Cash interventions to improve tuberculosis outcomes

Aaron Richterman, Jonathan Steer-Massaro, Jana Jarolimova, Liem Binh Luong Nguyen, Jennifer Werdenberg & Louise C Ivers

Department of Medicine, Brigham and Women’s Hospital, 75 Francis Street, Boston, MA 02115, United States of America (USA).
Department of Obstetrics and Gynecology, Boston University School of Medicine, Boston, USA.
Department of Medicine, Massachusetts General Hospital, Boston, USA.
Infection, Antimicrobials, Modelling and Evolution, Unité Mixte de Recherche 1137, INSERM, Paris, France.
Department of Pediatrics, Dell Children’s Hospital, Austin, USA.
Center for Global Health, Massachusetts General Hospital, Boston, USA.

Correspondence to Aaron Richterman (email: arichterman@partners.org).

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Abstract

Objective To assess cash transfer interventions for improving treatment outcomes of active pulmonary tuberculosis in low- and middle-income countries.

Methods We searched PubMed®, Embase®, Cochrane Library and ClinicalTrials.gov for studies published until 4 August 2017 that reported on cash transfer interventions during the treatment of active pulmonary tuberculosis in low- and middle-income countries. Our primary outcome was a positive clinical outcome, defined as treatment success, treatment completion or microbiologic cure. Using the purchasing power parity conversion factor, we converted the amount of cash received per patient within each study into international dollars (Int$). We calculated odds ratio (OR) for the primary outcome using a random effects meta-analysis.

Findings Eight studies met eligibility criteria for review inclusion. Seven studies assessed a tuberculosis-specific intervention, with average amount of cash ranging from Int$193–858. One study assessed a tuberculosis-sensitive intervention, with average amount of Int$101. Four studies included non-cash co-interventions. All studies showed better primary outcome for the intervention group than the control group. After excluding three studies with high risk of bias, patients receiving tuberculosis-specific cash transfer were more likely to have a positive clinical outcome than patients in the control groups (OR: 1.77; 95% confidence interval: 1.57–2.01).

Conclusion The evidence available suggests that patients in low- and middle-income countries receiving cash during treatment for active pulmonary tuberculosis are more likely to have a positive clinical outcome. These findings support the incorporation
of cash transfer interventions into social protection schemes within tuberculosis treatment programmes.

Introduction

Tuberculosis remains one of the top 10 causes of death worldwide, with the highest burden of disease in low- and middle-income countries. In these countries, the disease disproportionately affects the most vulnerable populations.

In 2015, the World Health Organization’s (WHO’s) End TB Strategy set the goal of a 90% reduction in tuberculosis deaths, an 80% reduction in tuberculosis incidence rate and zero catastrophic costs for tuberculosis-affected families by 2030. These goals explicitly acknowledge the need to both directly treat people infected with the disease and address social determinants of health to improve tuberculosis outcomes.

Social protection policies protect individuals or households during periods when they are unable to financially support themselves because of a range of conditions, such as illness or disability. Cash transfer interventions, defined as cash payments provided to selected beneficiaries by formal institutions, are one form of social protection that has been proposed in the setting of tuberculosis. Such interventions can either be tuberculosis-specific or tuberculosis-sensitive. Tuberculosis-specific interventions target directly tuberculosis patients and their households, and are typically incorporated into existing tuberculosis treatment programmes. A tuberculosis-sensitive intervention is part of a broader social protection scheme, potentially affecting tuberculosis outcomes by targeting communities and groups that are at high risk for tuberculosis. The effect on health outcomes, cost–effectiveness and feasibility of these two strategies are not well established and likely to vary based on the local social protection and health-care infrastructure.

As a review in 2011 on the effects of cash transfer interventions on tuberculosis outcomes in low- and middle-income countries was inconclusive, we assessed the current state of the evidence for such interventions. We were especially interested if cash transfer to people receiving treatment for active pulmonary tuberculosis affects their clinical outcomes.

Methods

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The review protocol is available from the corresponding author.
To identify studies on the use of cash transfer interventions during the treatment of active pulmonary tuberculosis in low- and middle-income countries, we searched the online databases PubMed®, Embase®, Cochrane Library and ClinicalTrials.gov. We used the search string “Tuberculosis” AND (“financial support” OR “token economy” OR “reimbursement” OR “economic burden” OR “incentives” OR “cash transfer” OR “enablers”) to identify studies published between the databases’ inceptions and 4 August 2017. We also manually reviewed reference lists of identified systematic reviews, relevant articles and abstracts from the Union World Conference on Lung Health 2011–2016.

