Li, X.; Kang, D.; Zhang, Ying; Wei, G.; Liu, W.; Fang, Li-Qun; Yang, H.; Cao, Wu-Chun
Epidemic trend of measles in Shandong Province, China, 1963-2005
Public Health, 2012; 126(12):1017-1023

*Manuscript

Epidemic trend of measles in Shandong Province, China, 1963–2005

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SUMMARY

Objectives: Although measles is a vaccine-preventable infectious disease and the measles vaccine is safe and effective, it still poses a serious threat to the health of children and susceptible populations in China every year. This study aimed to investigate the epidemiological characteristics of measles in Shandong Province, China, including its spatial distribution pattern, in order to have a precise prediction of measles epidemics for better public health strategic planning and resource allocation.

Study design: Longitudinal data study.

Methods: This study was based on the surveillance dataset of measles from all 17 regions (cities) in Shandong Province between 1963 and 2005. Geographical Information Systems and piecewise exponential smoothing of logarithmic transformed data were applied with consideration of the spatial and temporal features of the data. The parameters of epidemic peaks were estimated by filtering off the drifting long-term trends.

Results: Measles presented in almost all regions in Shandong Province with different spatial distribution over the 43-year study period. The incidence of measles was very high in the pre-vaccination period, with an average incidence of 617.61/100,000 population in 1963. With the implementation of vaccination, the average incidence of measles decreased to 3.63/100,000 population in 2005, the periodicity died out and the trend remained at a stable low level. Outbreaks have been reported recently.

Conclusions: This study identified the effects of different strategies on the incidence of measles observed in Shandong, China, and will provide valuable information to assist local and national public health policy making. There are still some challenges to improve vaccination coverage and efficacy in order to eliminate measles in China.

Strengthening surveillance will be essential in the framework of the anticipated global elimination campaign for measles.

Keywords:

Epidemic trend

Measles elimination

China

<A>Introduction

Measles is a severe respiratory infectious disease caused by measles virus. Unvaccinated populations are susceptible to measles virus.[1–3] Healthy and well-nourished children, if unvaccinated, are at risk of measles and its severe complications such as pneumonia, diarrhoea and encephalitis. Measles can be deadly in vulnerable populations, such as poorly nourished young children, especially those with insufficient vitamin A, or whose immune systems have been weakened by human immunodeficiency virus/acquired immunodeficiency syndrome or other diseases.[4] As such, the vast majority of measles deaths occur in developing countries.[5–8] Despite impressive global efforts, more than 400 children die worldwide every day from this vaccine-preventable infection.[8] Measles accounts for over 40% of the 1.4 million deaths each year due to vaccine-preventable diseases.[8,9]

The genotype of the measles virus is relatively stable in China. Genotype H_1 is the predominant indigenous measles virus genotype in mainland China, and H_{1a} is the predominant subgenotype in recent years in mainland China.[10–12] Infected individuals eventually acquire persistent natural immunity as human beings are the only host. The related vaccine is safe and effective. Global vaccination programmes have led to a worldwide decrease in the occurrence of measles,[13–15] with some areas documenting an interruption of transmission of the endemic virus.[16] Therefore, it is possible in both theory and practice to eliminate measles completely. Elimination of measles was recognized in World Health Organization American regions in 2000. The European, Eastern Mediterranean and Western Pacific (including China) regions have endorsed a plan to eliminate measles by 2010 and 2012, respectively.[15] In order to achieve this, it is important to investigate the character of measles epidemics and forecast the trend of measles precisely.

Early reports of measles cases in Shandong Province, China dated back to 1951.[17–19] Promotion of vaccination in pilot regions started in 1967. With the enforcement of vaccination among all newborn babies, measles outbreaks subsequently declined dramatically.[17,18]

This study aimed to reveal the spatiotemporal distribution and seasonality of measles from 1963 to 2005 in Shandong Province, given the changing strategies for the prevention and control of measles over this long period in China. By identifying high-risk regions, this study is of particular significance in order to improve current policies related to measles immunization and surveillance programmes, so that the task of eliminating measles can be completed successfully by the planned time.

<A>Methods

<B>Data source

Monthly confirmed cases of measles reported to the Centre for Disease Control and Prevention of Shandong (CDC) from 1963 to 2005 were reviewed. All the cases of measles data from 1963 to 2005 were obtained from the Shandong CDC. All measles cases were initially diagnosed by clinical symptoms. Patient blood samples were collected and sent to Shandong CDC laboratories for serological confirmation. All cases included in this analysis were laboratory confirmed. In China, measles is a nationally notifiable disease, and hospital physicians are legally required to report all cases of measles to the local health authority within 12 h. Therefore, the rate of under-reporting was very low throughout the study period and did not affect the results.

The total population of cases was analysed. Annual incidence rates (per 100,000 population) were calculated based on Shandong census data reported by the statistical yearbook of Shandong Province.[20]

<B>Data adjustment

Over the 43-year study period, there were some changes in municipal regions in Shandong Province. Therefore, justification was performed according to these changes. For example, Dongying, Weihai, Rizhao and Laiwu were separated from the adjacent regions in 1984, 1988, 1990 and 1993, respectively. Total populations and number of measles cases were adjusted accordingly.

