Heliyon 11 (2025) e41497

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Diabetes mortality burden attributable to influenza in China: A population-based time-series analysis

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ARTICLE INFO

Keywords:
Influenza
Diabetes mortality
Disease burden

ABSTRACT

Background: Previous studies have found an association between influenza, cardiovascular and cerebrovascular disease mortality, and all-cause mortality. And the vaccination of elderly diabetes is often recommended to reduce the risk of hospitalization and death. Nevertheless, no previous work has investigated the short-term impact of influenza on diabetes mortality in China. In this study, data from the national surveillance system was used to quantify the impact of influenza on diabetes-related mortality and provide guidance for the care of diabetes patients.
Methods: Data from the National Influenza Surveillance Center was collected for the period between 2015 and 2019 and weekly diabetes-related deaths were calculated from China's Disease Surveillance Points System (CDSP). A distributed non-linear lag model (DLNM) was used to 1] analyze the delayed impact of high influenza virus-positive rates on diabetes-related mortality, 2] calculate the relative risk of diabetes deaths caused by high influenza virus-positive rate, and 3] estimate the attributable risk of diabetes deaths caused by influenza in China.
Results: A total of 260 weeks of influenza weekly data from southern and northern China were included in this study. This resulted in 256,845 diabetes-related deaths with an average age of 73.36 years. During this period, the mean influenza virus-positive rate was 12.79 %. The relative risk of death from diabetes at high influenza positive rate was 1.33 (95 % CI [1.25, 1.40]) in southern China and 1.14 (95 % CI [1.08, 1.20]) in northern China for a 3-week lag. The estimated population attributable fraction (PAF) was 9.64 % (95 % CI [6.6 %, 12.55 %]) in southern China and 1.69 % (95 % CI [-0.04 %, 3.35 %]) in northern China. The present study suggest that reducing the influenza virus-positive rate to optimal levels could potentially prevent approximately 10,871 diabetes-related deaths annually.
Conclusion: A high influenza virus-positive rate is associated with an increased risk of diabetes-related mortality. Moreover, this effect is consistent across geographical areas and gender groups. Overall, the present study suggests that the risk of diabetes-related mortality attributable to influenza is high in China.

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https://doi.org/10.1016/j.heliyon.2024.e41497
Received 1 April 2024; Received in revised form 3 December 2024; Accepted 24 December 2024
Available online 27 December 2024

1. Introduction

Diabetes and its complications imposes substantial global health and economic burdens, which highlights the need for a closer examination and better understanding of its risk factors. Previous research shows an association between influenza and a higher risk of diabetes incidence [1]. Moreover, people with diabetes are more likely to be infected with influenza [2,3] and other serious respiratory infections [4,5]. Emerging evidence suggests a correlation between the prevalence of influenza-related respiratory diseases and increased mortality among individuals with underlying conditions such as cardiovascular diseases, cerebrovascular diseases, and diabetes [6–9].

Despite the risks, the prevention and care for influenza-related diseases in individuals with diabetes has not received sufficient attention, with low influenza vaccination coverage rates [10–12]. Currently, there is limited number of studies addressing the health risks of the diabetes population caused by influenza in China. Investigating the association relationship between influenza-related diseases and diabetes-related mortality could inform better care strategies for individuals with diabetes during influenza seasons.

The present study analyzed public health data to determine the impact of influenza epidemics on diabetes-related mortality in China. By quantifying the burden and identifying associated trends and patterns, this study aims to inform future public health initiatives, optimize resource allocation, and promote targeted prevention measures to protect individuals with diabetes during future epidemics and other public health emergencies.

2. Methods

2.1. Data collection

In this population-based ecological study, whole 31 provinces in mainland China were included. Based on different meteorological characteristics and cultural background, those provinces were categorized into southern and northern China (See supplementary Fig. 3). Weekly data on influenza virus-positive cases and diabetes-related deaths were collected for each region.

The data on influenza virus-positive rate were collected from the weekly report of the National Influenza Surveillance Center (https://ivdc.chinacdc.cn/cnic/zyzx/lgzb/) from 2015 to 2019 over whole 31 provinces. This public dataset reveals the weekly influenza epidemics situation of sentinel hospitals in southern and northern China (See Supplementary Fig. 3), including the influenza virus-positive rate of influenza virus detection and the proportion of influenza-like illness in outpatient visits (ILI).

