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Successful management of multidrug-resistant tuberculosis under programme conditions in the Dominican Republic

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SUMMARY

SETTING: The Dominican Republic is a high-incidence area for multidrug-resistant tuberculosis (MDR-TB; 6.6% of initial cases). Standardised treatment regimens for MDR-TB may be a potential solution.

OBJECTIVE: To present the effectiveness of standard regimens under routine national conditions.

DESIGN: We reviewed all MDR-TB patients treated under routine conditions from 29 August 2006 to 30 June 2010, showing interim and final outcomes. Patients were treated with regimens that were standardised or individualised based on previously received second-line anti-tuberculosis drugs.

RESULTS: Population description and culture conversion data are reported for the 289 MDR-TB patients. The median patient age was 31 years. Most had failed first-line treatment (72.6%). Culture negativity was obtained within 4 months (median 2 months) in 78.6%. Among the 150 patients treated between 2006 and 2008, 74% had favourable results on standardised and 66% on individualised regimens ($P = 0.211$). The efficacy of the standardised and individualised regimens was respectively 92.8% and 81% ($P = 0.056$). The relapse rate was approximately 1%. A median of five drug side effects occurred per patient. More than 2 months to culture conversion and bilateral cavitation on chest X-ray were found to be unfavourable outcome risk factors.

CONCLUSIONS: Standardised MDR-TB regimens may be effective at the national level, even in resource-poor settings.

KEY WORDS: Dominican Republic; multidrug-resistant tuberculosis; MDR-TB; standardised treatment; tuberculosis; TB

MULTIDRUG-RESISTANT TUBERCULOSIS (MDR-TB), defined as *Mycobacterium tuberculosis* strains with in vitro resistance to the two most effective anti-tuberculosis drugs, isoniazid (INH) and rifampicin (RMP), has become a major barrier to achieving successful tuberculosis (TB) control.[1] Among the estimated 500 000 new MDR-TB cases emerging annually worldwide, most are from low- and middle-income countries.[1,2] There are no randomised clinical trials showing the best drug combinations to achieve cure. Anti-tuberculosis treatment based on second-line drugs (SLDs) is less effective, more costly and associated with more adverse events than first-line regimens.[3,4] These difficulties are clearly greater in low- and middle-income countries, which have less access to care and affordable drugs. Even when SLDs are subsidised, programmatic challenges can prevent the completion of the required 18–24 months of treatment.[4] Despite these limitations, by following clinical management principles and with sufficient programme support, MDR-TB can be treated successfully.[5,6] Treatment success can vary from <50%[7–9] to >70%.[10–12]

The Dominican Republic is a Caribbean middle-income country with high rates of human immunodeficiency virus (HIV) co-infection (4.2%–8.3%) in the adult population.[13] The only survey available on drug resistance was published in 1998, where MDR-TB was diagnosed in 6.6% of new TB patients.[14] In April 2005, the World Health Organization (WHO)/Stop TB Partnership's Green Light Committee (GLC) approved an MDR-TB project in the country. The first patients initiated treatment at the end of August 2006.

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The present article assesses the implementation of MDR-TB treatment under routine low-resource programme conditions in the Dominican Republic in terms of effectiveness, side effects and risk factors associated with poor outcomes.

METHODS

This was a retrospective cohort study of all 289 MDR-TB laboratory-confirmed patients who started treatment in the Dominican Republic from 29 August 2006 until 30 June 2010. Only patients starting MDR-TB treatment within the programme for the first time were considered. Socio-demographic and clinical features are reported and the time to culture conversion is evaluated. Final treatment outcome (favourable or unfavourable) was available for the 150 patients entering treatment in 2006–2008. For those with favourable outcome, relapse at 6 months after treatment completion was assessed. Other variables evaluated included adverse drug reactions and risk factors for unfavourable outcome. The flow chart of enrolment of study patients is shown in Figure 1.

Drug susceptibility testing (DST) results were available only for failures on Category I or II treatment or cases with persistent TB after treatment in the private sector. Before 2011, the national reference laboratory only had the capacity to test resistance to first-line drugs. Sputum samples were treated with a modified Petroff method and cultured on Löwenstein-Jensen media. DST was performed using the proportion method according to Canetti et al.[15] At baseline, *M. tuberculosis* isolates were tested for susceptibility to INH (0.2 μg/ml), RMP (40 μg/ml), ethambutol (EMB; 2.0 μg/ml) and streptomycin (4 μg/ml).

