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Research Article

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Tuberculosis treatment outcome in a rural area of Senegal: a decade of experience from 2010 to 2019 by *StopTB Italia*

Niccolò Riccardi[1,2], Simone Villa*[1,3], Andrea Giacomelli[1,4], Mama M Diaw[1,5], Mamoud Ndiaye[1,6], Lamine Gning[1,6], Marta Robbiano[1], Riccardo Alagna[1,7], Laura Saderi[8], Antonio Di Biagio[1,9], Matteo Bassetti[1,9], Daniela M Cirillo[1,7], Giovanni Sotgiu[1,8], Luigi R Codecasa[1,10], Marie Sarr[11] & Giorgio Besozzi[1]

[1]Stop TB Italia, Milan, 20159, Italy
[2]Department of Infectious, Tropical Diseases & Microbiology (DITM), IRCCS Sacro Cuore Don Calabria Hospital, Negrar di Valpolicella, Verona, 37024, Italy
[3]Centre for Multidisciplinary Research in Health Science, University of Milan, Milan, 20122, Italy
[4]III Infectious Diseases Unit, ASST Fatebenefratelli Sacco, Milano, 20157, Italy
[5]Médecin coordonnateur lutte contre la TB, Région médicale de Thiès, Thiès, 21000, Sénégal
[6]District Sanitaire de Diofior/Département de Fatick, Diofior, 23400, Sénégal
[7]TB Supranational Reference Laboratory, IRCCS San Raffaele Scientific Institute, 20132, Milan, Italy
[8]Clinical Epidemiology & Medical Statistics Unit, Dept. of Medical, Surgical & Experimental Sciences, University of Sassari, Sassari, 07100, Italy
[9]Clinic of Infectious Diseases, IRCCS AOU San Martino-IST, Genoa, 16132, Italy
[10]Regional TB Reference Centre & Laboratory, Villa Marelli Institute/ASST Niguarda Ca' Granda, Milan, 20159, Italy
[11]National TB Programme, Dakar, 10200, Senegal
*Author for correspondence: simone.villa@unimi.it

Background: Tuberculosis (TB) unevenly affects individuals across the globe, especially in rural areas of low-income countries. Aim of the study was to assess the impact of social protection to increase TB awareness on treatment outcomes among TB patients in a rural area of Senegal. **Materials & methods:** The study, conducted in Fimela district (Senegal) from 1 January 2010 to 31 December 2019 and the intervention started from 31 January 2013, includes activities to increase awareness, active case finding, active follow-up and social protection. **Results:** Overall, 435 subjects – mainly male and young – were included in the analysis. Among TB cases, 94% had pulmonary involvement, 87% had no previous TB history, and 6% resulted positive HIV. Improved outcome was observed once intervention began (from 71 to 91%, $p < 0.001$); whereas mortality decreased (from 15 to 5%; $p < 0.001$), especially for those HIV co-infected for whom TB mortality rate dropped from 70 to 29%. **Conclusion:** After beginning the cooperation program, TB treatment success increased as a result of the decline of mortality, especially in people living with HIV.

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Keywords: *Mycobacterium tuberculosis* • rural area • social protection • treatment outcome • tuberculosis

Tuberculosis (TB) is the leading infectious disease cause of deaths worldwide, with 1.5 million deaths in 2018 [1]. In 2014 a new public health strategy was approved by the WHO to end TB by 2050. Three pillars define the core of the strategy, with the first one focused on 'integrated, patient-centered care and prevention', which can be partially assessed using the TB treatment success rate. The global treatment success rate is 85%. However, in some geographical areas (e.g., rural low-resource areas of Africa) it is very low [1–3].

The African region of WHO, in 2019, although saw a drop in TB deaths of 19% from 2015 to 2019, still accounted for a quarter of cases reported globally and the first region for TB incidence rate (226 per 100,000 population) [1]. Moreover, in this region known for the high HIV prevalence, a large of TB patients (86%) have now a documented HIV result; of whom the majority (88%) is in antiretroviral treatment (ART).

