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Higher cost of implementing Xpert MTB/RIF in Ugandan peripheral settings: Implications for cost-effectiveness

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SUMMARY

Setting—Initial cost-effectiveness evaluations of Xpert MTB/RIF (Xpert) for tuberculosis (TB) diagnosis have not fully accounted for realities of implementation in peripheral settings.

Objective—We evaluated costs and diagnostic outcomes of Xpert testing implemented at various healthcare levels in Uganda.

Design—We collected empirical cost data from five health centers utilizing Xpert for TB diagnosis, employing an ingredients approach. We reviewed laboratory and patient records to assess outcomes in these sites and ten sites without Xpert. We also estimated incremental cost-effectiveness of Xpert testing; our primary outcome was incremental cost of Xpert testing per newly detected TB case.

Results—The mean unit cost of an Xpert test was US$21 based on a mean monthly volume of 54 tests per site, though unit cost varied widely (US$16–58) and was primarily determined by testing volume. Total diagnostic costs were 2.4-fold higher in Xpert clinics compared to non-Xpert clinics, though Xpert only increased diagnoses by 12%. Diagnostic costs of Xpert averaged US $119 per newly detected TB case but were as high as US$885 in the lowest-volume center.

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Conclusion—Xpert testing can detect TB cases at reasonable cost but may double diagnostic budgets for relatively small gains, with cost-effectiveness deteriorating with lower testing volumes.

Keywords

tuberculosis; diagnostic tests; routine; molecular diagnostic techniques; cost-benefit analysis

INTRODUCTION

Tuberculosis (TB) is the leading single-agent infectious cause of death globally, responsible for 1.5 million deaths in 2014.[1] An estimated 3.6 million cases go unreported every year; reaching this "missing 3 million" is among the highest priorities for global TB control.[1] In 2010, the World Health Organization endorsed Xpert MTB/RIF (Xpert), a molecular TB diagnostic test that can provide results in two hours with minimal human resource requirements, higher sensitivity than sputum smear microscopy, and the ability to identify multi-drug resistant (MDR-) TB based on detected resistance to rifampin.[2,3] Scale-up has been rapid, with more than 10 million cartridges procured under concessional pricing in over 100 countries through 2014.[4,5] However, while sputum smear microscopy costs $1–$3 per test in most high-burden countries,[6] Xpert has been estimated to cost between $15 and $50 per test.[7–11] Thus, a key question is whether the improved accuracy of Xpert is worth the additional cost.

Initial economic evaluations suggested that Xpert is cost-effective, though estimations of incremental cost-effectiveness vary.[7,8,11–13] These earlier modeling studies largely assumed efficiently functioning laboratories that served as initial sites of Xpert scale-up. Over time, however, the focus of Xpert implementation has shifted to district and subdistrict levels,[14–16] where the cost of Xpert may be substantially higher because of lower testing volumes or additional costs associated with transport and installation.[17] Previous work in South Africa has suggested that point-of-treatment placement of Xpert could increase Xpert testing cost by 50% or more;[9] whether that additional cost, as well as the linkage between such additional cost and the potential for Xpert to improve diagnostic outcomes, generalizes to high-burden low-income settings remains uncertain.

Recent evidence has also suggested that Xpert, as implemented in African primary-care settings, may not improve treatment, morbidity, or mortality outcomes as much as initially expected.[18–20] Xpert effectiveness may be further reduced in non-trial settings because of equipment failure, uncertain electrical supply, ongoing calibration requirements, and unanticipated patterns of use (e.g., treatment monitoring).[9,17] It is thus important to collect data on both costs and outcomes of Xpert implementation in peripheral settings, particularly in high-burden, low-income countries where funding gaps suggest that affordability of Xpert remains a key question.[1] Here, we report on the costs of Xpert testing and corresponding diagnostic outcomes across regional hospitals, district hospitals and sub-district health centers in Uganda, a typical sub-Saharan African setting with high rates of TB and HIV/TB and the site of prior studies of Xpert's effectiveness[21] and cost-effectiveness.[11]

METHODS

Ethical considerations

This study received approval from institutional review boards at Makerere University College of Health Sciences in Kampala, Uganda, and Johns Hopkins Bloomberg School of Public Health in Baltimore, MD, USA.

