

Effect of the Bolsa Familia Programme on the outcome of tuberculosis treatment: a prospective cohort study



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Summary

Background Social protection interventions might improve tuberculosis outcomes and could help to control the epidemic in Brazil. The aim of this study was to evaluate the independent effect of the Bolsa Familia Programme (BFP) on tuberculosis treatment outcomes in Brazil.

Methods We prospectively recruited and followed up individuals (aged ≥ 18 years) who initiated tuberculosis treatment at 42 health-care centres across seven cities in Brazil, between March 1, 2014, and April 30, 2017. Patients were interviewed at health-care centres and information about individual characteristics, socioeconomic status, living conditions, lifestyle, and comorbidities was recorded. Patients were separated into two groups according to BFP beneficiary status: BFP (exposed) or non-BFP (not exposed). Treatment outcome (cure, dropout, death, or development of drug-resistant tuberculosis or treatment failure) was recorded after 6 months of therapy. Pearson's χ^2 test and ANOVA were used to compare tuberculosis treatment outcomes between the two groups, and we estimated the propensity score of being a beneficiary of the BFP using a logit model. We used multinomial regression models to evaluate the effect of the BFP on tuberculosis treatment outcomes.

Findings 1239 individuals were included in the study, of whom 196 (16%) were beneficiaries of the BFP and 1043 (84%) were not. After 6 months of treatment, 912 (87%) of 1043 patients in the non-BFP group and 173 (88%) of 196 patients in the BFP group were cured of tuberculosis, 103 (10%) patients in the non-BFP group and 17 (9%) patients in the BFP group had dropped out, and 25 (3%) patients in the non-BFP group and six (3%) patients in the BFP group had died. Three (<1%) of 1043 patients in the non-BFP group developed drug-resistant tuberculosis. Being a BFP beneficiary had a positive effect for cure (average effect 0.076 [95% CI 0.037 to 0.11]) and a negative effect for dropout (-0.070 [-0.105 to 0.036]) and death (-0.002 [-0.021 to 0.017]).

Interpretation BFP alone had a direct effect on tuberculosis treatment outcome and could greatly contribute to the goals of the WHO End TB Strategy.

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Introduction

Globally, tuberculosis remains a considerable threat to public health. In 2016, the disease was the leading cause of death due to infectious disease worldwide, with an estimated 10.4 million new cases and 1.4 million deaths.¹ In Brazil, where the burden of tuberculosis is high, 66706 new tuberculosis cases and 4543 deaths attributed to tuberculosis were reported in 2016.² Although the number of tuberculosis cases, and the associated incidence and mortality in Brazil has decreased in the past 15 years, important challenges remain for sustaining improvements in tuberculosis prevention and care. For example, the rate of cure for tuberculosis is low among patients who initiate treatment and the number of patients who discontinue treatment is high. In Brazil in 2016, the rate of cure for tuberculosis was 72% and the treatment dropout rate was 10%,

exceeding that recommended by WHO (<5%),^{1,2} which might perpetuate transmission and poor patient outcomes. A crucial barrier to improving tuberculosis treatment outcomes might be associated with unaddressed socioeconomic factors that affect either patient adherence to care or effectiveness of treatment.

The association between poverty and tuberculosis is evident in the global distribution of the disease; the 30 countries with the highest burden of tuberculosis are also those with largest social inequality measures and the lowest income per capita.^{1,3} Socioeconomic conditions and social determinants are well known risks for tuberculosis infection, reactivation, and for sustaining the epidemic within populations.⁴⁻⁶ Research to address the effect of poverty on tuberculosis outcomes and to understand further how targeted interventions might reduce tuberculosis risk is a burgeoning area of research.

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Research in context**Evidence before this study**

Evidence of the impact of cash transfers on tuberculosis outcomes is highly variable. We searched the Cochrane Library for relevant articles published from database inception to April 30, 2016, using the search terms “cash transfer” and “tuberculosis treatment”. We considered studies if they investigated material incentives in patients with active or latent tuberculosis. A Cochrane review showed that, at present, insufficient evidence exists to conclude that cash transfers can improve long-term adherence to tuberculosis treatment. However, studies in Ecuador, Moldova, and Peru suggest higher rates of cure among people who were beneficiaries of cash transfers than those who were not. In Brazil, the national conditional cash transfer scheme, the Bolsa Familia Programme (BFP), provides income assistance for impoverished households on the condition that beneficiaries participate in pro-health and educational activities. BFP has been associated with improved health outcomes, including nutrition, childhood mortality, and antenatal care for recipients, but the effect of this intervention on tuberculosis outcomes remains unclear. Retrospective secondary data from Brazil have shown the potential rate of cure among BFP beneficiaries during tuberculosis treatment was 7% higher than that of patients not exposed to BFP, with no improvement in other tuberculosis outcomes. These previous analyses were dependent on datasets with few variables available to control confounders, limiting their ability to assess causal associations between cash transfers and tuberculosis outcomes.

