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ABSTRACT

Background: **The introduction of Gene Xpert® MTB/RIF assay ("genexpert"; Cepheid, Sunnyvale, USA) (GeneXpert) in the diagnosis of Tb has been a practice changer not only in the speed of diagnosis but also in the early and prompt identification of rifampicin resistance. Data generated from the use of geneXpert is managed in the GeneXpert Laboratory Information Management System (GX-LIMS) as well as the Tuberculosis Information from Basic Units (TIBU). There is minimal knowledge on the interplay of the two platforms in the country.**

Objective: **To determine of the level of congruence between the GeneXpert laboratory management information system and the TIBU surveillance system for Kiambu county TB patients, 2014 -2016**

Design: **An analytic comparative cross-sectional study Setting: Kiambu County, Kenya Population: All patients notified into TIBU and entered in GX-LIMS within Kiambu County, 2014 -2016**

Results: **In the study period, there was a gradual increase in the number of GeneXpert tests done in Kiambu County. Patients tested in GX-LIMS were 171(2%), 1610(26%) and 6186 (78%) in 2014, 2015 and 2016 respectively. Of these, 60(4%), 209(16%) and 1272(83%) were notified into TIBU in the respective years. In the study period, 29 patients were Rifampicin resistant as per GX-LIMS, with 13 being notified into TIBU for care.**

Conclusion: **Our study showed that there is poor congruence between GX-LIMS and TIBU in Kiambu County. There is need for the development of unique patient identifiers that can be used to track and follow up patients from the point of testing in GX-LIMS to notification into TIBU for care. This will limit the number of patients lost to follow-up.**

INTRODUCTION

Successful treatment of Tuberculosis (TB) is dependent on timely diagnosis and rapid initiation of management. One of the key components towards patient-centered and integrated care in the End TB strategy by WHO is early diagnosis and universal drug susceptibility testing (DST)(1).

Several diagnostic and drug susceptibility modalities for TB are in use.

The gold standard for diagnosis of TB is mycobacterial culture. Others include chest X-ray, microscopic observation drug susceptibility, TB loop mediated is other mal amplification, and line probe assays. These are further discussed for the context of Kiambu County elsewhere (2).

Xpert® MTB/RIF assay ("genexpert"; Ceph eid, Sunnyvale, USA) is a technology that has been introduced in the armamentarium for diagnostics. Genexpert is an automated nucleic-acid-amplification test (NAAT) that detects Mycobacterium tuberculosis genes and genes associated with Rifampicin resistance in sputum in a single test. It has a sensitivity of 88% in high TB prevalence settings and specificity of 98% (2) and is suitable for all level laboratories requiring minimal hands to operate. It can detect up to 67% of smear negative TB cases(3). Genexpert test takes two hours to run thus patients can be diagnosed early enough upon clinical suspicion. This considerably reduces the time to initiate treatment and prevent transmission.

Kenya embraced use of genexpert in 2012, and in 2016, started the big step to ensure universal access. Kenya currently has 145 genexpert machines installed strategically to facilitate accessibility to many in need across the country mainly at county and sub-county referral hospitals and other private establishments. Facilities equipped with the machine are referred to as genexpert sites. For facilities that are non-genexpert sites, sample networking is facilitated to ensure optimal access to the genexpert site for prompt diagnosis and decision making.

In Kenya, genexpert data is managed in two systems. The genexpert laboratory management information system (GX¬LIMS) and the Tuberculosis Information from Basic Units (TIBU) (4). GX-LIMS is laboratory based and focuses on the actual genexpert tests done. It is a robust real-time system that provides results to clinicians and to the TB field managers rapidly allowing for prompt clinical decision making for patients. Currently, in practice, this occurs within two hours. It also has the advantage of providing case based data. Once a patient is presumed to have TB, the clinician fills the sputum/genexpert request form and the patient is referred to the laboratory for genexpert testing. Upon completion of a test, results are relayed back immediately via short message service (sms), email and hard copy platforms. These results are also documented in the hardcopy laboratory register. The genexpert machine itself has an automated online reporting system, and any test done on the genexpert machine is automatically reported in the GX-LIMS.

