Epidemiological characteristics of pulmonary tuberculosis among students in Guizhou, China: a retrospective study from 2010 to 2020

Jian Zhou 1, Xiaoxue Ma 2, Ting-Jia Lu 3, Yan Zhuang 2, Jin-Lan Li 2, Huijuan Chen 2

ABSTRACT

Objective: We described epidemiological characteristics of pulmonary tuberculosis (PTB) among students and evaluated susceptible populations and areas in Guizhou province and also to provide scientific suggestions for prevention and control.

Setting: Guizhou, China.

Design: This is a retrospective epidemiological study on PTB in students.

Methods: Data are from the China Information System for Disease Control and Prevention. We collected all PTB cases among the student population from 2010 to 2020 in Guizhou. Incidence, composition ratio and hotspot analysis were used to describe epidemiological and some clinical characteristics.

Results: A total of 37,147 new student PTB cases were registered among the population aged 5–30 years during 2010–2020. The proportions of men and women were 53.71% and 46.29%, respectively. Cases aged 15–19 years dominated (63.91%), and the proportion of ethnic groups was increasing during the period. Generally, the raw annual incidence of PTB among the population was increasing from 32.585 per 100,000 persons in 2010 to 48.872 per 100,000 persons in 2020 (\(\chi^2_{\text{raw}}=1283.230, \ p<0.001\)). March and April were the peak months of a year, and cases were clearly grouped in Bijie city. New cases were mainly identified via physical examination, and cases from active screening were still low (0.76%). Additionally, secondary PTB accounted for 93.68%, positive rate of pathogen was only 23.06%, and the recovery rate was 94.60%.

Conclusions: The population aged 15–19 years is the vulnerable population, and Bijie city is the susceptible area. BCG vaccination and promotion for active screening should be the priority of future PTB prevention and control. Tuberculosis laboratory capacity should be improved.

INTRODUCTION

Pulmonary tuberculosis (PTB) is a chronic respiratory infectious disease that seriously endangers human health, epidemic of PTB is serious in China, especially in the western province. 1, 2 Guizhou province is located in western China, with 88 counties. The research results in 2010 showed that the prevalence of active tuberculosis in Guizhou was 1226/100,000, until 2018, annual PTB cases reported in Guizhou were still more than 40,000 and the reported incidence was more than 100/100,000, among them, the number of students with PTB ranked the second among all occupations. 3 Recent studies have shown that the average annual incidence of PTB among students in Guizhou was 46.82/100,000, and the number of student cases accounts for 12.93% of the total cases, which is also higher than in other provinces in China. 4 Therefore, the prevalence of PTB among students in Guizhou is very serious.

There are 49 ethnic groups in Guizhou. The Guizhou Macro Economic Database system showed that among the resident population of Guizhou province, the Han population was 24,511,882, accounting for 63.56%, and the population of all ethnic minorities was 14,050,266, accounting for 36.44%. There were 20,865 schools of all types. WHO put forward a strategy to stop tuberculosis in 2006, which mentioned that we should focus on ethnic minorities. 5 Without early detection and containment, PTB infections in schools can

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study described the epidemiological characteristics of students with pulmonary tuberculosis (PTB) in Guizhou province, China, and discovered key populations and areas.
- Data are from the China Information System for Disease Control and Prevention, contained demographic information, diagnosis and treatment information of all students with PTB registered in Guizhou from 2010 to 2020.
- We investigated and analysed the reasons for the research’s results, and summarised the appropriate prevention and control measures for students with PTB.
- Main limitation of this study is that the incidence rates of various student populations and school types were not obtained.

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quickly spread across the campus. Most of the existing epidemiological studies on PTB among students are based on the occupation or outbreaks. Studies have shown that adolescents account for approximately 20% of PTB cases worldwide, some of which are student cases.

Therefore, it is necessary and urgent to describe the epidemiological characteristics of students with PTB in Guizhou, identify key populations and key areas and explore scientific and effective measures for the PTB prevention and control among students in Guizhou province.

METHODS

Study design and participants
PTB cases, registered in Guizhou from 1 January 2010 to 31 December 2020 were obtained from the China Information System for Disease Control and Prevention, and annual demographic information of students in Guizhou province came from Guizhou Provincial Bureau of Statistics. Inclusion criteria for this study were: (1) student, as long as their occupation is student in school, including primary school, middle school, high school, university; (2) diagnosis was PTB; (3) ≥ 5 years old. We excluded students who were too young and too old because they were not representative (those younger than 5 and older than 40).