Added value of this study

This is the first prospective study to investigate the impact of BFP, a national conditional cash transfer programme in Brazil,

on tuberculosis outcomes. The proportion of patients who were cured of tuberculosis was higher in the BFP group than the non-BFP group, which indicates the potential for a tuberculosis-sensitive social protection intervention to improve tuberculosis care. This finding is important since the global tuberculosis community has hypothesised that tuberculosis prevention and care strategies alone will not lead to achievement of the Sustainable Development Goals by 2030. Our analyses were based on a theoretical model of social determinants of tuberculosis developed by our group, which allows the assessment of direct and indirect effects of cash transfers on tuberculosis treatment outcomes. These models included adjustment for a variety of confounders and propensity score matching to prevent bias in the estimation of treatment effects from our observational data. Using propensity score matching, we evaluated paired individuals with the same attributes, who differed only in BFP beneficiary status (exposed or not exposed). Comparison of outcomes between groups demonstrates that rate of cure was higher and the proportion of patients who dropped out was lower in the BFP group than the non-BFP group.

Implications of all available evidence

Policy makers should consider optimising existing policies and resources for eligible patients with tuberculosis and reinforcing the protection of cash transfers benefits where they exist. Further studies should focus on elucidating the social and behavioural determinants that might affect the association between social protection interventions and the outcome of tuberculosis treatment, and the barriers and enablers of coverage and uptake of social benefits among individuals with low socioeconomic status and tuberculosis.

Social protection interventions aimed at reducing a patient's social or economic risk might improve tuberculosis outcomes and contribute to curbing the epidemic.⁷ Used in combination with tuberculosis prevention and care activities, social protection interventions are thought to have various synergistic effects on tuberculosis treatment outcomes.⁸ Improvement in living conditions, improved nutrition, better psychosocial health, and access to health services can reduce susceptibility to disease and improve access to good quality tuberculosis care.⁹ What is less clear is how best to implement social protection within the context of tuberculosis programmes to maximise the social, economic, and public health impact for susceptible patients.⁸ Although several studies from Nigeria,¹⁰ Moldova,¹¹ and Peru¹² have shown that financial incentives are effective in improving treatment success among patients with tuberculosis, the generalisability and use of social protection interventions is context dependent.

Brazil has one of the largest conditional cash transfer programmes in the world, focused on productive inclusion (ie, programmes aimed at alleviating poverty by increasing income and employment opportunities) termed the Brazil

Without Poverty Plan. The programme represents an unprecedented initiative to address social inequalities in Brazil,¹³ and is an extension of the Bolsa Familia Programme (BFP), which has been responsible for considerable improvements in socioeconomic conditions in Brazil since 2006.¹⁴ The BFP, a conditional cash transfer programme, provides financial aid for families defined as poor (per capita monthly income US\$25·60–51·20) with pregnant or lactating women or children and adolescents aged 17 years or younger, and all extremely poor families (per capita monthly income ≤\$25·60). The amount of money received per family is dependent on income and composition of the family, but all families receive at least a monthly basic benefit of \$25·60.¹⁵ BFP has been shown to reduce extreme poverty, alleviate social and economic inequalities,^{16,17} and improve public health outcomes, including improved nutritional status of the beneficiary population¹⁸ and reduced infant mortality.¹⁹ Lower tuberculosis incidence has been found to correlate with areas of high BFP coverage.²⁰ However, the association between BFP and tuberculosis treatment outcome remains unclear. Previously, secondary data²¹

have been retrospectively analysed to investigate the associations between BFP and tuberculosis outcomes in Brazil. These studies did not use an explicit theoretical model with adequate adjustment for confounding factors that influence treatment outcome. Therefore, the findings of these studies cannot be used to make inferences regarding the independent effect of BFP on tuberculosis treatment outcomes. Therefore, we did a prospective cohort analysis to evaluate the independent effect of BFP on tuberculosis treatment outcomes in Brazil.

Methods

Study design and participants

We did a prospective cohort study of individuals who had initiated treatment for tuberculosis at 42 health-care centres in seven cities (Manaus, Fortaleza, Recife, Salvador, Vitoria, Sao Paulo, and Porto Alegre) in Brazil between March 1, 2014, and April 30, 2017. The seven cities were selected because they had the highest incidence of tuberculosis nationally in 2012, and are highly representative of all administrative regions in Brazil, with regard to the socioeconomic and demographic composition of the population. Health-care centres were included if they had a treatment success rate for tuberculosis that was less than the WHO target of 85%, at least 20 individuals were diagnosed with tuberculosis at the centre in the year before data collection, and tuberculosis was treated in accordance with the National Tuberculosis Program of the Brazilian Ministry of Health recommendations.¹³ Health-care centres were excluded if there was an ongoing study at the health centre.