TIBU, on the other hand, is patient centered providing a national case-based reporting platform. It is a cloud-based electronic database that is used to notify patients to the National Tuberculosis Program. It collates patient based clinical data as entered from the primary sources, the patient record card and the TB facility register. It collects patient data, including the method used to diagnose TB at the onset of TB treatment which could be by clinical diagnosis (symptomatology and chest X-ray) or bacteriological confirmation (Sputum Smear Microscopy (SSM), Cultures, GeneXpert).The data is then available for analysis at national, county, sub-county and facility level.

Currently the two systems are viewed and analysed separately, though they are both managed by the National TB program. Generally, it is assumed that all patients diagnosed with TB using genexpert are put on treatment and notified into TIBU. This study therefore seeks to determine the level of congruence between GX-LIMS and TIBU in Kiambu County between 2014 and 2016.

MATERIALS AND METHODS

Study design: This is a retrospective analytical cross-sectional study done using data from the GX-LIMS and routinely collected TB data in TIBU.

Setting: Kiambu County, one of the 47 counties in Kenya covers an area of 2449.2 Km2.It is located centrally in the country, and is bordered by the capital, Nairobi County, to the south, and is divided into 12 subcounties, Gatundu North, Gatundu diagnosis (symptomatology and chest X-ray) or bacteriological confirmation (Sputum Smear Microscopy (SSM), Cultures, GeneXpert). The data is then available for analysis at national, county, sub-county and facility level. South, Githunguri, Juja, Kabete, Kiambaa, Kiambu, Kikuyu, Lari, Limuru, Ruiru and Thika. It is classified as a moderate TB burden county with a case notification of 240/100,000 in 2014.

GeneXpert was introduced first in Kiambu County in Thika level 5 hospital in May 2014. In 2015 there were three new geneXpert sites; -AIC (Africa Inland Church) Kijabe, Kiambu level 4and Tigoni Level 4 hospitals in May, June and November respectively.

