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NATIONAL SUMMIT ON TB DIAGNOSTICS

18-19 NOVEMBER 2013 / SHERATON HOTEL, PRETORIA

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Executive Summary

Thanks to strong political commitment, South Africa has been at the forefront of the roll out and use of new TB diagnostics, including liquid culture, Line Probe Assay and the Xpert MTB/RIF for rapid diagnosis of TB and resistance to rifampicin. Recent implementation of new diagnostic technology, coupled with ongoing local research, has generated a great deal of information and operational experience. Results have been shared at international conferences, but to only a limited extent locally. To that end, the National Department of Health (NDOH) and the USAID TB Program South Africa convened a National TB Diagnostics Summit as a platform/forum to facilitate the sharing of research findings to inform policy.

The National TB Diagnostics Summit took place on November 18-19, 2013. The purpose of the summit was for key stakeholders to review and discuss the state of TB diagnostics in South Africa and to create a roadmap for improving laboratory diagnosis of TB throughout the country. More than a hundred local and international participants attended, including representatives from the NDOH, the Department of Science and Technology, USAID, public and private laboratory service providers, diagnostic product manufacturers, funders, academics and researchers, and implementing partners.

Representatives from the NDOH, the USAID Mission in South Africa and University Research Co., LLC (URC) highlighted the relevance of effective TB diagnostics towards attainment of National Strategic Plan on HIV, STIs and TB 2012-2016 (NSP) targets. Public and private sector partners were urged to collaborate to achieve the desired sustainable results. The persistent challenge of high TB incidence in South Africa necessitates the use of new diagnostic tools to improve early identification, ensure faster initiation of treatment, and provide better support for patients.

The Summit was broken down into four main sessions as follows:

- Session 1: Introduction of new tests

  This session included an overview of new tests, and presentations on the uptake of TB laboratory diagnostics, the role of the private sector, testing in rural settings, and the introduction of new diagnostic technologies. Discussions centred on the utilisation of new algorithms, including costs, involvement of the medical aid schemes, non-compliance with the algorithm, the feasibility of the target of reducing time to treatment initiation to two days for DS-TB and five days for MDR-TB, and lack of inter-system operability of various patient databases, making difficult to track previous test results. It was agreed that improving the efficacy of the diagnostic processes in both the public and private sectors requires a combination of interventions.

- Session 2: Challenges in implementing the technologies

  Presentations included the clinical challenges in implementing the new technologies, challenges related to reaching all levels of the health system, measuring the challenges, evaluating GeneXpert rollout, and diagnosis of TB in children. Discussions covered the roll-out of a quality assurance programme for GeneXpert, the effect of GeneXpert on case detection, clinical lead times, location of the test, remote calibration, an effective algorithm, and issues related to cost effectiveness as a public health intervention.

- Session 3: Community, patients, civil society: Linking communities to services

  Presentations included issues related to access to health care, early diagnosis of TB and MDr. TB in the community setting, the high proportion of initial defaulters, the infectiousness of patients, the interface between community and PHC facilities, ineffective referral mechanisMs. between HIV clinics and TB clinics, the need for community-based integrated TB and HIV services, data quality, the need for an enabling policy, and revisiting the decentralization process. Discussions also addressed the role of NGOs working in the decentralized model and the amount of excellent TB operations research being undertaken across the country.

- Session 4: Key players in diagnostics: researchers, academics, private sector, manufacturers and medical schemes

  This session looked at what is in the pipeline for TB diagnostics both local and globally. It highlighted progress towards affordable point-of-care (POC) tests in resource-limited settings, early phase technology and biomarkers, and the importance of showing the impact of new tests on the burden of disease. Manufacturers BD Diagnostics (POC technology, collaboration with the NHLS to bring in second line drugs), Hain Life Science (new assays) and Cepheid HBDC (future molecular diagnostics, extended

warranty worldwide, on-site preventative maintenance, web-based training) all presented. The Department of Science and Technology (DST) reported on examining ways of supporting local research, development and innovation capacity in diagnostics and treatment for HIV, TB and malaria. South Africa is currently validating a new TB rapid test which is easy to use and will provide results in 30 minutes that will cost less than $4. This test will hopefully be available by 2015. The discussion covered training, health systeMs. strengthening, early diagnosis and linkages to care and treatment, identifying research gaps, and strengthening relationships with academia. The role of TB diagnostics in reaching "zero TB deaths" was also emphasized.

- Key recommendations

  Key recommendations generated from the 2013 Summit were as follows:

  1. Develop a generic national implementation framework for review and roll out of new diagnostic tests.
  2. Establish a multi-stakeholder national task team of experts to provide on-going guidance on the introduction of new tests/diagnostic procedures.
  3. Convene annual meetings to follow up on implementation.

This report on the 2013 Summit provides a summary of the session presentations, issues discussed, and recommendations reached.

Welcome

Mr. David Mametja, National Department of Health (DOH)

The National Strategic Plan on HIV, STIs and TB 2012-2016 (NSP) inforMs. the interventions by the Department of Health on the management and control of TB in the country. We are almost halfway through the implementation of this strategic plan. The targets are ambitious but we need to work towards attaining these targets in order to reduce the scourge of TB in South Africa. This is an important summit and the need to improve on the performance of the diagnostics is acknowledged. It is also important that the private sector is participating as the linkages between the public and private sector in relation to the management of TB have not received adequate attention in the past.

The expected outputs of this Summit are to:

- Provide recommendations on optimization of existing TB diagnostic technology;
- Provide recommendations on strengthening TB diagnostic and clinical management systems;
- Identify research priorities; and
- Reach consensus on a national TB diagnostic task team.

USAID Support

Ms. Catherine Brokenshire-Scott, United States Agency for International Development (USAID)

The United States Agency for International Development (USAID) is keen to support this important collaboration and commitment in tackling the scourge of TB. This event is supported by USAID, the South African National Department of Health (DOH) and the University Research Company (URC). The Summit provides the opportunity to review efforts made thus far on the management and control of TB with a special focus on diagnostics to make informed changes and improve future outcomes. A dedicated effort is needed amongst all partners to achieve the sustainable results that are so necessary.

TB Diagnostics – The Global Context

Dr. Refiloe Matji, University Research Co., LLC (URC)

The high incidence of TB remains a serious challenge in South Africa. While the focus for diagnosis has been on microscopy in the past, there have been many important developments such as Xpert MTB/RIF. Where these new diagnostic tools are placed is important. Patients at the community level therefore need to be considered in this planning.

One of the main challenges is that by the time people present at a facility, they already show evidence of serious symptoms. They then have to wait for testing to be done and again for the results of the tests. For MDr. TB, this can take a month or more from the time they present. There are many variables in the process resulting in these delays, in particular, transportation of specimens and results to and from the laboratory affecting the turnaround time.

While some people are close to a health facility, there are many who live some distance from a clinic and transport costs can be high. Many people cannot afford transport at all. There have been a number of local and international studies that highlight the high cost of accessing free health services. There may also be geographical impediments. The role of the community needs to be assessed since they can promote education on signs and symptoms, and encourage prevention and infection control.

Health care facilities need to focus on early identification, faster initiation of treatment, and support for patients. The key questions to be addressed include:

- Are we bringing services closer to the communities we serve?
- Can we reduce the high (30%) initial default rates?
- How can we reduce MDr. TB?

In Tanzania, there has been an interesting development in the use of African giant pouched rats which were trained to detect TB in patient sputum. This may not be ideal but the point is to begin to think creatively about the tools that are needed to promote the treatment and reduction of TB.

General Comments

1. Noting that initial screening is critical, and currently we screen ten people to identify one positive. We need a cost-effective way of screening to exclude expensive testing on the majority (±95%) of people who do not have TB. This would enable us to then use the expensive test for the identified high risk people.
2. There is currently no screening test available that has been validated and is suitable to screen patients and assist in narrow down the field to patients at highest risk on whom the Xpert MTB/RIF could then be used. Therefore it is best to focus on what is available and optimize its use. To manage TB into the future, a screening test at community level is needed.
3. Community health care workers should be encouraged to participate more actively in screening of TB. Communities should be encouraged to become more proactive in seeking TB screening services, while noting that limited finances often prevent people being able to access a health care facility for screening.
4. The NSP stipulates a further objective which is to ensure that all South Africans are screened for TB at least once a year, but how this will be achieved remains a challenge. The numbers needing to be screened could significantly escalate.
5. The use of GeneXpert has made a difference but not enough. People still have to go home and wait for their results and then come back to the health facility. The coverage of the National Laboratory Health Service (NHLS) is good but the roll-out of GeneXpert has not yet been evaluated. The placement of the GeneXpert should be assessed as well.
6. TB is a public health problem, so the focus must be both on the individual and on the health system overall.
7. New products are constantly being developed and tested and improved screening tools are expected in 2014.