Definitions
In this study, PTB cases were defined as tuberculosis lesions occurring in the lung tissues, trachea, bronchus and pleura, case types included both clinically diagnosed cases and confirmed cases. Ethnic groups included Han, Miao, Tujia, Buyi, Yi and ‘others’, besides Han, other ethnic groups are called ethnic minorities. Discovery methods include seeking medical advice for symptoms, referral, tracking, physical examination, recommendation, active screening and others (Seeking medical advice for symptoms: A PTB patient voluntarily visits the hospital because of related symptoms. Referral: A PTB patient is transferred from a non-designated hospital to a designated hospital. Tracking: Doctors find PTB patients according to clues and let him go to the hospital for treatment. Physical examination: PTB patients are detected during the physical examination. Recommendation: A PTB patient goes to the hospital after following the advice of others. Active screening: PTB patients identified through planned population screening. Other: Ways except above-mentioned six ways). Diagnostic types are classified by lesion location and include secondary PTB, tuberculous pleurisy, haematogenous disseminated PTB and Primary PTB (Secondary PTB: including infiltrative PTB, tuberculoma, caseous pneumonia, chronic fibrous cavitary PTB, etc. Tuberculous pleurisy: including dry pleurisy, exudative pleurisy and tuberculous empyema. Haematogenous disseminated PTB: including acute, subacute and chronic haematogenous disseminated PTB. Primary PTB: including primary syndrome and

<table>
<thead>
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<th>Classification of population</th>
<th>Number of cases</th>
<th>Proportion (%)</th>
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<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>19950</td>
<td>53.71</td>
</tr>
<tr>
<td>Female</td>
<td>17197</td>
<td>46.29</td>
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<td><strong>Age</strong></td>
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<tr>
<td>5–14</td>
<td>5660</td>
<td>15.24</td>
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<tr>
<td>15–19</td>
<td>23742</td>
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<tr>
<td>20–24</td>
<td>7466</td>
<td>20.10</td>
</tr>
<tr>
<td>25+</td>
<td>279</td>
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<td><strong>Ethnic group</strong></td>
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<td>Han</td>
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<td>Miao</td>
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<td>Tujia</td>
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<td>Buyi</td>
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<tr>
<td>Yi</td>
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<tr>
<td>Dong</td>
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</tr>
<tr>
<td>Gelao</td>
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<tr>
<td>Other</td>
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<td>3.27</td>
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<td><strong>Ways of discovery</strong></td>
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<td>Referral</td>
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<td><strong>Types of diagnosis</strong></td>
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<td>Secondary PTB</td>
<td>34800</td>
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<td>Tuberculous pleurisy</td>
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<td><strong>Aetiological results</strong></td>
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<tr>
<td>Negative</td>
<td>26917</td>
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<tr>
<td>Positive</td>
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<tr>
<td>Tuberculous pleurisy</td>
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<tr>
<td>No result</td>
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<td><strong>Treatment outcomes</strong></td>
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<td>35400</td>
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<tr>
<td>Cure</td>
<td>7696</td>
<td>20.56</td>
</tr>
<tr>
<td>Completing the course of treatment</td>
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<td>74.04</td>
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<tr>
<td>Adverse outcomes</td>
<td>2017</td>
<td>5.40</td>
</tr>
<tr>
<td><strong>Table 1 Basic characteristics of students with PTB in Guizhou province, 2010–2020 (n=37147)</strong></td>
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Successful treatment includes cure and completing the course of treatment.

PTB, pulmonary tuberculosis.
intrathoracic tuberculosis of lymph nodes, including caseous pneumonia and tracheobronchial tuberculosis in children). Aetiological results include negative, positive, tuberculous pleurisy, no result (aetiological results were based on sputum smears, sputum cultures and molecular biology tests). Treatment outcomes include cure, completing the course of treatment, successful treatment (cure+completing the course of treatment), adverse outcomes (which refers to treatment outcomes other than cure and completing the course of treatment, including adverse reactions, loss to follow-up, treatment failed, died and switch to multidrug resistance). Treatment failed: Treatment terminated or need for permanent regimen change of at least two anti-tuberculosis drugs because of: Lack of conversion by the end of the intensive phase; or bacteriological reversion in the continuation phase after conversion to negative; or evidence of additional acquired resistance to fluoroquinolones or second-line injectable drugs. Lost to follow-up: A patient whose treatment was interrupted for two consecutive months or more). \[14\] Definition of cure: For patients with sputum test were positive, complete the prescribed course of treatment, at least three times of sputum test, two consecutive times of negative sputum test results, one of which was at the completion of treatment. For patients with sputum test were negative, complete the prescribed course of treatment and have no positive sputum result during the treatment. Definition of completing the course of treatment: The patient completed the prescribed course of treatment without adverse outcomes, but did not reach the level of cure.

