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ORIGINAL ARTICLE

Profile and Treatment Outcomes of Patients with Tuberculosis: A Five-year Review of Patients on DOTS in Delta State, Nigeria

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Keywords:

Tuberculosis; DOTS; Case Detection; AFB Positive Rate; Treatment Success

ABSTRACT

Background: Tuberculosis (TB), the second leading cause of death among infectious diseases continues to be a major public health threat worldwide, more so in the developing world. Several strategies have been tried in the past to address its burden, including Directly Observed Therapy Short-course (DOTS), DOTS plus, and the Stop TB Strategy. Amid these efforts, TB is now listed amongst the top re-emerging diseases in the world. This study identified trends in TB case detection, major type of TB, patient demographics, AFB positive rates, and treatment outcomes within the period reviewed.

Methods: In this descriptive records review of years 2011-2015, existing data was extracted from tuberculosis central registers from all sites in Delta State, Nigeria. The data was analysed using winPEPI and EPIDATA software solutions and presented in tables and charts.

Results: Tuberculosis case detection declined between 2011 and 2015. Patients aged 25–34 years were the largest proportion. Males outnumbered females in total but the proportion of females was higher among 5 to 34 year olds. Treatment success rate improved from 68.3% in 2011 to 88.0% in 2014. Sputum AFB positive rate was <60% for 2011 – 2014 but rose above 70% in 2015. Prevalence of extra-pulmonary TB was 2% for all the years reviewed except 2013 which had a small variation. The proportion of patients lost to follow-up declined from 2011 through 2015.

Conclusion: The Delta State Tuberculosis Control Programme improved in case-holding. These gains need to be sustained to keep up with the stipulations of the National Tuberculosis Control Programme.

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INTRODUCTION

Mycobacterium tuberculosis infection is a major infectious cause of deaths globally, mostly in developing countries.[1] It is still the second leading cause of death among the infectious diseases and continues to be a major public health threat worldwide. It is a debilitating disease with a greater prevalence and severity in a background of reduced immunity. In more recent years, it has become even more

complex due to a rise in its drug-resistant strains, amidst a range of other issues including human immunodeficiency virus (HIV) co-infection and TB (tuberculosis) co-morbidities - diabetes, congestive heart failure, asbestosis, sarcoidosis, etc.[2] Several strategies for tuberculosis control were formulated through the mid-twentieth to the twenty-first centuries, namely DOTS, DOTS plus and the Stop TB strategy intended to reduce the burden of this disease.[3, 4] Amid all efforts to control TB, the tide is not abating; instead it is reappearing in almost epidemic proportions and now listed amongst the top re-emerging diseases, mainly because of increasing multi-drug resistance and co-infection with human immunodeficiency virus (HIV). Till date, no other disease in history matches the sheer magnitude of the misery inflicted by TB on the human race in terms of morbidity and mortality.[5]

In Nigeria, tuberculosis is one of the top public health problems, ranking fourth among the 30 high-burden TB countries in the world.[5] There were 90,447 TB cases notified in 2010 with 41,416 (58%) new smear positive cases, and a case detection rate of 40% in Nigeria.[6] Although targets were set to reverse the incidence, half the prevalence and mortality, diagnose 70 percent of new smear-positive cases and cure 85 percent of tuberculosis cases by 2015, for many countries, these targets were not achieved despite the current existence of interventions.[7, 8] New TB cases were estimated to be 10.6 million globally in 2016, with 1.4 million deaths and an additional 0.4 million deaths among persons co-infected with human immunodeficiency virus; 95% of these occurred in developing countries.[9] With the setting up of the national tuberculosis control programme in 1989 several strategies, including DOTS, have been adopted to combat the persistently high burden of TB in Nigeria.[10] However, the gains of such interventions only became profound in the last decade when STOP TB strategy was introduced so much that within a period of five years (2006-2010) the death rate from TB was halved.[6]