Panel Discussion – Introduction of New Tests

Panel Chair: Dr. Giorgio Roscigno

Introduction and Overview

Professor Mark Nicol, UCT/NHLS

Better testing is needed for the diagnosis of HIV-associated TB and early diagnosis of drug-resistant TB. In Gugulethu, it was shown that 25% of HIV positive patients commencing ARVs have TB despite having few symptoMs. and 80% had smear negative TB. There is a growing concern around the increase in Multi-Drug-Resistant TB (MDR-TB) and the threat to public health. While there have been improvements, in the reduction of time taken to treatment initiation, in Khayelitsha about 53% of patients died while waiting for results between Jan 2008 and June 2009.

A low cost triage test with high level of sensitivity is needed to rule out TB in the primary health care setting especially for HIV positive patients in care . A definitive test with a high sensitivity and specificity can then be used to diagnose TB and screen for MDR-TB in the identified high risk patients.

GeneXpert performance thus far has been good but its limitation is that it cannot be used as an exclusion test for TB in a patient with HIV. There is a need for further testing in HIV positive, Xpert negative patients. The main concerns with GeneXpert are that it i) has had no clear effect on mortality/outcome (Theron G, Lancet; XTEND results awaited), ii) has shown no substantial increase in case notification, iii) the impact on reducing time to treatment initiation is not yet clear. Therefore it needs to be used in a strong health care system with good follow up systeMs. to improve linkage to care.

GeneXpert has limited applicability for POC use and much more expensive compared to laboratory placement.

A study conducted in Khayelitsha has shown how the introduction of the rapid assays (LPA and Xpert MTB/RIF) has reduced the time to treatment initiation for drug resistant TB. The LPA however can only be used for direct testing of smear positive sputum or cultured isolates. There are new tests - MTBDRplus v2 which can be used on smear negative sputum, and MTBDRsl for second line DST.

There is a need to examine the indicators that must be measured in order to determine the impact of GeneXpert on mortality and outcomes, in particular MDR-TB.

Uptake of TB laboratory diagnostics

Professor Koleka Mlisana, UKZN/NHLS

The testing had previously been smear-based but with the increase in the HIV epidemic (high co-infection rates (65%), in medical wards this could be as high as 90%), the sensitivity of microscopy has dropped, with detection rates as low as 43%.

Introduction of the more sensitive tests (liquid culture, LPA and Xpert MTB/RIF) has improved the diagnosis of TB in HIV positive patients, while also improving the turnaround time for the diagnosis of drug resistant TB.

LPA (Version II) would be preferable for smear negative testing but evidence is limited and it is unclear where it will fit in the diagnostic algorithm. An analysis conducted in KZN showed that 50% of patients confirmed by Xpert as Rif resistant TB had a confirmatory test conducted within two weeks and 75% cumulatively within four weeks. The time to treatment initiation was within two weeks of diagnosis for 68% of the patients.

Challenges

- Lab safety issues
- High contamination rates (10 – 15%) with liquid culture
- High setup costs for the PCR lab
- Staff training
- Lack of political drive – no clear policy and lab request forMs. never finalised (incorporating LPA)
- Clinical training lagged behind introduction of the rapid assays, therefore most clinicians did not know what to do with the test results
- With the phased implementation, two algorithMs. (smear and Xpert MTB/RIF) were used causing confusion for both clinicians and laboratory personnel
- Lack of a system to check duplicate testing.
- There was no EQA program on implementation of the rapid assays.

The role of the private sector

Dr. Suleiman Hajee, Toga Laboratories

The sensitivity, rapid turnaround time, and technological advances of the molecular tests make compelling arguments for their widespread use as first-line tests. However, in the private sector, cost is the major barrier to more widespread utilization of the commercially available molecular tests like the GeneXpert. The Toga solution is to use a cheaper in-house molecular test as a screening

test, and if positive proceed with a commercial assay for confirmation of MDR-TB. Microscopy for AFB should be retained, for public health and infection control purposes.

Dr. Keshree Pillay, Lancet Laboratories

The GeneXpert has been used since 2009. The main challenge relates to the high costs of testing. There is pressure from clinicians and hospitals to conduct rapid specific and sensitive tests on smear negative patients because of the HIV prevalence. Since the endorsement of the use of GeneXpert by the WHO in 2010 the uptake has increased from 4 000 in 2009 to 60 000 in 2012. The algorithm is different from the DOH one in that microscopy is still the first line test and is followed by the Xpert MTB/RIF for all specimens.

Challenges

- Coordination and communication between public and private sector
- Standardisation of testing
- Waste of scarce resources by repeat testing between facilities

Testing in rural settings

Dr. Lorna Madurai, Global Laboratories

The private sector testing caters for medically insured and cash paying patients. The medical aid schemes are controlled by the Board of Health Care Funders, there is a chronic management plan for HIV patients, but TB is not considered a chronic disease therefore treatment is based on existing benefits. This anomaly must be addressed and TB must be included in the Prescribed Minimum Benefits within medical aids. There is no problem of over-testing in the private sector as it is very well governed. However, cost remains a big issue. The links between private and public sector collaboration should be promoted. The private sector must implement the national guidelines.

Introducing new diagnostic technologies

Dr. Nazir Ismail, NICD – NTBRL

The presentation highlighted the gaps in TB diagnosis and linkage to care and the importance of early diagnosis using the new rapid diagnostic tests (Xpert MTB/RIF, LPA) based on the WHO Policy recommendations. He shared the NHLS experiences with the roll out of the liquid culture, LPA and Xpert. Some of the requirements include the development of an evidence based algorithm, adequate infrastructure, staff – TB technicians and equipment taking into consideration the volume of tests to be conducted. There has been a 48% increase in the number of liquid cultures done since its introduction in 2007 and a 79% increase in first line DST by LPA since 2011. South Africa is leading globally in number of equipment and cartridges procured since the introduction of the Xpert MTB/RIF. The population coverage for Xpert is currently 84%. The NHLS is planning to introduce reflex testing (first and second line DST) for Rifampicin resistant TB.

Discussions and Comments

1. How are the algorithMs. being utilized? The private laboratories algorithMs. are determined by the costs; therefore expensive tests like GeneXpert cannot be used for screening. Since the private laboratories are constrained by the profit imperatives, greater efficiencies are needed to lower the costs of diagnosis. This can be addressed by getting buy in from the Medical schemes and lobbying the Department of Health to take the lead. It remains unclear how the reduction in costs in the private sector would change the overall role of the private sector in TB management and control. In the public sector there is non-compliance to the algorithm in that some doctors requested preferred tests instead of following the algorithm. The national target of time to treatment initiation for DS-TB is two days and for MDR-TB five days, is not realistic and needs to be reviewed. On the other hand the NHLS wants to program the diagnostic algorithm within their IT system to conduct reflex testing but the system is not conducive for this as the laboratory systeMs. are interlinked making it difficult to track previous test results on a patient. There has to be an evaluation of the existing diagnostic algorithMs. in order to determine which one is most efficient.
2. How to improve the efficacy of the diagnostic processes in both the public and private sectors? The private sector should be engaged in the development of the national diagnostic algorithMs. from the onset. Ongoing training is required in both the private and public sectors. A combination of interventions is required to improve the efficacy of the diagnostic processes, these include: i) the laboratory information systeMs. that are interfaced within the laboratory network, ii) implementation of the unique identifier and iii) improving communication between laboratory personnel and clinicians. The public sector can learn from the private sector on how to improve logistics and linkages. Ideally, all testing should be standardized across all sectors. All labs are accredited by South African National Accreditation System (SANAS); some labs do undergo assessments from organizations like Pharmaceutical Product Development (PPD) as per agreements with research partners.

Panel Discussion – Challenges in Implementing the Technologies

Panel Chair: Professor Maphoshane Nchabeleng, MEDUNSA

Introduction

Professor Lesley Scott, NHLS/Wits University

Infection hotspots include mines, prisons and transport routes, and these need to be addressed specifically. There is an increase in smear negativity and HIV co-infected TB patients where diagnosis is made too late. Smear sensitivity drops 25-40% with HIV. Since March 2011 there has been phased implementation in the public sector and 2.3 million tests done. Training of 916 laboratory staff and 3500 health care workers was done and 100 centres are reporting via website developed with SAFAID. Remote calibration is also being used. Work has been done to improve assay version changes and stock outs. SMs. printers have been installed 2096 SMs. printers in clinics to improve TAT. The programme needs to be expanded to mines and correctional services, using experts as the frontline.

Current challenges include non-adherence to algorithms, and no confirmatory tests for resistance being done. Multiple tests are requested on a single form, so there is a need to simplify the algorithm. On level of placement in clinics, GeneXpert is 46% more expensive if placed in clinics, where 2.5 staff members are needed to get 15 patients from test to treatment in one clinic in one day. Future assay changes and stock outs are a concern.

