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# Epidemiological characteristics and spatiotemporal distribution of hepatitis C in southeast coastal areas of China from 2015 to 2022

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## Abstract

**Objective** The purpose of this study was to analyze the epidemiological characteristics and spatial-temporal distribution characteristics of hepatitis C in Fujian Province, China, from 2015 to 2022, and to provide reference for the risk identification, early warning and prevention and control measures of hepatitis C in Fujian Province.

**Methods** The incidence data of hepatitis C in Fujian Province from 2015 to 2022 were collected from the China Information System for Disease Control and Prevention. Descriptive epidemiology method and JRP 4.9.1.0 software were used to analyze the epidemiological characteristics of hepatitis C in Fujian Province from 2015 to 2022. ArcGIS 10.8 software was used for spatial autocorrelation analysis of the reported incidence of hepatitis C, and SaTScan 10.1.3 software was used for spatio-temporal scanning analysis.

**Results** A total of 18,712 cases of hepatitis C were reported in Fujian Province from 2015 to 2022, and the annual reported incidence showed a decreasing trend (AAPC = -10.4,  $P < 0.001$ ). Males were more affected, accounting for 55.7% ( $n = 10,429$ ) of all reported hepatitis C cases compared to 44.3% ( $n = 8,283$ ) for females. Among all age groups, the number of cases in people aged 40–60 was the largest, accounting for 43.2%. Autocorrelation analysis showed that the reported cases of hepatitis C from 2015 to 2022 were clustered, and the global Moran's  $I$  values were all greater than 0 ( $P < 0.001$ ). Local autocorrelation analysis showed that the high-high concentration area of hepatitis C incidence was relatively fixed and concentrated in the Putian city. The spatial and temporal scanning analysis detected one largest possible agglomeration area, Xiuyu District of Putian city, and two type II agglomeration areas were mainly distributed in economically developed cities along the coastal line.

**Conclusion** The reported incidence of hepatitis C in Fujian province showed a downward trend from 2015 to 2022, and there were obvious epidemic characteristics and spatial-temporal clustering of hepatitis C. Attention should be

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paid not only to the key population of 40–60 years old males in rural areas and the key gathering areas in Putian City, but also to the incidence of hepatitis C in southeast coastal areas.

**Keywords** Hepatitis C, Epidemic characteristics, Joinpoint regression, Spatial-temporal clustering analysis

## Introduction

Hepatitis C is an infectious disease caused by hepatitis C virus infection (HCV). It can be transmitted through mother and child, blood and sexual contact. The onset is relatively hidden, the course of the disease is slow, and a considerable proportion of patients will have liver damage, cirrhosis and hepatocellular carcinoma and other complications [1]. According to the WHO report, there were approximately 58 million people with chronic hepatitis C worldwide in 2019, and approximately 290,000 people died from liver disease associated with HCV infection [2]. There were about 625,000 people infected with HCV in China in 2019, accounting for about 10% of the global HCV-infected population [3]. Hepatitis C has become a global public health problem, and previous studies have shown that HCV prevalence is significantly different due to social, geographical, customary and economic differences [4, 5]. Some researchers and scholars have conducted spatio-temporal analysis of HCV in mainland China from 2005 to 2011 and found that the distribution of hepatitis C cases was correlated with spatial factors and disease aggregation [6]. At present, China has incorporated hepatitis C cases into the automatic early warning information system of infectious diseases. It works with public opinion monitoring and sentinel doctors to establish a clustered warning mechanism for hepatitis C. In order to achieve the purpose of early detection and early disposal. Fujian Province is located in the southeast coastal area of China, with a relatively developed economy and a large floating population, which brings certain challenges to the prevention and control of hepatitis C. However, the spatio-temporal characteristics of hepatitis C in Fujian Province in the last decade is less documented. Therefore, this study will use geographic information system (GIS) and spatial statistics methods to analyze the surveillance data of hepatitis C in Fujian province from 2015 to 2022. We aimed to explore the epidemiological characteristics and spatial-temporal clustering of hepatitis C cases, and provide some scientific basis for risk identification and effective prevention and control of hepatitis C.