In Delta State, though the incidence was as high as 2500 new cases recorded in 2010, with intensified efforts towards elimination the figures for new TB cases have reduced significantly in subsequent years.[6] The policy of the national programme in Nigeria is for all patients to be treated free of charge using DOTS strategy for six months in pulmonary TB cases, and twelve months for TB meningitis and spine. In many developing countries including Nigeria, Sputum Smear Microscopy (SSM) is the most widely used test for the diagnosis of pulmonary tuberculosis in accordance with the *International Standards on Tuberculosis Care*.[11, 12] The implementation of DOTS, which has been long established in Nigeria, is practised through sites distributed in the various states of the country. Since the national programme has set targets and indicators for the tuberculosis control in Nigeria, it is imperative that we assess the performance of the Delta State TB programme. This would enable us identify its achievements and opportunity areas and enlighten stakeholders on the way forward. This study therefore aimed to provide a summary description of patients who received DOTS for tuberculosis in Delta State, Nigeria. The prevalence of tuberculosis, age/sex distribution, new smear positive cases, the major type of TB seen, and treatment outcomes including cure rates, failure, loss to follow up (LTFU) and death rates among tuberculosis patients managed at DOTS centres over a five–year period were reported.

METHODOLOGY

This descriptive study involving the use of pre-existing data (from January, 2011 through December, 2015) from all ninety-eight TB-

DOTS sites in the three senatorial zones of Delta State was conducted in a period from March - June, 2017.

Brief description of TB-DOTS in Delta state: There are 98 DOTS centres spread across all 25 LGAs in the state and a TB referral centre in Ethiope-East LGA. Each centre is manned by health workers who report to the Local Government TB Programme Control Officer who is accountable to the State TB Control Programme Coordinator.

Data collection: Data was extracted from a standardized and updated State Tuberculosis Central Registry using a proforma. The State Tuberculosis Central Registry from which data extracted was up-to-date at the time of this study and the challenge with missing data was circumvented.

Ethical consideration: Ethical clearance was obtained from the Ethical Review Board of Delta State Ministry of Health, Asaba before conducting this study. Patient confidentiality was maintained throughout the study as no information that could personally identify them was used.

Data analysis: Data was analysed to identify trends using Microsoft Excel, winPEPI and Epidata software solutions. The results were represented using frequency tables and charts.

RESULTS

The total number of TB patients seen at DOTS clinics in Delta State in the five years reviewed was 13,635. There was a steady yearly decline in the number of TB cases from 2011 to 2015: the count in 2011 was 3076 while that in 2015 was 2349. The rate of decline slowed down between 2014 and 2015. Each year, age group 25–34 years made up the highest proportion of patients presenting for treatment at DOTS clinics (average: males - 24.7%; female - 29.8%); while ages 0-4 years was the smallest proportion (average: males - 1.0%; female - 1.2%). Although the proportion of females was higher than the males, for age groups 5-14 (males: 2.1%, Females: 3.7%), 15-24 (males: 13.4%, females: 18.5%) and 25-34 (males: 24.7%, females: 29.8%) years, the relative number of males was consistently higher than that of females for all the years reviewed. (Table 1) Each year, age-group 25–34 years made up the modal age group of new sputum smear positive TB cases presenting at DOTS clinics. The next highest frequencies were seen in age groups 35-44 years and 15-24 years. There was less than an average of 1 (0.1%) case of sputum smear positive TB among 0–4 year olds in the 5 years reviewed. Sputum smear positive TB was more common among males for all age groups except among 5–34 years olds where the proportions were higher among females. (Table 2)

There was a consistent decline in the total number of TB cases seen each year: from 3076 in 2011 to 2349 in 2015; but the proportion of AFB positive cases fluctuated during the years reviewed. AFB+/N ratio were as follows: 2011: 51.8%, 2012: 56.4%, 2013: 54.0%, 2014: 56.1%, and 2015: 70.6%. (Figure 1) Although total number of TB patients on DOTS care was on the decline, the proportion of new patients registering into the program each year was on the increase from 2011 through 2015. The newly registered cases were 85.5% in 2011 and gradually rose to 97.8% in 2015 except for 2012 when newly registered cases constituted 93.9% which was higher than the newly registered cases in 2013. (Figure 2) The relative proportion of pulmonary tuberculosis (PTB) and extra-pulmonary tuberculosis (EPTB) cases that presented at DOTS centres in Delta State was nearly constant for the 5 years reviewed. Proportion of Extra-pulmonary TB was 2% of patients for all the years with a small variation in 2013. (Figure 3) Documented cure rate for patients ranged from 35.6% to 45.4% with the highest being in 2014. Treatment

