Subpopulations at Risk for Not Completing Once Weekly 12-Dose Regimen of Isoniazid plus Rifapentine for Treatment of Latent Tuberculosis Infection in United States TB Programs.

Nwabunie Nwana[1], Christine Ho[1], Amy Sandul[1], Sapna Morris[1], Suzanne Marks[1], and the 3HP Post-Marketing Group

[1]Division of Tuberculosis Elimination, Centers for Disease Control and Prevention (CDC), Atlanta, GA

Background

- Approximately 5–10% of persons infected with *Mycobacterium tuberculosis*, a condition known as latent tuberculosis infection (LTBI), will eventually develop active tuberculosis (TB) disease.
- Treatment of persons with LTBI is an important strategy for preventing progression to TB disease.

Objective

- To describe rhe risk of not completing treatment and associated characteristics in patients receiving 12 weekly, directly observed doses of isoniazid and rifapentine (INH-RPT) for LTBI treatment.
- To determine treatment discontinuation rates, and factors associated with discontinuing treatment.

Methods

- A prospective observational cohort of patients diagnosed with LTBI at 16 sites started treatment on INH-RPT between July 1, 2011, and December 31, 2013.
- Patients who were HIV-infected on anti-retroviral treatment, contacts to a TB patient having drug-resistant TB disease, diagnosed with active TB, or had a negative quantiFERON-TB Gold (QFT) test results were not eligible for treatment with INH-RPT and were excluded from analysis.
- Sites worked with CDC to develop patient-care data collection forms.
- Demographic information, treatment reason, and symptoms at each dose were collected from all eligible patients receiving directly-observed INH-RPT.
- At 10 of 16 sites, additional data on medical and social risk factors were collected.
- All patients who received treatment were monitored for adverse events (AE) using a standardized questionnaire.
- Treatment completion was defined as receipt of at least 11 of 12 doses of INH-RPT over 16 weeks.
- Data were entered into a Microsoft Access database and analyzed using SAS 9.3.
- We conducted descriptive analyses and reported relative risk (RR) associations with treatment discontinuation and their 95% confidence intervals (CI).

Contact Information

Nwabunie Nwana, MPH
Division of Tuberculosis Elimination
Centers for Disease Control and Prevention
MS E-10 , Atlanta, GA 30329
Phone no-404-639-8101
E-mail-vzv1@cdc.gov

Results

Figure 1. Flowchart of patients, July 1st 2011 – December 31st 2013, 16 sites

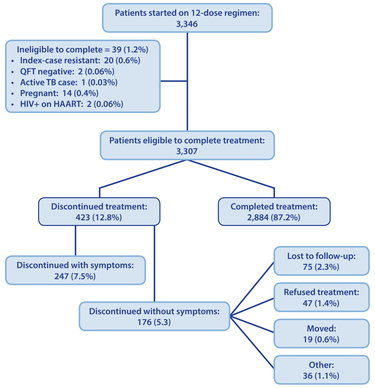
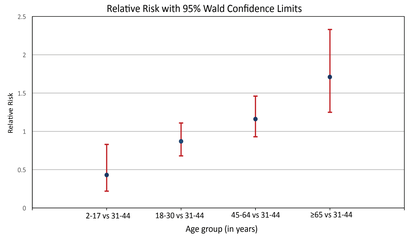
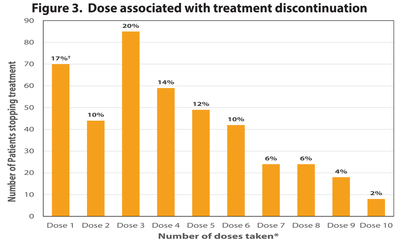


