

Homelessness and HIV: A Combination Predictive of Poor Tuberculosis Treatment Outcomes and in Need of Innovative Strategies to Improve Treatment Completion

Lina María Gómez,¹ Lizeth Andrea Paniagua-Saldarriaga,² Quinlan Richert,³ Yoav Keynan,^{4,5,6} Fernando Montes,⁷ Lucelly López,⁸ and Zulma Vanessa Rueda^{8*}

¹Secretaría de Salud de Envigado, Envigado, Colombia; ²Secretaría Seccional de Salud y Protección Social de Antioquia, Medellín, Colombia; ³Department of Internal Medicine, Max Rady College of Medicine, University of Manitoba, Winnipeg, Canada; ⁴Department of Medical Microbiology and Infectious Disease, University of Manitoba, Winnipeg, Canada; ⁵Department of Internal Medicine, University of Manitoba, Winnipeg, Canada; ⁶Department of Community Health Science, University of Manitoba, Winnipeg, Canada; ⁷Secretaría de Salud de Medellín, Medellín, Colombia; ⁸Facultad de Medicina, Universidad Pontificia Bolivariana, Medellín, Colombia

Abstract. Antioquia Department is the state with the highest burden of tuberculosis (TB) in Colombia. Our aim was to determine the risk factors associated with unsuccessful TB treatment in HIV-seropositive and homeless persons, compared with non-HIV-infected and non-homeless persons with TB. We conducted a retrospective cohort study using observational, routinely collected health data from all drug-susceptible TB cases in homeless and/or HIV-seropositive individuals in Antioquia from 2014 to 2016. Unsuccessful TB treatment was defined as individuals having been lost to follow-up, having died, or treatment failure occurrence during the study period. Successful treatment was defined as cure of TB or treatment completion according to the WHO definitions. We identified 544 homeless persons with TB (432 HIV– and 112 HIV+), 835 HIV+ persons with TB and non-homeless, and 5,086 HIV–/non-homeless people with TB. Unsuccessful treatment rates were 19.3% in HIV–/non-homeless persons, 37.4% in non-homeless HIV+ patients, 61.5% in homeless HIV– patients, and 70.3% in homeless HIV+ patients; all rates fall below End TB strategy targets. More than 50% of homeless patients were lost to follow-up. Risk factors associated with unsuccessful treatment were HIV seropositivity, homelessness, male gender, age ≥ 25 years, noncontributory-type health insurance, TB diagnosis made during hospitalization, and previous treatment for TB. These results highlight the challenge of treating TB in the homeless population. These findings should put an onus on TB programs, governments, clinicians, and others involved in the collaborative care of TB patients to pursue innovative strategies to improve treatment success in this population.

INTRODUCTION

The WHO's End Tuberculosis (TB) Strategy (ETS) calls for a 90% reduction in TB-related deaths, a 90% absolute reduction in TB incidence, and zero families facing catastrophic TB treatment-related costs, by 2035.¹ To ensure progress toward these goals, individualized national targets and monitoring are indicated. A treatment success rate of at least 85% and testing of 100% of TB-diagnosed patients for drug resistance and HIV coinfection are proposed by the WHO ETS as "targets that could apply in all countries."¹

Effective implementation of ETS requires an approach to monitor active TB cases, as well as treatment follow-up and case finding, according to each nation's unique epidemiological characteristics vis-à-vis TB incidence, prevalence, and risk factors. As per the WHO, "a detailed assessment of the national epidemiological and health system situation" is a prerequisite for the success of the strategy and should include an appraisal of the groups most afflicted by and susceptible to TB infection, along lines of age, gender, comorbidities, nutritional status, and tobacco and drug use.¹ In particular, collaborative HIV/TB identification and comanagement is a key action under ETS's first pillar—integrated, patient-centered care and prevention. Furthermore, ETS emphasizes the need for priority attention in groups at risk for poor treatment uptake and loss to follow-up.

In the case of Colombia, in 2016, there were 73,465 Colombians infected with HIV, and the department of Antioquia had the second highest prevalence for any department,

with an estimated 12,639 cases.² In 2017, an estimated 14,187 cases of TB were reported, of which 1,977 had HIV coinfection. In Antioquia, there were 2,603 TB cases (2,280 new cases and 323 previously treated cases).³ One of the problems identified during the development of Colombia's TB reporting program, especially in Antioquia, was the significant number of unsuccessful treatment outcomes, which has, to date, fallen short of the ETS proposed goals. The rate of TB treatment completion was 73%.

Homeless populations have a TB prevalence ratio that ranges between 34 and 452-fold higher compared with the same-country general population,⁴ and are frequently associated with multiple additional risk factors that lead to unsuccessful TB treatment and thus augmenting the risk of incomplete therapy. For example, a cross-sectional study, which followed rates of TB acquisition among homeless persons in the United States from 1994 to 2003, showed that fewer homeless than non-homeless TB patients completed treatment (77% versus 84%, respectively).⁵ In that same study, homeless TB patients also had a higher prevalence of injection drug use (IDU), and HIV coinfection, compared with non-homeless individuals. In another American study, homelessness was linked to 6% of TB cases and homeless individuals had a 10-fold increased risk of TB infection.⁶ In addition, the odds of being lost to follow-up have been significantly higher in HIV-positive individuals, migrants, intravenous drug users, alcohol abusers, and homeless people.⁷

Despite the fact that the link between homelessness and loss to follow-up is well established, there are limited data regarding what additional risk factors exist within the homeless population that put individuals at risk for failure to complete treatment. The aim of this study, therefore, was to determine the risk factors associated with unsuccessful TB

*Address correspondence to Zulma Vanessa Rueda, Escuela de Ciencias de la Salud, Universidad Pontificia Bolivariana, Calle 78B # 72A-109, Medellín, Colombia. E-mail: zulmaruedav@gmail.com

treatment in Antioquia's HIV-seropositive and homeless population, compared with homeless persons without HIV, and compared with non-HIV-infected and non-homeless people with TB.

