

**ASPIRING TO ZERO TUBERCULOSIS DEATHS
AMONG SOUTHERN AFRICA'S MINERS:
IS THERE A WAY FORWARD?**

Ashwin Dharmadhikari, Jonathan Smith, Edward Nardell,
Gavin Churchyard, and Salmaan Keshavjee

Tuberculosis notification rates among South African miners range from 4,000 to 7,000 per 100,000 people. These rates far exceed national tuberculosis notification rates for the general population. Tuberculosis mortality also surpasses deaths caused by mining accidents. These extraordinarily high rates of disease are unambiguously linked to a series of contributing factors, including exposure to silica dust, HIV infection, and poor working and living conditions. We argue that the only way to stop the transmission of this airborne disease is to treat the mine and its living quarters as one should any other congregate setting with individuals who have high rates of infection with drug-susceptible and drug-resistant strains of tuberculosis. This means implementing interventions that have been demonstrated to stop the spread of tuberculosis over the last 60 years: immediate treatment of active tuberculosis, concurrent treatment of latent tuberculosis disease to reduce the burden of active cases, and appropriate management of patients infected with HIV. Because tuberculosis is also a social disease, biomedical interventions must be coupled with improved living and working conditions. Achieving zero deaths from tuberculosis in the mines is possible if a clear commitment is made to a strategy that recognizes and ameliorates the biological and social antecedents to this epidemic.

On February 25, 1914, William Crawford Gorgas—the 22nd U.S. Surgeon General and a public health champion known for his efforts to eradicate yellow fever and malaria—presented a report to the British colonial government on his inspection of the gold and diamond mines of South Africa's Transvaal region and

Rhodesia. Gorgas and his team observed miners working long days, with little nourishment; in the evenings, they returned to living quarters consisting of rooms holding between 20 and 60 laborers in three-tiered bunk beds (1, 2). After spending three months visiting the Rand mines, where more than 200,000 miners worked, Gorgas reported that he “found the men were living in barracks closely strung together with a death rate of 30 to 35 per 1,000 [miners]”—deaths due to pneumonia, tuberculosis (TB), meningitis, and enteric fever. Gorgas’ report exposed the simple truth about why mine workers faced a two- to 10-fold risk of acquiring TB. He commented that such epidemics occur “in places where large numbers of men are herded together without sufficient breathing space” (1, 3). Autopsies of the “pneumonia” patients showed that they were actively infected with TB. According to studies conducted by local scientists, two factors contributed to the high mortality: exposure to disease by new arrivals and crowded living conditions (1). For Gorgas, the solution to the high mortality was simple: improve workers’ living conditions, improve their diet, and expand medical services so that those who are sick receive timely, appropriate care (2, 3).

Almost a century after the Gorgas report, TB remains a significant threat to the more than 500,000 workers in southern Africa’s mines. TB notification rates among South African miners range from 4,000 to 7,000 per 100,000 people (4, 5). These rates are almost exclusively tied to gold miners, and they exceed national TB notification rates for the general population more than 10-fold (5, 6). TB mortality at the mines also surpasses deaths caused from accidents, and miners have a 3.6 odds ratio of dying from TB compared with non-mine workers in the same geographical region (7–9).

These extraordinarily high rates of disease are unambiguously linked to a series of contributing factors working in concert with one another. Miners suffering from silicosis, an occupational lung disease most commonly associated with primary silica dust exposure in gold mines, face an almost three-fold risk of developing active TB compared to miners without silicosis (10–18). Infection with HIV, with prevalence among miners estimated at 25 percent to 30 percent, increases the risk of TB as much as five-fold (4, 16). The combination of the two—infection with HIV and exposure to silica—increases the TB incidence rate 15 times higher than in HIV-negative miners not suffering from silicosis (16).

As Gorgas’ report highlighted, poor living and working conditions further exacerbate the risk for TB. A significant number of miners are migrants, traveling between their rural home areas and densely populated mining communities. More than 100,000 workers in the mining industry come from Lesotho, Swaziland, Mozambique, or Botswana, and approximately 80 percent are concentrated in the gold mining industry (19). Between 50 percent and 60 percent of these men live in multiple-occupancy, single-sex hostels, with an average of six men per room (20, 21). Deep-level gold mine shafts are often only two to three meters wide and can reach up to several kilometers underground (22). This makes crucial TB preventative strategies, such as air circulation and ventilation aimed at

reducing silica dust, extremely difficult to implement, particularly in the cramped confines at the rock face. Personal protection equipment, required to enter the mineshaft, is little used in practice because of poor enforcement and because workers often remove the equipment as a result of the increased difficulty breathing in a hot, sweaty environment (23).