Figure 2. Association of age with treatment discontinuation



- 3346 patients started the regimen. 3307 were eligible to complete; of whom, 2400 provided data on medical and social risk factors.
- The overall treatment discontinuation rate was 13% (423/3,307) (Figure 1).
- Among patients starting treatment, 8% (247/3307) discontinued due to an AE attributed to the regimen (Figure 1). The median dose after which treatment was stopped was 4 doses (IQR: 2, 6) (Figure3).
- The risk of discontinuing treatment increased with age (Figure 2).
- Nausea was the most commonly reported symptom (Figure 4).
- The risk of discontinuation was greater for persons experiencing homelessness in the prior 12 months [ARR=1.71; 95% CI: 1.23-2.37], aged ≥ 65 [ARR=1.52; 95% CI: 1.11-2.09], incarcerated in the prior 12 months [ARR=1.35; 95% CI: 1.03-1.76], or had a history of smoking [ARR=1.41; 95% CI: 1.14-1.75].
- Persons having recent contact to an infectious TB patient [ARR=0.69; 95% CI: 0.53-0.90)] and students [ARR=0.41; 95% CI: 0.21-0.98] were more likely to complete treatment.
- There were no reported deaths during treatment.

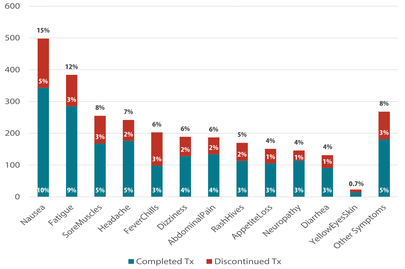
Figure 3. Dose associated with treatment discontinuation



*Patients who stopped therapy after dose 11 qualified as having completed treatment.

†Of all patients who stopped treatment (n=423), proportion that stopped at that dose.

Figure 4. Reasons for discontinuing INH-RPT treatment



†"Other" symptoms reported by one or more patients include: Dermatological-related Symptom, Gastro-Intestinal related Symptoms, Cough, Mental Health Symptom, Weight Loss, Blurred Vision, Flu-like Symptoms, Breathing Problem, Back Pain, Gynecological-related Symptoms, Chest Pain, Diaphoresis, Angioedema, Bleeding, Palpitation, Ease Bruising, Edema, Neurologic Symptoms, Hypotension, Flushing, Red Eyes, URI, Genitourinary Symptoms, Other Eye Symptom, Black Stool, Pain, Pneumonia, and Sepsis.

*Patients can have more than one symptom

Table 1. Patient profile, and analyses of factors associated with treatment discontinuation