MATERIALS AND METHODS

Study design. Retrospective cohort study using observational routinely collected health data.

Setting. Antioquia is a department of Colombia, in which there are currently 6,534,764 inhabitants.⁸ The health-care insurance in Colombia has two main types: a "subsidized" health-care plan (for those who cannot afford other forms of health-care coverage) and a "contributive" health-care plan (paid for by employees and employers). Ninety-two percent of the inhabitants of Antioquia have either subsidized or contributive health coverage.⁸

On diagnosis of TB, cases are reported to the National Public Health Surveillance System for Notification of Public Health Interest Events (SIVIGILA) by the involved health-care institution. The patient is transferred to her/his health-care provider, and once directly observed treatment short-course (DOTS) is initiated, the individual is registered in the TB Information System (SiTB). Tuberculosis diagnosis and treatment in Colombia is free for all patients. The diagnosis is made using sputum smears, cultures, and molecular diagnostic testing methods according to the availability of resources.

According to the last census of Antioquia's homeless population in 2013, there were 3,250 homeless persons registered in the department. Antioquia's homeless population system (HPS) is responsible for responding to the health needs of homeless individuals within the department. The HPS has dedicated centers where homeless individuals' basic health needs are addressed. Specifically for TB, there are dedicated physicians, nurses, psychologists, and social workers assigned within the program, in addition to four mobile teams that deploy around the city to identify homeless individuals with respiratory symptoms concerning for TB, and they communicate with homeless individuals about HPS's services, including TB care. The mobile teams are trained and empowered to order sputum smear microscopy.

In addition, Antioquia's network for TB has two TB-care-dedicated centers (day 1 center and 24-hour center) and one homeless shelter called Hermanos Desvalidos. The shelter oversees centralized TB treatment strategy and follow-up, and has a special unit for TB patients with a capacity for 60 hospitalized persons, including separate units for drug-susceptible and resistant TB treatment. In addition, homeless people concerned about TB infection have the option of presenting to one of 10 appropriately equipped public health institutions throughout Medellín. For emergencies, homeless persons can present to the emergency room from any health-care institution (private or public) in Antioquia. In all of the aforementioned hospitals, if a homeless person has any symptoms that suggest TB, the institution carries out all of the indicated investigations, and payment is made by the municipality of Medellín or the department of Antioquia.

Once TB is diagnosed, the patient enters into the DOTS program and undergoes medical evaluation, including basic blood tests and chest X-rays, followed by TB treatment and

epidemiological follow-up. Patients are encouraged (but not required) to complete their treatment regimen while staying in the homeless shelter to support adherence. Health-care access, including the aforementioned TB program, is free of charge for homeless individuals.

Inclusion criteria. All HIV-seropositive and/or homeless persons with drug-susceptible TB who had treatment initiated in Antioquia between January 2014 and December 2016 were eligible for inclusion in the study. All HIV and non-homeless persons with a confirmed TB diagnosis were included in the comparison group.

Exclusion criteria. For the bivariate and multivariate analyses, people reported as "not evaluated" for the TB treatment outcome, according to the WHO definitions and reporting framework for TB, 2013,⁹ were excluded from the study. Cases of drug-resistant TB (34 multidrug-resistant TB) were excluded from this study, as treatment of drug-resistant TB requires longer treatment duration, as well as different facilities and follow-up.

Data collection. The anonymized database was provided by the Secretaria Seccional de Salud y Protección Social de Antioquia. The SiTB database was created in Excel by the Department of Antioquia and includes all patients who are admitted to the TB program. Tuberculosis Information System data contain sociodemographic, epidemiological, and clinical variables collected at baseline and during routine follow-up until discharge from the program.

Definitions. The program used the WHO definitions⁹ for cured, treatment-completed, treatment-failed, died, not evaluated, relapse, treatment after failure, treatment after lost to follow-up, and other previously treated patients. Colombia considers loss to follow-up as a TB patient who did not start treatment or whose treatment was interrupted for one consecutive month or more.

Variables. We analyzed the following data—sociodemographic information: gender, age, health insurance, self-reported ethnicity and area of residence (urban center, rural, and scattered/remote rural), and membership in selected vulnerable subpopulations (prisoners, immigrants, displaced population, former illegal armed groups, and homeless). Homeless individuals were further analyzed according to whether they belonged to additional vulnerable groups; that is, homeless because of displacement from community of origin. Data on mental health status of the patients were not available in our database. Clinical information: diagnosis of TB made during hospitalization (yes or no), type of TB (pulmonary or extrapulmonary), extrapulmonary TB location, sputum smear (was performed, and if so, negative or 1 to 3+), culture result (negative or positive), comorbidities (HIV, diabetes, and chronic obstructive pulmonary disease), and patient registration group (new, relapse, previously treated patients after lost to follow-up, after failure, other previously treated patients, and transferred out). Other previously treated patients are those who have previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented. Treatment outcome was reported as cured, treatment completed, treatment failed, died, or lost to follow-up.

Analysis. The database in Excel[®] (Microsoft Corp., Redmond, WA) was exported to SPSS[®] version 21.1.1 (IBM Corp., Chicago, IL) and STATA[®] version 13.0 (StataCorp LLC, College Station, TX). We performed a descriptive analysis of the data.

