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Effectiveness of Community-Based Multidrug-Resistant Tuberculosis Treatment in Nigeria: A Retrospective Cohort Study

Dr Aliyu Abubakar[1] Dr Ali Davod Parsa[2] Dr Susan Walker[3]
1. School of Allied Health, Faculty of Health Education Medicine and Social Care, Anglia Ruskin University, Chelmsford, United Kingdom FHEMS-ARU
2. School of Allied Health, Faculty of Health Education Medicine and Social Care, Anglia Ruskin University, Cambridge, United Kingdom
3 School of Nursing and Midwifery, Faculty of Health Education Medicine and Social Care, Anglia Ruskin University, Chelmsford, United Kingdom.

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ABSTRACT: *Growing multidrug-resistant tuberculosis (MDR-TB) worldwide and new effective and affordable treatment modalities required exploring options such as the community model of MDR-TB treatment (CM), as introduced in Nigeria.To determine the most effective care model by comparing MDR-TB treatment outcomes at community-based sites with the hospital-based model of care in Nigeria.Treatment outcomes data were retrospectively accessed from the medical record of 423 MDR-TB patients to evaluate the effectiveness of HM and CM based on WHO criteria. Treatment success" is defined as the sum of cure and treatment completion. "Cure" is the "treatment completion" with at least three negative cultures taken at least 30 days apart after the intensive phase in the absence of "treatment failure. Predictors of treatment outcomes were also assessed on multivariate analysis. 423 patients (85% of the targeted sampling data) were available for analysis, of whom 272 (63.4%) had a conventional regimen, and 143 (33.8%) had a shorter treatment regimen. There is no significant difference in treatment outcomes between CM and HM; patients achieve similar treatment success in all models, 65.5% with HM compared to 68% at the CM (p = 0.608). Treatment failure was (4.1% versus 5.1%) in the HM versus CM, respectively; (p = 0.704). Death occurred in 20.9% of participants in the hospital model and 17.5% in the community model, and rates of Loss to follow-up were similar 9.5% HM vs 9.5% CM; (p = 0.704). On multivariate analysis, adjusting for age, HIV, sex, patient type, TB treatment history, resistance pattern, model of care and regimens, there was no change in treatment outcomes if patients were treated at the CM vs HM (adjusted odds ratio [aOR] 0.92; 95% CI 0.59 – 1.46, p = 0.735). MDR-TB patients with unknown HIV status (not on ART) were nine times more likely to have unsuccessful treatment outcomes compared with HIV-negative respondents (adjusted odds ratio [aOR] 8.83; 95% CI 1.79 – 43.60, p = 0.007). Similarly, HIV-positive respondents were 1.3 times more likely to have unsuccessful outcomes than HIV-negative (adjusted odds ratio [aOR] 1.26; 95% CI 0.71–2.26, p = 0.429, but the difference is not statistically significant. This retrospective study found that the community-based model is equally effective as care in a centralised hospital, based on similar treatment success rates, comparable default and death rates with hospital care and shorter time to treatment initiation at the community-based centres.*
***KEY WORDS**:* Community care, effectiveness, Hospital care, MDR-TB, Nigeria.

INTRODUCTION

Tuberculosis (TB) is a chronic infectious disease caused by *Mycobacterium tuberculosis (M. tuberculosis)* and the world's second deadliest infectious disease after COVID-19, ranking above HIV/AIDS (Trajman, et al., 2022). An estimated 10.6 million people globally developed

TB disease, with 1.6 million deaths in 2021 (Bagcchi, 2023). Advances made in the diagnosis and treatment of TB disease are threatened by the emergence of multidrug-resistant TB (MDR-TB), defined as TB caused by *M. tuberculosis* strains resistant to rifampicin and isoniazid, the two most effective first-line anti-TB drugs (Cho et al., 2022).

The trend of MDR-TB is rising in almost all regions of the world, and efforts to combat the disease are not commensurately rapid, taking a heavy toll on patients, communities and healthcare systems (Dheda et al., 2017). The proportion of TB cases with MDR-TB varies considerably among regions and countries, with a more significant burden in low and middle-income countries (LMICs) (Bada et al., 2019). Globally, an estimated 0.45 million people developed MDR-TB in 2021, an increase of 3.1% from 0.437 million in 2020 (Bagcchi, 2023). Over the past two decades, it has become apparent that the rising MDR-TB cases have continued to jeopardise the global efforts to cure patients and meet the ambitious targets of the End TB Strategy of ending TB by 2035 (Mirzayev et al., 2021; Gomez et al., 2021).

The effect of MDR-TB is detrimental to patients and healthcare systems, and only about 37% of estimated MDR-TB cases were enrolled for treatment in 2021, with low cure rates (Bagcchi, 2023).

MDR-TB treatment is more difficult for patients to tolerate than first-line anti-tuberculosis treatment due to the long duration of treatment, frequent medication toxicities and the daily administration of an injectable drug (Nunn et al., 2019). Treatment options for MDR-TB are few and, despite recent advancements, still involve long treatment, high pill counts of more than 14,000 pills for up to 20 months and painful injections (Sweeney et al., 2022). There have been changes in the treatment options available for people with MDR-TB, commencing with "Bangladesh regimen", a standardised shorter nine months treatment regimen that resulted in a relapse-free cure of 87.9% (Van Deun et al., 2010), followed by all-oral 9-month shorter regimens and 20-month longer regimens currently used in most countries. The most recent success is the recommendation of BPaL regimens, which contain bedaquiline, pretomanid, and linezolid, which are all-oral and only six months in duration (Berry, et al., 2022; Nyang'wa, et al., 2022), compared with 9-month shorter regimens and 20-month longer regimens currently used in most countries.

