The changing modes of human immunodeficiency virus transmission and spatial variations among women in a minority prefecture in southwest China
An exploratory study

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Abstract
Liangshan Yi Autonomous Prefecture in Southwest China has a high human immunodeficiency virus (HIV) prevalence rate. This study examined the changing modes of HIV transmission among women with new HIV infections and explored the spatial heterogeneities in the factors associated with heterosexual transmission in this minority region.

The data consisting of women with new HIV infections from 2011 to 2014 were collected from multiple sources. New infections were identified by BED capture enzyme immunoassay. The Bayesian hierarchical model was used to estimate the proportion of women with new HIV infections via heterosexual transmission across all townships in the Prefecture. A geographically weighted regression (GWR) model was utilized to investigate spatial variations in the sociodemographic characteristics associated with the changing modes of HIV transmission.

An analytical sample of 927 women with new HIV infections was constructed and utilized to investigate the changing mode of HIV transmission. The rate of heterosexual transmission among women with new HIV infections in 2011 was below 20%. However, by 2014 this rate dramatically increased to nearly 80%. Among sociodemographic characteristics, GWR results revealed significant ethnic differences in heterosexual HIV transmission between Yi women and women in other ethnic groups, with Yi women demonstrating a lower risk of infection through heterosexual transmission. However, such ethnic differences were observed only in 30% of the townships in the Prefecture. Moreover, having a primary education decreased the odds of heterosexual transmission, which was observed in about 56% of the townships. Also, being involved in occupations other than agriculture or animal husbandry and being single or married decreased the odds of HIV infection through heterosexual contact among women, which did not significantly vary across the Prefecture.

Heterosexual transmission was the predominant mode of HIV transmission among women in the Prefecture, and this transformation was clearly marked by a fast-growing trend and a spatial diffusion pattern. Spatial variations also existed in sociodemographic factors that were associated with the changing modes of HIV transmission.
1. Introduction

Liangshan Yi Autonomous Prefecture (shortened to Liangshan afterwards), located on the border of Sichuan and Yunnan provinces in Southwest China, is one of the most poverty-stricken regions in China. One of the major drug trafficking routes from the “Golden Triangle” to China passes through this Prefecture. As a result, the rate of human immunodeficiency virus (HIV) infection in the Prefecture has increased dramatically since the first HIV case was reported in 1995. By September 2017, the Prefecture exhibited the highest HIV prevalence rate in Sichuan province. It is widely accepted that this high prevalence of HIV infection is due primarily to intravenous drug use (IDU). However, in recent years, the number of new HIV infections among intravenous drug users has steadily declined. According to the Chinese HIV sentinel surveillance system (HSS), there was an uptrend in new HIV infections among women from 2011 to 2014, accounting for nearly 42% of all new HIV infections in the Prefecture. Given this shifting pattern in HIV infections, it is important to examine the changing mode of HIV transmission from IDU to heterosexual contact, its socioeconomic and demographic characteristics, and its spatial variations to develop, structure, and implement better informed and targeted as well as more effective prevention strategies and programs in the Prefecture.

Spatial heterogeneity in the changing mode of HIV transmission and in the factors associated with this changing mode of HIV transmission is noteworthy for several distinct reasons. First, as alluded to previously, the South-eastern townships in the Prefecture are located along the drug trafficking routes from the Golden Triangle region such that IDU is common in this area. It is well acknowledged that the sharing of equipment for IDU is both a substantial cause of HIV infection and a contributing factor to blood-borne transmission around the world. It has been estimated that as of 2017 about 17.8% of people aged 15 to 64 years who injected drugs (PWID) were living with HIV/AIDS worldwide. While the prevalence rate is generally low, China has witnessed a slight decline in the percentage of PWID living with HIV over the past several years. For example, the percentage of PWID living with HIV dropped from 6.33% in 2013 to 6.00% in 2014. Second, the level of economic development varies considerably across the townships in the Prefecture. In effect, some townships in the Prefecture remain the poorest in contemporary China because of the rugged mountainous terrain with a vulnerable ecological environment. Past research demonstrated that poverty was significantly associated with sexual risk behaviors, including inconsistent condom use and multiple sexual partners. Public health scholars have linked poverty with condom use decisions, and identified poverty as one of the most significant barriers to the negotiation of condom use. Third, the influence of cultural norms can have profound implications for HIV transmission and control. Liangshan is an ethnic minority region with more than 50% of its 4.873 million residents being of ethnic Yi, residing in 618 townships, 16 counties, and 1 county-level city. Dominant social norms and traditional values pertinent to HIV transmission, such as unsupportive attitudes toward condom use, condoned casual sex behavior, and arranged marriage within the same social status groups, remain strong among the Yi minority population, thus potentially exacerbating HIV infections spatially across the Prefecture. It is important to note that the distribution of the ethnic Yi population is not uniform in the Prefecture. In fact, the Yi population is primarily concentrated in the northeastern part of the region such that the influence of the Yi culture might be more prominent in the northeastern townships than their counterparts in other geographic locations.

