

Monitoring delays in diagnosis of pulmonary tuberculosis in eight cities in Colombia

David A. Rodríguez,¹ Kristien Verdonck,² Karen Bissell,³ Juan José Victoria,⁴ Mohammed Khogali,⁵ Diana Marín,⁶ and Ernesto Moreno⁷

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ABSTRACT

Objective. To measure time between onset of tuberculosis (TB) symptoms and start of treatment, and to identify factors associated with delay in eight Colombian cities.

Methods. Operational research with a retrospective analytical cohort design was conducted in 2014 using routinely collected data about new smear-positive pulmonary TB patients from eight cities in Colombia (Barranquilla, Bogotá, Bucaramanga, Cali, Cúcuta, Medellín, Pereira, and Villavicencio). Date of symptom onset was sourced from TB surveillance databases. Data on all other variables came from National TB Program (NTP) registers.

Results. There were 2 545 new cases of smear-positive pulmonary TB, but a plausible date of symptom onset was available for only 1 456 (57%). Median number of days between symptom onset and treatment start was 51 days (interquartile range: 27–101). A total of 72% of patients had a delay (> 30 days between symptom onset and treatment start), and 28% had a 3+ bacillary load at diagnosis. Based on multiple logistic regression, three factors were significantly associated with delay: being uninsured (odds ratio (OR): 1.30; 95% confidence interval (CI): 1.01–1.68) and having an unknown HIV status (OR: 1.81; CI: 1.04–3.17), which increased risk, and coming from a neighborhood with NTP-employed community health workers, which decreased risk (OR: 0.56; CI: 0.34–0.90).

Conclusions. Delays still prevent timely TB diagnosis and treatment in Colombia. As the country aims for TB elimination, delays must be reduced, especially in cities and vulnerable neighborhoods, to stop community transmission. The NTP should focus not only on the number of cases detected but also on how long it takes to detect them. To monitor interventions designed to reduce delays, additional dates in the process should be recorded routinely. In addition, reliability and completeness of data are crucial for monitoring.

Key words

Tuberculosis; tuberculosis, pulmonary; monitoring; epidemiological monitoring; community health workers; urban population; delayed diagnosis; operations research; Colombia.

- ¹ International Organization for Migration, Bogotá, Colombia. Send correspondence to: David Alejandro Rodríguez, davidalejorod@yahoo.es
- Institute of Tropical Medicine, Antwerp, Belgium.
 International Union Against Tuberculosis and Lung Disease, Paris, France.
- Fondo Financiero de Proyectos de Desarrollo, Bogotá, Colombia.
- Operational Research Unit, Operational Centre-Brussels, MSF-Luxembourg, Médecins Sans Frontières, Luxembourg City, Luxembourg.
- ⁶ Grupo de Investigación Demografía y Salud, Facultad Nacional de Salud Pública, Universidad de Antioquia, Medellín, Colombia.
- Ministerio de Salud y Protección Social, Bogotá, Colombia.

Reducing delays in the detection and treatment initiation for active forms of tuberculosis (TB) is crucial for achieving the two fundamental targets of TB control: 95% reduction in TB deaths (versus the statistics for 2015) and 90%

reduction in the 2035 TB incidence rate (fewer than 10 cases per 100 000 population) (1). Delays between symptom onset and diagnosis have been shown to contribute to the spread of the disease to domestic contacts (2). Prolonged delays in treatment initiation are likely to lead to more advanced disease, high mortality, and ongoing transmission in the community (3). Delays generally reflect a combination of patient delays in seeking health care and health care provider delays in making prompt and accurate diagnosis and in initiating treatment (4). Determinants of delays include sociodemographic and economic factors; stigma; time required to reach the health facility; poor quality of health care services (communication skills, organizational structure, attitudes, and knowledge of the TB control strategy among health care workers); seeking care from nonspecialized individuals; and visiting more than one health care provider before diagnosis (5, 6). The World Health Organization (WHO) post-2015 End TB Strategy reiterates the urgent need for National TB Programs (NTPs) to reduce such delays. It is therefore essential to identify when and where delays occur and to understand the reasons for them (7). However, if NTPs are to assess their progress in reducing such delays, they require the ability to monitor the length of time between the onset of symptoms and diagnosis, as well as the time taken from diagnosis to treatment initiation. In addition, the reasons for delays must be identified, and programmatic strategies that have been implemented specifically to address these issues must be evaluated (8-11). Many NTPs in Latin America are not currently monitoring delays on a routine basis.

