Original Article

Implementation challenges of a TB programme in rural northern mozambique: evaluation of 2012–2013 outcomes

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Background: We aimed to identify challenges and to propose solutions for the implementation of tuberculosis (TB) programmes in rural Sub-Saharan Africa (SSA) by evaluating the outcomes of the TB programme in the Ancuabe district in rural Northern Mozambique.
Methods: Retrospective descriptive study of the patients included in the TB programme in 2012–2013. Follow-up was continued till June 2014.
Results: Three hundred nineteen patients were registered, 62.1% male, mean age 36.3 (SD 14.4), estimated case detection rate (eCDR) of 24.24%. Two hundred seventy-two were new cases, 21 transferred-in, 11 back after lost to follow-up (LTFU), 10 relapsing TB, 5 previous treatment failures. 94.4% were tested for Human immunodeficiency virus (HIV), 41.9% HIV-positive. 87.5% of the new cases were pulmonary TB (PTB), 43.4% were HIV co-infected. Initial sputum results were available in 207 cases, with 145 smear-positive (SP) cases. Outcomes of new cases: 122 (44.9%) LTFU, 55 (20.2%) cured, 43 (15.8%) treatment completed (98–36%-treatment success), 31 (11.4%) died, 19 (7%) transferred out and 2 (0.7%) failures.
Conclusions: A low eCDR and high proportion of LTFU demonstrate that few patients were identified and had a low probability of complete treatment, suggesting a fragile health system. This raises the hypothesis that, probably, to improve TB health care in rural SSA, interventions should aim at improving health systems. Special attention should be given to social protection and compensation of the financial burden associated with TB.

Keywords: Tuberculosis, Directly observed treatment, Epidemiology, Mozambique

Introduction

Tuberculosis (TB) is one of the leading causes of mortality worldwide. In 2013, an estimated nine million people developed TB and 1.5 million died from the disease.[1] Mozambique is considered by the World Health Organisation (WHO) as a high TB/Human immunodeficiency virus (HIV) burden country. Reported TB figures are following an upward trend, and the estimated case detection rate (eCDR) remains stable at only 37%, the lowest among the high-burden countries.[1,2] Mozambique has a TB incidence of 552 ($CI_{95\%}$ 442–680)/100 000 population; 140 000 new cases every year. Of those, 81 000 are among people living with HIV (PLWH) and it is the leading cause of death among them.[3] The nationwide HIV prevalence is 12% and there are an estimated 1.6 million PLWH.[4] A thorough description of the Mozambican TB programme can be found elsewhere and is in line with WHO 2010 TB treatment guidelines.[5,6]

Implementation of TB programmes in rural areas is challenging. Mixed experiences have been reported from Malawi and Angola.[7,8] Rural areas may have the potential to act as reservoirs of undiagnosed TB

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cases[9] and because of lack of education,[10] difficulties in accessing care and the need for multiple visits,[11] diagnostic delays are frequent,[12] treatment outcomes are sub-optimal[13] and lost to follow-up (LTFU) rates high. This further suggests that rural areas might act as a possible source for the generation of multi drug-resistant TB (MDR-TB), given higher drug resistance rates have been repeatedly described in retreatment cases.[14,15]

Tuberculosis programmes in rural areas have been scarcely reported although the knowledge of the epidemiologic situation in such areas is key to design and implement TB control policies.[16] We aimed to evaluate the outcomes and identify implementation challenges of the TB programme in a remote rural African district.

Methods

Setting

The place of the study is Ancuabe, a rural district in the province of Cabo Delgado, one of the poorest provinces in Mozambique. Cabo Delgado has a population of 1.8 million inhabitants; 51.6% women. Eighty percent of the population lives in rural areas and the frequency of illiteracy is around 80 and 51% for women and men, respectively. Life expectancy is 36.7 years.[17]

Ancuabe has an extension of 4,606 km^2, with 118 926 inhabitants in 65 villages. HIV prevalence is about 5%.[18] The district has two type 1 health centers (HC) with 87 inpatient beds and the presence of a doctor and four type 2 HC that provide outpatient services. In the type 1 HC, a Chronic Diseases Unit and a TB clinic offer follow-up and treatment to patients living with HIV and TB. Patients could be followed up at the type 2 HC if they wish so. Tuberculosis diagnosis is based on clinical diagnosis and sputum smear microscopy. Access to chest X-ray is 120 km away. The majority of the health care services in Ancuabe are delivered by non-physician clinicians and they usually establish the diagnosis of both smear positive (SP) and smear negative TB cases.

