Monitoring contacts of tuberculosis patients by community health workers

Monitoramento de contatos de pacientes com tuberculose por agentes comunitários de saúde Monitoreo de contactos de pacientes con tuberculosis por agentes comunitários de salud

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Abstract

Objective: To analyze the monitoring of contacts of tuberculosis (TB) patients from the perspective of Community Health Workers (CHWs).

Methods: This was a descriptive, cross-sectional, qualitative study with CHWs from eight Primary Care Center in the Casa Verde/Cachoerinha/Limão Technical Health Supervision in the city of São Paulo, SP. Semi-structured interviews were conducted from June to July 2021. Health Surveillance was the conceptual framework and the statements were subjected to content analysis.

Results: The CHWs (51) had an average working time of 7.4 years and 169 families under their responsibility; they reported having already had cases of TB in the micro-area they worked in (68.7%) and had some training in the disease (70.6%). In general, the monitoring of contacts was not known by the participants, who also did not recognize this activity as a task for which they were responsible. Several difficulties were identified in the work routine, including: contacts' resistance to being assessed at appointments and carrying out the tests requested, accepting the possibility of having TB, not being able to access contacts, among others.

Conclusion: Ignorance of the need to monitor contacts can weaken the early detection of new cases of tuberculosis and latent tuberculosis infection, and contribute to maintaining the transmission of the disease. Given the importance of CHWs for this practice, and considering that they are an important link between the community and the health team, it is recommended that they be properly trained for the early identification of new TB cases and for the proper monitoring of contacts.

Resumo

Objetivo: Analisar o monitoramento de contatos de pacientes com tuberculose (TB) na perspectiva de Agentes Comunitários de Saúde (ACS).

Métodos: Estudo descritivo, transversal e qualitativo, com ACS de oito Unidades Básicas de Saúde da Supervisão Técnica de Saúde Casa Verde/Cachoerinha/Limão do Município de São Paulo, SP. Foram realizadas entrevistas semiestruturadas de junho a julho de 2021. A Vigilância à Saúde constituiu o referencial conceitual e os depoimentos foram submetidos a análise de conteúdo.

Resultados: Os ACS (51) tinham um tempo médio de atuação de 7,4 anos e 169 famílias sob sua responsabilidade; referiram já ter tido casos de TB na microárea de atuação (68,7%) e algum treinamento em relação à doença (70,6%). Em geral, o monitoramento de contatos não era conhecido pelos participantes, que também não reconheciam essa atividade como uma tarefa de sua responsabilidade. Várias dificuldades foram identificadas na rotina de trabalho, incluindo: resistência dos contatos em ser avaliados em consulta e realizar os exames solicitados, aceitar a possibilidade de ter TB, não conseguir acessar os contatos, dentre outras.

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Conflicts of interest: nothing to declare.

Conclusão: O desconhecimento da necessidade de monitorar os contatos pode fragilizar a detecção precoce de casos novos de Tuberculose e a Infecção Latente por Tuberculose, e contribuir para a manutenção da transmissão da doença. Dada a importância dos ACS para essa prática, e considerando que são um importante elo entre a comunidade e a equipe de saúde, recomenda-se sua devida instrumentalização para a identificação precoce de novos casos de TB e para o monitoramento adequado dos contatos.

Resumen

Objetivo: Analizar el monitoreo de contactos de pacientes con tuberculosis (TB) bajo la perspectiva de agentes comunitarios de salud (ACS).

Métodos: Estudio descriptivo, transversal y cualitativo, con ACS de ocho Unidades Básicas de Salud de la Supervisión Técnica de Salud Casa Verde/Cachoerinha/Limão del municipio de São Paulo, estado de São Paulo. Se realizaron entrevistas semiestructuradas de junio a julio de 2021. La Vigilancia de la Salud constituyó el marco conceptual y los testimonios fueron sometidos al análisis de contenido.

Resultados: Los ACS (51) contaban con un tiempo promedio de actuación de 7,4 años y 169 familias bajo su responsabilidad. Declararon haber tenido casos de TB en su microárea de actuación (68,7 %) y alguna capacitación relacionada con la enfermedad (70,6 %). En general, los participantes no conocían el monitoreo de contactos y tampoco reconocían esa actividad como una tarea bajo su responsabilidad. Se identificaron varias dificultades en la rutina de trabajo: resistencia de los contactos a ser evaluados en consulta y realizar los exámenes solicitados, aceptar la posibilidad de tener TB, no poder acceder a los contactos, entre otras.