Data volumes are in place and must now be linked to care, but how this will be done is not clear. Strengthening of health systeMs. is urgently required. On the costs of the revised models, many peripheral costs related to GeneXpert have pushed up costs, where costs at the laboratory are 50% lower than POC costs. For example, if there are 100 TB suspects, 20 will be TB positive. GeneXpert will pick up 16 and miss 4. So 84 suspects must be investigated via culture to positively identify the 4 patients who were missed.

Paediatric performance shows that 67% of sputum specimens are below the required volume. The WHO in 2012 recommended use of GeneXpert. It is also useful in reducing TTT where before GeneXpert use only 21% of patients were initiated within 5 days whereas since the use of GeneXpert 95% are initiated within 5 days.

Clinical challenges

Dr. Xavier Padanilam, Sizwe Hospital

The Sizwe Hospital is a dedicated MDR-TB facility. Experience indicates that a unique identifier is urgently required as many patients use different names, a range of tests is done in different hospitals, and the number of patients diagnosed in Gauteng with MDR-TB is higher because of the duplication of patients. The situation is exacerbated by migration in and out of Gauteng where there is a high level of inter-provincial movement. This leads to discrepancies in statistics and it is difficult to locate patients for treatment. Many patients also die because doctors make a diagnosis but do not refer to Sizwe for specialist treatment.

A key challenge is that laboratories do not report on mycobacterium TB and clinicians are then unable to make an informed decision. The laboratory should report fully and without omissions especially as regards mycobacterium TB since only then can the clinician provide an appropriate regimen.

GeneXpert is good when the smear is positive but when the smear is negative it is necessary to re-confirm the diagnosis. Smear negative culture takes 6-8 weeks, which means the patient could be on the wrong treatment for two months. In a hospital like Sizwe which does not have designated GeneXpert patients, this can lead to greater infection. Furthermore, GeneXpert is sometimes used on dead bacilli to assess progress of the disease but this is incorrect.

Reporting of mutational pattern for INH is needed that can guide clinicians, but most laboratories do not provide this essential information. Gauteng is the only province providing mutational information.

LPA for Second Line Drugs is not yet validated in terMs. of MDR-TB. If Second Line probes can be used then proper treatment can commence earlier rather than waiting for up to 8 weeks, and this can save a life.

New drugs should be tested as there are often very positive responses. Contamination and laboratory errors occur frequently, often after patients have been on a treatment, and these kinds of mistakes in the laboratory can impact on mortality. Significant morbidities can result from a wrong laboratory result.

Challenges related to reaching all levels of the Health System

Dr. Adeboyi Adelekan, CDC Laboratory Advisor

Having the required human capacity in place is key to ensuring Quality Assurance in delivery of health services. Even where a lot of training is done, people may still need to be mentored. Expensive equipment is in place and needs to be used appropriately and maintained adequately and this requires the required number of people to be properly trained. Calibration and periodic service of machinery is essential. However, the necessary technical expertise is not always available.

Supply chain management is important – consumables must be readily available and managed properly. For example, reagent must be carefully stored, and forecasts must be accurate to avoid stock outs. Biosafety level 3 is the minimum requirement, including temperature regulation.

Verification needs should be considered for a pilot study. What existing tests are being done and how are they linked to other networks? Draw on workflow analysis to optimize testing per site, and then scale up implementation. The strengthening of health systeMs. overall is important –the best equipment will not work in a weak system, and it is recognized that the laboratories do not contribute to the delays, yet there are delays in getting results back to patients. The blockages need to be accurately identified.

Quality assessment checks should be in place when introducing new technologies. A comprehensive Quality Assurance plan will address the details of testing from the first collection of sputum to return of results. Linkages are essential, as well as compatibility with existing systeMs. so as to avoid data quality concerns. It is necessary, therefore, to ensure that facilities are connected via internet.

Having new technology that is being badly applied has a greater negative impact than not having it at all and it is important therefore to ensure that new technologies are integrated with the existing testing environment. Quality Assurance processes must ensure value for money.

Measuring the Challenges

Dr. Pren Naidoo, Desmond Tutu TB Centre, Stellenbosch University

First assess and measure the challenges and then decide on implementation. In assessing new molecular diagnostic tests, the focus should not be on individual tests but rather on the impact on diagnostic algorithms, and how to move from targeted algorithMs. to a universal algorithm.

A key question is whether there are more TB cases being diagnosed, in the context of the high level of resources that have been directed to improving TB identification. Over a period of 2.5 years, the total number of people tested in 5 sub-districts was tracked, both in targeted and universal algorithms. The results indicated that there had been no change in the number of individuals evaluated. There has therefore not been an increase in the TB yield in Cape Town. The number of MDR-TB cases diagnosed was 188 in 2010 and 196 in Quarter 2 in 2013. There was previously an effective algorithm for smear-negative TB. The median treatment commencement time of 43 days in the targeted algorithm has been reduced to 17 days median to treatment in the universal algorithm. Laboratory turnaround time in the targeted algorithm was 25 days to less than day in the universal algorithm – this indicates 80% improvement in laboratory and 20% improvement in the health facility. However, when comparing two sets of facilities going from targeted to universal algorithm there is little change.

There was an increase in cost of 120% for presumptive TB cases, from R1.7 million to R3.7 million. The only real benefit in Cape Town has been a reduction in delay for MDR-TB cases. Laboratory results are completed in one day yet it takes 17 days to get patients to treatment due to operational blockages. The factors contributing to delay are all under the sphere of control of facility managers. There is a concern regarding the degree of agency and level of autonomy afforded to patients, where the results could in fact be sent directly to the patient. The current system assumes patients coming to facilities but this remains slow. It may also not be realistic to attach 5-day targets to chest x-rays and blood tests

In addition to the use of GeneXpert, the DISA system has also reduced delays but human capacity continues to present challenges. There is a need to allocate resources to training and capacity building of frontline staff in order to strengthen the health systems.

Evaluating GeneXpert rollout – Challenges in implementing TB diagnostic technologies

Dr. Kerrigan McCarthy, Aurum Health

Both formal and informal roll-out needs to be evaluated. It is preferable to use the diagnostic modalities that are currently available as well as feasible, rather than being overly aspirational. A current study that will become available early in 2014 has shown that the effectiveness of any diagnostic is the function of test performance.

It is important to keep in mind that TB can manifest anywhere and not only in the lungs. Sputum tests are then irrelevant. The kind of test being requested needs to be assessed. Furthermore, where tests are done, the connection between the primary health care facility where the patient first arrived and the referring doctor is often lost, and this is an important connection that needs to be maintained. A PHC that has a doctor in place with access to chest x-rays could follow up on this algorithm. The other possible approach is to examine potential indicators of TB, drawing on a range of symptoms, and include the use of microscopy.

Operationalizing new diagnostics, it is suggested that targeted testing is preferable. One of the challenges is getting results back to patients quickly. This could be addressed at the time of enrolment by ensuring informed consent, take a cell number and stay in contact, and follow up over time, at 2 months and 10 months. This will help to keep the patient in the system. The best way to do this is via a high quality of human interaction, trust, respect and availability. Fieldworkers are encouraged to know the patients and build on the clinic connection. Patients need to be assisted to understand TB, patient agency and involvement. Health care workers need to empower patients at the time sputum is taken, not when results arrive. Pre-counselling testing is recommended.

Societal factors include migration which is the biggest source of loss to follow-up and this can be mitigated by understanding and identifying patient risk of migration when taking the sputum.

Diagnosis of TB in children

Dr. Ute Feucht, Tshwane District/University of Pretoria

Many children are being lost to treatment. The TB epidemic manifests differently in children and the main difference for children is that, like HIV, TB comes from adults, rather than being a childhood disease. There is high exposure to TB for children but not all children with TB will have HIV as well. In South Africa, TB is strongly linked to high levels of malnutrition. There is a risk of both over-treatment and under-treatment of children with TB.

Paucibacillary disease has an impact on diagnosis, and doctors often do not diagnose correctly. There is a high level of infection in children under 5 who should get prophylaxis, and who are under greater threat if they are malnourished or otherwise compromised.

There is an increase in neonatal disease and also of maternal HIV and TB in pregnancy – therefore pregnant women should be screened for TB.

SymptoMs. in children are often non-specific so scoring systeMs. are useful in resource-constrained countries. Standardized clinical case definitions are vague and broad. TB diagnostics clarity must be improved at implementation level. The concepts of preventing TB and diagnosing and treating TB are often confused and must be clearly separated.

Greater clarity is needed on appropriate diagnostics, how they are used and at which level? For example, who will do an x-ray or read an x-ray? It has been proposed that screening be done by all HC facilities but at present children are not included. TB prophylaxis at facility level is not done, and there is a tendency to delay until children become ill and then go to hospital.