The decrease in Colombia's annual incidence rate has been minimal over the last three years (from 34 per 100 000 in 2011 to 32 per 100 000 in 2013 (12)), prompting policy-makers and program staff to renew efforts to measure the effectiveness of newly introduced interventions (7). Large increases in TB notifications have been observed across many settings (13). However, so far, it has not been possible to determine how the various interventions being implemented by the NTP and its partners may have contributed to these increases.

So far, four published studies have investigated delays in Colombia. One reported a delay of 120 days between onset of symptoms and diagnosis of pulmonary TB (14); the others reported on factors associated with delay (6, 15, 16). All were conducted in only one Colombian city and the sample sizes were small.

To contribute to the evidence, this study aimed to measure time between onset of TB symptoms and start of treatment, and to identify factors associated with delay in eight Colombian cities.

MATERIALS AND METHODS

Study design

This study consisted of operational research with a retrospective analytical cohort design conducted in 2014 using routinely collected data about new smear-positive pulmonary TB patients.

Study setting

Colombia is an upper-middle-income country with almost 48 million inhabitants. In 1993, the Colombian government launched health sector reform with the aim of improving equity of access to health care through the General System of Social Security in Health (Sistema General de Seguridad Social en Salud, SGSSS). The system is based on managed competition and comprises two insurance schemes: a contributory scheme for formal sector employees and those able to pay, and a subsidized scheme for the low-income population. Those who do not qualify for either scheme remain uninsured (17).

The Directly Observed Treatment, Short-course (DOTS) strategy was officially introduced in 2000. In 2006, the Ministry of Health launched its strategic plan "Colombia libre de tuberculosis" ("TB-free Colombia"), which adapted WHO's Stop TB strategy to the Colombian health system.

TB case detection in Colombia is passive. Patients with a cough for two weeks or longer are regarded as presumptive TB patients and have to submit three sputum specimens for smear microscopy. If the patient is diagnosed with smear-positive pulmonary TB, he or she is immediately registered for treatment. All new patients with pulmonary TB receive a standardized anti-TB treatment regimen of six months duration (18). Details of investigations and demographic and clinical observations are recorded in TB treatment cards and registers.

Independently from the NTP, information about TB patients is also collected by Colombia's National Public Health Surveillance System (Sistema de Vigilancia en Salud Pública, SIVIGILA). SIVIGLIA draws its information from the notification of particular health events of interest, including confirmed TB. Maintenance of the system is the responsibility of the Ministry of Health, the National Institute of Health (Instituto Nacional de Salud, INS), regional and municipal authorities, and insurance companies, among others.

Study sites

The study was conducted in eight cities of Colombia: Barranquilla, Bogotá, Bucaramanga, Cali, Cúcuta, Medellín, Pereira, and Villavicencio. According to official country statistics, the total number of inhabitants in these cities in 2014 was 15 887 713. The eight cities were selected for the following reasons: 1) 60% of the TB cases in Colombia come from these cities; 2) all of them have a reasonably good recording and reporting system, which is not the situation in other parts of Colombia; and 3) the Global Fund To Fight AIDS, Tuberculosis and Malaria ("Global Fund") (Geneva) has recently provided support to strengthen TB control activities in these cities, which has led to an improvement in the collection of routine data.

Study population

All individuals newly registered with smear-positive pulmonary TB from January through December 2014 in the eight cities were eligible for the study. Sample size was not calculated because a complete sample of the patient population in all eight cities, which were purposefully selected, was used.

Variables and data collection

The following demographic and clinical data were collected for all included patients: age; sex; HIV status; city; neighborhood with or without community health workers (CHWs) employed by the NTP ("NTP-CHWs"); type of health insurance (subsidized, contributory, or none); place of TB consultation (first, second, or third health care level); and smear positivity (1+, 2+, or 3+). The calculation of time periods was based

on three key dates: onset of respiratory symptoms, request of first sputum smear examination, and start of treatment. The date of first sputum request was used as a proxy for the date of TB diagnosis, which was not available. All variables were sourced from the individual TB patient register kept at the NTP, except for the date of onset of symptoms, which is not recorded by the NTP so was obtained from the TB surveillance database maintained at the local health directorate. To ensure sufficient quality of the TB patient register and the TB surveillance register, the two databases are linked using patients' national identity numbers. Patient lists are then cross-checked and duplicate entries removed. Other variables in the databases are not routinely cross-checked.