**Eligibility criteria**

We considered clinical trials and observational studies published in English, Spanish or French that assessed cash transfer interventions directed at people initiating treatment for microbiologically confirmed or clinically suspected active pulmonary tuberculosis. We used the WHO definition for tuberculosis and the 2017 World Bank’s classification of low- and middle-income countries. We included studies that reported standard outcomes of treatment completion, microbiologic cure or treatment success, which includes both treatment completion and cure.

**Study selection and data collection**

After removing duplicate records, two reviewers independently screened titles and abstracts of all records for inclusion in full-text review. After screening, two different reviewers independently applied eligibility criteria to each full-text article. Two reviewers then proceeded to data extraction using a standardized form created for the study (Box 1). Disagreements were settled by consensus among all authors.

To better understand the relative amount of cash distributed in the included studies, we converted the average and maximum possible amount of cash received per patient within each study into international dollars (Int$) using the purchasing power parity conversion factor, and then adjusted for inflation into 2016 Int$ with the local inflation conversion factor. If the average amount of cash received by patients in the intervention group was not reported in the article, we contacted the authors to provide the figures.

Because tuberculosis disproportionately affects the poorest households within a given context, we estimated the average amount of cash received per patient as a proportion of annual individual income by dividing the average amount of cash received per patient by the median
income per capita of the lowest quintile of that country from the time period of the study.\textsuperscript{11} Household-level income data were not available to estimate the interventions as proportion of annual household income.

**Assessment of bias**

For the randomized study, we assessed risk of bias using the Cochrane Collaboration Risk of Bias Tool, and defined a randomized study as overall high risk of bias if the trial met criteria for high risk of bias in more than one assessed domain.\textsuperscript{13} We assessed risk of bias within non-randomized studies using the Newcastle-Ottawa Scale, defining a non-randomized study as overall high risk of bias if it had zero stars in any of the three assessed categories.\textsuperscript{14} We generated a funnel plot to evaluate publication bias for studies included in the meta-analysis.

**Data analysis**

All identified studies were included in a qualitative synthesis. After excluding studies at overall high risk of bias, we generated summary effect measures using a random effects model for our primary outcome of interest, the odds ratio (OR) of a positive clinical outcome, defined as either a treatment success; treatment completion, if a study did not report treatment success; or microbiologic cure, if a study did not report treatment success or treatment completion. If a study reported ORs adjusted for potential confounders we included these ratios in our analysis. We assessed heterogeneity by using the Cochran’s $Q$ test and the $I^2$ statistic.

Among studies included in meta-analysis, we wanted to investigate sources of heterogeneity, including average amount of cash transfer, presence of non-cash co-intervention, treatment success rate in the control group, urban or rural setting, human immunodeficiency (HIV) prevalence, multidrug resistance (MDR) or extensive-drug resistance (XDR) tuberculosis prevalence and World Bank income classification. However, there was not enough information available to complete a random effects meta-regression model using any of these variables.

We used Comprehensive Meta-Analysis software version 3 (Biostat, Inc., Englewood, United States of America) and Review Manager Version 5.3 (The Cochrane Collaboration, London, United Kingdom of Great Britain and Northern Ireland) for data analysis.
Results

Study selection
We identified 1537 publications and after removal of 639 duplicates, we screened 898 titles and abstracts yielding 100 full-text articles to be assessed for eligibility. Of these full-text articles, 92 were excluded (Fig. 1). We included eight eligible articles: one randomized control trial,\textsuperscript{15} two non-randomized intervention studies,\textsuperscript{16,17} and five observational studies,\textsuperscript{18–22} comprising a total of 21,976 subjects.