Overview

We nested this evaluation of Xpert costs and TB diagnoses into a larger observational study of implementing TB diagnostic algorithms in Uganda.[22] Data were collected at 18 rural and urban health facilities from 2012–2014, selected to be representative of both geography and health system level: one national referral center (not included in this analysis), four regional referral centers, nine district hospitals, and four sub-district health centers. Xpert had been implemented in seven sites (plus the national referral center) at the time of evaluation, whereas the remaining 10 sites had laboratories capable of performing sputum smear microscopy. These 10 sites provided Xpert testing only as an offsite referral test from another health center (and only rarely). Here we compared five sites where Xpert was implemented (excluding two sites that served as referral centers) against the ten sites without Xpert.

Our primary aim was to measure costs and diagnostic outcomes related to Xpert testing as actually implemented in various levels of the Ugandan healthcare system in order to explore the primary drivers of Xpert cost-effectiveness in such settings. Because we did not measure the costs or outcomes of treatment, we did not attempt to estimate cost-effectiveness in terms of cost per disability-adjusted life year (DALY) averted, but rather used cost per diagnostic outcome (diagnosis of TB or rifampin-resistant TB) as a more proximal measure for exploring the key drivers of cost-effectiveness in these settings.

Empiric costing

We estimated diagnostic costs from the health system perspective using a unit-based "ingredients" approach. This method identifies and values all inputs required to perform diagnostic testing in order to develop a unit cost for each test. At five sites with Xpert implementation (two regional hospitals, one district hospital, and two sub-district [Level IV] health centers), we collected costs of overhead, building space, equipment, staff, reagents, and consumables related to Xpert testing and smear microscopy. We used a combination of laboratory personnel interviews, budgetary documentation reviews, procurement guides, and publically available product information. Overhead costs were allocated based on proportional space required for TB testing and percentage of staff time devoted to TB testing, as appropriate. To determine allocation of costs of shared resources between Xpert testing and non-Xpert testing, we directly observed time and motion of laboratory procedures at each site. For smear microscopy, we assumed an algorithm consisting of two smears per patient. Costs and diagnostic outcomes of TB culture (performed only rarely in these sites) were excluded.

We assumed that one person would require training in Xpert use per site per year, and that Xpert cartridge procurement and transportation would equal 10% of the US$9.97 cartridge list price, based on consultation with experts in Uganda. Cost of shipping the GeneXpert four-cartridge system was incorporated as a 10.9% markup of the ex-works list price.[23] Annual maintenance of GeneXpert was based on annual warranty cost[24] with a 5 year expected lifetime, whereas we assumed annual maintenance costs of all other durable equipment and building space to be 5% of total cost each year given assumed expected lifetime of 30 years. All future costs were discounted at 3% per year.[25] Costs were measured in 2014 currency and converted to US dollars using published exchange rates.

Estimation of diagnoses made

We reviewed 12 months of TB laboratory records, including electronic Xpert instrument logs and laboratory specimen registers, for Xpert testing volume and results of Xpert and smear microscopy at each site as reported previously.[22] Laboratory results and treatment data for 100 consecutive patients who provided sputum samples were also abstracted at each site in order to establish linkages between test results and treatment initiation. In order not to underestimate the cost-effectiveness of Xpert in diagnosing smear-negative TB, we assumed that Xpert tests run without a specific reason recorded were performed for the purpose of diagnosing TB over other reasons (e.g., treatment monitoring).

Analysis of outcomes

Primary cost outcomes were the cost per Xpert test performed and the incremental cost of diagnosis of a new TB case due to Xpert. Our primary effectiveness outcome was the number of positive Xpert tests performed on individuals without known pre-existing TB. A secondary effectiveness outcome was the number of Xpert tests indicating rifampin resistance among individuals not previously documented as having MDR-TB. For each Xpert site, we calculated the mean monthly cost of Xpert testing, mean number of incremental TB diagnoses, and thus the cost per diagnosis made. Finally, we compared mean facility-level estimates of monthly diagnostic costs and number of individuals started on TB treatment between sites with and without Xpert.