It can be difficult to get samples from children and so this is often overlooked. Furthermore, there are few guidelines on sample collection from children and these should be provided. The role of IMCI for HIV rollout must be refined for TB testing rollout with a focus on obtaining samples from children and renewing the focus on child health.

Discussion and Comments

1. Regarding Quality Assurance, was there a similar system for rollout of GeneXpert and what were the outcomes? How long does such a process take and what does it cost? Response: Some of the things were done. The EQA was in place at initiation of rollout and work was done on the algorithm at commencement. There had been a lot of preparatory work done but some things could not be anticipated, like stock-outs. It was hard to identify reasons for stock-outs but the lesson was that stock levels need to be measured more accurately. The audits showed that it was more cost-effective to keep certain functions in the laboratory rather than at POC.
2. The GeneXpert external quality assessment programme was in place before rollout including verification, so every item used in the field was tested to show fitness for purpose; this now forMs. ongoing quality assessment programmes via NHLS. Every instrument is linked to laboratory information systems, so results are reported in real time through a central data warehouse and then back to clinics and the SMs. printers to speed up TAT. Remote calibration is in place to check every module and remote connectivity allows for a real-time process that shows when every module was tested. This is a web-based programme at 100 sites. Quality standards for GeneXpert have always been in place.
3. There was an expectation that there would be an increase in case identification with GeneXpert, but in fact there was not a big increase in case detection. On time to diagnosis, shortening of laboratory time has contributed to reducing clinical lead times. On time to detection, GeneXpert has reduced the clinical diagnosis lag which lacks specificity. It is accepted that patients are being put on the correct treatment which costs more than diagnosis does. Response: All laboratories provide confirmed diagnosis although there is a timing issue to some extent. In terMs. of yield, this is not based only on patients being put on treatment but also the laboratory diagnosis. There was an effective algorithm in place and Cape Town has a good health infrastructure and high adherence to the algorithm for smear negative cases. This reinforces the importance of effective training of staff on the frontline so that results get back to patients more quickly.
4. Cost effectiveness is an issue even where there is a broad approach to test suspects. How can a more targeted approach be found where there an extensive array of facilities? Response: There is relative yield in different clinics. For example, one clinic might be low yield but testing a high number of people who were not symptomatic. It has been possible to show the linear proportion of yield based on the number of symptoMs. people have that are biologically plausible, but asymptomatic people may still have TB and pregnant women can be asymptomatic yet have culture-positive TB. This relates not only to cost effectiveness but also to how much TB can be prevented, and how health systeMs. can positively impact on transmission by identifying more cases of TB, as that is where cost effectiveness is balanced against the importance of intervention as a public health issue. It is not possible because of cost to screen the entire population but those with symptoMs. of more than two weeks' duration must be properly screened. There are 400 000 cases annually of TB testing, with about 200 000 smear positive cases seen in primary health care clinics, and the other 200 000 seen in hospital and via pulmonary diagnosis. A quarter of these have had a diagnosis of TB outside of their presentation clinic. The algorithm was functioning, but many people find themselves diagnosed with TB due to the natural progression of the disease.
5. Sero-studies have been done on the costs of reducing TB from laboratory and clinic but it is unclear whether it addressed interventions from a rural and urban setting perspective since there will be major differences and benefits. For example, to what extent can one compare the Eastern Cape and Gauteng? In the Eastern Cape because of the great distances it would be particularly important to have results provided the same day. It is important to keep the patient at the centre.

Panel Discussion – Community, Patients, Civil Society: Linking Communities to Services

Introduction

Many people do not enjoy adequate access to health care, yet there are 4790 health facilities across the country, of which a small fraction provides initiation of MDR-TB. There is a decrease in incidents of regular TB cases, but the numbers of MDR-TB are growing, reaching around 15 000 in 2012. This is a serious challenge. Of all those TB tests done in labs, 20% fall through the cracks with regular TB and half of those with MDR-TB do not commence treatment. This means many highly infectious patients remain in families and in communities.

Regarding the interface between community and diagnostics, most TB patients are at the PHC facilities. The number of people being screened for TB is much lower than the number of individuals being offered HIV testing. There are ineffective referral mechanisMs. between HIV clinics and TB clinics, including in the large public hospitals, and little synergy between the different clinic or hospital services and people are reluctant to access these services. Areas to be addressed related to poor linkages to patient care, concerns about lack of data, and the need for an enabling policy.

In Gauteng, for example, the numbers come from different facilities and not only public health. Patients who are poly-resistant often remain unconfirmed to mono-resistance. This relates to the inaccuracy of data. Approximately 3 000 TB patients are treated in a three-month period so the way patients are recorded is important. The numbers appear to be constantly increasing. Many TB patients are not linked to care, and even with poor data recording, high numbers are being diagnosed and not getting into care. The issue of decentralization could be revisited. The most appropriate technology to map patients needs to be examined.

The interface between Community and Diagnostics

Dr. Ribka Berhanu, Right To Care/Helen Joseph Hospital

Clinical trial settings are very different from real world settings. Solid information about which service delivery models work or not in TB treatment is best collected in programmatic settings.

There are many NGOs working in this field and a lot of TB operational research is being undertaken.

Right to Care operating at the Helen Joseph Hospital in Gauteng tested GeneXpert rollout feasibility. Two full-time staff were appointed to run 15 tests per day. Tracking for results in the same day was often difficult, and the way the clinic flow worked made it hard to accommodate the same-day delivery model.

Research indicates that POC testing is likely to be more expensive. Decentralized MDR-TB management has been discussed with average length of stay being 105 days at a cost per patient of R17164 – 90% of cost is not the usual cost drivers, but the direct hospitalization costs such as building and staffing, and only 2% of cost is related to drugs and diagnostics. The Helen Joseph Hospital in partnership with the City of Johannesburg is examining cost and outcomes of decentralized MDR-TB management and also promoting linkages.

Piloting clinical care models is an important role for NGOs, especially in light of the increase in TB patient numbers. The referral system presents challenges since not all patients sent to a referring hospital actually arrive there and not all clinics are equipped to deal with TB.

The project works closely with microbiologists who track every culture result obtained in the Hospital, and also assists the City of Johannesburg to trace patients and assign a final outcome and linkage if any positive TB culture emerged.

There is a free electronic system pilot presently under way that has been internally developed as a clinical tool and should not be considered a replacement for EDr. Previously paper records were used – but the new systeMs. allow for a better determination on patients including on referrals. The project is collaborating with Gauteng Provincial Health to expand the pilot. Most data is results data, information sent to the project and manual work, so there is a real need for an integrated electronic system.

NGOs provide a valuable link between academic, government, funder, and clinical interests, they have a greater capacity for innovation and flexibility, and they work at ideal sites and have better resources than government, and also have a strong Monitoring & Evaluation background to evaluate the work being done.

Early diagnosis of TB and MDR-TB in the community setting

Dr. Mokgadi Sinah Vlug, FPD

South Africa has not achieved its health targets and has to deal with a high burden of health costs. The TB epidemic is driven by multiple factors – a growing HIV epidemic, socioeconomic profile of very poor people, poor environmental conditions, and a dysfunctional health care system which is considered by many to present the greatest challenge. Further factors that exacerbate the situation are chronic illness and alcohol and substance abuse.

Diagnostic challenges include limited knowledge and training at community PHC level, especially with regard to staff having knowledge of policies and guidelines. Paediatric knowledge is identified as being particularly lacking.

There is poor management of smear negative patients, either not being put on treatment and no further investigation being done, or when referred up, they get lost in the system. Health care staff may exhibit stigma about TB and HIV, thereby marginalizing patients within the health system. There is a poor level of TB suspicion in non-HIV infected patients and in children, where patients are often treated for other illnesses but not for TB.

Community issues include a limited understanding of TB and how it is spread, not recognizing TB symptoMs. in children, late presentation of patients and patients lost to care and being difficult to locate, poor follow-up and low level of compliance unless very ill.

System issues include infrastructure probleMs. in PHC facilities that are often badly designed, with inadequate resources, poor communications and data collection tools, transport challenges related to specimens, and poor TAT from laboratory to clinician to patient.

The health status of those working in the health sector is often overlooked, yet it also contributes to the TB &HIV burden, since they are often at higher risk. Health Care Workers themselves have died from TB and also infected others, yet employee wellness programmes do not speak to this situation. What is required is the re-education of communities, and HCP need to provide proper information to inform better decisions, strengthen health systeMs. and QIP implementation to ensure integrated high quality delivery.

Linking communities to services

Dr. Tony Moll, Philanjalo, Tugela Ferry

TB is preventable and curable, yet in South Africa in 2012, 344 000 patients were diagnosed with TB and 14 000 with MDR-TB. Treatment outcomes are being improved but the spread has not been reduced. TB is a communicable disease that has direct links to situations of poverty. The pool of untreated cases in communities is the driver of a serious epidemic.