Study settings and populations
Table 1 summarizes the settings and populations of the included studies. With the exception of one study that took place in 1989–1990,\textsuperscript{17} the studies assessed cash transfer interventions between 2004 and 2015. The settings varied: one study took place in a rural clinic,\textsuperscript{17} one in a large rural secondary-care facility,\textsuperscript{16} four in urban centres,\textsuperscript{15,19–21} and two were nation-wide studies.\textsuperscript{18,22} Three of the studies took place in countries currently on the WHO list of high-burden countries for tuberculosis\textsuperscript{16,19,22,23} and two other studies were in a country currently considered high burden for MDR tuberculosis.\textsuperscript{15,21}

One study focused on migrant workers, a high-risk group within an urban centre.\textsuperscript{19} The remaining studies evaluated all tuberculosis patients identified within a given geographic or clinical service area. The control groups were either patients randomized to the non-intervention group,\textsuperscript{15} living in a non-intervention area,\textsuperscript{17,19} historical controls from the same population before the implementation of the intervention,\textsuperscript{16,18,21} eligible for the intervention but not yet receiving cash because of administrative delay\textsuperscript{22} or not eligible for the intervention because of insufficient financial need.\textsuperscript{20}

Prevalence of HIV seropositivity among the study populations was 0–15\% in the six studies reporting the outcome.\textsuperscript{15,16,14,17,18,22} Patients with MDR/XDR tuberculosis were excluded from four studies,\textsuperscript{16,18,19,22} two studies reported low prevalence (1–9\%),\textsuperscript{15,20} while two did not report on drug susceptibility.\textsuperscript{17,21} Five studies reported free care for tuberculosis,\textsuperscript{15,17,19,21,22} with the others not specifically commenting on the cost of care.\textsuperscript{16,18,20} Participants in seven studies received the WHO recommended directly observed therapy, short-course.\textsuperscript{24}

Tuberculosis-specific interventions
In total, seven studies evaluated tuberculosis-specific cash transfer interventions (Table 2).\textsuperscript{15–21} Six of these studies were at least partially conditional on clinic attendance or treatment
completion,\textsuperscript{15–20} and one did not report whether the intervention was conditional.\textsuperscript{21} Four studies described an additional transportation reimbursement.\textsuperscript{17–19,21}

Four studies did not report the average amount of cash received by patients in the intervention group. We contacted the authors of these studies and authors of two studies provided the amount,\textsuperscript{16,18} while this information was not available for other studies.\textsuperscript{19,20} The average amount of cash distributed ranged from Int$ 193–858. Two studies chose the amount of cash based on previous work estimating local tuberculosis-associated household costs,\textsuperscript{15,16} including the CRESIPT project in Peru, the only identified randomized control trial.\textsuperscript{15} The CRESIPT project distributed cash using bank deposit (hypothesizing that opening a bank account was empowering to the study subjects),\textsuperscript{15} whereas other studies used actual cash\textsuperscript{16,17,19,20} or did not report method of delivery.\textsuperscript{18,21} Four studies included some additional non-cash co-intervention, including home visits, community meetings, food vouchers and psychological intervention.\textsuperscript{15,17,18,21}

**Tuberculosis-sensitive interventions**

Only one study described a tuberculosis-sensitive intervention, a nation-wide retrospective cohort study in Brazil of tuberculosis patients in the *Bolsa Familia* programme. The programme is a monthly cash transfer to poor people that is conditional on attending antenatal care, nutrition and vaccine monitoring for their children and that their young children attend school.\textsuperscript{22} People with newly diagnosed non-MDR tuberculosis who received cash during treatment were compared to those who were eligible for cash at the time of treatment but did not receive it because of administrative delays. The average amount of total cash delivered to the intervention group was Int$ 101, representing an estimated 3.1\% of annual individual income. Cash could be claimed by the patient monthly using a designated bank card.

**Outcomes**

Most studies (5) reported the primary outcome of treatment success,\textsuperscript{15,16,18–20} one reported treatment completion\textsuperscript{21} and two reported microbiologic cure (Table 3).\textsuperscript{17,22} Four studies controlled for potential confounders.\textsuperscript{16,18,19,22} Two of the three studies that reported loss to follow-up found significantly less loss to follow-up in the intervention group.\textsuperscript{15,16,18} Of the four studies which reported mortality, none found a difference between the intervention and control groups.\textsuperscript{15–18}
Bias

Table 4 shows the risk of bias within individual observational studies and three studies met criteria for high overall risk of bias.\cite{17,20,21} We deemed the randomized control trial\cite{15} not to have a high overall risk of bias, as only the domain attrition showed high risk: 37% (105/282) of patients were lost to follow-up or not evaluated. The other six domains had a low risk. The funnel plot of studies included in meta-analysis did not show evidence of publication bias (Fig. 2; available at: http://www.who.int/bulletin/volumes/96/##/##-#####).

