# Report of the 18th Core Group Meeting of the TB/HIV Working Group Maputo, Mozambique, 12th April, 2013

The 18th Core Group meeting of the Global TB/HIV Working Group of the Stop TB Partnership was held in Maputo, Mozambique on 12 April 2013. The meeting followed a regional workshop to scale up collaborative TB/HIV activities in Africa from 10-11 April 2013 organised by the World Health Organization, with support from the President's Emergency Plan for AIDS Relief (PEPFAR). This offered the opportunity for more than 100 participants to attend the event, comprising Core Group members, key international and US Government partners as well as regional and national HIV and TB stakeholders including community and civil society representatives from 14 countries in the African region. Countries represented included Botswana, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, South Africa, Swaziland, Uganda, United Republic of Tanzania, Zambia, and Zimbabwe which collectively accounted for nearly 70% of the estimated global burden of HIV-associated TB in 2011.

Diane Havlir, Chair of the TB/HIV working Group chaired the meeting with Secretariat support from Haileyesus Getahun of the Stop TB Department of WHO. The aim of the Core Group Meeting was to assess the latest evidence, and identify challenges and opportunities to eliminate TB deaths among people living with HIV and define the direction of the TB/HIV Working Group over the coming years. The discussion focussed on three key areas of TB prevention, diagnosis and treatment. The Core Group members also discussed political and administrative issues about the future of the TB/HIV Working Group including the revision of its terms of reference and the selection of a new Chair in a closed meeting.

## Advances and next steps in TB Prevention

Using the model of Combination HIV Prevention, Lisa Nelson of WHO's HIV Department presented what is new in combination prevention of TB among people living with HIV followed by a commentary by Jonathan Golub of CREATE and Johns Hopkins University. Dr Nelson highlighted that whilst ART has a clear role in prevention of TB, whatever the CD4 count at ART initiation, (Suthar et al,) studies by Rangaka et al, Golub et al (Brazil), Golub et al (South Africa) and Samandari et al clearly show that ART has a much more significant impact in TB prevention when combined with Isoniazid Preventive Therapy (IPT) with protection rates of up to 97% particularly for skin test positives. New contrasting data on the durability of IPT protection was also presented. Golub et al demonstrated the durability of 6 months INH, with sustained protection for more than 6 years (80 months) in Brazil after an initial spike of risk, whilst randomised controlled trials in Botswana (Samandari et al) and the Thibela study in South Africa showed that life-long IPT might be necessary for durable protection in high burden settings. The promising potential of rifamycin-based regimens as shorter alternatives to isoniazid were also reviewed. Findings from studies by Sterling (NEJM 2011; 365:2155 and AIDS2012 MOAB0302) and Martinson et al showed similar efficacy, fewer hepatotoxic events, better tolerance and higher treatment completion rates with rifamycin-based regimens when compared with isoniazid. Dr Golub underlined the importance of targeted advocacy to increase the buy-in to IPT from health staff and patients, and demonstrated how provider belief in co-trimixazole and patient demand for ART have led to very impressive scale-up. It was further emphasized that the requirement for TST or IGRA presents a significant barrier to scale-up of preventive therapy in people living with HIV in resource-limited settings, due to reduced sensitivity in HIV positive clients, the need for staff training, inconvenience to patient, travel costs and the need for cold chain requirements or, in the case of IGRAs, the need for sophisticated

laboratory infrastructure. However, the benefits of TST screening were recognised where long term or life long use of IPT is necessary.

**Conclusions and next steps**

- *Efforts should be made to 'do the basics better than before' and scale up interventions that work and with a potential of population-level impact (e.g. ART, contact tracing)*
- *Scientific interest and funding should be maximised for research to yield shorter TB prevention regimens that are more tolerable to people living with HIV and improved tests to detect latent TB (e.g. the identification of a biomarker) and predict the risk of developing active TB disease.*
- *Appropriate infection control measures in health facilities with adequate triage procedures for TB and MDR-TB suspects as well as developing community-based strategies as alternatives to hospitalization, were stressed as essential for curbing TB transmission to patients, healthcare workers and their communities.*
- *Timely identification of active tuberculosis was also highlighted as a crucial component of the combined strategy to stem the transmission of tuberculosis with active case-finding of both TB and HIV in households of TB patients and those suspected of TB and target populations such as miners as promoted in the 2012 Recommendations for investigating contacts of persons with infectious tuberculosis in low- and middle-income countries and the WHO TB screening guidelines (2013).*
- *Future efforts should focus on preventing TB in those at greatest risk of developing disease, as part of targeting efforts and knowing your epidemic*.