## Methods

### Data collection and processing

Hepatitis C is one of the statutory Class B infectious diseases in China, and the state stipulates that all medical institutions should report the information of confirmed HCV patients (including clinically diagnosed cases and laboratory-confirmed cases) to the Internet-based China

Disease Control and Prevention Information System (CISDCP) within 24 h. Through the infectious disease surveillance system of the CISDCP, hepatitis C cases with current addresses in 88 counties (cities, districts) of Fujian province and the final examination time from January 1, 2015 to December 31, 2022 were included in the study. It includes both clinically diagnosed cases and laboratory-confirmed cases. At the same time, multiple reported cases, suspected cases and cases from unknown counties were excluded. The information collected includes case number, national standard code of current residence address, date of onset, date of diagnosis, date of final trial, case classification, occupation, age, gender, and other characteristics.

The population data of each county (city, district) in each year were derived from the statistical yearbook of Fujian. The vector map and geographic coordinate data of Fujian were obtained from the National Center for Basic Geographic Information (<https://www.ngcc.cn/ngcc/>). The database of hepatitis C incidence (including geocoding, number of cases and time of onset), geographic information database (including geocoding, longitude and latitude) and demographic information database (including geocoding, year and population) were constructed at county (city, district) level. Each database is connected with the geocode of the county (city, district) as the key filed. Reported incidence of hepatitis C = number of reported cases of hepatitis C in the current year / number of permanent residents in 88 counties (cities and districts) in Fujian Province\*100,000.

### Joinpoint regression analysis

Joinpoint regression program (JRP) 4.9.1.0 software was used to construct the Joinpoint regression analysis with year as the independent variable and the reported hepatitis C cases as the dependent variable, and the optimal regression model was fitted [7]. Their annual percentage change (APC) and average annual percentage change (AAPC) were calculated. If  $APC > 0$ , it indicates an upward trend, and if  $APC < 0$ , it indicates a downward trend [8]. A  $p$  value  $< 0.05$  was considered statistically significant.

### Spatial autocorrelation analysis

ArcGIS 10.8 software was used to conduct global and local spatial autocorrelation analysis [9]. In the global autocorrelation analysis, global Moran's  $I$  was used to measure the spatial correlation and difference degree of hepatitis C in Fujian province, and  $Z$  value was Moran's  $I$

test statistic. Under the test level of  $\alpha = 0.05$ , the absolute value of  $Z$  was greater than or equal to 1.96, it is suggested that there is spatial clustering of reported cases of hepatitis C. The Moran's  $I$  value was generally between  $-1$  and  $+1$ , and the larger the absolute value was, the stronger the degree of clustering distribution was. When Moran's  $I > 0$ , it indicates that the distribution is spatially positively correlated. When Moran's  $I < 0$ , it indicates that there is a spatial negative correlation. When Moran's  $I = 0$ , it indicates a random distribution without regional aggregation. Cluster and outlier analysis modules were used to further explore four types of spatial aggregation patterns in the whole region: high-high, high-low, low-high and low-low.

### Spatiotemporal aggregation analysis

The spatiotemporal scanning statistic is to create a spatiotemporal two-dimensional scanning cylinder on the map, the bottom surface of the cylinder is the spatial range of detection, and the height of the cylinder represents the time interval of scanning [10]. The location and size of the cylinder will change continuously. The log-likelihood ratio (LLR) is calculated by using the actual number of cases and the theoretical number of cases in the scan window. When the LLR value is larger and the  $P$ -value is less than 0.05, the incidence in this area can be considered to be clustered.

SaTScan 10.1.3 software was used for spatial-temporal scanning analysis. The scanning time was from January 2015 to December 2022, the time interval was "month", the regional overlap was "none", the maximum risk population was set as 30% of the total population, and the number of Monte Carlo simulation was 999. The LLR constructed by the actual and theoretical numbers inside and outside the scanning window was used to describe the degree of aggregation. The cluster area with the largest LLR value was classified as the Class I cluster area, while the other cluster areas with statistical significance were the Class II cluster area. ArcGIS 10.8 software was used to visualize the aggregation area.

## Results

### Epidemic profile

From January 2015 to December 2022, a total of 18,712 cases of hepatitis C were reported in 88 counties (cities and districts) in Fujian province, including 3,488 clinically diagnosed cases (18.4%) and 15,264 laboratory-confirmed cases (81.6%). The average annual reported incidence was 5.95 per 100,000 population. The reported incidence of hepatitis C decreased from 8.56 per 100,000 population in 2015 to 4.05 per 100,000 population in 2022, showing an overall decreasing trend ( $APC = -10.4$ ,  $P < 0.001$ ). At the same time, when we conducted a time period study for 2017–2022, we found that the annual

reported incidence of hepatitis C in 2020–2022 was significantly lower than that in 2017–2019 ( $\chi^2$  trend = 23.49,  $P < 0.01$ ). There was a statistically significant difference in the incidence rates reported each year, during the period 2015–2022 (Fig. 1).

