Towards elimination of tuberculosis in New Zealand

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ABSTRACT

New Zealand could be the first country in the world to eliminate tuberculosis (TB). We propose a TB elimination strategy based on the eight-point World Health Organization (WHO) action framework for low incidence countries. Priority actions recommended by the WHO include 1) ensure political commitment, funding and stewardship for planning and essential services; 2) address the most vulnerable and hard-to-reach groups; 3) address special needs of migrants and cross-border issues; 4) identify active TB and undertake screening for latent tuberculosis infection (LTBI) in recent TB contacts and selected high-risk groups, and provide appropriate treatment; 5) optimise the prevention and care of drug-resistant TB; 6) ensure continued surveillance, programme monitoring and evaluation and case-based data management; 7) invest in research and new tools; and 8) support global TB prevention, care and control. In New Zealand, central government needs to take greater responsibility for TB policy and programme governance. Urgent action is required to prevent TB in higher risk groups including Māori communities, and to enable immigration screening to detect and treat LTBI. Clinical services need to be supported to implement new guidelines for LTBI that enable better targeting of screening and shorter, safer treatment regimens. Access to WHO recommended treatment regimens needs to be guaranteed for drug-resistant TB. Better use of existing data could better define priority areas for action and assist in the evaluation of current control activities. Access to GeneXpert® MTB-RIF near the point of care and whole genome sequencing nationally would greatly improve clinical and public health management through early identification of drug resistance and outbreaks. New Zealand already has a world-class TB research community that could be better deployed to assist high-incidence countries through research and training.

Tuberculosis (TB) remains a disease of public health significance to New Zealand. Progress in reducing TB incidence has stalled for more than a decade, with between 276 and 308 cases notified each year.[1] Inequities are a major feature of the epidemiology of TB in New Zealand, with people born overseas and Māori and Pacific peoples disproportionately affected. New Zealand could be the first country in the world to eliminate TB, thereby ending a public health threat and providing a template of success for other countries. We envisage a centrally coordinated TB strategy that uses enhanced surveillance and laboratory tools to promptly diagnose and successfully manage TB cases. Additionally it would more effectively focus preventive efforts on risk groups to reduce TB incidence and achieve disease elimination.

Public health impact of TB in New Zealand

Despite a relatively low overall incidence of 6.3 notifications per 100,000 population, TB remains a disease of public health significance in New Zealand because of the intensive work required to trace contacts and supervise treatment. Drug resistance also magnifies the public health impact of the disease as it causes increased treatment duration, costs and side effects, and requires prolonged isolation. Furthermore, the overall incidence belies substantially higher risk in certain populations. In 2016, the annual incidence in the Asian ethnic group was 32.7 per 100,000, 30 times greater the in the European and Other ethnic group and in Māori was eight time higher than in the European and Other ethnic group.[1]

ISSN 1175-8716

The high incidence of TB in Asian New Zealanders likely reflects a high proportion of recent migrants from countries where TB is common. In 2016 79% of TB notifications in New Zealand were in people born overseas,[1] despite long-term migrants undergoing radiological screening to exclude active TB disease. It is likely TB in migrants represents re-activation of LTBI acquired from having lived in high-incidence TB countries. Consistent with this, isolates in migrants to New Zealand seldom are closely genetically related, and usually reflect the TB strains prevalent in their country of origin.[2] TB can occur anytime over their lifetime but usually occurs within five years of migration. Although good management of cases and contacts means transmission outside the home is infrequent, the children of certain migrants are at risk.[3]

Elimination of TB as a public health problem is defined as <1 notified TB case per million population per year.[4] This is the rate at which it is considered that the disease cannot sustain itself in a population. In New Zealand 'pre-elimination', defined as a rate of approximately 10 per 1,000,000, has been achieved in the European and Other ethnic group. This comparatively low incidence in some sectors of the community illustrates inequities and shows that TB elimination is an achievable goal if TB risk factors and barriers to care are systematically addressed. We use the WHO action framework for low incidence countries to identify key actions for New Zealand to take.[4] New Zealand could be the first country in the world to eliminate TB, thereby providing a template of success to other countries.

