Diagnosis and treatment of common infectious diseases in severely ill sub-Saharan African patients

Studies from a hospital floor

Bos, J.C.

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Chapter 2

Tuberculosis diagnostic process management of patients in a referral hospital in Mozambique in comparison with the 2007 WHO recommendations for the diagnosis of smear-negative pulmonary tuberculosis and extra-pulmonary tuberculosis

Bos JC, Smalbraak L, Macome AC, Gomes E, van Leth F, Prins JM

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Abstract

Background In sub-Saharan African countries with large numbers of HIV positive tuberculosis (TB) patients, the high proportion of smear-negative pulmonary TB (SNTB) and extra-pulmonary TB (EPTB) continues to contribute to a delay in TB diagnosis and treatment. Information about the clinical management of individuals with presumptive TB in this setting is however limited. We evaluated the TB diagnostic process of adult patients with presumptive TB in a referral hospital in Mozambique according to the 2007 WHO recommendations for the diagnosis and treatment of SNTB and EPTB in HIV prevalent and resource-poor settings.

Methods This is a retrospective, cross-sectional study, using medical records of patients admitted in June and July 2009.

Results Overall, 514 patient records were screened, providing 234 presumptive TB patients. There were 70 deaths (29.9%). The evaluation of danger signs was never complete. HIV status was known for 175/234 (74.8%) patients, 140 (80.0%) of whom were HIV-positive. A sputum smear microscopy (SSM) result was obtained for 59/234 (25.2%) patients. SSM results were positive in 8/59 (13.6%) patients. Chest radiography was done in 150/234 (64.1%) patients and 103 were abnormal (68.7%). A total of 66 patients (28.2%) received TB treatment.

Conclusion The TB diagnostic process in this Mozambican hospital remained largely incomplete according to the WHO recommendations and few patients with presumptive TB were identified as TB patients. Deficiencies as described should prompt reconsideration of WHO guideline implementation with an emphasis on health system strengthening as well as on guideline contents and feasibility.
**Introduction**

Tuberculosis (TB) is responsible for the majority of deaths among HIV-infected adults. Sub-Saharan African countries have been severely affected by the HIV epidemic and up to 70% of patients with TB in this part of the world are co-infected with HIV.\(^1\) TB/HIV co-infected patients have higher mortality rates than HIV-uninfected TB patients. In HIV high-prevalence settings, the disproportionate increase of smear-negative pulmonary TB (SNTB) and extra-pulmonary TB (EPTB) is thought to contribute significantly to a delay in TB diagnosis and treatment, especially among patients with advanced HIV infection.\(^2\) In order to tackle this delay, the WHO revised its algorithm for the diagnostic handling of presumptive SNTB in HIV prevalent resource-constrained settings in 2007, and expanded case definitions for EPTB.\(^5\) Nevertheless, for SNTB, diagnosis and TB treatment initiation decision-making continue to rest mainly on the detection of acid-fast bacilli (AFB) in sputum, and on the interpretation of radiologic features on the chest radiograph (CXR), diagnostic tools with low sensitivity and low specificity as well as high inter-reader and intra-reader variability, respectively.\(^6\) With the use of Xpert MTB/RIF molecular testing, which was recommended by the WHO in 2011, a more sensitive diagnostic tool can be introduced at a larger scale in some areas, although many sites continue to depend on the clinical-radiological algorithm.\(^8\) As for EPTB, a clear algorithm is lacking altogether.

The performance of the 2007 WHO algorithm has been evaluated in ambulant as well as in seriously ill patients. A South African study was able to demonstrate improved survival after the introduction of the algorithm through earlier TB treatment initiation, but both this study and a Kenyan evaluation acknowledged the presence of serious limitations in the diagnosis of SNTB in the absence of a sensitive, point-of-care diagnostic test.\(^9\)\(^,\)\(^10\)

Importantly, information about how health systems in TB/HIV high-burden countries actually deliver services in the light of these weaknesses is sparse.\(^11\) Little is known about the capacity of health care facilities to follow the proposed TB diagnostic process, whereas inadequacies in this process may have significant negative effects on TB diagnosis and treatment delay, and, ultimately, on mortality. Mozambique ranks amongst the countries with the highest TB burden, with an estimated prevalence of 490 per 100 000 population/year and with 60% of tested TB patients being HIV-positive.\(^1\) At the same time, TB case detection rate is low (34%) and healthcare worker capacity and TB laboratory capacity are limited. In Mozambique, there is a similar lack of information about the diagnostic management of persons with presumptive TB, where such information could serve as a starting point for local policy change. *Hospital Central da Beira* (HCB), Beira, Mozambique, is the second
largest governmental referral hospital in the country. It was one of the first hospitals to offer HIV testing and antiretroviral treatment (ART) and it continues to manage high numbers of HIV-infected patients with presumptive TB.