### Population distribution characteristics

From 2015 to 2022, a total of 10,429 cases of hepatitis C in men and 8,283 cases in women were reported in Fujian Province, with a sex ratio of 1.3:1. The average annual reporting rate for males was significantly higher than that for females. The AAPC was  $-7.5$  for males and  $-10.9$  for females, with  $P$  values less than 0.001, indicating that the annual average change trend was statistically significant. Hepatitis C cases are distributed among all age groups, with the highest reported incidence in people aged 40 to 60 years. The occupational distribution was mainly farmers, domestic workers and unemployed people, and the proportion of farmers was nearly half of the total cases. The remaining demographic characteristics are shown in Table 1.

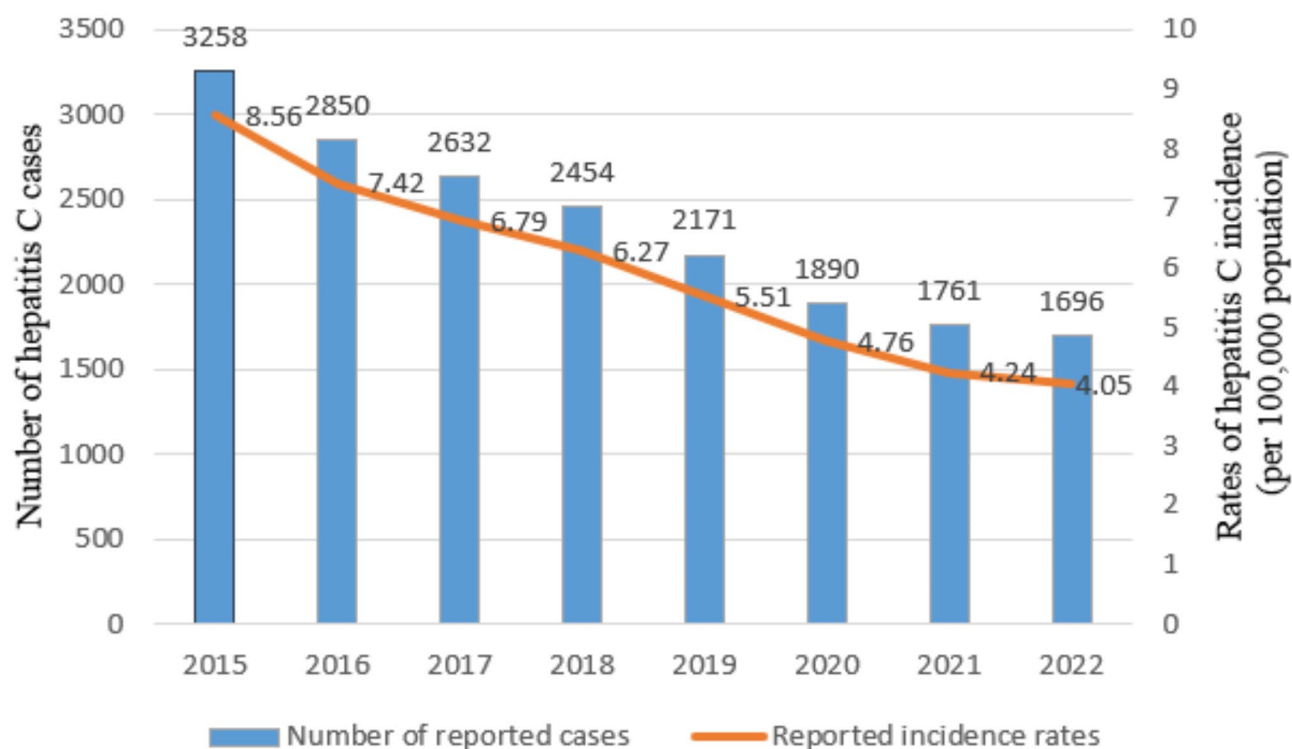
### Spatial autocorrelation analysis

The results of global spatial autocorrelation analysis of reported incidence of hepatitis C in Fujian from 2015 to 2022 are shown in Table 2. It showed that the annual Moran's  $I$  values were significantly different, indicating that the reported incidence of hepatitis C in Fujian province were non-randomly distribution. Each year the value of Moran's  $I$  was greater than 0 and the  $P$  values were less than 0.001. This suggests that the incidence of hepatitis C in Fujian province has a certain spatial aggregation.