Political commitment, funding and stewardship for planning and essential services

New Zealand has no central governance of TB control. Since 2001, responsibility for diagnosis, infection prevention, treatment and operational public health services, including TB, has been devolved to 20 district health boards (DHB) and 12 regional public health units respectively. A national TB advisory group comprising experienced practitioners from these operational units served as a source of technical advice and informal input into programme governance, but was disbanded in 2010. While the government has committed to TB elimination via endorsement of the UN Sustainable Development Goals,[5] in practice there is no coordinated mechanism to deliver on this commitment.

To achieve TB elimination, TB policy development and government coordination would need to be prioritised by the Ministry of Health. Currently there is not a single official whose role focuses on TB. This means TB initiatives occur on an *ad hoc* basis as other priorities and outbreaks permit. A policy for TB elimination is lacking and there is no mechanism for planning the delivery of effective national TB diagnostic services and real-time surveillance infrastructure. Responsibility for aspects of TB control is fragmented across agencies, and as a result the Ministry lacks direct control over medicines supply, surveillance and immigration screening. TB is the archetypal communicable disease of public health significance, which requires central coordination from the Ministry of Health.

Finally, despite New Zealand having a consortium-based initiative for eradication of bovine TB in animals with funding of $80M per year,[6] funding for human TB control is not ring-fenced. Public health units face a number of priorities and are insufficiently resourced for directly observed therapy to be consistently offered throughout the country.

Eliminating TB in Māori

Since the time of European colonisation of New Zealand, TB has had a significant impact on Māori communities. In 1769 the Māori population was 100,000 and in 1820 it had fallen to 42,000.[7] Although the contribution TB played in this decrease is not fully known, it is recognised that even up into the early 1900s, TB was one of the most common causes of premature death within Māori communities. In 1935 Dr Harold Turbott published a report of a high-quality prevalence survey in Māori in the Waiapu valley, East Coast.[8] The prevalence of LTBI was 48.5%, including 81% of all those aged 16 years and over. It is likely that there remains a large reservoir of LTBI in at least older Māori, which will continue to reactivate and cause disease regularly, perpetuating endemic transmission. New

Zealand's isolation means TB may have undergone a founder effect. This means isolates will appear to be part of 'outbreaks' when they are not. A recent whole genome sequencing (WGS) study of 'Rangipo' strains thought to be linked epidemiologically showed that three of the six were not in fact the same strain.[9]

Within Māori, reactivation of LTBI is likely to be promoted by higher rates of comorbidities like cancer and diabetes compared to non-Māori.[10] Timely diagnosis, care and prevention of transmission will be impacted on by higher rates of overcrowding and the added barriers that Māori have accessing health services in their current configuration. For example, Māori are more likely than non-Māori to not see a general practitioner because of cost, less likely to be referred on to specialist services and more likely to experience racism in the health system.[11,12] Yet control of TB requires significant engagement with the health sector for diagnosis, contact tracing and treatment.

Work with Māori communities is required to better understand existing TB strains and the relative contribution of LTBI reactivation versus recent transmission in driving higher TB incidence in Māori. Urgent action is needed to reduce poverty and improve housing for Māori. The professional community of TB clinicians also needs to improve its competence when engaging with Māori individuals and communites to deliver culturally appropriate care.

Addressing the needs of migrants and cross-border issues

Currently migrants applying for a visa to work, live or study in New Zealand are screened for TB using chest radiographs. This screening detects prevalent pulmonary TB, but not LTBI. Data from a number of sources indicate that most TB cases in New Zealand arise from reactivation of LTBI acquired overseas. First, active TB on arrival is unlikely to explain TB cases that develop more than two years after screening,[13] and 75% of TB cases in migrants to New Zealand are diagnosed more than two years after arrival.[1] Second, genotyping confirms infection in New Zealand is uncommon in migrants.[2] Third, we audited the screening records of 120 TB cases occurring within two years of their immigration medical and found 41% had a recent normal x-ray, meaning that a substantial proportion of early cases could also arise from reactivation of LTBI (unpublished data). Screening migrants from high TB incidence countries for LTBI is the initiative that will most substantially reduce TB in New Zealand and is a necessary step for TB elimination.

