiwan—namely IPD, influenza with severe complication, and tuberculosis—using data from the open database of Taiwan's Centers for Disease Control and Prevention (CDC).

2. Methods

2.1. The policies used to control COVID-19 in Taiwan

Since January 15, 2020, when the Taiwan government officially declared COVID-19 as a category 5 notifiable infectious disease (identified by the authority as an emerging infectious disease or syndrome that may affect national health, necessitating the establishment of prevention or preparedness plans, with a requirement to report to the authority within 24 h after diagnosis), until May 1, 2023, when the government officially downgraded COVID-19 to a category 4 notifiable infectious disease (recognized by the authority as a known infectious disease or syndrome for which monitoring of the epidemic or implementation of prevention is necessary, with only severe and critical cases required to be reported to the authority within 24 h), numerous policies used to control COVID-19 in Taiwan changed over time, such as the relaxation of the criteria for de-isolation, principal of triage, duration of home quarantine, and reopening of borders. After reviewing all epidemic prevention policy articles on the Taiwan CDC website in the past 3 years, the relatively critical decision-making milestones were identified and are summarized in Fig. 1.

2.2. Source of data

In Taiwan, a total of 73 infectious diseases are classified as notifiable infectious diseases. Regular, frequent, and timely information regarding individual cases is considered necessary for the prevention and control of the diseases. Associated data can be collected through the National Notifiable Disease Surveillance System. Therefore, data obtained in this study is publicly available through the open database established by the Taiwan CDC website.[22]

2.3. Study period and data analysis

Based on the evolution of epidemic prevention policies (Fig. 1), we divided Taiwan's COVID-19 prevention policies into three phases for the year 2021, 2022, and 2023 (Fig. 2). These three phases represent the following policies: for 2021, "Strict epidemic policies and strategies for the control of COVID-19 and border control; " for 2022, "The gradual easing of pandemic restrictions for COVID-19 and the progressive relaxation of entry and exit controls; " and for 2023, "Thoroughly ending the era of strict epidemic prevention for COVID-19 officially."

We then utilized the Taiwan National Infectious Disease Statistics System available on the Taiwan CDC website to retrieve the confirmed case numbers for the three above mentioned diseases across the three stages and to explore the age distribution of IPD cases from 2021 to 2023.[23]

2.4. Statistical analysis

During the study period, the total population of Taiwan in 2021, 2022, and 2023 were 23,375,314, 23,264,640, and 23,278,642 people, respectively.[24] First, we calculated the annual incidence rate for the three diseases by dividing the total number of reported cases each year by the total population of Taiwan in that year. The unit is the number of people infected per 100,000 populations. Also, we utilized data from the

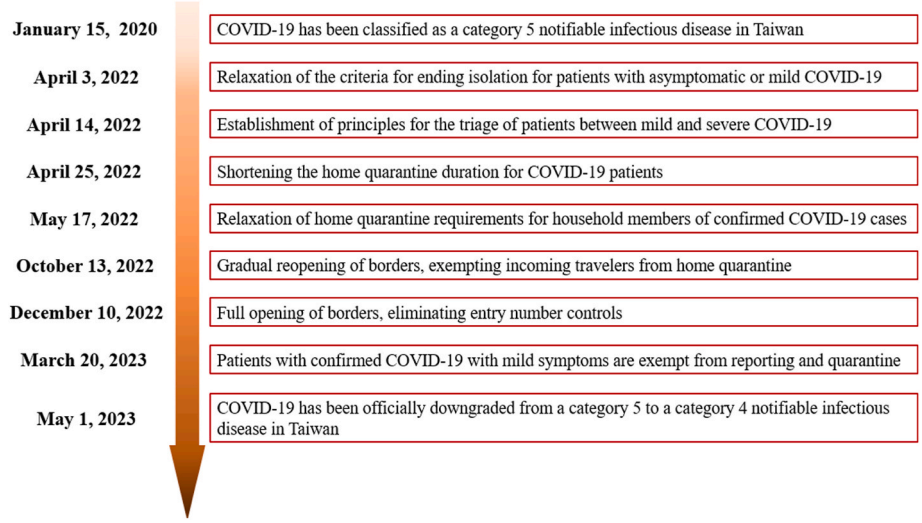

Fig. 1. The progression of policies used to control COVID-19 in Taiwan from January 15, 2020 to May 1, 2023.

