

## Care strategies for controlling drug-resistant tuberculosis: integrative literature review

*Estratégias assistenciais para o controle da tuberculose drogarresistente: revisão integrativa da literatura*

*Estrategias asistenciales para el control de la tuberculosis farmacoresistente: revisión integradora de la literatura*

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### ABSTRACT

**Objective:** from the scientific literature, to identify care strategies for controlling drug-resistant tuberculosis. **Method:** this integrative literature review examined relevant research on the research question – What is the scientific evidence on care strategies for controlling drug-resistant tuberculosis? – by searching Latin American and Caribbean Health Sciences Information, Medical Literature Analysis, *Índice Bibliográfico Español en Ciencias de la Salud* and *Banco de Dados em Enfermagem*, between January and March 2020. Ten articles were included in order to discuss findings that answered the research question, after meeting the inclusion and exclusion criteria. **Results:** of studies published in the past five years, 80% addressed care strategies for controlling drug-resistant tuberculosis and 20% revealed shortcomings in care for patients with the disease. **Conclusion:** the literature review identified several care strategies for controlling drug-resistant tuberculosis, particularly by decentralized diagnosis and shared treatment, allowing expanded, comprehensive patient care.

**Descriptors:** Health Promotion; Patient Care Team; Patient-Centered Care; Tuberculosis, Multidrug-Resistant.

### RESUMO

**Objetivo:** identificar, na literatura científica, estratégias assistenciais para o controle da tuberculose drogarresistente. **Método:** revisão integrativa da literatura, com análise de pesquisas relevantes sobre a questão norteadora: Quais são as evidências científicas sobre as estratégias assistenciais para o controle da tuberculose drogarresistente? Busca realizada nas bases Literatura Latino-Americana e do Caribe em Ciências da Saúde, *Medical Literature Analysis*, *Índice Bibliográfico Espanhol en Ciencias de la Salud* e *Banco de Dados em Enfermagem*, entre janeiro e março de 2020. Foram incluídos dez artigos para discussão dos resultados que responderam à questão da pesquisa, atendendo aos critérios de inclusão e exclusão. **Resultados:** nos estudos publicados nos últimos cinco anos, 80% abordaram estratégias assistenciais para o controle da tuberculose drogarresistente e 20% evidenciaram falhas na assistência aos portadores da doença. **Conclusão:** a revisão da literatura identificou várias estratégias assistenciais para o controle da tuberculose drogarresistente, com destaque para a descentralização do diagnóstico e tratamento compartilhado, possibilitando uma atenção ampliada e integral aos pacientes.

**Descritores:** Promoção da Saúde; Equipe de Assistência ao Paciente; Assistência Centrada no Paciente; Tuberculose Resistente a Múltiplos Medicamentos.

### RESUMEN

**Objetivo:** identificar, en la literatura científica, estrategias de asistencia para el control de la tuberculosis farmacoresistente. **Método:** se trata de una revisión integradora de la literatura, con análisis de investigaciones relevantes sobre la cuestión rectora: ¿Cuáles son las evidencias científicas sobre las estrategias de asistencia para el control de la tuberculosis farmacoresistente? La búsqueda fue realizada en las bases Literatura Latinoamericana y del Caribe en Ciencias de la Salud, *Medical Literature Analysis*, *Índice Bibliográfico Español en Ciencias de la Salud* y *Banco de Datos en Enfermería*, de enero a marzo de 2020. Se incluyeron diez artículos para discutir los resultados que respondieron a la pregunta de la investigación, cumpliendo con los criterios de inclusión y exclusión. **Resultados:** en los estudios publicados en los últimos cinco años, el 80% abordó estrategias de atención para el control de la tuberculosis farmacoresistente y el 20% mostró fallos en la atención de los pacientes con la enfermedad. **Conclusión:** la revisión de la literatura identificó varias estrategias asistenciales para el control de la tuberculosis farmacoresistente, con énfasis en la descentralización del diagnóstico y tratamiento compartido, permitiendo una atención ampliada e integral a los pacientes.