The results of local spatial autocorrelation analysis showed that from 2015 to 2022, the high incidence areas of hepatitis C in Fujian Province were only distributed in the counties/districts under the jurisdiction of Putian City, among which the high-high aggregation areas of Chengxiang District, Xiuyu District and the north shore Economic Development zone of Meizhou Bay existed for 8 consecutive years. Licheng District temporarily dropped out of the high-high clustering area and became a low-high clustering area only in 2021, and was a high-high clustering area in the other years. Five high-low clustering areas were found, including Jianyang district of Nanping City, Xinluo district, Liancheng county and Wuping county of Longyan City, and Taining county of Sanming City. A total of 24 low-low accumulation areas were found, mainly distributed in different counties/regions of Zhangzhou City, Quanzhou City, Sanming City, Longyan City and Nanping City, as shown in Fig. 2.

### Spatial-temporal clustering analysis

Spatial-temporal scanning was performed on the reported hepatitis C cases in each county (city, district)



**Fig. 1** Epidemiological trends of hepatitis C in Fujian Province, China from January 2015 to December 2022

**Table 1** Demographic characteristics of hepatitis C cases in Fujian from 2015 to 2022

Characteristics	Number of cases [Percentage (100%)]							
	2015	2016	2017	2018	2019	2020	2021	2022
Gender								
Male	1745(53.6)	1598(56.1)	1431(54.4)	1316(53.6)	1237(57.0)	1036(54.8)	1044(59.3)	1022(60.3)
Female	1513(46.4)	1252(43.9)	1201(45.6)	1138(46.4)	934(43.0)	854(45.2)	717(40.7)	674(39.7)
Age (years)								
< 10	50(1.53)	45(1.58)	39(1.48)	29(1.18)	17(0.78)	27(1.43)	6(0.34)	18(1.06)
20~<40	946(29.0)	799(28.0)	692(26.3)	575(23.4)	497(22.9)	412(21.8)	330(18.7)	299(17.6)
40~<60	1267(38.9)	1147(40.3)	1078(41.0)	1060(43.2)	1011(46.6)	825(43.7)	835(47.4)	869(51.2)
60~<80	820(25.2)	719(25.2)	674(25.6)	656(26.7)	526(24.2)	534(28.3)	521(29.6)	443(26.1)
≥ 80	175(5.37)	140(4.92)	149(5.66)	134(5.46)	120(5.53)	92(4.87)	69(3.92)	67(3.95)
Occupation								
Farmer	1512(46.4)	1313(46.1)	1236(47.0)	1216(49.6)	963(44.4)	923(48.8)	773(43.9)	642(37.9)
Commercial service	94(2.89)	91(3.19)	68(2.58)	90(3.67)	97(4.47)	113(5.98)	122(6.93)	171(10.1)
Housework and unemployment	771(23.7)	651(22.8)	556(21.1)	528(21.5)	544(25.1)	416(22.0)	403(22.9)	471(27.8)
Unknown	354(10.9)	301(10.6)	298(11.3)	222(9.05)	184(8.48)	129(6.83)	152(8.63)	134(7.90)
Others	527(16.2)	494(17.3)	474(18.0)	398(16.2)	383(17.6)	309(16.3)	311(17.7)	278(16.4)

of Fujian province from January 2015 to December 2022, and a total of three possible spatial-temporal clustering areas were detected, including one most likely clustering area and two type II clustering areas, as shown in Table 3; Fig. 3. The most likely clustering area was Xiuyu district of Putian City, and the clustering time span was January 2015 to September 2018. The first type II cluster was mainly distributed in the northeast and central part of Fujian Province, covering the period from January 2015 to August 2018. The second type II cluster mainly

covered most counties/districts in Xiamen and a few counties/districts in Quanzhou and Zhangzhou, and the time span was from January 2015 to September 2018. Comprehensive analysis showed that the clustering areas of hepatitis C in Fujian province were mainly in the main urban areas and surrounding counties/districts of the eastern coastal cities, and the clustering time span was relatively long.