Two treatment regimens were used for MDR-TB: 1) the standardised regimen, for patients who had never previously received SLDs, comprised kanamycin (KM), ofloxacin (OFX), ethionamide, cycloserine and pyrazinamide.[3,4] EMB was added if DST showed susceptibility. In 2010, OFX was replaced by levofloxacin and KM by capreomycin (CPM). 2) Individualised regimens were given to those who had received SLDs or if they were in contact with a case who had received SLDs. All individualised regimens were based on at least four drugs that had not been used previously. As many patients had received fluoroquinolones, only 19 regimens incorporated fluoroquinolones. All individualised regimens included one injectable (KM or CPM), and most included para-aminosalicylic acid.[3,4,16] All treatments were supplemented with vitamin B6 (50 mg). Drugs with unclear efficacy (Group 5 drugs)[3,4,16] and surgery were unavailable.

The length of treatment of both regimens was

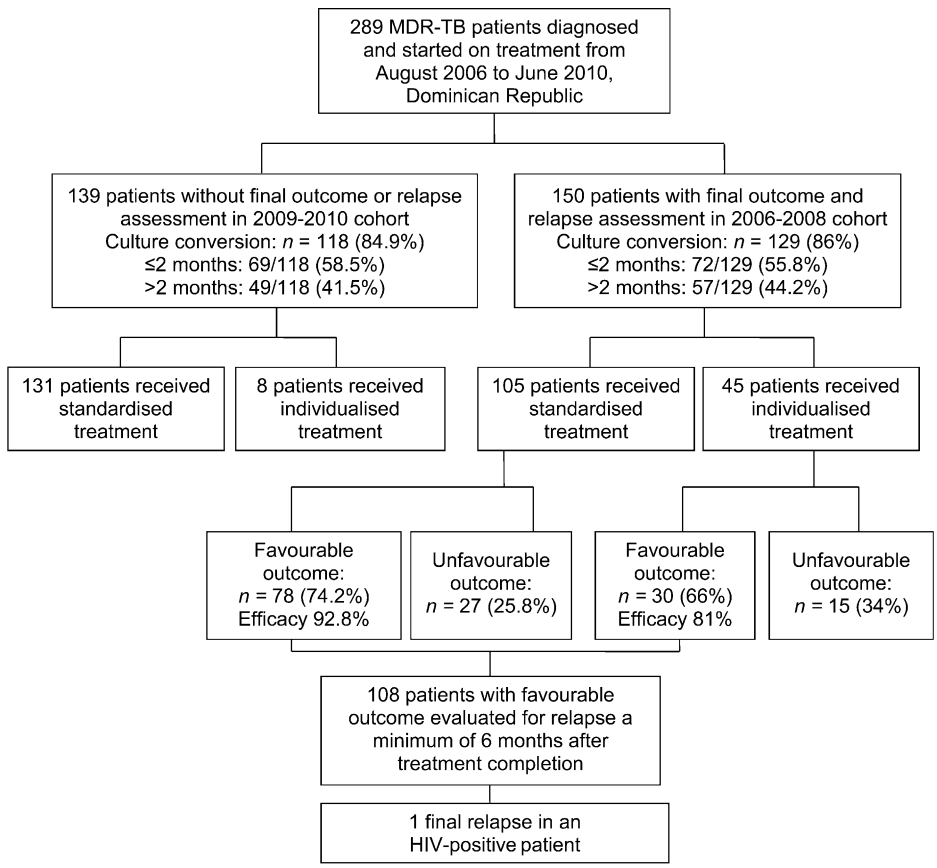

Figure 1 Enrolment, outcome and follow-up of study patients. MDR-TB = multidrug-resistant tuberculosis; HIV = human immunodeficiency virus.

18–24 months. All but four of the patients began hospital-based treatment. Anti-tuberculosis medications were given under directly observed treatment (DOT) in the morning without splitting the doses. Patients remained hospitalised until they became sputum smear-negative, and tolerance to drugs was observed. All patients received at least 6 months of an intravenous injectable given daily in the initial phase. Depending on time to culture conversion or lack of adherence to treatment, some cases received the injectable for a longer period. Oral agents were continued throughout the continuation phase. After discharge, patients continued treatment in selected primary health care centres with staff trained in MDR-TB management.

