

## Tuberculosis treatment outcomes among peri-urban children receiving doorstep tuberculosis care

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### SUMMARY

**OBJECTIVE:** To determine the optimal tuberculosis (TB) management strategy for children living in peri-urban, resource-limited settings.

**DESIGN:** We compared TB treatment outcomes among children aged 0–15 years receiving doorstep care ( $n=82$ ) with those of a historical group ( $n=97$ ) receiving clinic-based care.

**RESULTS:** The doorstep care and clinic-based groups had similar age and sex profiles; treatment default rates

were 3.7% (3/82) vs. 38.1% (37/97,  $P < 0.0001$ ), treatment completion rates were 65.9% (54/82) vs. 51.6% (50/97,  $P = 0.01$ ), and cure rates were 13.4% (11/82) vs. 2.1% (2/97), respectively ( $P < 0.0001$ ).

**CONCLUSION:** Children living in peri-urban communities had improved TB treatment outcomes with doorstep care.

**KEY WORDS:** tuberculosis; doorstep care; peri-urban; TB; South Africa

IN 2012, APPROXIMATELY 6% of the global tuberculosis (TB) burden occurred in children aged 0–15 years.<sup>1</sup> While TB mortality rates among human immunodeficiency virus (HIV) infected children is largely unknown, the 74 000 TB deaths among HIV-negative children accounted for 8% of global TB deaths.<sup>1</sup> In South Africa, childhood TB accounts for 15–20% (47 571 cases) of the total number of TB cases, and is among the top five causes of death in children aged <15 years.<sup>2</sup> In 2006, 29 801 TB cases were reported among children aged 0–7 years in South Africa, accounting for 8% of all TB cases notified.<sup>3</sup> The TB impact on child health impedes South Africa's efforts to attain the Millennium Development Goals (MDG) 4 and 6 pertaining to child health.<sup>4</sup>

The optimal management strategy for childhood TB is largely unknown. The World Health Organization's (WHO's) Stop TB Strategy, which advocates for directly observed treatment (DOT) under decentralised TB care,<sup>1</sup> makes no special considerations for children. Resource constraints have meant that clinic-based TB care remains the routine approach, even among children.<sup>5</sup> Despite the successes of DOT,<sup>5</sup> a meta-analysis suggested that this strategy was not superior to self-administration.<sup>6</sup> Studies evaluating the impact of alternative approaches to childhood TB care in this setting are scarce.

We compared TB treatment outcomes among children receiving doorstep TB care with those of a historical group receiving clinic-based care in the same peri-urban community.

### METHODS

We conducted a retrospective analysis of clinic records of 82 children aged 0–15 years enrolled in a pilot Centre for the AIDS Programme of Research in South Africa (CAPRISA) doorstep TB care programme from 2008 to 2011. This was compared with a historical group of 92 children from the same peri-urban community receiving clinic-based TB care from 2005 to 2008. This peri-urban community included residents from low-cost state housing and adjacent informal squatter settlements.

The doorstep TB care programme was a health care intervention that formed part of the CAPRISA community-based treatment programme, aimed at enhancing TB treatment access and adherence. A total of 516 adult and childhood ambulatory TB cases were referred for doorstep TB on presentation at either one of the two local primary health care clinics for TB diagnosis or treatment follow-up. TB was diagnosed based on sputum analysis and chest X-ray. Following counselling, parents or guardians provided consent for the enrolment of the children into care.

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**Table 1** Baseline characteristics comparing children receiving doorstep TB care and those receiving clinic-based care

Variable	Doorstep TB care (n = 82) n (%)	Clinic-based TB care (n = 97) n (%)	P value
Male	44 (53.7)	54 (55.7)	0.80
Age, years			
<1	13 (15.9)	13 (13.5)	0.60
1–6	53 (64.6)	67 (69.1)	0.45
7–15	16 (19.5)	17 (17.6)	0.72

TB = tuberculosis.

The addresses were then verified. Trained community care givers or nurses supervised two to three home visits per week and recorded basic clinical history, evaluated treatment adherence, completed the TB treatment card, offered TB-specific health education, addressed issues relating to poor adherence, dispensed TB medication and arranged follow-up visits. All patients and their guardians were counselled on the need for TB screening in the household and for HIV testing, and where permission for testing was obtained, HIV testing and TB screening were performed.

