### **Round table**

### Reaching the targets for tuberculosis control: the impact of HIV

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**Abstract** In 1991, the 44th World Health Assembly set two key targets for global tuberculosis (TB) control to be reached by 2000: 70% case detection of acid-fast bacilli smear-positive TB patients under the DOTS strategy recommended by WHO and 85% treatment success of those detected. This paper describes how TB control was scaled up to achieve these targets; it also considers the barriers encountered in reaching the targets, with a particular focus on how HIV infection affects TB control.

Strong TB control will be facilitated by scaling-up WHO-recommended TB/HIV collaborative activities and by improving coordination between HIV and TB control programmes; in particular, to ensure control of drug-resistant TB. Required activities include more HIV counselling and testing of TB patients, greater use and acceptance of isoniazid as a preventive treatment in HIV-infected individuals, screening for active TB in HIV-care settings, and provision of universal access to antiretroviral treatment for all HIV-infected individuals eligible for such treatment. Integration of TB and HIV services in all facilities (i.e. in HIV-care settings and in TB clinics), especially at the periphery, is needed to effectively treat those infected with both diseases, to prolong their survival and to maximize limited human resources.

Global TB targets can be met, particularly if there is renewed attention to TB/HIV collaborative activities combined with tremendous political commitment and will.

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Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

#### Introduction

In 1991, the 44th World Health Assembly (WHA) recognized the importance and previous neglect of tuberculosis (TB), and set two key global targets to be reached by 2000: 70% case detection of acid-fast bacilli smear-positive TB patients under the then-new DOTS strategy recommended by WHO, and 85% treatment success for those detected.<sup>1,2</sup> Achieving these targets would significantly decrease TB prevalence and reduce TB incidence by approximately 10% per year in the absence of any major change in TB epidemiology.<sup>3-6</sup> By 2000, 148 countries had adopted the WHO DOTS strategy and 27% of the estimated global TB cases were being treated in a DOTS programme.2 Despite this progress, it became clear that the WHA targets would not be met by 2000, and the achievement date was deferred to 2005.2

# Setting the stage: scaling up TB control

In an effort to scale up global TB control to reach the WHA targets, the STOP TB Partnership was launched in 2000 and the first Global Plan to Stop TB, covering the years 2001-2005, was implemented.3 Between 1990 and 2004, the global TB prevalence decreased from 297 to 229 per 100 000 (including those positive for HIV).7 During this time, many countries received technical assistance to improve their national TB programmes, and 4.5 million patients were treated with anti-TB drugs procured through the Global Drug Facility, which was established to facilitate treatment with good quality, inexpensive TB drugs. 8 Second-line drug prices were reduced by 95% via the Green Light Committee, which promotes access to, and rational use of, second-line drugs for multidrug-resistant TB (MDR-TB).9 By July 2005, more than 36 projects managing drug-resistant TB in the context of DOTS programmes had been initiated, with more than 10 000 patients treated appropriately for MDR in more than 27 countries.<sup>4</sup>

As HIV continued to worsen the burden of TB, the TB/HIV working group of the STOP TB partnership provided guidance to help countries design and implement collaborative TB/HIV activities. 10 By the end of 2003, 29 of the 41 countries with the highest prevalence of HIV-associated TB had a national policy for collaboration between their TB and HIV programmes, and 16 had a national TB/HIV coordinating body key steps towards implementation.<sup>4</sup> In 2006, progress in meeting the target numbers was substantial: case detection reached 59% (more than 57 countries met the case detection target), and treatment success reached 84% (more than 60 countries met the treatment target) (Chris Dye, WHO, unpublished data). By late 2006, the global TB epidemic was at the threshold of decline (Chris Dye,

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WHO, unpublished data); however, only 25 countries have reached both of the 1991 WHA targets for TB control; particularly problematic are the low treatment success rates reported from Africa (72%) and Europe (75%).<sup>7</sup>

To meet the 1991 WHA targets, the US \$56 billion Global Plan to STOP TB, 2006–2015 was formulated and disseminated. Fulfilling this second plan will reach the 1991 targets. It will also achieve target 8 of Millennium Development Goal (MDG) 6— "to have halted by 2015, and begun to reverse, the incidence of [all forms] of TB". It will also meet the STOP TB Partnership's 2015 targets, which are to halve TB prevalence and death rates from the 1990 baseline, and eliminate TB (incidence < 1/1 000 000) as a global public health problem by 2050.

