ABSTRACT

Background: While the incidence of tuberculosis (TB) is declining globally, the rate of decline is far too slow to meet the 2035 end TB targets. Use of rapid molecular diagnostics that can be deployed in peripheral settings has the potential to address gaps in TB care cascade, improve case detection, and ultimately limit the on-going transmission of the disease.

Methods: We assessed the costs and affordability of 2 commercial nucleic acid amplification test (NAAT)—loop-mediated isothermal amplification assay for TB (TB-LAMP) and Xpert MTB/RIF (Xpert)—used at the peripheral laboratories in Malawi and Vietnam. Costs were assessed from the health service provider perspective using bottom-up method. Categorized documentation of resources uses for each diagnostic test was done using a standardized time-and-motion form directly observing each laboratory procedure. Affordability was assessed as a proportion of total first-year implementation and operational costs of respective diagnostics against the national TB program budget for 2014.

Results: Unit costs of TB-LAMP and Xpert varied depending on the daily test volumes and the test kit costs were the primary cost driver. Unused equipment capacity costs were also an important cost driver at low testing volumes and was more significant for Xpert. Weighted average per-test cost of nationwide implementation of respective diagnostics was between $14.37–$15.85 for TB-LAMP and $20.06–$26.86 for Xpert for Vietnam and Malawi. Both NAATs would account for a significant portion of or exceeded the national TB program budget if complete nationwide roll-out to peripheral laboratory were considered.

Conclusion: While TB-LAMP is a lower cost alternative to Xpert as an upfront NAAT for TB in peripheral settings, cost-utility against Xpert and other alternatives and optimized implementation strategies must be carefully evaluated through additional model-based studies to better inform policy and program decisions to expand the coverage of rapid diagnostics for TB.

Keywords: Cost analysis; Affordability; Diagnosis; Nucleic acid amplification techniques; Tuberculosis
INTRODUCTION

Although the global incidence of tuberculosis (TB) is declining, it continues to be the top single most infectious disease cause of deaths globally, with more than 10 million people impacted by the disease and an estimated 1.6 million people dying from TB (300,000 among human immunodeficiency viruses [HIV]-positive people). This phenomenon is largely driven by countries with highest TB burdens where delays in diagnosis and linkage to proper care continue to fuel disease transmission and undermine TB control efforts. Likewise, introduction of novel technologies and public health interventions that can improve delays in the TB care cascade are critical in achieving the 2035 end TB targets.

The majority of countries facing the highest TB disease burden are low-and-middle income countries where sputum smear microscopy (SSM) remains as a primary bacteriologic diagnostic tool in peripheral settings. While it is relatively cheap to perform, its performance is highly variable based on a technician’s experience, quality of the sample, and has limited diagnostic value for children, HIV-positive patients, and those suspected of drug-resistant (DR) TB. Xpert MTB/RIF assay (Xpert; Cepheid, Sunnyvale, CA, USA)—the first World Health Organization (WHO) approved commercialized cartridge-based nucleic acid amplification test (NAAT) utilizing a common GeneXpert testing platform—has widely been adopted by high TB burden countries, but its coverage and utility is limited to centralized locations (intermediate level laboratories or higher).

As an alternative to Xpert and as a replacement test for SSM, the LoopampTM MTBC Detection assay (loop-mediated isothermal amplification assay for TB [TB-LAMP], developed by Eiken Chemical Co., Ltd. Tokyo, Japan), a closed-tubed rapid NAAT for the detection of Mycobacterium tuberculosis, also received conditional recommendation by the WHO in 2016. Furthermore, testing procedures and hands-on involvement of laboratory personnel is no more complicated than that of Xpert. Considering its comparable diagnostic performance and favorable operational characteristics, TB-LAMP has the potential to address important gaps in the TB diagnostic cascade in high TB burden countries.

In this study we evaluated and compared the economic costs and affordability of nationwide implementation of TB-LAMP assay with that of Xpert in peripheral TB laboratories in 2 high TB burden countries—Malawi and Vietnam.