Anti-tuberculosis treatment was monitored using a doorstep TB care card. Very sick patients were visited by a professional nurse on request, and were referred to another health facility, if required, along with those patients who wished to relocate. These patients were documented as transferred out. All patients visited the clinic at the end of the intensive and continuous phases of anti-tuberculosis treatment for sputum and clinical evaluation.

A total of 560 adult and childhood TB cases were receiving clinic-based care. The clinic-based group received care from the local primary health care clinic per routine practice. Patients were expected to visit the clinic once a month to collect their medications. Clinic cards contained only basic demographic and TB outcome data. A follow-up date was given on the patient's clinic card. Patients could visit the clinic if they felt unwell or had queries regarding their medication.

Both groups were administered the standard treatment regimen, i.e., 2 months of rifampicin (RMP), isoniazid (INH), pyrazinamide and ethambutol, followed by 4 months of INH and RMP. Multidrug-resistant, extensively drug-resistant and extra-pulmonary TB cases were not included in this study.

Treatment outcomes for both groups were defined as recommended in the 2014 South African TB Control Programme Guidelines and the 2013 WHO TB outcomes classification.<sup>7,8</sup>

#### Statistical analysis

Data are presented as proportions. A sample *t*-test and a sample binomial test were used to compare TB

**Table 2** Childhood TB treatment outcomes in the doorstep TB care group and the clinic-based care group

TB outcome	Doorstep TB care (n = 82) n (%)	Clinic-based TB care (n = 97) n (%)	P value
Treatment success	65 (79.3)	52 (53.7)	<0.0001
Cure	11 (13.4)	2 (2.1)	<0.0001
Completed treatment	54 (65.9)	50 (51.6)	0.01
Defaulted	3 (3.7)	37 (38.1)	<0.0001
Transferred out	5 (6.1)	3 (3.1)	0.22
Relocated	9 (11.0)	4 (4.1)	0.01
Death	0	1 (1.0)	—

TB = tuberculosis.

treatment outcome data between groups. Statistical analyses were performed using SAS, version 9.2 (Statistical Analysis System, Cary, NC, USA).

The study was approved by the University of KwaZulu-Natal Biomedical Research Ethics Committee, Durban, South Africa (Ref: E248/05).

## RESULTS

### Baseline characteristics

Overall, childhood TB accounted for 82 of 516 (15.9%) cases in the doorstep TB care group and 97/560 (17.3%) cases under the clinic-based care programme. In the doorstep and clinic-based care programmes, the mean age was respectively 3.9 years (interquartile range [IQR] 1–5) ( $P = 0.91$ ) vs. 3.5 years (IQR 1–5) ( $P = 0.51$ ); most children were between the ages of 1 and 6 years (64.6% vs. 69.2%), with a male predominance (53.7% vs. 55.7%) (Table 1).

### TB treatment outcomes

In the doorstep TB and clinic-based TB care programmes, treatment success (cure and completion) rates were respectively 79.3% (65/82) and 53.7% (52/97) ( $P < 0.0001$ ), treatment completion rates were 65.9% (54/82) and 51.6% (50/97) ( $P = 0.01$ ) and cure rates were 13.4% (11/82) and 2.1% (2/97), ( $P < 0.0001$ ) (Table 2). Children receiving doorstep TB care had significantly lower treatment default rates (3/82, 3.7%) than those who received clinic-based TB care (37/97, 38.1%,  $P < 0.0001$ ). Transfer out and relocation occurred more frequently in the doorstep vs. the clinic-based care group (respectively 5 [6.1%] vs. 3 [3.1%] and 9 [11%] vs. 4 [4.1%]). Patients who transferred out or relocated did not have their TB treatment outcomes evaluated. There was one death among the patients receiving clinic-based care.