In part because of these conditions, it is estimated that 89 percent of miners are latently infected with TB (20). These individuals collectively represent a large population of individuals who develop active TB. Not only are rates of new TB infections high, but the rate of recurrent TB infection in the gold mining industry, whether or not complicated by silicosis, is more than twice the rate in the general population. Charalambous and colleagues showed that among 609 gold mine workers followed for a median of 1.02 years after a first cured episode of TB, 57 developed recurrent disease. Re-infection was demonstrated by genotyping in 69 percent of those with isolates recovered from both the first and subsequent TB episodes (24–26).

The high TB rates seen in the mines exist within a peculiar paradox. By and large, the industry is very aware of the problem and, compared to the surrounding population, several mining facilities possess excellent tertiary care, including more than 40 hospitals and clinics, 350 full-time doctors, and 3,500 other medical personnel (22). Improved health and wellness programs are especially evident in larger mining companies, such as AngloGold Ashanti (AGA) and Gold Fields, who have taken innovative steps to combat TB and HIV. Companies like AGA promote active case-finding of patients with TB through bi-annual chest X rays—using both stationary and mobile clinics—that are performed on all miners working underground or in otherwise “dust risk work” positions (27). The company also promotes case-finding at each point of contact in its health care system. In addition, AGA recently acquired a modern TB laboratory at its West Vaal Hospital, capable of mycobacterial culture and drug susceptibility testing (27, 28). In the larger mining companies, factors that increase miners’ susceptibility to TB, namely silica dust exposure and infection with HIV, are also addressed. These mines use a series of engineering, administrative, and personal controls to manage silica dust in the mineshaft, integrate TB and HIV diagnostic and treatment services, as well as a shift toward family-style housing that is less dense. Gold Fields, for instance, is aiming to build 890 two-bedroom homes in an effort to reduce the social and contextual factors associated with HIV vulnerability among migrants and to reduce the dense living conditions associated with TB transmission. This is part of the company’s “24 Hours in the Life of a Gold Fields Employee” program, which includes various initiatives around occupational health and safety, health care, living conditions, nutrition, education, and sport and recreation (29).

Despite laudable efforts by some companies, TB rates in the industry continue to remain at epidemic levels and are considered a human rights crisis (30). Many of the positive measures remain localized within only a few mines and have yet

to be disseminated industry-wide. Additionally, the sheer force of transmission overwhelms measures that are effective in other populations. For instance, given the occupational hazards and factors contributing to TB, even exceeding the World Health Organization's cure rate target of 85 percent seems insufficient for interrupting transmission; similarly, because of the presence of drug-resistant strains, achieving treatment adherence of up to 98 percent among miners treated for drug-susceptible disease does not stop the transmission of drug resistance (31, 32). On August 18, 2012, the heads of state from the 15 member countries of the Southern Africa Development Community (SADC) met in Maputo, Mozambique, and signed the *Declaration on Tuberculosis in the Mining Industry*, calling for zero deaths from TB in the region's mines (33, 34). The TB crisis in the region is staggering, but given the experiences of companies like AGA and Gold Fields, the resources of the industry, and recent diagnostic developments, we believe significant movements toward achieving zero deaths can be realized.

In this article, we call for exploration of an approach to stopping the transmission of this airborne disease that treats mines and associated living quarters as one would any other congregate setting with individuals who have high rates of infection with drug-susceptible and drug-resistant strains of TB. This means implementing critical biomedical interventions that have been demonstrated to stop the spread of TB: rapid diagnosis using new diagnostic tests, linked to early treatment of active TB with the appropriate medicines (including second-line anti-TB drugs for multi-drug-resistant TB [MDR-TB]). Coupled with the treatment of latent TB disease and appropriate management of patients infected with HIV, we are confident this strategy would enhance current approaches. Additionally, because TB is also a social disease, as Gorgas and his colleagues suggested a century ago, biomedical interventions must be coupled with improved living conditions, working conditions, and nutrition. In the following sections, we argue that by adopting strategies that target the transmission of TB—borrowed from the clinical environment, but extrapolated to other congregate settings—it will be possible to move toward the goal of achieving zero deaths from TB in the mines.

