Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

Int J Tuberc Lung Dis. Author manuscript; available in PMC 2024 November 26.

Published in final edited form as:

Int J Tuberc Lung Dis. 2024 November 01; 28(11): 521–526. doi:10.5588/ijtld.23.0599.

Reasons for acceptance or nonparticipation in iAdhere: a trial of latent TB infection treatment

K.N. Chapman Hedges[1], **N. Scott**[1], **R. Belknap**[2], **S.V. Goldberg**[1], **M. Engle**[3], **A. Borisov**[1], **J. Mangan**[1]

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

[2]Public Health Institute at Denver Health, Denver, CO, USA

[3]University of Texas Health Science Center at San Antonio, Division of Infectious Diseases, San Antonio, TX, USA.

SUMMARY:

BACKGROUND: Understanding the motivations behind clinical trial participation can help enhance recruitment strategies and determine the generalizability of trial results. This study focuses on the reasons for participating in or declining the Tuberculosis Trials Consortium Study 33 (iAdhere), a clinical trial on the treatment of latent tuberculosis infection (LTBI).

METHODS: A quantitative evaluation was conducted among screened patients to ascertain their reasons for participating or not in the iAdhere trial. The study gathered data from enrolled participants and those who chose not to enroll.

RESULTS: Among 1,002 enrolled individuals, 290 participants provided 749 reasons for enrolling. The most common reasons included access to shorter treatment regimens (56%), avoiding progression to TB disease (45%), and improving health (21%). Of the 670 eligible persons who chose not to enroll, 551 individuals provided 800 reasons, with the most common being a preference for standard therapy (17%), disinterest in study medication or TB therapy (both 13%), and the inconvenience of daily observed treatment (12%).

CONCLUSION: The desire for shorter treatment options and preventing active disease motivates participation in LTBI trials. The diverse reasons for declining enrolment suggest the importance of developing targeted recruitment strategies. These findings support exploring shorter treatment regimens and can guide future recruitment efforts.

Keywords

latent tuberculosis infection; randomized clinical trial; recruitment; decision making; motivation

Correspondence to: Kimberley N Chapman Hedges, Division of TB Elimination, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, 1600 Clifton Road, NE, H24-5, Atlanta, GA 30329, USA. khedges@cdc.gov.

Clinical trials registration: The primary trial, TBTC Study 33 iAdhere, is registered with ClinicalTrials.gov (NCT01582711).

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

INTRODUCTION

Efficient recruitment of eligible participants is essential for the success of clinical trials. The generalizability of trial results may be limited if sociodemographic groups are not well represented among participants.[1] In the United States, racial and ethnic minorities remain underrepresented in trials, potentially perpetuating health disparities.[2,3] Despite the 1993 National Institutes of Health Revitalization Act, which aimed to increase minority enrolment, only modest improvements have been observed.[2] Thus, understanding the reasons for and against participation, particularly among underrepresented groups, is crucial for successful recruitment.

Persons with latent TB infection (LTBI) are not physically ill and cannot transmit TB; however, without preventative therapy, approximately 10% of those with LTBI may develop active TB disease.[4] Therefore, there is less urgency for treatment, additional testing, or frequent medical monitoring than with active TB disease treatment. Furthermore, LTBI treatment is often provided at no cost in many U.S. jurisdictions, potentially reducing motivation to participate in LTBI treatment trials.[5]

Underrepresented groups have cited removing financial barriers, providing education about the condition, providing rapid access to care and treatment, and increasing health monitoring as reasons for enrolment.[6–10] However, limited research exists on whether these reasons apply to LTBI trials.[11] Additionally, the reasons for declining participation are not well understood.

To explore motivations for and against trial enrolment, particularly among underrepresented groups, we evaluated the reasons provided by candidates screened for the iAdhere trial, TB Trials Consortium (TBTC) Study 33. This trial demonstrated that self-administered therapy without reminders was non-inferior to directly observed treatment (DOT) in the United States.[12]

