Temporal trends and shifts of 24 notifiable infectious diseases in China before and during the COVID-19 epidemic

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Abstract

The COVID-19 epidemic and the subsequent implementation of public health and social measures (PHSMs) have markedly reshaped the transmission dynamics of infectious diseases. In this study, we analyzed the impact of PHSMs on 24 notifiable infectious diseases (NIDs) in mainland China and utilized multiple time series models to forecast transmission trends under hypothetical scenarios without PHSMs or epidemic. Our findings revealed distinct seasonal patterns in the incidence of different NIDs categories. Among these categories, respiratory infectious diseases exhibited the most substantial response to PHSMs, while bloodborne and sexually transmitted diseases demonstrated more moderate effects. Furthermore, we identified 8 NIDs, including hand, foot, and mouth disease (HFMD), dengue fever, malaria, pertussis, scarlet fever, mumps, and rubella, as being highly susceptible to the impact of PHSMs. PHSMs, such as travel restrictions, played a crucial role in mitigating the transmission of zoonotic diseases such as dengue fever and malaria. Interestingly, the easing of PHSMs did not lead to a notable resurgence in NIDs, likely due to the continued practice of self-isolation. Our findings highlight the varied impact of PHSMs on different infectious diseases and emphasize the need for developing sustainable, long-term strategies, such as vaccine development, for their prevention and control.

Background

During the COVID-19 epidemic, the emergence of various SARS-CoV-2 variants have reshaped the transmission dynamics of other infectious diseases. Notably, influenza activity in the United States experienced a significant 98% reduction before May 2020. This decline is largely attributed to the widespread implementation of public health and social measures (PHSMs) to combat COVID-19. For instance, the widespread use of face masks and enforcement of physical distancing have effectively reduced the transmission of respiratory infectious diseases by limiting the spread of respiratory droplets. Additionally, travel restrictions have successfully controlled the spread of diseases that are bloodborne, sexually transmitted, or zoonotic in nature. Furthermore, improved hand hygiene practices have indirectly contributed to a 31% decrease in the transmission of intestinal infectious diseases.

Despite many published studies have analyzed the impact of PHSMs on notifiable infectious diseases (NIDs), a substantial knowledge gap persists in our understanding of this relationship. Most of these studies have primarily focused on the impact stricted PHSMs during early stage while often overlooking the potential impact of varying durations. Additionally, most published studies have predominantly concentrated on the impact of PHSMs on common respiratory and intestinal infectious diseases, with limited quantitative analysis regarding their effects on bloodborne, sexually transmitted, and zoonotic diseases. Notably, following the Chinese government ended “dynamic zero-COVID” policy and discontinued all PHSMs, an outbreak of the Omicron BA.2 variant emerged. However, limited research has been conducted to analyze the patterns of other infectious diseases throughout this period.
In this study, we employed multiple models to identify the most appropriate model for analyzing the transmission trends of 24 NIDs. Using these selected models, we project the transmission trends of 24 NIDs in a hypothetical scenario without PHSMs, while also assessing the influence of SARS-CoV-2 transmission. We compare these predictions with real-world data to thoroughly analyze the impact of different periods on 24 NIDs. Additionally, we conduct a quantitative analysis to decipher the correlation between PHSMs and NIDs, incorporating a PHSMs index into our investigation. Moreover, we delve into the lagged effects of PHSMs on NIDs through a detailed cross-correlation analysis. The findings of this study offer crucial insights for future strategies in the prevention and control of NIDs.

Results

From January 2008 to March 2023, a total of 94,073,113 cases of 24 NIDs were reported in mainland China. Among them, the most prevalent were intestinal infectious diseases, with 44,626,189 cases (47.40%). Bloodborne and sexually transmitted diseases followed, with 28,884,038 cases (30.70%), and respiratory infectious diseases accounted for 19,419,118 cases (20.60%). The last reported was natural focal disease, with only 1,143,788 cases (1.22%) (Fig. 1A). The diseases with the highest number of reports were HFMD (26.90%), hepatitis B virus (HBV) (17.80%), other infectious diarrhea (16.20%), and tuberculosis (15.10%). These four diseases combined accounted for a total of 76.00% of the 24 notifiable infectious diseases. Among them, HFMD and other infectious diarrhea are classified as level III infectious diseases according to China's law, while HBV and tuberculosis are classified as level II infectious diseases (Fig. 1A).