The aim of our study was to evaluate the clinical TB diagnostic process of adult patients who were admitted with presumptive TB to the internal medicine wards of HCB in Beira, Mozambique, whilst investigating the extent to which the TB diagnostic process and subsequent TB treatment assignment matched with the 2007 WHO recommendations for the diagnosis of SNTB and EPTB in resource-poor HIV-prevalent settings.

**Methods**

**Study area**

This study was conducted at the HCB, a 733-bed governmental health facility. The HCB has 260 internal medicine beds, admitting up to 1500 patients monthly, and a separate TB ward with another 50 beds, admitting 10-20 patients each month. HCB is located in the coastal capital of the central Sofala Province. A network of health centres throughout the country delivers primary care, whilst hospitals such as HCB serve as provincial referral healthcare institutions, providing care for a population of 1.7 million living in Sofala province. However, patients may present directly to HCB. Until 2010, HCB performed the detection of AFB as the only TB-specific diagnostic procedure and TB culture was only available in the national TB reference laboratory in Mozambique’s southern capital of Maputo and could therefore only be done in selected individual cases and whenever drug-resistant TB was suspected. In the HCB, the equipment and technique for sputum induction with hypertonic saline and flexible bronchoscopy are not available.

Mozambican hospitals use a national routine (‘opt out’) HIV testing policy, which includes routine informed HIV testing for all patients during hospital admission, unless declined. Patients diagnosed with TB in the hospital start TB treatment on the ward and, once discharged, are referred back to their nearest health center for follow-up.

**Study design**

A cross-sectional study using patient records from consecutive patients at discharge on two of the four internal medicine wards in HCB was performed. One female and one male ward were randomly selected. Patient records of all discharged patients were reviewed daily during a 7-week period in June-July 2009. Discharge included transfer to other hospital wards or to other healthcare facilities, as well as death.
Data on patient demographics, HIV status, reason for admission and final diagnosis were collected from all patient records.

Patient records containing specific clues that would raise suspicion of incident TB were selected for further review. A patient was defined as a patient with presumptive TB when one or more of the following clues for incident TB were recorded in a patient record: TB diagnosis on admission or at discharge; taking TB treatment on or during admission; TB-specific diagnostics done at any time during admission; or the presence of a chronic respiratory syndrome, with or without the specific mentioning of TB presumptive diagnosis by the attending medical officer. A chronic respiratory syndrome was defined as any cough, chest pain or difficulty with breathing that lasted for ≥2 weeks preceding admission. A presumptive TB diagnosis was defined as the mentioning of TB as a possible diagnosis as stated anywhere in a patient record by the attending medical officer. Patient records of patients with presumptive TB were evaluated for TB diagnostic process measures, TB diagnostic test results and subsequent TB treatment.

**Ethical approval**

Ethical approval was obtained from the Mozambican National Committee of Bio-Ethics, through its subcommittee, seated in Beira (ref. nr.: 001/10/SCBE). In addition, a letter of support was obtained from the general director of HCB.