METHODS

Settings

We conducted a comprehensive cost analysis of TB-LAMP and Xpert assays performed in peripheral laboratories in Malawi and Vietnam from the health service provider perspective. We incorporated a time-and-motion (TAM) study to directly observe and quantify all resource use for every relevant laboratory procedure for each diagnostic. Empiric cost data of respective NAATs were collected at select peripheral TB laboratories operating within multi-functional primary care clinics (Ndirande in Malawi and Ung Hoa in Vietnam). Both laboratories performed 10–20 SSM tests per day (5 working days for Ung Hoa and 2 days for Ndirande for TB), which were medium to high workload laboratories. As independent diagnostic performance evaluation sites for TB-LAMP, these laboratories were the only laboratories in respective countries that were concurrently performing Xpert assays at the
time of our assessment (At Ndirande site, Xpert was being offered as a routine test for select patients based on national diagnostic guideline).

**Identification, measurement, and valuation of resources used**

We assessed the costs of each diagnostic test using a bottom-up costing method. Between February and April of 2015, we collected all data on relevant resources used to perform each test, including overhead (utilities, furniture, administrative, and operational costs) and building costs, staff salaries, laboratory equipment and capital assets, procurement costs of laboratory chemicals and consumables (Appendix 1). Actual resource-use data for each laboratory procedure was assessed based on the TAM study, using a standardized form completed by study staff directly observing and quantifying time and resources used for each step of the procedure diagnostic tests (Fig. 1). As laboratory staff members at the study sites did not experience with TAM study, our study staff provided a brief overview of goals and methods of the study prior to engaging in the data collection. The TAM study was conducted multiple times over several working days at each laboratory to observe varied batch sizes of patient samples under routine working conditions. To overcome generalizability and representativeness of our study site, we observed a range of minimum to maximum testing volumes reflective of daily workloads at a wide range of peripheral TB laboratories (between 1 and 14 tests) for the 2 diagnostics.

**Cost analysis**

For each batch size observed, unit cost was assessed based on the ‘ingredients’ approach multiplying the quantities of resource-use collected from TAM observations by unit cost/prices of each resource. Costs associated with the use of laboratory equipment, building space, and other capital assets directly and indirectly utilized for each test were assessed as time-associated costs (annuitized) based on their purchased-new prices (in 2014), expected useful life years (Appendix 2), and an annual discount rate of 3%. Overhead costs were allocated based on the total staff hands-on time (for administrative overheads) and total procedural time (for infrastructural overheads). For each testing volume, we assessed and added unused daily equipment processing capacity (56 for TB-LAMP and 16 for Xpert) to calculate overall unit cost of each diagnostic test. For example, if only 2 tests were performed

---

**Fig. 1.** Laboratory procedures for TB-LAMP and Xpert assays observed using TAM method. Sample preparation methods and testing/reaction steps for TB-LAMP and Xpert involved multiple procedural steps that were generalized to the ‘squares’ represented in the diagram above. Each ‘square’ represented independently observable continuously performed laboratory procedure for each diagnostic test. Resource-use data for each procedural step were collected based on direct observation and standardize time and motion forms. LAMP = loop-mediated isothermal amplification; TB-LAMP = loop-mediated isothermal amplification assay for tuberculosis; Xpert = Xpert MTB/RIF.

---

https://e-jghs.org

https://doi.org/10.35500/jghs.2019.1.e22
per day on average, we assumed a total of 6 hours out of possible 8 hours (75%) of useful
equipment operations as both tests have a total equipment run-time of 2 hours per batch/
test. The daily fraction of annual unused equipment capacity was then multiplied by the daily
cost of relevant laboratory equipment (e.g. GeneXpert IV system, $15.13 per day) to calculate
daily costs associated with unused equipment capacity (0.75 × $15.13 = $11.34). All costs
were evaluated based on 2014 United States Dollars (USDs); where data was available in local
currency, and conversion was done based on average UN exchange rate to the USD.16

To estimate weighted average per-test costs post nationwide roll-out of the test, we first
estimated the total number of peripheral laboratories in the respective countries:160
in Malawi and 920 in Vietnam, based on the WHO guideline for diagnostic coverage of
microscopy centers (1 per 100,000 population). Then we summarized workload categories
into 3 categories based on mean daily testing volumes: low (less than 4 tests), medium
(between 5 and 9 tests), and high (10 or more tests). Distribution of laboratories in respective
workload categories were assumed to be at 60%, 30%, and 10%, respectively, and were varied
for sensitivity analyses. We then multiplied volume-based average unit cost with estimated
proportion of peripheral laboratories in each workload category and summed these estimates
to compute weighted per-test cost.

