

3.2: Enhancing synergy: Responding to tuberculosis epidemic among people who use drugs

About the authors:

Dr Christian Gunneberg and Dr Haileyesus Getahun work in the Stop TB Department at the headquarters of the World Health Organization in Geneva, Switzerland.

The authors would like to thank Annette Verster for her input into this chapter.

Introduction

Tuberculosis (TB) is a major infectious disease responsible for over one million global adult deaths each year. These fatalities are preventable as TB is almost always curable if diagnosed and treated early. The estimated 15.9 million people who inject drugs around the world have a higher risk of developing TB than the general population. For the estimated 3 million people who inject drugs and are living with HIV, the risk is even higher. Prison populations, often including significant numbers of people who use drugs, are also at increased risk of developing TB. UN agencies recommend including TB prevention, diagnosis and treatment as part of an integrated and comprehensive harm reduction package inside and outside prisons. Attainment of international HIV/AIDS targets such as universal access and the millennium development goals will require the provision of TB services to marginalised groups such as people who inject drugs and prisoners.

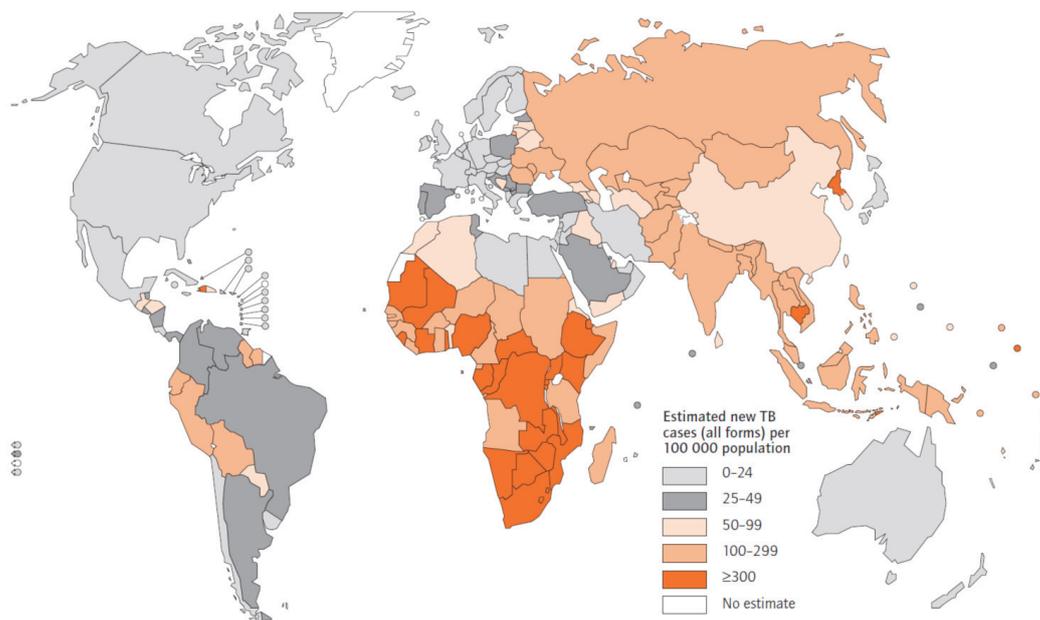
This chapter reviews the epidemiology of TB and the TB and HIV co-infection among drug-using populations and explores the international response in policy and implementation to address these epidemics. While TB services are being integrated into wider efforts to scale up HIV and harm reduction services in some countries, these are few and not proportionate to the scale of the problem. Access to harm reduction interventions and general health care for people who inject drugs remains low in most countries. For prison populations, access to these services is even lower. There is an urgent need for increased collaboration between TB, HIV, drug treatment and harm reduction services and health services in the criminal justice system in order to address this issue.

TB and HIV co-infection among people who use drugs

TB is a mycobacterial infectious disease spread from person to person by droplet transmission through the lungs (e.g. when coughing). Transmission does not result in disease in nine out of ten people who are infected, so that around one-third of the global population is infected with 'sleeping' or latent TB and for most of them nothing else happens. Only one in ten people with latent infection will develop TB disease during their lifetime. However, among people with compromised immune systems, such as those living with HIV, one in ten TB infections each year will result in development of the disease.