Conclusión: La falta de conocimiento de la necesidad de monitorear los contactos puede debilitar la detección temprana de nuevos casos de tuberculosis y de infección por tuberculosis latente, lo que contribuye a mantener la transmisión de la enfermedad. Dada la importancia de los ACS para esta práctica y considerando que son un importante eslabón entre la comunidad y el equipo de salud, se recomienda que sean debidamente preparados para la identificación temprana de nuevos casos de TB y para el monitoreo adecuado de los contactos.

Introduction =

Tuberculosis (TB) can be prevented and cured, but its prevalence is still significant, making it a major public health problem. In 2021, 10.6 million people worldwide were affected by the disease. The COVID-19 pandemic has reversed years of progress in its control and the number of deaths has risen for the first time in more than a decade: 1.5 million in 2020 and 1.6 million in 2021.⁽¹⁾

Brazil is among the 30 countries with a high TB burden, including TB associated with the Human Immunodeficiency Virus (TB-HIV), both of which must be controlled as a matter of priority, according to the WHO.⁽²⁾ In 2021, the incidence of TB was 48.0/100,000 inhab. (104,000 new cases); in 2020, there were 6,000 deaths (TB mortality coefficient in HIV-negative: 2.8 cases/100,000 inhab.).⁽³⁾

This data highlights the importance of control measures aimed at reducing the number of cases, detecting and treating them early and monitoring their contacts. The Brazilian Ministry of Health (MoH) recommends that all contacts be systematically assessed, defining them as all people exposed to those diagnosed with TB, whether at home, work, long-term care institutions, school, etc. (4)

Contact investigation is an effective strategy for detecting TB cases and helps to control the disease and prevent people from becoming ill. (5) Although evaluation is widely recommended, it has not been

valued in practice as a source of identifying new cases. What's more, there is evidence that surveillance in the home is gaining ground by extending into social spaces and seeking to build the social networks of the individual with TB.⁽⁶⁾ In 2021, the percentage of examinations of contacts of new cases of pulmonary TB, with laboratory confirmation, in Brazil, was 69.1%; in the State of São Paulo, 80.7%; and in the Municipality of São Paulo, 56.1%.⁽⁷⁾

The Global Strategy to Combat TB calls for the intensification of contact assessment and the incorporation of new technologies for the diagnosis of Latent Tuberculosis Infection (LTBI). (8) LTBI is identified mainly through contact monitoring, and refers to individuals infected with Mycobacterium tuberculosis who do not have active disease. Although not all of them will become ill with the active form of TB, they remain a reservoir that can be reactivated in the event of a compromised immune response. (9) In order to meet the targets of this strategy, the National Plan to End Tuberculosis adopted the proportion of contacts examined (of new pulmonary tuberculosis cases with laboratory confirmation) as an indicator, setting a target of assessing 90% of them.(2)

In this context, we highlight the importance of studies that make it possible to understand any difficulties encountered by health professionals, especially Community Health Workers (CHWs), who continuously monitor users in the territory of the

health unit where they work. (10,11) Therefore, the aim of this study was to analyze contact monitoring in Primary Care Center (PCC) from the perspective of community health workers.

Methods =

This was a cross-sectional, descriptive study with a qualitative approach, carried out in eight PCC with a Family Health Strategy in the Casa Verde/Cachoerinha/Limão Technical Health Supervision (THS) of the Northern Regional Health Coordination of São Paulo, SP.

The sample was intentional and one CHW from each PCC team was interviewed by lot, totalling 51 participants. When the study was carried out, there were 51 FHS teams in the region, and each PCC had 4-9 teams. Working as a CHW for at least one year was the inclusion criterion, and CHWs on sick leave or vacation were the exclusion criterion.

Data collection took place in June-July 2021, through an individual semi-structured interview (recorded on portable audio, in a private environment at the CHW's workplace), which was previously scheduled with the health unit manager. An instrument designed for this study was used, containing questions about the CHW's sociodemographic profile and their experience with TB; in addition, eight guiding questions were asked which sought to capture their way of acting in relation to contact monitoring, as well as other aspects of their experience with TB patients. The statements were subjected to content analysis (12) following the stages of pre-analysis, coding, categorization and inference. (13) Excerpts from the statements are identified by E (CHW interviewed) and sequential number (according to the order in which the interview was conducted).