Analysis and statistics

Data were extracted from the TB patient register and the TB surveillance databases and imported into Epi Info™ version 7.1.2.0 (Centers for Disease Control and Prevention (CDC), Atlanta, Georgia, United States). Numbers and proportions of patients and their characteristics were described. Mean and standard deviation (SD) were used to summarize numerical variables with a normal distribution; median and interquartile range (IQR) were used for variables with an nonnormal distribution.

If the date of onset of symptoms was missing or implausible (i.e., onset of symptoms occurred after the first sputum smear request), time periods were not calculated. For cases that did include a plausible date, time from onset of TB symptoms to request for a first sputum smear examination and time from request for first sputum smear to start of treatment were calculated, along with the median and IQR of the number of days for each time period. The Kruskal–Wallis test was used to compare both time periods across different groups of patients.

The proportion of patients with delay (defined as > 30 days between onset of symptoms and start of treatment) was also calculated. The 30-day cutoff period was based on global benchmarks and has been used previously (19). Bivariate and multiple logistic regression were used to explore the association between demographic,

clinical, and health system factors and the presence of delay. Differences at the 5% level (P < 0.05) were regarded as significant. Stata 10.0^{TM} (StataCorp, College Station, Texas, United States) was used for the statistical analysis.

Ethics

Ethics approval was received from both the Ethics Committee of the Universidad de Antioquia (Medellín) and the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease (Paris). Because this was a retrospective study based on routine program information, informed consent was not needed. The confidentiality of the study subjects was protected and individual data not shared.

RESULTS

There were 2545 new cases of smear- positive pulmonary TB. Table 1 shows the demographic, clinical, and health system characteristics of the patients. The mean age was 43 years (± 19 SD) and 64% were men. The largest group was from Medellín (28%), followed by Cali (19%). A total of 145 cases came from prioritized neighborhoods where NTP-employed CHWs are active. A total of 40% were covered by the contributory health insurance scheme, 49% by the subsidized scheme, and a minority (10%) had no insurance. In 47% of the patients, sputum smear tests were not done at the first level of the health system. The sputum smear test gave 3+ results in 28% of the study population. HIV status was known for 2 292 patients; 10% of them were HIV-positive.

The date of onset of symptoms was missing for 339 patients (13%) and implausible (i.e., it was after the sputum smear was requested) for an additional 750 (29%) patients. For the remaining 1 456 patients (57%), time periods were calculated. For all 1 456 patients, the median duration of time between onset of respiratory symptoms and request of first sputum smear was 36 days (IQR: 18-89); after that, it took a median of 6 days (IQR: 3–12) to start TB treatment. The median total time for all 1 456 patients between onset of symptoms and start of treatment was 51 days (IQR: 27-101). Table 2 shows these time

TABLE 1. Demographic and clinical characteristics of 2 545 smear-positive pulmonary tuberculosis patients from eight cities, Colombia, 2014

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Negative 2 051 (80)	Negative	2 051	(80)
Confirmed positive 229 (9)		229	
One ELISA ^b positive 12 (0)		12	٠,
Patient did not accept testing 3 (0)	Patient did not accept testing	3	(0)
Missing 250 (10)	Missing	250	(10)

Source: prepared by the authors based on the study results.

periods stratified by demographic, clinical, and health system characteristics.

There were significant differences in time periods when patients from different cities were compared: total times were shorter in Villavicencio and Cúcuta and longer in Bucaramanga and Medellín. The time between onset of symptoms and first sputum smear request was significantly shorter for patients coming from neighborhoods with NTP- employed CHWs compared to the rest of the study population. In addition, patients with a 3+ smear test result had a longer

^a NTP-CHW: community health care worker (CHW) supported by the National Tuberculosis Program (NTP).

^b Enzyme-linked immunosorbent assay.