Long-term trends of NIDs before epidemic

During the pre-epidemic period, the epidemiology of intestinal infectious diseases was characterized by pronounced seasonality, with monthly incidence increasing predominantly during the summer and fall month. However, this pattern of seasonality is not universally applicable to all intestinal infectious diseases (Fig. 2A). Specific diseases such as hepatitis E virus (HEV), dysentery, typhoid and paratyphoid fever each exhibited their own distinct seasonal fluctuations. HEV reached its annual peak from January to May, while typhoid and paratyphoid fever and dysentery had their peak seasons from May to November (Supplementary Appendix 1). HFMD was notable for its biannual peaks and the remarkable alternating pattern it exhibited across odd and even years. Due to the significantly higher incidence of HFMD relative to other intestinal infectious diseases, this biennial alternation heavily influenced the aggregate trend observed in intestinal infectious diseases (Fig. 2A, Supplementary Appendix 1). Additionally, hepatitis A virus (HAV) demonstrated more pronounced seasonality before 2012, which subsequently diminished, accompanied by a steady decline in monthly incidence after 2012. A particularly severe outbreak in October 2010 led to 231,167 reported infections of Acute hemorrhagic conjunctivitis (AHC), as documented in Supplementary Appendix 1.

The temporal distribution of natural focal diseases from 2008 to 2020 demonstrates seasonality analogous to that of intestinal infectious diseases, yet with attenuated peak magnitudes. Five out of
seven natural focal diseases (excluding dengue fever and hydatidosis) displayed clear seasonality patterns (Fig. 1B, Fig. 2B). Typhus was prevalent throughout the year, with lower incidence in the spring but high peaks primarily occurring in the autumn before 2014. In the context of malaria, the gradual success of eradication efforts has been reflected in a decreasing incidence trend, particularly after 2011. The peak seasons of natural focal diseases shifted forward, with brucellosis, hemorrhagic fever with renal syndrome (HFRS), and Japanese encephalitis emerging as the primary contributors. These diseases reported case numbers in close proximity (Fig. 1A) and had peak seasons spanning March to July, October to January, and June to September, respectively (Supplementary Appendix 1). This distribution pattern led to a more homogenized seasonality curve, lacking the sharp peaks traditionally associated with natural focal diseases. It’s worth noting that there was an outlier in September and October 2014 (Fig. 1B), which can be primarily attributed to a dengue fever outbreak. During this period, there were 19,178 and 23,525 cases reported, respectively, which represent a substantial deviation from the 1,480 and 1,665 cases reported in the corresponding months of the preceding year, 2013 (Supplementary Appendix 1).

In the pre-pandemic period, bloodborne and sexually transmitted infections demonstrated a recurrent annual trough in February, yet the epidemiological data did not reveal distinct seasonal peaks. The monthly incidence for these diseases oscillated between 10,000 and 20,000 cases from 2008 to 2017. A notable inflection point occurred in 2018, where a sustained increase in incidence rates was documented (Fig. 1B). This increase was not exclusively attributed to a rise in the number of infectious disease cases but rather stemmed from a significant upsurge observed across all five bloodborne and sexually transmitted diseases. The fluctuating pattern observed in bloodborne and sexually transmitted diseases was mainly driven by HBV, which displayed peak seasons in January and March each year since 2012 and continued until 2023. Conversely, respiratory infectious diseases maintained a minimal seasonal variation, with monthly incidences hovering around 10,000 cases. Before 2013, rubella constituted a significant portion of the more virulent respiratory disease cases. However, with the gradual decline in rubella incidence, the seasonality of respiratory infectious diseases diminished (Fig. 2D, Supplementary Appendix 1).

Both bloodborne and sexually transmitted diseases and respiratory infectious diseases showed an increase in the proportion of cases during the winter and spring seasons, accounting for over 50% of all reported cases (Fig. 1C). This proportion tapered below 50% in the summer and autumn months, as a rise in the prevalence of intestinal infectious diseases. Nonetheless, during the PHSMs period I and PHSMs period II, there was a noticeable decrease in reported cases of intestinal infectious diseases. Bloodborne and sexually transmitted diseases, as well as respiratory infectious diseases, experienced a sharp decline in the first three months of 2020 but exhibited a rapid resurgence to prior levels, highlighting the limited impact of PHSMs on these diseases. Consequently, during the PHSMs periods, these diseases continued to represent most of the reported cases, consistently surpassing the 50% threshold (Fig. 1C).