## The latest on TB diagnosis and next steps

Haileyesus Getahun of the Stop TB Department gave an overview of the latest in diagnostic technologies, highlighting research gaps and challenges in timely detection of HIV-associated TB in his presentation on what is new in TB diagnosis. A commentary was provided by Helen Ayles of the London School of Hygiene. Evidence from recent autopsy studies presented at CROI 2013 by Martinson et al, Some et al and Mutevidzi et al demonstrated that undetected TB is a major contributor to HIV-associated mortality and that it is therefore crucial to increase efforts to ensure early diagnosis. It was stressed how Xpert MTB/RIF has revolutionized the diagnosis of HIV-associated TB including rifampicin resistance among people living with HIV with a potential to replace the century-old microscopy. However, it was noted that microscopy is still the most accessible diagnostic tool as well as the mainstay for monitoring response to treatment in smear positive cases. It was also noted that there is a yawning gap in the development pipeline until at least 2016 for a point of care test. Nevertheless, it was recognised that Xpert MTB/RIF has high sensitivity in detecting HIV-associated pulmonary TB (Steingart et al), and also has utility in detecting extrapulmonary TB (Lawn and Zumla). In addition, it was highlighted that the use of Xpert as a screening tool among people living with HIV has resulted in 45% increase in TB diagnosis compared to microscopy (Lawn et al). It was also noted that the WHO recommended algorithm included in the Xpert implementation manual might be improved by introducing a repeat Xpert test at an earlier stage for those cases that are not diagnosed from the first Xpert test. Delay between onset of symptoms and diagnosis of TB was shown to be quite common in HIV treatment settings as shown by Coimbra et al and van Lettow et al. Results from a number of reviewed studies demonstrated the use of Urine TB-LAM to enhance TB diagnosis among PLHIV and showed contrasting results (Drain et al, Dheda et al and van Rie et al). However increased sensitivity was consistently found in detecting TB in people with low CD4 counts of less than 50. This was explained by the fact that urinary excretion of LAM correlates with MTB burden in the body and is therefore an indicator for clinical prognosis (Lawn et al). However, cross-reactivity with *Candida* species and normal oral flora containing LAM-like molecules and Urine LAM's poor sensitivity and specificity in pleural and pericardial and cerebrospinal fluid were highlighted as critical limitations (Dheda et al). Its role as an adjunct diagnostic test combined with other tools such as Xpert MTB /RIF and microscopy was also explored (Shah et al).

The importance of "combination diagnosis" of TB among PLHIV was echoed by Dr Ayles who warned against throwing out existing tools such as florescent microscopy and digital X-ray or culture and called for the retention of a strong laboratory workforce through training and appropriate task-shifting. Concern was expressed about the expanding practice of using a rifampicin resistance result from Xpert MTB/RIF as a proxy to MDR-diagnosis among PLHIV without any clinical indication or established exposure to MDR case in the African setting. Particular concern was expressed about additive adverse effects of ART and second line anti-TB drugs.

**Conclusions and next steps.**

- *The use of Xpert MTB/RIF has to be expanded as a primary TB diagnostic test for PLHIV and its role as a screening tool to rule in active TB in high TB/HIV burden settings has to be explored.*
- *The WHO guidelines on the management of smear negative TB among PLHIV need to be updated taking into consideration the role of MTB/RIF in the diagnosis of both pulmonary and extrapulmonary TB.*
- *Caution needs to be exercised while using rifampicin resistance results from Xpert MTB/RIF to initiate MDR treatment in the African context, and clinical condition and exposure to risk factors (e.g. exposure to MDR-TB case, previous treatment of TB etc.) of PLHIV need to be considered.*
- *The absence of a more sensitive, low cost, low technology screening algorithm that can be used at community level was underlined as a key research gap.*

## Improving combined TB and HIV treatment

Diane Havlir, the Chair of the TB/HIV Working Group briefed on the landscape of new developments in combined TB and HIV treatment. Jefter Mxotshwa of Network of African People living with HIV South African Region (NAPSAR) provided commentary from the community perspective. Dr Havlir highlighted the risk of mortality that increases with each day when ART initiation is delayed beyond two weeks after the start of TB treatment in TB/HIV patients with a CD4 count of less than 50. Although TB IRIS complicates the earlier management of HIV-associated TB and requires closer supervision, the overall mortality benefits of earlier ART far outweigh the much lower risk of morbidity and mortality from TB IRIS. She stressed that a system has to be established to monitor the earlier initiation of ART among TB patients at a programme level in order to minimise mortality. A closer analysis of the cascade of care for people living with HIV and TB at each level of healthcare from the perspective of both the provider and the patient needs to be developed and monitored. Mr Mxotshwa reiterated Dr Havlir's call for simplification of the cascade of care, stating that health, as a fundamental human right, is the duty of governments to maintain and they should therefore ensure that adequate funding is allotted and measures are taken to correct over-burdened health services in order that silos are destroyed and that time spent by people living with HIV in queues is reduced. The engagement of communities was also underlined as key to supporting adherence, reducing loss to follow-up and supporting the patient's psycho-social needs including among migrants, intravenous drug users and prisoners.