TABLE 2.Time from onset of respiratory symptoms to sputum smear request and start of treatment in 1 456 new smear-positive pulmonary tuberculosis patients, Colombia, 2014

		Days from onset of symptoms to smear request	Days from smear request to treatment start	Total days from onset of symptoms to treatment start	
Characteristic	n	Median (IQRa)	Median (IQR)	Median (IQR)	
Total number (%)	1 456	36 (18–89)	6 (3–12)	51 (27–101)	
Sex		,	, ,	,	
Men	538	39 (20-91)	6 (2–13)	51 (31-101)	
Women	918	35 (17–89)	6 (2–13)	51 (27–103)	
Age group (years)					
< 5	7	13 (7–109)	3 (3–37)	30 (13-116)	
5–14	15	45 (30–76)	7 (4–15)	68 (38–102)	
15–24	274	34 (20–76)	5 (3–12)	51 (29–102)	
25-49	581	38 (21–89)	5 (2–13)	59 (30–108)	
50-64	339	39 (17–96)	7 (4–15)	43 (19–121)	
≥ 65	239	33 (13–98)	5 (2–11)	43 (19–121)	
City		` ,	,	,	
Barranguilla	190	32 (16-69)	9 (5-17) ^b	45 (30-83) ^b	
Bogotá	229	36 (16–113)	3 (1–8)	42 (21–121)	
Bucaramanga	96	41 (14–100)	9 (34–17)	60 (24–112)	
Cali	306	44 (21–96)	6 (2–12)	57 (31–110)	
Cúcuta	116	35 (13–75)	3 (2–8)	39 (21–80)	
Medellín	368	36 (22–95)	7 (4–16)	61 (32–105)	
Pereira	52	37 (16–78)	5 (2–13)	42 (28–92)	
Villavicencio	99	31 (15–60)	3 (1–5)	37 (19–64)	
Neighborhood with NTP-CHW ^c		` '	` '	,	
Yes	79	28 (14-61) ^d	5 (3–11)	36 (23-62) ^d	
No	1377	37 (18–92)	6 (3–12)	52 (29–104)	
Type of health insurance		` ,	,	,	
Contributory	593	38 (16-91)	5 (2-11)	51 (26-103)	
Subsidized	742	35 (17–85)	4 (2–10)	45 (25–94)	
No insurance	121	36 (16–99)	5 (2–13)	60 (27–122)	
Health system level		, ,	` ,	,	
First	679	35 (17-81)	6 (2-13)	47 (29–96)	
Second	246	46 (20–99)	6 (3–12)	53 (28–111)	
Third	531	37 (17–91)	6 (2–14)	53 (27–105)	
Bacillary load		` '	,	,	
1+	626	32 (15-74)d	6 (3–14)	45 (24-92)d	
2+	405	39 (20–92)	5 (3–12)	54 (30–102)	
3+	425	45 (19–102)	6(3–12)	59 (29–115)	
HIV test	-	- (/	- (- /	(/	
Negative	1 185	38 (17-90) ^d	6 (3–12)	52 (27-102)	
Positive	121	31 (17–60)	7 (3–17)	49 (25–90)	
Not known ^e	150	35 (19–93)	6 (3–14)	51 (31–114)	

Source: prepared by the authors based on the study results.

time and HIV-positive patients had a shorter time between onset of symptoms and first sputum smear request (Table 2).

For 72% of the study population, the total time between onset of symptoms and start of treatment was > 30 days, which was defined as "delay." Table 3 shows the proportion of patients with a delay, by various demographic, clinical, and health system characteristics. In multiple logistic regression, three factors were significantly associated with delay: being uninsured (odds ratio (OR): 1.30; 95% confidence interval (CI): 1.01–1.68) and having an unknown HIV status (OR:

1.81; CI: 1.04–3.17), which were risk factors, and coming from a neighborhood with NTP-employed CHWs, which was protective (OR: 0.56; CI: 0.34–0.90).

DISCUSSION

This was the first study in Colombia to combine routine data from the NTP and the national surveillance system to study time from symptom onset to treatment in patients with pulmonary TB. Despite efforts by the NTP to ensure that patients are diagnosed early and started promptly on treatment, the median time between symptom onset and treatment

start was 51 days, 72% of patients had more than one month of delay, and 28% of the cases had a bacillary load of 3+ at the time of diagnosis. This is of great concern because it indicates that even if the TB case detection rate is high, community transmission is most likely ongoing (9).

