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## **Eliminating Latent Tuberculosis in low burden settings: Are the principal beneficiaries to be disadvantaged groups or the broader population?**

**Degeling, C., J. Denholm, P. Mason, I. Kerridge and A. Dawson (2017)**

Correspondence to Dr Chris Degeling, Centre for Values, Ethics and the Law in Medicine, Level 1, Medical Foundation Building, K25, University of Sydney, NSW 2006, Australia;  
[chris.degeling@sydney.edu.au](mailto:chris.degeling@sydney.edu.au)

### **Abstract**

Tuberculosis (TB) remains a leading cause of morbidity and mortality worldwide, and the burdens of this disease continue to track prior disadvantage. In order to galvanise a co-ordinated global response, the World Health Organisation has recently launched the *End TB Campaign* that aims to eliminate TB by 2050. Key to this is the introduction of population screening programmes in low burden settings to identify and treat people who have latent TB infection [LTBI]. The defining features of LTBI are: that it is not an active disease but confers an increased risk of disease; the socially disadvantaged are those most in danger; and, uncertainty persists as to who will be harmed or benefitted from screening-led prophylactic interventions. Systematic screening programmes that include surveillance, case-finding and treatment of asymptomatic individuals inevitably redistribute the risk of harms and the potential for benefits within a population. The extent to which those targeted within such programmes should be exposed to higher levels of risk in the pursuit of individual or community benefits requires careful consideration prior to implementation. As currently construed, it remains unclear who stands to benefit most from how LTBI screening in high income countries is being organised, and whose health is being prioritised: members of disadvantaged groups or the broader community. Unless the aims of LTBI screening programmes in these settings are made transparent and their prioritisation ethically justified, there is a significant danger that such a targeted intervention will further disadvantage those who have the least capacity to bear the burdens of TB elimination.

## Introduction

Tuberculosis (TB) remains a leading cause of morbidity and mortality, with an estimated 10.4 million new cases and 1.4 million deaths occurring globally in 2015.(1) While the numbers remain large, these figures represent a major advance. The global rates of TB mortality have declined by 47% since 1990, with most of these gains made in high burden settings. Despite this progress, the most recent *Global Tuberculosis Report* highlights that detection and treatment gaps remain – with more than a third of new TB cases remaining undiagnosed or unreported. In light of this impact upon human health the elimination of TB (defined as an annual incidence of less than 1 case per million of population) would be a major achievement. In July 2014, the World Health Organisation released the *Framework towards tuberculosis elimination in low-incidence countries*, as a central component of the *End TB Strategy* to eliminate TB globally by 2050.(2) Interim targets for attaining this goal have been set at a 40/60% reduction in the TB incidence rate by 2025/30.

The *WHO End TB Strategy* has 3 pillars, each of which are intended to promote co-ordinated actions that address specific drivers of the global burden.(3) The first pillar of the strategy focuses on providing integrated, patient-centred care and prevention. The second concentrates on promoting measures such as social protection, poverty alleviation and enhanced epidemiological surveillance to address the social dimensions of health. The third intends to provide the intellectual and financial impetus for rapid diagnostic and therapeutic innovation. When combined, the 3 pillars should do much to ameliorate many of the key structural, technological and socio-cultural barriers to effective and sustained TB control, and, over-time, will create the conditions where elimination is possible. Importantly, the overall success of the End TB strategy will depend on global investment in providing sufficient health coverage and social protection for populations in low income countries and on the development of new tests and treatments suitable for use in these high-burden and low resources settings.(3)

A historical reluctance to address global poverty, and present constraints on technologies and healthcare resources, mean that most of the early gains in TB elimination are likely to be achieved in low burden settings such as North America, Australasia and the European Union.(4) In these low-burden countries the rates of TB transmission are typically very low and TB cases tend to cluster in disadvantaged groups such as migrants, prisoners, the homeless, indigenous peoples and those living in poor housing and poverty.(5) Most people who develop active TB in these low-burden settings have done-so following the re-activation of previously latent TB infection [LTBI].(6) This means that the identification and management of latent LTBI is a critical component of the first pillar of the new post-2015 *End TB Strategy*.(7)