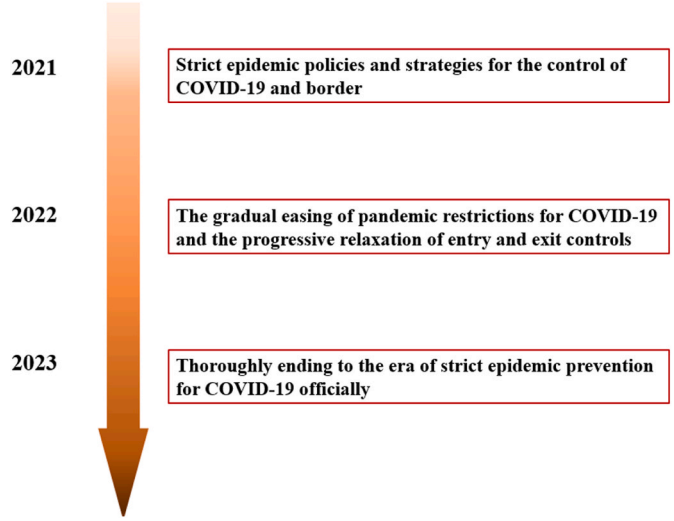

Fig. 2. The division of Taiwan's COVID-19 prevention policies into three phases in 2021, 2022, and 2023, respectively.

same source with the same method to calculate the annual incidence rate for tuberculosis from 2005 to 2023.[22,24]

Second, to evaluate the variation in total cases across different year-month combinations for each disease, we employed the Kruskal–Wallis test. This non-parametric method was used to assess statistical differences among all the time periods for each disease individually. The Kruskal–Wallis test results suggested that there are no statistically significant differences in the total cases across different year-month combinations for each of the diseases, as indicated by p-values >0.05.[25]

Third, to analyze the annual trends in the incidence of IPD and influenza with severe complication for the year 2023, we used the joinpoint regression model. While this method was initially developed for cancer surveillance, it has been validated for analyzing various infectious disease patterns.[26–28] This model enabled the identification of significant changes in incidence, specifically pinpointing the months with peak and trough occurrences. The analysis was performed using the joinpoint Trend Analysis Software, version 5.1.0, provided by the National Cancer Institute in the U.S.

3. Results

Table 1 summarizes the reported case numbers of IPD, influenza with severe complication, and tuberculosis across the three phases in 2021, 2022, and 2023. Overall, the annual case number for both IPD and influenza with severe complication increased with time. For IPD, the total case number in 2021 was 196 people, increasing to 200 and 287 people in 2022 and 2023, respectively. The annual incidence rate per 100,000 populations were 0.84, 0.86, and 1.23 in 2021, 2022, and 2023, respectively. There were only 1 and 22 reported cases of influenza with severe complication in 2021 and 2022, respectively, which surged to 1058 cases in 2023. The annual incidence rate per 100,000 populations were 0.004, 0.095, and 4.55 in 2021, 2022, and 2023, respectively. However, the reported cases of tuberculosis showed a decreasing trend with time, from 7062 cases in 2021–6576 cases in 2022, and 6422 cases in 2023. The annual incidence rate per 100,000 populations were 30.2, 28.3, and 27.6 in 2021, 2022, and 2023, respectively.

We found that both IPD and influenza with severe complication had a trend of increasing every year. However, IPD showed a slightly increasing trend without a statistically significant difference ($p = 0.111$) (Fig. 3A). Only influenza with severe complication showed a statistically significant increasing trend with a remarkably steep slope (p value $<$ 0.001) (Fig. 3B). In contrast, tuberculosis exhibited a slightly decreasing trend over the years although without statistically significant difference ($p = 0.114$) (Fig. 3C).

