Title: Implementation of Isoniazid Preventive Therapy (IPT) in South Africa, 2011

Authors:

J. C. Chehab *, K. Vilakazi-Nhlapo †, P. Vranken * A. Peters *, J. D. Klausner *

* Centers for Disease Control and Prevention, South Africa

† National Department of Health, Pretoria, South Africa

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None.

Corresponding Author Contact Information:

Chehab, C. Joel, MPH

2nd Floor CBE building

Brooklyn

P.O. Box 9536
0001, Pretoria

South Africa

Email: ChehabJ@sa.cdc.gov

Tel: +27 (0) 12 424 9000 (ext. 9021)

Fax: +27 (0) 12 346 4286
SUMMARY

SETTING: Public Health Facilities in South Africa

OBJECTIVE: To assess the current implementation of Isoniazid Preventive Therapy (IPT) in South Africa, 2011

DESIGN: Cross-sectional study of 50 randomly selected facilities in South Africa. Trained interviewers administered a standardized questionnaire per facility on aspects of IPT policy, implementation and recording and reporting. We calculated and compared descriptive statistics by province and facility type.

RESULTS:

Of the 49 participating sites, 35 provided IPT (71%). By province: absent (0%) in all Western Cape facilities, and available in few Mpumalanga (40%) and Limpopo (20%) sites, resulting in 46% of eligible HIV-infected patients in February 2011 initiated on IPT. Implementation by facility type was 27% among community health centers. Of facilities with TB/HIV committees, 85% offered IPT compared to 59% of those without TB/HIV committees (p=0.1217). Possession of the 2010 South African National IPT guidelines was statistically significantly associated with sites providing IPT (84% versus 29%; p=0.006).

CONCLUSION:

IPT implementation in South Africa, as of February 2011, has begun. TB/HIV on-site committees and presence of guideline availability were strongly associated with IPT
uptake. More operational studies are needed to improve IPT implementation among HIV-infected patients in South Africa.

KEYWORDS: Tuberculosis; HIV; co-infection; integration; prevention

Word count: 199
INTRODUCTION

Globally, the HIV and Tuberculosis (TB) epidemics are profoundly intertwined: HIV is the leading risk factor associated with developing active TB, and the latter is the leading cause of death and morbidity among HIV-infected individuals [1]. This is particularly evident in South Africa, home to the highest number of HIV-infected patients and one of the highest TB incidences worldwide [2]. Co-infection rates in South Africa are high with as many as 80% of TB patients in Kwazulu-Natal province estimated to be HIV positive [3].

Since the 1990s, several randomized clinical trials found Isoniazid Preventive Therapy (IPT) to be effective in preventing active TB among HIV-infected individuals [4-7]. A Cochrane review of 11 randomized trials showed a 33% protective effect of IPT against active TB [8] and another study showed that protection increased to 64% among individuals with positive Tuberculin Skin Tests (TST) [9]. In 1999, the World Health Organization (WHO) recommended adding IPT to existing HIV care packages, and initiating all HIV-infected individuals with confirmed latent TB infection or TB exposure on IPT [10]. The newest WHO guidelines recommend that in settings with high rates of TB transmission among HIV-infected individuals, all HIV-infected people where TB has been ruled out should be initiated on IPT [11].

In 2010, the South African National Department of Health (NDOH) revised their guidelines on Tuberculosis Prevention Therapy among HIV-infected individuals accordingly, recommending that all eligible HIV-infected individuals be initiated irrespective of TST [12]. Together with Infection Control and Intensive Case-Finding
policies, Isoniazid Preventive Therapy forms WHO’s Three I’s, and South Africa’s core strategy to combat the spread of TB [11-14]. Despite an abundance of scientific evidence and clear guidelines in place, IPT implementation has been slow worldwide, with only 30,000 people living with HIV having started IPT in 2007 [1]. No national assessment had been conducted since the revised guidelines to determine the level of implementation of IPT in South Africa.

We aimed to assess the current implementation of IPT in South Africa.

**STUDY POPULATION AND METHODS**

*Study population*

We assessed 49 public medical facilities in high HIV prevalence districts in South Africa’s nine provinces from March 1st to March 31st 2011.