In light of these geosocial and geo-cultural diversities, there is a good reason to anticipate the township-level heterogeneity in the mode of HIV transmission and in the factors associated with the mode of HIV transmission in the Prefecture. Unfortunately, to the best of our knowledge, no study to date has systematically investigated such notable spatial heterogeneity. To fill this research void, the present study is designed to accomplish 2 specific research goals that are outlined below.

First, to properly visualize the aforementioned township-level spatial heterogeneity in the changing mode of HIV transmission in the Prefecture, a database comprising women with new HIV infections was constructed through multiple sources to minimize the township-level small sample size problem. This small sample size related problem may result in unstable and unreliable estimates as well as their corresponding maps. To help attenuate this potential problem, Bayesian hierarchical model was employed to estimate and map the proportion of heterosexual transmission among women with new HIV infections. Second, the geographically weighted regression (GWR) model was used to link sociodemographic characteristics to the changing mode of HIV transmission among women with new HIV infections at the township-level. To achieve these research goals is contextually important and relevant because this minority region has been devastated by the HIV/AIDS epidemic and extreme poverty since the 1990s.

2. Methods

2.1. Data collection

To compile a comprehensive and accurate HIV/AIDS database consisting of women who were newly infected with HIV from 2011 to 2014 in Liangshan, multiple data sources for detecting HIV in Liangshan were considered and triangulated (ie, cross-checked and validated). These data sources included:

1. provider-initiated HIV testing & counseling (PITC) service,
2. voluntary counseling and testing (VCT) service,
3. HSS, and
4. recent scientific studies conducted in the prefecture.

PITC has been routinely recommended by health care providers in the prefecture to patients who attended health care facilities as a standard component of medical care. If patients agreed to HIV testing, health care facilities would provide HIV testing service. Through such routinized testing services, the

Abbreviations: FSW = female sex workers, GWR = geographically weighted regression, HIV = human immunodeficiency virus, HIV/AIDS = human immunodeficiency virus/acquired immune deficiency syndrome, HSS = HIV sentinel surveillance, IDU = injecting drug user, ORs = odds ratios, PITC = provider-initiated HIV testing & counseling, PWID = people who injected drugs, VCT = voluntary counseling and testing.

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newly infected female cases were reported. This study secured the service records from health care facilities throughout the Prefecture. Likewise, new female infection cases were also identified and obtained from the VCT service as this service included individuals who sought HIV testing and counseling service on their own initiative. Moreover, new female infection cases were obtained from the HSS that monitors the HIV epidemic among IDUs, female sex workers (FSW), attendants at the sexually transmitted disease clinics, and pregnant women. Established in 1995, HSS has 1888 sentinel sites within 300 cities across 31 provinces in China. Finally, recent research projects conducted in the prefecture were also consulted to corroborate the new female HIV infection cases collected from the above data sources. To avoid duplicates, every new infection case was coded with a unique ID number. It must be noted that if women who were hospitalized and diagnosed with AIDS, they were not included in this study unless they received services provided by PITC.

For the present study, the BED capture enzyme immunoassay was utilized, which identified and confirmed a total of 1074 women with new HIV infections residing in 618 townships, 16 counties, and 1 county-level city from 2011 to 2014. Out of these women with new HIV infections, 927 cases were retained to constitute the analytical sample for the present study as these cases had complete information on age, ethnicity, occupation, educational level, marital status, and more importantly, the mode of HIV transmission. All the information was obtained at the time of blood sample collection. The data collection was approved by the Ethics Committee of the Center for Disease Control and Prevention of the Liangshan Yi Autonomous Prefecture.