In Colombia, the issue of delayed diagnosis has been reported before. A study in Bucaramanga in 2002–2003 found a median time of 120 days between onset of symptoms and diagnosis of TB (14), and a study in Cali in 2005–2006 found a median time of 66 days (16). In Medellín, in 2007, almost half of the study subjects

^a IQR: interquartile range.

^b P < 0.01; Kruskal–Wallis test.

[°]NTP-CHW: community health care worker (CHW) supported by the National Tuberculosis Program (NTP).

 $^{^{}d}$ 0.01< P < 0.05; Kruskal–Wallis test.

 $^{^{\}rm e}\,\mbox{Not}$ done, patient did not accept, or information not available.

TABLE 3. Time delays between onset of respiratory symptoms and start of antituberculosis treatment in relation to socio-demographic, clinical, and health system factors among patients with smear-positive pulmonary tuberculosis (n = 1456), Colombia, 2014

	(≤ 30	delay) days) = 411	Delay (> 30 days) n = 1 045			
Characteristic	No.	(%)	No.	(%)	Crude ORa (CIb)c	Adjusted OR (CI) ^d
Total number (%)	411	(28)	1 045	(72)		
Sex						
Men	277	(67)	641	(61)		
Women	134	(33)	404	(39)	1.30 (1.02-1.66) ^e	1.28 (1.00-1.65)
Age group (years)						
< 15	5	(1)	17	(2)	1	1
15–49	232	(S 7)	623	(59)	0.79 (0.29-2.17)	0.83 (0.30-2.34)
≥ 50	174	(42)	405	(39)	0.69 (0.25-1.90)	0.75 (0.27–2.11)
City		, ,		,	,	,
Barranguilla	52	(13)	138	(13)	1	1
Bogotá	72	(18)	157	(15)	0.82 (0.54-1.26)	0.87 (0.55-1.35)
Bucaramanga	27	(7)	69	(7)	0.96 (0.56-1.66)	0.98 (0.55-1.73)
Cali	75	(18)	231	(22)	1.16 (0.77–1.75)	1.18 (0.76–1.82)
Cúcuta	41	(10)	75	`(7)	0.69 (0.42–1.13)	0.68 (0.41–1.15)
Medellín	88	(21)	280	(27)	1.20 (0.80–1.79)	1.24 (0.81–1.91)
Pereira	16	(4)	36	(3)	0.85 (0.43–1.66)	1.03 (0.51–2.06)
Villavicencio	40	(10)	59	(6)	0.56 (0.33-0.93) ^e	0.60 (0.35–1.04)
Neighborhood with NTP-CHW ^f		(,		(0)	0.00 (0.00 0.00)	0.00 (0.00 1.01)
No	378	(92)	999	(96)	1	1
Yes	33	(8)	46	(4)	0.53 (0.33-0.84) ^e	0.56 (0.34-0.90) ^g
Type of health insurance		(-)		(- /	(**************************************	(
Contributory	179	(44)	414	(40)	1	1
Subsidized	195	(47)	547	(52)	0.98 (0.64–1.50)	1.09 (0.69–1.72)
No insurance	37	(9)	84	(8)	1.21 (0.95–1.54)	1.30 (1.01–1.68) ^g
Health system level	٠.	(0)	٠.	(0)	(0.00)	(
First	190	(46)	489	(47)	1	1
Second	65	(16)	181	(17)	1.08 (0.78–1.50)	1.05 (0.75–1.47)
Third	156	(38)	375	(36)	0.93 (0.73–1.20)	0.90 (0.70–1.16)
Bacillary load	100	(00)	0.0	(00)	0.00 (0.70 1.20)	0.00 (0.70 1.10)
1+	196	(48)	430	(42)	1	1
2+	105	(25)	300	(28)	1.30 (0.99–1.72)	1.32 (0.99–1.77)
3+	110	(27)	315	(30)	1.31 (0.99–1.72)	1.33 (0.99–1.78)
HIV test	110	(21)	010	(00)	1.01 (0.00 1.72)	1.00 (0.00 1.70)
Negative	335	(82)	850	(31)	1	1
Positive	42	(10)	79	(8)	1.35 (0.91–2.00)	1.29 (0.86–1.95)
Not known ^h	34	(8)	116	(11)	1.81 (1.06–3.10)	1.81 (1.04–3.17) ⁹

Source: prepared by the authors based on the study results.

had a delayed diagnosis, which was defined as more than 44 days between symptom onset and TB diagnosis (15). Similar observations have been made in other Latin American countries (20, 21).

