Community-based rifapentine and isoniazid preventive treatment among household contacts of drug-susceptible tuberculosis patients in urban settings of Bangladesh: A Demonstration Project

Challenge TB Project Bangladesh
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CHALLENGE TB

Acknowledgments

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Acronyms and Abbreviations

3HP	once weekly dose of isoniazid rifapentine for three months
CTB	Challenge TB
CXR	chest X-ray
DOT	directly observed treatment
DSCC	Dhaka South City Corporation
DS-TB	drug-susceptible TB
INH	iso nicotinyl hydrazide (isoniazid)
IPT	isoniazid preventive treatment
MDR-TB	multidrug-resistant TB
NGO	nongovernment organization
NTP	National Tuberculosis Control Program
PT	preventive treatment
PTB	pulmonary TB
TB	tuberculosis
USAID	US Agency for International Development
WHO	World Health Organization

Executive Summary

In 2018, Bangladesh committed to enrolling 969,300 individuals on preventive treatment (PT) for tuberculosis (TB) by 2022. It is crucial to expand the PT program among all age groups at risk of developing TB. However, evidence on effective programmatic approaches for PT in resource-constrained settings like Bangladesh is lacking. We aimed to develop a feasible programmatic approach for PT in Dhaka, Bangladesh. Between February 2018 and January 2019, we enrolled 883 index pulmonary TB (PTB) patients from 12 directly observed treatment (DOT) centers under National Tuberculosis Control Program (NTP) in Dhaka. We enumerated household contacts of those index patients and counseled them to visit the selected health facilities for screening and evaluation. We performed symptomatic verbal screening for TB, clinical evaluation, and chest X-ray (CXR) among the contacts to rule out active TB. Individuals identified with TB were initiated on TB treatment at NTP treatment centers, and individuals who did not have TB were counseled to start PT. Household contacts who were ruled out as TB-free and consented to take part were enrolled for PT using a 12-dose weekly isoniazid and rifapentine (3HP) regimen at the community level and were followed through treatment completion. During the study period, 883 index PTB patients were counseled to bring eligible household contacts (n=3,193) to the health facility. Of these contacts, 2,149 (67%) visited the facilities. We performed CXR on 1,804 contacts (84%) to rule out active TB, and 39 (2%) were identified with TB and initiated treatment. We counseled 1,673 (93%) eligible contacts for PT and of those, 1,216 (73%) agreed and initiated PT using 3HP. The mean age of participants was 27, and 56% were female. Among the 1,216 who enrolled for PT, 1,175 contacts (97%) completed PT with no serious adverse events. No significant differences were observed for PT completion in terms of age, gender, education, occupation, or household income.

This study demonstrated that identification of potential household contacts for PT in urban areas and high treatment completion could be achieved through a well-designed, community-based program involving appropriately trained health workers. The awareness creation, counseling and rigorous follow-up, convenient weekly regimen, shorter treatment duration, and minimal adverse events are crucial to achieving higher PT adherence. The community-based approach of PT using 3HP seems feasible to scale up at the national level and can be used to reach the committed target for PT.

Contents

1. Introduction

1.1. Background

The primary mode by which TB spreads is person to person, and it is estimated that one person with TB can infect up to 15 individuals each year until that patient is started on treatment and rendered noninfectious. Studies have documented an infection rate of 30–50% among household contacts of infectious adults, while in children under 5, that rate can be as high as 72%.[1–4] Of those infected with TB, 10% develop the disease during their lifetime; the risk for those with living with HIV and not receiving antiretroviral treatment is 10–15%.[5,6] The rate of development of TB among infected household contacts under 5 years of age is between 15% and 20%.[7,8]

A World Health Organization (WHO) study by Dye et al. has shown that to meet WHO 2050 elimination targets, TB infection treatment will need to be incorporated in TB programs, as merely treating active disease will not result in a significant reduction in the burden given the large number of individuals infected with TB. These patients will continue to give rise to TB cases due to reactivation.[9] Both etiological routes of TB disease—prevention of transmission through early diagnosis and treatment of active disease and treatment of TB infection—will have to be addressed to significantly reduce the burden and move toward the elimination targets.

Individuals infected with TB but free from TB disease or individuals with a history of exposure who are at high risk of developing TB should receive TB PT to stop the progression from infection to disease.[10] People infected with TB are potential future active disease cases. Estimates suggest that roughly 10% of immunocompetent people infected with TB will eventually fall ill with active TB. Without treatment, approximately 5% of people with normal immune systems who have been infected with TB will develop the disease in the first two years after infection, and another 5% will develop the disease later in life.[11] Even if health systems could find and instantly treat every new TB patient, the epidemic would remain unchecked. Drastically shrinking the number of people who are infected with TB is the only way to eliminate the disease. This will require reducing the burden of infectious TB by early and active case finding; protecting people from exposure to the TB bacteria; and treating people who have been exposed to TB with PT, preferably with shorter regimens.

One of the most efficient uses of PT is in the context of household and other close contact investigations, which is a critical activity for TB programs for two reasons. First, it allows the efficient and early identification of others in a TB patient's home who are also sick with TB and require immediate treatment but may yet be undiagnosed and treated (missed cases). Second, it allows programs to efficiently identify others at home who may benefit from the treatment of latent TB infection to prevent its progression to disease and death.