Study population

This is a retrospective descriptive study of the results of the TB programme in Ancuabe. All TB patients – independent of age – entering the TB programme from January 2012 to December 2013 were included. Transferred-in cases were excluded from the analysis as the information before the registration in Ancuabe was not available.

Data collection

We collected the data from March to June 2014. The information enclosed in the TB registry books was introduced into an electronic database by the study investigators. It was checked for completeness and consistency by comparison with the treatment charts.

Variables

We recorded demographic data: age, sex and place of residence. The clinical variables compiled were as follows: type of TB (pulmonary/extra-pulmonary); pre-diagnostic situation in terms of previous TB treatment, LTFU or relapse. Other clinical variables included were HIV status, including antiretroviral treatment (starting date if available) and trimethoprim/sulfamethoxazole prophylaxis. To report on the microbiological results the date and result of the initial and subsequent sputum smears was introduced. We recorded type of case and outcomes following the WHO guidelines (before 2013 modifications) and Mozambican TB programme definitions (Tables 1 and 2) [5,6] and finally, end of treatment date.

Rates

We calculated the eCDR as the number of patients registered divided by the number of estimated incident cases. We used the WHO estimate for incident cases.[19] The sputum completion rate was calculated as the number of patients with a sputum result available at 2 months of follow-up divided by the number of patients that were SP at baseline (excluding those who died or were transferred out). The sputum conversion rate was calculated as the number of patients with a negative smear at 2 months divided by the number of patients that had a smear result available at 2 months of follow up and were SP at start.

Analysis

We analysed basic demographic characteristics, type of TB diagnosed, eCDR and rate of sputum smear positivity. Two-month sputum smear completion rate as well as sputum smear conversion rate was obtained. We analysed the proportions of different

Table 1 Case definitions used in the study.

Type of case	Definition
New case	When diagnosis was established and the patient had never received TB treatment or had previously received treatment for <1 month
Relapsing TB	A microbiologically positive TB case, who had previously been treated and cured of a TB episode (i.e. sputum smear negative and clinical resolution)
Back after lost to follow-up	When patients had abandoned treatment for 2 months or longer, and were microbiologically positive
Previous treatment failure	A patient that restarted a new TB treatment, after showing unsuccessful results with a previous regimen (ensuring correct compliance)
Transferred-in	Those who arrived from another health facility to continue or start TB treatment

Table 2 Outcomes definitions used in the study.

Outcomes	Definitions
Cure	Assumed when there was an initial positive sputum smear which veered to negative and completed 6 months of treatment
Treatment completed	When there was proof that the patient had completed 2 months of intensive phase treatment and at least 4 months of continuation phase treatment, but sputum smear had not been done or the result was not available
Treatment failure	Was acknowledged when the patient had a positive sputum smear at the fifth month of treatment
Transferred out	When the patient was transferred to another facility out of the district to continue the treatment (which could happen at any stage of follow-up)
Death	Death for any reason during treatment
Lost to follow-up	A patient that had abandoned the treatment for more than 2 months or if no outcome at all for the TB treatment was registered after the treatment time had been completed

patient outcomes. This analysis was repeated and stratified by sex, age, HIV status and smear positivity status.

We used SPSS v20 (SPSS Inc, Amonk, NY, USA). Quantitative variables were described using mean (standard deviation) for those that had normal distribution, or median (interquartile range) for those that did not. Qualitative variables were described with proportions. We used chi square (or Fisher's exact test, when needed) for the comparison of qualitative variables; and for variables with non-normal distribution, we used the Mann–Whitney U non-parametric test.