The US has screened child migrants for LTBI for over a decade. The UK National Institute for Health and Care Excellence recommends LTBI screening for all migrants from countries with an incidence >40 per 100,000 without age restriction following an analysis of cost-effectiveness.[14] In Australia the National Tuberculosis Advisory Committee recommends LTBI screening for migrants under 35 years of age from countries with an incidence >100 per 100,000 or >40 per 100,000 when resources permit.[15] International studies find the prevalence of LTBI in migrants is correlated with TB incidence in their country of origin.[16,17] Similar studies are needed in New Zealand to determine the most appropriate target population and to determine the resource required to provide quality LTBI treatment services equitably. Screening could be initiated during the immigration medical, a positive test should prompt a referral for treatment, and not influence immigration decisions. Implementing LTBI screening and treatment for migrants to New Zealand would have the single greatest impact in reducing TB incidence, addressing an important health disparity for the migrant community and progressing us towards TB elimination.

Undertake screening for active TB and LTBI in TB contacts and selected high-risk groups, and provide appropriate treatment

Public health units perform TB contact tracing to find active and LTBI in recently exposed contacts. Outside of contact tracing, LTBI screening and management in New Zealand has been unnecessarily complex. Firstly, many health sector employers implement large-scale screening of employees with interferon gamma release assays (IGRA) of low-risk individuals. Positive results in low-risk populations like this are most likely to be false positives, and

Figure 1: Who should be tested for LTBI?

- TB case contacts.
- Recent migrants from high-incidence countries.
- People with immune suppression due to HIV infection, TNF-α inhibitors or solid organ transplant, irrespective of TB exposure.
- People with immune suppression due to renal failure, haemodialysis, corticosteroid use and cancer with a history of possible TB exposure.
- Healthcare workers with a history of possible TB exposure.

From Guidelines for Tuberculosis Control in New Zealand, 2019.

the testing is wasteful. Secondly, previous guidelines lacked clarity on the interpretation of tests and did not issue specific recommendations on who should be treated.

New Guidelines for TB control in New Zealand published by the Ministry of Health seek to simplify the approach to LTBI.[18] *The Guidelines* underscore that IGRA and tuberculin skin test are largely equivalent in their performance, except in BCG vaccinated people in whom IGRA is preferred. *The Guidelines* specify clinical populations to be targeted for LTBI screening, and, if they test positive, treated (see Figure 1). New regimens for treatment of LTBI are also recommended, enabling shorter and safer treatment.

The Guidelines provide the framework for better targeted testing. It is clear that clinicians managing individuals with HIV, cancer or renal failure, transplant patients, or those receiving corticosteroids or TNF-α inhibitors must have a systematic approach to TB risk assessment and screening. Laboratories should use these indications as the basis for demand management for IGRA testing. New regimens enable faster and safer treatment of LTBI than previously possible with isoniazid alone. For example,

Capital and Coast District Health Board, has streamlined the management of LTBI in a fortnightly registrar-led clinic. Patients can start treatment at their first (and usually only) clinic visit with follow-up by scheduled telephone visits. This combined with shorter treatment regimens mean the non-attendance rate has fallen from 45% to 16%, and more patients can be treated with the same staff resource.

Optimise the prevention and care of drug-resistant TB

Over the decade ending 2016 the rate of MDR-TB among culture confirmed cases was 1.3%. While the number of referrals to the TB clinical network has increased in the last year, more recent surveillance data is needed to confirm if MDR-TB rates are increasing.

The priority issue in MDR-TB management relates to funding for WHO-recommended second-line antimycobacterial medicines. Historically, the Ministry of Health has guaranteed funding for all aspects of TB care because of the potentially catastrophic consequences of outbreaks. As new treatments for MDR-TB have been developed, the Ministry convened the TB Clinical Network to provide expert advice, including assessing the need for expensive new agents such as bedaquiline.[19]

Over the last 18 months WHO have revised their MDR-TB recommendations,[20] based on a metaanalysis of individual level data from several trails that showed bedaquiline reduced treatment failure by 70%. The new guidelines recommend a combination of highly effective bacteriocidal drugs, including bedaquline, and discourage the use of amikacin due to significant adverse reactions, such as hearing loss in a third of recipients even with therapeutic and audiometry monitoring.[21]

Over time, the TB Clinical Network's role in approving use of bedaquiline has been taken over by PHARMAC. The public health considerations that underpinned guaranteed drug funding have given way to a focus on reducing drug costs. Bedaquiline can only be accessed for MDR-TB if the patient faces exceptional clinical circumstances such as extensive drug resistance (XDR-TB) or an absolute contraindication to or intolerance of other second-line agents. In other words, for most MDR-TB cases bedaquiline is not available until the patient starts to lose their hearing. This is harmful and risks treatment failure and secondary transmission, and is

a false economy as amikacin treatment is as expensive as bedaquilline once the administration costs are considered.[22] The public health considerations in the supply of these essential medicines are poorly incorporated into Pharmac's decision making process, and an urgent review is needed.