HIV fuels the TB epidemic so a community-based must integrate TB and HIV. There are powerful TB prevention strategies including intensive Case Finding and infection control and this should be community-based.

Case studies show that in Sub-Saharan Africa, intensive Case Finding works well. This promotes an understanding of who to target and what yield to expect. For example, of 946 sputum samples, 37 would be TB-positive, of which 11 would be MDR-TB so overall it is necessary to screen 147 patients to find 1 TB case. Yield varies according to the population setting which is high in prisons, where only 38 were screened to find 1 case, and lower at taxi ranks, where 148 people were screened to find 1 case.

In health care settings 70% of TB cases were HIV positive but in communities over 90% of TB cases were HIV negative. Household contacts present a high yield group, where for every 13 index patients and every 61 household contacts screened, 1 MDR-TB case was identified.

At Tugela Ferry, 1211 adults started ARV and all were screened for TB – this indicated 345 new TB cases. There were 200 new cases identified in two years in health care settings. However, as a result of community interventions, there was a dramatic decrease in new infections. It is advisable to screen at community level and use the portable CD4 counter to stream patients into appropriate care.

Linking patients to treatment services

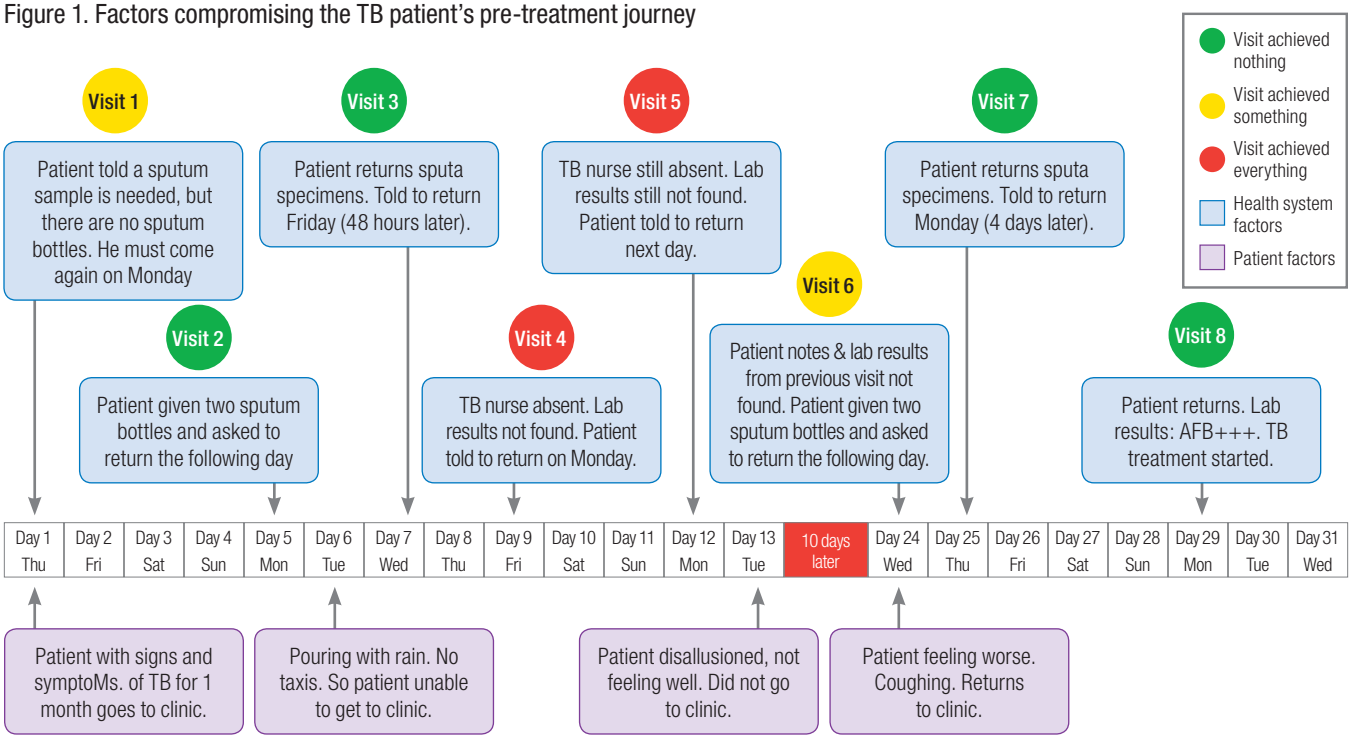
Marian Loveday, Medical Research Council

A 4-year study was done at decentralized MDR-TB sites with all 4 sites given the same guidelines and training. Yet outcomes were quite different. At the centralized site 54% and 58% achieved successful outcomes. At the four decentralized sites, successful outcomes were lower. The reasons for unsuccessful outcomes varied. This is similar to how GeneXpert has been implemented, with site variations. It is useful to understand therefore, that the rollout of a programme is done very differently at different sites. If a new programme can integrate into health systeMs. that exist it

usually strengthens the health systems. Between 2004 and 2011 it took 100 days from diagnosis to treatment – with the introduction of four decentralized sites, the time went down to 72 days, so taking it closer to communities improved delivery. By 2011-2012 with GeneXpert it was down to 21 days. There are many variable factors that compromise the MDR-TB patient journey as explained in Figure 1.

At one state facility - 813 patients were listed, of which 213 could not access their folders. This is an accurate reflection of the scenario that people face on the ground, resulting in the patient receiving 42% incomplete treatment, 42% full treatment and 16% no treatment. Effectively, the patient was cured in spite of the health care system, not because of it!

Figure 1. Factors compromising the TB patient's pre-treatment journey



Discussions and Comments

1. As well as having 16 mobile teams, what other methods were used to bring TB under control? Response: Many interventions took place – strict infection control policies in the hospital, decongesting wards, waiting areas ventilated, extra resources from the DOH, human resource support and technical assistance from Brown University, promoting a decentralized community model and household content tracing, and improved transport.
2. This district had the second highest cure rate in the country, the TB programme is working well, even though this is also one of the poorest districts in the country so it provides an excellent example of what is possible.
3. South Africa has done well to reduce time to initiation from 70 to 21 days, but we are now in an era when we can put patients on treatment in 2 days and the tools are available. What are the blockages in other areas? Response: There is a high level of infection in the community and an understanding is needed that real interventions must happen at community level. For example, in measuring the high rate of infection at taxi ranks and then looking at public transportation, many taxis are in poor condition and in cold months the windows are closed all the time, which promotes infection. How can communities lobby for improvements in transport or hospital waiting rooms, amongst others?
4. What is the role of private hospitals and health care workers in communities? There is a public health crisis around TB but the message from the politicians is not clear, and they do not provide guidance on how this challenge must tackled with a high level of political commitment. Response: Our professional people are very visible and could promote public awareness about TB, handing information out on street corners, for example, as happens with other information. There should be TB flyers handed out at every intersection. The challenges of the TB programme are the same challenges of the health system overall. If the PHC clinics are not fully supportive then there is less possibility of success in eradicating TB. For example, in Germany in 1945, after the Second World War, there was a serious TB problem and this was addressed through a concerted information campaign to raise awareness.

Panel Discussion – Key Players in Diagnostics: Researchers, Academics, Private Sector, Manufacturers, and Medical Schemes

Introduction to New Diagnostics

Professor Andrew Whitelaw

Progress is being made towards decentralized affordable field-friendly POC NAATs for TB, and some are well-suited for use in resource-limited settings. Antigen detection is used but sensitivity trends to be sub-optimal especially in patients with high CD4 counts. This means there is a "rule in rather than rule out" process which is not conducive to accurate screening. It can be used better in hospital settings.

For detection of resistance, the molecular approach is recommended with improvements already under way. In the diagnostic landscape of South Africa, GeneXpert remains the selected rapid diagnostic test. Second line assay works reasonably well as an add-on but cost and operational implications are not yet fully assessed.

Early phase technology includes volatile organic compounds, various NAATs including for DST, VOCs such as e-noses and rats and further equipment is under development. Biomarkers play a differentiation role but there are presently no commercial biomarkers available. Point Of Care tests should be 80% in smear negative results, with same-day results. There are various specimen types and simple minimal training is needed, but currently no test offers all of this.

It is important to demonstrate the impacts that a specific test has on burden of disease. Discussion is needed around WHO endorsement, when to adopt a specific test, how to choose for the settings, whether the test is a replacement or an add-on and how to use it. It is important to be able to measure impact, including cost effectiveness.

What is on the horizon for TB diagnostics, global and local?

Dr. Glaudina Loots, Department of Science and Technology

Rather than taking a clinician's view, or a laboratory view, the patient should be at the centre. People who have used their last money on transport to reach a clinic are the clients who must have immediate care and quick results. The DACST has a health innovation unit that examines ways to support local research and development and innovation capacities. Areas of study include HIV, TB, malaria, diagnostics, treatment, building clinical capacity, and promoting local manufacturing.