**Descriptores:** Promoción de la Salud; Grupo de Atención al Paciente; Atención Dirigida al Paciente; Tuberculosis Resistente a Múltiples Medicamentos.

## INTRODUCTION

Drug-resistant tuberculosis (DR-TB) is a severe form of tuberculosis (TB) that can range from mono-resistance (resistance to a first-line antibiotic) to extensive drug-resistance (XDR-TB), that is, resistance to the first-line drugs as well additional resistance to any fluoroquinolone and to at least one of the three second-line injectable

medications (amikacin, kanamycin, or capreomycin). It is noteworthy that, even with the recommended and standardized therapy scheme, the occurrence of resistance to antituberculosis drugs has been increasing disease severity<sup>1</sup>.

The rapid increase of DR-TB in recent years imposes concerns on the health authorities and managers. They recognize the potential risk of the available therapeutic regimens becoming ineffective, imposing the need to use adequate care strategies for disease control that go beyond drug treatment<sup>2</sup>.

DR-TB is complex and involves social, cultural, political and economic factors that favor the development of resistance to different drugs. In addition to that, there is also inherent contamination with already resistant bacteria<sup>1</sup>.

Currently, 30 countries concentrate 95% of the global TB cases, among which is Brazil, as a representative of the American Continent<sup>3</sup>. It is estimated that in 2017, worldwide, 7.1% of the new TB cases and 7.9% of the previously treated cases were resistant to the main drugs available. The number of DR-TB cases increases every year in the countries that concentrate the TB cases, such as Brazil, China, Russia and India, among others<sup>1-3</sup>.

To reverse the current situation, the World Health Organization (WHO) proposed the End TB Strategy worldwide, including access to adequate care and adherence to free treatment available in the health services. Therefore, the context of the TB patient, the strengthening of humanized care and the integration with the multiprofessional team must be considered. In this strategy, Nursing plays a historical leading role in welcoming the patients and in their adherence to the treatment of the disease<sup>4</sup>.

It is necessary for the nurse, together with the other professionals working in the assistance provided to the TB patient, to know the care strategies for adherence to the treatment. It is indispensable to increase the integration and appreciation of the individuals affected by the disease as co-responsible subjects for their treatment, in order to generate care quality, reduce the abandonment rate and, consequently, break the disease transmission chain, which is configured as a relevant social phenomenon<sup>5</sup>.

In this perspective, it is important to know the current and innovating strategies of the assistance provided to DR-TB patients, which turn them into leading actors of their care in the construction of knowledge and actions to achieve a cure<sup>4</sup>. The objective of this study is to identify, in the scientific literature, care strategies for the control of drug-resistant tuberculosis.

## METHOD

This is an integrative literature review with a descriptive approach to fully understand the phenomenon, by means of the analysis of relevant research studies supporting decision-making in assistance. This research was developed in six stages: 1<sup>st</sup>) identification of the theme and definition of the research guiding question; 2<sup>nd</sup>) literature search and careful sampling selection; 3<sup>rd</sup>) data categorization; 4<sup>th</sup>) critical analysis of the studies included; 5<sup>th</sup>) interpretation of the integrative review results; and 6<sup>th</sup>) review report and knowledge synthesis<sup>6,7</sup>.

The guiding question emerged from the PICO strategy, acronym for: P - Population, I - Intervention, C - Comparison, O - Outcomes<sup>7</sup>. The following was attributed in this study: P - Patients with DR-TB; I - Assistance provided to the patient with DR-TB; C - It was not applied, as this was not a comparative study; and O - Control of DR-TB. Consequently, the research guiding question was formulated as follows: What is the scientific evidence about the care strategies for the control of drug-resistant tuberculosis?

The search for the selection of the publications took place from January to March 2020 in four databases: LILACS (*Literatura Latino-Americana e do Caribe em Ciências da Saúde*), MEDLINE (Medical Literature Analysis), IBECs (*Índice Bibliográfico Español en Ciencias de la Salud*), and BDEF (*Banco de Dados em Enfermagem*).

