

# ClinicalTrials.gov *PRS*

## Protocol Registration and Results System

ID: 68722 Implementation of an Integrated Care Strategy for Children Contacts of Patients With Tuberculosis

NCT04331262

### Protocol Registration Preview

This is a rough approximation of how the Protocol Registration will appear on the ClinicalTrials.gov public web site.

## Implementation of an Integrated Care Strategy for Children Contacts of Patients With Tuberculosis



The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier:  
NCT04331262

Recruitment Status: Recruiting  
First Posted: \*  
Last Update Posted: \*

\* Date not available in PRS

### Sponsor:

Corporacion para Investigaciones Biologicas

### Collaborators:

Universidad Pontificia Bolivariana  
Universidad de Antioquia  
Secretaría de Salud de Medellín  
Secretaría Seccional de Salud y Protección Social de Antioquia  
Hospital Pablo Tobón Uribe

**Information provided by (Responsible Party):**

Corporacion para Investigaciones Biologicas

**Study Description**

---

**Brief Summary:**

**Introduction:** childhood tuberculosis continues to be a major public health problem, despite the fact that the visibility of the epidemic in this population group has increased, studies are still lacking that can resolve the gaps that persist.

**Objective:** To design, implement and evaluate an integrated care strategy for children under five years old household contacts of patients with smear positive pulmonary tuberculosis in Medellín and the Metropolitan Area.

**Methodology:** quasi-experimental study, in which around 300 children household contacts of patients with smear positive pulmonary tuberculosis from Medellín and the Metropolitan Area will be evaluated, who will be recruited in a period of one year. A subgroup of these children, estimated at 85, who require treatment for latent tuberculosis, will be offered to receive treatment for latent tuberculosis under a integrated care strategy that includes some modifications to the currently standardized scheme in Colombia, with rifampicin treatment daily oral route for four months, follow-up under the project scheme with the availability of a nurse, general practitioner, specialists, care by professionals from other disciplines such as social work, psychology, and nutritionist, and the provision of incentives (transport and food assistance). This strategy will be compared with isoniazid treatment according to the standardized scheme in the country, which was received by a cohort of children between 2015 and 2018. The study has the CIB Research Ethics Committee approval.

**Expected results:** this project is expected to contribute with greater local evidence of integrated care strategies that allow greater compliance with treatment for latent tuberculosis in children, so that there is a real impact in the control of childhood tuberculosis and in the reduction of tuberculosis reservoirs in order to achieve the goals proposed by the World Health Organization's End TB Strategy.

Condition or disease
Latent Tuberculosis

**Detailed Description:****Objective:**

To design, implement and evaluate an integrated care strategy for children under five years old household contacts of patients with smear positive pulmonary tuberculosis in Medellín and the Metropolitan Area.

**Methodology:**

## Study design

Quasi-experimental study with a one-year follow-up, which will include a cohort of children household contacts of patients with smear positive pulmonary TB from Medellín and the Valle de Aburrá Metropolitan Area, to carry out the contact tracing and treatment for latent TB in those who is indicated, and who will receive the intervention of the integrated care strategy. Compliance with the treatment achieved with this strategy will be compared with compliance achieved with the treatment with isoniazid in the 2015-2018 cohort.

The integrated care strategy for contact children of patients with smear positive pulmonary TB will have the following components:

- Diagnostic tests (TST, IGRAS, standardized chest x-ray, gastric aspirate, induced sputum, smear microscopy, culture in solid and liquid media, Xpert Ultra MTB/RIF).
- Staff: Nursing assistant, General practitioner, Specialist (pediatrician, ID specialist, radiologist), Other disciplines (nutritionist, psychology, social worker).
- Supply of scheme treatment with daily rifampicin for four months.
- Provision of social assistance and/or incentives (transport, food assistance).
- Patient-centered care based on primary health care (active monitoring, permanent education and contact, among others).

## Operational hypothesis

The proportion of treatment compliance for latent TB in contact children of patients with smear positive pulmonary TB in Medellín and the Metropolitan Area who receive the integrated care strategy is greater than the proportion of treatment compliance for children who received isoniazid in the 2015-2018 cohort.

## Study population

Sample: the sample will be children under five years old household contacts of patients with smear positive confirmed pulmonary TB from Medellín and the Metropolitan Area notified to the surveillance system during 2020, in whom treatment for latent TB is indicated.

## Sample

Sampling type: it will correspond to an Incidental Sampling, since the children of the study will be recruited as new cases (incidents) of smear positive confirmed pulmonary TB identified in Medellín and the Metropolitan Area.

Sample size: all children household contacts of smear positive pulmonary TB patients from Medellín and the Metropolitan Area will be follow-up initially for a period of one year, according to previous studies it is estimated that around 250 to 300 children will be assessed with a proportion of estimated infection of 73.5%.

