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Effectiveness of community-based DOTS strategy on tuberculosis treatment success rates in Namibia

D. Kibuule,* T. W. Rennie,* N. Ruswa,† F. Mavhunga,† A. Thomas,† R. Amutenya,† M. R. Law,‡ G. Günther,§ E. Ette,¶ B. Godman,# R. K. Verbeeck*

*School of Pharmacy, Faculty of Health Sciences, Ministry of Health and Social Services (MOHSS), University of Namibia, Windhoek, †National Tuberculosis and Leprosy Programme, Ministry of Health and Social Services, Windhoek, Namibia; ‡Centre for Health Services and Policy Research, School of Population and Public Health, University of British Columbia, Vancouver, British Columbia, Canada; §Tuberculosis Clinic, Katutura Intermediate Hospital, MOHSS, Windhoek, Namibia; ¶Anoixis Corporation, Natick, Massachusetts, USA; #Department of Laboratory Medicine, Division of Clinical Pharmacology, Karolinska Institutet, Karolinska University Hospital Huddinge, Stockholm, Sweden

SUMMARY

SETTING: DOTS is a key pillar of the global strategy to end tuberculosis (TB).

OBJECTIVE: To assess the effectiveness of community-based compared with facility-based DOTS on TB treatment success rates in Namibia.

METHODS: Annual TB treatment success, cure, completion and case notification rates were compared between 1996 and 2015 using interrupted time series analysis. The intervention was the upgrading by the Namibian government of the TB treatment strategy from facility-based to community-based DOTS in 2005.

RESULTS: The mean annual treatment success rate during the pre-intervention period was 58.9% (range 46–66) and increased significantly to 81.3% (range 69–87) during the post-intervention period. Before the intervention, there was a non-significant increase (0.3%/year) in the annual treatment success rate. After the intervention, the annual treatment success rate increased abruptly by 12.9% ($P < 0.001$) and continued to increase by 1.1%/year thereafter. The treatment success rate seemed to have stagnated at ~85% at the end of the observation period.

CONCLUSION: Expanding facility-based DOTS to community-based DOTS increased annual treatment success rates significantly. However, the treatment success rate at the end of the observation period had stagnated below the targeted 95% success rate.

KEY WORDS: TB treatment outcome; population-based; policy analysis

TUBERCULOSIS (TB) REMAINS a significant health problem in many low- and middle-income countries. In 2015, there were 10.4 million cases of TB worldwide, leading to an estimated 1.8 million fatalities.[1] The disease is particularly prevalent in sub-Saharan African countries such as Namibia, where the case notification rate (CNR; i.e., the number of new and relapse TB cases notified in one year) was 489 cases per 100 000 population in 2015.[2] A major strategy to reduce TB incidence has been DOTS, which was implemented in Namibia in 1995. Directly observed treatment (DOT), i.e., standardised anti-tuberculosis drug regimens administered to patients under direct observation, remains a critical strategic goal of DOTS implementation in Namibia.[3,4]

TB case identification and optimisation of treatment outcomes through DOTS are the key global strategies to 'end TB' in Namibia by 2035.[1,4] Unsuccessful treatment outcomes however, are important risk factors for the development of drug-resistant TB, a condition that is extremely difficult and expensive to treat.[5–9] In the past decade, community-based DOTS has improved treatment outcomes in Namibia and worldwide.[9,10] Nevertheless, Namibia, an upper-middle-income country in southern Africa with a population of 2.2 million, remains one of the countries with the highest TB incidence in the world.[1,2,10]

Facility-based DOTS (FB-DOTS) was thus scaled-up to all public health facilities in Namibia between 1991 and 1995 as a strategy to control TB and improve treatment outcomes.[10,11] In Namibia, FB-DOTS refers to the availability of DOT and related services only at health facilities (pre-2005); CB-DOTS refers to the extension of DOTS services extended to villages and households through community-based health workers.

Correspondence to: Dan Kibuule, Department of Pharmacy Practice and Policy, School of Pharmacy, University of Namibia, Private Bag 13301, Pionierspark, Windhoek, Namibia. e-mail: dkibuule@unam.na
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Assessment of the FB-DOTS strategy in Namibia in 2002 showed that, since its introduction in 1991–1995, TB incidence rates had not declined and the treatment success rate (TSR; i.e., the proportion of cures or treatment completions in a given year) was at its lowest in 2004.[10] FB-DOTS was therefore scaled-up to CB-DOTS under the first national TB and Leprosy Medium-Term Plan I (MTP-I) implemented from 2004 to 2009.[12] Access to high-quality CB-DOTS was further expanded to all regions, public and private workplaces, and integrated with community-based human immunodeficiency virus (HIV) care. This was enhanced, with improved quality of bacteriological assessments and standardisation of DOTS services such as treatment and DOT support, among others, under MTP-II (2010–2016) to empower DOT supporters in each community to deliver quality DOT services.[13,14] TSR targets under MTP-I and MTP-II were respectively 85% and 90%.[12,13]

With implementation of MTP-I in 2004, an electronic TB database was started to closely monitor treatment outcomes. The objective of the present study was to compare the annual rates of treatment success, cure and treatment completion before (1996–2004) and after (2005–2015) MTP implementation to assess the effectiveness of CB-DOTS and to improve TB treatment outcomes.