TB disease affects and destroys mainly the lungs, but may also spread to other parts of the body such as lymph nodes, bones and kidneys. Symptoms usually develop gradually during the course of the disease and include coughing (for more than two weeks), fever, night sweats and weight loss. In approximately half of the cases (less if HIV co-infected), TB can be diagnosed by examining sputum stained with a dye under a microscope, a test that has been used for over a century. Where sputum examination is negative, diagnosis is more difficult, requiring a clinician's decision to treat based on clinical signs and symptoms, aided where available by culture of sputum or other tissues, X-rays and other tests. Line-probe assays and LED microscopy are exciting recent developments with the potential to increase early diagnoses from sputum examinations. However, a diagnostic point of care test that reliably distinguishes TB infection from disease, and diagnoses this disease correctly every time, remains elusive.

Map 3.2.1: Estimated TB incidence rates in general population per 100,000, 2008



Accurate diagnosis and treatment of TB is literally a matter of life or death. If left untreated, over half of people with TB will die within two years and one-third will develop chronic debilitating symptoms. For people living with HIV, the death toll rises to over 80% within a year. HIV-related TB is more difficult to diagnose, as immuno-suppression also suppresses symptoms and signs. Only around one-third of HIV-positive TB patients can be diagnosed by sputum microscopy, making the role of a symptom-based clinical diagnosis even more important in the case of people living with HIV. Actively screening for TB, early TB treatment or TB prevention using isoniazid preventive therapy (IPT) and infection control measures, in addition to the early provision of antiretroviral therapy (ART) and co-trimoxazole preventive treatment (CPT), are therefore lifesaving interventions among people living with HIV.

The treatment of drug-sensitive TB involves four drugs, usually given in combination tablets for a period of up to six months, with patient support from health workers, community or family to ensure treatment adherence. Drug-resistant tuberculosis requires a two-year treatment with more expensive drugs, which also cause more side effects.

The extent of the TB epidemic

Worldwide, more than nine million people develop TB every year. In 2008 the estimated global TB incidence rate was 139 per 100,000 population, which equates to 9.4 million (range: 8.9–9.9 million) new TB cases.^{1 2}

The TB epidemic increased during the 1990s and has only recently peaked. The 2008 figures show an 11% and 40% increase in TB incidence rates and TB cases respectively in comparison with 1990 estimates. This global increase in rates was largely the result of increases in the Sub-Saharan African and European regions and was mainly due to the HIV epidemic. The HIV epidemic in Europe has been primarily driven by injecting drug use. In Sub-Saharan Africa, mirroring the HIV epidemic, TB incidence and death rates have

a This refers to the European region as defined by the WHO, which corresponds to Europe and Eurasia in this report.

doubled and the numbers of TB cases and deaths have tripled in comparison with estimated figures in 1990. Globally, incidence rates have been declining slowly since 2004, by less than 1% annually, although the number of TB cases is still rising as a result of increases in population size. More than half (55%) of the estimated number of TB cases in 2008 were in Asia, followed by Africa (30%). Alongside HIV, TB is the leading cause of adult death from infectious disease. In 2008 the number of deaths estimated to have occurred from TB without HIV was 1.3 million and a further 520,000 TB deaths were related to HIV.¹ TB causes one-quarter of the 2.1 million annual deaths among the 33.4 million people living with HIV.^{1 3}

TB rates are high among people who inject drugs, a situation primarily linked to the high rates of HIV in this group. However, drug use was identified as a risk factor for TB even before the HIV epidemic.