The many stakeholders need to be brought together as Strategic Health Innovation Partnerships to promote synergies, and collegial work, drawing on international experiences. Collaborative research is a key component.

It is important to identify what is presently being done at universities that can be drawn on. South Africa is doing a lot of biomarker research because of easy access to clinical trial opportunities. An interesting project relates to rapid testing in 30 minutes, costing under $4 and easy to administer. This is presently being validated. Links that will hold interest for corporates such as Novartis are being promoted and there have been a number of successes in a short period.

Mr. Peter Mehlape, BD Diagnostics

Regarding POC technologies, a recent survey was done on what patients and health care systeMs. wanted in 23 African and Asian countries, in particular around TB and HIV. Whatever the test that must be done, patients want simple, easy, cheap tests and the health systeMs. want tests that require limited infrastructure. In the past 5 years a CD4 POC product has been produced that can be used without a doctor and this is being expanded to TB POC products that will be accessible in the last mile of health care with limited infrastructure.

Capacity for POC technology has been built that is of world class standards and can be brought to developing countries in a viable way. The collaborative approach has worked well, and valuable experience has been shared. The CD4 POC products took some time to develop but provided valuable lessons going forward that will inform the TB POC product development. There is collaboration with the NHLS to bring in second line drugs.

Mr. David Hain, Hain Life Science

A comprehensive range of microbacterial test systeMs. provide rapid and easy test options. South Africa is an important market and there is strong collaboration. An important test currently being marketed is for second line drugs – this was drawn from what was available at the time and it does exactly what is expected from the assay. The probe is very accurate and there is a new version of the Line Probe Assay (Version II). There are also tests for NTMs. which are important in South Africa.

New assays are under development – fluorescence-based multiplex – in a single tube that will be customer-friendly and go into laboratories easily. With the new drug regimes, there needs to be discussion around what drugs should be tested in the future. It is important to be aware that new resistant markers are emerging and design accordingly. Therefore vanguard studies are being done – an assay can be designed based on new technologies, but in designing such an assay it is important that the scientific community makes input on what is needed. Research must inform product development and public-private partnerships are useful in this regard.

Mr. Paul Steuperaert, Cepheid HBDC

This is a high growth company with innovative approaches. Future products include the 50-pack of GeneXpert which is much cheaper and easier to use and store. There is an extended warranty worldwide, on-site preventative maintenance, and simpler calibration. Web-based training for users is provided around the world and a user-friendly approach is promoted.

On rollout of national programmes, there has been expert MDR-TB provision in HBDC countries which includes installation and training. Accurate monitoring of system usage is important. User functionality support is available free to all users, and relates to any instrument sold. Going forward, simplified installation and settings with remote upgrade, and appending data to test results, as well as Excel export is possible. Administration will include external application interface, data share with other institutions, and assistance with system replacement or relocation. This is the future for defining molecular diagnostics—any test, any time, any sample, any place!

Discussions and Comments

1. A concern in South Africa is that we focus on training people who perform the different tests but health care workers also need to know when to request a test and why. How can a manufacturer contribute to guiding health care workers in knowing when to request a test? Response: Extensive training has already been done in South Africa that has been well received and there are monthly training updates as well as support platforms.
2. At hospital level, using GeneXpert has been challenging as modules start to fail over time, usually after the warranty has expired, and 30% of modules are replaced after 2-3 years of use. This has a serious impact on budget. What is intended for cost of maintenance and replacement of this equipment? Response: Module failure is an issue that must be avoided at all costs, and this is being addressed at the international level. In South Africa a new repair and calibration centre was established with new tests that are more rigorous, such as 17 hours of non-stop testing on a single module before it is validated. Expert calibration will improve performance. There is also remote calibration service. Current failure rate is 4% that is constantly being worked on. However, end users must also play a role in maintaining quality, especially in rural settings.
3. It is not only a question of training, but assessing the entire stakeholder chain and educating and informing all stakeholders, including funders and clinicians. They need to be included in processes at the outset to ensure their commitment to a new way of working. They need to buy into the new technology and see its value.

In summary, Dr. L Mvusi noted that the key outcomes that are expected from the Summit relate to examining the existing tests and the extent to which these are currently being optimized, and where there are gaps, there must be discussion as to how these can be addressed.

The health systeMs. must be strengthened so as to improve diagnostics and early diagnosis and promote linkages to care and treatment, including a higher level of compliance with treatment.

Research gaps need to be identified and relationships with academia, and indeed with all stakeholders, strengthened.

It is clear that in introducing new tests, the implementation has not been consistent and there were unexpected challenges. There was a lack of commitment from provinces, districts, health care workers and the patients themselves that has impacted on outcomes. It is important that all stakeholders are equally informed and

The Role of TB Diagnostics in Reaching Zero TB Deaths

Dr. Sanni Babatunde, WHO

The World Health Organisation embraces a vision of a world free of TB and this is what we must all aspire to. The intention is that many of us will become unemployed in 2035 because we will have attained our goals!

What should we be targeting into the future? It is necessary to draw on the draft 2015 strategy which will be adopted in 2014. The target is fewer than 10 TB cases per 100 000 population for 2035—this provides a baseline figure. To achieve this will require innovative principles and thinking based on the three pillars of high quality integrated care and prevention; bold policies and supportive systems; and intensified research and innovation.

If the current trajectory can be optimized with the addition of social stability and other positive influencers, then there will be a decline of 10% a year, but even in this positive scenario the goals will not be achieved. There is a need to improve not only diagnostics but also the entire health systeMs. continuum. Diagnostics is important but a comprehensive approach goes beyond that. The term Universal Health Coverage speaks to access, quality, and fullest possible access for patients. Social protection plays a key role and requires a comprehensive package that optimizes tools and promotes Universal Health Care, and this will contribute to a 10% decline in incidence. This requires innovative, strong health and surveillance systeMs. that can be measured. New R&D outcomes are also an important factor.

On the role of TB diagnostics, the TB infection pool is 2 million people at present. It is important to prevent expansion of this number by early case detection and good TB management, including treatment. This is a key role for the health systems. Shorter duration of treatment will contribute to better treatment management. High specificity is needed and the necessary tools are available.

South Africa has good GeneXpert coverage which reduces TAT in laboratories, but this has not contributed to improved treatment initiation. Any patient benefit is unclear because while the laboratory processes are acceptable, the main opportunities for improvement are found in the space between the laboratory and the patient.

Technology endorsed by the WHO indicates a significant shift in the accessibility of a good TAT testing environment. It is important to keep in mind that that TB is both pulmonary and extra-pulmonary and therefore the most appropriate test is required to ensure accurate detection. An ongoing concern remains the delay in TAT with test results, and the higher level expertise required to analyse the tests and influence the outcomes. Public health diagnostic evaluation for TB also requires revised policy recommendations that are based on the use and outcomes of updated technology. A new focus is now possible on the diagnosis and treatment of adults and children, including presumptive MDR/HIV associated with TB.

The main recommendation is that GeneXpert should be used rather than traditional microscopy for initial testing. It is important to agree on the kind of diagnostic approach to be promoted in order to move towards zero incidence, and draw on the existing diagnostic tools to attain this. GeneXpert appears to be that option.

Discussions and Comments

1. The WHO figures seem to indicate a downward trend in TB infections but this is not the case, and there is definitely an upward trend. The WHO recommendations are good but an activist model is needed in South Africa.
2. GeneXpert is recommended in certain situations as first line instead of microscopy. Can molecular testing also be used as this is cheaper than GeneXpert? Response: Not all molecular testing is acceptable because the assessment is based on GeneXpert in comparison with the gold standard.
3. The WHO and NDOH finalized extensive reviews which covered all provinces and based on the findings it is possible to assess where diagnostics fits in. Response: With a review it will be seen that this linked up with what the WHO study indicates, that the burden is beyond the excerptor only and has to do with other components that were not reviewed. To attain the proper perspective there is a need to know what the current South African TB burden is. The WHO asserts that the basis for activation and arriving at this particular estimate is still not entirely clear and triangulation is needed to derive accurate meaning. For the health sector review, it will provide a picture of what the health sector can do to improve the TB situation based also on external factors.
4. There are two things relevant for the URC – the unique identifier and patients not returning for results. Data from NHLS showed 14 000 MDR-TB cases but these are not all patients so the challenge is to improve the process to quantify both testing and treatment. The other concern is that there are districts where one third of people with TB symptoMs. had a smear taken but did not come back for results yet these are infectious patients. This means there are 30-40% of tested patients who are infectious and we now cannot find them. Response: The NHLS in conjunction with the CPW is making a significant effort to address duplication in the absence of a unique identifier – although everyone agrees that a unique identifier is critically needed.