Summary effect measures

Fig. 3 shows the forest plot of the remaining tuberculosis-specific studies after excluding studies at high overall risk of bias. Patients receiving tuberculosis-specific cash transfer were more likely to have a clinical positive outcome than patients in the control groups (OR: 1.77; 95% confidence interval: 1.57–2.01), with $I^2 = 0\%$ ($Q$ test $P = 0.44$).

Discussion

The findings of this systematic review and meta-analysis suggest that cash transfer interventions for patients in low- and middle-income countries initiating tuberculosis treatment may improve clinical outcomes. All studies reported improvement in treatment outcomes. However, the overall evidence is weak because we only identified one eligible randomized control trial. Additionally, half of the studies included some non-cash co-intervention and thus some of the positive effects seen may be related to the pooled effects of cash and non-cash interventions.

There are several possible mechanisms by which cash transfer interventions may improve clinical outcomes for tuberculosis patients during treatment.\cite{6,25} Both tuberculosis-specific and tuberculosis-sensitive cash transfer interventions can act as direct poverty-reduction measures by offsetting costs caused by the disease. These costs include both direct costs of treatment such as clinic fees, medication costs, travel and/or food, as well as indirect costs incurred through loss of wages. In particular, catastrophic costs, defined as tuberculosis-related costs which exceed 20% of the household’s annual income, have been associated with adverse clinical outcomes.\cite{1,2,26} Two studies have found that, on average, a person with tuberculosis in a low- and middle-income country will experience catastrophic costs as a result of the illness.\cite{2,27} In this review, one tuberculosis-specific intervention provided cash equivalent to 173% of estimated annual individual income,\cite{17} four provided cash equivalent to 10–20% of estimated annual individual income,\cite{15,16,18,21} and two of these studies also reported the intervention as percentage of annual household income, between 3–6%.\cite{15,21} The single tuberculosis-sensitive intervention we
identified provided cash equivalent to 3.8% of estimated annual individual income. The difference between tuberculosis-specific and tuberculosis-sensitive interventions may reflect the findings that sensitive interventions are less likely to be effective and affordable by countries for offsetting tuberculosis-associated catastrophic costs than specific interventions.\textsuperscript{27} However, tuberculosis-sensitive interventions also have the advantage of a broader poverty reduction impact, which might improve household economic resilience before a household member develops active tuberculosis infection.

Beyond simply offsetting costs, cash transfer interventions may also serve as an additional incentive for health-seeking behaviour, particularly when distribution is conditional on clinical follow-up or medication adherence.\textsuperscript{28–30} Several systematic reviews have found a positive effect of conditional cash transfers in low- and middle-income countries on health behaviours and outcomes, including increased use of preventative services, improved childhood nutritional status, decreased self-reported episodes of illness and decreased HIV prevalence.\textsuperscript{25,30,31} Another systematic review found that the impact of unconditional cash transfers on health services use and health outcomes was uncertain.\textsuperscript{28} None of the interventions we identified had a completely unconditional cash transfer intervention. The incentive of a conditional intervention may be particularly important in tuberculosis care, where consistent adherence to a multiple-drug regimen for a prolonged treatment course is essential for optimal treatment outcomes. However, a meta-analysis of the effect of incentives and/or enablers on medication adherence in tuberculosis was largely inconclusive, but primarily identified studies in high-income countries, where financial interventions may have less effect.\textsuperscript{32} Tuberculosis-sensitive interventions are likely to lack a tuberculosis-specific incentive, although they may include other conditional elements unrelated to tuberculosis, as in the case of the \textit{Bolsa Familia} programme.\textsuperscript{22}

The study designs between the studies included in the review showed substantial heterogeneity. However, there was no measured heterogeneity within the subset of studies with tuberculosis-specific interventions that were not at high overall risk of bias. Although factors related to the population, setting and intervention could cause heterogeneity in the effect size of the interventions, the available information from the limited number of studies did not allow us to determine the impact of these variables.

Whether cash transfers or goods and services, such as direct provision of food, vocational training, psychologic support and housing programmes, are preferable to improve health-related
and other outcomes is currently under debate.\textsuperscript{33–35} A recent meta-analysis found that non-cash socioeconomic interventions, predominantly food provision, may improve clinical outcomes in active tuberculosis.\textsuperscript{36} To better understand which forms of social protection are most effective at improving clinical outcomes for tuberculosis, non-cash strategies should be studied comparatively and in combination with cash transfer interventions.