Uncertainty analysis

We directly measured costs and diagnostic outcomes, and therefore did not need to use parameter values from literature. Nevertheless, our sample size of five Xpert sites still leads to uncertainty in our estimates as a reflection of other similar Ugandan clinics. To capture this uncertainty, we adopted a probabilistic approach in which we drew 10,000 samples of testing volume, Xpert unit cost (as a function of testing volume), and number of newly diagnosed TB and MDR-TB cases (as a function of testing volume). Testing volume was modeled as a gamma distribution to reflect the zero bound and right skew observed in our data. In each simulation, we calculated the diagnostic cost per Xpert test positive for TB and diagnostic cost per Xpert test positive for rifampin resistance. We also compared the cost-effectiveness of TB testing in simulated sets of nine small-volume facilities (<20 tests per month) against single large-volume facilities (> 20 tests per month; mean nine times larger than small-volume facilities).

RESULTS

Unit cost of Xpert

Across the five sites evaluated, the mean unit cost of Xpert was US$21 based on an observed mean monthly volume of 54 tests per site (Figure 1). Reagents (including the Xpert cartridge) and equipment comprised 93% of this unit cost, which varied from US$16 to US $58 across sites. The primary driver of this variation was testing volume, which tended to be higher in regional and district hospitals and lower in sub-district health centers. If all five facilities operated under their lowest-volume conditions observed over the 12-month periods, the estimated mean unit cost would rise from US$21 to US$65 (Table 1).

Xpert diagnostic costs and outcomes

The estimated monthly incremental diagnostic cost of Xpert testing at each site ranged from US$590–US$2098 (Table 2). Regional and district-level hospitals had higher total costs for the overall Xpert testing program per month due to larger volumes of Xpert testing. On average, of the 54 Xpert tests per site per month, 9.6 were positive for TB and 0.5 indicated rifampin resistance, though variation across sites was substantial. The diagnostic cost per positive Xpert test on patients not known to have TB averaged US$119 (range US$80–885), whereas the diagnostic cost per positive test for rifampin resistance among those without known pre-existing resistance averaged US$1383 (range US$896–7081), reflecting the smaller number of rifampin-resistant cases diagnosed. Cost per positive diagnosis was highest in sites with lowest volumes of testing.

Figure 2 presents the estimated incremental costs and diagnoses due to Xpert by comparing costs, number of diagnoses, and number started on treatment at Xpert versus non-Xpert sites. The total cost of TB diagnosis per month averaged US$1679 per Xpert site. Total TB diagnostic costs were 2.4-fold higher in clinics with Xpert testing compared to those without (US$702, based on our empiric estimate of US$1.41 per sputum smear). However, Xpert resulted in an estimated 5.3 incremental diagnoses per site per month, an incremental yield of only 12%. While treatment initiations were 31% higher in Xpert versus non-Xpert sites, rates of treatment initiation after diagnostic testing at Xpert and non-Xpert sites were similar at 87% and 89%, respectively.

Uncertainty analysis

Figure 3 presents the distribution of costs per Xpert test positive for TB and per test positive for rifampin resistance across 10,000 simulated months of testing. The median cost per Xpert test positive for TB was US$106. Among simulations in which Xpert testing volume was less than 20 per month per site, this median diagnostic cost was $918, versus $138 among simulations in which monthly testing volume was at least 20.

DISCUSSION

This economic investigation of Xpert implementation across regional, district, and sub-district health centers in Uganda suggests that costs and impact of Xpert testing vary widely across sites and levels of the health system, with a strong dependence on testing volume. For example, the diagnostic cost per positive Xpert test ranged from US$80 in the highest-volume site to US$885 in the lowest-volume site. Xpert testing accounted for more than 60% of all diagnostic costs but was responsible for no more than 12% of new TB diagnoses. As Xpert is increasingly implemented in lower-volume settings, it may become less cost-effective.