Data collection was conducted by means of queries in the databases accessed through the Virtual Health Library (*Biblioteca Virtual em Saúde*, BVS) portal with the help of a librarian, and using the following Descriptors in Health Sciences (*Descritores em Ciências da Saúde*, DeCS): Multiple Drug-Resistant Tuberculosis and its respective synonyms: Drug-Resistant Tuberculosis, Pharmacoresistant Tuberculosis; Patient-Centered Care; Health Promotion; Patient Care Team.

Four search strategies were conducted in the databases with the subject descriptor, using the Boolean operators AND and OR: 1) "Tuberculose Resistente a Múltiplos Medicamentos" OR "Tuberculose Resistente a Drogas" OR "Tuberculose Farmacorresistente" AND "Assistência Centrada no Paciente"; 2) Tuberculose Resistente a Múltiplos Medicamentos OR "Tuberculose Resistente a Drogas" OR "Tuberculose Farmacorresistente" AND "Promoção da Saúde"; 3) "Tuberculose Resistente a Múltiplos Medicamentos" OR "Tuberculose Resistente a Drogas" OR "Tuberculose Farmacorresistente" AND "Equipe de Assistência ao Paciente"; 4) Tuberculose Resistente a Múltiplos Medicamentos OR "Tuberculose Resistente a Drogas" OR "Tuberculose Farmacorresistente" AND "Assistência Centrada no Paciente" OR "Promoção da Saúde".

The criteria for inclusion in the literature review were established as follows: original articles published in full in the last five years (2015-2019), available in electronic format, and in Portuguese, English and/or Spanish. Duplicate studies were excluded, as well as literature reviews, reflective studies, experience reports, and those that did not adhere to the research guiding question.

The articles were selected in three stages carried out between peers. In the first stage, which began with a search in the selected databases by crossing the descriptors, 8,041 articles were identified, of which 1,665 met the inclusion criteria. In the second stage, 1,558 articles were excluded after reading the main titles. By applying the exclusion criteria, 97 articles were excluded after reading the abstracts, for not adhering to the research question, thus resulting in 10 articles for the third stage. In this stage, the articles were read in full according to what is shown in the flowchart for the selection of the studies based on the PRISMA<sup>7</sup> model (Figure 1).