While the difference between active TB and LTBI is both clinically and biologically ambiguous, the distinction has important epidemiological, socio-cultural and ethical dimensions.(8) People with LTBI do not have an active infection; they are asymptomatic carriers and pose no immediate risk to others. LTBI is a potential disease for some and an inconsequential infection in the vast majority of people who carry the mycobacteria. People with LTBI can, however, pose a risk to others in the future if their infection becomes active (the lifetime risk for someone with LTBI of developing active disease being between 5 and 15%).(4)

The initial focus of the *End TB Strategy* on identifying and treating people with LTBI in low burden settings is a major departure from past efforts at global TB control and prevention. Interventions organised under *The Stop TB Campaign* concentrated on identifying and

delivering effective treatment to individuals with active disease in locations where the burden of active disease is high.(9) In contrast, it is estimated that globally 1 in 3 people have LTBI (10) – so the *End TB Strategy* is a major escalation in the scale and scope of TB control.

The case for screening disadvantaged groups for LTBI is that their rates of re-activation are much higher. For example in the USA, as in other low burden countries, individuals with LTBI / HIV co-infection face up to a sixty-fold increase in the relative risk of reactivation when compared to someone with LTBI. Reactivation becomes more likely the greater the burden of immunosuppressive comorbid disease for people living with diabetes mellitus or organ transplants.(11) The contextual dimensions of TB infection, such as social disadvantage and deprivation are also important determinants of LTBI reactivation. Recent migrants from low and middle-income countries are relatively economically disenfranchised, and at substantially higher risk of active TB than non-migrants. The risk is highest shortly after arrival, but persists at levels higher than non-migrants lifelong.(12, 13) The late diagnosis of re-activated TB is also a common occurrence amongst marginalised people, and is associated with worse outcomes for the individual, and in the case of pulmonary TB with a potential transmission risk to the public. The risk to others from reactivation is not insignificant. It has been estimated that between 5-7% of new TB cases in low burden countries like Australia are due to transmission from individuals with reactivated LTBI, with most cases primarily affecting family members and close social contacts.(14)

In this paper we explore some of the relevant ethical issues to consider when contemplating introducing systematic LTBI screening programmes that include surveillance, case-finding and treatment of asymptomatic individuals. We argue that such programmes, which we refer to as LTBI screening in this paper for brevity, inevitably redistribute the risk of harms and the potential for benefits within a population. The extent to which those targeted within such programmes should be exposed to higher levels of risk in the pursuit of individual or community benefits requires careful consideration. As currently construed, it remains unclear who stands to benefit most from how LTBI screening in high income countries is being organised, and whose health is being prioritised: members of disadvantaged groups or the broader community. Unless the aims of the LTBI screening programme in these settings are made transparent and their prioritisation ethically justified, there is a significant danger that such a targeted intervention will further disadvantage those who have the least capacity to bear the burdens of TB elimination.<sup>1</sup>

### **The nature of population screening**

The idea of screening otherwise healthy people for LTBI so as to prevent the harms of future disease – both for the individual being tested and their communities – is seductive. But it is important to realise that screening asymptomatic people for early disease or heightened disease risk can create both benefit and harm. Systematic screening redistributes risk across a population. Some people who may otherwise go on to develop active disease receive earlier interventions, providing benefits to them and potentially their communities. Others, however, who may not have developed active disease, receive treatments that are of no real benefit to them, and might actually cause them harm. As we cannot compare the alternate future of each individual based on his or her decision about whether or not to be tested, it is

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<sup>1</sup> It should be noted that when we refer to populations or communities (and any associated risks and benefits) that attach to such collective groups, we remain neutral on questions of social ontology. Nothing in this paper hangs on whether such a group is or is not ‘more than’ an aggregate of the individuals comprising that group. All ‘group’ talk can be translated into ‘individual constituent’ talk if the reader wishes.

impossible to know who will have truly benefited and who will have actually been harmed by screening-led interventions.(15) Because programmes can be organised so as to minimise the risk of potential harms for individuals at the expense of maximising the potential benefits for populations, or *vice versa*, the most fundamental issue is to determine exactly what the primary purpose of a systematic screening programme ought to be.(16)