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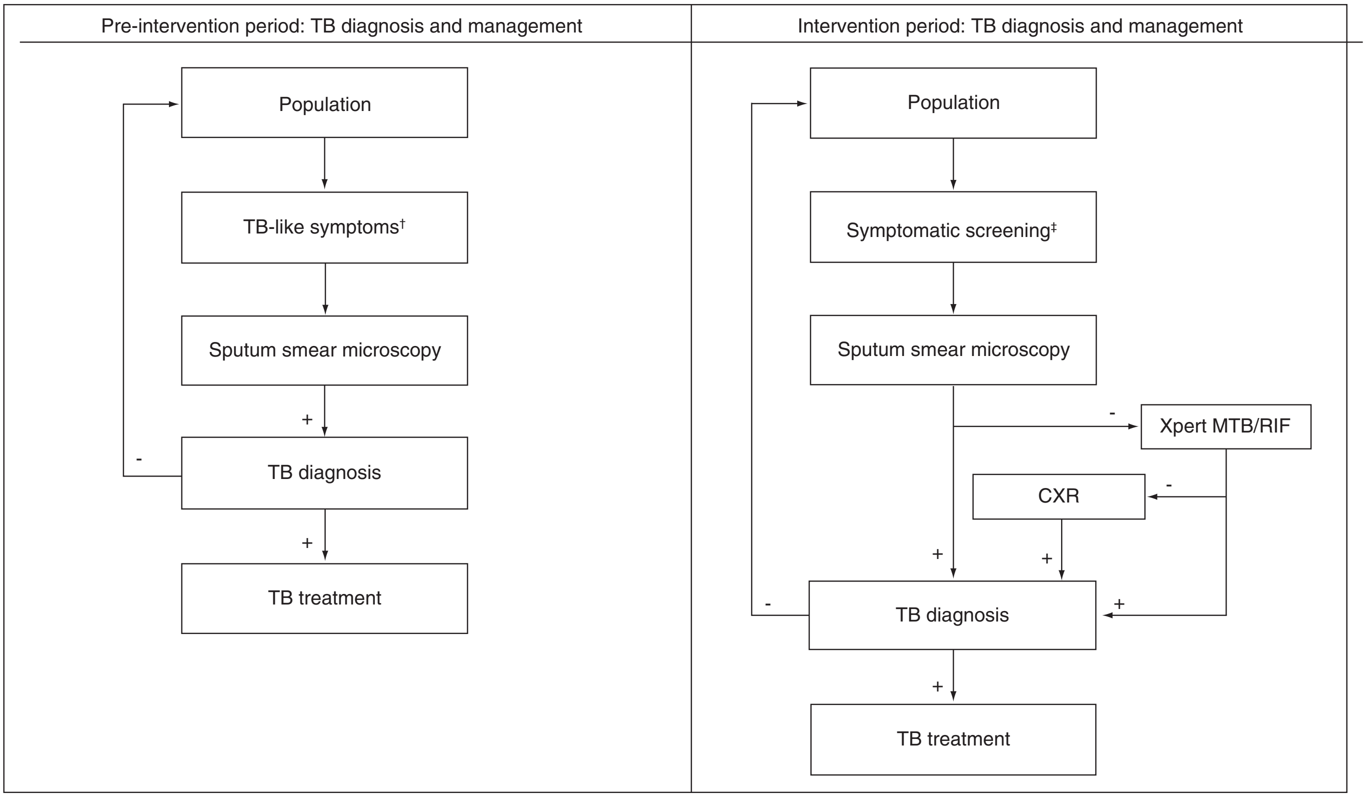

Figure 1. Flowchart of tuberculosis diagnosis and management before and during StopTB Italia intervention in place at the Health Centre of Diofior, in the Fimela district, Fatick region, Senegal.
†Patients were self-referred to the Health Centre of Diofior during the pre-intervention period.
‡Symptomatic screening for TB-like symptoms was performed by local women (badieu'ngox) trained by StopTB Italia Onlus medical staff.