METHODS

Data collection

Quantitative population-level data on annual TB rates of treatment success, cure (i.e., the proportion of pulmonary TB cases [PTB; TB with lung parenchymal involvement] with bacteriologically confirmed TB at the start of treatment whose sputum was smear- or culture-negative in the last month of treatment), treatment completion (i.e., the proportion of TB cases in a given year who completed anti-tuberculosis treatment without bacteriological evidence of success) and case notification for all cases of TB registered from 1995 to 2015 were extracted from the annual reports of the National Tuberculosis and Leprosy Programme (NTLP) of the Namibia's Ministry of Health and Social Services (MOHSS).[11] In Namibia, treatment success for extra-pulmonary TB (EPTB; i.e., TB disease at sites other than lung parenchyma) is reported as the proportion of patients with or without aspirate bacteriological or cytology/histology results who are clinically well after completion of 6–8 months of treatment.[11] The National Institute of Pathology, Windhoek, Namibia, an accredited laboratory, performs all bacteriological testing for TB cases at all DOTS sites in Namibia. A 'cured' case is confirmed by a medical officer base on TB guidelines, which are implemented at all DOT sites with supported training. These annual rates are based on aggregates of quarterly reports collated from district and regional TB case registers. The annual rates were validated against the World Health Organization (WHO) Analytical Country Summaries for TB, as well as the data reported by the World Bank, United States Agency of International Development (USAID) and the Global Fund.[1] Twenty validated annual TSR, and CNR from 1995/1996 to 2014/2015 for PTB, EPTB, drug-susceptible TB (DS-TB) and drug-resistant TB (DR-TB) cases were included in the study. Annual rates reported before 1995 were excluded because there was no systematic reporting on TB outcomes before establishment of the NTLP in 1991.[10,11]

During the study period, case definitions for 'cure' and 'treatment completion' did not change; DOTS services were provided free of cost and treatment support as the only incentive during CB-DOTS.

Statistical analysis

An interrupted time series (ITS) analysis was conducted to establish the underlying trend in TB treatment success, cure and completion rates for all TB cases from 1996 to 2015. The effect of implementation of a countrywide CB-DOTS in Namibia in 2005 (the intervention and the treatment success, cure and completion rates) was also assessed using ITS.[15] The ITS analysis is explained in more detail in the Appendix 'Segmented regression model for treatment success, cure and completion rate'. Comprehensive description of implementation of FB-DOTS in Namibia and scale-up to CB-DOTS under the first and second National TB and Leprosy MTP-I and MTP-II can be found in the Appendix 'Facility-based and community-based DOTS in Namibia'.*

Ethics

Data reported in public documents by the health authorities of Namibia were used as the primary source to assess the effectiveness of an intervention at the population level. Ethical approval for the study was obtained from the human ethics committees of the MOHSS, and the University of Namibia, both in Windhoek, Nambia.

RESULTS

The annual number of case notifications by TB category and the TSR, CNR and population covariates from 1996 to 2015 are shown in respectively Figures 1 and 2. The mean (± SD) TSR during the pre-intervention period was 58.9 ± 6.9%, but varied considerably from year to year (range 46–66) (Figure 2). After the implementation of CB-DOTS in 2005, a slow but steady increase in the annual TSR was

* The appendix is available in the online version of this article, at http://www.ingentaconnect.com/content/iuatld/ijtld/2019/00000023/00000004/art000 .....

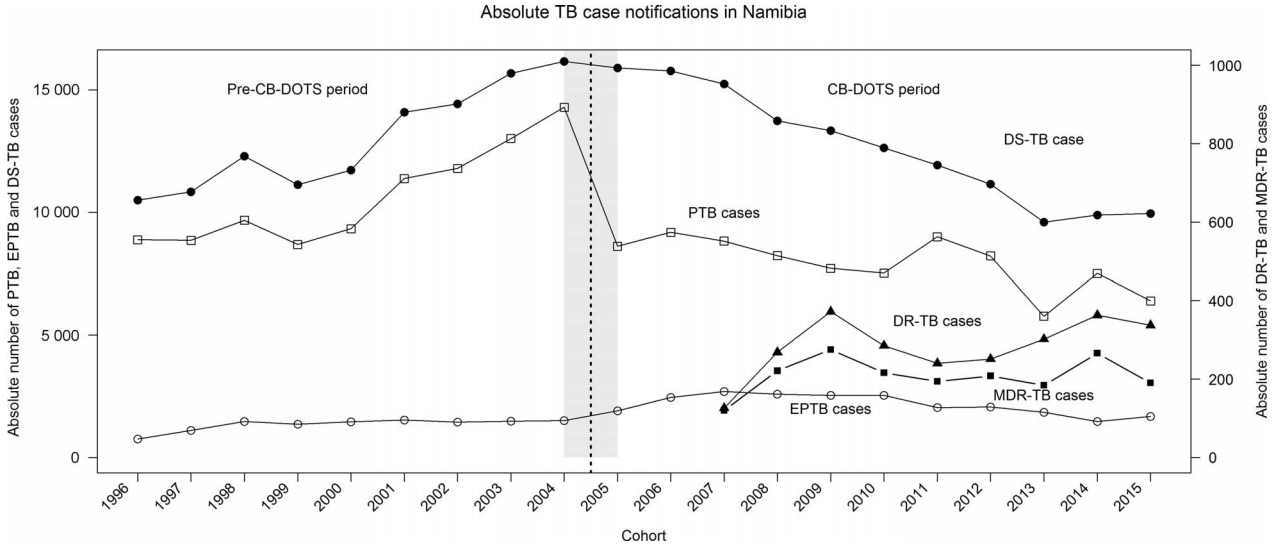

Figure 1 Absolute TB case notifications in Namibia, 1996–2015. ● = DST-TB; ▲ = DR-TB; ■ = MDR-TB; □ = PTB; ○ = EPTB; PTB = pulmonary tuberculosis; EPTB = extra-pulmonary TB; DST-TB = drug-susceptible TB; CB-DOTS = community-based DOTS; DR-TB = drug-resistant TB; MDR-TB = multidrug-resistant TB.

observed: during MTP-I, this was on average 76.4 ± 4.8% and during MTP-II 85.3 ± 1.4% ($P < 0.001$). During the post-CB-DOTS implementation period, the mean annual TSR was significantly higher than during the pre-intervention period. After implementation of the CB-DOTS strategy, the CNR, which had been around 800 per 100 000 population just before the intervention, started to decline gradually to 436/100 000 in 2015. A significant inverse correlation ($r = -0.65$, $P = 0.001$) was found between the CNR and TSR.