While beyond the scope of this review, the impact of cash transfer interventions on household and national or subnational outcomes, like contact screening and overall tuberculosis incidence, must also be considered. For example, a multivariable analysis found that municipalities in Brazil with higher coverage by the \textit{Bolsa Familia} programme had a significant reduction in tuberculosis incidence compared to those with lower coverage.\textsuperscript{37}

In conclusion, we found some evidence that cash transfer interventions improve treatment outcomes in patients with active pulmonary tuberculosis in low- and middle-income countries, although the overall quality of this evidence is low. These findings support calls by WHO and others to incorporate cash transfer interventions into social protection schemes within tuberculosis treatment programmes.\textsuperscript{1,6} In addition, high-quality research is needed to better understand the effectiveness of tuberculosis-specific and tuberculosis-sensitive cash transfer interventions, including understanding of the optimal amount, conditional feature, delivery method and implementation strategy.

\textbf{Acknowledgements}
JJ, LBN and JW contributed equally to this work.

\textbf{Competing interests:}
None declared.

\textbf{References}


35. Leroy JL, Gadsden P, Rodríguez-Ramírez S, de Cossío TG. Cash and in-kind transfers in poor rural communities in Mexico increase household fruit, vegetable, and micronutrient consumption but also lead to excess energy consumption. J Nutr. 2010 Mar;140(3):612–7. https://doi.org/10.3945/jn.109.116285 PMID:20089777


### Box 1. Type of data extracted from identified studies on cash interventions to improve tuberculosis outcome

We extracted data on location; urban and rural setting; time frame; study design; number of subjects; age and gender of participants; HIV prevalence; number with microbiologically confirmed tuberculosis; number with confirmed or suspected MDR and XDR tuberculosis; type of usual care for tuberculosis; annual individual or household income; whether the intervention was conditional; tuberculosis-specific or sensitive intervention; concurrently implemented co-interventions; primary and secondary outcomes.

HIV: human immunodeficiency virus; MDR: multidrug resistant; XDR: extensively-drug resistant.
Table 1. Design, setting and population of included studies in the systematic review on cash interventions to improve tuberculosis clinical outcomes, 1991–2017