In Senegal, TB treatment success rate, despite the national high average rate (87%), displays a great variability (ranging from 58.5 to 94.5%) [4] with rural areas dominated by poor disease awareness and unreliable TB epidemiological data [5,6].

Strengthening healthcare system is the key ingredient to increase TB treatment success rate and to improve TB surveillance [1,3]. Nevertheless, it also requires the collaboration of non-governmental organizations in the short period to rapidly implement efficient healthcare services [7,8].

Social protection and universal health access can mitigate social and economic hardships, which hinder access to quality healthcare services. Therefore, in many low- and middle-income countries social protection measures, as non-income-producing cash transfer interventions (CTIs), has been investigated and proved effective in improving TB treatment outcome [9].

Since 2013, the Italian non-governmental organization *StopTB Italia Onlus* has been supporting the Senegalese National Tuberculosis Programme (NTP) to deliver appropriate treatment after diagnosis [1,10,11]. Data regarding TB incidence and treatment outcomes in Senegal are already known. However, data for rural areas, like the Fimela district, are likely to be unreliable and inconsistent. Our study aims to fill the gap of knowledge of TB diagnosis and care in Senegalese rural districts and to provide a model to improve treatment outcomes in similar rural districts.

Materials & methods

The study period included a pre-intervention phase followed by the *StopTB Italia Onlus* intervention (Figure 1). The study was conducted in the Fimela district, Senegal, from 1 January 2010 to 31 December 2019. The study period in the analysis was divide in two phases: pre-intervention (until 31 January 2013) and the intervention period during which *ad hoc* actions took place (from 31 January 2013). The data recording and the study itself is still ongoing. The observation was censored on 31 December 2019.

Ethical disclosure

The study was endorsed by the NTP of Senegal on 16 August 2012 (registration no. S00257). Waiver of consent was applied due to the retrospective nature of the study. All individuals with sputum smear-positive for *Mycobacterium tuberculosis* were included in the study. Exclusion criteria were the following: lack of registration of the TB case in the TB register or missing completion of follow-up before the 31 December 2019.

Study setting

The intervention took place in Fimela district, an administrative district of the region of Fatick located in the southwest part of the northern outcrop of Senegal. There is only one tertiary level healthcare centre, the Health Centre of Diofior (HCD), serving the whole Fimela district, an area of 1115 km^2.

Study population

The Fimela district has an estimated population of 80,599 people (population density: 72 inhabitants per km^2), mostly by farmers and merchants living in rural and sub-urban settings, organized in villages.

Intervention & study procedures

Before *StopTB Italia Onlus* mediation ('pre-intervention period'), TB diagnosis relied on autonomous referral of patient to the HCD (the patient goes to the HCD for general screening, independently of the symptoms) and sputum smear microscopy alone; whereas, since 1 February 2013 ('intervention period'), diagnosis depended on trained woman (*badieu'ngox*) actively looking monthly, house-to-house, for suggestive symptoms (productive cough for at least 10 days, fever, weight loss and night sweats) using a symptom screening tool in villages [7,12,13]. Moreover, idiomatic brochures listing the symptoms suggestive for TB according to WHO (i.e., productive cough for 10 days or more, fever, weight loss and night sweats) were distributed annually in all villages to raise awareness of the disease. Due to high illiteracy levels, the idiomatic brochures were expressly created by *StopTB Italia Onlus*. All referred presumptive TB cases underwent sputum smear microscopy, whereas culture was not performed due to structural laboratory limitations and to long distance to the regional supranational laboratory (~150 km). The Xpert MTB/RIF was used as a second-level tool for those sputum smear negative with high clinical TB suspicion [9]. Chest radiography was the third-level diagnostic tool for those negative to both sputum smear microscopy and Xpert MTB/RIF due to the high cost of films. The description and comparison of the activities for TB diagnosis and management are displayed in Figure 1. Those who received a TB diagnosis were offered HIV testing, and subsequently linked to outpatient HIV care if positive. All patients who started TB treatment underwent follow-up visits and sputum smear microscopy at the first, second, fifth and sixth month. An economic support of 20,000 FCFA ≈US$30–40 (namely, Franc of the French Community of Africa) was granted to all patients who completed treatment to stimulate the retention-in care. The financial amount depended on the income of an agricultural cooperative managed by former TB patients under the supervision of the HCD and *StopTB Italia Onlus* [7].