Figure 1:
Map of the counties in Kenya

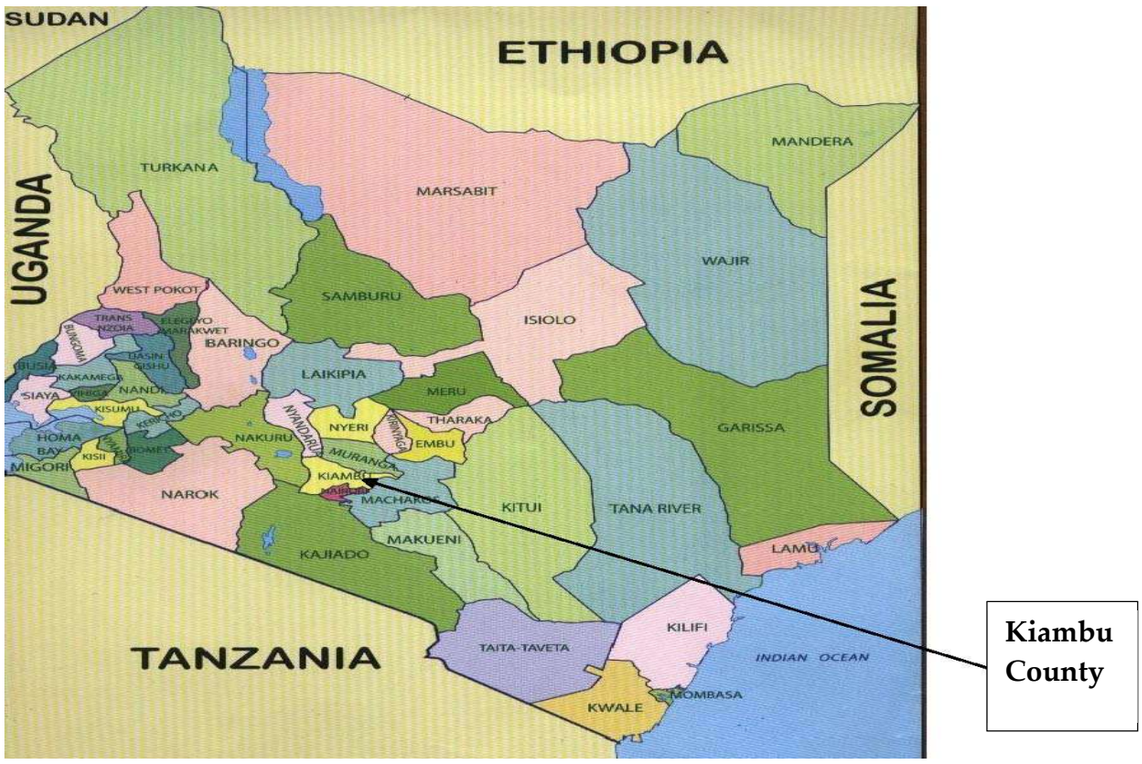
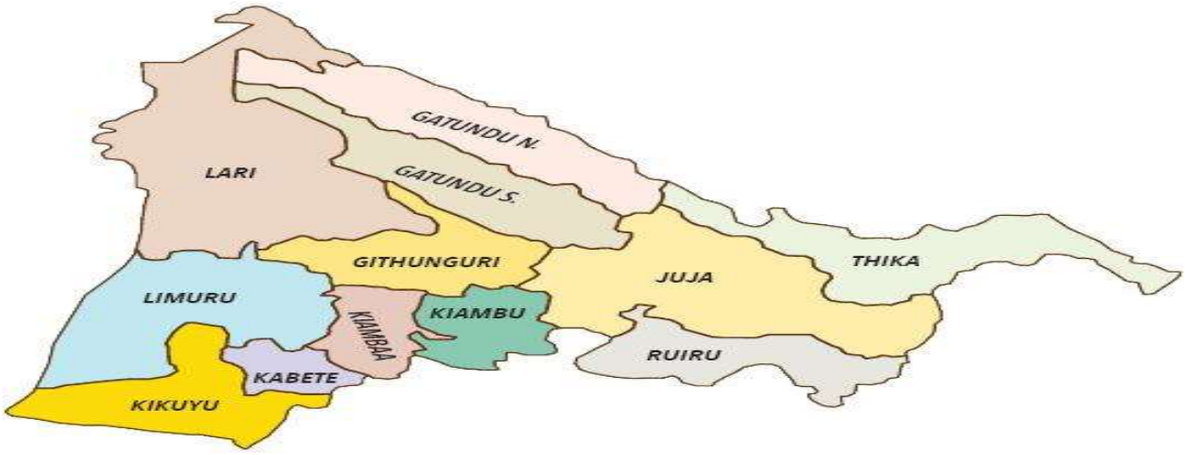


Figure 2:
Map of the sub-counties in Kiambu County



Context: Though patient management is reported at county level, patients are free to be tested in one county, and receive treatment in another. As such, a patient could be tested by the geneXpert at Thika level 5 hospital and therefore be recorded into GX-LIMS in Kiambu county and then go to a medical facility in Nairobi county for treatment and be notified into TIBU in Nairobi County

Study population: The study population are patients who were diagnosed as having TB using geneXpert seen in Kiambu County between 2012 and 2016 that have been captured by the GX-LIMS, and those notified in TIBU

Data collection: Data was extracted from both GX-LIMS and TIBU for the period of review. Databases were described using all the data found therein, but congruence was evaluated using only the Rifampicin resistance (Rif-resistance data). Only data for Kiambu County was extracted

Data management and analysis: TIBU has internal consistency checks to ensure that data entry errors are minimized. The National TB Program to ensure data consistency conducts quarterly data review meetings, data quality audits and biannual performance review meetings. The datasets from GX-LIMS and TIBU available in excel files were imported into STATA Version 13 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP) for cleaning using pre-developed cleaning do-files. Descriptive analysis was then done where continuous data were summarized by means (±SD) and Medians as appropriate. Categorical data was summarized using percentages. Due to the limited sample size(n=29), splitting the numbers further into different categories further reduces the sample size and limits our ability to compute error estimates. As such, the aim of the analysis was to provide a more descriptive rather than analytic or inferential picture. All this data was then presented using tables and graphs.