Group Work Reports

Group One: Introduction of new tests (liquid culture, LPA & GeneXpert)

Group proposals, Discussions and Comments

- The NHLS and the private laboratories should collaboration data sharing and Quality Assurance.
- The current regulatory framework for laboratories is limited. Therefore there is a need for a statutory body for labs – that includes a multi-stakeholder expert group. For example there are certain tests that are too costly and should only be allowed in specific contexts. The NDOH does have recommendations regarding laboratories and prescribed tests but this is not statutory and not well enforced.
- The private sector should comply with the national TB diagnostic algorithms
  - However the private sector costs are too high, medical schemes are reluctant to pay for the test, and patients cannot afford to pay.
  - NDOH should engage private funders on cost reductions for GeneXpert tests.
- The NDOH should encourage operational research on newly introduced tests, in order to assess their impact on outcomes, patient delays in seeking care and the time to treatment initiation.
- A better tracking system should be implemented to prevent duplication. Explore use of a unique identifier (e.g. Identification number, thumb prints, etc.)
- Accelerate the implementation of a single request form which must be aligned with the algorithm and level of care. The form should integrate NDOH and NHLS requirements.
- The sample collection from patients and storage at facility level need to be improved.
- The NDOH must standardize practice as far as possible throughout provinces. For example, consider changing from collecting one specimen to two upfront, similar to the Western Cape approach, but this could be considered in a programme that has a good system of linkage to care.
  - There are two components to this discussion— one is the issue of the baseline smear in GeneXpert positive cases, and could that part of the algorithm be dropped? However, the smear result is still essential for contact investigation and bacteriological monitoring. The matter is presently under review by the NDOH where case definition will be reviewed with regard to notification requirements.
- The NDOH must invest in improved IT systeMs. to ensure that all facilities have a computer and internet to facilitate access to the results.
- There is a need to create a strong local evaluation system for new tests, which is inclusive of the private sector. Where appropriate, new tests can be endorsed and implemented locally without waiting for WHO approval.
- Develop linkages across the board, such as the South African Health Products Regulatory Authority (SAHPRA) for registration of new technologies, and the Office of Health Standards and Compliance which evaluate the quality elements.
- Leverage the power of the new diagnostics to improve the health system overall and strengthen linkages to care.

Recommendations

- Propose the development of a generic implementation framework within which the review and rollout of all new diagnostics is undertaken and this to be developed with the involvement of all stakeholders, for example, the private sector will contribute innovation and efficiencies.
- NDOH should consider establishing a voluntary regulatory body that will oversee development of the regulatory framework for all laboratories (private and public) based on international norMs. and standards.
- NDOH should consider appointing a national laboratory co-ordinator who will oversee liaison between DOH and public and private laboratories.

Group Two: Challenges in implementing the technologies

Group Discussions and Comments

- Adopt a standardized national referral form that will capture basic information to communicate to the hospital. This form would contain the following information: smear negative results, HIV status as well as chest x-rays for the facility to commence the correct treatment.
- Proper sputum collection, as well as transportation of specimens has proven to be a problem in the past.
- Encourage induction of sputum in children with TB.

- Collection of two specimens upfront saves a lot of time for MDR-TB confirmation
- The definition for turnaround time (TAT) was agreed upon as the time taken from sample collection to when the results reach the clinician again. The proposed targets for TAT were 5 days for drug susceptible TB and 10 days for drug resistance TB. The proposed TAT for culture is 6 – 8 weeks.
- Healthcare workers and laboratory staff need to be trained on the diagnostic algorithm.
  - Training sessions with healthcare workers on the pre-analytical process is important.
  - There is a gap in training of clinicians
  - There should be follow up support and mentoring after training
- A unique identifier should be used for patients to avoid duplication of tests.
- There should be an effort to strengthen ward-based outreach teams.

Recommendations

- NHLS needs to process sputum samples over weekends, instead of only processing samples received on a Friday on the next Monday.
- The processes that were followed when implementing new tests should be reviewed in order to establish what has been done, identify gaps and then develop a framework / strategy to address the gaps.
- There should be an effort to strengthen ward based outreach teams.
- Develop systeMs. to monitor turnaround times.

Group Three: Community, patients, civil society: Linking communities to services

Group Discussions and Comments

- Training of community health workers and communities is important
  - Treatment adherence counselling
- Social mobilization
  - Use community dialogues to address stigma, discrimination and Xenophobia
- Clarify the role of stakeholders such as faith based organisations (pastors preaching healing and to stop medication) and ward councillors.
- There must be coherent messages communicated to avoid confusion.
- Strengthen public/private partnerships within communities.
- Right to care is not sufficiently prioritized.
- Ward based Outreach TeaMs. – but this had little impact on the TB programme.
- Managing the influx of migrant patients from outside South Africa seeking treatment for MDR-TB remains a challenge.
- Guidelines must be revised to include the role of clinics and home based carers in the decentralization of MDR-TB management.
- Train professional nurses on the IMCI strategy to improve TB diagnosis in children under 5.

Recommendations

- Strengthen the functionality of clinic committees and hospital boards
- Screening at community level must target high risk groups
- Explore options to improve access to testing at community level
- Strengthen linkage to care
- Develop tools for monitoring community TB care

Group Four: Key players in Diagnostics: Researchers, Academics, Private Sector, Manufacturers, Medical Schemes

Group Discussions and Comments

- The private sector focuses on cost issues – but this is correct because when on medical aid patients must have access to the best tests – those with TB must be diagnosed and managed creatively under medical aids.
- In house tests must go through robust evaluation, and there must be regulated standards to evaluate against.
- No government body evaluating technology/tests. Although tests done internationally, local studies are wanted. European manufacturers use European and American standards for thorough evaluation and products then carry CE mark. Need to know where local tests are required to take place.
- Currently manufacturers have education and training teaMs. for all levels of medical personnel in laboratory and health facilities. They are willing to provide training at no cost but have to be requested to do so. Coordinated approach should include all manufacturers to share knowledge.

- Currently NHLS makes decisions on placement of new tests, with very little consultation, especially with provincial departments on what equipment is placed where.

Recommendations

- Consultation with district and provinces on closing the gap between diagnostics and implementation
- Strong national leadership is essential to drive the process of adoption and implementation of new technologies equitably across all provinces.
- Training of health care workers should be centrally organized and coordinated, driven by the DOH with the support of the private sector.
- All academic and research institutions should be involved in pre- and post-marketing research for new tests.
- Create a national repository of data including publications on basic research.
- Set priorities for operational research to evaluate the implementation of new tests
- Develop a framework/guidelines for registration procedures of new technologies.
- Establish a national body to review new tests/ technology

Recommendations

The report, recommendations and presentations will be shared electronically.

Next Steps:

1. Report to the quarterly meeting with all provinces and partners on 27 and 28 November and present findings and also circulate within NDOH. Follow up on tasks on what to operationalize from this meeting.
2. The expectation is to provide an implementation plan, talk about progress, and evaluate new evidence that might have become available.
3. A recommendation is that there must be a national task team that will advise how best to introduce these tests. Also request approval within the Department for appointment of such a team and contact individuals regarding terMs. of reference of this team and circulate for input and suggest candidates.
4. It is hoped that the team will be representative but not overly large.
5. It is suggested that another meeting of this nature be convened a year from now – we need to assess if this is too soon or not soon enough. General agreement was that the meeting would be useful with an expanded agenda that has feedback from the field.
6. We are committing to the TB programme in that next week provinces will already take up some of the points raised here – this forMs. part of health systeMs. strengthening to be incorporated into coming year plans.
7. When we meet again we must have clear guidelines about what we will need to do and how to assess our progress. Outline the recommendations from this meeting and those organizations or people would have to say what they have done and share the challenges and learnings. We need to have begun to implement recommendations.
8. Timeline for all the suggested work – report for inputs by 1st week December to circulate for comment from participants. Friday 13thDecember to provide feedback to Convenors who will then consolidate for early in 2014.

Closure

The Summit shared a high level of technical expertise in a short time and the exceptional quality of all inputs into this important area of work is acknowledged. TB Diagnostics have long experienced challenges and the opportunity to host such a Summit and include a wide range of stakeholders is very welcome. It is hoped that the recommendations and inputs from this meeting will also contribute to the guidelines that are presently in development.

