Management of Isoniazid Preventive Therapy in Southern Lima, Peru: An Analysis of Health Center Characteristics

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Research Article

Keywords: Contacts, Chemotherapy, latent tuberculosis, isoniazid, children, adolescents

Posted Date: January 18th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-143791/v1

Abstract

Background: Prevention of TB through the use of preventive treatment is a critical activity in the elimination of TB. Health personnel are a key element in achieving proper management of isoniazid preventive therapy (IPT) for TB contacts. This study aims to determine the association between health center characteristics and indicators of TB contact care management with isoniazid preventive therapy in southern Lima.

Methods: We conducted an ecological study. Through the review of medical records, we identified children and adolescent contacts of tuberculosis patients, who initiated IPT between 2016 and 2018. We assessed bivariate associations between clinic staffing and IPT initiation and completion using binomial logistic regression with robust standard errors.

Results: We included 977 contacts, among whom 69% took more than a week to start IPT and 41% did not complete IPT. For those who did successfully complete IPT, 58% were not medically evaluated with three follow-up appointments. While completion of IPT and 3 clinical appointments was better among health centers with more physicians and nurses, these differences were not statistically significant. Contact sex was associated with initiating IPT (p=0.005), and contact age was associated with completion of IPT (p=0.025) and completion of clinical evaluations (p=0.041).

Conclusion: There are significant gaps in IPT management in health centers of southern Lima, Peru, but insufficient staffing of health centers may not be responsible. Further research is needed to identify how IPT management can be improved, including through improving training and staffing.

Background

Tuberculosis (TB) is one of the world's leading causes of mortality – in 2019, it was estimated that nearly 10 million people developed the disease [1]. In the region of the Americas, only 65% of estimated TB cases are detected by health systems, and pediatric TB accounts for 5.5% of total cases [2]. Peru has the second highest number of TB cases among countries in the Americas [2].

Given such a high disease prevalence, prevention of TB through the use of preventive treatment is critical for elimination strategies [3]. Contacts of TB patients are a priority group for preventive treatment because of their high risk of developing TB disease [4]. Prompt initiation of preventive treatment, appropriate monitoring, and support for contacts can reduce the risk of developing TB in exposed individuals [5].

Appropriate staffing and training of health personnel are important factors in improving TB prevention and management [6]. The World Health Organization (WHO) recommends that countries assess health system infrastructure, staffing of healthcare workforce, and training to implement contact tracing and preventive treatment in health centers [5]. More evidence is needed to support fair and adequate

distribution of human resources in health centers, based on the prevalence of TB and risk of transmission in a given area.

Although the proper implementation of international standards for TB prevention could prevent the deaths of thousands of children and adolescents around the globe [7], initiation and maintenance of preventive treatment is poor [8]. Various countries have reported non-compliance with policies aimed at medical management of TB contacts [9]. Most research that focuses on TB contacts in minors less than 18 years of age evaluates the administration of the purified protein derived (PPD) skin test and completion of a 24-week course of isoniazid preventive therapy (IPT) [10–12]. There are fewer studies that evaluate other aspects of TB contact care, such as the timely onset of IPT and proper clinical evaluation with follow-up medical appointments [13]. Peruvian TB guidelines indicate that TB contacts 19 years or younger should receive a PPD test and 24 weeks of IPT if the PPD result is positive. For TB contacts less than five years of age, the guidelines recommend IPT without requirement of a PPD test [14].

Weak health systems hinder TB control efforts [15]. The WHO classifies the health workforce as an essential building block for strong health systems. This includes a sufficient, competent, and equitably distributed group of healthcare workers that can improve health outcomes [16]. Healthcare workers are especially vital in resource-constrained areas, such as Lima, where social determinants of health such as transportation, health-seeking behaviors, and material resources have been shown to impede patient access to care [17, 18]. In 1990, Peru's National TB Program (NTP) became a national health priority, and since then there have been increased funds and political commitment to the NTP [19]. Despite this, however, Lima continues to face a lack of qualified and well-trained staff in the city's most impoverished areas, where the public health system may lose healthcare staff to private or international health bodies [20].

