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Examining the cost of community-based tuberculosis treatment in South Africa

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SUMMARY

SETTING: While South Africa has improved access to tuberculosis (TB) treatment and care, the 2015 treatment success rate for multidrug-resistant TB (MDR-TB) remains low, at 55%. Community-based TB treatment and care improves patient retention compared to the standard of care alone.

OBJECTIVE: To assess the cost of a USAID-funded community-based TB model in Nelson Mandela Bay Health District (NMBHD), Eastern Cape Province, South Africa compared to the national standard of care alone.

DESIGN: We estimated the cost of community-based DR-TB treatment and adherence support compared to the standard of care alone.

RESULTS: Average overall costs were US$2827 lower per patient on the community-based model than the standard of care alone.

CONCLUSION: The per-patient cost of the community-based model is lower than the standard of care alone. Assuming the costs and effects of a community-based model implemented in NMBHD were observed at a larger scale, implementing the model could reduce overall health system costs.

KEY WORDS: drug-resistant TB; patient retention; cost; effects; South Africa

BASED ON INCIDENT CASES, South Africa is one of the top 20 high multidrug-resistant tuberculosis (MDR-TB) burden countries according to the World Health Organization (WHO).[1] Despite a "clear, consistent and sustained downward trend in TB case notifications" due to improved coverage of antiretroviral (ART) drugs, the country was estimated to have 322 000 incident TB cases (567 per 100 000 population) in 2017, of which 7336 cases were laboratory-confirmed MDR-TB.[1] While South Africa has demonstrated improvements in access to drug-resistant TB (DR-TB) treatment and care, in part by increasing the number of treatment sites from 17 in 2011 to 664 in 2016, the treatment success rate for MDR-TB remains low, at 55%.[1]

Effectiveness of community-based TB treatment and care in the Southern Africa region is well-documented through better treatment success, reduced time-to-treatment initiation and reduced time-to-conversion compared to traditional care models.[2–7] While these community-based models are effective, the costs of community-based models of care in South Africa have not been well-assessed among DR-TB patients, especially in the context of evolving treatment regimens, clinical guidance and patient management standards in the country.[8–10]

The US Agency for International Development (USAID) TB South Africa Project developed a novel model of community-based care which engages local non-governmental organisations (NGOs) and civil society organisations (CSOs) to deliver high-quality, person-centred DR-TB care. This paper examines the additional upfront cost associated with the community-based model of care and compares these costs to the standard of care.

STUDY POPULATION AND METHODS

Study population

The intervention group included 25 patients (56% male, 44% female) from Nelson Mandela Bay Health District (NMBHD) in Eastern Cape Province, South Africa, at least 15 years of age from the most recently available DR-TB cohort (2015) through the South African electronic DR-TB register (EDR.Web). While patients in the community-based intervention were managed by a single NGO, the NGO collaborates with patients at multiple facilities in the district based

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on caseloads and demand. These patients also received the standard of care, which includes a monthly visit to the DR-TB facility for medication pick up, ongoing sputum testing and general patient management. The comparison group included the remaining 404 DR-TB patients (60.6% male, 39.4% female) in the 2015 NMBHD DR-TB cohort available through EDR.Web who were at least 15 years of age. The sum of the intervention group and comparison group represents all DR-TB patients on treatment for the 2015 cohort who were at least 15 years of age.

Standard of DR-TB care in South Africa

Based on the most recently available TB management guidelines, diagnosis and early management of DR-TB in South Africa includes diagnosis using a rapid diagnostic tool (including Xpert® MTB/RIF; Cepheid, Sunnyvale, CA, USA).[10] New diagnoses are reported to the National Health Laboratory Service (NHLS) within 24 h of diagnosis and patients should start treatment within 5 days of initial diagnostic sputum collection.[10] Patients are diagnosed at a primary health care (PHC) facility after referral of diagnostic sputum sample to a laboratory for testing. Upon diagnosis, patients are referred to MDR-TB hospitals for treatment initiation and development of a patient management plan. Treatment continues at the PHC facility with monthly evaluation at the MDR-TB unit, although the number of visits patients make to the facility, use of DOT, frequency of medication pickup and other patient-side factors vary at the facility level. Ongoing monitoring for DR-TB patients includes adherence counselling and treatment support, education and patient motivation, psychosocial support, and early identification, management and reporting of adverse events.[10]

