

LETTER
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## Use of chest radiography in the 22 highest tuberculosis burden countries

To the Editor:

An estimated 9 million new tuberculosis (TB) cases and 1.5 million deaths were caused by *Mycobacterium tuberculosis* in 2013 [1], more than 80% of which occurred in the 22 highest TB burden countries (HBCs). Among the confirmed incident cases, 4.9 million were pulmonary TB (PTB), of which 58% were bacteriologically confirmed. For many of these cases, chest radiography (CXR) was used as an important tool for triaging, particularly in smear-negative patients, to select patients for further microbiological workup with culture or Xpert MTB/RIF (Cepheid, Sunnyvale, CA, USA) [2, 3]. For the diagnosis of 42% of PTB cases who were microbiologically negative, CXR was often used to support the clinical decision, particularly in children [1, 4].

CXR has high sensitivity 98% (95% CI 95–100%) for detecting abnormalities associated with PTB [5]. Due to its modest specificity 75% (95% CI 72%–79%), it is recommended that all patients with CXR suggestive of TB should have microbiological confirmation [6]. However, limited guidance is available for the optimised use of CXR in different algorithms (e.g. triage), which leaves room for varied clinical practice. In order to achieve the World Health Organization (WHO) End TB strategy goals, the current practice of CXR use in clinical care needs to be better understood and further optimised [4]. We conducted a survey to assess where and how CXR is used for TB control in the 22 HBCs.

This survey was conducted between December 2014 and March 2015 through a structured questionnaire with a mix of open and multiple-choice questions, covering topics such as use of CXR in the diagnosis of PTB and paediatric TB, frequency of use as a diagnostic test, cost, and major challenges associated with its use. Survey questions differentiated between use of CXR in the private and public sectors. The questionnaire was sent *via* email to one National TB Programme (NTP) representative, and two or three expert practitioners with extensive clinical experience either in the public or the private sector, or both, in each of the 22 HBCs. Respondents were instructed to focus on the "typical" use of CXR for TB diagnosis for different indications at different levels of the healthcare setting in the country with which they were familiar. We compared the responses with the recommendations on the use of CXR in national guidelines of the 22 HBCs [7]. As there was variability among respondents, the majority response was used and "inconsistent" was coded if no consensus was reached.

We contacted 200 representatives and received 77 (39%) completed surveys, with at least two responses from each of the HBCs. Given the limited responses from the private sector practitioners, we report here only on the use of CXR in the public sector. As shown in table 1, in 19 (86%) countries, CXR was an integral part of national guidelines for TB diagnosis, with 13 (59%) recommending CXR for all persons with presumed TB. South Africa, along with five other countries (86%), reported CXR to be used for further evaluation of TB only in a subset of patients, *i.e.* those who either cannot produce sputum, or have negative sputum smears or Xpert MTB/RIF results. Eight (36%) countries reported the use of Xpert MTB/RIF in all persons with suspected TB irrespective of CXR findings, whereas seven (32%) recommended using CXR as a triage test to select patients prior to testing with Xpert MTB/RIF. 10 (46%) countries reported that CXR was used for systematic screening, of which five (50%) used them for screening household contacts. 16 (73%) countries reported that trained readers only performed CXR interpretation, while others reported unknown or inconsistent results. Although CXR is not recommended as a sole tool for diagnosis of TB [6], Bangladesh and Cambodia reported that CXR was used as such in >50% of the cases and seven (32%) other countries reported that sometimes (10–50%) CXR was used as the only tool to diagnose TB.

Conventional (film-based) CXR was used in 19 (86%) countries and semidigital radiographs in two (9%) countries. Out of the 22 countries, none indicated use of a complete digital radiography system. CXR was most commonly used in district-level health centres (91%) and referral hospitals (86%). No country reported availability of CXR in microscopy centres; and only two (9%) countries reported availability in primary care clinics.