According to the current NTP guidelines, only children younger than 5 and people living with HIV are eligible for isoniazid preventive treatment (IPT). The recommended PT now is isoniazid given daily for at least six months. However, PT completion rates are often low because of the long duration of treatment.[12] Recent WHO guidelines recommend shorter regimens that ease the burden on both patients and health systems. One of the recently recommended regimens is 3HP. This regimen has fewer adverse events and better treatment completion rates.[13–16] The experience with this regimen in a low-resource programmatic setting is lacking, but given once weekly dosing and higher completion

rates as observed in trials, it is expected to improve adherence and address the operational challenges with IPT.

Relevant to this project, WHO issued new recommendations:

1. PT of non-HIV-infected adult contacts in high-incidence settings
2. Use of 3HP in high-burden settings
3. A daily dose of isoniazid rifampicin for three months is an option for children and adolescents younger than 15 years in countries with a high TB incidence

There is useful information in these guidelines on adverse event risks and monitoring (including data and references) and ethical considerations, which provides a firm basis for the current project.

Bangladesh TB Perspective

Bangladesh is one of the world's 30 high TB burden countries, with an annual incidence of 364,000 cases and a treatment coverage rate (notified cases/estimated incidence) of 67%.[17] Approximately 59,000 people die of TB in Bangladesh each year. Another significant challenge is multidrug-resistant TB (MDR-TB), with an estimated 8,400 cases per year.[17] The findings from the 2015–16 National TB Prevalence Survey show large socioeconomic and geographic differences—TB prevalence rates are higher in urban areas (316/100,000) than in rural areas (270/100,000) and among men and the elderly.[18] These high rates of TB in urban areas and among high-risk groups may be due to overcrowded living conditions with poor housing in slum areas, high levels of poverty, and limited access to quality TB services. Based on this evidence, the 2018–2022 National Strategic Plan for TB calls for an approach that targets cities and at-risk populations.

Bangladesh has made significant progress in its fight to prevent, detect, and treat TB. The NTP of Bangladesh, along with its partners, has been maintaining good basic TB control services and has a 67% case detection rate and excellent treatment outcomes.[17] Despite promising achievements, an estimated 120,000 active TB cases remain missing every year in Bangladesh,[17] and addressing TB infection equitably and comprehensively is a challenge. This is particularly true in urban settings like Dhaka, where universal access to quality diagnostic services and treatment is overstressed by myriad factors, such as an influx of rural-to-urban migrants and the complexity of the urban health care infrastructure, with overlapping services from the public and private sectors and nongovernment organizations (NGOs) and a less clear patient pathway. Moreover, systematic information on TB transmission, treatment, and prevention, as well as a cascade of TB care for urban populations, is lacking. There is a crucial need to enhance case finding (specifically missing cases) and improve the care pathway of TB in urban settings. In addition to existing interventions, new perspectives and innovative ways of addressing TB treatment and control are needed as the disease persists.

In October 2017, the Government of Bangladesh, with support from the US Agency for International Development (USAID) and the Challenge TB (CTB) project, launched the Zero TB Cities Initiative with strong political commitment to end TB and signed a declaration with a call to action "uniting to make our cities TB free." To lay a strong foundation for the Zero TB Cities Initiative, the NTP and CTB undertook a set of activities focused on urban Dhaka to support the Government to better prevent latent TB infection from becoming active disease, identify missing TB patients, and treat them according to the national guidelines, thus saving lives. The urban TB initiative used the comprehensive, evidence-driven interventions of the search, treat, and prevent strategy. The initiative builds on existing

platforms and relies on multistakeholder engagement, including coalitions of local governments, businesses, civil society, and multiple funders under the leadership of the NTP.[19]

For the prevent aspect of the comprehensive search, treat, and prevent strategy, this demonstration project on PT was designed and based on the Ministry of Health and Family Welfare, Bangladesh, and the NTP's strategic priorities and followed extensive discussions with the key leadership at the Directorate General of Health Services, the NTP, and key stakeholders. A qualitative study on barriers to and facilitators of existing PT in Bangladesh was conducted prior to this demonstration project initiation and informed the development of the intervention package. Several meetings with key managers and technical experts at the NTP, including the line director, were held, and it was agreed to develop an effective intervention model for contact tracing and PT using 3HP.

1.2. Objectives

General objective:

- To inform the development of an effective programmatic approach to contact investigation and preventive treatment in Bangladesh based on the latest WHO guidelines for the management of latent TB infection and contact investigation

Specific objectives:

- To test the feasibility of phone calls and/or home visits and counseling efforts for contact investigation and preventive treatment among household contacts of index drug-susceptible TB (DS-TB) patients in an urban setting
- To measure the effectiveness of household contact investigation by introducing verbal screening and counseling interventions among all eligible household contacts of a selected sample of index DS-TB patients and detect additional positive TB patients early among target populations through proposed interventions
- To implement a 12-dose 3HP weekly regimen for treatment of TB infection among household contacts of index DS-TB patients and assess the uptake of the 3HP regimen
- To determine the completion rate of PT with 3HP by structured directly observed follow-up and counseling interventions

2. Methods

2.1. Design

A prospective intervention was conducted to quantify the effect of contact investigation and determine the acceptability of PT with 3HP among eligible household contacts of index DS-TB patients.