The primary outcome was the assessment of the treatment success (cured and treatment completion) defined according to 2016 WHO definitions [11]. The secondary outcomes were the assessment of death, and loss to follow-up rates during the treatment period.

Statistical analysis

Qualitative variables were described with absolute and relative (percentage) frequencies, whereas nonparametric quantitative variables were summarized with medians and interquartile ranges. Chi-square and Fisher's exact tests were used to detect any statistical differences in the comparison of qualitative data when appropriate. Quantitative variables were compared with Mann–Whitney test. A two-tailed p-value <0.05 was considered statistically significant. Computations were performed with the statistical software STATA version 16 (StataCorp, TX, USA). Geospatial data were displayed using ArcGIS® software by Esri.

Results

Overall, 446 patients were diagnosed with TB; however, 11 were excluded because they were still on treatment at the moment of data analysis. A total of 122 (28%) and 313 (72%) patients were recruited during the pre-intervention and intervention periods, respectively. The geospatial distribution of TB cases diagnosed during the study period is displayed in Figure 2, with most of the cases diagnosed in people living at Diofior (n = 79), Palmarin (n = 64), Samba dia (n = 40) and Fimela (n = 31).

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Figure 2. Geospatial distribution of place of residency of tuberculosis cases diagnosed during the study period, from 2010 to 2019 (n = 392).

Baseline characteristics at TB diagnosis

Patients were generally male (287; 66%) and young (median [interquartile ranges] age of 35 [24–53] years) (Table 1). Annual reported cases ranged from 31 to 61 cases, with a peak in 2014. Pulmonary TB was the main form, accounting for 375/400 (94%); HIV co-infection was documented in 24/392 individuals (6%). The majority were new TB cases (345; 87%), although some had either previously interrupted treatment (17; 4%) or were transferred out (16; 4%). Sputum smear microscopy was used to diagnose 353/410 (86%) pulmonary TB cases, whereas 82/435 (23%) required further investigation through Xpert MTB/RIF and 91/100 (91.0%) resulted positive although with no mutation to rifampicin detected. Chest radiography was found positive in 66/183 (36%) patients.

Notably, during the pre-intervention period, the proportion of HIV diagnosis was higher (11 vs 5%; p = 0.030).

TB treatments & follow-up

Treatment of TB relied on a standard therapeutic regimen with 2 months of rifampicin, isoniazid, ethambutol and pyrazinamide followed by 4-month of isoniazid and rifampicin combined (369/401 patients; 92%), while streptomycin was added during the induction phase for failure and/or retreatment patients. Sputum smear conversion after 2-months from anti-TB treatment initiation was observed in 335/353 (95%) subjects.

Twelve (12/24; 50%) subjects with HIV co-infection were treated with ART. Noteworthy, in the pre-intervention phase, only 4/10 (40%) of HIV co-infected were treated with ART (tenofovir disoproxil/lamivudine/efavirenz as a first line-single tablet regimen q.d.), whereas the number increased during the intervention period (8/14; 57%).

Table 1. Baseline patients characteristics.