2.2. Variables

The dependent variable for this study was the mode of HIV/AIDS transmission among women with new HIV infections in the Prefecture from 2011 to 2014. This variable was dummy-coded with 1 indicating heterosexual transmission and 0 representing all other modes of transmission. This variable was dummy-coded with 1 indicating heterosexual transmission and 0 representing all other modes of transmission. The independent variables included age, ethnicity, marital status, educational level, and occupation. Age was measured in years as a continuous variable; ethnicity was dummy-coded as 1 = other ethnicities and 0 = Yi; marital status was dummy-coded as 1 = single or married with divorced and 0 = widowed; educational level was dummy-coded as 1 = primary school or above and 0 = no formal education; occupation was dummy-coded as 1 = other occupations and 0 = peasant and/or herdsman. The zero category was consistently used as the reference group. Furthermore, the residential location of each case was represented by the latitude and longitude of the centroid of the township it belongs to. The sample characteristics and bivariate associations with the dependent variable are reported in Table 1.

2.3. Statistical modeling

As indicated above, the mode of transmission among women with new HIV infections was identified by cross-validating multiple data sources, including a variety of monitoring records, medical check-up reports, IDU history records, and sexual-behavior surveys. Since these newly identified cases came from different townships that might be affected by varying degrees of socioeconomic conditions, spatial and cultural factors such as proximity to Yunnan province and the Golden Triangle region, the Bayesian hierarchical model was utilized to estimate the proportion of the heterosexual transmission from 2011 to 2014. The implementation of the Bayesian hierarchical model is described below in detail.

Because this study focuses on heterosexual transmission among women with new HIV infections, the mode of transmission was classified as heterosexual versus other modes of HIV transmission. As such, the underlying proportion of the mode of HIV transmission was estimated using a beta distribution. In the present study, the hyperparameters were expressed as $\alpha$, $\beta$, which determine the beta distribution for the proportion of women with new HIV infections through heterosexual contact. The proportion of such HIV infections was presented by $\theta$. To obtain the posterior distribution of $\theta$, a vector of hyperparameters, $(\alpha, \beta)$, was drawn from its marginal posterior distribution, $p(\alpha, \beta | y)$, and the parameter vector $\theta$ was drawn

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Sociodemographic characteristics of women with new HIV/AIDS infection in Liangshan Yi Autonomous Prefecture: 2011 to 2014 (n = 927).</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Heterosexual transmission case</td>
</tr>
<tr>
<td></td>
<td>N</td>
</tr>
<tr>
<td>Age</td>
<td>489</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Yi</td>
<td>432</td>
</tr>
<tr>
<td>Other ethnicities</td>
<td>57</td>
</tr>
<tr>
<td>Employment</td>
<td></td>
</tr>
<tr>
<td>Peasant and herdsman</td>
<td>428</td>
</tr>
<tr>
<td>Other occupations</td>
<td>61</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>84</td>
</tr>
<tr>
<td>Married</td>
<td>352</td>
</tr>
<tr>
<td>Divorced or widowed</td>
<td>53</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>No formal education</td>
<td>266</td>
</tr>
<tr>
<td>Primary school</td>
<td>188</td>
</tr>
<tr>
<td>Junior high school or above</td>
<td>35</td>
</tr>
</tbody>
</table>

Age is shown in mean (SD) format.
HIV/AIDS = human immunodeficiency virus/acquired immune deficiency syndrome.
from its conditional posterior distribution, \( p(\alpha, \beta, \gamma) \), given the values of \( \{\alpha, \beta\} \).