Affordability analysis
Affordability of nationwide roll-out of TB-LAMP or Xpert was assessed as a percentage of
the total first-year operational costs of the nationwide implementation out of the reported
annual national budget for TB for 2014. For each test, the total first-year operational cost per
laboratory workload category was assessed using the budgeting table adapted from the WHO
Xpert implementation manual (Appendix 3),17 the estimated annual testing volume, and the
total number of peripheral laboratories in each workload category. The first-year operational
cost included procurement of necessary laboratory equipment (e.g. LF-160 incubator for
TB-LAMP and GeneXpert systems for Xpert), testing kits and laboratory consumables only.
For Xpert, we assumed all peripheral laboratories would procure 1 GeneXpert IV (GX4, with
capacity to test 16 test per day) system. We excluded costs associated with implementation
and recurrent training and quality assurance program costs as data was unavailable at the
time of our assessment.

Ethics
This study received approvals from local government authorities and organizations to review
financial records. No Institutional Review Board approval was needed as the study did not
utilize patient relevant information nor recruited patients for the study. Eiken Chemicals
Co., Ltd. and Cepheid did not provide any financial support and had no role in the designing,
analyzing, and writing of this manuscript.

RESULTS
Per-test costs for TB-LAMP and Xpert varied depending on daily testing volumes (Table 1).
Factoring all laboratory-based procedures, TB-LAMP cost between $10.39–$19.25 in Malawi
and $10.08–$17.55 in Vietnam for samples processed between 2 and 14 per operating day.
Differences in per-test costs for Xpert was greater between the low (1 sample) and high
volumes (14)—$13.40–$48.01 in Malawi and $13.49–$30.60 in Vietnam—due to high costs
associated with unused equipment capacity at lower testing volumes. Per-test costs were
higher in Malawi as a result of lower number of operating days for TB diagnosis (2 days per week) compared to Vietnam (5 days per week). This led to much greater unused equipment capacity costs in Malawi, where for Xpert, this figure was as high as $30.69 per test (more than twice the estimate for same test volumes in Vietnam).

The weighted national average per-test cost was significantly higher for Xpert than TB-LAMP in both countries: in Malawi, Xpert per-test cost was $11 more expensive (70% higher) than TB-LAMP. The differences in costs were mainly driven by high costs associated with unused equipment capacity for the GX4 system in low volume laboratories. As GX4 system can simultaneously test up to 4 samples per run (2 hours per run), daily test volumes higher than 4 tests requires for multiple runs. This resulted in consistently higher overhead, building space use, and staffing costs than TB-LAMP. For both tests, reagent and chemicals (mainly TB-LAMP test kit and Xpert cartridge) were the single largest cost driver (Table 2).

First-year implementation and operational costs of TB-LAMP were $8,427, $14,170, and $26,348 at a low, medium, or high-volume laboratory, respectively. For Xpert, these costs were more than 3 times higher ($27,627; $40,621; and $57,775, respectively) than for TB-LAMP, largely due to high equipment cost of the GX4 system. When assuming complete roll-out at all peripheral laboratories, the TB-LAMP first-year cost accounted for 35% of total national TB program budget for 2014 in Malawi while it exceeded the budget by more than 5/11 times.

