NON ADHERENCE TO TUBERCULOSIS TREATMENT IN SÃO PAULO STATE: REFLECTIONS ON HEALTH MANAGEMENT AND NURSING

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THE AUTHOR'S CONTRIBUTION STATEMENT

Lair Bianchi de Melo and Marcelo de Castro Meneghim were responsible for study conceptualization; Karine Laura Cortellazzi and António Carlos Pereira made data curation and Methodology; Lair Bianchi de Melo, Marcelo de Castro Meneghuim and Emílio Prado da Fonseca were responsible for Writing – original draft; Antonio Carlos Pereira, Karine Laura Cortellazzi Mendes and Márcia Regina Dal Medico Verdi writing – review & editing.

ABSTRACT

Objective: To associate abandonment of tuberculosis treatment with the variables of access to health services in the state of São Paulo was estimated. **Methods**: was an epidemiological observational study with data to individuals diagnosed with tuberculosis, residing in the state of São Paulo in the period 2012 to 2017. Generalized Estimating Equations models were used to analyze the relationships between independent variables and noncompliance with tuberculosis treatment over time. **Results**: A prevalence of over 12% of noncompliance with tuberculosis treatment was identified. Individuals residing in medium and large-sized municipalities had, 2.64 (95% CI: 2.15-3;24) and 4.48 (CI 95%: 4.62-5.55) times more risk, respectively, of abandoning TB treatment when compared with those living in small cities (p<0.05). Moreover, presence of Psychosocial Care Centers did not contribute to the reduction of treatment abandonment [1.20 (1.03-1.40) p<0.05]. **Conclusions**: Was an association between municipal size and abandonment of tuberculosis treatment.

Descritores: Tuberculose; Enfermagem; Aderência ao Tratamento; Avaliação de Resultados em Cuidados de Saúde; Gestão em Saúde.

Descriptors: Tuberculosis; Nursing; Treatment Adherence and Compliance; Outcome Assessment; Managed Care Programs.

Descriptores: Tuberculosis; Enfermería; Cumplimiento y Adherencia al Tratamiento; Evaluación de Resultado en la Atención de Salud; Gestión en Salud.

INTRODUCTION

Abandonment of tuberculosis (TB) treatment is a complex issue for disease control. Abandonment of TB treatment is defined as the behavior of an individual who, after starting treatment for the disease, failed to attend the health unit for a period longer than 30 consecutive days[1]. In 2017, the percentage of tuberculosis treatment abandonment in Brazil was 14.1%, above the 5% target recommended by the WHO[2-3]. In the state of São Paulo, the percentage of abandonment is around 10.0% and the state is responsible for 23.5% of cases in Brazil[4-5].

The scientific literature has pointed out the late diagnosis of TB, decentralization of treatment and failure in the organization of health services as factors that have a negative effect on achieving cure of the disease[6-7]. Furthermore, inequalities in primary care coverage in medium and large cities and high demand for diagnosis in secondary care are obstacles to obtaining treatment. A set of organizational and regional factors that favor the abandonment of treatment have been observed, and these are potentiated by individual conditions, social inequities and difficulties in accessing health services[4].

In addition, the studies have focused on analysis of persistent factors in the abandonment of TB treatment with emphasis on individual characteristics, thereby providing important information to enable identification of individuals at greater risk for abandonment (non-adherence) of treatment[8-10]. However, recent studies have sought to analyze the influence of organizational and contextual factors on access to TB treatment[11-13]. One study found that the highest treatment abandonment/dropout rates were concentrated in the Southeastern regions[10]. This approach has encouraged new studies that consider access to health services and the size of municipalities as modulating and indispensable factors in the assessment of treatment abandonment. Furthermore, analyses of the magnitude of impacts resulting from this abandonment and its reduction, makes it necessary to apply methods that enable an understanding of disease distribution dynamics; risk of contracting diseases and disorders related to them, as well as their non-random regional variations over a given period of time.