The complete intervention of the integrated care strategy (with medication, incentives and active follow-up) will be provided to a subgroup of children who require treatment for latent tuberculosis, and who will also be selected incidentally, according to their willingness to participate. To calculate the sample size of this subgroup, compliance with the treatment with isoniazid in the 2015-2018 cohort of 59% was considered, hoping that the proposed strategy achieves at least 80% of compliance (expected goal), with a confidence level of 95% and a power of 80%, it is estimated that a group of at least 75 children will be required in the proposed comprehensive care strategy (sample size calculated with Epidat version 4.2), an

additional 10% will be estimated due to loss to follow-up, so the total number of children to enter the integrated care strategy will be 85.

## Description of interventions

The intervention will be the integrated care strategy, in which the effects of interventions established in the regulations of the TB program at the national level will be observed, such as the diagnosis and administration of treatment for latent TB in children household contacts of patients with pulmonary TB, with two main modifications, the supply of daily oral rifampicin for four months self-administered scheme (instead of daily oral isoniazid for nine months self-administered scheme), and provision of incentives such as transport and food assistance (monthly food supplies). In addition to this, immune response tests will be performed measuring interferon gamma production levels (QuantiFERON®-TB Gold Plus - QFT Plus test) and tuberculin skin test (TST).

## Procedures

- Standardization of the personnel that will participate in the study will be carried out both in data collection and in clinical assessment and information processing.
- Children recruitment: children will be recruited through contact with the tuberculosis control program of the Health Authorities of Medellín, and other municipalities in the Metropolitan Area that agreed to participate, which will immediately supply their information on children under five years old household contacts of pulmonary TB patients recruited by the program through epidemiological visits to the homes of patients with pulmonary tuberculosis recently diagnosed and reported to the program. The staff of the health authorities will request authorization from those responsible for the children to share the information with the study staff. Additionally, the staff of the health authorities will support in socializing the project to promote the participation of children.
- By telephone contact, it will start the informed consent process to participate in the study to the parents or guardians of children under five years old identified as household contacts of smear positive confirmed TB patients from the municipalities of Medellín and the Metropolitan Area, that meet the inclusion criteria and that do not have exclusion criteria.
- According to what was previously found, the first two information collection formats will be filled in by telephone with the variables corresponding to the index case (person with TB of whom the child under five years old is contact) and some variables corresponding to the child.
- During the same phone call, an appointment will be assigned, during which the doctor will carry out the basic clinical assessment with a complete physical examination, tests for latent TB will be performed. Trained health personnel will apply tuberculin and take the reading at 72 hours, previously taking a blood sample (5 ml sample of blood taken through a puncture in the vein) for evaluation of interferon gamma production in response to CFP-10, ESAT-6 and PHA antigens (QuantiFERON®-TB Gold Plus-QFT Plus test), as well as biomarker determination. This last test will also be performed on a urine sample. A radiological chest study will be performed to rule out active disease with a standardized reading. The first children with criteria for treatment for latent TB will be invited to participate in the integrated care strategy, in which they will receive care from the project by Nursing Assistant, General Practitioner, Specialists (pediatrician, ID specialist, child radiologist), Other disciplines (nutritionist, psychology, social worker), Treatment provision scheme with daily rifampicin for four months, Supply of social assistance and / or incentives (transport, food assistance), Patient-centered care based on primary health care (active monitoring, education and permanent contact, among others).

- Children with clinical and / or radiological criteria for active TB during the year of follow-up and uptake will receive studies to confirm the diagnosis of active TB, taking samples of induced sputum (two samples) and aspirating gastric juice (two samples) with smear, Xpert MTB/RIF Ultra test, and culture in solid and liquid media to the collected samples. Stool and urine samples will also be taken.
- Children who receive treatment for latent TB under the integrated care strategy will have a monthly clinical assessment during the period they receive the medication, to detect side effects, observe compliance with the treatment, identify the development of active disease (in those who present respiratory symptoms will be performed the same tests as in children with suspected initial active TB). Liver function tests will be performed after two months of treatment to detect liver adverse effects. Biomarkers will also be measured in a blood sample, as well as in urine. At the end of the treatment, a blood biomarker study will be performed again.

## Research site

Children will be assessed at CIB medical office for clinical and epidemiological conditions and to rule out the diagnosis of tuberculosis and confirm the diagnosis of latent TB; in those who enter the integrated care strategy, treatment compliance and side effects will be assessed, with a clinical assessment at the time of intake, monthly while receiving medication (rifampin four months) and 12 months after the initial assessment; immune response (TST and IGRA) at baseline will also be evaluated; as defined in the procedures.

Chest radiography (including standardized reading) and sampling of induced sputum and gastric juice aspirate will be performed at the Pablo Tobón Uribe Hospital, the samples will be processed at the Corporation for Biological Research (CIB). Liver function tests will be taken at CIB, and processed in Laboratorio Echavarría.

**Data analysis** To describe the characteristics of children's exposure to TB, a univariate analysis will be carried out, which will include the variables corresponding to the index case, the child's exposure, and other epidemiological variables. Frequencies distribution and proportions estimation will be carried out for the qualitative variables such as sex, socioeconomic stratum, system of affiliation to the social security system in health, history of BCG vaccination, bacteriological study and other variables.