Most countries have adopted a hospital treatment model (HM) where patients are admitted to specialised hospitals to allow enhanced monitoring of adverse drug reactions and treatment compliance (WHO, 2011). Unfortunately, resource limitations and lack of hospital capacity often force patients to wait for several months before initiation of treatment, which might favour transmission.

To address these challenges, the WHO recommends a community treatment model for MDR-TB (CM), which involves utilising family members, neighbours, community healthcare support workers (CHSWs), or former TB patients to observe and support the patients throughout the treatment period directly (WHO, 2016). Alternative community-based treatment could increase MDR-TB treatment capacity limited by hospital bed availability, reduce the time to treatment initiation and make treatment more accessible by being closer to

patients (Loveday et al., 2015). Although the recommendation by WHO to practise CM was based on a limited number of uncontrolled trials (WHO, 2011), it has since been adopted by many countries with favourable outcomes (Weiss et al., 2014; Loveday et al., 2015; Wai et al., 2018; Yin et al., 2018; Dunga et al., 2019). Despite this recommendation, the National tuberculosis programme in Nigeria largely uses hospital-based MDR-TB treatment to allow close monitoring of adverse events and adherence (Musa et al., 2016; Bieh, Weigel and Smith, 2017; Bada et al., 2019). However, in practice, adopting this model in resource-limited settings implies that patients with MDR-TB must wait for hospital beds to become available (Fitzpatrick and Floyd 2012).

In Nigeria, the hospital-based MDR-TB model entails in-patient care for the initial eight months of treatment with a longer regimen and four months with a shorter regimen that allows for monitoring of adverse drug reactions and ensures adherence (Bada et al., 2019).

Patients enrolled on HM in Nigeria are cared for by nurses trained to care for MDR-TB patients. They remain in care in a specially built ward for the intensive phase. Physicians attend to these patients for about 15 minutes per week during the intensive phase.

In the community-based model, patients receive intensive phase care in their homes and community centres from trained healthcare providers. They visit them daily to observe and administer medications (Musa et al., 2016) and concurrently provide psychosocial support to the patients.

During the continuation phase, patients in both arms receive CM in community health centres and experience the same exposure and outcomes. Patients are seen monthly by a physician.

Evidence about the relative effectiveness of the CM versus HM is limited in Nigeria (Musa et al., 2016). Previous similar studies relied on secondary data from the systematic reviews of studies outside Nigeria (Bassili et al., 2013; Weiss et al., 2014) or outcomes of community-based treatment without hospital comparison (Wai et al., 2018; Yin et al., 2018). Those conducted in Nigeria were limited to comparing culture conversion (Oladimeji et al., 2014), the outcome in the intensive phase (Oyefabi et al., 2020) or the qualitative experience of hospital-based patients (Bieh, Weigel and Smith, 2017). However, policymakers also need in-country information on the potential clinical efficacy of CM compared to HM for scaling up at the programmatic level.

The “treatment success” is defined by WHO as the proportion of patients cured or completed treatment. The WHO defines “cure” as treatment completion without evidence of failure and with at least three consecutive negative cultures taken at least 30 days apart after the intensive phase. Treatment completion – a patient completes treatment without evidence of failure but no record of three or more consecutive negative cultures taken at least 30 days apart after the intensive phase.

Effectiveness data are part of the evidence needed to inform decisions about how to scale up MDR-TB treatment in Nigeria and other LMICs.

The present study evaluates the community-based model of MDR-TB care based on treatment success (clinical effectiveness) compared to care in a hospital setting in Nigeria and predictors of treatment outcome.

METHODS

Study design

Routinely collected data from the MDR-TB register and patients' medical records were retrospectively analysed to evaluate and compare the clinical effectiveness of CM versus HM from Nigerian perspectives, programme characteristics, and clinical progression for MDR-TB patients treated in hospital compared to community. The WHO definitions of treatment outcomes were used to assess the clinical effectiveness of HM vs CM.

Study settings

The study was conducted in North-Western Nigeria, covering the three most populous states in the region (Kano, Kaduna, and Katsina), with the highest prevalence of MDR-TB and economic deprivation. Nigeria has a GDP per capita of US $2,065.7 (Basak, et al., 2022) and unequal wealth distribution, with about 50% of the 200 million Nigerian population living below the international poverty line of $1.90 per day (Ikem and Akintayo, 2022).

sample size and sampling strategy

The sample size was estimated using G power statistical software (Faul et al., 2009) based on two proportions of treatment success, HM 66.7% and CM 58%, based on previous studies (Loveday et al., 2015; Fitzpatrick and Floyd, 2012) using Fischer exact test. An estimated sample size of 510 was calculated, which was deemed sufficient to achieve 80% power to detect the effectiveness differences between CM and HM, with a significance alpha level of 0.05 and effect size based on the absolute difference between the two proportions (8.7%). Of the total 510 patients targeted sample size, data of 423 patients (85%) of the targeted sample size were available for analysis (Figure 1 enrolment flow chart).