**Data management and analysis**

The clinical diagnostic workup of a patient with presumptive TB was evaluated for the inclusion of four basic steps in the 2007 WHO algorithm for the diagnosis of TB in seriously ill patients in HIV-prevalent settings: (i) evaluation of the presence of danger signs through the baseline measurement of body temperature, respiratory rate, pulse rate and ambulatory state measurement; (ii) obtaining an HIV test result; (iii) obtaining a sputum smear microscopy (SSM) result; and (iv) performance of a CXR. CXRs were reviewed by an experienced study physician, who was blinded to the patient’s clinical background. Any abnormal CXR was considered to be suspect for active TB. Furthermore, obtaining other TB-specific as well as TB-non-specific diagnostic test results was documented. Other TB-specific diagnostic tests included needle aspiration cytology, biopsy Ziehl-Neelsen staining and histology, and TB culture. Non-specific TB diagnostic tests were defined as pleural, ascitic, pericardial or spinal fluid analysis. Pleural, pericardial and ascitic fluid analysis was considered positive when the white blood cell count (WBC) differential analysis showed ≥50% lymphocytes and the total protein level was >30 g/L or the protein fluid/blood ratio was >0.5. In the case of spinal fluid analysis, a test was considered positive when the protein liquor/blood ratio was >25×10⁻³.
A patient’s workup matched the WHO recommendations when the evaluation of the presence of danger signs, obtaining an HIV test result, a TB-specific test result and a CXR had all been performed. A workup of a patient with presumptive TB did not match WHO recommendations whenever one of the aforementioned steps was missing or incomplete. TB treatment variables including final hospital diagnosis, TB treatment initiation and TB treatment according to TB diagnostic test results were subsequently evaluated for all patients with presumptive TB.

Data were analyzed using STATA v.12 software (StataCorp LP, College Station, Texas, USA). Differences in the distribution of categorical variables between TB suspect patients with and without a chronic respiratory syndrome were compared using $\chi^2$ analysis where appropriate. A p-value <0.05 was considered significant.

Results

Study population

A total of 514 patient records were reviewed and 234 (45.5%) met the criteria for patients with presumptive TB (Table 1). The median age was 36 years (IQR: 27-44 years) and 137/234 patients (58.5%) were female. Of the 234 patients with presumptive TB, 114 (48.7%) were mentioned to have a chronic respiratory syndrome on admission and 48 (20.5%) were on ART on admission. 70/234 patients (29.9%) with presumptive TB died during their hospital stay.

TB diagnostic process

Evaluation of danger signs: Body temperature was evaluated in 147/234 cases (62.8%) cases and was the most frequently evaluated baseline measurement. A patient’s ambulatory state was never evaluated (Table 2). HIV test result: HIV status was known for 175/234 patients (74.8%) with presumptive TB, among which 140 (80.0%) patients were HIV-positive.

SSM result: SSM was requested for 93/234 patients (39.7%) and a result was obtained for 59/234 patients (25.2%) (Figure 1). Of 93 SSM requests, 34 (36.6%) were left without a result, although possible reasons for this lack were not mentioned in the patient’s file. Only 8/59 (13.6%) SSM results were positive. Transfer to the TB ward took place for six patients with a positive SSM 3-9 days after admission, whereas the remaining two patients remained on the ward: one patient died on the ward without TB treatment after 8 days of hospital stay and the other patient was diagnosed with pneumonia and was sent home without TB treatment after 7 days. A total of 175/234 patients (74.8%) either had no positive SSM result or no SSM result at all. There was no difference between patients with and without a chronic respiratory syndrome with regard to the total amount of requested SSMs.
[49/114 (43.0%) and 44/120 (36.7%); p=0.65] and with regard to the SSM positivity rate [4/27 (14.8%) and 4/32: 12.5%; p=0.54).

**Chest radiography:** A CXR was done for 150/234 patients (64.1%), of which 103 (68.7%) were abnormal, and therefore suspect for incident TB. In this group, 20/103 patients (19.4%) had unilateral pleural effusion and 9/103 patients (8.7%) either had cavitary or miliary disease, all radiologic abnormalities generally regarded as being highly consistent with active TB. The proportion of abnormal CXRs did not differ according to the presence or absence of a chronic respiratory syndrome [56/85 (65.9%) and 47/65 (72.3%); p=0.4].

**Table 1. Patient characteristics.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All (n=514)</th>
<th>Presumptive TB (n=234)</th>
<th>No presumptive TB (n=280)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) [median (IQR)]</td>
<td>36 (27-48)</td>
<td>36 (27-44)</td>
<td>38 (27-50)</td>
</tr>
<tr>
<td>Female</td>
<td>309 (60.1)</td>
<td>137 (59.1)</td>
<td>172 (61.0)</td>
</tr>
<tr>
<td>HIV test result - positive</td>
<td>333 (64.8)</td>
<td>175 (74.8)</td>
<td>158 (56.4)</td>
</tr>
<tr>
<td>Chronic respiratory syndrome</td>
<td>-</td>
<td>114 (48.7)</td>
<td>-</td>
</tr>
<tr>
<td>ART</td>
<td>76 (14.8)</td>
<td>48 (20.7)</td>
<td>28 (9.9)</td>
</tr>
<tr>
<td>Death</td>
<td>164 (31.9)</td>
<td>70 (29.9)</td>
<td>94 (33.3)</td>
</tr>
</tbody>
</table>

Data are in n (%) unless otherwise stated. IQR: interquartile range; ART: antiretroviral treatment.