TABLE 1
Sociodemographic data according to homeless and non-homeless (HIV+ or HIV-) groups

	Homeless people with HIV, N = 112		Homeless people without HIV, N = 432		HIV-infected individuals, N = 835		Non-HIV/non-homeless group, N = 5,086	
	n	%	n	%	n	%	n	%
Gender								
Male	98	87.5	329	76.2	691	82.8	2,937	57.7
Age (years)								
≤ 24	12	10.7	45	10.4	95	11.4	1,066	21.1
25–44	72	64.3	193	44.7	474	56.8	1,651	32.7
≥ 45	28	25.0	194	44.9	266	31.9	2,328	46.1
Drug users	21	18.8	70	16.2	5	0.6	108	2.1
Health insurance								
Contributory	4	3.6	10	2.3	374	44.8	2,581	50.7
Subsidized	75	67.0	252	58.3	416	49.8	2,296	45.1
None	33	29.5	170	39.4	45	5.4	209	4.1
Population group								
Prisoners	0	0.0	0	0.0	7	0.8	82	1.6
Immigrants	0	0.0	0	0.0	2	0.2	3	0.1
Displaced persons	0	0.0	0	0.0	3	0.4	36	0.7
Former members of illegal armed groups	0	0.0	0	0.0	1	0.1	1	0.1
Disabled	0	0.0	0	0.0	1	0.1	21	0.4
Health-care workers	0	0.0	0	0.0	1	0.1	81	1.9
Occurrence area								
Urban center	102	98.1	380	97.2	673	93.2	3,869	90.4
Rural municipality	2	1.9	9	2.3	27	3.7	214	5.0
Scattered/remote rural	0	0.0	2	0.5	22	3.0	198	4.6

The main outcome used in this study was unsuccessful treatment, defined as loss to follow-up, death, or failure. Successful treatment included cure or treatment completion. Bivariate and multivariate analyses were used to estimate the relative risks and their 95% CIs of the association between the unsuccessful treatment and sociodemographic and clinical characteristics. For the multivariate analysis, we did a binomial regression model. As there were 583 people with a “not evaluated” outcome, 274 with unknown HIV status, and additional missing data on different variables, there were 4,910 patients included in the multivariate model.

Ethical considerations. There is written approval from the Health State Authority of Antioquia to use the SIVIGILA and SiTB databases for the years 2014–2016. In addition, the protocol was approved by the Ethics Committee of Universidad Pontificia Bolivariana and the Pan American Health Organization.

RESULTS

The total number of patients diagnosed with TB in the Department of Antioquia during the time period of the study was 6,739, of whom 544 were homeless persons (112 had HIV+ serological status and 432 had HIV- serological status); 835 patients were HIV+ and were non-homeless; and 5,086 people were HIV-/non-homeless. There were 274 people with unknown HIV status (HIV testing not completed in 191 and without data in 83).

Sociodemographic features. The population was overwhelmingly young, male, and from urban areas of Antioquia (Table 1).

Clinical-demographic features. There was a low rate of self-reported drug use. When drug use was reported, however, it was highest in the HIV+ and HIV- homeless groups.

Among homeless people with HIV, 48.2% had incomplete prior therapy because of being lost to follow-up after a

previous TB episode and 30.3% were lost to follow-up among homeless individuals without HIV (Table 2).

In the HIV+ non-homeless group, 38.9% (325/835) had preexisting HIV+ status and 61.1% (510/835) were newly diagnosed. Among the HIV+ homeless population group, 49.1% (55/112) were previously aware of their HIV+ status and 50.9% (57/112) were newly diagnosed.

In terms of treatment outcomes, the highest success rate was in the non-HIV and non-homeless group at 80.7%, followed by the HIV+ non-homeless group at 62.6%, the HIV- homeless group at 38.5%, and 29.7% in the HIV+ homeless group (Table 2).

Risk factors. A previous diagnosis of TB was shown to be associated with decreased successful treatment across all HIV/homeless groups, with HIV+ homeless patients having the lowest rates of treatment success (Figure 1).

The site where the current TB diagnosis was made was a risk factor for unsuccessful treatment. As illustrated in Figure 2, in all groups, TB diagnosed during hospitalization had lower rates of successful treatment, as compared with when the diagnosis was made in an outpatient setting.

In the multivariate analysis, the risk factors associated with unsuccessful TB treatment were male gender, homelessness, HIV seropositivity, age ≥ 25 years, having subsidized or no health insurance, previous treatment for TB, and primary diagnosis of TB made during inpatient hospitalization (Table 3).

DISCUSSION

This study demonstrates that successful treatment targets recommended by the WHO ETS¹ are not presently met in Antioquia in any of the HIV/homeless categories. The rates of successful treatment are worst in the HIV+ homeless population, followed by the HIV- homeless population and then the HIV+ non-homeless group. This effect is influenced in part by other risk factors identified in this study: male gender,

TABLE 2
Clinical and treatment outcome data according to homeless and non-homeless (HIV+ or HIV-) groups

Characteristics	Homeless people with HIV, N = 112		Homeless people without HIV, N = 432		HIV-infected/non-homeless individuals N = 835		Non-HIV/non-homeless group, N = 5,086	
	n	%	n	%	n	%	n	%
Time from onset and TB notification, median (quartile 1–quartile 3), n	24 (4.5–111) n = 76		31.5 (6–93) n = 298		43 (15–92) n = 507		49 (21–102) n = 3,118	
Type of TB								
Pulmonary TB	102	91.1	429	99.3	586	70.2	4,194	82.5
Extrapulmonary TB	10	8.9	3	0.7	249	29.8	892	17.5
Sputum smear was recorded in database	102	91.1	418	96.8	521	62.4	3,829	75.3
Sputum smear results								
Negative	32	31.4	73	17.4	195	37.4	731	19.1
1+	58	56.9	285	67.9	269	51.6	2,503	65.4
2+	6	5.9	25	6.0	22	4.2	265	6.9
3+	6	5.9	37	8.8	35	6.7	330	8.6
Positive TB culture result was recorded in database	16	14.3	106	24.5	170	20.4	1,047	20.6
Classification of TB patients ⁹								
New TB patients	41	36.6	264	61.1	676	81	4,558	89.6
Relapse	11	9.8	27	6.3	43	5.1	182	3.6
Previously treated patients after lost to follow-up	54	48.2	131	30.3	91	10.9	236	4.6
Previously treated patients after failure	0	0	2	0.5	0	0	9	0.2
Other previously treated patients*	4	3.6	5	1.2	10	1.2	59	1.2
Transferred out	2	1.8	3	0.7	15	1.8	42	0.8
Treatment outcome								
Cured	13	11.6	91	21.1	108	12.9	1,740	34.2
Complete	17	15.2	65	15.0	348	41.7	2,031	39.9
Lost to follow-up	63	56.3	229	53.0	146	17.5	533	10.5
Treatment failed	0	0.0	4	0.9	10	1.2	30	0.6
Death	8	7.1	16	3.7	117	14.0	341	6.7
Not evaluated	11	9.8	27	6.3	106	12.7	411	8.1

TB = tuberculosis.