The marginal posterior distribution of \( \alpha, \beta \) was computed algebraically using the conditional probability formula, which was written as:

\[
P(\alpha, \beta | y) = \frac{p(\alpha, \beta, y)}{p(\alpha, \beta)}
\]

Here, the joint posterior distribution of all parameters \( p(\alpha, \beta, \gamma) \) and the \( \theta \)'s conditional posterior distribution \( p(\theta | \alpha, \beta, y) \) were denoted by formulas (2) and (3), respectively:

\[
p(\alpha, \beta) \propto p(\alpha, \beta, \gamma) \prod_{i=1}^{I} \left( \frac{\gamma(x_i + \beta + n_i)}{\Gamma(\gamma + 1)} \right)^{n_i} (1 - \theta_i)^{\beta - 1} \prod_{i=1}^{I} \left( \frac{\gamma(x_i + \gamma)}{\Gamma(\gamma + 1)} \right)^{y_i} \prod_{i=1}^{I} \left( 1 - \theta_i \right)^{\gamma - 1}
\]

\[
p(\theta | \alpha, \beta, y) = \prod_{i=1}^{I} \left( \frac{\gamma(x_i + \beta + n_i)}{\Gamma(\gamma + 1)} \right)^{n_i} \left( 1 - \theta_i \right)^{\beta + n_i - y_i} \prod_{i=1}^{I} \left( \frac{\gamma(x_i + \gamma)}{\Gamma(\gamma + 1)} \right)^{y_i} \prod_{i=1}^{I} \left( 1 - \theta_i \right)^{\gamma - 1}
\]

In these 2 formulas, \( y_i, n_i, \) and \( \theta_i \) represent the number of women with new HIV infections through heterosexual transmission, the sample size, and the proportion of heterosexual transmission among women with new HIV infections in \( j \)th township, respectively.

By substituting (2) and (3) into the formula in (1), the marginal posterior distribution of \( \alpha, \beta \) can be obtained through:

\[
p(\alpha, \beta | y) \propto p(\alpha, \beta) \prod_{i=1}^{I} \left( \frac{\gamma(x_i + \alpha + \beta + n_i)}{\Gamma(\gamma + 1)} \right)^{n_i} \left( 1 - \theta_i \right)^{\beta - 1} \prod_{i=1}^{I} \left( \frac{\gamma(x_i + \gamma)}{\Gamma(\gamma + 1)} \right)^{y_i} \prod_{i=1}^{I} \left( 1 - \theta_i \right)^{\gamma - 1}
\]

To obtain a proper posterior distribution of \( \alpha, \beta \), a diffuse hyperprior density was set as:

\[
p(\alpha, \beta) \propto (\alpha + \beta)^{-5/2}
\]

With the data collected from the Prefecture, we computed the density function in (4) with hyperprior density in (5). Next, 10,000 hyperparameter \( (\alpha, \beta) \) draws were simulated from their normalized marginal posterior distribution. For each township \( j \) \( (j = 1, \ldots, J) \), \( \theta_i \) was sampled from its conditional posterior distribution, \( p(\theta_i | \alpha, \beta, y, \gamma) \sim \text{Beta}(\alpha + y_i, \beta + n_i - y_i) \) as proposed by Gelman. All these analytical procedures were implemented using R version 3.3.3.

Additionally, a GWR model was used to explore spatial variations in the effects of the independent variables on the mode of new female HIV transmission. The model was specified as: Logit \( (p_i) = \sum_k \beta_k \gamma(u_i, v_i) x_{k,i} \) where the \( p_i \) is the estimated probability that the dependent variable is 1, that is, heterosexual HIV transmission among women with new HIV infections, \( \beta_k \) signifies the estimated effects of independent variable \( k \) for individual \( i \), \( (u_i, v_i) \) represents the \( x,y \) coordinates of individual \( i \), and \( x_{k,i} \) indicates a set of independent variables \((k = 1, \ldots, K)\) for individual \( i \). GWR version 4.08 was used to implement the GWR model.

3. Results

3.1. Sociodemographic characteristics

As expected, Table 1 revealed that the vast majority (90.4%) of women with new HIV infections were of Yi ethnic origin. They were primarily engaged in agricultural or animal husbandry activities as farmers or herdsmen (83.1%). About 3 quarters (74.4%) of these women with new HIV infections were married and more than half of them (51.8%) had no formal education at the time of diagnosis. These sociodemographic characteristics were significantly associated with the mode of HIV transmission \( (P < 0.05) \). The spatial distribution of cases and variables are shown in figures included in the appendix, http://links.lww.com/MD/6D41.