The WHO recommendations for TB diagnosis in children highlight that CXR is a useful diagnostic tool [8]. 13 (59%) countries confirmed this recommendation by WHO and valued CXR as crucial for the diagnosis of TB among paediatric patients [9]. 19 (86%) countries indicated that CXR is routinely used to

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TABLE 1 Usage of chest radiography (CXR) in the 22 high tuberculosis burden countries

| Country                     | Active case finding       | Integral component<br>of diagnostic<br>algorithms in NTP<br>guideline | How often<br>CXR used | Frequency of<br>prescribing ATT<br>solely based on<br>CXR findings | Use as an<br>adjunct test<br>for HIV | Availability of portable CXR | Availability of<br>computer aided<br>diagnostic<br>software | Average<br>price NTP<br>pays for CXR<br>USD | Routinely used<br>in diagnosis of<br>paediatric<br>patients |
|-----------------------------|---------------------------|---|-----------------------|--|--------------------------------------|------------------------------|---|---|---|
| Afghanistan                 | Inconsistent <sup>#</sup> | Yes, as a follow-up<br>for smear-negative<br>cases                    | Sometimes<br>(10–50%) | Sometimes  | Unknown                              | Yes                          | Inconsistent  | 1.50-3.00                                   | Yes   |
| Bangladesh                  | No <sup>¶</sup>           | Yes   | Often (>50%)          | Sometimes  | Yes                                  | Yes                          | Inconsistent  | 5.00-7.00                                   | Yes   |
| Brazil                      | Yes <sup>+</sup>          | Yes   | Sometimes<br>(10–50%) | Sometimes  | Yes                                  | Yes                          | No  | 4.63  | Yes   |
| Cambodia                    | Yes                       | Yes   | Often (>50%)          | Rarely   | Yes                                  | Yes                          | No  | Unknown <sup>§</sup>                        | Yes   |
| China                       | Yes                       | Yes   | Sometimes<br>(10–50%) | Sometimes  | Inconsistent                         | Yes                          | Yes   | 10.00-18.00                                 | Yes   |
| DRC                         | Yes                       | Yes   | Rarely<br>(<10%)      | Inconsistent   | Inconsistent                         | No                           | No  | 15.00-20.00                                 | Inconsistent  |
| Ethiopia                    | No                        | Yes   | Inconsistent          | Rarely   | Yes                                  | Unknown                      | No  | 3.00-5.00                                   | Yes   |
| India                       | No                        | Yes, as a follow-up for smear-negative cases                          | Rarely<br>(<10%)      | Rarely   | Yes                                  | Yes                          | No  | 1–4   | Yes   |
| Indonesia                   | No                        | Inconsistent  | Inconsistent          | Inconsistent   | Yes                                  | Yes                          | No  | 5.00  | Inconsistent  |
| Kenya                       | No                        | Yes   | Rarely<br>(<10%)      | Rarely   | Yes                                  | Yes                          | Inconsistent  | Unknown                                     | Yes   |
| Mozambique                  | No                        | Yes   | Inconsistent          | Sometimes  | Yes                                  | No                           | No  | 12.00                                       | No  |
| Myanmar                     | Yes                       | Yes   | Rarely<br>(<10%)      | Rarely   | Yes                                  | Yes                          | Inconsistent  | 5.00  | Yes   |
| Nigeria                     | No                        | Yes   | Rarely<br>(<10%)      | Sometimes  | Yes                                  | Yes                          | Inconsistent  | 5.00-15.00                                  | Yes   |
| Pakistan                    | Unknown                   | Yes, as a follow-up for smear-negative cases                          | Rarely<br>(<10%)      | Rarely   | Yes                                  | Yes                          | No  | 1.00-5.00                                   | Yes   |
| Philippines                 | Yes                       | Yes   | Sometimes<br>(10–50%) | Inconsistent   | Yes                                  | Yes                          | No  | 3.00-5.00                                   | Yes   |
| Russian Federation          | Yes                       | Yes   | Rarely<br>(<10%)      | Rarely   | Inconsistent                         | Yes                          | Inconsistent  | Unknown                                     | Yes   |
| South Africa                | No                        | No  | Sometimes (10–50%)    | Sometimes  | Yes                                  | Yes                          | No  | Unknown                                     | Yes   |
| United Republic of Tanzania | Unknown                   | Yes   | Inconsistent          | Sometimes  | Yes                                  | No                           | No  | 5.00-6.00                                   | Yes   |
| Thailand                    | Yes                       | Yes   | Inconsistent          | Sometimes  | Yes                                  | Yes                          | No  | 3.00-6.00                                   | Yes   |
| Uganda                      | No                        | Yes   | Rarely<br>(<10%)      | Sometimes  | Yes                                  | No                           | No  | 4.00-5.00                                   | Yes   |
| Vietnam                     | Yes                       | Yes   | Rarely<br>(<10%)      | Rarely   | Yes                                  | Yes                          | No  | 1.50-3.50                                   | Yes   |
| Zimbabwe                    | No                        | Yes   | Rarely<br>(<10%)      | Sometimes  | Yes                                  | Yes                          | No  | 20.00-30.00                                 | Yes   |