It is essential to generate evidence about health personnel staffing at the primary care level of decision-making in attempts to reduce health inequities and improve TB prevention. The objective of the study is to determine the association between health center characteristics, including available human resources, and effective IPT management in southern Lima.

Methods

Study design and setting

In 2018, we conducted an ecological study to analyze the relationship between staffing of health centers and indicators of effective IPT management in southern Lima, Peru. The public health system in Peru is divided into regional health networks, which are managed by a Directorate of Integrated Networks (DIN) office. This study was conducted in the regional health network of southern Lima, under management of the Lima South DIN. In total, this DIN manages 136 health centers located in 13 city districts, covering a combined population of 1,860,382 people.

We conducted this study in 46 health centers in the Lima South DIN, located in 6 districts of Lima Metropolis (Fig. 1). These health centers were purposively sampled because they treat approximately 80% of the TB cases in the Lima South DIN and represent a range of health center levels and caseloads [21]. Each health center had a designated TB treatment program that was regulated by the NTP.

Data collection

The outcomes of interest were indicators of the quality of IPT management, assessed at the patient level. We extracted data from health records for patients meeting the following criteria: individuals 18 years of age or younger who initiated IPT and were family members or home contacts of patients receiving treatment for TB between 2016 and 2018. We excluded contacts whose information was not legible, whose start date of IPT treatment was unknown, who were diagnosed with TB after initiating IPT, and/or who suspended IPT for other medical reasons.

We evaluated the following indicators IPT management quality: 1) time between initiation of TB treatment in the index case and initiation of IPT in the contact; 2) completion status of IPT, considered complete when the contact took isoniazid for 24 weeks or 168 doses; and 3) clinical evaluation of contacts, which was considered complete when the contact attended two medical appointments during IPT and one follow-up medical appointment after IPT completion.

Health center-level predictors of interest were: 1) physician staffing; 2) nurse staffing; 3) number of TB cases that the health center reported in 2016; and 4) level of health center care, defined as I-2 for an outpatient health clinic, I-3 for health centers without overnight beds, and I-4 for health centers with overnight beds. In addition, we evaluated associations between age and sex of the contacts and indicators of IPT management quality. We obtained information on physician and nurse staffing from the Lima South DIN administrative office and information on contacts from their health records.

Statistical analysis

To assess the significance of bivariate associations between predictors and outcomes, we generated p-values using a binomial logistic regression with robust standard errors to account for clustering at the health center level. Statistical analysis was performed using SAS v9.4.

Ethical approval.

The study was approved by the Institutional Ethics Committees of the Maria Auxiliadora University (Nº 005-2019). A waiver of informed consent was granted because data were collected from routine medical records in a way that did not permit the identification of patients.

Results

We identified 1010 contacts that met the inclusion criteria and obtained information from 977 (99%). Of these, 772 individuals were contacts of index patients with sputum smear-positive TB. Table 1 describes

the sociodemographic and clinical characteristics of contacts. Overall, 616 (63%) contacts were under 5 years of age, 551 (56%) were male, and 925 (95%) were contacts of index patients with pulmonary TB.

Table 2 shows a description of the health centers included in the study. 41% of health centers had a full-time physician and 13% had 2 or more nurses working in the TB service. 46% of health centers reported serving between 25–49 TB patients per year.

Table 3 shows results from the bivariate analysis. While completion of IPT and 3 clinical appointments was better among health centers with more physicians and nurses, these differences were not statistically significant. There were also no significant differences in IPT management indicators based on health center caseload or level. The percentage of female contacts who had delayed IPT initiation (31%) was significantly larger than male contacts (24%) who delayed ($p = 0.005$). IPT completion was significantly greater ($p = 0.025$) in contacts age 5 and older (64%) compared to contacts under 5 years of age (56%). In addition, the percentage of contacts aged 5 and older who completed medical evaluations for IPT (46%) was statistically higher ($p = 0.041$) than contacts under 5 years of age (35%).