Each patient underwent clinical and laboratory evaluations before enrolment, monthly during the initial phase of treatment, including smear and culture, and bimonthly during the continuation phase. Basic baseline laboratory tests included a complete blood count, hepatic and renal function and HIV testing (Determine®, Abbott Diagnostic Division, Hoofddorp, The Netherlands). Audiometric, psychiatric and ophthalmological evaluations and thyroid stimulating hormone tests were not available.

The main study outcomes were time to culture conversion and whether the patient was cured or completed treatment (favourable outcome) according to definitions in international MDR-TB guidelines.[4] A relapse assessment was performed by clinical and bacteriological screening at 3, 6 and 12 months after cure or completion of treatment.

All information used was routine data from clinical records and operational files, in accordance with WHO guideline forms and definitions.[4] Information was retrospectively reviewed, and data were collected and entered into Excel 2003 (Microsoft, Redmond, WA, USA) by programme staff from January to June 2011. All reported *P* values were two-sided. $P = 0.05$ was considered statistically significant. Clinically relevant risk factors were analysed applying Cox proportional hazards model to generate association estimates with unfavourable outcome and 95% confidence intervals (CIs). The proportionality of risks in the Cox models were verified using Schoenfeld plots.[17] Analyses were performed using *R* statistical package, version 2.12.1 (R Foundation for Statistical Computing, Vienna, Austria).

Ethics committee approval

Ethical approval was provided by the local authorities and by the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease.

RESULTS

A total of 289 MDR-TB patients were included. The median age was 31 years (interquartile range [IQR]

Table 1 Characteristics of a cohort of 289 patients with MDR-TB at treatment initiation, Dominican Republic

Characteristic	Patients *n* (%)	Median [IQR]
Sex		
Male	156 (54)	
Female	133 (46)	
Age, years		31 [24.5–40.0]
Diabetes mellitus	28 (9.7)	
HIV	12 (4.5)	
Incarceration	24 (8.3)	
Substance abuse	34 (11.8)	
MDR-TB contacts	46 (15.9)	
Use of SLDs in the past	37 (12.8)	
Group condition		
Failure on Category II treatment	101 (34.9)	
Failure on Category I treatment	109 (37.7)	
Others	19 (6.6)	
Relapse	28 (9.7)	
New	22 (7.6)	
Default	10 (3.5)	
BMI, kg/m^2 ($n = 71$)		
Men		20.96 [18.9–23.6]
Women		18.18 [15.6–23.6]
Men with BMI <20	17 (21.2)	
Women with BMI <18.5	14 (20)	
Haemoglobin, g/dl*		
Men		12.5 [11.3–12.5]
Women		10.7 [10–12]
Men with <13 g/dl	66 (43.3)	
Women with <12 g/dl	82 (61.7)	
CXR pattern ($n = 270$)		
Bilateral cavitation	128 (44.3)	
Unilateral cavitation	98 (33.9)	
Abnormal CXR without cavitation	46 (15.9)	
EMB-susceptible ($n = 274$)	146 (50.5)	
Delay in treatment from the time of diagnosis, months		7.3 [4.2–12.0]
Number of patients included per year		
2006 (starting end of August)	24 (8.3)	
2007	57 (19.7)	
2008	69 (23.9)	
2009	89 (30.8)	
2010 (until the end of June)	50 (17.3)	
Type of treatment		
Standardised	135 (46.7)	
Standardised+EMB	101 (34.9)	
Individualised	53 (18.3)	
Time to culture conversion, months		2 [2–3]†
0–2	141 (48.8)	
3–4	84 (29)	
5–6	22 (7.6)	
⩾7	3 (1)	
Never converted‡	39 (13.5)	
Total	289 (100)	

*Data on some of the characteristics were missing for some patients. Data on total haemoglobin levels were available for 90 patients; normal or abnormal haemoglobin values were available for 259 patients.
†Median time to conversion in months. Includes only those achieving conversion.
‡Patients who never culture converted: early deaths and defaults plus real treatment failures.
MDR-TB = multidrug-resistant tuberculosis; IQR = interquartile range; HIV = human immunodeficiency virus; SLD = second-line drugs; BMI = body mass index; CXR = chest X-ray; EMB = ethambutol.