<B>Phase partition of measles epidemics

Referring to the historical periods of control of measles in China, combined with different strategies in Shandong Province,[17–19] the epidemic evolved from 1963 to 2005 in five stages:

Stage I: Early period prior to vaccination (1963–1966). Incidence of measles was in a natural infection state.

Stage II: Promotion of measles vaccination (1967–1978). No refrigerant equipment was available over this time period, and the measles vaccine was unstable at high temperatures. The measles vaccine had to be used all at once to ensure effective immunity. Usually, vaccination was available twice a year for each region, when all children were gathered for immunization with a very low (approximately 20%) coverage rate, so the artificially acquired immunity could be completed in 5 years.

The number of immunized children in each county is required to be reported to Shandong CDC by law, based on the immunization card for each child collected by staff at local (village) clinics. Staff at the Shandong CDC then collated the data and estimated the average coverage rate using the total number of actually immunized children divided by the total number of children who should be immunized. The vaccination coverage in Stages III, IV and V was evaluated using the same method (please contact the corresponding author for further information on estimation).

Stage III: Planned regular vaccination (1979–1997). There were two phases in this period. Before 1985, planned vaccination was extended in experimental units. From 1985 onwards, all of Shandong Province was covered. The estimated vaccination coverage was increased to 80%. The surveillance sites were developed in 1994 in Shandong Province.

Stage IV: Accelerated measles control (1998–2004). Surveillance networks were established to provide support to surveillance sites and strengthen vaccination coverage (e.g. supplementary immunization activities, coupled with further efforts to improve routine measles vaccination coverage). The estimated vaccination coverage was approximately 90%.

Stage V: Measles elimination (2005–). This period observed the achievement and maintained a high coverage of vaccination. The first dose of measles-containing vaccine was ensured among all children by the age of 8 months in every region through routine immunization services. A second opportunity for measles immunization (or through a second routine dose) was provided for all children. Surveillance systems were reinforced to ensure vaccination coverage of 95%.

<B>Analysis approaches

Descriptive analyses, piecewise exponential smoothing technique and a time series analysis were performed based on the above five stages with different measles control strategies.

Measles epidemics are affected by the method of immunity prevention. In order to discuss the approach to forecast the incidence of the disease, this study attempted to use piecewise exponential smoothing analysis to separate the season term and trend term of the incidence of measles.[21]

Logarithmic transformation was performed because of the incidence trend.[21] Rather than keep the initial five stages, the dataset was regrouped into three time periods (i.e. 1963–1976, 1977–1986 and 1987–2005) because these time periods had similar decreasing trends in the incidence of measles, which improved the effectiveness of forecasting.

The exponential smoothing model[21] was developed to construct the basic model, which allows examination of the effects of seasonality and long-term trends:

$$y_t = \beta_0 + \beta_1 t + \sum_{i=1}^{11} \delta_i IND_{ti} + \varepsilon_t$$

where β is the regression coefficient for trend term, δ_i is the seasonal effect for the i^{th} month, IND_{ti} is denoted the instruct function for i^{th} month t^{th} year, and ε_t is the residuals. Based on the least mean square error, optimization of the smoothing coefficient was achieved.

The exponential smoothing technique was adopted as this is a time series analysis based on a moving average, which is the preferred technique for forecasting purposes, controlling for potential confounding of seasonality and long-term trends. In addition, using a recent database, the model has a good fit and is able to forecast future trends in the incidence of measles.

<A>Results

<B>Epidemic trend and features of measles in Shandong Province

Overall, there were 4,793,983 notified cases of measles in Shandong Province China over the 43-year study period.

Fig. 1 shows the temporal pattern of the incidence of measles in Shandong Province from 1963 to 2005. The overall declining trend is clear, with the annual average incidence decreasing from 617.61/100,000 population in 1963 to 3.63/100,000 population in 2005. The highest annual average incidence was 1260/100,000 in 1965. Before 1985, there was a 3–4-year periodic recurrent pattern, distributed in 1970–1973, 1976–1977 etc., which means there was a peak in incidence every 3 or 4 years. Since 1985, the incidence of measles has remained at a relatively low level.

<insert Fig 1 near here>

<B>Seasonality of measles records (1963–2005)

Fig. 2 shows the seasonal distribution throughout the study period. Peaks in the incidence of measles mainly occurred from March to May each year.

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<B>Spatial distribution of the incidence of measles

Fig. 3 shows the trend in the incidence of measles in different regions and periods. Stage I had the highest incidence, ranging from 1205.15/100,000 population to 481.31/100,000 population. The incidence in Stage II had decreased dramatically compared with Stage I. The incidence in Stage IV was the lowest, ranging from 2.82/100,000 population to 0.04/100,000 population. Notably, the incidence of measles increased in Stage V, and was approximately 3.4 times higher than the incidence in Stage IV.

<insert Fig 3 near here>

Measles was observed in almost all regions in Shandong Province, but the spatial distribution varied over the 43-year study period. In Stage I, measles broke out in all regions and the incidence was very high, especially in Jinan and Qingdao. In Stage II, the incidence was also higher in Heze and Linyi in the west of Shandong Province. In Stage III, the incidence of measles decreased significantly. Outbreaks of measles were reported in Heze, Zaozhuang and Linyi, located in the west of Shandong Province. In Stages IV and V, high-risk regions were found in Binzhou, in the north of Shandong Province (note: Dongying, Weihai, Rizhao and Laiwu were separated from the adjacent regions in 1984, 1988, 1990 and 1993, respectively).