Tuberculosis exhibited almost no discernible seasonal change, as seen in Table 1, with reported cases being evenly distributed throughout all the four seasons of the year. However, we noticed that the reported cases of IPD in these 3 years were predominantly observed during winter and spring. In contrast, during the influenza surge in 2023, the number of reported cases for influenza with severe complication had peaked in the summer.

The analysis of annual trends of IPD and influenza with severe complication for the year 2023 was performed using the joinpoint regression model. For IPD, the joinpoint was identified at September 2023, with the monthly percent change (MPC) showing a decrease of 7.3 % per month from January to September ($p = 0.002$) and an increase of 27.7 % per month after September ($p < 0.001$). This indicates that September had the lowest incidence of IPD during the year (Fig. 4A). On the other hand, influenza with severe complication cases peaked in August 2023, as evidenced by the joinpoint at August and the significant MPC of 35.0 % per month from January to August ($p < 0.001$). After August, the trend reversed, with cases decreasing by 19.6 % per month

Table 1
The reported case numbers and annual incidence rate of invasive pneumococcal disease, influenza with severe complication, and tuberculosis across three phases in 2021, 2022, and 2023.

	Case of numbers								
	Invasive pneumococcal disease			Influenza with severe complication			Tuberculosis		
Month	Year								
	2021	2022	2023	2021	2022	2023	2021	2022	2023
January	27	14	30	0	0	17	565	538	462
February	36	13	28	0	0	18	499	423	477
March	30	16	27	1	0	16	687	569	633
April	16	13	21	0	0	76	640	576	487
May	24	17	27	0	0	92	582	551	623
June	12	18	21	0	0	115	503	462	581
July	8	15	21	0	0	116	478	571	539
August	10	8	19	0	0	163	600	599	565
September	7	17	9	0	0	168	645	622	527
October	7	15	26	0	2	116	610	514	534
November	10	20	22	0	11	69	648	590	505
December	9	34	36	0	9	92	605	561	489
Total	196	200	287	1	22	1058	7062	6576	6422
Annual incidence rate per 100,000 populations	0.84	0.86	1.23	0.004	0.095	4.55	30.2	28.3	27.6

Note: During the study period, the total population of Taiwan in 2021, 2022, and 2023 were 23,375,314, 23,264,640, and 23,278,642 people, respectively[24].

