Author's response to reviews

Title: Designing and implementing a social protection intervention to enhance TB control: operational evidence from the CRESIPT project in Lima, Peru

Authors:

Tom Wingfield (tomwingfield@hotmail.co.uk)
Delia Boccia (delia.boccia@lshtm.ac.uk)
Marco Tovar (marco.tovar@ipsyd.org)
Doug Huff (dhuff@tulane.edu)
Rosario Montoya (mrmontoyav@gmail.com)
James J Lewis (james.lewis@lshtm.ac.uk)
Carlton A Evans (carlton.evans@ifhad.org)

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Author's response to reviews: see over
Dear Dr Jonathan Golub, Victorino Silvestre, and the editorial team of BMC Public Health,

We are grateful for your favourable consideration of our manuscript and for the helpful and constructive reviews received. We believe that this innovative research has important implications for your readers because it describes the design, implementation, and refinement of one of the world’s very first TB-specific socioeconomic interventions to improve TB care, cure, and prevention.

The World Health Organisation’s (WHO) post-2015 End TB Strategy explicitly identifies socioeconomic interventions as a key pillar of global TB control. In addition, the strategy mandates that “zero TB-affected households should face catastrophic costs by 2020”. However, WHO acknowledges that evidence concerning socioeconomic interventions to mitigate catastrophic costs and enhance TB control is extremely limited. In order to generate new knowledge to inform this global policy, we implemented a novel TB-specific socioeconomic intervention that included cash transfers and supported TB prevention and cure in 32 shantytowns in Callao, Peru. This innovative study built on our previous peer-reviewed research publications (all available on Pub Med):

- Wingfield et al (2014), “TB, sunlight, vitamin D, & household crowding.” *JID*;210(5):774-783; and

As described above, socioeconomic interventions are now part of global TB policy and, as evidenced during our recent involvement in an expert consultation at WHO in Geneva, both we and our colleagues in the WHO’s global TB program sincerely believe that this manuscript is an important and necessary document with which to guide policy-makers and national TB program implementers. While socioeconomic interventions and conditional cash transfers continue to be used in HIV and maternal health, the absolute dearth of evidence in the field of TB, means that this timely, unique paper describing a TB-specific intervention is of considerable value for the wider TB community. Indeed, WHO TB strategists are aiming to use this published evidence to inform international partner organisations and key stakeholders about future implementation of this policy change.

Below is a response letter to the reviewers’ comments that we received on the 24th of June 2014. We have uploaded our resubmission (with and without tracked changes) to your online submission system. Our responses are in italics labelled “author response”. All updates to the manuscript are written in red with speech marks and the corresponding section specified. Line and
page numbers that are given for the new manuscript text correspond to those in the attached document without tracked changes.

This material has not and will not be submitted for publication elsewhere so long as it is under consideration by BMC Public Health. The material is original and has not already been published. As mentioned in the original cover letter, all authors participated in the study and concur with the submission and subsequent revisions submitted by the corresponding author.

We are grateful for the reviewers’ constructive comments and for Victorino Silvestre’s assistance throughout the submission process. We believe that the manuscript is now optimal thanks to this process and look forward to the updated version of this seminal article as a potential publication in BMC Public Health.

If you need any further information please do not hesitate to contact me.

Yours sincerely,

Tom Wingfield MBChB(Hons) MRCP PhD(c) DTM&H
Innovation For Health And Development PhD Fellow and Infectious Diseases Specialist Registrar
Imperial College London, UK and Universidad Peruana Cayetano Heredia, Lima, Peru
Comments to the author: Reviewer 1, Cesar Ugarte-Gil, 1st March 2015

Reviewer 1 comment: Interesting paper about an important topic in tuberculosis control.

Author response: We thank the reviewer for their positive review of the article, which has led to it being improved for publication.

Reviewer 1 comment: Ethical issues: I’m pretty sure CRESIPT has IRB approval, however should be stated because the intervention has some risks to the participants.

Author response: We agree with the reviewer’s comment and have now moved the following confirmation of ethical approval from its previous position in the document end notes to Pages 6-7, Lines 180-183, of the Methods section:

“Ethical Approval. Approval was granted by the ethics committees of the Callao Ministry of Health, Peru; Asociación Benéfica PRISMA, Peru; and Imperial College London, UK. All interviewed participants gave written informed consent to participate in the study and for subsequent publication of anonymised data.”