**Short-term trends of NIDs during epidemic**
During PHSMs period I, the government implemented the most stringent measures and all NIDs were in a low endemic phase, it was difficult to determine whether the decrease was a natural phenomenon or a result of the PHSMs. Therefore, separate time series models were established for each disease, and the best model was selected using the normalized composite index. The optimal models for AHC, dysentery, brucellosis, Japanese encephalitis, and malaria were found to be neural network models. For dysentery, the performance advantage of the neural network model over the hybrid model was small (1.38 vs. 1.35) (Fig. 3). Upon evaluation of the prediction outcomes, the neural network model produced a singular value, prompting the use of the hybrid model for subsequent forecasts. Consequently, the hybrid model was utilized to forecast 5 diseases: HEV, HFMD, dysentery, gonorrhea, and syphilis. Among all the optimal models, the most used model was seasonal autoregressive integrated moving average (SARIMA) model, which was the most frequently employed, being applied to 8 NIDs, including typhoid and paratyphoid fever, other infectious diarrhea, HFRS, acquired immune deficiency syndrome (AIDS), HCV, pertussis, scarlet fever, and mumps. Notably, the prophet model was not utilized for any of the diseases.

By comparing the forecasted result with the actual incidence data, it was observed that during PHSMs period I, apart from HAV, which had virtually no change in reported cases (+1.89%), other NIDs were significantly affected. The diseases that experienced the most substantial decreases were dengue fever, rubella, Japanese encephalitis, and HFMD, with reductions of 1861.01 (-94.71%), 6594.62 (-79.50%), 22.61 (-79.03%), and 120,048 (-77.68%) cases, respectively (Fig. 4). Clustering analysis of different diseases during PHSMs period I revealed that scarlet fever was also significantly impacted, as it had a seasonal peak in April-May 2020, which directly disappeared (Fig. 5J, Fig. 4). Regarding the primary mode of transmission, respiratory infectious diseases were most severely affected, with a wide heterogeneity in relative risk (RR), ranging from 0.13 to 0.72. Among them, tuberculosis showed the least impact, with a median RR of 0.72 (IQR: 0.64 to 0.73) (Fig. 5H, Supplementary Appendix 2). In contrast, the impact on the five bloodborne and sexually transmitted diseases was relatively stable, with the median of RR ranging from 0.49 to 0.79 (Fig. 5F, Supplementary Appendix 2).

From April 2020 onwards, during PHSMs period II, the Chinese government shifted from its "dynamic zero-COVID" policy and relaxed intercity travel restrictions. During this period, the patterns of disease epidemics exhibited distinct trends, which can be broadly categorized into four types. The first type includes diseases such as HAV, typhoid and paratyphoid fever, AHC, dysentery, other infectious diarrhea, AIDS, HCV, syphilis, scarlet fever, tuberculosis, and mumps. These diseases demonstrated a seasonal or jagged pattern with an overall decreasing trend in prevalence (Fig. 4A, 4C, 4D, 4E, 4G, 4O, 4R, 4S, 4U, 4V, 4W). The second type, represented by rubella, dengue fever, and malaria, experienced a substantial reduction in incidence, reaching very low levels, and lost their seasonal variation (Fig. 4I, 4X, 4L). The third type is commonly observed among natural focal diseases and bloodborne and sexually transmitted diseases. These diseases maintained their seasonal or jagged patterns with little overall change or even an increase in reported cases. Examples include brucellosis, HFRS, Japanese encephalitis, hydatidosis, typhus, gonorrhea, and HBV (Fig. 4H, 4J, 4K, 4M, 4N, 4P, 4Q). The final type of disease exhibited a decrease in prevalence followed by a gradual recovery to a normal trend. This category includes HEV,
HFMD, and pertussis (Fig. 4B, 4F, 4T). Clustering analysis using the RR grouped the 24 NIDs into two categories. Pertussis, dengue fever, rubella, mumps, and scarlet fever were identified as diseases highly susceptible to PHSMs. The remaining 18 NIDs were considered less affected by PHSMs (Fig. 5K). Dengue fever and rubella were most strongly impacted by PHSMs during PHSMs period II, maintaining extremely low levels of prevalence, with RR values of 0 (IQR: 0-0.01) and 0.04 (IQR: 0.02–0.09) respectively (Fig. 5D, 5H). Typhus, HEV, and gonorrhea were less affected, with RR values of 1.00 (IQR: 0.76–1.23) for typhus (V = 247, P = 0.99) and 1.00 (IQR: 0.91–1.11) for gonorrhea (V = 252, P = 0.95). Brucellosis experienced a significant increase with an RR of 1.62 (IQR: 1.39–2.04), being the only NID with an RR significantly greater than 1 (P< 0.001).