Tuberculosis was defined on the basis of at least one positive smear using acid-fast bacilli microscopy or culture or rapid molecular tuberculosis test, and also any suspected case that did not meet the laboratory confirmation criterion but presented test results or histological findings suggestive of tuberculosis (pulmonary or extra-pulmonary).²²

Participants were aged 18 years or older, had microbiological diagnosis of tuberculosis by sputum smear microscopy and culture or Xpert MTB/RIF assay (Cepheid, Sunnyvale, CA, USA) and had initiated treatment for tuberculosis. Individuals who had resistant or multidrug-resistant tuberculosis, had been treated for more than 6 months for a previous episode of tuberculosis, or had received treatment in another unit for more than 30 days were excluded. Previously trained health-care workers enrolled participants during their visits to the health-care centres. Individuals were interviewed at the time of treatment initiation. All individuals provided written informed consent. The study was approved by the ethics committee of the Federal University of Espirito Santo.

Procedures

All participants were prospectively followed up for the entire tuberculosis treatment course. Trained health-care

workers did surveys and health assessments at enrolment, and during the second and sixth month of tuberculosis treatment, with the exception of Salvador, where data collection was coordinated by a team from the Federal University of Bahia (Salvador, Brazil). Information about individual characteristics (sex, age, ethnicity), socioeconomic status (years of education, occupational status, monthly income, household goods), living conditions (sewerage system, waste collection, housing conditions), current lifestyle (smoking status, alcohol use, and illicit drug use), comorbidities (eg, HIV or AIDS, diabetes, kidney disease), anthropometric data, allergies, presence of bacillus Calmette-Guérin scar, previous history of tuberculosis (date of diagnosis, disease type, pharmaceutical regimen, results of examination during treatment, adverse drug reactions, response to directly observed therapy), and coverage of health insurance and receipt of social benefit (type, values) was recorded.

Treatment outcome was recorded after 6 months of therapy, when a patient is expected to be cured by the basic regimen of tuberculosis treatment. If the individuals did not complete the treatment within 6 months, they were followed up with monthly visits at the health centres until treatment completion (according to medical criteria) or if follow-up was not possible, they were removed from the study. The treatment outcome of individuals who transferred to another health service or municipality not included in the study during treatment was recovered via requests from the municipal health secretaries of each capital.

Receipt of cash transfers through the BFP was the main exposure of interest. Participants were classified as exposed (ie, BFP beneficiaries) or not exposed (ie, individuals who did not receive cash transfers from the BFP).

Outcomes were based on definitions adopted by the Brazilian Ministry of Health¹³ and were classified as favourable or unfavourable. Cure was defined as a favourable outcome, whereas dropout (treatment interrupted for ≥ 30 days), death during tuberculosis treatment from any cause, and development of drug-resistant tuberculosis or treatment failure (culture-confirmed resistance to streptomycin, isoniazid, rifampicin, or ethambutol) were defined as unfavourable outcomes. Cure was defined as medical discharge of individuals with pulmonary tuberculosis who completed their treatment and had two negative sputum smear tests, or clinical improvement and normal physical examination in patients for whom sputum smear testing was not done. Patients with extra-pulmonary tuberculosis were considered to be cured when they completed their treatment and had clinical improvement, radiological evidence, or other complementary examinations.

Statistical analysis

We required a sample size of 1200 to detect a difference in treatment outcomes of 10% between individuals that

	Non-BFP (n=1043)	BFP (n=196)	p value*
Sex			0.753
Men	513 (49%)	94 (48%)	
Women	530 (51%)	102 (52%)	
Age (years)	40 (29–53)	35 (26–45)	<0.0001
Skin colour			0.002
White	299 (29%)	33 (17%)	
Black	233 (22%)	54 (27%)	
Brown	498 (48%)	109 (56%)	
Indigenous	13 (1%)	0 (0%)	
Education (years)			<0.0001
0–3	213 (20%)	42 (21%)	
4–7	255 (24%)	63 (32%)	
8–10	170 (16%)	43 (22%)	
11–14	317 (31%)	46 (24%)	
>14	88 (9%)	2 (1%)	
Occupation			0.006
Employed or student	593 (57%)	94 (48%)	
Unemployed	316 (30%)	82 (42%)	
Retired	134 (13%)	20 (10%)	
Individual income (US\$)	241 (90–392)	160 (0–265)	<0.0001
Sewage system	958 (92%)	168 (86%)	0.006
Waste collection	1007 (97%)	184 (94%)	0.146
Lifestyle			
Tobacco smoker	175 (17%)	26 (13%)	0.221
Alcohol use	300 (29%)	48 (24%)	0.222
Illicit drug use	120 (12%)	33 (17%)	0.037
HIV or AIDS	339 (32%)	64 (33%)	0.967
Comorbidities†	199 (19%)	40 (20%)	0.665
Health insurance	246 (24%)	14 (7%)	<0.0001

Data are n (%) or median (IQR). BFP=Brasilia Familia programme. *Pearson's χ^2 test was used to compare proportions and ANOVA was used to compare medians.
†Excluding HIV or AIDS.

