**Supplemental Figure 1: Base case pre-Xpert algorithm for diagnosing TB among PLHIV who are not at high risk for MDR TB at sites without access to GeneXpert**

\* Contraindications to IPT include active hepatitis, heavy alcohol consumption and peripheral neuropathy

† If patient cannot produce sputum, diagnosis may be made using CXR and clinical assessment alone. Culture using a lymph node aspirate is also possible.

**Clinical assessment & smear microscopy (3x) & CXR†**

Smear-positive

Smear-negative; CXR suggestive of TB / clinical suspicion of TB

Smear-negative; CXR not suggestive of TB

Start TB treatment

 (Start/continue CPT & ART)

* Start IPT if no contraindications\*
* Refer to IPT algorithm

Start TB treatment

(Start/continue CPT & ART)

OI present; treat OI

**One of the following symptoms within the last 4 weeks:**

* Cough, anytime of any duration
* Fever, anytime of any duration
* 2 weeks or more of drenching night sweats
* Weight loss

No OI present; reassess for TB, as needed

No symptoms present

Evaluate for other OI;
Culture (sputum or lymph node aspirate)

Culture-positive

Culture-negative present

Patient can produce sputum

Patient cannot produce sputum

**Clinical assessment & CXR†**

TB diagnosed (clinical judgment)

No TB diagnosed

**Supplemental Figure 2: Post-Xpert algorithm for diagnosing TB among PLHIV who are not at high risk for MDR TB**

\* Contraindications to IPT include active hepatitis, heavy alcohol consumption and peripheral neuropathy

\*\* Refer to PLA algorithm of work up for diagnosing TB among PLHA without Xpert

**Gene-Xpert**

**(1 Sample, first sample)**

MTB detected

RIF resistance detected

MTB detected

RIF resistance not detected

MTB not detected

Start SLD empirical

 (Start/continue CPT& ART)

* Start IPT if no contraindications\*
* Refer to IPT algorithm

Any symptoms and patients can produce sputum

Start FLD

(Start/continue CPT& ART)

Chest X-ray

Clinical assessment\*\*

TB likely

Not likely TB

Refer to OI clinic

Culture & DST

(2 samples)

If not MDR-TB

If MDR-TB

Adjust regimen base on DST result

Continue MDR-TB regimen

**One of the following symptoms within the last 4 weeks:**

* Cough, anytime of any duration
* Fever, anytime of any duration
* 2 weeks or more of drenching night sweats
* Weight loss

If no clinical response with other treatment

=> repeat Xpert

No symptoms present

**Supplemental Figure 3: Base case pre-Xpert algorithm for diagnosing MDR TB, including PLHIV who are at high risk for MDR TB,at sites without access to GeneXpert**

**Do they have any one of the following criteria?**

* All pulmonary TB re-treatment cases
* Sputum non converter at month 2 or 3 of TB treatment
* Symptomatic close contacts of known MDR-TB

**Culture + DST (2x)**

MTB detected

Susceptible to all FLD

Start/continue FLD

(Determine HIV status & manage accordingly)

Continue/start MDR-TB regimen

(Determine HIV status & manage accordingly)

Confirmed

MDR-TB

Non MDR resistance

Adjust regimen based on DST result

(Determine HIV status & manage accordingly)

MTB detected

Resistance to any FLD

**Supplemental Figure 4: Post-Xpert algorithm for diagnosing MDR TB, including among PLHIV who are at high risk for MDR TB**

****

**Supplemental Box 1: Examples of per-procedure cost calculations by input type**

*Note: For each input category below, an example of a single input from that category is provided to illustrate the calculations used to attribute a share of the cost of that input to each procedure. The examples provided are not comprehensive of all inputs used in each procedure.*

Input: Personnel

**Cost per Xpert MTB/RIF test of lab chief technician time** = ($120 salary per month x 10% time per month spent on Xpert MTB/RIF tests)/40 Xpert MTB/RIF tests conducted per month = **$0.30**

Input: Single-use Supplies

**Cost per Xpert MTB/RIF test of test cartridge** = ($120 per pack/10 cartridges per pack) x 1 cartridge per Xpert MTB/RIF test = **$12**

Input: Multiple-use Supplies

**Cost per Xpert MTB/RIF test of disinfectant** = $8 per bottle/(3 months of use per bottle x 40 Xpert MTB/RIF tests conducted per month) = **$0.07**

Input: Equipment

**Cost per Xpert MTB/RIF test of GeneXpert 4-module instrument** = [($17,500 purchase price per instrument-($0 resale value/(1.03(5 years of useful life))))/4.5797 annuity factor based on 3% discount rate and 5 years of useful life]/(40 Xpert MTB/RIF tests conducted per month x 12 months) = [($17,500-($0))/4.5797]/(480) = **$7.96**

Input: Equipment maintenance

**Cost per Xpert MTB/RIF test of biosafety cabinet maintenance** = [$1,000 per year/(40 Xpert MTB/RIF tests conducted per month x 12 months)] x (100% use for Xpert MTB/RIF testing) = **$2.08**