In December 2022, the Chinese government shifted from the "dynamic zero-COVID" policy and adopted a new approach aimed at coexisting with the virus during the epidemic period. Similar to the trend observed when strict PHSMs were implemented in 2020, all four categories of communicable diseases exhibited a pattern of initial sharp decline followed by an increase in cases (Fig. 2). Even brucellosis, which had consistently high growth during PHSMs period II, saw its RR drop to 0.89 in December 2022. Clustering analysis revealed that the other 23 NIDs were significantly impacted (Fig. 5L). However, the impact on bloodborne and sexually transmitted diseases remained relatively limited, with syphilis being the most affected, with an RR value of 0.54 (IQR: 0.44–0.71).

**Relation between PHSMs strength and relative risk**

During the implementation of strict PHSMs, similar results to those observed during the epidemic period were achieved in PHSMs period I. However, in PHSMs period II, the number of reported cases increased due to a lower intensity of PHSMs implementation compared to PHSMs period I, coupled with seasonal peaks. Clustering analysis identified 8 NIDs that were highly influenced by PHSMs interventions (Fig. 5I, 5K). These diseases primarily involved respiratory infectious diseases (4 NIDs) and natural infectious diseases (3 NIDs), while no diseases from the bloodborne and sexually transmitted diseases category were included, aligning with the overall trend (Fig. 1B).

Among these diseases, only HFMD displayed a high prevalence and significant susceptibility to the impact of PHSMs, evidencing the most substantial cumulative decline in reported instances during the periods of PHSM implementation when compared to other NIDs. Specifically, HFMD experienced a reduction of 3,131,840 cases (52.80%). Additionally, 7 NIDs exhibited both a low incidence and minimal susceptibility to PHSM influences, including dengue fever, Japanese encephalitis, malaria, pertussis, scarlet fever, mumps, and rubella. Cross-correlation analysis indicated that the correlation coefficients between PHSMs stringency and the RR for HFMD, malaria, scarlet fever, and mumps occurred in the same month, with correlation coefficient values of 0.22, 0.66, 0.25, and 0.23 respectively. However, for dengue fever and malaria, the correlation coefficient values displayed two peaks: one in the same month and another with a 3-month lag. Both peaks in dengue fever had similar correlation coefficient values (0.18 vs. 0.20). Similarly, Japanese encephalitis exhibited two high correlation coefficient values in the same
month and with a 6-month lag (0.18 vs. 0.23). In the case of rubella, no lag time showed a weak association or higher strength. Notably, there was no observed positive correlation for pertussis (Fig. 6).

**Discussion**

In this study, we conducted a modeling study on NIDs, which were categorized into four groups based on their primary mode of transmission. To evaluate the impact of PHSMs on the dynamics of these 24 NIDs, an ensemble model was employed to comparatively analyze the transmission characteristics across three distinct periods: PHSMs period I, PHSMs period II, and the epidemic period. Furthermore, we aimed to evaluate the impact of PHSMs on the dynamics of these 24 NIDs. Our findings revealed distinct seasonal patterns in the incidence of different NID categories, exhibiting variations across the studied periods. Comparative analysis of predicted and actual data identified 8 NIDs susceptible to PHSMs, including HFMD, dengue fever, Japanese encephalitis, malaria, pertussis, scarlet fever, mumps, and rubella (Fig. 5J, 5K). Notably, rubella and malaria exhibited a close-to-elimination incidence across the three periods (Fig. 5C, 5J). The decline in malaria cases was primarily attributed to stringent travel restrictions, while the decrease in rubella can be attributed to the increased coverage of MR (measles and rubella) and MMR (measles, mumps, and rubella) vaccine\(^{17,18}\).

Cross-correlation analysis revealed the highest relative correlation coefficients for HFMD, dengue fever, malaria, scarlet fever, and mumps occurring within the same month, suggesting these diseases were immediately impacted following the implementation of PHSMs. This can be attributed to the immediate effectiveness of PHSMs in controlling the spread of these diseases, which are primarily transmitted through direct contact and respiratory droplets. The quick response of these diseases to PHSMs may also be related to their relatively short incubation periods, which allows for a rapid reflection of changes in transmission dynamics following the implementation of PHSMs. However, Japanese Encephalitis, categorized under susceptible NIDs, may demonstrate a larger RR due to its low monthly incidence (Fig. 4K) and the potential instability of the model, where minor modifications can induce significant RR fluctuations. Despite Rubella having a brief incubation period, the actual case count approaches nullity due to the synergistic effect of vaccines and PHSMs (Fig. 4X), rendering its RR relatively insensitive to variations in PHSMs.