Characteristic	N=3,307 (%)	Number of patients not completing (%)	Univariates and Multivariate Analyses of Factors Associated with Treatment Discontinuation			
			RR (95%) CI)	p value	Adjusted RR (95% CI)	p value
Gender						
Male	1,768 (53.5)	211 (11.9)	0.87 (0.73, 1.04)	0.1141		
Female	1,539 (46.5)	212 (13.8)	reference			
Age Categories (years)						
Median [IQR]	36 [26, 50]					
(2-17)	167 (5.1)	9 (5.4)	**0.43 (0.22, 0.83)**	**0.0118**	0.55 (0.28, 1.07	0.0767
(18-30)	1,037 (31.4)	113 (10.9)	0.87 (0.68, 1.11)	0.2544	0.86 (0.68, 1.11)	0.2294
(31-44) REF	957 (28.9)	120 (12.5)	reference		reference	reference
(45-64)	945 (28.6)	138 (14.6)	1.16 (0.93, 1.46)	0.1893	1.03 (0.83, 1.30)	0.7447
≥65	201 (6.1)	43 (21.4)	**1.71 (1.25, 2.33)**	**0.0008**	**1.52 (1.11, 2.09)**	**0.0094**
Race/Ethnicity						
Hispanic	754 (22.9)	69 (9.2)	0.84 (0.61, 1.17)	0.3072	0.88 (0.63, 1.25)	0.4819
Non-Hispanic White	729 (22.1)	127 (17.4)	**1.60 (1.20, 2.14)**	**0.0013**	1.22 (0.90, 1.66)	0.1983
Non-Hispanic Black	1,200 (36.4)	161 (13.4)	1.23 (0.93, 1.63)	0.1406	0.89 (0.65, 1.20)	0.4424
Asian REF	543 (16.5)	59 (10.9)	reference		reference	reference
Other	74 (2.2)	7 (9.5)	0.87 (0.41, 1.83)	0.7154	0.80 (0.38, 1.69)	0.5594
Treatment Reason†						
Contact	827 (25.0)	71 (8.6)	**0.60 (0.47, 0.77)**	**<0.0001**	**0.69 (0.53, 0.90)**	**0.006**
Converter	806 (24.4)	131 (16.2)	**1.39 (1.15, 1.68)**	**0.0007**		
Corrections	519 (15.7)	66 (12.7)	0.99 (0.78, 1.30)	0.956	**1.35 (1.03, 1.76)**	**0.0317**
Homeless	181 (5.5)	34 (18.8)	**1.51 (1.10, 2.07)**	**0.0109**	**1.71 (1.23, 2.37)**	**0.0014**
Foreign-born	1,237 (39.2)	126 (9.7)	**0.66 (0.54, 0.80)**	**<0.0001**		
Refugee	132 (4.0)	19 (14.4)	1.13 (0.74, 1.73)	0.5705		
Health Care Worker	502 (15.2)	84 (16.7)	**1.38 (1.11, 1.72)**	**0.0036**		
Student	130 (3.9)	7 (5.4)	**0.41 (0.20, 0.85)**	**0.0165**	**0.45 (0.21, 0.98)**	**0.0434**
Employment	213 (6.4)	32 (15.0)	1.19 (0.85, 1.66	0.308		
Long-term Care Facility Resident	47 (1.4)	6 (12.8)	1.00 (0.47, 2.12)	0.9959		
Any Poprisk	1,540 (46.6)	220 (14.3)	**1.24 (1.04, 1.49)**	**0.0165**		
Medical Conditions†	**N=2400 (%)**					
Diabetes	177 (7.4)	29 (16.4)	1.20 (0.85, 1.70)	0.3099		
Chronic Renal Disease	30 (1.3)	6 (20.0)	1.45 (0.70, 2.99)	0.314		
Immunocompromised	91 (3.8)	9 (9.9)	0.70 (0.38, 1.32)	0.2752		
Hepatitis	59 (2.5)	13 (22.0)	1.61 (0.99, 2.63)	0.0565		
Chronic Lung Disease	78 (3.3)	19 (24.4)	**1.80 (1.20, 2.70)**	**0.0043**		
Mental Health Problems	127 (5.3)	28 (23.0)	**1.64 (1.17, 2.32)**	**0.0046**		
Hypertension	305 (12.7)	44 (14.5)	1.05 (0.78, 1.41)	0.7651		
Other Medrisk	572 (23.8)	90 (15.7)	0.82 (0.63, 1.07)	0.1437		
Any Medrisk	777 (32.4)	126 (16.2)	**1.27 (1.04, 1.56)**	**0.0212**		
Behavioral Risk Factors†						
Alcoholism	211 (8.8)	35 (16.6)	1.22 (0.88, 1.68)	0.2268		
Current or Past Smoker	537 (22.4)	102 (19.0)	**1.53 (1.24, 1.89)**	**<0.0001**	**1.41 (1.14, 1.75)**	**0.0015**
IDU Drug Use	22 (0.9)	5 (20.8)	1.51 (0.69, 3.31)	0.305		
Non-IDU Drug Use	157 (6.5)	28 (17.8)	1.31 (0.92, 1.86)	0.1305		
Any Substance risk	664 (27.7)	120 (18.1)	**1.47 (1.20, 1.81)**	**0.0002**		

Abbreviations: N: number of respondents for the indicated factor; CI: Confidence Interval; RR: relative risk; ARR: adjusted relative risk;

‡ Not mutually exclusive; Bolded confidence intervals indicate a statistically significant association at the .05 significance level; Univariate analyses test the association between the indicated factor and discontinuation of 3HP; Multivariate analyses for demographic factors and treatment indications show the association between the indicated factor and discontinuation of 3HP while controlling for all other factors listed in the model and the potential effect of the site; Multivariate analyses for medical conditions and behavioral risk factors show the association between the indicated factor and discontinuation of 3HP while controlling for age.

† Denominator is patient count for standard and comprehensive tiers, N = 2,400

Conclusions

- The use of directly observed INH-RPT to treat LTBI resulted in a low treatment discontinuation rate (13%).
- Homeless persons, older adults, persons with history of incarceration, and smokers were at greater risk for discontinuation of LTBI treatment. Nevertheless, treatment completion rates in these subpopulations were high.

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Division of Tuberculous Elimination

CS260079-A