Table 2 Outcomes of a cohort of 150 patients with multidrug-resistant tuberculosis by year of entry into treatment and type of treatment, Dominican Republic

Characteristic	Total *n* (%)	Cure *n* (%)	Treatment completed *n* (%)	Treatment success *n* (%)	Failure *n* (%)	Death *n* (%)	Default *n* (%)	Treatment efficacy*	*P* value†
Results by year of treatment entry									0.656
2006	24 (16)	18 (75)	0	18 (75)	3 (12.5)	3 (12.5)	0		
2007	57 (38)	40 (70.2)	1 (1.8)	41 (71.9)	6 (10.5)	5 (8.8)	5 (8.8)		
2008	69 (46)	45 (65.2)	4 (5.8)	49 (71)	4 (5.8)	9 (13)	7 (10.1)		
Results by type of treatment									0.211
All standardised	105 (70)	73 (69.5)	5 (4.7)	78 (74.2)	6 (5.7)	12 (11.4)	9 (8.6)	92.8	
Standardised	55 (36.7)	40 (72.7)	3 (5.4)	43 (78.2)	4 (7.3)	6 (10.9)	2 (3.6)	91.5	
Standardised+EMB	50 (33.3)	33 (66)	2 (4)	35 (70)	2 (4)	6 (12)	7 (14)	94.6	
All individualised	45 (30.3)	30 (66)	0	30 (66)	7 (15.6)	5 (11.1)	3 (6.7)	81	
Total	150	103 (68.6)	5 (3.3)	108 (72)	13 (8.6)	17 (11.3)	12 (8)	89	

*Calculated as cured + treatment completed/(cured + treatment completed + failures).
†Pearson's χ^2 test.
EMB = ethambutol.

24.5–40.0), with similar sex proportions (54% men). Most of the patients were from Santo Domingo, the capital city (71.6%). Most (72.6%) had previously failed treatment, 9.7% had relapsed and 3.5% had defaulted from treatment; 7.6% were new incident MDR-TB cases. A high proportion of the sample population (15.9%) were contacts of MDR-TB patients. Approximately 7% had no information on previous treatment, as most were from the private sector.

At least 37 patients had used SLDs in the past, particularly fluoroquinolones. Twelve (4.5%) were HIV-infected. Illicit substance abuse was recorded for 34 (11.8%) and 24 (8.3%) had a history of incarceration. On chest X-ray, 78.2% of the patients had cavitation, and for the 259 with an available haemoglobin test, levels were low in 57.1% (<13 g/dl for men and <12 g/dl for women, Table 1).

The median time between requesting DST and starting treatment was 7.3 months (IQR 5.4–14.2); however, this delay steadily decreased over the years. Most patients were treated using a standardised regimen (81.7%). Culture conversion was obtained in 250 patients (86.5%). The median time to culture conversion was 2 months (IQR 2–3), and 78.6% of patients had achieved culture negativity by the fourth month. There were no statistically significant differences in speed of conversion as regards type of regimen or year of treatment. Among the 39 cases (13.5%) who did not convert, 17 were early deaths, 10 defaulted from anti-tuberculosis treatment, and one completed treatment (MDR-TB confirmed by biopsy). Only 11 of those who did not convert were assumed to be failures (nine of these were from the early cohorts, 2006–2008).

Final outcome data were available for all 150 patients who entered into treatment during 2006–2008. Of these, 129 (86%) achieved culture conversion. Overall, 72% (n = 108) achieved a favourable outcome within a median treatment time of 20.7 months (IQR 19–22). Table 2 summarises these results by year of entry and type of treatment. Among the 105 MDR-TB patients who received the standardised regimen, a favourable outcome (cured or completed treatment) was achieved by 74.2% (78.2% standardised vs. 70% standardised+EMB). Of the 45 (30%) patients who received individualised regimens, 66% had favourable outcomes. There were no statistically significant differences in outcome or survival time by type of treatment or previous use of SLDs. Appendix Figure A.1 shows the survival curve by type of MDR-TB regimen.*

Treatment efficacy was calculated as the sum of cured + treatment completed divided by the sum of cured + treatment completed + failures. According to the results for the 150 patients with final outcomes, overall treatment efficacy was 89%. The efficacy of the individualised regimen was 81%, while the efficacy of the standardised regimen was 92.8% (P = 0.056).

