

Scale-up of isoniazid preventive therapy in PEPFAR-assisted clinical sites in South Africa

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SUMMARY

We reviewed the implementation of isoniazid preventive therapy (IPT) in South Africa from January 2010 to March 2011. The South African National Department of Health distributed revised IPT guidelines in May 2010 to increase IPT use in eligible human immunodeficiency virus (HIV) infected patients. We found a dramatic in-

crease in the absolute numbers of patients reported to have been initiated on IPT (from 3309 in January–March 2010 to 49130 in January–March 2011), representing an increase in the proportion (1.0–10.5%) of potentially eligible HIV-infected patients started on IPT.

KEY WORDS: IPT; tuberculosis; HIV; PEPFAR

SOUTH AFRICA has the third highest incidence of tuberculosis (TB) in the world, and accounts for the greatest global burden of TB and human immunodeficiency virus (HIV) co-infection.^{1,2} Over 60% of individuals with active TB in South Africa are co-infected with HIV. TB is the most common opportunistic infection in HIV-infected individuals, and is responsible for about one in five HIV-related deaths in South Africa.³ Isoniazid preventive therapy (IPT) has been shown to be highly effective in these patients.⁴ In a study of HIV-positive gold miners in South Africa, IPT was shown to reduce the incidence of active TB by 38%.⁵ Munseri et al. assessed IPT acceptance and adherence among HIV-infected patients in Tanzania, and found high rates (87%) of IPT adherence when counseling, follow-up and reimbursement for travel were provided.⁶ The World Health Organization (WHO) has recommended IPT as part of a comprehensive HIV/AIDS (acquired immune-deficiency syndrome) care strategy since 1998, and has set 2015 as a target year for the provision of IPT to all eligible HIV-infected patients.¹

In May 2010, the South African National Department of Health (NDOH) issued updated recommendations for IPT for all HIV-infected individuals without symptoms of active TB or medical contraindications, based on the WHO guideline on intensified case finding and IPT, making South Africa an early implementer of this policy.⁷ Suspected active TB is the presence of one or more of the following symptoms: current cough (≥ 24 h), fever, loss of weight and drenching night sweats. Patients with none of these symptoms and no

contraindications (active liver disease or active alcohol abuse) should be started on IPT.⁸

The US President's Emergency Plan for AIDS Relief (PEPFAR) was launched in 2003 as an emergency response to the HIV/AIDS epidemic. PEPFAR's agreement with the South African government supports improvement of the national HIV and TB response, primarily through cooperative agreements with over 150 non-governmental organizations (NGOs), faith-based organizations and universities.⁹ PEPFAR requires its award recipients to submit quarterly programmatic data from each of the assisted clinical facilities. In 2010, PEPFAR awardees reported on approximately 82% of all patients receiving antiretroviral therapy in South Africa.¹⁰

We report on IPT uptake among HIV-infected patients in PEPFAR-assisted South African health facilities from January 2010 to March 2011.

METHODS

PEPFAR awardees have submitted quarterly monitoring data through a web-based system since 2005 (MySQL, MySQL AB, Uppsala, Sweden). As of January 2010, the reported indicators included the number of patients initiated on IPT per clinical facility.

We analyzed PEPFAR monitoring data for the period from 1 January 2010 to 31 March 2011. Symptom-screened HIV-infected patients receiving care and treatment services who were not diagnosed with active TB were considered potentially eligible for IPT. We compared data by period and province.

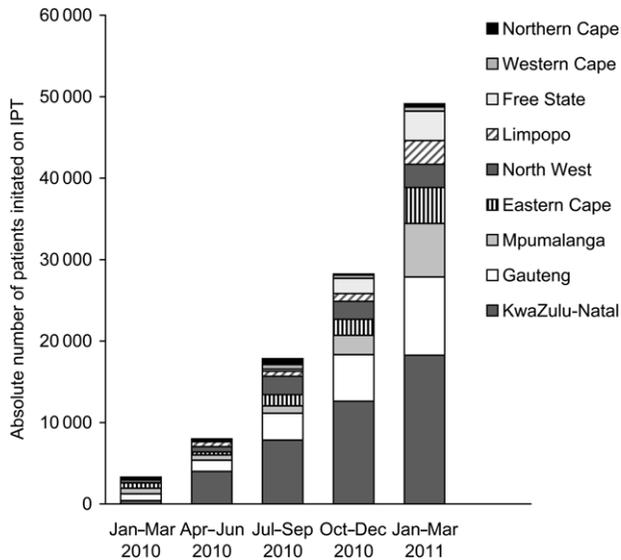


Figure Patients initiated on IPT per quarter, by province, South Africa, January 2010–March 2011. IPT = isoniazid preventive therapy.

In accordance with US regulations, the Centers for Disease Control and Prevention determined the collection of data and subsequent analyses to be a non human subjects research activity.

RESULTS

In January–March 2010, 3309 (1.0%) of 317797 potentially eligible patients in PEPFAR-assisted clinical facilities initiated IPT. This number and proportion increased to 49130 (10.5%) of 467137 potentially eligible patients in January–March 2011, a more than 14-fold increase, with an average increase of 9164 new patients per quarter initiated on IPT (Figure). During the quarter January–March 2011, the Eastern Cape Province demonstrated the highest proportion of IPT use, with 4431 (25.3%) of the 17492 potentially eligible patients initiated on IPT, while the Western Cape Province demonstrated the lowest use (539/29698, 1.8%). Patients potentially eligible to initiate IPT in Eastern Cape were 25.9 (95% confidence interval 23.8–28.2) times as likely as those in Western Cape to initiate IPT.