Table 1: Baseline characteristics of the study population

received cash transfers from the BFP (BFP group) and those that did not receive BFP (non-BFP) with 86% power with 5% significance (appendix).

In our study database, tuberculosis treatment outcome as a variable had the highest frequency of missing data (14%). The mean proportion of missing data for other variables was 5%. We imputed missing data using the missForest algorithm. Random forest is an ensemble learning method that combines the predictions from multiple decision trees to produce more accurate predictions.²³ We used MICE random forest with 1000 trees. The imputation analysis was done using the R Project program (version 3.3.3).

Categorical variables including sex, ethnicity, years of education, occupation, sewerage system, waste collection, lifestyle, HIV or AIDS, comorbidities, and health insurance were presented as absolute and relative frequencies (%). Continuous variables (age and individual income) were presented as median (IQR). Pearson's χ^2 test was used

	Non-BFP (n=1043)	BFP (n=196)	p value*
Cure	912 (87%)	173 (88%)	0.774
Dropout	103 (10%)	17 (9%)	..
Death	25 (3%)	6 (3%)	..
Drug-resistant tuberculosis	3 (0%)	0 (0%)	..

Data are n (%). *Pearson's χ^2 test was used to compare proportions between the two groups for all outcomes.

Table 2: Tuberculosis treatment outcome among the study population

to compare the differences between proportions for categorical variables and ANOVA was used to compare differences between medians for continuous variables.

The variables included in the data analysis were selected a priori on the basis of a directed acyclic graph, which shows how variables potentially confound the direct effect of BFP on tuberculosis treatment outcome.

Propensity score indicates the probability of an individual being allocated to the exposed or non-exposed group on the basis of the covariates measured.²⁴ Since BFP allocation was not random, a single comparison between beneficiaries and non-beneficiaries is not appropriate, because the effect of BFP could be associated with background characteristics, which might differ between groups. Thus, we used propensity score matching to overcome this limitation, which estimates the conditional probability of an individual being a beneficiary, according to their observed characteristics.²⁴ We estimated the propensity score of being a BFP beneficiary using a logit model. The predictors in the propensity score model included the minimal number of variables needed to estimate the direct effect of the BFP on tuberculosis treatment outcome, according to the directed acyclic graph: socioeconomic status (household goods, years of education, monthly individual income, and unemployment), environmental characteristics (waste collection and house condition), behaviour (smoking status and illicit drug use), comorbidities, and access to health-care services (private health insurance and type of health-care service during treatment).

We used multinomial regression models to assess the effect of the BFP on tuberculosis treatment outcomes, which included cure as the reference category. The first model was unadjusted, the second model was adjusted by a minimal set of variables identified in the directed acyclic graph, and the third model was adjusted by the estimated propensity score as a continuous variable. To verify the performance of the built propensity score, the second and the third models were compared. The estimation of variance–covariance matrix of all models was accounted for by the clustered distribution of our sample.

The average effect of being a BFP beneficiary on tuberculosis treatment outcome was estimated by a logistic model using propensity score matching^{25,26} in a

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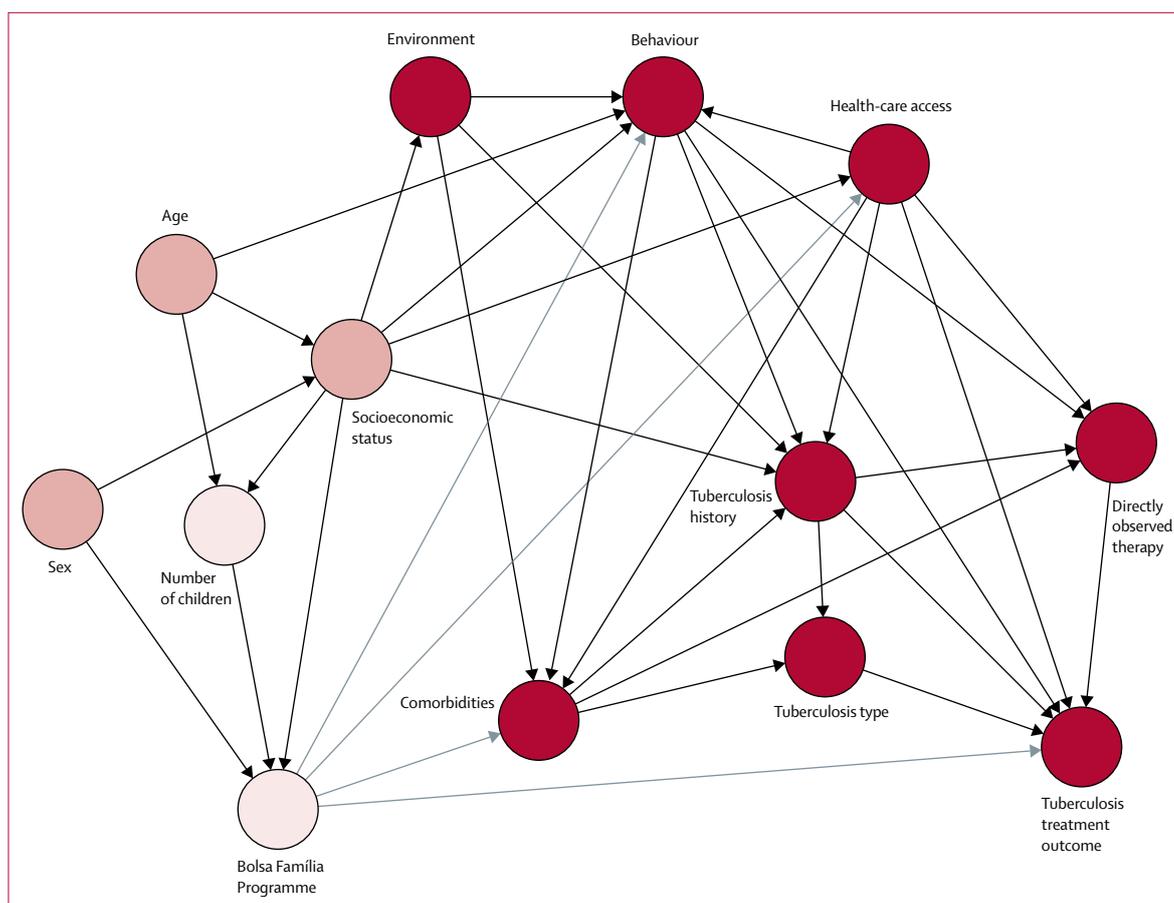