METHODS

Setting and study participants

The iAdhere study was an open-label, international, multicenter, phase IV randomized controlled clinical trial (www.clinicaltrials.gov/show/NCT01582711). The primary objectives were to compare adherence between DOT and self-administered therapy (SAT) using a 3-month weekly regimen of isoniazid and rifapentine (3HP) among persons diagnosed with LTBI and to evaluate the use of short messaging service (SMS) reminders. During the iAdhere study, TBTC staff screened patients initially eligible for enrolment at 12 sites, including nine in the United States and one each in Hong Kong, South Africa, and Spain. Eligible patients who provided informed consent were enrolled. Details on enrolment criteria, participant descriptions, and main trial results are available elsewhere.[12]

During the iAdhere study, we conducted a quantitative evaluation to assess reasons for nonparticipation among screened patients who were not enrolled. As the study progressed, an evaluation of motivations for enrollment was also incorporated.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Non-enrollment form

Study staff prospectively recorded non-identifying demographic and clinical information using a standardized non-enrolment form for screened individuals who were not enrolled. The reasons for nonparticipation, as volunteered by the individual, were noted. The non-enrolment form (Supplementary Data 1: https://figshare.com/s/a3c6fc49a3f7cd68496e) categorized individuals as 1) protocol ineligible, 2) eligible but not enrolled due to study staff decision, or 3) not enrolled by their own choice. Those not enrolled by their choice were further categorized into eight groups: research-related concerns, communication issues, individual beliefs related to TB, clinic or staff factors, work or school factors, medication or health concerns, individual lifestyle or family factors, or other (with details requested). Manually entered 'other' reasons were reclassified and counted among the listed reasons where applicable. Demographics and country of birth were used to stratify reasons for non-enrolment.[13]

Motivations to enroll form

Following a protocol amendment during the iAdhere trial, the Motivations to Enroll form was distributed to sites and implemented with the last 30% of enrolled participants between January and April 2014. This form was used during enrolment or any study visit up to 120 days post-enrolment (Supplementary Data 2: https://figshare.com/s/a3c6fc49a3f7cd68496e). A literature review of study recruitment and prior TBTC experience informed the form's development. Thirty coordinators across 10 sites completed the form. Participants were asked an open-ended question to elicit their reasons for participation. Staff transcribed each participant's answer and checked relevant reasons on a list of responses grouped into health-related benefits, psycho-social benefits, financial benefits, the opinion of others, altruism, miscellaneous, and other categories. To minimize bias, staff asking these questions were different from site staff who screened and enrolled study participants. Study staff did not read responses back to the participants.

Data analysis

The analysis population included all screened individuals who either enrolled or did not enroll due to personal choice. Sociodemographic data were used to identify the characteristics of those who enrolled, and descriptive statistics (counts, frequencies, and proportions) were reported for reasons for enrolment and non-enrolment. χ^2 tests and odds ratios (ORs) from univariable logistic regression were used to estimate the association strength between characteristics of enrolled and non-enrolled individuals. Characteristics with a $P < 0.20$ were further analyzed using a multivariable logistic regression model, employing Firth's penalized likelihood approach to account for small sample sizes.[14–16] The focus was on an association model to understand participants' motivations based on demographic data. All tests were two-tailed, with $P < 0.05$ considered statistically significant in the multivariable model. Analyses were performed using SAS v9.4 (SAS Institute, Cary, NC, USA).

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Ethics statement

The study protocol and the amendment for collecting data on motivations for study participation were reviewed and approved by the Institutional Review Boards (IRBs) of the Centers for Disease Control and Prevention (CDC; Atlanta, GA, USA) and participating institutions.[12] To comply with CONSORT (Consolidated Standards of Reporting Trials) recommendations and confirm trial representativeness, limited demographic data without identifying information were recorded for screened but not enrolled persons.[17]

RESULTS

Study population

From September 2012 to April 2014, 2,176 individuals were screened, with 46% (n = 1,002) enrolling and 54% (n = 1,174) not enrolling. Among the non-enrolled, 19% (n = 408) were ineligible, 4% (n = 96) were not enrolled by site choice (110 reasons documented), and 31% (n = 670) were not enrolled by personal choice (Figure).

Associations between sociodemographic characteristics and enrollment

Table 1 details characteristics stratified by those who enrolled versus those who did not enroll by personal choice. The multivariable model, controlling for other factors, showed that age was significantly associated with enrolment. Those aged ≥65 years were less likely to enroll (adjusted OR [aOR] 0.52, 95% confidence interval [CI] 0.32–0.85). Hispanic ethnicity was associated with higher enrolment rates (aOR 1.67, 95% CI 1.34–2.08) than non-Hispanic ethnicity. Additionally, candidates in South Africa (aOR 1.92, 95% CI 1.19–3.12) and Hong Kong (aOR 2.42, 95% CI 1.31–4.48) were more likely to enroll compared to those screened in the United States.[13] Individuals born in the screening country were also more likely to enroll (aOR 1.33, 95% CI 1.06–1.67).