EFFECTIVE DIAGNOSIS AND TREATMENT IS THE FIRST STEP IN PREVENTING DEATHS

From a clinical perspective, the first step in combating TB and preventing deaths is identifying TB patients early and initiating the correct treatment as close to the time of diagnosis as possible. This strategy has dual benefits. First, it allows patients with TB to get on treatment sooner and to experience lower risks of progressive lung destruction, morbidity, and mortality. Lung function declines more rapidly in miners presenting with advanced TB and more significantly with each successive episode of TB (35, 36), making delayed diagnosis and its impact on the miner's endurance a mining workforce supply issue as well as a

health issue. In addition, unsuspected TB patients (i.e., those who have active disease but have not yet been identified as such) pose a high risk of transmission to others (37). Second, timely diagnosis and treatment initiation convert patients who are infectious or potentially infectious into non-infectious patients (38, 39). Treatment must be effective, meaning that the *M. tuberculosis* bacilli isolated from the patient's sputum must be susceptible to the drug regimen administered. Ineffective therapy is not only dangerous for the patient, but facilitates ongoing transmission of resistant strains.

The clinical evidence for this approach to TB transmission control has been very well-characterized, but largely forgotten in the present day. For example, in a seminal study involving five years of follow-up of household contacts of index patients with TB treated in Madras, India, in the 1960s, incidence rates among household contacts of patients treated at home from the time of initiation of therapy versus household contacts of those treated in sanatoria at the time of treatment initiation were similar (40). This study provided some of the earliest evidence that effectively treated patients with drug-susceptible TB are not sources of ongoing transmission. The effect of chemotherapy initiation on preventing further transmission to contacts was rapid, since the index cases in the home-based treatment group returned home at the start of treatment. For the interested reader, a review by Rouillon provides an excellent summary of this body of evidence and emphasizes the key point that the elimination of infectiousness among patients with TB occurs even *before* the conversion of sputum smears and cultures to negative (41).

More recently, there is evidence to suggest the impact of treatment on stopping transmission also occurs rapidly in MDR-TB patients (42). In the United States, MDR-TB patients have been treated at home without evidence of further transmission (43). The percentage of TB cases at the mines found to be MDR-TB is almost twice that of the general population (3.6% vs. 1.9%), and exogenous primary infection is the primary mode of transmission (5, 31). This highlights the need for early diagnosis of MDR-TB patients and rapid initiation of treatment.

Although diagnosis of TB remains a challenge—especially early diagnosis of drug-resistant disease—new developments show promise. The mining industry has traditionally used mass miniature chest X ray (CXR) radiography to detect TB cases, but has recently switched to use of fixed and mobile digital chest radiography. Semi-annual radiographic screening for active TB among miners using miniature chest X ray has been shown to reduce the extent of disease at diagnosis and mortality during the first two months of treatment, compared to an annual radiographic screening program (44). The sensitivity of this approach is increased when combined with symptom-based screening, especially among HIV-infected miners (45, 46). Yet, radiography, with or without symptom screening, does not identify drug-resistant strains of TB. In contrast, a new, rapid, automated molecular diagnostic test for *M. tuberculosis* and rifampin resistance (Xpert MTB/Rif) has been shown to have high sensitivity and specificity for TB

(86% to 90% sensitivity; 97% specificity) and rifampin resistance (93% sensitivity; 100% specificity), even among smear-negative patients and HIV-infected patients (47). Screening for TB among gold miners using Xpert MTB/Rif alone, an approach that does not require much laboratory infrastructure and is easily decentralized, has greater sensitivity than using sputum smear microscopy alone or symptom screening and chest radiography combined (46, 48).

Delayed presentation of TB symptoms poses a particular risk given the high density and close proximity of working and living conditions of the mine and peri-mine areas. A rapid, effective diagnostic such as Gene Xpert MTB/Rif could allow medical staff at the mines to more readily identify patients with TB and initiate appropriate treatment. This would simultaneously identify TB and, when present, drug resistance, reducing the high levels of exogenous infection or re-infection thought to be driving the epidemic in mining communities (31). In keeping with recent South African policy guidelines (49), we think it would be more effective to expand the use of such decentralized, rapid diagnostic approaches in the mining industry—at the places where miners work and live, but also at the facilities where they receive medical care for the conditions (such as HIV and silicosis) that put them at high risk of TB—than to continue relying on current methods of screening and diagnosis, such as annual radiological exams (45, 49).

The potential benefits for the mining industry of this type of approach to TB and MDR-TB incidence in the mining industry—finding patients early and putting them on the correct treatment—cannot be overstated: if successful, active case-finding and improved treatment would likely lead to a significant reduction in the force of transmission in crowded settings when infectious individuals are converted into non-infectious ones with early initiation of the correct treatment. The mining industry needs to move quickly to test rapid approaches to effective diagnosis and the initiation of appropriate treatment, with the aim of eliminating one of the most significant risk factors for TB among miners.