OBJECTIVE

To associate abandonment of tuberculosis treatment with the variables of access to health services in the state of São Paulo in the period from 2012 to 2017.

METHODS

Ethical aspects

This study was a research with the updating of secondary data in the public domain, a letter for its exemption was obtained from the Research Ethics Committee of FOP/Unicamp. Patient consent was waived because the study was conducted with secondary data.

Study design, period and place

This an epidemiological observational study (Strobe checklist tool), using secondary data in the public domain available on the Ministry of Health/DATASUS website, of individuals diagnosed with tuberculosis, receiving care from the public or private system, in the period from January, 2012 to December, 2017, in São Paulo state[13].

Population or sample, inclusion and exclusion criteria

For the purposes of this study, the recommendation of the Ministry of Health for abandoning TB treatment was considered; that is, after starting treatment for TB, the individual remained absent from the health unit for a period longer than 30 days[1]. São Paulo state has 645 municipalities with a total population of 41,262,199 inhabitants[14]. The number of individuals confirmed with tuberculosis was 117,121, and of these, 14,178 abandoned treatment for the disease. Individuals with transfers to other states, changes in diagnosis were excluded, that is, individuals who, during the course of treatment, had their diagnosis of tuberculosis discarded, drug-resistant tuberculosis and change in treatment scheme. Individuals who were transferred to other states, whose diagnosis of tuberculosis was discarded during the course of treatment, who had drug-resistant tuberculosis and underwent a change of treatment regimen were excluded from the study. In the period studied, 14,178 individuals abandoned Tuberculosis treatment in São Paulo state.

Study protocol

For the purposes of this study, the recommendation of the Ministry of Health for abandoning TB treatment was considered; that is, after starting treatment for TB, the individual remained absent from the health unit for a period longer than 30 days[1]. Chart 1 presents the independent variables studied and their definitions.

Chart 1 - Definition of independent variables of the study

Source:	Independent variable	Definitions
IBGE2010	Size of Municipality	Small size (from 1 to 22.000 inhabitants) Medium size (from 22.001 to 100.000 inhabitants) Large size (over 100.000 inhabitants)
IBGE 2010	HDI (Human development Index)	HDI lower than 0.74 HDI ≥ 0.74
IBGE 2010	GDP per capita (Expressed in Reais)	GDP per capita lower than $27,247.00 GDP per capita≥ $27,247.00
DPC	Percentage of population coverage by primary care	Coverage <77.68% and > 77.68%
DPC	Percentage of population coverage by the Family Health Strategy (FHS)	All municipalities in the state considered as being classified into: Coverage of 0-58.0% and >58.0% by FHS
CNES	CAPS	% of cities with CAPS
CNES (National Register of Health Establishments)	SAE	% of cities with SAE (sanitation, water and sewage systems)

Source: IBGE: Brazilian Institute of Geography and Statistics[14]; CNES: National Register of Health Establishments[15]; Department of Primary Care: Family Health Strategy (FHS)[16].

Analysis of results and statistics

Initially descriptive data analyses were performed. For this purpose, frequencies and percentages were calculated for the categorical variables and measures of central tendency. Generalized Estimating Equations (GEE) models were used to analyze the relationships between independent variables and noncompliance with tuberculosis treatment over time. For the multiple analysis, two blocks of variables were considered, block 1 with the year and economic variables and block 2 with the variables of coverage and presence of health services. The Poisson distribution was considered and the gross and adjusted relative risks were estimated. Quality of the adjustment was assessed by QIC (Quasilikelihood under the Independence model Criterion). In all analysis a significance level of 5% was considered. (SAS Institute Inc. 2019. SAS® Studio 3.8: User's Guide. Cary, NC: SAS Institute Inc).

RESULTS

Tables 1 to 3 show the descriptive results of the study. In the period between 2012 and 2017, the diagnoses of 117,121 individuals with tuberculosis were confirmed in the state of São Paulo, of whom 14,178 (12.11%) abandoned treatment. In small-sized municipalities, there was higher prevalence of this occurrence, with a total of 401 cases (62.2%). In the period studied (2012-2017), the year 2014 showed the highest percentage of abandonment with 13.04%.