Ethical considerations

The data presented here were collected as part of a larger study for the evaluation of TB diagnostic techniques approved by the Mozambican National Bioethics committee and by the University of Barcelona ethics committee.

Results

A total of 319 patients were registered in the TB programme, with 658 yearly expected cases (if we accept the WHO estimate on incidence as a good approximation), yielding an eCDR of 24.24% ($CI_{95\%}$21.9–26.6%). Male patients accounted for 62.1%, with a mean age of 36.3 (SD 14.4) years. There were 272 (85.3%) new cases, 21 (6.6%) transferred-in [excluded from further analysis], 11 (3.4%) returning from LTFU, 10 (3.1%) relapsers and 5 (1.6%) treatment failures. Of the included, 263 (88.3%) had pulmonary TB (PTB) and 35 (11.7%) extra-pulmonary TB (EPTB). 94.4% of the patients were tested for HIV and 132 (41.4%) were identified HIV positive. Of those, 97.0% received trimethoprim/sulfamethoxazole prophylaxis and 71.9% received antiretroviral treatment (ART).

New cases

Of the 272 new cases, 238 (87.5%) were PTB and 34 (12.5%) EPTB (Characteristics in Table 3). One hundred and eighteen (43.4%) were HIV infected. Outcomes (Fig. 1, Table 4) of those 272 patients were 122 (44.9%) LTFU, 55 (20.2%) cured, 43 (15.8%) treatment completed [98–36%-treatment success], 31 (11.4%) dead, 19 (7%) transferred out and 2 (0.7%) failure. Initial sputum results were available in 210 (77.2% of new cases) cases, with 148 of patients being SP (54.4%; $CI_{95\%}$48.3–60.4%). Of those, 78 (52.7%; $CI_{95\%}$44.3–60.9% sputum completion rate) had a sputum control after the intensive phase. Excluding dead and transferred out this yields a sputum completion rate of 86.67% ($CI_{95\%}$ 79.1–94.2). Sixteen patients remained positive, resulting in a sputum conversion rate of 79.5% ($CI_{95\%}$ 68.8–87.8%). Of the 272 patients who should have completed the treatment, only 40 (27% of SP cases) and 22 patients (14.8% of SP cases) had a sputum control at months 5 and 7, respectively. Two of those resulted SP at 5 months and two at 7 months.

Previously treated cases

Of the 26 previously treated cases, 25 (96.2%) were PTB and 7 (26.9%) were HIV co-infected (characteristics in Table 3). Outcomes (Fig. 1) of the 22 patients that should have finished treatment were 10 (45.4%) LTFU, 7 (31.8%) cured, 3 (13.6%) treatment completed [10–45.4%-treatment success], 1 (4.5%) dead, 1 (4.5%) failure. Initial sputum results were available in 20 patients (76.9%), and 16 (61.5%) were SP cases. Of those, 7 (43.7%) had a sputum control after intensive phase (2 SP). Of the 22 patients who should have completed the treatment by the end of the study period, only 4 had a sputum control at month 8 (31.8%) (2 SP).

Pediatric cases

Ten (3.7% of the total number of new cases) cases of TB were diagnosed in patients <15 years of age, of which 50% were EPTB; five had sputum or gastric aspirate smear microscopy of which one was found positive. Six out of 10 were LTFU, 2 had successful treatment outcomes (treatment completed) and 2 were reported dead.

Stratified analysis

When stratifying the analysis by gender, men were more likely to be HIV positive (53.6 vs 46.4%; $P=0.02$), and SP (76.6 vs 64.1% $P=0.039$) compared to women (Table 5, Fig. 2).

Table 3 Clinical characteristics of the patients included in the study.