Reviewer 1 comment: Sample size and population: How did the authors decide to stop at 149 participants?

Author response: As the reviewer notes, we had omitted to mention the power of the study and hence the cohort size required. In order to resolve this, we have expanded Lines 184-191, Page 7 of the methods section to read:

“Sample Size. The main outcome of the study (reported elsewhere) was completion of TB chemoprophylaxis in household contacts of TB patients. TB patients had an average of five contacts and 25% of those eligible for TB chemoprophylaxis completed it. Therefore, a priori, we calculated that 312 patients would give statistical power of 80% to detect a 33% increase in the primary outcome comparing intervention versus control households with two-sided 5% significance. The 312 patients recruited were randomly assigned in a 1:1 ratio to the intervention arm (normal standard of care from National TB Program plus socioeconomic intervention) and control arm (normal standard of care from National TB Program).”

In addition, Page 10, Lines 262-264, of the results section now read:

“As per the a priori sample size calculations and study protocol, 312 consecutive TB patients from the study site were recruited of whom 149 were randomized to receive the socioeconomic intervention.”

Reviewer 1 comment: Are these consecutive patients are all the same (pulmonary and full-sensitive TB) or there are also MDR-TB patients, extra-pulmonary patients, HIV-TB patients. If is a mix of patients here, can you explain how this affect the calculation of cost and consequently the value of cash transfer? Also could be interesting to see how many percentage of TB patients with comorbidities such as diabetes and/or drug abuse you expect and how this affect the value of cash transfer.

Author response: It is indeed important to highlight the differential comorbidities of the TB patient cohort. While we have not focused on drug addiction or mental illness, we have now elaborated on those patients who had diabetes, MDR TB and HIV-TB coinfection. Accordingly, we have expanded Page 10, Lines 268-269, of the Results section to respond to this comment:

“Of the 133 participants, 9/133 (7%) had MDR TB, 5/133 (4%) were HIV positive, and 7/133 (5%) were diabetic.”
In terms of how comorbidities might affect the value of the conditional cash transfers, Figure 3 expands on the differential values of the transfers for patients who have HIV-TB co-infection and/or MDR TB. In addition, we have alluded to this issue in Lines 348-353, Page 14, of the Discussion section:

“Hard-to-reach populations and/or difficult urban settings such as those in which our intervention was implemented, may be characterised by violence, illegal drug use and severe marginalisation that are also associated with TB. These populations and those with comorbidities (such as diabetes, HIV and mental illness) and/or resistant TB may require differential levels of intervention including prolonged or enhanced conditional cash transfers and social support. Future studies may investigate the barriers, feasibility and impact of delivering TB-specific socioeconomic interventions to challenging, vulnerable groups in such settings.”

Reviewer 1 comment: Percentages and number of people didn’t participate: The authors said in page 8 in Results part: "17/148 (11%) patients declined to participate, died prior to recruitment, or were recruited and subsequently lost to follow up”, I suggest to put the number and percentage in each category, to have a better idea of the people who didn’t participate. If is possible a flowchart can help.

Author response: We agree that clarification of specific patient numbers and loss-to-follow-up rates is essential and are grateful to the reviewer for highlighting this omission. We have updated Lines 264-265, Page 10, of the Results section accordingly and believe it now gives more detailed information concerning the reasons for people not participating and resolves the need for a flow chart:

“12/149 (8%) patients declined to participate, 2/149 (1%) died prior to recruitment, and 2/149(1%) were recruited and subsequently did not complete follow up.”

Comments to the author: Reviewer 2, Prashant Yadav, 16th June 2015

Reviewer 2 comment: This paper provides an assessment of the operational design and implementation of a conditional cash transfer schemes (and other components) for TB affected families in poor settings. The paper studies a problem of interest and impact for TB programs globally. The authors conduct a comprehensive literature review of the literature on CCTs and the literature on TB and social protection.

Author response: We are grateful to the reviewer for their positive comments concerning the background literature review conducted for this article.

Reviewer 2 comment: However, in its current form, the manuscript provides limited advancement or contribution to the scientific questions regarding the value of CCT for TB, which the CRESPIIT project will demonstrate once its results are available. I do recognize the value in a paper that critically assesses the main design and implementation challenges associated with conditional cash transfer in the context of TB.

