Understanding the gaps in DR-TB care cascade in Nigeria: A sequential mixed-method study

Charity Oga-Omenka a,b,c,*, Jody Boffa d,e, Joseph Kuye f, Patrick Dakum g,h, Dick Menzies c,i, Christina Zarowsky h,j

a The School of Public Health of the University of Montreal (ÉSPUM), Montreal, Quebec, Canada
b Centre de recherche en santé publique, Université de Montréal (CReSP), Canada
c McGill University International TB Centre, Montreal, Quebec, Canada
d Dahdaleh Institute for Global Health, York University, Toronto, Canada
e Centre for Rural Health, School of Nursing and Public Health, College of Health Sciences, University of KwaZulu-Natal, Durban, South Africa
f National Tuberculosis and Leprosy Control Program, Abuja, Nigeria
g Institute of Human Virology, Nigeria
h University of Maryland School of Medicine, Baltimore, MD, USA
i School of Public Health, University of the Western Cape, South Africa

ARTICLE INFO

Keywords:
TB Care Cascade
Nigeria
Access to healthcare
Drug-resistant tuberculosis
Mixed-methods
Diagnosis and treatment

ABSTRACT

Background: Despite the availability of free drug-resistant tuberculosis (DR-TB) care in Nigeria since 2011, the country continues to tackle low case notification and treatment rates. In 2018, 11% of an estimated 21,000 cases were diagnosed and 9% placed on treatment. These low rates are nevertheless a marked improvement from 2015 when only 3.4% were diagnosed and 2.3% placed on treatment of an estimated 29,000 cases. This study describes the Nigerian DR-TB care cascade from 2013 to 2017 and considers factors influencing gaps in care.

Methods: Our study utilized a mixed-method design. For the quantitative component, we utilized the national diagnosis and treatment databases, as well as the World Health Organization’s estimates for prevalence to construct a 5-year care cascade: numbers of patients at each level of DR-TB care, including incident cases, in 2013 and 2017. Using retrospective data for patients diagnosed in 2015, we performed the Fisher’s exact test to determine the association between patient (age and gender) and provider/patient (region- north or south) variables, permitting a closer look at the gaps in care revealed across the 5 years. Barriers to care were explored using framework thematic analysis of 57 qualitative interviews and focus group discussions with patients, including 5 cases not initiated on treatment from the 2015 cohort, treatment supporters, community members, healthcare workers and program managers in 2017.

Results: A 5-year analysis of cascade of care data shows significant, but inadequate, increases in overall numbers of cases accessing care. On average, between 2013 and 2017, 80% of estimated cases did not access testing; 75% of those who tested were not diagnosed; 36% of those diagnosed were not initiated on treatment and 23% of these did not finish treatment. In 2015, children and patients in Northern Nigeria had odds of 0.3 [95% CI 0.1-0.7] and 0.4 [0.3-0.5] of completing treatment once diagnosed; while males were shown to have a 1.34 [95% CI 1.0-1.7] times greater chance of completing treatment after diagnosis. The main themes from qualitative data identified barriers to care along the care cascade at individual, family and community, as well as health systems levels. At the individual level, a lack of awareness of the true cause of disease and the availability of ‘free’ care was a recurring theme. Family interference was found to be a particular challenge for children and women. At the health system level, low index of suspicion, lack of rapid diagnostic tools and human resource shortages appeared to limit patients’ access.

Conclusions: Any gains in diagnostic technology and shorter regimens are lost with inadequate access to DR-TB services. The biggest losses in the Nigerian cascade happen before treatment initiation. There is a need for urgent...
1. Introduction

Rifampicin- or multidrug-resistant tuberculosis (DR-TB) actively infected an estimated 484,000 people and took 214,000 lives in 2018, threatening to reverse years of advances in global TB prevention and control [1–3]. Drug resistance is an ongoing challenge, especially in settings where healthcare systems are fragmented, suggesting gaps in the care cascade [3,4].

Nigeria accounts for 4% of the global DR-TB burden and 27% of the incidence in Africa [3]. While the World Health Organization (WHO) estimates that 4.3% of new and 15% of previously-treated people with TB in Nigeria have drug-resistant TB [3], others have suggested that the incident rate of DR-TB is much higher [5,6]. In a meta-analysis of 8,002 adult TB patients from across the country, Onyedum et al found 32% of new (734/2892) and 53% of previously treated people (1467/5020) had DR-TB [5]. Gehre et al found 32% (9/28) and 66% (58/88) respectively in Lagos state [6].

Furthermore, Nigeria has particularly low notification and treatment rates of DR-TB. WHO estimates that only 11% of people with DR-TB were diagnosed and 9% placed on treatment in 2018, compared to the 39% diagnosis and 32% treatment rates globally [3]. The 2012 Nigerian National Survey found 75% of smear-positive cases presented with TB symptoms meeting the National criteria for screening (cough for two weeks or more) who had not been previously diagnosed, reflecting some missed opportunities for TB diagnosis [3,7]. According to the WHO, Nigeria contributes 12% of the global DR-TB diagnosis gap, defined as the gap between the number of new cases reported and the estimated incident cases [3].

In order to meet the End TB targets, Nigeria’s diagnosis rates and treatment coverage need to be 90% or more with a drug susceptibility testing (DST) coverage of 100% [3]. The TB care cascade outlines a series of necessary steps and services each patient must go through to achieve a positive health outcome. This includes accessing testing, receiving a diagnosis, initiating treatment, completing treatment and surviving at one year of follow-up [8].

Identifying gaps in the DR-TB care cascade in a given setting enables targeted interventions at the stages of the care cascade where losses and drop-outs occur most frequently. Currently, information on factors contributing to gaps in DR-TB care in Nigeria is limited. Our study aimed to estimate the gaps along the DR-TB care cascade and to identify barriers to care from the perspectives of patients, their relatives and DR-TB care providers as their first point of initial care-seeking for respiratory conditions and fever [13,14]. Patients, after onset of symptoms, visited private pharmacies (79%), traditional healers (10%), and private hospitals (10%) [14]. Despite this, only 11% of total TB notifications come from the private sector, or less than 3% of estimated incidence [13].

Nigeria adopted the use of GeneXpert MTB/RIF (Xpert) technology in 2011 in several national reference laboratories, increasing access to DR-TB diagnosis [15,16]. Prior to this, diagnosis for TB relied mostly on smear microscopy, culture, molecular line probe assay and drug susceptibility testing [17,18]. Initially, GeneXpert use was reserved for testing HIV patients, presumed DR-TB cases, children, and extra pulmonary TB cases [18,19]. Treatment for DR-TB patients began with a hospital-based model in 2010 and evolved to include community-based DR-TB treatment initiation in 2013 [15,17]. By the end of 2015, the country had scaled GeneXpert testing to 201 sites, from 7 sites in 2011, expanded testing algorithms to include all presumed TB cases, implemented DR-TB treatment in facilities within 16 States and community DR-TB initiation in 27 States, with support from the Global Fund and other partners [17,18]. At the end of 2015, 12% of Gene Xpert sites and 16% of DR-TB hospital bedspaces were in 3 privately owned facilities [18].

