ABSTRACT
Objective: To analyze the influence of multimorbidity on the treatment outcome of new cases of pulmonary tuberculosis.
Method: A population-based analytical study, using secondary data, collected from the database of the Notification Disease Information System, of new cases of pulmonary tuberculosis in the state of Rio Grande do Sul between 2013 and 2016. The relationship between multimorbidity and the outcome was analyzed with Multinomial Logistic Regression.
Results: Multimorbidity was present in 37.0% of the cases. Of these, the Relative Risk (RR) was 1.7 for treatment abandonment and 2.9 for death. HIV had an RR of 2.1 for dropout and of 3.9 for death. The higher the number of comorbidities, the higher the RR for unfavorable outcomes.
Conclusion: Multimorbidity influences on unfavorable outcomes of the treatment for tuberculosis.
Keywords: Tuberculosis. Multimorbidity. Comorbidity. Treatment outcome. Epidemiological monitoring.

RESUMO
Objetivo: Analisar a influência da multimorbidade no desfecho do tratamento de casos novos de tuberculose pulmonar.
Métodos: Estudo analítico de base populacional, utilizando dados secundários, coletados no banco de dados do Sistema de Informação de Enfermidades de Notificação de casos novos de tuberculose pulmonar ocorridos no estado do Rio Grande do Sul entre os anos de 2013 e 2016. A relação entre a multimorbidade e o desfecho foi analisada com Regressão Logística Multinomial.
Resultados: A multimorbidade esteve presente em 37,0% dos casos. Destes, o risco relativo (RR) foi de 1,7 para o abandono do tratamento e de 2,9 para o óbito. O HIV apresentou um RR de 2,1 para o abandono e de 3,9 para óbito. Quanto maior o número de comorbidades, maior será o RR para os desfechos desfavoráveis.
Conclusões: A multimorbidade influencia nos desfechos desfavoráveis do tratamento da tuberculose.
Palavras-chave: Tuberculose. Multimorbidade. Comorbidade. Resultado do tratamento. Vigilância epidemiológica.

RESUMEN
Objetivo: Analizar la influencia de la multimorbilidad en el resultado del tratamiento de nuevos casos de tuberculosis pulmonar.
Método: Estudio analítico de base poblacional, en el que utilizan datos secundarios, recopilados de la base de datos del Sistema de Información de Enfermedades de Notificación, de nuevos casos de tuberculosis pulmonar en el estado de Rio Grande do Sul entre 2013 y 2016. La relación entre la multimorbilidad y el resultado se analizó con regresión logística multinomial.
Resultados: Se registró multimorbilidad en el 37,0% de los casos. De estos, el riesgo relativo (RR) fue de 1,7 para el abandono del tratamiento y de 2,9 para la muerte. El VIH tuvo un RR de 2,1 para el abandono y de 3,9 para la muerte. A mayor cantidad de comorbilidades, mayor será el RR correspondiente a resultados desfavorables.
Conclusión: La multimorbilidad influye en los resultados desfavorables del tratamiento de la tuberculosis.
Palabras claves: Tuberculosis. Multimorbilidad. Comorbilidad. Resultado del tratamiento. Monitoreo epidemiológico.
INTRODUCTION

Tuberculosis is an infectious disease of chronic evolution which is directly related to the socioeconomic aspects of the population and represents a serious public health problem worldwide. According to the World Health Organization (WHO), it is among the top 10 death causes in the world, overcoming infection by HIV\(^1\). In 2016, 10.4 million people worldwide developed tuberculosis and 1.8 million died by the disease\(^2\).

Brazil is part of the group of countries that concentrate 50% of the disease burden in the world; in 2015, 69 thousand people fell ill in the country and 4.5 thousand died from tuberculosis\(^3\). In 2015, 69,569 new cases of tuberculosis were reported, representing an incidence coefficient of 33.5 cases per 100,000 inhabitants (inhab.), and there were 4,534 deaths due to the disease\(^4\).

To reverse this scenario, from 2015 onwards, the WHO, together with STOP TB and with the Tuberculosis Control Programs of priority countries, has been investing in the "End TB" strategy, which aims to eliminate tuberculosis as a public health problem (<1 case per 100,000 inhabitants) and to reduce deaths by 95% by 2035\(^2\).