Author response: We agree with the reviewer that the results of the CRESIPT project will be vital to evaluate the impact of this socioeconomic intervention on TB control at a community level. Moreover, of relevance to this comment, we have also produced two manuscripts (both submitted elsewhere) concerning the preliminary results of CRESIPT that report: the impact of the intervention on completion of TB treatment and chemoprophylaxis; and the extent to which the intervention mitigated TB-related and catastrophic costs. We believe that these manuscripts will be complementary to the current manuscript, which we agree is valuable in terms of its focus on design and implementation of TB-specific conditional cash transfers rather than their impact. While we strongly agree with Reviewer 2 that impact evidence is necessary, such evidence will not alone be sufficient to address the existing knowledge gaps surrounding the use of conditional cash transfer for TB control. Operational evidence policy papers are
urgently needed so that implementers will know how to utilise these interventions in their own setting. By providing an extensive descriptions of the key operational decisions made and strategies adopted in the intervention, this article will have great value to help policy implementers and decision-makers to navigate the complex challenges surrounding the planning, designing, of TB-specific socioeconomic interventions including conditional cash transfers. Thank you for this comment.

Reviewer 2 comment: In its current form this manuscript does not provide a critical assessment that can clearly and effectively inform future study designers in this area. Many of the challenges presented appear more like a discussion without any clear scientific synthesis to inform the design of future studies.

Author response: The CRESIPT study is the first of its kind in the world and thus there is extremely limited existing rigorous evidence to critically assess. As specifically alluded to in the article, important lessons can be learnt from the experience of conditional cash transfers in HIV and maternal medicine. However, the majority of evidence from these fields is from the grey literature and HIV and TB, which clearly have different epidemiological profiles and require distinct responses. This makes the generation of new evidence and sharing of operational experiences, such as in our article, very important. Specifically, the WHO now recommend that TB control programs include social protection activities but there is almost no published evidence or experience to inform how this should be done. Our manuscript directly addresses this knowledge gap by systematically reviewing the literature and describing the processes that we utilised, what worked and what did not. We therefore strongly believe that this manuscript effectively informs future study and program designers in this area.

In order to address Reviewer 2’s comment, we have comprehensively reorganised the structure of the article and as requested in Reviewer 2’s further comments detailed below, updated the text. Specifically, we have clarified in the main text the content of the updated Tables 2 and 3 and Box 1, which we believe do indeed offer a scientific synthesis of the limited available evidence, with which to inform the design of future studies:

Lines 162-165, Page 6: “Table 2 summarises the critical review of the available evidence that occurred during the planning process, and the manner in which this review subsequently informed the main operational design and implementation decisions relating to some of the main aspects of the cash transfer intervention, including: existing cash transfer schemes, conditionality, and transfer size.”

Lines 278-280, Pages 10-11: “The lessons that emerged are grouped into successes, challenges and refinements in Table 3, which aim to inform the design of future studies and, ultimately, allowed us to identify persisting knowledge gaps in this field (Box 1).”

We are grateful to Reviewer 2 for this comment and the specific suggestions below, which have helped the narrative flow, readability, and potential impact of the article.

Reviewer 2 comment: The methods, results and discussion section can benefit from restructuring. In a paper of this form, the methods section should perhaps be concise and briefly describe the interviews, focus groups, meetings, workshops and other operational instruments used to study the operational challenges. The results and discussion should get into how each component of the intervention was established. The appropriate design of the intervention is intended to be a result of this paper so it should not be a method.

Author response: In response to Reviewer 2’s constructive comment, we have improved the structure of the methods and results section.

The methods section is, as requested, now more concise. It is divided into sections entitled:

“Intervention objectives” that briefly gives an overview of the project’s goals (which are also appropriately elaborated upon in Figure 1); and
“Intervention planning” that summarises, as also requested by Reviewer 1, our previous related research and consultations, acceptability assessment, ethical approval, and sample size calculations. These themes are further expanded upon in both Table 1 and Figure 2.

As suggested by Reviewer 2, the Results section now focuses on how each component of the cash transfer intervention was established and is therefore entitled “Results: designing and implementing the intervention”.