Ethics Approval: This study was approved by the Moi University College of Health Sciences (MU/CHS) and Moi Teaching & Referral Hospital (MT&RH) Institutional Review Board (IREC).

RESULTS

Within TIBU 17.9 %(2110) of those notified are aged 40-49yr, and 17.2%(2031) are 15-24 years. In GX-LIMS, 44.8 %(3568) of the tests done had no age indicated. In TIBU, 64.4%(7605) of those notified were male. In GX-LIMS, 56.1% (2464) were male. In TIBU, 65.9 %(7780) of those notified were HIV negative. In GX-LIMS, 61.2%(2702) had their HIV status as "not done", as in table 1.

Table 1

Demographic and Clinical indicators found both in TIBU and GX-LIMS in Kiambu County, 2014-2016

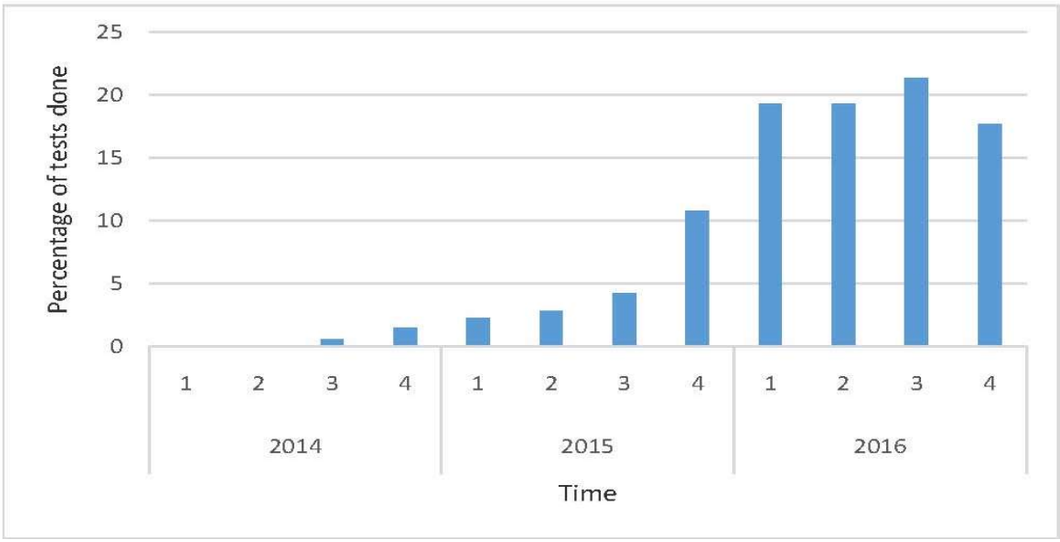
	TIBU (%)	**GX-LIMS (%)**
Age	(n=11787)	(n= 7967)
<5	4.1	1.7
5_9	1.4	1.4
10_14	1.4	1.5
15_24	17.2	6.6
25_29	14.9	6.3
30_34	15	7.9
35_39	13.7	7.3
40_49	17.9	11.6
>50	13.4	10.9
Missing	0	44.8
Sex	(n=11808)	(n=4392)
Female	35.6	43.9
Male	64.4	56.1
HIV Status	(n=11808)	(n=4417)
Declined	0.2	0.2
Not Done	5.1	61.2
Negative	65.9	7.9
Positive	28.8	30.8

A total of 7967 geneXpert tests were done in Kiambu County from 2014 to 2016 as documented in GX-LIMS. Of the 20 patient types described in GX-LIMS, 35.3% (1561) were new patients. There were no tests done in the quarter of 2014. In the second quarter of 2014, 7 (0.1%) were done. By quarter three of 2016, 1700 (21.3%) tests were done in as shown in figure 1.