2. Methodology

2.1. Study setting

2.1.1. National and TB program context

Nigeria, with an estimated 193 million people in 2016 [9], has 36 States and one Federal Capital Territory, across 6 geopolitical zones: North-Central, North-East, North-West, South-East, South-South and South-West [10]. In 2016, there were an estimated 34,140 health facilities in Nigeria- with 88% of them primary, 11% secondary and 0.13% tertiary [11,12]. Of these, 67% were public-funded and 33% private sector health facilities, excluding patent medicine vendors (PMVs) and private pharmacies [11]. In terms of geopolitical distribution of health facilities, the North-East had 18.6, North-West 14.4, North-Central had 25.8, South-West 20.4, South-East 23.4 and South-South 14.0 health facilities/100,000 population [11].

Although only 33% of treatment facilities were privately owned, studies found that 66–92% of the time, new TB patients visited private providers as their first point of initial care-seeking for respiratory conditions and fever [13,14]. Patients, after onset of symptoms, visited PMVs (79%), traditional healers (10%), and private hospitals (10%) [14]. Despite this, only 11% of total TB notifications come from the private sector, or less than 3% of estimated incidence [13].

2.1.2. Study data sources and contexts

The WHO TB estimates for Nigeria were derived from the 2012 National TB prevalence and the 2010 DR-TB surveys, 2000–2008 notification data, and Standards and Benchmark Assessments for 2013 and 2017 [7,20–22]. Additional secondary quantitative data were derived from national databases for diagnosis and treatment collected by the National TB and Leprosy Control Program (NTBLC) from public and private facilities.

The qualitative interviews were conducted in the South-West and North-Central geopolitical zones. Patient and provider interviews were conducted in 2017 from two of the largest DR-TB treatment centers in Nigeria, with 48 and 34 beds, respectively: Sacred Heart Hospital (SHH) in Ogun State and the Jos University Teaching Hospital (JUTH) in Plateau State. Two large treatment facilities were purposively selected to differ based on location and sector (one privately owned facility in the South – SHH; and a public facility in the North – JUTH) to maximise external validity.

2.2. Study design and methods

Our sequential mixed-methods study (Fig. 1) utilised the following methods: a review of Nigeria’s DR-TB cascade over 2013–2017 using data from WHO Global TB Reports [20–24], a cohort analysis of patients diagnosed in 2015, and a qualitative study based on semi-structured individual interviews with a purposive sample of respondents. We used the Mixed Methods Appraisal Tool (MMAT) [25] to conceptualize, develop and interpret findings from this study [26].

The purpose of this sequential transformative mixed methods study [27] was to understand the health system and patient barriers and facilitators to the DR-TB care cascade. The quantitative phase explored health system and patient factors associated with gaps in the DR-TB care continuum. The qualitative phase enhanced the understanding of the health system and patient-related factors for these gaps.

2.3. Quantitative data collection and analysis

The WHO TB Nigeria estimates used national TB prevalence (2012) and DR-TB (2010) surveys, Standard and Benchmark Assessment (2013, 2017), and TB notifications (2000–2018) [28]. We elected to analyse the
2015 cohort of diagnosed patients because this was the most recent year with available, complete, cleaned and deduplicated treatment outcome data from DR-TB in the national treatment register, allowing for further insights on gaps in care revealed across the 5 years. The primary results of this analysis have been published elsewhere [29].

We used two approaches to describe the DR-TB care cascade according to categories outlined by Subbaraman [8]. As a first step, we extracted the following data for Nigeria from annual WHO TB reports from 2013 to 2017 [20–24] utilising a denominator-numerator unlinked methodology [8,30]: 1) Estimated DR-TB incident cases (defined by the WHO as the TB cases arising in a given time period, usually one year), 2) Number of individuals with DR-TB who accessed TB tests, 3) Number of individuals with DR-TB who were successfully diagnosed as having drug-resistant TB, 4) Number of individuals registered on DR-TB treatment and 5) Number of patients who completed TB treatment. Recurrence-free survival, the final step of the TB care cascade, was not included as there was insufficient data to measure this. Unlike other years, DR-TB incident cases for Nigeria were not explicitly stated in the WHO annual reports for 2013 and 2014 [23,24]. Rather, we calculated DR-TB incidence based on the 2.9% of new TB events estimated by the WHO for these years. National program data is disaggregated for age, sex and geopolitical zone. We used notification data to describe the same for incidence and testing access [18]. The outcome indicators, including sources of data are described in the Appendix.

Our second approach is cohort-based, and is a denominator-denominator linked method [8,30]. Recurrence-free survival was also not included because of a lack of data. The additional retrospective data was collected from 2 different web-based databases for all patients diagnosed with DR-TB in 2015. The diagnosis (GxAlert) receives results from Xpert machines on diagnosed patients. The e-TB Manager database has records for all patients placed on TB treatment. Treatment initiation records were tracked from January 2015 to August 2017 (20–32 months after diagnosis). Preparatory processes, including the handling of missing data, have been discussed in a prior publication [29].

We utilised VassarStats, a computational statistics website, (www.vassarstats.net) to perform descriptive statistics and tests for association. We used Pearson’s chi-squared test to determine associations and Fisher’s exact test to compare differences between categorical variables.

2.4. Qualitative data collection and analysis

Our qualitative study involved interviews of patients, relatives, and providers in Ogun and Plateau states, as well as program managers in Benue and Abuja, the Federal Capital Territory (FCT). A total of 57 interviews were conducted in these States, including 10 focus group discussions (FGDs), 12 key informant interviews (KIIs) - including 5 phone
interviews - and 35 in-depth interviews (IDIs). The five (5) phone interviews were conducted using contact information for patients who were diagnosed but whose treatment start dates were not found in the treatment register to contrast with patients who were already on treatment. There were a total of 127 unique interviewees (Fig. 1).

We asked providers to describe the program structure, challenges and strengths, as well as their perception of access barriers and facilitators. Patients and their treatment supporters were asked to describe barriers and facilitators to accessing DR-TB care that they, their relative or someone they knew had experienced. Community interviews explored common beliefs and practices around TB among the general population. We grouped themes into the different stages of DR-TB care based on participants description of barriers and facilitators they faced as they navigated the care process, although they were not specifically asked to match these factors to all the stages.

Government and program managers at the central level were asked about national policies and resources available for DR-TB control and how these resources were distributed nationally and within each State. They were also asked about the strengths and challenges within the program and how these might have affected different groups of patients.

All interviews were conducted between September and November 2017 by CO, using interview guides developed by the research team and piloted at the beginning of the data collection. Initial entry meetings were held with national and state coordinators, as well as clinic managers at both treatment meetings to discuss overall objectives of the research and sampling strategies. Participants were selected based on their role in the DR-TB program and availability during the interview timeframe. Informed consents were written or verbally acknowledged before each interview. All interviews with patients were conducted outdoors in the treatment centers with patients who had been on treatment for more than two weeks. Interviews were conducted in English and respondents were encouraged to respond in or ask for translation into Nigerian pidgin, Yoruba or Hausa as needed. Interviews were audio-recorded and transcribed. There were instances of responses translated from the Yoruba language, the predominant language in the South West of Nigeria and pidgin English by translators fluent in those languages. Transcripts were sent back to 17 participants who had earlier agreed to be contacted for accuracy checking. Six participants responded, with 2 requesting minor revisions, and transcripts were revised accordingly prior to analysis.

We used a framework approach involving both inductive and deductive thematic analysis [31]. Codes were inductively derived and assigned to new themes or deductively derived from themes identified from an initial systematic review of barriers and facilitators to DR-TB care [32]. Interviews were coded by the first author (CO) with the help of 2 assistants. All themes and codes were double-checked by CO. Other members of the research team checked the thematic analysis for overall alignment with study objectives. Transcripts were coded with aid of Quirkos software, version 1.6.1.