Figure 1: Direct acyclic graph of the association between being a beneficiary of the Bolsa Familia Programme and tuberculosis treatment outcome

The directed acyclic graph was built based on models by Hernan and Robins²⁷ and on a previous theoretical model used to determine tuberculosis treatment outcomes.^{8,28} This strategy uses sets of arrows to characterise causal associations between exposures and outcomes and, additionally, identify relationships among covariates that influence the exposure or outcome. In this type of graph, causes are often referred to as ancestors. In this way, the directed acyclic graph allowed us to select an appropriate set of confounding variables as well as to identify collider variables on a non-causal or biasing pathway, to be retained within the model.^{27,29} Light red circles indicate ancestors of exposure. Dark red circles indicate ancestors of outcome. Red circles indicate ancestors of exposure and outcome. Grey lines indicate a causal pathway. Black lines indicate a biasing pathway.

1:1 ratio (pairs of observations were considered a match if the absolute difference in the propensity score was <0.05). In this analysis, outcomes were dichotomous (cure vs not cured; dropout vs not dropout; and death vs not death). The propensity score balance was analysed before and after matching. Statistical analysis was done using Stata (version 14.0).

Role of the funding source

The funders of the study had no role in study design, data collection, data interpretation, or writing of the report. The corresponding had full access to all the data in the study and had final decision to submit for publication.

Results

We enrolled 1252 individuals, of whom 13 were excluded during the follow-up period because they were diagnosed with another disease and thus were considered false-positives. We included 1239 individuals in the analysis,

of whom 196 (16%) were beneficiaries of the BFP and 1043 (84%) were not. Baseline characteristics of the study population are shown in table 1.

After 6 months of treatment, 912 (87%) of 1043 patients in the non-BFP group and 173 (88%) of 196 patients in the BFP group were cured of tuberculosis, 103 (10%) patients in the non-BFP group and 17 (9%) patients in the BFP group had dropped out, and 25 (3%) patients in the non-BFP group and six (3%) patients in the BFP group had died (table 2). Three ($<1\%$) of 1043 patients in the non-BFP group developed drug-resistant tuberculosis.

We identified the minimum number of variables required to test the hypothesis of a direct BFP effect on tuberculosis treatment outcomes (figure 1). Multinomial regression models using cure as the reference category showed that the relative risk of dropping out was 0.65 (95% CI 0.41–1.03) and the relative risk of death was 1.13 (0.31–4.12) in the BFP group when compared with the non-BFP group (table 3).

	Cure	Dropout	Death
Unadjusted RR (95% CI)	1 (ref)	0.97 (0.63–1.47)	1.60 (0.58–4.42)
Adjusted RR (95% CI)*	1 (ref)	0.62 (0.37–1.05)	1.14 (0.31–4.18)
Adjusted RR (95% CI)†	1 (ref)	0.65 (0.41–1.03)	1.13 (0.31–4.12)

RR=relative risk. *Adjusted for socioeconomic status (household goods, years of education, monthly individual income, and unemployment), environmental characteristics (waste collection and house condition), behaviour (smoking status and illicit drugs use), comorbidities, and health-care services access (private health insurance and type of health-care service during treatment). †Adjusted for continuous propensity score estimated by socioeconomic status (household goods, education, monthly individual income, and unemployment), environmental characteristics (waste collection and house condition), behaviour (smoking status and illicit drug use), comorbidities and health-care services access (private health insurance and type of health-care service during treatment).