TB and people who use drugs

Although there is a lack of global data, the available research suggests that TB presents a major challenge for people who use drugs. Studies among HIV-negative drug users from the United States and Europe suggest a rate of TB between six and ten times that of the general population. For example, in a study from 1973 (prior to the impact of the HIV epidemic) carried out in New York in twenty methadone treatment centres, researchers found a TB disease prevalence rate among drug users of 1,372 per 100,000 citywide against a general population rate of 86.7 per 100,000.⁴ In Amsterdam some fifteen years later, a study found that the incidence of TB in HIV-negative drug users was 180 per 100,000, six times higher than in the overall Amsterdam population in the same period.⁵

Both injecting and non-injecting drug use is associated with elevated TB infection rates. Approximately half the people who inject drugs (both those living with HIV and those not) in a Spanish study tested positive for TB infection.⁶ A study from the US also showed crack cocaine users to be at an equally high risk for TB

Table 3.2.1: Summary of data from ten countries with 70% of global total of injecting drug users (IDU) living with HIV

Name of country	Number of people who inject drugs ³²	HIV prevalence among people who inject drugs ³²	Number of IDU living with HIV	Percentage of global total number of IDUs living with HIV	Proportion of IDUs living with HCV	Incident TB rate per 100,000
Russia	1,825,000	37.15%	677,988	22.6%	68-95%	110
Brazil	800,000	48%	384,000	12.8%	40-70%	48
US	1,857,354	15.57%	289,190	9.6%	35%	4
China	2,350,000	12.3%	289,050	9.6%	61%	98
Ukraine	375,000	41.8%	156,750	5.2%	70-90%	102
Indonesia	219,130	42.5%	93,130	3.1%	60-98%	228
Thailand	160,528	42.5%	68,224	2.3%	90%	142
Kenya	130,748	42.9%	56,091	1.9%	42%	353
Viet Nam	135,305	33.8%	45,733	1.5%	10-81%	171
Italy	326,000	12.1%	39,446	1.3%	42-90%	7
TOTAL	8,179,065		2,099,602	70%		

infection as people who inject drugs.⁷ Rates of TB infection were found to be similar among HIV-positive and HIV-negative injecting drug users in a two-year prospective study. The rate of development of TB in HIV-negative injecting drug users also appears to be higher than the rate of TB in the general population.⁸

TB prevalence rates vary greatly between countries and this variation is likely to be reflected in TB rates among drug using populations. Figure 3.2.1 shows the national variations in rates of TB in 2007, with a twentyfold difference in rates between the US (4/100,000) and China (98/100,000), both countries with sizable numbers of people who inject drugs (see Table 3.2.1).⁹

Using the mid-point estimates of data gathered by the Reference Group to the UN on HIV and Injecting Drug Use,¹⁰ ten countries (see Table 3.2.1) with almost half of the global number of people who inject drugs, also have over two-thirds (70%) of the global estimated numbers of injecting drug users living with HIV. The overall TB rate in the people who inject drugs in these countries would be somewhere between 700 and 1,220 per 100,000, assuming that TB rates in HIV positive people are twenty-five times higher than the background population rates, and taking the rates of HIV-negative drug users as between one and ten times the background population rates of TB. Overall there would be between 54,000 and 90,000 TB cases annually among the seven million drug users in these countries. The general population TB rates in these countries vary between 4 and 353 per 100,000.¹¹ More data are needed on TB rates among drug users in these countries, especially those with high rates of TB, in order to improve the estimation of the burden of TB disease in drug users.

Several factors are likely to increase the vulnerability to TB infection of people who inject drugs, including high rates of incarceration, homelessness and poverty. The rates of TB disease in prisons can be more than thirty times higher than those outside prisons.¹³ Poor nutrition associated with heavy drug use is also likely to add to susceptibility to TB. Although all these factors are

important contributors to the overall rates of TB in drug users, it is the presence of HIV that is the most important contributing factor to the TB epidemic among this population.

TB and HIV co-infection among people who inject drugs

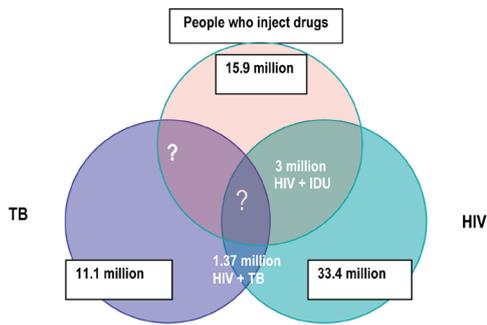
TB prevalence rates among people living with HIV are twenty to thirty times higher than among people who are HIV-negative. This is due to the increased risk of progression from TB infection to TB disease: from one in ten during a lifetime in HIV-negative people to one in ten annually for people living with HIV.