Reasons for non-enrolment based on individual choice

Among the 670 persons who did not enroll due to individual choice, 551 (87%) responded and reported 800 reasons for declining enrolment (Table 2). The most common reasons included a preference for the standard treatment regimen (n = 91, 17%), disinterest in study medications (n = 72, 13%), disinterest in LTBI therapy (n = 72, 13%), inconvenience of DOT (n = 67, 12%), concerns about the number of pills per dose (n = 55, 10%), unwillingness or inability to follow study requirements (n = 54, 10%), concerns about participating in research studies (n = 47, 9%), apprehensions regarding medication side effects (n = 40, 7%), reluctance to be randomized (n = 39, 7%), and inconvenience due to the number of visits (n = 38, 7%).

Motivations for enrolment

Of the 1,002 individuals enrolled in iAdhere, 290 (29%) completed an enrolment motivations form, providing 749 reasons for participating. This group had more females (54.5%) than males (45.5%) and fewer individuals identifying as Black (24.5%), Asian (17.2%), or of multiple racial groups (0.7%) than those identifying as White (57.6%) (Table 3 (see https://figshare.com/s/281c9ef70f762147bf11). The top reasons for participation were

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

access to shorter treatment regimens (*n* = 162, 56%), avoiding progression from LTBI to active TB disease (*n* = 131, 45%), improving personal health (*n* = 61, 21%), convenience or ease of once-weekly dosing (*n* = 39, 13%), faster access to care or treatment (*n* = 25, 9%), recommendation by a physician or nurse (*n* = 25, 9%), access to new or potentially superior drugs (*n* = 23, 8%), a protocol that was not inconvenient or intrusive (*n* = 23, 8%), enabling early detection of problems (*n* = 22, 8%), and helping others with the same diagnosis (*n* = 19, 7%).

Reasons were analyzed in the context of sociodemographics, including education, employment status, and birth in a country with a high TB burden. Table 3 (see https://figshare.com/s/281c9ef70f762147bf11) illustrates differences in the top reasons for participation among these groups. Generally, the main reasons for enrolling aligned across all groups, emphasizing the importance of highlighting these factors during recruitment.

DISCUSSION

This evaluation examined the reasons for and against participating in an LTBI treatment trial among those screened. The findings can inform recruitment strategies for future LTBI trials. Few differences were found across age, ethnicity, country of screening, and country of birth when comparing enrolled individuals with those who declined enrolment. The most common reasons for participation—access to shorter treatment regimens, avoiding progression to active TB disease, improving health, and the convenience of once-weekly dosing—were closely related to the original objectives of the iAdhere study. Recruitment efforts should emphasize these reasons, especially since they are relevant across various populations and settings. Trust and rapport with healthcare professionals also emerged as a key motivator for enrollment.

The primary reasons for declining participation included concerns about study medications, reluctance to undergo treatment or participate in research, and the inconvenience of DOT, which aligns with previous reports from investigators conducting TB trials.[18, 19] These issues highlight the need for clear, accessible information about the safety and benefits of study regimens. Addressing logistical concerns, such as the inconvenience of DOT, can also improve participation rates. The availability of alternatives such as electronic DOT (eDOT) might mitigate these concerns.[20]

Limitations

Self-reported data may be subject to recall bias, particularly when collected up to 120 days post-enrollment. Additionally, interactions with study staff and the design of data collection forms might have influenced the responses, leading to socially desirable answers. The study's size and site variability limited the assessment of these effects.