completion rate without documented cure fluctuated between 32.7% and 43.2% between 2011 and 2015. Treatment success rate therefore varied between 68.3% and 88.6%. Loss to follow-up rate was disproportionately high in 2011 at 25% compared to the other years which were below 10%. Death rate was similar for the 5 years reviewed ranging from 4.3% to 5.4 %. (Table 3)

DISCUSSION

The control of tuberculosis continues to be topical as the burden and complexity of the disease is still a source of much concern both globally and locally. This review of TB records in Delta State, Nigeria showed a steady decline in the total number of TB cases seen at DOTS centres over the 5 years reviewed. This decline is likely due to consistency in control efforts in the last decade, and this finding is consistent with the reports of the CDC for the United States in 2014.[13] It is important that strategies that have worked be reinforced for better performance, and if new strategies are to be introduced, they must have been proven to out-perform these. Sex distribution with respect to prevalence of tuberculosis in this study was similar to that from a study conducted within same Delta State[14] and in other studies in western and eastern Nigeria where the prevalence of tuberculosis amongst males was generally greater than that of females.[15–17] This finding is also in keeping with some studies from outside Nigeria where male predominance was observed.[18,19]

The World Health Organization asserts that prevalence of tuberculosis is higher in females in countries like Nigeria where the prevalence of HIV is above 1%.[20] It would appear that the findings of this study contradict that mindset, and that would be surprising especially as the prevalence of HIV in Nigeria is 3.2% and 4.1% in Delta State, the location of this review.[21] However, a closer observation reveals that although the total number of male patients was generally more than that of females, for ages 5-34 years, the collective proportion of females with TB and positive for AFB was consistently greater than that of males for all the 5 years reviewed. This is more consistent with the WHO assertion of a female preponderance in high burden HIV countries.[20] This could likely be the effect of HIV and due to the fact that transgenerational sex and marriage are somewhat common in this environment.[22,23] Public health authorities and other stakeholders must add the findings of this study to their cache of amoury to engender social change in matters like this that so clearly impact on public health negatively.

The decline in TB cases as well as the increasing trend of AFB positive cases over the five years was unlike findings from a similar study in Enugu State which showed a rising trend of TB cases despite a decline in the proportion of AFB positive cases.[15]AFB positive cases in this study were disproportionately higher in 2015 and did not align with the generally decreasing TB trend. This may have been due to the recent introduction of Xpert MTB/Rif in the diagnosis of TB. The findings of this study with respect to sex and age patterns of sputum smear positive PTB correlate with reports from a recent study in southern Nigeria,[24] and are consistent with the documented global epidemiology of the disease.[25] It is not at all surprising that the rate of positive AFB tests were very low among children generally and almost virtually nil amongst under-fives. Diagnosing TB in children continues to pose a great challenge to TB management globally as it is difficult to collect sputum samples from children, and even when sputum is produced, it is usually "*paucibacillary*" and thus smear negative.[26] This has rendered the current modalities for diagnosis of tuberculosis insufficient for use in children. New modalities like the Quantiferon Gold test

which use biomarkers expressed in other body fluids are being perfected for use in TB diagnosis.[26] They will definitely reduce diagnostic dilemmas which are currently a common trend among children and immune-suppressed persons.