DISCUSSION

Our analysis demonstrated that IPT uptake had increased substantially among potentially eligible patients from January 2010 to March 2011 at PEPFAR-assisted sites in South Africa following the release of the South African national IPT guidelines. Although the absolute number of patients initiating IPT increased, the overall proportion of potentially eligible patients on IPT was low. Differences in reported use among provinces demonstrated varying degrees of

guideline implementation across the country. The differences in uptake among provinces suggest the need to identify factors that contribute to these differences as well as efforts to align provincial policy with the national policy.

The observed rapid increase in IPT use was supported through increased training, the use of clinic-based registers, assurance of isoniazid (INH) supplies and routine quarterly evaluation by the NDOH TB program.

Our analysis was subject to several limitations. The data represent patients who initiated IPT, but neither adherence nor outcomes were assessed. As the true denominator was unknown, we estimated it as HIV-infected patients who were not diagnosed with active TB. However, we do not know if all patients were actually screened for TB or if they were ineligible for other reasons, such as medical contraindications. The proportion of patients receiving IPT among those potentially eligible may therefore be an underestimation. Our data collection methods do not allow for disaggregation below the province level. Although these data represent the majority of facilities in South Africa, they may not be generalizable to non-PEPFAR-assisted clinical sites.

IPT is one arm of the WHO recommended ‘Three I’s’ strategy to control TB, which also includes intensified case finding and improved infection control measures.⁷ Ultimately, the integration of the Three I’s with additional interventions will be necessary to control TB. While there has been no evidence of an increase in IPT-related adverse affects, toxicity or INH resistance, continued monitoring of those outcomes is critical. Expansion of programs to further increase IPT coverage is urgently needed in South Africa. Enhanced monitoring of IPT uptake, quality improvement activities for tracking IPT use at the clinic level, providing supervision and mentoring may accelerate IPT implementation. Over time, we expect that the increase will plateau as the number of those eligible for IPT approaches implementation targets. Lessons learned from our evaluation suggest that policy creation and dissemination are critical elements to increasing implementation by stakeholders.

Acknowledgement

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References

- 1 World Health Organization. Global tuberculosis control, 2010. WHO/HTM/TB/2010.7. Geneva, Switzerland: WHO, 2010.
- 2 Getahun H, Gunneberg C, Granich R, Nunn P. HIV infection

- associated tuberculosis: the epidemiology and the response. *Clin Infect Dis* 2010; 50 (Suppl 3): 201–207.
- 3 Corbett E L, Watt C J, Walker N, et al. The growing burden of tuberculosis: global trends and interactions with the HIV epidemic. *Arch Intern Med* 2003; 163: 1009–1021.
 - 4 Samandari T, Agizew T B, Nyirenda S, et al. 6-month versus 36-month isoniazid preventive treatment for tuberculosis in adults with HIV infection in Botswana: a randomized, double-blind, placebo-controlled trial. *Lancet* 2011; 377: 1588–1598.
 - 5 Grant A D, Charalambous S, Fielding K L, et al. Effect of routine isoniazid preventive therapy on tuberculosis incidence among HIV-infected men in South Africa. *JAMA* 2005; 293: 2719–2725.
 - 6 Munseri P J, Talbot E A, Mtei L, Fordham von Reyn C. Completion of isoniazid preventive therapy among HIV-infected patients in Tanzania. *Int J Tuberc Lung Dis* 2008; 12: 1037–1041.
 - 7 World Health Organization. Guidelines for intensified tuberculosis case finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings. Geneva, Switzerland: WHO, 2010.
 - 8 National Department of Health. Guidelines for tuberculosis preventive therapy among HIV-infected individuals in South Africa. Pretoria, South Africa: NDOH, 2010. <http://www.rhru.co.za/Resources/Documents/2010%20TB%20Prophylaxis%20Guidelines.pdf> Accessed April 2012.
 - 9 The United States President's Emergency Plan for AIDS Relief. Partnership framework in support of South Africa's National HIV & AIDS and TB response 2012/13–2016/17 between the Government of the Republic of South Africa and the Government of the United States of America. Washington DC, USA: PEPFAR, 2010. <http://www.pepfar.gov/frameworks/southafrica/161215.htm> Accessed April 2012.
 - 10 Statistics South Africa. Mid-year population estimates, 2011. Pretoria, South Africa: Statistics South Africa, 2011. <http://www.statssa.gov.za> Accessed April 2012.

R É S U M É

En Afrique du Sud, nous avons passé en revue la mise en œuvre du traitement préventif à l'isoniazide (IPT) à partir de 2010 jusqu'en mars 2011. Le Département National de Santé d'Afrique du Sud avait distribué des directives révisées sur l'IPT en mai 2010 en vue d'augmenter son utilisation chez les patients éligibles infectés par le VIH. Nous avons noté une augmentation drama-

tique des nombres absolus de patients signalés comme ayant été mis sous IPT (de 3309 entre janvier et mars 2010 à 49 130 entre janvier et mars 2011), ce qui représente une augmentation (depuis 1,0% jusqu'à 10,5%) de la proportion des patients infectés par le VIH et potentiellement éligibles pour l'IPT réellement mis sous IPT.

R E S U M E N

En el presente estudio se evaluó la administración del tratamiento preventivo con isoniazida (IPT) entre enero del 2010 y marzo del 2011 en Sudáfrica. El Departamento Nacional de Salud de Sudáfrica distribuyó las directrices sobre el IPT en mayo del 2010, con el propósito de incrementar su uso en los pacientes aptos, infectados por el virus de la inmunodeficiencia humana (VIH). Se

observó un aumento considerable del número absoluto de pacientes que inició el tratamiento (de 3309 entre enero y marzo del 2010 a 49 130 entre enero y marzo del 2011), lo cual corresponde a una mayor proporción (1,0% a 10,5%) de los posibles pacientes aptos infectados por el VIH que comenzaron el IPT.