Table 1
Sociodemographic and clinical descriptions of TB Contacts, 2016–2018 (N = 977).

Characteristics	Category	N (%)
Sociodemographic contact characteristics		
Contact age range	Under 5 years old	616 (63)
	5 to older years	361 (37)
Contact sex	Male	551 (56)
	Female	426 (44)
Clinical characteristics of the Index case		
Tuberculosis Diagnosis	Pulmonary	925 (95)
	Extrapulmonary	52 (5)
Sputum smear microscopy result	Positive	772 (79)
	Negative	205 (21)
Treatment completion	Successful	833 (85)
	Not successful	135 (14)
	No information	9 (1)

Table 2
Health Center Information (N = 46)

Characteristic	Category	Number of Primary Health Center, n (%)
Physician Staffing	1 Full-time	19 (41)
	1 Part-time	27 (59)
Nurse Staffing	≥ 2 Full Time	13 (28)
	1 Full time or Part-time	33 (72)
Number of TB cases per year	≥ 50	10 (22)
	25–49	21 (46)
	≤ 24	15 (33)
Health Center Level of Care	I-2 (Outpatient Clinic)	26 (57)
	I-3 (Health Center)	9 (20)
	I-4 (Health Center with overnight beds)	11 (24)
Management of IPT.		

Table 3
Indicators of IPT quality and management by Health Center (N = 977)

Indicator	Description	Total Number	Delayed < 7 days in beginning IPT*		Completed IPT		Completed 3 clinical appointments for IPT	
			n (%)	P	n (%)	P	n (%†)	P
Age of Contact	< 5	616	179 (29)	0.110	343 (56)	0.025	157 (46)	0.041
	≥ 5	361	87 (24)		230 (64)		81 (35)	
Sex of Contact	Male	551	132 (24)	0.005	320 (58)	0.579	138 (43)	0.378
	Female	426	134 (31)		253 (59)		100 (40)	
Physician staffing	1 Full time	581	147 (25)	0.353	346 (60)	0.795	148 (46)	0.331
	1 Part Time	396	118 (30)		227 (57)		80 (35)	
Nurse staffing	≥ 2 Full Time	467	134 (29)	0.607	303 (64)	0.148	144 (48)	0.245
	1 at Full Time or Part Time	510	510 (26)		270 (53)		93 (35)	
Number of TB cases per year	≥ 50	399	103 (26)	Ref	243 (61)	Ref	102 (42)	Ref
	25–49	374	113 (30)	0.376	215 (57)	0.722	80 (37)	0.712
	≤ 24	204	50 (25)	0.663	115 (56)	0.687	46 (49)	0.640
Health Center Level of Care	I-2	401	98 (24)	Ref	245 (61)	Ref	108 (44)	Ref
	I-3	207	64 (31)	0.435	107 (52)	0.452	34 (32)	0.338

*The statistical evaluation excludes 41 contacts with insufficient data to determine days of delay to initiate IPT

†Out of those who completed IPT

Indicator	Description	Total Number	Delayed < 7 days in beginning IPT*		Completed IPT		Completed 3 clinical appointments for IPT	
	I-4	369	104 (28)	0.492	221 (59)	0.900	96 (43)	0.962
*The statistical evaluation excludes 41 contacts with insufficient data to determine days of delay to initiate IPT								
†Out of those who completed IPT								

Discussion

The study found that no association between health center level, staffing, caseload, and management of IPT in pediatric contacts of TB patients. The lack of an association between health center characteristics and IPT completion could be mediated through the role of caregivers for children, and whether children experience adverse events in treatment, as reported in other studies [22–24]. Services within the health center may only indirectly influence IPT completion. In addition, because we only collected data for children who initiated IPT, we may have missed children most affected by lack of resources for IPT management – those who never initiated treatment. Other studies have shown the greatest gaps in contact management to occur during the identification and screening process [25, 26]. These activities require trained staff, capacity to complete radiographic imaging, and supplies for PPD testing – conditions that vary with the level of health center. Our findings contrast with a previous study in Lima, Peru, which reported that contacts attending health centers with high caseloads were less likely to complete IPT [13].