2.2. Setting

The project was implemented in zones 3, 4, and 5 of Dhaka South City Corporation (DSCC) and involved 12 NTP-linked TB treatment facilities (annex A) that treat TB disease as per the national guidelines and report data to the NTP.

2.3. Intervention Population and Geographical Coverage

The intervention group comprised 3,193 eligible household contacts of all 883 index DS-TB patients diagnosed and enrolled for treatment at the 12 selected NTP-linked TB treatment facilities between January and July 2018. The patients and their families lived and received treatment in DSCC zones 3, 4, and 5. The individuals enrolled for PT were followed up until treatment completion.

2.4. Implementation Period

February 2018 to May 2019.

2.5. Identification of At-Risk Populations

Inclusion criteria:

- Household contacts of a DS-TB patient diagnosed and enrolled for treatment at the NTP-linked TB treatment facilities between January and July 2018
- Household contacts of a DS-TB patient receiving treatment from an NTP-linked TB treatment facilities and residing in DSCC zone 3, 4, or 5
- All age groups excluding 0 to 2 years old

Exclusion criteria:

- Already receiving TB disease treatment at the time of the initial household contact investigation
- Women who are pregnant or expect to become pregnant within the implementation period

2.6. Sample Size and Enrollment

A purposive sample of all individuals with DS-TB who were newly diagnosed and registered with 12 NTP-linked TB treatment facilities for TB treatment between January and July 2018 were considered eligible for this study. During this period, 883 individuals newly diagnosed with DS-TB were selected

from these 12 treatment centers and enlisted with contact details (address and mobile phone number) by the project field workers/supervisors.

The field supervisor interviewed each index patient by phone to enumerate the household contacts and encouraged them to bring their household contacts to the nearest health facility for contact screening and clinical evaluation (figure 1).

The project treatment counselors also contacted the index TB patients by phone, counseled them about the need for screening and evaluation, and requested them to bring their family members to the selected health facility for contact screening and subsequent clinical evaluation. Once contacts arrived at the facility, the counselors conducted verbal screening for the presence of TB symptoms, and the medical officer conducted a clinical assessment. Based on the advice of the doctor, the contacts were tested by GeneXpert (if sputum was available) and CXR to rule out TB disease as per the NTP protocol. When active TB disease was detected, project field staff connected the patient with an NTP-linked TB treatment facility close to his or her home for treatment initiation.

Contacts who did not have active TB were informed and counseled by the treatment counselor to take PT with 3HP. Individual contacts were given the opportunity to ask questions during the counseling process and to discuss the program with other family members and friends before agreeing to initiate PT. Individuals with a previous history of treatment, project staff, and NGO staff reviewed the NTP records to identify previous treatment and outcome before starting PT. If the individual had not completed treatment, was not declared cured/treatment completed, or did not have documented proof, he or she was referred to the TB treatment unit for further evaluation before being cleared for PT.

In instances where the household contacts did not come for evaluation or were reluctant to come within one week of the index patient diagnosis, the project counselors made at least three reminder phone calls, followed by household visits by NGO health workers.

2.7. Providing Treatment

The household contacts who were willing to participate in the project and met the inclusion criteria were considered eligible. Before treatment initiation, the counselor counseled each eligible contact and the parents of eligible children regarding the effectiveness of treatment; its benefits, potential side effects, and safety; and the importance of completion.

The project physician then prescribed eligible contacts over two years of age with 3HP (table 1).

Table 1. PT regimen for contacts of susceptible TB patients*

Age	Drug(s)	Dose	Duration
>2–15 years	INH and rifapentine	INH: 15mg/kg Rifapentine: 300-450mg	Once weekly for 12 weeks
15 years and older	INH and rifapentine	INH: 15mg/kg Rifapentine: 450–900mg	Once weekly for 12 weeks

***WHO** latent tuberculosis infection updated and consolidated guidelines for programmatic management, 2018.

The process flow for TB treatment and PT in the project is shown in figures 1 and 2.