Clinical characteristics	New cases $n = 272$ n (%)	Previously treated $n = 26$ n (%)	P-value
Median age (IQR)	34 (25.3–45)	34 (28.8–40.3)	0.573
Gender (men)	163 (60.1)	20 (76.9)	0.116
Pulmonary TB	238 (87.8)	25 (96.2)	0.436
HIV prevalence	117 (43.2)	7 (26.9)	0.107
Sputum completion rate	78 (52.7)	7 (43.7)	0.253
Sputum conversion rate	62 (79.5)	5 (71.42)	0.934
Treatment success	98 (36.4)	10 (45.4)	0.257

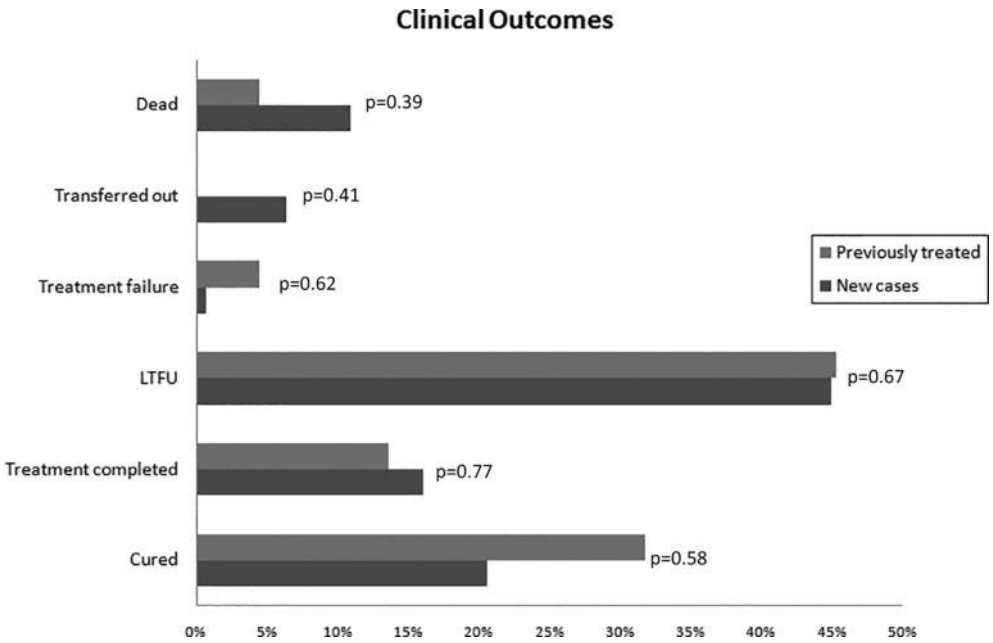


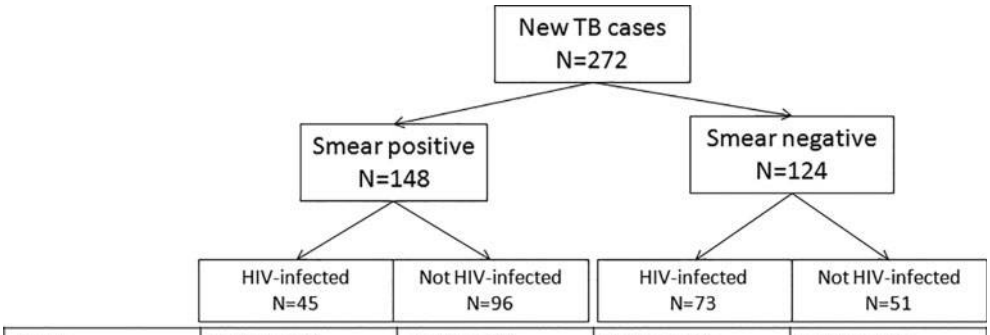
Figure 1 Clinical outcomes: new cases vs previously treated patients.

Table 4 Treatment outcomes and confidence intervals for new TB patients.

Outcome	New patients $n = 272$	$CI_{95\%}$
Dead	11.4% (31)	8–13%
Transferred out	6% (19)	4–11%
Treatment failure	0.7% (2)	0.1–3%
LTFU	44.9% (122)	39–51%
Treatment completed	15.8% (43)	12–21%
Cured	20.2% (55)	16–25%

Table 5 Sex, age and HIV status in TB population analysis.