The results of the final (i.e., after correction for autocorrelation) segmented regression model of the TSR, CNR, cure and treatment completion rates for all DS-TB cases are given in Table 1 and Figure 3A. The model estimated TSR at the beginning of the pre-intervention period (β_0) at 58.0% and the CNR at 596.7/100 000. During the pre-intervention period, the annual change in the TSR, CNR and cure rate (β_1) was positive, indicating an increase in trend, which was statistically significant for only the cure rate ($P = 0.0172$). The treatment completion rate during the pre-intervention period showed a slight, non-significant decrease. Conversely, during the pre-intervention period, the CNR increased significantly by 23.9/100 000 cases/year. After the intervention, treatment

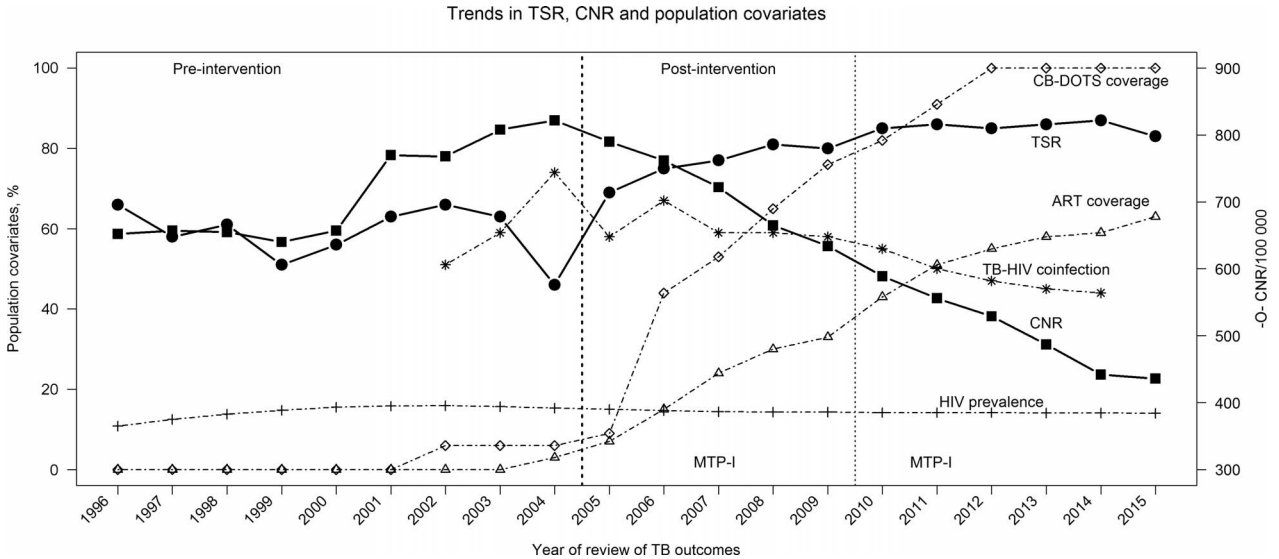

Figure 2 Trends in the TSR, CNR and population covariates, Namibia, 1996–2015. Data source: annual MOHSS National TB and Leprosy reports, Global TB reports and WHO TB database.[1,2] ○ = CNR), ◇ = CB-DOTS coverage; + = adult HIV prevalence; △ = ART coverage; ✶ = HIV prevalence among TB patients; ● = TSR; TSR = treatment success rate; CNR = case notification rate; CB-DOTS = community-based DOTS; ART = antiretroviral therapy; TB = tuberculosis; HIV = human immunodeficiency virus; MTP = medium-term plan; MOHSS = Ministry of Health and Social Services; WHO = World Health Organization.

Table 1 Estimated coefficients for the interrupted time series analysis of the TSR, cure rate, treatment completion rate and CNR*

	Pre-intervention level (β_0)		Pre-intervention trend (β_1)		Post-intervention level change (β_2)		Post-intervention trend change (β_3)	
	Estimated % (95%CI)	P value	Estimated % (95%CI)	P value	Estimated % (95%CI)	P value	Estimated % (95%CI)	P value
PTB								
All PTB cases								
TSR	62.1 (59.4 to 64.9)	<0.001	0.9 (0.3 to 1.3)	0.003	5.6 (2.2 to 8.9)	0.003	0.2 (−0.4 to 0.8)	NS
Cure rate	26.1 (19.8 to 32.3)	<0.001	0.95 (−0.2 to 2.1)	NS	7.7 (−0.01 to 15.32)	NS	0.8 (−0.6 to 2.2)	NS
Completion rate	36.0 (31.1 to 41.0)	<0.001	−0.2 (−1.04 to 0.72)	NS	−2.4 (−8.5 to 3.7)	NS	−0.6 (−1.7 to 0.5)	NS
New smear-positive PTB cases								
TSR	64.8 (61.8 to 67.8)	<0.001	0.5 (−0.004 to 1.070)	NS	7.1 (3.4 to 10.8	0.002	0.6 (−0.1 to 1.2)	NS
Cure rate	44.2 (37.1. 51.5)	<0.001	0.9 (−0.4 to 2.1)	NS	12.1 (3.2 to 21)	0.017	0.3 (−1.3 to 1.9)	NS
Completion rate	20.5 (15.6 to 25.5)	<0.001	−0.3 (−1.2 to 0.6)	NS	−5.4 (−11.4 to 0.7)	NS	0.2 (−0.9 to 1.3)	NS
Retreatment (smear-positive) PTB cases								
TSR	63.3 (58.8 to 67.8)	<0.001	−0.5 (−2.6 to 1.5)	NS	2.5 (−2.9 to 8.0)	NS	2.2 (1.2 to 3.1)	<0.001
Cure rate	41.5 (30.0 to 53.0)	<0.001	−0.04 (−1.9 to 1.8)	NS	0.1 (−13.9 to 14.3)	NS	3.4 (0.9 to 5.9)	0.018
Completion rate	22.0 (11.5 to 32.4)	<0.001	1.6 (0.9 to 2.3)	NS	2.4 (−10.5 to 15.2)	NS	−0.9 (−3.2 to 1.4)	NS
Smear-negative patients PTB cases								
Completion rate	57.7 (53.7 to 61.7)	<0.001	1.6 (0.9 to 2.3)	<0.001	6.1 (1.2 to 11.0)	0.028	−1.1 (−2.0 to −2)	0.024
Extra-pulmonary TB cases								
Completion rate	61.3 (55.5 to 66.8)	<0.001	0.1 (−0.8 to 1.1)	NS	10.4 (3.7 to 17.1)	0.008	1.3 (0.1 to 2.6)	0.044
Drug-susceptible TB cases†								
TSR	58 (53.6 to 62.9)	<0.001	0.3 (−0.7 to 1.2)	NS	12.9 (6.8 to 18.9)	<0.001	1.1 (0.1 to 2.1)	0.046
Cure rate	37.2 (34.1 to 40.4)	<0.001	0.9 (0.2 to 1.5)	0.017	−18.6 (−22.5 to −14.7)	<0.001	1.0 (0.2 to 1.7)	0.020
Completion rate	17.8 (15.5 to 20.1)	<0.001	−0.06 (−0.5 to 0.4)	NS	24.3 (21.6 to 27)	<0.001	0.05 (−0.5 to 0.6)	NS
MDR-TB cases								
TSR			NA‡		−21.3 (−52.9 to 10.4)	NS	4.9 (3.0 to 6.9)	<0.001
CNR, /100 000	596.7 (553.1 to 640.3)	<0.001	23.9 (16.4 to 31.5)	<0.001	10.1 (−39.1 to 59.2)	NS	−60.6 (−70.6 to −50.7)	<0.001