The research team comprised two senior scientists (CZ and DM) with extensive experience in social, implementation science and TB research; a PhD researcher (CO) and post-doctoral fellow (JB) with over 15 years of combined implementation and mixed-methods research experience in HIV/AIDS and TB in sub-Saharan Africa; a DR-TB National program manager (JK), implementing partner and seasoned researcher in Nigeria (PD); and a research assistant who was a recent science graduate fluent in Yoruba and the pidgin English widely spoken in Nigeria. The research assistant was trained over 2 weeks on qualitative interview skills before fieldwork. None of the researchers were directly involved in patient management for DR-TB.

2.5. Ethics

The National Health Research Ethics Committee of Nigeria (NHREC/01/01/2007) and the Research Ethics Committee (CER) of the University of Montreal Hospital (17.060) granted ethical approval for this study. An additional ethical approval was obtained from the Research Ethics Committee (CER) of sciences and health of the University of Montreal (CERSES-19-098-D). All interview participants gave written or verbal informed consent.

3. Results

3.1. Quantitative results

3.1.1. Changes in DR-TB care cascade in Nigeria, 2013–2017

Our data shows a gradual increase in numbers retained across all stages of the cascade between 2013 and 2017. Graphs showing each stage of the DR-TB care cascade from 2013 to 2017 are described in more detail below.

Estimated incidence varied between 2013 and 2017 due to differences in measurements (Appendix 1). According to the WHO, Nigeria DR-TB incidence estimates fell from 29,000 in 2015 to 20,000 in 2016 (a reduction of 32%) when data on the prevalence of HIV among prevalent TB cases derived from the 2012 national prevalence surveys from Nigeria was used to re-estimate TB incidence ([21], p.24). We have elected to use a 5-year average of estimated incidence.

The increases in cases diagnosed and treated over the 5 years was statistically significant (p < 0.0001) (Fig. 2). In step 5, treatment success rate stayed relatively the same from 76.9% in 2013 to 76.7% in 2016. Data were unavailable on the number of patients diagnosed in 2017 who completed treatment.

Percentage retained, which is the ratio between patients who completed treatment and the estimated incidence for the year, increased from 1.5% to 4.8% between 2013 and 2016, representing a 3-fold increase.

The percentage losses between each stage of care are shown in Fig. 3. On average, between 2013 and 2016, 80% of estimated DR-TB patients did not gain access to testing for TB or drug susceptibility. Three-quarters of those who were tested were never diagnosed. Of those diagnosed, 35% were not initiated on treatment, and 23% of those treated did not complete treatment. The biggest losses over these years were in testing and diagnosis access, as more than 60% of those diagnosed were treated, and went on to complete their treatment.

3.1.2. Characteristics of patients within the DR-TB care cascade in 2015

Data sources for the cascade steps and gaps for patients diagnosed in 2015 are shown in Table 1.

The DR-TB diagnosis and treatment data for 2015, disaggregated by age, sex and geopolitical location, gives a closer look into the gaps in care (Table 2). Among the 29,000 people estimated to have TB of any form in 2015, 4700 were estimated as DR-TB cases among notified pulmonary TB cases. The WHO estimates these as the DR-TB patients expected to be found among all notified pulmonary TB patients for a given year, if all notified pulmonary TB patients were tested for Rif-resistance using WHO-recommended diagnostic tests [36]. This is different from the absolute number of patients tested for DR-TB (with or without a positive result) in the year. Subbaraman et al, 2019 [8] (Table 1) recommends using this estimate of DR-TB among notified pulmonary TB cases as a proxy for the total number of DR-TB patients who likely accessed testing during the same period. Of these, 996 were diagnosed with DR-TB, 660 were treated and 511 completed treatment.

The association between age, sex and geopolitical zone and proportion through the cascade of care was shown to be statistically significant. Using the Fisher’s exact probability test, children had lower odds than adults (0.3, 95% CI 0.1–0.7), males had 1.34 (95% CI 1.0–1.7) greater odds than females, and patients in the north had lower odds than those in the south (0.4, 95% CI 0.3–0.5) to move from diagnosis to treatment completion. A further analysis of this cohort are presented in a previous publication [29].
**Fig. 2.** Trends in DR-TB Care Cascade in Nigeria 2013–2017.

**Fig. 3.** Average Retention and Losses in DR-TB Care Cascade in Nigeria.
Predominantly, this related to a number of uncertainties about TB and to testing and diagnostic gaps, which were identified as the major barriers at the health system level. We present several examples, especially for personal influences operating at the family or community level, and finally

3.2.1. Factors influencing gaps in care

Our qualitative analysis focused on the first four cascade of care steps – testing access, diagnosis, treatment initiation and completion. From the perspective of patients and treatment supporters, several factors influenced access to care at each stage of the cascade. The interviews with providers were mostly in agreement with the factors identified by patients and their relatives.

Our results presented below and in Fig. 4, group themes influencing each stage of the care cascade into individual/patient factors, interpersonal influences operating at the family or community level, and finally at the health system level. We present several examples, especially for testing and diagnostic gaps, which were identified as the major barriers in the quantitative results.

3.2.2. Gap 1: accessing to TB diagnostics

Many respondents described individual delays in accessing testing. Predominantly, this related to a number of uncertainties about TB and to symptom minimization, being unaware of available care and the use of alternative care as a first option. For example, one FGD participant indicated:

“For me, when I started coughing, I was thinking that maybe it’s [a] normal cough, two and three days, you use [cough syrup] and it will go….”

Others were unclear about where to get tested:

“…this TB is killing people a lot. For many people that I know, realising later that it was this sickness that killed [them], and they did not know of this centre or to go to another centre” (Patients FGD).

For many, initial care seeking involved alternatives to the public sector. For example, many patients or their loved ones described first seeking care through “prayer houses,” traditional healers, or through the private sector:

“[When this illness started], I went to private hospitals, and they did not see anything wrong with me, I went to church and they said it was spiritual attack. Then I went to a [health] centre and they were not straight for….” (Patients FGD)

There were also instances of patients resisting further testing. One healthcare worker described patient fears related to long hospital stays if
they were found to be positive:

“We actually want[ed] him to come for [a drug resistance] test but some other people [had] ...cornered him [to say] by the time you go, they are going to put you in the treatment center and you may not come out till so, so period, so the patient refused [to come back]” (HCW KII).

When asked what could have helped them or their loved one get earlier access to testing, respondents indicated clearer information about TB and where to access reliable testing services at no cost to patients. One family member described his perspective of care in private hospitals, where he felt his loved one had unnecessarily perished:

“The problems I have noticed are amongst the private hospitals. They don’t diagnose [when] people have TB. They give wrong medications to people with DR-TB, which worsens their cases. They will be treating malaria, typhoid [fever]... making some mistakes costing people their lives. But, assuming the knowledge of TB is everywhere... it will be easy for [private hospitals] to diagnose and treat it” (Patient relative KII).

All participant groups repeatedly highlighted the need for increased community awareness around TB and availability of free services.

“Before coming here I was not aware ... that there is TB care here ...[and] that everything is free. I didn’t believe that ...my mummy asked if I would come I said no, I was not coming but [eventually I came]... [my health] has improved... The patients coming here are happy ... that is why we are suggesting radio advertisement or TV ...” (Patient FGD).