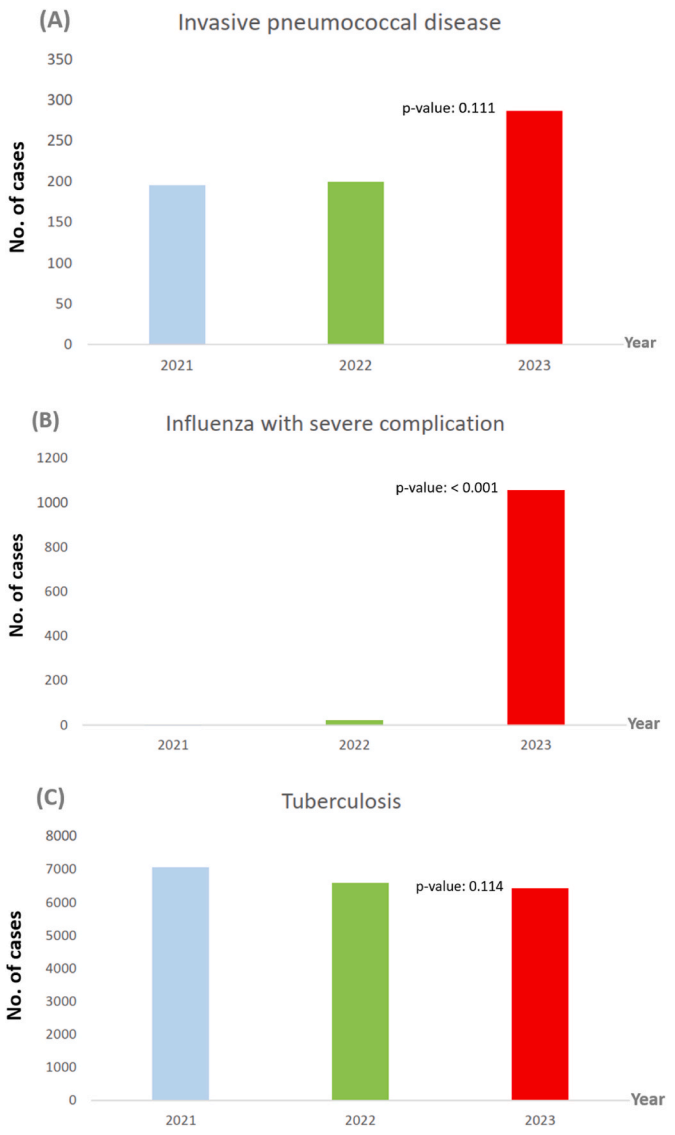

Fig. 3. Annual case number of invasive pneumococcal disease (A), influenza with severe complication (B) and tuberculosis (C).

until December, although this decrease was not as statistically significant ($p = 0.07$) (Fig. 4B).

In addition, we found no imported cases of IPD and tuberculosis over the 3-year period. However, while there were no imported cases of influenza with severe complication reported in 2021 and 2022, there were 28 cases of overseas imports in 2023. Fig. 5 shows the geographic distribution of the countries of these 28 overseas imported cases, and the majority were found to be from East Asia and Southeast Asia.

Fig. 6 shows the age distribution of IPD cases from 2021 to 2023, based on data from the Taiwan CDC website.[23] Over these three years, while there were few cases among children under 10 years old, most cases occurred in elderly individuals, particularly those aged 75 and above.

Finally, Fig. 7 presents the annual tuberculosis incidence rates from 2005 to 2023. While tuberculosis incidence had been steadily declining since 2005, the post-pandemic period after 2021 showed a slower rate of decrease, especially following the complete lifting of epidemic prevention policies in 2023.

4. Discussion

This is the first epidemiological analysis of infectious respiratory diseases in Taiwan after the COVID-19 pandemic. COVID-19, ravaged the world and severely impacted people globally, resulting in millions of deaths,[29] including up to 17,668 people in Taiwan.[30] However, as the situation with COVID-19 stabilized, governments gradually lifted pandemic-related restrictions and opened borders. Based on data from the Taiwan CDC on notifiable infectious diseases, we found that with the easing of policies, there has been a rapid spread of respiratory infectious diseases, particularly IPD and influenza with severe complication. This clinical finding is consistent with those of studies on the epidemiology of respiratory infections in other countries in the post-pandemic era.[13–21,31]

In Taiwan's post-pandemic era, reported cases of IPD and influenza with severe complication have increased annually, with influenza with severe complication showing a statistically significant yearly rise. This increase can be attributed to several factors: the relaxation of pandemic policies, declining adherence to non-pharmaceutical interventions (NPIs) such as personal protection, environmental measures, social distancing, and travel restrictions, and impaired lung function from previous SARS-CoV-2 infections.[32] Furthermore, long COVID (a syndrome affecting people recovering from acute COVID-19 infection) can cause multi-organ functional deterioration with chronic inflammation, leading to decreased activity levels and weakened immunity, potentially increasing susceptibility to respiratory infections.[33,34] A Taiwanese cohort study found that more severe acute COVID-19 infections were associated with more intense long COVID symptoms and poorer health-related quality of life over time.[35]

"Population immunity", also known as "herd immunity", refers to the indirect protection from an infectious disease that occurs when a population becomes immune through vaccination or previous infection.[36] This concept encompasses both a threshold required to reduce infection incidence and a level of immunity that prevents the spread of new infections.[37] During the COVID-19 pandemic, the implementation of NPIs significantly reduced the number of cases of transmissible respiratory diseases. However, this phenomenon is a double-edged sword. From the perspective of immunity debt, the reduction in infectious cases leading to decreased population immunity could facilitate a large outbreak of infectious diseases in the post-COVID-19 pandemic era.[38] Nonetheless, in Taiwan, passive immunity provided by vaccinations for COVID-19, influenza, and pneumococcal diseases has increased compared to previous years, both among those eligible for free vaccines and those who need to pay for it themselves.[39,40] Despite vaccination, however, the number of cases of IPD and influenza with severe complication continued to rise, suggesting that relaxed pandemic policies and the gradual neglect of NPIs are the main reasons for the yearly increase in respiratory infectious diseases.