Community-based model

The community-based model links patients to treatment supporters for daily adherence support, side-effect reporting and subsequent referral to facilities, household contact tracing, and awareness building activities at the district level. Treatment supporters are managed through local NGOs and CSOs which also manage DR-TB nurses, data managers and project managers. NGOs are provided performance-based grants by the USAID TB South Africa Project and are paid monthly based on patient referral and patient support targets. NGOs work directly with multiple facilities to receive DR-TB patient referrals (after patients have been diagnosed at a PHC facility and referred to a treatment initiation site) for subsequent follow up and management.[10] Once referred to NGOs by the facility in which they initiated DR-TB treatment, patients are visited at their home by DR-TB treatment supporters daily. Treatment supporters report to DR-TB nurses at least weekly. A novel mHealth solution, ConnecTB, assists treatment supporters, DR-TB nurses and programme managers in assuring treatment adherence and side-effect monitoring among intervention patients.[11] Individualised treatment regimens for intervention patients are stored on the secure, cloud-based ConnecTB system for easy reference by DR-TB treatment supporters, who can then mark that medication has been taken, report any side effects and manage household contact tracing activities. This model is shown in Figure 1.

Estimating costs associated with TB care in South Africa

Costs were assessed from a health systems perspective, which does not consider wider household or economy-level impacts of TB. These costs and sources are given in Table 1. DR-TB treatment cost was the same in both groups and was estimated using a community-based clinic model in KwaZulu-Natal, South Africa by Loveday et al. This estimate was used in lieu of published cost data from Eastern Cape and was considered an acceptable proxy for the province given the resemblance between the care described in the Loveday et al. estimate and the treatment standard experienced by patients in Eastern Cape. Furthermore, the KwaZulu-Natal setting was considered an acceptable proxy for Eastern Cape as the TB incidence and other statistics in both provinces have been similar, especially in recent years.[12] The Loveday et al. estimate included monthly clinic visits, outpatient department (OPD) visits, tests and medications, and was considered similar to the standard described above.[2]

Other costs included the cost of death and the cost of loss to follow-up, both with subsequent death and subsequent survival (and onward transmission). The cost of death was taken from Pooran et al. and was based on the cost of removing a body from facility premises.[13] Loss to follow-up costs included DR-TB treatment, DR-TB hospitalisation and extensively drug-resistant TB (XDR-TB) treatment estimates. DR-TB treatment costs were estimated using Loveday et al. We added the cost of treating one DR-TB patient, assuming that a DR-TB patient who is lost to follow-up (LTFU) could spread DR-TB to up to 15 people, one of whom would acquire active TB disease (1-15-1 assumption).[2,13] Taking estimates from Gandhi et al. for MDR-TB and XDR-TB patients as an example of high prevalence of primary MDR-TB and XDR-TB transmission in KwaZulu-Natal, South Africa, the 1-15-1 assumption was used to describe higher lifetime probability of TB transmission among LTFU patients.[14–16] Assuming that 30% of LTFU patients would survive for some time without treatment, we estimated that half of these patients (i.e., 15% of all LTFU) would return to the health system and require hospitalisation. We added the cost