**Statistical analysis**

The incidence of PTB among students is equal to the number of students with PTB divided by the total number of students in the same year. Positive rate of pathogens is equal to the number of pathogenic positive cases divided by the total number of cases. Successful treatment rate is equal to the number of successfully treated cases divided by the total number of cases (successfully treated cases include those cured and completed the course of treatment). We used composition ratio to describe characteristics of gender, age, ethnic group and time of PTB among students in Guizhou. In addition, in order to know the ability of clinical diagnosis and treatment of PTB among students, we also analysed discovery ways, aetiological results, diagnosis results and treatment outcomes. Disparities in incidence trend for subgroups were analysed.
through the trend $\chi^2$ test with the IBM SPSS V.22.0. Spatial clustering, especially hot spot analysis, was estimated by the Getis-ORD $Gi^*$ through the ArcMap V.10.2 software, where Getis-ORD $Gi^*$ is a well-accepted algorithm to assess and depict high-value or low-value clustering problems of local spatial attribute values.\textsuperscript{15 16} The cold spot region represents not only the low value itself, but also the low value around the cold spot region, which is a concentrated area of low values. We defined $\alpha=0.05$ as the significance level and the $p$ value was two-sided, $p<0.05$ was considered statistically significant.

**RESULTS**

**Participant characteristics**

A total of 37,147 students with PTB in Guizhou from 2010 to 2020 were included in this study, including 19,950 men and 17,197 women (men:women=1.16:1). The number of PTB among students aged 15–19 years was the largest, with 23,742 (63.91%). The number of Han cases was the largest, with 24,188 (65.11%), followed by Miao, with 4,547 (12.24%). The ways that cases were discovered showed that the proportion of seeking medical advice for symptoms was the largest (35.07%), followed by referral, and active screening was only 0.76%. Diagnosis results showed that secondary PTB accounted for 93.68%, and tuberculous pleurisy accounted for 3.33%. Aetiological results showed that the positive rate of pathogens was only 23.06%. Treatment results showed that the successful treatment rate was 94.60%, the cure was 20.56%, completing the course of treatment was 74.04% and the adverse outcome was 5.40% (table 1).

**Population characteristics of PTB among students in Guizhou**

The ratio of male to female students with PTB was 1.31 in 2010, 1.308 in 2015 and 1.16 in 2020 (figure 1A). The results of our study showed that the proportion of student cases aged 15–19 years increased first and then decreased,
in general, the proportion increased from 56.11% in 2010 to 61.34% in 2020. In addition, we can clearly see that the proportion of student cases aged 5–9 years was decreasing, from 4.45% in 2010 to 1.47% in 2020, and the proportion of students cases aged 10–14 years decreased from 17.35% in 2010 to 13.30% in 2020 (figure 1B). We counted the number of PTB cases for each age, and the largest number of cases was 18 years old, followed by 17 years old and the third was 16 years old (figure 1C). The changes in ethnic composition ratio demonstrated that the proportion of Han students with PTB was the largest but gradually decreased, and the proportion of ethnic minorities was increasing, among which the proportion of Yi and Gelao increased significantly, followed by Miao (figure 1D).

**Temporal characteristics of PTB among students in Guizhou**

The incidence of PTB among students in Guizhou showed an upward trend from 2010 to 2020, from 32.585/100 000 in 2010 to 48.872/100 000 in 2020 ($\chi^2_{\text{trend}}=1283.230$, $p<0.001$), and the highest incidence was 52,960/100 000 in 2018 (figure 2A). A monthly number of student cases showed that the peak number of student with PTB was in March or April each year, but the peak in 2020 was in June (figure 2B).

**Spatial characteristics of PTB among students in Guizhou**

We drew the hot spot map of the number of students with PTB in Guizhou in 2010, 2015 and 2020. We can see that the hot spots were all concentrated in the western part of Guizhou and the number of hot areas was increasing, there were four hot spots in 2010 (99% confidence), and they all belong to Guizhou’s Bijie city (figure 3A). Seven areas became hot spots in 2015 (99% confidence), of which five belonged to Bijie city and two belong to Liupanshui city (figure 3B). There were eight hot spots in 2020 (99% confidence), of which six belong to Bijie city and two belong to Liupanshui City. There were five cold spots in 2020 (95% confidence), all of which were in Guiyang City (figure 3C).