* Other previously treated patients are those who have previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented.

age ≥ 25 years, having subsidized or no health insurance, previous treatment for TB, and TB diagnosis made during hospitalization. We also found that HIV is newly diagnosed at the time of TB diagnosis in > 50% of homeless individuals and in more than 60% of non-homeless individuals.

Our study reveals an alarmingly high percentage of unsuccessful treatment in homeless people with or without HIV

mainly as a result of being lost to follow-up at any time after the commencement of treatment. These findings are consistent with what is demonstrated in the literature regarding the connection between unsuccessful TB treatment, homeless populations, and HIV.^{7,10} Explanations for this finding are lack of awareness regarding TB within homeless populations, lack of a high index of suspicion in health-care personnel at the

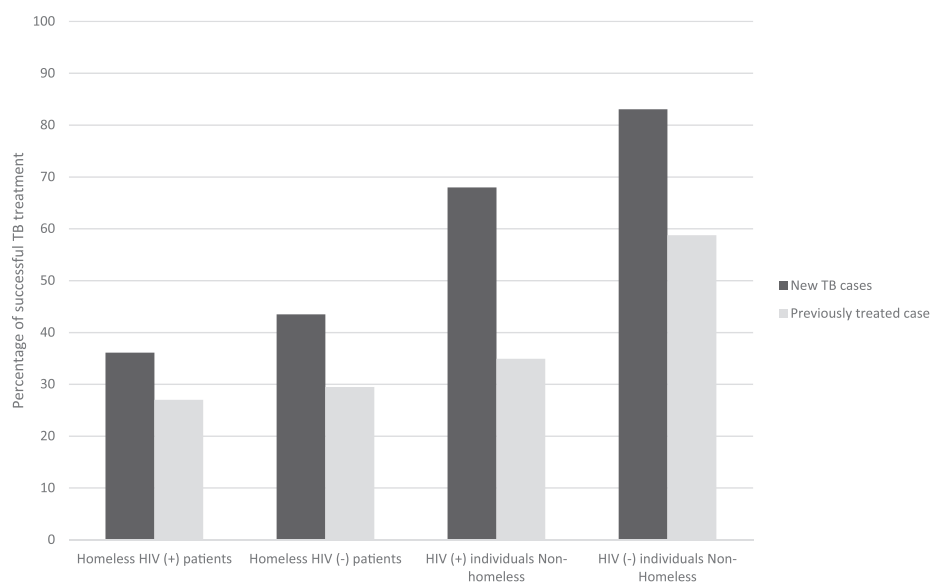


FIGURE 1. Success of antituberculosis (TB) treatment in homeless and non-homeless patients (HIV+ and HIV-) according to new or previously treated TB case.