<table>
<thead>
<tr>
<th>Author, publication year</th>
<th>Year of study</th>
<th>Study design and setting</th>
<th>Usual care</th>
<th>% male</th>
<th>% smear positive</th>
<th>% HIV</th>
<th>% MDR tuberculosis</th>
<th>Intervention group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tuberculosis-specific interventions</strong></td>
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</tr>
<tr>
<td>Farmer et al., 17 1991</td>
<td>1989–1990</td>
<td>Cluster non-randomized intervention study in a clinic in rural Haiti</td>
<td>Free care, no community health workers or DOTS</td>
<td>33</td>
<td>100</td>
<td>5</td>
<td>NR</td>
<td>People with newly diagnosed tuberculosis from sector adjacent to clinic</td>
<td>People with newly diagnosed tuberculosis from outside sector adjacent to clinic</td>
</tr>
<tr>
<td>Chirico et al., 20 2011</td>
<td>2004–2008</td>
<td>Retrospective cohort in one health district of Buenos Aires, Argentina</td>
<td>51% of patients receiving DOTS, cost of care NR</td>
<td>57</td>
<td>NR</td>
<td>6</td>
<td>0.91</td>
<td>All people with newly diagnosed tuberculosis reported to national tuberculosis control programme</td>
<td>People with newly diagnosed tuberculosis who did not get the intervention because deemed not to have the financial need, chosen at random among all people who did not get the intervention</td>
</tr>
<tr>
<td>Rocha et al., 21 2011</td>
<td>2007–2010</td>
<td>Cohort with historical control in eight shantytowns in Lima, Peru</td>
<td>DOTS, free care</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>People with newly diagnosed tuberculosis from households in the national tuberculosis programme where intervention had been implemented</td>
<td>People with newly diagnosed tuberculosis from households in the national tuberculosis programme where the intervention had not yet been implemented</td>
</tr>
<tr>
<td>Ciobanu et al., 18 2014</td>
<td>2008, 2011</td>
<td>Nation-wide retrospective cohort with historical control in the Republic of Moldova</td>
<td>DOTS, cost of care NR</td>
<td>69</td>
<td>36</td>
<td>3</td>
<td>0</td>
<td>Adults with drug-susceptible tuberculosis registered for treatment in 2011 (after introduction of incentives)</td>
<td>Adults with drug-susceptible tuberculosis registered for treatment in 2008 (before introduction of incentives)</td>
</tr>
<tr>
<td>Lu et al., 19 2015</td>
<td>2006–2010</td>
<td>Retrospective cohort in Shanghai, China</td>
<td>DOTS, free care</td>
<td>63</td>
<td>100</td>
<td>NR</td>
<td>0</td>
<td>Migrants treated for smear-positive pulmonary tuberculosis living in one of the eight districts providing cash</td>
<td>Migrants treated for smear-positive pulmonary tuberculosis living in one of the nine districts not providing cash</td>
</tr>
<tr>
<td>Study Authors</td>
<td>Year</td>
<td>Study Design</td>
<td>Study Setting</td>
<td>Intervention 1</td>
<td>Intervention 2</td>
<td>Cost of Care 1</td>
<td>Cost of Care 2</td>
<td>Cost 1</td>
<td>Cost 2</td>
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</tr>
<tr>
<td>Ukwaja et al., 16 2017</td>
<td>2014</td>
<td>Prospective pre-and post-intervention in a large, rural, secondary-care facility, Nigeria</td>
<td>DOTS, cost of care NR</td>
<td>54</td>
<td>55</td>
<td>15</td>
<td>0</td>
<td>All registered people receiving first-line anti-tuberculosis treatment at study site during 3-month period of intervention</td>
<td>All registered people receiving first-line anti-tuberculosis treatment at study site during 3-month period without financial package</td>
</tr>
<tr>
<td>Wingfield et al., 15 2017</td>
<td>2014–2015</td>
<td>Cluster randomized control trial in thirty-two contiguous shantytowns in Callao, Peru</td>
<td>DOTS, free care</td>
<td>62</td>
<td>70</td>
<td>5</td>
<td>9</td>
<td>People starting treatment for tuberculosis administered by the national tuberculosis programme, randomized to receive the socioeconomic support intervention</td>
<td>People starting treatment for tuberculosis administered by the national tuberculosis programme, randomized not to receive the socioeconomic support intervention</td>
</tr>
<tr>
<td>Torrens et al., 22 2016</td>
<td>2010</td>
<td>Nation-wide retrospective cohort in Brazil</td>
<td>Free diagnostics and treatment for all patients. Tuberculosis patients only enrolled into directly observed therapy if judged to be able to complete treatment</td>
<td>50</td>
<td>NR</td>
<td>7</td>
<td>0</td>
<td>People with newly diagnosed non-MDR tuberculosis recorded in the national database who received cash during treatment</td>
<td>People with newly diagnosed non-MDR tuberculosis recorded in the national database who were eligible for cash interventions but only started to receive them after treatment due to administrative delays</td>
</tr>
</tbody>
</table>