The treatment for tuberculosis is effective and available free of charge by the Unified Health System; however, the cure is achieved on average only by 70% of those affected, staying below the 85% recommended by the WHO to ensure the control of the disease. As for the unfavorable outcomes, 11.3% abandoned treatment and 1,077 individuals acquired resistant multi-drug tuberculosis in 2014\(^5\). These results are attributed to the barriers related to the socioeconomic, behavioral and clinical characteristics of those affected, to the sensitivity profile of the tuberculosis bacillus, and also to the care received in the health services and to the prolonged use of medication\(^6\).

Among the clinical conditions, studies show that the presence of another disease is associated with the unfavorable outcomes of the tuberculosis treatment, among which are HIV, diabetes mellitus and chronic kidney conditions\(^6-8\). However, no studies were found that observed the relationship between multimorbidity and the outcome of the treatment for the disease. Multimorbidity is conceptualized as the presence of two or more diseases in the same individual, is considered a public health problem due to the increasing prevalence and to the reduction in the quality of life and life expectancy of the individual\(^9-11\).

The relevance of this study is noteworthy since multimorbidity is associated with low percentages of adherence to drug therapy, relating to polypharmacy due to the difficulty of integration among the health services. These aspects imply an increase in the use of services, generating costs for the affected individual and for the health system. Multimorbidity care requires a network of interconnected services, with decentralized health actions for Primary Care, which must act as a protagonist of care, with family health teams that enable care centered on people's needs\(^10-12\).

This study aims to contribute to the alignment of the health policies aimed at individuals with tuberculosis who present multimorbidity. Thus, it aimed to analyze the relationship between the presence of multimorbidity and the treatment outcome of new cases of pulmonary tuberculosis.

METHODS

An analytical, longitudinal, and population-based study, using secondary data collected in the database of the Notification Disease Information System (Sistema de Informação de Agravos de Notificação, SINAN), regarding new cases of pulmonary tuberculosis that occurred in the state of Rio Grande do Sul between 2013 and 2016.

The state of Rio Grande do Sul is located in the South of Brazil, with a territorial area of 281,731.445 km\(^2\), and a population of 11,322.895 inhabitants distributed among the 497 municipalities that make up the state\(^13\). The SINAN concentrates the individual notification of the occurrence of diseases and illnesses from the national list of compulsorily notifiable diseases\(^14\), among which is tuberculosis. After confirmation of the diagnosis, the health professional responsible for the detection/treatment of the disease, regardless of the level of attention, registers the case by completing the epidemiological investigation form (ficha de investigação epidemiológica, FNI) for tuberculosis.

In order to have access to the data of this study, a request of the SINAN database was made, concerning the notifications of tuberculosis in the state of Rio Grande do Sul, to the General Coordination sector of the National Program for the Control of Tuberculosis. This Program authorized the use of the database and availed it in Excel, for the years 2013 to 2017. The database was received in July 2018, containing 31,317 tuberculosis case records. The data from the database are entered from the compulsory notification forms, which gather sociodemographic information, diagnosis, and types of tuberculosis, morbidities, examinations, treatment, and treatment outcome.

In selecting the variables of interest for the present study, the following were used as inclusion criteria: notifications/ investigations of lung tuberculosis cases with entry record as a new case; the notification period being restricted from 2013 to 2016, since the cases referring to the year 2017 were not yet complete. Notifications that had the registration of
change in diagnosis and/or transfer as an outcome of the treatment were also excluded. The change of diagnosis for the disease not being tuberculosis, and in the case of transfer because the final outcome of the case was not obtained, due to transfer to another treatment site, which presents a new entry in the database.

The study’s dependent variable was the treatment outcome (cure/abandonment/death/multi-drug resistance). The independent variables were grouped into: Sociodemographic characteristics - age (in years old); gender (female/male); skin color (white/non-white); education (illiterate/incomplete elementary school/complete elementary school/complete high school/complete higher education); area of residence (rural/urban); receives government benefit (no/yes); institutionalized population (no/yes); street population (no/yes). Multimorbidity - multimorbidity (no/yes); number of morbidities apart from tuberculosis (none/one/two/three or more); HIV (no/yes); diabetes (no/yes); mental illness (no/yes); illicit drugs (no/yes); smoking (no/yes); alcoholism (no/yes). Type of treatment - (DOT/Self-applied).