### Table 1. Unit-cost, unused equipment capacity costs, and overall per-test costs of TB-LAMP and Xpert by varied daily testing volumes

| Daily testing volume | Malawi | Xpert | Vietnam | Xpert |
|----------------------|--------|-------|---------|-------|
|                      | TB-LAMP |       | TB-LAMP |       |
|                      | Unit cost | Unused equipment capacity | Total per-test cost | Unit cost | Unused equipment capacity | Total per-test cost | Unit cost | Unused equipment capacity | Total per-test cost |
| 1                    | -       | -    | 17.32   | 30.69  | 48.01 |
| 2                    | 17.88   | 1.37 | 19.25   | 14.56  | 28.20 |
| 4                    | 13.38   | 0.68 | 14.06   | 13.02  | 26.08 |
| 6                    | 11.74   | 0.46 | 12.20   | 13.79  | 26.59 |
| 7                    | 11.54   | 0.39 | 11.93   | 14.96  | 26.90 |
| 10                   | 10.65   | 0.27 | 10.92   | 13.53  | 24.46 |
| 14                   | 10.19   | 0.20 | 10.39   | 13.40  | 23.79 |

We assessed per-test costs based on the fraction of total TB laboratory operational days (2 days for Malawi and 5 days for Vietnam per week) out of possible 250 annual operational days.

TB-LAMP = loop-mediated isothermal amplification assay for tuberculosis; Xpert = Xpert MTB/RIF.

*Complete laboratory procedure for 1 sample testing for TB-LAMP was not observed during the time-and-motion study.

### Table 2. Weighted national average per-test cost (US$ 2014) of TB-LAMP and Xpert test for Malawi and Vietnam, inclusive of unused equipment daily testing capacity

| Costs per resource category | Malawi | Xpert | Vietnam | Xpert |
|-----------------------------|--------|-------|---------|-------|
| TB-LAMP                     |        |       | TB-LAMP |       |
| Overhead                    | 0.30   | 0.53  | 0.18    | 0.29  |
| Building space              | 0.03   | 0.09  | 0.01    | 0.01  |
| Equipment use               | 0.47   | 2.65  | 0.08    | 1.03  |
| Unused equipment capacity   | 0.77   | 11.04 | 0.32    | 4.59  |
| Staff                       | 0.24   | 0.40  | 0.16    | 0.26  |
| Reagents and chemicals      | 11.82  | 11.48 | 11.82   | 11.48 |
| Consumables*                | 1.13   | 0.93  | 1.18    | 0.97  |
| Registration                | 1.03   | 1.03  | 0.49    | 0.49  |
| Repeat test cost*           | 0.16   | 0.17  | 0.14    | 0.13  |
| Weighted national average   | 15.85  | 26.86 | 14.37   | 20.06 |

TB-LAMP = loop-mediated isothermal amplification assay for tuberculosis; Xpert = Xpert MTB/RIF.

*For both TB-LAMP and Xpert, we assumed 1% rate for invalid, uninterpretable result requiring repeat testing;
*For TB-LAMP, 1 of the 3 test kits required (pipette 60 set, approximately $0.50 per test) was classified as consumables, instead of reagents and chemicals.

https://doi.org/10.35500/jghs.2019.1.e22
DISCUSSION

In this study, we evaluated the cost and affordability of TB-LAMP and Xpert assays as potential upfront bacteriologic tests for TB deployed at peripheral laboratory level in high TB burden, low resource settings represented by Malawi and Vietnam. TB-LAMP cost between $10.39–$19.25 in Malawi and $10.08–$17.55 in Vietnam and $13.40–$48.01 in Malawi and $13.49–$30.60 in Vietnam for Xpert. Test kit costs were the single most important cost driver for both tests, but at lower testing volumes, costs associated with unused equipment capacity became an important cost driver. Given significantly more expensive equipment costs for Xpert, TB-LAMP was consistently cheaper to operate and implement at peripheral laboratories than Xpert. However, given the high up-front costs of equipment and significantly more expensive test kits compared to SSM, complete roll-out of TB-LAMP or Xpert to peripheral laboratories will likely put a significant burden on and could far exceed the annual national TB program budget.

Variabilities in the unit-costs of diagnostic tests, clinical services, or public health interventions resulting from differences in operations, implementation practices, service volumes and economies of scale have been reported previously.16-21 In our study, we further describe this variability along with an assessment of key cost drivers at different daily testing volumes. However, at lower testing volumes, Xpert costs were considerably more expensive due to the low utilization rate of the GeneXpert system (almost ten times the cost of TB-LAMP equipment). Furthermore, depending on the amount of TB laboratory operational days, unused equipment capacity costs can account for more than $30 per-test (i.e. the laboratory in Malawi with 2 operating days per week for TB) at very low-test volumes. This was further reflected in the weighted national average per-test cost of the 2 tests, resulting in at least $5 to $10 higher in cost for Xpert compared to TB-LAMP.