Of the tests done, 1663(20.9%) tested positive. In the study period, 1663 Rif-resistance tests were done, 29(1.7%) of which were positive. A description of the TIBU database has been done elsewhere (5)

Figure 1

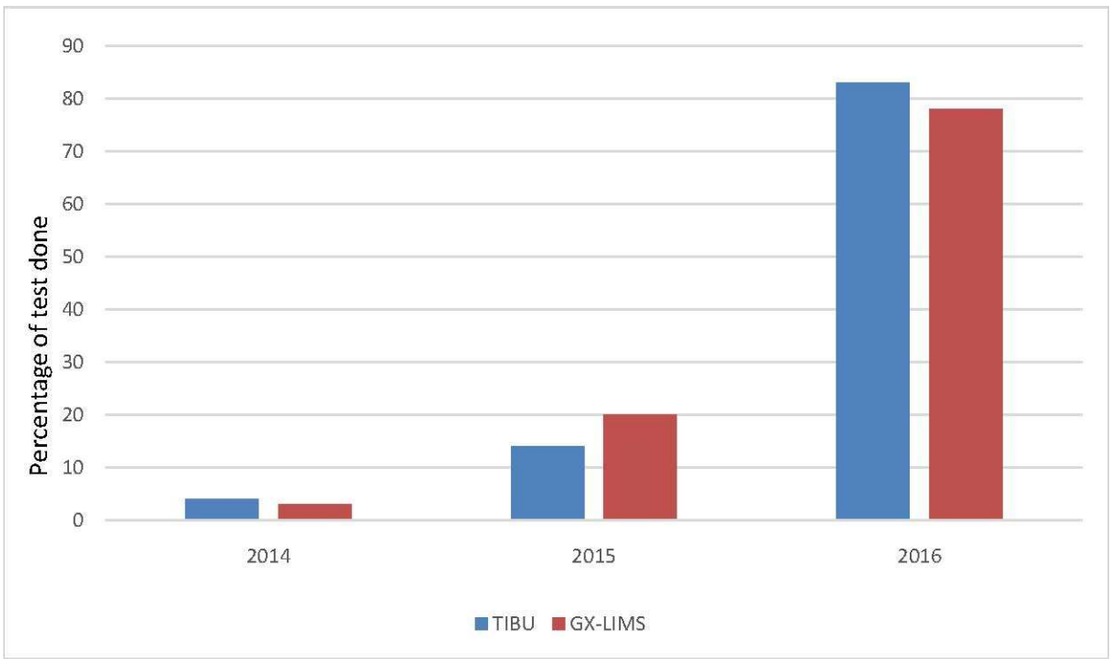
Quarterly Trend of geneXpert tests documented in the GeneXpert Laboratory Information Management System (GX-LIMS) in Kiambu County, 2014 to 2016.



In TIBU, of the 1541 patients notified based GX-LIMS, were in 2016 as shown in figure 2. 6186(78%) were also in 2016 as on geneXpert, 1272(83%)