We found that 72% of contacts initiated IPT at least 7 days after the index patient began TB treatment, representing a delay in IPT initiation. This is greater than a study conducted in Cuba, which reported that 23% of contacts initiated contact control late [10]. Another study in Taiwan found an association between delay in initiation of TB treatment and health system characteristics, such as living in long-term care facilities and initial visit at a primary care clinic [27]. Considering that 79% of children included in our study were contacts of patients with sputum smear-positive TB, the delay in initiation of IPT places children at greater risk for developing TB disease.

Although preventive treatment for contacts is recommended in most countries [28], completing preventive treatment with 6 months of isoniazid is a challenge. The reported completion of IPT in this study (59%) is similar to other studies conducted in Peru [11–13] and Ecuador [29], and greater than studies from South Africa [25] and Ethiopia [23]. The fact that IPT completion is suboptimal across a range of settings suggests that this aspect of contact management continues to be a challenge for clinical teams, particularly for nurses who are often charged with contact follow-up. One strategy that could improve treatment completion is the adoption of shorter 3 or 4-month preventive regimens that have shown better completion compared to isoniazid [30, 31].

Medical evaluation of contacts is important for detecting and preventing TB disease. Our study found that the majority of contacts who completed IPT were not clinically evaluated with the recommended three follow-up appointments. This is similar to what was reported in another study in Lima that provided community support to improve TB contact management [12]. Another recent study in Peru included all contacts in their analysis, both those receiving IPT and those not, and reported only 5% completed three follow up appointments [13]. Unlike TB patients who receive directly observed therapy in clinic, contacts do not regularly attend health centers, which may represent a barrier to completing these medical appointments.

This study includes several limitations. We only collected data on contacts who completed IPT. We did not evaluate the percentage of contacts who were eligible for but did not receive IPT. This subset of contacts may have been more affected by health center resources and staffing. Future research might evaluate the association between health center characteristics and poor prescription of IPT, a recognized gap in TB contact care in Peru [12]. Additionally, we collected clinical data from paper-based, abbreviated medical charts, and excluded charts that did not contain complete information. We attempted to improve data collection by also reviewing index case records and long-form medical records of contacts. We included health centers with higher TB caseloads, and so results reported may not apply to health centers with fewer TB cases.

Conclusions

We collected information from health centers that together report 80% of the total TB cases from the Lima South DIN. This study showed no association between health center characteristics and indicators of IPT management, suggesting that gaps in management of contacts who initiate IPT may not be due to insufficient staffing. However, contact sex was associated with delay in initiating IPT and age was associated with completion of IPT and clinical follow-up appointments.

Health-providing institutions must promote ongoing training of health personnel to reduce gaps in contact management and subsequent TB infection in children. Further research is needed to improve the management of TB contact monitoring and management.

List Of Abbreviations

TB: tuberculosis

WHO: World Health Organization

IPT: isoniazid preventive therapy

NTP: Peru’s National TB Program

DIN: Directorate of Integrated Networks

Declarations

Ethics approval and consent to participate:

This study was approved by the Maria Auxiliadora University.

Consent for publication:

Not applicable

Availability of data and materials:

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests:

The authors report no competing interests.

Funding:

None

Authors' contributions:

RZC, and JZH conceptualized the study. RZC, MBM, and JZH collected the data. CMY analyzed the data. RZC and LBV wrote the first draft of the manuscript. All other authors revised it critically and approved the submitted version.

Acknowledgements:

Not applicable

References

1. Global Tuberculosis Report 2019. https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-report-2019. Accessed 11 Nov 2020.
2. Organización Panamericana de la Salud. Tuberculosis en las Américas. Informe regional 2019 - OPS/OMS |. http://www.paho.org/es/documentos/tuberculosis-americas-informe-regional-2019.