The concept of Health Surveillance was the reference point for the study, considering that it refers to the practice that organizes work processes to tackle health problems in a given territory. (14)

The project was approved by the Research Ethics Committee of a Public Higher Education Institution (# 4.601.966) (Certificate of Submission

for Ethical Appraisal: 41891621.6.0000.5392) and the Ethics Committee of the Health Department of the Municipality of São Paulo (# 4.697.559) (Certificate of Submission for Ethical Appraisal: 41891621.6.3001.0086).

Results =

In order to facilitate understanding and for didactic purposes only, since they make up the interviews as a whole and are dependent on each other in their interpretation, the results are presented by content categories.

The profile of the CHWs interviewed

A total of 49 (96.4%) interviewees were women (average age: 40.6 years); the majority self-declared as white (19; 37.2%), followed by brown (17; 33.3%). The majority (35: 68.6%) had completed high school. The average time they had worked as CHWs was 7.4 years, and the average number of families they were responsible for was 169. As for their experience with tuberculosis, most of them (36; 70.6%) reported having received training and/or guidance on a daily basis, especially from the team nurse, and 68.7% (35) said they had had cases of tuberculosis in their micro-area of work (Table 1).

Table 1. Study participants' experience with tuberculosis (Casa Verde, Limão and Cachoeirinha; São Paulo, SP)

Indicators	Variables	n(%)
Have you ever had cases of tuberculosis in your	yes	35(68.7)
micro-area?	No	16(31.3)
How many patients had tuberculosis?	0	16(31.3)
	1-4	30(58.9)
	5-8	2(3.9)
	9-12	1(1.9)
	13-16	2(3.9)
Has there been training on tuberculosis?	Yes	36(70.6)
	No	15(29.4)

Perception of CHWs on actions with contacts of TB patients

The participants described how they perceived the flow of care at the health unit and pointed out actions for monitoring contacts of patients with TB, such as guidance on avoiding transmission, main-

taining surveillance and summoning them for care and tests at the PCC. They pointed out that contacts were first welcomed at the PCC and were given information about the disease, its symptoms and the tests needed to detect it (E14, E40, E41, E45).

Welcoming and clearing up doubts, because many people still have doubts about the disease in general; clarifying, welcoming, clearing up any doubts, information; reinforcing care and meeting the needs in question, including guidance for the patient and family (E40).

Some guidelines, especially on the need to isolate the sick person and their private objects, are mistaken and show the precarious understanding of the illness when the correct therapy is put in place:

I think there should be isolation of the family, everyone should wear a mask, like with COVID, because it's a disease... tuberculosis is a serious disease... but I think social isolation should include the whole family (E6).

From another perspective, some CHWs reported that contacts are not necessarily assessed at the PCC after undergoing tests and having negative results (E17, E20, E23, E26, E32, E35, E38, E39, E47), even though scheduling was prioritized by the team, so they were seen on the same day they sought the service (E44, E50).

The CHWs advise the contacts to come to the PCC, saying that they have no difficulties with this activity (E1, E4, E5, E6, E8, E9, E11, E12, E13, E15, E16, E19, E20, E22, E24, E25, E27, E29, E30, E33, E38, E39, E40, E41, E43, E45, E46, E47, E50, E51). However, they stated that the realization of this orientation was independent of their will (E13, E30, E40, E45, E51).

I don't think it would be difficult; I go there and now we have a tablet that we work with; we also have WhatsApp contacts with the patients... we have no difficulty talking to them, either in person or on the tablet (E6).

No, no difficulty at all, not least because it's our role to provide guidance and visit these families on a monthly basis... and always persist in providing guidance; one day the person will end up coming to the unit (E46).

I don't think there's any difficulty in giving advice, but coming to the clinic depends on each family (E30).

... and sometimes the person doesn't see the risk either, they're afraid... (E51).

According to the CHWs, contact surveillance takes place during home visits, and they believe that they are the bridge between the PCC and the families, bringing information about any changes to the health team (E4, E5, E6, E8, E16, E32, E39), as well as understanding the need for contact tracing and assessment at the PCC (E10, E11, E24, E31, E46, E48).