Successful implementation of the Global Plan depends on implementation of the new 6-point STOP TB strategy recommended by WHO. This strategy promotes use of the new International Standards for Tuberculosis Care 11,12 to engage all care providers (including those in the private sector) in delivering high-quality care. It specifically addresses HIV-associated TB, MDR-TB and other challenges, and strengthens human rights and health systems. However, the plan also relies on new diagnostic tests, new drugs and TB vaccines being developed by or before 2015.

Through the successful implementation of the new plan, 50 million patients will be treated using DOTS and/or tested for drug-resistant TB in the context of DOTS programmes. Countries will achieve comprehensive TB control for their entire populations, through improved quality of TB treatment and care services (including TB laboratories) and implementation of community DOTS initiatives. Although the second global plan lays out an ambitious strategy for achieving the global TB targets, it acknowledges that these targets may not be reached in eastern Europe or Africa, due to the complexities of managing and treating both MDR-TB and HIV and their implications for case detection and treatment success, as described below.

# Barriers to meeting the TB control targets

Long-standing barriers to the achievement of the global targets include neglect of TB control by governments, lack of financial and human resources to provide supervision and quality control, weakened health systems, poorly managed TB control programmes, poverty, population growth and a significant increase in drug-resistant TB (particularly MDR-TB) and recently, extensively drug-resistant TB (XDR-TB).<sup>13</sup> A lack of new diagnostic tools has impeded progress in global TB control. Perhaps the greatest challenge to achieving the global TB targets, however, has been the ever-expanding HIV epidemic and the resulting increases in HIV-associated TB.

In 2005, in large part due to Africa's uncontrolled epidemic of HIVassociated TB, African health ministers declared TB a regional emergency.4 Approximately 38% of African TB patients are estimated to be HIV-infected.<sup>7,14</sup> This TB/HIV syndemic has seriously compromised even historically strong national TB programmes in many countries.<sup>7</sup> TB programmes are overwhelmed by an increasing volume of HIV-associated TB cases and by the need to manage cases and ensure treatment completion. Furthermore, TB is the leading cause of death among HIV-infected persons, and HIV is the strongest predictor of progression from latent TB infection to active disease. 4,15-17 Thus, TB programmes that were nearing the WHA-set global TB targets have seen their cure and completion rates worsen.7

The TB/HIV syndemic has also had a tremendous impact on human resources. 4,18-20 In a workforce that has remained the same or decreased, the increased overall number of TB patients has weakened TB programmes' infrastructure and increased poor TB outcomes such as treatment default, death and the emergence of XDR-TB.21 The HIV-associated TB epidemic has led to an increasing incidence of smearnegative and extrapulmonary TB;7 these forms of TB do not contribute to the case-detection targets and are more complicated to diagnose. Furthermore, smear-negative TB has a worse prognosis than smear-positive TB among those who are also HIV-infected. 16,22,23

#### TB/HIV collaborative activities

To address the impact of HIV-associated TB and facilitate the achievement of both old and new global TB targets, we must scale up the WHO-recommended TB/HIV collaborative activities and push for closer coordination of these activities between HIV and TB control programmes. The WHO 2006 report on global TB control notes that 32 of

41 countries with a high burden of HIVpositive TB cases have reported on their TB/HIV collaborative activities for the last three years.7 In 2004, 23 countries had appointed a TB/HIV focal person within their national TB programme, 17 had a formal system for referring patients from HIV to TB services, 20 had a policy to carry out intensified TB case-finding among people with HIV, 18 had a policy to provide HIV testing and counselling for all TB patients, 20 had a policy to provide cotrimoxazole preventive therapy to HIV-positive TB patients and 21 had a policy to provide antiretroviral therapy to HIV-positive TB patients.7

