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Loss to follow-up in tuberculosis treatment and its relationship with patients' knowledge of the disease and other associated factors

Pérdida de seguimiento del tratamiento de la tuberculosis y relación con el conocimiento del paciente y otros factores asociados

Aylana De S. Belchior[1], Evelyne Marie T. Mainbourg[2] and
Maria J. Ferreira-Gonçalves[3]

1 Escola de Enfermagem de Ribeirão Preto, Universidade de São Paulo. Pará State University and Amazonas Federal University. Ribeirão Preto, São Paulo, Brazil.   aylanabelchior14@gmail.com
2 Instituto Leônidas & Maria Deane/Fiocruz. Manaus, Amazonas, Brazil. evelyne.mainbourg@gmail.com
3 Instituto Leônidas & Maria Deane/Fiocruz. Universidade Federal do Amazonas. Manaus, Amazonas, Brazil. jaciremagoncalves@gmail.com

ABSTRACT

Objective To identify factors associated with loss to follow-up in Tuberculosis (TB) treatment, including patients' level of knowledge regarding treatment of this disease.
Methods 42 loss to follow-up cases and 84 control cases that were finishing the sixth month of their first treatment for tuberculosis were selected for this study. Primary data were gathered through interviews, while secondary data were obtained from the notification form of the disease, between December 2011 and April 2012. Factors associated with loss to follow-up were analyzed by means of a conditional logistic regression multivariate model for matched case-control groups.
Results No significant differences were observed between loss to follow-up cases and controls regarding socioeconomic factors, lifestyle, clinical condition, treatment-related behaviors and the access of patients to sources of information on TB. In the regression multivariate analysis, significant associations with retreatment after loss to follow-up that were detected include: scarce knowledge on tuberculosis, lack of adherence to consultation during the current treatment, noncompliance with follow-up consultation deadline, smoking and HIV negative.
Conclusion When compared to controls, cases undergoing TB retreatment after loss to follow-up have less knowledge on the disease, which is a sign for the professionals responsible for health education of the need to invest more time and efforts in activities that help the patient understand the disease and its treatment, as well as to have higher levels of adherence. In addition, noncompliance with the follow-up consultation deadline, failure to attend consultations during the current

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treatment and smoking are also factors that may be influenced by poor knowledge on the disease, which leads to the treatment loss to follow-up.

Key Words: Tuberculosis, health education, medication adherence, patient drop-outs, epidemiologic factors (*source: MeSH, NLM*).

RESUMEN

Objetivo Identificar los factores asociados con la pérdida del seguimiento en el tratamiento de la tuberculosis (TB), incluyendo el nivel de conocimiento de los pacientes sobre el tratamiento de esta enfermedad.
Métodos Se seleccionaron 42 casos de pérdida de seguimiento y 84 controles que se encontraban terminando el sexto mes de su primer tratamiento contra la TB. Los datos primarios fueron recolectados mediante entrevistas, mientras que los secundarios, a partir del formulario de notificación de la enfermedad, entre diciembre de 2011 y abril de 2012. Se utilizó modelo multivariado de regresión logística condicional para analizar los factores asociados con la pérdida del seguimiento entre grupos de casos y controles emparejados.
Resultados No hay diferencias significativas entre los casos y controles en cuanto a factores socioeconómicos, estilos de vida, condición clínica, comportamientos relacionados con el tratamiento de la enfermedad, así como el acceso a fuentes de información sobre tuberculosis. En el análisis de regresión se observaron las siguientes asociaciones significativas con el retratamiento después de la pérdida del seguimiento: bajo conocimiento sobre tuberculosis, falta de adherencia a la consulta en el tratamiento actual, incumplimiento de la fecha límite de la consulta de seguimiento, tabaquismo y VIH negativo.
Conclusión En comparación con los controles, en los casos de retratamiento de la enfermedad después de la pérdida del seguimiento presentan menor conocimiento sobre tuberculosis, lo que es una señal, para los profesionales responsables de la educación sanitaria, de la necesidad de invertir más tiempo y esfuerzos en actividades que lleven al paciente a comprender la enfermedad y su tratamiento, así como para obtener mayores niveles de adherencia Además, incumplir la fecha límite de las consultas de seguimiento, no asistir a las consultas del actual tratamiento y el tabaquismo también son factores que pueden estar influenciados por el escaso conocimiento de estos pacientes acerca de su enfermedad, lo lleva a la pérdida del seguimiento del tratamiento.