*Methods*

A multistage sampling method was used. Firstly, we systematically selected the single district in each province with the highest HIV prevalence. In Kwazulu Natal, two districts were selected as it had the highest HIV prevalence and double the number of districts of other provinces [15]. Secondly, each sub-district per selected district was assigned a number and one sub-district randomly selected using the random number generator on stattrek.com. Thirdly, all facilities per selected sub-district were assigned a number, stratified by facility type- Community Health Center, Primary Health Clinic or District Hospital. Using the random number generator mentioned above, a random sample of three primary health clinics, one community health center and one hospital per sub-
district was chosen. This ratio was chosen to approximate the current distribution of public medical facilities in South Africa. The lists of facilities used for this sampling was provided by the South African National Department of Health.

We determined the availability of the latest national guidelines, as well as the presence of dedicated TB/HIV committees within each facility. Those committees were defined as specific on-site bodies to enable TB and HIV integration with management from both the TB and HIV sections within each facility.

We also determined the training of staff in TB and HIV, defining trained staff as any permanent facility staff trained in at least IPT and TB Infection control since January 2010.

Finally, we sought out the major reasons for not initiating patients on IPT. In an effort to assess the quality of counseling offered, we asked each facility to report the four most important facts about IPT that were covered in their counseling sessions. We defined the four essential aspects of IPT as adherence, reporting of side effects, reporting of symptoms of tuberculosis, and stopped or reduced alcohol intake during treatment.

**Questionnaire**

A team composed of five members of the Centers for Disease Control and Prevention and the South African NDOH created a standardized anonymous survey. The survey contained questions on various aspects of IPT implementation, including guideline availability, service provision, supply, and reporting and recording of routine data.

**Data collection**
Ten teams of interviewers were trained by the Principal Investigator in the use of the standardized questionnaire prior to the assessment. Each data collection team was responsible for conducting the assessment in 5 sites.

The questionnaires were administered to the TB and HIV focal person in each selected facility. Information reported by interviewees was systematically verified by collecting routine data from facility registers for TB and HIV information.

Data Analysis

Questionnaire data were directly entered into an Epi-Info 3.5.1 database for analysis (Centers for Disease Control and Prevention, Atlanta, GA), and descriptive statistics were calculated and compared by province and facility type, using Chi-Square.

Ethical considerations

The Centers for Disease Control and Prevention determined that the collection of routine data and its analysis for this study was a non-research activity in accordance to United States Federal regulations. Further, the South African National Department of Health waived the need for local human subjects’ review.

RESULTS

Facilities

Of the 50 facilities randomly selected, 49 (98%) participated in the survey. The missing site was a facility in Northern Cape, which had merged with another selected site situated on the same premises shortly prior to data collection.
**Service availability**

Of the 49 participating facilities, 35 (71%) provided IPT. Implementation varied significantly by province: none of the sites in Western Cape, 20% of Mpumalanga and 40% of Limpopo sites offered IPT. Table 1 shows the distribution by province among our sample.

Stratified by facility type, community health centers were the least frequent implementers of IPT with only 56% of 10 offering IPT as opposed to 77% of 29 and 80% of 10 public health clinics and district hospitals respectively.

Survey participants not implementing IPT (n=14) reported no clear guidance or commitment from authorities (29%) and concerns of INH resistance (21%). Western Cape followed national IPT guidelines but required that patients be given a Mantoux test and be positive in order to be initiated on IPT. Regardless of Mantoux results, no patient had been initiated on IPT in the five facilities assessed in that province in February 2011.

**Guidelines availability**

The 2010 National IPT guidelines were available in 39 (80%) out of the 49 participating facilities. Table 1 shows little variation by province, with the notable exception of Western Cape where none of the facilities had the latest guidelines. Of the survey participants, 64% reported using the latest guidelines. Facilities having the 2010 IPT guidelines were almost three times as likely to offer IPT than those who did not (84%; 29%, p=0.006).
**IPT initiation**

In the month prior to the survey, 46% of eligible patients were initiated on preventive therapy in the 35 facilities implementing IPT. Those 616 patients had been diagnosed HIV-infected that month, screened negative for tuberculosis and were deemed eligible to initiate therapy. Implementation by facility type was lowest among community health centers where only 27% of eligible patients were initiated on INH.