ADDRESSING LATENT TUBERCULOSIS AND HIV IN MINERS

The long-term efficacy of isoniazid preventive therapy (IPT) in preventing progression to TB among latently infected individuals in endemic settings is dampened by the extent to which these individuals continue to be exposed to active TB cases. Results from several large studies of IPT in HIV-infected individuals show that although IPT provides short-term reduction in the incidence of active TB, the benefit wanes significantly after IPT ends, including in the mines (50–55). Thus, treatment of latent disease should be given continuously and must be closely tied to the correct and rapid treatment of active TB (50, 51). Miners exposed to isoniazid-resistant strains of TB, for whom IPT will presumably have no effect and for which there is currently no standard therapy, are at

particular risk (56). Urgent research needs to be conducted into the appropriate post-exposure prophylaxis for this group. For migrants, coordination of prophylaxis therapy will remain a challenge, but may be facilitated by rigorous exit examinations (an existing requirement) as well as education and emphasis on the importance of this intervention.

Similarly, the early treatment of HIV is a critical part of averting TB deaths and continued transmission of TB. Substantial evidence has demonstrated that treating HIV infection at higher CD4-count thresholds in individuals than was previously believed to be appropriate, along with more aggressively extending antiretroviral uptake and coverage within communities, helps reduce the incidence of opportunistic infections (including TB), reduce morbidity and mortality associated with HIV, and prevent HIV transmission to uninfected individuals in endemic settings such as South Africa (57, 58). Given how significantly HIV infection increases the risk of progression from latent to active TB, and given how prevalent both conditions are among South African mine workers, it is imperative that HIV testing and early treatment initiation be included as an essential component of the struggle against TB.

URGENT NEED FOR IMPROVED HOUSING FOR MINERS

The efforts described above will fall short if not accompanied by improvements in miners' living conditions. Described by South Africa's Department of Mineral Resources as "appalling" in its 2009 assessment report, housing conditions in the South African mining industry remain notoriously poor, with the majority of men living in multiple-occupancy, single-sex hostels with crowded, unsanitary conditions and poor nutritional standards—an enabling environment for the spread of TB (20, 21, 59–61). Men not staying in the hostels typically elect to take a housing or "living out" allowance, although no information exists on the adequacy of these provisions. Anecdotal evidence suggests that the plurality of miners retain these stipends and opt to live in informal settlements surrounding the mine, creating conditions similarly conducive to the spread of communicable diseases, including TB (60, 62, 63). Both living situations create physical and social conditions that provide high-pressure environments for TB infection that extend well beyond the working hours in the mineshaft (64, 65).

Aware of housing's contribution to the spread of disease, South Africa's Mineral and Petroleum Resources Development Act of 2002 and Section 28 of the South African Constitution states there must be adequate housing and conditions standards for the minerals industry (66, 67). In addition, other legal acts, including the Mining Charter of 2004 and recommendations from the Department of Housing, have provided the guidance and resources necessary to accelerate the industry's move toward appropriate housing (61, 68, 69). Some companies, such as Gold Fields, have displayed reasonable progress in improving housing

standards and have strived for family-style housing and accommodation (29). However, a 2009 investigation by the Department of Mineral Resources into the efficacy of the 2002 act demonstrated that for the industry as a whole, only 26 percent of companies provide adequate housing and only 29 percent have improved standards of housing (61). The industry average for number of individuals per hostel was reduced from 16 to four per room; however, the probe reiterated that this number remains unacceptably high and that the same unhygienic living conditions that have characterized the industry for decades remain present (61).

There is an abundance of literature describing the positive impact that improved housing conditions have on HIV transmission and, subsequently, on TB infection rates (59, 70–72). Notably, data indicate that non-migrating partners have a substantially lower HIV prevalence compared to miners who return home two to four times a month (17.8% vs. 27.7%, respectively) (70, 71), suggesting the industry should not simply improve living conditions, but also facilitate family-style housing to achieve optimal results. This increase in family relocation would reduce migrant labor, but may encounter resistance for cultural and economic reasons, especially the risk of losing a family's rural home.

ECONOMIC IMPACT

In light of the SADC declaration, the World Bank is investigating the cost of potential interventions to address TB in the mining industry (60, 73). This investigation was presented on March 7, 2012, at the Regional Stakeholder Consultation Meeting on Tuberculosis in the Mining Sector in Johannesburg, coordinated by SADC, the World Health Organization, and the International Organization for Migration (60, 73). Preliminary estimates show current annual costs to the South African government and the mining industry for treatment of TB, including drug-resistant forms, to be \$140.9 million (all dollar amounts in U.S. dollars) and \$253.1 million, respectively, for a combined total of \$361.7 million. These preliminary estimates are only for the marginal cost of patient care such as treatment and hospitalization. Furthermore, the report estimates that the industry loses an additional \$568.4 million in productivity and training as a result of attrition of miners affected by TB (73). On top of losses by the companies, the World Bank estimates miners lose an estimated \$320 million per year in lost wages because of TB morbidity, as miners are too ill to fill their shifts. The loss of income often translates into families having to choose economic survival over important priorities such as nutrition and children's education, contributing to the relentless cycle of poverty seen throughout the region.