Palabras Clave: Tuberculosis, educación en salud, cumplimiento de la medicación, pacientes desistentes del tratamiento, factores epidemiológicos (*fuente: DeCS, BIREME*).

Tuberculosis (TB) still remains a challenge for public health, since, due to its lengthy treatment, it is a disease difficult to control. In fact, an important number of patients are lost to follow-up in treatment of this condition soon after its onset (1-2), on average, up to three months of treatment (3).

According to the data from the Information System for Notifiable Diseases (Sinan), in 2011, there was 7.4 % of loss to follow-up in TB treatment in Brazil, while in the state of Amazonas it was 8.7 %, and in its capital city, Manaus, 9.3 %, percentages that are above the 5 % deemed acceptable by the World Health Organization (WHO) for TB control (4).

Loss to follow-up in TB treatment is defined as failing to attend the health center for more than 30 consecutive days after the scheduled date of return (4). This phenomenon has been related to mortality caused by TB, disease incidence and multidrug resistance, which leads to reduced cure rates and a decreased effectiveness of TB control programs (1-2).

Factors associated with loss to follow-up in TB treatment more frequently studied are those related to the patient (1,5) and the characteristics of health services (6). Aspects generally related to the patient include: economic factors, difficulties faced in the adherence to TB treatment, comorbidities and health conditions such as diabetes, acquired immune deficiency syndrome (AIDS), drug addiction, alcoholism and smoking, poor health status, adverse effects derived from medications, and patients' lack of motivation (1,5,7). On the other hand, factors related to health services to be highlighted include: difficulties experienced by patients in order to access health facilities and services, need for hospitalization, drawbacks arising from the training and continuing education given to health professionals, resources availability to improve patients' adherence rates, delay in the starting of TB treatment, long waiting times to receive medical consultations, professionals' failure to advise patients on TB treatment and shortage of physicians, which in turn causes low levels of medical consultation availability (6,8-9).

Studies that focus on the knowledge, attitudes and practices of patients regarding TB note that providing the patient and his/her family with proper information on the disease, in addition to a good relationship between patients and health staff dealing with TB cases, greatly reduce the likelihood of loss to follow-up (3,10-11). Therefore, a poor level of knowledge on the disease in a patient often poses a problem to control any pathological condition (10). Nevertheless, just a few studies (2,10,12-13) address aspects related to knowledge on TB among patients. Furthermore, studies that specifically address the relationship between the knowledge of patients regarding TB and loss to follow-up in its treatment have not been reported.

A better understanding of this issue may provide the health staff with means to improve their work practices; therefore it is necessary to recognize that health education on TB must be a part of medical consultations in this context. Thus, this study aims to identify the factors that are associated with loss to follow-up in TB treatment, including the knowledge level on TB of patients undergoing treatment for this disease.

METHOD

This is a matched case-control study conducted to compare patients undergoing TB treatment (cases of retreatment after loss to follow-up) to new cases nearing completion of the 6-month standard treatment (controls) assuming they have had a successful treatment, since the basic treatment for TB finishes after the sixth month is concluded.

Data were collected in the Reference Center in Sanitary Pulmonology (CREPS, for its acronym in Portuguese) in Manaus, Amazonas, Brazil. CREPS annually determines around 70 % of TB diagnoses in the Manaus and it is the referral center for TB treatment in the state of Amazonas for cases of retreatment after loss to follow-up.

The inclusion criterion for controls completing the first treatment was that these patients were undergoing TB treatment in primary health centers (PHCs) covering the area where cases (retreatment for TB) selected in this study underwent TB treatment for the first time, so that sociodemographic characteristics similarity between cases and controls was ensured. This way, the place where the first treatment was received was the matching variable used as recruitment criteria. No other variables were used to pair the cases and controls.

The sample size was calculated based on the total number of cases of retreatment after loss to follow-up in TB treatment (n=42) in CREPS in 2011; each case was paired with two controls, including the universe of cases. The control group consisted of 84 patients who were finishing their first treatment for TB (six months) during field research (from December 2011 to April 2012) in order to have access to both cases and controls at the same time of their treatments. In PHCs where there was more than one eligible control, a draw was randomly made in order to choose the patient.