**Table 2** Global Spatial autocorrelation analysis of reported incidence of hepatitis C in Fujian, China from 2015 to 2022

Year	Moran's I	Z-value	P-value
2015	0.563	11.400	<0.001
2016	0.343	10.937	<0.001
2017	0.326	10.218	<0.001
2018	0.343	10.543	<0.001
2019	0.370	8.486	<0.001
2020	0.296	8.877	<0.001
2021	0.489	9.544	<0.001
2022	0.367	7.381	<0.001

## Discussion

The overall incidence of hepatitis C in Fujian Province showed a downward trend from 2015 to 2022, and the annual reported incidence rate was 5.95/100 000, which was at the low epidemic level in China during the same period [11]. Since the implementation of online direct reporting of hepatitis C in Fujian Province in 2005, the reported epidemic situation of hepatitis C showed an increasing trend year by year until 2015, which may be related to the standardization of online reporting, the level of diagnosis and treatment and the continuous improvement of detection capacity [12]. The annual incidence of hepatitis C has decreased year by year since 2015, which on the one hand may be related to the improvement of people's awareness of self-protection and voluntary medical treatment. On the other hand, it may be related to the country's continuous improvement and standardization of the infectious disease reporting system, the improvement of the quality of case reporting, the reduction of heavy and missing cards, and the implementation of the new hepatitis C diagnostic criteria in 2018 [13]. It is worth noting that the downward trend of the hepatitis C epidemic in 2020–2022 is more obvious than that in 2017–2019, which may be related to the reduction of personnel flow and the decline of people's willingness to seek medical treatment after the Chinese government has taken epidemic containment measures since the outbreak of the novel coronavirus in 2020 [14, 15].

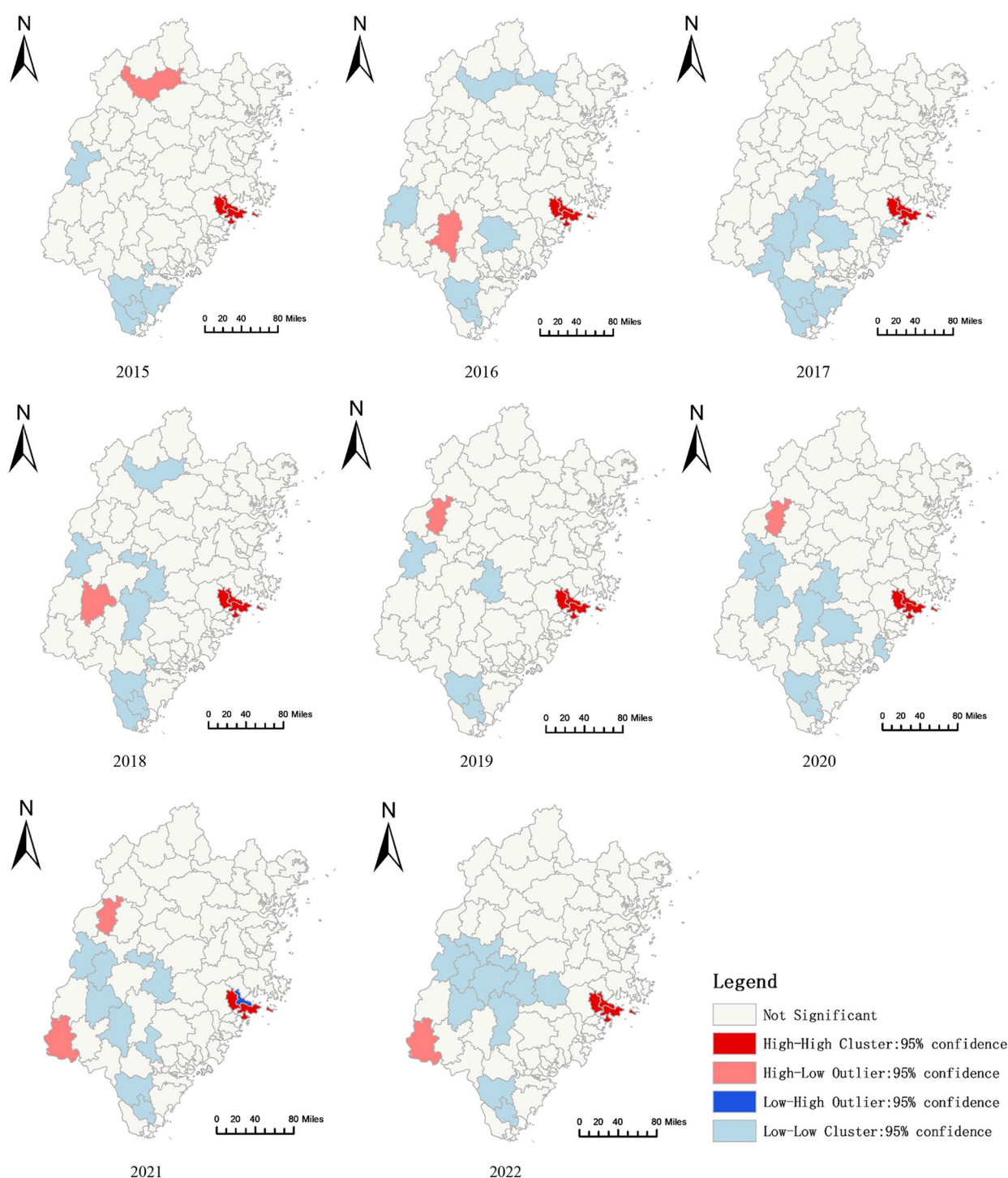
From the perspective of population distribution, the incidence of hepatitis C in males was higher than that in females in Fujian province, and the highest incidence was reported in 40–60 years old group. The occupation distribution of hepatitis C patients was mainly farmers, household workers and unemployed workers. The results are similar to those of some domestic and foreign scholars [16–18]. The higher number of male patients may be related to the traditional Chinese concept of “men in charge of the outside and women in charge of the inside”, which leads to men have a wider range of social activities, a higher socioeconomic status, and a greater possibility of high-risk behaviors [19]. The three groups with the