Table 1 - Characteristics of municipalities in the State of São Paulo.

Variable	Frequency (%)
Size of Municipality	
Small	401 (62.2%)
Medium	169 (26.2%)
Large	75 (11.6%)
Municipalities with CRATOD in 2017	107 (16.6%)
	Median
	(minimum and maximum Value)
Population	12737 (805-11253503)
HDI in 2010	0.74 (0.64-0.86)
GDP per capita	25305 (8262-324935)

[1]CRATOD: Reference Center for Alcohol, Tobacco and Other Drugs (Centro de Referência de Álcool, Tabaco e outras Drogas)

Table 2 - Characteristics of cases of abandoned pulmonary tuberculosis treatment/dropout in the State of São Paulo from 2012 to 2017, abandoned treatment and characteristics of patients who dropped out.

Variable	Result within period
Cases confirmed (n)	11.7121
Abandoned	14.178
% of abandonment/dropout (%)	12.11
% cases of AIDS among abandoned treatments/ dropouts (%)	16.10
% cases of HIV among those who abandoned treatments/ dropouts (%)	17.30
% cases of Alcoholism among those who abandoned treatments/ dropouts (%)	30.18
% cases of substance addicts among those who abandoned treatments/ dropouts (%)	38.51

Table 3 - Confirmed cases of tuberculosis in the State of São Paulo from 2012 to 2017, abandoned treatments/ dropouts and characteristics of patients who abandoned treatments/dropped out.

Year	Number of cases confirmed	Number of abandoned treatments/dropouts	Percentage of abandoned treatments/dropouts
2012	18156	1999	11.01
2013	19254	2325	12.08
2014	19280	2514	13.04
2015	19699	2328	11.82
2016	19600	2388	12.18
2017	21132	2624	12.42
Total	117121	14178	12.11

Table 4 presents the associations of the percentage of abandonment of TB treatment in relation to individuals diagnosed with TB. After adjustment, the size of the municipality and the presence of

CAPS - (Psychosocial Care Centers) remained in the final model (p<0.05). Medium and large municipalities had, 2.64 (95%CI: 2.15-3;24) and 4.48 (CI 95%: 4.62-5.55) respectively, times more risk of abandoning TB treatment when compared with those in small municipalities (p<0.05). Furthermore, municipalities with CAPS (Psychosocial Care Centers - Centros de Atenção Psicossocial) have 1.20 (1.03-1.40) times more risk of abandonment than municipalities that do not have CAPS (p<0.05).

Table 4 - Analyses (crude and adjusted) of the associations with the percentage of abandonment of treatment/dropout in relation to confirmed individuals with tuberculosis in the State of São Paulo from 2012 to 2017.

Caegory	$Raw OR ([#]CI 95%)	p-value	([$]Adjusted OR ([#]CI 95%)	p-value
		Block 1		
Year		1.01 (0.99-1.03)	0.2481	
Population	<22291	Ref		
	≥[&] 22291	3.63 (3.05-4.32)	<0.0001	
	Small	Ref	Ref	Ref
Size	Medium	2.81 (2.33-3.40)	<0.0001	2.64 (2.15-3.24) <0.0001
	Large	4.85 (4.10-5.75)	<0.0001	4.48 (4.62-5.55) <0.0001
MHDI	<0.74	Ref		