There is some evidence that the relative risk of TB may be elevated among HIV-positive drug users compared with the general population. The relative risk of developing TB in people living with HIV (as compared with the general population) in countries where HIV infection is primarily linked to drug use is 27.6 versus 20 in those countries with generalised epidemics.¹ This is most likely because vulnerable populations, such as people who use drugs, have TB exposure factors in addition to HIV that increase their level of TB, relative to the country population they come from.

In 2008 there were an estimated 1.37 million new cases of TB and 520,000 TB deaths among all people living with HIV.¹ There are no data on what proportion of this is related to drug use. However, if the rate of TB among people living with HIV who inject drugs is assumed to be the same as that among other people living with HIV, it would suggest that perhaps as many as 140,000 cases of TB (5 per 100 injecting drug users) with 52,000 deaths (2 per 100 people who inject drugs) occurring annually among the more than three million people living with HIV who inject drugs.

Projecting from what is known about the estimated interactions between the TB and HIV epidemics and their relationship with injecting drug use, the gaps in knowledge are in the estimated numbers of drug users who have TB and HIV-related TB (see Figure 3.2.2).

Figure 3.2.2: The interaction between TB, HIV and injecting drug use



Estimate of number of people with TB¹
 Estimate of number of people living with HIV²
 Estimates of numbers of people who inject drugs¹⁰

TB is a leading cause of death among injecting drug users living with HIV. Globally, approximately 520,000 people died from HIV-related TB in 2008, which was nearly one in three TB deaths (29%). TB also contributed to 26% of the estimated HIV deaths occurring globally. Both all-cause and TB-associated mortality rates are several-fold higher among injecting drug users living with HIV than in other people living with HIV.^{14 15}

Data from Ukraine, where the HIV epidemic is largely among people who use drugs, suggest high death rates from HIV due to TB. A retrospective study showed TB to be the leading cause of death among people living with HIV, accountable for approximately 58% of all causes of death in people living with HIV in Ukraine.¹⁶ Reports from TB registers in Latin American countries, where much HIV-related TB is found among drug-using populations, show that 20% of TB patients living with HIV and undergoing treatment died. This rate was approximately five times higher than the rate of death in TB patients without HIV (4%) and occurred in countries with a comparatively high ART coverage among people living with HIV.^b

Hepatitis C and TB

The majority of people who inject drugs are living with hepatitis C virus (HCV) (see Chapter 3.1 on viral hepatitis). In the nine countries that are home to half of all people who inject drugs, the prevalence of HCV is very high (see Table 3.2.1). It appears that over two-thirds of all people who inject drugs are living with HCV, regardless of their HIV status. The estimates of HCV prevalence among drug users living with HIV are even higher.¹⁷

Data on the proportion of people who inject drugs who have co-infection with HCV and TB are not available. However, the majority of people who inject drugs living with TB, regardless of their HIV status, will also have HCV. People co-infected with HCV should not be denied lifesaving TB treatment and ART, although more careful monitoring of hepatic side effects is needed during the treatment of TB and HIV and during concurrent treatment for HCV.¹⁸

The threat of multidrug-resistant TB

Multidrug-resistant tuberculosis (MDR TB) is TB that has developed resistance to some or all drugs used in treatment, usually as a result of poor treatment in the past. Globally, approximately 500,000 cases are estimated to exist. Effective treatment of MDR TB takes longer and is more expensive than that of treatment-sensitive TB.

The evidence for increased risk of MDR TB in people who use drugs is indirect. There are no studies that have directly measured the prevalence of MDR TB in drug users. As mentioned above, there is a link between higher rates of MDR TB and prison populations. There is also a growing evidence base for the link between HIV and MDR TB, and this also applies to drug users with HIV.¹⁹ Major outbreaks of MDR TB in congregate settings such as prisons or health institutions have occurred repeatedly, especially among people living with HIV.

