Active case finding in tuberculosis-affected households: time to scale up

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In 2017, 10 million people developed tuberculosis, of whom approximately 4 million were not diagnosed, treated, or notified to national tuberculosis programmes (NTP).[1] Of the remaining 6 million, many experienced substantial delays in accessing and receiving appropriate care.[1] This unacceptable situation leads to unnecessary disability and loss of life, and impedes tuberculosis control because of onward transmission at a household and community level. To rectify these shortcomings and eliminate tuberculosis, new strategies are urgently required to enhance tuberculosis case detection.

WHO endorses two complementary approaches to improve tuberculosis case detection: active case finding (ACF) and systematic screening of household contacts.[2,3] Household contacts of people with tuberculosis are a group at high risk of acquisition of tuberculosis infection and development of tuberculosis disease. Most incident tuberculosis cases within the household occur in the first 2 years following the diagnosis of the index patient.[4] Household-level interventions that identify contacts with latent tuberculosis infection and tuberculosis disease and provide appropriate preventive therapy or treatment can break the chain of onward transmission.[5] Thus, such interventions have the potential to reduce the prevalence of tuberculosis at a community level, especially in low-income and middle-income countries with a high tuberculosis burden.[6] In *The Lancet Global Health*, Thomas Lung and colleagues[7] report the findings of an economic evaluation conducted alongside a large trial of an ACF intervention in Vietnam.

ACT2 was a large, cluster randomised trial[8] that recruited 25 707 household contacts of 10 964 patients with tuberculosis in 70 districts of Vietnam. Household contacts in intervention districts were invited to be screened for tuberculosis (consisting of physical examination, chest radiograph, and symptom questionnaire) at a local clinic at enrolment, then at 6 months, 12 months, and 24 months. Household contacts in control districts received standard care. Lung and colleagues estimated the number of disability-adjusted life years (DALYs) averted in the intervention group over 24 months.[8]

The trial results showed that, in the study sites, an additional 1084 registered tuberculosis cases (95% CI 721–1410) and 1154 (776–1495) smear positive tuberculosis contacts per 100 000 people were identified over the 24-month follow-up period in the intervention group compared with the control group, respectively. The estimated incremental cost-effectiveness ratio was US$544 (95% CI 330–1375) per DALY averted and the investigators conducted several sensitivity analyses around model inputs. Although these findings might not be generalisable to other settings—especially to low-income countries or those with high rates of HIV and tuberculosis co-prevalence—the findings, nonetheless, remain important. ACT2 is one of the first rigorous trials to show that an ACF intervention integrated into NTP activities not only increased tuberculosis case detection and reduced all-cause mortality[8] but was also cost-effective. The authors conclude that ACF in tuberculosis-affected households should be considered for wider implementation and scale-up in Vietnam.

Despite proven benefits and endorsement by WHO, ACF interventions tailored towards tuberculosis-affected households have not been widely adopted or integrated into NTP activities in high-burden settings.[9] The reasons behind this low implementation are complex and include health systems that have restricted, overstretched resources; NTPs that work mainly within a static model of health-care provision in clinics and hospitals; and tuberculosis care and prevention that occurs predominantly through passive case finding rather than active case finding, community engagement, and outreach. Another important factor underlying the gap between global policy and national-level implementation of ACF and systematic household screening interventions is the lack of robust economic data available to NTPs to support them to make the most locally-appropriate decisions concerning allocation of resources.[10] Indeed, most extant data supporting ACF interventions was derived from non-randomised observational and modelling studies, rather than being empirical data from pragmatic trials. Lung and colleagues' research[7] highlights the wider importance of incorporating well planned, economic evaluation

into the design of randomised trials, both in the field of tuberculosis and more widely.[11]

For more on the **CRESIPT project** see http://www.ifhad.org

Building on this research, innovative developments in health economic evaluations should be assimilated into the planning and design of randomised trials addressing tuberculosis. First, analyses should go beyond the standard, narrow evaluation of the effect of interventions on health outcomes only (eg, disease-related deaths or cases averted) and examine the effect on non-health outcomes. Extended cost-effectiveness analysis (ECEA) takes into account the effect of an intervention on both health and non-health outcomes, including out-of-pocket expenditures averted, financial risk protection provided, and distributional consequences across socioeconomic strata.[12,13] ECEA is highly pertinent to tuberculosis given that poorer people are often underserved by health and social services and disproportionately affected by tuberculosis infection, disease, catastrophic tuberculosis-related costs, and adverse treatment outcomes.[14,15] Developing simple, user-friendly scores to estimate individual or household risk of tuberculosis, adverse tuberculosis clinical outcomes, or financial shock could ensure that potential interventions reach those most in need and offer the best value for money.[16] Second, existing economic evaluations of interventions targeted at tuberculosis-affected households often underestimate their cost-effectiveness. This is mainly because health outcomes are estimated at a patient or individual level rather than at a household level, despite the household being either the unit of randomisation in the trial or the expressed target of an intervention. Other reasons for this underestimation are that rates of onward transmission of tuberculosis (either intra-household or extra-household) are not incorporated into calculations; duration of data collection or time to final follow-up is often insufficient; and, as in Lung and colleagues' study,[7] data on household contacts' rates of tuberculosis preventive therapy or tuberculosis treatment completion are not frequently included in analyses. More accurate and representative estimates of household-level rather than individual-level health and non-health outcomes are required. Finally, ongoing community-based studies are now evaluating the broader economic consequences of ACF interventions from both a health system and a societal perspective, including mitigation of catastrophic costs of tuberculosis-affected households (eg, the EU-funded IMPACT-TB project in Nepal and Vietnam) and the role of innovations to complement ACF, including socioeconomic support, empowerment, and stigma reduction for tuberculosis-affected households (eg, the CRESIPT trial in Peru[17]).

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In Vietnam, Lung and colleagues[7] have shown that an NTP-delivered ACF intervention targeted to tuberculosis-affected households was not only clinically impactful but also cost-effective. This evidence highlights the importance of economic evaluation in trials and supports the potential scale-up of ACF in Vietnam. These findings should motivate researchers, implementers, and policy makers to evaluate similar ACF models in diverse settings.

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