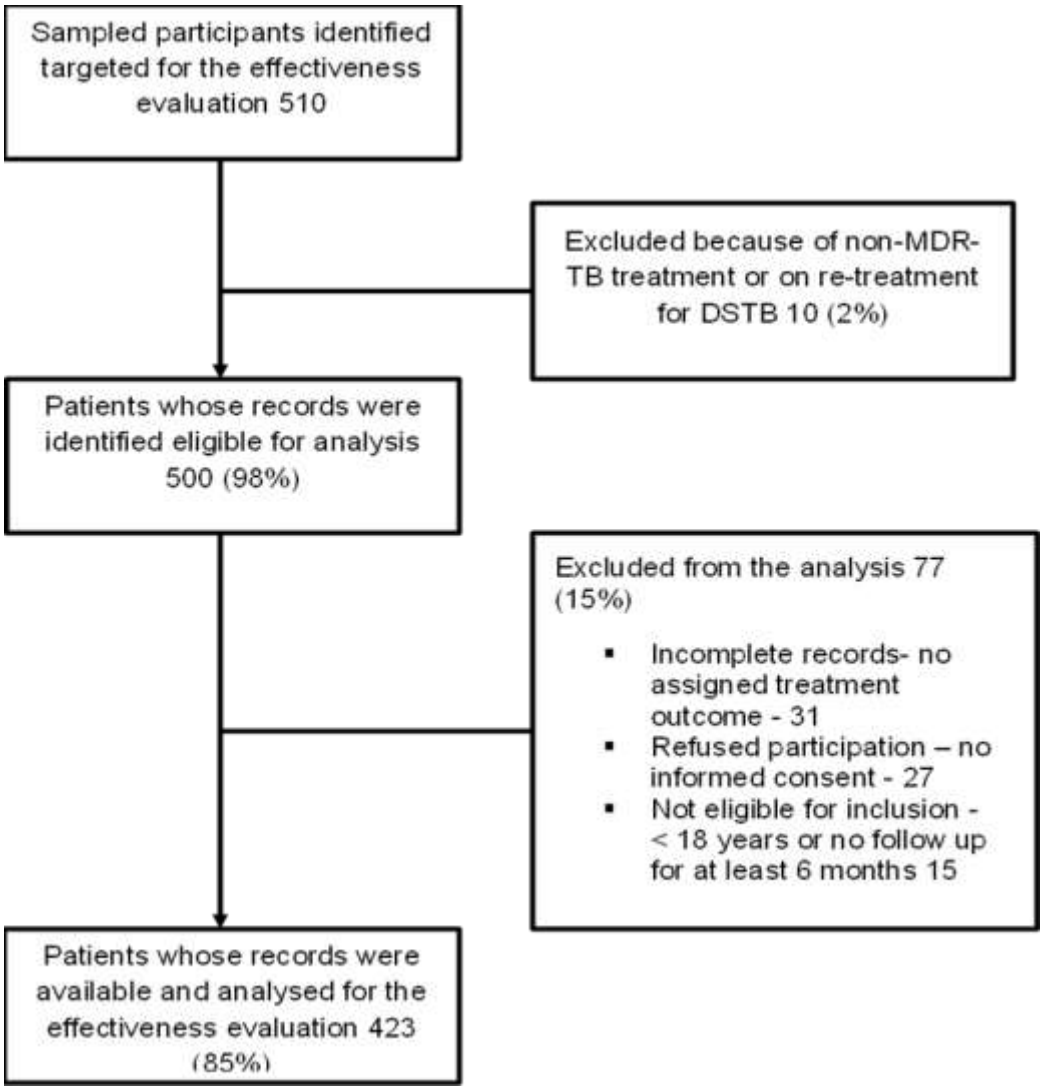

Figure 1 Enrolment flowchart

Participants identification and enrolment

All diagnosed MDR-TB patients aged 18 years that received either community or hospital treatment according to the Nigerian NTP guidelines were eligible to participate. Participants were identified through the MDR-TB register and medical records with the help of MDR-TB focal persons. Patients were eligible if they received a conventional or shorter regimen according to the Nigerian NTP guidelines, adapted from the WHO (2016) MDR-TB treatment guidelines. Patients were excluded if they were less than 18 years old, did not qualify for the WHO definition of MDR-TB, and had missing treatment outcome records.

We retrospectively collected baseline data, clinical characteristics and progression, and final treatment outcomes of MDR-TB patients treated either in the community or hospital between January 2012 and December 2018. The earlier limit period of 2012 was when CM commenced

in Nigeria. The closing date of 2018 allowed the completion of treatment and at least six months follow-up period, considering the duration of MDR-TB treatment and the period of this study's fieldwork.

MDR-TB treatment protocol in Nigeria

Patients diagnosed with MDR-TB were enrolled on either HM or CM (Bada et al., 2019). The selection into either treatment arm in Nigeria is by chance and does not bias the outcome or the cost of care (Musa et al., 2016). Nevertheless, the effect of confounding factors on treatment outcomes was adjusted during the analysis.