Table 3: Unadjusted and adjusted multinomial logistic regression analysis of the association of being a beneficiary of the Bolsa Familia Programme and tuberculosis treatment outcomes

	Coefficient	95% CI	p value
Cure	0.076	0.037 to 0.116	<0.0001
Dropout	-0.070	-0.105 to -0.036	<0.0001
Death	-0.002	-0.021 to 0.017	0.836

*Calculated with a logistic model using propensity score (estimated by the predictors: index of household goods, education, monthly individual income, unemployment, waste collection, house condition, current tobacco smoke, illicit drug use, comorbidities, private health insurance, and type of health-care service during treatment) matching in a 1:1 ratio.

Table 4: Average effect* of being a beneficiary of the Bolsa Familia Programme on the outcome of tuberculosis treatment

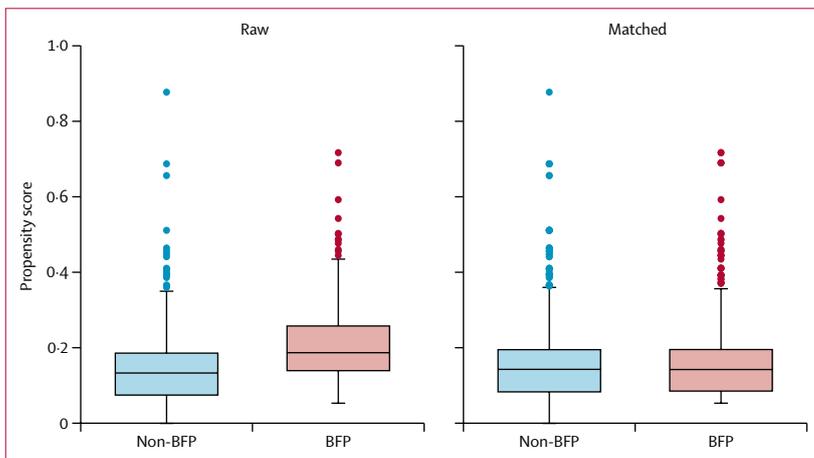


Figure 2: Box plots of propensity scores before and after matching in the BFP and non-BFP groups Box and whiskers plots indicate median with IQR (boxes) and range (whiskers). Dots are statistical outliers. BFP=Bolsa Familia Programme.

Being a BFP beneficiary had a positive effect for cure (average effect 0.076 [95% CI 0.037 to 0.116]) and a negative effect for dropout (-0.070 [-0.105 to -0.036]) and death (-0.002 [-0.021 to 0.017]; table 4). These results indicate that the rate of cure is 7.6% higher in the BFP group than the non-BFP group and the proportion of patients who dropped out was 7% lower in

the BFP group than the non-BFP group. To estimate the average effect of the BFP on treatment outcomes, individuals were matched according to propensity score (figure 2), which increased the comparability of the groups.

Discussion

Patients who were BFP beneficiaries were more likely to be younger, to be of mixed race, to use illicit drugs, to be less educated, and to have a lower individual monthly income, and were less likely to have health insurance than patients who were not BFP beneficiaries. Beneficiaries of BFP demonstrated greater social vulnerability providing justification for the programme. Families living in poverty not only have a low income, but have fewer opportunities to improve living conditions because their access to education is limited, which subsequently affects employment opportunities. In Brazil, more than 80% of adults (aged >25 years) from families who are beneficiaries of BFP are poorly educated (15.8% are illiterate and 65.3% do not complete primary school), which reduces employment opportunities and limits access to public utility services.³⁰ Our results also demonstrated an association between individuals who dropped out and poor education, unemployment, and use of illicit drugs. Our data highlight the social and economic disadvantages experienced by patients with tuberculosis (with or without BFP), supporting the rationale for interventions that address these potentially unmet social needs.

Although the proportion of patients in the BFP and non-BFP groups who were cured of tuberculosis was not significantly different (87% in the non-BFP group vs 88% in the BFP group, p=0.774), propensity score matching showed that rate of cure was 7.6% higher in the BFP group than the non-BFP group and the proportion of patients who dropped out was 7% lower in the BFP group than the non-BFP group. Additionally, the prospective study design, which included face-to-face interviews enabled the production of a directed acyclic graph with a large number of variables that demonstrated a causal association between exposure (BFP group) and outcome (outcome of tuberculosis treatment). This method enabled adjustment for a large number of comorbidities, such as those associated with socioeconomic status, environmental characteristics, and behaviour. In this analysis, a small difference was identified between the adjusted models and non-adjusted models for these variables. The comparison of adjusted and unadjusted models increased the reliability of our results.