Further, the study did not stratify non-enrolment by specific risk factors for developing active TB or collect some characteristics (e.g., educational attainment) for non-enrolled participants, potentially affecting the generalizability of the results. The quantitative nature of the study also limits the depth of understanding that could be gained from qualitative methods like focus groups or interviews.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

CONCLUSION

Addressing the barriers to and motivations for enrolment is crucial to ensure representativeness in clinical trials. Participants were motivated by the prospect of shorter treatment regimens and preventing active TB disease, highlighting the need for continued research into shorter treatments. Recruitment materials should compare standard and study regimens and emphasize health improvements and disease prevention benefits. Future research could explore whether emphasizing these aspects during recruitment enhances enrolment rates.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The authors thank all study participants and those screened but not enrolled in TBTC Study 33 iAdhere. The authors also appreciate the contributions of the TBTC site staff and the technical and editorial review provided by W Carr, R Boyd, A Vernon, R Traxler, and C K Smith.

This trial was funded by the Centers for Disease Control and Prevention (CDC; Atlanta, GA, USA), National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Division of TB Elimination (Bethesda, MD, USA). Sanofi (Paris, France) provided rifapentine and funding for pharmacokinetic testing. From 2007 to 2016, Sanofi donated US$2.9 million to the CDC Foundation to support rifapentine research, providing salary support for KNCH and NAS from 2013 to 2017.

Preliminary results of this evaluation were presented at a poster presentation at the American Thoracic Society (ATS), CDC/ATS Poster Session, Denver, CO (May 2015), and at The International Journal of Tuberculosis and Lung Disease (Paris, France). Poster Discussion at the 45th Union World Conference in Barcelona, Spain (November 2014).

Reference

1. Bartlett C, et al. The causes and effects of socio-demographic exclusions from clinical trials. Health Technol Assess. 2005;9(38):iv, ix–x, 1–152.
2. Turner BE, et al. Race/ethnicity reporting and representation in US clinical trials: a cohort study. Lancet Reg Health Am. 2022;11: 100252.
3. Camidge DR, et al. Race and ethnicity representation in clinical trials: findings from a literature review of Phase I oncology trials. Future Oncol. 2021;17(24):3271–3280. [PubMed: 34047192]
4. Centers for Disease Control and Prevention. Deciding when to treat latent TB infection. Atlanta, GA, USA: CDC, 2018.
5. Sutherland HJ, et al. What attitudes and beliefs underlie patients' decisions about participating in chemotherapy trials? Med Decis Making. 1998;18(1):61–69. [PubMed: 9456210]
6. Carroll R, et al. Motivations of patients with pulmonary arterial hypertension to participate in randomized clinical trials. Clin Trials. 2012;9(3):348–357. [PubMed: 22388077]
7. Locock L, Smith L. Personal benefit, or benefiting others? Deciding whether to take part in clinical trials. Clin Trials. 2011;8(1):85–93. [PubMed: 21163854]
8. McCann SK, Campbell MK, Entwistle VA. Reasons for participating in randomized controlled trials: conditional altruism and considerations for self. Trials. 2010;11:31. [PubMed: 20307273]
9. Schmotzer GL. Barriers and facilitators to participation of minorities in clinical trials. Ethn Dis. 2012;22(2):226–230. [PubMed: 22764647]
10. Voytek CD, Jones KT, Metzger DS. Selectively willing and conditionally able: HIV vaccine trial participation among women at "high risk" of HIV infection. Vaccine. 2011;29(36):6130–6135. [PubMed: 21704110]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

11. Hedges KNC, et al. Nonparticipation reasons in a randomized international trial of a new latent tuberculosis infection regimen. Clin Trials. 2020;17(1):39–51. [PubMed: 31690107]
12. Belknap R, et al. Self-administered versus directly observed once-weekly isoniazid and rifapentine treatment of latent tuberculosis infection: a randomized trial. Ann Intern Med. 2017;167(10):689–697. [PubMed: 29114781]
13. World Health Organization. Global tuberculosis report, 2015. Geneva, Switzerland: WHO, 2015.
14. Devika S, Jeyaseelan L, Sebastian G. Analysis of sparse data in logistic regression in medical research: a newer approach. J Postgrad Med. 2016;62(1):26–31. [PubMed: 26732193]
15. Firth D. Bias reduction of maximum likelihood estimates. Biometrika. 1993;80(1):27–38.
16. Heinze G, Schemper M. A solution to the problem of separation in logistic regression. Stat Med. 2002;21(16):2409–2419. [PubMed: 12210625]
17. Schulz KF, Altman DG, Moher D. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomized trials. Ann Intern Med. 2010;152(11):726–732. [PubMed: 20335313]
18. Craig SR, et al. Altruism, scepticism, and collective decision-making in foreign-born U.S. residents in a tuberculosis vaccine trial. BMC Public Health. 2018;18(1):535. [PubMed: 29685114]
19. Lamunu D, et al. Reasons for nonparticipation in an international multicenter trial of a new drug for tuberculosis treatment. Int J Tuberc Lung Dis. 2012;16(4):480–485. [PubMed: 22640513]
20. Burzynski J, et al. In-person vs electronic directly observed therapy for tuberculosis treatment adherence: a randomized noninferiority trial. JAMA Netw Open. 2022;5(1): e2144210.
21. Bonevski B, et al. Reaching the hard-to-reach: a systematic review of strategies for improving health and medical research with socially disadvantaged groups. BMC Med Res Methodol. 2014;14:42. [PubMed: 24669751]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