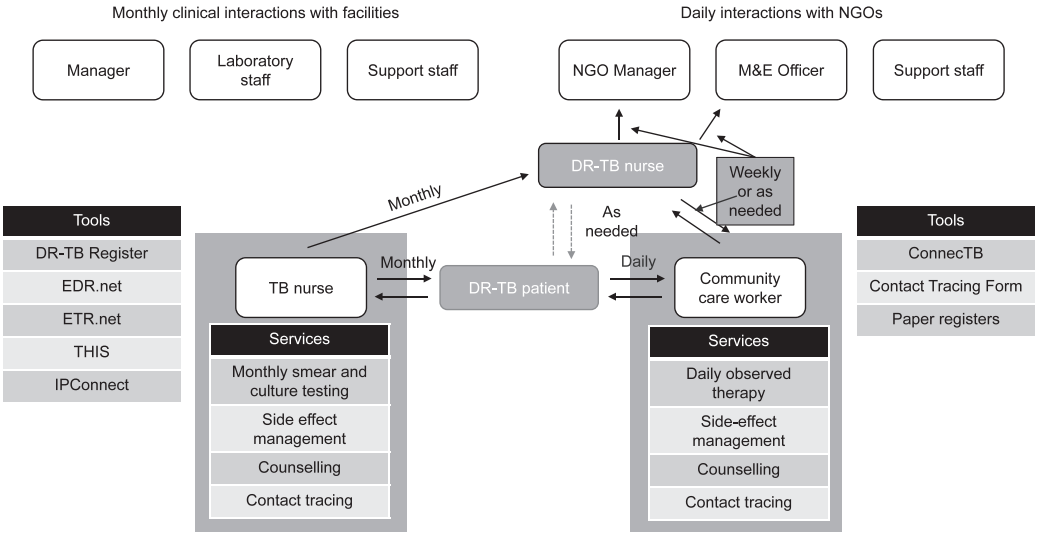

Figure 1 The TB South Africa Project NGO Model (DR-TB). NGO = non-governmental organisation; M&E = monitoring and evaluation; DR-TB = drug-resistant TB; TB = tuberculosis.

of treating 0.5 MDR-TB patients (under a decentralised MDR-TB treatment estimate from Loveday et al.).[2,17] Using estimates from Gandhi et al. suggesting that DR-TB patients previously exposed to anti-TB therapy are at 2.5 times greater odds of developing XDR-TB than the general population, we assumed that half of LTFU patients who survive (15% of all LTFU) would develop XDR-TB. We added the cost of treating 0.5 XDR-TB patients (using Pooran et al.'s inpatient XDR-TB treatment estimate) to the estimated cost of LTFU.[15] These estimates do not consider onward transmission of XDR-TB. Table 2 describes cost calculations per outcome.

Additional intervention costs included NGO management costs, which were represented by dividing the monthly grant payment by the number of daily visits in the month (the target on which payments are based), and ConnecTB costs.

Assessing the added value of the community-based model

Eight outcomes of interest were identified, as shown in Figure 2. Patients were categorised based on group (intervention or comparison). Patients were further categorised based on retention in care; either as LTFU or continued on follow-up (CFU). Finally, patients

Table 1 Additional costs under the community-based model (per patient)

	Cost US$	Source
Treatment and treatment-related costs		
MDR-TB clinic, community-based treatment	6 739	Loveday et al.
Additional treatment costs (only for forward transmission among LTFU)		
MDR-TB hospital-based treatment	19 484	Loveday et al.
XDR-TB treatment	26 392	Pooran et al.
Additional intervention costs		
NGO costs, total	918	TB South Africa Project
DOT visits	842	TB South Africa Project
ConnecTB costs: maintenance	4	TB South Africa Project
ConnecTB costs: airtime	48	TB South Africa Project
ConnecTB costs: tablets	24	TB South Africa Project
Health system costs		
Death	28	Pooran et al.
Loss to follow-up	29 677	Composite estimate: cost of DR-TB treatment + 0.5*MDR-TB hospitalisation + 0.5*XDR-TB hospitalisation

MDR-TB = multidrug-resistant tuberculosis; XDR-TB = extensively drug-resistant TB; NGO = non-governmental organisation; DOT = directly observed treatment.

Table 2 Total cost under the intervention and standard of care

	Conditional probability	Cost elements (US$)	Patients *n*	Cost US$
Intervention costs			25	214 437
LTFU	0.04			
Death (among LTFU)	0.70	ConnecTB cost ($918) + cost of death ($28) + Cost of DR-TB LTFU (DR treatment [$6 739] + 0.5*MDR hospitalisation [0.5*19 484] + 0.5*XDR hospitalisation [0.5*26 392])	0.7	21 436
Survival (among LTFU)	0.30*	ConnecTB cost ($918) + Cost of DR-TB LTFU (DR treatment [$6 739] + 0.5*MDR hospitalisation [0.5*19 484] + 0.5*XDR hospitalisation [0.5*26 392])	0.3	9 189
Receiving treatment (CFU)	0.96*			
Death (among CFU)	0.08	ConnecTB cost ($918) + cost of death ($28) + DR treatment ($6 739)	2	14 756
Survival (among CFU)	0.92*	ConnecTB cost ($918) + DR treatment ($6 739)	22	169 067
Standard of care costs			404	4 607 429
LTFU	0.20			
Death	0.70	Cost of death ($28) + cost of DR-TB LTFU (DR treatment [$6 739] + 0.5*MDR hospitalisation [0.5*19 484] + 0.5*XDR hospitalisation [0.5*26 392])	57	1 705 088
Survival	0.30*	Cost of DR-TB LTFU (DR treatment [$6 739] + 0.5*MDR hospitalisation [0.5*19 484] + 0.5*XDR hospitalisation [0.5*26 392])	25	730 054
Receiving treatment (CFU)	0.80*			
Death	0.25	Cost of death ($28) + DR treatment ($6 739)	82	555 561
Survival	0.75*	DR treatment ($6 739)	240	1 616 726