Fig. 4 suggests that the effect of seasonality was consistent in Stages I–III, while the effect of trend was dramatically different. In Stage I (1963–1976), namely the natural infection period and the initial stage of measles vaccination, periodic outbreaks were observed. In Stage II (1977–1986), measles vaccination was promoted, the rate of outbreaks declined and periodicity died out. In Stage III (1987–2005), the enforced vaccination procedures reduced the number of outbreaks, and the incidence remained at a stable low level.

<insert Fig 4 near here>

<A>Discussion

This study identified seasonality and periodicity of the incidence of measles before measles vaccination, when measles virus was in a natural infectious state. Consistent with observations from other countries,[3] there were outbreaks of measles every 3–4 years in Shandong Province.[22] After implementation of measles vaccination activities, especially programme immunity, the number of epidemics decreased and incidence declined quickly.

The variation in vaccination efforts in different regions led to an imbalance in the incidence of measles across the regions. From Stage II to Stage IV, the incidence of measles remained high. The reasons may include lower economic status of local residents, low vaccination coverage and poor surveillance networks in these regions. The reason for the high incidence of measles in Binzhou in Stage V was mainly due to an outbreak that accounted for 80% of the total cases in Shandong Province.[23] Increasing numbers of immigrants could be another reason for the increased incidence of measles in Stage V.[23] The flow of immigrants between local regions caused the spread of the disease from rural regions to cities. The incidence of measles in Zaozhuang was high from 1994 to 2004. Zaozhuang is in the south of Shandong Province, the density of the population is low compared with other regions, and the population had a relatively low socio-economic status. In addition, vaccination coverage was low at that time. However, the incidence of measles decreased gradually in Zaozhuang from 2005, but remained high in Bingzhou. One of the strengths of this study is the combined piecewise exponential smoothing technique of time series analysis, and the consideration of different stages of strategies in prevention and control to identify dynamic features of the measles epidemic. This method may be useful to study other vaccine-preventable infectious diseases (e.g. chincough, lockjaw and diphtheria) because it can separate the seasonality and trend terms in different stages, expose the epidemic's dynamic character and thus give a reasonable forecast for the future. This method provides a high-quality, stable evaluation for precise prediction.

Based on the trend analysis data from previous years in this study, the measures of prevention at different stages had a tremendous effect on the epidemic dynamics of measles. According to the results of the last stage, the incidence of measles should remain at a stable low level. Progress towards measles elimination in 2012 in Shandong Province is a little pessimistic. Some measures should be strengthened to eliminate measles, especially from the Government at all levels and strategic planning of public health. Efforts from the Government should be reinforced to widen immunization coverage by routine vaccination projects, to enhance disease surveillance, and to prevent and control outbreaks.

As a vaccine-preventable infectious disease, an effective surveillance system is crucial to ensure the elimination of measles.[24–26] This would serve as an early warning system, identifying public health emergencies, guiding public health policy and strategies, documenting the impact of an intervention or progress towards specified public health targets/goals, and monitoring the epidemiology of a condition to set priorities. It should be acknowledged that in addition to detection and notification, a surveillance system would also assist in the collection and consolidation of pertinent data, investigation and confirmation (epidemiological, clinical and/or laboratory) of cases or outbreaks, routine analysis and creation of reports, feedback of information to those providing the data, and feed-forward (i.e. the forwarding of data to more central levels) reporting of data to the next administrative level.

This study has some limitations. Firstly, it is acknowledged that due to the lack of the annual population structure from all the study areas over the lengthy time period, standardization of the incidence of measles over the years was not possible. Secondly, different time-mathematical models used to analyse time series data of infectious diseases (e.g. the seasonal autoregressive integrated moving average model[27]) may have influenced the results. In order to improve forecasting ability of the incidence of measles, one of the directions for future study is comparison with various mathematical models. Considering the complicated effect factors for the transmission of measles in Shandong, another limitation of this study is that some potential confounding factors (e.g. changes in population structure, immigration and socio-economic status) could not be included in this study due to data availability. It is recommended that collaboration within multisectoral government offices is necessary to improve the strategic planning of prevention and control of measles in China.

<A>Conclusions

This study has discovered the various effects of different strategies on the incidence of measles in Shandong, China, which will provide valuable information to assist local public health policy making and can also be applied at national level. There are still some challenges to improve vaccination coverage and efficacy in order to eventually eliminate measles in China. Strengthening surveillance will be essential in the framework of the anticipated global elimination campaign for measles.

Ethical approval

None sought.

Funding

This study was supported by the National Science Fund for Distinguished Young Scholars (Grant No. 30725032), the Special Program for Prevention and Control of Infectious Diseases (Grant Nos. 2008ZX10004-012 and 2009ZX10004-720), and the Natural Science Foundation of China (No. 305903740). This study was also supported by Shandong Provincial Natural Science Fund (No. ZR2010HM126).

Competing interests

None declared.

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Fig. 1–Average annual incidence of measles in Shandong Province, 1963–2005.

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Fig. 2–Average monthly incidence of measles in Shandong Province, 1963–2005.

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Fig. 3–Spatiotemporal distribution of the incidence of measles in 17 municipal regions in different stages.

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Fig. 4–Seasonality and trend effect of the incidence of measles in different stages.