In order to collect data regarding the knowledge of patients about the disease, an instrument consisting of five questions, applied after a pilot pre-test, was carried out: "How is TB transmitted?", "How is TB treated?", "How

long does TB treatment last?", "Can TB treatment be disrupted as soon as I feel better?", and "How is TB prevented?". Knowledge level evaluation was made based on the number of correct answers each patient scored.

If a patient scored up to three correct answers he or she was classified into the "limited knowledge" category, but if the number of correct answers was four or five he or she was placed under the "proper knowledge" category. This criterion was adopted because this information was deemed to be primary, i.e., every patient undergoing TB treatment should know about it. Socioeconomic variables, lifestyle, difficulties in follow-up during treatment and characterization of the health service with regard to follow-up information and activities of patients undergoing treatment were included.

The bivariate analysis used a Chi-squared test for categorical variables (McNemar) or a trend test for ordered variables (an extension of the Wilcoxon rank-sum test), and paired t-Student's test for continuous variables with statistical significances smaller than 0.05. The conditional logistic multivariate model for matched case-control groups was adjusted according to the automated stepwise backward method by means of the full model, containing all significant variables in the bivariate logistic analysis (P <=0.20). Only those variables with a significance level smaller than 5 % were included in the final model, as well as control variables. Odds ratio (OR) was used as an association measure, while interactions and potential confounders such as sex, age and educational level were tested.

The study was approved by the Research Ethics Committee of Amazonas Federal University, under the Certificate of Presentation for Ethical Consideration (CAAE, for its acronym in Portuguese) 0441.0.115.000-11. In addition, participants of the study have signed a free and informed consent form.

RESULTS

126 patients participated in the study. Out of the 62 patients who were cases of retreatment after loss to follow-up in 2011, 20 could not be included due to the following reasons: admission to an intensive care unit, failure to contact them, homelessness, refusal to participate in the research, change of address, and being in jail.

Table 1 shows the characterization of TB patients. It indicates a more limited knowledge on TB among cases of retreatment after loss to fol-

low-up when compared to new cases (controls) whose TB was cured in their first treatment (P=0.047). Most cases and controls reported they were not visited at home by professionals from the Family Health Strategy (FHS) during their current treatment, with a higher prevalence among controls. Cases missed more consultations than controls did. In terms of compliance with the deadline of follow-up consultation there is a significant difference between cases and controls, as most of the cases of retreatment returned for consultation before the time recommended by the Brazilian Ministry of Health, a situation justified by the strategy of anticipating visits that was adopted by the public health service.

The sample population was predominantly male (66.7 % of cases and 58.3 % of controls), with a proportion of two men for every woman among cases and 1.67 to 1 among controls. The average age of cases was 41.1 years (±15.3), while for control group (new cases) it was 39.7 years (±14.5), i.e., there is not a statistically significant difference (Table 1).

The average number of years attending school was higher in controls (new cases) than in cases (P=0.011). More than half of cases of retreatment after loss to follow-up only attended school from one to eight years, while more than half of controls reported having studied for nine or more years.

Table 1. Bivariate analysis of TB patients' characterization, information and knowledge on TB between cases and their matched controls. Manaus, Brazil, 2011

Variables	Cases of retreatment after loss to follow-up n (%)	Controls completing the first treatment n (%)	Test	P-value
Sex				
Male	28 (36.4)	49 (63.6)	X^2=19.4	<0.001[c]
Female	14 (28.6)	35 (71.4)		
Age group (years)				
≤ 29	11 (31.4)	24 (68.6)	z = -0.4	0.729[b]
30 to 49	20 (33.3)	40 (66.7)		
≥ 50	11 (35.5)	20 (64.5)		
Mean (standard deviation)	41.1 (15.3)	39.7 (14.5)	t = -0.5	0.606[a]
Educational level (years attending school)				
Illiterate	6 (54.5)	5 (45.5)	z = -2.3	0.019[b]
1 to 8	23 (39.0)	36 (61.0)		
≥ 9	13 (23.2)	43 (76.8)		
Mean (standard deviation)	5.9 (3.7)	7.9 (4.2)	t = 2.6	0.011[a]
Income[d]				
No income	9 (37.5)	15 (62.5)	z = -0.1	0.906[b]
< 1 minimum wage	4 (22.2)	14 (77.8)		
1 to 2 minimum wages	24 (36.4)	42 (63.6)		
> 2 minimum wages	5 (27.8)	13 (72.2)		