The seasonal variations in NIDs observed before the pandemic can primarily be attributed to the interplay between transmission models and behavioral patterns\(^{19,20}\). Respiratory diseases, such as mumps, exhibited higher prevalence during the winter\(^{21,22}\). This phenomenon can be ascribed to increased indoor gatherings in enclosed spaces without physical distancing, facilitating virus transmission\(^{23}\). Additionally, the low humidity and temperature during winter were crucial factors increasing vulnerability to upper respiratory tract infections\(^{24}\). Some studies have suggested that seasonal variations can impact immune responses, potentially rendering individuals more susceptible to infections during specific times of the year\(^{25,26}\).
The substantial decrease of 24 NIDs during PHSMs period I (Fig. 1B) can be attributed to a confluence of factors. Stringent PHSMs enacted by the Chinese government served as an effective barrier to interpersonal contact and disease transmission. Parallelly, the advent of the Omicron BA.2 pandemic significantly heightened public awareness and vigilance towards infectious diseases, prompting the widespread adoption of protective behaviors. The reduction in NIDs observed during this period can be partially attributed to the decreased mobility of infected individuals, coupled with an increased propensity to wear masks. Additionally, compliance with PHSMs extended even to susceptible individuals, even in the absence of government enforcement. This collective adherence significantly contributed to the observed decrease in the transmission of respiratory viruses, underscoring the effectiveness of PHSMs in the containment of infectious diseases.

However, the impact of PHSMs varied across diseases with different modes of transmission. Respiratory infectious diseases, notably HFMD and mumps, displayed a pronounced susceptibility to PHSMs. Conversely, the impact on bloodborne and sexually transmitted diseases was more limited, consistent with previous research findings. In the case of most respiratory diseases, the implementation of PHSMs significantly curtailed their transmission (Fig. 5E), reaffirming previous studies on the efficacy of PHSMs in controlling these diseases. This reduction can be attributed to the primary transmission route of these diseases, i.e., respiratory droplets, which can be effectively managed by measures such as mask-wearing, physical distancing, and improved ventilation. In contrast, bloodborne and sexually transmitted diseases, primarily transmitted through direct contact with infected bodily fluids, may not be as effectively mitigated by these measures. It is important to note, however, that while the median of RR for AIDS, syphilis, HCV, and HBV were generally less than 1, indicating a reduced impact, this does not imply that these diseases were entirely unaffected (Fig. 5E). Interestingly, the incidence of gonorrhea increased during 2021 (Fig. 3P), potentially due to its relatively short incubation period (1–9 days), which resulted in quick responses to PHSMs. In contrast, diseases such as AIDS, syphilis, HCV, and HBV, which typically exhibit longer incubation periods (over a month), may experience a substantial delay between symptom onset and reporting.

Travel restrictions have a profound impact on the transmission dynamics of zoonotic infectious diseases, particularly those with short incubation periods and high susceptibility to imported cases, such as dengue fever and malaria. These diseases are primarily transmitted by mosquitoes. The winter season, which creates an inhospitable environment for mosquitoes, naturally suppresses the spread of these diseases throughout most regions of mainland China. During the study periods, stringent international travel restrictions, combined with the synchronization between the isolation period and the incubation period for imported cases of dengue fever and malaria, frequently facilitated the detection of these cases during quarantine. Consequently, local outbreaks of these diseases were markedly decreased during PHSMs periods. However, a contrasting pattern was observed in the case of brucellosis, another zoonotic infectious disease. The monthly incidence of brucellosis recorded a significant surge during PHSMs periods. This divergence can potentially be ascribed to the enforcement of various PHSMs which may have inadvertently impeded farmers’ timely access to veterinary services, thereby escalating the risk of
brucellosis transmission among livestock. Furthermore, the epidemic may have precipitated food shortages in rural areas, spurring an increase in home breeding or poultry farming. This surge in close human-animal interactions, particularly with brucellosis-infected animals, may have inadvertently amplified the risk of human infection.

Our study has several limitations. Firstly, we focused on 24 NIDs instead of all infectious disease, particularly leaving a gap in the study of respiratory diseases. While influenza was excluded due to its reliance on sentinel surveillance, this does not undermine the overall conclusion of the study. Respiratory diseases continue to exhibit high incidence and are notably susceptible to PHSMs. The selection of 24 high-incidence NIDs for this study is indicative of the broader trends observed across all NIDs. Additionally, the reported incidence may be influenced by reporting biases, delays between reporting and disease onset, and data quality concerns. These factors potentially affect the accuracy of the predictions generated by our model. Thirdly, the association between model selection and disease types remains nebulous and may be influenced by seasonality, warranting adjustments tailored to individual disease characteristics. Finally, inherent limitations of time-series models must be acknowledged. These include the inability to capture sudden, unexpected events and the direct impact of intervention measures on disease transmission. These models also rely on assumptions about data being stationary and following certain trends. Therefore, when comparing our results with those from other studies, it is essential to consider these limitations with due diligence.