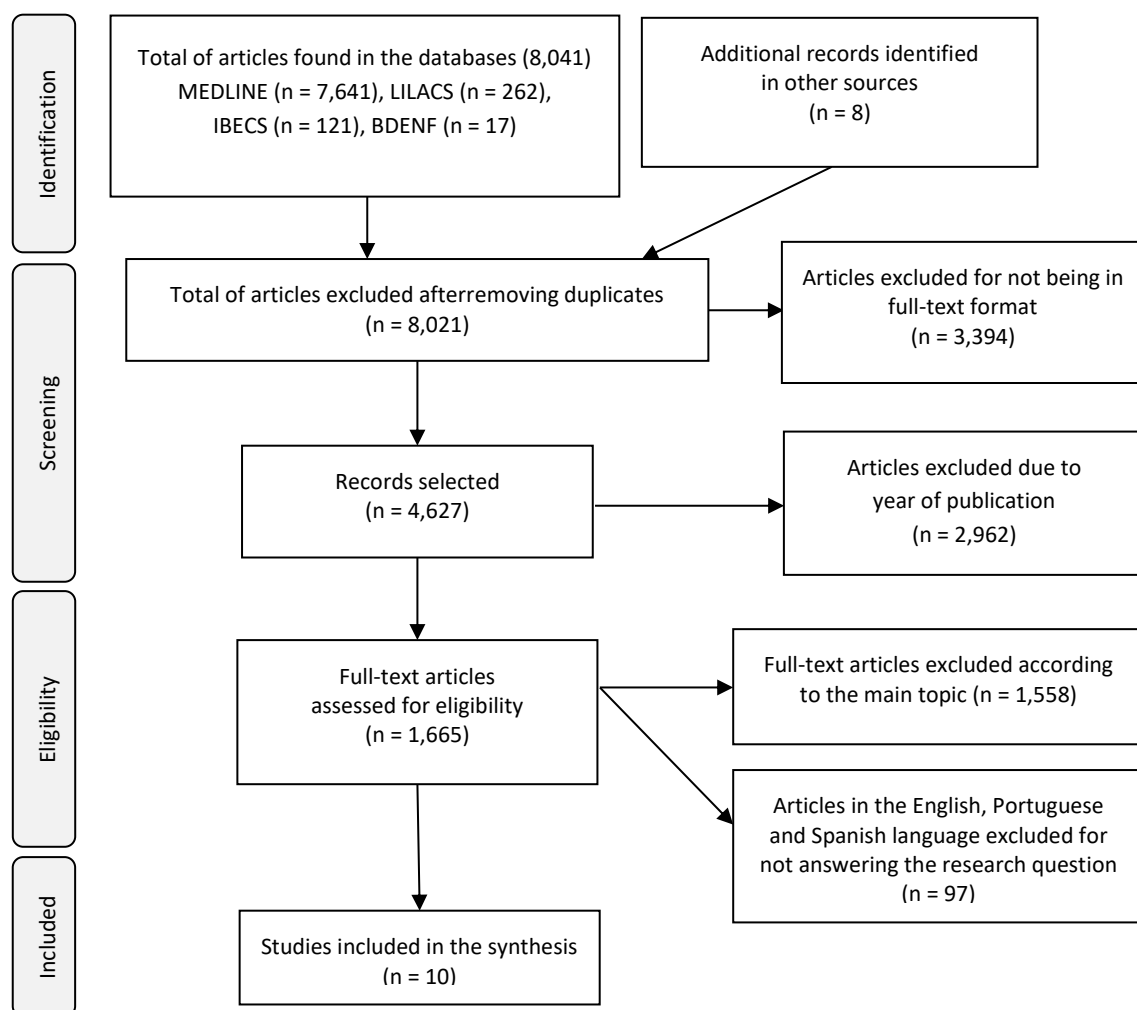


FIGURE 1: Flowchart for the selection of the articles based on PRISMA<sup>7</sup>. Manaus, AM, Brazil, 2020

## RESULTS AND DISCUSSION

The articles included in this integrative review were published in international journals from 2015 to 2019. Some of the countries where the studies were conducted are recognized by the WHO as with priority in the application of care strategies for the control of tuberculosis (TB) and of drug-resistant tuberculosis (DR-TB). The nine articles in English and the one in Spanish are described in Figure 2, in relation to title, country and nature of the study, general objective, journal where it was published and Qualis-CAPES.