DOTS: directly observed therapy, short course; HIV: human immunodeficiency virus; MDR: multidrug resistant; NR: not reported.
<table>
<thead>
<tr>
<th>Author, year</th>
<th>Cash transfer intervention</th>
<th>Conditional intervention; method of cash delivery</th>
<th>Maximum cash, Int$&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Average cash, Int$&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Average cash as percent of annual income&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Additional interventions&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Tuberculosis-specific interventions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Daily visits by community health worker during first month. Food supplements for first 3 months. If patient did not attend appointment, someone from clinic went to household to investigate None</td>
</tr>
<tr>
<td>Farmer et al., 17, 1991</td>
<td>Monthly cash transfer and travel reimbursement</td>
<td>Mixed: travel reimbursement conditional on clinic attendance, monthly transfer not conditional because clinic staff would come to homes of patients missing clinic visits; cash Yes: clinic visits; cash delivered by bank employee after patient presented documentation of programme enrolment</td>
<td>900</td>
<td>900</td>
<td>173</td>
<td></td>
</tr>
<tr>
<td>Chirico et al., 20, 2011</td>
<td>Monthly cash during period of treatment equal to low civil service salary For patients not otherwise protected by other social safety net benefits Cash transfers for transportation, poverty reduction, and other tuberculosis-associated costs.</td>
<td></td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Microcredit loans, vocational training, microenterprise activities (e.g. raising animals, home-based manufacturing), food transfers, home visits, community workshops, psychological assessment Vouchers for food/hygiene products, other support (clothes, wood for cooking). Provided to only a subset of the intervention group None</td>
</tr>
<tr>
<td>Rocha et al., 21, 2011</td>
<td></td>
<td>NR</td>
<td>NA</td>
<td>291</td>
<td>17 (5.5)&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Ciobanu et al., 18, 2014</td>
<td>Combination of smaller monthly cash, larger cash at treatment completion, and variable transport reimbursement Monthly cash transfer and transportation subsidy</td>
<td>Yes: clinic visits and/or treatment completion; NR</td>
<td>773</td>
<td>489</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Lu et al., 19, 2015</td>
<td></td>
<td>Yes: clinic visits; cash delivered by programme staff at community health centre or district centre for disease control</td>
<td>253</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Description</td>
<td>Yes: [Activity 1]</td>
<td>[Activity 2]</td>
<td>[Activity 3]</td>
<td>[Activity 4]</td>
<td>[Activity 5]</td>
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</tr>
<tr>
<td>Ukwaja et al., 2017</td>
<td>Monthly cash transfer equivalent to median direct cost for tuberculosis care.</td>
<td>Clinic visits</td>
<td>Cash delivered at clinic by trained staff member</td>
<td>193</td>
<td>193</td>
<td>11</td>
</tr>
<tr>
<td>Wingfield et al., 2017</td>
<td>Cash transfers throughout treatment to defray average household tuberculosis-associated costs, estimated to be 10% annual household income in this setting</td>
<td>Details unspecified; deposit into bank account</td>
<td></td>
<td>436</td>
<td>355</td>
<td>13 (3.6)</td>
</tr>
<tr>
<td>Torrens et al., 2016</td>
<td>Monthly cash to female head of household as part of Bolsa Familia programme</td>
<td>Attendance at prenatal, postnatal monitoring sessions Nutrition and vaccine monitoring for children School attendance; Withdrawal using designated debit card distributed by programme</td>
<td>222</td>
<td>101</td>
<td>3.1</td>
<td>None</td>
</tr>
</tbody>
</table>

Int$: international dollars; NA: not available; NR: not reported.

\(^a\) We converted the average amount of cash received per patient into Int$ purchasing power parity conversion factor, and then adjusted for inflation into 2016 dollars with the local inflation conversion factor.\(^11\)

\(^b\) Estimated percentage of annual individual income, unless otherwise specified

\(^c\) Additional interventions did not involve cash.

\(^d\) Reported percentage of annual household income.
Table 3. Outcomes of included studies in the systematic review on cash interventions to improve tuberculosis clinical outcomes, 1991–2017

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Outcome indicatora</th>
<th>Sample size</th>
<th>No. patients of with primary outcome</th>
<th>OR (95% CI)</th>
<th>Adjusted covariates</th>
<th>Secondary outcomes (intervention versus control)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tuberculosis-specific interventions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Farmer et al., 17</td>
<td>Microbiologic cure</td>
<td>30</td>
<td>30</td>
<td>13</td>
<td>79.08 (4.42–1413.33)</td>
<td>None</td>
</tr>
<tr>
<td>1991</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chirico et al., 20</td>
<td>Treatment success</td>
<td>804</td>
<td>847</td>
<td>750</td>
<td>666</td>
<td>1.19 (1.03–1.37)</td>
</tr>
<tr>
<td>2011</td>
<td>Treatment completion</td>
<td>307</td>
<td>1554</td>
<td>298</td>
<td>1414</td>
<td>3.28 (1.65–6.51)</td>
</tr>
<tr>
<td>Rocha et al., 21</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Ciobanu et al., 18</td>
<td>Treatment success</td>
<td>2378</td>
<td>2492</td>
<td>2081</td>
<td>1964</td>
<td>2.00 (1.61–2.22)a</td>
</tr>
<tr>
<td>2014</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lu et al., 19</td>
<td>Treatment success</td>
<td>3290</td>
<td>2413</td>
<td>NR</td>
<td>NR</td>
<td>1.65 (1.40–1.95)b</td>
</tr>
<tr>
<td>Study</td>
<td>Outcomes</td>
<td>Success Rate</td>
<td>CI/Rate</td>
<td>Effect Size</td>
<td>Risk Factors</td>
<td>Loss to Follow-Up</td>
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<tr>
<td>----------------------------</td>
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<td>----------------------------------</td>
<td>------------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>Ukwaja et al., 2017</td>
<td>Treatment success</td>
<td>121</td>
<td>173</td>
<td>104</td>
<td>123</td>
<td>2.30 (1.20–4.30)</td>
</tr>
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<td></td>
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<td></td>
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<tr>
<td>Wingfield et al., 2017</td>
<td>Treatment success</td>
<td>135</td>
<td>147</td>
<td>87</td>
<td>78</td>
<td>1.60 (0.99–2.59)</td>
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<tr>
<td>Tuberculosis-</td>
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<td></td>
<td></td>
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<tr>
<td>sensitive interventions</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Torrens et al., 2016</td>
<td>Microbiologic cure</td>
<td>5788</td>
<td>1467</td>
<td>4752</td>
<td>1128</td>
<td>1.07 (1.04–1.11)</td>
</tr>
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</tbody>
</table>