Figure 2

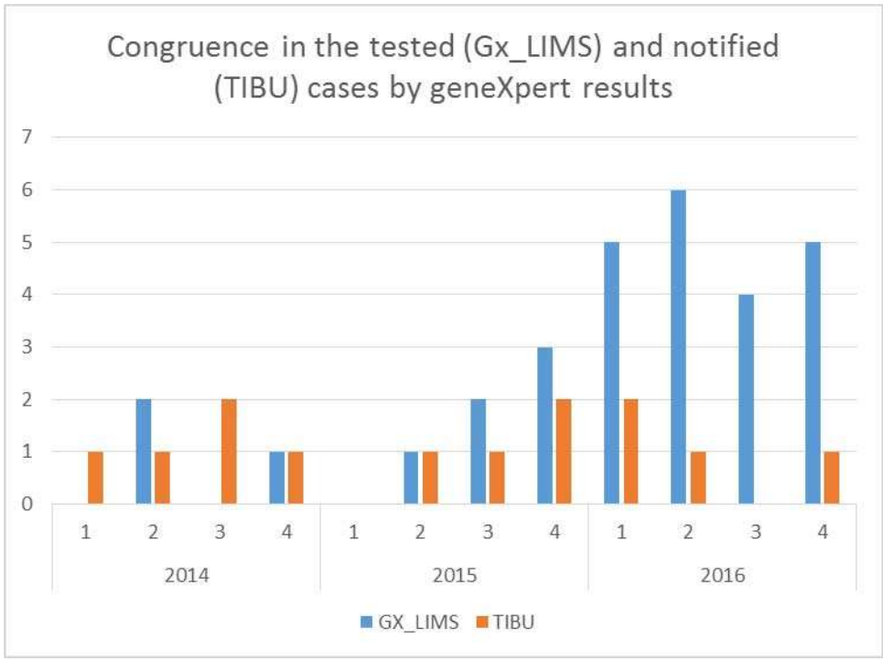
GeneXpert tests done as notified in TIBU and recorded on GX-LIMS in Kiambu County, 2014 -2016



In Kiambu County from 2014 to 2016, 29 quarter 4 and 2015 quarter 2 when one patients were diagnosed as having Rif-patient was diagnosed same period thereafter notified in TIBU as in figure 3. in TIBU, 13 were identified as having Rif-resistance. There was congruence in 2014 quarter 4 and 2015 quarter 2 when one patient was diagnosed in GX-LIMS and thereafter notified in TIBU as in figure 3.

Figure 3

Congruence in the cases of Rifampicin resistance tested in GX-LIMS and those notified in TIBU in Kiambu County, 2014-2016.



DISCUSSION

There is a gradual rise in the number of geneXpert tests done in Kiambu County from the third quarter of 2014 to the third quarter of 2015.The fourth quarter of 2015 and the first of 2016 saw the number of tests done increase by 78%. The gradual rise could be attributed to the increasing number of geneXpert sites in Kiambu County, with the sharp rise being due to the inclusion of Kiambu level 4 hospital which is the second largest hospital in the county.

As per the GX-LIMS data, one in five patients who had a geneXpert done was positive for TB. Of those positive, 1.7% had Rif-resistance. This is below 3.7% Rif-resistance rate found in the area classified as "low-risk" for drug resistance in Kwa Zulu-Natal (6). All (100%) of the patients who were TB positive also had a Rif-resistance test done.

The quality of data in GX-LIMS is poor. Majority of the tests done neither had age indicated, nor was the HIV test done. This is likely an issue of data entry into geneXpert since similar indicators in TIBU had no missing data. This can be explained by possible lethargy of laboratory staff to key in the relevant details for each patient.

They may have a huge workload as these staff are also involved in normal routine laboratory duties. Additionally, since GXLIMS is not as directly involved in patient managed as TIBU, there may not be proper supervision to ensure that the data collected is of high quality. In the study period, only twice in twelve quarters was there perfect congruence in the number of patients tested as being Rif-resistant in GX-LIMS and notified into TIBU. For the rest of the period, the trend was that more patients were tested than those notified. This could be explained by the stigma associated with TB(7) leading patients to seek diagnosis away from their homes. Additionally, proximity to Nairobi will have many patients from Nairobi going to geneXpert sites in Kiambu, but opting to have TB treatment sites closer to their homes. Finally, one cannot rule out the possibility of patients who after diagnosis are lost to follow-up and not started on treatment (8).