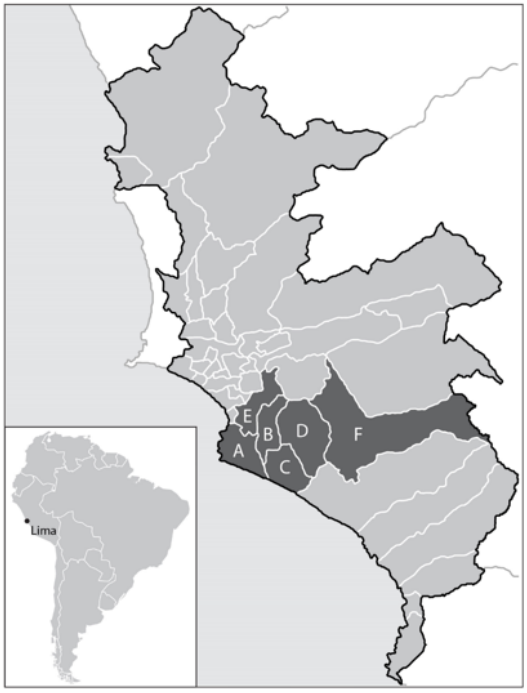
Accessed 26 Nov 2020.

3. Rangaka MX, Cavalcante SC, Marais BJ, Thim S, Martinson NA, Swaminathan S, et al. Controlling the Seedbeds of Tuberculosis: Diagnosis and Treatment of Tuberculosis Infection. Lancet Lond Engl. 2015;386:2344–53.
4. Global Tuberculosis Programme. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. 2018. http://www.ncbi.nlm.nih.gov/books/NBK531235/. Accessed 11 Nov 2020.
5. Domínguez J, Latorre I, Santin M. Diagnosis and therapeutic approach of latent tuberculosis infection. Enferm Infecc Microbiol Clin. 2018;36:302–11.
6. Bezerra e Silva SY, Rodrigues de Medeiros E, Balbino da Silva S, Chacon de Matos Neta MN, Lima de Souza N, Galvão Pinto ÉS. Capacitações sobre tuberculose e sua associação com competências desenvolvidas no controle da doença. Rev Recien - Rev Científica Enferm. 2020;10:129–36.
7. Dodd PJ, Yuen CM, Becerra MC, Revill P, Jenkins HE, Seddon JA. Potential effect of household contact management on childhood tuberculosis: a mathematical modelling study. Lancet Glob Health. 2018;6:e1329–38.
8. Grace SG. Barriers to the implementation of isoniazid preventive therapy for tuberculosis in children in endemic settings: A review. J Paediatr Child Health. 2019;55:278–84.
9. Hill PC, Rutherford ME, Audas R, van Crevel R, Graham SM. Closing the policy-practice gap in the management of child contacts of tuberculosis cases in developing countries. PLoS Med. 2011;8:e1001105.
10. Muñoz Peña R, Estela Reynel PG, Abreu Suárez G, González Valdés JA, Rodríguez Vargas LE. Control de foco de tuberculosis en menores de 15 años. Rev Cuba Pediatría. 2014;86:189–99.
11. Wingfield T, Tovar MA, Huff D, Boccia D, Montoya R, Ramos E, et al. A randomized controlled study of socioeconomic support to enhance tuberculosis prevention and treatment, Peru. Bull World Health Organ. 2017;95:270–80.
12. Yuen CM, Millones AK, Contreras CC, Lecca L, Becerra MC, Keshavjee S. Tuberculosis household accompaniment to improve the contact management cascade: A prospective cohort study. PLOS ONE. 2019;14:e0217104.
13. Otero L, Battaglioli T, Ríos J, De la Torre Z, Trocones N, Ordoñez C, et al. Contact evaluation and isoniazid preventive therapy among close and household contacts of tuberculosis patients in Lima, Peru: an analysis of routine data. Trop Med Int Health TM IH. 2020;25:346–56.
14. MINSA. Norma técnica de salud para la atención integral de las personas afectadas por tuberculosis. 2013. http://www.tuberculosis.minsa.gob.pe/newtb/Archivos/norma_tecnica.pdf. Accessed 28 Jun 2020.
15. Atun R, Weil DEC, Eang MT, Mwakyusa D. Health-system strengthening and tuberculosis control. Lancet Lond Engl. 2010;375:2169–78.
16. World Health Organization. Everybody’s business: strengthening health systems to improve health outcomes: WHO’s frmaework for action. Geneva: World Health Organization; 2007.