Unlike the trends for IPD and influenza with severe complication, the reported number of tuberculosis cases has been consistently decreasing. Tuberculosis is an important notifiable infectious disease in Taiwan, and regular professional meetings are held to develop and revise therapeutic guidelines for tuberculosis. In recent years, the government increased the budget for treating latent tuberculosis. The Directly Observed Treatment, Short-course (DOTS) strategy, unique to Taiwan, aims to ensure that tuberculosis patients take their medication regularly under strict supervision, helping them recover on schedule and preventing the spread of multidrug-resistant bacteria, thereby protecting the public.[41,42] Based on these long-standing government strategies, the reported number of tuberculosis cases has predictably continued to decrease even in the post-COVID-19 pandemic era.

According to the Taiwan National Infectious Disease Statistics System, there is a discrepancy between reported cases of influenza with severe complication and weekly deaths from influenza-related pneumonia. Intriguingly, while reported cases of influenza with severe complication decreased significantly from 2020 to 2022, the weekly death toll from influenza-related pneumonia did not show a corresponding decline.[43] This discordant pattern may be attributed to delayed medical treatment and under detection during the pandemic, as

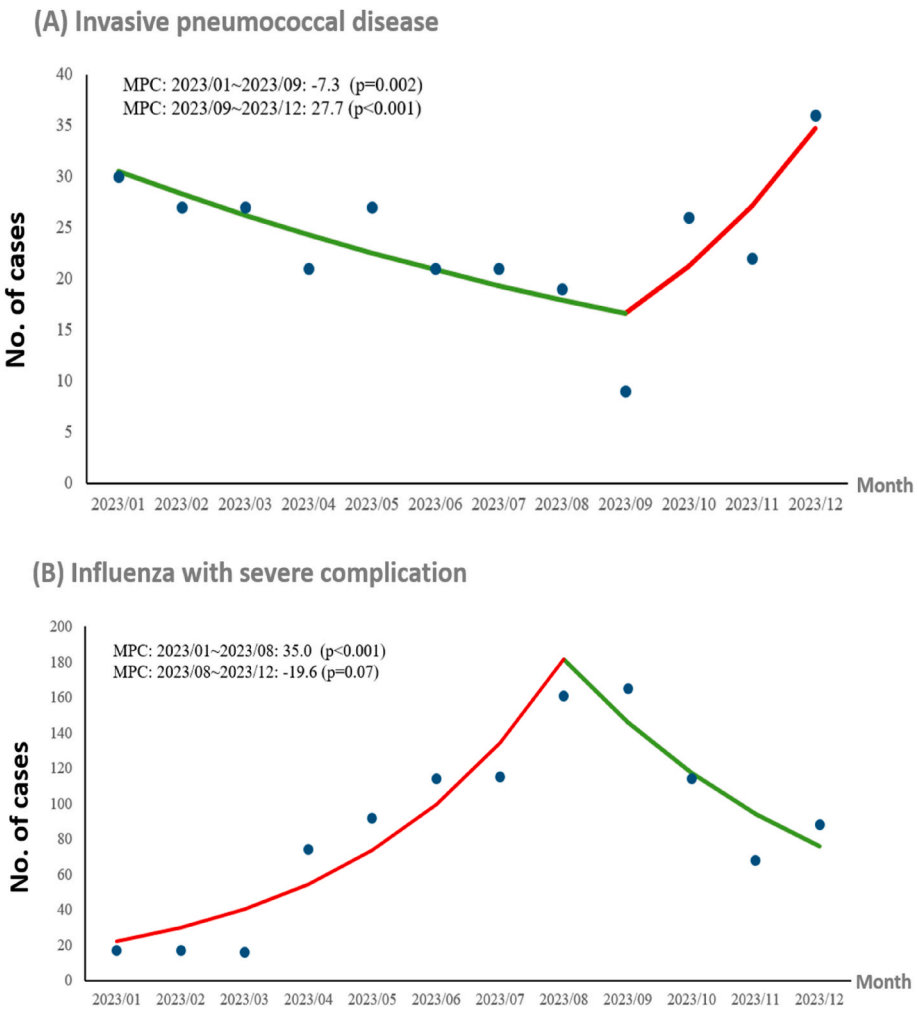

Fig. 4. Joinpoint regression model for the investigation of the seasonality of invasive pneumococcal disease (A) and influenza with severe complication (B) in 2023. Note. MPC, monthly percent change