To adjust the impact of temperature [18] on diabetes-related mortality and influenza epidemics, we also included temperature data in the model. The mortality data during the period from January 2015 to December 2019 were obtained from China's Disease Surveillance Points system (DSPS), which is administrated by the Chinese Center for Disease Control and Prevention. The detailed descriptions of the sampling and development of the DSPS were published elsewhere [13–15]. From 2013, this system comprises 605 communities from 322 cities and covers a population of 323.8 million (24.3 % of the total population in China). The current DSPS is considered to be representative at the national and provincial levels and data from this system have been extensively used to assess the disease burden at both regional and national levels in China [15–17]. Diabetes-related deaths are identified as those with a primary cause coded E10-E14, according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10). Using address codes from the death registration card, deaths were categorized as occurring in southern or northern China. Weekly diabetes-related mortality was then calculated separately for each region.

The temperature data from various cities, including daily average temperature, daily minimum temperature, daily maximum temperature, and relative humidity, were obtained from the National Meteorological Center (http://data.cma.cn). Weekly average temperature was then calculated for each city. Finally, the average weekly temperature for southern and northern China was calculated by averaging the weekly temperatures of all cities within each region. Missing data in the weekly influenza-positive rates (0.3 % of total) were imputed using adjacent value interpolation. No missing data were present in the mortality or temperature datasets.

2.2. Statistical analysis

The association between influenza and diabetes mortality was investigated using a two-stage analysis, which has been widely applied in assessing the effects of environmental risk factors, such as air pollution and temperature, on mortality [18–20]. This approach primarily focuses on evaluating the association of the lagged effects of environmental risk factors and diabetes deaths. The impact of influenza epidemics on public health is similar to that of environmental risk factors, namely, any individuals exposed in the real world may potentially be affected by the influenza virus. In the first stage, region-specific non-linear and lagged effects of temperature on weekly diabetes-related death counts were analyzed using a distributed lag non-linear model (DLNM) combined with quasi-Poisson regression. The following covariates were included in the model: (1) a natural cubic spline with 6 degrees of freedom (df) for weeks was used to control for long-term trend, including seasonality and other potential socioeconomic changes from 2015 to 2019; (2) a natural cubic spline with 3 df for mean temperature was used to control for potential confounding effects. In order to fully capture the effects of influenza on mortality, the maximum lag of 3 week was used. This choice was motivated by previous studies indicating that the effects of influenza appear after some delay and persist for several weeks, and evaluated by model akaike information criterion (AIC) (see Supplementary Table 1). The relative risks (RR) of the influenza-mortality association over a 3-week lag period were plotted for both southern and northern China, comparing the risk at each influenza virus-positive rate to that at the low virus-positive rate. The low and high virus-positive rates were defined as the 2.5th and 97.5th percentiles of the region-specific influenza virus-positive rates, respectively. In the second stage, a random-effect meta-analysis was used to obtain the pooled effects of high virus-positive rates on diabetes-related mortality across the two regions. This analysis was based on restricted maximum likelihood. The effect estimates among individual characteristics were pooled separately.

For stratified analyses, the distributed lag non-linear models were fitted after stratifying by several demographic and socioeconomic factors: age (<50, 50–65, 65–75, >75), sex (male and female), marriage (married, widowed, divorced and unmarried). The maximum lag for influenza virus-positive rates was varied from 0 to 5 weeks to check the robustness of our main findings (i.e. sensitivity analysis).

To further characterize influenza-attributable diabetes-related mortality, the population attributable fraction (PAF) was calculated for each week and region [21]based on the RR associated solely with differences in influenza activity in each specific region. The PAF reflects the proportion of diabetes deaths attributable to influenza. Equation (1) describes the calculation of weekly PAFs.

$$wPAF_{ra} = \frac{RR_a - 1}{RR_a}$$

where r is the region, and a is the weekly influenza activity a given region. RR_a is the relative risk associated with influenza activity a. To evaluate the potential public health impact of the estimates, the annual reduction (H) in diabetes-related mortality attributable influenza was calculated, assuming the influenza virus-positive rate was reduced to an optimal level, H is defined as $H_y = wPAF_y \times N_y$ where N_y is the total number of diabetes deaths in China at year y which were calculated by multiplying the total population size and national-average mortality of each cause in China.