highest proportion of hepatitis C in Fujian Province were consistent with those in Hubei and Jilin Province [20, 21]. The largest proportion of farmers may be due to the large base of Chinese farmers, the large mobility of migrant workers, and the weak awareness of health [22, 23]. The highest incidence in the 40–60 years age group may be related to the occult nature of hepatitis C development and the cumulative effect of risk factors [24, 25]. Therefore, accurate and comprehensive intervention measures should be formulated for such key populations, including increasing the intensity of testing, health education, and regulating medical behavior.

Based on the spatial autocorrelation analysis of counties (districts), the results showed that the distribution of hepatitis C epidemics in Fujian Province from 2015 to 2022 had a significant spatial clustering, and the clustering area had a slight change. The distribution of high-high clustering areas of hepatitis C cases was relatively fixed, concentrated in the area under the jurisdiction of Putian City, and the clustering lasted for a long time, which may be related to the existence of more previous cases in Putian city, residents' living habits and economic life. Studies have shown that the sharing of syringes and infusion sets and nonstandard disinfection of medical instruments existed in local rural health centers for a long time before 2000, which led to a high incidence of hepatitis C infection in some counties and villages in Putian City. The local government subsequently launched the hepatitis C screening “Liver Net Action” program, which promoted more hepatitis C infections to be detected [26, 27]. The low-low clustering areas of hepatitis C cases were mostly distributed in the jurisdiction of mountainous cities in Fujian province (including Longyan city, Sanming city and Nanping city), which may be related to the less developed economy and relatively low medical conditions in mountainous cities [28]. Therefore, this study suggests that it is particularly important to strengthen the public's self-protection awareness, continuously improve the medical environment, and eliminate hepatitis C through effective treatment.

Spatiotemporal detection and analysis methods have been proved to play an important role in the transmission of infectious diseases [29, 30]. This study further confirmed that Xiuyu district of Putian City was the most likely clustering area of hepatitis C cases by using SaTScan for spatio-temporal scanning analysis. The results are consistent with the spatial autocorrelation analysis. At the same time, other spatial and temporal aggregation areas were also detected, which were mainly distributed in the cities along the eastern coast of Fujian Province. The aggregation time had no obvious seasonal characteristics, and the time span was about 3 years. Similar to some domestic scholar's research results, this may be because hepatitis C is a chronic infectious disease





**Fig. 2** Yearly local spatial autocorrelation analysis of hepatitis C incidence at the county level in Fujian Province, China, 2015–2022

and seasonal changes have little effect on transmission [31–33]. In rural areas of Putian City, there were many hepatitis C patients and hidden infections due to unsafe medical behavior in the early years [27]. Therefore, Xiuyu District became the largest possible cluster area, and its surrounding districts Licheng district, Chengxiang

District, Hanjiang district and Xianyou County became the second cluster area. Xiamen as a deputy provincial city, Fuzhou as the provincial capital city, the economy is relatively developed, relatively rich medical resources, relatively high level of diagnosis and treatment, hepatitis C screening rate and diagnosis level continue to improve,