* Indicates that the field is calculated through the other values in the tree and is not a directly input estimate. Estimates for LTFU and death were used to derive estimates for CFU and survival, respectively, by subtracting these estimates from 1.
LTFU = loss of follow-up; DR-TB = drug-resistant tuberculosis; CFU = continued on follow-up; MDR-TB = multidrug-resistant TB; XDR-TB = extensively drug-resistant TB.

were categorised based on mortality: either death or survival. Actual values were used for LTFU, resultant CFU and death among those CFU in both the standard of care and the intervention. Literature estimates were used for death and survival proportions among those LTFU.[17] Conditional probabilities were then used to ascribe a theoretical number of patients to the eight outcomes.

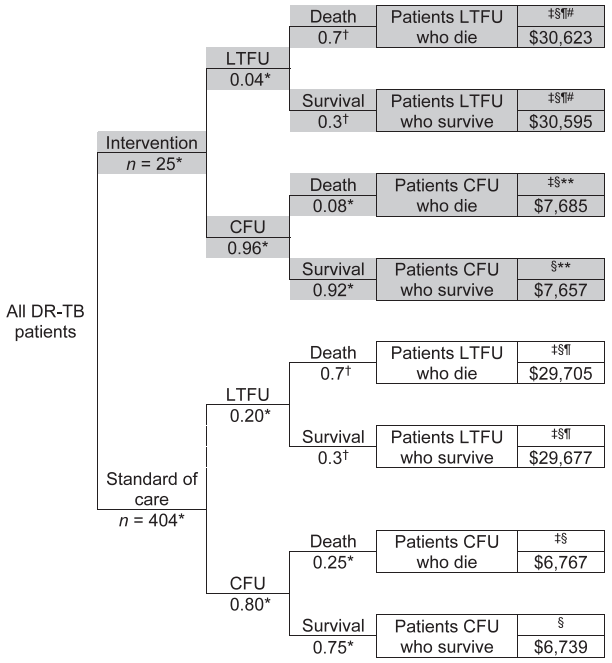

Figure 2 Model schematic with costs and effects. The following estimates are noted where used: *EDRWeb; †ERS; ‡Pooran; §Loveday; ¶Gandhi; #TB South Africa Project Whitebook. DR-TB = drug-resistant tuberculosis; LTFU = loss of follow-up; CFU = continued on follow-up.

As described in Table 2, the cost of each outcome was multiplied by the theoretical number of patients experiencing each outcome, and the sum of the total costs for each of the four outcomes per intervention (intervention group and standard of care) was taken. This sum was then divided by the total number of patients in the respective group to derive an average per-patient cost for both the standard of care and intervention.

Sensitivity analyses

We varied different key cost inputs and conditional probabilities to understand the variability and uncertainty in our measurements. For each selected input or conditional probability, we selected extreme high and low values and then calculated the per-patient incremental cost of the intervention compared to the standard of care.

RESULTS

Cost estimation

Costs for the standard of care and additional costs unique to the intervention, assessed using programmatic data are given in Table 1.[2,13,15] The average cost DOT visits for DR-TB patients (assuming 2 years of treatment) was calculated at US$842, using the average of all 1 176 272 TB South Africa Project NGO patient visits and payments (totalling

Table 3 Cost-per-patient under the intervention and standard of care models

	Average cost per patient US$
Intervention costs	8 577
LTFU	
Death (among LTFU)	30 623
Survival (among LTFU)	30 595
Receiving treatment (CFU)	
Death (among CFU)	7 685
Survival (among CFU)	7 657
Standard of care costs	11 405
LTFU	
Death	29 705
Survival	29 677
Receiving treatment (CFU)	
Death	6 767
Survival	6 739

LTFU = loss of follow-up; CFU = continued on follow-up.