All statistical analyses were performed using R, V.3.6.1 (R Foundation for Statistical Computing, Vienna, Austria, https://www.R-project.org/

3. Results

3.1. Summary of descriptive statistics

The baseline characteristics of influenza and diabetes-related mortality in northern and southern China are shown in Table 1. Overall, there were more diabetes-related deaths in southern China than that in northern China for the period between 2015 and 2019. The average age of death was also higher in southern than in norther China (74.13 in southern China vs 72.02 in northern China), and the proportion of elderly individuals over 75 years old was also higher in southern China (53.4 %) compared to northern China (46.0 %). The average influenza virus-positive rates was higher in southern China (14.58 %) compared to that in northern China (11.01 %), same like the average ILI. The average temperature was nearly 8° higher in southern China than in northern China. The higher proportion of elderly individuals and the elevated influenza virus-positive rate suggest a greater burden of influenza-related diseases in southern China compared to northern China.

Table 1
Baseline characteristics.

	Overall	North	South	*P*
Deaths	256845	94360	162485	
Marriage name (%)				<0.001
unspecified	1937 (0.8)	666 (0.7)	1271 (0.8)	
widowed	69045 (26.9)	24854 (26.3)	44191 (27.2)	
married	172461 (67.1)	63071 (66.8)	109390 (67.3)	
unmarried	7313 (2.8)	2637 (2.8)	4676 (2.9)	
divorce	6089 (2.4)	3132 (3.3)	2957 (1.8)	
Age group (%)				<0.001
0-49	11612 (4.5)	4693 (5.0)	6919 (4.3)	
50-64	47802 (18.6)	20413 (21.6)	27389 (16.9)	
65-74	67285 (26.2)	25810 (27.4)	41475 (25.5)	
75+	130146 (50.7)	43444 (46.0)	86702 (53.4)	
AGE (mean (SD))	73.36 (12.37)	72.02 (12.34)	74.13 (12.31)	<0.001
Gender (%)				<0.001
Female	134361 (52.3)	48850 (51.8)	85511 (52.6)	
Male	122484 (47.7)	45510 (48.2)	76974 (47.4)	
Years (%)				<0.001
2015	36721 (14.3)	13606 (14.4)	23115 (14.2)	
2016	46020 (17.9)	16773 (17.8)	29247 (18.0)	
2017	54313 (21.1)	19880 (21.1)	34433 (21.2)	
2018	65264 (25.4)	22984 (24.4)	42280 (26.0)	
2019	54527 (21.2)	21117 (22.4)	33410 (20.6)	
Flu rate				
ILI (%, mean (SD))	3.20 (0.84)	2.95 (0.83)	3.45 (0.78)	<0.001
Positive rate (%, mean (SD))	12.79 (12.53)	11.01 (13.28)	14.58 (11.47)	0.001
Tempture				
Mean tempture (mean (SD))	14.40 (10.10)	10.62 (11.20)	18.18 (7.08)	<0.001

3.2. Lag pattern and cumulative effects of influenza on diabetes-related mortality

As shown in the time series plot of influenza virus-positive rates and diabetes mortality (see Supplementary Fig. 1), a temporal correlation was found between the weekly number of diabetes-related deaths and the weekly influenza virus-positive rate in both southern and northern China from 2015 to 2019. The exposure-response curves of influenza-positive rate and weekly diabetes-related deaths in different regions, indicate that a high influenza virus-positive rates leads to a delayed increase in diabetes-related mortality (see Fig. 1a and b). This effect is more pronounced in southern China, suggesting that high influenza-positive rates lead to a higher relative risk of diabetes-related deaths. In northern China, a similar trend is observed, but the impact is not significant at lower influenza virus-positive rate. After adjusting for regional differences through meta-analysis, high influenza virus-positive rates are still associated with an increased risk of delayed diabetes-related mortality (see Fig. 1 c). The effect of influenza virus-positive rate on diabetes-related mortality is not linear, it becomes significant when the influenza prevalence exceeds 27 %. Furthermore, when the influenza prevalence exceeds 34 %, this effect is even greater.