Variables	Cases of retreatment after loss to follow-up n (%)	Controls completing the first treatment n (%)	Test	P-value
Knowledge				
Up to 3 correct answers	27 (49.1)	28 (50.9)	X^2=3.9	0.047[c]
4 or 5 correct answers	15 (21.1)	56 (78.9)		
Faced difficulties to comply with the treatment				
Yes	41 (34.5)	78 (65.5)	X^2=0.9	<0.001[c]
No	1 (14.3)	6 (85.7)		
Greatest difficulties to comply with the treatment				
Malaise	23 (31.9)	49 (68.1)	z = 0.6	0.520[b]
Lack of money	11 (37.9)	18 (62.1)		
Lack of attention from professionals	3 (60.0)	2 (40.0)		
Medicine x alcohol	4 (30.8)	9 (30.8)		
Clinical form				
Pulmonary	39 (37.9)	64 (62.1)	z = -2.3	0.022[b]
Extrapulmonary	3 (13.6)	19 (86.4)		
Pulmonary + Extrapulmonary	0 (0.0)	1 (100.0)		
Received home visits by professionals from the FHS in the current treatment				
Yes	13 (56.5)	10 (43.5)	X^2=9.3	0.002[c]
No	29 (28.2)	74 (71.8)		
Person who taught the patient on taking medication				
Nurse	31 (37.4)	52 (62.4)	X^2=27	<0.001[c]
Physician	11 (25.6)	32 (74.4)		
Record of missing consultation during the current treatment				
Yes	23 (59.0)	16 (41.0)	X^2=0.3	0.61[c]
No	19 (21.8)	68 (78.2)		
Time to return to the scheduled consultation				
≥30 days	9 (15.5)	49 (84.5)	X^2=15	<0.001[c]
< 0 days	33 (48.5)	35 (51.5)		
Seropositivity for HIV				
Positive	1 (10.0)	9 (90.0)	z = -1.5	0.123[b]
Negative	20 (54.1)	17 (45.9)		
Not conducted or in progress	21 (26.6)	58 (73.4)		
Lifestyle				
Smoking	27 (50.9)	26 (49.1)	X^2=2.9	<0.08[c]
Alcohol use	16 (41.0)	23 (59.0)	X^2=0.2	0.66[c]
Drug use	5 (62.5)	3 (37.5)	X^2=29	<0.001[c]

[a] Paired student t-test; [b] trend test; [c] McNemar test; [d] Minimum wage is around US$ 308.00 within the period of fieldwork; TB = Tuberculosis; FHS = Family Health Strategy; HIV = human immunodeficiency virus; CI = Confidence Interval; OR = Odds Ratio

Table 2 shows the results of the conditional logistic multivariate model for matched case-control groups. In the crude analysis, the abandon of treatment is associated with the following variables: return to consultation, failure to attend consultations in the current treatment, poor knowledge on TB, smoking, home visits by professionals performed during the current treatment, educational level, drug use and HIV test result. In turn, in the adjusted analysis home visit by professionals, educational level and drug use variables lost significance. Variables associated with loss to follow-up in treatment in the adjusted model were return to consultation (wrong deadline, adjusted OR=4.3), failure to attend the consultation in the current treatment (yes, adjusted OR=3.2), limited knowledge on TB (up to three questions, OR=3.2), smoking (smoker or former smoker, OR=4.0) and negative result in the HIV test (OR=2.7). According to Hausman's test (P=0.4), the multiple regression model showed a good adjustment.