	Men (%)	Women (%)	P value
HIV positive	53.6	46.4	$P = 0.02$
Smear positive	76.9	63.8	$P = 0.039$
	<15 years old (%) (3.7%)	>15 years old (%) (96.3%)	
EPTB	44.4	10.7	$P = 0.002$
Smear positive	20	72.8	$P = 0.01$
	HIV + (%)	HIV − (%)	
Smear negative	67.2	32.8	$P < 0.001$
Age >40	34.3	38.6	$P = 0.012$
Male sex	53.6	46.4	$P = 0.02$
LTFU	40	47.4	$P = 0.14$
Deaths	12	10.3	$P = 0.14$



LTFU	11(24.4%)	45(46.9%)	35(47.9%)	27(52.9%)
Dead	10(22.2%)	12(12.5%)	5(6.8%)	4(7.8%)
Failure	1(2.2%)	1(1%)	None	None
Transfered out	2(4.4%)	5(5.2%)	6(8.2%)	4(7.8%)
Treatment completed	4(8.9%)	5(5.2%)	22(30.1%)	11(25%)
Cured	17(37.7%)	28(29.2%)	5(6.8%)	5(9.8%)

Figure 2 Stratified analysis of treatment outcomes according to sputum smear and HIV status.

When stratifying the TB cases by age group, only 10 (3.7%) patients were children under 15 years of age and these appeared to have EPTB more often (44.4 vs 10.7%; $P=0.002$) and resulted SP (20 vs 72.8%; $P=0.01$) less frequently.

People living with HIV with TB co-infection were more likely to have a negative sputum smear (67.2 vs 32.8%, $P<0.001$). Furthermore, they were younger (34.3 vs 38.6 years, $P=0.012$) and more frequently men (53.6 vs 46.4%, $P=0.02$). HIV-infected patients treatment outcomes were different compared to non HIV-infected patients because of a lower percentage of LTFU (40 vs 47.4%) ($P=0.14$) and a higher proportion of deaths (12 vs 10.3%) ($P=0.14$). Nevertheless, these differences were not statistically significant.

Discussion

Through documenting outcomes of TB patients from a single district in one of the poorest areas of the world, we provide a much needed insight into the ground realities, unbiased by research interventions.

We describe the whole patient pathway from diagnosis and treatment start to final outcomes. While almost 95% of the TB patients received an HIV test – highlighting the successful integration efforts of HIV and TB within such context – the high percentage of defaulters, the low-estimated eCDR (WHO target=70%)[20] and low proportion of treatment success (36.4%) signal major challenges in patient detection and follow-up. These results are in line with the national TB programme outcomes and reflect the main challenges of the programme in such low-income country.[1]

We observed a sputum completion rate of 86.67%, with a sputum conversion rate of 79.8%. The sputum completion rate is in line with reported rates from other African countries and the sputum conversion rate reached the WHO standard of at least 75% among new PTB and is in line with other reports from similar settings.[13,21]

An adequate rate of HIV screening (94.4%) was found, with 43.4% HIV-positive. This is a slightly lower proportion of HIV co-infection than those published in other previous studies in Mozambique (Manhiça).[22] We also found a high percentage (97%) of HIV-infected patients on trimethoprim/sulfamethoxazole prophylaxis. The number of co-infected patients receiving ART (71.96%) was lower than the Stop TB partnership target of 100% for 2015;[20] however, as it has also been observed in previous studies,[22] HIV patient records are a better source to provide ART status and we could be underestimating the real value.

Only 10 (3.7%) cases of TB were diagnosed in patients under 15 years of age, and with poor outcomes. These cases are likely only a small fraction of the total number of paediatric cases.[23] According to Jenkins *et al.*, considering the TB incidence in Mozambique, we could expect around 12% of TB cases to be paediatric cases.[24] New diagnostic strategies in this age group are needed and new culture and molecular techniques are emerging as promising resources.[25,26] Moreover, vulnerability of children in this context is high and is probably also influencing the outcomes.