Consistent with prior studies performed under conditions of greater resource availability,[19,26] we found that implementation of Xpert in Uganda (a country with fewer resources and outside a trial setting) led to few incremental TB diagnoses relative to the current standard based on sputum smear. We augment this understanding by correlating diagnostic outcomes with the incremental cost of Xpert, which constituted over 60% of diagnostic costs in sites utilizing Xpert. In our uncertainty analysis simulations, the median cost per new TB case detected was US$106; however, this increased when considering Xpert implementation in sites with low testing volume. These findings may help inform decision-makers about the appropriateness of Xpert deployment in different settings.

Prior analyses have estimated the mean unit cost of Xpert to vary within US$20–$30 depending on country deployed,[11] while others have also noted that testing volume is an important contributor to cost variations.[9,10] Our analysis builds on this by describing the degree of variability that could be observed even within the same health system. This research suggests that there is likely a threshold testing volume – and thus, a threshold level of healthcare system – at which Xpert should be implemented. Such thresholds may raise concerns about trade-offs between equity and efficiency in peripheral settings, especially as some apparent cost savings from a more centralized referral system may in fact represent costs shifted away from the health system and instead toward patients who would have to travel further, wait longer for results, and delay treatment initiation. Cost-effectiveness of Xpert testing at lower-volume centers could potentially be improved with increased volume of patients referred for testing, such as through facility-based screening and other intensified case-finding initiatives.[27,28] Alternatively, referral networks could be further developed to deliver sputum specimens efficiently to more centralized sites,[29,30] an approach which must consider quality of available transport networks and potential for pre-treatment loss to follow-up while awaiting results. Novel lower-cost platforms for Xpert testing (e.g., Xpert Omni,[31] Alere q[32]) may also aid in cost-effective decentralization of testing. Future research should evaluate the appropriate healthcare level for Xpert implementation in different economic and epidemiological settings, investigate the economic impact of alternative approaches in peripheral settings, and evaluate trade-offs between patient costs and healthcare system costs when placing Xpert centrally versus peripherally.

Our study has several limitations. First, we only included costs of Xpert and sputum smear microscopy in estimating diagnostic costs, excluding ancillary evaluation (e.g., chest X-ray, antibiotic trials) costs. As a result, we likely underestimate the true diagnostic program cost at both Xpert and non-Xpert sites. Second, we took as our primary effectiveness outcome the observed number of positive Xpert tests not performed on those with known TB, which may overestimate the incremental value of Xpert. Third, HIV status was not reliably logged in patient records. We were therefore unable to evaluate the differential costs and impact on diagnoses from Xpert testing within this important sub-group.[33] Finally, we measured costs from the healthcare perspective and did not incorporate patient costs. Including patient costs would increase overall estimates of diagnostic and treatment costs, though the incremental cost due to Xpert might differ according to diagnostic algorithm (e.g., whether testing is same-day).

In summary, this analysis demonstrates that Xpert diagnostic costs and impact on TB and MDR-TB diagnoses made can vary widely at different levels of the same healthcare system, with cost-effectiveness deteriorating substantially in low-volume settings. As Xpert is scaled up to sites with increasingly lower testing volumes, more attention must be paid to proper placement within the healthcare system and the development of alternative strategies to make peripheral implementation more cost-effective. Future policy guidance for Xpert and emerging TB diagnostic tests[34] should carefully consider the economic realities of testing in peripheral settings when recommending implementation strategies.

