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Reasons for non-participation in an international multicenter trial of a new drug for tuberculosis treatment

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SUMMARY

SETTING—Clinical trials can provide a high standard of patient care and contribute to scientific knowledge; however, only a fraction of the patients screened participate and receive treatment as part of a trial.

OBJECTIVE—To explore reasons why patients were not enrolled in an international tuberculosis (TB) treatment trial and to compare experiences among study sites.

DESIGN—An analysis of reasons why patients were not enrolled was conducted among patients screened for a TB clinical trial at 26 sites in North and South America, Africa, and Europe.

RESULTS—Staff at study sites screened 1119 potential candidates for the trial: 61% (n = 686) were not enrolled due to 1) failure to meet eligibility criteria (n = 405, 59%), 2) site's decision (n = 168, 24%), or 3) candidate's choice (n = 113, 16%). Study staff recorded a total of 144 reasons for why they believed patients chose not to participate, including concerns over research (28%), conflicts with work or school (21%), and lifestyle and family issues (20%). Socio-demographic and geographic factors also influenced participation.

CONCLUSION—Increased evaluation of screening outcomes and of specific interventions, such as improved education and communication about trial procedures, may increase the efficiency of screening and enrollment in clinical trials.

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RÉSUMÉ

Des essais cliniques peuvent garantir un niveau élevé de soins des patients et contribuer aux connaissances scientifiques; toutefois, une fraction seulement des patients dépistés participent à un essai et reçoivent le traitement au sein de celui-ci.

Explorer les raisons pour lesquelles les patients n'ont pas été recrutés dans un essai international de traitement de la tuberculose (TB), et comparer les expériences d'un site à l'autre.

On a mené une analyse des raisons pour lesquelles les patients n'ont pas été recrutés pour un essai clinique TB parmi les patients dépistés dans 26 sites d'Amérique du Nord et du Sud, d'Afrique et d'Europe.

Le personnel des sites d'étude ont dépisté 1119 candidats potentiels pour l'essai; 61% d'entre eux n'ont pas été recrutés (n = 686) pour les raisons suivantes : 1) absence des critères d'éligibilité (n = 405, 59%); 2) décision du site (n = 168, 24%); ou 3) choix du candidat (n = 113, 16%). Le personnel de l'étude a signalé au total 144 raisons pour lesquelles ils pensaient que les patients avaient choisi de ne pas participer à l'essai, notamment des préoccupations concernant la recherche (28%), des incompatibilités avec le travail ou l'école (21%) et des problèmes de style de vie et de famille (20%). La participation a également été influencée par des facteurs socio-démographiques et géographiques.

L'efficience du dépistage et du recrutement dans les essais cliniques pourrait être améliorée par une augmentation de l'évaluation des résultats du dépistage et par des interventions spécifiques telles qu'une amélioration de la formation et de la communication concernant les procédures de l'essai.

RESUMEN

Los ensayos clínicos pueden ofrecer a los pacientes una atención sanitaria de gran calidad y contribuir a mejorar los conocimientos científicos; sin embargo, solo una pequeña proporción de los pacientes seleccionados participan y reciben tratamiento como parte de un ensayo clínico.

Investigar las razones por las cuales los pacientes no participaron en un estudio clínico terapéutico internacional sobre la tuberculosis (TB) y comparar las experiencias entre los diferentes centros del estudio.

Se llevó a cabo un análisis de las razones por las cuales los pacientes preseleccionados en el marco de un estudio clínico de la TB no se incluyeron en el estudio en 26 centros de Norteamérica, Suramérica, África y Europa.

El personal del estudio en los centros escogió a 1119 candidatos posibles; 61% (n = 686) de ellos no participaron en el estudio clínico: 1) por no cumplir con los criterios de inclusión (n = 405, 59%); 2) por decisión del centro (n = 168, 24%); o 3) por opción del candidato (n = 113, 16%). El personal del estudio consignó 144 razones que, en su opinión, llevaron a los pacientes a tomar la decisión de no participar, entre ellas las dudas sobre la investigación (28%), las incompatibilidades laborales o escolares (21%) y los problemas relacionados con el estilo de vida y con la familia (20%). Los factores sociodemográficos y geográficos también influyeron en la participación.

