

in vitro [8], clinical data including Bangladesh regimen experience support its efficacy [7, 9, 10], and for some patients (as in our case) clofazimine represents the only effective drug, exclusion of clofazimine from salvage therapy would greatly limit treatment efficacy. Patients due to receive a regimen with QT prolonging drugs (*i.e.* bedaquiline, delamanid, clofazimine and moxifloxacin) alone or in combination should receive ECG and electrolytes monitoring before and during treatment, so as not to lose therapeutic benefit. If QTc prolongation above 500 ms occurs, one of the QTc prolonging drugs should be promptly discontinued.



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First case, concerns and challenges of treatment of severe XDR-TB with both delamanid and bedaquiline <http://ow.ly/8e4l303i0LH>

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Tuberculosis prevention must integrate technological and basic care innovation

To the Editor:

ALBERT *et al.* [1] advocate for a multipronged approach in rolling out new diagnostic technology for tuberculosis (TB), stating “diagnostic tests alone, if not implemented with a comprehensive package of accompanying tools and within the context of a strengthened health system, may fail to demonstrate the expected benefit”. This is a lesson learned from those who have walked this path before us; one should not be too complacent to ignore basic strategies in the face of escalating technological advances in our field.



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A telling example from the history of TB research and development serves as a potent reminder that technological innovation is ineffective in isolation. In 1917, due to the First World War, the Dutch company, Royal Philips, began developing X-ray equipment following supply chain cuts from Germany. Royal Philips eventually developed a portable X-ray capable of high-quality lung tissue images. In 1932, Royal Philips began TB screening among their staff, then their families, and eventually the entire population of the city of Eindhoven (figure 1). This community-wide screening programme helped reduce TB rates in Eindhoven. By the 1940s, Eindhoven had less than half the TB incidence of cities like Amsterdam, Utrecht and Haarlem [2]. Remarkably, this dramatic reduction preceded the availability of antimicrobials. Treatment was a strict regimen of rest, diet, exercise and fresh air. Without lifestyle and dietary innovations, new diagnostic technologies such as radiography would have been ineffectual in controlling TB.

A hundred years on, the global TB epidemic persists and the innovative research and development community is struggling to deal with the increasing prevalence of drug-resistant TB. This calls for a re-visit to these basic innovations, with a greater focus on prevention of acquisition of infection and progression from latent to active disease. Whilst there are parallels between the TB epidemics of a hundred years ago and the present day, a significant difference is the nature of epidemiological transition and rapid urbanisation, driving the coexistence of infectious and non-communicable diseases, now occurring particularly in low- and middle-income countries. Basic and integrated innovations that address shared risk factors for TB and emerging non-communicable diseases are needed to improve overall health profiles. Nutritional and behavioural innovations that address exposures such as alcohol abuse, tobacco smoke, cooking fuels, diabetes and vitamin D deficiency, in addition to interventions in the built and natural environment, are going to become even more important. Clinicians at the frontlines of TB care in the developing world are often left trying to implement antimicrobial therapy in contexts of dense urban overcrowding, food insecurity and air pollution. Population growth and climate change are further exacerbating the global TB burden. Rolling out technological innovations in the absence of adequate nutrition and basic patient support services could very well serve the rise of drug-resistant TB.

In the contemporary TB research landscape, “innovation” has become almost synonymous with vaccine, biomarker and drug discovery. However, any of these technological innovations will require appropriate implementation within the context of the community they are targeted at. The coexistence of a variety of underlying morbidities, each an independent risk factor for TB, also indicates that the research community developing new technologies must test these technologies in a variety of populations and co-morbidity