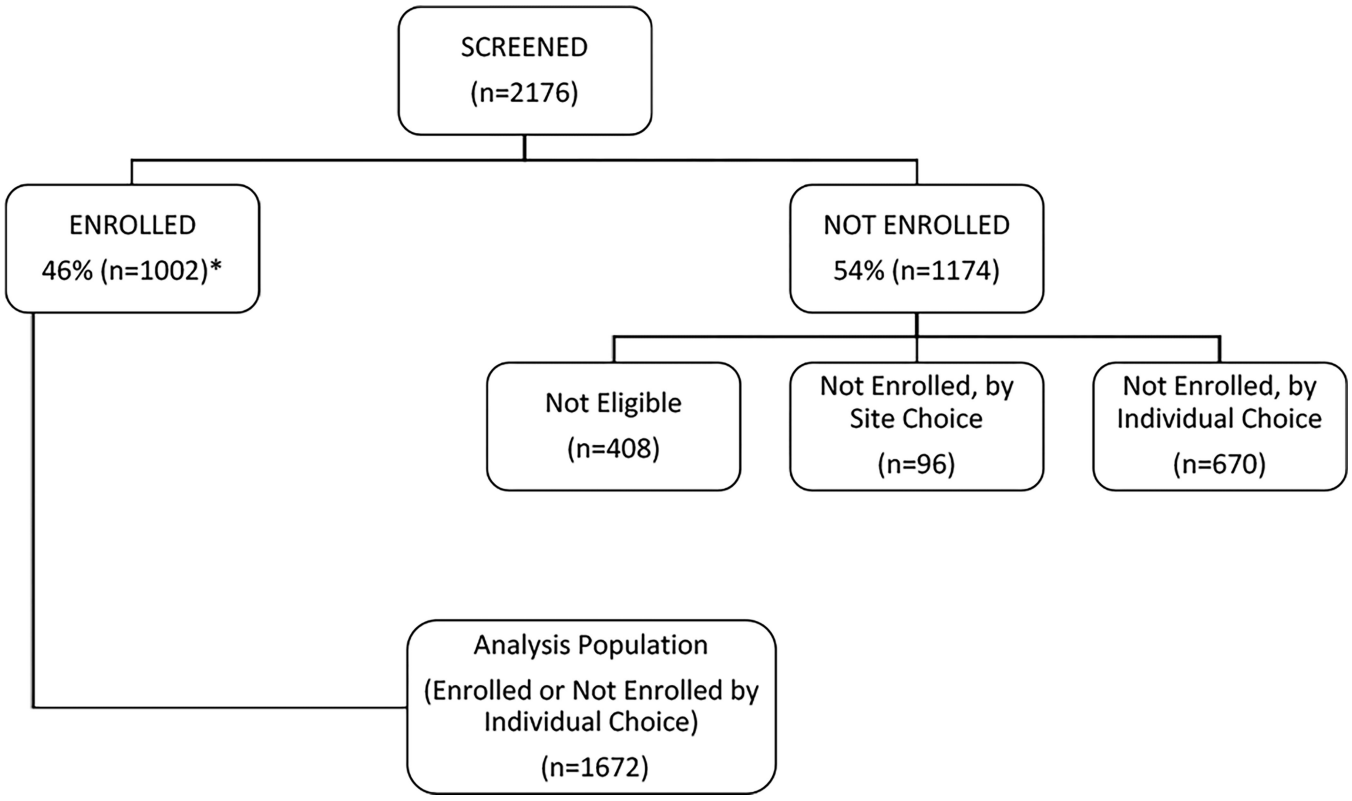

Figure.