**Other TB-specific diagnostic tests:** Other TB-specific test results were obtained for 4/234 patients (1.7%) with presumptive TB. Three results were biopsy histology reports and one was a TB culture result. Only one biopsy result confirmed a TB diagnosis. The single TB culture result came back negative.

**Non-specific TB diagnostic tests:** Although analysis of bodily fluids was requested for 17 patients with presumptive TB (7.3%), only one (0.4%) patient had a complete test result with a lymphocyte count as well as either a protein level or a protein ratio.

None of the workups of patients with presumptive TB were complete according to WHO recommendations, whilst a total of 32/234 (13.7%) included an SSM result as well as a CXR.
**Table 2.** TB diagnostic process analysis for patients with presumptive TB (n=234).

<table>
<thead>
<tr>
<th>TB diagnostic workup step</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Danger signs complete evaluation respiratory rate</td>
<td>75 (32.1)</td>
</tr>
<tr>
<td>Body temperature</td>
<td>147 (62.8)</td>
</tr>
<tr>
<td>Pulse rate</td>
<td>99 (42.3)</td>
</tr>
<tr>
<td>Ambulatory state</td>
<td>0 (0)</td>
</tr>
<tr>
<td>HIV test result present</td>
<td>175 (74.8)</td>
</tr>
<tr>
<td>SSM result requests</td>
<td>59 (25.2)</td>
</tr>
<tr>
<td>Other TB specific tests</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>NAC</td>
<td>0 (0)</td>
</tr>
<tr>
<td>BPZN</td>
<td>0 (0)</td>
</tr>
<tr>
<td>BPA</td>
<td>3 (1.3)</td>
</tr>
<tr>
<td>TB culture requests</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>TB non-specific tests</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Lumbar punction</td>
<td>9 (3.9)</td>
</tr>
<tr>
<td>Pleural tap</td>
<td>4 (1.7)</td>
</tr>
<tr>
<td>Ascitic tap</td>
<td>4 (1.7)</td>
</tr>
<tr>
<td>Pericardial tap</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

**Figure 1.** TB treatment assignment of patients with presumptive TB according to sputum smear microscopy and chest radiography result.

TB diagnosis and treatment

Among patients with presumptive TB, a total of 66/234 (28.2%) received TB treatment. There was no difference between patients with and without a chronic respiratory syndrome with regard to receiving TB treatment [25/114 (21.9%) and 41/120 (34.2%); p=0.65]. Of 66 patients receiving TB treatment, 48 (73%) had a TB
diagnosis at discharge. Moreover, 30/66 patients (45%) were already on TB treatment on admission and continued this treatment throughout their hospital stay without modification. The 36 patients who initiated TB treatment during admittance started treatment at an average 7.4 days (range 1-30) after admission.

Of the eight patients with a positive SSM result, six (75%) received TB treatment (Figure 1). In the large remaining group of 226 patients without a (positive) SSM result this number was 60 (26.5%). Of the 226 patients without a (positive) SSM result, 96 (42.5%) had an abnormal CXR, of which 25 (26%) were assigned to TB treatment; for the 47/226 patients (20.8%) who had a normal CXR and the 83/226 patients (36.7%) who had no CXR at all, these numbers were 10/47 (21.3%) 25/83 (30.1%), respectively. Among the nine patients with cavitory or miliary disease, six (66.7%) patients were assigned to TB treatment.

The only patient with a lymph node biopsy result confirming a TB diagnosis was put on TB treatment.

**Discussion**

This study is the first Mozambican study to report on in-hospital TB diagnostic process management and one of few sub-Saharan African efforts to evaluate this topic. It clearly demonstrates that diagnostic process management according to the 2007 WHO recommendations in a referral hospital in Mozambique, is poor. For a large group of patients with presumptive TB, TB-specific, as well as TB-non-specific test results did not become available during the whole of a patient's hospital stay. In the absence of a (positive) TB-specific test result, the TB diagnosis and treatment decision-making process remained largely unclear, with a small proportion of patients with presumptive TB being identified as TB patients, even when CXR results were compatible with incident TB.