The characteristics of the children in the 2015-2018 and 2020-2022 cohort will be compared using the Z test for the difference in proportions for the qualitative variables and using the Mann-Whitney U test for the quantitative variables according to the normality of those variables estimated with the Shapiro Wilk test. The characteristics of the index cases and the characteristics of the children household contacts will be analyzed separately.

To examine the cellular immune response to M. tuberculosis, a univariate analysis will be carried out. The proportion of response to the TST will be calculated according to categories in <5 mm, between 5 and 10 mm and ≥10 mm, and the prevalence of positive response with cutoff point ≥5 mm. Proportion of interferon gamma production (QuantiFERON®-TB Gold Plus - QFT Plus) will be calculated according to the categories of positive and negative results.

The total agreement between the two immunological tests will be analyzed, as well as the different possibilities of discordance. The kappa index will also be calculated. The prevalence ratio of TST ≥5 mm and / or positive QFT will be calculated, and a bivariate analysis will be made with the characteristics of exposure to TB in children, adjusting for the index case cluster using Poisson regression. Subsequently, the multivariate analysis will be performed adjusting for the variables that met the Hosmer-Lemeshow criterion in the bivariate analysis (p-value <0.25).

A description of the characteristics of the treatment for latent TB will be made, a univariate analysis of the characteristics of the treatment for latent TB will be made, by estimating proportions, the qualitative variables related to the characteristics of the administration of the treatment, side effects (appearance of symptoms such as gastrointestinal or allergic) and treatment compliance (temporary or permanent suspension, cause of treatment suspension).

The difference in treatment compliance proportions between the 2015-2018 and 2020-2022 cohorts will be calculated, with 95% confidence.

## Study Design

---

Study Type: Observational

Estimated Enrollment: 300 participants

Observational Model: Other

Time Perspective: Prospective

Official Title: Tuberculosis en Niños: Implementación de Una Estrategia de Cuidado Integral Para Los Niños Contacto de Pacientes Con Tuberculosis Pulmonar Bacilífera

Actual Study Start Date: July 26, 2021

Estimated Primary Completion Date: July 2022

Estimated Study Completion Date: December 2022

## Groups/Cohorts

---

Number of groups: 1

## Outcome Measures

---

Primary Outcome Measure:

1. Treatment Compliance [Time Frame: 4 months]

Proportion of treatment compliance

## Eligibility Criteria

---

Ages Eligible for Study: up to 5 Years

Sexes Eligible for Study: All

Gender Based: No

Accepts Healthy Volunteers: No

Sampling Method: Non-Probability Sample

## Study Population

Universe: the study universe are children under five years old household contacts of patients with smear positive confirmed pulmonary TB from Medellín and the Metropolitan Area, in whom treatment for latent TB is indicated.

Sample: the sample will be children under five years of age household contacts of patients with smear positive confirmed pulmonary TB from Medellín and the Metropolitan Area notified to the surveillance system during 2020, in whom treatment for latent TB is indicated.

Sampling type: it will correspond to an Incidental Sampling, since the children of the study will be recruited as new cases (incidents) of smear positive confirmed pulmonary TB appear in Medellín and the Metropolitan Area.

## Criteria

Inclusion Criteria:

Inclusion criteria for initial evaluation (clinical and paraclinical)

- Child under five years of age.
- Household contact of smear positive confirmed pulmonary tuberculosis patient.
- That the parents or legal guardian sign the informed consent.
- To live in Medellín or the Metropolitan Area of the Aburrá Valley.

Diagnostic criteria for latent tuberculosis

- Asymptomatic child.
- Normal clinical assessment, without clinical signs of active TB.
- Normal chest x-ray.
- Response to the tuberculin skin test (TST)  $\geq 5$  mm and / IGRA (QuantiFERON®-TB Gold Plus - QFT Plus) positive.

Inclusion criteria to start treatment for latent tuberculosis infection

- Having a diagnosis of latent tuberculosis or
- Being in immunological window period.

Exclusion Criteria:

Exclusion criteria for receiving treatment for latent tuberculosis

- Having symptoms or signs of active TB and that the disease has not been ruled out.
- Having basic liver disorder.

Exclusion criteria for performing induced sputum

- Having severe asthma.

## Contacts and Locations

---

**Contacts**

Dione Benjumea, Dr      573007759022      [dionebenjumea@gmail.com](mailto:dionebenjumea@gmail.com)

**Locations****Colombia**

Corporación para Investigaciones Biológicas

Medellín, Colombia

**Recruiting**

Contact: Diana Maldonado      5746051808      [coordinaciondeproyectos@cib.org.co](mailto:coordinaciondeproyectos@cib.org.co)

**Investigators**

Study Director:      Jaime Robledo, Dr      Corporacion para Investigaciones Biologicas

**More Information**

---

Responsible Party:      Corporacion para Investigaciones Biologicas

ClinicalTrials.gov Identifier: NCT04331262

Other Study ID Numbers:      68722

Last Verified:      August 2021

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD: No

Human Subjects Protection Review Board Status: Approved