* Durbin-Watson statistic for TSR data = 2.9 (lag = 3, $P = 0.034$); Durbin-Watson statistic for CNR data = 1.3 (lag = 1, $P = 0.012$).
† β_w (impact of the wild point in 2004, i.e., unexplained low treatment success rate): TSR, −13.6 (–21 to –6.4), $P = 0.002$; cure rate, 27.4 (–36 to –20.1), $P < 0.001$; and treatment completion rate, 12.0 (6.5 to 17.5), $P < 0.001$.
‡ No data on MDR-TB in the pre-intervention period to make comparisons.
TSR = treatment success rate; CNR = case notification rate; CI = confidence interval; PTB = pulmonary tuberculosis; NS = not significant; MDR-TB = multidrug-resistant TB; NA = not applicable.

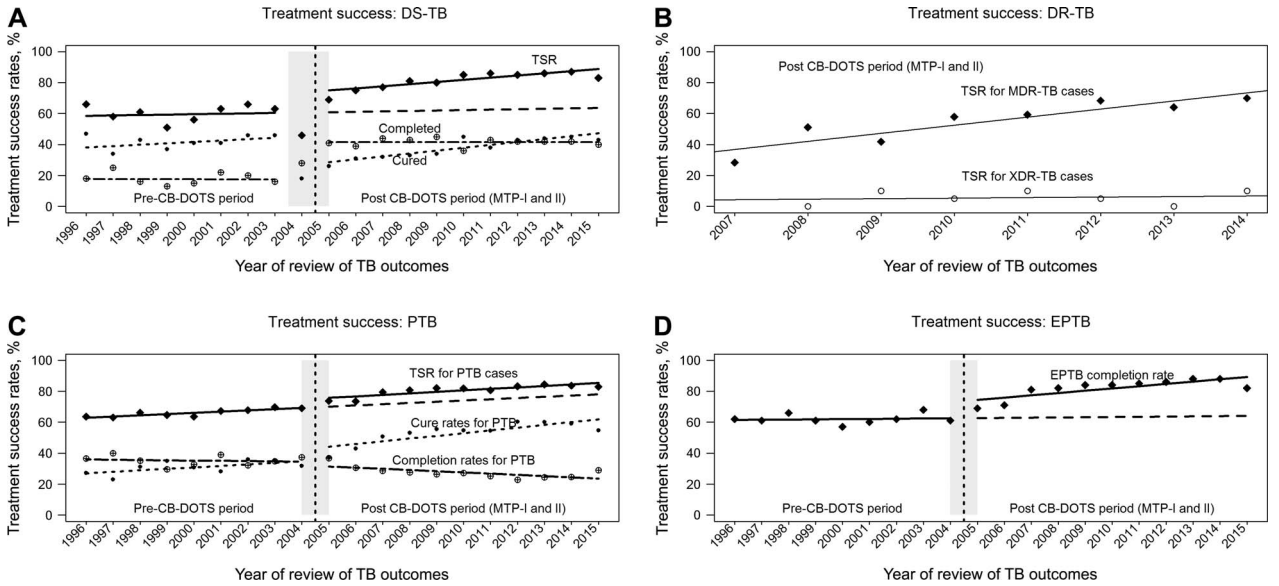

Figure 3 Interrupted time series analysis of the annual TSR (black square), cure rate (black circle) and treatment completion rate (diamond with dot). **A)** Treatment success in DS-TB cases; **B)** treatment success in drug-resistant TB cases; **C)** treatment success in PTB cases; **D)** treatment success in EPTB cases. The predicted pre- and post-intervention trends, based on the final segmented regression model, are shown by the lines. DS-TB = drug-susceptible tuberculosis; TSR = treatment success rate; CB-DOTS = community-based DOTS; DR-TB = drug-resistant TB; MTP = medium-term plan; MDR-TB = multidrug-resistant TB; XDR-TB = extensively drug-resistant TB; PTB = pulmonary TB; EPTB = extra-pulmonary TB.

success and treatment completion rates (β_2) increased abruptly and significantly ($P < 0.001$) by respectively 12.9% and 24.3% from the estimated level at the end of the pre-intervention period (e.g., the TSR increased from 60.9% to 68.0%; Figure 3A). In contrast, the cure rate dropped abruptly after the CB-DOTS intervention by 18.6% ($P < 0.001$). The immediate post-intervention change in the CNR was not statistically significant (Table 1). After the intervention, the trend in the annual TSR, cure and completion rates (β_3) increased; however, this was only statistically significant for the TSR and cure rate. The post-intervention trend in the CNR decreased significantly 60.6/100 000 notifications per year. The wild point (i.e., unexpected and unexplained drop in the TSR) at 2004 was associated with a significant drop in treatment success and cure rates ($P < 0.001$), but not treatment completion rate (Figure 3A).

After the intervention, there was a significant ($P < 0.005$) immediate increase in level and/or annual rates for treatment outcomes for pulmonary vs. extra-pulmonary (Figure 3C and 3D, Table 1) and DST-TB vs. DR-TB (Figure 3A and 3B, Table 1) and the different classes of PTB categories (new smear-positive, retreatment and smear-negative cases; Table 1, Figure 4A–D).