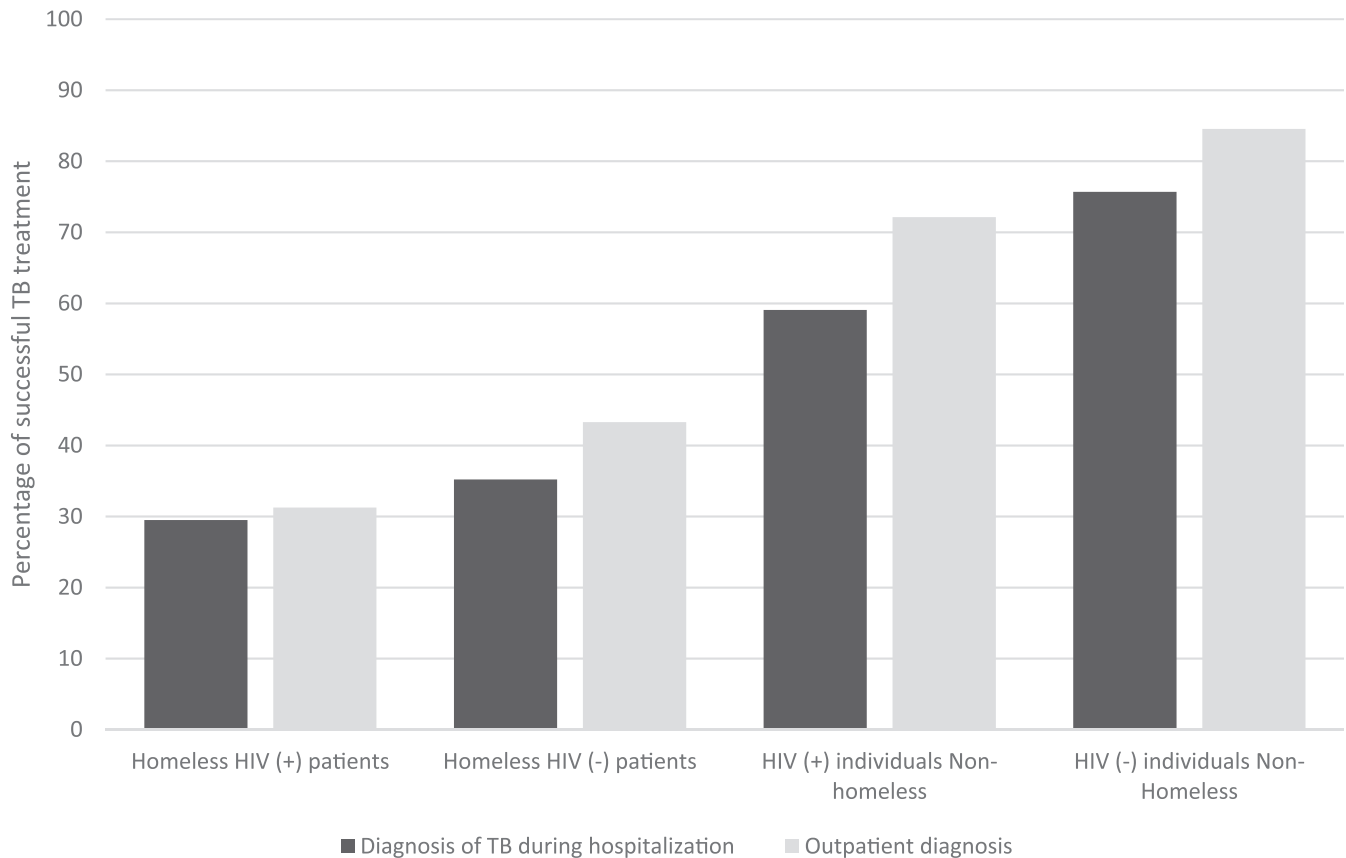


FIGURE 2. Success of antituberculosis (TB) treatment in homeless and non-homeless patients (HIV+ and HIV-) according to whether diagnosis of TB was made in inpatient or outpatient setting.

primary care level,¹¹ discrimination toward the homeless, TB, and/or HIV-related stigmatization by the community and/or health-care personnel,^{11,12} alcohol^{13,14} or drug addiction,¹⁵ mental health diagnosis,¹⁶ complex social interactions, and

comorbidities that impede health-care seeking and adherence.^{5,17-21}

In addition to the high percentage of unsuccessful treatments, a history of previously treated TB translated to lower

TABLE 3
Factors associated with the non-successful treatment of TB in homeless and non-homeless (HIV+ or HIV-) patients

Characteristic	Unsuccessful treatment/TB patients,* n (%)	Relative risk (95% CI)	Adjusted relative risk (95% CI)
Female gender	452/2,302 (19.6)	1	1
Male gender	1,181/3,854 (30.6)	1.56 (1.42-1.72)	1.26 (1.14-1.40)
Non-HIV and Non-homeless group	904/4,675 (19.3)	1	1
HIV+ and non-homeless	273/729 (37.4)	1.94 (1.73-2.16)	1.54 (1.37-1.76)
HIV- and homeless	249/405 (61.5)	3.17 (2.89-3.50)	1.67 (1.48-2.06)
HIV+ and homeless	71/101 (70.3)	3.64 (3.16-4.18)	1.65 (1.39-2.38)
Age (years)			
≤ 24	237/1,175 (20.2)	1	1
25-44	672/2,279 (29.5)	1.46 (1.28-1.67)	1.19 (1.03-1.38)
≥ 45	718/2,686 (26.7)	1.33 (1.16-1.51)	1.19 (1.04-1.37)
Health insurance			
Contributive	354/2,765 (12.8)	1	1
Subsidized	1,049/2,926 (35.9)	2.80 (2.51-3.12)	2.36 (2.07-2.67)
None	230/465 (49.5)	3.86 (3.38-4.42)	2.56 (2.16-3.04)
Nondrug users	1,534/5,935 (25.8)	1	
Drug users	99/221 (44.8)	1.73 (1.49-2.02)	0.90 (0.72-1.14)
Primary diagnosis of TB			
Outpatient	496/2,466 (20.1)	1	1
During patient's hospitalization	872/2,643 (33.0)	1.64 (1.49-1.80)	1.43 (1.30-1.57)
New TB case	1,161/5,260 (22.1)	1	1
Previously treated patient	454/838 (54.2)	2.45 (2.27-2.66)	1.65 (1.49-1.82)
TB type			
Extrapulmonary TB	210/1,076 (19.5)	1	1
Pulmonary TB	1,423/5,080 (28.0)	1.44 (1.26-1.63)	1.22 (1.06-1.41)

TB = tuberculosis.

* The denominator is different to the previous tables because of "Not evaluated" outcome, unknown HIV status, and/or missing data.

rates of success across all groups, in particular in the homeless population, where we found that one half of HIV+ homeless people and one-third of HIV- homeless people were previously incompletely treated patients. Higher rates of failure among patients previously treated for TB have been illustrated by others.²²⁻²⁵ A cohort study on homeless patients with TB in Poland found that a significant number of homeless TB patients had been treated for TB in the past compared with non-homeless patients.²¹ In that study, homeless patients also had lower rates of treatment success, although the study did not differentiate patients according to HIV status.²¹ Being lost to follow-up (currently or in a previous treatment) raises concerns for the emergence of drug-resistant TB,²⁶ and consequently higher mortality in the homeless population than in the general population.²⁷

On the other hand, the relationship in our cohort between insurance plan and treatment success is of interest, as having any type of insurance besides contributive was a risk factor for unsuccessful treatment. Depending solely on a subsidized insurance plan is likely associated with lower socioeconomic status and barriers to health-care access because this type of plan is only available to those unable to buy into a contributive-type insurance plan. This finding is consistent with a Japanese study that found unemployment and lack of insurance to be risk factors for TB death.²⁸

Another risk factor for unsuccessful treatment was having TB diagnosed in hospital (versus in the outpatient setting). We think the main explanations for this finding might be attributed to more complicated TB cases presenting in-hospital, the frequent association with incomplete prior TB therapy, low awareness of the disease among patients, and the lack of a high index of suspicion in primary care clinical personnel; therefore, a high percentage of TB diagnoses is attained in high-complexity hospitals. However, the diagnosis made in hospital could also be explained because of 1) the free access to diagnostics and care in hospitals that are contracted by health authorities, in a population that frequently has no access to primary care otherwise; and 2) because a significant proportion of homeless individuals have had a prior diagnosis of TB with incomplete therapy because of being lost to follow-up, the index of suspicion may be higher, contributing to the early diagnosis among the homeless. These facts could be an explanation for the finding of the shortest time between first onset of symptoms and TB notification in homeless HIV+ people.