US$1 908 041 from January 2016 to December 2018). Also, the cost of the ConnecTB mHealth solution which included annual maintenance, tablets and airtime was calculated at US$76 per DR-TB patient (assuming 2 years of treatment). The total additional cost per patient on the intervention was US$918.

Added value of the community-based model

Conditional probabilities and cost calculations for outcomes in both groups are given in Table 2. In the intervention group, 56% ($n = 14$) were cured or completed treatment, 8% ($n = 2$) died and 4% ($n = 1$) were LTFU. In the standard of care group, 50% ($n = 201$) were cured or completed treatment, 25% ($n = 103$) died and 20% ($n = 82$) were LTFU.

The estimated per-patient costs for each outcome are shown in Table 3. The overall average cost per patient was lower per intervention patient, at US$8577, than standard of care patients, at US$11 405, representing an average cost savings of US$2827 per intervention patient.

As shown in Table 4, these results are generally robust based on sensitivity analyses examining various cost inputs and conditional probabilities. Incremental cost is reported for extreme high and low values for a given cost input or conditional probability. Incremental cost is the additional per patient cost for the intervention compared to the standard of care group. Results were most sensitive to LTFU. The incremental cost for the intervention was lowest with the highest cost per patient LTFU values, and cost parity between groups was reached at US$12 330. The incremental cost of the intervention was positive for LTFU costs lower than US$12 330. Similarly, the incremental cost of the intervention was lowest in scenarios where the difference between LTFU in the intervention and the standard of care was largest. The incremental cost of the intervention was negative for between-group LTFU differences, as small as 3.98%.

DISCUSSION

This paper assesses the costs of implementing a novel community-based DR-TB care model in South Africa under current treatment regimens and programmatic management guidelines. Results show that while the intervention costs an estimated US$918 per patient, patients who were managed under the community-based model had lower LTFU during treatment, which yields a per-patient savings of US$2827 compared to the standard of care under this specific LTFU proportion. While the incremental cost of the intervention increases with a smaller difference in LTFU between groups, targeted scale-up to other high DR-TB burden districts has the potential to replicate these programmatic gains.

Scaling the model to include more DR-TB patients in South Africa requires multiple enabling factors. Commitment and capacity of the national programme and local NGOs and CSOs are critical to ensure sustainability of this model. District- and

Table 4 Sensitivity analyses

Parameter	High value %	Incremental cost of the intervention	Mid value %	Incremental cost of the intervention US$	Low value %	Incremental cost of the intervention US$	Cost parity or parity value* %
Cost inputs (par-patient costs reported), US$							
Cost of LTFU	50 000	6 139	15 000	435	100	1 993	12 330
Cost of DR-TB hospitalisation	30 000	3 684	20 000	2 869	1 000	1 321	—
Cost of XDR-TB treatment	30 000	3 121	25 000	2 714	1 000	758	—
Cost of ConnecTB	5 000	1 255	3 000	745	100	3 645	3 745
Conditional probabilities (per-patient costs reported)							
Difference in LTFU between groups	30	5 972	15	2 529	1	684	3.98
LTFU (standard of care)	30	7 710	15	4 267	1	1 054	—
Difference in death between groups	50	2 834	25	2 829	1	2 823	—
Death among LTFU	90	2 828	50	2 826	1	2 824	
Death among CFU (intervention group)	50	2 816	10	2 826	1	2 829	
Death among CFU (standard of care)	50	2 833	10	2 824	1	2 825	—

* Parity value describes the value at which cost parity is achieved.
LTFU = loss of follow-up; DR-TB = drug-resistant tuberculosis; CFU = continued on follow-up.

facility-level buy-in should also be considered at the outset of expansion activities to ensure a shared understanding of the model. Finally, the level of support provided to each patient should be considered and adjusted to allow for maximum human resource flexibility at the NGO level.

The authors believe that the cost benefits of this model would be preserved in the context of a universal shorter treatment regimen in South Africa. As cost savings in this intervention were primarily driven through reduced LTFU, these savings would be maintained in the context of a shorter treatment regimen using bedaquiline in place of injectable agents. As reported by Zhao et al., a 2018 retrospective cohort of MDR-TB patients in South Africa for whom bedaquiline was used in place of second-line injectable agents (SLIs) experienced similar proportions of LTFU compared to those given SLIs (10.5% vs. 12.5%; $P = 0.57$).[18] Furthermore, the need for more extensive monitoring tests (including echocardiograms and audiology monitoring) during bedaquiline treatment requires more individualised patient management to maintain low LTFU, such as the type provided through the community-based model.