Taking the 97.5th percentile of the influenza virus-positive rates (42 %) as indicative of an influenza epidemic the estimated relative risk (RR) of diabetes-related deaths after a 3-week lag was calculated. The RR values are 1.33 (95 % CI [1.25, 1.41]) for southern China, 1.14 (95 % CI [1.08, 1.20]) for northern China and 1.23 (95 % CI [1.06, 1.43]) for China overall (Table 2).

For sensitivity analysis, we evaluated the cumulative effects under different lag periods and the impact of influenza ILI rates on diabetes-related mortality. The impact of influenza epidemics on diabetes-related mortality is not immediate but shows a time-lagged effect. The weekly time-lagged impact analysis (see Supplementary Fig. 2, Table 2) suggests that high influenza-positive rates are associated with an increased risk of diabetes-related mortality after a 3-week lag. However, no significant risk increase is observed in the first two weeks. The relative risk remains stable at 4-week and 5-week lags. This trend is consistent in both northern and southern China. Same time-lagged effect can be found in the exposure-response curves of ILI rates and weekly diabetes-related mortality (see

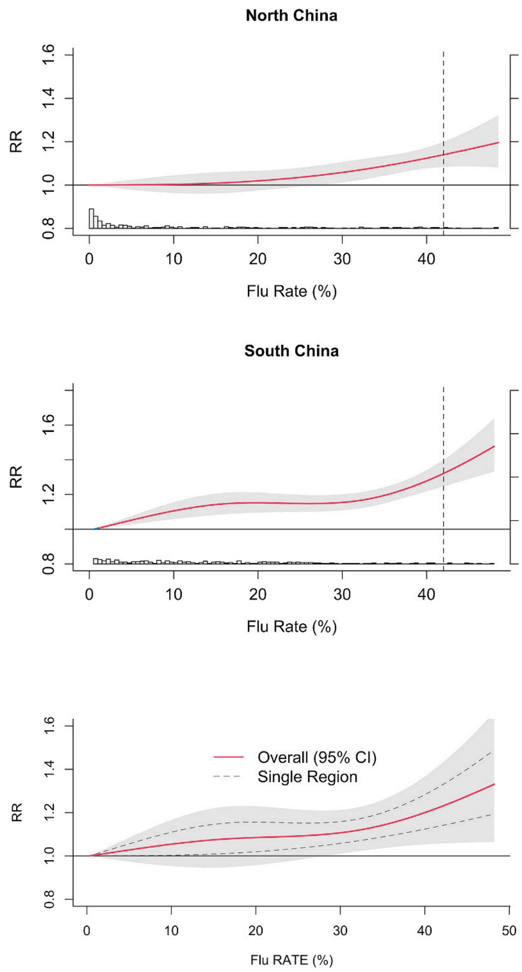

Fig. 1. Exposure-response curves illustrating the relationship between influenza positivity rates and diabetes-related mortality with a lag of 0–3 weeks. a. northern China. b. southern China. c. Meta-analysis results of the influenza virus-positive rate on diabetes mortality with a lag of 0–3 weeks. In all pannels, black lines represent the effect estimates and the gray shaded areas indicate the 95 % confidential intervals.

Table 2
Relative risk of diabetes-related mortality during an influenza epidemic (influenza virus-positive rate = 42 %), stratified by individual characteristics.