Characteristics	Overall (n = 435)	Before-intervention (n = 122)	During the intervention (n = 313)	p-value
Females, n (%)	148 (34.0)	42 (34.4)	106 (33.9)	0.910
Age at diagnosis, median in years (IQR)	35 (24–53)	32 (23–46)	36 (25–56)	0.005
TB form, n (%)	400 (92.0)	122 (100.0)	275 (87.9)	0.780
– Pulmonary/extra pulmonary-TB	375 (93.8)	115 (94.3)	260 (93.5)	
– Extra-pulmonary TB	22 (5.1)	7 (5.7)	15 (6.5)	
Type of patient, n (%)	398 (91.5)	122 (100.0)	276 (88.2)	0.020
– New	345 (86.7)	107 (87.7)	238 (86.2)	
– Relapse	1 (0.3)	0 (0.0)	1 (0.4)	
– Failure	8 (2.0)	1 (0.8)	7 (2.5)	
– Restart treatment after interruption	17 (4.3)	0 (0.0)	17 (6.2)	
– Transferred	16 (4.0)	10 (8.2)	6 (2.2)	
– Other	11 (2.8)	4 (3.3)	7 (2.5)	
Sputum smear microscopy, n (%)	410 (94.3)	116 (95.1)	294 (93.9)	
– Positive results (n)	353 (86.1)	105 (90.5)	248 (84.4)	0.100
Xpert MTB/RIF, n (%)	100 (23.0)	1 (0.8)	99 (31.6)	
– Positive results (n)[†]	91 (91.0)	1 (100.0)	90 (90.9)	1.000
Chest radiography, n (%)	183 (42.1)	10 (8.2)	173 (55.3)	
– Patients with positive CXR (n)	66 (36.1)	10 (100)	56 (32.4)	<0.0001
HIV testing, n (%)	392 (90.1)	91 (74.6)	301 (96.2)	
– HIV positive (n)	24/392 (6.1)	10 (11.0)	14 (4.7)	0.030
– On ART	12 (50.0)	4 (66.7)[‡]	8 (100.0)[§]	0.170[¶]

[†]All patients positive at Xpert MTB/RIF were rifampicin susceptible (*rpoB* gene negative).
[‡]Data on ART prescription is not reported in four patients with HIV co-infection.
[§]Data on ART use is unknown in six patients with positive HIV result.
[¶]p-value is computed excluding the missing values.
ART: Antiretroviral treatment; CXR: Chest radiography; IQR: Interquartile range; RIF: Rifampicin; TB: Tuberculosis.

TB outcomes

Treatment outcomes are displayed in Table 2.

During the study period, treatment success was achieved by 373/435 (86%) individuals, whereas 32 (7%) died, ten (2%) were lost to follow-up, and five (1%) failed. Among HIV co-infected, treatment success was halved when compared with the rate of HIV-negative subjects (334/368; 91%) ($p < 0.001$). Likewise, deaths were ninefold higher in those with HIV co-infection (11/24; 46%) in contrast with those of the HIV-negatives (18/368; 5%) ($p < 0.001$). The majority of people living with HIV who had a successful treatment were under ART (7/11; 64%), whereas only 4/11 (36%) who died were exposed to ART.

During the intervention an increase in treatment success rate was observed compared with the baseline (91 vs 71%; $p < 0.001$). In people living with HIV treatment success rate increased from 20 to 64% ($p = 0.047$) (Tables 3 & 4).

Discussion

The present study shows the importance of self-sustainable social protection measures in improving TB treatment outcomes in a rural and resource-limited setting. Social protection was found to be effective in improving treatment outcome among TB patients, especially for those co-infected with HIV, for whom a lower death rate was reported. Social protection and other broader interventions aimed to address proximal determinants of TB progression and deterioration (e.g., poverty, undernutrition, accessibility to healthcare services) are pivotal measures to couple with tools widely used in NTP (e.g., active case finding), especially to retain TB patients in care in low- and middle-income regions and break the cycle of TB and poverty [11,12].