The key ethical issue here is whether efforts to determine the disease/risk status of individuals are a *means to*, or the *goal of*, the programme. When case finding activities are directed toward the secondary prevention of a non-communicable disease, it is often the case that *means* and *goal* align so closely that the difference between them is negligible. However, screening for a communicable disease can bring the *means* and *goal* of a specific programme into tension. This is because screening for communicable disease can be directed towards primary prevention, secondary prevention or both. The choices then faced occur on two interrelated dimensions:

- i) whether the screening programme should be organised in order to prioritise the provision of benefits to individuals or the populations to which they belong; and,
- ii) whether the ultimate goal of the screening programme is to improve the quality and length of the lives of people who are at higher risk of active disease, or to detect individuals with abnormalities such that every potential case is found and any risk removed.

Complicating these considerations are aetiological and contextual factors. The nature of the disease being screened for, and the likelihood and scale of potential harms and benefits, have a significant bearing on how the ultimate purpose of the programme should be framed, and how any potential harms and benefits incurred in its practice will be distributed. For example, screening programmes for highly communicable diseases that cause minor harms to most individual participants are easier to justify ethically if they prevent significant harm to many others (thereby promoting population health); whereas screening programmes for non-communicable diseases might be unethical if they unnecessarily harm, burden or inconvenience a large number of participants with inconsequential disease for the benefit of a few.

The resources available to targeted individuals and their communities, and the social, cultural and economic context within which they live, are also important considerations. Depending on what you think the ultimate goal of screening a population for a specific condition is, you might arrive at different conclusions as to how a programme should be organised to achieve this ambition. In making this determination, it is important that both harms and benefits are treated fairly, and that the contingent features of programmes are not treated as necessary features. A hierarchy of goals for screening for active TB has been described where the primary benefits being pursued are directed towards individuals, and the *means* and *goals* are closely aligned.(17) Yet as we move towards TB elimination it remains unclear who stands to benefit most from LTBI screening in low burden countries, and whose health is being prioritised – members of disadvantaged groups or the broader community?

### **The harms and benefits of LTBI screening programmes**

LTBI screening programmes have potential benefits for individuals and populations. The early detection and treatment of LTBI through screening can reduce morbidity, and, in some instances, be life saving. This benefit can accrue for people with LTBI identified through screening programmes, and these individual benefits could aggregate for the broader population who individually and as a group, could enjoy greater productivity and a lower risk of TB infection. Other benefits for individuals found to have LTBI can include simpler and less

toxic preventive interventions, and less overall disruption to their health and quality of life were they to develop active disease (and endure subsequent treatment). Earlier intervention could conceivably also be of benefit to individuals and populations if they free up resources that can be allocated elsewhere to address other pressing social, economic or health problems. Removing the burdens that TB can add to the lives of those at extreme social, economic and material disadvantage would be a watershed in global health. (3, 5)

Framed in these terms, the logic of LTBI prevention is compelling. However the available screening tests for LTBI only identify the presence of *risk* or the *possibility* that disease may occur; they do not allow you to accurately predict who will develop clinical disease at some future point, even amongst groups at higher risk. Any further specification is difficult because uncertain combinations of mycobacterial, host and environmental risk factors determine an individual's progression from LTBI to active TB. This indeterminacy in the prognostic value of LTBI case finding is compounded by uncertainties about the effects of treatment as there is currently no test available to confirm that the treatment for LTBI has been successful for a specific individual. This makes it difficult to claim that a medical intervention has saved someone with LTBI from active TB, and thereby also protected the community. Anti-tuberculous therapy, which typically involves taking a dose of the pharmaceutical isoniazid (INH) daily for 6 - 9 months, also carries risks of physical harms. While INH is generally well-tolerated, it frequently causes headaches, rashes, and fevers and may cause hepatitis in about 1 in 200 patients.(4) While newer, short-course treatment for LTBI are in use in some countries, side effect profiles are not significantly different.(18) As a consequence, even in high-income countries such as Canada and the USA, treatment completion is often hampered by drug intolerance and inconvenient clinical schedules.(19) The incidence of potentially life threatening side effects such as hepatitis is likely to be much higher, and the long-term consequence more devastating when treatments are given to disadvantaged individuals – people who have limited capacities to deal with the social and psychological burdens of a LTBI diagnosis or the impositions and potential harms associated with its medical management.