A higher number of male TB cases were found. And they were also more likely to have SP TB. This is consistent with findings from other settings and speaks of the consistency of our data.[27]

Only 36.4% of the new TB cases had a successful outcome (i.e. cured or treatment completed), whereas the percentage of adverse outcomes (deaths and

LTFU) was disturbingly high (57.1%). The high proportion of LTFU in this study represents a constant risk of MDR-TB emergence. Thus, specific measures to increase retention are needed to avoid the generation of resistance.

This is a retrospective observational study with its attendant limitations. We could observe that data quality and collection at health centre level were weak, with missing data in the registries not being infrequent. Nevertheless, the search for data and transcription into the database was thorough and exhaustive from the paper based registries as well as from the individual patient charts. We believe that the results presented are the best possible and reflect the district reality. However, generalisability of these results to other settings is questionable and lessons learnt as well as conclusions drawn from this evaluation may not be applicable everywhere. Nonetheless, this district is a rural African district with all its intrinsic complications and conditionings and probably in many settings challenges and solutions could be similar.

Our results highlight the difficulties in carrying out successful TB programmes in poor settings of Sub-Saharan African (SSA) rural areas, and point out that most steps of the TB care need improvements. In a broad view, what the data are telling us is that the health system as a whole is quite fragile. Bringing up the hypothesis that, probably, interventions that could have the biggest impact would be those that aimed at the health system as a whole or at least had a strong component of health system strengthening. Otherwise, interventions are unlikely to be completely successful. One such example is the recent experience of GeneXpert introduction in the provinces of Sofala and Manica in Mozambique. This was an urban setting, and a quite impressive 69% increase in TB diagnosis was achieved. Nevertheless, 33% of the extra patients detected did not start treatment. And even worse, 53% of those with Rifampicin resistance did not start treatment.[28] Raising the question whether it is ethical to expand only diagnostic services when the health system is not able to cope with the extra cases.[29] Nevertheless, for rural settings, with structural difficulties for standard GeneXpert installation, same-day sputum microscopy approach could be an alternative as it has demonstrated to have the same diagnostic accuracy as the traditional 2 days sampling and has also been endorsed by WHO. Its implementation has recently been adopted in Mozambique and may help to increase the eCDR.

The WHO DOTS strategy was encouraged during the study period. However, although studies have suggested that it may improve patients' outcomes and it is widely recommended,[30–32] there is no conclusive evidence that it improves outcomes.[33] It has also been stated that a too rigid application could have a harmful effect if patients are facing big difficulties to access health services.[33] This could have been an issue in Ancuabe, as the Community DOT programme was not functioning at time of evaluation because of lack of staff and resources and DOT at a health centre level was encouraged during the intensive phase. Drugs were provided free of charge in fixed-dose combinations but stock outs occurred regularly. Ambulatory TB care was free but often provided by overloaded and therefore unmotivated non-physician clinicians that did not undertake patient education nor counselling. The community support programme was practically non-existent. No food incentives or transport support was available. Patients could only be admitted at a common medical ward. Application of the END TB strategy with integrated patient-centred care and bold supportive systems could help improve this situation.[34] It seems reasonable that the efforts should start at improving treatment outcomes and follow-up. For that, expanding social protection and poverty alleviation actions may come to use. Schemes for compensating the financial burden associated with illness, such as social welfare payments, cash transfers, transport, and/or food vouchers, could be helpful, as well as ensuring a logistic system that could guarantee availability of drugs.

Once treatment outcomes are improved, and the system could guarantee a correct follow-up of the patients, efforts could be moved towards actions for earlier diagnosis and better diagnosis (ie rapid tests and drug susceptibility testing).

To improve paediatric TB results, it seems imperative to increase clinical awareness of TB clinicians, as well as to perform screening of TB patients' household contacts. Implementation of the new WHO guidelines with broad screening approaches, new diagnostic techniques and active case finding may reduce the magnitude of under-diagnosis in this vulnerable population.[35]

Conclusions

Challenges were found in almost every step of TB care in our setting. Our data suggest that to improve TB health care in rural SSA, it seems necessary to implement interventions with horizontal design aiming at improving the health systems in all of their components. It seems that special attention should be given to social protection and compensation of the financial burden associated with TB.