A large proportion of this economic burden can be eliminated if mines introduce efforts to intensify case-finding, improve treatment, and reduce factors that exacerbate TB infection. Preliminary investigations by the World Bank on

behalf of SADC estimate that implementing measures that address these factors yields a total annual benefit of \$783 million for mines and miners, including gains as a result of fewer cases and increases in productivity and earned wages (60, 73, 74).

SUMMARY AND POLICY RECOMMENDATIONS

Today, mining is responsible for an estimated 760,000 cases of TB in the general population of sub-Saharan Africa each year; aside from HIV, mining is the largest driver of the TB epidemic (75). The SADC aspiration for zero deaths among miners provides an important opportunity to investigate different strategies to stem the tide of TB among miners and, subsequently, TB in the context of the region's broader epidemic. It is now possible to screen patients for TB and drug-resistant strains at most mining health facilities. It is possible to perform regular screening of workers—through biannual symptom screening, X ray, and DNA-based testing as needed—and it is possible to ensure patients receive treatment appropriate to a specific strain of TB. By making the investment to improve diagnostics and care at the mine, mining companies will ultimately see a financial benefit in terms of productivity and retaining highly skilled workers, along with the obvious social and moral benefit of reducing morbidity and mortality among miners. Many facilities are capable of initiating treatment for HIV immediately upon diagnosis, not just at the CD4 = 350 threshold; almost all facilities are able to deliver preventive therapy to patients who are eligible. If these biomedical interventions are coupled with realistic plans to phase out high-density housing and replace it with single-occupancy or family-style housing—a step that will ameliorate the social and environmental factors that increase a miner's risk for contracting both TB and HIV—we are almost certain that a positive effect will be observed (27–29, 73, 76–78).

The financial incentive is present for the industry and for national health services, and the moral imperative is clear. The previous century was characterized by an egregious lack of discipline in addressing TB in the mining industry, which was rooted in apartheid-era social and economic policies that severely oppressed black miners. Today, with improved diagnostics and the potential for rapid initiation of appropriate treatment, coupled with enormous economic and moral incentives, there remains little excuse for inaction. Achieving zero TB deaths in the mining industry, however, will require governments, industry, organized labor, and civil society to work together closely to implement a strategy reflective of TB as a biosocial phenomenon, considering both the pathogen that causes the disease and the social conditions that give rise to its transmission and entrenchment in certain communities. A century after the Gorgas report, its advice is still valid: improve workers' living conditions, improve their diet, and expand diagnostic and medical services so that those already sick receive timely and appropriate care (2, 3).