Our study population consisted of adults with an estimated high HIV prevalence. The in-hospital mortality among patients with presumptive TB was high, but was similarly high in the non-presumptive TB group. This is likely to be due to a high prevalence of other severe, HIV-related disease, such as cryptococcosis, malignancies and invasive bacterial disease, although we can certainly not exclude that a considerable number of patients in the non-presumptive TB suspect group was in fact suffering from TB. Among patients with presumptive TB, the use of ART was common and this raises the question whether incident TB may have been overlooked during the phase of ART initiation. A substantial number of presumptive TB patients was already on TB treatment on admission. Although this could indicate that patients were admitted for non-TB-related disease, there were only two patients
in this group that did not have criteria for incident TB other than being on TB treatment. This observation is of concern, as it may be an indication for the presence of drug-resistant TB.

The baseline evaluation of danger signs was largely incomplete, and individual vital signs were done for less than one-half of the patients with presumptive TB. Obviously, this negatively impacts clinical assessment and follow-up of patients in general. We did not include process measures such as the availability of medical equipment in our study, but it is our observation that there is a lack of (adequate) equipment, such as thermometers, scales and blood pressure meters. Despite the use of the routine ‘opt-out’ HIV testing policy, HIV status remained unknown for many patients throughout their hospital stay. Although the HIV screening coverage appeared to be somehow better among presumptive TB patients, still, an important opportunity to target HIV care and treatment was probably lost.

A striking absence of SSM results was observed in 75% of the patients with presumptive TB owing to lacking SSM requests and a failure to retrieve SSM results. One could argue that a large group of presumptive TB patients may in fact have been presumptive EPTB patients and that therefore the amount of SSM requests was low. Although we cannot exclude this, the low yield of SSM results found in patients with a chronic respiratory syndrome does not support this. In addition, the amount of other TB-specific and non-specific test requests and results was also low. Although data providing information about possible causes of the absence of SSM results were not collected, we suppose that various explanations exist, such as poor sputum production in individual (very ill) patients, inadequate sputum-obtaining procedures, sputum sample transport delays and compromised (administrative) handling of sputum samples, including the reporting of the results.14

Finally, a CXR was missing for approximately 40% of patients with presumptive TB, whereas the CXR is a proposed diagnostic tool in the WHO algorithm for the diagnosis of PTB as well as EPTB. We suspect that several factors play a role in the cause of this gap, namely: necessary chemical products being out of stock, dysfunctional equipment, patients presenting in the hospital when radiologic services are not available, and, not unimportantly, hesitation and delay in the severely ill, who’s CXRs can only be done with proper assistance during (transport to) radiologic procedures.

In our study population, neither a positive SSM result alone, nor any SSM result in combination with a positive CXR would prompt TB treatment initiation. Adding other positive TB-specific or non-specific test results to the equation did not alter
this picture. The fact that a positive CXR did not guide TB treatment initiation does not have to come as a surprise, as there is no consensus about the true value of the CXR in pulmonary TB and EPTB diagnosis in the severely ill, and the CXR appearance can vary according to the degree of immune suppression in HIV-infected patients with confirmed TB.\textsuperscript{15} In diagnostic workups of severely ill patients with a high suspicion for TB, especially in an HIV-prevalent setting where many severe opportunistic diseases may present with radiologic abnormalities, CXR results are not very likely to prove or exclude incident TB.\textsuperscript{16} The diagnostic value will therefore also depend on agreement about the use of CXR results in the decision-making process: either a low-threshold strategy that labels a large range of radiologic abnormalities as suspicious of TB, or a high-threshold strategy limiting such suspicion to a select group of abnormalities that have proven to be more specific for active TB. In the current study, we chose a low-threshold strategy, although we did perform a separate analysis for patients with CXR abnormalities generally regarded as being highly specific for incident TB, such as a miliary pattern and the presence of cavities. Also here, the presence of strong evidence for incident TB did not result in a uniform-decision making process with regard to TB treatment initiation. Clearly, for this study population, a CXR interpretation strategy with a subsequent TB treatment assignment policy was missing. It is important to mention that the 2007 WHO guidelines do not contain specific information guiding clinicians in this respect other than the need to use ‘sound clinical judgment’ when confronted with ‘suggestive CXRs’ in TB suspects with negative sputum results. Based on the current study results and on other reports about the difficulty of CXR interpretation in a setting where TB-specific diagnostic tools are sparse, we feel that the positioning of the CXR in the TB diagnostic process needs to be much more clearly defined.