Es posible mejorar la eficiencia de la selección inicial y de la inclusión de los pacientes en los ensayos clínicos si se fomenta la evaluación del resultado de la preselección y se realizan

intervenciones específicas, por ejemplo mejorar la comunicación con los pacientes y ofrecer una mayor educación sobre los procedimientos de los estudios clínicos.

Keywords

tuberculosis; non-participation; clinical trial; moxifloxacin; anti-tuberculosis agents

Understanding reasons for non-participation in clinical trials is useful in planning international multicenter trials and optimizing strategies for successful recruitment. Information about study candidates who are ineligible or who decline to participate can help assess the generalizability of study outcomes to other populations and settings. CONSORT (Consolidated Standards of Reporting Trials) guidelines for randomized clinical trials call for completeness of reporting, including accounting of the population screened but not enrolled, to allow accurate interpretation of the data provided by the trial and recognition of its limitations.[1] Appropriate recording and reporting of challenges faced while recruiting participants into research trials can help in devising non-coercive strategies to overcome problems of low recruitment.

Many published reports on recruitment experiences in clinical trials fail to mention specific reasons for non-participation.[2] To understand reasons why patients do not enroll in tuberculosis (TB) treatment trials, we examined data from a prospectively collected log of reasons for non-participation in a recent large international TB treatment trial.

STUDY POPULATION AND METHODS

Setting and study participants

This study considered patients with acid-fast bacilli in a sputum smear and suspected pulmonary TB screened for enrollment into Tuberculosis Trials Consortium (TBTC) Study 28, a multicenter, double-blind, Phase 2 clinical trial.[3] TBTC Study 28 compared the safety and efficacy of two treatment regimens containing rifampin, ethambutol, and pyrazinamide, plus either moxifloxacin (MFX) or isoniazid, during the first 2 months of anti-tuberculosis treatment. Enrollment criteria, a description of the participants and the main trial results have been published.[3]

The protocol was approved by the institutional review boards of the sponsor, the US Centers for Disease Control and Prevention (CDC), and all study sites.

Patients who met the inclusion criteria and gave informed consent were enrolled and randomized as participants at 26 TBTC sites in Brazil (1 site), Canada (2 sites), South Africa (1 site), Spain (1 site), Uganda (1 site) and the United States (20 sites).

Measures and data analysis

Demographic and clinical information about screened patients who were not enrolled was entered by study staff at each site into a standardized non-participation database. For analysis, age groups were categorized as ≤35 years or >35 years. Region of birth was categorized based on the World Health Organization (WHO) regional groups.[4] Study staff

recorded one of three reasons for non-participation: 1) protocol-ineligible (failure to meet inclusion/exclusion criteria), 2) site staff decision (for example, if the patient had a history of non-adherence or lived too far away for directly observed therapy), or 3) patient's choice. Details about patients who were protocol-ineligible or who were not enrolled due to site decision were not further specified. Patients' reasons for declining enrollment were recorded by study site staff in the nonparticipation database, checking all applicable reasons for each patient, based on information volunteered at screening encounters. These data were collected prospectively, as specified in the protocol.

Each non-participation category was examined for frequencies. Socio-demographic data for all screened patients (enrolled and not enrolled) were merged and analyzed using χ^2 tests and odds ratios (ORs) from univariate logistic regression to estimate the strength of association (Stata version 10, Stata Corp, College Station, TX, USA). All tests were two-tailed, and $P \leq 0.05$ was considered statistically significant.

Ethics statement

TBTC Study 28 was approved by the institutional review boards of the CDC and participating institutions, and were registered with Clinicaltrials.gov (Study 28: NCT00144417).

RESULTS

Study population

Between February 2006 and March 2007, 1119 patients were screened for participation. Table 1 shows selected characteristics (stratified by enrolled vs. non-enrolled patients). Of those screened, the majority were male (69%), and had a median age of 34 years (range 12–93); 491 (44%) patients were aged >35 years. Patients were screened at trial sites in Africa (n = 546, 49%), North America (n = 516, 46%), Spain (n = 32, 3%) and Brazil (n = 25, 2%). Of the 516 patients screened in North America, place of birth was known for 405; of these, 150 (37%) were born in the United States or Canada and 255 (63%) were foreign-born, with the largest proportion born in the Americas other than the United States or Canada (n = 123, 30%). Ethnicity was known for 477 of the patients screened in North America; 64% (n = 303) were non-Hispanic. Race was reported for 483 patients screened at North American sites; half of these were white (n = 242, 50%).