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Figure(s)
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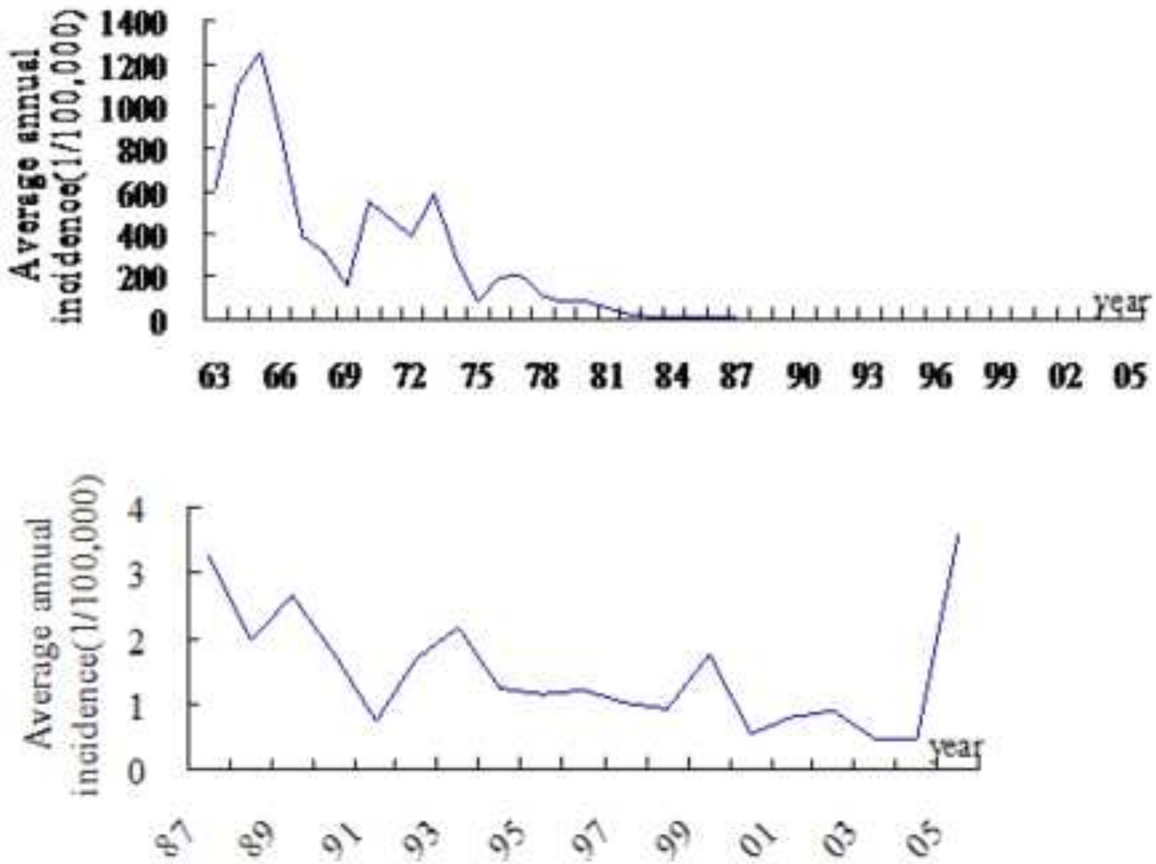