To increase treatment success in HIV-infected individuals and homeless people, a combination of well-established and innovative approaches is needed. Although the ETS does not explicitly provide recommendations for the treatment of homeless TB patients in particular, careful adherence to these guidelines on the part of health-care providers will lead to improved rates of treatment success in these patients. For example, the ETS recommends a 6-month treatment regimen over an 8-month or longer treatment regimen for HIV-infected population,¹ which is likely to be deemed more favorable for most patients in our cohort. The ETS also recommends a variety of patient care and support options for TB patients, including health education and counseling, tracers or digital medication monitoring, material and psychological support to patients, and directly observed treatment or video-observed therapy options.¹ Again, we are optimistic that these interventions would be helpful in improving

treatment success rates in our homeless and HIV+ patient group, but the caveat must be given that the ETS only recommends these interventions on a conditional basis, given the very low to moderate quality of available evidence, especially in these specific populations.

It should also be noted that certain ETS recommendations will in all likelihood prove to be barriers to treatment adherence in our homeless patients—for example, the recommendation of daily treatment over thrice weekly treatment¹ may be harder to adhere to for patients who are homeless.

In a 2017 systematic review, de Vries et al.¹¹ outlined recommendations to improve TB program adherence in hard-to-reach populations, including homeless populations. Their recommendations are germane to our study population and are as follows: 1). The introduction of awareness-raising programs that address local perceptions to enhance early case finding and reduce delay in health-care seeking; 2). to organize interactive community sensitization programs that target stigmatizing attitudes and actions; 3). support and social networks, multidisciplinary teams that integrate existing social services, substances abuse programs with TB care, and trained care providers who are sensitive to gender and culture; and 4). continuous training of health-care providers on TB and computer-based decision support.

Given the vulnerable status of the involved populations, and in addition to previous recommendations, innovative and open-minded harm reduction strategies will be required on the part of care providers, governments, and TB programs to improve adherence and, hence, the chances of TB treatment completion. A 2013 systematic review of integrated HIV/TB and IDU care highlighted the successes of administering integrated HIV/TB care within needle and syringe exchange programs and opioid substitution programs, despite the overall barrier of staffing inefficiencies in these areas.²⁹ The same review emphasized the improved uptake of screening and prevention with the use of incentivized care at integrated treatment centers.²⁹ In addition, incentive-based strategies and culturally sensitive care will further improve uptake.

Multipronged approaches that address the barriers to the completion of therapy, based on social context, are likely to be rewarded with higher success rates. The provision of financial incentives has been explored with moderate and variable success on active TB treatment completion.³⁰ One study illustrated superior results for latent tuberculosis infection (LTBI) prophylaxis completion when cash incentives were compared with noncash incentives given to marginally housed individuals.³¹ In a study from Moldova, success among recipients of several different types of incentives (small and bigger cash amounts, food and hygiene product vouchers, travel reimbursement, and other support such as clothes and wood) was higher (95% versus 58%) than that among the group that received no incentives.³² Similarly, a study from rural Nigeria documented a significant increase in treatment completion with monetary incentive.³³ Such strategies could be applied to ongoing TB treatment in a similar fashion.

This study had several limitations. First, many potential confounders were not measured because of the retrospective study design, such as tobacco use, nutritional status, differentiation between IDU versus non-IDU, CD4⁺ T-cell count, viral load, mental health disease, and utilization of homeless shelters. These variables could be examined in follow-up studies where the data are available. Data on drug use appear

to be unreliable in this study, especially considering that a previous article reported 77.2% of drug dependence in this population,¹⁶ and a census in 2009 of homeless people in Medellín and other municipalities found that 74.4% (2,516/3,381) of homeless individuals were users of illegal drugs,³⁴ and drug use has been identified by others as a risk factor for defaulting on treatment.⁷ Furthermore, there are missing data in the used databases on TB culture results.

In conclusion, we have found unacceptably low treatment success rates among homeless and/or HIV-infected individuals. Having subsidized or no health insurance, a previous diagnosis of TB, and having TB diagnosed in hospital were additional risk factors for unsuccessful TB treatment. The data presented here should be used to formulate a plan for preemptively identifying those at risk for unsuccessful TB treatment, to improve treatment success rates within these marginalized and underserved groups. The results highlight the challenges among homeless populations and point to gaps in provision of care outside of the hospital. Failure to specifically address this population may jeopardize attempts to attain WHO targets for the general population. To achieve improved treatment completion, there is a need for a humanized and integrated approach with enhanced and innovative strategies for homeless individuals, with enhanced linkage to care and incentives for treatment completion.

Received April 9, 2018. Accepted for publication January 4, 2019.

Published online March 11, 2019.