All patients received a standardised treatment regimen consisting of eight months intensive phase and a 12-month continuation phase (longer regimen) or nine months standardised shorter regimen consisting of a 4-month intensive phase and a 5-month continuation phase (shorter regimen) (FMoH, 2017; Bada et al., 2019). Patients on a 20-month conventional regimen received pyrazinamide, levofloxacin/moxifloxacin, kanamycin, prothionamide and cycloserine supplemented by kanamycin during the initial 8-month intensive phase. Patients on shorter regimen received moxifloxacin, clofazimine, ethambutol, and pyrazinamide administered over nine months, supplemented by kanamycin, high-dose isoniazid, and prothionamide in the first four months of the intensive phase similar to Bangladesh regimen (Van Deun et al., 2010). Subsequently, bedaquiline replaced kanamycin to achieve all oral longer and shorter regimens (Cox et al., 2020).

Outcome of interest

Clinical charts were reviewed to obtain data on demographics, clinical findings, treatment regimens, and laboratory results. The primary outcome of interest is the difference in the effectiveness between HM and CM. The measure of effectiveness used is the treatment success based on MDR-TB treatment outcome variables as defined by the WHO (2013) (Table 1).

Table 1 WHO treatment outcome definitions

Outcome variables	Definitions
Cure	Completion of treatment as recommended by the guidelines without evidence of failure, and with 3 or more consecutive negative culture results taken at least 30 days apart during continuation phase
Treatment completion	Completion of treatment according to the guidelines but without bacteriological documentation of cure
Treatment success	The percentage of patients in whom the treatment outcome was either cured or completed, i.e., % successful = no. of patients cured + no. of patients completed treatment/ total no. who initiated treatment x 100
Treatment failure	Patient with 1 or more positive culture during continuation phase of treatment, or if any one of the final 3 cultures was positive, or if more than 1 drug in the treatment regimen was replaced, or if treatment was terminated due to adverse events or absence of clinical improvement or evidence of acquired resistance to fluoroquinolones or second-line injectable drugs
Loss to follow-up	Interruption in treatment for 2 or more consecutive months for any reason
Death	Patient who died for any cause during MDR-TB treatment
Unsuccessful treatment	The percentage of patients in whom the treatment outcome was died, loss to follow-up or failed treatment i.e. % unsuccessful = no. of patients died + no. of patients loss to follow-up + no. of patients failed treatment /total no. who initiated treatment x 100
Not evaluated	A patient with no assigned treatment outcome, including patients transferred out to another facility whose treatment outcome is unknown

MDR-TB = Multidrug-resistant TB

Source: WHO, (2013)

Data management and analysis

EpiData Version 3.1 (EpiData Association, http://www.epidata.dk, EpiData Association, Odense, Denmark) was used to set up the data entry system. Data on baseline information (age,

HIV status, type of TB patient, site of TB, pattern of resistance regimens treatment models), clinical progression (date of sputum collection, culture results) and final treatment outcome of MDR-TB patients were retrieved retrospectively through patients' medical records and the MDR-TB Register. Treatment outcome variables were used to categorise patients into "treatment success" if their final treatment outcome was cure or treatment completion and "unsuccessful treatment" if their final treatment outcome was treatment failure, loss to follow-up, or death.

Anonymised data were exported to SPSS version 26.0 (SPSS Inc., Chicago, IL, USA) for cleaning and analysis, and results with $p < 0.05$ were considered statistically significant.

Categorical variables, including MoC and type of regimens used across the different treatment models, were summarised using frequencies (proportions), and continuous variables were summarised using medians inter-quartile ranges (IQR) and mean standard deviation [SD] stratified by the model of care. Mean [SD] was used when the data assumed a normal distribution and median (IQR) for non-normally distributed data. Independent t-test or ANOVA was performed to compare continuous variables when the data assumed a normal distribution and non-parametric tests (Mann–Whitney U test) for non-normally distributed data (Kim, 2015).

Chi-square was used to assess the association and compare categorical variables, and Fisher's exact tests when the minimum expected counts in the Chi-square table exceeded. A multivariate logistic regression model was constructed to assess the effect of risk factors on successful and unsuccessful treatment outcomes. Treatment regimens and models of care were the main explanatory variables while adjusting for sex, age, patient type, site of diagnosis, resistance pattern, HIV status, model of care and regime.

Ethical approval

Ethical approval was given by the Nigerian National Health Research Ethics Committee (NHREC) (NHREC Approval Number NHREC/01/01/2007-12/06/2018) (Appendix 7) and by the Anglia Ruskin University Faculty of Health Education Medicine and Social Care Research Degrees Ethics Sub Committee (FHEMS-FREP) in April 2018 (Appendix 8).