In an earlier global assessment of costs associated with Xpert implementation, increasing Xpert coverage to test all presumptive TB patients was reported to be approximately 5 times the cost of conventional diagnostics in most of the countries assessed, but the affordability

---

Table 3. Total cost and affordability of national roll-out of TB-LAMP compared to Xpert assay in Malawi and Vietnam

| Workload categories | No. of labs | TB-LAMP |  | Xpert |  | National TB budget (%) | TB-LAMP |  | Xpert |  | National TB budget (%) |
|---------------------|------------|---------|---|-------|---|------------------------|---------|---|-------|---|------------------------|
| Low (≤ 4 tests per day) | 96 | $808,994 | 14 | $2,652,200 | 47 | 460 | $4,651,715 | 64 | $15,250,150 | 209 |
| Medium (> 4 and < 10 tests per day) | 48 | $680,167 | 12 | $1,949,850 | 34 | 280 | $3,910,963 | 54 | $11,211,638 | 154 |
| High (≥ 10 tests per day) | 16 | $421,584 | 7 | $924,400 | 16 | 180 | $2,424,106 | 33 | $5,315,300 | 73 |
| Total | 160 | $1,910,745 | 34 | $5,526,450 | 97 | 920 | $10,986,784 | 151 | $31,777,088 | 435 |

We further varied the distribution of low (50%–70%), medium (25%–35%), and high volume (5%–15%) labs. These results are available in Appendix 4 and Appendix 5.

TB = tuberculosis; WHO = World Health Organization; Lab = laboratory; TB-LAMP = loop-mediated isothermal amplification assay for tuberculosis; Xpert = Xpert MTB/RIF.
was dependent on how much the country spent on TB care and control. Similarly, our current analyses indicate that the magnitude of the budget-impact of nationwide roll-out of each of the tests is further dependent on the overall coverage (assessed as total number of implementing peripheral laboratories). Likewise, in Vietnam where the TB program budget relative to population size (surrogate for total number of peripheral laboratories) is vastly small compared to Malawi, costs of the first-year operations of the nationwide TB-LAMP roll-out would far exceed the annual TB program budget despite it being a considerably cheaper alternative to Xpert. Given the significance of the budget implications of the nationwide roll-out of TB-LAMP or Xpert, decision-makers should further seek evidence on optimized placement strategies and their associated costs, operational and epidemiologic impact as countries aim to modernize TB diagnostics at the peripheral level.

There are several important limitations that should be noted for interpretation and generalizability of our findings. First, representativeness of the laboratories in which we collected empiric cost data may not be generalizable to other peripheral laboratories in Malawi and Vietnam. Furthermore, our estimates for weighted average per-test costs and assessment of affordability were based on a hypothetical distribution of peripheral TB laboratory network estimates based on the WHO’s recommendation of 1 microscopy laboratory per 100,000 population. Likewise, our cost estimates may be an over estimate of the actual costs of procurement of equipment and test kits required for the first-year operation at peripheral laboratories. However, given that our affordability assessment does not include costs associated with quality control programs and implementation training, the degree of over-estimation may likely be offset by these additional programmatic costs.

Second, we did not assess costs against the diagnostic performance, relevant TB epidemiology, and other important factors associated with increasing the coverage of NAATs in these 2 countries. Given TB-LAMP’s limitation in diagnosing DR TB, ongoing global efforts to scale-up Xpert coverage, and the development of simpler, innovative NAATs with capacities to detect DR-TB, cost-utility of TB-LAMP must be evaluated against Xpert and other alternatives in additional modeling studies to better inform the position and utility of TB-LAMP in high TB burden settings. This is particularly important as new tool uptake has proven to be slow and technological innovation alone will not likely address many gaps in the TB care cascade in high burden countries.