Demographics of screened patients: enrolled and not enrolled

Of the total patients screened, 61% were not enrolled. Median age was 32 years among enrollees and 35 years among non-enrollees. The percentage of females not enrolled (65%) was similar to the percentage of males not enrolled (60%). Comparing the two highest enrolling countries, a higher proportion were enrolled in Uganda, 47% (202/433), than in the United States, 35% (149/425; Table 1). The lowest proportion enrolled was at the two study sites in Canada, 7% (6/91), mostly attributed to ineligibility (70/85, 82%; Table 2). Within North America, enrollment did not differ significantly by Hispanic ethnicity. Within every race category in North America, more patients were not enrolled than enrolled. Among North American Black patients, 27% (40/147) were enrolled, compared to 34% (81/242) of

White patients. Within North America, 24% (9/37) of Blacks born in Africa were enrolled, while 38% (27/71) of Blacks born in North America were enrolled. None of these latter differences were statistically significant.

Association between socio-demographic characteristics and non-participation

The percentage not enrolled was significantly higher among patients aged >35 years than among younger patients (Table 1). This difference was most pronounced at the Uganda site, where 49% (166/342) of patients aged ≤35 years were not enrolled compared to 71% (65/91) of those aged >35 years. There was a significant association between the country or region where a candidate was screened and non-participation. Compared to patients screened in Uganda, patients from other sites were more likely to be non-participants (South Africa OR 1.6, 95% confidence interval [CI] 1.0–2.5; United States OR 1.6, 95%CI 1.2–2.1; Canada OR 12.4, 95%CI 5.1–30.3). Among patients screened in North America, failure to enroll varied non-significantly by place of birth.

Reasons for non-participation

Of the 686 patients not enrolled, 405 (59%) were protocol-ineligible, 168 (24%) were not enrolled by site decision, and 113 (16%) declined by personal choice (Table 2). Among the 26 sites that screened patients for Study 28, 15 (58%) enrolled less than half of the patients they screened. Twenty-five sites recorded ‘protocol-ineligible’ as the most common reason for not enrolling a patient; however, in Kampala, Uganda, the highest enrolling site, the most common reason was site staff decision.

Table 3 shows the reasons volunteered by patients who declined to enroll by personal choice. For 113 patients, 144 reasons were recorded. Study staff did not record any reasons for eight patients and recorded more than one reason for 18 patients (two to six reasons per patient). Forty responses (28%) were related to research, 30 (21%) reported potential conflict with work or school, and 29 (20%) attributed nonparticipation to patient lifestyle/family issues. Fourteen patients (10%), including 12 in Africa, declined to enroll because of the requirement that participants agree to be tested for human immunodeficiency virus (HIV). Other reasons for candidate non-participation included perceived communication barriers, location of clinic or study site, and various concerns about study medication. Belief that the bacille Calmette-Guérin vaccination would protect them from TB was not given as a reason for non-participation by any patients.

Non-enrollment was attributed to ineligibility more often among older patients (≤35 years: n = 180, 52%; >35 years: n = 225, 67%) and to site choice (≤35 years: n = 100, 29%; >35 years: n = 68, 20%), and patient choice more often among younger patients (≤35 years: n = 66, 19%; >35 years: n = 45, 13%). Concerns about work or school were more commonly cited by patients aged ≤35 years (n = 22, 25%) than by older patients (n = 8, 15%). Concerns about lifestyle or family were also more commonly cited by younger patients (n = 21, 24%) than by older patients (n = 8, 15%). The dominant lifestyle and family concerns were stigmatization due to TB and taking TB medicine (≤35 years: n = 4, 5%; >35 years: n = 1, 2%), and refusal to be tested for HIV (≤35 years: n = 11, 12%; >35 years: n = 3, 6%). Only one patient, aged ≤35 years, attributed declining to worries about medication side effects.

DISCUSSION

We examined the reasons for non-participation in a large, multicenter international TB treatment trial among patients screened for enrollment, as site staff considered them likely to be eligible and appropriate study candidates.[5] Information from this study may help to improve recruitment efficiency for future studies, with caution, to protect the basic principles of informed consent.