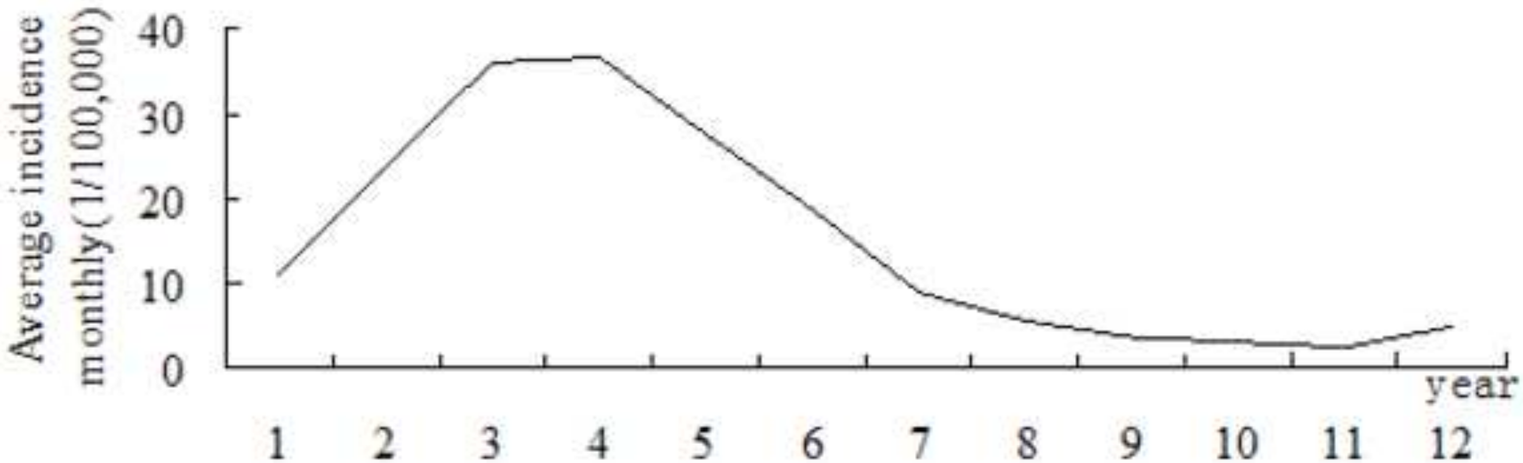
Average incidence monthly(1/100,000)
40
30
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year
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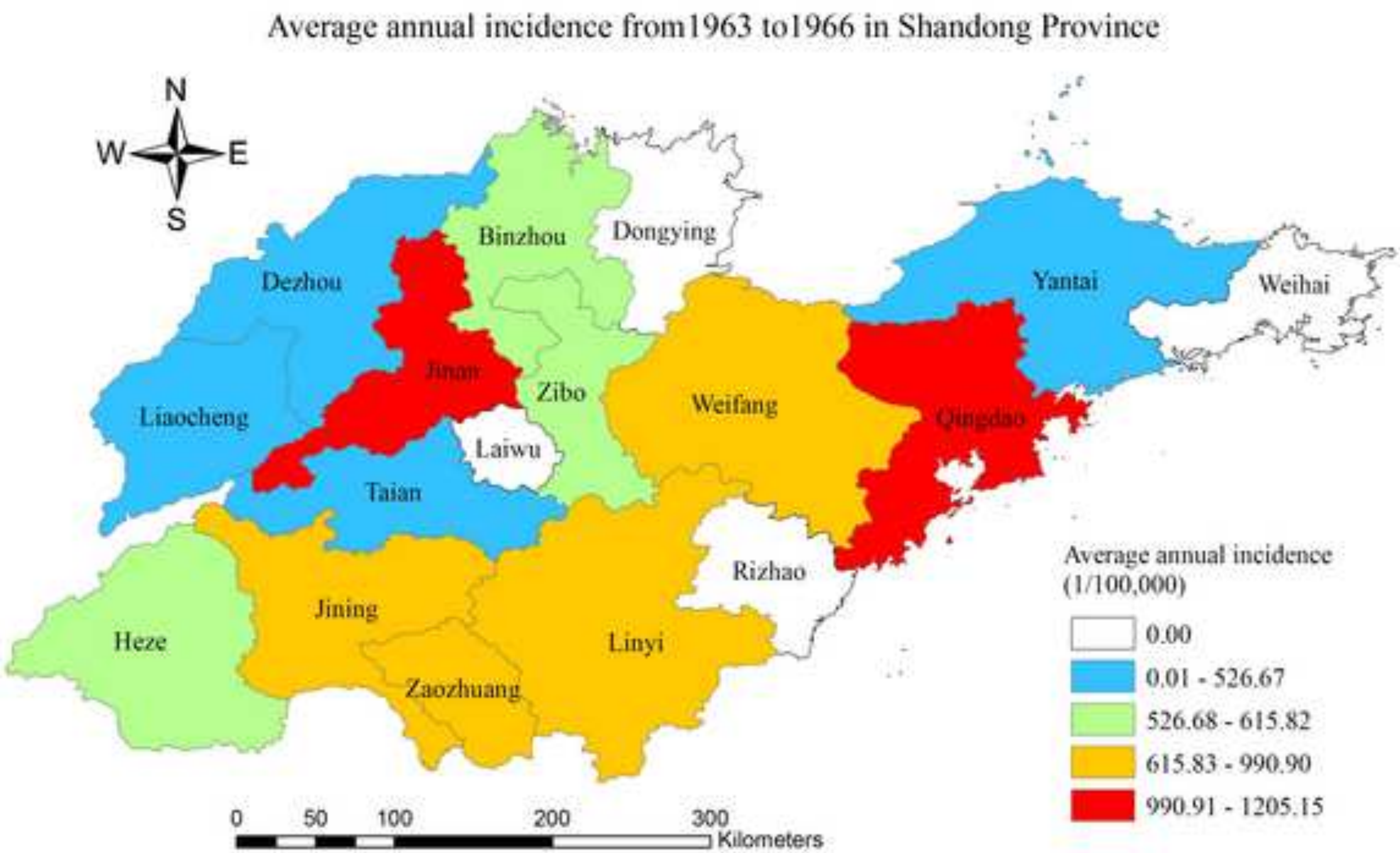