Other potential harms from the large-scale treatment of LTBI are the promotion of further drug resistance. Even as current evidence suggest this is unlikely (4) – if it occurs this harm will profoundly affect individuals, their communities and future populations. Concern about the possibility of emergent drug resistance has spurred examination of alternatives to treating those who screen positive for LTBI including monitoring of individuals with LTBI and treating them only if they develop evidence of TB reactivation. However, even if people at the highest risk from LTBI in low-burden settings are willing to commit to participate in long-term surveillance, some harms posed by LTBI screening persist. Furthermore, even offering a test to an individual can have far-reaching consequences for their future.(20) The psychological and social impacts of screening are often discounted and rarely investigated.(21) Being labelled with a disease or told you are at elevated risk of a condition can do more than cause stress and anxiety – it can change a person's ability to support themselves, how they think of themselves and their social identity.(8, 22) The harms experienced by individuals can also aggregate to affect the health of current and future populations – through exacerbating rather than alleviating the relative social and economic disadvantage of participants. Described in these terms the case for promoting LTBI screening programmes in disadvantaged groups seems far from overwhelming, but the potential for harm to individuals is not sufficient justification not to screen. For every harm caused by screening there is potentially a compensatory benefit that can be provided. If the harms of LTBI screening programmes are necessary features of the intervention, then the provision of such benefits to those affected could promote circumstances where meeting the needs of

the population does not place excessive burdens on individuals.

It might be objected that many of the potential problems that we have pointed out could be met by ensuring that an informed decision to agree to or refuse involvement in LTBI screening is obtained from potential participants. However, as we discuss below, although consent is important, it is not the answer to all of these potential problems. For example, an individual cannot agree to belong to a disadvantaged group and any inequities that may be attached to such a position, they cannot agree to the existence of any additional risks of group stigma if they are part of a migrant community, they cannot consent to the way that a LTBI screening programme is constructed, or the aims of such a programme if it focuses on population-level outcomes. Individuals can, of course, agree or refuse treatment for their LTBI within the programme, but once such a public health programme is established and focused on TB elimination, it will be a strong individual who is able to refuse participation, especially if they are from a prior disadvantaged group.

In the simplest terms, it will always be necessary to trade-off different factors when setting up a targeted LTBI screening programmes. There is a danger that the focus in high-income settings is on pursuing the benefits of screening, rather than weighing this against necessary protections for participating individuals and relevant high-risk social groups such as migrants from high-burden countries.(5,7) A possible alternative programme, for example, would be one that focused on minimised the potential harms to individuals through offering non-onerous long term surveillance to LTBI-positive members of vulnerable groups – treating any that develop active disease – rather than prophylactically treating every case in the targeted group. The individual harms that would be minimised by such an alternative include that otherwise healthy people are not exposed to the risks of iatrogenic injury through treatment, the social, economic and psychological burdens of undertaking prophylactic treatment and the broader social and psychological impacts of being labelled as having TB. The population benefits being sacrificed through this arrangement are the protective benefits of eliminating as much TB as possible from the broader community so that eventually the risks and costs of active TB are so small that these resources can be allocated elsewhere and the populations previously at risk can live longer and more productive lives as a collective, and we no longer have the impacts of syndemic illness and disease from TB in these already disadvantaged groups.(23)

#### **Implications for LTBI screening programmes in low burden settings**

The potential for substantial and enduring population level benefits appears to provide much of the underlying rationale for TB Elimination. But if case finding and treatment of LTBI amongst disadvantaged groups in low burden settings is a *means* rather than a *goal* of TB elimination, it is necessary both to provide a sound ethical justification for the intervention proposed and to explicitly identify the redress/compensation that will be offered to those who experience harms, burdens or even inconveniences.(24) There are emerging models for how public health programmes that seek to benefit populations at the expense of individuals can be constructed so as to be ethical. Drawing on scholarship in research ethics, Jaffe and colleagues (25) have, for example, proposed that these types of programmes can ‘ethically proceed’ under the following conditions:

1. That participants give valid consent
2. The risk of [net] harm to participants of the intervention is low
3. That if there is an alternative way of achieving the same benefits that does not use participants as a *means* to an *end*, then those means should be used.
4. The public health benefit is large enough to justify the risk of harm to participants.