“My advice is that there should be awareness through the radio or television that whoever that coughs should visit hospital that it is free because when charges are involved many will run. Many listen to radio in car or homes or television. [Someone can say], my friend you have been coughing for a week and I heard on radio that it is free in the hospital. It will create awareness” (Patient FGD).

Providers also reinforced the need for more awareness, similar to what exists in the HIV program.

“One thing I can say is that, it is just the awareness, for [patients] to know that this TB has to be diagnosed and where to get the treatment... I think that the major thing ... that [TB] is existing, and [services] are free......” (HCW KII).

“...The awareness is not much, they should ...make people aware of TB, like ... they did for HIV. ...the awareness is not as much as that of HIV. And TB is killing more than HIV” (HCW KII).

Several family and community influences were reported to prevent access to testing. Respondents cited instances in which patients’ parents or spouses acted as a barrier to appropriate care, sometimes because of their own beliefs in alternate care, a lack of awareness about the TB symptoms or available services. These are discussed further in cross-cutting themes below.

A number of health system barriers were identified including inadequate coverage of services, inadequate human resource, lengthy care procedures, and misdiagnosis due to low index of suspicion in both public and private hospitals. The attitude of public healthcare workers was also a cited as a barrier.

“The first day I went for [a] test.....they chased me out that I should go and stay by the window...I felt embarrassed ...why should I be disgraced to stay outside ...they ordered me to buy [a] handkerchief to cover my mouth ... they chased me away” (Patients FGD).
3.2.3. Gap 2: from testing to diagnosis

Participants mentioned several patient-level reasons for difficulty getting diagnosed after testing. A predominant theme was preference for private sector care or long wait times for test results in the public sector, which led to the seeking of alternate care elsewhere. A second important theme was not being able to pay transportation costs to return for appointments.

“I got there for sputum culture, at government hospital they said [for] this test, you will have to come back for it. They will have to be giving us [a] date to come back for the sputum, they will say come back another day, if you get there again they will say you came late, and this thing is disturbing me up to the extent that I could not walk, people will have to hold me, until they said go somewhere else” (Patients’ FGD).

At the interpersonal level, there were instances of families removing patients from the care cascade to seek alternatives in traditional healing and prayers, or the patients themselves preferring alternative care to the public sector. Participants recalled knowing patients who died before they could initiate treatment.

“… Sometimes [the problem] is waiting... you brought the sample and most of the time is the DOTS people will not give ... accurate ... information. They [will] say ... drop your sample in the lab ... and go and ... come back tomorrow or come back on Friday, [and] today is [only] Monday...[they will say] come back next week (HCW KII).

“Sometimes [the problem] is waiting... you brought the sample and most of the time is the DOTS people will not give ... accurate ... information. They [will] say ... drop your sample in the lab ... and go and ... come back tomorrow or come back on Friday, [and] today is [only] Monday...[they will say] come back next week (HCW KII).

“Some [government] hospitals ... were always postponing appointments, treating people like animals...they shout on us not to stand somewhere, touch anything, or ... go out, come back tomorrow, up to the extent that I had given up ... but ... a month after I got the test after disturbing them, but some people do not have the perseverance to do what I did... ... please help us to explain to [HCWs] to treat [patients] well” (Patients FGD).

3.2.4. Gap 3: from diagnosis to treatment

Barriers to treatment initiation occurred at individual, family and health system levels, many of which were also cross-cutting, such as preference for private sector care. At the individual level, some participants recalled knowing patients who died before they could initiate treatment due to delayed diagnosis. A few instances were cited of patients refusing treatment or giving false addresses because of fear of long treatment duration or belief in alternative care, particularly traditional or spiritual healing.

“Sometimes … there are some people … they [say they] know what their problem is. [They] came to [the hospital but] gave [a] fake address and phone number ... I think this quarter alone ... I have lost 3 [patients] like that. The last conversation we had was that they know their problem was [a spiritual attack] from their village and [they] are going to [the church]. … Sometimes [for this] group of people you cannot account for them, because …when you call …the number will not connect” (HCW KII).

There were particular instances of adult females living with their parents, who were prevented from accessing treatment. In one instance, the duration of treatment was a barrier, and the parent thought going to a prayer house would bring faster results. In another instance, the father believed his daughter was already healed by prayer and not in need of any medication.

Family responsibilities and fear of separation, school and work conflicts were also mentioned as barriers to starting treatment.

At the health system level, limited hospital bed spaces to admit patients in the initial phase of treatment contributed to delays in treatment. HCWs also mentioned staff workload and low motivation, due to unpaid salaries, resulting in slow case management.

“From the provider’s side is a lack of motivation. Imagine you are going to attend to a patient every day for … 20 months, that means you abandon almost all you have to do for that patient. And in a situation where salaries are not forthcoming and the support from the [funding] partners are [much]. The program pays the DOTS providers [USD] communication allowance monthly but there is a very good package for the patients [105 USD]. … Most of the providers in the face of no salaries will … evry what the patients are getting... So, from the provider side this is one of the major challenges” (HCW KII).

3.2.5. Gap 4: from treatment initiation to treatment completion

At the individual level, several respondents mentioned that adverse drug reactions were a major issue with adhering to the treatment regimen. These led to some instances of patients losing hope or becoming anxious and refusing further treatment or dying while on treatment.

“[An elderly man], … when he sees the tray for drugs, … he will start vomiting, ha! even when they have not given him, as soon as he sees it, he starts vomiting, … even nurse or doctor, when he sees them he will just start vomiting, and finally he said he wants to go, … if he even sees the color of the doctors or nurses uniform he will be so afraid… he said it is better for him to go [home] and die... maybe he is dead but we don’t know... they gave him [the] paper to sign out of treatment...and he signed out and left” (Patients FGD).

An initial 8 months hospitalization was the standard practice before 2013 and is still used for certain high risk patients e.g. pediatric cases and those who are pregnant or have co-morbidities. Transitioning between the initial hospital phase and continuation in outpatient care was also another point at which patients dropped off treatment, sometimes due to miscommunication or poor understanding of the process.

“…a lack of information caused my stopping the treatment, due to... lapses on their sides... because... after they discharged me I was [told] to go [to] the community- who are the community I don’t know... [that] is their medical term...[I] am not a medical person. How do I get to know all those things? …that was how I actually stopped... taking my medication” (Patients FGD).

Weak linkages and referral systems led to patients dropping off treatment when moving between facility and home. One instance involved a prisoner released from jail who was subsequently lost to follow-up.

3.2.6. Cross-cutting barriers across the care cascade

Several cross-cutting barriers were identified. At the individual level, these included attributing symptoms to other causes or perceptions about healthcare which led to a preference for alternative care at all levels of the cascade.
The major cross-cutting themes on interpersonal influences were related to the influence of parents, spiritual leaders and to a lesser degree, husbands. Although predominantly negative, these experiences were sometimes positive.

“My pastor, he told me to come to the [treatment center], that this cough I am coughing that he has seen someone that was coughing the same and had been collecting drugs for six month and it stoped. It was my pastor that knew about it and ask me to come.” (Patients FGD).

“We have had a case of a pastor who refused ... a member of his church from taking drugs for DR-TB when the patient actually has DR-TB. He refused vehemently that it was not a disease to be cured like that, that it was a special [problem]. But ... eventually [the pastor] himself came down with DR-TB and died” (HCW KII).

Parental influence was a particular problem across the care cascade, affecting even adult patients, especially if they were female. This was often due to the parents own perception of better results with alternative care.