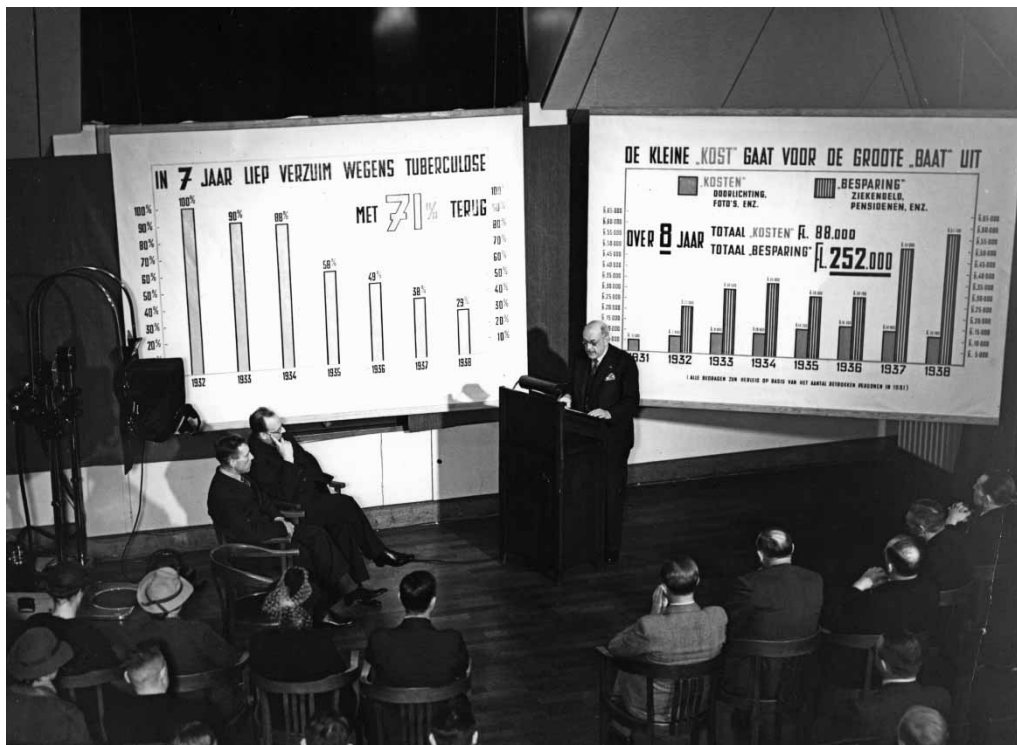


FIGURE 1 A speech by Anton Philips to celebrate the 100 000th radiograph scan for tuberculosis, on May 4, 1939. Figure reproduced with permission from the Philips Company Archives.

backgrounds. Despite this need for understanding the inter-relationship of co-morbidities, interventional research studies often exclude the majority of these individuals who are most at risk. This includes pregnant women and children, and persons with diabetes and HIV infection. Often-insufficient demographic information is captured to analyse the effect of contextual factors such as alcohol abuse, smoke exposure, and nutritional deficiencies on research outcomes. If taken into account, an integrated treatment approach addressing nutritional, behavioural and social interventions together with the new technology could then be assessed.

New technology alone cannot solve the TB epidemic. Innovative, integrated and community-driven solutions, which apply a primary health care approach, and are not purely based on technological innovation, will be required to stop the persistence of TB.



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Without societal, lifestyle and dietary innovations, new technologies will be ineffectual in stopping tuberculosis <http://ow.ly/IgY3303bgdU>

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From the authors:

P.H. Mason and colleagues highlight the fact that “new technology alone cannot solve the [tuberculosis] epidemic” and that integrated and community-driven solutions are needed to meet tuberculosis (TB) care and treatment goals. The authors highlight an example of community-wide screening using portable radiography in the pre-antibiotic treatment era, with patients being prescribed rest, diet, exercise and fresh air, leading to a reduction in TB prevalence in the intervention area. We concur with the authors’ view that a focus purely on introducing new technologies, be they diagnostics, drugs or vaccines, will not have the desired impact on patient outcomes or public health. In our article, we put forward the proposition that a holistic solution is needed to ensure adequate impact of new diagnostics on patient-important outcomes [1]. For TB patients, especially those with multidrug-resistant disease, who require extremely long and arduous treatment regimens, social support, adequate diet and management of other pre-existing conditions, are essential components of a patient’s care, without which patients are unlikely to be successfully treated.

This view is also clearly reflected in the World Health Organization (WHO) End TB strategy [2] pillars: 1) integrated care and prevention (which includes treatment of comorbidities), 2) bold policies and support systems (including social protection, poverty alleviation and actions on other determinants of TB), and 3) intensified research and innovation. Importantly, intensified research and innovation encompasses development of new technologies including drugs, vaccines and diagnostics, but also innovations in implementation to optimise impact. Indeed, the WHO End TB strategy targets for decline in global TB incidence rely on the introduction of new tools, including a point-of-care test for active TB and latent TB infection, by 2025, without which global targets will remain unmet [2].

However, the continued focus on development of new tools should be matched by an equally vigorous drive towards innovation in implementation, with a strong focus on providing patient-centred care. Implementation research must address how novel diagnostics can be better integrated into healthcare