In conclusion, our study provides a comprehensive assessment of costs and affordability of TB-LAMP compared to Xpert as a potential alternative upfront peripheral NAAT in high TB burden countries. While TB-LAMP costs are considerably lower than that of Xpert, its lack of DR-TB detection capacity and on-going scale-up efforts of Xpert may limit the cost-utility of TB-LAMP, particularly in settings with high DR-TB prevalence. Furthermore, given high costs associated with increasing coverage of NAATs as primary diagnostics for TB in high TB burden settings, overall utility of NAATs and their placement strategies to address highly variable and copious health system gaps for TB must be assessed to better inform resource allocation in low resource and high TB burden settings.

REFERENCES

1. World Health Organization. Global Tuberculosis Report 2018. Geneva: World Health Organization; 2018.
2. Sreeramareddy CT, Panduru KV, Menten J, Van den Ende J. Time delays in diagnosis of pulmonary tuberculosis: a systematic review of literature. *BMC Infect Dis* 2009;9(1):91.

3. Houben RM, Menzies NA, Sumner T, Huynh GH, Arinaminpathy N, Goldhaber-Fiebert JD, et al. Feasibility of achieving the 2025 WHO global tuberculosis targets in South Africa, China, and India: a combined analysis of 11 mathematical models. *Lancet Glob Health* 2016;4(11):e806-15.

4. Sohn H, Sinhuwattanawibool C, Rienthong S, Varma IK. Fluorescence microscopy is less expensive than Ziehl-Neelsen microscopy in Thailand. *Int J Tuberc Lung Dis* 2009;13(2):266-8.

5. Boehrke CC, Nabeta P, Hillemann D, Nicol MP, Shenai S, Krapp F, et al. Rapid molecular detection of tuberculosis and rifampin resistance. *N Engl J Med* 2010;363(11):1005-15.

6. World Health Organization. *Automated Real-Time Nucleic Acid Amplification Technology for Rapid and Simultaneous Detection of Tuberculosis and Rifampin Resistance: Xpert MTB/RIF Assay for the Diagnosis of Pulmonary and Extrapulmonary TB in Adults and Children*. Geneva: World Health Organization; 2013.

7. Weltzien AE, Kew J, Marcellino J, Mabey D, Ebeno J, et al. Evaluation of a simple loop-mediated isothermal amplification test kit for the diagnosis of tuberculosis. *Int J Tuberc Lung Dis* 2011;15(9):1211-7, i.

8. Sohn H, Minion J, Albert H, Dheda K, Pai M. TB diagnostic tests: how do we figure out their costs? *Expert Rev Anti Infect Ther* 2009;7(6):723-33.

9. Hendriks ME, Kundu P, Boers AC, Bolarinwa OA, Te Pas MJ, Akande TM, et al. Step-by-step guideline for disease-specific costing studies in low- and middle-income countries: a mixed methodology. *Glob Health Action* 2014;7(1):23573.

10. Vassall A, Sweeney S, Kahn J, Gomez GG, Bollinger L, Marsee E, et al. Reference case for estimating the costs of global health services and interventions. https://ghcosting.org/pages/standards/reference_case. Updated 2017. Accessed November 17, 2017.

11. Walker D, Kumararanyake L. Allowing for differential timing in cost analyses: discounting and annualization. *Health Policy Plan* 2002;17(1):112-8.

12. Cunnama L, Sinanovic E, Rampa L, Foster N, Berrie L, Stevens W, et al. Using top-down and bottom-up costing approaches in LMICs: the case for using both to assess the incremental costs of new technologies at scale. *Health Econ* 2016;25 Suppl 1:S3-66.

13. Obure CD, Guinness L, Sweeney S, Initiative I, Vassall A. Does integration of HIV and SRH services achieve economies of scale and scope in practice? A cost function analysis of the Integra Initiative. *Sex Transm Infect* 2016;92(2):130-4.

14. Turner HC, Truscott JE, Fleming FM, Hollingsworth TD, Brooker SJ, Anderson RM. Cost-effectiveness of scaling up mass drug administration for the control of soil-transmitted helminths: a comparison of cost function and constant costs analyses. *Lancet Infect Dis* 2016;16(7):838-46.
21. Sarin S, Huddart S, Raizada N, Parija D, Kalra A, Rao R, et al. Cost and operational impact of promoting upfront GeneXpert MTB/RIF test referrals for presumptive pediatric tuberculosis patients in India. PLoS One 2019;14(4):e0214675.