“I had an experience…… a patient … was ... asked ... to go and do... a [further testing] ...the mother insisted that it is ...a spiritual attack...and all effort to ensure that. the patient takes treatment, failed” (HCW KII).

In one instance, a phone interview was cut short when the participant, who had not yet initiated treatment, was interrupted by her father, who cut the line after demanding that the interviewer never contact her again. Her brother called the line ten minutes later:

“The man who spoke with you earlier is [the patient]‘s father. God has healed [her], she is totally well now. Her father does not want to hear [from] you or, anyone who talks about DR-TB so, keep off for the sake of peace.” (Relative to patient not initiated on treatment).

Healthcare workers and program managers also mentioned the lack of female autonomy to seek care without their husbands' approval.

“Women... of course, you know some women depend on their husbands... There are [wives] that [can't] go out, even when she is sick... and the husband [might] feel like taking her to the hospital is just ... maybe [a] waste [of] time, until the sickness [has made her bedridden].” (HCW KII).

When female patients were asked directly, none of them mentioned that this was a factor. However, one FGD participant mentioned that her husband’s persistence was key to her diagnosis.

At the health system level, predominant themes addressed the attitudes, knowledge and skills of providers, which affected linkage and retention in care for DR-TB patients and brings to bear the importance of targeting control efforts at different stages of the care cascade.

Attitudes of healthcare workers, from the perspectives of patients, were predominantly negative before diagnosis.

“When this [illness] started... when I went for [a] test ... I was treated anyhow, like sit here, leave here, shouting, and I fought them to stop chasing me ... and embarrassing me”. (Patients FGD).

Health workers became much more supportive once patients began treatment, and this was the same across interviews from different centers.

“...they are taking [good] care of us. We [get our medications] and collect injections at the right time; if anything happens to us or we feel anything, we go to meet them. They [joke] with us, allowing us to realise that we are still humans and that there is still hope for us here...” (Patients FGD).

“They attend to us as if we are their [relatives]. There is no stigmatisation... I don’t know of other centres but they don’t separate themselves [from us here]. If at times we [don’t] use our mask, they talk to us ... attend to us. They don’t ... shout at us [or] make us feel different” (Patients FGD).

The provision of free DR-TB care and patient financial support was mentioned repeatedly by patients and their relatives as the main facilitator to care.

“...when I remember [what I went] through [with] my daughter, how they [referred] us from [one hospital] to [another]. [An] ordinary razor blade, before they will give you ... you go and pay in to the [hospital] account ... but, I thank God for [the program]. They make me to be the happiest woman on this earth because [to] lose a child of ... 15 years [would] not [have been] easy but today they put laughter into my own family... Thank you.” (Treatment supporters FGD).

“The day they gave me the result and said it was TB, I was like ah, and I started thinking that where do I want to get money, I told my husband and he was worried. The doctor then said that whatever we are using here will be free of charge...” (Patient FGD).

“I used to hear that they heal people with cough at this place, but I was like, ‘how much will I [pay] there?’ but when I heard it was free, that was what gave me the opportunity to come here” (Patient FGD).

3.2.7. Program strengths

Overwhelmingly, patients cited the free care and financial support provided by the program as the major facilitators of access, enabling them to focus on getting better, without the added worries of compensating for lost livelihoods due to the effects of the illness itself and workplace stigma. Other strengths of the program were the patient education and counseling sessions.

On the other hand, healthcare workers mentioned teamwork and coordination, pooling of resources from implementing partners, the use of technology e.g. WhatsApp messaging within the team to improve patient tracking and GeneXpert results notifications.

“If there are treatment issues, treatment interruption, so that the community based officers [can intervene] immediately and to also respond. If there are drug reactions you know who to call it could also be the doctor, it could be [someone else]. We already have like a coordinated referral system and also we use the WhatsApp very well where you just throw [in any question] and you can be sure there will be a quick response.” (HCW KII)

4. Discussion

Our mixed methods analysis of the DR-TB care cascade in Nigeria contributes to the understanding of the main factors influencing access and retention in care for DR-TB patients and brings to bear the importance of targeting control efforts at different stages of the care cascade.

Although numbers improved over the period of study, only 2.5% of people with DR-TB successfully navigate the DR-TB care cascade in Nigeria. The vast majority do not even make it to formal providers. Our qualitative data suggests there is a lack of awareness regarding TB in general, and specifically around main symptoms, where and how to access free testing, and that TB is curable with appropriate treatment. However, there was a 3-fold increase in the ratio of patients who
interventions. For example, at each level of the cascade, patient beliefs and gender roles impeding access to TB care for women [53,54].

Our data suggest that this may relate to how people are treated in the public sector or alternative explanations about what causes the symptoms. However, some patients may be lost to follow-up due to poor linkages between the private and the public sector. Respondents mentioned that knowing someone with knowledge about TB and available services was instrumental in getting them into care, similar to studies from South Africa and India [37,38].

Interventions to improve program visibility through community awareness, as suggested by the participants, and engaging the private sector, including with spiritual and traditional healers, have been shown to dramatically improve TB case finding (up to 100%) in resource-limited settings like Nigeria [39–41].

Our data suggest an estimated three quarters of DR-TB patients are lost at Gap 2 due to misdiagnosis or inadequate provider index of suspicion, poor provider attitudes, clinic and laboratory challenges and the poor linkages between the private and public sector. Patients also mentioned fear of prolonged treatment. Provider training and supervision contributed to significant increases in case finding in India and Ethiopia [40,42].

According to the care cascade, the majority of people diagnosed with DR-TB (64%) went on to initiate treatment and 78% of these finished treatment. Gaps 3 and 4, treatment enrolment and completion, were sometimes due to individual beliefs and perceptions about healthcare, and fear of treatment, as well as work and family commitments. This highlights the need to continuously counsel patients, especially on adherence and potential side effects, and to address the opportunity costs of accessing care, as this has been shown to improve retention in care [43]. The financial support given to patients was repeatedly cited as a major facilitator at this stage and needs to be sustained.

Related to treatment completion, patients’ mental health and the toll from medication side effects were underscored by several respondents. The toxicities of DR-TB medications and their effects on patients’ outcomes is widely documented [25,44,45]. The current revision in WHO guidelines to shorter oral regimens will potentially improve patient adherence to treatment, as side effects reduce [46,47]. Several studies have made a case for psychosocial support for DR-TB patients [48–50].

Although DR-TB incidence was higher in adult males, women and children faced particular challenges in accessing care due to a lack of autonomy and adverse gender norms. Our cross-cutting findings of instances of family members preventing TB care for their family members is not very common in the literature, although some studies have reported marriages ending as a result of a TB diagnosis for the woman [51,52]. We found one study in India, where parents prevented their daughter’s TB treatment enrolment to avoid stigma and a cancelled marriage [44]. Other studies from Nigeria have found similar adverse gender roles impeding access to TB care for women [53,54].

While each level had unique barriers, addressing the cross-cutting barriers could serve as a first step for policy change and targeted interventions. For example, at each level of the cascade, patient beliefs and perceptions about the symptoms and the path to cure determined whether they persisted to treatment completion or not. Patients and providers repeatedly recommended improving community awareness on TB. This would likely have impact across the continuum of care, as evidence from other countries show [55,56]. Data management and correctly tracking patients by verifying contact information is another area that could have cross-cutting impact on the cascade of care [57,58].