This study also revealed interesting information about programmatic issues. The Colombian NTP has begun employing CHWs to improve detection of presumptive TB and treatment adherence, a strategy that has been implemented and evaluated in diverse settings (22, 23). The NTP-employed CHWs are supervised by

nurses or managers from TB treatment health care facilities who oversee guardian-supervised, home-based DOTS in the community. The CHWs and health care managers that supervise them work exclusively for the NTP. This strategy has been implemented in a few selected neighborhoods where socioeconomic conditions are precarious and the risk of TB is high. As shown in the results reported here, patients from the selected neighborhoods start treatment earlier than the rest of the study population. Although this finding

alone is not sufficient to determine the effectiveness of the NTP-CHW strategy, it does seem to indicate that the strategy is making a difference in the time to testing/treatment, and thus warrants further analysis (24).

Another interesting finding was that the majority of cases are being diagnosed at the second and third health care level. This raises important questions about whether medical staff working at the primary care level are sufficiently aware of the symptoms of TB and the procedure to follow for organizing a sputum smear test. It may also reflect the lack of coverage of sputum microscopy at the primary health care level (25).

Strengths and limitations

The study had a number of strengths. The study population is large, as the eight cities included in the study notify more than half of the country's TB cases. These cities have a relatively good recording system and receive additional technical support for data management through the Global Fund. In addition, the linkage made between the NTP data and the national surveillance system data was reliable, because it was based on patients' national identity numbers. However, the date of onset of symptoms was missing or implausible for about 42% of the patients. As a consequence, these patients could not be included in the evaluation of delay, which may have affected the internal validity of the study. The findings about the factors associated with delay should therefore be interpreted with caution. In addition, the routinely collected program data do not allow a detailed analysis of the reasons for delay, and no information was available about patients who were not notified. Nevertheless, this study shows the potential for using the length of delay as an important indicator of the effectiveness of specific interventions that are intended to reduce the delay between symptom onset, request for sputum smear, and start of TB treatment (9).

Conclusions

For patients in whom the date of symptom onset was known, the median time between symptom onset and start of treatment was 51 days. Three factors were identified as being significantly and independently associated with delay: being uninsured and having an

a OR: odds ratio.

^b CI: 95% confidence interval.

^c The crude ORs were calculated using bivariate logistic regression and indicate the strength of the association between each of the socio-demographic, clinical, and health system factors and the presence of diagnostic delay.

^d The adjusted ORs were calculated using one multiple logistic regression model that included all socio-demographic and health system factors.

e P < 0.05; X2 test.

^f NTP-CHW: community health worker (CHW) supported by the National Tuberculosis Program (NTP).

⁹ P < 0.05: Wald test.

^h Not done, patient did not accept, or information not available.

unknown HIV status, which increased the chance of delay, and coming from a neighborhood with NTP-employed CHWs, which decreased the chance of delay.

The findings of this study have three important implications for policy and practice: 1) there is an urgent need for the NTP to implement measures to reduce the long delays in getting patients diagnosed and started on treatment; 2) TB program monitoring should include variables that adequately measure delay and allow program managers to explore the reasons for delay; and 3) reliability and completeness of program data are crucial for monitoring. Therefore, the authors propose that NTP monitoring focus not only on counting how many cases are being detected but also on how long it takes to detect these cases. If the date of symptoms onset is considered an important variable that allows for measurement of delays, the most efficient means of improving the collection of that information must be determined.