**Conclusions and next steps:**

- *A system has to be established to monitor the earlier initiation of ART among TB patients within two weeks at a programme level.*
- *A model for analysis of the cascade of care for PLHIV with TB needs to be developed and monitored at each level to identify critical gaps and solutions.*
- *Qualitative research need to be promoted to assess the patients' needs, the provider-led and system bottlenecks as well as the enablers to scale-up.*

## Strategic vision and administrative issues of the Working Group

### Revision of the terms of reference (TOR)

The Core Group members reviewed the significant progress and key contributions of the Working Group over the last five years to the global TB/HIV response, particularly in promoting the development and implementation of evidence based policies and programme guidance, defining critical gaps and promoting research, raising the global visibility and mainstreaming TB into the global HIV agenda. The Core Group members noted the expiration of the current TOR of the Working Group by the end of 2013 and agreed to develop the next TOR that expands until 2020 with a strategic vision of eliminating TB deaths among people living with HIV.

The following were key issues discussed for consideration in the new TOR:

- *Quantify the definition of elimination for TB deaths among people living with HIV through informed consensus, based on broader discussion and consultation including learning from lessons and experiences of other similar initiatives (e.g. elimination of mother to child transmission of HIV).*
- *Develop a clear strategy that gives due consideration to intensified national actions including generous and effective mobilisation of resources and innovations addressing local context and needs.*
- *Identify settings where more people living with HIV are dying (e.g. hospitals) and where less diagnosis of TB and HIV is occurring (e.g. community structures, prisons) and develop comprehensive response strategies.*
- *Develop linkages with existing targets and initiatives (e.g. MDGs, Universal Health Coverage, post-2015 development agenda) and use them as fora to promote the TB/HIV agenda.*
- *Promote implementation science research to enhance accurate documentation, monitoring and evaluation of programme implementation. Particular emphasis needs to be given on how to collect accurate data at a facility level and transmit it smoothly and correctly including through the use of modern technologies.*
- *Advocate for massive TB research in the context of HIV and without HIV, particularly focusing on research activities that will lead to the development of a point of care diagnostic tool for both latent TB infection and active disease. New and shorter drugs and drug regimens should be also be a focus.*
- *Focus on specific groups with high prevalence of HIV such as adolescents, drug users, prisoners, men having sex with men and commercial sex work is needed, particularly for integrating TB prevention and earlier diagnosis.*

### Administrative and structural issues

The Core Group members reviewed the administrative, political and structural issues related to the Working Group and the on-going changes within the Stop TB Partnership. Core Group members noted that the atmosphere around these issues, which had been a source of extreme concern about the future of the Working Group (Beijing CG meeting report) is now improving. The significant contribution of the Working Group in advancing the causes of the Partnership are now valued and there have been communications to that effect over the last couple of months, which were shared with members of the Core Group. Dr Amy Bloom, a long standing member of the Core Group was thanked for her proactive engagement as Interim Board Chair during the complex reform process and in helping communicate changes with the related implications to the different working Groups of the Partnership. The Core Group members appreciated the work done by the Chair, Dr Diane Havlir of University of California in San Francisco, in her two consecutive terms that will finish by the end of 2013 and the Secretariat at WHO for the significant achievements and progress in the global TB/HIV response. It was agreed that the WHO will continue as the Secretariat of the Working Group and the next chair of the Working Group should come from the HIV community. Although the fate of sub-groups within the Partnership structure is yet to be addressed, it was recognised that the Infection Control Subgroup, which has been functioning as an autonomous body within the TB/HIV Working Group still has a critical role in the advancement of the TB infection control agenda. The

Chair of the Infection Control Sub-group, Dr Bess Miller, expressed her concern of the lack of financial and administrative support for the Sub-group particularly after the departure of the TB infection control focal point at WHO following structural changes of the organisation. Core Group members agreed to the proposition by the Chair of the Sub-group to explore all possible measures to revitalise the functionality of the sub-group including identifying itself as an independent entity or merging with other Working Groups.

**Conclusion and next steps**

- *The next TOR of the Working Group should aim at eliminating TB deaths among PLHIV and should extend between 2014-2020. The revision of TOR should also include the revision of standing institutional and rotating individual membership of the Core Group.*
- *As the current community representatives in the Core Group have already finished their term of membership, guidance should be sought from the Board or Secretariat of the Partnership. In the absence of such guidance, the Secretariat of the Working Group is encouraged to define selection methods in consultation with the Core Group.*
- *WHO will continue as the Secretariat of the Working Group with the revision of the TOR.*
- *The next Chair of the Working Group should be someone with leadership qualities, commitment and time from the HIV community who can further take the TB agenda into HIV research and implementation.*
- *A Core Group sub-committee will serve in the revision of the TOR and the search for the chair of the Working Group*
- *The TOR revision should be finished following iterative process and broad based consultation in due course before the end of 2013.*