As requested, this section has been improved to detail the chronological development of the intervention including:

“Designing the conditional cash transfers” which details under separate subtitles cash transfer targeting, delivery, size, conditions, levels, and responsiveness; and

“Implementation of the conditional cash transfers” which details setting up cash transfers in terms of banks, accounts, and administration, and also recruitment of patients and cash transfers achieved. We believe that this extensive restructuring meets Reviewer 2’s helpful comments and has improved the manuscript’s flow and accessibility.

Reviewer 2 comment: The paper should discuss the impact of cash transfer via banks in greater detail. Should future researchers look at alternative means of CCT implementation due to the challenges encountered? How significant was the challenges? Are there other issues that need to be explored because first time bank account users will have other difficulties and may not value the cash the same way as others due to higher perceived transaction costs?

Author response: This is a valuable point that we have expanded on in the original manuscript. In the Results section of the original manuscript, there are three paragraphs that elaborate on the system we set up for bank transfers, Lines 237-260, Pages 9-10, and read:

“Banks: Of 10 banks visited, formal meetings were organised with four that aimed to: create a relationship with the bank to achieve sustainable cash transfers throughout the study; identify charge-free appropriate accounts; create a “virtual” way of opening accounts to minimize paperwork, time spent “in branch”, and travel-related patient costs; establish a mutually suitable day on which to accompany patients to open accounts; and to clarify the bank’s accessibility in our study sites (i.e. branches and agencies).

The banks we consulted raised similar concerns about the proposed intervention, including: infection risk; cash transfer flow; and difficulties opening accounts with patients who have no national identification, fixed abode, or are illiterate. We initially chose one bank that appeared to be more likely to overcome these issues because it had a social inclusion department with previous involvement in successful microfinance initiatives.

Opening bank accounts: Recruited patients with a negative sputum smear microscopy test (indicating low infectiousness) were accompanied by our project staff to open a bank account. The account holder’s details were then relayed to our project office with a copy of the bank’s original documents. In the case that the patient was a minor, did not have legal capacity, wished for another household member to be the named bank account holder, or had prolonged sputum smear positivity, then a household member was selected by the patient or household. Patient transport and time costs were reimbursed by our project.

Cash transfer administration: The patient’s incentive card (Supplementary Figures 1a and 1b) was updated by the field nurses when each condition was achieved. Confirmation of completion was made through liaison with the patient, review of CRESIPT project records (e.g. participatory community meeting attendance) and Peruvian National TB Program records and treatment cards (e.g. medication...
adherence verification). Signed incentives cards were returned to a project administrator who double digitized the data. Thus, a weekly list of patients, their bank account details, and required transfers was generated. The same day, this list was submitted electronically to a member of the social inclusion department of the bank, and the virtual transfers made. The transaction codes and receipts generated were double digitized in the CRESIPT project database and delivered to the patients in the health post by the CRESIPT field nurses.”

While it is beyond the scope of this article to review all the alternative means of conditional cash transfer implementation in detail, we have now expanded Lines 361-377, Page 14-15 of the Discussion section within the confines of acceptable word limit accordingly. This involved a further literature search, the references for which have been added to the manuscript bibliography. Specific mention is made of how this logistical challenge was overcome, use of potential bank providers, use of potential non-bank providers, and considerations concerning implementation of conditional cash transfer schemes:

“The new bank-provider, while not having a specific social inclusion department, provided improved coverage and accessibility because of a greater density of agency micro-branches in local shops that facilitated participant transactions. While the new bank-provider overcame the challenges described above, these experiences have led us to question whether banks are the most appropriate delivery strategy. Indeed, conditional cash transfer programs in Sub-Saharan Africa have predominantly used specified pay points to pay participants in cash rather than banks which may be less accessible to the poor and may have user fees. However, banks have been the favoured partner agent in existing conditional cash transfer programs in Peru (JUNTOS), Brasil (Bolsa Familia), and Mexico (Progresa) with the co-ordination of national cash transfer programs being centralised through national banks in these countries. This level of coordination may only be suitable in countries with comparatively developed financial infrastructure, information and communications technologies, and accessibility to bank branches or micro-agencies. We have reviewed other modalities of conditional cash transfers in greater detail elsewhere. Future research into implementation of socioeconomic interventions may compare the effectiveness and cost-effectiveness of cash delivery mechanisms including mobile phone vouchers, mobile banking, automated or other pay points, or innovative strategies, for which rigorous evidence is currently lacking. To achieve optimal impact, implementers of conditional cash transfer programs may work more closely with the local communities and civil societies to establish how a program can be adapted to be appropriate and acceptable in that specific setting.”