Variable	Category	RR (95% CI)	p-value	RR (95% CI)	p-value
	$\geq^{\&}$ 0.74	1.83 (1.56-2.15)	<0.0001		
GDP per capita	<27.247	Ref			
	$\geq^{\&}$ 27.247	1.43 (1.22-1.66)	<0.0001		
			Block 2		
%[1]CAB	<77.68	1.93 (1.68-2.22)	<0.0001		
	$\geq^{\&}$ 77.68	Ref			
			Block 2		
% FHS[2]	<58.0	1.87 (1.61-2.16)	<0.0001		
	$\geq^{\&}$ 58.0	Ref			
CAPS[3]	Does not have	Ref			
	Has	2.55 (2.21-2.93)	<0.0001	1.20 (1.03-1.40)	0.0204
SAE[4]	Does not have	Ref			
	Has	2.08 (1.85-2.33)	<0.0001		

Median of sample *Reference category $^{\$}$Relative Risk [#] 95% Confidence Interval. CAB: Percentage of coverage by primary care; CESF: Percentage of coverage by the Family Health Strategy; CAPS:

Psychosocial Care Centers; SAE: Specialized Care Service QIC (empty model) =7536,89; QIC (block 1 model)=6785,32; QIC (final model)=6783.97

DISCUSSION

Abandonment of TB treatment, influenced by individual conditions, social inequities or difficulty in gaining access to health services, is a factor that interferes with the cure and control of the disease, mainly because it causes drug resistance[4,17]. Rates of prevalence of treatment abandonment of over 10% were similar to those of a previous study[10]. An ecological study with national data identified the existence of high-risk areas concentrated mainly in the Southeastern region[10]. We point out that the disease is transmissible and the individual who abandons treatment is capable of contaminating, on average, 10 to 15 people per year[10].

The results of this study showed that individuals residing in large cities had a higher risk of abandoning treatment/dropout. Therefore, when using factors such as municipal socioeconomic, health service structure and access variables, it is possible to better understand the distribution of the event studied. The results pointed out a high prevalence of abandonment of antituberculosis drug therapy in the state of São Paulo during the period studied. Treatment abandonment was also observed to be heterogeneously distributed according to municipal size and in a non-random manner. Moreover, there were high-risk areas concentrated mainly in medium and large-sized municipalities. In the state of São Paulo, TB treatment is performed in secondary care in the majority of cases[8]. In large-sized municipalities, actions to control TB are more focused on secondary care and private services. This can make it difficult to obtain access to services/medication, counseling, consequently making adherence increasingly difficult, and leading to treatment abandonment[18].

In the present study, the presence of Psychosocial Care Centers (CAPS/CAPS Alcohol and drugs –AD) and sanitation/water/sewage in the municipalities did not contribute to reducing the risk of abandoning TB treatment. A possible factor to justify this situation may be the centralization of actions for TB control in secondary care, resulting in late diagnosis and difficulty in (barriers to) obtaining access to care[9,18]. Another hypothesis for this finding would be that individuals living in larger municipalities access this service as a "gateway" to other health conditions and end up abandoning treatment as a whole because Psychosocial Care Centers (CAPS) are not the appropriate referral service for TB treatment[19]. Furthermore, a cross-sectional study conducted with patients who returned to TB treatment after abandonment in the city of Belém, Pará, indicated that the use of illicit drugs was the most prevalent (predictive factor) for abandonment of TB treatment[12].

Decentralization of TB treatment to primary care could result in a decrease in treatment abandonment due to better adherence to treatment, since patients' proximity to the basic health unit would favor monitoring, individual's transport to the unit, active search for a unit and the bond patients create with the unit[20]. Adoption of strategies for accessing treatment performed in the PHC (port of entry), with the administration of medications performed at the health unit through DOT (Directly Observed Treatment), and flexible schedules for medical appointments could prevent individuals from disrupting their daily routine, loss of time at their employment and consequent abandonment of treatment[20-22].

This study revealed that the prevalence of TB treatment abandonment remained constant and above 10%, even with the implementation of the DOT strategy throughout the studied period (2012-2017) in the State of São Paulo. This finding revealed that the actions developed need to be reviewed, especially in medium and large cities (higher risk)[10,12]. Reports have indicated that the possible failure of DOT could lead to individuals developing drug-resistant TB or drug-resistant TB (DR-TB), which can make it more difficult to manage the disease[12]. In individuals with drug-resistant TB, it is unclear whether those who are submitted to DOT show better results when compared with those who perform self-administered treatment[12]. The persistence of high rates of treatment abandonment, irrespective of the type of treatment, reinforces the perspective of transmissibility, treatment costs, morbidity, mortality and resistance to therapy[10].