Published literature over the last two decades suggest that institutional outbreaks of MDR TB primarily affect people living with HIV, with a significantly higher mortality rate and short survival period.^{20 21} The outbreaks were largely linked to poor infection-control practices and occurred before the availability of ART.¹⁹ However, the initiation of ART does not necessarily improve survival time, with mortality rates of over 80% within weeks of MDR TB detection.²²

One hospital outbreak in Portugal in the 1990s was among drug users living with HIV.²³ Data from this outbreak showed that among the ninety-five cases of HIV-related MDR TB, most people died before the diagnosis could be established. Epidemiological data from DNA fingerprinting analysis supported the conclusion that the transmission of MDR TB occurred among injecting drug users living with HIV who were exposed to infectious TB cases on open wards in the HIV unit. Improved infection control measures on the HIV unit and the use of empirical therapy with six drugs, once patients were suspected to have TB, reduced the incidence of MDR TB from 42% of TB cases in 1996 to 11% in 1999.

People who use drugs need to have access to treatment for MDR TB. Places where drug users congregate, including prisons and health care settings for substitution therapy or drug treatment, need to implement airborne infection control measures in order to counteract the risk of person to person transmission of TB, including MDR TB.

^b This information is derived from unpublished data from 2007 in the WHO Global Tuberculosis Database.

Prisons and TB

The problems of TB and HIV among people who inject drugs are intensified by incarceration. There are between eight and ten million people in places of detention in the world. Because many people are detained for short periods of time, the actual numbers who pass through prisons and places of detention each year is many times higher. Detainees are often housed in overcrowded facilities with inadequate ventilation, hygiene and sanitation. The food that is provided can be unappealing and nutritionally inadequate. Health services may be weak or absent. The vast majority of prisoners and detainees around the world have no access to harm reduction measures or condoms, despite evidence that sex and drug use occur within these institutions across the globe. Such conditions are ripe for the outbreak of epidemic diseases, including TB and HIV (see Chapter 3.5 on prisons).

Much higher levels of active TB disease, thirty times or more, are reported within prisoner and detainee populations compared with those outside prisons.²⁴ Some prison programmes have found high levels of MDR TB, up to one-third of all cases.²⁵ A study from the Samara region in Russia reported TB rates of 37.3% in prison, twice as high as in the civilian population.²⁶ High rates of TB in prisons and places of detention are made worse by late diagnosis and inadequate treatment of infectious cases, due to lack of adherence or treatment support, high transfer rates of prisoners and gaps in continuity of care upon release. Prison health is often forgotten or given a low priority.

It needs to be remembered that the problem of TB and poor health of prisoners and detainees will not stay confined to prisons. Prison staff and visitors should be considered part of the prison population with respect to the transmission of infectious diseases such as TB. Prison health must be seen as a public health concern and health systems should be coordinated to ensure continuity and equivalence of care. This is most evident in the spread of MDR TB, an increasingly recognised threat to effective TB control.

The global policy response to TB

Since the early 1990s, the provision of high-quality Directly Observed Treatment Short-Course (DOTS) has been central to responding to TB epidemics around the world. This requires the provision of services for early detection and diagnosis of TB through quality-assured bacteriology, followed by standardised TB treatment with supervision and patient support, using an effective drug supply, with monitoring and evaluation, including treatment outcomes and impact measurements.

The Stop TB Strategy, published in 2006 by the WHO, lays down additional elements for a comprehensive framework for TB control, including the involvement of all care providers, empowering people living with TB and communities, the treatment of MDR TB and TB/HIV co-infection and addressing highly vulnerable groups such as prisoners and people who use drugs.²⁷

The Global Plan to Stop TB, published by the Stop TB Partnership (a global and multisectoral alliance of partners fighting TB), provides a budgeted work plan and lays down targets and milestones to achieve the millennium development goals related to TB.²⁸ People who use drugs are one of the groups that may not be easily reached through routine TB services alone, and the high proportion of drug users living with HIV also need the TB/HIV services detailed in the policy for TB/HIV collaborative services.²⁹ This highlights the need for TB patients to be screened for HIV and for the provision of HIV services, including early co-trimoxazole and ART for those TB patients living with HIV. For people living with HIV, it recommends regular screening for TB, provision of IPT and infection control measures in all congregate settings and especially in health facilities treating people living with HIV.