5. Data on harm to participants must be collected during implementation so that increasingly accurate estimates of risk and harm can be provided.
6. An appropriate independent body scrutinizes the programme.

Whilst it is not clear in regards to LTBI that the benefits to populations are always 'at the expense' of individuals, given the uncertainties, constraints and trade-offs described above, it is clear to us that there are three issues intrinsic to the ethical practice of active case finding for LTBI in disadvantaged groups that need to be addressed.

*i) To what extent is the primary purpose of LTBI screening programmes to promote individual or population benefit?*

TB was one of the first conditions targeted by mass population screening, and continues as part of many immigration health-screening programmes. In this context screening for active TB is explicitly directed at benefiting the population of the potential receptor state by policing TB mobility.(26) In contrast, recent proposals to systematically screen populations in high-burden settings for active disease are more closely aligned to providing benefits to individuals, with the anticipation that populations will also reap rewards from lower transmission rates and burdens of morbidity.(17) In the case of LTBI screening programmes, encouraging individuals to take on burdens for the good of society mandates some form of reciprocal arrangements.(27) It is laudable, therefore, that the guidelines of the WHO's *End TB campaign* insist that enhanced social protection and health coverage for disadvantaged groups subject to targeted LTBI screening must be part of the intervention – as pay off for participation.(4, 5) What priority, if any, the LTBI screening programme is placing on population benefits needs to be described, explained and negotiated with those involved and ethically justified, as does any potential burdens the pursuit of these population benefits places on individual participants and targeted communities.

*ii) How should we measure, classify and compare net harms and net benefits?*

Key concerns in evaluating any screening intervention are the certainty with which the individuals identified through screening progress to active disease and whether earlier detection leads to more effective treatment.(16) In the case of LTBI, the outcomes of interest are both at the individual and community levels through potential impacts on progression to re-activation and transmission. Treating population benefits fairly is necessary, but makes these evaluations more complicated. The harms and benefits of screening also have unique social, economic and cultural dimensions. More work is needed on the social and psychological impact of a LTBI diagnosis within the context of the lived experience of disadvantaged groups such as migrant communities before any accurate estimation of the balance of harms and benefits for individuals and populations can be made.(28) Isolated cross-sectional or case-control studies are not sufficient. The examination and evaluation of the harms experienced by participants must continue as a central and iterative feature of any LTBI screening programme's on-going implementation. Efforts to develop new predictive tests and alternative measures such as enhanced surveillance of migrant groups for active cases must also remain on the table for consideration until we are sure that the public health benefits from LTBI screening are sufficiently large before we ask those from disadvantaged groups to take on the burdens.

*iii) How should we manage ambiguity in the concept of latent infection?*

LTBI is a risk for developing TB, it is not an active disease itself. Except for immune-compromised people in high risk groups such as people living with HIV, we cannot know which individuals with LTBI will benefit from prophylactic treatment. In the absence of diagnostic and prognostic certainty, claims and assumptions that all individuals who are

identified and treated for LTBI through screening have been saved from active TB must be resisted. Given that at least a third of the world have LTBI, by this logic a lot of people will need saving. Similarly, encouraging individuals to accept treatment for their LTBI without informing them of the ambiguity, the risks and uncertainties inherent in the definition, diagnosis and treatment of LTBI is profoundly unethical. Whether individuals are to be treated as *means* or *a goal* for TB elimination, the current ambiguity surrounding LTBI is a barrier to the success of efforts to ensure that those targeted for screening make an informed choice to participate. Experience with other screening programmes indicates that members of disadvantaged groups such as migrants can be difficult to access and struggle to meet efforts to provide them with information and shared decision-making processes.<sup>(29)</sup> If LTBI screening in disadvantaged groups is to be pursued then communication tools and decision aides need to be developed in order to support potential participants to make decisions that reflect their priorities and values. At the same time it remains incumbent upon those offering screening to ensure that those who choose to risk harms for the good of the population are adequately compensated should these harms eventuate.