Table 2. Conditional logistic regression analysis of knowledge on TB and other factors associated with loss to follow-up in treatment among TB patients. Manaus, Brazil, 2011

Variables	Crude OR	(CI 80 %)	Adjusted OR	(CI95 %)
Return to consultation				
Correct deadline	1.0		1.0	
Wrong deadline	5.2	(2.9-9.4)	4.3	(1.2-14.7)
Missed a consultation in the current treatment				
Yes	5.2	(2.9-9.6)	3.2	(0.9-10.8)
No	1.0		1.0	
Knowledge				
Up to 3 correct answers	3.6	(2.1-6.2)	3.3	(1.1-9.8)
4 or 5 correct answers	1.0		1.0	
Smoking				
Smoker or former smoker	4.5	(2.6-8.0)	4.0	(1.2-13.8)
Non-smoker	1.0		1.0	
Home visit by professionals				
Yes	2.8	(1.6-5.1)	-	-
No	1.0			
Education (years attending school)	0.9	(0.8-0.9)	-	-
Drug use				
Yes	5.0	(1.7-14.6)	-	-
No	1.0			
Result of anti-HIV serology				
Positive	0.4	(0.9-1.5)	-	-
Negative	2.6	(1.5-4.3)	2.7	(0.9 - 8.2)
In progress or not conducted	1.0		1.0	

TB=Tuberculosis; HIV=human immunodeficiency virus; OR=odds ratio; CI=confidence interval

DISCUSSION

In this study it was possible to identify that, in addition to other factors widely known to be associated with loss to follow-up in TB treatment, there is higher

prevalence of low knowledge levels on TB in cases of retreatment after loss to follow-up than in new cases completing the final phase of their treatment.

Although there is no statistical significance regarding sex, it is worth noting the predominance of men who experienced loss to follow up in treatment during the study, which confirms TB incidence profile. Therefore, this predominance is also a reflection of the disease incidence, usually 60 % in men. Other studies have also found that most cases of loss to follow-up were men, something that is attributed to their greater detachment from health services (8,10-11).

There were no differences in mean age between cases and controls because of the profiles of the cases enduring the disease: most of patients with TB are young adults. In consequence, health professionals must pay more attention to provide care to this population, which is economically active and could fail to attend treatment on time due to difficulties related to leaving their workplace or, as shown in this research, due to the lack of knowledge on TB.

It is important to say that although the difference between the groups regarding years attending school was two years (with an average of 5.9 years for cases and 7.9 years for controls), this situation may be related to the level of knowledge on TB. However, health professionals must advise patients on the different aspects of disease, regardless of their education level, since abilities developed over the years attending school may facilitate understanding of several aspects of life, but they are not specific about knowledge on TB. Thus, all patients must be targeted by health education strategies addressing TB.

The authors in this study expected to find a relationship between schooling and level of knowledge on the disease, but such relationship was not observed. The fact that educational level increases is not enough to provide patients with proper knowledge on TB, therefore, health professionals must work taking into account health education strategies, as counseling, and health education have proven effective in increasing cure rates, as well as in decreasing loss to follow-up rates (14).

The low level of knowledge on the disease, together with other factors, contributes to loss to follow-up in treatment. These factors include: the low number of home visits made by professionals and missing consultations during the current treatment or returning to follow-up consultation in a period ≥ 30 days. Thereby, the need to invest in measures promoting greater

knowledge on TB in patients and relating it to the other factors identified here should be stressed. If a patient knows the importance of returning to consultation on the scheduled date, as well as other TB general aspects, his or her potential adherence will increase.

The assumption that patients with an inferior knowledge on TB are those experiencing loss to follow-up in treatment more frequently was confirmed in this study as those with a rather limited knowledge are three times more prone to be a case of retreatment after loss to follow-up (adjusted OR=3.3).

Literature on this subject is consistent in considering that access to information on the disease is an important factor for treatment adherence, while ignorance of the possibility of cure may encourage loss to follow-up (15-16). Findings of other authors were confirmed in this study as it was observed that a low level of knowledge on TB is associated with loss to follow-up (11-12,16).

Health education is an important strategy for reducing rates of loss to follow-up in treatment, because lack of information or its improper assimilation contributes to difficulties in the compliance of treatment. From this perspective, health education becomes an important tool to encourage self-care (15).

So, in order to provide information on TB to the patient it is necessary to understand his or her needs and to identify and overcome his or her difficulties (13,15,17). Given this context, nurses play a key role in TB control, since one of their duties, according to the National TB Control Program in Brazil (4), is providing patients with home visits, which enables an interpersonal contact that allows the identification of patients' needs and difficulties.