Patients were screened in North America, Africa, Brazil, and Spain. Fewer than 40% of those screened were enrolled. Screening location was associated with enrollment rate more strongly than race or ethnicity (in North America); place of birth was also associated with enrollment in some regions. The largest category for non-enrollment was protocol ineligibility. The proportion of patients not enrolling due to ineligibility varied by country, from 39% in Uganda to 100% in Brazil (Table 2). These differences may reflect the available pool of candidates for TB studies in a low-prevalence vs. a high-prevalence country. Evaluation of which eligibility criteria were not met might help to understand recruitment practices at sites and to guide pre-enrollment screening procedures in future clinical trials.

More detailed data were collected from patients who declined participation by their own choice. Patients most frequently declined to participate due to concerns about enrolling in research trials, including the efficacy of experimental study medication, due to concerns about the convenience and timing of visits, and over a reluctance to undergo HIV testing, particularly in Africa.

Observed or hypothesized reasons for nonparticipation in clinical trials have been reported by others; these included inconvenient study visits and procedures, reluctance to become experimental subjects, logistical issues, and the requirements of informed consent.[5–7] Our findings are similar to those of previous studies. Enrollment might increase if prospective participants are given additional educational information about the research, with appropriate caution to avoid coercion.[8] Differences among methods of providing research information may also influence understanding and recruitment.[9] Well-designed recruitment strategies should be responsive to participant and TB program needs, in addition to the requirements of the clinical trial itself.

Nearly one third (28%) of the candidates who declined to participate in our trial had concerns about the research procedures, such as the efficacy of experimental drugs, the volume of blood drawn for tests, and the complexity of the informed consent process. While patients may be interested in participating in clinical trials, they often do not have a good understanding of the trial for which they are recruited.[8] Researchers can address this barrier through patient education, by presenting and conducting clinical trials with transparency, and by discussing protective measures for research subjects. Patients participate in clinical trials for a variety of reasons, including perception of personal benefit and altruistic reasons.[10] A recent study found that ‘willingness to help others and to contribute towards furthering medical knowledge’ featured strongly among the reasons people gave for being interested in participating in a clinical trial.[11]

We also found that patients decline to participate due to potential conflicts with work or school. Among those declining participation, 30 (21%) had busy work or school schedules, and of these 23 (76%) reported that the number of study visits was inconvenient or expressed concerns over repercussions for missing school or work. These scheduling concerns were similar to those identified in several non-TB clinical trials.[7,8,12] Concerns may be offset by compensation for travel and inconvenience or by a more convenient schedule for visits than typically offered by public or private clinics.[13] These concerns may also apply to acceptance of TB treatment in general, and may suggest a need for improved access to health care systems if treatment is to be successful.

Reasons related to patient lifestyle, beliefs and attitudes regarding TB disease or research were also cited as the basis for non-participation. Of these, 67% expressed concerns about stigma associated with having TB and fears about undergoing HIV testing, which appears to be more important in Africa (21%), where HIV infection is more prevalent, than in North America (3%). Patient perceptions of study drugs and protocol-required procedures may negatively influence participation in clinical trials. Age appears to affect patient choice to decline in expected ways, with more young patients declining because of work or school, lifestyle or family, and fear of stigmatization. Addressing patients' beliefs and attitudes about TB and concerns about research may improve recruitment. Improved health education and community awareness programs about TB may increase participation in subsequent clinical trials.

Limitations

Our study has several limitations. This analysis has limited generalizability across socio-demographic groups due to the small numbers of patients in some groups. The recruitment of patients was not uniformly distributed across all geographic sites, with particularly heavy enrollment in two African sites and in North America. Although study site region was significantly associated with non-participation, this study had limited power to explore factors at individual sites affecting enrollment. There were also differences in language, study staff, and styles for presenting the study. Although a standardized form was used to record patients' reasons for declining, it was completed by site staff only after the interview; therefore, differences among screeners in evaluating patients' reasons for declining may have yielded inconsistencies. Study candidates were not directly administered questionnaires about participation, as this would have required additional consent, possibly further reducing the response rate and imposing an extra burden on patients when they are already heavily burdened by new diagnosis and treatment for TB. Bias could have been introduced by staff recording reasons for declining study participation, rather than by patients providing such reasons anonymously.

Future research on why patients decline participation in clinical trials could include qualitative surveys to facilitate the design and validation of standardized self-administered questionnaires. Questionnaires that are self-administered have less interviewer impact, can help to 'minimize bias and maximize precision', and are thus less susceptible to information bias from influences such as social desirability.[14,15] A study candidate might provide an answer that would impart a more socially desirable but false impression than he or she might

record confidentially.[16] Recent reviews have pointed out the greater reliability of questionnaires and patient diaries over interviews.[15,17] Furthermore, this study did not collect the specific reasons why patients were found to be ineligible, nor the specifics of why sites declined to enroll patients. Collecting additional details in these categories could improve our understanding of factors influencing recruitment.