On the health system level, in addition to improving coverage and access to GeneXpert testing, our findings suggest that training providers to recognize individuals at risk for DR-TB and on stigma and discrimination could play a role in reducing the very large gaps 1 and 2 in the care cascade [59,60]. Additionally, healthcare providers felt under-resourced and unsupported to provide adequate care, agreeing with findings in a recent study from India [61].

The significant gaps in accessing testing and diagnostic services noted in our data agrees with findings on DR-TB cascades in India and Madagascar, where Gaps 1 and 2 were reportedly the biggest gaps in DR-TB care [62,63]. These findings are in contrast with the South Africa DR-TB care cascade showing treatment initiation and completion were the biggest challenges [64].

Our findings suggest TB policy implications. Increasing patient awareness of TB symptoms and available services is an important first step for TB control in Nigeria, since case finding is reliant on patients recognizing their symptoms and presenting to a public health facility with TB services. This is supported by other studies from Nigeria, calling for improved public communication around TB [65–67]. Mass awareness campaigns have been used successfully in South Africa and other settings to create awareness, reduce stigma, and improve case finding [56,68,69]. Improving accessibility to healthcare facilities with TB testing and treatment could include active case-finding, mobile TB clinics and working with the private sectors to ensure adequate support for referring TB patients for appropriate testing. Interventions might also include behavioural change messages, advocacy with community leaders and gatekeepers [70]. Improving access to TB care services for women and children need to consider adverse cultural gender and parental norms, especially those that could prevent them from accessing healthcare. Integrating current policies to protect the rights of women and children to access TB care could potentially improve their health protection [71,72].

4.1. Comparing different sources of data

Findings from the quantitative data were generally in agreement with qualitative findings. Overall, the quantitative findings indicating that males and adults were more likely to progress through the various steps of the cascade were reflected in the qualitative themes showing parental and spousal influence impacting access to care and disadvantaging women and girls, as well as children. Several studies from Africa, including Nigeria, and Asia have shown similar barriers to TB care for women, children and rural dwellers [53,54,73–77].

While the data from the 2015 cohort indicated regional differences in access, we were not able to identify major themes related to this, besides the operationalizing of case findings in the different hospital teams, including the use of WhatsApp group messaging. These differences will need to be further explored.

There were differences between the cohort and the cascade of care results with regards to children. The cohort analysis [29] showed children were more likely than adults to initiate treatment once diagnosed in the South-West zone, but not at the national-level. One likely reason might be the particular attention given to initiate pediatric patients on treatment once tested within the South-West zone. This earlier treatment initiation in children might not be a complete contradiction as the cascade analysis showed a reduced likelihood of progressing from tested to treatment outcome, and not just treatment initiation alone.
4.2. Study strengths and limitations

Using qualitative interviewing permitted an in-depth understanding of the problem of access from the differing perspectives of individuals affected. It is not always the case that the views of patient and their relatives align with those of providers. One strength of this study was that it sought to elicit and compare these different perspectives. In our study, we found that, while health workers mentioned cases where a lack of female autonomy was a barrier to care, female participants themselves did not identify this as a problem. This difference in opinions may have been due to the way the female participants perceived autonomy and cultural norms.

Our study has some limitations. The quantitative data for incidence and access to testing are estimates using routine data. This may have introduced bias into cascade gaps because as estimates, they do not account for the changing patient populations at each stage of the cascade [8]. The cohort analysis used in the second step links diagnostic to treatment registers and tracks patients to treatment completion. This may have minimized bias in the cascade estimates at the later stages of the cascade.

Besides 2015, data for the other years used in the cascade estimation and analysis did not show the contribution of the private sector to notifications and treatment numbers. As a large number of Nigerian TB patients seek care first in the private sector, this lack of a clear understanding of the private sector contribution is a limitation of this analysis. If a significant number of people who first present to the private sector are appropriately managed, but not notified to the National TB Program, our estimates at various stages may be overestimated.

There were other limitations due to its qualitative study design [78]. A large amount and range of interview data made analysis complex and impossible to present in its entirety. Also, based on the fact that we conducted interviews in only 2 out of 6 geopolitical zones in Nigeria, the extent to which our results are generalizable to other parts of the country is largely unknown. Additionally, given their status as ‘missing’, we were unable to seek direct feedback from people who did not present to health centres. Although the perceptions of those receiving care provide insight into the reasons for these gaps, we may have missed potential factors that affect the large proportion of losses at the first stage.

Although participants were further probed and their responses reconfirmed, we cannot exclude the possibility of recall and reporting biases. We addressed this by triangulating sources, location and interview methods. There was an overall consistency in the themes emerging from the different sources of data. Finally, we did not conduct interviews in Northern Nigeria beyond the central geopolitical zone. There is a possibility that particular contexts in these regions were not explored.

5. Conclusion

Our study has shown that, although there is noticeable progress in access to DR-TB care in Nigeria between 2013 and 2017, this is not nearly enough to meet the End TB targets. On average, less than 3% of estimated incident cases ever make it to treatment completion. This presents serious implications for TB control in Nigeria. Major bottlenecks persist in accessing diagnostic testing and getting diagnosed. Treatment initiation rates also remain sub-optimal.

To reduce gaps in testing and diagnosis, the National TB program needs to make concerted efforts to improve community awareness about symptoms and available resources, private sector engagement and training of providers, and data management, including patient tracking systems.

Gaps in treatment enrolment and completion at the health system level will require increasing access to services and improved coverage, especially for remote locations, as well as policies to protect workers in need of healthcare. The National TB control program also needs to consider specific approaches to address the barriers faced by children and women in accessing services.

Funding

COO received funding for field work through the Global Fund New Funding Model MDRTB Grant (Global Fund to Fight AIDS, Tuberculosis and Malaria: NFM MDRTB Grant), with funds provided through IHVN as the Principal Recipient. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Ethical Statement

The National Health Research Ethics Committee of Nigeria (NHREC/01/01/2007) and the Research Ethics Committee (CER) of the University of Montreal Hospital (17.060) granted ethical approval for this study. An additional ethical approval was obtained from the Research Ethics Committee (CER) of sciences and health of the University of Montreal (CERSES-19-098-D). All interview participants gave written or verbal informed consent.

CRediT authorship contribution statement

Charity Oga-Omenka: Conceptualization, Methodology, Formal analysis, Visualization, Writing - original draft. Jody Boffa: Methodology, Writing - original draft. Joseph Kuye: Software, Validation, Writing - review & editing. Patrick Dakum: Resources, Writing - review & editing. Dick Menzies: Methodology, Supervision, Writing - original draft. Christina Zarewsky: Conceptualization, Methodology, Supervision, Writing - original draft.

Acknowledgements

The authors thank the National TB and Leprosy Control Program (NTBLCP) of the Federal Ministry of Health (in Abuja, Plateau and OgunState), the International Research Center for Excellence (IRCE) of the Institute of Human Virology Nigeria (IHVN) for granting access to the National database and for support in the process of data collection.

The contents of this publication are solely the responsibility of the authors and do not necessarily represent the official views of the Global Fund, NTBLCP or IHVN.