Procedure unit cost in each evaluation site

Unit cost per Xpert MTB/RIF test = Sum of the cost per Xpert MTB/RIF test for each type of personnel, supplies, equipment, and equipment maintenance used in Xpert MTB/RIF testing at that site

**Supplemental Table 1. Unit costs per procedure assuming identical average monthly procedure volumes across sites (costs in 2017 U.S. dollars)\***

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Procedure** |  | **BTB** | **MKB** | **MR OD** | **CENAT** |
| **Clinical diagnostic assessment** | Unit Cost | US$1.84 | US$1.22  |  |  |
| *Procedure Volume* | *500* | *500* |  |  |
| **Chest x-ray, automatic development** **(\*manual development)** | Unit Cost | US$2.28 | US$2.14(US$2.06\*) |  |  |
| *Procedure Volume* | *200 (chest)**350 (all x-rays)* | *200 (chest)**350 (all x-rays)* |  |  |
| **Smear Microscopy – FM** | Unit Cost | US$2.54 | US$1.93 |  |  |
| *Procedure Volume* | *300* | *300* |  |  |
| **Smear Microscopy – ZN** | Unit Cost |  |  | US$1.26 |  |
| *Procedure Volume* |  |  | *140* |  |
| **Xpert** | Unit Cost | US$40.40 | US$37.11 |  |  |
| *Procedure Volume* | *25* | *25* |  |  |
| **Liquid Culture – MGIT** | Unit Cost | US$22.83 |  |  | US$20.50 |
| *Procedure Volume* | *112* |  |  | *112* |
| **Follow-on work up for positive MGIT results and MTB identification** | Unit Cost | US$14.72 |  |  | US$16.60 |
| *Procedure Volume**(Follow-on work-ups)* | *23* |  |  | *23* |
| *Procedure Volume**(MTB identification)* | *28* |  |  | *28* |
| **DST** | Unit Cost |  |  |  | US$44.26 |
| *Procedure Volume* |  |  |  | *23* |

*\* Assuming that both sites performed the monthly procedure volume of the lower-volume site; these hypothetical unit costs and volumes are highlighted.*

* ***BTB:*** *Battambang Provincial Referral Hospital;* ***MKB****: Mongkol Borei Provincial Referral Hospital;* ***MR OD:*** *Mong Russey Operational District Hospital;* ***CENAT:*** *National TB Control Program Lab*
* *At the time of the study, GeneXpert instruments did not operate at maximum possible capacity every day at either the BTB or MKB site due to low specimen volumes received.*

**Supplemental Table 2. Personnel cadre and share of monthly time per procedure at study sites**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Procedure** |  | **BTB** | **MKB** | **MR OD** | **CENAT** |
| **Clinical diagnostic assessment** | Clinician | 0.00313 | 0.00313 |  |  |
| Nurse | 0.00313 | 0.00104 |  |  |
| Volunteer | 0.00156 |  |  |  |
| **Chest x-ray, automatic development** **(\*manual development)** | Nurse | 0.00052 | 0.00052(\*0.00052) |  |  |
| Radiographer | 0.00133 | 0.00104(\*0.00143) |  |  |
| **Smear Microscopy – FM** | Nurse | 0.00200 |  |  |  |
| Cleaner | 0.00040 |  |  |  |
| Lab assistant |  | 0.00167 |  |  |
| Lab technician | 0.00034 | 0.00167 |  |  |
| Lab chief | 0.00024 | 0.00023 |  |  |
| Lab supervisor | 0.00001 |  |  |  |
| **Smear Microscopy – ZN** | Lab technician |  |  | 0.00121 |  |
| Lab supervisor |  |  | 0.00050 |  |
| **Xpert** | Lab assistant |  | 0.00500 |  |  |
| Lab technician | 0.00175 |  |  |  |
| Lab chief | 0.00300 | 0.00280 |  |  |
| Lab supervisor | 0.00006 |  |  |  |
| **Liquid Culture – MGIT** | Lab technician | 0.00035 |  |  | 0.00042 |
| Lab chief | 0.00024 |  |  |  |
| Lab supervisor | 0.00001 |  |  | 0.00046 |
| **Follow-on work up for positive MGIT results and MTB identification** | Lab technician | 0.00070 |  |  |  |
| Lab specialist |  |  |  | 0.00031 |
| Lab chief | 0.00028 |  |  |  |
| Lab supervisor | 0.00001 |  |  | 0.00092 |
| **DST** | Lab specialist |  |  |  | 0.01304 |
| Lab supervisor |  |  |  | 0.00120 |

* ***BTB:*** *Battambang Provincial Referral Hospital;* ***MKB****: Mongkol Borei Provincial Referral Hospital;* ***MR OD:*** *Mong Russey Operational District Hospital;* ***CENAT:*** *National TB Control Program Lab*