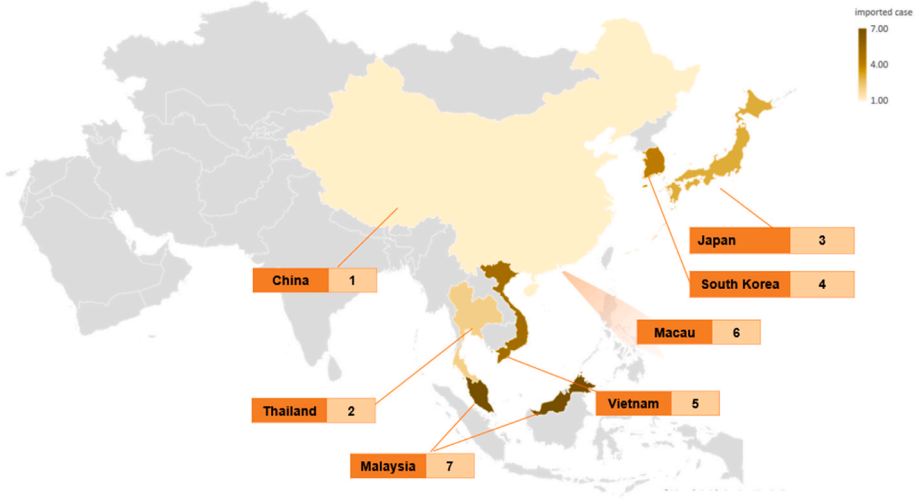

Fig. 5. The geographic distribution of the imported cases of influenza with severe complication in 2023.

people feared contracting COVID-19 in hospitals. Consequently, when patients did present to emergency departments during the pandemic, their illnesses may have been more severe than in pre-pandemic times, resulting in persistently high mortality rates.

Similarly, despite decreasing incidence rates, tuberculosis mortality rates remained stable according to Taiwan CDC.[44] We may also attribute this phenomenon to the delay of medical treatment and under detection, as mentioned above. Although government tuberculosis policies have

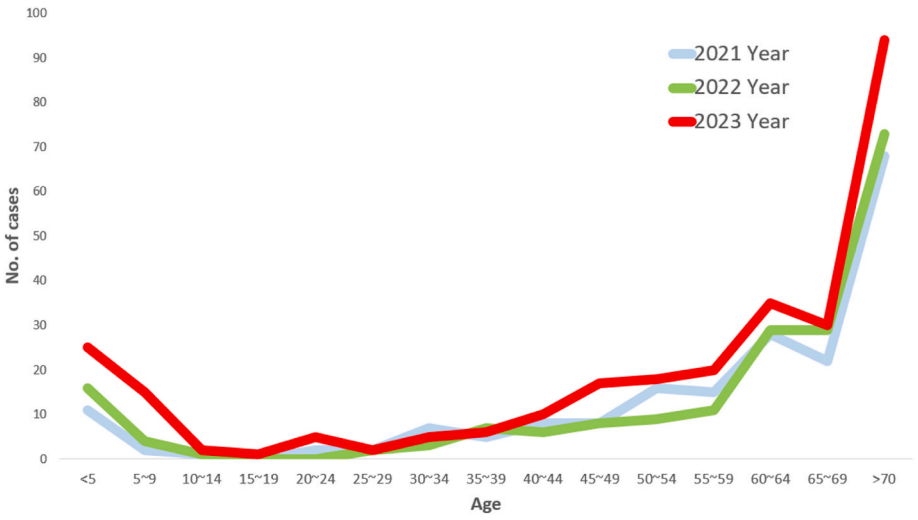

Fig. 6. The age distribution of invasive pneumococcal disease (IPD) cases from 2021 to 2023.