17. Bonadonna LV, Saunders MJ, Zegarra R, Evans C, Alegria-Flores K, Guio H. Why wait? The social determinants underlying tuberculosis diagnostic delay. PloS One. 2017;12:e0185018.
18. Bonadonna LV, Saunders MJ, Guio H, Zegarra R, Evans CA. Socioeconomic and Behavioral Factors Associated with Tuberculosis Diagnostic Delay in Lima, Peru. Am J Trop Med Hyg. 2018;98:1614–23.
19. Bonilla C, Bayona J. Building political commitment in Peru for TB control through expansion of the DOTS strategy. Bull World Health Organ. 2007;85:402.
20. Enarson DA, Billo NE. Critical evaluation of the Global DOTS Expansion Plan. Bull World Health Organ. 2007;85:395–8.
21. MINSA. Plan de Intervención de Prevención y Control de Tuberculosis en Lima Metropolitana y Regiones priorizadas de Callao, Ica, La Libertad y Loreto, 2018 - 2020. 2018. https://www.gob.pe/institucion/minsa/normas-legales/187412-247-2018-minsa. Accessed 2 Aug 2020.
22. Rutherford ME, Ruslami R, Maharani W, Yulita I, Lovell S, Van Crevel R, et al. Adherence to isoniazid preventive therapy in Indonesian children: A quantitative and qualitative investigation. BMC Res Notes. 2012;5:7.
23. Garie KT, Yassin MA, Cuevas LE. Lack of Adherence to Isoniazid Chemoprophylaxis in Children in Contact with Adults with Tuberculosis in Southern Ethiopia. PLoS ONE. 2011;6. doi:10.1371/journal.pone.0026452.
24. Chang Sh, Eitzman Sr, Nahid P, Finelli Ml. Factors associated with failure to complete isoniazid therapy for latent tuberculosis infection in children and adolescents. Journal of infection and public health. 2014;7. doi:10.1016/j.jiph.2013.11.001.
25. Black F, Amien F, Shea J. An assessment of the isoniazid preventive therapy programme for children in a busy primary healthcare clinic in Nelson Mandela Bay Health District, Eastern Cape Province, South Africa. S Afr Med J. 2018;108:217–23.
26. Laghari M, Sulaiman SAS, Khan AH, Talpur BA, Bhatti Z, Memon N. Contact screening and risk factors for TB among the household contact of children with active TB: a way to find source case and new TB cases. BMC Public Health. 2019;19. doi:10.1186/s12889-019-7597-0.
27. Chen C-C, Chiang P-H, Chen Y-H, Fan I-C, Chan T-C. Patient and health care system characteristics are associated with delayed treatment of tuberculosis cases in Taiwan. BMC Health Serv Res. 2019;19:846.
28. Rodriguez CA, Sasse S, Azzawi S, Becerra MC, Yuen CM, Yuengling KA. A systematic review of national policies for the management of persons exposed to tuberculosis. Int J Tuberc Lung Dis. 2017;21:935-935–40.
29. Chacón A, Alarcón E, López L. Factores asociados al cumplimiento de la terapia preventiva con isoniacida en niños en Quito, Ecuador (2014-2016 y 2018). Rev Panam Salud Pública. 2019;43. doi:10.26633/RPSP.2019.97.

30. Macaraig MM, Jalees M, Lam C, Burzynski J. Improved treatment completion with shorter treatment regimens for latent tuberculous infection. Int J Tuberc Lung Dis Off J Int Union Tuberc Lung Dis. 2018;22:1344–9.
31. Cruz AT, Starke JR. Completion Rate and Safety of Tuberculosis Infection Treatment With Shorter Regimens. Pediatrics. 2018;141.