CI: confidence interval; GDP: gross domestic product; HIV: human immunodeficiency virus; lbs: pounds; MDR: multidrug resistant; NR: not reported; OR: odds ratio; US$: United States dollars.

a The definitions of the outcomes were: treatment success was positive clinical outcome; treatment completion was if a study did not report treatment success; and microbiologic cure was if a study did not report treatment success or treatment completion.

b Derived from multivariable regression models.
Table 4. Bias within included observational studies in the systematic review on cash interventions to improve tuberculosis clinical outcomes, 1991–2017

<table>
<thead>
<tr>
<th>Study, year</th>
<th>Category, no. of stars</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Selection(^a)</td>
<td>Comparability</td>
</tr>
<tr>
<td>Farmer et al.,(^17) 1991</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Chirico et al.,(^20) 2011</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Rocha et al.,(^21) 2011</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Ciobanu et al.,(^18) 2014</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Lu et al.,(^19) 2015</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Torrens et al.,(^22) 2016</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Ukwaja et al.,(^16) 2017</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

\(^a\) A study could be awarded a maximum of four stars for this category.
\(^b\) A study could be awarded a maximum of two stars for this category.
\(^c\) A study could be awarded a maximum of two stars for this category.

Note: We used Newcastle-Ottawa Scale to assess bias in observational studies. The more stars the study received the lower the risk of bias.
Fig. 1. Flowchart showing the selection of studies on cash interventions to improve tuberculosis clinical outcomes, 1991–2017

1528 records identified through database search
- 1210 from Pubmed
- 65 from Embase
- 46 from The Cochrane Library
- 7 from ClinicalTrials.gov

9 additional records identified through review of references

1537 total identified records

639 duplicates removed

898 titles and abstracts screened

798 records excluded

100 full-text articles assessed for eligibility

92 full-text articles excluded
- 40 were an ineligible study type
- 3 focused on latent or MDR/XDR tuberculosis
- 9 concerned food incentives
- 4 concerned incentives to providers only
- 7 did not concern cash intervention during treatment
- 13 had no relevant outcome
- 3 had no comparator group
- 8 were in a high income country
- 2 evaluated the same population as another study
- 1 was not in English, Spanish, or French

3 studies had high overall risk of bias

8 studies included in qualitative synthesis

4 studies of TB-Specific Interventions (included in meta-analysis)

1 study of a TB-Sensitive Intervention
Fig. 2. Publication bias of studies included in the meta-analysis on cash interventions to improve tuberculosis clinical outcomes, 1991–2017

OR: odds ratio; SE: standard error.
Note: The dashed vertical line represents the summary OR generated through random effects meta-analysis.
Fig. 3. Likelihood of a positive clinical outcome for tuberculosis-specific cash interventions to improve tuberculosis clinical outcomes, 1991–2017

<table>
<thead>
<tr>
<th>TB-Specific Interventions</th>
<th>OR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciobanu et al, 2014</td>
<td>2.00 [1.61–2.22]</td>
</tr>
<tr>
<td>Lu et al, 2015</td>
<td>1.65 [1.40–1.95]</td>
</tr>
<tr>
<td>Ukwaja et al, 2017</td>
<td>2.30 [1.20–4.30]</td>
</tr>
<tr>
<td>Wingfield et al, 2017</td>
<td>1.60 [0.99–2.59]</td>
</tr>
<tr>
<td>Total</td>
<td><strong>1.77 [1.57–2.01]</strong></td>
</tr>
</tbody>
</table>

CI: confidence interval; OR: odds ratio.

Note: We excluded three studies with a high overall risk of bias.17,20,21