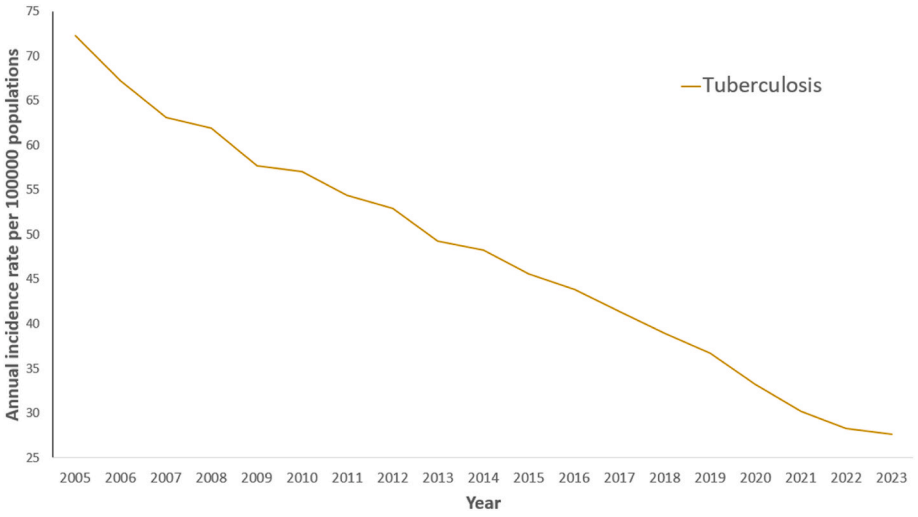

Fig. 7. The annual incidence rate of tuberculosis cases from 2005 to 2023.

been effective, leading to declining case numbers since 2005,[45,46] the reduction in incidence has slowed significantly in the post-pandemic period compared to pre-pandemic levels (Fig. 7). This deceleration likely stems from multiple factors: (1) delayed healthcare access and under detection, enabling community spread; (2) uneven allocation of medical resources due to COVID-19 management priorities; and (3) potential tuberculosis reactivation in patients with COVID-19-weakened immune systems.[47] As pandemic-related restrictions ease and NPI adherence declines, tuberculosis transmission has resumed within communities. In Taiwan, the persistent slowdown in tuberculosis incidence reduction necessitates proactive interventions to prevent a potential resurgence in the near future.

According to the Joinpoint regression analysis of annual influenza with severe complication in 2023, the reported case numbers had peaked in summer (August) in Taiwan. This weird seasonality is an interesting phenomenon, unlike the typical prevalent season of winter and spring for influenza and other respiratory infectious diseases.[48] The timing of this peak (in August), immediately following full reopening after withdrawal of COVID-19 prevention policies in our country in March 2023, suggested that the resurgence of social interactions may be one reason for this unusual trend. Based on Taiwan CDC data, between 2022 and 2023, type A influenza was predominant in the community, with A/H1N1 and A/H3N2 strains co-circulating. Antigenic analysis revealed that nearly all H1N1 and H3N2 viruses matched the vaccine strains. Additionally, the less frequently isolated type B influenza strains showed 100 % match with vaccine strains.[43] Therefore, the reliable passive immunity provided by influenza vaccines cannot explain the surge in influenza with severe complication during summer 2023. Another possible reason may be the lack of population immunity to influenza due to extremely low number of reported cases from previous pandemic years, which enabled the large outbreak of this infectious disease very rapidly in the post-COVID-19 pandemic era. Additionally, the reopening of borders and the increasing number of people traveling abroad not only contributed to the 28 imported cases of influenza with severe complication in 2023, but also suggested that during summer, which is the travel season, the influx of influenza virus from abroad would increase, contributing to a peak in reported cases of influenza with severe complication.

