**Title Page: Wingfield et al Invited Comment for Lancet**

**Title: Addressing social determinants to end tuberculosis**

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Leave no one behind. This is the overarching pledge of the Sustainable Development Goals; a pledge which is far from being realised. In 2016, over 4 million people with tuberculosis (TB) were estimated to be undiagnosed, or their care was unknown. In the same year, nearly a fifth of the people who were diagnosed and known to be treated for TB had adverse outcomes, including 1.3 million deaths.1 One reason that millions of people affected by TB are left behind is a lack of coordinated, international action to combat poverty and inequality.

Despite renewed interest in addressing the social determinants of TB, there remains stark global disparity in disease burden and access to TB care.2 Low- and middle-income countries bear the highest TB burden1 and people with TB are often vulnerable, impoverished, and suffer financial shock.3 Conversely, countries with higher gross domestic product, human development indices, and/or social protection expenditure per capita have lower TB prevalence.4–6 The World Health Organisation’s (WHO) 2015 End TB Strategy acknowledges the need to reduce inequalities in TB prevention and care, including through provision of social protection and poverty alleviation for TB-affected households.7 For the past two decades, we have been working with impoverished peri-urban shantytown communities of Callao, Peru, to generate evidence on feasibility, acceptability, and impact of social and economic (‘socioeconomic’) support for TB-affected people.

We did a cohort study of TB-affected households and defined a threshold above which costs of accessing “free” TB care became catastrophic, predicting loss-to-follow-up and death.3 This threshold was endorsed in the End TB Strategy, which mandated that “zero TB-affected families should face catastrophic costs by 2025”. However, little rigorous evidence is available to guide costs mitigation strategies for TB-affected households. The Innovative Socioeconomic Interventions Against TB (ISIAT) project addressed this knowledge gap by offering a panel of diverse psychosocial and economic support to TB-affected households.8 The most acceptable, feasible components of ISIAT were then combined into a standardised intervention, consisting of integrated social support (household visits and participatory community meetings) and economic support (conditional cash transfers), evaluated in the Household-Randomised Evaluation of a Socioeconomic Intervention to Prevent TB (HRESIPT). HRESIPT showed that patients offered the intervention were more likely to achieve treatment success,9 their contacts more likely to initiate preventive therapy,10 and the household less likely to incur catastrophic costs.11 The intervention was simplified further and its impact and cost-effectiveness on long-term cure, TB case-finding and risk-targeted TB prevention12 is being assessed in the Community Randomized Evaluation of a Socioeconomic Intervention to Prevent TB (CRESIPT) trial. However, whatever CRESIPT’s results, several important questions remain largely unaddressed.

First, while socioeconomic support have had positive impacts on TB-affected households in a few settings including Peru, their wider transferability is unknown. Socioeconomic interventions are likely to benefit from adaptation to, and evaluation in, settings with diverse patient demographics (e.g. rates of poverty, substance abuse, HIV, and TB drug resistance), health and social care systems, and infrastructure.

Second, current global policies focus on providing TB-affected households with economic support to prevent catastrophic costs. Indeed, economic incentives and enablers for TB have a long history. However, it is striking that in ISIAT, HRESIPT, and CRESIPT, participants consistently valued social support more highly than economic support.13,14 This is important because: social support is, generally, much less expensive than economic support but may be more labour intensive; psychosocial support may have a similar impact on TB prevention and outcome measures to economic or combined support;15 unlike economic support, which has its own target in the End TB Strategy in the form of the catastrophic costs, social support lacks a global indicator and is in danger of being overlooked; and there has been no robust trial evaluating social vs economic vs socioeconomic support vs standard of care for TB-affected households. The interesting feedback results from Peru highlight the potential value of engaging TB-affected households and civil-society to establish what type of socioeconomic support communities would find valuable, acceptable, locally-appropriate, and sustainable.

Third, cost-opportunity and cost-effectiveness of socioeconomic support for TB-affected households are likely to depend on targeting strategies focused on specific beneficiaries but relevant analyses are lacking. This leaves an evidence gap concerning the optimal allocation of already scarce resources. For example, it is unknown whether a relatively expensive, labour-intensive intervention for high-risk groups such as those who are homeless, currently/formerly incarcerated, living in extreme poverty, or who have MDR-TB, would be more cost-effective and impactful on National TB Programs’ (NTPs) rates of TB treatment success than a cheaper, more modest intervention that supported all TB-affected households.

Fourth, it is not known how a disease-orientated approach which provides “TB-specific” support focused on TB-affected households, as in ISIAT, HRESIPT and CRESIPT, may complement and be complemented by “TB-sensitive” approaches. TB-specific approaches focus on supporting households post-diagnosis and throughout treatment, and their success is measured by short-term predominantly TB-related indicators. TB-sensitive approaches involve strengthening national social protection strategies and adapting them to be more inclusive to people at risk of TB infection and disease, such as Brasil’s Bolsa Familia social welfare program, which has been associated with improved TB treatment outcomes and reduced TB incidence.16,17 Although initially expensive,18 TB-sensitive interventions may lead to improved long-term population outcomes in health (including TB), food security, and poverty-alleviation. Thus, a combination of TB-sensitive and TB-specific support is likely to be the most impactful approach to comprehensively address the social determinants of TB, while improving wellbeing.