Overall screened and enrolled versus not enrolled by individual choice.* *Among Enrolled participants (*n* = 11,002): motivation to enroll form not completed by *n* = 712 (71%); motivation to enroll form completed by *n* = 290 (29%).

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 1.

Characteristics of persons screened: enrolled and not enrolled.

	Enrolled Total n (Col %)	Not enrolled Individual choice n (Col %)	Univariable OR (95% CI)*	*P*-value	Multivariable OR (95% CI)*	*P*-value
	1,002	670				
Sex						
Male	520 (51.9)	353 (52.7)	1.00 (reference)			
Female	482 (48.1)	317 (47.3)	1.03 (0.85–1.26)	0.7516		
Age group, years†						
35–64	525 (52.4)	374 (55.8)	1.00 (reference)			
18–34	447 (44.6)	254 (37.9)	1.25 (1.02–1.54)	0.0296	1.20 (0.97–1.49)	0.0864
≥65	30 (3.0)	42 (6.3)	0.51 (0.32–0.83)	0.0070	0.52 (0.32–0.85)	0.0096
Race						
White	518 (51.7)	315 (47.0)	1.00 (reference)			
Black/African American	250 (25.0)	163 (24.3)	0.93 (0.73–1.19)	0.5699		
Asian	200 (20.0)	164 (24.5)	0.74 (0.58–0.95)	0.0189		
Other	34 (3.4)	28 (4.2)	0.74 (0.44–1.24)	0.2488		
Ethnicity						
Non-Hispanic	607 (60.6)	453 (67.6)	1.00 (reference)			
Hispanic	393 (39.2)	208 (31.0)	1.41 (1.15–1.74)	0.0012	1.67 (1.34–2.08)	<.0001
Unknown‡	2 (0.2)	9 (1.3)				
Country of screening						
US	774 (77.2)	558 (83.3)	1.00 (reference)			
Spain	100 (10.0)	70 (10.4)	1.03 (0.74–1.42)	0.8676	1.11 (0.79–1.54)	0.5563
South Africa	83 (8.3)	28 (4.2)	2.11 (1.36–3.28)	0.0009	1.92 (1.19–3.12)	0.0078
Hong Kong	45 (4.5)	14 (2.1)	2.26 (1.24–4.15)	0.0083	2.42 (1.31–4.48)	0.0050
Born in country of screening						
No	603 (60.2)	462 (69.0)	1.00 (reference)			
Yes	399 (39.8)	208 (31.0)	1.42 (1.16–1.75)	0.0009	1.33 (1.06–1.67)	0.0129
Unknown§	—	15 (2.2)				
Born in country with high TB burden¶						
Non-high-burden	753 (75.1)	467 (69.7)	1.00 (reference)			
High-burden	249 (24.9)	188 (28.1)	0.82 (0.66–1.03)	0.0817		
Unknown§	—	15 (2.2)				

*Logistic regression using Firth's Penalized Likelihood Estimates was used to generate *P*-values, ORs, and 95% CIs, comparing enrolled to not enrolled patients by patient choice.

†6 participants were ≤17 years old and did not enroll due to ineligibility

‡Not interpretable since data not collected

§Not applicable since there were no unknown responses among participants who enrolled.

¶The high-burden countries listed by the WHO in 2015[13] were Afghanistan, Bangladesh, Brazil, Cambodia, China, the Democratic Republic of the Congo, Ethiopia, India, Indonesia, Kenya, Mozambique, Myanmar, Nigeria, Pakistan, the Philippines, the Russian Federation, South Africa, Thailand, Uganda, the United Republic of Tanzania, Viet Nam, and Zimbabwe.

CI = confidence interval; OR = odds ratio.

Author Manuscript
Author Manuscript
Author Manuscript
Author Manuscript

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 1a.

Characteristics of persons screened in the United States: enrolled and not enrolled.