...it's a disease that's caught in the air... So the more care the CHWs can take with this family and the closer they can look, I think it's very important (E6).

I think you also have to screen people who live together and probably have close contact, not least because sometimes you end up sharing cutlery in the same house, the same glass... (E24).

Surveillance takes the form of identifying symptoms, even in patients who have already been clinically assessed and whose tests are unchanged (E13, E24, E35).

...we've been monitoring, the doctor too, the nurse too, ... if we notice that the person isn't very well, we call the nurse: "look XXX, it's like this: this patient isn't very well, he's bad, he's got a cough; he's arrived with his mother; shouldn't we do the tests again?" (E13)

The need to submit contacts to laboratory tests was not mentioned in only 6 statements (E2, E5,

E8, E24, E30, E42). The majority of CHWs said that contacts had undergone the "TB test", the BK (referring to the Rapid Molecular Test for TB or the sputum smear test), or X-rays (E12, E13, E15, E18, E20, E21, E36, E37, E44, E48, E50).

However, only 15 CHWs mentioned that one of the tests that contacts should undergo is the Protein Purified Derived (PPD), the Tuberculin Test (E3, E8, E12, E13, E18, E21, E22, E26, E36, E37, E40, E41, E42, E43, E48). Even when they mentioned PPD, most were unaware of its purpose; some couldn't remember what it was called, saying only that it was carried out elsewhere (reference PCC) (E3, E8, E41, E42, E43).

Still on the subject of tests, some CHWs said that the tests carried out on adult contacts were different from those carried out on children (E5, E8, E12, E13, E16, E18, E20, E24, E26, E33, E37, E40, E42, E47, E49).

...in children, the PPD is done; and in adults, the X-ray is usually done for those who don't have symptoms; when they still have symptoms, they ask for the BK to see if they have the disease, but in children it's just the PPD (E26).

According to the CHWs, the tests for contacts are requested in advance by the team's doctor or nurse, and then the CHW delivers the requests and a bottle for collecting the sputum (E13, E18, E20, E29, E21, E27, E33, E40, E48). Although most of the CHWs accurately mentioned the operational system for carrying out tests on contacts, some were uncertain about its flow (E6, E9, E28, E51).

Despite the variety and complexity of the actions carried out by CHWs in the territory, and their appreciation of their work, some of them considered it not to be part of their job, such as scheduling appointments at the request of patients (E33, E34, E46):

...I like it because... although there are always some who... it's happened to me several times, not once or twice; they demand a role from us that isn't ours; they sometimes demand a caregiver role; they don't understand our role, what is our role? that we're

limited, that we're not here for that; often, we even do things we shouldn't in order to help the family, but even then there's ingratitude; it happens a lot; there are people who demand too much of us; it wears you down a lot, a lot, and I try to deal with it patiently and wisely, because it's difficult... (E33).

Perception of CHWs on the treatment of LTBI

The CHWs showed a limited understanding of the treatment of ILTB, which is fundamentally relevant in monitoring contacts, but they didn't show any differences in conduct in relation to treatment in the case of TB (E7, E21, E29, E30, E38, E43, E47, E48, E49), with the exception of just three mentions (E43, E47, E48).

...in my case, I know that my doctor treated the patient, but he also gave medication to the family as well (E7).

I think it's going to the doctor, doing tests; I don't know; there was once a patient on our team who was also given medication by the family (E30).

...the mother and the niece took the medication for three months, in the case of the asymptomatic patient the medication is different from the one who was in contact, it's a lot less time and it's another medication, the one who has tuberculosis already detected, he has to take four pills, the other one doesn't, it's a much smaller dose and it's a lot less time... (E43).

It's the PPD and he takes the test and, if there's a slight reaction, he sometimes starts the prophylaxis treatment as well (E47).

CHWs' perception of difficulties in caring for TB contacts

In this regard, the CHWs pointed out: resistance on the part of contacts to undergo tests (E4, E7, E9, E12, E17, E21, E22, E26, E32, E35, E38, E44, E46, E48, E49) and to accept the possibility of having TB (E18); PPD being offered only at the referral unit (E12, E26); not being able to access con-

tacts (absent from home, didn't live in the area covered by the PCC or didn't understand Portuguese, in the case of immigrants) (E14, E16, E18, E28, E31, E38); and the need to work, which limits the chances of going to the PCC (E6, E8, E14, E28).