A key role may have been played by *badieu'ngox* involved in active case finding and disease awareness of the general population: they can improve early TB diagnosis and treatment outcomes because increased patients' adherence [14]. Likewise, comparable finding of studies with a similar design (i.e., either employment of nonhealthcare workers

Table 2. Treatment, follow-up, and outcomes patients affected with tuberculosis at the Health Centre of Diofior, Senegal.

Characteristic	Overall (n = 435)	Before-intervention (n = 122)	During the intervention (n = 313)	p-value
Days from diagnosis to treatment initiation, median (IQR)	1 (0–2)	1 (0–3)	1 (0–2)	0.130
TB treatment regimens, n (%)	401 (92.2)	122 (100.0)	279 (89.1)	0.020
– RHZE	369 (92.0)	116 (95.1)	253 (90.7)	
– HRZ	5 (1.3)	3 (2.5)	2 (0.7)	
– SHRZE	27 (6.7)	3 (2.5)	24 (8.6)	
Treatment duration, median in days (IQR)	184 (181–190)	182 (180–187)	185 (182–275)	0.003
Sputum smear microscopy at follow-up, n (%)				
– Sputum smear at 2 months	361 (83.0)	91 (74.6)	270 (86.3)	0.470
– Negative results (n)	335 (92.8)	86 (94.5)	249 (92.2)	
– Sputum smear at 5 months	330 (75.9)	81 (66.4)	249 (79.6)	
– Negative results (n)	325 (98.5)	81 (100.0)	244 (98.0)	0.340
– Sputum smear at 6 months	321 (73.8)	83 (68.0)	238 (76.0)	
– Negative results (n)	318 (99.1)	83 (100.0)	235 (98.7)	0.570
Treatment outcome, n (%)				
– Treatment completed	71 (16.3)	6 (4.9)	65 (20.8)	<0.0001
– Cured	302 (69.4)	81 (66.4)	221 (70.6)	0.390
– Treatment success	373 (85.7)	87 (71.3)	286 (91.4)	<0.0001
– Death	32 (7.4)	18 (14.8)	14 (4.5)	<0.0001
– Lost to follow-up	10 (2.3)	8 (6.6)	2 (0.6)	0.001
– Transferred out	15 (3.5)	8 (6.6)	7 (2.2)	0.040
– Failure	5 (1.2)	1 (0.8)	4 (1.3)	1.000

E: Ethambutol; H: Isoniazid; IQR: Interquartile range; R: Rifampicin; S: Streptomycin; TB: Tuberculosis; Z: Pyrazinamide.

Table 3. Comparison of treatment outcomes before and during the StopTB Italia project implementation in people living with HIV (n = 24).

Characteristic	Before intervention (n = 10)	During the intervention (n = 14)	p-value
Treatment success	2 (20.0)	9 (64.3)	0.047
Death	7 (70.0)	4 (28.6)	0.10

Table 4. Comparison of treatment outcomes between those positive and negative to HIV (n = 392).

Characteristic	HIV-negatives	HIV-positives	p-value
Before intervention, n (%)	81 (100.0)	10 (100.0)	
– Treatment success	66 (81.5)	2 (20.0)	<0.0001
– Death	8 (9.9)	7 (70.0)	<0.0001
– Others	7 (8.6)	1 (70.0)	–
During *StopTB Italia* intervention, n (%)	287 (100.0)	14 (100.0)	
– Treatment success	268 (93.4)	9 (64.3)	<0.0001
– Death	10 (3.5)	4 (28.6)	0.002
– Others	9 (3.1)	1 (7.1)	–

TB: Tuberculosis.

for TB awareness and retention in care or CTIs or both), supporting our results were previously reported for other rural areas of different sub-Saharan countries [15,16].