	Enrolled Total n (Col %)	Not enrolled Individual choice n (Col %)	Univariable OR (95% CI)*	*P*-value	Multivariable OR (95% CI)*	*P*-value
Sex						
Male	383 (49.5)	289 (51.8)	1.00 (reference)			
Female	391 (50.5)	269 (48.2)	1.10 (0.88–1.36)	0.4065		
Age group, years†						
35–64	433 (55.9)	323 (57.9)	1.00 (reference)			
18–34	317 (41.0)	199 (35.7)	1.19 (0.95–1.49)	0.1401	1.20 (0.95–1.51)	0.1289
≥65	24 (3.1)	36 (6.5)	0.50 (0.29–0.86)	0.0115	0.50 (0.29–0.85)	0.0114
Race						
White	453 (58.5)	263 (47.1)	1.00 (reference)			
Black/African American	162 (20.9)	128 (22.9)	0.74 (0.56–0.97)	0.0293		
Asian	130 (16.8)	140 (25.1)	0.54 (0.41–0.72)	<.0001		
Other	29 (3.7)	27 (4.8)	0.62 (0.36–1.08)	0.0896		
Ethnicity						
Non-Hispanic	407 (52.6)	358 (64.2)	1.00 (reference)			
Hispanic	367 (47.4)	192 (34.4)	1.68 (1.34–2.10)	<.0001	1.73 (1.37–2.17)	<.0001
Unknown‡	—	8 (1.4)	0.05 (0.00–1.07)	0.0553	0.08 (0.00–1.86)	0.1159
Born in the country of screening						
No	518 (66.9)	395 (70.8)	1.00 (reference)			
Yes	256 (33.1)	149 (26.7)	1.31 (1.03–1.67)	0.0284	1.33 (1.04–1.70)	0.0218
Unknown§	—	14 (2.5)	0.03 (0.00–0.49)	0.0147	0.03 (0.00–0.61)	0.0218
Born in a country with high TB burden¶						
Non-high-burden	645 (83.3)	401 (71.9)	1.00 (reference)			
High-burden	129 (16.7)	143 (25.6)	0.56 (0.43–0.73)	<0.0001		
Unknown§	—	14 (2.5)	0.02 (0.00–0.40)	0.0100		

*Logistic regression using Firth's Penalized Likelihood Estimates was used to generate *P*-values, ORs, and 95% CIs, comparing enrolled to not enrolled patients by patient choice.

†6 participants were ≤17 years old and did not enrol due to ineligibility.

‡Not interpretable since data not collected.

§Not applicable since there were no unknown responses among participants who enrolled.

¶The high-burden countries listed by the WHO in 2015 were Afghanistan, Bangladesh, Brazil, Cambodia, China, the Democratic Republic of the Congo, Ethiopia, India, Indonesia, Kenya, Mozambique, Myanmar, Nigeria, Pakistan, the Philippines, the Russian Federation, South Africa, Thailand, Uganda, the United Republic of Tanzania, Viet Nam, and Zimbabwe ($n = 14$).

CI = confidence interval; OR = odds ratio.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 2.

Detailed reasons for nonparticipation.*

Reasons for not enrolled by individual choice	Category	Patients Total n (Col%)
Patient prefers regular medication/treatment	Medication health	91 (16.5)
Patient is not interested in study medications	Medication health	72 (13.1)
Infected with TB, but not interested in TB therapy	Patient LTBI beliefs	72 (13.1)
DOT is inconvenient	Medication health	67 (12.2)
Worried about number of pills required per dose	Medication health	55 (10.0)
Non-compliant (passive refusal: patient did not return calls, return to clinic, etc.)	Patient family other	54 (9.8)
Worried about enrolling in any clinical research studies	Research	47 (8.5)
Patient worried about medication side effects	Medication health	40 (7.3)
Patient does not want to be randomized	Research	39 (7.1)
Number of visits not convenient	Work school	38 (6.9)
Missing work or school could otherwise be a problem	Work school	36 (6.5)
Too busy or too much stress right now	Patient family other	31 (5.6)
Moving/traveling	Patient family other	31 (5.6)
Transportation, travel to or parking not convenient	Clinic staff	24 (4.4)
Worried about impact on other medical problems or medications	Medication health	17 (3.1)
Not infected with TB	Patient LTBI beliefs	13 (2.4)
Prefers alternative therapy/treatment (for example, with another doctor, medical facility or different drug regimen)	Medication health	10 (1.8)
Family member against enrolment	Patient family other	10 (1.8)
Worried about losing income	Work school	10 (1.8)

*Reasons shown where >1% of total reasons reported.

LTBI = latent TB infection.