There are disturbing similarities between the results of this study and results recently presented in a Malawian review set in a tertiary hospital. Where we found approximately 75% of TB-specific test results and 40% of CXRs to be missing. the Malawian study demonstrated that SSM results and CXRs were missing for approximately 50% and 60% of presumptive pulmonary TB patients, respectively.\textsuperscript{17} Investigators in this study also found that as little as 3% of presumptive SNTB suspects eventually received TB treatment, and that of 11 patients with a CXR suggestive of TB, only two were started on TB treatment. The proportion of patients with presumptive TB receiving TB treatment in the current study was higher at 28%, but this included a substantial number of patients already on TB treatment on admission. There was an important difference between this study and the Malawian one in that the latter focused on presumptive pulmonary TB patients only, whereas the current study also included patients with presumptive EPTB, a group that is
thought to contribute substantially to the high numbers of patients with presumptive TB found in HIV/TB co-infected patients. A South African study examining medical records of deceased patients with a ‘TB Process-Based Performance Review tool’ to identify missed opportunities for early and accurate TB diagnosis in four different hospitals found that SSMs and CXRs were omitted in up to 85% and 38%, respectively.\(^1\) Finally, a prospective Zimbabwean study investigating hospital TB services for patients with presumptive TB in four local referral hospitals in 1999 reported severe shortcomings in the diagnostic in-patient process.\(^2\) Although this study only provided general process scores, it did demonstrate that diagnostic process deficiencies go hand in hand with structural deficiencies.

Apparently, severe inadequacies in the local implementation of proper TB diagnostic policies with subsequent poor in-hospital TB diagnostic service delivery is neither limited to one country, nor to one health care facility. This is an important observation as it may impact TB diagnostic and TB treatment delay to a significant extent, independent of the performance of TB diagnostic and TB treatment algorithms. According to the WHO, keeping health systems on track requires a strong sense of direction at all levels in the presence of health information, finances, health workforce capacity and regulated access to medical products. As for HCB in Beira and in Mozambique, we suppose that deficiencies exist in all of these health-system building blocks.\(^3\) We propose to continue to create (local) awareness through operational research followed by local policy change. At the same time, it may be rational to reconsider local feasibility of existing guidelines and discuss further expansion of criteria for severely ill patients with presumptive TB in resource-poor HIV-prevalent settings on a global level. A 2012 systematic review evaluating research on implementation of interventions in TB control in low- and middle-income countries clearly showed that there are substantial gaps in published evidence for the effectiveness of diagnostic algorithms for the rule-in or rule-out of SNTB.\(^4\)

There are limitations to our study. The study was based on patient record review and reflects TB case handling as performed and recorded by different responsible healthcare workers with different interpretations and motives that may or may not be (uniformly) recorded. The data may therefore be incomplete and not fully accurate. Also, we did not include an evaluation of local system errors and we can therefore not come up with evidence based, local recommendations for improvement. We do however believe that this study provides an important insight in the magnitude of local TB diagnostic process management deficiencies. Finally, we recognize that the sample size was small for the detection of differences in the distribution of SSM requests and CXRs between patients with presumptive TB with or without a chronic
respiratory syndrome. Other studies demonstrating a comparable absence of SSMs and CXRs in the diagnostic workup of presumptive PTB patients do however support the apparent lack of difference found in our study.\textsuperscript{17,19}

In conclusion, in this referral hospital in Mozambique, where the burden of HIV infection and TB is high, the diagnostic trajectory according to the 2007 WHO recommendations remains largely incomplete for most patients with presumptive TB, with a major lack of TB-specific- as well as non-specific test requests and results and CXRs. In the absence of a TB-specific test result and of a fixed CXR interpretation strategy, TB treatment assignment appeared to have been random, whilst treatment was started in only a small proportion of patients. Even when new sensitive TB diagnostic tools will become widely available in the future, inadequacies in the implementation of the whole of the TB diagnostic chain will have to be addressed more carefully, with an emphasis on health system strengthening as well as on guideline contents and feasibility.

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