These issues are also summarised in Tables 2 and 3 as per the original submitted manuscript.

Reviewer 2 comment: Are the authors suggesting that the method used to establish cash transfer amount appropriate? Should it be based on the distribution of catastrophic expenditures as in this intervention or are they suggesting use some other basis to determine that. It is not clear after reading the discussion.

Author response: We thank Reviewer 2 for this important comment. On page 15, Lines 378-391, we have now specifically mentioned the thresholds that we used to define this research’s cash transfer amount, which were appropriate for the local setting:

“Cash transfer size: During focus group discussions, the internal research committee debated what the most important objective of cash transfers is: mitigating TB-related costs; avoiding catastrophic costs; or reducing poverty-related TB risk factors. This confounded deciding the cash transfer amounts. To address this challenge, we analysed TB patients’ costs, which demonstrated that direct out-of-pocket expenditure was 10% of that household’s annual income. These results, together with additional data characterising annual household income for TB-affected households in the study site, informed the cash transfer amount necessary to match direct out-of-pocket expenditure and subsequently avoid catastrophic costs.”

In addition to the above, we have now made it clearer that we would suggest using a pragmatic and operationally-feasible “costs-mitigation” rather than “poverty-reduction” approach. We have also
improved the revised manuscript to be more cautious in our recommendations by noting that the threshold used in this impoverished Peruvian setting may be inappropriate for other settings, especially in other continents that have distinct TB epidemics (e.g. sub-Saharan Africa, which has a TB profile including high prevalence of TB-HIV co-infection). Lines 384-391, Page 15 now read:

“The optimal cash transfer size is likely to depend on the intervention setting and proposed outcomes of the intervention. This will require baseline evaluation of local TB-related costs prior to planning for and implementing cash transfers of suitable amounts. Further research is required to evaluate how cash transfer size affects intervention impact and cost-effectiveness. It is noteworthy that the strategy we adopted in this research was a “costs-mitigation” rather than a “poverty-reduction” strategy and involved a cash transfers amount that was appropriate and feasible for the local setting. While long-term poverty reduction would be an appealing additional goal, this would likely require greater socioeconomic support than national TB programs could afford.”

Reviewer 2 comment: There are areas where the authors make judgements such as “…therefore we recommend combining unconditional money transfer…” These statements are prescriptive enough that future study designers would take them into consideration, while in reality there is no evidence in this study (except in some interviews) to inform that.

Author response: We thank Reviewer 2 for this comment. As Reviewer 2 notes above, this paper critically assesses the main design and implementation challenges associated with conditional cash transfer schemes. The recommendations that can be made in an implementation evaluation paper such as this are thus necessarily experiential. Moreover, in our systematic review of similar TB-specific socioeconomic interventions (Boccia et al, IJTLD 2011), we found only a handful of studies providing rigorous evidence on the subject and so these new findings contribute to a limited existing knowledge base. Therefore, while we maintain that the experiential findings we present are important and may be useful to policy-and decision-makers, we agree that it is essential to temper any prescriptive recommendations by recognising the limitations of this qualitative appraisal of the implementation process and that such recommendations relate to a specific, local setting and may not be reproducible or applicable in other settings. We believe that we have resolved these issues in the following improved sections of the text:

Lines 422-426, Pages 16-17: “Consequently, on the basis of this qualitative evaluation of the implementation process, we suggest designing relevant incentives to be more equitable and responsive to household size: a fixed amount added to the patient’s cash transfer for each member of their household completing the condition. In this way, larger households will receive the same amount per household member as smaller households.”

Lines 409-412, Page 16: “Learning from this setting-specific qualitative feedback, in the planned CRESIPT study in these same communities, we will combine unconditional monthly cash transfer provided to all TB patients taking treatment with supplementary conditional cash transfers for meeting project and National TB Program conditions.”

END OF AUTHOR RESPONSE LETTER

We are very grateful to both reviewers for their constructive comments that have improved the article that we now believe is ready to be published in BMC Public Health. While we believe the present manuscript to be modified optimally, please do not hesitate to contact us if we can assist you further with the review process.

Yours sincerely,
Tom Wingfield (on behalf of the co-authors)