**Clinical characteristics of PTB among students in Guizhou**

The discovery methods of these student cases showed that the proportion of seeking medical advice for symptoms, tracking and recommendation decreased, the proportion of physical examinations increased significantly and the proportion of active screening increased but remained very small (figure 4A). The diagnostic types showed that the proportion of secondary PTB and tuberculous pleurisy increased, and the proportion of haematogenous disseminated PTB and primary PTB decreased (figure 4B). In addition, our study found that primary PTB was mainly concentrated in students aged 7–14 years (206/277, 74.37%), secondary PTB was mainly concentrated in students aged 15–20 years (25,601/34,800, 73.57%) and tuberculous pleurisy was mainly concentrated in students aged 15–19 years (817/1236, 66.10%). The aetiological results showed that the positive rate of pathogens was low, but decreased first and then increased, while the proportion of negative results increased first and then decreased. The proportion of tuberculous pleurisy increased overall, and the proportion of those without aetiological results significantly decreased (figure 4C).

The treatment outcomes of these student cases with PTB showed that the proportion of completing the course of treatment first increased and then decreased, the proportion of cured cases first decreased and then increased and the successful treatment rate was more than 90% each year (figure 4D).
DISCUSSION
Epidemiology
Existing data and studies showed that the ratio of male to female population in Guizhou was about 1.05:1, and the ratio of male to female PTB cases was 1.88:1, which is consistent with the finding of previous studies that men are more likely to become PTB cases than women.3 17 18 However, our results showed that the ratio of male to female among students with PTB is 1.16 to 1, which was different from the whole population, which indicated that there may be no difference in the possibility of male and female students become PTB cases. 15-year-old to 19-year-old student cases with PTB accounted for the most, which were mainly concentrated in 16 to 18 years old, these students are almost all high school students, and their proportion was rising, which suggests that high school student is a key population, the reason may be that many Chinese high school students have heavy study, lack of rest, lack of exercise and high mental stress,19–21 which lead to them have lower resistance and are more likely to be infected with mycobacterium tuberculosis and become PTB cases. The proportion of students cases with PTB under 14 years old was decreasing, especially in children aged 5–9 years old, the reason is probably that the policy of free BCG vaccination for newborns has been consistently implemented in Guizhou, and with the improvement of people’s health awareness, the BCG vaccination rate of newborns has also increased than before, which has largely reduced the PTB incidence among children.22–24 Second, with the rapid social and economic development and social attention to children’s health, as well as the progress of medical conditions, children’s physical health were also better than before,25 26 which was one of the reasons for the decline in the proportion of children with PTB. Existing studies have shown that the incidence of PTB in Han was significantly higher than that in ethnic minorities.27 28 Our results showed the number of Han cases was very large, but the proportion gradually decreased, and the proportion of ethnic minorities gradually increased, after the investigation, it was found that the proportion of ethnic minority population in Guizhou was gradually increasing. In addition, the reason for the obvious increase in Yi and Gelao cases was due to the increase in their population’s proportion, but special living habits, lifestyles and genetic differences of the population could not be excluded.29 30

March or April was the peak of the registration of PTB among student in Guizhou, the reason was that March and April was the time of physical examination before China’s high school and college entrance examination, so a large number of students with PTB were found through physical examination, followed by March 24 is World Tuberculosis Day, which raises people’s awareness of seeking healthcare. However, the peak in 2020 appeared in June, because the epidemic of COVID-2019 in early 2020, Guizhou was in the state of stopping production and school from February 2020 to April 2020, and no medical or diagnostic services related to tuberculosis were carried out during this period, which began to recover gradually in May, so June was the peak in 2020.3 31 The incidence of PTB among students in Guizhou showed an upward trend from 2010 to 2020, the main reason was...
Guizhou gradually increased the detection of PTB among students since 2015, China and Guizhou have formulated and implemented the norms and guidelines on PTB prevention and control in schools, which were targeted at all types of schools (including primary, middle, high schools, universities and various vocational schools). Guizhou has implemented physical examination for freshmen entrance and health examination to discover PTB cases. Therefore, the number and incidence of PTB among students in Guizhou have increased significantly since 2015, and this result also suggested that there may be many undiscovered PTB cases among students in Guizhou.