The main limitations of this study are the small number of participants in the intervention group ($n = 25$), and the fact that data were collected using routinely available cohort data. The data are subject to certain biases, including possible self-selection into the intervention arm and inability to control for baseline characteristics, including age, sex and HIV status. Even considering these limitations, those who were more likely to be LTFU could have been selected systematically to receive more individualised case management, which would attenuate the effect of the intervention. These limitations do raise generalisability concerns for blanket policy recommendations, but the results remain useful for districts with similarly high DR-TB burdens.

Based on the sensitivity analysis, results are most affected by proportion of patients LTFU, in which the incremental cost of the intervention is positive for differences in LTFU smaller than 3.98% and for LTFU costs below US$12 330. This finding clarifies the scope and type of scale up that should be pursued for this model. Districts with high DR-TB burden and a high proportion of LTFU patients would be ideal candidates for expansion, as the opportunity to reduce LTFU is highest in these districts. We expect to continue scale up of the community-based model within USAID TB South Africa Project-supported districts during project implementation. Continued government buy-in at the district and provincial levels will be essential to sustainable implementation.

CONCLUSIONS

The community-based model has a lower per-patient cost than the standard of care alone among the patients observed in NMBHD, Eastern Cape, South Africa. The model should be further expanded, especially in high-burden DR-TB districts like NMBHD. Further expansion should also include criteria to individualise the level of support provided to each patient based on a patient's likelihood of being LTFU to maximise use of human resources and further minimise costs to the health system. Continued, targeted scale up of the community-based model can improve treatment outcomes, reduce LTFU and reduce costs to the health system in South Africa.

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RÉSUMÉ

CONTEXTE : Si l'Afrique du Sud a amélioré l'accès au traitement et à la prise en charge de la tuberculose (TB), le taux de succès du traitement en 2015 de la TB multirésistante (MDR-TB) reste faible à 55%. La prise en charge communautaire de la TB améliore la rétention des patients comparée au traitement standard seul.

OBJECTIF : Evaluer le coût d'un modèle de TB à base communautaire financé par l'USAID dans le district de santé de la Nelson Mandela Bay (NMBHD), province du Cap Est, Afrique du Sud, comparé au standard de soins national seul.

SCHÉMA : Nous avons estimé le coût du traitement de la TB résistante en communauté et le soutien à l'adhérence comparés au traitement standard seul.

RÉSULTATS : Les coûts d'ensemble moyens par patient ont été plus faibles de 2827 USD dans le modèle à base communautaire comparé au traitement standard seul.

CONCLUSION : Le coût par patient du modèle à base communautaire est plus faible que le traitement standard seul. Si ces coûts et les effets d'un modèle à base communautaire mis en œuvre au NMBHD étaient adoptés à plus grande échelle, ce modèle pourrait réduire les coûts d'ensemble du système de santé.

RESUMEN

MARCO DE REFERENCIA: Suráfrica ha mejorado el acceso al tratamiento y la atención de los pacientes con tuberculosis (TB); sin embargo, en el 2015 la tasa de tratamiento exitoso de la TB multirresistente (MDR-TB) permaneció baja, en un 55%. El tratamiento y la atención comunitarios de la TB mejoran la retención de los pacientes, en comparación con la aplicación exclusiva de la norma nacional de atención.

OBJETIVO: Evaluar el costo de un modelo de atención comunitaria de la TB financiado por la USAID en el distrito sanitario Nelson Mandela del Cabo Oriental (NMBHD) en Suráfrica y compararlo con la norma nacional de atención exclusiva.

MÉTODO: Se estimó el costo del tratamiento comunitario de la TB farmacorresistente y la ayuda al cumplimiento terapéutico y se comparó con la aplicación exclusiva de la norma nacional de atención.

RESULTADOS: El promedio de los costos globales por paciente fue 2827 USD más bajo en el modelo comunitario, comparado con el enfoque exclusivo de la norma asistencial.

CONCLUSIÓN: El costo por paciente del modelo comunitario es inferior al de la norma de atención exclusiva. Si se admite que los costos y los efectos de un modelo comunitario aplicado en NMBHD se pueden lograr en una escala más amplia, la ejecución del modelo podría reducir los costos globales del sistema de salud.