Acknowledgments: This research was carried out through the Structured Operational Research and Training Initiative (SORT IT), a global alliance led by the Special Programme for Research and Training in Tropical Diseases (TDR), UNICEF/UNDP/World Bank/WHO. The program SORT IT Colombia, where this research was conducted, was developed and executed jointly by the following committee: the Communicable Diseases Research Program of the Department of Communicable Diseases and Health Analysis (CHA) at the Pan American Health Organization (PAHO), the Universidad Pontificia Bolivariana, Medellín (Colombia), and the International Organization for Migration (Colombia); the initial work plan was prepared and approved by the National Technical Committee of TB in Colombia consisting of the Ministerio de Salud y Protección Social (MSPS), Instituto Nacional de Salud de Colombia (INS), Pan American Health Organization (PAHO Colombia), International Organization for Migration (IOM), the Liga Antituberculosa Colombiana y de Enfermedades Respiratorias (LAC), Financial Fund of Development projects (FONADE), and TB Group of the Country Coordinating Mechanism for Colombia (MCP). The staff who supported the training and analysis were professors of the Universidad Pontificia Bolivariana, Medellín, the Universidad de Antioquia, and the Universidad del Cauca from Colombia, Ministry of Health of Brazil, Instituto Nacional de Enfermedades Respiratorias (INER) of Argentina. We thank our funders: The SORT IT program was funded by The Global Fund to Fight AIDS, TB, and Malaria through the TB project that TB Group of the Country Coordinating Mechanism for Colombia (MCP) presented in the 10th round to The Global Fund. Specifically, this activity was approved as a strategy of sustainability and closure of the project in territories that were prioritized because of their having the highest burden of TB in Colombia.

Disclaimer: The content of this article does not reflect the official opinion of the Gobernación de Antioquia, or Secretaría Seccional de Salud y Protección social de Antioquia, or Secretaría de Salud de Envigado. Responsibility for the information and views expressed in this article lies entirely with the authors. The funders did not play any role in the design of the study, the compilation and analysis of the data, the decision to publish, or the writing of the article.

Authors' addresses: Lina María Gómez, Secretaría de Salud de Envigado, Envigado, Colombia, E-mail: lini2992@hotmail.com. Lizeth

Andrea Paniagua-Saldarriaga, Secretaria Seccional de Salud y Protección Social de Antioquia, Medellín, Colombia, E-mail: lpaniagua8@yahoo.es. Quinlan Richert, Department of Medical Microbiology and Infectious Disease, Max Rady college of medicine, University of Manitoba, Winnipeg, Canada, E-mail: umricheq@myumanitoba.ca. Yoav Keynan, Department of Medical Microbiology and Infectious Disease, University of Manitoba, Winnipeg, Canada, Department of Internal Medicine, University of Manitoba, Winnipeg, Canada, and Department of Community Health Sciences, University of Manitoba, Winnipeg, Canada, E-mail: yoav.keynan@umanitoba.ca. Fernando Montes, Secretaría de Salud de Medellín, Medellín, Colombia, E-mail: fernando.montesz@gmail.com. Lucelly López and Zulma Vanessa Rueda, Facultad de Medicina, Universidad Pontificia Bolivariana, Medellín, Colombia, E-mails: lucelly@gmail.com and zulmaruedav@gmail.com.

REFERENCES

1. World Health Organization, 2014. *Global Strategy and Targets for Tuberculosis Prevention, Care and Control after 2015*. Geneva, Switzerland: WHO. Available at: http://www.who.int/tb/post2015_strategy/en/. Accessed February 13, 2018.
2. Cuenta de Alto Costo, 2016. *Situación del VIH en Colombia 2016*. Bogotá, Colombia: CAC. Available at: https://cuentadealtocosto.org/site/images/Publicaciones/CAC.Co_2017_06_13_Libro_Sit_VIH_2016_V_0.1.pdf.pdf. Accessed February 13, 2018.
3. Instituto Nacional de Salud, 2018. *Informe del Evento Preliminar de Tuberculosis Hasta el Período Epidemiológico XIII Colombia, 2017*. Bogotá, Colombia: INS. Available at: <http://www.ins.gov.co/buscadoreventos/SitePages/Evento.aspx?Event=7>. Accessed February 13, 2018.
4. Beijer U, Wolf A, Fazel S, 2012. Prevalence of tuberculosis, hepatitis C virus, and HIV in homeless people: a systematic review and meta-analysis. *Lancet Infect Dis* 12: 859–870.
5. Haddad MB, Wilson TW, Ijaz K, Marks SM, Moore M, 2005. Tuberculosis and homelessness in the United States, 1994–2003. *JAMA* 293: 2762–2766.
6. Bamrah S, Yeik Woodruff RS, Powell K, Ghosh S, Kammerer JS, Haddad MB, 2013. Tuberculosis among the homeless, United States, 1994–2010. *Int J Tuberc Lung Dis* 17: 1414–1419.
7. Nunes C, Duarte R, Veiga AM, Taylor B, 2017. Who are the patients that default tuberculosis treatment?—space matters! *Epidemiol Infect* 145: 1130–1134.
8. Ministerio de Salud y Protección Social, 2018. *Cifras Aseguramiento en Salud*. Bogotá, Colombia: Ministerio de Salud y Protección Social. Available at: https://public.tableau.com/views/CifrasAseguramientoenSalud_0/Aseguramiento?:embed=y&:showVizHome=no&:host_url=https%3A%2F%2Fpublic.tableau.com%2F&:embed_code_version=2&:tabs=no&:toolbar=yes&:animate_transition=yes&:display_static_image=no&:display_spinner=no&:display_overlay=yes&:display_count=yes&:publish=yes&:loadOrderID=0. Accessed October 27, 2018.
9. World Health Organization, 2014. *Definitions and Reporting Framework for Tuberculosis*. Geneva, Switzerland: WHO. Available at: <http://www.who.int/tb/publications/definitions/en/>. Accessed March 20, 2018.
10. van Hest R, Ködmön C, Verver S, Erkens CGM, Straetemans M, Manissero D, de Vries G, 2013. Tuberculosis treatment outcome monitoring in European Union countries: systematic review. *Eur Respir J* 41: 635–643.
11. de Vries SG et al., 2017. Barriers and facilitators to the uptake of tuberculosis diagnostic and treatment services by hard-to-reach populations in countries of low and medium tuberculosis incidence: a systematic review of qualitative literature. *Lancet Infect Dis* 17: e128–e143.
12. Davila JA, Cabral HJ, Maskay MH, Marcus R, Yuan Y, Chisolm N, Belton P, McKeithan L, Rajabuin S, 2018. Risk factors associated with multi-dimensional stigma among people living with HIV/AIDS who are homeless/unstably housed. *AIDS Care* 30: 1335–1340.
13. Imtiaz S, Shield KD, Roerecke M, Samokhvalov AV, Lönnroth K, Rehm J, 2017. Alcohol consumption as a risk factor for