A predominance of pulmonary tuberculosis, as seen in this study (98%), was also reported by studies of patients treated at DOTS centres in South-western Nigeria, Eastern Nigeria, and Europe where 94.8%, 86.5% and 80.3% of the patients had pulmonary tuberculosis, respectively.[17, 27, 28] Hospital wide infectious disease profiles have shown PTB to still present a high burden in many settings. In fact, prevalence rates from reviews in North-West Ethiopia, Kano Nigeria, and Saudi Arabia were 14.7%, 43.8%, 10.3%, respectively.[29–31] However, the high prevalence could be due to over diagnosis of PTB largely from reliance on chest X-ray reports, case definitions and clinical findings instead of the standard AFB or Xpert MTB/Rif tests. Extra-pulmonary tuberculosis was more prevalent in other studies in Ibadan, Oyo State, and Nnewi, Anambra State, Nigeria and another study in Europe with a prevalence of 15.6%, 13.5% and 19.3%, respectively,[27, 28, 32] than in this review where only about 2% had EPTB each year for the five years reviewed. The reason for this could be over diagnosis or higher co-infection with HIV in those studies. A higher prevalence of 51.2% and 56.2% of EPTB, have been recorded in studies in north-west Ethiopia.[30, 33] The reasons for this is not immediately obvious although it is possible that EPTB is under-diagnosed in the setting of this study because of the difficulties involved with sample collection for diagnosing EPTB and maybe because AFB is not sufficient for this purpose.

This study revealed that over a period of five years, the proportion of patients who had successfully completed their TB treatment gradually increased from 68.3% in 2011 to 88.0% in 2014 and some decline in 2015. This finding is in contrast with findings of a study in Southern Ethiopia where successful completion of TB treatment declined from 68% to 50% over a period of ten years.[34] Documented cure rate for patients in this review fluctuated between 35.6% and 45.4% which was rather inconsistent and low compared to the WHO recommended TB cure rate of 85%.[10]However, this corroborated findings from a study conducted in Eku, Delta State, Nigeria where the cure rate was 45.7%.[14] This finding is probably a result of the inconsistencies in the system of provision of DOTS services in Delta State. These inconsistencies could have included poor record keeping, [35] lack of or poor follow-up services and reminder systems, and possibly, inconsistencies with timing of clinics. Several studies from India, Pakistan, Iraq and Mexico reported varying cure rates; 42.9%, 55%, 63.5%, 69.6% and 82.7% respectively.[19, 36–39] Also, the efficacy of current TB drugs is in question and there is ongoing research to produce more effective drugs for TB treatment.[26] There may also be a need to expand services for testing and management of drug-resistant TB in Delta State; as this may improve cure rates.

The loss to follow-up rate of patients attending DOTS clinics observed in this study, steadily declined from 25% to 4.3% for the first four years. However, there was a slight increase to 6.1% in the fifth year. These findings were mostly lower than values obtained from Eku, Delta State where loss to follow-up (LTFU) rate was observed to be 12.9% over a five-year period.[14] This implies that LTFU is generally better in other parts of Delta State than at Eku which is only one of the ninety-eight DOTS centres in Delta State. LTFU in this study was worse compared to that observed in North-

West Ethiopia where it was reportedly low at 2.5%.[34] The differences observed between these studies may be attributed to the general challenges observed in the delivery of health care services, including DOTS in Nigeria.

The treatment failure rate in this study was below 3% for the years reviewed and similar to 2.7% reported from a previous study in eastern Nigeria.[27] This suggests that TB drug resistance may be low in Delta State even though it is among the high burden States for TB in Nigeria.[40] Death rate among TB patients observed in this study ranged from 4.3% to 5.4%. These rates were similar to those from studies conducted in Abuja, Nigeria and Felige, Ethiopia where death was reported to be 4.9% and 5.8%, respectively. [30, 41] Slightly lower mortality rates of 3%, 2.7%, and 3.6% recorded from previous studies in Mexico and India indicate a likely generally better outcome of treatment for patients in those countries.[38, 39, 42] However, these findings were in contrast to reports from a study in Saudi Arabia where TB mortality rate was 18%.[31] Although death rate in this study was markedly lower than that in the Saudi Arabian study; the probable reason for this could be because more than half of the patients in the Saudi study had associated co-morbidities. It also needs to be borne in mind that the treatment outcomes of patients lost to follow-up are unknown.

Conclusion

Tuberculosis is common in all age groups in Delta State but most prevalent in the third and fourth decades of life but treatment outcomes do not meet the WHO recommendations. Although prevalence has been on the decline since 2011, documented cure rates leave much to be desired. Extra-pulmonary Tuberculosis rate has been stable at about 2% but this may actually be due to under-diagnosed. In the active years of life, females bear a higher burden of TB. This finding may need further exploration and social interventions to curb it if the suspected underlying factors are identified.