Table 2 shows the impact of population covariates on TSR, cure and completion rates. During the post-intervention period, the increased national CB-DOTS and/or antiretroviral therapy (ART) coverage significantly increased the TSR for all TB cases (Table 2). The impact of time-varying covariates on treatment, cure and treatment completion rates for all TB cases was more significant with increased CB-DOTS and ART coverage (Table 2). HIV prevalence significantly reduced TSR, cure and completion rates among cases with DST-TB by respectively 4.4%, 3.0% and 2.9%. The declining CNR had virtually no impact on treatment outcomes, but marginally increased the treatment completion rates among PTB and DST-TB.

After the intervention, the annual TSR seemed to increase non-linearly and tended towards a maximum, which was estimated at 92.4% (95% confidence interval [CI] 87.7–97.1; r^2 0.961) of current interventions (Appendix 'Prediction of the maximum possible treatment success rate under community-based DOTS', Figure 5). However, the approach to this estimated maximum treatment rate is very slow, with a 90% TSR estimated to be reached in 2025.

DISCUSSION

As recommended by the WHO, DOT is used in many countries to deliver anti-tuberculosis treatment.[3,4,6] The effectiveness of CB-DOTS vs. FB-DOTS (or clinic DOTS) has not been systematically assessed to date. Wright et al. carried out a review and meta-analysis of eight studies before 2015 to compare treatment outcomes under CB-DOTS vs. FB-DOTS.[9] They concluded that CB-DOTS had a higher TSR, with a pooled odds ratio of 1.54 (95%CI 1.01–2.36, $P = 0.046$). FB-DOTS was introduced in Namibia in 1991 and was universally accessible at all public health facilities in 1996; it was later expanded in

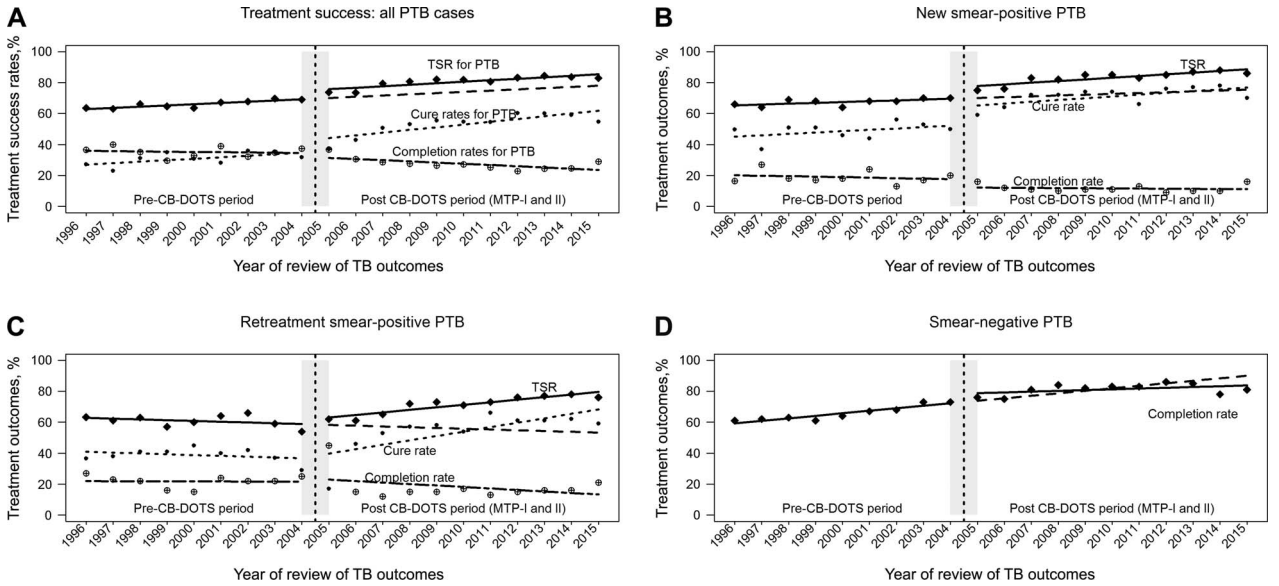

Figure 4 Interrupted time series analysis of the annual treatment success rates (black diamond), cure rates (black circle) and treatment completion rates (diamond with dot) by PTB categories (new smear-positive PTB cases, retreatment PTB cases and smear-negative PTB patients). The predicted pre- and post-intervention trends based on the final segmented regression model are shown by the lines. **A)** Treatment success in all PTB cases; **B)** treatment success in new smear-positive PTB cases; **C)** treatment success in retreatment smear-positive PTB cases; **D)** treatment success smear-negative PTB cases. TSR = treatment success rate; PTB = pulmonary TB; CB-DOTS = community-based DOTS; MTP = medium-term plan; TB = tuberculosis.

2005 to CB-DOTS. Before the implementation of CB-DOTS, the annual TSR in Namibia was ~60% but showed high variability from year to year (range 46–66). During the same period, the CNR slowly increased from 652 to 822/100 000, which is among the highest in the world.[2] The first year after the introduction of CB-DOTS, the TSR and completion rate, but not the cure rate, showed a significant increase compared with the pre-intervention success rate. A review of MTP-I in 2010 attributed the suboptimal cure rates to the persistence of inadequate access to quality TB diagnostic services and direct observation of anti-tuberculosis treatment due to the geographic vastness of the country (second lowest population density in the world), which impeded not only patient-level CB-DOTS coverage but also the quality and turnaround time of TB direct microscopy results in remote areas and among highly mobile populations.[12] Introduction of the electronic TB database in 2005 as a component of CB-DOTS may have increased reporting of treatment outcomes, which may explain the abrupt rise in the TSR between 2004 and 2005. During the post-intervention period, TSRs continuously increased by 1.1%/year from 69% in 2005 to 88% at the end of 2015.