WHO, UNAIDS and UNODC have identified the key elements of the harm reduction package and include TB as one of the key areas to be addressed.³⁰ The three agencies also recognised that the provision of services for TB and HIV among drug users required additional guidance and, in 2008, collectively launched policy guidelines for the integrated delivery of TB and HIV services for injecting and other drug users.¹⁷ This guidance makes thirteen recommendations in support of improving integrated services, providing a package of care and overcoming barriers to its implementation (see Figure 3.2.3). The guidelines are intended for people providing services for the population of drug users who have the most problematic patterns of use and who have the greatest risk of HIV and TB. These are people who use opiates, cocaine or amphetamine-type stimulants in a dependent or harmful way, in particular those who inject.

The guidelines recommend that services should have a more coordinated response to the needs of people who use drugs. Services should provide access to prevention, treatment and care services at all entry points. This requires collaborative planning between HIV, TB, specialist drug services and the criminal justice system. In particular, health services should provide treatment adherence support for people who use drugs. Co-morbidities, such as HCV, should not be a barrier to TB and HIV treatment services. Prisoners living with HIV, TB or drug dependency need to have the same access to treatment and care as people outside prisons, as should drug users who are migrants, homeless or otherwise marginalised. In addition, continuity of care on transfer in and out of places of detention is essential.

The guidelines were launched at the International AIDS Conference in Mexico City in 2008 and are available in Russian, Chinese and Spanish. Since their launch, they have been deliberated on at global workshops involving activists, programme managers of TB/HIV, health in prison, harm reduction and drug treatment services from high-burden countries, and are informing the implementation of services locally.¹⁷

Figure 3.2.3: Recommendations from the policy guide for integrated TB and HIV services for injecting and other drug users

A	Joint planning service providers
	<ol style="list-style-type: none"> 1. National local coordination body 2. Plans with roles and responsibilities and monitoring and evaluation 3. Human resources and training available 4. Support to operational research
B	Package of care
	<ol style="list-style-type: none"> 5. TB infection control plans in care settings 6. Case finding protocols at services that people who use drugs attend 7. Treatment services for TB and HIV available 8. Isoniazid preventive therapy (IPT) available for TB prevention 9. HIV prevention available (harm reduction package)
C	Overcoming barriers
	<ol style="list-style-type: none"> 10. Integrated services (link TB/HIV treatment with harm reduction) 11. Equivalence of care in prisons 12. Adherence support measures 13. Comorbidity not to be used to withhold treatment

TB services for people who use drugs

A total of 5.7 million incident TB cases were notified by national TB control programmes globally in 2008. This amounts to 62% of all estimated TB cases worldwide. These are being treated by national TB programmes using DOTS, with an average cure rate of 86%.¹ It is not known what proportion of people who use drugs globally have had TB diagnosed or treated successfully. There is evidence that drug users make poor use of general health services. US data suggest that a substantial proportion of injecting drug users living with HIV receive their HIV diagnosis late and have a lower chance of survival than people who acquired the virus via another transmission route.³¹

As recently as 2005 in Eastern Europe and Central Asia, people who inject drugs accounted for over 70% of HIV cases but represented only 24% of the people receiving ART.³² Data collected for the WHO's universal access report in 2009 suggest that of 92 low- and middle-income countries that reported information on programmes and policies targeting injecting drug users, only 30 were providing needle and syringe programmes in 2008, 26 reported providing opioid substitution therapy (OST) and 26 reported access to HIV testing.³³ With regard to the prevention, diagnosis and treatment of TB in services aimed at people who inject drugs, a ratio of two to one countries replied that these were not available to drug users.³²

Much more needs to be done to integrate TB and HIV services with those aimed at people who use drugs. As shown elsewhere in this report, there has been increasing focus on people who inject drugs within recent years and the scale-up of key harm reduction interventions such as OST programmes has been reported in many countries, including China, Vietnam and Indonesia, with a gradual move towards integrating these with HIV services. Integration with HIV and TB services is not yet the norm, although examples of good practice have been reported from countries such as Spain, Brazil and Ukraine.