RESULTS

Baseline Demographic and Clinical Characteristics

Overall, 423 patients (85% of the targeted sampling data) were available for analysis, of whom 275 (65%) were treated at community centres (receiving CM), and 148 (35%) received HM (Table 2). The majority, 272 (63.4%), had the conventional regimen, while a third (n = 143, 33.8%) had a shorter treatment regimen (Table 3). In total, 311 (73.5%) of the study participants were male, and 112 (26.5%) were female (Table 2). There was no significant difference among the groups (community versus hospital) regarding sex and age (26.2% female in the CM versus 27.0% female in the HM; $p = 0.851$). The mean [SD] ages of community-based and hospital-based patients were 33.35 [11.655] and 32.59 [10.343] years; ($p = 0.512$), respectively (Table 2). Similarly, when participants in aggregate (receiving “all regimens”,

ARG) were re-grouped based on treatment regimen and MoC, their mean [SD] ages in years were:

- Conventional regimen (CVRG)
  - 31.70 [9.271] in hospital, 33.80 [11.162] in the community; (p = 0.116) (table 6.2)
- Shorter regimen (SHRG)
  - 34.48 [12.561] in hospital, 32.69 [12.514] in the community; (p =.0.432) (table 6.3)

There is no significant difference between HM and CM based on their TB treatment history (p = 0.116) (Table 2). Similarly, among the 98.6% of study participants whose HIV status was known, HIV-TB co-infection rates were relatively low (14.3% CM versus 13.1% HM) (p = 0.227) (Table 2).

Characteristics	Model Type		Total (n=423) n (%)	p-value
	Hospital, ARG(n=148) n (%)	Community, ARG(n=275) n (%)		
Sex				
Male	108 (73.0)	203 (73.8)	311 (73.5)	0.851[c]
Female	40 (27.0)	72 (26.2)	112 (26.5)	
Age, years mean [SD]	32.59 [10.34]	33.35 [11.66]	33.08 [11.21]	0.512[t]
Patient type				
New	33 (22.4)	89 (33.2)	122 (28.8)	0.116[f]
Relapse	37 (25.2)	50 (18.7)	87 (20.6)	
TALFO	16 (10.9)	25 (9.3)	41 (9.7)	
Treatment after failure (TAF)	11 (7.5)	39 (14.6)	50 (11.8)	
Other previously treated	24 (16.3)	51 (19.0)	75 (17.7)	
Transferred-in	1 (0.7)	0	1 (0.2)	
PUPH	25 (17.0)	14 (5.2)	39 (9.2)	
Site of TB				
Pulmonary	146 (98.6)	272 (98.9)	418 (98.8)	1.000[f]
Extra-pulmonary	2 (1.4)	3 (1.1)	5 (1.2)	
Resistance pattern				
MDR-TB	144 (97.3)	272 (98.9)	416 (98.3)	0.246[f]
Pre-XDR-TB	4 (2.7)	3 (1.1)	7 (1.7)	
HIV status				
Positive	19 (13.1)	39 (14.3)	58 (13.7)	0.227[f]
Negative	122 (82.4)	233 (85.7)	355 (83.9)	
Unknown	4 (2.7)	0	4 (0.90)	

The majority of the respondents (98.8%) had pulmonary TB, while 1.2% had extra-pulmonary TB, and there is no significant difference among the groups regarding the site of the disease (98.6% versus 98.9% had pulmonary TB among CM and HM patients, respectively) (p = 1.000) (Table 2). Among the 98.6% of total study participants whose HIV status was known, HIV-TB co-infection rates were relatively low (14.3% CM versus 13.1% HM) (p = 0.227) (Table 2). However, when participants were categorised based on treatment regimens and models, the rates of HIV-TB co-infection were similar among CVRG patients (Table 3) but higher among HM than CM SHRG patients (15.9% versus 5.1%, p = 0.047) (Table 4).Table 2: Baseline demographic and clinical characteristics between HM and CM (all regimens combined)

[f] =Fisher's Exact test, [c] =Chi square test, [t] =*t*-test, TALFO = treatment after loss to follow-up; PUPH = patient with unknown previous TB treatment history; MDR-TB = multidrug-resistant tuberculosis; Pre-XDR-TB = pre-extensively drug resistant-TB; ARG All regimens; HIV = Human immune deficiency virus.

Source: Author

Table 3: Baseline demographic and clinical characteristics between HM and CM (conventional regimen)

Characteristics	Model Type		Total (n=272) n (%)	p-value
	Hospital CVRG(n=98) n (%)	Community CVRG(n=174) n (%)		
Sex				
Male	68 (69.4)	132 (75.9)	200 (73.5)	0.245[c]
Female	30 (30.6)	42 (24.1)	72 (26.5)	
Age, years mean [SD]	31.70 [9.27]	33.80 [11.16]	33.04 [10.55]	0.116[t]
Patient type				
New	14 (14.4)	43 (25.6)	57 (21.5)	0.246[f]
Relapse	25 (25.8)	39 (23.2)	64 (24.2)	
TALFO	10 (10.3)	20 (11.9)	30 (11.3)	
Treatment after failure (TAF)	7 (7.2)	23 (13.7)	30 (11.3)	
Other previously treated	17 (17.5)	32 (19.0)	49 (18.5)	
Transferred-in	1 (1.0)	0	1 (0.4)	
PUPH	23 (23.7)	11 (6.5)	34 (12.8)	
Site of TB				
Pulmonary	97 (99.0)	172 (98.9)	269 (98.9)	1.000[f]
Extra-pulmonary	1 (1.0)	2 (1.1)	3 (1.1)	
Resistance pattern				
MDR-TB	98 (100.0)	174 (100.0)	272 (100.0)	-
Pre-XDR-TB	0	0	0	
HIV status				
Positive	12 (12.5)	34 (19.9)	46 (17.2)	0.222[f]
Negative	81 (84.5)	137 (80.1)	218 (81.6)	
Unknown	3 (3.1)	0	3 (1.1)	

[f] =Fisher's Exact test, [c] =Chi square test, [t] =*t*-test, TALFO = treatment after loss to follow-up; PUPH = patient with unknown previous TB treatment history; MDR-TB = multidrug-resistant tuberculosis; Pre-XDR-TB = pre-extensively drug resistant-TB; CVRG = Conventional regimen; HIV = Human immune deficiency virus.

