

Title: Digital adherence technology for tuberculosis treatment: focus on livelihoods as well as lives

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Dear Editor,

We read with interest the recent paper by Arinaminpathy et al estimating the potential impact of adherence technologies on tuberculosis (TB) in India.¹ We wish to highlight an important aspect of TB burden that these technologies have the potential to address which has not been widely acknowledged or investigated. Patient-centered TB care can only be achieved by reducing the economic burden that “free” care puts on individuals and their households. The third pillar of the End TB strategy, of 0% of people with TB facing catastrophic costs,² is often overlooked relative to TB incidence and mortality. Patient-incurred costs are considered catastrophic if total costs are 20% or more of annual household income due to TB disease. By the end of 2019, 49% (varying at country level from 19-83%) of people with TB were still faced with these costs.² TB affects the poorest most, who are least able to absorb these costs, and it is therefore important to monitor the distribution of TB care-associated costs and outcomes by socio-economic status.³ To reach the goal of reducing catastrophic costs and to address the true burden of TB, we need to ensure that TB care is more affordable by reducing direct and indirect patient-incurred costs.

Digital adherence technologies (DATs), that monitor and remind patients to take medication, are a promising tool to reducing these costs by enabling individualised patient care, potentially reducing health facility visits required under Directly Observed Therapy Short course (DOTs) and accompanying income loss. Given that TB treatment success is already high, approximately 85% globally,² and failure is a result of a variety of underlying factors, epidemiological impact may be limited. However, the often-overlooked economic impact of these tools through providing patient-centered care likely overshadows their direct epidemiological benefit. In Table 1, we compare for five high TB burden countries treatment outcomes, number of health facility visits and catastrophic costs incurred. This highlights the high proportion of TB patients experiencing catastrophic costs and the burden of repeated health facility visits, as opposed to already low treatment failure rates. While there is limited variation in treatment success (and even less scope for DATs to solve the underlying problem), the number of visits do vary, and could contribute to reducing patient costs.

The economic burden of TB care is driven by income loss as well as the cost (due to travel and time off work) of collecting medication at the facility.³ DATs could lead to a schedule of fewer treatment visits, which may empower patients to continue productive activities. In addition, if DATs lead to better patient support and treatment adherence, previous evidence suggests that this may increase wellbeing and treatment success, and therefore reduce income losses from being too ill to work.⁴

Unfortunately, the current evidence of both the epidemiological or patient-cost impact of DATs is limited, and likely to be highly setting-specific due to differences in number of health facility visits and treatment success in the standard of care, as illustrated in Table 1.⁵ There is also no existing evidence on the distributional effect of DATs by socioeconomic status yet. If only the rich benefit from DATs, due to differences in the distribution of phone ownership between socio-economic status groups, the utility of DATs in improving treatment outcomes and reducing patient costs among those most affected by TB are undermined.⁶ It is therefore vital that we understand the impact of DATs across different socioeconomic status groups, thus improving their ability to improve equity by reducing barriers to their use and effectiveness among some groups.

It is key that these questions are addressed in pragmatic studies, as achieving the potential of digital tools will be dependent on how they are adapted to routine care, and how their use shapes the behaviour of patients and providers. Previous pragmatic TB studies have demonstrated that guidelines and reality may differ strongly when it comes to the patient experience;⁷ if patients were already attending the health facility less than is currently reported or if clinicians don't act on the information from DATs, then we may see a lower than expected impact of DATs in reducing patient costs. If trials require access to a mobile phone, usually required for complete engagement with DATs, they will exclude the vital experiences of those patients without such access, usually those with less resources, where TB patients and those at risk of catastrophic costs are likely overrepresented⁶. Rather than ignore the problem, we need studies that explore provision of phone access in the intervention where necessary.

The importance of evidence on digital technology to support TB care has become increasingly clear during the COVID-19 pandemic, as tools to support patients while their movements are restricted.² While it may be tempting to simply implement DATs widely, the lack of pragmatic evidence means that the effectiveness, acceptability and cost implications of the variety of tools available is unknown.

As we look to fill these gaps, our focus should be to achieve maximum benefit for a patient's livelihood, as well as their health.

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Declaration of Interests:

The authors report no conflicts of interest.

Author Contributions:

CFM, NF, RMGJH and KLF conceptualized this piece. CFM and NF drafted the manuscript. All authors read and revised the draft manuscript.

References:

1. Arinaminpathy N, Chin DP, Sachdeva KS, et al. Modelling the potential impact of adherence technologies on tuberculosis in India. *Int J Tuberc Lung Dis* 2020; **24**(5): 526-33.
2. World Health Organization. Global Tuberculosis Report 2020. Geneva, Switzerland, 2020.
3. Tanimura T, Jaramillo E, Weil D, Raviglione M, Lonnroth K. Financial burden for tuberculosis patients in low- and middle-income countries: a systematic review. *Eur Resp J* 2014; **43**(6): 1763-75.
4. Kastien-Hilka T, Abulfathi A, Rosenkranz B, Bennett B, Schwenkglenks M, Sinanovic E. Health-related quality of life and its association with medication adherence in active pulmonary tuberculosis- a systematic review of global literature with focus on South Africa. *Health Qual Life Outcomes* 2016; **14**: 42.
5. Subbaraman R, de Mondesert L, Musiimenta A, et al. Digital adherence technologies for the management of tuberculosis therapy: mapping the landscape and research priorities. *BMJ global health* 2018; **3**(5): e001018.
6. Saunders MJ, Wingfield T, Tovar MA, et al. Mobile phone interventions for tuberculosis should ensure access to mobile phones to enhance equity – a prospective, observational cohort study in Peruvian shantytowns. *Trop Med Int Health* 2018; **23**(8): 850-9.
7. Vassall A, Siapka M, Foster N, et al. Cost-effectiveness of Xpert MTB/RIF for tuberculosis diagnosis in South Africa: a real-world cost analysis and economic evaluation. *The Lancet Global health* 2017; **5**(7): e710-e9.
8. World Health Organization. World Health Organization Global TB Database. <https://www.who.int/tb/country/data/download/en/> (accessed 27 November 2020).
9. Assebe LF, Negussie EK, Jbaily A, Tolla MTT, Johansson KA. Financial burden of HIV and TB among patients in Ethiopia: a cross-sectional survey. *Bmj Open* 2020; **10**(6): e036892.
10. Mudzengi D, Sweeney S, Hippner P, et al. The patient costs of care for those with TB and HIV: a cross-sectional study from South Africa. *Health policy and planning* 2017; **32**(suppl_4): iv48-iv56.

Table 1: Epidemiological and economic context in five high TB burden countries. Data for 2019 publicly available from the World Health Organization, except where indicated otherwise.⁸ In comparison, delivery of treatment support with the use of DATs could require as few as six health facility visits for monthly collection of medicines.

Country	Number of TB case notifications in 2019	Treatment success rate in new & relapse cases in the public sector	Typical number of health facility visits for patients starting first-line TB treatment	Patients facing catastrophic costs
Ethiopia	112 597	88%	76	40% ⁹
Philippines	419 102	83%	62	35%
South Africa	222 350	71%	6	47% ¹⁰
Tanzania	82 166	92%	18	45%
Ukraine	28 539	77%	195	-