Unfavourable outcomes (defined as death, failure or default) occurred in 28% of the 150 patients: 11.3% died, 8.7% failed and 8% defaulted. Death occurred at a median of 7 months after initiating treatment (IQR 3–7), default mostly occurred at 7.5 months (IQR 3.25–17), and failure occurred mainly at 14 months (IQR 12.5–20.5). Among the two HIV-infected cases, one was cured and the other defaulted.

In univariate analysis (Appendix Table A.1), culture conversion after >2 months was found to predict an unfavourable outcome, with a hazard ratio of 2.65 (95%CI 1.37–5.29, P = 0.005). Low haemoglobin and bilateral cavitation on chest X-ray were also predictive of an unfavourable outcome, but with borderline significance. After adjusting for potential confounders in the final multiple regression model,

*The Appendix is available in the online version of this article at http://www.ingentaconnect.com/content/iuatld/ijtld/2013/00000017/00000004/art00017

conversion after >2 months ($P = 0.011$) and bilateral cavities ($P = 0.031$) were significantly associated with unfavourable outcome (Appendix Table A.1).

All but two patients reported some kind of adverse event, with a median of five side effects per patient (IQR 3–6). Most cases presented mild and manageable adverse events, mainly gastrointestinal disturbances. In only one case did the causative anti-tuberculosis medication need to be suspended (psychotic episode); treatment was resumed without cycloserine once the patient's condition had stabilised. A complete description and frequency of the side effects are shown in Appendix Table A.2 and Figure A.2.

A relapse assessment was performed in the 108 patients with a favourable outcome. At least 6 months of follow-up was considered acceptable;[18] however, 83.3% were followed for >1 year (range 8–34 months). Of these patients, 100 were asymptomatic, 4 died, 2 were symptomatic and 2 were lost to follow-up. Overall, only one case was confirmed as an MDR-TB relapse.

DISCUSSION

The question of whether national TB programmes should invest in SLDs and MDR-TB management has been widely discussed.[19] Only when MDR-TB was recognised as a global epidemic was there a need to face this problem under programme conditions.[20] Our experience in the Dominican Republic, working under programme conditions with many limitations, can be considered encouraging, as the country has achieved treatment successes (72%) comparable to the best experiences published to date with individualised management in reference and high-resource settings.[10,12,21–25] Moreover, the success rates are higher than that estimated for GLC-approved programmes (60%),[22] and higher than those gathered in the two meta-analyses analysing MDR-TB treatment outcomes.[5,6] In the meta-analysis published by Johnston et al.,[5] including 31 programmes from 21 countries, a treatment success rate of 62% (95%CI 57–67) was achieved, while in the meta-analysis published by Orenstein et al., studies that combined treatment duration of at least 18 months and DOT throughout had significantly higher pooled success rates (69%) than those who did not (58%).[6] Our experience seems to confirm these results, as the use of DOT and prolonged treatment achieved a similar outcome (72%). Conversely, our experience achieved higher results with standardised regimens than those reported in the meta-analysis (74.2% vs. 54%), while patients in our study who received individualised treatment achieved similar outcomes (66% vs. 64%). At the time of the study, access to some SLDs was limited and high-dose fluoroquinolones were not indicated. Patients receiving individualised treatment may have had *M. tuberculosis* strains with a more extensive pattern of resistance. All of these factors could have contributed to the relatively reduced effectiveness of individualised regimens.

Before 2010, patients waited many months to enter into treatment. Some died during the delay, and the rest were aware of that. This may be why our patients were particularly adherent and able to endure side effects. In addition, as these patients had lived with the disease for many years, some kind of survival effect may have existed.

Regarding the efficacy of the regimens used, our overall result of 89% is among the highest published.[3] The median time to achieve culture negativity, also a reflection of efficacy, was as early as 2 months (IQR 2–3), similar to the 58–99 days published in the TBNET (Tuberculosis European Network) systematic review.[26] The effectiveness of the regimen might have been even better, with fewer deaths and defaults, had intensive care and social support accompanied the treatment.

In the multivariate analysis, only conversions that took place after 2 months ($P = 0.008$) and bilateral cavities ($P = 0.032$), factors not usually analysed in other studies, were significantly associated with unfavourable outcome. Bilateral cavitation was linked to death (15%) and failures (10%), while culture conversion after 2 months was found to be an even stronger risk factor for both (15.6% death, 16.9% failures). Borderline significance was obtained for low haemoglobin ($P = 0.075$), which has been shown to be a worse outcome predictor in other studies.[10,23] Using an EMB-containing standardised regimen also acted as a borderline significant risk factor ($P = 0.054$). Nonetheless, we believe that adding EMB was not in itself a risk factor for defaulting, but a result of residual confounding.