	lag 0		lag 0–3 week		lag 0–5 week	
	RR	**95 % CI**	**RR**	**95 % CI**	**RR**	**95 % CI**
Overall China	1.11	[1.01, 1.27]	1.23	[1.06, 1.43]	1.24	[1.01, 1.51]
North China	0.96	[0.85, 1.08]	1.14	[1.08, 1.20]	1.12	[1.06, 1.19]
Gender						
Male	1.07	[0.93, 1.23]	1.18	[1.11, 1.25]	1.18	[1.1, 1.26]
Female	0.86	[0.74, 1.01]	1.11	[1.04, 1.18]	1.07	[0.99, 1.15]
Age						
0-49	1.1	[0.73, 1.65]	1.11	[0.94, 1.31]	1.08	[0.89, 1.32]
50-64	1.07	[0.87, 1.31]	1.23	[1.13, 1.34]	1.22	[1.11, 1.35]
65-75	0.94	[0.76, 1.15]	1.08	[1.00, 1.16]	1.02	[0.92, 1.12]
75+	0.83	[0.7, 0.98]	1.13	[1.06, 1.21]	1.08	[0.99, 1.17]
Marriage name						
Unmarried	0.56	[0.34, 0.95]	1.01	[0.82, 1.24]	0.93	[0.73, 1.18]
Married	1	[0.88, 1.15]	1.13	[1.07, 1.20]	1.12	[1.05, 1.2]
Divorce	1.08	[0.65, 1.77]	1.2	[0.98, 1.47]	1.13	[0.89, 1.43]
Widowed	0.87	[0.71, 1.06]	1.14	[1.05, 1.24]	1.11	[1.01, 1.23]
South China	1.18	[1.02, 1.36]	1.33	[1.25, 1.41]	1.38	[1.29, 1.47]
Gender						
Male	1.19	[1.01, 1.41]	1.33	[1.25, 1.42]	1.38	[1.29, 1.49]
Female	1.16	[0.99, 1.36]	1.31	[1.23, 1.40]	1.37	[1.27, 1.47]
Age						
0-49	0.79	[0.54, 1.16]	1.1	[0.94, 1.28]	1.14	[0.96, 1.35]
50-64	0.93	[0.74, 1.16]	1.17	[1.07, 1.28]	1.19	[1.08, 1.31]
65-74	1.12	[0.9, 1.41]	1.29	[1.19, 1.38]	1.2	[1.09, 1.33]
75+	1.02	[0.82, 1.27]	1.36	[1.27, 1.46]	1.34	[1.22, 1.47]
Marriage name						
Unmarried	1.23	[0.78, 1.95]	1.23	[1.03, 1.48]	1.28	[1.05, 1.57]
Married	1.19	[1.02, 1.39]	1.32	[1.24, 1.41]	1.37	[1.27, 1.46]
Divorce	1.03	[0.61, 1.74]	1.3	[1.06, 1.59]	1.33	[1.06, 1.67]
Widowed	1.12	[0.92, 1.36]	1.32	[1.23, 1.43]	1.41	[1.29, 1.53]

Supplementary Fig. 4).

3.3. Effect of influenza on diabetes-related mortality by individual characteristics

Subgroup analysis reveals that the impact of influenza epidemics on the delayed risk of diabetes-related mortality is generally consistent across gender groups (see Fig. 2). Nevertheless this effect is not significant among younger individuals (0–45 years old).High influenza virus-positive rates are associated with an increased relative risk of diabetes-related mortality among young individuals (0–45 years old) in both southern (1.10; 95 % CI [0.94, 1.28]) and northern China (1.11; 95 % CI [0.94, 1.31]), but this effect is not statistically significant. Additionally, in northern China, no positive correlation was observed between diabetes-related mortality and influenza epidemics among individuals aged 65–75 years.

The estimated relative risk for different gender subgroups shows the similar results as for the general population, indicating that influenza epidemics increase the relative risk of diabetes-related mortality across all populations. However, it appears that unmarried individuals and younger groups may have a relatively lower risk during periods of influenza prevalence, which is likely influenced by age-related factors.

3.4. Attributable burden of diabetes-related mortality to influenza

Based on the estimated RR value of diabetes-related deaths associated with influenza virus-positive rates and the weekly reported influenza virus-positive rates, the population attributable fraction (PAF) of diabetes-related deaths attributable to influenza epidemics was estimated for southern and northern China from 2015 to 2019 (Table 3). The burden of influenza epidemics on diabetes-related deaths is substantially higher in southern China compared to northern China. Approximately 9.64 % (95 % CI [6.6 %, 12.55 %]) of diabetes-related deaths in southern China can be attributed to influenza epidemics, while in northern China this figure is 1.69 % (95 % CI [−0.04 %, 3.35 %]). For China overall the mean PAF of diabetes-related deaths attributable to influenza epidemics is 5.47 % (95 % CI [−1.84, 12.05]).