Study title	Country(ies) where the study was conducted	Nature of the study	General objective	Journal	Qualis
Quality of tuberculosis care in high burden countries: the urgent need to address gaps in the care cascade <sup>8</sup>	India	Systematic Review	To describe the current evidence on the quality of TB treatment in high-burden countries.	Int. J. Infect. Dis.	A3
Tuberculosis care strategies and their economic consequences for patients: the missing link to end tuberculosis <sup>9</sup>	Ethiopia	Cross-sectional study	To determine the economic consequences of the DOT strategy for TB patients.	Infect. Dis. Poverty.	A1
Using Patient Pathway Analysis to Design Patient-centered Referral Networks for Diagnosis and Treatment of Tuberculosis: The Case of the Philippines <sup>10</sup>	Philippines	Methodological according to Patient Pathway Analysis (PPA)	To provide evidence on the possible gaps in the provision of services that may be contributing to the persistent prevalence of tuberculosis.	J. Infect. Dis.	A1
Team approach to manage difficult-to-treat TB cases: Experiences in Europe and beyond <sup>11</sup>	Portugal, Belarus, Belgium, France, Mexico and United Kingdom	Multicenter Comparative Analysis	To describe the different experiences with the TB Consilium, both at the international level and in some of the countries where this experience is successful.	Pulmonology	A1
Model of care and risk factors for poor outcomes in patients on multi-drug resistant tuberculosis treatment at two facilities in eSwatini (formerly Swaziland), 2011–2013 <sup>12</sup>	Swaziland	Retrospective and observational cohort study	To report the treatment outcomes of a cohort of MDR-TB patients enrolled between 2011 and 2013.	PLoSOne	A1
Home is where the patient is”: a qualitative analysis of a patient-centred model of care for multi-drug resistant tuberculosis <sup>13</sup>	Uganda	Qualitative and exploratory	To determine the acceptability and accessibility of home treatment for MDR-TB.	BMC Health Serv. Res.	A2
Cost-effectiveness of a comprehensive programme for drug-resistant tuberculosis in China <sup>14</sup>	China	Cohort study	To investigate the cost-benefit ratio of a comprehensive drug-resistant TB program launched in four sites in China in 2011.	Bull. World Health Organ.	A1
“My Favourite Day Is Sunday”: Community Perceptions of (Drug-Resistant) Tuberculosis and Ambulatory Tuberculosis Care in KaraSuu District, Osh Province, Kyrgyzstan <sup>16</sup>	Kyrgyzstan	Qualitative Validation through triangulation	To understand the perception of TB and DR-TB, in order to improve the efficacy and acceptance of the Doctors Without Borders (DWB) intervention.	PLoSOne	A1
WHO strategies for the management of drug-resistant tuberculosis <sup>17</sup>	Mexico	Qualitative Descriptive Exploratory	To explain how to apply the WHO priority actions to control multidrug-resistant tuberculosis (MDR-TB).	Arch. Bronconeumol.	B1
‘Whole person’ approach used in complex TB case <sup>18</sup>	New Zealand	Case study	To explore the importance of a multidisciplinary team (MDT) when dealing with a patient with drug-resistant tuberculosis.	Kai Tiaki Nursing New Zealand	B4

Key: Ref. – Reference.

FIGURE 2: Descriptive chart of the articles included in the literature review study, Manaus-AM, Brazil, 2020.

Regarding the publication area, one was in Nursing, one in Health Services, two in Epidemiology, two in Science and Medicine and four in Infectology. Of the studies conducted, 80% addressed care strategies for the control of TB and of DR-TB, and 20% evidenced failures in the assistance provided to the individuals affected by the disease and monitored by the health services.

The studies showed that there are several care strategies that can be effectively used for the prevention and control of DR-TB. However, the failures occurring in care have resulted in an increase in the number of DR-TB cases over time<sup>8-10</sup>.

Access to the proper DR-TB diagnosis and treatment in the health services is the core strategy to provide adequate assistance to the patients. Absence or delay in diagnosis by the rapid molecular test for tuberculosis - Xpert MTB/RIF - results in inappropriate therapeutic courses of action, which aggravate the patient's condition. This test is essential to detect not only the presence of *Mycobacterium tuberculosis* genetic material, but also the main gene associated with resistance to rifampicin<sup>8</sup>.

The studies highlighted that the consequences of TB diagnosis without access to the aforementioned test are inadequate initial treatment and monitoring, favoring the transmission of resistant strains. The delay in improving the clinical condition leads to the patient abandoning the treatment, with the consequent need to initiate a new one, longer and with more toxic medications<sup>8,10</sup>.

After establishing proper diagnosis and treatment in a timely manner, Directly Observed Treatment (DOT) becomes an essential and widely used strategy nowadays for the prevention and control of DR-TB, as it avoids the use of incorrect medications and treatment interruption. However, a study suggests the application of a new DOT strategy, based on the patients' reality in their community and applied by the Primary Health Care (PHC) team, using an adequate model for the provision of complex care<sup>8</sup>.