### Age-stratified TB outcomes

Treatment completion outcomes showed the greatest improvement among children aged <1 year under doorstep TB care (10/13, 76.9%) vs. clinic-based care

**Table 3** Age-stratified TB treatment outcomes for doorstep TB care and clinic-based TB care

	Doorstep TB care				Clinic-based TB care			
	<i>n</i> (%)				<i>n</i> (%)			
Age group, years	<1	1–6	7–12	13–15	<1	1–6	7–12	13–15
Treatment outcome								
Cured	1 (7.7)	4 (7.5)	4 (36.4)	2 (40)	0	0	2 (13.3)	0
Completed treatment	10 (76.9)	37 (69.8)	5 (45.5)	2 (40)	1 (7.7)	44 (65.7)	4 (26.7)	1 (50)
Defaulted	1 (7.7)	2 (3.8)	0	0	10 (76.9)	19 (28.4)	7 (46.7)	1 (50)
Transferred out	0	4 (7.5)	1 (9.1)	0	0	2 (3)	1 (6.7)	0
Relocated	1 (7.7)	6 (11.3)	1 (9.1)	1 (20)	1 (7.7)	2 (3)	1 (6.7)	0
Death	0	0	0	0	1 (7.7)	0	0	0
Total	13 (100)	53 (100)	11 (100)	5 (100)	13 (100)	67 (100)	15 (100)	2 (100)

TB = tuberculosis.

(1/13, 7.5%) (Table 3). The greatest reduction in treatment default rates was among children aged 7–12 years, from 46.7% (7/15) among those on clinic-based care to 0% (0/11) among those on doorstep TB care. Provision of doorstep TB care had no impact among the 7–12 and 13–15 year age groups who relocated or transferred out, where both outcomes increased from 6.7% (1/15) in clinic-based care to 9.1% (1/11) in doorstep care.

#### *HIV co-infection*

Data on the HIV status of the patients were only available for the doorstep TB care group. Of 82 patients, 36 (44%) had known HIV status, 15 of whom were verified by the health care worker. There were 21/82 (26%) non-HIV-infected (17 unverified) children. Of the 46 children (56%) not tested for HIV, the guardians of 30 children said that the child could be tested after completion of TB treatment. These numbers are too small to comment on the association of HIV co-infection with TB treatment outcomes.

## DISCUSSION

The improved treatment success rates among children receiving doorstep TB care compared to clinic-based care suggest that the former should be the preferred strategy for childhood TB management. The greatest impact on the treatment success rates was achieved in the <1-year age group (Table 3). Limited data are available for a comparison of TB outcomes, and specifically treatment completion and treatment default rates, among children aged <1 year and those aged 7–12 years. Available age-stratified TB outcome data from a retrospective study of over 2000 children conducted in Ethiopia demonstrated similar TB treatment completion, default and transfer out rates among children aged <4 years compared to rates among children aged <6 years in our study.<sup>9</sup> While the Ethiopian study also demonstrated significantly higher mortality among children aged <5 years ( $P < 0.001$ ) and among those with HIV co-infection ( $P <$

0.001),<sup>9</sup> we have insufficient data to make this comparison.

We attribute the extremely low TB cure rates in our population to the recognised challenges associated with detecting TB in very young children.<sup>1</sup> Although the treatment success rate among those receiving doorstep TB care was higher than among those receiving clinic-based care, they do not reach the WHO and country target of 85%.<sup>1,7</sup> A study from India among children aged  $\geq 12$  years enrolled in the more resource-intensive conventional DOTS programme showed a 94.6% treatment success rate.<sup>10</sup> The low TB treatment success rate among children enrolled in clinic-based care, as seen in this study, is in line with findings from studies conducted in Botswana, Malawi and India.<sup>11,12</sup> In the South African context, where childhood TB accounts for approximately 13% of the total South African TB burden,<sup>1</sup> children are a vulnerable group requiring attention. Current TB management efforts are largely clinic-based, and will not enable us to reach the MDG 4 and 6 targets for child health.

While the impact of HIV co-infection, malnutrition, immunosuppression and TB drug resistance<sup>13</sup> on TB outcomes were not evaluated in this study, we highlight notable improvements in TB treatment outcomes and a significant reduction in the treatment default rate among children accessing doorstep anti-tuberculosis treatment. More patients had a record of transfer out or relocation in the doorstep TB care programme as opposed to clinic-based care, most likely due to reporting bias. This is also evident from the higher rates of transfer out and relocation. Furthermore, TB outcomes in these patients were not evaluated in both study groups due to resource constraints. It is reasonable to suggest that migration patterns typical of peri-urban populations, as seen elsewhere in India and globally,<sup>5,14</sup> influence the recording of treatment outcomes.