Figure 1. The process of treatment for TB disease and preventive treatment

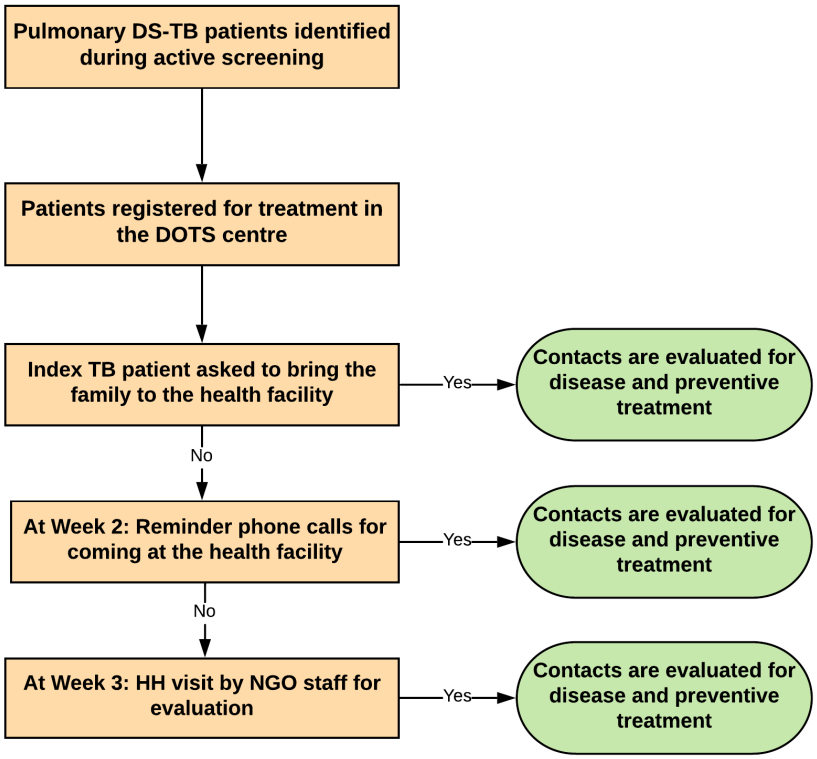
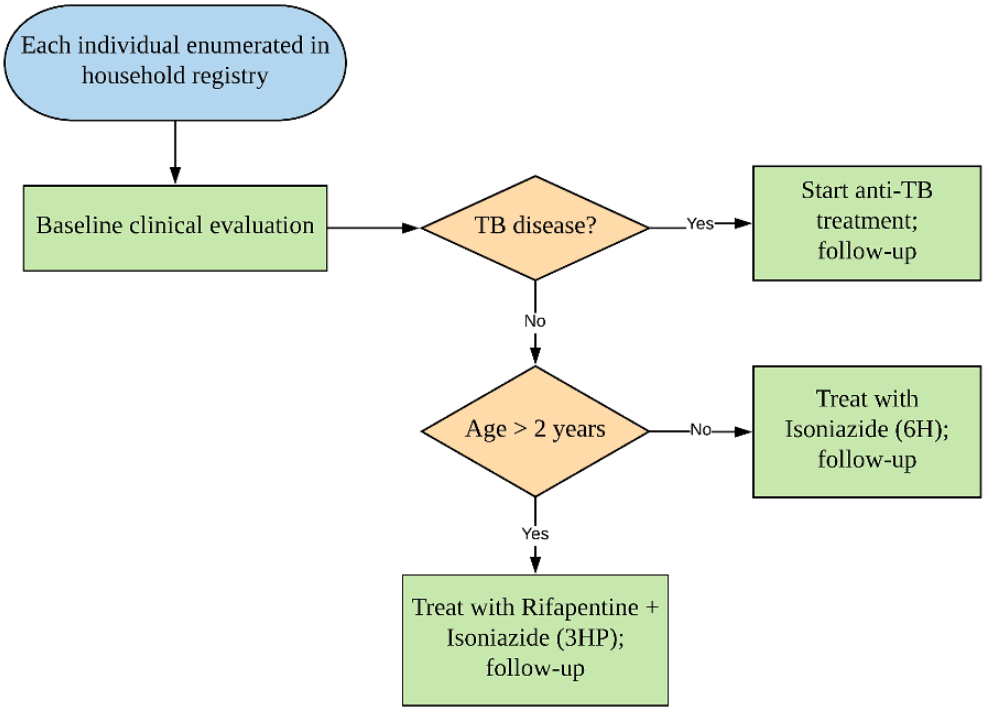


Figure 2. Treatment of TB disease and infection in exposed households



2.8. Monitoring Treatment Adherence and Adverse Events

Project staff routinely monitored the individuals receiving treatment during monthly visits and explained the disease process, the treatment rationale, and the importance of completing treatment. Participants receiving 3HP were advised to contact their health care provider at any time and to immediately stop PT if they experienced symptoms such as anorexia, nausea, vomiting, abdominal discomfort, persistent fatigue or weakness, dark-colored urine, pale stools, jaundice, cutaneous reactions, hypersensitivity reactions, or gastrointestinal intolerance.

- An NGO volunteer treatment supporter visited the participant at home weekly for DOT.
- The volunteer treatment supporter was trained to recognize signs of typical 3HP adverse events and to refer patients to appropriate care.
- Project treatment counselors called the person taking infection treatment on the day the medication was due and the day after the medication was supposed to be taken to ensure that dosages were not missed.
- Project field supervisors visited all households monthly, quantified adherence, inquired about adverse events, and recorded the results on forms developed by CTB.
- If either the treatment supporter or field supervisor identified a possible adverse event, they immediately referred the participant to the hospital for clinical evaluation.
- Contacts on the 3HP regimen were encouraged to visit every month for follow up evaluation by a physician and counselor until the end of PT.
- The health provider and/or treatment counselor recorded all adverse events using standardized data collection tools.

2.9. Field Team and Data Collection

A field team that included field supervisors, treatment counselors, and a physician was engaged to identify eligible household contacts and initiate PT. The field supervisors collected the list of index TB patients from the selected facilities and enumerated the household contacts. The treatment counselor then counseled the index TB patients and the household contacts on the risk of developing TB and the importance of PT. The physician ensured that all the contacts were clinically evaluated and either ruled out as not having active TB disease or initiated on PT.

A local NGO that has community-based health programs in the intervention areas was also involved in this project. The NGO health workers were engaged specifically for raising community awareness on PT, performed household visits, and facilitated hospital visits of household contacts for initial evaluation and during PT. Along with their routine household visits, they also followed up with individuals on PT for adverse drug reactions and immediately reported any adverse events to the project medical officer.