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REFERENCES

- 1. World Health Organization. Global tuberculosis report 2014. Geneva: WHO; 2014. Available from: http://apps.who.int/ iris/bitstream/10665/137094/1/ 9789241564809_eng.pdf?ua=1 Accessed on 16 August 2015.
- 2. World Health Organization and Stop TB Partnership. The Stop TB strategy: building on and enhancing DOTS to meet the TB-related Millennium Development Goals. Geneva: WHO; 2006. Available from: http://whqlibdoc.who.int/hq/2006/WHO_HTM_STB_2006.368_eng.pdf?ua=1 Accessed on 16 August 2015.
- 3. Begun M, Newall AT, Marks GB, Wood JG. Contact tracing of tuberculosis: a systematic review of transmission modelling studies. PLoS One. 2013;8(9): e72470.
- Storla DG, Yimer S, Bjune GA. A systematic review of delay in the diagnosis and treatment of tuberculosis. BMC Public Health. 2008;8:15.
- 5. Li Y, Ehiri J, Tang S, Li D, Bian Y, Lin H, et al. Factors associated with patient, and diagnostic delays in Chinese TB patients: a systematic review and meta-analysis. BMC Med. 2013;11:156.
- Jaramillo E. Pulmonary tuberculosis and health-seeking behaviour: how to get a delayed diagnosis in Cali, Colombia. Trop Med Int Health. 1998;3(2):138–44.
- 7. Uplekar M, Weil D, Lonnroth K, Jaramillo E, Lienhardt C, Dias HM, et al. WHO's new end TB strategy. Lancet. 2015; 385(9979):1799–801.

- 8. Storla DG, Yimer S, Bjune GA. Can treatment delay be utilized as a key variable for monitoring the pool of infectious tuberculosis in a population? J Infect Dev Ctries. 2010;4(2):83–90.
- 9. Yimer SA, Holm-Hansen C, Storla DG, Bjune GA. Tuberculosis management time: an alternative parameter for measuring the tuberculosis infectious pool. Trop Med Int Health. 2014;19(3):313–20.
- 10. Uys PW, Warren RM, van Helden PD. A threshold value for the time delay to TB diagnosis. PLoS One. 2007;2(8):e757.
- 11. Blok L, Creswell J, Stevens R, Brouwer M, Ramis O, Weil O, et al. A pragmatic approach to measuring, monitoring and evaluating interventions for improved tuberculosis case detection. Int Health. 2014;6(3):181–8.
- World Health Organization. Annex 4: Key indicators for the world, WHO regions and individual countries. In: WHO. Global tuberculosis report 2013. Geneva: WHO; 2013. Available from: http://apps.who. int/iris/bitstream/10665/91355/1/ 9789241564656_eng.pdf Accessed on 7 October 2014.
- 13. Kranzer K, Afnan-Holmes H, Tomlin K, Golub JE, Shapiro AE, Schaap A, et al. The benefits to communities and individuals of screening for active tuberculosis disease: a systematic review. Int J Tuberc Lung Dis. 2013;17(4):432–46.
- Cáceres-Manrique Fde M, Orozco-Vargas LC. Demora en el diagnóstico de tuberculosis pulmonar en una región de Colombia. Rev Salud Publica (Bogota). 2008;10(1):94–104.

- 15. Gaviria MB, Henao HM, Martínez T, Bernal E. Papel del personal de salud en el diagnóstico tardío de la tuberculosis pulmonar en adultos de Medellín, Colombia. Rev Panam Salud Publica. 2010;27(2):83–92.
- 16. Rojas CM, Villegas SL, Piñeros HM, Chamorro EM, Durán CE, Hernández EL, et al. Características clínicas, epidemiológicas y microbiológicas de una cohorte de pacientes con tuberculosis pulmonar en Cali, Colombia, Colombia. Biomedica. 2010; 30(4):482–91.
- 17. Arbeláez MP, Gaviria MB, Franco A, Restrepo R, Hincapié D, Blas E. Tuberculosis control and managed competition in Colombia. Int J Health Plann Manage. 2004; 19 Suppl 1:S25–43.
- 18. World Health Organization. Treatment of tuberculosis: guidelines 4th ed. Geneva: WHO; 2010. Available from: http://apps. who.int/iris/bitstream/10665/44165/1/9789241547833_eng.pdf?ua=1&ua=1 Accessed on 17 August 2015.
- 19. Pirkis JE, Speed BR, Yung AP, Dunt DR, MacIntyre CR, Plant AJ. Time to initiation of anti-tuberculosis treatment. Tuber Lung Dis. 1996;77(5):401–6.
- 20. Lambert ML, Delgado R, Michaux G, Volz A, Speybroeck N, Van Der Stuyft P. Delays to treatment and out-of-pocket medical expenditure for tuberculosis patients, in an urban area of South America. Ann Trop Med Parasitol. 2005;99(8):781–7.
- 21. Macq J, Solis A, Ibarra M, Martiny P, Dujardin B. The cost of medical care and