Presentations can be accessed via the following link: http://tbsouthafrica.org/node/267

National Summit on TB Diagnostics: AGENDA

DAY 1 (18 November 2013) Program Directors: Dr. Lindiwe Mvusi & Dr. Refiloe Matji

TIME	ACTIVITY	PRESENTER
08:30 – 09:00	Registration	
09:00 – 10:00	Welcome and Introductions	Session chair: Mr. David Mametja (DOH)
	USAID Support	Ms. Catherine Brokenshire-Scott (USAID)
	TB Diagnostics, Global context	Dr. Refiloe Matji (URC)
	• NDOH priorities and challenges on TB diagnostics in South Africa • Objectives of the summit	Dr. Yogan Pillay (DOH)
10:00 – 10:15	TEA BREAK	
10:15 – 11:40	Panel Discussion Session I: Introduction of new tests (liquid culture, LPA & GeneXpert)	Panel Chair: Dr. Giorgio Roscigno
	Session introduction	
	• What are the key issues in TB diagnosis? • How were the currently available tests in SA introduced? • What was the rationale? • What lessons have been learnt? • How are the algorithMs. being used? • What is the role of private sector?	Panel Members: • Prof. Koleka Mlisana (UKZN/NHLS) • Dr. Jan van Rooyen (Ampath) • Dr. Peter Cole (Lancet), • Dr. Lorna Madurai (Global Labs) • Dr. Suleiman Hajee (Toga Labs) • Dr. Nazir Ismail (NICD)
11:40 – 13:00	Panel Discussion Session II: Challenges in implementing the technologies	Panel Chair: Prof. Maphoshane Nchabeleng (MEDUNSA)
	Session introduction	Prof. Wendy Stevens (NHLS/WITS)
	Challenges related to reaching all levels of the Health System? • Quality Assurance challenges • Clinical challenges • Operational challenges • Diagnosis of TB in children	Panel Members: • Dr. Adeboyi Adelekan (CDC) • Dr. Xavier Padanilam (Sizwe Hospital) • Dr. Pren Naidoo (DTTC) • Dr. Kerrigan McCarthy (Aurum) • Dr. Ute Feucht (Tshwane District/UP)
13:00 – 13:45	LUNCH	
13:45 – 15:05	Panel Discussion Session III: Community, patients, Civil Society Linking communities to services	Panel Chair: Mr. David Mametja (DOH)
	Session introduction	Dr. Norbert Ndjeka (DOH)
	• Interface between community and Diagnostics • Access to TB Screening and HIV testing • Early Diagnosis of TB and MDr. TB • Linking patients to treatment services	Panel Members: • Dr. Rebecca Berhanu (Right to Care) • Dr. Sinah Vlug (FPD) • Dr. Tony Moll (Philanjalo) • Marian Loveday (MRC)
15:05 – 15:20	TEA BREAK	

TIME	ACTIVITY	PRESENTER
15:20 – 16:40	Panel Discussion Session IV: Key players in Diagnostics Researchers, Academics, Private Sector, Manufacturers, Medical Schemes	Panel Chair: Dr. Refiloe Matji (USAID TB Program, URC)
	Session introduction	Prof. Andrew Whitelaw
	• What is on the horizon for TB diagnostics- globally and in South Africa? • What are the roles of the public, private and the research sectors? • What do we need?	Panel members: • Dr. Giorgio Roscigno • Ms. Glaudina Loots (DST) • Mr. Peter Mehlape (BD Diagnostics) • Mr. David Hain (Hain Lifescience), • Mr. Paul Steuperaert (Cepheid) • (Roche, TBC)
16:40 – 17:00	What role will TB diagnostics play in getting to Zero TB Deaths?	Dr. Sanni Babatunde (WHO)
17:00-17:10	Closing Remarks	Chairperson- David Mametja
18:30-20:00	DINNER	

DAY 2 (19 November 2013) Program Directors: Dr. Lindiwe Mvusi & Dr. Refiloe Matji

TIME	ACTIVITY	PRESENTER
08:30 – 09:00	Recap Day 1	Chairperson
09:00 – 09:20	Working Group (WG)Instructions	Facilitator (TBC)
09:20 – 10:00	Group Work	Group Facilitators
10:00 – 10:15	TEA / COFFEE BREAK	
10:15 – 12:00	Group Work continuation	Group Facilitators
12:00:13:30	Feedback presentations	
	WG 1	Group representative
	WG 2	Group representative
	WG 3	Group representative
	WG4	Group representative
13:30 – 14:30	LUNCH BREAK	
14:30-15:30	Feedback Presentations continued	
15:30–16:30	Way Forward	Chairperson
16:30 – 17:00	Closure and Departure	David Mametja (DOH)

List of Participants

Name	Organization
Ms. Dakhile Ndiwalane	URC
Dr. Dawie Theron	PDOH
Mr. David Hain	Hain Lifescience
Mr. David Mametja	NDOH
Mr. Detlef Siewert	BD Diagnostics
Dr. Dimakatso Moloi	PDOH
Dr. Donna Jacobs	URC
Ms. Duduzile Mbambo	PDOH
Mr. Banele Dlamini	URC
Ms. Smita Kumar	USAID
Mr. Elvis Ngobeni	PDOH
Ms. Evelyn Mhlope	URC
Dr. Frederick Balagadde	K-RITH
Dr. Giorgio Roscigno	NEXT
Ms. Glaudina Loots	DST
Dr. Harold Hlophe	PDOH
Dr. Faizan Ismail	NHLS
Mr. Iain Sharp-Paul	Cepheid
Dr. Keshree Pillay	Lancet
Prof. Koleka Mlisana	NHLS
Dr. Kerrigan McCarthy	Aurum
Dr. Kgomotso Vilakazi	NDOH
Mr. Dirk Smit	Hain Lifescience
Dr. Leigh Berrie	NHLS
Ms. Lerato Legoabe	URC
Ms. Lessie Mnisi	USAID
Dr. Limenako Matsoso	URC
Dr. Lindiwe Mvusi	NDOH
Dr. Lorna Madurai	Global Laboratories
Mr. Sebaka Molapo	NHLS
Prof. Maphoshane Nchabeleng	Medunsa
Ms. Marian Loveday	MRC
Prof. Mark Nicol	NHLS
Dr. Martie van der Walt	MRC

Name	Organization
Ms. Maswikana Sithole	URC
Mr. Mokete Phungwayo	NDOH
Dr. Mpho Ratshikana-Moloko	URC
Dr. Muhammad Osman	City of Cape Town
Mr. Musawenkosi Simelane	URC
Dr. Sibongile Mahlangu	NHLS
Mr. Marlon Burgess	MDG
Mr. Sicelo Dlamini	NDOH
Mr. Garvon Molefe	NDOH
Ms. Eva Kobola	PDOH
Mr. Masala Silinda	NDOH
Dr. Nazir Ismail	NHLS
Mr. Neil Barker	Cepheid
Ms. Nellie Gqwaru	USAID
Dr. Nesri Padayatchi	CAPRISA
Ms. Nicole van der Westhuizen	PDOH
Dr. Norbert Ndjeka	NDOH
Ms. Nomsa Sebitlo	URC
Ms. Nonkululeko Nkomo	URC
Dr. Ntombi Mhlongo-Sigwebela	URC
Prof. Nulda Beyers	DTTC
Ms. Nokwazi Madhlala	NDOH
Mr. Paul Steuperaert	Cepheid
Dr. Peter Cole	Lancet
Mr. Peter Mehlape	BD Diagnostics
Mr. Philemon Phatedi	PDOH
Mr. Philippe Jacon	Cepheid
Mr. Phumlani Ximiya	NDOH
Dr. Pren Naidoo	DTTC
Dr. Mokgadi Sinah-Vlug	FPD

Name	Organization
Ms. Nadine Zama	MRC
Ms. Patricia Ntsele	NDOH
Mr. Raymond Mabope	NDOH
Dr. Rebecca Berhanu	Right to Care
Dr. Refiloe Matji	URC
Prof. Rob Warren	University of Stellenbosch
Dr. Robert Makombe	URC
Dr. Sanni Babatunde	WHO
Mr. Simphiwe Mayaphi	URC
Dr. Suleiman Hajee	Toga
Ms. Sineli Shabalala	NDOH
Ms. Thandeka Dayimani	URC
Mr. Thulani Mbatha	URC
Dr. Tiyani Mabunda	PDOH
Dr. Tony Moll	Church of Scotland Hospital (COSH)
Ms. Tumi Mbengo	URC
Ms. Ursula de Kok	BD Diagnostics
Prof. Wendy Steven	NHLS
Prof. Wesley Scott	Wits University
Dr. Xavier Padalinum	NDOH
Mr. Zanoxolo Mbundu	Hain Lifescience
Dr. Varough Deyde	CDC
Dr. Beki Magazi	University of Pretoria (UP)
Dr. Ute Feucht	UP/DOH Tshwane
Dr. Francesco Balletti	Italian Cooperation
Mr. Thulani Tukulu	Faranani Healthcare
Ms. Georgina Wessie	URC
Ms. Fikile Dlongolo	URC
Dr. Adeboye Adelekan	CDC
Ms. Alvera Swartz	PDOH
Dr. Andrew Shija	MP NDOH
Prof. Andrew Whitelaw	NHLS
Prof. Anne Grobler	NWU
Ms. Catherine Brokeshire-Scott	USAID
Ms. Cindy Dladla	URC
Dr. Claudio Marra	URC
Ms. Elizabeth Matsepe	FPD