The field team and NGO health workers received training from the project before they were engaged in the process. Training sessions included orientation on PT, algorithms related to verbal screening, counseling, clinical and laboratory evaluations, treatment regimen, and follow-up during PT.

2.10. Data Collection Instruments

The data were collected using structured and semistructured questionnaires. Data are presented in a cascade of steps with indicators measuring the proportion of people moving from one step to the next (figure 3). The indicators measure the steps from the identification of index patients to household contacts evaluated for TB disease and started and completed 3HP to determine the acceptability and to quantify the effect of contact investigation and PT among the target sample.

2.11. Data Analysis

All data were analyzed using the Statistical Package for Social Sciences, version 20 (SPSS Inc., Chicago, IL, USA). The data were cleaned for entry errors, and any missing values were entered before conducting the analysis. The descriptive statistics were used to report the data. Age-adjusted PT completion with a 95% confidence interval (CI) was calculated for the whole sample. A p-value of <0.05 was considered significant.

2.12. Ethical Considerations

The formal ethical approval for this study was obtained from the Bangladesh Medical Research Council (Registration Number 127 14 06 2018). In addition, this demonstration project was approved by the National TB Technical Committee of the NTP. Written informed consent for participation was obtained by project staff prior to enrollment into the study from adults and from guardians/parents of children. All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee. All participants enrolled in this study received free services, including investigation and PT with 3HP.

3. Results

During the study period, we enumerated household contacts of 883 index patients and counseled all 3,193 contacts to visit the health facility. A total of 2,149 (67%) contacts visited the health facilities through the combined efforts of phone calls, counseling, and household visits by project staff and NGO workers. We performed CXR on 1,804 contacts (84%) to rule out active TB and identified 131 (7%) who were ineligible for preventive treatment with 3HP. Among those, 39 (2%) contacts had active TB, and we initiated treatment for all of them through NTP-linked treatment facilities. Further, 92 (5%) children aged under age 2 were enrolled for routine IPT. We identified 1,673 (93%) eligible contacts and approached all of them about PT using 3HP. We initiated PT for the 1,216 (73%) contacts who agreed. Of those on 3HP, 1,175 contacts (97%) completed PT. Among the 41 (3%) contacts who did not complete PT, 32 (78%) refused after treatment initiation, 6 (15%) migrated out to a different area where the intervention was not available, and the remaining 3 (7%) had 3HP stopped by the physician.

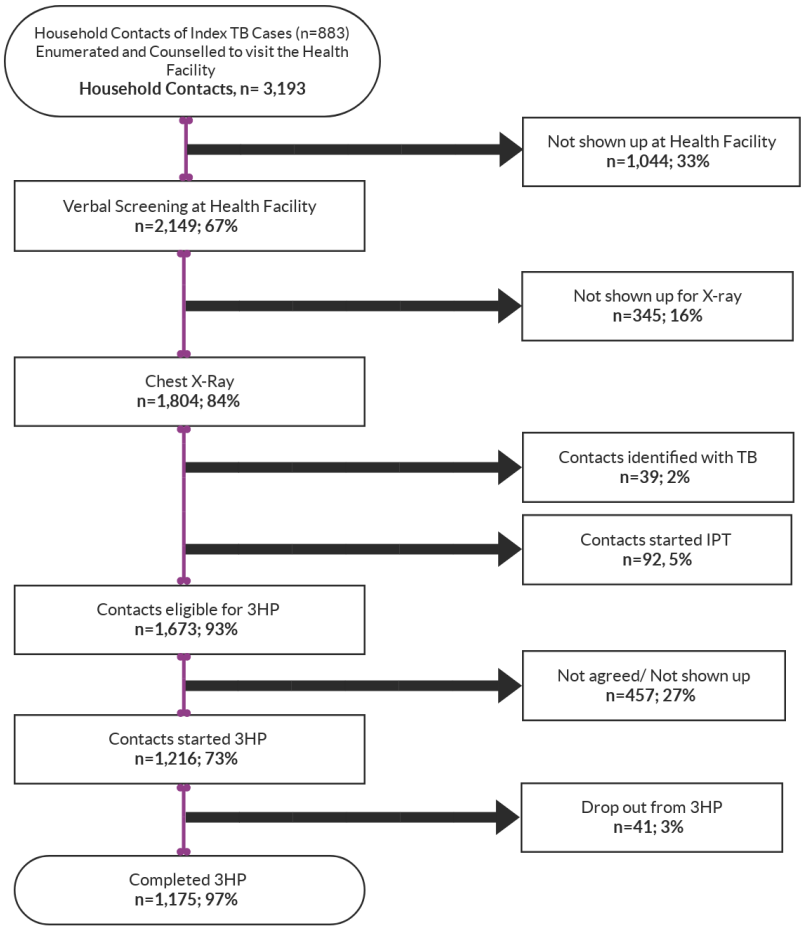


Figure 3. The care cascade of participants taking 3HP through the demonstration project