The database was analyzed by means of the Stata® 13.0 software. Initially, the descriptive analysis was performed, with distribution of absolute and relative frequencies for the categorical variables, and the mean and standard deviation for the continuous variables. To identify the relationship of the occurrence of the independent variables in the treatment outcome, the multinomial logistic regression analysis was used. In the adjusted analysis, the variables that presented an association with the outcome \( p \leq 0.05 \) were inserted in the models. Models containing the dependent variable and the independent variables by groups were used: sociodemographic characteristics and multimorbidities. The confidence interval used was 95%.

In conducting this study, although the proposal was not sent to the Research Ethics Committee for being a production based on secondary data collection, the ethical principles of research with human beings were respected\(^{15}\), since there was no access to personal data identifying the user.

### RESULTS

Table 1 shows that between 2013 and 2016, in the state of Rio Grande do Sul, 14,323 new cases of pulmonary tuberculosis were reported to the SINAN, with a record of treatment outcome by cure, death, abandonment, or infection by a multi-drug-resistant bacillus. Among these, 67.0% (9,596) were male, with a mean age of 41.6 years old (SD=17.1), ranging from zero to 107 years old, 71.3% (9,894) with white skin color, 57.4% (6,364) with incomplete elementary education, and 6.2% (449) received government benefit. As for the place of residence, it was verified that 95.5% (13,255) lived in the urban area, 13.5% (825) as institutionalized population, and 4.2% (354) were homeless.

Table 2 shows the description of the variables related to the presence of multimorbidity, type of treatment, and treatment outcome of the cases. The presence of multi-morbidity was verified in 37.0% (4,587) of the cases, with 6.7% (838) presenting two or more morbidities besides tuberculosis, with emphasis on HIV with 17.7% (2,308) cases, and on smoking with 31.2% (2,547).

Regarding the treatment, 25.3% (3,073) performed Directly Observed Treatment (DOT). As for the treatment outcome, a favorable outcome was observed with 71.3% (10,208) of cure and 28.7% (4,115) with unfavorable outcomes.

Table 3 shows the multinomial logistic regression analysis performed between the characteristics of multimorbidity and the treatment outcome. In this analysis, the Relative Risk (RR) in obtaining an unfavorable outcome rises in the presence of multimorbidity. For the abandonment of treatment being of 1.7 \( (CI=1.6 - 1.9; p<0.001) \) times higher, for death 2.9 \( (CI=2.5 - 3.3; p<0.001) \) times higher, and for the multi-drug resistance 2.5 \( (CI=1.9 - 3.1; p<0.001) \) times higher among those affected by multimorbidity, when compared to those without other diseases.

It was verified that as the number of morbidities in the person with pulmonary tuberculosis increases, so does the RR in obtaining unfavorable treatment outcomes. In the case of the abandonment outcome, the RR obtained in the presence of two morbidities besides tuberculosis stands out, which was 2.5 \( (CI=2.1 - 2.9; p<0.001) \) times higher for the abandonment of treatment. For the death outcome, it was identified that, as the number of morbidities besides tuberculosis increases, the RR is 7.4 \( (CI=4.4 - 12.4; p<0.001) \) times higher to obtain the death outcome among those who have three or more chronic conditions besides tuberculosis when compared to those who had only tuberculosis. Regarding the outcome of multi-drug resistance, there was statistical significance concerning the presence of two morbidities besides tuberculosis, the RR of multi-drug resistance being 3.3 \( (CI=2.3 - 4.9; p<0.001) \) times higher.

In the analysis of the outcome in relation to the presence of illnesses and associated diseases (HIV, mental illness and diabetes mellitus), we obtained a relative risk of abandonment outcome over the cure outcome of 2.1 \( (CI=1.9 - 2.4; p<0.001) \) times for cases of HIV infection, compared to those without it. The existence of diabetes mellitus represented a protective factor in relation to the abandonment of treatment, with a relative risk of 0.5 \( (CI=0.4 - 0.7; p<0.001) \). And the existence of mental illness had no statistical significance. Whereas having HIV represented a relative risk of 3.9 \( (CI=3.3 - 4.6; p<0.001) \).
Table 1 – Sociodemographic characteristics of the new cases of pulmonary tuberculosis reported between 2013 and 2016 in the state of Rio Grande do Sul, Brazil (N=14,323), 2018