Home visits are not properly provided to TB patients. However, conveying clear information during home visits and providing support to transport patients to health centers are factors that also contribute to TB treatment adherence (18). Nevertheless, in our study, patients were treated at primary health care centers that were close to their homes.

When asked about returning to their consultations, most cases of retreatment after loss to follow-up reported they returned for consultation before the time recommended by the Brazilian Ministry of Health, namely, 30 days. Since these cases had a history of loss to follow-up, professionals from this service adopted a strategy consisting of reducing consultation

deadlines. When compared to controls, it was observed that returning to consultation within the deadline was not a big issue.

TB treatment control and a proper follow-up require the patient to return to consultation once a month to access medicines and every two months to monitor the evolution of clinical and etiologic diagnosis, as recommended by the National TB Control Program (4). A possible strategy to encourage patients to return to the health center and shorten the time between visits is reducing the time between medical consultations, especially at the beginning of the treatment. This way, during the first month of treatment, patients must attend medical consultations on a weekly basis, in the second month they must do it every two weeks, and from the third month until the end of the treatment, once a month. This strategy resulted in a decreased loss to follow-up in TB treatment in a pilot study conducted in a city in southeastern Brazil (19). However, this strategy requires much more organization by professionals in health services.

Ideally, in every return, health professionals should emphasize the importance of treatment and its adherence, and use strategies to ensure this adherence, since loss to follow-up mainly occurs within the first three months of treatment (3). Therefore, health professionals must focus on advising on TB during this period.

The association of smoking with loss to follow-up in treatment coincides with the findings of another research (20). Perhaps due to smoking itself, the evolution of the disease is exacerbated when combined with the effects of medicines, which drives the patient to feel unwell and to be lost to follow-up. As smoking is addictive, the patient might find easier quitting TB treatment than quitting smoking. Therefore, in cases where there is an association between smoking and TB, the National TB Control Program should consider working along with other professionals qualified to help in smoking cessation (20).

The Health Ministry of Brazil recommends performing an anti-HIV serology test in all cases diagnosed with TB (4). In practice, however, this does not happen. Findings in this study showed that over half of patients did not get tested for HIV, which evidences difficulties faced in service delivery and patient monitoring. This factor has an impact on loss to follow-up because if the patient does not have an adequate follow-up regarding his

or her examination, he or she might feel helpless or lacking proper health care, which would end up in a case of loss to follow-up in TB treatment.

These results confirm other studies results, but they also show that the patient's knowledge on TB is associated with loss to follow-up. Despite that in this study such knowledge was determined through simple and direct questions on TB, it is known that adherence to treatment is also permeated by the attitudes and habits of the individual, which not always are the product of knowledge. However, this approach to this topic has not been affected by the study and it may reveal the role of knowledge as a factor that interferes with adherence to TB treatment.

The following factors associated with loss to follow-up were: return to consultation after the scheduled time, failure to attend scheduled consultations in the current treatment, poor knowledge on TB, smoking and negative anti-HIV serology. These findings remind us of the need for professionals to get to know their patients in order to deal with potential risks of loss to follow-up. It is also crucial to give appropriate tools to patients so that, by acquiring knowledge, they can also become a subject of their treatment and cure, instead of mere objects subjected to the actions taken by health professionals.

The results obtained in this study may promote reflections in health professionals by providing information that helps health teams to intensify educative actions and contributes to improve health actions targeting patients undergoing TB treatment. This study may expand discussions on this subject by making contributions not only in teaching and research scenarios, but mainly in the improvement of care services by considering the need to keep patients attending treatment until the disease is cured, with an emphasis on health education •

REFERENCES

1. Garrido MS, Penna ML, Perez-Porcuna TM, de Souza AB, Marreiro LS, Albuquerque BC, et al. Factors associated with tuberculosis treatment default in an endemic area of the Brazilian Amazon: a case control-study. PLoS One. 2012;7(6):e39134. http://doi.org/brnx.

2. Muture BN, Keraka MN, Kimuu PK, Kabiru EW, Ombeka VO, Oguya F. Factors associated with default from treatment among tuberculosis patients in Nairobi province, Kenya: a case control study. BMC Public Health. 2011;11:696. http://doi.org/bwbpjq.

3. Hoa NB, Sokun C, Wei C, Lauritsen JM, Rieder HL. Time to unsuccessful tuberculosis treatment outcome, Cambodia, China, and Viet Nam. Public Health Action. 2012;2(1):15-20. http://doi.org/brnz.