Figures



City Districts	Contacts Identified	%
A. Chorrillos	112	11.5
B. San Juan de Miraflores	266	27.2
C. Villa El Salvador	349	35.7
D. Villa Maria del Triunfo	237	24.3
E. Surco	5	0.5
F. Pachacamac	8	0.8
Total	977	100

Figure 1

Study districts Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

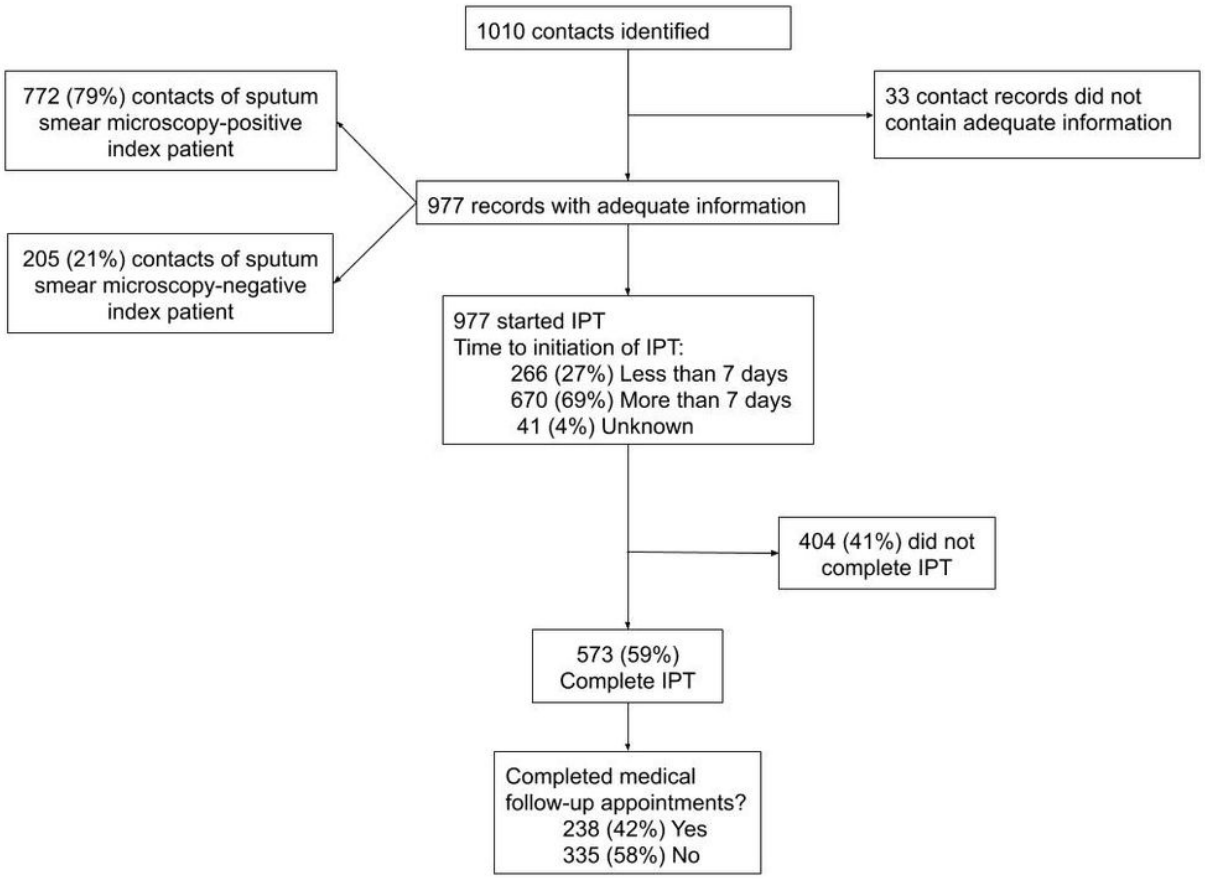


Figure 2

Flow diagram of data collection