| Variable (N)                        | n    | %  |
|-------------------------------------|------|----|
| **Gender (14,322)**                 |      |    |
| Female                              | 4,726| 33.0|
| Male                                | 9,596| 67.0|
| **Age in years old (14,159)**       |      |    |
| 0 to 17                             | 617  | 4.4 |
| 18 to 30                            | 3,733| 26.3|
| 31 to 40                            | 2,951| 20.7|
| 41 to 50                            | 2,520| 17.7|
| 51 to 59                            | 2,037| 14.4|
| 60 and older                        | 2,301| 16.5|
| **Skin color (13,885)**             |      |    |
| White                               | 9,894| 71.3|
| Non-white                           | 3,991| 28.7|
| **Schooling (11,099)**              |      |    |
| Illiterate                          | 514  | 4.6 |
| Incomplete Elementary               | 6,364| 57.4|
| Complete Elementary                 | 2,365| 21.3|
| Complete Secondary                  | 1,498| 13.5|
| Higher Education Degree             | 358  | 3.2 |
| **Government Benefit (7,244)**      |      |    |
| No                                  | 6,795| 93.8|
| Yes                                 | 449  | 6.2 |
| **Area of residence (13,885)**      |      |    |
| Rural                               | 630  | 4.5 |
| Urban                               | 13,255| 95.5|
| **Institutionalized population (6,271)** |      |    |
| No                                  | 5,422| 86.5|
| Yes                                 | 825  | 13.5|
| **Street population (8,436)**       |      |    |
| No                                  | 8,082| 95.8|
| Yes                                 | 354  | 4.2 |

Source: SINAN’s database (2013-2016), 2018.
Table 2 – Characteristics of multimorbidity, type of treatment and treatment outcome of the new cases of pulmonary tuberculosis, notified between the years 2013 and 2016 in the state of Rio Grande do Sul, Brazil (N=14,323), 2018

| Variables (n)                                      | n   | %   |
|---------------------------------------------------|-----|-----|
| Presence of multimorbidity (12,396)                |     |     |
| No                                                 | 7,809 | 63.0 |
| Yes                                                | 4,587 | 37.0 |
| Number of morbidities (12,396)                     |     |     |
| Only tuberculosis                                  | 7,809 | 63.0 |
| Tuberculosis +1                                     | 3,749 | 30.3 |
| Tuberculosis +2                                     | 759  | 6.1  |
| Tuberculosis and 3 others or more                   | 79   | 0.6  |
| HIV (13,049)                                       |     |     |
| No                                                 | 10,741 | 82.3 |
| Yes                                                | 2,308 | 17.7 |
| Mental Illness (13,618)                            |     |     |
| No                                                 | 13,130 | 96.4 |
| Yes                                                | 488  | 3.6  |
| Diabetes (13,426)                                  |     |     |
| No                                                 | 12,373 | 92.2 |
| Yes                                                | 1,053 | 7.8  |
| Illicit drugs (8,205)                              |     |     |
| No                                                 | 6,926  | 84.4 |
| Yes                                                | 1,279 | 15.6 |
| Smoking (8,168)                                    |     |     |
| No                                                 | 5,621  | 68.8 |
| Yes                                                | 2,547 | 31.2 |
| Alcoholism (13,579)                               |     |     |
| No                                                 | 11,364 | 83.7 |
| Yes                                                | 2,215 | 16.3 |
| Directly Observed Treatment (12,126)               |     |     |
| No                                                 | 9,053  | 74.7 |
| Yes                                                | 3,073 | 25.3 |
| Treatment outcome (14,323)                         |     |     |
| Cure                                               | 10,208 | 71.3 |
| Abandonment                                        | 2,379  | 16.6 |
| Death                                              | 1,384  | 9.7  |
| Multi-drug resistance                              | 352   | 2.4  |

Source: SINAN's database (2013-2016), 2018.
p<0.001) times higher for the death outcome. Having mental illness and diabetes had no statistical significance. The RR for the multi-drug-resistance outcome was 3.1 (CI=2.3 - 4.1; p<0.001) times higher in cases with HIV infection, and there was no statistical significance in the presence of mental illness and diabetes mellitus.