REFERENCES

1. Chaves-Carballo, E. *The Tropical World of Samuel Taylor Darling: Parasites, Pathology, and Philanthropy*. Sussex Academic Press, Portland, 2007.
2. Fassin, D. *When Bodies Remember: Experiences and Politics of AIDS in South Africa*, University of California Press, 2007.
3. General Gorgas. Home from South Africa. *New York Times*, April 2, 1914. <http://query.nytimes.com/mem/archive-free/pdf?res=F30710FB355D13738DDDAB0894DC405B848DF1D3> (accessed September 9, 2012).
4. Churchyard, G. J., et al. Mycobacterial disease in South African gold miners in the era of HIV infection. *Int. J. Tuberc. Lung Dis.* 3(9):791–798, 1999.
5. Republic of South Africa, Department of Health. *Tuberculosis Strategic Plan for South Africa, 2007-2011*. Pretoria, 2008.
6. World Health Organization. *Global Tuberculosis Control: WHO Report*. Geneva, 2011.
7. Murray, J., et al. Cause of death and presence of respiratory disease at autopsy in an HIV-1 seroconversion cohort of southern African gold miners. *AIDS* 21(Suppl. 6): S97–S104, 2007.
8. Murray, J., et al. Effect of HIV on work-related injury rates in South African gold miners. *AIDS* 19(17):2019–2024, 2005.
9. Reid, P. J., and Sluis-Cremer, G. K. Mortality of white South African gold miners. *Occup. Environ. Med.* 53(1):11–16, 1996.
10. Cowie, R. The epidemiology of tuberculosis in gold miners with silicosis. *Am. J. Respir. Crit. Care Med.* 150:1460–1462, 1994.
11. teWaternaude, J. M., et al. Tuberculosis and silica exposure in South African gold miners. *Occup. Environ. Med.* 63(3):187–192, 2006. doi: 10.1136/oem.2004.018614.
12. Hnizdo, E., and Murray, J. Risk of pulmonary tuberculosis relative to silicosis and exposure to silica dust in South African gold miners. *Occup. Environ. Med.* 55(7): 496–502, 1998.
13. South African Native Affairs Commission. *Report: 1903–1905*. Limited Printers, Cape Town, 1905.
14. Hoffman, F. *The Problem of Dust Phthisis in the Granite-Stone Industry*. U.S. Bureau of Labor Statistics, Washington, DC, 1922.
15. Allen, P. *Report of Tuberculosis Survey of the Union of South Africa*. Government Printer, Cape Town, 1924.
16. Corbett, E. L., et al. HIV infection and silicosis: The impact of two potent risk factors on the incidence of mycobacterial disease in South African miners. *AIDS* 14(17):2759–2768, 2000.
17. Churchyard, G. J., et al. Silicosis prevalence and exposure-response relations in South African gold miners. *Occup. Environ. Med.* 61(10):811–816, 2004. doi: 10.1136/oem.2003.010967.
18. Rees, D., and Murray, J. Silica, silicosis and tuberculosis. *Int. J. Tuberc. Lung Dis.* 11(5):474–484, 2007.
19. Rees, D., et al. Oscillating migration and the epidemics of silicosis, tuberculosis, and HIV infection in South African gold miners. *Am. J. Ind. Med.* 53(4):398–404, 2010. doi: 10.1002/ajim.20716.

20. Hanifa, Y., et al. Prevalence of latent tuberculosis infection among gold miners in South Africa. *Int. J. Tuberc. Lung Dis.* 13(1):39–46, 2009.
21. AngloGold Ashanti. *West Wits Country Report 2008*. Johannesburg, 2008.
22. Williams, B. G., et al. Occupational health, occupational illness: Tuberculosis, silicosis and HIV on the South African mines. In *Occupational Lung Disease: An International Perspective*, ed. D. Banks and J. Parker. Chapman and Hall, London, 1998.
23. National Institute of Occupational Health: Mine Health and Safety Council. *What Does Silicosis Reduction Mean to Mineworkers?* Johannesburg, 2010.
24. Charalambous, S., et al. Contribution of reinfection to recurrent tuberculosis in South African gold miners. *Int. J. Tuberc. Lung Dis.* 12(8):942–948, 2008.
25. World Health Organization. *Global Tuberculosis Control*. Geneva, 2011.
26. Basu, S., et al. The production of consumption: Addressing the impact of mineral mining on tuberculosis in southern Africa. *Global. Health* 5:11, 2009. doi: 10.1186/1744-8603-5-11.
27. AngloGold Ashanti. *Case Study: TB Control at AngloGold Ashanti Health, Applying Best Practice*. AngloGold Report to Society 2007–Regional Health. Johannesburg, 2007.
28. Lilly MDR-TB Partnership. *Outstanding Business Action to Stop Tuberculosis: How Companies Contribute to the Global Fight*. New York, 2009.
29. Gold Fields, Ltd. *Gold Fields Limited Annual Report 2010, Sustainability Report*. Johannesburg, 2010.
30. Kistnasamy, B., et al. *RE: Calling for Urgent Action on TB in the South African Mining Sector*. http://www.ghdonline.org/uploads/26.03.09_Letter_to_DME_DOH_from_experts.pdf (accessed June 14, 2011).
31. Calver, A. D., et al. Emergence of increased resistance and extensively drug-resistant tuberculosis despite treatment adherence, South Africa. *Emerg. Infect. Dis.* 16(2): 264–271, 2010. doi: 10.3201/eid1602.090968.
32. Godfrey-Faussett, P., et al. Tuberculosis control and molecular epidemiology in a South African gold-mining community. *The Lancet*. 356(9235):1066–1071, 2000. doi: 10.1016/s0140-6736(00)02730-6.
33. Southern African Development Community. *Declaration on Tuberculosis in the Mining Sector*. [http://www.stoptb.org/assets/documents/news/Declaration on Tuberculosis in the Mining Sector2012English.pdf](http://www.stoptb.org/assets/documents/news/Declaration%20on%20Tuberculosis%20in%20the%20Mining%20Sector2012English.pdf) (accessed September 1, 2012).
34. Baleta, A. Southern African declaration targets TB in mining sector. *The Lancet*. 380(9849):1217–1218, 2012. doi: 10.1016/s0140-6736(12)61698-5.
35. Ross, J., et al. Excess lung function decline in gold miners following pulmonary tuberculosis. *Thorax* 65(11):1010–1015, 2010. doi: 10.1136/thx.2009.129999.
36. Hnizdo, E., et al. Chronic pulmonary function impairment caused by initial and recurrent pulmonary tuberculosis following treatment. *Thorax* 55(1):32–38, 2000.
37. Kantor, H. S., et al. Nosocomial transmission of tuberculosis from unsuspected disease. *Am. J. Med.* 84(5):833–838, 1988.
38. Riley, R. L., et al. Infectiousness of air from a tuberculosis ward. Ultraviolet irradiation of infected air: Comparative infectiousness of different patients. *Am. Rev. Respir. Dis.* 85:511–525, 1962.
39. Riley, R. L., et al. Aerial dissemination of pulmonary tuberculosis. A two-year study of contagion in a tuberculosis ward. *Am. J. Epidemiol.* 142(1):3–14, 1959.