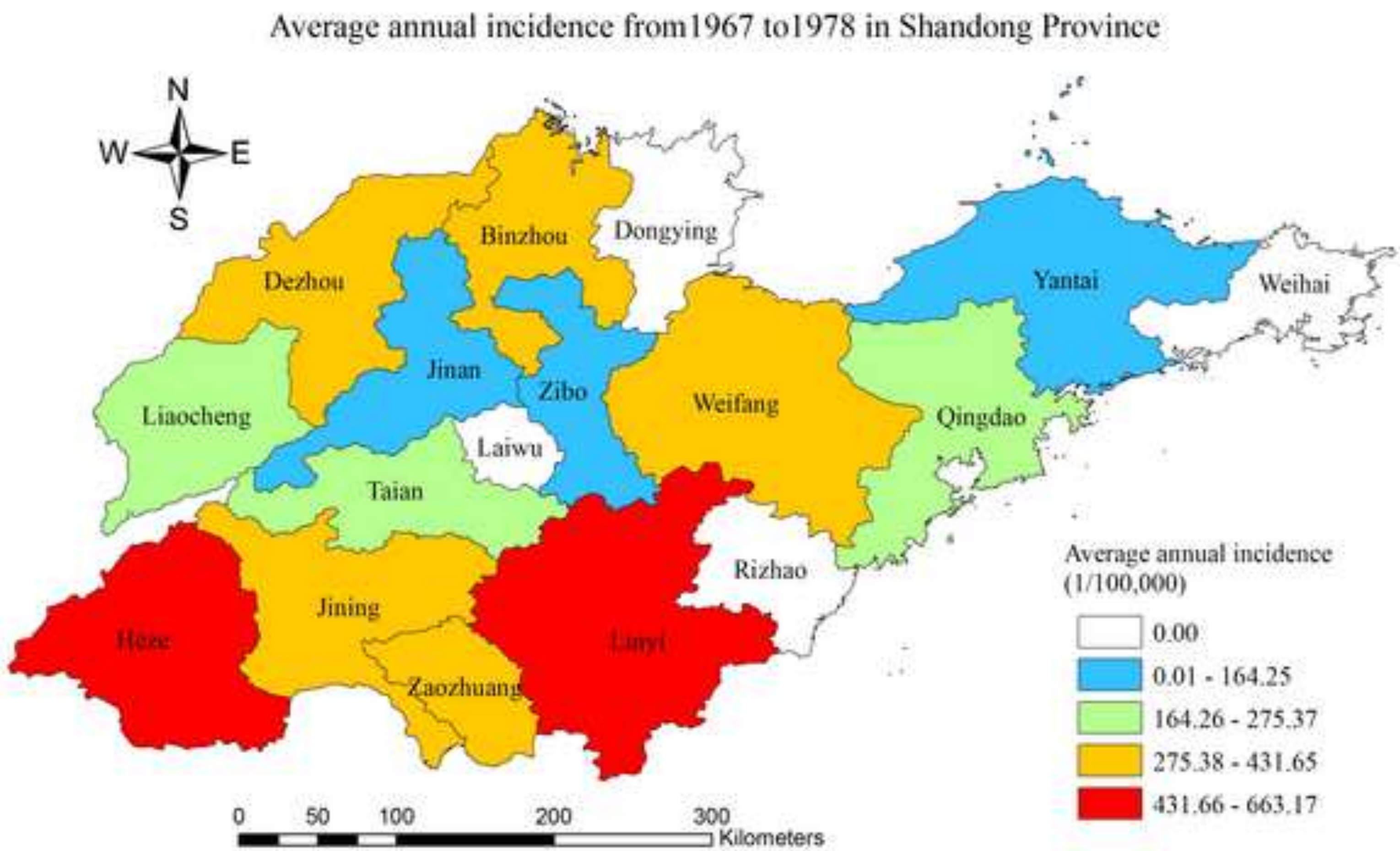
Average annual incidence from1967 to1978 in Shandong Province
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Dezhou
Yantai
Weihai
Jinan
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Weifang
Liaocheng
Qingdao
Laiwu
Taian
Rizhao
Jining
Heze
Linyi
Zaozhuang
Average annual incidence (1/100,000)
0.00
0.01 - 164.25
164.26 - 275.37
275.38 - 431.65
431.66 - 663.17
0
50
100
200
300
Kilometers