22. Cazabon D, Pande T, Kik S, Van Gemert W, Sohn H, Denkinger C, et al. Market penetration of Xpert MTB/RIF in high tuberculosis burden countries: a trend analysis from 2014-2016. Gates Open Res 2018;2:35.

23. Pai M, Nicol MP, Boehme CC. Tuberculosis diagnostics: state of the art and future directions. Microbiol Spectr 2016;4(5).

24. Pai M, Furin J. Tuberculosis innovations mean little if they cannot save lives. Elife 2017;6:e25956.

25. Pai M, Schumacher SG, Abimbola S. Surrogate endpoints in global health research: still searching for killer apps and silver bullets? BMJ Glob Health 2018;3(2):e000755.

26. Cox V, Cox H, Pai M, Stillo J, Citro B, Brigden G. Health care gaps in the global burden of drug-resistant tuberculosis. Int J Tuberc Lung Dis 2019;23(2):125-35.
Appendix 1. TB diagnostics cost data elements and relevant data sources

| Data element                          | Cost items                                                                 | Source of data collected                                                                 |
|---------------------------------------|----------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| Physical infrastructure               | Building construction                                                      | Construction contractors/government estates and building planning office/recent laboratory construction budget |
| Capital assets                        | Maintenance contracts for all laboratory equipment requiring periodic maintenance | Laboratory financial records/laboratory or hospital accounts office/service contractors |
|                                       | Laboratory equipment                                                       | Manufacture catalogues, purchase records, FIND concessionary price list                  |
|                                       | Medical equipment                                                          | Manufacture catalogues, purchase records                                                |
| Chemicals, reagents, consumables & drugs | All types of chemicals and reagents utilized for diagnostic methods evaluated/drugs used for TB specific and non-specific clinical practice | Laboratory and clinic financial records/manufacturer catalogue (must include all costs associated with procurement, usually at 25% of the catalogue price) |
|                                       | All types of general laboratory and medical consumables (e.g. latex gloves, syringe, etc.) | Laboratory financial records/manufacturer catalogue (must include shipping costs)        |
| Human resources                       | Laboratory staff salaries                                                   | Government salary scale/laboratory or hospital accounts office                           |
|                                       | Laboratory staff allowances and benefits                                    | Government salary scale/laboratory or hospital accounts office                           |
|                                       | Staff training off-site                                                     | Laboratory records/interview                                                              |
| Training & quality assurance          | Relevant internal and external quality assurance program                    | Estimated at 5% of per-test cost, tested in sensitivity analysis for ranges between 2%–10% |

TB = tuberculosis; FIND = Foundation for Innovative New Diagnostics.

Appendix 2. Assumed expected life years for laboratory capital assets

| Types of capital asset    | Examples                                      | Expected/depreciable life (rangea) |
|---------------------------|-----------------------------------------------|------------------------------------|
| Buildings                 | Building structures/infrastructures           | 30 yr                              |
| Equipment                 | Powered laboratory or medical equipment       | 10 yr (5–15 yr)                    |
|                           | Non-powered multi-purpose equipment           | 2 yr (1–5 yr)                      |
|                           | Laboratory glassware                          | 2 yr (1–5 yr)                      |
|                           | Administrative equipment and computers        | 5 yr (2–10 yr)                     |

aA 1-way sensitivity analysis was conducted using this range.