The anarchic use of SLDs in the past was notably frequent in the early years of implementation. The use of individualised regimens fell from 58.3% in 2006 to only 16% in 2010. It appears that the introduction of MDR-TB treatment by the National Tuberculosis Control Programme has reduced the uncontrolled use of anti-tuberculosis SLDs, making individualised regimens, which are often more lengthy and much more expensive, less necessary. The proportion of side effects (median five per patient) observed was greater than in other studies,[27,28] but treatment had to be interrupted for only one patient. Aggressive treatment of side effects and correct drug dosages might have been crucial in preserving treatment activity.

The current study is subject to several limitations, mainly due to use of routine data and resource constraints. Some key information, such as the number of drugs to which each patient was resistant and other potential risk factors, is missing, and data on specific causes of death or default during treatment were unavailable. However, other typical factors associated with worse outcome in MDR-TB management were

probably not significant due to the size of our population. The relapse assessment was performed with many restrictions and with inconsistent availability of culture confirmation in asymptomatic patients. Furthermore, the lack of funding made it impossible to assess the role of reinfection. Nonetheless, the use of routine data and field limitations do not diminish the interest of the findings; on the contrary, they bring them closer to the reality of MDR-TB in low- and middle-income countries.

In conclusion, based on programme conditions and with effective standardised treatment, successful, low-cost MDR-TB management can be achieved even in resource-constrained settings with high initial MDR-TB rates. The overall 86.4% culture conversion and 74.3% treatment success rates achieved with standardised treatment regimens in the Dominican Republic are good examples.

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Conflict of interest: none declared.

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APPENDIX

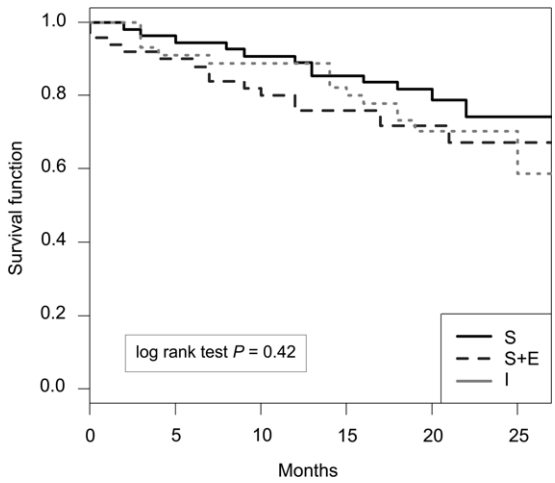

Figure A.1 Kaplan-Meier survival estimates and treatment length in a cohort of 150 patients with multidrug-resistant tuberculosis, Dominican Republic, by type of treatment regimen.

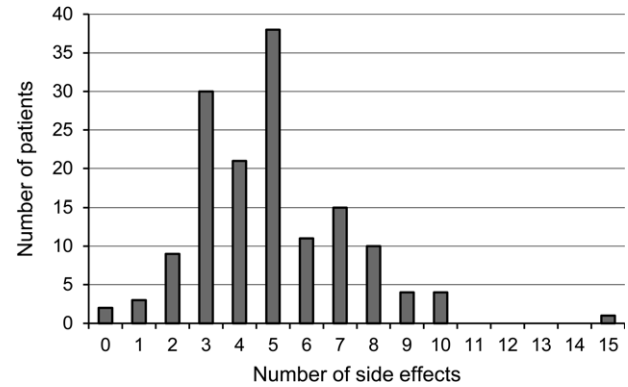

Figure A.2 Number of adverse events reported per case in a cohort of 150 multidrug-resistant tuberculosis patients, Dominican Republic.