Appendix
Table A1
The DR-TB care cascade and process indicators (Subbaraman et al., 2019).

| Cascade stage | Outcome indicators for cascade steps | 2013 Cases [Range] | 2014 Cases [Range] | 2015 Cases [Range] | 2016 Cases [Range] | 2017 Cases [Range] | Process indicators used | Methods used for process indicators |
|---------------|--------------------------------------|--------------------|--------------------|--------------------|--------------------|--------------------|------------------------|-------------------------------------|
| Stage 1:      | Reaching health facilities and accessing a TB test |                      |                    |                    |                    |                    | Gap 1: Number of individuals with TB who did not reach health facilities and access a TB diagnostic test |
| Step 1:      | Number of individuals with incident or prevalent DR-TB in the population | 590,000 [340,000-880,000] | 570,000 [340,000-870,000] | 586,000 [345,000-890,000] | 407,000 [266,000-579,000] | 418,000 [273,000-594,000] | Population-based TB prevalence survey (2012) | WHO TB Burden Estimate using extrapolations from 2012 prevalence survey, yearly notification data and expert opinion on case detection gaps |
| Step 2:      | Number of individuals with DR-TB who accessed TB tests | 17,100 [9,900-25,500] | 16,500 [9,900-25,200] | 29,000 [15,000-43,000] | 20,000 [12,000-29,000] | 24,000 [14,000-36,000] | Estimated number of individuals with DR-TB | Estimation of Incidence of RIF-resistance in the annual tuberculosis burden |
| Step 3:      | Number of individuals diagnosed with DR-TB | 3700 [2,800-4,600] | 3300 [2,500-4,200] | 4700 [3700-5700] | 5200 [4100-6200] | 5400 [4200-6500] | Number of individuals with DR- TB who were successfully diagnosed as | Identified through National Gene Xpert register (GX Alert) |
| Stage 2:      | Diagnosis |                      |                    |                    |                    |                    | Gap 2: Number of individuals with TB who accessed a TB diagnostic test but did not get successfully diagnosed | Health system–related delays in diagnosis |
| Stage 3:      | Linkage to treatment |                      |                    |                    |                    |                    | Gap 3: Number of individuals diagnosed with TB who did not get registered in treatment | Delays in treatment initiation |
| Step 3:      | Number of individuals diagnosed with DR-TB | 669 | 798 | 996 | 1691 | 2300 | Number of individuals with DR-TB who were successfully diagnosed as | Identified through National Gene Xpert register (GX Alert) |

(continued on next page)
Table A1 (continued)

| Cascade stage | Outcome indicators | Methodology and data for outcome indicators | Reference |
|---------------|--------------------|-------------------------------------------|-----------|
| Stage 3: Post-treatment national | Number of individuals who are drug-sensitive TB treatment response | Qualitative interviews with patients and/or their caregivers | [33] NTBLCP/FMOH. DR-TB Program Data. [Program data]. 2015. |
| | Number of patients who completed DR-TB treatment | | [31] Organization WH. Engaging private health care providers in TB care and prevention: a landscape analysis. World Health Organization; 2018. |
| | Number of patients who received and completed DR-TB treatment | | [30] Makinde OA, Sale A, Ayankogbe O, Boone D. Distribution of health facility in Nigeria: implications and options for universal health coverage. Int J Health Plann Manage 2018;33(4):e1179–92. |
| | Number of patients who are drug-sensitive TB treatment response | | [29] PharmAccess. A Closer Look at the Healthcare System in Nigeria. In: PharmAccess, editor. 2016. |
| | Number of patients who completed DR-TB treatment | | [28] Creswell JW, Clark VP, Garrett A. Advanced mixed methods research. Handbook of mixed methods in social and behavioural research. Thousand Oaks, CA: Sage; 2003. p. 209–40. |
| | Number of patients who received and completed DR-TB treatment | | [27] Gehre F, Otu J, Kendall L, Forson A, Kwara A, Kudzawu S, et al. The emerging threat of pre-extensively drug-resistant tuberculosis in West Africa: preparing for large-scale tuberculosis research and drug resistance surveillance. BMC Med 2016; 14(1):160. |
| | Number of patients who are drug-sensitive TB treatment response | | [26] Cazabon D, Suresh A, Oghor C, Qin ZZ, Kik SV, Denkinger CM, et al. Assessing the effectiveness of Xpert MTB/RIF in the diagnoses of TB among HIV smear-negative TB patients in Nigeria. J Health Popul Plan Dev 2019;42(1):1–5. |
| | Number of patients who completed DR-TB treatment | | [25] Hong QN, Furst T, Gourley S, Otu J, Forson A, Kwara A, et al. Achieving high treatment success for multidrug-resistant TB in Africa: initiation and scale-up of MDR TB care in Ethiopia—an observational cohort study. Thorax 2017;72(12):1188–9. |
| | Number of patients who received and completed DR-TB treatment | | [24] WHO. Global tuberculosis report 2015. World Health Organization; 2015. |
| | Number of patients who are drug-sensitive TB treatment response | | [23] Glaziou P, Sismanidis C, Zignol M, Floyd K. Methods used by WHO to estimate the global burden of TB disease. Geneva: Global TB Programme, WHO; 2016. |
| | Number of patients who completed DR-TB treatment | | [22] WHO. Global tuberculosis report 2017: World Health Organization; 2017. |
| | Number of patients who received and completed DR-TB treatment | | [21] WHO. Global tuberculosis report 2016. 2016. |
| | Number of patients who are drug-sensitive TB treatment response | | [20] WHO. Global tuberculosis report 2017: World Health Organization; 2017. |
| | Number of patients who completed DR-TB treatment | | [19] WHO. Global tuberculosis report 2016. 2016. |
| | Number of patients who received and completed DR-TB treatment | | [18] WHO. Global tuberculosis report 2017: World Health Organization; 2017. |
| | Number of patients who are drug-sensitive TB treatment response | | [17] WHO. Global tuberculosis report 2016. 2016. |
| | Number of patients who completed DR-TB treatment | | [16] WHO. Global tuberculosis report 2017: World Health Organization; 2017. |
| | Number of patients who received and completed DR-TB treatment | | [15] WHO. Global tuberculosis report 2016. 2016. |
| | Number of patients who are drug-sensitive TB treatment response | | [14] WHO. Global tuberculosis report 2017: World Health Organization; 2017. |
| | Number of patients who completed DR-TB treatment | | [13] WHO. Global tuberculosis report 2016. 2016. |
| | Number of patients who received and completed DR-TB treatment | | [12] WHO. Global tuberculosis report 2017: World Health Organization; 2017. |
| | Number of patients who are drug-sensitive TB treatment response | | [11] WHO. Global tuberculosis report 2016. 2016. |
| | Number of patients who completed DR-TB treatment | | [10] WHO. Global tuberculosis report 2017: World Health Organization; 2017. |
| | Number of patients who received and completed DR-TB treatment | | [9] WHO. Global tuberculosis report 2016. 2016. |
| | Number of patients who are drug-sensitive TB treatment response | | [8] WHO. Global tuberculosis report 2017: World Health Organization; 2017. |
| | Number of patients who completed DR-TB treatment | | [7] WHO. Global tuberculosis report 2016. 2016. |
| | Number of patients who received and completed DR-TB treatment | | [6] WHO. Global tuberculosis report 2017: World Health Organization; 2017. |
| | Number of patients who are drug-sensitive TB treatment response | | [5] WHO. Global tuberculosis report 2016. 2016. |
| | Number of patients who completed DR-TB treatment | | [4] WHO. Global tuberculosis report 2017: World Health Organization; 2017. |
| | Number of patients who received and completed DR-TB treatment | | [3] WHO. Global tuberculosis report 2016. 2016. |
| | Number of patients who are drug-sensitive TB treatment response | | [2] WHO. Global tuberculosis report 2017: World Health Organization; 2017. |
| | Number of patients who completed DR-TB treatment | | [1] WHO. Global tuberculosis report 2016. 2016. |
C. Ogo-Omenka et al.