3.2. Bayesian hierarchical analyses

By using Bayesian hierarchical models to estimate the proportion of heterosexual transmission among women with new HIV infections in the Prefecture, the marginal posterior distributions for all 4 years were computed. Figure 1 displays the hyper-parameters \( (\alpha, \beta) \) and grids for the 4 years under this study, namely, \( (\alpha, \beta) \in [0.2, 2] \times [0.2, 5] \) for 2011, \( (\alpha, \beta) \in [1.7, 26] \times [1.5, 17] \) for 2012, \( (\alpha, \beta) \in [1, 17] \times [1, 21] \) for 2013, and \( (\alpha, \beta) \in [1.7, 37] \times [0.4, 9] \) for 2014. Figure 2 reports the distribution of the estimated rates of heterosexual transmission among women with new HIV infections from 2011 to 2014 for the sampled townships, respectively. As can be observed from the figure, there was a significant upward trend in the rates of heterosexual transmission during the 4-year period. In spite of the minor fluctuations in 2012 and 2013, the rates for most townships in 2011 were under 0.25, whereas the rates for all townships in 2014 were around 0.80. Moreover, Figure 3 displays the posterior average rates of heterosexual transmission among women with new HIV infections across all townships during the 4-year period. It appeared that the number of women with new HIV infections through heterosexual transmission increased over time: 111, 139, 163, and 172 (not shown in the figure), respectively, from 2011 to 2014. It can be seen from the figure that the higher rates of heterosexual transmission in 2014 were extended to the western and southern townships in addition to the northeastern part of the region where there is a greater concentration of the Yi population.

3.3. GWR analyses

Results GWR analyses are shown in Table 2 and Figure 4. A careful examination of Table 2 suggests that Yi women were less likely to be infected through heterosexual transmission as compared with women with new HIV infections in other ethnic groups. However, this ethnic difference was salient only in about 30% of the townships, especially in the northeastern and/or southern parts of the Prefecture (see Fig. 4). Stated differently, in the remaining 70% of the townships, it was Yi women with new HIV infections that accounted for much of the shift in the mode of HIV transmission from IDU to heterosexual contact. Moreover, as Table 2 indicated, women with new HIV infections engaging in other occupations were less likely to be infected through heterosexual transmission for all townships (100%) than their agricultural and herdsman counterparts, with the odds ratios (ORs) ranging from 0.52 to 0.55 \( (P < 0.05) \). This is particularly true for women residing in the western part of the Prefecture (see Fig. 4). It is also observed that net of other sociodemographic characteristics, being single or married (vs divorced or widowed) decreased the odds of heterosexual transmission for all women with new HIV infections, with the adjusted ORs ranging from 0.31 to 0.38 \( (P < 0.05) \) for unmarried women and from 0.30 to
0.35 (P < 0.05) for married women, respectively (see Table 2). As shown in Table 2 and Figure 4, these marital status effects were present throughout the prefecture (100%) but stronger in the northern townships. Furthermore, in more than half of the townships (55.56%), having primary school education (vs no formal education) was negatively associated with the odds of heterosexual transmission, which was particularly pronounced in the northeastern part of the prefecture (see Fig. 4). However, there was no significant difference between those who had a junior high school education or above and those who had no formal education (see Table 2). Finally, age was statistically insignificant, thus subsequently being removed from Table 2. Spatial variations in the significant sociodemographic predictors are mapped and highlighted in Figure 4.

4. Discussion
Our study revealed that there was a rapid shift in the mode of HIV transmission among women with new HIV infections living in Liangshan from 2011 to 2014. The results from the Bayesian hierarchical model showed that the proportion of heterosexual transmission among women with new HIV infections increased from about 20% in 2011 to approximately 80% in 2014, suggesting that the mode of female HIV infection in this minority region had undergone a dramatic transformation. Taken together, these findings demonstrate that the predominant mode of women with new HIV infections in Liangshan had shifted to heterosexual transmission, and this shift could partially explain why HIV incidence among women in the Prefecture soared from 2011 to 2014, which accounted for almost 42% of all new HIV infections during this period of time.13

As indicated by previous studies, the prevalence of people living with HIV in the Yi minority regions in China ranged from 2.88% to 9.46% in the 2000s.12 If heterosexual contact was the predominant mode of female HIV transmission, then it could be argued that women in these high prevalence minority regions, especially those who are poorly educated, could face serious challenges in protecting themselves from being infected.17,20 Although HIV/AIDS prevention work should continue to focus on such high-risk populations as drug abusers and FSW, earnest attention must be given to heterosexual women who are increasingly at risk for HIV infection through their sexual activities.