As for the illicit drugs, the RR of abandonment of treatment was 3.1 (CI=2.6 - 3.7; p<0.0001) times higher among those who used illicit drugs and 1.3 (CI=1.1 - 1.6; p=0.003) times higher among alcoholics. Smoking was of no statistical significance. For the death outcome, only alcoholism presented statistical significance with an RR of 1.5 (CI=1.2 - 1.9; p<0.0001) times higher than those who did not consume the substance. In the multi-drug-resistant infection outcome, there was no statistical significance for the conditions evaluated.

**DISCUSSION**

The population under study presented characteristics similar to the results of research studies conducted in Brazil, Ethiopia and Bangladesh. These similarities, in each scenario, reinforce that tuberculosis is a pathology directly linked to social vulnerability, and that it primarily affects males of working age.

We acknowledge that the profile of those affected is closely related to the tuberculosis treatment outcome; in the case of the presence of multi-morbidity, there is an increased risk of obtaining the unfavorable outcome. In this study, multimorbidity was present in 37% of the cases, with smoking (31.2%) and HIV (17.7%) being the most common morbidities, as identified by other researchers. The HIV, tuberculosis and smoking triad poses a global health...
challenge, and there is evidence that its presence increases the risk of Latent Tuberculosis Infection (LTI) progressing to the situation of active disease. Apart from causing a delay in the negativity of the sputum examination, and unfavorable outcomes such as non-adherence to treatment, cases of failure of the basic treatment scheme, and the multi-drug resistance\textsuperscript{7,8,17–18}.

The epidemiological relevance of TB/HIV co-infection lies on the fact that a person living with HIV (PLHIV) is 28 times more likely to develop active tuberculosis than a person non-infected by HIV\textsuperscript{2}. Therefore, it is recommended to investigate LTI, with universal treatment for all PLHIV with CD4 below 350 cel/mm regardless of whether the tuberculin test or Interferon Gamma Release Assay is carried out \textsuperscript{12,19}. The diagnosis of LTI makes it possible to indicate the prophylactic treatment and, consequently, the reduction of the risk of developing the active disease, the treatment of which is more complex, costly and with a more unfavorable prognosis.

When analyzing the outcomes achieved with the treatment of lung tuberculosis, 71.3% of the cases were cured, 16.6% abandoned the treatment and 9.7% were concluded in death. These results corroborate the indicators observed in the national scenario, with regard to the failure in achieving the targets proposed by the WHO of 85% cure and a maximum of 5% abandonment of treatment\textsuperscript{2}. Such results may be related to the model of care offered during treatment since in this study only 25% of the cases were followed up with Directly Observed Treatment (DOT). We must note that the DOT variable was excluded from the model due to the low percentage of individuals who performed the follow-up.

DOT is considered a priority tool in the control of tuberculosis, with which the reception and the link between the person being treated and the health service and its professionals would be provided, enabling targeted attention to the needs of the subjects, and contributing to modify factors that may impair the adherence to the treatment, thus achieving the outcome of cure\textsuperscript{17,20}. In this sense, we draw the attention to the need for investment in the expansion of the DOT coverage in the scenario under study, which will make it possible to improve the indicators of cure and abandonment.

In this research, it was verified that multimorbidity increased the RR in obtaining an unfavorable outcome with treatment, being 2.9 times higher for death. This relates to evidence that multimorbidity is associated with poor quality of life, and with the high frequency of prolonged hospitalizations\textsuperscript{10–12}.

Moreover, as the number of morbidities besides tuberculosis increased, the RR rises to an unfavorable outcome in the treatment. The individual with three or more morbidities besides tuberculosis has an RR 7.4 times higher for death, and the fact of having two morbidities besides tuberculosis raised the RR for abandonment by 2.5 times and, for Multi-drug resistance, by 3.3 times when compared to people who had only tuberculosis. Studies that have sought to evaluate this relationship are scarce, not allowing for a comparison of these results with other populations.

There is the difficulty of the current health system in promoting attention focused on the needs of individuals according to the number of morbidities that affect them. As a result, polypharmacy (use of five or more medications) and the adverse events resulting from it occur and, as a consequence, non-adherence and abandonment of treatment. In addition to the frequent use of health services, especially in specialized care, which reproduces a fragmented attention, focusing on the clinically dominant disease, disregarding the totality of the individual\textsuperscript{10–12}.