40. Kamat, S., et al. A controlled study of the influence of segregation of tuberculosis patients for one year on the attack rate of tuberculosis in a 5-year period in close family contacts in South India. *Bull. World Health Organ.* 34:517–532, 1966.
41. Rouillon, A., et al. Transmission of tubercle bacilli: The effects of chemotherapy. *Tubercle.* 57(4):275–299, 1976.
42. Dharmadhikari, A., et al. Impact of standardised treatment on the infectiousness of MDR-TB patients in South Africa. Presented at the 42nd World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease, Abstract Number OP-581-29, Lille, France, 2011.
43. Burgos, M., et al. Treatment of multidrug-resistant tuberculosis in San Francisco: An outpatient-based approach. *Clin. Infect. Dis.* 40(7):968–975, 2005. doi: 10.1086/428582.
44. Churchyard, G. J., et al. Twelve-monthly versus six-monthly radiological screening for active case-finding of tuberculosis: A randomised controlled trial. *Thorax* 66(2): 134–139, 2011. doi: 10.1136/thx.2010.139048.
45. Day, J. H., et al. Screening for tuberculosis prior to isoniazid preventive therapy among HIV-infected gold miners in South Africa. *Int. J. Tuberc. Lung Dis.* 10(5): 523–529, 2006.
46. Lewis, J., et al. HIV infection does not affect active case finding of tuberculosis in South African gold miners. *Am. J. Respir. Crit. Care Med.* 180:1271–1278, 2009.
47. Boehme, C. C., et al. Rapid molecular detection of tuberculosis and rifampin resistance. *N. Engl. J. Med.* 363(11):1005–1015, 2010. doi: 10.1056/NEJMoa0907847.
48. Dorman, S. E., et al. Performance characteristics of the Cepheid Xpert MTB/RIF Test in a tuberculosis prevalence survey. *PLoS ONE* 7(8):e43307, 2012. doi: 10.1371/journal.pone.0043307.
49. Republic of South Africa National Department of Health. *Management of Drug-Resistant Tuberculosis: Policy Guidelines.* Pretoria, 2010.
50. Martinson, N. A., et al. New regimens to prevent tuberculosis in adults with HIV infection. *N. Engl. J. Med.* 365(1):11–20, 2011. doi: 10.1056/NEJMoa1005136.
51. Samandari, T., et al. 6-month versus 36-month isoniazid preventive treatment for tuberculosis in adults with HIV infection in Botswana: A randomised, double-blind, placebo-controlled trial. *The Lancet* 377(9777):1588–1598, 2011. doi: 10.1016/s0140-6736(11)60204-3.
52. Quigley, M. A., et al. Long-term effect of preventive therapy for tuberculosis in a cohort of HIV-infected Zambian adults. *AIDS* 15(2):215–222, 2001.
53. Johnson, J. L., et al. Duration of efficacy of treatment of latent tuberculosis infection in HIV-infected adults. *AIDS* 15(16):2137–2147, 2001.
54. Churchyard, G. Community-wide Isoniazid Preventive Therapy Does Not Improve TB Control among Gold Miners: The Thibela TB Study, South Africa. Abstract presented at 19th Conference on Retroviruses and Opportunistic Infections, Seattle, 2012.
55. Fielding, K. Individual-level effect of isoniazid preventive therapy on risk of tuberculosis in the Thibela TB study. Abstract 150bLB presented at Conference on Retroviruses and Opportunistic Infections, Seattle, 2012.
56. Mlambo, C. K., et al. Genotypic diversity of extensively drug-resistant tuberculosis (XDR-TB) in South Africa. *Int. J. Tuberc. Lung Dis.* 12(1):99–104, 2008.
57. Cohen, M. S., et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N. Engl. J. Med.* 365(6):493–505, 2011. doi: 10.1056/NEJMoa1105243.