Source: Author

Table 4: Baseline demographic and clinical characteristics between HM and CM (shorter regimen)

Characteristics	Model Type		Total (n=143) n (%)	p-value
	Hospital SHRG (n=44) n (%)	Community SHRG (n=99) n (%)		
Sex				
Male	34 (77.3)	70 (70.7)	104 (73.0)	0.416[c]
Female	10 (22.7)	29 (29.3)	39 (27.0)	
Age, years mean [SD]	34.48 [12.56]	32.69 [12.51]	33.24 [12.51]	0.432[t]
Patient type				
New	19 (43.2)	46 (46.9)	65 (14.4)	0.440[f]
Relapse	12 (27.3)	11 (11.2)	23 (25.8)	
TALFO	5 (11.4)	5 (5.1)	10 (10.3)	
Treatment after failure (TAF)	3 (6.8)	14 (14.3)	17 (7.2)	
Other previously treated	3 (6.8)	19 (19.4)	22 (17.5)	
Transferred-in	-	-	-	
PUPH	2 (4.5)	3 (3.1)	5 (23.7)	
Site of TB				
Pulmonary	43 (97.7)	98 (99.0)	141 (98.4)	0.522[f]
Extra-pulmonary	1 (2.3)	1 (1.0)	2 (1.6)	
Resistance pattern				
MDR-TB	44 (100.0)	98 (99.3)	142 (99.7)	1.000[f]
Pre-XDR-TB	0	1 (0.7)	1 (0.3)	
HIV status				
Positive	7 (15.9)	5 (5.1)	12 (8.4)	0.047[f]
Negative	37 (84.1)	94 (94.9)	131 (91.6)	
Unknown	-	-	-	

[f] =Fisher's Exact test, [c] =Chi square test, [t] =*t*-test, TALFO = treatment after loss to follow-up; PUPH = patient with unknown previous TB treatment history; RR-TB = rifampicin-resistant tuberculosis; MDR-TB = multidrug-resistant tuberculosis; Pre-XDR-TB = pre-extensively drug resistant-TB; SHRG = Short regimen; HIV = Human immune deficiency virus.

Source: Author

Table 5 compares CM and HM patients according to the patient type, treatment regimens and MoCs using Chi-square tests. The proportion of new cases and patients with previous TB treatment history treated with conventional regimens were 14.4% and 25.6% and 85.6%, and 74.4%; p =0.033 for HM and CM, respectively. The difference narrowed down in the shorter

regimen, with no significant difference between new cases and patients with a previous history of TB treatment, 43.2% vs 56.8% HM and 46.9% vs 53.1% CM, for new and previous TB treatment history, respectively (p= 0.678).

Table 5: Comparison of patient type by previous TB treatment history (treatment regimen and MoC)

Regime and Model type	Patient type: New n (%)	Patient type: Patient with previous TB treatment history n (%)	P-value
ARG			
Hospital	33 (22.4)	114 (77.6)	0.221[c]
Community	89 (33.2)	179 (66.8)	
CVRG			
Hospital	14 (14.4)	83 (85.6)	0.033[c]
Community	43 (25.6)	125 (74.4)	
SHRG			
Hospital	19 (43.2)	25 (56.8)	0.678[c]
Community	46 (46.9)	52 (53.1)	

[c] =Chi square test, CVRG = ARG = All regimens; Conventional regimen; SHRG = Short regimen

Source: Author

Treatment outcomes

This analysis found that there is no statistically significant difference in treatment success between CM and HM; patients achieve similar treatment success in all models, and CM is, therefore, as effective as HM. Overall, the success was 65.5% with HM compared to 68% at the CM (p = 0.608) (Table 6). A higher percentage of patients died in the HM (20.9%) compared to the 17.5% in the CM, although the difference is not significant (p = 0.704) (Table 6). Similar proportions of patients were cured (50.7% versus 48.4%) or had treatment failure (4.1% versus 5.1%) in the HM versus CM, respectively; (p = 0.704c) (Table 6). Treatment outcomes were categorised based on regimens, using Chi-square and Fisher's Exact tests to test the sensitivity of the difference in treatment outcomes between HM and CM. Despite changes in the regimens, there was no significant difference in treatment outcomes between HM and CM. The proportion of successful treatment was 66.3% HM and 68.4% CM p=0.727 CVRG, and 68.2% HM and 67.7% CM p= 0.952 SHRG (Table 6).