Disclaimer Statements

Contributors PEW-J and AM-C designed the study, collected the data, performed the analysis, and wrote

the manuscript. JL-G contributed to the design of the study, supervised the data collection, checked the data for completeness and consistency, supervised the data analysis, and contributed to the manuscript. TMP-P contributed to the interpretation of the data and writing of the manuscript. MH contributed to the writing of the manuscript. JE contributed to the preparation of the manuscript. MAM contributed to the manuscript and interpretation of data. RA reviewed the statistical analysis and contributed to the manuscript. CA overviewed the statistical analysis and contributed to the interpretation of the data and writing of the manuscript.

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Conflicts of interest None declared.

Ethics approval The data presented here were collected as part of a larger study for the evaluation of TB diagnostic techniques approved by the Mozambican National Bioethics committee and by the University of Barcelona ethics committee.

References

1 WHO. Global tuberculosis report 2014. 2014. Available from: http://www.who.int/tb/publications/global_report/en/.
2 García-Basteiro AL, López-Varela E, Manhiça I, Macete E, Alonso PL. Mozambique faces challenges in the fight against tuberculosis. Lancet. 2014;383:215–6.
3 UNAIDS. Global report: UNAIDS *report on the global AIDS epidemic 2013*. Geneva: UNAIDS; 2013.
4 WHO. Epidemiological fact sheet on HIV and AIDS core data on epidemiology and response *Mozambique*. Geneva: WHO; 2008.
5 WHO. Treatment of tuberculosis: guidelines. 4th ed 2010. Available from: http://whqlibdoc.who.int/publications/2010/9789241547833_eng.pdf.
6 Ministerio da Saúde de Moçambique. Tuberculose. Actualização para Docentes das Instituçoes de Formaçao. Maputo. 2011 (Jul);1–92.
7 Mboma SM, Houben RM, Glynn JR, Sichali L, Drobniewski F, Mpunga J, *et al.* Control of (multi) drug resistance and tuberculosis incidence over 23 years in the context of a well-supported tuberculosis programme in rural Malawi. PLoS One. 2013;8:e58192.
8 López T, Moreno M, Salvador F, Zacarías A, Carvalho Rd, Tomás E, *et al.* Tuberculosis diagnosed in a rural setting in Angola. Accuracy of follow-up sputum smears to predict outcome. Pathog Glob Health. 2013;107:5–10.
9 van't Hoog AH, Laserson KF, Githui WA, Meme HK, Agaya JA, Odeny LO, *et al.* High prevalence of pulmonary tuberculosis and inadequate case finding in rural western Kenya. Am J Respir Crit Care Med. 2011;183:1245–53.
10 Tobin EA, Okojie P-W, Isah E. Community knowledge and attitude to pulmonary tuberculosis in rural Edo state. Nigeria. Ann Afr Med. 2013;12:148–54.
11 Harries AD, Nyirenda TE, Godfrey-Faussett P, Salaniponi FM. Defining and assessing the maximum number of visits patients should make to a health facility to obtain a diagnosis of pulmonary tuberculosis. Int J Tuberc Lung Dis. 2003;7:953–8.
12 Finnie RK, Khoza LB, van den Borne B, Mabunda T, Abotchie P, Mullen PD. Factors associated with patient and health care system delay in diagnosis and treatment for TB in Sub-Saharan African countries with high burdens of TB and HIV. Trop Med Int Health. 2011;16:394–411.
13 Kayigamba FR, Bakker MI, Mugisha V, Gasana M, Schim van der Loeff MF. Sputum completion and conversion rates after intensive phase of tuberculosis treatment: an assessment of the Rwandan control program. BMC Res Notes. 2012;5:357.
14 Samo Gudo P, Cuna Z, Coelho E, Maungate S, Borroni E, Miotto P, *et al.* Is MDR-TB on the rise in Mozambique? Results of a national drug resistance survey. Eur Respir J. 2011;38:222–4.