Progress has been made, but in reality we are dismally behind in all countries. WHO estimates that 125 000 TB patients were HIV tested in high-HIV-prevalence settings in Africa by the end of 2005 (Chris Dye, WHO, unpublished data). For 2006, however, the new global plan calls for 600 000 TB patients to be counselled and tested in these settings, and for 29 million TB patients to be counselled and tested overall by the end of 2015. Furthermore, once detected, these HIV-infected TB patients must receive cotrimoxazole preventive therapy and antiretroviral treatment. 10

Although isoniazid preventive therapy (IPT) has been demonstrated to reduce the risk for TB among those with HIV infection,<sup>24</sup> only Botswana has attempted nationwide scale-up of this important intervention.<sup>25</sup> Many national programmes are reluctant to implement this activity due to cost, fear of not excluding active disease and logistic challenges. Successful achievement of the new global plan will require approximately 3 million HIV-positive individuals to be treated with IPT.<sup>4</sup>

HIV care settings, such as voluntary counselling and testing centres, comprehensive care clinics and centres to prevent mother-to-child transmission of HIV represent ideal settings for identifying persons with active TB; screening for active TB should be increasingly incorporated into these areas. 10,26,27 Indeed, addressing TB should be a core function of HIV services. The second global plan calls for the TB screening of 210 million people living with HIV/AIDS by the end of 2015.4 However, to properly screen for TB among HIV-positive individuals, TB diagnostic capability needs to be strengthened, far beyond direct sputum-smear microscopy.<sup>23,28</sup> Microscopy often performs poorly even when correctly executed, and is less useful among HIV-positive individuals than among those uninfected, because of the high proportion of smear-negative TB among those infected with HIV.<sup>23,29</sup> WHO has proposed a new smear-negative TB screening algorithm in the context of HIV;29 however, this algorithm relies on the availability of chest X-ray and sputum culture for these patients. Thus, to properly diagnose and reduce TB in the context of HIV, improved and higher-quality diagnostic services, including sputum cultures, will have to be made widely available.30 Such strengthening of TB laboratory capacity will also greatly improve the ability to detect MDR-TB and XDR-TB, which in turn will help to achieve the 1991 and global plan targets in those countries where MDR-TB is preventing TB control progress, such as in eastern Europe. Furthermore, the HIV care setting is key for the initiation of urgently needed IPT programmes.

Finally, one of the most important interventions for the control of HIV-associated TB is the provision of universal access to antiretroviral (ARV) treatment for all eligible HIV-infected individuals. Freatment for HIV prevents or slows progression from latent infection to TB disease, and also leads to better treatment outcomes in patients who already have TB. However, ARV treatment must be initiated early in the course of an HIV infection, and the coverage and compliance with ARV

treatment must be extremely high to truly prevent additional TB cases. <sup>32</sup> Currently, 15 000 HIV-infected TB patients are reported to be on ARV treatment in high-HIV settings in Africa (Chris Dye, WHO, unpublished data). The global plan calls for 200 000 coinfected persons to be on ARV in 2006 in these settings, and the enrolment of 3 million HIV-positive TB patients into ARV treatment programmes by the end of 2015.<sup>4</sup>

## TB-HIV service integration's impact

Integration of TB and HIV services in all facilities (i.e. in HIV-care settings and in TB clinics), especially at the periphery, is needed to treat effectively those infected with both diseases, to prolong their survival and to maximize limited human resources.<sup>33</sup> Diagnosing and treating TB disease in HIV-care settings will help to increase case detection and improve rates of TB treatment completion; infection control will be paramount in this context. Likewise, treating HIV (with cotrimoxazole and/or ARV) and TB together in TB treatment and care settings is logistically easier for the patient, and will also help to strengthen the follow-up and treatment completion rates for TB treatment. It is often difficult to achieve this integration operationally at the programme level, given differing resources and agendas of control programmes for TB and HIV/AIDS. Yet strengthening basic TB control in this way is critical to managing TB in the context of HIV, and

will also help to "turn off the faucet" of MDR-TB, a product of poor TB control and incomplete treatment.<sup>34</sup>