Appendix 3. A worked-out example annual budget for complete roll-out of TB-LAMP into peripheral laboratories in Vietnam, including initial implementation costs

| Row label | Category | Item | Cost (USD) | Comment                                                                 |
|-----------|----------|------|------------|-------------------------------------------------------------------------|
| A         | Equipment| LF-160 incubator (LAMP) | $2,002.21 | Estimated cost for shipment to Vietnam                                  |
| B         | Equipment| Shipping | $450.82 | Cost of 12.5 kits needed to run tests for 1,500 samples (96 tests/kit) |
| C         | Consumables| MTBC detection kit | $11,437.42 | Cost of 20 kits needed to run tests for 3,500 samples (90 tests/kit) |
| D         | Consumables| PURE DNA extraction kit | $15,011.73 | Cost of 12.5 kits needed to run tests for 1,500 samples (1 pipette + 385 pipette tips/kit) |
| E         | Consumables| Pipette-60 set | $1,429.46 | To run 1 sputum sample                                                  |
| F         | Consumables| Per test | $7.97 | Number varies depending on country                                      |
| G         | Consumables| Average number of working days per year | 250 | Number varies depending on country                                      |
| H         | Consumables| Average number of patients per day (medium volume labs) | 14 | Number varies depending on working hours and country                   |
| I         | Consumables| Average number of tests per year | 3,500 | Number varies depending on working hours and country                   |
| J         | Estimated total cost for installation | | $2,453.03 | A + B                                                                  |
| K         | Estimated running costs/year               | | $27,878.61 | C + D + E                                                              |
| L         | Total per lab                             | | $30,331.64 | J + K                                                                  |

USD = United States Dollar; LAMP = loop-mediated isothermal amplification; lab = laboratory.
Appendix 4. Total cost and affordability of national roll-out of TB-LAMP compared to Xpert assay in Malawi and Vietnam, lower distribution of low volume laboratories

| Workload categories | Malawi | Vietnam |
|---------------------|--------|---------|
|                     | No. of labs | TB-LAMP | Xpert | No. of labs | TB-LAMP | Xpert |
|                     |          | Total 1st yr cost | National TB budget (%) | Total 1st yr cost | National TB budget (%) | Total 1st yr cost | National TB budget (%) | Total 1st yr cost | National TB budget (%) |
| Low (< 4 tests per day) | 80 | $674,162 | 12 | $2,210,167 | 39 | 460 | $3,876,429 | 53 | $12,708,458 | 174 |
| Medium (> 4 and < 10 tests per day) | 56 | $471,913 | 8 | $1,547,117 | 27 | 280 | $2,713,500 | 37 | $8,895,921 | 122 |
| High (≥ 10 tests per day) | 24 | $202,248 | 4 | $663,050 | 12 | 180 | $1,162,929 | 16 | $3,812,538 | 52 |
| Total | 160 | $1,348,323 | 24 | $4,420,333 | 78 | 920 | $7,752,858 | 106 | $25,416,917 | 348 |
| Total national TB program budget (2014) | $5,700,000 | $7,300,000 |

TB = tuberculosis; TB-LAMP = loop-mediated isothermal amplification assay for tuberculosis; Xpert = Xpert MTB/RIF; Lab = laboratory.

Appendix 5. Total cost and affordability of national roll-out of TB-LAMP compared to Xpert assay in Malawi and Vietnam, higher distribution of low volume laboratories

| Workload categories | Malawi | Vietnam |
|---------------------|--------|---------|
|                     | No. of labs | TB-LAMP | Xpert | No. of labs | TB-LAMP | Xpert |
|                     |          | Total 1st yr cost | National TB budget (%) | Total 1st yr cost | National TB budget (%) | Total 1st yr cost | National TB budget (%) | Total 1st yr cost | National TB budget (%) |
| Low (< 4 tests per day) | 112 | $941,826 | 17 | $3,094,233 | 54 | 644 | $5,427,001 | 74 | $17,791,842 | 244 |
| Medium (> 4 and < 10 tests per day) | 40 | $337,081 | 6 | $1,105,083 | 19 | 230 | $1,938,215 | 27 | $6,354,229 | 87 |
| High (≥ 10 tests per day) | 8 | $67,416 | 1 | $221,017 | 4 | 46 | $387,643 | 5 | $1,270,846 | 17 |
| Total | 160 | $1,348,323 | 24 | $4,420,333 | 78 | 920 | $7,752,858 | 106 | $25,416,917 | 348 |
| Total national TB program budget (2014) | $5,700,000 | $7,300,000 |

TB = tuberculosis; TB-LAMP = loop-mediated isothermal amplification assay for tuberculosis; Xpert = Xpert MTB/RIF; Lab = laboratory.