- tuberculosis: meta-analyses and burden of disease. *Eur Respir J* 50: 1–13.
14. Raviglione M, Poznyak V, 2017. Targeting harmful use of alcohol for prevention and treatment of tuberculosis: a call for action. *Eur Respir J* 50: 1700946.
 15. Nyamathi A, Sands H, Pattatucci-Aragón A, Berg J, Leake B, 2004. Tuberculosis knowledge, perceived risk and risk behaviors among homeless adults: effect of ethnicity and injection drug use. *J Community Health* 29: 483–497.
 16. Hernández Sarmiento JM et al., 2013. Tuberculosis among homeless population from Medellín, Colombia: associated mental disorders and socio-demographic characteristics. *J Immigr Minor Health* 15: 693–699.
 17. Wolitski RJ, Kidder DP, Fenton KA, 2007. HIV, homelessness, and public health: critical issues and a call for increased action. *AIDS Behav* 11 (Suppl 6): 167–171.
 18. Gelberg L, Gallagher TC, Andersen RM, Koegel P, 1997. Competing priorities as a barrier to medical care among homeless adults in Los Angeles. *Am J Public Health* 87: 217–220.
 19. Hwang SW, Ueng JJM, Chiu S, Kiss A, Tolomiczenko G, Cowan L, Levinson W, Redelmeier DA, 2010. Universal health insurance and health care access for homeless persons. *Am J Public Health* 100: 1454–1461.
 20. Ranzani OT, Carvalho CRR, Waldman EA, Rodrigues LC, 2016. The impact of being homeless on the unsuccessful outcome of treatment of pulmonary TB in São Paulo state, Brazil. *BMC Med* 14: 41.
 21. Korzeniewska-Koseła M, Kuś J, Lewandowska K, Siemion-Szcześniak I, 2015. Tuberculosis in homeless persons in Poland. *Przegl Epidemiol* 69: 445–451, 575–580.
 22. Hamusse SD, Demissie M, Teshome D, Lindtjørn B, 2014. Fifteen-year trend in treatment outcomes among patients with pulmonary smear-positive tuberculosis and its determinants in Arsi Zone, Central Ethiopia. *Glob Health Action* 7: 25382.
 23. Gafar MM, Nyazema NZ, Dambisya YM, 2014. Factors influencing treatment outcomes in tuberculosis patients in Limpopo province, South Africa, from 2006 to 2010: a retrospective study. *Curationis* 37: 1169.
 24. Sinshaw Y, Alemu S, Fekadu A, Gizachew M, 2017. Successful TB treatment outcome and its associated factors among TB/HIV co-infected patients attending Gondar University Referral Hospital, northwest Ethiopia: an institution based cross-sectional study. *BMC Infect Dis* 17: 132.
 25. Eshetie S, Gizachew M, Alebel A, van Soolingen D, 2018. Tuberculosis treatment outcomes in Ethiopia from 2003 to 2016, and impact of HIV co-infection and prior drug exposure: a systematic review and meta-analysis. *PLoS One* 13: e0194675.
 26. Shimouchi A, Ohkado A, Matsumoto K, Komukai J, Yoshida H, Ishikawa N, 2013. Strengthened tuberculosis control programme and trend of multi-drug resistant tuberculosis rate in Osaka city, Japan. *Western Pac Surveill Response J* 4: 4–10.
 27. Uchimura K, Ngamvithayapong-Yanai J, Kawatsu L, Ohkado A, Yoshiyama T, Shimouchi A, Ito K, Ishikawa N, 2013. Characteristics and treatment outcomes of tuberculosis cases by risk groups, Japan, 2007–2010. *Western Pac Surveill Response J* 4: 11–18.
 28. Uchimura K, Ngamvithayapong-Yanai J, Kawatsu L, Ohkado A, Yoshiyama T, Ito K, Ishikawa N, 2015. Permanent employment or public assistance may increase tuberculosis survival among working-age patients in Japan. *Int J Tuberc Lung Dis* 19: 312–318.
 29. Grenfell P, Baptista Leite R, Garfein R, de Lussigny S, Platt L, Rhodes T, 2013. Tuberculosis, injecting drug use and integrated HIV-TB care: a review of the literature. *Drug Alcohol Depend* 129: 180–209.
 30. Lutge EE, Wiysonge CS, Knight SE, Sinclair D, Volmink J, 2015. Incentives and enablers to improve adherence in tuberculosis. *Cochrane Database Syst Rev* 9: CD007952.
 31. Tulskey JP, Hahn JA, Long HL, Chambers DB, Robertson MJ, Chesney MA, Moss AR, 2004. Can the poor adhere? Incentives for adherence to TB prevention in homeless adults. *Int J Tuberc Lung Dis* 8: 83–91.
 32. Ciobanu A, Domete L, Soltan V, Bivol S, Severin L, Plesca V, Van den Bergh R, Kumar A, de Colombani P, 2014. Do incentives improve tuberculosis treatment outcomes in the Republic of Moldova? *Public Health Action* 4: S59–S63.
 33. Ukwaja KN, Alobu I, Gidado M, Onazi O, Oshi DC, 2017. Economic support intervention improves tuberculosis treatment outcomes in rural Nigeria. *Int J Tuberc Lung Dis* 21: 564–570.
 34. Ruiz-Restrepo J; Centro de Estudios de Opinión, Secretaria de Bienestar Social de Medellín, 2010. Censo de habitantes de calle y en calle de la ciudad de Medellín y sus corregimientos. *Sociol En Sus Escen* 21: 2–175.