Ensure continued surveillance, programme monitoring and evaluation and case-based data management

Active TB is a notifiable disease in New Zealand and annual surveillance reports provide a comprehensive description of TB cases and trends with respect to time, person and place as well as basic clinical, drug susceptibility and molecular typing analysis. There are various ways in which better use of existing data and additional data collection could support TB elimination in New Zealand.[23] Firstly, including TB notifications in the government's integrated data infrastructure with linkage with health, demographic and immigration datasets[24] would enable periodic analytic studies. These could better define risk factors for TB in New Zealand and would be especially useful for identifying how immigration screening (and access to funded treatment) could be improved. Secondly, performance indicators for case management and contact investigations should be developed and routinely applied by clinical and public health services for information on quality of care. Thirdly, new data on LTBI prevalence in Māori and other risk populations are needed to better understand the potential for future disease and guide prioritisation for intervention.

Invest in new tools

Over the last decade there have been significant advances in the laboratory diagnosis of TB, and the testing for drug susceptibility. The introduction of the molecular tests Xpert MTB/RIF (Cepheid, Sunnyvale, CA, US) and Xpert MTB/Rif Ultra assay now make it possible to very rapidly diagnose TB and identify resistance from clinical samples. This allows TB to be confirmed more rapidly, and results in better use of isolation. *The Guidelines for TB control in New Zealand* recommend a Xpert® MTB-RIF is performed on all smear positive samples,[18] and this needs to be available in regional laboratories to ensure the benefits of rapid diagnosis are achieved equitably.

The introduction of WGS offers many potential benefits such as providing a greater discrimination of strain relatedness, reducing unnecessary contact tracing and identifying links not established through contact tracing processes. It also supplements phenotypic drug susceptibility testing by providing rapid identification of resistance gene mutations to a wide range of drugs.[25,26] Unlike the rapid PCR tests which should be available close to patient care, WGS should be centralised allowing for expertise in the interpretation of results to support both public health and clinical decision making. Interpretation of WGS data used in case and outbreak management needs supported training for clinicians and public health staff with regular regional and national meetings to discuss findings. Models like this exist in Australia and the UK, which shows close liaison between public health, clinicians and laboratory scientists in the interpretation and application of such findings is essential. There is widespread support for a national reference laboratory providing rapid, consistent and well-interpreted results available to multidisciplinary teams.

Support global TB prevention, care and control and invest in research

Like many communicable diseases of significance in New Zealand, TB is a persistent reminder that we are connected to the wider world. Even if we can achieve elimination, we will remain vulnerable to re-entry of *M. tuberculosis*. Therefore, New Zealand needs to play a role in addressing TB on a global scale. New Zealand indicated readiness to work towards global TB elimination through adopting the sustainable development goals. New Zealand funding should go towards enhancing TB control in Low and Middle Income Countries through the New Zealand Aid Programme. This can focus on the Asia-Pacific region, which has the highest TB burden globally and the source of a substantial proportion of cases identified in New Zealand. New Zealand TB experts could play an active role in prioritising and implementing projects and are in a strong position to train TB control programme staff on scholarships in a broad array of disciplines. New Zealand has also

invested in TB research through joining the e-Asia initiative since 2014. There is a critical mass of TB-focused researchers in New Zealand who are part of the global research community, studying immune protection,[27] vaccine development,[28] new drug development,[29] diagnostics[30] and public health. These research efforts should be enhanced by more investment. Furthermore, New Zealand TB experts should be encouraged and enabled to contribute their expertise to global bodies.