Figure(s)
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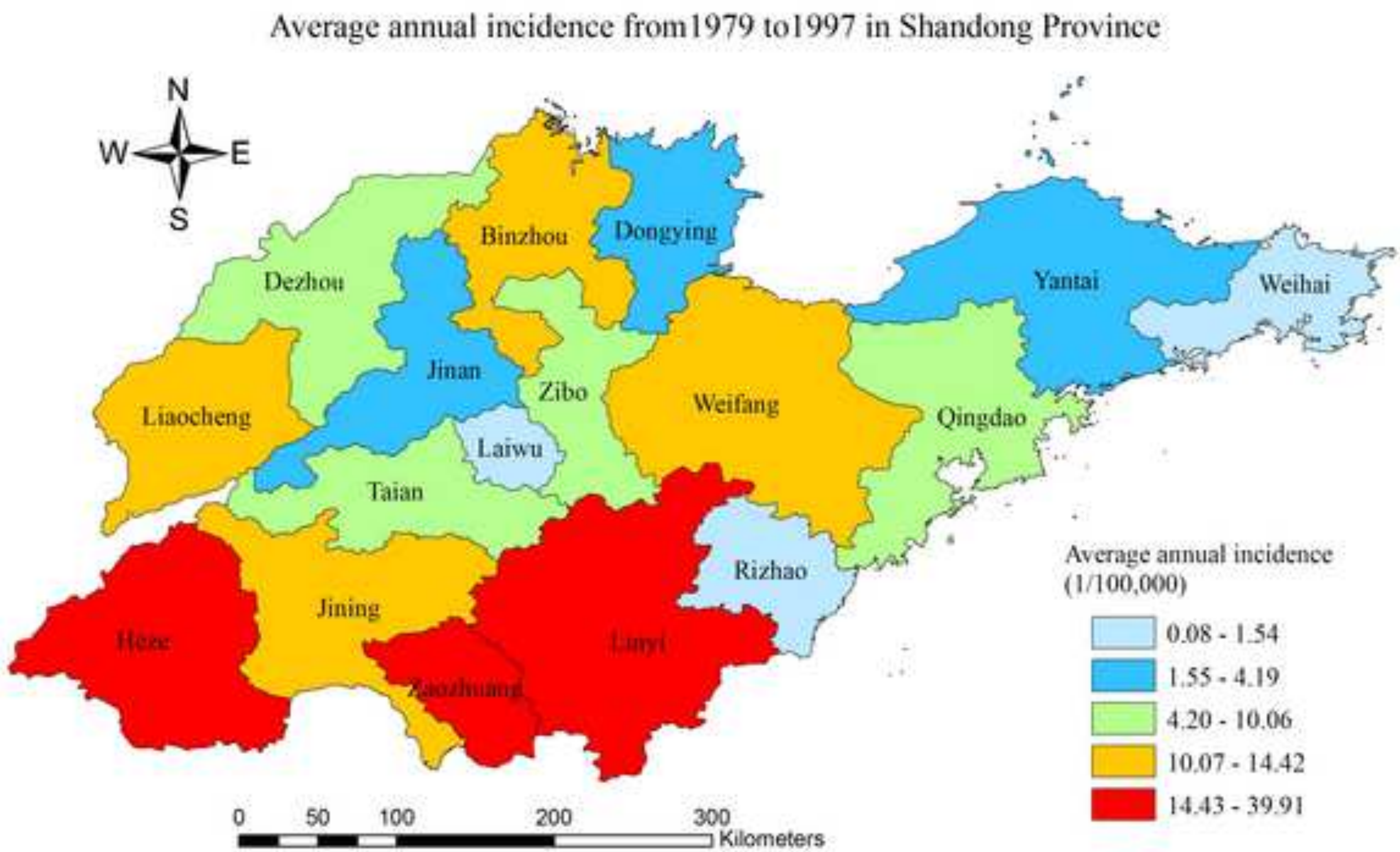