In the Philippines, the strategy used was the implementation of a National Nurse Development Program, with training for DOT application in the community. The result was greater capacity for local clinical care and treatment with the most complex line of therapeutic regimen, including second-line injectable drugs delivered by PHC nurses. This strategy allowed the patients not to undergo long treatments in specialized centers far from their families and communities<sup>10</sup>.

A multicenter study carried out in Belarus, Belgium, France, Mexico, Portugal and the United Kingdom, pointed to the use of the "Global TB Consilium", a global technological strategy of free electronic clinical consulting offered by the Global TB Network (GTN), for all the services and programs that work with complex TB cases, such as DR-TB and XDR-TB. The service provides the physicians with detailed and coordinated expert opinions on these complex cases, and the qualified experts respond within 48 hours of case submission<sup>11</sup>.

To improve the clinical outcomes for DR-TB at the local level, the TB Consilium technology strategy assists the several countries in the training and counseling of the professionals who treat these patients in their communities. In addition to that, they promote unified monitoring of the case, reducing the risk of diagnosis errors and of inadequate patient monitoring<sup>11</sup>. This procedure shows that technology is fundamental for the adequate and uniform management of the DR-TB cases in different world contexts.

The diagnosis, treatment and monitoring carried out by trained professionals, using technology in the local context, increases the cure rate, reducing low adherence to the DR-TB treatment, which is often attributed to the centralized care model in some specialized centers. Thus, the patients need to leave the area or community where they live in search of these centers, which are mostly located far from their homes. This difficulty leads many of them to abandon the treatment due to lack of financial conditions to pay for the commute and to support their families<sup>10</sup>.

Thus, the need for decentralized care at the local level and patient- and community-centered for the control of DR-TB is evident. A study carried out in Ethiopia recommends this strategy for the treatment of DR-TB. It also shows that many patients abandon the treatment, even developing Extensively Drug-Resistant Tuberculosis (XDR-TB), for having to undergo a complex treatment, far from their family and community context, and lacking the necessary social and economic conditions<sup>9</sup>. As a consequence of the difficulties experienced by the patients after DR-TB diagnosis, only half of them undergo DOT and successfully complete the treatment<sup>8-9</sup>.

Another aspect of greater complexity, such as the management of patients with DR-TB in a population with high rates of human immunodeficiency virus (HIV) co-infection, requires more effective and more tolerated treatment regimens. The comprehensive patient-centered care model provided by the home health teams, including psychosocial support, is indicated. This model has contributed with effective results in the treatment of these individuals<sup>12</sup>.

Assistance centered on the DR-TB patients was also assessed in a rural community in Uganda, with an emphasis on their home context. In this study, the patients from the rural community and the multiprofessional team chose home patient-centered care as the preferred location for both, when compared to hospital care, due to three main reasons: the home is seen as more conducive to patient recovery, allows for greater psychosocial support, and enables more free time for patients and caregivers to carry out other activities, reducing psychological stress<sup>13</sup>.

The studies evidence that all the countries, even those with limited resources, must apply the care strategy of comprehensive assistance to the patients. This implies providing broad coverage of the health services with financial and nutritional incentives, in order to avoid subsequent expenditures as a consequence of treatment abandonment. The fact that the patients are distanced from their work activities due to the disease makes them face serious financial and psychological problems<sup>9,10,12</sup>.

In a comprehensive research study carried out in China through a program with 73 patients, based on a detailed review of the medical records after they have completed six months of treatment, the effectiveness of the program was highlighted for including rapid screening, standardized care and financial protection, effectively improving the individual DR-TB results<sup>14</sup>.

Another study conducted in eSwatini (formerly Swaziland) with DR-TB patients showed that the care administered by a community-based clinic for the individuals affected by this disease in their homes was effective in several settings, with high cure rates. This strategy is feasible and safe, allowing broader factors influencing health to be addressed, including psychosocial support. In addition to that, community assistance models are from three to four times more economical than the hospital approaches<sup>12</sup>.