Conclusion

By eliminating TB we can address the stark inequities that characterises this illness, particularly among Māori compared to others born in New Zealand. It is evident that LTBI screening of migrants from high TB incidence countries will be necessary to achieve TB elimination, whereas for Māori, further study is urgently needed to determine the appropriate action. Other priority actions include the implementation of LTBI screening recommendations for high-risk clinical populations. Ensuring laboratory capability to rapidly diagnose TB and identify drug resistance and clusters is needed. Disease intelligence needs to be extended beyond surveillance to analytic studies and periodic programme evaluation. The management of TB case contacts and other clinical populations has been streamlined, but quality projects and audit are required to ensure this is implemented.

Strong leadership by the Ministry of Health will be necessary, and can begin with the development and implementation of a TB elimination plan to prioritise these goals. New Zealand has a depth of scientific and clinical expertise in TB that can assist this implementation.

Competing interests:
Dr Perumal reports and works as the local Medical Officer of Health for TB control in the Auckland Region.

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www.nzma.org.nz/journal-articles/towards-elimination-of-tuberculosis-in-new-zealand

REFERENCES:

1. Institute of Environmental Science. Tuberculosis in New Zealand 2016 [Internet]. Porirua; 2019. Available from: http://surv.esr.cri.nz/PDF_surveillance/AnnTBReports/TBannualreport2016.pdf
2. Yen S, Bower JE, Freeman JT, Basu I, O'Toole RF. Phylogenetic lineages of tuberculosis isolates in New Zealand and their association with patient demographics. The International Journal of Tuberculosis and Lung Disease. 2013; 17(7):892–7.
3. Marx FM, Fiebig L, Hauer B, Brodhun B, Glaser-Paschke G, Magdorf K, et al. Higher Rate of Tuberculosis in Second Generation Migrants Compared to Native Residents in a Metropolitan Setting in Western Europe. PLoS One 2015; 10(6):e0119693.
4. Lonnroth K, Migliori GB, Abubakar I, D;Ambrosio L, de Vries G, Diel R, et al. Towards tuberculosis elimination: an action framework for low-incidence countries. The European respiratory journal 2015; 45(4):928–52.
5. United Nations. United Nations General Assembly Resolution A/Res/70/1: Transforming our world: the 2030 Agenda for Sustainable Development. Resolution adopted by the General Assembly on 25 September 2015..
6. OSPRI Consolidated Financial Statements [Internet]. 2018 [cited 2019 Sep 9]. Available from: http://ospri.co.nz/assets/Uploads/Documents/OSPRI-Consolidated-Financial-Statements-201718.pdf
7. Pool I. Death rates and life expectancy - Effects of colonisation on Māori [Internet]. Te Ara - the Encyclopedia of New Zealand. Available from: http://teara.govt.nz/en/death-rates-and-life-expectancy/page-4
8. HB Turbott. Tuberculosis in the Māori, East Coast, New Zealand. Wellington: Department of Health; 1935.
9. Colangeli R, Arcus VL, Cursons RT, Ruthe A, Karalus N, Coley K, et al. Whole Genome Sequencing of Mycobacterium tuberculosis Reveals Slow Growth and Low Mutation Rates during Latent Infections in Humans. PlosONE 2014; 9(3):e91024. Available from: http://dx.plos.org/10.1371/journal.pone.0091024
10. Ministry of Health New Zealand. Wai 2575 Māori Health Trends Report. Wellington New Zealand; 2019.
11. Health Quality & Safety Commission New Zealand. A window on the quality of Aotearoa New Zealand's health care 2019 – a view on Māori health equity [Internet]. 2019. Available from: http://www.hqsc.govt.nz/assets/Health-Quality-Evaluation/PR/Window_2019_web_final.pdf
12. Harris R, Tobias M, Jeffreys M, Waldegrave K, Karlsen S, Nazroo J. Effects of self-reported racial discrimination and deprivation on Māori health and inequalities in New Zealand: cross-sectional study. Lancet. 2006; 367(9527):2005–9.
13. Walter ND, Painter J, Parker M, Lowenthal P, Flood J, Fu Y, et al. Persistent latent tuberculosis reactivation risk in United States immigrants. American Journal of Respiratory and Critical Care Medicine 2014; 189(1):88–95.
14. National Institute for Excellence in Health and Care. Tuberculosis: Prevention, diagnosis, management and service organisation [Internet]. National Institute for Health and Care Excellence; 2016. Available from: http://www.nice.org.uk/guidance/NG33
15. National Tuberculosis Advisory Committee. National position statement for the management of latent tuberculosis infection [Internet]. Vol. 41, Communicable diseases intelligence quarterly report. 2017. Available from: http://www.health.gov.au/internet/main/publishing.nsf/Content/cdi4103-d
16. Menzies NA, Hill AN, Cohen T, Salomon JA. The impact of migration on tuberculosis in the United States. The International Journal of Tuberculosis and Lung Disease. 2019; 22(12):1392–403.
17. Pareek M, Watson JP, Ormerod LP, Kon OM, Woltmann G, White PJ, et al. Screening of immigrants in the UK for imported latent tuberculosis: a multicentre cohort study and cost-effectiveness analysis. Lancet Infectious Diseases. 2011; 11(6):435–44.
18. Ministry of Health New Zealand. Guidelines for Tuberculosis Control in New Zealand, 2019. Wellington: Ministry of Health New Zealand; 2019.