The actions described above for scaling-up TB/HIV activities will also help to address the action plan put forward by the recently convened WHO Global Task Force on XDR-TB.<sup>35</sup> Integrated services and overall better TB control, including manual laboratory services, will help to manage and treat MDR- and XDR-TB patients and will allow better investigation of cases and contacts. Scaling-up TB/HIV collaborative activities will also help to promote universal access to ARV treatment for all TB patients, another critical action for managing and controlling XDR-TB.<sup>35</sup>

#### **Conclusion**

Implementation of the above activities is the only way to achieve the global targets. Implementation and scale-up of these activities is critical if these targets are to be reached in eastern Europe and Africa, two places that the Global Plan to STOP TB 2006–2015 has suggested will not meet the targets. Failure to meet the targets in eastern Europe and Africa would be disastrous for global TB control overall. All targets can be met in all countries through these activities, provided that renewed attention to TB/HIV collaborative activities is combined with political commitment and will.

Competing interests: None declared.

#### Résumé

#### Incidence du VIH/sida sur la réalisation des objectifs de la lutte antituberculeuse

En 1991, la 44° Assemblée mondiale de la Santé a fixé deux objectifs essentiels à la lutte mondiale contre la tuberculose (TB) à atteindre d'ici 2000 : détection, dans le cadre de la stratégie DOTS préconisée par l'OMS, de 70 % des cas de TB à frottis positif pour les bacilles acido-alcoolorésistants et succès du traitement chez 85 % des cas détectés. Le présent article décrit le passage à l'échelle supérieure de la lutte antituberculeuse pour réaliser ces objectifs. Il étudie aussi les obstacles rencontrés dans cette réalisation, en s'intéressant particulièrement à l'impact des infections à VIH sur la lutte antituberculeuse.

Il sera plus facile de renforcer la lutte contre la TB en élargissant les activités de collaboration TB/VIH recommandées par l'OMS et en améliorant la coordination entre les programmes de lutte anti-VIH et anti-TB, notamment pour endiguer les TB pharmacorésistantes. Il est entre autre nécessaire de renforcer les activités de conseil et de dépistage concernant le VIH auprès des malades tuberculeux, d'élargir l'utilisation et l'acceptation

de l'isoniazide comme traitement préventif chez les individus infectés par le VIH, de dépister les tuberculoses actives dans les établissements dispensant des soins liés au VIH/sida et d'offrir un accès universel au traitement antirétroviral à tous les individus porteurs du VIH remplissant les critères pour bénéficier d'un tel traitement. Une intégration des services accueillant les malades tuberculeux et de ceux affectés au VIH/sida s'impose dans tous les établissements (à savoir des unités de soins en rapport avec le VIH et de celles de traitement de la TB), et tout particulièrement dans les établissements périphériques, pour traiter avec efficacité les personnes atteintes des deux maladies, prolonger leur survie et tirer la maximum de moyens humains limités.

La réalisation des objectifs mondiaux de la lutte antituberculeuse suppose en particulier un regain d'intérêt pour les activités de collaboration TB/VIH, accompagné d'une volonté et d'un investissement très forts sur le plan politique.

#### Resumen

#### Logro de las metas de control de la tuberculosis: impacto del VIH

En 1991, la 44ª Asamblea Mundial de la Salud estableció dos metas decisivas para la lucha mundial contra la tuberculosis con miras al año 2000, a saber, detectar el 70% de los casos bacilíferos en el marco de la estrategia de DOTS recomendada por la OMS, y tratar satisfactoriamente el 85% de los casos detectados. En este artículo se describe cómo se expandió la lucha antituberculosa para lograr esas metas, analizándose también los obstáculos que se interpusieron en el camino, en particular la influencia de la infección por VIH en el control de la enfermedad.