Paradoxically, reported cases of influenza with severe complication peaked in late August 2023, followed by a declining trend through December 2023 (Fig. 4B). Although this decrease was not statistically significant ($p = 0.07$) according to the joinpoint regression model, we believe this decline can be attributed to multiple factors: the recovery of population immunity following the summer influenza wave, people's

voluntary adoption of NPIs such as mask-wearing based on their COVID-19 experience, and the influenza vaccination campaign that began in October 2023.[49]

However, IPD retained its seasonality, being prevalent in winter and summer. Joinpoint regression analysis of annual IPD in 2023 showed that the reported case number was at the dip point in September, thereby suggesting that its incidence wound gradually increase to peak numbers during the colder climate. This finding is consistent with that observed in our previous clinical practice,[50] but is contrary to the seasonality of influenza with severe complication in 2023. It is possibly due to the protection offered by vaccination administered in the past few years. Different from the influenza vaccine that has a short protective duration of less than one year,[51] the protection provided by pneumococcal vaccine can last for several years, even lifelong.[52] Hence, there will be no lack of population immunity anymore, making IPD still can maintain its seasonality in the post-COVID-19 pandemic era. These findings reveal significant seasonal shifts in the patterns of occurrence of each disease in 2023.

As shown in Fig. 6, the age distribution of IPD cases remained consistent from 2021 to 2023.[23] During these three years, while there were few cases among children under 10 years old, most cases occurred in elderly individuals, particularly those aged 75 and above. Moreover, IPD susceptibility and reported cases increased with age. The thorough implementation of publicly funded pneumococcal vaccination for infants in Taiwan has achieved nearly 100 % coverage since 2015,[53] explaining the low number of IPD cases among children under 10. However, although elderly vaccination rates increased from 41 % in 2021 to 49.1 % in 2023, the overall pneumococcal vaccine coverage among the elderly remains low, contributing minimally to population immunity.[54,55] Besides, the introduction of pneumococcal vaccine in Taiwan has altered serotype distribution, with significant increase in non-vaccine-types, particularly 15A and 23A.[56] Also, different *S. pneumoniae* serotypes may exhibit varying antimicrobial resistance patterns.[57] Hence, continuous monitoring of the number of IPD cases, along with their associated serotypes and antimicrobial resistance patterns, is of critical and paramount importance in the post-pandemic era.

Taiwan, like other countries, has entered the post-pandemic era as the situation is under control. However, the virus has not disappeared from the world, and we must remain vigilant.[58–60] Moreover, we cannot neglect other respiratory infectious diseases and vaccinations for influenza and pneumococcal disease must be taken seriously. Although there are no longer strict policies to prevent the spread of disease, other NPIs, such as wearing masks, hand hygiene, alcohol disinfection, and workplace prevention measures, must not be forgotten.[61]

The main limitation of this study was the inability to accurately identify the number of people vaccinated against influenza and pneumococcal disease in Taiwan, which prevented a detailed analysis of the vaccination coverage rate and its correlation with respiratory diseases.

5. Conclusions

The relaxation of COVID-19 preventive measures in Taiwan has led to a significant resurgence of respiratory infectious diseases, especially influenza with severe complication, which showed a statistically significant surge in 2023. Reported cases of IPD also increased annually, with a prominent trend of the increased incidence as the increasing age, peaking in winter and spring, while influenza had an unusual summer peak, likely due to resumed social interactions, lack of population immunity, and increased international tourism. In contrast, tuberculosis cases continued to decline, reflecting effective public health interventions, however, it is worth noting that the reduction in the annual incidence rate of tuberculosis has slowed down in the post-pandemic era. These findings underscore the need for sustained vigilance and robust strategies, including vaccination and NPIs, to manage respiratory infections in the post-pandemic era. Future research should focus on the impact of vaccination coverage and the reimplementation of preventive measures to mitigate these infections.

CRediT authorship contribution statement

Jin-Wei Liu: Writing – original draft, Formal analysis, Data curation, Conceptualization. **Ya-Wen Tsai:** Formal analysis, Data curation. **Chih-Cheng Lai:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Hung-Jen Tang:** Writing – review & editing, Supervision, Data curation, Conceptualization.

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