

Editorial**Ending Tuberculosis by 2030: United Nations High Level Meeting Commitments***Farzana Ismail^{1,2}, Shaheed Vally Omar¹ and Nazir Ahmed Ismail^{1,2,3}**International Journal of Human and Health Sciences Vol. 03 No. 02 April'19 Page : 51-53
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On the 26th of September 2018, the United Nations (UN) General Assembly hosted its first ever high-level meeting (HLM) on tuberculosis under the theme - "United to end tuberculosis: an urgent global response to a global epidemic"¹. This was a historic event, gathering Heads of States and Ministers of Health from around the globe to commit themselves to accelerate efforts to end the tuberculosis (TB) epidemic by 2030. It follows on from the End TB Strategy adopted by the World Health Organization (WHO) that has set targets for 2030 and 2035 which are linked to the sustainable development goals². These targets are to achieve a 90% reduction in TB deaths, 80% reduction in TB incidence by 2030 and zero TB affected households that experience catastrophic costs related to TB, compared with the 2015 baseline.

Tuberculosis is among the top 10 causes of death globally with 1.6 million people estimated to have died from the disease in 2017 alone³. Developing countries are disproportionately affected with 99% of TB associated deaths occurring in these countries⁴. The global burden of TB is estimated to be 10.0 million (range 9.0-11.1 million), while only 6.4 million were formally notified as being on treatment. This highlights a massive gap of 3.6 million TB cases undetected and untreated, which threatens any potential for ending TB. Bangladesh, China, Democratic Republic of Congo, Indonesia, India, Nigeria, Pakistan, Philippines, South Africa and United Republic of Tanzania are the top ten contributors to this gap and collectively account for 80% of the missing 3.6 million³. Despite the extensive burden of disease, positive signs of decline are observed globally with an annual reduction of 2% observed in recent years. The greatest declines seen have been in sub-Saharan

Africa (4-8%), attributed to the aggressive roll out of anti-retroviral treatment that has achieved significant control of the HIV epidemic in the region. Despite these above global average declines, achieving the 2030 target would require a TB incidence reduction of 10% per annum².

Fundamental to driving the change is the requirement of strong political commitment, commensurate with appropriate resources made available. The UN-HLM on TB has achieved this objective by getting countries to commit themselves to ending the TB epidemic. The signed declaration has laid bold actions covering efforts at finding and treating TB, raising the importance of using preventative therapy on scale and addressing the unfolding crisis with drug resistant TB and the neglected paediatric TB epidemic.

Through the UN-HLM initiative, countries have committed to cumulatively diagnose and treat 40 million of TB patients over the period 2018-2022¹, with pre-set allocations for each country⁵. Major advancements in diagnosing TB are available, with the current front line test the Xpert MTB-Ultra assay, a second-generation technology that can detect TB in 88% of culture positive cases in under 90 minutes⁶. Several new competitor products are also on the horizon which is very encouraging³. Unfortunately, adoption and scale up of the new molecular technologies have been lagging and will need to be prioritised. Of concern is the persistence of missed opportunities, especially linking communities to care and treatment. Greater efforts towards patient education and screening for TB is needed to address this issue.

The second key deliverable is to ensure that 30 million individuals receive TB preventative therapy. Such a strategy is not new, however, in

1. Center for Tuberculosis, National Institute for Communicable Diseases, National Health Laboratory Services, Johannesburg, South Africa
2. Department of Medical Microbiology, University of Pretoria, Pretoria, South Africa
3. Department of Internal Medicine, University of Witwatersrand, Johannesburg, South Africa

Correspondence to: Prof Nazir Ahmed Ismail, 1Center for Tuberculosis, National Institute for Communicable Diseases, National Health Laboratory Services, Johannesburg, South Africa. 1 Modderfontein Road, Sandringham, 2131, Johannesburg, South Africa. E-mail: naziri@nicd.ac.za

2017 only 36% of those eligible received preventative therapy⁴. Using a combination therapy of rifapentine and isoniazid for 3 months given once a week (12 doses) has been shown to be as efficacious as 9-months of isoniazid preventative treatment which is very encouraging⁷, while a more recent study has shown that just one month of the combination therapy could do equally well⁸. Such shorter courses could potentially improve adherence and possibly simplify the implementation of this deliverable. Key priority groups for preventative therapy, which include HIV positive individuals who do not have active TB, and all household contacts of TB, not restricted to children under 5 years of age. This latter target group is relatively new and 20 of the 30 million to receive preventative therapy are for this group, potentially minimising future incident cases of TB.

Drug resistant TB, unlike drug susceptible TB is predicted to continue to increase over time⁹ and is a declared public health crisis by WHO. One third of global deaths due to antimicrobial resistance are attributable to multi-drug resistant TB (MDR-TB)⁴. Success rates among MDR-TB have been dismal with only 55% of patients achieving successful outcomes, while it is only 34% among those with extensively drug resistant TB (XDR-TB)³. On the positive side, two new drugs have been introduced for treatment of this challenging condition after a lag of 40 years. Bedaquiline, a diarylquinoline with a novel mechanism of action against *Mycobacterium tuberculosis*, has shown significant impact; halving mortality compared to standard of care¹⁰, while favourable outcomes among those who received a bedaquiline containing regimen was 73%¹¹. The second novel agent Delamanid, a dihydro-nitroimidazooxazole, had shown good overall safety and efficacy in earlier trials, however the recent Phase 3 clinical trial results did not show any improvement with a success rate of 77.1% in the Delamanid containing arm compared with 77.6% in the placebo arm¹². Of note, the overall success in both arms was notably higher compared to routine data from the same settings.

Another advancement has been the establishment

of policies for reduction in treatment duration with newer short regimens used for 9 months rather than 24-months, in a specific category of patients¹³. Thus, the potential to dramatically improve the situation for M/XDR-TB is now. The commitment at the UN-HLM is to ensure that 1.5 million patients between the periods of 2018-2022 with drug resistant TB will receive shorter regimens and the new drugs. Implementation of these new recommendations is urgent if this public health crisis is to be resolved.

An often-neglected component of TB control is paediatric TB. The UN-HLM has made a specific allocation for this form of TB⁴. Of the 40 million TB patients 3.5 million of these should be children as well as 4 of the 30 million individuals placed on preventative therapy should comprise of those at greatest risk exposed to an active adult TB case - children younger than 5 years of age. Addressing paediatric TB has long-term impact and is important when considering the 2030 deadline. Furthermore, child friendly regimens are still severely lagging behind and is now included as important focus in the declaration. There are currently various clinical trials underway incorporating the two new drugs (Bedaquiline and Delamanid) as part of the drug resistant TB regimen for paediatric TB, however, these currently are restricted to children 6 years and older.

In summary, although the End TB Strategy by WHO has set ambitious targets, the recent commitments achieved at the UN-HLM combined with advancements made to date in TB control offer hope. The last decade has seen several new developments in diagnostics and treatment, which need accelerated roll out to ensure that we not only control TB but also end TB. However, even with exceptional implementation it is a tough ask. Therefore, the need for additional commitments towards further research and development, particularly focusing on a vaccine either as primary or secondary protection. If successful, this additional intervention could realise what has seemed as a distant dream. The slogan "*leave no one behind*" is still relevant and everyone, every organization and every country needs to actively play its part.

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