Other factors that interfere in these dynamics are related to individuals who use alcohol and other drugs and late diagnosis; that is, the delay in seeking care[23]. This could be influenced by the fact that patients are referred to secondary care for treatment, making access to it more difficult[24]. Horizontalization of vertical processes in health actions could contribute to reduction in TB abandonment, by improving the level of communication, training and reducing the risk factors presented herein[25,26]. The National Mental Health Policy[27] and technical note 11/2019 emphasize the importance of comprehensive and multidisciplinary/ professional treatment for individuals[28].

Moreover, in medium and large-sized municipalities, the (units of) health services are present in larger numbers at the three levels of care, which could favor TB control[10]. Whereas the intra-urban socioeconomic inequality has made it more difficult for the individuals assigned to the more populous municipalities to gain access to them, while smaller municipalities tend to provide easier access to health equipment for the community[10]. In addition, the findings of this study corroborate the finding of a previous study[10]. In which the greater demand for services and greater potential for transmitting the disease could occur in more populous municipalities. This confirmed the relevance of (considering) each spatial cut, the different social contexts and living conditions in the analysis of TB treatment abandonment[29].

Study limitations

Possible under-reporting, absence of some data in the information system, and inconsistencies in the databases used. The study showed the need to rethink secondary care represented by CAPS/CAPS-AD and sanitation/water/sewage (SAEs) to reduce cases of treatment abandonment for the disease.

CONCLUSIONS

A prevalence of over 12% of abandonment of TB treatment was identified in the state of São Paulo during the period studied. Furthermore, the increase in the size of the municipality contributed to the abandonment of treatment whereas the presence of Psychosocial Care Centers (CAPS)/ and sanitation/ water/ sewage (SAEs) in the municipalities made no contribution to reducing the abandonment of TB treatment.

SUPPLEMENTARY MATERIAL

Repository Data: Fonseca EP, Melo LB, Cortellazzi KL, Verdi MRDM, Meneghim MC, Pereira AC. NON-ADHESION TO TUBERCULOSIS TREATMENT IN THE STATE OF SÃO PAULO: 2012-2017. Figshare [Internet]. 2022 [cited 2022 Nov 01] Available from: https://doi.org/10.6084/m9.figshare.21520809.v4.

CONFLICT OF INTERESTS STATEMENT

The authors declare that there is no conflict of interest of authors, reviewers, editors, journals and publishers whether identified before or after publication.

REFERENCES

1. Ministério da Saúde (MS). Secretaria de Vigilância em Saúde. Departamento de Vigilância das Doenças Transmissíveis: Manual de Recomendações para o Controle da Tuberculose no Brasil. Brasília: Ministério da Saúde; 2019. https://bvsms.saude.gov.br/bvs/publicacoes/manual_recomendacoes_controle_tuberculose_brasil_2_ed.pdf

2. Ministério da Saúde (MS). Secretaria de Vigilância em Saúde. Departamento de Vigilância Epidemiológica: Boletim Epidemiológico: Perspectivas Brasileiras para o fim da tuberculose como problema de saúde pública. Brasília: Ministério da Saúde; 2018. https://www.cevs.rs.gov.br/upload/arquivos/201804/18151437-boletim-epidemiologico-ms-tuberculose-2018.pdf

3. World Health Organization (WHO). Global strategy and targets for tuberculosis prevention, care and control after 2015. Geneva: WHO; 2013. https://apps.who.int/iris/handle/10665/172828