To compare with previous studies that explored spatial variations in the risk factors associated with the mode of HIV infection,6 this study also examined the spatial heterogeneity in the socioeconomic and demographic factors associated with heterosexual HIV transmission among women with new HIV infections. One surprising finding was that compared to women in other ethnic groups, Yi women were less likely to be associated
with HIV infection through heterosexual transmission. However, this unanticipated ethnic difference was observed only in 30% of the townships, especially in several eastern counties where heroin use and addiction were common among Yi women. Although public health scholars in China continue to observe differences between Yi women and women in other ethnic groups,[34–36] our study showed that heterosexual activities had become a common mode of HIV transmission for women with new HIV infection living in most townships in Liangshan. Also, we suggest that findings regarding ethnic differences in this study should not be generalized without caution to other minority regions in China, where Yi minority population size is less than that in Liangshan.

As to marital status, we found that divorced or widowed women were more likely to be infected through heterosexual transmission than those who were married or single. This is not surprising given the traditional custom for the widowed to marry her husband’s brother who is known to have been HIV positive. Moreover, because women’s social status remains low with little or no right to negotiate condom use,[37] casual sex and sex without condom persist in this minority region.[27,38,39] This widespread casual sex behavior without consistent condom use might be the central reason for the growing proportion of heterosexual transmission among women, especially among divorced or widowed Yi women.

In addition to marital status, the association between educational attainment and the mode of HIV transmission among women with new HIV infections was found in several northeastern townships. As such, the effects of educational attainment on HIV transmission varied spatially in Liangshan. As discussed previously, the northeastern part of Liangshan is one of the highest HIV-infected areas. As such, education may have a disproportionate effect on HIV transmission since improved education is known to lead to more condom use and less frequent casual sex.[40,41] This finding confirms that the government’s HIV prevention efforts should be harmonized with their targeted poverty alleviation efforts as well as their drive to improve education in this minority region.

5. Study limitations

There were several limitations in this study. First, even though we made concerted efforts to collect every identified and confirmed HIV case involving a woman with new HIV infection in the prefecture by triangulating multiple data sources, it was possible...
that some of the female IDUs had been left out from the present study, given the difficulty to track them over a 4-year period from 2011 to 2014. However, the amount of bias due to this data omission is arguably small as the IDU has been steadily declined in the prefecture and nationwide [3,42]. In addition, patients who were hospitalized and diagnosed with AIDS but did not utilize services provided by PITC were not included in the present study. By the same token, women who were stigmatized and were not monitored by HSS would be omitted from this study as well. Second, when the proportion of heterosexual transmission among women with new HIV infections was estimated, the sample size for several townships was relatively small. This could be due to the fact that some newly infected cases could not be accurately classified as heterosexual transmission. Although Bayesian hierarchical model partially avoided extreme estimates due to the small-sample biases, a slight amount of such biases might still exist. Last but not least, because the number of variables in the constructed database was limited for the present study, future research should include and investigate more risk or protective factors that are potentially associated with the changing mode of HIV transmission among women in Liangshan or other Yi minority areas.

6. Conclusion
Over the past few years, heterosexual transmission has become the predominant mode of HIV transmission among women in Liangshan. This shift in the mode of HIV transmission over a period of 4 years is characterized by a noteworthy spatial diffusion pattern. That is, overtime the rates of heterosexual
transmission have expanded beyond the northeastern townships to the western and southern parts of the prefecture. In addition, sociodemographic factors that are associated with this changing mode of HIV transmission also exhibit spatial variations. These findings suggest that future intervention strategies and programs should be spatially structured and culturally competent to better serve targeted populations in this minority region.

Author contributions

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Supervision: Shujuan Yang.

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Writing – original draft: Chenghan Xiao.

Writing – review & editing: Chenghan Xiao, Danping Liu, Xiaoxi Xu, Peng Jia, Shujuan Yang.

References