Table A.1 Univariate and multivariate analysis of risk factors associated with unfavourable outcome during treatment in a cohort of 150 patients with multidrug-resistant tuberculosis, Dominican Republic

Risk factor	Patients with unfavourable outcome *n/N* (%)	Univariate analysis* Crude HR (95%CI)	*P* value†	Multivariate analysis* adjusted HR (95%CI)‡
Sex				
Female	23/80 (28.7)	1		
Male	19/70 (27.1)	1.01 (0.55–1.85)	0.984	—
Age, years				
⩽30	20/78 (25.6)	1		
>30	22/72 (30.6)	1.21 (0.66–2.24)	0.54	—
Diabetes mellitus				
No	38/136 (27.9)	1		
Yes	4/14 (28.5)	1.16 (0.41–3.27)	0.775	—
Substance abuse				
No	35/132 (26.5)	1		
Yes	7/18 (38.9)	1.60 (0.71–3.61)	0.261	—
Contact with MDR-TB case				
No	35/121 (28.9)	1		
Yes	7/29 (24.1)	0.79 (0.35–1.79)	0.571	—
Use of SLDs in the past				
No	32/119 (26.9)	1		
Yes	10/31 (32.3)	1.05 (0.51–2.15)	0.889	—
BMI				
Normal	9/40 (22.5)	1		
Low	13/31 (41.9)	1.93 (0.82–4.52)	0.13	—
Haemoglobin				
Normal	10/49 (20.4)	1		
Low	29/74 (39.2)	2.04 (1.00–4.20)	0.051	2.13 (0.93–4.92)
CXR findings				
Abnormal CXR without cavitation	4/26 (15.4)	1		
Unilateral cavitation	14/51 (27.5)	1.77 (0.58–5.42)	0.315	—
Bilateral cavitation	22/60 (36.7)	2.64 (0.91–7.68)	0.075	3.62 (1.12–11.65)
EMB-susceptible				
Yes	22/80 (27.5)	1		
No	20/70 (28.5)	0.89 (0.48–1.65)	0.718	—
Delay in treatment after diagnosis, months				
⩽10	19/75 (25.3)	1		
>10	23/75 (30.7)	1.19 (0.65–2.18)	0.584	—
Type of treatment				
Standardised	12/55 (21.8)	1		
Standardised+EMB	15/50 (30)	1.56 (0.73–3.33)	0.252	2.62 (0.98–7.02)
Individualised	15/45 (33)	13.46 (0.68–3.17)	0.334	—
Speed of conversion, months				
⩽2	11/72 (15.3)	1		—
>2	31/72 (40.3)	2.65 (1.33–5.29)	0.005	2.69 (1.25–5.78)
Side effects				
⩽5	27/104 (26)	1		
>5	15/46 (32.6)	1.35 (0.72–2.56)	0.351	—

*Cox proportional-hazards regression analyses.
†Log-rank test.
‡The multivariate model included haemoglobin levels, CXR findings, conversion delay, type of treatment, age, treatment delay, SLDs used in the past, illicit drug abuse, diabetes mellitus and contact with MDR-TB case. The variable BMI was not included in the multiple logistic regression model due to the large number of missing values. EMB susceptibility, sex and number of side effects also disrupted the proportionality of the analysis, and were not included.
HR = hazard ratio; CI = confidence interval; SLD = second-line drugs; BMI = body mass index; CXR = chest X-ray; EMB = ethambutol.

Table A.2 Adverse events reported per case in a cohort of 150 patients with multidrug-resistant tuberculosis, Dominican Republic

Organ or system affected	Description of side effect	Frequency *n* (%)
Gastrointestinal	Nausea	144 (96)
	Vomiting	104 (69.3)
	Loss of appetite	51 (34)
	Gastritis	47 (31.3)
	Abdominal pain	46 (30.6)
	Diarrhoea	7 (4.6)
	Constipation	1 (0.7)
Oto-vestibular	Dizziness (motion sickness)	54 (36)
	Hearing loss reported by patient	31 (20.6)
	Tinnitus	12 (8)
	Otalgia	2 (1.3)
Musculoskeletal	Arthralgia (joint pain)	46 (30.6)
Neurological	Peripheral neuropathy	41 (27.3)
	Headache	45 (30)
	Abnormal tremors or shaking	3 (2)
	Vision loss confirmed by physician	1 (0.7)
	Convulsions	1 (0.7)
Neuro-psychiatric	Anxiety	35 (23.3)
	Insomnia	15 (10)
	Depression diagnosed by physician	11 (7.3)
	Psychotic episodes with visual or auditory hallucinations	4 (2.6)
Dermal	Dermatitis and cutaneous eruption	21 (14)
	Alopaecia	1 (0.7)
Renal	Hypokalemia (potassium <3.5 mEq/l)	8 (5.3)
	Renal failure (creatinine >141 mmol/l)	6 (4)
	Hyponatraemia (sodium <136 mEq/l)	1 (0.7)
Cardiovascular	Tachycardia and/or palpitations reported by the patient with or without findings on ECG	8 (5.3)
Endocrine and metabolic	Mastalgia and gynaecomastia (breast pain or increase in size reported by patient)	3 (2)
	Hyperglycaemia (glycaemia >120 mg/dl)	1 (0.7)
	Amenorrhoea	1 (0.7)
Hepatic	Elevation of serum transaminases (<5 times normal levels without other signs of hepatitis)	2 (1.3)
Genitourinary	Dysuria	1 (0.7)