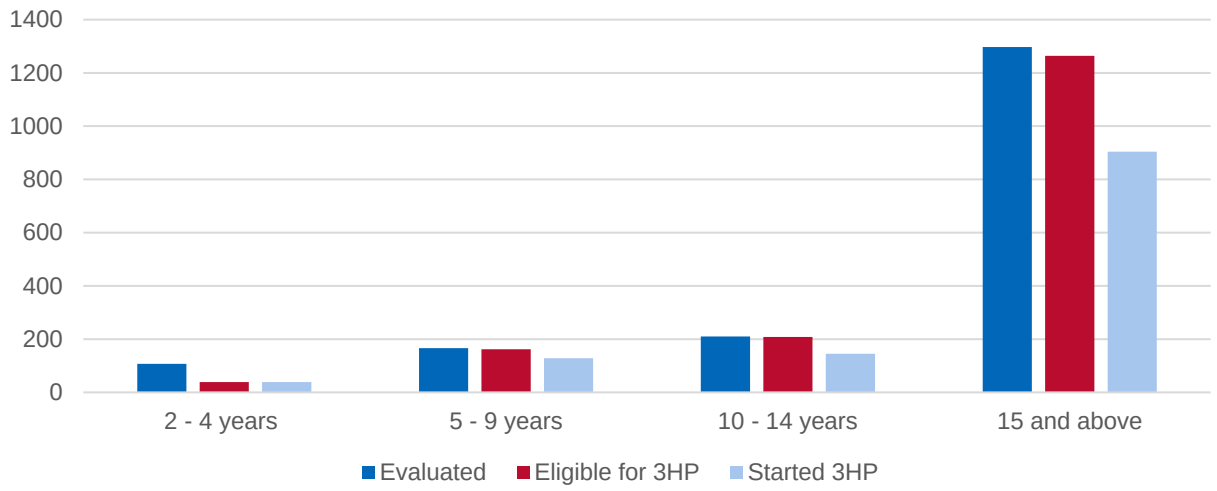
Table 2 shows the sociodemographic characteristics of household contacts verbally screened at the health facilities and household contacts who initiated PT. The mean age of the contacts was 21 for those who were verbally screened and 27 for those who initiated PT. Among those verbally screened, 46% were male and 54% were female, and of those who initiated PT, 44% were male and 56% were female. Regarding type of TB, 25% were bacteriologically positive and 13% were clinically diagnosed. Diabetes was the predominant comorbidity among contacts. It was observed that the majority of contacts needed two phone calls from the project staff to get them to the facilities for verbal screening.

Table 2. Sociodemographic profile of household contacts of index TB patients verbally screened (n=2,149) and enrolled for PT (n=1,216)

	Household Contacts Verbally Screened (n=2,149)	Household Contacts Initiated PT (n=1,216)
Age		
Mean age, SD	21	27
2–4	65 (3%)	40 (3.3%)
5–9	193 (9%)	127 (10.4%)
10–14	291 (13.5%)	145 (12%)
15 and above	1,600 (74.5%)	904 (74.3%)
Gender		
Male	971 (45.2%)	541 (44%)
Female	1,178 (54.8%)	675 (56%)
Type of TB in index PTB patient		
Contacts of bacteriologically positive TB index	2,006 (93%)	1,186 (97.5%)
Contacts of clinically diagnosed TB patients	143 (7%)	30 (2.5%)
Comorbidity		
No comorbidity	1,472 (68.5%)	1,194 (98.2%)
Diabetes mellitus	35 (1.6%)	16 (1.3%)
Hypertension	469 (22%)	4 (0.3%)
Asthma	14 (0.7%)	1 (0.1%)
Thyroid dysfunction	159 (7.4%)	1 (0.1%)

The age breakdown of household contacts enrolled on 3HP shows that that majority of contacts who were clinically evaluated, found eligible, and initiated PT were 15 years and older (figure 4).

Figure 4. Age breakdown of household contacts evaluated, eligible for, and initiated on 3HP treatment, February 2018–January 2019



The intervention efforts applied for contact investigation and PT enrollment showed that the majority of household contacts who were contacted/approached came to the health facilities for verbal screening based on phone calls made to the index patients by the project staff (59.2%) (table 3).

Table 3. Uptake of contact investigation and preventive treatment by type of interventions

Interventions applied	Total HH contacts N=3,193	HH contacts conducted verbal screening n (%)	Performed CXR after verbal screening n (%)	Household contacts received preventive treatment after CXR n (%)
Phone calls only	3,193	1,890 (59.2%)	1,705 (90.2%)	1,150 (67.4%)
Phone calls and counseling	1,303	196 (15.0%)	80 (40.8%)	54 (67.5%)
Phone calls, counseling, and home visit	1,107	63 (5.7%)	19 (30.2%)	8 (42.1%)
	Total	2,149 (67.3%)	1,804 (83.9%)	1,216 (67.4%)

Second to this was a combined phone calls and counseling efforts conducted by project staff and treatment counselors (15%). A combination of phone calls, counseling, and home visit efforts by project staff, treatment counselors, and NGO health workers was required to bring in 5.7% of the contacts for contact investigation and verbal screening.

The project team enumerated 3,193 household contacts of 883 enlisted index TB patients and counseled them for verbal screening. CXR was performed on 84% (1,804 out of 2,149) of the contacts who were verbally screened to rule out active TB. Of those, 1,673 (93%) contacts were found to be eligible and 1,216 (73%) initiated treatment. The overall adherence and treatment completion rate was 97% (1,175) among the household contacts enrolled for PT (table 4).