La eficacia de la lucha antituberculosa se verá potenciada por la expansión de las actividades en colaboración contra la coinfección tuberculosis/VIH recomendadas por la OMS y por la mejora de la coordinación entre los programas de control del VIH y de la tuberculosis, en particular de los destinados a combatir la tuberculosis farmacorresistente. Las actividades requeridas abarcan una intensificación del asesoramiento y pruebas del VIH para los pacientes con tuberculosis, un mayor uso y aceptación

de la isoniazida como tratamiento preventivo de las personas infectadas por el VIH, el cribado de la tuberculosis activa en los entornos de atención de la infección por VIH, y el acceso universal a la terapia antirretroviral para todos los seropositivos que reúnan las condiciones para recibir ese tratamiento. Es necesario integrar los servicios contra la tuberculosis y el VIH en todos los establecimientos (esto es, en los entornos de atención para los infectados por el VIH y en los consultorios antituberculosos), especialmente en la periferia, para poder tratar eficazmente a quienes sufren ambas infecciones, a fin de prolongar su supervivencia y de maximizar unos recursos humanos limitados.

Es posible alcanzar las metas mundiales de control de la tuberculosis, sobre todo si se presta una renovada atención a las actividades colaborativas en materia de tuberculosis/VIH con el respaldo de un enorme compromiso y voluntad políticos.

#### ملخص

### تحقيق أهداف مكافحة السل: أثرها على الإيدز

حول الإيدز وإجراء اختباراته على مرضى السل، مع استخدام أكثر وقبول أكبر للإيزوينازيد كمعالجة وقائية تعطى للأفراد المصابين بالإيدز، وتحري السل في المواقع التي تقدم بها الرعاية لمرضى الإيدز، وإتاحة شاملة للمعالجة بمضادات الفيروسات القهقرية المسببة للإيدز لجميع المصابين بعدوى الإيدز والمؤهلين لتلك المعالجة. إن التكامل بين خدمات مكافحة السل وخدمات مكافحة الإيدز في جميع المرافق (مثل مواقع تقديم الرعاية لمرضى الإيدز وعيادات مكافحة السل)، ولاسيما في المناطق المحيطية، أمر تمس الحاجة إليه لتحقيق المعالجة الفعّالة للمصابين بكلا المرضين، ولإطالة فترة بقائهم أحياء، ولزيادة المؤورد البشرية المحدودة.

إن الهدفين العالميين لمكافحة السل يمكن تحقيقهما، ولاسيما إذا ما تم إيلاء اهتمام كاف للأنشطة التعاونية بين السل والإيدز إلى جانب الإرادة والتزام السياسي الهائل.

في عام 1991، وضعت جمعية الصحة العالمية الرابعة والأربعون هدفين رئيسيين للمكافحة العالمية للسل كان ينبغي تحقيقهما عام 2000؛ وهما كشف 70 بالمئة من المرضى بالسل الإيجابي اللطاخة لعصيات مقاومة للحمض ممن يخضعون لاستراتيجية المعالجة القصيرة الأمد تحت الإشراف المباشر التي توصي بها منظمة الصحة العالمية، والنجاح في معالجة 85% ممن تم اكتشافهم. وتصف هذه الورقة كيفية النهوض بمكافحة السل لتحقيق هذين الهدفين؛ كما تولي هذه الورقة اهتماماً خاصاً للعوائق التي تقف دون تحقيق هذه الأهداف، مع تركيز خاص على تأثير العدوى بفيروس الإيدز على مكافحة السل.

إن المكافحة الحازمة للسل يمكن أن تصبح أكثر سهولة بالنهوض بالأنشطة التعاونية بين السل والإيدز التي توصي بها منظمة الصحة العالمية، وبتحسين التنسيق بين برامج مكافحة السل وبرامج مكافحة الإيدز، ولاسيما في ضمان مكافحة السل المقاوم للأدوية. وتتضمن الأنشطة المطلوبة المزيد من التوعية

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