Table 6: Treatment outcomes and clinical progression of all participants (all regimens combined)

Regime and Model type	Treatment outcome					P-value
	Cure n (%)	Treatment completion n (%)	Loss to Follow-up n (%)	Treatment failure n (%)	Died n (%)	
ARG						
Hospital	75 (50.7)	22 (14.9)	14 (9.5)	6 (4.1)	31 (20.9)	0.704[c]
Community	133 (48.4)	54 (19.6)	26 (9.5)	14 (5.1)	48 (17.5)	
CVRG						
Hospital	48 (49.0)	17 (17.3)	10 (10.2)	1 (1.0)	22 (22.4)	0.527[f]
Community	90 (51.7)	29 (16.7)	16 (9.2)	8 (4.6)	31 (17.8)	
SHRG						
Hospital	27 (61.4)	3 (6.8)	3 (6.8)	3 (6.8)	8 (18.2)	0.094[f]
Community	43 (43.4)	24 (24.2)	10 (10.1)	6 (6.1)	16 (16.2)	

[c] =Chi square test; [f] =Fisher's Exact test; ARG = All regimens; CVRG = Conventional regimen; SHRG = Short regimen; MoC = Model of care.

Source: Author

A multivariable model was constructed to explore interaction, assessing the factors associated with successful and unsuccessful treatment outcomes. Treatment regimens and models of care were considered the main explanatory variables.

Table 7: Factors associated with unsuccessful treatment outcome (final model without interaction term)

Factors	uOR	95% CI	p-value	aOR	95% CI	p-value
Age ≥ 45	1.03	1.01 – 1.05	0.001	1.03	1.10 – 1.05	0.002
Sex						
Female*	Ref			Ref		
Male	1.24	0.77 – 1.98	0.373	0.97	0.58 – 1.62	0.903
Patient type						
New case*	Ref			Ref		
Previous TB history	1.44	0.90 – 2.30	0.125	1.44	0.86 – 2.40	0.166
Site of diagnosis						
Pulmonary TB*	Ref			Ref		
Extra-pulmonary TB	3.11	0.51 – 18.83	0.217	2.46	0.38 – 16.07	0.349
HIV status						
Unknown vs Negative*	8.91	1.86 – 42.64	0.006	8.83	1.79 – 43.60	0.007
Positive vs Negative*	1.24	0.67 – 2.260	0.429	1.26	0.71 – 2.26	0.494
Model of care						
Hospital-based*	Ref			Ref		
Community-based	0.89	0.59 – 1.37	0.608	0.92	0.59 – 1.46	0.735
Regime						
Shorter regimen*	Ref			Ref		
Conventional regimen	1.01	0.65 – 1.56	0.969	0.87	0.54 – 1.40	0.568

uOR = Unadjusted Odds Ratio, aOR = Adjusted Odds Ratio, Ref*=Reference (source: Author)

On multivariate analysis, adjusting for age, HIV status, sex, patient type, previous TB treatment history, resistance pattern, site of diagnosis, model of care and regimens, there was no change in effect on MDR-TB treatment outcomes if patients are treated at the community-based site (adjusted odds ratio [aOR] 0.92; 95% CI 0.59 – 1.46**,** p = 0.735) (Table 7). Regardless of the site, there was no effect modification on MDR-TB treatment outcomes of patient type and sex status, patient with previous TB history (adjusted odds ratio [aOR] 1.44; 95% CI 0.86 – 2.40, p = 0.166), male sex (adjusted odds ratio [aOR] 0.97; 95% CI 0.58 – 1.62 p = 0.903). HIV status was a significant predictor of treatment outcome in the univariate (P=0.004). In multivariate, MDR-TB patients with unknown HIV status (not on ART) were nine times more likely to have unsuccessful treatment outcomes compared with HIV-negative respondents (adjusted odds ratio [aOR] 8.83; 95% CI 1.79 – 43.60, p = 0.007). HIV-positive respondents were 1.3 times more likely to have unsuccessful outcomes compared to HIV-negative (adjusted odds ratio [aOR] 1.26; 95% CI 0.71–2.26, p = 0.429 (P=0.429) (table 7).

DISCUSSION

Analysis of patients' treatment data in this research showed that CM treatment outcomes were similar to those of HM in Nigeria. Patients in both models achieved similar cure rates and treatment success. Thus, CM is equally effective as HM, as evidenced by similar treatment success (68% versus 65.5%, p = 0.608), relatively similar default rate and treatment failure (9.5% versus 9.5%,) and (4.1% versus 5.1%) (respectively).

The effectiveness findings obtained in this research are comparable to two systematic reviews: one on CM treatment outcomes by Weiss et al. (2014) and one on the "effectiveness of hospital and ambulatory-based management" of MDR-TB by Bassili et al. (2013). However, the latter was based on the analysis of heterogeneous secondary data, while the former was limited to outcomes of CM without comparison with HM.

Similarly, the findings were consistent with those on the effectiveness of community-based directly observed treatment reported from urban Tanzania (Wandwalo, Robberstad and Morkve, 2005), South Africa (Johnston et al., 2009) and Myanmar (Wai et al., 2018). However, the findings in this research differed in that the results of Wandwalo, Robberstad and Morkve (2005) were based on DS-TB. Although Johnston et al. (2009) did address MDR-TB and reported a similar treatment success rate of 62%, their report was based on a systematic review of secondary data influenced by unadjusted confounding factors. Additionally, none of the previous studies looks at the effectiveness difference regarding treatment regimens and models (CVRG versus SHRG and HM versus CM).