NTP: National Tuberculosis Programme; ATT: antituberculosis treatment; USD: US dollar; DRC: Democratic Republic of Congo. #: respondents provided discrepant results where no consensus could be reached; 11: the majority of respondents indicated CXR is used; 15: the respondents were unable to answer the question.

diagnose PTB in paediatric patients, with Mozambique being the only country reporting that it is not routinely used in paediatric patients.

Use of CXR for the purpose of monitoring response to therapy in all or most cases of PTB was reported in nine (41%) countries. However, as results from CXR has been shown possibly to be misleading for treatment monitoring purposes, the International Standard for Tuberculosis Care recommends CXR only as an adjunct for treatment monitoring that cannot replace microbiological evaluation [10]. Five (23%) countries follow these guidelines and use CXR for monitoring only in cases of smear- or culture-negative TB.

Respondents were asked about the average price for an NTP to conduct a CXR on a patient (interpretation not included). The cost varied greatly, with the median being US dollars (USD) 5.00 (interquartile range USD 7.50). Cost was also included as one of the major challenges (15 countries, 68%) for further rollout of CXR in addition to inadequate access to technology such as digital radiography/mobile vans (16 countries, 73%) and shortage of qualified readers such as radiologists (13 countries, 59%).

Overall, these results indicate that most countries are using CXR primarily for the diagnosis of sputum smear-negative PTB patients and paediatric patients, and as a screening tool to select patients prior to testing with Xpert MTB/RIF test. Conventional (film-based) radiographs are the most commonly used technology. Limited access to digital radiography technologies and trained readers were identified as major obstacles to greater use of CXR in TB control.

Our survey was not intended to collect data on every clinical setting in each country. We acknowledge that there may be large variations across different regions and settings within a country, and our data only reflect the typical use of CXR across different settings. The results, as such, may be overoptimistic, as we were not able to elucidate a clear picture from the even less regulated private sector. The limited response rate of 39% could be attributed to the requirement of an Internet connection and the fact that the survey was in English. A field study using the help of local workers to assess the current practice of CXR use in representative settings might allow for collection of more accurate results.

Despite the limitations of this study, the survey demonstrated the varied use of CXR in the diagnostic evaluation of TB suspects and in screening of high-risk populations, and an urgent need to develop guidelines to inform the best algorithms with CXR and strategies that overcome the barriers of cost and lack of human resources. Low-cost digital radiography and computer-aided diagnosis, if proven to be equal to or better than human readers, may have great potential to overcome the listed barriers. Furthermore, clear global and national policies must be put into place to assure standardised use of CXR.



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CXR is used widely in the 22 highest TB burden countries but we need strategies for cost and human resources http://ow.ly/RT7fq

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