CONCLUSIONS

Timely and efficient recruitment has important implications for clinical trials.[2] Longer trials cost more, and patients want their contributions of time and effort to provide societal benefits as quickly as possible. In an international multicenter TB treatment trial, concerns about research, worries related to work or school, and patient lifestyle or family issues were the most important stated reasons for patients choosing not to enroll. Although multiple factors influence patients' decisions to participate in clinical trials, improved communication between patients and site personnel about the nature and procedures involved in participating in clinical trials may be needed. Clear explanations of clinical trials to patients should address patients' concerns. Increased evaluation of screening outcomes can help to ensure the best use of resources and deliver the greatest benefits to patients, TB control programs and trial groups.

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Table 1

Socio-demographic characteristics of participants screened*

	Total (*N* = 1119, 100%) *n* (col %)	Enrolled (*n* = 433, 38.7%) *n* (row %)	Not enrolled (*n* = 686, 61.3%) *n* (row %)	*P* value	χ^2 estimates OR (95%CI)
All sites					
Sex					
Female	346 (31)	123 (36)	223 (65)	0.16	1.2 (0.9–1.6)
Male	773 (69)	310 (40)	463 (60)		Reference
Age group, years					
≤35	626 (56)	280 (45)	346 (55)	0.00†	Reference
>35	491 (44)	153 (31)	338 (69)		1.8 (1.4–2.3)
Unknown	2 (0)	0	2 (100)	—	—
Median [IQR]	34 [26–46]	32 [25–41]	35 [27–50]		
Study site country					
Brazil	25 (2)	21 (84)	4 (16)	0.00†	0.2 (0.1–0.5)
Canada	91 (8)	6 (7)	85 (93)		12.4 (5.1–30.3)
South Africa	113 (10)	40 (35)	73 (65)		1.6 (1.0–2.5)
Spain	32 (3)	15 (47)	17 (53)		1.0 (0.5–2.0)
Uganda	433 (39)	202 (47)	231 (53)		Reference
USA	425 (38)	149 (35)	276 (65)		1.6 (1.2–2.1)
North America only					
Place of birth (North America vs. other)‡					
USA/Canada	150 (29)	58 (39)	92 (61)	0.84	Reference
All other	255 (49)	96 (38)	159 (62)		1.0 (0.7–1.6)
Not reported/unknown	111 (22)	1 (1)	110 (99)	—	—
Place of birth (North America vs. WHO regions)‡					
USA/Canada	150 (29)	58 (39)	92 (61)	0.04†	Reference
Africa	38 (7)	10 (26)	28 (74)		1.8 (0.8–3.9)
Americas (other than US and Canada)	123 (24)	59 (48)	64 (52)		0.7 (0.4–1.1)
Eastern Mediterranean	10 (2)	1 (10)	9 (90)		5.7 (0.7–46.0)

	Total (*N* = 1119, 100%) *n* (col %)	Enrolled (*n* = 433, 38.7%) *n* (row %)	Not enrolled (*n* = 686, 61.3%) *n* (row %)	*P* value	χ^2 estimates OR (95%CI)
Europe	10 (2)	2 (20)	8 (80)		2.5 (0.5–12.3)
South–East Asia	16 (3)	5 (31)	11 (69)		1.4 (0.5–4.2)
Western Pacific	58 (11)	19 (33)	39 (67)		1.3 (0.7–2.5)
Not reported/unknown	111 (22)	1 (1)	110 (99)	—	—
Ethnicity					
Non-Hispanic	303 (59)	90 (30)	213 (70)	0.09	Reference
Hispanic	174 (34)	65 (37)	109 (63)		0.7 (0.5–1.1)
Not reported/unknown	39 (8)	0	39 (100)	—	—
Race					
White	242 (47)	81 (34)	161 (67)	0.39	Reference
Black	147 (28)	40 (27)	107 (73)		1.3 (0.9–2.1)
Asian/Hawaiian/Pacific Islander	81 (16)	25 (31)	56 (69)		1.1 (0.7–1.9)
American Indian/Alaskan Native	13 (3)	6 (46)	7 (54)		0.6 (0.2–1.8)
Not reported/unknown	33 (6)	3 (9)	30 (91)	—	—

[*] Totals and percentages may not always add up due to rounding.