[36] Global health observatory (GHO) data. 2020 [Internet]. 2020. Available from: http://www.who.int/data/gho/indicator-metadata-registry/imr-details/1364,

[37] Naidoo P, Van Nickerk M, Du Toit E, Beyers N, Leon N. Pathways to multidrug-resistant tuberculosis diagnosis and treatment initiation: a qualitative comparison of patients’ experiences in the era of rapid molecular diagnostic tests. BMC Health Serv Res 2015;15(1):488.

[38] Yadav SK, Damor R, Kanharia S, Tiwari M. Assessment of knowledge and treatment seeking behaviour among tuberculosis and multi-drug resistant tuberculosis patients: a case control study. IOSR J Dent Med Sci 2015;14(7):t66-71.

[39] Sharma N, Taneja D, Pagare D, Sahar R, Vashist R, Ingle G. The impact of an IEC campaign on tuberculosis awareness and health seeking behaviour in Delhi, India. Int J Tuberc Lung Dis 2005;9(11):1259-65.

[40] Yasin MA, Datiko DG, Tulloch O, Markos P, Aschalew M, Shargie EB, et al. Barriers and delays in tuberculosis diagnosis and treatment services: does gender matter? Tuberculosis Res Treatment 2014;2014.

[41] Colvin C, Muyagabon J, Munuo G, Lyimo J, Oren E, Mkomwa Z, et al. Evaluation of community-based interventions to improve TB case detection in a rural district of Tanzania. Global Health: Sci Pract 2014;2(2):219-25.

[42] Ambe G, Lonroth K, Djohlia Y, Copeaux J, Zignol M, Borremans N, et al. Every provider counts: effect of a comprehensive public-private mix approach for TB control in a large metropolitan area in India. Int J Tuberc Lung Dis 2005;9(5):562-8.

[43] Law S, Dafty A, O’Donnell M, Padasatchi N, Calzavara L, Menzies D. Interventions to improve retention-in-care and treatment adherence among patients with drug-resistant tuberculosis: a systematic review. Eur Respir J 2019;53(1).

[44] Deshmkhd RH, Dhande D, Sachdeva KS, Sreenivas A, Kumar A, Satyanarayana S, et al. Patient and provider reported reasons for lost to follow up in MDR-TB treatment: a qualitative study from a drug resistant TB Centre in India. PLoS One 2015;10(6).

[45] Awofeso N. Anti-tuberculosis medication side-effects constitute major factor for poor adherence to tuberculosis treatment. Bulletin of the World Health Organization. 2008. p. 86-8-D.

[46] Abidi S, Achar J, Neino MMA, Bang D, Benedetti A, Brode S, et al. Standardised shorter regimens versus individualised longer regimes for rifampin-or multidrug-resistant tuberculosis. Eur Respir J 2020;55(3).

[47] WHO. Rapid Communication: Key changes to the treatment of drug-resistant tuberculosis. World Health Organization. Geneva, Switzerland. 2019.

[48] Thomas BE, Shanmugam P, Malaisamy M, Ovung S, Suresh C, Subbaraman R, et al. Understanding pretreatment loss to follow-up of tuberculosis patients: an explanatory qualitative study in Chennai, India. BMJ Global Health 2020;5(2):e001974.

[49] Abidi S, Achar J, Neino MMA, Bang D, Benedetti A, Brode S, et al. Standardised shorter regimens versus individualised longer regimes for rifampin-or multidrug-resistant tuberculosis. Eur Respir J 2020;55(3).

[50] WHO. Rapid Communication: Key changes to the treatment of drug-resistant tuberculosis. World Health Organization. Geneva, Switzerland. 2019.

[51] Ibrahim LM, Hadejia IS, Nguku P, Dankoli R, Waziri NE, Akhimien MO, et al. Barriers and delays in tuberculosis diagnosis and treatment services: does gender matter? Tuberculosis Res Treatment 2014;2014.

[52] Subbaraman R, Nathavitharana RR, Satyanarayana S, Pai M, Thomas BE, Chadha VK, et al. The tuberculosis cascade of care in India’s public sector: a systematic review and meta-analysis. PLoS Med 2016;13(10):e1002149.

[53] Naidoo P, Theron G, Mangxa M, Chiwot VN, Vaughan L, Brey ZO, et al. The South African tuberculosis care cascade: estimated losses and methodological challenges. J Infect Dis 2017;216(suppl_7). S702-S13.

[54] Hassan A, Olukolade R, Ogjobu Q, Afolabi S, Okwuonye I, Kusimo O, et al. Knowledge about tuberculosis: a precursor to effective TB control—findings from a follow-up national KAP study on tuberculosis among Nigerians. Tuberculosis Res Treatment 2017;2017.

[55] Jonso G, Mbabwe PT. Global tuberculosis burden: is Nigeria losing the war? J Biol Med Clin Pract 2018;1(1):xvi.

[56] Babanlou OE, Bismark EC, Amarchi NE, Gabriel EI, Olanike A-UR. Determinants of treatment delays among pulmonary tuberculosis patients in Emuagu Metropolis, South-East, Nigeria. Health 2015;7(1):1106.

[57] Golub JE, Mohan C, Comstock G, Chasson RE. Active case finding of tuberculosis: historical perspective and future prospects. Int J Tuberc Lung Dis 2005;9(11):1183-203.

[58] Meiring C, van Helden PD, Goosen WJ. TB control in humans and animals in South Africa: a perspective on problems and successes. Front Veterinary Sci 2018;5:298.

[59] Oishi D, Chukwu J, Nwafor C, Chukwu NE, Meka AO, Anyim M, et al. Support and unmet needs of patients undergoing multidrug-resistant tuberculosis (MDR-TB) treatment in southern Nigeria. Int J Health Plann Manage 2019.

[60] Federal Ministry of Health NU. Women and children’s rights in Nigeria: A wake up call - Situation assessment and analysis. Abuja, Nigeria; 2002.

[61] Kuma SW, Yero BU. An analysis of gender inequality and national gender policy in Nigeria. Int J Sci Eng Res 2013;4(1):1-23.

[62] Karim F, Islam MA, Chowdhury A, Johansson E, Diwan VK. Gender differences in delays in diagnosis and treatment of tuberculosis. Health Policy Plans 2007;22(5):329-34.

[63] Okeibunor J, Onyeneho N, Chukwu J, Post E. Where do tuberculosis patients go for treatment before reporting to DOTS clinics in southern Nigeria. Tanzania J Health Res 2007;9(2):94-101.

[64] Tarimo GB. Delay in seeking care among tuberculosis patients attending tuberculosis clinics in Rungwe district. Tanzania: Muhimbili University of Health and Allied Sciences; 2012.

[65] Sullivan BJ, Esmaiili BE, Cunningham CK. Barriers to initiating tuberculosis treatment in sub-Saharan Africa: a systematic review focused on children and youth. Global health Action 2017;10(1):129017.

[66] Yang W-T, Gounder CR, Akande T, De Neve J-W, McIntyre KN, Chandrasekhar A, et al. Barriers and delays in tuberculosis diagnosis and treatment services: does gender matter? Tuberculosis Res Treatment 2014;2014.

[67] Hoddinok P, Hoddinok H, (eds.). The strengths and limitations of case study research. learning and skills development agency conference at Cambridge; 2001.