Based on the total population size and national-average mortality rates for each cause in China [22], it is estimated that reducing the influenza-positive rate to optimal levels could potentially result in approximately 10,871 fewer diabetes-related deaths annually.

4. Discussion

The present population-based study investigated the association between diabetes-related mortality and influenza epidemics using

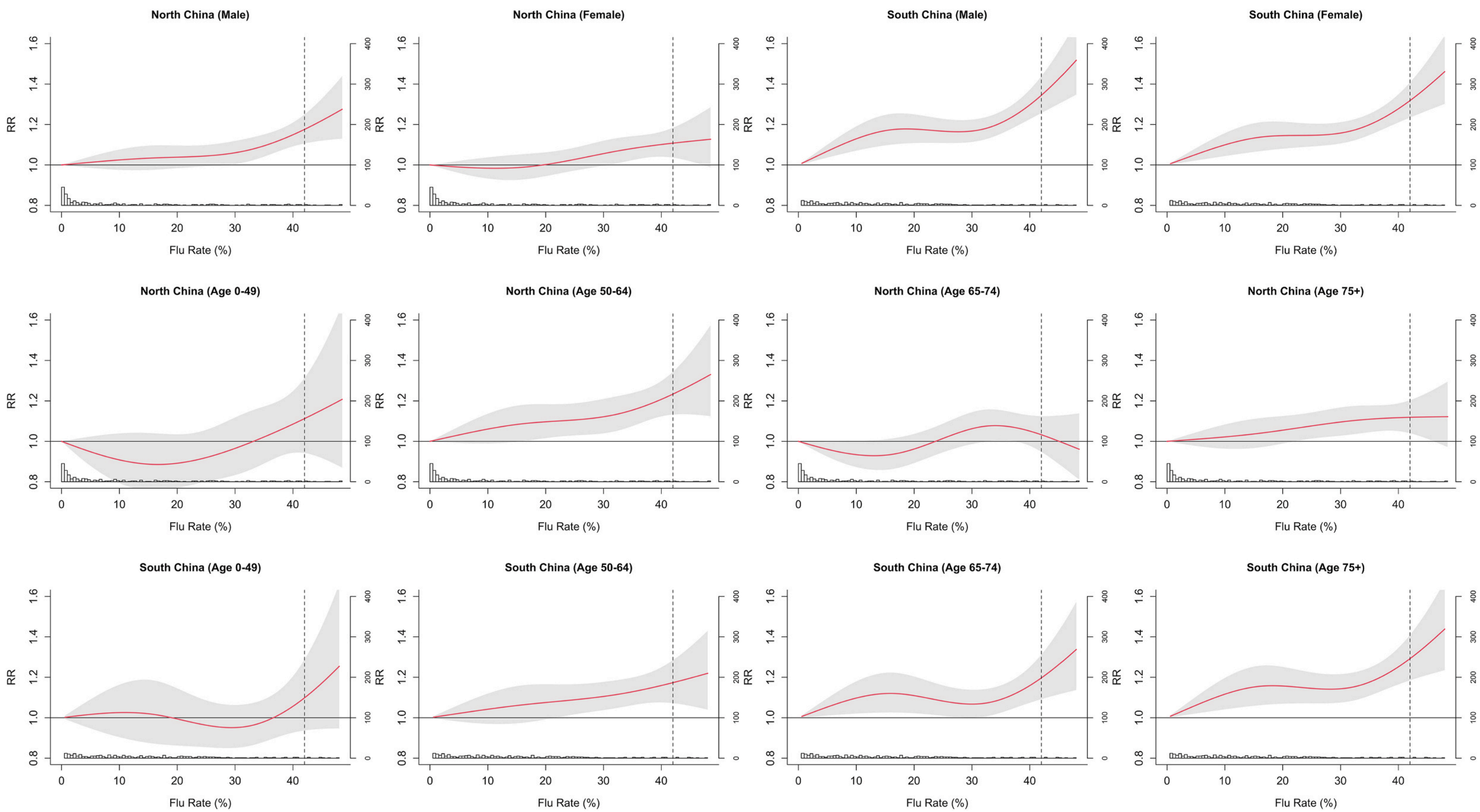

Fig. 2. Exposure-response relationship between weekly influenza virus-positive rates and weekly diabetes-related deaths in different gender groups and different age groups.