Recommendation

Public health authorities and other stakeholders could act on the findings of this study to improve TB (pulmonary and extra-pulmonary) diagnosis by adopting innovative modalities to reduce diagnostic delays and dilemmas commonly experienced in TB management and care in the state.

Conflict of interests

The authors do not have any conflict of interest

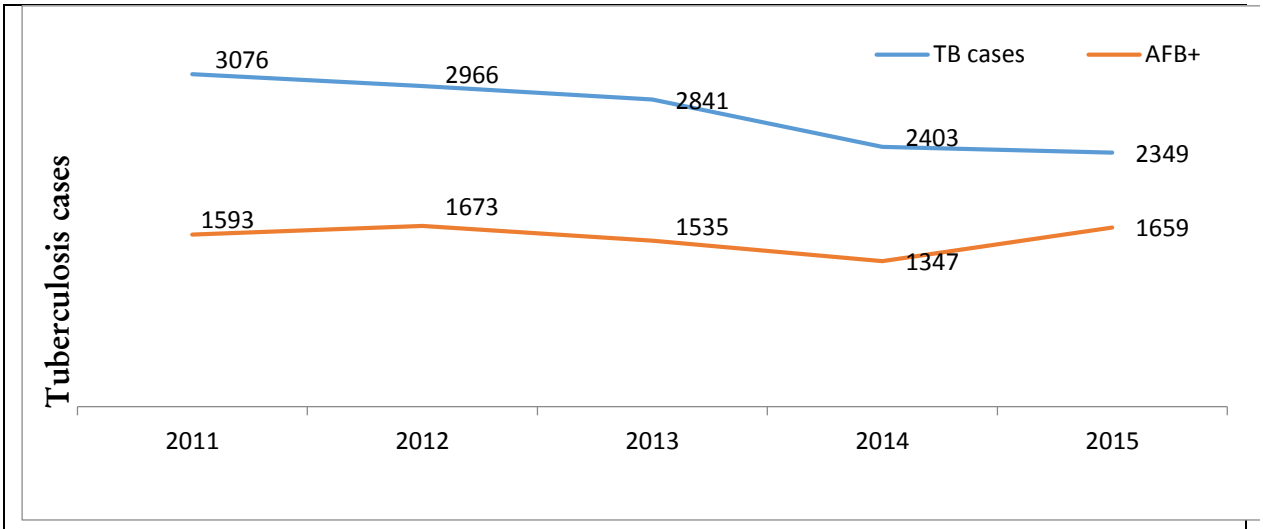
Table 1: Distribution of TB patients at DOTS centres in Delta State from 2011 - 2015