Finally, we need to consider how socioeconomic support will be funded (e.g. governmental, charitable, crowd-sourcing), by whom it will be delivered (e.g. NTPs, the third sector, civil-society), how it might be enhanced by streamlined service delivery (e.g. ambulatory care, decentralisation, out-of-hours services), and the timeframes, indicators, and outcome measures used to judge its success (e.g. TB-related, broader health outcomes, psychosocial and economic impact).

In conclusion, socioeconomic interventions for TB-affected people can be achievable and impactful8,9 but require local adaptation tailored to meet the needs of diverse populations and underserved groups. Ensuring that no one is left behind requires turning rhetoric into reality: to end TB, medicines must be integrated with socioeconomic interventions that fight poverty.

**References**

1. World Health Organization. Global Tuberculosis Report. http://apps.who.int/iris/bitstream/10665/259366/1/9789241565516-eng.pdf?ua=1. Published 2017.

2. Collaborators Q. Healthcare Access and Quality Index based on mortality from causes amenable to personal health care in 195 countries and territories, 1990-2015: A novel analysis from the Global Burden of Disease Study 2015. *Lancet*. 2017:1990-2015. doi:10.1016/S0140-6736(17)30818-8.

3. Wingfield T, Boccia D, Tovar M, et al. Defining catastrophic costs and comparing their importance for adverse tuberculosis outcome with multi-drug resistance: a prospective cohort study, peru. *PLoS Med*. 2014;11(7):e1001675. doi:10.1371/journal.pmed.1001675.

4. Janssens J, Rieder H. An ecological analysis of incidence of tuberculosis and per capita gross domestic product. *Eur Respir J*. 2006;32(5):1415-1416.

5. Siroka A, Ponce NA, Lönnroth K. Association between spending on social protection and tuberculosis burden: a global analysis. *Lancet Infect Dis*. 2015;3099(15):1-7. doi:10.1016/S1473-3099(15)00401-6.

6. Reeves A, Basu S, McKee M, Stuckler D, Sandgren A, Semenza J. Social protection and tuberculosis control in 21 European countries, 1995-2012: A cross-national statistical modelling analysis. *Lancet Infect Dis*. 2014;14(11). doi:10.1016/S1473-3099(14)70927-2.

7. Uplekar M, Weil D, Lonnroth K, et al. WHO’s new End TB Strategy. *Lancet*. 2015:1799-1801. doi:10.1016/S0140-6736(15)60570-0.

8. Rocha C, Montoya R, Zevallos K, et al. The Innovative Socio-economic Interventions Against Tuberculosis (ISIAT) project: an operational assessment. *Int J Tuberc Lung Dis*. 2011;15 Suppl 2(5):S50-7. doi:10.5588/ijtld.10.0447.

9. Wingfield T, Tovar M, Huff D, et al. Socioeconomic support to improve initiation of tuberculosis preventive therapy and increase tuberculosis treatment success in Peru: a household-randomised, controlled evaluation. *Lancet*. 2017:16. doi:10.1016/S0140-6736(17)30412-9.

10. 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(4):270-280. doi:10.2471/BLT.16.170167.

11. Wingfield T, Tovar MA, Huff D, et al. The economic effects of supporting tuberculosis-affected households in Peru. *Eur Respir J*. 2016;48(5):1396-1410. doi:10.1183/13993003.00066-2016.

12. Saunders MJ, Wingfield T, Tovar MA, et al. A score to predict and stratify risk of tuberculosis in adult contacts of tuberculosis index cases: a prospective derivation and external validation cohort study. *Lancet Infect Dis*. 2017;17(11):1190-1199. doi:10.1016/S1473-3099(17)30447-4.

13. Wingfield T, Boccia D, Tovar M a., et al. Designing and implementing a socioeconomic intervention to enhance TB control: operational evidence from the CRESIPT project in Peru. *BMC Public Health*. 2015;15(1):810. doi:10.1186/s12889-015-2128-0.

14. Wingfield T, Tovar M, Huff D, et al. Feedback from TB-affected households’ receiving a socioeconomic intervention in Peruvian shantytowns: acceptability of social versus economic support according to poverty level. In: *International Union Against Tuberculosis and Lung Disease*. Vol SOA-436-14. ; 2017.

15. van Hoorn R, Jaramillo E, Collins D, Gebhard A, van den Hof S. The Effects of Psycho-Emotional and Socio-Economic Support for Tuberculosis Patients on Treatment Adherence and Treatment Outcomes - A Systematic Review and Meta-Analysis. *PLoS One*. 2016;11(4):e0154095. doi:10.1371/journal.pone.0154095.

16. 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(7):790-796. doi:10.5588/ijtld.16.0599.

17. Torrens AW, Rasella D, Boccia 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(3):199-206. doi:10.1093/trstmh/trw011.

18. Rudgard WE, Evans CA, Sweeney S, et al. Comparison of two cash transfer strategies to prevent catastrophic costs for poor tuberculosis-affected households in low- and middle-income countries: An economic modelling study. *PLoS Med*. 2017;14(11):e1002418. doi:10.1371/journal.pmed.1002418.