### **Concluding remarks**

Evaluating the ethical dimensions of LTBI screening programmes requires a consideration of the burdens and benefits for asymptomatic individuals against the potential for TB transmission and harm to others, including future populations. Targeted LTBI screening of a specific sub-population will certainly benefit some members of that group – those who would have gone on to develop active TB. However, such a programme will certainly also harm other individuals – those who screen positive and receive treatment but would never have developed active TB. In addition, targeting specific groups might also harm others who do not have LTBI at all, through the effects of perceptions about the group being targeted (e.g. migrants from high-burden TB countries), through social stigma and other negative social and cultural effects, even where such a programme also providing benefits to the broader population by reducing the incidence of and costs of active TB disease. Working out how all of this might cash out is the key issue. What we need is greater empirical evidence about both potential risks and benefits and community perceptions of them.

Important to all these considerations is that the harms caused by screening programmes are iatrogenic – they would not have existed without participation. The key ethical and public health challenge in pursuing TB elimination in low burden settings is that the risks of screening, surveillance, case-finding and treatment will fall upon those already marginalised and those who often have least access to health care resources. This potential for iatrogenic harms adds an extra dimension of responsibility that is not present in other clinical encounters where a patient with symptoms is seeking medical assistance. However the prioritisation of population benefits over the harms experienced by individuals does not necessarily entail that a screening programme is unethical. As long as alternative approaches to TB elimination are judged to provide insufficient population benefits, asking individuals and their communities to take on this burden for the common good might be ethically appropriate. Programmes can be organised such that any acceptance of necessary harms to individual or communities from systematic screening is entirely contingent upon the availability of measures that ameliorate or counteract these burdens. Care must be taken to ensure that necessary and contingent features of screening programmes complement one another such that participants and populations are treated fairly. Problems will arise if there is insufficient effort to characterise what all of these burdens are, and explain to those being targeted for screening the nature and the value of the benefits being pursued. As a team comprised of clinicians, bioethicists and anthropologists, we assert that we are being wilfully blind if we simply focus on the ‘lives’ saved and do not consider the potential for other



unwanted effects from the focus on LTBI-screening as a means to achieve progress towards TB elimination.

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### **References**

1. WHO. Global Tuberculosis Report. Geneva: World Health Organization 2016.
2. WHO. Documentation for World Health Assembly 67. Geneva World Health Organization; 2014.
3. Uplekar M, Weil D, Lonnroth K, Jaramillo E, Lienhardt C, Dias HM, et al. WHO's new End TB Strategy. *The Lancet*. 2015;385(9979):1799-801.
4. Getahun H, Matteelli A, Abubakar I, Aziz MA, Baddeley A, Barreira D, et al. Management of latent Mycobacterium tuberculosis infection: WHO guidelines for low tuberculosis burden countries. *European Respiratory Journal*. 2015:ERJ-01245-2015.
5. Lönnroth 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. *European Respiratory Journal*. 2015;45(4):928-52.
6. Toms C, Stapledon R, Waring J, Douglas P. Tuberculosis notifications in Australia, 2012 and. *Commun Dis Intell* 2015;39(2):E217–E35.
7. WHO. Global Tuberculosis Report. Geneva: World Health Organization 2015.
8. Denholm J, Matteelli A, Reis A. Latent tuberculous infection: ethical considerations in formulating public health policy. *The International Journal of Tuberculosis and Lung Disease*. 2015;19(2):137-40.
9. Stop TB Partnership. The Global Plan to Stop TB. Geneva, Switzerland World Health Organization; 2006.
10. Dye C, Scheele S, Dolin P, Pathania V, Raviglione MC. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. *JAMA*. 1999;282(7):677-86.
11. Horsburgh Jr CR, O'Donnell M, Chamblee S, Moreland JL, Johnson J, Marsh BJ, et al. Revisiting rates of reactivation tuberculosis: a population-based approach. *American journal of respiratory and critical care medicine*. 2010;182(3):420-5.
12. 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.
13. McBryde ES, Denholm JT. Risk of active tuberculosis in immigrants: effects of age, region of origin and time since arrival in a low-exposure setting. *Medical Journal of Australia*. 2012;197(8):458.
14. Lavender C, Globan M, Kelly H, Brown L, Sievers A, Fyfe J, et al. Epidemiology and control of tuberculosis in Victoria, a low-burden state in south-eastern Australia, 2005–2010. *The International Journal of Tuberculosis and Lung Disease*. 2013;17(6):752-8.
15. Barratt A, Irwig L, Glasziou P, Cumming RG, Raffle A, Hicks N, et al. Users' guides to the medical literature: XVII. How to use guidelines and recommendations about screening. *Jama*. 1999;281(21):2029-34.