	Sex of patients Frequency (%)											
	2011		**2012**		**2013**		**2014**		**2015**		**Average no. (%)**	
Age-group (years)	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**
0-4	24 (1.3)	16 (1.3)	15 (0.9)	14 (1.1)	18 (1.1)	18 (1.5)	15 (1.1)	13 (1.3)	8 (0.6)	5 (0.5)	16 (1.0)	13 (1.2)
5-14	38 (2.1)	39 (3.2)	43 (2.5)	64 (5.1)	32 (2.0)	48 (4.0)	22 (1.6)	28 (2.8)	33 (2.4)	31 (3.3)	34 (2.1)	42 (3.7)
15-24	220 (12.0)	228 (18.5)	243 (14.3)	214 (17.0)	222 (13.8)	222 (18.1)	203 (14.4)	188 (18.9)	183 (13.1)	198 (20.9)	214 (13.4)	210 (18.5)
25-34	517 (28.0)	402 (32.6)	425 (25.0)	379 (30.0)	395 (24.5)	362 (29.5)	351 (24.9)	297 (30.0)	279 (21.2)	248 (26.1)	393 (24.7)	338 (29.8)
35-44	419 (22.7)	246 (20.0)	396 (23.2)	282 (22.3)	396 (24.5)	252 (20.5)	337 (24.0)	221 (22.3)	337 (24.1)	221 (23.3)	377 (23.6)	244 (21.5)
45-54	290 (15.7)	143 (11.6)	265 (15.6)	143 (11.3)	264 (16.4)	154 (12.5)	227 (16.1)	118 (11.9)	270 (19.3)	131 (13.8)	263 (16.5)	138 (12.2)
55-64	172 (9.3)	88 (7.1)	165 (9.7)	91 (7.2)	140 (8.7)	89 (7.2)	133 (9.4)	60 (6.0)	161 (11.5)	59 (6.2)	154 (9.7)	78 (6.9)
≥65	164 (8.9)	70 (5.7)	152 (9.0)	75 (6.0)	146 (9.1)	83 (6.7)	122 (8.7)	68 (6.8)	129 (9.2)	56 (5.9)	143 (9.0)	70 (6.2)
Sub-total	**1844 (60.0)**	**1232 (40.0)**	**1704 (57.5)**	**1262 (42.5)**	**1613 (56.8)**	**1228 (48.2)**	**1410 (58.7)**	**993 (41.3)**	**1400 (59.6)**	**949 (40.4)**	**1594 (58.5)**	**1133 (41.5)**
Total	**3076 (100.0)**		**2966 (100.0)**		**2841 (100.0)**		**2403 (100.0)**		**2349 (100.0)**		**2727 (100.0)**	

Note: Age group 0-4 years is a different interval from the others just to show the relative frequency of under-fives; Averages were rounded up to whole numbers because they refer to humans

Table 2: Distribution of new smear positive cases from 2011 – 2015

	Sex of patients											
	Frequency (%)											
Age-group (years)	2011		2012		2013		2014		2015		Average No. (%)	
	M	F	M	F	M	F	M	F	M	F	M	F
0-4	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)
5-14	9 (1.0)	21 (3.4)	13 (1.3)	20 (3.0)	8 (0.9)	13 (2.0)	11 (1.4)	10 (1.8)	14 (1.4)	16 (2.4)	11 (1.2)	16 (2.6)
15-24	147(15.1)	163(26.3)	175 (17.3)	148(22.5)	132(14.9)	158(24.4)	136(17.0)	121(22.2)	143(14.3)	160(24.2)	147(15.7)	150(23.9)
25-34	307(31.6)	219(35.3)	282 (27.8)	215(32.6)	260(29.3)	204(31.5)	209(26.1)	181(33.2)	225(22.6)	189(28.5)	256(27.4)	202(32.2)
35-44	231(23.7)	120(19.4)	258 (25.4)	154(23.4)	229(25.8)	137(21.2)	205(25.6)	121(22.2)	253(25.4)	154(23.3)	235(25.2)	137(21.9)
45-54	155(16.0)	54 (8.7)	158 (15.6)	63 (9.6)	134(15.1)	72 (11.1)	121(15.1)	62 (11.4)	192(19.3)	76 (11.5)	152(16.3)	65 (10.4)
55-64	68 (7.0)	23 (3.7)	72 (7.1)	32 (4.9)	72 (8.1)	37 (5.7)	68 (8.5)	28 (5.1)	103(10.3)	35 (5.3)	76 (8.1)	31 (4.9)
≥65	55 (5.6)	20 (3.2)	56 (5.5)	27 (4.1)	53 (6.0)	26 (4.0)	51 (6.3)	23 (4.2)	66 (6.6)	32 (4.8)	56 (6.0)	26 (4.1)
Sub-total	**973(61.1)**	**620(38.9)**	**1014(60.6)**	**659(39.4)**	**888(57.9)**	**647(42.1)**	**801(59.5)**	**546(40.5)**	**997(60.1)**	**662(39.9)**	**934(59.8)**	**627(40.2)**
Total	**1593 (100.0)**		**1673 (100.0)**		**1535 (100.0)**		**1347 (100.0)**		**1659 (100.0)**		**1561 (100.0)**	



AFB+/N Ratio (%)	51.8	56.4	54.0	56.1	70.6

N refers to the total number of tuberculosis patients seen each year consecutively for the 5 years reviewed