[†] Indicates χ^2 *P* values and OR that are statistically significant at 5%.

[‡] Grouped by the six WHO member regions; USA/Canada considered as a reference for the analysis.

OR = odds ratio; CI = confidence interval; IQR = interquartile range; WHO = World Health Organization

Table 2

Reasons for non-participation by country

	Protocol-ineligible *n* (row %)	**Not enrolled by site staff decision *n* (row %)**	**Enrollment declined by patient's choice *n* (row %)**
Brazil	4 (100)	0	0
Canada	70 (82)	7 (8)	8 (9)
South Africa	45 (62)	2 (3)	26 (36)
Spain	8 (47)	3 (18)	6 (35)
Uganda	91 (39)	110 (48)	30 (13)
USA	187 (68)	46 (17)	43 (16)
Total	405 (59)	168 (24)	113 (16)

Table 3

Reasons for non-participation by candidate's choice *

	Total† (*n* = 144, 100%) *n* (col%)	Africa (*n* = 57, 40%) *n* (col%)	North America (*n* = 70, 49%) *n* (col%)
Research	40 (27.8)	14 (24.6)	24 (34.3)
Worried about enrolling in any clinical research studies	25 (17.4)	13 (22.8)	11 (15.7)
Worried about efficacy of experimental arm	11 (7.6)	0	11 (15.7)
Worried about blood draw	2 (1.4)	0	2 (2.9)
Length and/or complexity of obtaining informed consent	2 (1.4)	1 (1.8)	0
Communication	6 (4.2)	0	6 (8.6)
Does not understand language available for translation	3 (2.1)	0	3 (4.3)
Understands English, but does not understand study	2 (1.4)	0	2 (2.9)
Unable to communicate for other reasons (e.g., illiterate, mental or neurologic incapacity, etc.)	1 (0.7)	0	1 (1.4)
Patient TB beliefs	1 (0.7)	0	1 (1.4)
Not infected with TB	1 (0.7)	0	1 (1.4)
Clinic/staff	4 (2.8)	4 (7.0)	0
Has trouble keeping medical appointments in general	1 (0.7)	1 (1.8)	0
Travel to/parking at clinic not convenient	3 (2.1)	3 (5.3)	0
Work/school	30 (20.8)	15 (26.3)	6 (8.6)
Number of visits not convenient	20 (13.9)	14 (24.6)	3 (4.3)
Worried about supervisor's/teacher's response to missed work/school	3 (2.1)	0	0
Missing work or school could otherwise be a problem	5 (3.5)	0	2 (2.9)
Worried about losing income	2 (1.4)	1 (1.8)	1 (1.4)
Medication/health	10 (6.9)	2 (3.5)	7 (10.0)
Patient worried about medication side effects	1 (0.7)	0	1 (1.4)
Worried about duration of medication required	1 (0.7)	0	1 (1.4)
Worried about number of pills required per dose	2 (1.4)	0	1 (1.4)
Does not take any medicine in general	3 (2.1)	2 (3.5)	1 (1.4)
Primary care or other physician's concerns about TB in this patient	3 (2.1)	0	3 (4.3)
Patient lifestyle, family, other	29 (20.1)	18 (31.6)	8 (11.4)
Family member against enrollment	2 (1.4)	0	2 (2.9)
Worried about stigmatization due to TB or taking TB medicine	5 (3.5)	5 (8.8)	0
Displeased with recommendation not to drink alcohol while on TB treatment	1 (0.7)	0	0
Perceived potential conflict with recreational drug use	1 (0.7)	0	0
Too much stress now	4 (2.8)	0	3 (4.3)
Worried about use of barrier methods of birth control	1 (0.7)	1 (1.8)	0
Children or other dependents make clinic attendance difficult	1 (0.7)	0	1 (1.4)
Declines to be tested for HIV	14 (9.7)	12 (21.1)	2 (2.9)
Other reasons	16 (11.1)	4 (7.0)	12 (17.1)
Unknown	8 (5.6)	0	6 (0.1)

* Patients who chose to decline could provide multiple reasons; 113 patients provided a total of 144 reasons, with 8 not specified.

[†]Total includes 15 responses from Spain and Brazil.

TB = tuberculosis; HIV = human immunodeficiency virus