Yes, ... to bring them in, there's going to be a little bit of rejection from them... because until then, they don't accept it; it's very difficult; they don't have that; they don't even accept that they have tuberculosis, you know? to bring in, it's very difficult; there are some patients who are very difficult to bring in for a common test (E22).

Even if we ask, say, "Is everything okay? Does anyone have a cough?" "Oh, I'm just coughing a little bit", just a little bit, but you'll see how many days it's been, especially if you're Bolivian, they don't want to stop working, ... they don't want to waste time coming to the clinic to get tested; meanwhile, they're contaminating the others, the others who are working around them (E18).

... the only difficulty I find is with the PPD, because sometimes I have a family that is very poor and, when they had tuberculosis, they had to get tested at another unit (E26).

... the difficulty would be if they had to work; that many say: I can't go to the unit, because I have to go to work (E6).

There's always that family, there's that person who lives there, who works... who's afraid of, I don't know, getting a statement or doesn't want to stop working to come, there's always going to be one who's going to be more trouble... (E8).

Absence of symptoms, extrapulmonary TB (E26, E38), contacts from outside the family, e.g. friends, also make it difficult to monitor contacts (E2, E10, E23, E26, E38).

...there are some people who don't bother... they don't take care... because they haven't had any symptoms, I don't think they'd come, I think it's

important for family members to come, but I think friends... I don't know if they'd come (E2).

Discussion

Contact monitoring, the focus of this study, is not carried out systematically. There is uncertainty among the CHWs about the flow and access to the service, including their attributions. Most CHWs don't recognize monitoring as their responsibility, which compromises the proposal of Health Surveillance.

The CHWs have a number of duties in TB control, including the following: being aware of the main signs and symptoms of TB in all meetings with the community; referring suspected cases; carrying out an active search for respiratory symptoms (RS) as a priority; advising the population on the transmission and prevention measures of the disease; monitoring the vaccination status of children and referring children under 5 years of age without a BCG vaccination record to the PCC, as well as advising and referring contacts of TB patients for clinical assessment and possible treatment at the PCC. (15) Although some of these attributions were mentioned in this study, the participants did not give advice to the general population about the disease, but restricted themselves to families affected by TB, even with restrictions. Nor was it noted that the active search for FS is a priority strategy for CHWs; and the identification of the vaccination status of children under 5 was not mentioned.

It was possible to identify a certain misunderstanding regarding the flow of care for respiratory symptomatic patients and contacts of TB patients. If contacts show symptoms, it is recommended to rule out active tuberculosis through diagnostic tests, such as the Rapid Molecular TB Test (RMS-TB) or bacilloscopy; once it is certain that the contact does not have the disease, ILTB should be investigated.⁽⁴⁾

With regard to tests carried out by contacts, almost all the subjects in the study mentioned that the TRM-TB or the sputum smear test should be carried out; some of them mentioned the need for contacts to have a chest X-ray and about a third

reported that the PPD should also be carried out, which shows a lack of knowledge. (4) Despite the current practice of using the PPD, most of the participants were unaware of its purpose. The PPD test is used routinely and is a delayed-type hypersensitivity reaction to mycobacterial antigen. (4)

Another worrying point, mentioned by some CHWs, is that contacts should not necessarily return to the PCC for evaluation if they have undergone tests (bacilloscopy and/or chest X-ray and/or PPD) whose results were negative. As the majority of CHWs did not report PPD as the main test to be carried out on contacts, this could mean that this group will supposedly have TB ruled out, and ILTB treatment will not be considered, with negative repercussions for disease control. However, one of the difficulties mentioned is that there are few PCCs that carry out PPD. In fact, when the study took place, the STS was made up of 13 PCC and only one of them carried out this test.