Other studies conducted in Nigeria reporting outcomes for community-based MDR-TB care have documented similar success rates, but their findings were limited to sputum culture conversion during the intensive phase, not the final treatment outcome (Oyefabi et al., 2020; Oladimeji et al., 2014). A few that reported the final treatment outcome either relied on secondary data outside Nigeria (Musa et al., 2016; Bada et al., 2019) or did not provide a model comparison as explored in this research (Dunga et al., 2019).

Findings from this research support the WHO recommendation of CM, as the introduction of CM, would have the capacity to increase patient treatment enrolment by more than double,

using limited resources, which would help in closing the MDR-TB treatment enrolment gap as Nigeria is among the top 10 countries that reported for 72% of MDR-TB treatment enrolment gap globally (WHO, 2022). CM may address patient needs more successfully, as care closer to home is easier to access, more convenient, allows family and peer support, and promotes improved mental health outcomes. In addition, it enables more flexibility for patients and their families to seek earning opportunities and sustain some economic productivity.

Furthermore, when extrapolating the findings for the shorter regimen, the success rate was 69.2% compared to 64% for the conventional regimen and noticed more MDR-TB patients without prior treatment history under the shorter regimen. The better treatment outcomes observed in shorter regimens could be due to improved MDR-TB control over the last few years due to the establishment of new therapeutics. The 69.2% success rate for the shorter regimen observed in this study was much lower than the 84.4% success rate reported in Bangladesh (Van Deun et al., 2010; Aung et al., 2014). This may be due to different healthcare settings. The increased number of MDR-TB cases without any prior TB treatment history witnessed under the shorter regimen may be attributed to the increased community transmission of a resistant strain of MDR-TB (Walker, et al., 2018). Another possible explanation may be due to non-random allocation or reactivation from the growing reservoir of latent MDR infection. However, the global prevalence of latent MDR-TB infection remains low (0.3%). Nevertheless, it plays a significant role in the global MDR-TB epidemics because MDR M tuberculosis strains are resistant to most recommended therapies for people with latent infection (Knight, et al., 2019).

Multivariate analysis of our data showed no significant association between treatment outcomes and sex, residence, type of MDR-TB and category of the patient treated, consistent with the findings reported by Teferi et al. (2021) in Southern Ethiopia and the results of predictors of MDR-TB treatment outcomes in Portugal (Oliveira et al. 2021). Similarly, in the data presented in this research, advancing age and HIV-coinfection increased the odds of an unsuccessful outcome in the multivariate analysis, which is consistent with the results of predictive factors of unfavourable treatment outcomes for MDR-TB in Brazil by Bhering, Duarte and Kristki (2019). When participants were categorised based on treatment regimens and models, the rates of HIV-TB co-infection were higher among HM compared to CM SHRG patients. The higher rate of HIV-positive patients on the shorter regimen may be due to increasing awareness and improved testing capacity for HIV among MDR-TB patients on shorter regimens in recent years compared to limited testing capacity for HIV and reduced awareness among MDR-TB patients in previous years when longer regimen was conceived. The knowledge of risk factors of unfavourable outcomes identified from this research would improve patients' clinical management in Nigeria and enhance treatment success.

Limitations

The WHO standardised definitions of treatment outcomes were used to estimate treatment success. However, these definitions have some limitations, including underestimating the cure secondary to the difficulty of many patients to produce sputum after months of effective treatment and improper assessment of the failure rate by not taking into account relapse after treatment that is not recognised because of loss to follow-up (Guenther, et al., 2016; Lange, et

al., 2018). Similarly, patients classified as a loss to follow-up based on the WHO definitions of treatment outcome may have an unknown outcome and subsequent source of infection due to bacteriological reversion (Mitnick et al., 2016). Thus, TB-net (Tuberculosis Network European Trials Group) proposed simplified treatment outcome definitions for MDR-TB which consider the 6-month culture status and include one year of follow-up after treatment (Guenther, et al., 2016). In addition to overcoming the difficulty of assessing outcomes in TB patients who cannot produce sputum during the later stages of treatment.

Despite efforts to recruit a more representative sample, community-based patients were more represented than hospital-based patients in the study population. The low number of hospital patients may be due to the limited capacity to accommodate patients in all the MDR-TB treatment centres, as per the Nigerian NTP. However, efforts were made to recruit almost all accessible participants from MDR-TB hospitals. Furthermore, with the recent recommendation of six months BPaL regimens for the treatment of MDR-TB, the findings from this research may differ from that of BPaL regimes in terms of duration, drug composition and effectiveness. However, it will take time to transition to new regimens due to cost implications, training and logistics, particularly in LMICs, including Nigeria, with limited resources.

CONCLUSION

This analysis suggests that the community-based model is equally effective as care in a centralised hospital, based on similar treatment success rates, comparable default and death rates with hospital care and shorter time to treatment initiation at the community-based sites. Even in HIV coinfection, the community-based model increased treatment success. As alternative models of care for patients are encouraged by the WHO, we recommend regular monitoring and support of community health workers to ensure that services are equitable, guidelines are adhered to, quality of care is optimal, and the possibility of treatment success is improved.

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