Table 4. Cascade data on contact investigation, screening, evaluation, and enrollment for and completion of preventive treatment (February 2018–January 2019)

Indicators	n/Total	%
Household contacts enumerated and counseled to visit health facilities		3,193
Undergone verbal screening	2,149/3,193	67
CXR performed	1,804/2,149	84
Contacts identified with active TB	39/1,804	2.2
Contacts eligible for 3HP	1,673/1,804	93
Contacts started 3HP	1,216/1,673	73
Contacts completed 3HP	1,175/1,216	97

Table 5 illustrates the results of analyses examining the associations between PT completion and demographic variables of the respondents. PT completion was found to be slightly higher among those between 5 and 15 years of, women, and participants with low household income. Surprisingly, the completion rate was also higher among participants with no formal education. However, none of these demographic variables were statistically significant.

Table 5. Factors associated with treatment completion among household contacts

Variables	Number of contacts completed treatment/total enrolled[a]	% of contacts completed treatment (95% CI)[a]	*P* value
Age (years)			
Below 5	39/40	97.5 (92.7–102.3)	
Below 15	265/272	97.4 (95.5–99.3)	.657
15 and above	871/904	96.6 (95.1–97.6)	
Gender			
Male	518/541	95.8 (94.0–97.5)	
Female	657/675	97.3(96.1–98.5)	.128

Variables	Number of contacts completed treatment/total enrolled[a]	% of contacts completed treatment (95% CI)[a]	*P* value
Education			
No education	64/66	97.0 (92.8–101.1)	
Primary or less	327/336	97.3 (95.6–99.1)	.857
Secondary and above	784/814	96.3 (95.0–97.6)	
Household Income (Taka)			
Below 10,000	4/4	100 (100–100)	
10,000 and above	1,171/1,212	96.6 (95.6–97.6)	.708
Occupation			
Self-employed and business	135/138	97.8(95.4–100.3)	
Service	223/232	96.1 (93.6–98.6)	
Unemployed	10/10	100 (100–100)	
Housewife	330/341	96.8 (94.9–98.7)	.933
Student	444/461	96.3 (94.6–98.0)	
Dependant child	33/34	97.1(91.4–102.7)	

[a] Proportions and P-values derived from Chi-squared/Fisher's exact test (computing row percentages among the variables).

Among the household contacts enrolled for PT, 3% (n=41) did not complete the treatment. The most common reason for noncompletion of PT was refusal to continue treatment due to side effects or fear of side effects (n =32, 78%). Furthermore, 14.6% migrated to areas where 3HP intervention was not available. Only a small proportion (n=3, 7.3%) were advised by a doctor to stop treatment due to unusual events experienced during PT (table 6).

Table 6. Reasons for noncompletion of preventive treatment

	Total N (%)
Refused after treatment initiation due to side effects	32 (78%)
Treatment not completed due to out migration	6 (14.6%)
PT stopped by physician due to unfavorable events	3 (7.3%)
Total	41

Only 65 (5%) household contacts experience adverse events during the entire course of treatment (table 7). There were no major adverse events or any hospitalization reported among the enrolled household contacts. For all reported adverse events, only symptomatic management resolved the presenting issues. Most of the adverse events were reported in patients 15 years of age and older (51, 78%) and among females (35, 54%). Among the self-reported adverse events, the prevalent symptoms were weakness (22, 34%) and vomiting (21, 32%). Of the three contacts who stopped PT due to suggestion from the physician, one was hypertensive and had poor adherence to antihypertensive medication and two female patients had altered menstrual cycles.

Table 7. Adverse events among household contacts while on 3HP PT in Dhaka city, February 2018–January 2019

Variables	Household Contacts Reported Adverse Events (n=65)
Age (in years)	
2–4	1 (2%)
5–9	7 (11%)
10–14	6 (9%)
15 and above	51 (78%)
Gender	
Male	30 (46%)
Female	35 (54%)
Frequency symptoms	
Weakness	22 (34%)
Vomiting	21 (32%)
Nausea	17 (26%)
Dizziness	12 (18%)
Flu-like symptoms	11 (17%)
Headache	8 (12%)
Itching	3 (5%)
Shortness of breath	3 (5%)

We estimated the cost of systematic contact evaluation and provision of PT with 3HP for contact ages 5 and above over a 12-month period. Children under 5 years of age were given IPT as per the national program guidelines and were not included in the current cost estimate. Of the 3,193 household contacts, 2,149 were evaluated for TB disease and 1,216 were initiated on PT (table 8).

The costs were calculated from the program's perspective (table 9). We had 8 full-time project staff and 20 part-time NGO personnel working to support the patients. We paid the monthly salary for all full-time staff (one medical officer, two field supervisors, three treatment counselors, one field operations manager, and one data research associate). Part-time staff costs included travel allowance provided to health workers who supported patients through household visits.

Project operational costs, such as training of all personnel, preparatory and data sharing meetings with NTP and stakeholders, and transport for project personnel to follow up with patients at home, were included. To rule out TB disease during systematic contact evaluation, all household members were asked for a CXR and other test as suggested by the hospital medical officers. Most of the investigation costs were borne by the project.