58. Tanser, F., et al. Effect of ART on Rate of New Infections in a Hyper-Endemic, Rural Population: South Africa. Paper 136LB presented at the 19th Conference on Retroviruses and Opportunistic Infections, Seattle, 2012.
59. Gebrekristos, H. T., et al. Estimating the impact of establishing family housing on the annual risk of HIV infection in South African mining communities. *Sex. Transm. Dis.* 32(6):333–340, 2005.
60. World Bank. *Costing of Potential Policy Choices to Eliminate TB from the Mines in South Africa*. Unpublished working report. Pretoria, February 2012.
61. Republic of South Africa Department of Mineral Resources. *Mining Charter Impact Assessment Report*. Pretoria, 2009.
62. Bench Marks Foundation. *Principles for Global Corporate Responsibility for Measuring Business Performance. Discussion Document: Mining and Community Engagement Principles*. http://www.bench-marks.org.za/campaigns/mining_community_engagement.pdf (accessed October 1, 2012).
63. Steward, D. How will future historians view Markiana? *Politicsweb*, September 28, 2012. <http://www.politicsweb.co.za/politicsweb/view/politicsweb/en/page71651?oid=329465&sn=Detail&pid=71651> (accessed October 1, 2012).
64. Farmer, P. Social scientists and the new tuberculosis. *Soc. Sci. Med.* 44(3):347–358, 1997.
65. Mutatkar, R. K. Public health problems of urbanization. *Soc. Sci. Med.* 41(7):977–981, 1995.
66. Republic of South Africa. *Mineral and Petroleum Resources Development Act, Act No. 23922*. Pretoria, 2002.
67. Constitution of the Republic of South Africa. Pretoria, 1996.
68. Republic of South Africa Department of Minerals and Energy. *Housing and Living Conditions Standard for the South African Minerals Industry*. Gazette No. 32166. Pretoria, April 2009.
69. Republic of South Africa. *Government Gazette No. 2661*. Pretoria, August 13, 2004.
70. Lurie, M. N., et al. Who infects whom? HIV-1 concordance and discordance among migrant and non-migrant couples in South Africa. *AIDS* 17(15):2245–2252, 2003. doi: 10.1097/01.aids.0000088197.77946.ba.
71. Lurie, M. N., et al. The impact of migration on HIV-1 transmission in South Africa: A study of migrant and non-migrant men and their partners. *Sex. Transm. Dis.* 30(2):149–156, 2003.
72. Deloitte on Mining & Metals. *Taking the Gamble out of Mining-Related Risk*. South Africa, 2006.
73. Osewe, P. Costing of Potential Policy Choices to Eliminate TB from the Mines in the SADC Region: A Case Study of South Africa. Presented by the World Bank at the SADC Consultation Meeting on TB in the Mining Industry, Johannesburg, South Africa, March 7, 2012. <http://siteresources.worldbank.org/INTSOUTHAFRICA/Resources/world-bank-costing-of-policy-options-presentation-for-sadc-consu.pdf> (accessed September 1, 2012).
74. World Health Organization Stop TB Partnership. *Tuberculosis and Mining: A Challenge to a Key Southern African Economic Sector*. Geneva, 2012.
75. Stuckler, D., et al. Mining and risk of tuberculosis in sub-Saharan Africa. *Am. J. Public Health* 101(3):524–530, 2011. doi: 10.2105/ajph.2009.175646.

76. Gold Fields, Ltd. *24 Hours in the Life of a Gold Fields Employee Program*. http://www.goldfields.co.za/sus_housing.php (accessed September 15, 2012).
77. AngloGold Ashanti. *Intensified Efforts to Reduce Dust Levels at South Africa Operations Start to Show Results*. Report to Society Case Studies 2007, Occupational Safety and Health. Johannesburg, 2007.
78. Republic of South Africa Department of Mineral and Energy Affairs. *Commission of Inquiry into Safety and Health in the Mining Industry, Vol. 1*, R. N. Leon (Chairperson). Pretoria, 1995.

Direct reprint requests to:

Ashwin Dharmadhikari, MD
Brigham and Women's Hospital
Harvard Medical School
641 Huntington Avenue, Suite 3A03
Boston, MA 02115

adharmadhikari@partners.org