Integration of HIV/TB services for people who use drugs in Ukraine

With more than 1.5% adult HIV prevalence, Ukraine has been hard hit by the Eastern European HIV epidemic, largely driven by unsafe injecting drug use. The epidemic has had high mortality rates, with TB being the major cause of mortality among people living with HIV. The positive news is that Ukrainian civil society and government have made great progress in building a strong network of harm reduction services and providing HIV prevention, care and treatment to thousands of people with Global Fund to Fight AIDS, Tuberculosis and Malaria and state funding. However, despite the rapid scale-up of ART (from reaching 200 people in 2003 to approximately 10,000 out of 43,000 people living with HIV in 2008), TB has continued to be a major cause of mortality even for people receiving ART.

In order to support drug users in using services, civil society organisations, in collaboration with the Ministry of Health, are working to expand the provision of OST to over 150 sites, including TB centres, TB hospitals and ART clinics. New models of integrated care are being developed, such as 'one-stop shops' with multidisciplinary teams licensed to provide OST, DOTS treatment of TB and ART, as well as the provision of social support and low-threshold services integration. At least five of these pilot sites were operating by 2009.

Efforts are also under way to draw the prison services into the integrated treatment scale-up. The state of HIV services in the prison system has been lacking, quality drug treatment is more the exception than the rule and TB is widespread, with high rates of MDR TB, poor treatment access, lack of adherence and/or lack of social support. Using Global Fund Round 6 funding, prisons are being encouraged to set up harm reduction services integrated with HIV and TB treatment services.

Next steps and recommendations

TB and HIV services are slowly scaling up in many countries, often alongside harm reduction services such as OST programmes, but there is a need to increase service cross-referral and integration.¹³ This should be accompanied by the documentation of best practice in the provision of training and development of integrated services for TB/HIV and drug treatment/harm reduction, including collaboration with the criminal justice system.

Routine data on health service utilisation and outcome monitoring of people who use drugs is severely lacking and is needed for the planning and management of services, as well as for advocacy. This shortfall needs to be addressed through surveys and routine data collection.

Increased resources and political commitment for scaling up integrated services for people who use drugs, including TB, is essential. Drug user and harm reduction activists need to become more vocal in demanding access to these services.

The Global Fund is an increasingly important funding source for TB and HIV programmes, particularly for people who inject drugs. The international harm reduction community, including civil society and government, must take the opportunity the Global Fund provides to catalyse engagement in the provision of integrated services for drug users.