The actual cost of android phone-based electronic data collection tool development, including mobile phones and internet bills, incurred by the project were also included in the costing analysis.

Table 8. Household contacts evaluated and initiated on preventive treatment

Number of index patients	883
Household contacts enumerated	3,193
Household contacts verbally screened	2,149
Household contact evaluated	1,804
Household contacts diagnosed with TB	39
Household contacts initiated on preventive treatment	1,216

Finally, the actual cost of rifapentine procurement from the Global Drug Facility and the associated shipment costs as incurred by the project were included. We also included the cost of isoniazid even

though the project received it free from the NTP. Data were extracted/collected from the project's financial records and analyzed in Microsoft Excel. The costs were estimated in Bangladesh Taka and converted into US dollars (conversion rate used USD 1=BDT 83). [20]

Table 9. Cost of household contact investigation and preventive treatment with 3HP in Bangladesh

Cost Categories	Program costs (USD)	N used for each cost category (N)	Cost per household contact evaluated and initiated on preventive treatment (USD)
Personnel	84,705	2,149	39
NGO staff stipend	9,253	2,149	4
Transport and communication allowance	11,219	2,149	5
Training	2,248	2,149	1
Mobile app development cost	2,235	2,149	1
Equipment (mobile phone, laptop, printer)	9,806	2,149	5
TB diagnostic investigations	14,215	1,804	8
Rifapentin procurement and shipment	62,579	1,216	51
INH procurement	1,882	1,216	2
Project cost and cost per household contact evaluated and initiated on preventive treatment	198,142		116

Cost Implications for Scale Up

We believe that the cost per patient evaluated and initiated on treatment if scaled in Bangladesh will be lower than in the pilot. This is primarily due to human resources that already exist within the government system and through the Global Fund grant. Additional personnel such as treatment counselors may be recruited if needed. The data collection application has been developed by the project, so the NTP will only incur a one-time cost of integrating it into the DHIS2 system. The costs of the TB investigation were supported through the project. In the current program, smear microscopy and GeneXpert tests are provided free by the government; however, CXR, which is used to rule out TB among household contacts, is an out-of-pocket expenditure. The NTP may need to evaluate this and consider building the cost of CXR into its budget so it is not a barrier for household contact evaluation.

4. Discussion

The convenient weekly regimen and shorter treatment duration were preferred and played an important role in the decision of household contacts to accept the initiation of PT. The programmatic interventions, which included counseling of index TB patients and their families on the importance of PT, reminder phone calls to take the medication, and home visits from the community health workers to support treatment adherence resulted in a 97% PT completion rate. The adverse events from the PT regimen were few, which also contributed to the limited drop-outs.

Several other studies that included a shorter PT regimen showed better completion rates. One study reported fewer drop-outs from PT using 3HP even after having higher incidence of adverse events compared to PT using isoniazid. Involvement of community health workers in treatment adherence was found to be beneficial in other settings too.

The majority of the contacts who initiated PT were adults, but in the national program we do not provide PT to adults. This demonstration project revealed that adults are ready to take PT when prescribed by the physicians. We observed a higher percentage of women initiating PT. It is encouraging to see that women were free to participate in the PT program as there is a perception in the community that the head of household plays a crucial role in the health care seeking behavior of female family members.

The NTP should consider the preference and compliance of the contacts who will be enrolled for PT. The completion of PT needs to be ensured when it is initiated. The benefits of PT outweigh the potential harm that can result from the side effects of the PT drugs. A weekly regimen using 3HP was found to be feasible as a self-administered treatment procedure as direct observation could be a barrier to implementation.

Prevention of active TB disease by PT is a critical component of the WHO End TB Strategy. With the commitments made during the United Nations High-Level Meeting to treat more than 900,000 individuals with PT, it is essential to expand the current PT practice in all age groups. With the feasibility of using 3HP under this project, it is well demonstrated that this can be considered a means to achieve this target. Considering the high completion rate of PT among the study sample, the cascade of care for managing the household contacts who initiated PT and also the interventions implemented to support the PT can be adopted by the national program.

5. Conclusions and Recommendations

This study demonstrated that identification of potential household contacts for PT in urban areas and high treatment completion could be achieved through a well-designed, community-based program involving appropriately trained health workers. The awareness creation, counseling and rigorous follow-up, convenient weekly regimen, shorter treatment duration, and minimal side effects are crucially important to achieve a higher PT adherence. The community-based approach of PT using 3HP seems feasible to scale up at the national level and can be used to reach the committed target for PT.

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7. Annex I

7.1. LIST OF HEALTH FACILITIES

Hospital-Based DOT Corners

1. Dhaka Medical College and Medical Hospital, Dhaka
2. Sir Sallimullah Medical College and Medical Hospital, Dhaka
3. Dhaka National Medical College Hospital, Dhaka
4. Sharkari Karmachari Hospital, Dhaka
5. Mugda Medical College and Medical Hospital, Dhaka
6. Holy Family Red Crescent Medical College, Dhaka

NGO Clinics

1. Concern Women for Family Development, Begumganj
2. Concern Women for Family Development, Doyaganj
3. Concern Women for Family Development, Gandaria
4. Concern Women for Family Development, Lalbagh
5. Concern Women for Family Development, Rayerbazar
6. Concern Women for Family Development, Wari