4. Ministério da Saúde (MS). Secretaria de Vigilância em Saúde. Departamento de Vigilância das Doenças Transmissíveis. In: Brasil Livre da Tuberculose: Plano Nacional pelo Fim da Tuberculose como Problema de Saúde Pública. Brasília: Ministério da Saúde; 2017. https://bvsms.saude.gov.br/bvs/publicacoes/brasil_livre_tuberculose_plano_nacional.pdf

5. Ministério da Saúde (MS). Secretaria de Vigilância em Saúde. Departamento de Vigilância Epidemiológica: Boletim Epidemiológico: Perspectivas Brasileiras para o fim da tuberculose como problema de saúde pública. Brasília: Ministério da Saúde; 2021. https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/boletins/epidemiológicos/especiais/2021/boletim-tuberculose-2021_24.03

6. Machado ACFT, Steffen RE, Oxlade O, Menzies D, Kritski A, Trajman A. Fatores associados ao atraso no diagnóstico da tuberculose pulmonar no estado do Rio de Janeiro. J Bras Pneumol. 2011;37(4):512-20. https://doi.org/10.1590/S1806-37132011000400014

7. Wysocki AD, Ponce MZ, Brunello MEF, Beraldo AA, Vendramini SHF, Scatena LM, et al. Atenção Primária à Saúde e tuberculose: avaliação dos serviços. Rev Bras Epidemiol. 2017;20(1):161-75. https://doi.org/10.1590/1980549720170010014

8. Junior RT, Rodolpho L, Leonor CM, Gasparetto RM. Clinical and epidemiological profile of tuberculosis in an urban area with high human development index in southeastern Brazil. Time series study. Sao Paulo Med J. 2017;135 (5):413-19. https://doi.org/10.1590/1516-3180.2016.0260210317

9. Sacramento DS, Lavor DCBS, Oliveira LRT, Gomes APBL, Gonçalves MJF. Organização dos serviços de saúde para o diagnóstico e tratamento dos casos de tuberculose em Manaus, Amazonas, 2014. Epidemiol Serv Saude. 2019;28(2):e2017500. https://doi.org/10.5123/S1679497420190000200007

10. Soeiro VMM, Caldas AJM, Ferreira TF. Abandono do tratamento da tuberculose no Brasil, 2012-2018: tendência e distribuição espaço-temporal. Cien Saude Colet. 2022;27(3):825-36. https://doi.org/10.1590/1413-81232022273.45132020

11. Poersch K, Costa JSD. Fatores associados ao abandono do tratamento da tuberculose: estudo de casos e controles. Cad Saude Colet. 2021;29(4):485-49. https://doi.org/10.1590/1414-462X202129040

12. Sousa GJB, Garces TS, Pereira MLD, Moreira TMM, Silveira GM. Padrão temporal da cura, mortalidade e abandono do tratamento da tuberculose em capitais brasileiras. Rev Lat Am Enfermagem. 2019;27:e3218. https://doi.org/10.1590/1518-8345.3019.3218

13. Ministério da Saúde (MS). Departamento de Informática do SUS- DATASUS. Notificações de casos de Tuberculose no Estado de São Paulo entre 2012 e 2017. Tuberculose no Estado de São Paulo [Internet]. 2019 [cited 2019 Jul 10]. Available from: http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sinannet/cnv/tubercbr.def

14. Ministério do Planejamento, Orçamento e Gestão. Instituto Brasileiro de Geografia e Estatística (IBGE): Censo Demográfico 2010. Rio de Janeiro: IBGE; 2011. https://censo2010.ibge.gov.br/

15. Cadastro Nacional de Estabelecimentos de Saúde (CNES). Ministério da Saúde [Internet]. 2020 [cited 2021 May 05]. Available from: http://cnes2.datasus.gov.br/Mod_Ind_Unidade.asp?VEstado=35

16. Sistema de Informação e Gestão da Atenção Básica (e-Gestor). Ministério da Saúde [Internet]. 2021 [cited 2021 Apr 01]. Available from: https://egestorab.saude.gov.br/paginas/acessoPublico/relatorios/relHistoricoCoberturaAB.xhtml