As the risk of progression to active TB is greatest among children aged <2 years,<sup>15</sup> it was not surprising to find that approximately 81% of TB cases in this study were aged  $\geq 6$  years, in line with other studies

conducted elsewhere.<sup>9,16</sup> The 2012 South African Integrated Schools' Health Policy, which uses schools as a first point of care,<sup>17</sup> therefore misses the majority of childhood TB cases. The optimal mechanism for detection of these cases under the health programme would be via the Integrated Management of Childhood Illnesses programme and the Expanded Programme of Immunization. In addition, initiatives to address retention gaps are necessary even with doorstep care programmes. Patient education on disclosing pending relocation, improved communication between patients and health care workers (HCWs), and between HCWs of different facilities, will enable seamless transfer of patients between facilities.

### Limitations

There are important limitations in this study. The generalisability of our findings is limited, as the study was restricted to selected clinics serving a geographically defined population. Due to inadequate documentation, we are unable to report on outcomes by TB site and smear status or on efforts in household TB contact tracing. In addition, HIV testing rates in children were low due to challenges in obtaining consent from parents and guardians, making it impossible to obtain a true estimate of the impact of HIV co-infection on TB outcomes in this group. The inability to determine cure and mortality rates among the clinic-based care group was likely due to poor TB tracing systems and lack of programme mechanisms for the detection of treatment default. While the number of treatment defaulters in the doorstep care programme was lower, no further follow-up of treatment defaulters and those who transferred out was possible in either group due to poor patient communication of impending relocation and restricted geographic coverage of the programme. Additional potential bias include ascertainment bias, as data were collected over different periods of time in the two groups, and due to the retrospective nature of the analysis of the clinic-based care group, only demographic data for sex and age were available for comparison. Further research evaluating the impact of doorstep care on TB outcomes is required. Analysis stratified by HIV status, nutrition level, clinical presentation and site of TB, and availability of mycobacteriological data and treatment features, will provide further data on the utility and generalisability of such a strategy to resource-limited settings, where these co-existing features are common.

In conclusion, doorstep TB care led to an increase in TB cure and completion rates among children as compared to clinic-based care; however, treatment success rates remain below WHO targets. The system

should be strengthened to ensure retention of children in TB treatment programmes.

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Conflicts of interest: none declared.

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**RESUME**

**OBJECTIF :** Déterminer la meilleure stratégie de prise en charge de la tuberculose (TB) pour les enfants vivant dans des zones périurbaines aux ressources limitées.

**SCHEMA :** Nous avons comparé les résultats du traitement de la TB chez des enfants âgés de 0–15 ans, bénéficiant de soins à domicile ( $n = 82$ ) à un groupe historique ( $n = 97$ ) recevant leur traitement dans un centre de santé.

**RÉSULTATS :** Le groupe recevant les soins à domicile et le groupe traité en centre de santé avaient une répartition

par âge et par sexe similaire ; les taux d'abandon ont été de 3,7% (3/82) contre 38,1% (37/97 ;  $P < 0,0001$ ), les taux d'achèvement du traitement ont été de 65,9% (54/82) contre 51,6% (50/97 ;  $P = 0,01$ ) et les taux de guérison ont été de 13,4% (11/82) contre 2,1% (2/97), respectivement ( $P < 0,0001$ ).

**CONCLUSION :** Les enfants vivant dans des communautés périurbaines ont eu de meilleurs résultats du traitement antituberculeux avec une prise en charge à domicile.

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**RESUMEN**

**OBJETIVO:** Determinar la estrategia óptima de tratamiento de la tuberculosis (TB) en los niños que viven en los entornos periurbanos de recursos limitados.

**MÉTODOS:** Se compararon los desenlaces del tratamiento antituberculoso en los niños de edad de 0–15 años que recibieron atención domiciliaria ( $n = 82$ ) con un grupo de referencia histórico que recibió atención en un servicio ambulatorio ( $n = 97$ ).

**RESULTADOS:** El grupo de atención domiciliaria y el grupo que acudió al servicio ambulatorio presentaron

características semejantes de edad y sexo; las tasas de abandono del tratamiento fueron 3,7% (3/82) contra 38,1% (37/97), respectivamente ( $P < 0,0001$ ); las tasas de compleción del tratamiento fueron 65,9% (54/82) y 51,6% (50/97;  $P = 0,01$ ); y las tasas de curación 13,4% (11/82) contra 2,1% (2/97;  $P < 0,0001$ ).

**CONCLUSIÓN:** Los niños que viven en comunidades periurbanas alcanzan desenlaces más favorables del tratamiento de la TB cuando reciben atención domiciliaria.

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