**Table 3** Result of Spatiotemporal scanning of hepatitis C incidence in Fujian, China, 2015–2022

Cluster Type	Number of Clustering areas	Cluster districts and counties	Gathering time (year/month)	Observed cases	Expected cases	Relative risk	Log likelihood ratio	P-value
Most likely cluster	1	Xiuyu	2015/01-2018/09	2542	39.72	73.91	8245.35	< 0.001
Secondary cluster1	23	Minqing, Minhou, Yongtai, Gutian, Gulou, Youxi, Jian'ou, Jin'an, Taijiang, Cangshan, Yanping, Hanjiang, Mawei, Luoyuan, Dehua, Lianjiang, Pingnan, Xianyou, Changle, Fuqing, Chengxiang, Jiaocheng, Licheng	2015/01-2018/08	3612	1721.67	2.36	895.34	< 0.001
Secondary cluster 2	10	Tong'an, Jimei, Xiang'an, Huli, Haicang, Changtai, Siming, Nan'an, Anxi, Jinjiang	2015/01-2018/09	1933	729.10	2.84	722.04	< 0.001

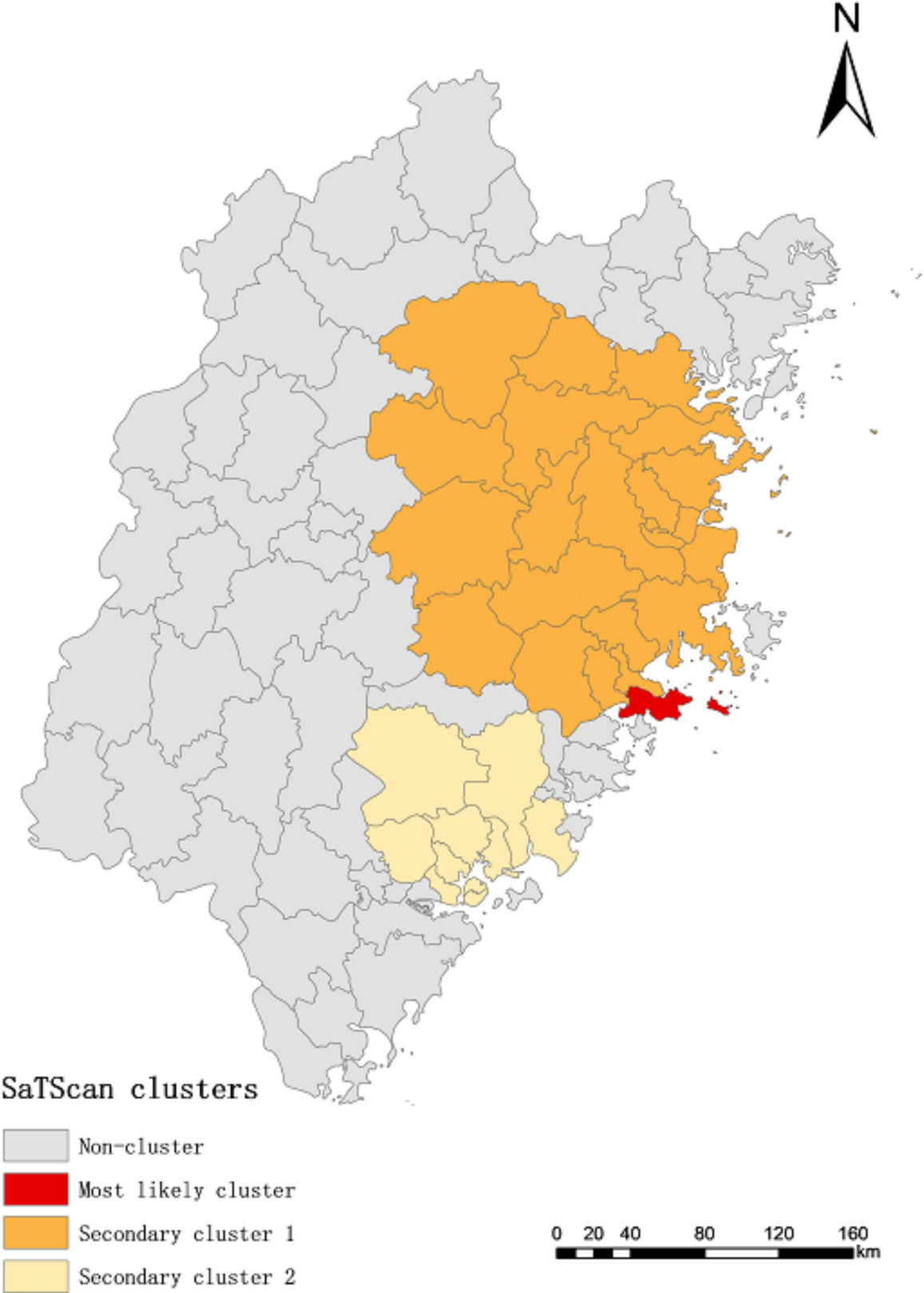
so the reported incidence of hepatitis C is relatively high. Ningde and Quanzhou, as coastal cities, have rapid industrial and economic development and large mobility of migrant workers, which to a certain extent promotes the spread of sexually transmitted diseases [34]. This is also consistent with the research results of Shaoqi Ning et al. [35]. Therefore, some districts and counties in Fuzhou, Xiamen, Ningde and Quanzhou became the type II clustering areas of hepatitis C epidemic. This study suggests that the presence of a large number of patients with hepatitis C, liquidity of floating population is probably the main reason for the existence of the spatiotemporal clustering areas.