17. Rocha DS, Adorno, RCF. Abandono ou descontinuidade do tratamento da tuberculose em Rio Branco, Acre. Saude Soc. 2012;21(1):232-45. https://doi.org/10.1590/S0104-12902012000100022

18. Araújo AJ, Lima PM, Silva CEL, Davina SR, Menezes BL, Bertolozzi MR, et al. Avaliação de ações de controle da tuberculose em um município brasileiro de grande porte. Rev salud publica. 2019;21(1):77-83. https://doi.org/10.15446/rsap.V21n1.67140

19. de Paiva JPS, Magalhães MAFM, Leal TC, da Silva LF, da Silva LG, do Carmo RF, et al. Time trend, social vulnerability, and identification of risk areas for tuberculosis in Brazil: An ecological study. PLoS One. 2022;17(1):e0247894. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0247894

20. Cortez AO, Melo AC, Neves LO, Resende KA, Camargos P. Tuberculose no Brasil: um país, múltiplas realidades. J Bras Pneumol. 2021;47(2):e20200119. http://dx.doi.org/10.36416/1806-3756/e20200119

21. Silva DR, Mello FCQ, Migliori GB. Série tuberculose 2020. J Bras Pneumol. 2020; 46(2):e20200027. https://doi.org/10.36416/1806-3756/e20200027

22. Pereira JC, Silva MR, Costa RR, Guimarães MDC, Leite ICG. Profile and follow-up of patients with tuberculosis in a priority city in Brazil. Rev Saude Publica. 2015; 49:6. https://doi.org/10.1590/S0034-8910.2015049005304

23. Junges JR, Burille A, Tedesco J. Tratamento Diretamente Observado da tuberculose: análise crítica da descentralização. Interface - Comunic, Saude, Educ.2020; 24:e190160. https://doi.org/10.1590/Interface.190160

24. Dantas DNA, Enders BC, Oliveira DRC, Vieira CENK, Queiroz AAR, Arcêncio RA. Fatores associados ao atraso na procura por atendimento pelo doente de tuberculose. Rev Bras Enferm. 2018; 71(Suppl1):646-51. http://dx.doi.org/10.1590/0034-7167-2016-0680

25. Andrade HLP, Ramos ACV, Crispim JA, Neto MS, Arroyo LH, Arcêncio RA. Spatial analysis of risk areas for the development of tuberculosis and treatment outcomes. Rev Bras Enferm. 2021;74(2):e20200564. https://doi.org/10.1590/0034-7167-2020-0564

26. Beraldo AA, Andrade RLP, Orfão NH, Silva-Sobrinho RA, Pinto ESG, Wysocki AD, et al. Adherence to tuberculosis treatment in Primary Health Care: perception of patients and professionals in a large municipality. Esc Anna Nery. 2017;21(4):e20170075. https://doi.org/10.1590/2177-9465-EAN-2017-0075

27. Ministério da Saúde (MS). Secretaria Executiva. Coordenação Nacional de DST/Aids. A política do Ministério da Saúde para a atenção integral a usuários de álcool e outras drogas. Brasília: Ministério da Saúde; 2003. https://bvsms.saude.gov.br/bvs/publicacoes/politica_atencao_alcool_drogas.pdf

28. Ministério da Saúde (MS). Nota Técnica nº 11/2019-CGMAD/DAPES/SAS/MS. MS [Internet]. 2019 [cited 2021 Jun 05]. Available from: http://pbpd.org.br/wp-content/uploads/2019/02/0656ad6e.pdf.

29. Aragão, FBA, Arcêncio RA, Fuentealba-Torres M, Carneiro TSG, Souza LLL, Alves YM, et al. Impact of social protection programs on adults diagnosed with Tuberculosis: systematic review. Rev Bras Enferm. 2021;74 (3):e20190906. https://doi.org/10.1590/0034-7167-2019-0906

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