ECG = electrocardiogram.

RÉSUMÉ

CONTEXTE : L'incidence de la tuberculose multirésistante (TB-MDR) est élevée en République Dominicaine (6,6% de cas initiaux). Des régimes standardisés de traitement de la TB-MDR peuvent constituer une solution.

OBJECTIF : Exposer l'efficience des régimes standards dans les conditions nationales de routine.

SCHÉMA : Nous avons revu l'ensemble des patients TB-MDR traités dans des conditions de routine entre le 29 août 2006 et le 30 juin 2010 ainsi que les résultats intermédiaires et finaux. Les patients ont bénéficié de régimes standardisés ou individualisés en fonction de l'utilisation antérieure de médicaments antituberculeux de deuxième ligne.

RÉSULTATS : Nous rapportons la description de la population et les données de négativation des cultures chez les 289 patients TB-MDR. L'âge médian des patients était de 31 ans ; chez la plupart d'entre eux, le traitement par les médicaments de première ligne avait échoué (72,6%). On a obtenu une négativation des cultures dans 78,6% des cas à 4 mois (valeur médiane 2 mois). Parmi les 150 patients traités entre 2006 et 2008, les résultats ont été favorables chez 74% avec un régime standardisé et chez 66% avec un régime individualisé ($P = 0,211$). Les efficacités respectives du régime standardisé et individualisé ont été de 92,8% et de 81% ($P = 0,056$). Le taux de rechute a été d'environ 1%. On a noté une valeur médiane de cinq effets collatéraux des médicaments par patient. Les facteurs de risque de résultats défavorables ont été une durée supérieure à 2 mois avant la négativation des cultures et la présence de cavités bilatérales au cliché thoracique.

CONCLUSIONS : Les régimes TB-MDR standardisés peuvent être efficaces au niveau national, même dans des contextes à ressources limitées.

RESUMEN

MARCO DE REFERENCIA: La República Dominicana es un país de alta tasa de tuberculosis multidrogorresistente (TB-MDR; 6.6% de los casos iniciales). Los tratamientos estandarizados pueden ser una potencial solución para la TB-MDR.

OBJETIVO: Presentar la efectividad de los regimenes estandarizados en condiciones rutinarias a nivel nacional.

DISEÑO: Se revisaron los pacientes tratados de TB-MDR en condiciones de programa desde el 29 de agosto de 2006 al 30 de junio de 2010 mostrando resultados provisionales y finales. Los pacientes recibieron tratamientos estandarizados o individualizados según el uso previo de medicamentos antituberculosos de segunda línea.

RESULTADOS: Se describe una población de 289 pacientes con TB-MDR y se reporta su tiempo de conversión de cultivo. La mediana de edad de los pacientes fue de 31 años, la mayoría procedentes de tratamientos fallidos con medicaciones de primera línea (72,6%). La negativización del cultivo fue obtenida en 4 meses por el 78,6% (mediana 2 meses). De los 150 pacientes tratados entre 2006 y 2008, obtuvieron resultados favorables el 74% de los que recibieron tratamiento estandarizado y el 66% de los que recibieron individualizados ($P = 0,211$). La eficacia de los regímenes estandarizados e individualizados fue 92,8% y 81% respectivamente ($P = 0,056$). La tasa de recaídas fue aproximadamente del 1%. Hubo una mediana de cinco efectos adversos por cada paciente. Más de 2 meses en negativizar el cultivo y la presencia de cavitación bilateral en la radiografía de tórax resultaron como factores de riesgo independientes.

CONCLUSION: Los regimenes estandarizados pueden ser efectivos para el tratamiento de la TB-MDR a nivel nacional, incluso en países de escasos recursos.