Time-varying covariates such as CB-DOTS coverage, HIV prevalence and ART coverage only marginally affected TB treatment outcome rates for all TB cases. However, the effect of other potentially important covariates, such as the quality and availability of anti-tuberculosis medicines and drug resistance patterns, could not be tested due to the lack of appropriate data. Not surprisingly, improvement in the TSR after implementation of CB-DOTS, alongside other MTP interventions, was accompanied by a gradual decrease in the CNR from 822/100 000 at the end of the pre-intervention period to 436/100 000 one decade later. This decrease in the annual CNR was inversely correlated to the TSR (r^2 0.46, $P = 0.0011$) and other factors, such as improved programmatic detection of new TB cases and preventative control measures through community-based TB care as well as the improved access to quality DOTS services nationwide. However, improvement of the treatment outcome rates following the expansion of FB-DOTS to CB-DOTS falls short of the targets set by the NTLP/MOHSS under MTP-I and MTP-II. TSR targets under MTP-I and MTP-II were respectively 85% and 90%. Although the MTP-I programme target was met, at the end of 2015 the treatment rate had seemingly stagnated around ~85%, which falls short of the MTP-II target of 95%. Even if the success rate had continued to increase during that final year at the projected 1.1%/year, the 90% target would still not have been reached. Moreover, the success rate data were clearly levelling off towards the end of the MTP-II programme. Based on the data, it would still take several decades to reach the predicted theoretical maximum success rate of ~92%.

It is clear that the CB-DOTS strategy alone will not be able to 'end TB'. Other factors, which cannot be controlled by CB-DOTS, must be used to explain why the TSRs are stagnating at ~90%. Similar

Table 2 Impact of population time-varying covariates on the TSR, cure, treatment completion and CNR

	CNR /100 000		National adult HIV prevalence %		CB-DOTS coverage (% districts)		National ART coverage (% districts)	
Population covariate	Estimated* % (95%CI)	P value	Estimated* % (95%CI)	P value	Estimated* % (95%CI)	P value	Estimated* % (95%CI)	P value
PTB								
All PTB cases								
TSR	0.1 (−0.3 to 0.5)	NS	−0.7 (−2.1 to 0.7)	NS	0.1 (0.02 to 0.2)	0.015	0.3 (−0.02 to 0.6)	NS
Cure rate	−0.7 (−1.5 to 0.1)	NS	0.6 (−2.7 to 3.9)	NS	0.3 (0.2 to 0.5)	0.001	0.7 (0.05 to 1.39)	0.037
Completion rate	0.8 (0.3 to 1.4)	0.007	−1.3 (−3.8 to 1.3)	NS	−0.2 (−0.4 to −0.08)	0.006	−0.52 (−1.1 to 0.03)	NS
New smear-positive PTB cases								
TSR	0.02 (−0.4 to 0.5)	NS	−0.7 (−2.4 to 1.0)	NS	0.12 (0.001 to 0.23)	0.047	0.24 (−0.15 to 0.63)	NS
Cure rate	−0.4 (−1.5 to 0 to 7)	NS	−0.8 (−4.9 to 3.2)	NS	0.3 (−0.08 to 0.54)	NS	0.37 (−0.59 to 1.3)	NS
Completion rate	0.4 (−0.3 to 1.2)	NS	0.1 (−2.6 to 3.0)	NS	−0.2 (−0.36 to 0.02)	NS	−0.30 (−0.94 to 0.35)	NS
Retreatment (smear-positive) PTB cases								
TSR	0.15 (−0.5 to 0.8)	NS	0.8 (−1.7 to 3.3)	NS	0.11 (−0.07 to 0.29)	0.204	0.17 (−0.42 to 0.76)	NS
Cure rate	−0.95 (−2.6 to 0.7)	NS	2.5 (−4.0 to 8.9)	NS	0.7 (0.45 to 1.02)	<0.001	1.52 (0.21 to 2.83)	0.026
Completion rate	1.1 (−0.3 to 2.6)	NS	−1.8 (−7.7 to 4.1)	NS	−0.6 (−0.9 to −0.4)	<0.001	−1.25 (−2.49 to −0.01)	0.048
Smear-negative patients PTB cases								
Completion rate	0.25 (−0.4 to 0.8)	NS	−1.8 (−3.4 to 0.3)	NS	0.2 (0.06 to 0.33)	0.007	0.7 (0.3 to 1.1)	0.001
Extra-pulmonary TB cases								
Completion rate	0.04 (−0.8 to 0.9)	NS	−1.5 (−4.5 to 1.5)	NS	0.3 (0.1 to 0.5)	0.004	0.72 (0.09 to 1.35)	0.026
Drug-susceptible TB cases								
TSR	0.1 (−0.001 to 0.1)	NS	−4.4 (−7.7 to −1.1)	0.021	0.5 (0.1 to 0.9)	0.032	0.8 (0.3 to 1.2)	0.004
Cure rate	0.04 (−0.02 to 0.09)	NS	−3.0 (−4.8 to 1.2)	0.005	0.5 (0.2 to 0.7)	0.003	0.5 (0.2 to 0.8)	0.003
Completion rate	0.1 (0.04 to 0.14)	0.001	−2.9 (−4.4 to −1.4)	0.002	0.1 (−0.2 to 0.4)	NS	0.05 (−0.3 to 0.4)	NS

* The impact, i.e., the percentage change that a covariate had on the treatment outcome after implementation of CB-DOTS in 2015.
TSR = treatment success rate; CNR = case notification rate; CI = confidence interval; HIV = human immunodeficiency virus; CB-DOTS = community-based DOTS; ART = antiretroviral therapy; PTB = pulmonary tuberculosis; NS = not significant.

studies in other countries have concluded that stagnation of TSRs below the 95% target may favour DR-TB, and modifications to the DOTS strategy have been recommended.[16–19] In low- to middle-income countries such as Namibia, the effectiveness of DOTS is compromised by false-negative smear results, the limited monitoring of bacteriological endpoints and the growing burden of DR-TB.[20–24] CB-DOTS should therefore be improved by implementing additional strategies to identify patients at risk of poor treatment outcomes to reach the WHO goal to 'end TB' by 2035. These additional community-based measures should focus on ways to improve treatment monitoring and outcomes in TB patients with comorbidities such as HIV infection and diabetes mellitus, in childhood TB, in malnourished patients and in other or mobile patient groups with an increased risk of treatment failure.[17,21,25–30] In addition, use of treatment completion as a surrogate measure of treatment success should be validated across all TB cases in the context of programmatic challenges. In addition, some communities/patients may require personalised rather than standardised DOTS approaches to optimise treatment outcomes.