4. Brasil. Brazilian Ministry of Health. Manual of recommendations for tuberculosis control in Brazil/ Manual de Recomendações para o Controle da Tuberculose no Brasil. Brasília: Ministério da Saúde. 2011. Avaliable from: https://goo.gl/Ru9Zl. Accessed on September 1, 2014.

5. Shiotani R, Hennink M. Socio-cultural influences on adherence to tuberculosis treatment in rural India. Glob Public Health. 2014;9(10):1-13. http://doi.org/brn2.

6. Brasil PE, Braga JU. Meta-analysis of factors related to health services that predict treatment default by tuberculosis patients. Cad Saude Publica. 2008;24 (Suppl 4):s485-502. http://doi.org/fsm5sm.

7. Slama K, Tachfouti N, Obtel M, Nejjari C. Factors associated with treatment default by tuberculosis patients in Fez, Morocco. East Mediterr Health J. 2013;19(8):687-93.

8. Oliveira NF, Gonçalves MJ. Social and environmental factors associated with the hospitalization of tuberculosis patients. Rev Lat Am Enfermagem. 2013;21(2):507-14. http://doi.org/brn3.

9. Rodrigues ILA, Monteiro LL, Pacheco RH, da Silva SE. [Abandonment of tuberculosis treatment among patients co-infected with TB/HIV]. Rev Esc Enferm USP. 2010;44(2):383-7. http://doi.org/cxz99t.

10. Maciel E, Seixas C, Moraes E, Fregona G, Dietze R. [The knowledge of tuberculosis patients about their disease: a case-control study]. Cad Saude Colet. 2005;13(3):593-604.

11. Tachfouti N, Slama K, Berraho M, Elfakir S, Benjelloun MC, El Rhazi K, et al. Determinants of tuberculosis treatment default in Morocco: results from a national cohort study. Pan Afr Med J. 2013;14:121. http://doi.org/brn4.

12. Hoa NP, Chuc NT, Thorson A. Knowledge, attitudes, and practices about tuberculosis and choice of communication channels in a rural community in Vietnam. Health Policy. 2009;90(1):8-12. http://doi.org/chmk38.

13. Ma E, Ren L, Wang W, Takahashi H, Wagatsuma Y, Ren Y, et al. Demographic and Socioeconomic Disparity in Knowledge About Tuberculosis in Inner Mongolia, China. J Epidemiol. 2015;25(4):312-20. http://doi.org/brn5.

14. M'Imunya JM, Kredo T, Volmink J. Patient education and counselling for promoting adherence to treatment for tuberculosis. Cochrane Database Syst Rev. 2012;(5):CD006591. http://doi.org/brn6.

15. Oblitas FY, Loncharich N, Salazar ME, David HM, Silva I, Velásquez D. Nursings role in tuberculosis control: a discussion from the perspective of equity. Rev Lat Am Enfermagem. 2010;18(1):130-8. http://doi.org/c77hmb.

16. Tola HH, Tol A, Shojaeizadeh D, Garmaroudi G. Tuberculosis Treatment Non-Adherence and Lost to Follow Up among TB Patients with or without HIV in Developing Countries: A Systematic Review. Iran J Public Health. 2015;44(1):1-11.

17. Hino P, Takahashi RF, Bertolozzi MR, Villa TC, Egry EY. Family health team knowledge concerning the health needs of people with tuberculosis. Rev Lat Am Enfermagem. 2012;20(1):44-51.

18. Farias de Oliveira J, Antunes MBC. [Announced tuberculosis treatment abandonment in a family health unit of Recife: the user's perspective]. Rev APS. 2012;15(1):4-13.

19. Bergel FS, Gouveia N. [Frequent return as a novel strategy for tuberculosis treatment adherence]. Rev Saude Publ. 2005;39(6):898-905. http://doi.org/fh6zkw.

20. Chiang Y-C, Lin Y-M, Lee J-A, Lee C-N, Chen H-Y. Tobacco consumption is a reversible risk factor associated with reduced successful treatment outcomes of anti-tuberculosis therapy. Int J Infect Dis. 2012;16(2):e130-e5. http://doi.org/dqg7g9.