19. Diacon AH, Pym A, Grobusch MP, de los Rios JM, Gotuzzo E, Vasilyeva I, et al. Multidrug-Resistant Tuberculosis and Culture Conversion with Bedaquiline. New England Journal of Medicine. 2014; 371(8):723–32.

20. World Health Organisation. Consolidated guidelines on drug-resistant tuberculosis treatment. Geneva:WHO; 2019.

21. Peloquin CA, Berning SE, Nitta AT, Simone PM, Goble M, Huitt GA, et al. Aminoglycoside Toxicity : Daily versus Thrice-Weekly Dosing for Treatment of Mycobacterial Diseases. Clinical Infectious Diseaseess 2004; 38(11):1538–1544.

22. McNaughton A, Blackmore T, McNaughton H. Comprehensive cost of treating one patient with MDR/pre-XDR-TB in Wellington, New Zealand. European Respiratory Journal [Internet]. 2016; 48(4):1256–9. Available from: http://erj.ersjournals.com/lookup/doi/10.1183/13993003.00876-2016

23. Theron G, Jenkins HE, Cobelens F, Abubakar I, Khan AJ, Cohen T, et al. Data for action: collection and use of local data to end tuberculosis. The Lancet [Internet]. 2015; 386(10010):2324–33. Available from: http://www.thelancet.com/article/S0140673615003219/fulltext

24. Milne BJ, Atkinson J, Blakely T, Day H, Douwes J, Gibb S, et al. Data Resource Profile: The New Zealand Integrated Data Infrastructure (IDI). International Journal of Epidemiology. 2019; 48(3):677–677e.

25. The CRyPTIC Consortium and the 100 000 Genomes Project. Prediction of Susceptibility to First-Line Tuberculosis Drugs by DNA Sequencing. New England Journal of Medicine 2018; 379(15):1403–15.

26. 6. Basu I, Bower JE, Roberts SA, Henderson G, Aung HL, Cook G, et al. Utility of whole genome sequencing for multidrug resistant Mycobacterium tuberculosis isolates in a reference TB laboratory in New Zealand. New Zealand Medical Journal. 2018; 131(1487):15–22.

27. Verrall AJ, Schneider M, Alisjahbana B, Apriani L, van Laarhoven A, Koeken VACMV, et al. Early clearance of Mycobacterium tuberculosis is associated with increased innate immune responses. J Infect Dis [In Press]. 2019; doi:10.1093/infdis/jiz168

28. Steigler P, Daniels NJ, McCulloch TR, Ryder BM, Sandford SK, Kirman JR. BCG vaccination drives accumulation and effector function of innate lymphoid cells in murine lungs. Immunology and Cell Biology. 2018; 96(4)379–389.

29. Hards K, McMillan DGG, Schurig-Briccio LA, Gennis RB, Lill H, Bald D, et al. Ionophoric effects of the antitubercular drug bedaquiline. Proceedings of the National Academy of Sciences of the United States of America. 2018; 115(28):7326–31.

30. Mulholland CV, Ruthe A, Cursons RT, Durrant R, Karalus N, Coley K, et al. Rapid molecular diagnosis of the Mycobacterium tuberculosis Rangipo strain responsible for the largest recurring TB cluster in New Zealand. Diagnostic Microbiology and Infectious Disease. 2017; 88(2):138–40.