- people's health-seeking behaviour before being suspected of tuberculosis in three local health systems, Nicaragua. Int J Tuberc Lung Dis. 2004;8(11):1330–6.
- 22. Perry HB, Zulliger R, Rogers MM. Community health workers in low-, middle-, and high-income countries: an overview of their history, recent evolution, and current effectiveness. Annu Rev Public Health. 2014;35:399–421.
- 23. Prado TN, Wada N, Guidoni LM, Golub JE, Dietze R, Maciel EL. Cost-effectiveness
- of community health worker versus homebased guardians for directly observed treatment of tuberculosis in Vitória, Espírito Santo State, Brazil. Cad Saude Publica. 2011;27(5):944–52.
- 24. Odendaal WA, Lewin S. The provision of TB and HIV/AIDS treatment support by lay health workers in South Africa: a time-and-motion study. Hum Resour Health. 2014;12:18.
- 25. Arbeláez MP. La reforma del sector salud y el control de la tuberculosis en Colombia.

In: Yadón ZE, Gürtler RE, Tobar F, Medici AC, editors. Descentralización y gestión del control de las enfermedades transmisibles en América Latina. Buenos Aires: Pan American Health Organization; 2006.

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RESUMEN

Supervisión del retraso en el diagnóstico de la tuberculosis pulmonar en ocho ciudades de Colombia *Objetivo.* Medir el lapso entre la aparición de los síntomas de tuberculosis y el comienzo del tratamiento y reconocer los factores que se asocian con este retraso en ocho ciudades de Colombia.

Métodos. Investigación operativa con un estudio de cohortes analítico retrospectivo realizado en el 2014, a partir de los datos corrientes consignados en los casos nuevos de tuberculosis pulmonar con baciloscopia positiva en ocho ciudades de Colombia (Barranquilla, Bogotá, Bucaramanga, Cali, Cúcuta, Medellín, Pereira y Villavicencio). La fecha de aparición de los síntomas se obtuvo de las bases de datos de vigilancia de la tuberculosis. Los datos sobre todas las demás variables provinieron de los registros de Programa Nacional contra la Tuberculosis.

Resultados. Se registraron 2 545 casos nuevos de tuberculosis pulmonar con baciloscopia positiva, pero solo se contó con una fecha verosímil de aparición de los síntomas en 1 456 casos (57%). La mediana del número de días entre la aparición de los síntomas y el comienzo del tratamiento fue 51 días (intervalo intercuartil: de 27 a 101). En 72% de los pacientes se comprobó un retraso (más de 30 días entre la aparición de los síntomas y el comienzo del tratamiento) y en 28% de los casos se observó una carga bacilar de 3+ en el momento del diagnóstico. Según el análisis de regresión logística multivariante, tres factores se asociaron de manera significativa con el retraso, a saber: la falta de seguro de enfermedad (razón de posibilidades [OR]: 1,30; intervalo de confianza [IC] de 95%: de 1,01 a 1,68) y el desconocimiento de la situación frente al virus de la inmunodeficiencia humana (OR: 1,81; IC de 95%: de 1,04 a 3,17), factores que aumentaron el riesgo de retraso y el hecho de provenir de un vecindario donde operan agentes sanitarios de la comunidad empleados por el Programa Nacional contra la Tuberculosis, que disminuyó el riesgo (OR: 0,56; IC: de 0,34 a 0,90).

Conclusiones. Los retrasos todavía obstaculizan el diagnóstico y el tratamiento oportuno de la tuberculosis en Colombia. Al buscar la eliminación de la tuberculosis en el país es preciso disminuir los retrasos, sobre todo en las ciudades y los vecindarios vulnerables, con el objeto de interrumpir la transmisión en la comunidad. El Programa Nacional contra la Tuberculosis debe prestar atención no solo al número de casos detectados, sino también al tiempo que precisa su detección. Con el propósito de llevar a cabo un seguimiento de las intervenciones encaminadas a disminuir los retrasos, es necesario registrar de manera sistemática otras fechas de la evolución clínica. Además, la fiabilidad y la integridad de los datos registrados constituyen aspectos primordiales del seguimiento.

Palabras clave

Tuberculosis; tuberculosis pulmonar; monitoreo; monitoreo epidemiológico; agentes comunitarios de salud; población urbana; diagnóstico tardío; investigación operativa; Colombia.