Our results are consistent with those of previous studies,¹⁰⁻¹² which investigated the effect of incentives as a method of social protection on the outcomes of tuberculosis treatment in low-income countries. A study in Nigeria¹⁰ showed that patients with tuberculosis who received \$15 per month during treatment had a success rate that was approximately 15% higher than those who

did not receive the incentive ($p=0.003$). This effect might have been partly due to the lower proportion of patients who were lost to follow-up in the group who received the incentive than the control group during the intervention period (20.2% vs 5.0%, $p<0.001$). Similar results were reported in a retrospective cohort study done in Moldova,¹¹ which showed that provision of incentives (eg, cash, food vouchers, travel reimbursement) to patients with tuberculosis significantly improved treatment success rates by approximately 10%. Loss to follow-up (5% vs 10%, $p<0.001$), death (5% vs 6%, $p=0.03$), and failure (2% vs 5%, $p<0.001$) were also lower in the group receiving social protections than the group that did not receive them. A randomised controlled study in Peru¹² evaluating the effect of conditional cash transfers (\leq \$230 per household) aimed at enhancing tuberculosis prevention and treatment, showed that cash transfers improved treatment outcomes: 64% of patients in the intervention group versus 53% in the control group were treated successfully (unadjusted odds ratio 1.6 [95% CI 1.0–2.6]). These studies demonstrate the potential impact of novel financial incentives or social support in improving tuberculosis treatment outcomes in a variety of social contexts.

A limitation of the study was non-random selection of BFP beneficiaries, which prevented comparison of the non-BFP and BFP groups because the effect of BFP could be associated with background characteristics that might vary between groups. We used a logistic model with propensity score matching^{25,26} to verify the average effect of BFP on the outcome of tuberculosis treatment as a strategy to overcome this limitation.

Our results show that BFP alone appears to be sufficient to have a direct effect on tuberculosis treatment outcome. One hypothesis is that this effect could increase even further if the programme specifically targeted patients with tuberculosis in addition to families of low socioeconomic status. Additionally, the number of BFP recipients in the population who have tuberculosis is low (only 13.1% of patients with tuberculosis are BFP beneficiaries²¹), highlighting the need for implementation of health policies and programmes to reduce and minimise the negative effects of poverty on tuberculosis treatment outcomes. A key component of the WHO End Tuberculosis Strategy and the UN Sustainable Development Goals agenda is to improve the health and wellbeing of individuals through multisectorial interventions that jointly address issues of health and poverty. Modelling studies demonstrate that global expansion of social protections could decrease the incidence of tuberculosis by 76%.³¹ Social protection interventions, including expansion of existing programmes such as the BFP, could be a crucial for achieving these goals.

Contributors

BR-S, MNS, and ELNM conceptualised and designed the study. JGNO, BR-S, RLL, CMMS, WGdSF, KCdS, KVfDA, GSdA, SMP, and ELNM collected data. KVfDA, GSdA, and SMP developed the questionnaires.

BR-S analysed and interpreted data. JGNO, RLL, CMMS, WGdSF, and KCdS drafted the manuscript. BR-S, MNS, PBS, LWR, CL, and ELNM revised the Article critically for important intellectual content. All authors approved the final version of the manuscript.

Declaration of interests

We declare no competing interests.