15 Nunes EA, De Capitani EM, Coelho E, Joaquim OA, Figueiredo IR, Cossa AM, *et al.* Patterns of anti-tuberculosis drug resistance among HIV-infected patients in Maputo, Mozambique, 2002-2003. Int J Tuberc Lung Dis. 2005;9:494–500.
16 WHO. Report of the commission on macroeconomics and health. Macroeconomics and health: investing in health for economic development. Geneva: WHO; 2001.
17 Gaspar C. Estatísticas do Distrito de Ancuabe. Available from: http://www.ine.gov.mz/ResourceCenter/Default.aspx 2012.
18 Ali Abubacar A, Macurire Z, David L, Garcia Santanta J, Mario Mopola E, Jules Aime B. Relatorio da supervisão especifica dos programas de ITS/HIV/SIDA, PTV e TB. Direção Provincial de Saúde de Cabo Delgado. Pemba; 2012.
19 WHO. Global tuberculosis report 2013. 2013. Available from: http://www.who.int/tb/publications/global_report/en/.
20 WHO. The global plan to stop TB 2011-2015. Geneva: WHO; 2011.
21 Adams L, Bergstrom K, Bleed D, Colvin C, Eckert E. Compendium of indicators for monitoring and evaluating national tuberculosis programs. 2014. Available from: http://www.popline.org/node/239605.
22 Brouwer M, Samu Gudo P, Mage Simbe C, Perdigao P, . Are routine tuberculosis programme data suitable to report on antiretroviral therapy use of HIV-infected tuberculosis patients? BMC Res Notes. 2013;6:23.
23 Praygod G, Todd J, McDermid JM. Early childhood tuberculosis in northwestern Tanzania. Int J Tuberc lung Dis. 2012;16:1455–60.
24 Jenkins HE, Tolman AW, Yuen CM, Parr JB, Keshavjee S, Pérez-Vélez CM, *et al.* Incidence of multidrug-resistant tuberculosis disease in children: systematic review and global estimates. Lancet. 2014;383:1572–9.
25 Pérez-Porcuna TM, Ascaso C, Ogusku MM, Abellana R, Malheiro A, Quinco P, *et al.* Evaluation of new strategies for the diagnosis of tuberculosis among pediatric contacts of tuberculosis patients. Pediatr Infect Dis J. 2012;31:e141–6.
26 Cuevas LE, Petrucci R, Swaminathan S. Tuberculosis diagnostics for children in high-burden countries: what is available and what is needed. Paediatr Int Child Health. 2012;32(Suppl 2):S30–7.
27 Rhines AS. The role of sex differences in the prevalence and transmission of tuberculosis. Tuberculosis. 2013;93:104–7.
28 Cowan J, Michel C, Manhiça I, Monivo C, Saize D, Creswell J, *et al.* Lessons from the implementing rapid testing for tuberculosis in Mozambique. Bull World Health Organ. 2015;93:125–30.
29 Dirlikov E, Raviglione M, Scano F. Global tuberculosis control: toward the targets and beyond. Ann Intern Med. 2015;163:52–8.
30 Say L, Raine R. A systematic review of inequalities in the use of maternal health care in developing countries. Bull World Health Organ. 2007;85:812–9.
31 Hopewell PC, Pai M, Maher D, Uplekar M, Raviglione MC. International standards for tuberculosis care. Lancet Infect Dis. 2006;6:710–25.
32 Suárez PG, Watt CJ, Alarcón E, Portocarrero J, Zavala D, Canales R, *et al.* The dynamics of tuberculosis in response to 10 years of intensive control effort in Peru. J Infect Dis. 2001;184:473–8.
33 Volmink J, Garner P. Directly observed therapy for treating tuberculosis. Cochrane Database Syst Rev. 2007;4:3–34. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003343.pub3/abstract/.
34 WHO. Global strategy and targets for tuberculosis prevention, care and control after 2015. Geneva: WHO; 2015.
35 WHO. Guidance for national tuberculosis programmes on the management of tuberculosis in children. 2014. Available from: http://www.who.int/tb/publications/childtb_guidelines/en/.