**TB/HIV training of staff**

Of the 49 facilities assessed, 38 (78%) had at least one staff member recently trained in TB and HIV integrated services. Of facilities implementing IPT, 83% had at least one recently trained staff. These figures stratified by province are shown in table 1.

75% of facilities had no doctors trained and 84% had at no nurses trained in TB and HIV integrated services since January 2010.

**TB/HIV committees**

Out of our sample of 49 facilities, 20 (41%) had such committees. Facilities with TB/HIV committees were more likely to offer IPT that those that did not among our sample (85% versus 59%). There was great variation by provinces, and is shown in table 1.

**IPT counseling**

All 35 facilities offering IPT also offered patients counseling prior to initiation on therapy. Table 2 illustrates the distribution of counseling content among facilities providing counseling.
Of the 35 facilities providing counseling to IPT patients, 30 (86%) covered two or more essential topics, 54% three topics or more, and only 6 (17%) covered all four essential topics. Only 3% did not cover any of the essential topics. The four essential topics were covered to varying degrees among those 35 facilities: 97% of them counseled on the importance to adhere to the treatment for its entire duration, 66% on the need to immediately report any side effects, 29% on the importance to immediately report any signs or symptoms of TB, and only 9% on the need to reduce or stop alcohol intake during course of treatment.

**IPT Recording and Reporting**

IPT data was recorded in 34 of the 35 (97%) facilities - the exception being one primary health clinic in Mpumalanga. There was no official IPT register available for facilities at the time of assessment, yet 20 of the 34 facilities (59%) had made their own allowing them to record patient information and IPT data throughout treatment. Of those sites, 33 (97%) also reported IPT monthly statistics, except for one primary health clinic in North West province. We investigated separately recording practices for ART patients, and found that among the sites providing IPT (N=35), 27 (77%) initiated ART patients on IPT. Recording of IPT information for ART patients among these facilities was poorer, with only 21 of 27 sites (78%) doing so.

**DISCUSSION**

Our study assessed the implementation of IPT in South Africa in early 2011. Our data shows that IPT is being partly implemented. We found that 71% of randomly selected medical facilities implemented IPT and that in February 2011, 46% of eligible newly
diagnosed HIV-infected patients were initiated on preventive therapy. In this survey, many of the sites not implementing IPT did so either because of lack of provincial policy, guidance from authorities or fear of INH resistance. This lends support to current literature indicating that facility staff’s concerns about INH resistance due to a failure to rule out active Tuberculosis is a major barrier to IPT implementation [14-19]. Some of those concerns might be due to inexperienced staff or other organizational barriers, and some studies have suggested that clinical opinion leaders could be instrumental in changing fears about INH resistance [20-22].

We found that facilities where the 2010 National IPT guidelines were available were almost three times as likely to offer the preventive therapy, confirming findings that developing operational guidelines and strong policy presence are essential for effective IPT implementation [23-26].

The lack of association between recent staff training in TB and HIV integration and IPT implementation was not expected. Overall, recent training in TB and HIV among core staff in our sample sites was poor: although most surveyed sites had at least one recently trained staff, only some facilities had at least one trained doctor or nurse. This is of particular concern since the latter are key in initiating patients on ART and TB and IPT treatment [9,27]. More training of public clinical facility staff is needed in TB and HIV Integration.

Further, while effective communication and joint decision-making between managers of TB and HIV services on site seems paramount to efficient integration of these services, only a minority of sampled sites had official TB/HIV coordination bodies. We did not find
an association between having TB/HIV committees and increased IPT uptake, but believe that such an association would have been likely with a larger sample size.