Our research revealed that the implementation of PHSMs in response to various SARS-CoV-2 variants can significantly impact the transmission dynamics of most infectious diseases. Intriguingly, the relaxation of all PHSMs by the Chinese government did not trigger a significant resurgence in NIDs. Instead, widespread self-isolation practices adopted by the population after infection with the Omicron BA.2 variant restrained the transmission of other infectious diseases. This period of restricted transmission was, however, followed by a more extensive spread of diseases such as influenza and mycoplasma pneumoniae. Our findings emphasize that while PHSMs can provide an effective short-term solution in controlling the spread of infectious diseases, their long-term application may inadvertently lead to a decrease in population immunity, thus creating a potential environment conducive to large-scale outbreaks. For a more sustainable and long-term management of infectious disease transmission, it is imperative to prioritize the development and widespread implementation of effective vaccines, similar to the successful approach observed with the MMR vaccine.

**Methods**

This study adopts a modeling methodology to examine the patterns of 24 NIDs in mainland China, excluding Hong Kong SAR, Macau SAR, and Taiwan province. The diseases under analysis include pertussis, HCV, HEV, brucellosis, dengue fever, tuberculosis, rubella, AHC, HAV, dysentery, gonorrhea, HFRS, AIDS, mumps, syphilis, malaria, various other infectious diarrheal diseases, typhoid and paratyphoid fever, HBV, HFMD, scarlet fever, Japanese encephalitis, hydatidosis, and typhus. For analytical purposes, these diseases are categorized into 4 groups based on their primary modes of transmission: intestinal
infectious diseases, respiratory infectious diseases, zoonotic infectious diseases, and bloodborne and sexually transmitted diseases. Specifically, bloodborne and sexually transmitted diseases include gonorrhea, HBV, HCV, and syphilis. Intestinal infectious diseases include AHC, dysentery, HAV, HEV, HFMD, other infectious diarrheal diseases, and typhoid and paratyphoid fever. Zoonotic infectious diseases comprise brucellosis, dengue fever, HFRS, hydatidosis, Japanese encephalitis, malaria, and typhus. Lastly, respiratory infectious diseases include mumps, pertussis, rubella, scarlet fever, and tuberculosis (Fig. 1A).

Data Collection

The data was collected from the monthly Notifiable Infectious Diseases Reports published by the National Health Commission of China. These reports aggregate data derived from the National Notifiable Disease Surveillance System, which was established in 2004. The study period spans from January 2008 to July 2023. To align with the different phases of the SARS-CoV-2 epidemic in China, the study period is divided into distinct periods. The period from January 2008 to December 2019 is referred to as the pre-epidemic period. January 2020 to March 2020 is categorized as the PHSMs I period, April 2020 to October 2022 as the PHSMs II period, and November 2022 to March 2023 as the epidemic period. Additionally, a dashboard has been created to facilitate readers in querying and downloading the data used in this study (https://kanggle.shinyapps.io/NIDs/).

Throughout the years, the National Notifiable Disease Surveillance System has undergone continuous enhancements, and as of October 2023, it encompasses data from 41 NIDs. However, we have only included 24 infectious NIDs while excluding 17 NIDs in this study due to data defects: monkeypox, a newly emerging infectious disease, was only incorporated into the NIDs from September 2023 and lacks historical monitoring data. Influenza, due to its detection method involving specialized sentinel monitoring, also has been excluded. Furthermore, diseases such as plague, cholera, rabies, anthrax, H7N9 avian influenza, highly pathogenic avian influenza in humans, poliomyelitis, SARS, diphtheria, filariasis, and leprosy have been virtually eliminated, with reported cases nearing zero. Similarly, schistosomiasis, leptospirosis, meningococcal meningitis, and visceral leishmaniasis, although still having reported cases, exhibit low prevalence, rendering them unsuitable for time series modeling and thus have been excluded. Measles, nearing elimination status in China, and having a relatively low number of reported cases, has also not been included in the analysis.