In conclusion, the present study indicated that CB-DOTS is more effective than FB-DOTS in increasing TB TSR. In Namibia, the CB-DOTS strategy however was not, and will not be, able to reach the target of 95% success rate. Additional measures, such as bacteriologic monitoring among patients at risk of therapeutic failure, is critical to 'end TB' by 2035. We are currently exploiting the extensive electronic TB database of the NLTP/MOHSS to identify significant predictors of poor TB treatment outcome in Namibia.

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APPENDIX

Segmented regression model for treatment success, cure and completion rate

An interrupted time series analysis was carried out to assess the effectiveness of a community-based DOTS (CB-DOTS) strategy on the treatment success rate (TSR), case notification rate (CNR), cure and treatment completion rates in all cases. Interrupted time series analysis is a valuable study design for evaluating the effectiveness of population-level health interventions that have been implemented at a clearly defined point in time.[15] In this design, the pre-intervention regression level and trends in the outcome measures act as controls for the post-intervention segment.[15] The intervention was expansion of facility-based DOTS (FB-DOTS) to CB-DOTS in Namibia. The effective time for implementation of the CB-DOTS strategy was set at 2005, 1 year after implementation of medium-term plan I (MTP-I). This considered a 1-year phase-in period as a full cycle of completion of DOTS lasting 6–8 months for a patient with drug-susceptible TB and reporting of the TSR in the subsequent year. Outcome variables were the TSR (defined as the percentage of patients who were cured and completed DOT in the particular year under review), treatment completion rate and annual CNR.[11] The impact of CB-DOTS on TSR, cure and completion rates, and covariates such as human immunodeficiency virus (HIV) prevalence, CB-DOTS and antiretroviral therapy (ART) coverage, was determined by changes in the level (β_2) and trend (β_2) in the treatment outcome in the pre- and post-intervention period after 2005 by a segmented regression model using RStudio v 3.3.2 (RStudio, Boston, MA, USA), as detailed below.

The following segmented regression model was used to determine the level and trend changes in tuberculosis (TB) treatment success, cure and completion:

$$Y_t = \beta_0 + \beta_1 * T + \beta_2 * X_t + \beta_3 * T * X_t + \beta_w * T * X_t + e_t$$

Y_t is the outcome (i.e. TSR or CNR at time t), T the time (in years) that elapsed since the start of the study, X_t a dummy variable indicating the pre-intervention period (coded 0) or the post-intervention period (coded 1); β_0, the estimated baseline outcome at $T = 0$; β_1, estimated pre-intervention outcome trend (the change in outcome with time); β_2, estimated change in outcome immediately after the intervention, compared with the outcome at the end of the pre-intervention period; β_3, estimated change in the post-intervention outcome trend compared with the pre-intervention outcome trend; β_w, estimated impact of the wild point in 2004 (the unexpectedly low TSR and cure rate, or unexpectedly high completion rate, in 2004 relative to preceding years), which was excluded from the final model; and e_t, random variability not explained by the model. The TSR in 2004 was modelled as a wild point because there was an abrupt drop in the TSR in that year relative to the preceding years (1996–2004). This unexpected drop in the TSR may have been due to the transition from the FB-DOTS to the CB-DOTS policy, the high incidence of TB and HIV in that year, as well as programmatic problems caused by the move to fixed-dose combination (FDC) anti-tuberculosis medicines. The impact of population time-varying covariates such as TB incidence, HIV prevalence and ART coverage on the TSR and/or CNR were modelled individually as $\beta_i * T * X_i$, alongside the Y_t parameters. Adjustment for serial autocorrelation was carried out using the Durbin-Watson statistic and an autocorrelation parameter was included in the segmented regression model.

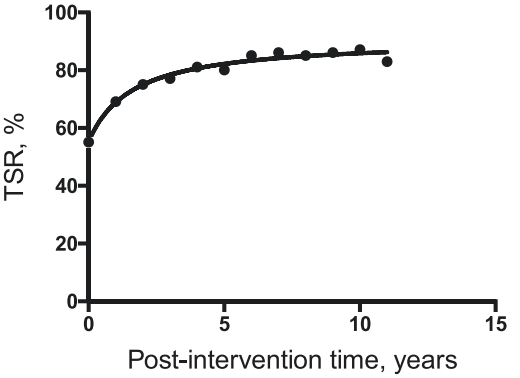

Figure A The maximum effect model fitted the post-intervention TSRs very well ($r^2 = 0.961$) with a predicted maximum TSR of 92.4%. TSR = treatment success rate.

Facility-based and community-based DOTS in Namibia

Namibia achieved countrywide DOTS coverage at all public health facilities—42 hospitals, 34 health centres and 244 clinics—by 1996.[12] Nonetheless, geographic access to DOT was limited because many patients live too far from clinics (up to 50 km) to come for daily clinic DOT; this led to inadequate tracing of treatment interrupters. There was hardly any provision for CB-DOT.[12] Furthermore, the high pill burden (9–12 tablets/day) of first-line, single-drug DOT formulations compromised the adherence to treatment and effectiveness of medications, particularly among patients on co-medication for TB and HIV. Moreover, sputum smear examination services were insufficient at hospitals (long distances between the 30 laboratories and hospitals, irregular specimen collection and smear result turnaround time beyond 48 h) and unavailable in health centres and clinics. This negatively impacted the utility of sputum smear microscopy for diagnosis and treatment follow-up. In 2004, Namibia reported the emergence of drug-

resistant TB (DR-TB), the lowest TSR and highest CNR for TB.[12]