It must be acknowledged that our study has some limitations. Firstly, like other case reportable studies, data were derived from the infectious disease surveillance system of the CISDCP. The reliability of research results has a lot to do with the accuracy and standards of reporting. For example, there may be underreporting, concealing and duplicate reporting of case reports. And because the early symptoms of hepatitis C infection are not obvious, some infected people have not been discovered. These would underestimate the prevalence of hepatitis C. The country issued new diagnostic criteria in 2018, which may have led to changes in data quality before and after promulgation. Secondly, scanning statistical analysis requires various model assumptions about the variation and distribution of spatio-temporal data. In practice, the assumed distribution of parameter data is sometimes invalid. This is a limitation of spatial scan statistics [36]. Finally, some potential influencing factors were not included in the analysis in this study, such as demographic characteristics and socioeconomic information. In the future, we will continue to work on the

impact of hepatitis C infection and transmission, taking into account relevant factors.

## Conclusion

In summary, the reported incidence of hepatitis C in Fujian Province showed a downward trend year by year from 2015 to 2022, and the incidence of hepatitis C showed obvious population epidemic characteristics and spatial-temporal aggregation. Thus, we suggest that in the prevention and control of hepatitis C epidemic in the future, a series of measures should be taken according to the epidemic characteristics and spatial and temporal distribution characteristics of the population. First of all, we should increase the efforts to publicize the harm of hepatitis C and increase the way to popularize the knowledge of hepatitis C prevention and treatment. Promote health education, self-protection and screening awareness among key rural populations aged 40 to 60 years. Secondly, blood quality management norms and medical device application hygiene norms should be strictly formulated and implemented to reduce the probability of iatrogenic infection. At the same time, it is necessary to actively carry out the elimination of hepatitis C patients in the key city of Putian, screen and manage the key population in the epidemic area, and manage the source of infection as much as possible. Finally, optimizing the allocation of medical and health resources and improving the ability of medical institutions at all levels to diagnosed and treat hepatitis C is also an indispensable part of the prevention and treatment work.



**Fig. 3** Spatiotemporal clusters of hepatitis C at the county level in Fujian, China, 2015–2022



## Acknowledgements

This study was supported by the Fujian Provincial Center for Disease Control and Prevention. We would like to thank Fujian Research and Training Grants for Young and Middle-aged Leaders in Healthcare.

## Author contributions

XJF and LW conceived and designed the study. LW and LQL analyzed the data and wrote the main manuscript. LXL and LZQ contributed to the analysis tools. WSB, ZMY contributed to data collation and interpretation. PYJ and LYX helped to draft the manuscript. XJF provided advice and critically reviewed the manuscript. All authors read and approved the final manuscript.

## Funding

This research was funded by The Major Health Research Project of Fujian Province (No.2021ZD01001).

## Data availability

The data used and /or analyzed in this study are available upon reasonable request from the corresponding author.

## Declarations

### Ethical approval and consent to participate

Ethics committee approval was not specifically required for this study because this study only focused on population-level analysis and any information that could reveal the privacy of the subjects of this study was removed prior to data analysis.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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Received: 24 April 2024 / Accepted: 10 March 2025

Published online: 21 March 2025

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