Student PTB cases were mainly concentrated in western Guizhou, Bijie city, and the number of hot spot areas was gradually increasing, the reason for this result was that the population of each county in Bijie city was far more than that in other counties, but the economic, educational conditions and people’s health awareness in Bijie city were slightly worse than those of other cities, as a result, the number of students with PTB in Bijie city was large. Second, Guizhou has gradually paid more attention to PTB prevention and control in Bijie city, and the government and health departments have increased funds for the entrance physical examination and active screening of freshmen, which has led to a large number of students PTB cases being discovered. So we have reason to think that there may be many undiscovered student’s PTB cases in Bijie city from the results of our study. In addition, it is worth noting that Guiyang city had also implemented the entrance physical examination for many years, there were some cold spots in 2020, the reason was Guiyang city was the capital city of Guizhou, and its medical, economic and educational conditions and people’s health awareness were better than other areas, so those policies were being implemented very well there.

Clinical diagnosis and treatment

The proportion of physical examinations in the way of discovery has increased significantly, which was the result of the entrance physical examination and health examination of freshmen implemented for many years in Guizhou. Our preliminary work and investigation results found that PTB outbreaks occurred frequently in Guizhou in the past 10 years, and we carried out active screening in Bijie city, where PTB outbreaks frequently occurred, which led to many students with PTB were discovered, so it is necessary to carry out active screening in areas with very serious tuberculosis epidemics such as Guizhou. Existing studies have shown that active screening can discover a large number of PTB cases in areas with a high incidence of PTB. In addition, Guizhou requires schools to carry out screening of close contacts immediately after the occurrence of PTB cases in the class, including those who are in the same class and dormitory with the cases, and gradually expand the scope of screening in the whole school until no new PTB cases are discovered. However, our research results showed that although the proportion of active screening has increased, it accounts for only 0.76%, the reason was that although the Center for Disease Control and Prevention has increased the attention and effort to active screening of school students, there was still insufficient funding, and the enthusiasm and cooperation of education departments for an active screening of PTB in schools was not enough, and the active screening of PTB in students was not free, so some teachers and parents were not willing to participate in the work, which led to the slow progress of active screening.

Aetiological examination is an important basis for the diagnosis of PTB, and the positive rate of pathogen is an important indicator to reflect the diagnostic ability and level of tuberculosis laboratory in a region. Our study found that the positive rate of pathogens in students with PTB was only 23.06%, which was much lower than the results of the whole population in Guizhou, and also lower than the results of other provinces in China. But the positive rate of pathogens showed an upward trend, the reason was that Guizhou Provincial Center for Disease Control and Prevention was gradually improving the ability of tuberculosis laboratory, carrying out the quality control on tuberculosis laboratory and the quality control on aetiological negative result, so the positive rate of pathogens was gradually increasing. However, the number of tuberculosis laboratory personnel in many Guizhou’s counties was insufficient, and whose ability was not high, laboratory facilities were not good enough, so the comprehensive ability of the laboratory was lower than that of other provinces in China.

The proportion of secondary PTB increased, and primary PTB decreased, this result conforms to the overall trend of PTB prevention and control, and the results of our research also showed that the age of primary PTB cases was mainly concentrated in 7–14 years old, secondary PTB mainly concentrated in 15–20 years old, which means that the primary PTB mainly mostly occurs in children and secondary PTB mostly occurs in teenagers. The proportion of tuberculous pleurisy increased, which should be noted.

The treatment outcomes showed that the treatment ability for PTB in Guizhou was good, with a successful treatment rate of 94.60%, which was better than other provinces in China and some other countries. The reason was Guizhou continuously strengthened the construction of clinical treatment ability and achieved good effects. Second, the treatment course of PTB cases was more than 6 months, and farmers accounted for the majority of PTB, students had better compliance than farmers during the treatment process, and students often had easier to completing the treatment course, so the successful treatment rate of students was higher than that of other groups.
CONCLUSIONS

The gender difference in PTB among students is milder than that of the whole population. 15–19 years old students, high school students and those who are Yi and Gelao minorities are the susceptible population. Bijie city is the highest-risk area. It is necessary to continue to implement BCG vaccination, physical examination, health examination for freshmen and active screening. The financial investment for PTB prevention and control in schools should be increased, and medical and health departments, education departments and other relevant departments should strengthen cooperation for students PTB. The treatment ability of PTB in Guizhou has gotten effective results but accelerating improvement of tuberculosis laboratory capacity and training of laboratory personnel are still in high demand.

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