Treatment for LTBI consists of therapy for individuals infected with Mycobacterium tuberculosis who have not manifested active disease, and is one of the main strategies for interrupting the chain of transmission. (9) Some CHWs pointed out that contacts had been treated for LTBI, but showed insufficient knowledge and misunderstandings about the difference between TB and LTBI. To diagnose LTBI, it is necessary to rule out active disease and carry out PPD or the Interferon-Gamma Release Assay (IGRA). (9) The latter, like PPD, makes it possible to assess the cell-mediated immune response, while the former assesses this response in vitro. PPD was the only method made available by SUS for the management of LTBI in public health units, but in 2023 IGRA was made available for some situations, such as its use in children who are contacts of TB patients.(16,17)

The difficulties in managing contacts are corroborated by a study carried out in Vitória (ES). (10) and in Ribeirão Preto (SP). The latter concluded that changing the status of CHWs from transmitters of information to the health team to participants in TB control is a complex process, since work practice must be associated with technical knowledge and political competence, which go beyond person-

al experiences.⁽¹⁸⁾ This was also reported in a study carried out in South Africa, highlighting a lack of resources and training, low community acceptance, misunderstandings between contact tracing activities and other TB care, as well as a lack of prioritization of contact monitoring over other activities.⁽¹⁹⁾

The CHWs recognize that they must carry out contact surveillance during home visits, seeking to identify signs and symptoms, and act as a bridge between the family and the PCC. The Family Health Strategy has made it possible to decentralize the actions of the PNCT and home visits should include active search and identification of respiratory symptoms, and failure to carry out these actions compromises health surveillance. (20,21)

It's important to note that CHWs see themselves as a bridge between the PCC and the community. Their role is to integrate the community into the health services in an attempt to facilitate communication, acting as interlocutors, as they know the territory they work in, experience the daily lives of the families living in the region, which can facilitate the health surveillance and promotion work carried out by the whole team and, with this, it is recognized that there is potential to reorient the care model. (22)

In fact, the work of the CHWs involves a broader approach to the family, establishing and maintaining links with the health service. Their work is essential for identifying respiratory symptoms (RS) and diagnosing TB, although this work is not without its difficulties. (23)

In addition to those mentioned above, the difficulties in monitoring contacts included their refusal to accept the possibility of contracting the disease, their refusal to undergo tests due to the absence of signs and symptoms, and the restriction of some contacts to take time off work. These difficulties are similar to those found in a study in Campina Grande (PB). (24)

Another issue pointed out was the care provided to immigrant contacts, especially with regard to their limited understanding of the language. It's important to remember that international immigration has become one of the biggest challenges to public health; migrants have faced other difficulties besides the language barrier in accessing

health services, such as lack of information, low perception of health and self-care, lack of qualified professionals for the specific demands of this population, etc. (25,26) In a study carried out in Barcelona (Spain), in areas with a high concentration of immigrants, the presence of community workers was important, as they contributed to a significant increase in contact tracing of patients with pulmonary TB, with positive bacilloscopy and in all clinical forms of TB. (27)

Although the majority of CHWs said that they had no difficulty in advising contacts about the importance of seeking health services in order to be assessed, they mentioned that not all of them went to the PCC. In line with the low rates of contact assessment, a study carried out in Ethiopia also found that the proportion of contacts screened was low (20%), pointing to the need to improve home visits. (28) In contrast, a study carried out in Recife (PE) found that the majority of CHWs actively sought out contacts, gave advice on tuberculosis prevention and referred them for evaluation at the PCC. (21)

The diagnosis of extrapulmonary TB was also mentioned by the CHWs as a difficulty, since it is a non-transmissible form of the disease. Even so, it is necessary to investigate contacts in order to discover the source case and interrupt the chain of transmission. (4)

The results of this study revealed one side of the contact monitoring carried out by the CHWs, revealing limitations to its implementation and gaps in the knowledge of these professionals, such as the need to isolate patients, even if they are unaware of the therapeutic follow-up situation. In addition, this study points to other weaknesses, such as the low supply of PPD in the territory and incomplete assessment of contacts by the PCC, highlighting that knowledge of these gaps can help to improve the work of the health team and guide strategies to overcome them, as well as helping nurses to understand the potential and weaknesses of the work of CHWs in primary health care.

Since the results of this study are restricted to one health region in the city of São Paulo, it is recognized that this is a limitation and therefore cannot be generalized.

Conclusion

CHWs are essential in the FHS and in monitoring contacts. However, the shortcomings observed in their knowledge can corroborate the low rates of evaluation, lead to losses in the early diagnosis of TB and ILTB, and the permanence of the chain of transmission of the disease. They should be trained on the subject, and methodological resources should be used to reach this category of workers.

Collaborations

Venancio JMP, Bertolozzi MR, Orlandi GM and França FOS contributed to the conception of the project, analysis and interpretation of the data, writing of the article, relevant critical review of the intellectual content and approval of the final version to be published.

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