A study carried out in Brazil corroborates the others, highlighting that accessibility to the health service must be valued, for the performance of effective diagnoses and treatments. The greater the number of basic health units and PHC professionals trained to apply the TB control strategies, the more effective the search and detection of cases will be and the earlier treatment and supervision will be initiated, favoring cure and the interruption of the transmission chain<sup>15</sup>.

The active search and notification of new TB cases is an essential strategy that must be promoted by PHC. The individuals with respiratory symptoms, together with their family members, must be motivated to undergo the test and, if the disease is confirmed, undergo treatment as quickly as possible, with an effective therapeutic regimen and with the shortest possible treatment time. Awareness-raising strategies adapted to each vulnerable group must always be used<sup>16</sup>.

Health promotion is also highlighted in the studies as an important care strategy that must be worked on throughout patient care. A study emphasizes that, even in its resistant form, TB is curable if correctly diagnosed and treated. Comprehensive monitoring and guidelines are indispensable, which explain the disease and its entire course from treatment to cure, provided by the multiprofessional team, as part of the elaboration of the care plan<sup>13</sup>.

Some studies emphasized the strategies to control DR-TB recommended by the WHO, with four of them standing out: DR-TB prevention, administering high-quality treatments to patients with sensitive TB; expansion of the rapid tests for DR-TB detection; provision of intermediate access to effective treatment and adequate care; and prevention of transmission, using infection control in the health institutions<sup>8,10,12,17</sup>.

Another especially important care strategy is the approach with the multidisciplinary care team for DR-TB patients, for adequate assistance: holding regular meetings; favoring the review of patient care; allowing for a comprehensive and patient-centered approach, with clear team communication; contributing to the planning of adequate care and assistance; and strengthening the bond between the professional and the user<sup>18</sup>.

The studies revealed care failures, such as: late access to diagnosis and treatment, centralization of DR-TB diagnosis and treatment in specialized centers, inadequate use of the therapy schemes, absence of strategies to combat the social vulnerabilities, and lack of permanent education for the health teams and of education in health for the patients, the family members and the community<sup>8-10</sup>.

For the failures identified, the strategies used to overcome them were as follows: diagnosis and treatment shared between the reference institutions for DR-TB and PHC; active and permanent search of individuals with respiratory symptoms, with access to the rapid molecular test for tuberculosis in PHC; community-based DOT; permanent education of the multiprofessional team for clinical care and drug administration; use of information technologies such as the TB *Consilium* for the management of cases in an adequate and uniform manner; and education in health for the users, the family members and the community, as well as financial, nutritional and psychological support for the patients affected by the disease<sup>8-14,16-18</sup>.



It is noteworthy that, in addition to the pharmacological treatment, the quality of the care routinely offered to DR-TB patients in different countries of the world, especially in those with a high burden of tuberculosis both in the public and private sectors, should be valued, with strategies that convert patients into allies in all the stages for the elaboration of their care plan, ensuring universal, equal and continuous care and treatment for disease control<sup>12</sup>.

### Study limitations

The scarcity of studies on the theme in the data sources selected stands out as a limitation of this study, since further studies may be available in other information sources not consulted in this research. In addition, no educational technology was identified for the individuals affected by the disease, even knowing its importance for the empowerment and monitoring of users in the health care network. It is recommended that further research studies be carried out with expansion of searches in the databases, allowing access to a wider range of knowledge that can strengthen the use of fundamental strategies for the prevention and control of DR-TB.

### CONCLUSION

Through this literature review, it was possible to identify several strategies for the control of DR-TB, with emphasis on diagnosis decentralization and conduction of shared treatments, enabling broader and comprehensive care for the patients. These strategies must be applied in all the health services, aiming at eliminating assistance failures that contribute to spreading the disease.

The patients must be at the center of the care plan, as leading actors and co-responsible for their treatment and for the well-being of their families and communities, their sociocultural peculiarities and potentials having to be respected.

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