References

1. WHO (2009) *Global Tuberculosis Control. A Short Update to the 2009 Report*. Geneva: WHO.
2. Kitayaporn D et al. (1996) Survival of AIDS patients in the emerging epidemic in Bangkok, Thailand. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology*. 11(1): 77–82.
3. UNAIDS (2009) *Report on the Global AIDS Epidemic. Joint United Nations Programme on HIV/AIDS, 2009*. Geneva: UNAIDS.
4. Reichman LB et al. (1979) Drug dependence, a possible new risk factor for tuberculosis disease. *Archives of Internal Medicine* 139(3): 337–9.
5. Keizer ST et al. (2000) How does tuberculosis relate to HIV positive and HIV negative drug users? *Journal of Epidemiology and Community Health* 54(1): 64–8.
6. Portu JJ et al. (2002) Tuberculin skin testing in intravenous drug users: Differences between HIV-seropositive and HIV-seronegative subjects. *Addiction Biology* 7(2): 235–41.
7. Malotte CK et al. (1998) Tuberculosis screening and compliance with return for skin test reading among active drug users. *American Journal of Public Health* 88(5): 792–6.
8. Selwyn PA et al. (1989) A prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection. *New England Journal of Medicine* 320(9): 545–50.
9. WHO (2009) *Global Tuberculosis Control: Epidemiology, Strategy and Financing*. Geneva: WHO.
10. WHO, UNAIDS, UNICEF (2009) *Towards Universal Access: Scaling Up Priority HIV/AIDS Interventions in the Health Sector. Progress Report 2009*. Geneva: WHO.
11. WHO (2008) *Global Tuberculosis Control: Surveillance, Planning and Financing*. Geneva: WHO.
12. WHO (2009) *Scoping document: a review of viral hepatitis and HIV co-infection among injecting drug users and assessment of priorities for future activities* (unpublished)
13. WHO Regional Office for Europe (2007) *Status Paper on Prisons and Tuberculosis*. Copenhagen: WHO Regional Office for Europe.
14. Sylla L et al. (2007) Integration and co-location of HIV/AIDS, tuberculosis and drug treatment services. *International Journal of Drug Policy* 18(4): 306–12.
15. Kourbatova EV et al. (2006) Risk factors for mortality among adult patients with newly diagnosed tuberculosis in Samara, Russia. *International Journal of Tuberculosis and Lung Disease* 10(11): 1224–30.
16. Ministry of Health Committee on Response to HIV/AIDS, Ukrainian National AIDS Centre, LV Hromashevsky Institute for Epidemiology and Communicable Disease of AMS of Ukraine (2008) *Causes of Death of HIV-Positive People in Ukraine Study Report*. Kiev: STI/HIV/AIDS Programme, WHO Country Office in Ukraine.
17. Personal communication with Annette Verster, HIV Department, WHO, on systematic review of viral hepatitis being conducted by WHO.
18. WHO, UNAIDS, UNODC (2008) *Policy Guidelines for Collaborative TB and HIV Services for Injecting and Other Drug Users: An Integrated Approach*. Geneva: WHO.
19. Nunn P et al. (2007) TB drug resistance: Is it really a threat to Africa? *Ethiopian Medical Journal* 45(4): 399–404.
20. Wells CD et al. (2007) HIV infection and multidrug-resistant tuberculosis: The perfect storm. *Journal of Infectious Diseases* 196(Suppl. 1): S86–107.
21. Gandhi NR et al. (2006) Extensively drug-resistant tuberculosis as a cause of death in patients co-infected with tuberculosis and HIV in a rural area of South Africa. *Lancet* 368(9547): 1575–80.
22. Gandhi NR et al. (2010) HIV coinfection in multidrug- and extensively drug-resistant tuberculosis results in high early mortality. *American Journal of Respiratory and Critical Care Medicine* 181(1): 80–6.
23. Hannan MM et al. (2001) Investigation and control of a large outbreak of multi-drug resistant tuberculosis at a central Lisbon hospital. *Journal of Hospital Infection* 47(2): 91–7.
24. Dara M et al. (2009) *Guidelines for Control of Tuberculosis in Prisons*. Tuberculosis Coalition for Technical Assistance and International Committee of the Red Cross.
25. WHO (2000) *Tuberculosis Control in Prisons: A Manual for Programme Managers*. Geneva: WHO.
26. Ruddy M et al. (2005) Rates of drug resistance and risk factor analysis in civilian and prison patients with tuberculosis in Samara Region, Russia. *Thorax* 60(2): 130–35.
27. WHO (2006) *The Stop TB Strategy*. Geneva: WHO.
28. Stop TB Partnership (2006) *The Global Plan to Stop TB (2006–2015): Actions for Life, Towards a World Free of Tuberculosis*. Geneva: WHO.
29. WHO (2004) *Interim Policy on Collaborative TB/HIV Activities*. Geneva: WHO.
30. Donoghoe MC et al. (2008) Setting targets for universal access to HIV prevention, treatment and care for injecting drug users (IDUs): Towards consensus and improved guidance. *International Journal of Drug Policy* 19(Suppl. 1): S5–14.
31. Grigoryan A et al. (2009) Late HIV diagnosis and determinants of progression to AIDS or death after HIV diagnosis among injection drug users, 33 US States, 1996–2004. *PLoS One* 4(2): e4445.
32. WHO (2006) *Antiretroviral Therapy for HIV Infection in Adults and Adolescents: Towards Universal Access. Recommendations for a Public Health Approach*. Geneva: WHO.
33. Mathers BM et al. (2008) Global epidemiology of injecting drug use and HIV among people who inject drugs: A systematic review. *Lancet* 372(9651): 1733–45.