Table 3
PAF of diabetes-related mortality caused by influenza epidemic in 2015–2019.

	PAF (%)	95 % CI	Annual Reduction in Deaths
Overall China			
Mean	5.47	[-1.84, 12.05]	10871
2015	4.24	[-2.96, 10.75]	6855
2016	5.52	[-1.73, 12.07]	10029
2017	5.75	[-3.12, 13.72]	12196
2018	4.58	[-0.75, 9.37]	9151
2019	7.26	[-0.63, 14.33]	16121
North China			
Mean	1.69	[-0.04, 3.35]	–
2015	0.12	[-1.09, 1.3]	–
2016	0.2	[-1.03, 1.37]	–
2017	1.51	[-0.76, 3.73]	–
2018	2.5	[0.69, 4.19]	–
2019	4.14	[1.99, 6.16]	–
South China			
Mean	9.64	[6.6, 12.55]	–
2015	8.18	[5.39, 10.86]	–
2016	9.3	[6.12, 12.35]	–
2017	10.86	[7.27, 14.29]	–
2018	9.66	[7.31, 11.89]	–
2019	10.19	[6.92, 13.34]	–

a DLNM combined with quasi-Poisson regression. The results suggest a strong correlation between diabetes-related deaths and influenza epidemics in the period from 2015 to 2019. Both phenomena exhibit seasonal patterns and a certain degree of lag. Based on the association analysis using the DNLM model, an increase in respiratory tract samples testing positive for influenza virus is associated with a higher diabetes-related mortality rate. At an influenza virus-positive rate of 42 %, the RR of diabetes-related mortality within three weeks was found to be 1.33 (95 % CI, [1.25, 1.41]) in Southern China and 1.14 (95 % CI, [1.08, 1.20]) in Northern China. Meta-analysis, adjusting for regional differences, confirmed that increased influenza-positive rates were significantly associated with elevated relative risk of diabetes-related mortality. However, influenza peaks do not always result in a high risk of diabetes mortality. For instance, the summer influenza peak in southern China in 2015 did not result in a high risk of diabetes mortality, additional research may be needed to assess and evaluate this phenomenon. Based on these findings, the population attributable fraction (PAF) of diabetes-related deaths attributable to influenza was estimated for the period from 2015 to 2019. The results indicated that influenza epidemics contribute to a substantial number of annual diabetes-related deaths, highlighting the significant challenges posed by influenza epidemics to diabetes management and care.

Regional comparisons of influenza-related diabetes mortality showed significant differences between southern and northern China, with the south experiencing a greater burden than the north. Specifically, the average influenza-positive rate was estimated to be 3.57 % higher in the south than that in the north. Consequently, the resulting attributable mortality in southern China was estimated at 7.97 % (95 % CI [2.01 %, 13.94 %]), substantially higher than the 1.43 % (95 % CI [−1.82 %, 4.69 %]) estimated for northern China. The results of the present study also show that whereas the risk for the elderly was the most pronounced, the impact of influenza epidemics on the young group was found to be not significant. This observation is consistent with existing research findings [23–26]. This geographical and population differences highlight the need for targeted interventions and better care measures. Further promotion and implementation of influenza vaccination strategies, particularly tailored to regional and age-specific needs, may be beneficial.

Influenza virus infection has been associated with higher risk of death among individuals with diabetes, Relevant studies have elaborated the relevant mechanism, studies in Canada [27] and Poland [28] have found that influenza can lead to additional attributable deaths from diseases such as cardiovascular diseases, respiratory diseases, cancer and metabolic diseases. Our research is the first time to investigate the short-term effects of influenza prevalence on diabetes mortality using national surveillance data in China, and it estimates the annual disease diabetes-related mortality attributable to influenza epidemics. Several studies have investigated the underlying mechanisms of this relationship. Obesity and diabetes are known to induce inflammation of adipose tissue. This inflammatory state may increase susceptibility to systemic infections, including influenza [29,30]. Additionally, infection with influenza virus has been shown to impact insulin sensitivity, affect the blood brain barrier [31], and disrupt glycemic control in individuals with diabetes. These effects can increase the risk of severe comorbidities such as immune aging (age-related immune dysfunction) and inflammatory aging, which may lead to poor immune response in elderly individuals. These conditions may worsen in patients with metabolic comorbidities [32]· Consequently, elderly individuals with diabetes face greater health risks during influenza epidemics.