The CB-DOTS strategy, which was designed to mitigate the persistently high CNR and low TSR despite the countrywide implementation of FB-DOTS between 1995 and 2004, and which was effectively implemented in Namibia in March 2005 under MTP-I (2004–2009) and MTP-II (2010–2015) for TB and leprosy constituted 'the intervention' in the interrupted time series analysis. The strategic goal of CB-DOTS was to improve TB diagnosis, cure and treatment completion through universal access at geographic and patient levels to high-quality community-based TB care. In particular, CB-DOTS aimed to increase the TSR for all patient categories from 65% to 85% by 2009 and to 90% by 2015. To achieve these goals, the CB-DOTS implementation framework designated the National Tuberculosis and Leprosy Programme (NTLP) and health districts ($n = 34$), as the coordination and implementing units, to work in partnership with up to 14 community-based organisations (CBOs) implementing TB or HIV care. The budget for implementing CB-DOTS was funded by the Government of the Republic of Namibia (51%), the Global Fund (19%) and US Agency for International Development (3%), among others through subgrants to the CBOs. This framework also paved the way for the introduction of FDC drugs for first-line anti-tuberculosis treatment, CB-DOTS training manual and national course, adoption of the World Health Organization guidelines for TB treatment for supporters and universal access to high-quality, low-cost DOT regimens; revised TB guidelines to improve case management and community-based DOT cards to track treatment outcomes were introduced.[10,12] By 2015, CB-DOTS coverage had scaled-up one pilot region (Omaheke in 2004) to 12 regions and 27 districts during MTP-I and to all 14 regions and 34 health districts during MTP-II; 529 community health workers (CHWs) (TB cases $\sim$ 1:25 or 529/13 147) were deployed. A team of community-based persons comprising CHWs (community DOT supervisors and facility and DOT nurses), DOT field promoters and community DOT supporters implement the CB-DOTS programme at each health district unit. The CBOs assist the district unit in early identification of TB cases and DOT provision in the community. DOT supporters such as family/relatives, workplace peers or CHWs directly observe the administration of the TB medication at community DOT points, at home and workplaces. For example, in the Omaheke region there were 954 DOT supporters, 858 supervisors and 1189 DOT providers in 2015. In addition, access to quality CB-DOTS services was expanded and scaled-up during MTP-II (2010–2015) to all 14 regions and 34/34 health districts, all 13 regional prisons, collaborative integration in all CBOs and sites implementing community-based HIV care, public-private workplace partnerships and mobile CB-DOT clinics. The quality of CB-DOTS was enhanced by scaling up quality-assured bacteriology laboratories from 30 (1 laboratory per 67 000 people) in 2004 to 36 out of 80 in 2015 to increase case detection, publishing a CB-DOTS training manual and implementing World Health Organization guidelines for TB treatment supporters to standardise treatment with supervision and patient support, creating a system for effective supply and management of anti-tuberculosis drugs as well as a monitoring and evaluation system for effective measurement.

Prediction of the maximum possible treatment success rate under community-based DOTS

To estimate the maximum TSR that could theoretically be expected based on the observed post-intervention TSRs, non-linear regression analysis was carried out using the following model predicting the maximum outcome as a function of time after the intervention:

$$TSR = A + \frac{TSR_{max} \cdot T}{T_{50} + T}$$

in which A is the TSR level during the intervention estimated by the segmented regression model, TSR_{max}, the maximum treatment effect rate, T_{50}, the time at which the outcome is 50% of TSR_{max}, and T, the time (in years) after the intervention. For all statistical tests, $P \leqslant 0.05$ was considered significant.

RÉSUMÉ

CONTEXTE : Le DOTS est un pilier de la stratégie mondiale visant à mettre fin à la tuberculose (TB).

OBJECTIF : Evaluer l'efficacité des DOTS basés en communauté comparée à celle des DOTS basés en structures de santé en termes de taux de succès du traitement de la TB en Namibie.

MÉTHODE : Les taux annuels de succès du traitement de la TB, de guérison, d'achèvement du traitement et de notification des cas ont été comparés entre 1996 et 2015 par analyse de série chronologique interrompue. L'intervention a consisté en extension par le gouvernement de Namibie de la stratégie de traitement de la TB par DOTS en communautés par rapport aux DOTS en structures de santé en 2005.

RÉSULTATS : Le taux de succès annuel du traitement pendant la période précédant l'intervention a été de 58,9% (fourchette 46–66) et a significativement augmenté à 81,3% (fourchette 69–87) pendant la période suivant l'intervention. Avant l'intervention, il y a eu une augmentation non significative (0,3%/an) du taux de succès annuel du traitement. Après l'intervention, le taux de succès annuel du traitement a augmenté brutalement de 12,9% ($P < 0{,}001$) et a continué à augmenter de 1,1%/an par la suite. Ce taux de succès semble avoir ensuite stagné autour de 85% à la fin de la période d'observation.

CONCLUSION : L'expansion des DOTS en structures de santé vers les DOTS en communauté a significativement augmenté le taux annuel de succès du traitement. Ce taux a cependant stagné à la fin de la période d'observation restant inférieur à l'objectif de 95% de succès.

RESUMEN

MARCO DE REFERENCIA: El esquema de DOTS es uno de los pilares esenciales de la estrategia mundial para poner fin a la tuberculosis (TB).

OBJETIVO: Evaluar la eficacia del DOTS comunitario comparado con el DOTS basado en un centro asistencial, en materia de tasas de éxito terapéutico en Namibia.

MÉTODOS: Se compararon las tasas anuales de éxito terapéutico, curación, compleción del tratamiento y de notificación de casos de 1996 al 2015, mediante un análisis de series temporales interrumpidas. La intervención consistió en el mejoramiento de la estrategia de tratamiento antituberculoso por parte del gobierno de Namibia, con el cambio del DOTS basado en los centros de atención por el DOTS comunitario en el 2005.

RESULTADOS: El promedio de la tasa anual de éxito terapéutico en el período anterior a la intervención fue 58,9% (entre 46% y 66%) y aumentó de manera significativa a 81,3% (entre 69% y 87%) durante el período posintervención. Antes de la intervención se observó un incremento no significativo de la tasa anual de éxito terapéutico (0,3% por año). Después de la intervención esta tasa aumentó súbitamente un 12,9% ($P < 0{,}001$) y en adelante, el aumento continuó con un ritmo de 1,1% por año. La tasa de éxito terapéutico se estacionó en 85% al final del período de observación.

CONCLUSIÓN: La ampliación del DOTS basado en los establecimientos hacia un DOTS comunitario aumentó las tasas anuales de éxito terapéutico. Sin embargo, al final del período de observación la progresión de este indicador se detuvo por debajo de la meta fijada de una tasa de éxito anual del 95%.