Limitations

The survey was a rapid assessment and thus included few facilities in each province, limiting generalizability. The small sample size further limited the power of the survey, and may have prevented us from finding statistical significance in differences that truly did exist. The data suggest that greater sample size might have shown an association between factors such as staff training in TB/HIV and on-site TB/HIV committees and increased IPT uptake. In addition, facilities were selected in the districts with the highest antenatal HIV prevalence, which might not be representative of areas with lower HIV prevalence. We sought to maximize external validity through random sampling and selecting a range of facility types in each province which approximated national distribution. Finally, Kwazulu-Natal had twice the number of study sites selected compared to other provinces, but also had double the number of districts compared to most other provinces and the highest overall HIV prevalence in 2008 [15]. Northern Cape only had four study sites as two of the facilities initially selected merged into a single entity shortly before data collection.

Conclusion

Our study demonstrated that some progress is being made towards IPT implementation in South Africa, where almost half of eligible patients were initiated in February 2011. The presence of the latest guidelines, with their simplified algorithms to identify and initiate eligible patients on IPT, was associated with better IPT uptake. The barriers to
IPT implementation were practitioner’s fear of INH resistance and lack of clear guidance from authorities. Few of our survey participants had on-site TB/HIV committees and recent TB/HIV training remained low, particularly among nurses and doctors. One of the keys to efficient integration of TB and HIV services might be effective communication between facility TB and HIV coordinators, and updated staff knowledge in TB and HIV integrated services. Further studies are needed to investigate the effects of on-site TB/HIV coordination bodies and staff training on IPT implementation.

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### Table 1: Distribution TB/HIV services and policy in selected sites, South Africa, 2011

<table>
<thead>
<tr>
<th>Province</th>
<th>Total # of selected sites (N=49)</th>
<th>Availability of IPT to HIV-infected individuals (N=49)</th>
<th>Availability of May 2010 IPT guidelines (N=49)</th>
<th>Staff trained in TB/HIV services since January 2010 (N=49)</th>
<th>Facilities having dedicated TB/HIV committees (N=49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern Cape</td>
<td>5</td>
<td>5 (100%)</td>
<td>4 (80%)</td>
<td>3 (60%)</td>
<td>1 (20%)</td>
</tr>
<tr>
<td>Free State</td>
<td>5</td>
<td>4 (80%)</td>
<td>5 (100%)</td>
<td>5 (100%)</td>
<td>4 (80%)</td>
</tr>
<tr>
<td>Gauteng</td>
<td>5</td>
<td>5 (100%)</td>
<td>5 (100%)</td>
<td>4 (80%)</td>
<td>2 (40%)</td>
</tr>
<tr>
<td>Kwazulu-Natal</td>
<td>10</td>
<td>9 (90%)</td>
<td>4 (80%)</td>
<td>7 (70%)</td>
<td>5 (50%)</td>
</tr>
<tr>
<td>Limpopo</td>
<td>5</td>
<td>1 (20%)</td>
<td>4 (80%)</td>
<td>4 (80%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Mpumalanga</td>
<td>5</td>
<td>3 (40%)</td>
<td>4 (80%)</td>
<td>4 (80%)</td>
<td>3 (60%)</td>
</tr>
<tr>
<td>North West</td>
<td>5</td>
<td>5 (100%)</td>
<td>5 (100%)</td>
<td>4 (80%)</td>
<td>2 (40%)</td>
</tr>
<tr>
<td>Northern Cape</td>
<td>4</td>
<td>3 (75%)</td>
<td>4 (100%)</td>
<td>4 (100%)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>Western Cape</td>
<td>5</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>3 (60%)</td>
<td>1 (20%)</td>
</tr>
</tbody>
</table>
Table 2: Number of essential aspects of IPT covered in counseling (n=35)

<table>
<thead>
<tr>
<th>Number of essential topics*</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 topics</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>1 topics</td>
<td>4 (11%)</td>
</tr>
<tr>
<td>2 topics</td>
<td>11 (31%)</td>
</tr>
<tr>
<td>3 topics</td>
<td>13 (37%)</td>
</tr>
<tr>
<td>4 topics</td>
<td>6 (17%)</td>
</tr>
<tr>
<td>Total</td>
<td>35 (100%)</td>
</tr>
</tbody>
</table>

* 4 Essential topics included adherence; reporting side effects; reporting of tuberculosis signs/symptoms; alcohol reduction/elimination during treatment
References