Previous studies have shown that influenza vaccination provides protection for diabetes patients, reduces their respiratory infection rate [33], lowers the incidence of chronic kidney disease and dialysis [34], and reduces hospitalization and all-cause mortality in diabetes patients [35]. Some developed countries have found that increasing the rate of vaccination against influenza can provide significant protection for diabetes patients [36,37]· Nevertheless, the coverage of influenza vaccination in developing countries remains low [10,11]. The findings from the present study highlight the urgent need for developing and implementing strategies to improve influenza vaccination rates among individuals with diabetes.

Several limitations should be acknowledged in the present study. Firstly, the temporal resolution of the data poses a constrain. Both influenza and mortality data were aggregated on a weekly basis, which prevents the analysis of intra-week variations in influenza and mortality rates. Moreover, potential temperature fluctuations within a week were not captured in the present study, which may introduce some degree of information bias. Despite these limitations, the weekly data resolution aligns with reported lag between influenza exposure and increased mortality risk for diabetes, cardiovascular and cerebrovascular diseases in previous studies Secondly, the present study, only considered the differences between the south and the north of China. Despite this limitation, the results reveal regional differences between the north and the south, including the age distribution of diabetes-related deaths and the rate of influenza prevalence. Future studies with access to more detailed regional and municipal epidemic surveillance data may evaluate finer regional differences. Thirdly, the present study analyzed data from 2015 to 2019 and did not consider the specific measures for the prevention and control of infectious diseases implemented by the Chinese government during the COVID-19 epidemic. In addition, the diabetes-related risk of death may have changed from 2019 till now. Thus, there present study does not capture any potential changes in the relationship between influenza and disease-related risk of death from 2019 to date. Fourthly, due to the lack of relevant population baseline data, we were unable to estimate an accurate mortality rate. We used the number of deaths instead of the mortality rate in the DLNM model, Considering that the total population of China did not change significantly from 2015 to 2019, and since we are assessing the relative risk changes under different influenza epidemics, the total number of deaths can effectively reflect this impact. Fifthly, The flu season may coincide with the prevalence of other viruses and environmental risk factors that could impact the mortality of diabetes patients, but currently, we do not have data to incorporate them into our model. The observed association between influenza and delayed mortality in diabetes may be due to climate differences in winter infection mortality cycles, with influenza being just one of many circulating pathogens, We also found that proportion of all deaths was highest in 2018, additional research may be needed to assess and evaluate diabetes mortality and excess diabetes mortality in China in 2018. Finally, population-based ecological studies present inherent limitations when considering their applicability to clinical and care practice. Whereas these studies provide insights on overall trends and associations, specific cohort studies and clinical trials based on real world data are needed to better characterize the relationship between influenza infections and diabetes-related risk of death.

In conclusion, the present study reveals an association between influenza and a higher diabetes-related risk of death in China. This effect is largest in southern China and among elderly individuals with diabetes. The findings from this study highlight the need for more targeted policies to address the significant public health challenges posed by influenza epidemics. An effective approach could be to increase influenza vaccination rates among high-risk populations.

CRediT authorship contribution statement

Suijun Tong: Writing – original draft, Investigation, Formal analysis, Data curation. **Peng Yin:** Writing – review & editing, Resources, Investigation, Data curation. **Jianhong Li:** Writing – review & editing, Methodology, Investigation. **Zhenping Zhao:** Writing – review & editing, Validation, Supervision, Methodology. **Yuchang Zhou:** Writing – review & editing, Methodology. **Maigeng Zhou:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Investigation, Data curation.

Data availability statement

The data used in this study is confidential and subject to data protection regulations. Due to the sensitive nature of the data, it is not publicly available.

Declaration of competing interest

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

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e41497.

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