Acknowledgments

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References

- 1 WHO. Global tuberculosis report 2016. Geneva: World Health Organization, 2016.
- 2 Brasil Ministério da Saúde. Secretária de Vigilância em Saúde. Indicadores prioritários para o monitoramento do Plano Nacional pelo Fim da Tuberculose como Problema de Saúde Pública no Brasil. Boletim Epidemiológico, 2017. http://bvsms.saude.gov.br/bvs/publicacoes/brasil_livre_tuberculose_plano_nacional.pdf (accessed June 23, 2017).
- 3 The World Bank. World Bank country and lending groups. 2016. <https://datahelpdesk.worldbank.org/knowledgebase/articles/906519> (accessed March 6, 2017).
- 4 Maciel EL, Reis-Santos B. Determinants of tuberculosis in Brazil: from conceptual framework to practical application. *Rev Panam Salud Publica* 2015; **38**: 28–34.
- 5 Lönnroth K, Jaramillo E, Williams BG, Dye C, Ravignone M. Drivers of tuberculosis epidemics: the role of risk factors and social determinants. *Soc Sci Med* 2009; **68**: 2240–46.
- 6 Dye C, Lönnroth K, Jaramillo E, Williams BG, Ravignone M. Trends in tuberculosis incidence and their determinants in 134 countries. *Bull World Health Organ* 2009; **87**: 683–91.
- 7 Lönnroth K, Glaziou P, Weil D, Floyd K, Uplekar M, Ravignone M. Beyond UHC: monitoring health and social protection coverage in the context of tuberculosis care and prevention. *PLoS Med* 2014; **11**: 1001693.
- 8 Hargreaves JR, Boccia D, Evans CA, Adato M, Petticrew M, Porter JDH. The social determinants of tuberculosis: from evidence to action. *Am J Public Health* 2011; **101**: 654–62.
- 9 Boccia D, Hargreaves J, Lönnroth K, et al. Cash transfer and microfinance interventions for tuberculosis control: review of the impact evidence and policy implications. *Int J Tuberc Lung Dis* 2011; **2**: 37–49.
- 10 Ukwaja KN, Alobu I, Gidado M, Olajumoke O, Oshi DC. Intervention of economic support improves outcomes of tuberculosis treatment in rural Nigeria. *Int J Tuberc Lung Dis* 2017; **21**: 564–70.
- 11 Ciobanu A, Domete L, Soltan V, et al. Do incentives improve tuberculosis treatment outcomes in the Republic of Moldova? *Public Health Action* 2014; **4**: 59–63.
- 12 Wingfield T, Tovar MA, Huff D, et al. A randomized controlled study of socioeconomic support to enhance tuberculosis prevention and treatment, Peru. *Bull World Health Organ* 2017; **95**: 270–80.
- 13 Brasil Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância Epidemiológica. Manual de Recomendações para o controle da Tuberculose no Brasil. Brasília: Ministério da Saúde, 2011.
- 14 Paim J, Travassos C, Almeida C, Bahia L, Macinko J. The Brazilian health system: history, advances, and challenges. *Lancet* 2011; **377**: 1778–97.
- 15 Ministério do Desenvolvimento Social e Agrário. Bolsa Família: como funciona. Assistência Social. 2015. <http://mds.gov.br/assuntos/bolsa-familia/o-que-e/como-funciona> (accessed March 10, 2017).
- 16 Ministério do Desenvolvimento Social e Combate à Fome. Secretaria Nacional de Renda de Cidadania—Programa Bolsa Família: uma década de inclusão e cidadania. 2013. http://www.ipea.gov.br/portal/images/stories/PDFs/livros/livros/livro_bolsafamilia_10anos.pdf (accessed June 23, 2017).
- 17 Hoffmann R, Ney MG. The recent fall in income inequality in Brazil: analysis of PNAD data, demographic censuses and national accounts. *Económica* 2008; **10**: 7–39 (in Portuguese).
- 18 Santos ML, Vendramini SHF, Gazetta CE, Oliveira SAC, Villa TCS. Pobreza: caracterização socioeconômica da tuberculose. *Rev Latino Am Enfermagem* 2007; **15**: 762–67.

- 19 Rasella D, Aquino R, Santos CA, et al. Effect of a conditional cash transfer programme on childhood mortality: a nationwide analysis of Brazilian municipalities. *Lancet* 2013; **382**: 57–64.
- 20 Nery JS, Rodrigues LC, Rasella D, et al. Effect of Brazil's conditional cash transfer programme on tuberculosis incidence. *Int J Tuberc Lung Dis* 2017; **21**: 790–96.
- 21 Torrens AW, Rasella D, Bocchia D, et al. Effectiveness of a conditional cash transfer programme on TB cure rate: a retrospective cohort study in Brazil. *Trans R Soc Trop Med Hyg* 2016; **110**: 199–206.
- 22 Ministério da Saúde. Secretaria de Vigilância em Saúde. Coordenação-Geral de Desenvolvimento da Epidemiologia em Serviços. Guia de Vigilância em Saúde. 2ª edição. Brasília: Ministério da Saúde, 2017.
- 23 Shah AD, Bartlett JW, Carpenter J, et al. Comparison of random forest and parametric imputation models for imputing missing data using MICE: a CALIBER study. *Am J Epidemiol* 2014; **179**: 764–74.
- 24 Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivar Behav Res* 2011; **46**: 399–424.
- 25 Dehejia RH, Wahba S. Propensity score-matching methods for nonexperimental causal studies. *Rev Econ Stat* 2002; **84**: 151–61.
- 26 Hirano K, Imbens GW, Ridder G. Efficient estimation of treatment effects using the estimated propensity score. *Econometrica* 2003; **71**: 1161–89.
- 27 Hernan MA, Robins JM. Causal inference. Boca Raton: CRC Press, 2017.
- 28 Maciel EL, Reis-Santos B. Determinants of tuberculosis in Brazil: from conceptual framework to practical application. *Rev Panam Salud Publica* 2015; **38**: 28–34.
- 29 Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. *Epidemiology* 1999; **10**: 37–48.
- 30 Ministério do Desenvolvimento Social e Combate à Fome. Instituto de Pesquisa Econômica Aplicada (Ipea). Bolsa Família 2003–2010: avanços e desafios. Brasília: Ipea, 2010.
- 31 Carter DJ, Glaziou P, Lönnroth K, et al. The impact of social protection and poverty elimination on global tuberculosis incidence: a statistical modelling analysis of Sustainable Development Goal 1. *Lancet Glob Health* 2018; **6**: e514–22.