16. Harris R, Sawaya GF, Moyer VA, Calonge N. Reconsidering the Criteria for Evaluating Proposed Screening Programs: Reflections From 4 Current and Former Members of the U.S. Preventive Services Task Force. *Epidemiologic Reviews*. 2011;33(1):20-35.
17. Lönnroth K, Corbett E, Golub J, Godfrey-Faussett P, Uplekar M, Weil D, et al. Systematic screening for active tuberculosis: rationale, definitions and key considerations [State of the art series. Active case finding/screening. Number 1 in the series]. *The International Journal of Tuberculosis and Lung Disease*. 2013;17(3):289-98.
18. Sterling TR, Villarino ME, Borisov AS, Shang N, Gordin F, Bliven-Sizemore E, et al. Three months of rifapentine and isoniazid for latent tuberculosis infection. *New England Journal of Medicine*. 2011;365(23):2155-66.
19. Menzies D, Long R, Trajman A, Dion M-J, Yang J, Al Jahdali H, et al. Adverse events with 4 months of rifampin therapy or 9 months of isoniazid therapy for latent tuberculosis infection: a randomized trial. *Annals of internal medicine*. 2008;149(10):689-97.
20. Woolf SH, Harris R. The harms of screening: New attention to an old concern. *JAMA*. 2012;307(6):565-6.
21. DeFrank JT, Barclay C, Sheridan S, Brewer NT, Gilliam M, Moon AM, et al. The psychological harms of screening: the evidence we have versus the evidence we need. *Journal of general internal medicine*. 2015;30(2):242-8.
22. Aronowitz RA. The converged experience of risk and disease. *Milbank Quarterly*. 2009;87(2):417-42.
23. Farmer P. *Infections and Inequalities: The Modern Plagues*: University of California Press; 2001.
24. Denholm JT, McBryde ES, Brown GV. Ethical evaluation of immigration screening policy for latent tuberculosis infection. *Australian and New Zealand Journal of Public Health*. 2012;36(4):325-8.
25. Jaffe HW, Hope T. Treating for the Common Good: A Proposed Ethical Framework. *Public Health Ethics*. 2010;3(3):193-8.
26. Horner J, Wood JG, Kelly A. Public health in/as 'national security': tuberculosis and the contemporary regime of border control in Australia. *Critical Public Health*. 2013;1-14.
27. Silva DS, Dawson A, Upshur RE. Reciprocity and Ethical Tuberculosis Treatment and Control. *Journal of Bioethical Inquiry*. 2016,13(1):75-86.
28. Tomás BA, Pell C, Cavanillas AB, Solvas JG, Pool R, Roura M. Tuberculosis in migrant populations. A systematic review of the qualitative literature. *PLoS ONE*. 2013;8(12):doi:10.1371/journal.pone.0082440.
29. Tangka FK, O'Hara B, Gardner JG, Turner J, Royalty J, Shaw K, et al. Meeting the cervical cancer screening needs of underserved women: the National Breast and Cervical Cancer Early Detection Program, 2004–2006. *Cancer Causes & Control*. 2010;21(7):1081-90.