Considering the varying intensities of PHSMs during different periods, we utilize the stringency index to measure the overall intensity of PHSMs nationwide. The stringency index is a composite measure based on thirteen policy response indicators, including school closures, workplace closures, travel bans, testing policies, contact tracing, face coverings, and vaccine policies. It is rescaled to a value from 0 to 100.

Model building

A single time series model alone is insufficient to capture the epidemic patterns of all 24 diseases, due to the diverse epidemiological characteristics and temporal distribution of different infectious diseases.
Therefore, the ensemble forecasts, encompassing neural network model, Bayesian structural time series model, prophet model, exponential smoothing (ETS) model, SARIMA model, and hybrid model that combine SARIMA, ETS, STL (seasonal and trend decomposition using loess), and neural network components. Each model demonstrates advantages depending on the specific epidemic characteristics of different diseases. The neural network model excels in capturing nonlinear trends and complex relationships. Prophet model automatically handles long-term trends, seasonality, and holiday effects. Bayesian structural time series models address uncertainty and randomness, the ETS model is suitable for smoothing data and short-term forecasting, while the SARIMA model considers trends, seasonality, and autoregressive terms simultaneously. By combining the weighted averages of the neural network, STL, ETS, and SARIMA models, a hybrid model can better capture the epidemic trends of different infectious diseases.

**Neural network model**

We utilized a feed-forward neural network with lagged inputs and a single hidden layer, containing half as many neurons as the input layer. Multiple networks were trained with distinct initial random weights, and their forecasts were averaged. The network was calibrated for single-step predictions, while multi-step projections were derived recursively\textsuperscript{40}.

**Bayesian structural time series models**

These models were executed using the 'bsts' package in R (version 4.3.1, R Core Team, Vienna, Austria), incorporating structural components for trend, seasonality, and regression effects. Priors were selected via the empirical Bayes method, and we conducted 500 MCMC simulations to ensure convergence\textsuperscript{41, 42, 43}.

**Prophet Model**

Prophet employs an additive model to fit non-linear trends with components for yearly, weekly, and daily seasonality, as well as holidays. It excels with data exhibiting strong seasonal patterns and copes well with missing data, trend shifts, and atypical values, available in R\textsuperscript{44}.

**ETS model**

The ETS model's three parameters were automatically determined using a log-likelihood optimization criterion, guided by the Akaike Information Criterion (AIC)\textsuperscript{45, 46}.

**SARIMA Model**

The SARIMA model's parameters \((p, d, q) \times (P, D, Q)s\) were systematically selected using a stepwise algorithm informed by the AIC, facilitated by the 'auto.arima' function in R\textsuperscript{46}.

**Hybrid Model**
Our hybrid approach synthesizes the predictive power of SARIMA, ETS, STL, and neural network models. By assigning weights to each base model's forecast according to its out-of-sample error rate and normalizing them to sum to unity, we recalibrate these weights annually to better align with the evolving disease patterns\textsuperscript{47}.

To estimate the baseline epidemic trend of the 24 NIDs from January 2020 to January 2023 (without PHSMs and SARS-Cov-2 transmission), this study uses monthly NIDs incidence from January 2008 to December 2017 as the training set for baseline modeling, and data from January 2018 to December 2019 as the test set to evaluate the performance of different models. To assess the performance of these models on the test sets, three evaluation indicators are utilized: root mean square error (RMSE), R-squared, and mean absolute error (MAE). As these indicators hold varying degrees of significance, the study first calculates the negative values of RMSE and MAE, followed by the application of z-normalization using the provided formula to transform them into standardized values:

\[
Z_{m,d} = \frac{x_{RMSE,m,d} - \mu_{RMSE,d}}{\sigma_{RMSE,d}} + \frac{x_{R2,m,d} - \mu_{R2,d}}{\sigma_{R2,d}} + \frac{x_{MAE,m,d} - \mu_{MAE,d}}{\sigma_{MAE,d}}
\]

**Statistical Analysis**

After establishing the optimal model, this study trained the model using data from 2008 to 2019. The model was then applied to predict the incidence of various infectious diseases during three different periods. By comparing the predicted results with the actual incidence, the study calculated the RR of PHSMs for different NIDs. The formula for calculating RR is the ratio of the incidence during PHSMs to the incidence without PHSMs:

\[
RR = \frac{I_a}{I_m}
\]

The value of RR determines the impact of PHSMs on the risk of disease incidence. RR less than 1 indicates that PHSMs can reduce the risk, while RR greater than 1 indicates that PHSMs can increase the risk. The significance of the difference between RR and 1 was assessed using two-sample Wilcoxon tests with a significance level of 0.05.