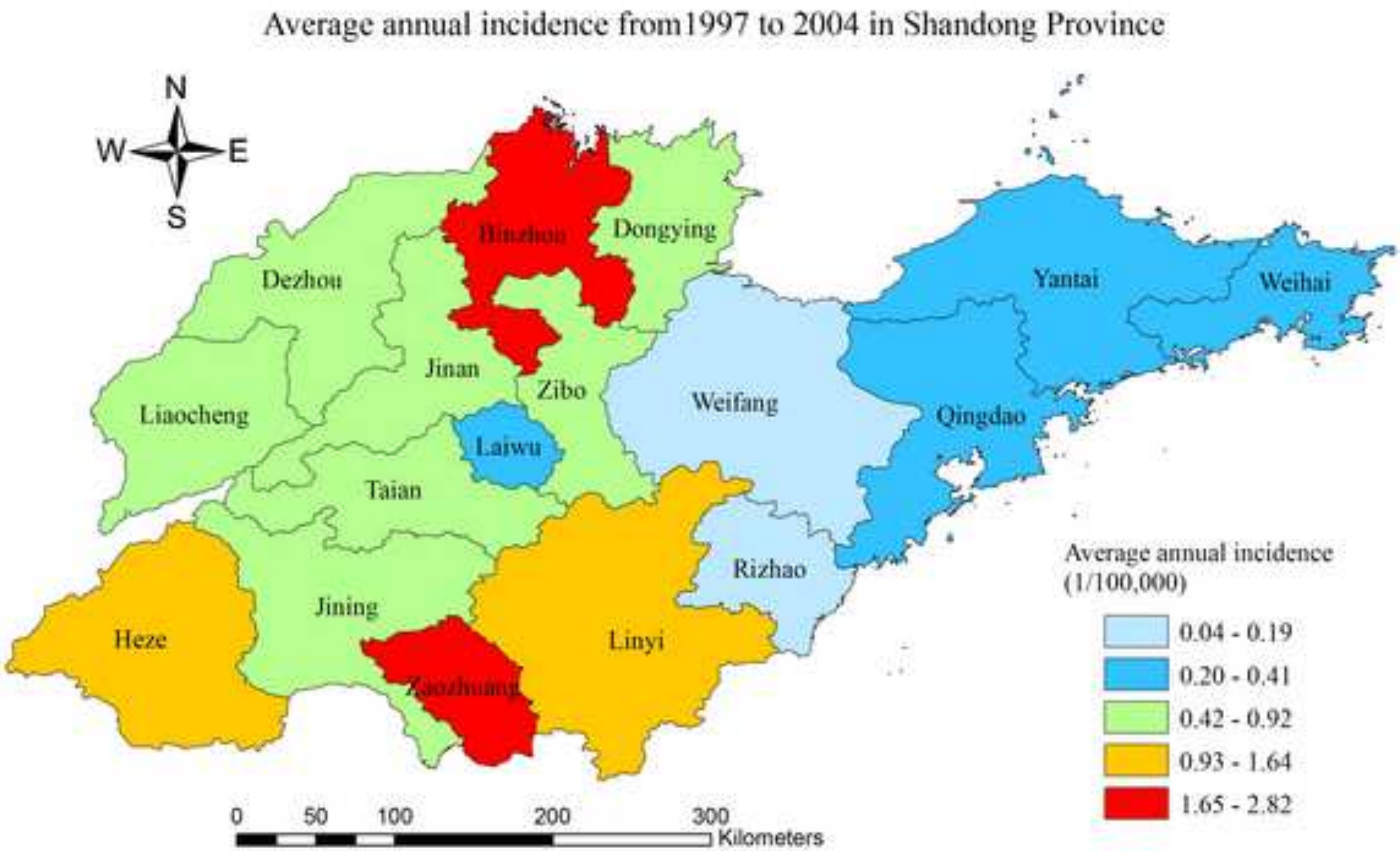
Average annual incidence from1997 to 2004 in Shandong Province
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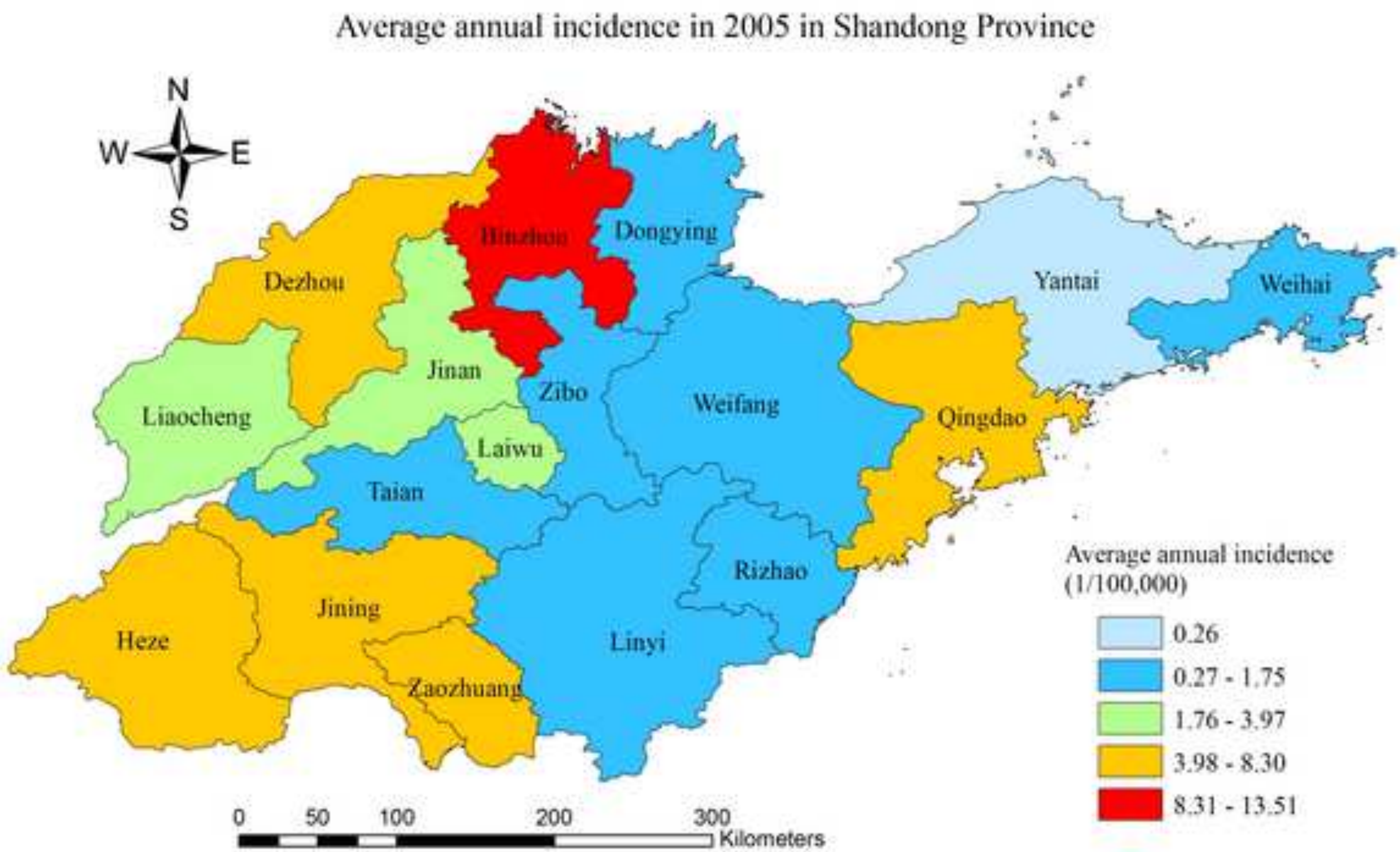
Yantai
Weihai
Qingdao
Rizhao
Jining
Heze
Linyi
Zaozhuang
0
50
100
200
300
Kilometers
Average annual incidence
(1/100,000)
0.04 - 0.19
0.20 - 0.41
0.42 - 0.92
0.93 - 1.64
1.65 - 2.82


Average annual incidence in 2005 in Shandong Province
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Binzhou
Dongying
Dezhou
Yantai
Weihai
Jinan
Zibo
Weifang
Liaocheng
Qingdao
Laiwu
Taian
Rizhao
Jining
Heze
Linyi
Zaozhuang
Average annual incidence
(1/100,000)
0.26
0.27 - 1.75
1.76 - 3.97
3.98 - 8.30
8.31 - 13.51
0
50
100
200
300
Kilometers

Figure(s)
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