Co-infection with HIV remains, however, one of the most detrimental factors associated with unfavorable TB treatment outcomes. Many negative elements can be associated with the HIV co-infection in this geographical area: HIV care and support services are virtually absent (11% of healthcare facilities in Fatick region) [17] because concentrated in urban and distant areas; social stigma may hinder HIV screening, diagnosis, and treatment; drug–

drug interaction between TB treatment and ART are poorly addressed in those treated for HIV, only 7% healthcare facilities in the whole country providing ART to people living with HIV [17,18]. However, since the intervention period, 96% of the TB patient has been screened for HIV in line with the regional statistics (100%) and higher to the national one (84%) of 2016 [17]. Therefore, efforts must be made in strengthening and expanding HIV care services in this rural area to allow patient to be treated and prevent them to drop the treatment. We suggest enhanced treatment follow-up for patients with HIV/TB co-infection in order to increase treatment success and stable suppressed viral load.

Cash transfer as a form of social protection was firstly applied for improving health outcome in people living with HIV/AIDS, where its effect on HIV outcome were scarcely documented [19]. Our study, therefore, contributes in expanding the knowledge, even though partially to those with TB, of nonincome producing CTIs application in people living with HIV/AIDS.

The collaboration between *StopTB Italia Onlus* and the NTP at the HCD represents the first attempt aimed at improving the epidemiological assessment in the Fimela district, highlighting a high notification rate in the areas of Diofior, Palmarin, Samba dia and Fimela (Figure 2). No cases of *rpoB* mutations, the gene encoding for the β-subunit of the mycobacterial RNA polymerase and is associated to rifampicin resistance, were detected with Xpert MTB/RIF and, given the high rate of treatment success, rifampicin-resistant TB seems not to pose a threat in this setting compared with urban area of Senegal where DR-TB was 0.5% of new TB cases and 17.9% in previously treated cases in 2014, according to the National Tuberculosis Control Program.

Our results may be used to strengthen case finding and to provide social protection to more vulnerable population in other resource-constrained geographical areas [1,20,21].

The study has several limitations related to selection bias and potential confounders (e.g., environmental changes during the study period). First, before the start of the cooperation, patients were self-referred to HCD; whereas, later, patients were referred to the HCD by *badieu'ngox* during case-finding activities. Consequently, in the second phase of the study patients have been selected according to clinical manifestation. Second, data collection was stimulated at the beginning of 2013, therefore data before the intervention could be incomplete. Third, during this decade, additional changes not captured in our study may have contributed in mitigating social and economic difficulties associated with TB and its treatment completion. The implementation of road infrastructures, access to safe water and sanitation, and availability of electricity could have played a key role. However, those improvements were recently implemented, and then their contribution could have been less prominent in influencing treatment outcome. Last but not least, the so-called 'observer effect' regarding the intervention phase cannot be excluded.

Our study suggested that social protection, in the form of CTIs, is effective in improving treatment outcome in patients affected by TB, including for those HIV co-infected especially when ART is also provided. Nevertheless, additional interventions are required to further improve TB early detection and treatment outcomes, such as the implementation of strategies for TB infection diagnosis and treatment, as well as the extension of this model to similar settings [22–25].

Conclusion

Our study showed that during the implementation of a multifaceted intervention, combined with social protection and disease awareness activities, TB treatment outcome was found to improve, especially for HIV co-infected patients in a rural area of Senegal. We present a simple, self-sustainable model which could be scaled-up in other rural settings.

Summary points

- Poor tuberculosis (TB) treatment outcome affects low- and middle-income countries, especially in rural settings.
- Social protection is a key component in interrupting the cycle of TB transmission by improving TB care.
- Our intervention took place in Health Centre of Diofior serving the Fimela district of the Fatick region, Senegal between 2010 and 2019.
- Active case finding and treatment adherence was performed in villages by trained women (*badieu'ngox*).
- Social protection coupled with TB awareness displayed to play a role in reducing TB mortality and improve outcome.
- Those who benefit the most were individuals with HIV co-infection, because antiretroviral treatment was be started.

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Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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Ethical conduct of research

The study was endorsed by the NTP of Senegal on 16 August 2012 (registration no. S00257). Waiver of consent was applied due to the retrospective nature of the study.

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