To comprehensively understand the influence of PHSMs on the incidence of NIDs, we further explored the association between the stringency index and RR. Considering the variations in incubation periods of different infectious diseases and potential lag effects of PHSMs, this study utilized a generalized additive model to analyze the combined effects of the monthly stringency index, both without and with a lag of 1 to 6 months, on disease incidence and reduction ratios. The monthly stringency index was treated as a factor that mirrors the stringency of the current PHSMs. Concurrently, the stringency index with a lag of 1 to 6 months was incorporated into the model to account for potential lag effects of PHSMs\textsuperscript{48}. By incorporating these factors into the model, the study investigated the relationship between the stringency index and disease incidence and RR, as well as the influence of lag effects. The correlation coefficient
value less than 0.2 was considered unrelated, 0.2 to 0.4 indicated a weak association, 0.4 to 0.6 indicated moderate association strength and values greater than 0.6 indicated a strong association\textsuperscript{49}.

Moreover, cluster analysis was utilized to classify different NIDs based on RR and monthly incidence, aiming to further analyze the relationship between disease incidence and susceptibility. To ensure the reliability and reproducibility of our findings, we used hierarchical k-means clustering based on Euclidean distance and Ward.D2 method. In the clustering process, the Ward.D2 method was first utilized to split the hierarchical tree into k clusters. Subsequently, the centroids of each cluster were calculated and served as the initial cluster center for the k-means clustering algorithm based on Euclidean distance\textsuperscript{50}. Using this approach, 24 NIDs were classified into four categories: high incidence with high susceptibility, high incidence with low susceptibility, low incidence with high susceptibility, and low incidence with low susceptibility. All statistical analyses were conducted using R.

**Declarations**

**Data availability**

The monthly incidence data of 24 NIDs used in this study is accessible through the GitHub repository (https://github.com/xmusphlkg/code_PHSM). Furthermore, a shiny dashboard has been developed to enhance data sharing and exploration, which can be accessed via the following link (https://kanggle.shinyapps.io/NIDs/). This interactive interface enables visualization and analysis of the data utilized in this study.

**Code availability**

The R code used for statistical analysis and Fig. generation is also available at the GitHub repository (https://github.com/xmusphlkg/code_PHSM).

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**Author contribution**
Conceptualization: TMC, TXX, KGL, JR, LL. Investigation: HJW, YKZ, RXZ. Methodology: KGL, LL, JR, TMC, HJW. Software: KGL, YKZ, HJW, ZCZ, HL. Validation: KGL, LL, TXX. Writing - original draft: KGL, JR, LL. Writing - review & editing: TMC, RXZ, BA, YW, HMQ, TXX. All authors read and approved the final manuscript.

Competing interests
The authors declare that they have no competing interests.

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**Figures**

**Figure 1**

Temporal trends and cumulative incidence of four categories of notifiable infectious diseases (NIDs) in China from January 2008 to July 2023. (A) Cumulative incidence of 24 NIDs, categorized by their...
respective modes of transmission, over the period from January 2008 to July 2023. The size and color of each circle represent the cumulative incidence and severity levels, respectively. AIDS including human immunodeficiency virus infections. Dynthesia includes bacterial dysentery and amoeba dysentery. (B) Epidemic curves for the 4 categories of NIDs, were segmented into four distinct periods: the pre-epidemic period (January 2008 to December 2019), the PHSMs period I (January 2020 to March 2020), the PHSMs period II (April 2020 to October 2022), and the epidemic period (November 2022 to March 2023). (C) Percentage of monthly incidences for the 4 categories of NIDs.
Figure 2

Temporal variation in the monthly incidence of notifiable infectious diseases (NIDs) in China from January 2008 to July 2023. (A) Intestinal infectious diseases. (B) Blood borne and sexually transmitted diseases. (C) Respiratory infectious diseases. (D) Zoonotic infectious diseases. The heatmap represents normalized monthly incidence data for each NIDs, with color intensity corresponding to the normalized monthly incidence. Instances where the normalized monthly incidence exceeds the range of -5 to 10 are highlighted with a black box.

Figure 3

Figure 4

Figure 5

incidence. Cluster tree of 24 NIDS risk ratios during PHSMs period I (January 2020 to March 2020) (J), PHSMs period II (April 2020 to October 2022) (K), and the epidemic period (November 2022 to March 2023) (L). In these panels, red and green represent higher and lower risk ratios.

Figure 6

Cross-correlation analysis of 8 notifiable infectious diseases (NIDs) susceptible to PHSMs.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplementary1.docx
- Supplementary2.xlsx