We consider that, in order to fully care for individuals with tuberculosis and other associated morbidities, a networked health system is required. Having the Family Health Strategy (FHS) as the care coordinator, with the management of the clinic supported by the Chronic Conditions Care Model\textsuperscript{10–12} focused on the individual, considering the totality of his/her health needs, in order to achieve adherence to treatment.

Regarding the analysis of the isolated influence of each morbidity with the treatment outcome, it was observed that people who consume illicit drugs (3.1), co-infected TB/HIV (2.1) and alcoholics (1.3) showed a rise in the RR to obtain the treatment abandonment outcome. These results are in line with other studies\textsuperscript{13–14,18,20}.

The health professionals interviewed in a study conducted in São Paulo in 2016 declared that, in order to avoid the abandonment of tuberculosis treatment by people who use illicit and illicit drugs, it is essential to reduce drug use during treatment, in addition to psychological activities aimed at resolving the stigma of the disease\textsuperscript{20}. People co-infected with TB/HIV face the consequences of polypharmacy, with the use of anti-retroviral therapy and of the tuberculostatics, which sometimes cause severe and intolerable adverse reactions, generating interruption in the use of drugs, leading to the abandonment of treatment and to the induction of multi-drug resistance\textsuperscript{17,18,20}.

It was verified that diabetes mellitus acted as a protective factor for the abandonment of treatment. This result is opposed to a literature review, which concluded that the risk of death and abandonment of treatment is significantly higher if the person is diabetic\textsuperscript{17,17}. The adherence to the treatment identified in this study may be related to a prior relationship a person living with diabetes mellitus has with the health services, in addition to the possibility of the person’s self-responsibility for their ongoing drug treatment.
Regarding the death outcome, it was verified that HIV co-infection and alcoholism increased the risk by 3.9 and 1.5 times, respectively. Alcoholism directly influences the clinical evolution of the disease, since the treatment of tuberculosis allied to alcoholism potentiates the possible damages to the liver, besides the nutritional deficiency and the social factors imbricated in the alcoholism problem comes to contribute to this outcome8,17).

As for HIV, co-infection has also increased the risk (3.1) of multi-drug resistance. Both unfavorable outcomes are believed to occur due to impaired immunity and to the likely interaction between the drugs used for dual treatment20,21. Thus, the planning of actions for TB/HIV co-infected persons should prioritize the subject in its entirety, taking into account the systematic assessment of viral load with CD4 cell count and verification of the interaction of drugs used, as well as performing health education and surveillance8-10,20.

So, the results of this study reflect the urgency of reorganizing the care provided to subjects with tuberculosis, considering the other existing comorbidities. There is an urgent need to strengthen Primary Health Care, with health actions focused on the needs of the subjects.

**CONCLUSIONS**

It was identified that multimorbidity was present in 37.0% of the new cases of pulmonary tuberculosis in the state of Rio Grande do Sul between 2013 and 2017. The most common morbidity was HIV; and, among use of substances, smoking was predominant. As for the outcomes, 71.3% of cure, 16.6% of abandonment and 9.7% of deaths were observed. People with multi-morbidity presented a Relative Risk (RR) of 1.7 to abandon treatment, and of 2.9 to die. The Relative Risk increased significantly as the number of morbidities that the individual also rose. The relation of the morbidities with the unfavorable outcomes showed that HIV presented significant results in relation to abandonment and death; in relation to substance consumption, illicit drugs also presented a significant relation to the increased risk of abandonment.

The results found in this study warn of the importance of considering the presence of multimorbidity in planning the treatment of the person with tuberculosis, since it was possible to verify that the presence of multimorbidity and the number of existing diseases influence the outcome of the disease treatment, abandonment of treatment and death standing out. In view of the results found, new studies are recommended to evaluate this relationship, in addition to the inclusion of the topic of multimorbidity in the discussion scenarios of the tuberculosis control policy in Brazil and worldwide. Studies are also recommended that evaluate the association of other morbidities in the outcome of the treatment for tuberculosis, since only the diseases and behavioral conditions pre-established in the SINAN research sheet were analyzed.

As limitations of the study, the use of secondary data from the SINAN is highlighted, data which are collected by different professionals from all over the country, hindering a quality control process in the data collection, thus generating inconsistencies and incompleteness in some variables. Another factor considered as a limitation of the study was the impossibility to observe the behavior of other diseases for the treatment outcome since the filling in of this variable presented a high amount of inconsistencies.

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