STRENGTHS AND LIMITATIONS OF THE STUDY

There was a lack of unique patient identifiers that could link patients in the TIBU and GX-LIMS databases. The use of names was not adequate due to duplication. Resultantly, further analysis and patient tracking, even from a national perspective looking across counties was not possible. However, this study on GX-LIMS is a first of its kind regionally. Additionally, both platforms have robust data quality assurance mechanisms. Due to the large sample size findings can be generalized to similar counties in Kenya and beyond in regions with similar settings. Finally, the study adhered to the (Strengthening the Reporting of Observational studies in Epidemiology) STROBE guidelines (9).

To improve the quality of data in GX-LIMS, the NTLD-P needs to clearly identify the role that this database plays in the management of TB in Kenya. Further, there is need for unique patient identifiers across the different databases. This will allow for all patients in GX-LIMS to be followed up in TIBU nationally, ensuring that all who test positive are tracked and put on treatment, regardless of where they are tested. Indicators included in GX-LIMS should complement those in TIBU, and additionally have a defined purpose in patient care. Laboratory technicians directly handling the geneXpert machines need sensitization to understand the importance of the geneXpert data. Regular data audits are required to ensure that the data is adequate.

In conclusion, GX-LIMS and TIBU are databases that ideally should complement each other and act as back-ups for each other in case one or the other was to fail, as well as be a mechanism for counter checking the accuracy of each other. From a programmatic perspective, all patients identified as being positive for TB on GXLIMS should be followed up to ensure that they are started on treatment and hence notified in TIBU.

This loss to follow-up has far reaching implications as these patients are often in the community at best considering where to go for treatment and at worst in denial and spreading the disease.

There is need, therefore, for the development of unique patient identifiers across platforms to allow for the identification and follow-up of patients at a programmatic level.

Conflict of Interest: None

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REFERENCES

1. World Health Organisation. The End TB Strategy [Internet]. Geneva; 2015. Available from: http://www.who.int/tb/End_TB_brochure .pdf?ua=1
2. Steingart KR, Schiller I, Horne DJ, Pai M, Boehme CC, Dendukuri N. Xpert® MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. Cochrane database Syst Rev. 2014;1.

3. Behr MA, Warren SA, Salamon H, Hopewell PC, Ponce De Leon A, Daley CL, et al. Transmission of Mycobacterium tuberculosis from patients smear-negative for acid-fast bacilli. Lancet. 1999;353(9151):444–9.
4. National Tuberculosis Leprosy and Lung Disease Program. National Strategic plan for Tuberculosis, Leprosy and Lung Health 2015 – 2018. Nairobi; 2014.
5. Mwancha-Kwasa C, Karumbi J, Kilonzo M., Gwako G, Ondieki D, Tanui L, et al. Variations in methods of diagnosis amongst patients at initiation of tuberculosis treatment in Kiambu County between 2012 and 2016.
6. Christine L. Heidebrecht, Laura J. Podewils, Alexander Pym, Thuli Mthiyane TC. Assessing Local Risk of Rifampicin-Resistant Tuberculosis in KwaZulu-Natal, South Africa Using Lot Quality Assurance Sampling. PLoS One [Internet].2016;Available from: http://journals.plos.org/plosone/article?id =10.1371/journal.pone.0153143
7. Courtwright A, Turner AN. Tuberculosis and Stigmatization: Pathways and Interventions. Public Health Rep [Internet]. 2010; Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/ PMC2882973/h
8. Tollefson D, Ngari F, Mwakala M, Gethi D, Kipruto H, Cain K, et al. Under-reporting of sputum smear-positive tuberculosis cases in Kenya. INT J TUBERC LUNG DIS [Internet].2016;Availablefrom:https://www.ncbi.nlm.nih.gov/pubmed/2 7725044
9. Von Elm, Erik; Altman, Douglas G; Egger, Matthias; Pocock, Stuart J; Gøtzsche, Peter C; Vandenbroucke JP.The Strengthening the Reporting of Observational Studies in Epidemiology(STROBE)statement: guidelines for reporting observational studies. Lancet [Internet].2007;Availablefrom:http://www.thelancet.com /pdfs/journals/lancet/PIIS014067360761602X.pdf