Figure 1: Comparison of total number of tuberculosis patients with no. of AFB+ Cases

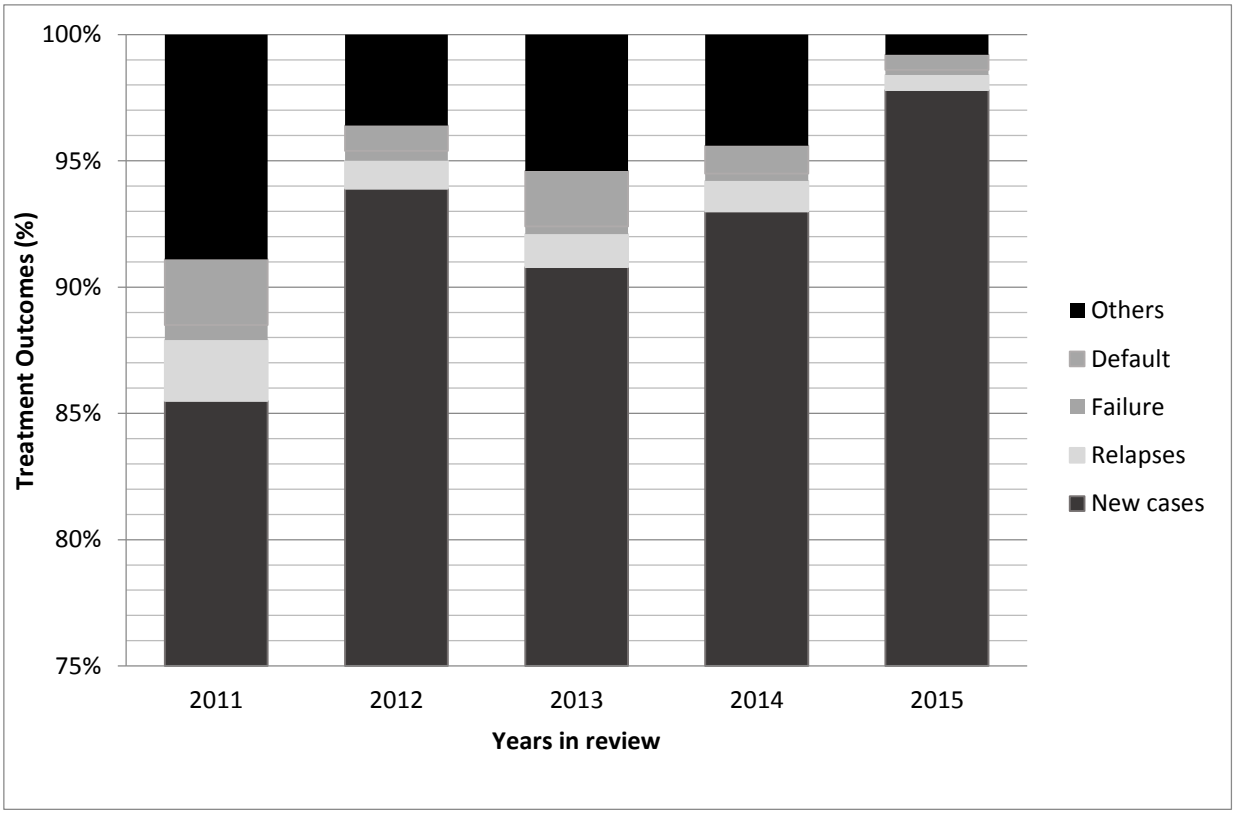


Figure 2: Categories of patients registered for TB-DOTS treatment in Delta State

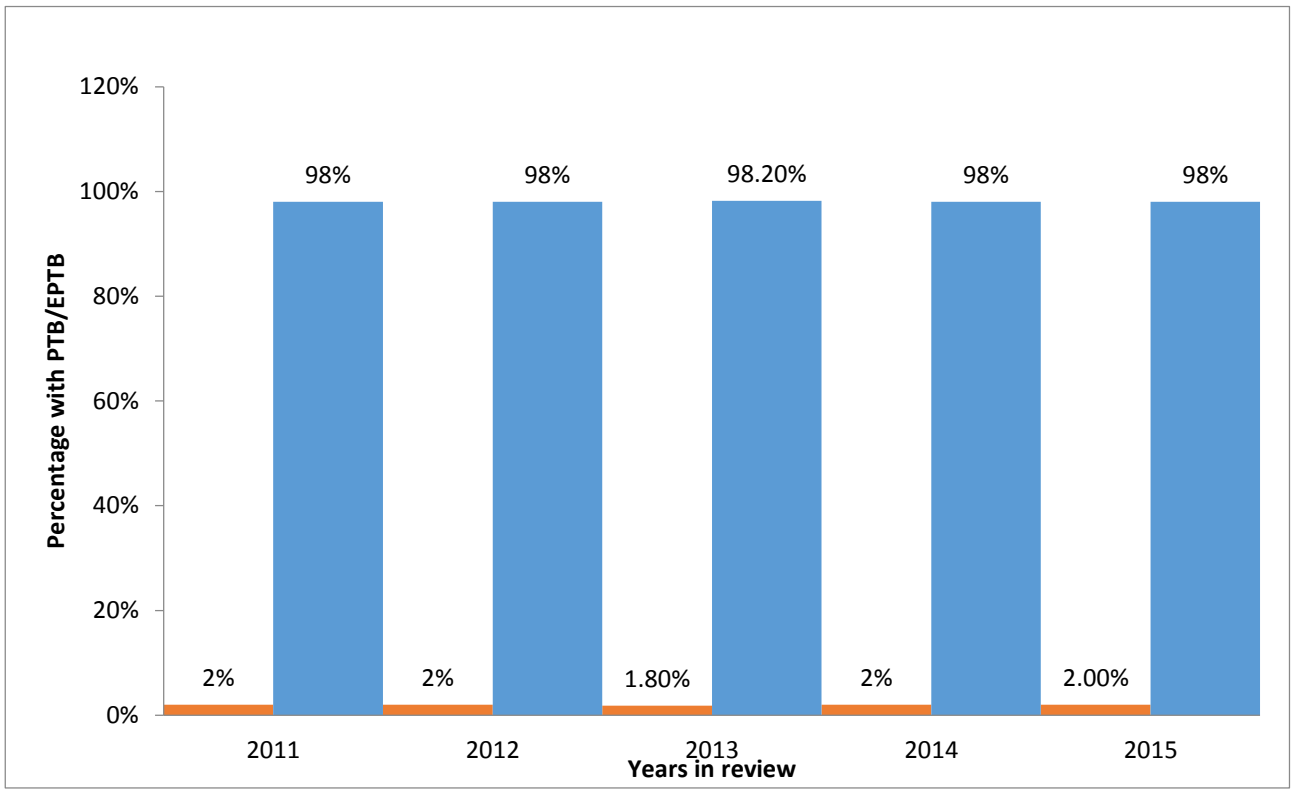


Figure 3: Proportions of Pulmonary and Extra-pulmonary Tuberculosis at DOTS Clinics

Table 3: Trends in treatment outcomes for all new cases of tuberculosis in Delta State

Outcomes	Years in review Frequency (%)				
	2011 (n=1593)	**2012 (n=1673)**	**2013 (n=1535)**	**2013 (n=1347)**	**2015 (n=1659)**
Cured (a)	567 (35.6)	706 (42.2)	682 (44.4)	611 (45.4)	720 (43.40
Treatment completed (b)	521 (32.7)	709 (42.4)	642 (41.9)	574 (42.6)	717 (43.2)
Treat failure	11 (0.7)	17 (1.0)	17 (1.1)	11(0.8)	15 (0.9)
Loss to follow-up	398 (25.0)	107 (6.4)	71 (4.6)	58 (4.3)	101 (6.1)
Transfer	27 (1.7)	54(3.2)	40 (2.6)	23 (1.7)	25 (1.5)
Died	69 (4.3)	80 (4.8)	83 (5.4)	70 (5.2)	81 (4.9)
Treatment success (a + b)	1088 (68.3)	1415 (84.6)	1324 (86.3)	1195 (88.0)	1437 (86.6)

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