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References

1. World Health Organization. Global tuberculosis report 2015. 2015. http://www.who.int/tb/publications/global_report/en/
2. World Health Organization. Policy statement Geneva, Switz World Heal …. 2011. Policy statement: automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF.
3. 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(1):CD009593.doi: 10.1002/14651858.CD009593.pub3 [PubMed: 24448973]
4. World Health Organization. [Accessed July 20, 2015] TB diagnostics and laboratory strengthening. http://who.int/tb/laboratory/mtbrifrollout/en/. Published 2015
5. World Health Organization. [Accessed July 20, 2015] WHO monitoring of Xpert MTB/RIF roll-out: Orders of GeneXperts and Xpert MTB/RIF cartridges. http://apps.who.int/tb/laboratory/xpertmap/. Published 2014
6. Whitelaw A, Peter J, Sohn H, et al. Comparative cost and performance of light-emitting diode microscopy in HIV-tuberculosis-co-infected patients. Eur Respir J. 2011; 38(6):1393–1397. DOI: 10.1183/09031936.00023211 [PubMed: 21659413]
7. Abimbola TO, Marston BJ, Date Aa, Blandford JM, Sangrujee N, Wiktor SZ. Cost-Effectiveness of Tuberculosis Diagnostic Strategies to Reduce Early Mortality Among Persons With Advanced HIV Infection Initiating Antiretroviral Therapy. JAIDS J Acquir Immune Defic Syndr. 2012; 60(1):e1–e7. DOI: 10.1097/QAI.0b013e318246538f [PubMed: 22240465]
8. Meyer-Rath G, Schnippel K, Long L, et al. The impact and cost of scaling up genexpert MTB/RIF in South Africa. PLoS One. 2012; 7(5)doi: 10.1371/journal.pone.0036966
9. Schnippel K, Meyer-Rath G, Long L, et al. Scaling up Xpert MTB/RIF technology: the costs of laboratory- *vs*. clinic-based roll-out in South Africa. Trop Med Int Heal. 2012; 17(9):1142–1151. DOI: 10.1111/j.1365-3156.2012.03028.x
10. Pantoja A, Fitzpatrick C, Vassall A, Weyer K, Floyd K. Xpert MTB/RIF for diagnosis of tuberculosis and drug-resistant tuberculosis: A cost and affordability analysis. Eur Respir J. 2013; 42(3):708–720. DOI: 10.1183/09031936.00147912 [PubMed: 23258774]

11. Vassall A, van Kampen S, Sohn H, et al. Rapid diagnosis of tuberculosis with the Xpert MTB/RIF assay in high burden countries: A cost-effectiveness analysis. PLoS Med. 2011; 8(11)doi: 10.1371/journal.pmed.1001120

12. Andrews JR, Lawn SD, Rusu C, et al. The cost-effectiveness of routine tuberculosis screening with Xpert MTB/RIF prior to initiation of antiretroviral therapy: a model-based analysis. AIDS. 2012; 26(8):987–995. DOI: 10.1097/QAD.0b013e3283522d47 [PubMed: 22333751]

13. Menzies NA, Cohen T, Lin HH, Murray M, Salomon JA. Population Health Impact and Cost-Effectiveness of Tuberculosis Diagnosis with Xpert MTB/RIF: A Dynamic Simulation and Economic Evaluation. PLoS Med. 2012; 9(11)doi: 10.1371/journal.pmed.1001347

14. Cox HS, Mbhele S, Mohess N, et al. Impact of Xpert MTB/RIF for TB Diagnosis in a Primary Care Clinic with High TB and HIV Prevalence in South Africa: A Pragmatic Randomised Trial. PLoS Med. 2014; 11(11):1–12. DOI: 10.1371/journal.pmed.1001760

15. Sachdeva KS, Raizada N, Sreenivas A, et al. Use of Xpert MTB/RIF in decentralized public health settings and its effect on pulmonary TB and DR-TB case finding in India. PLoS One. 2015; 10(5): 1–18. DOI: 10.1371/journal.pone.0126065

16. Hanrahan CF, Clouse K, Bassett J, et al. The patient impact of point-of-care vs. laboratory placement of Xpert MTB/RIF. Int J Tuberc Lung Dis. 2015; 19(7):811–816. [PubMed: 26056107]

17. Abdurrahman ST, Emenyonu N, Obasanya OJ, et al. The hidden costs of installing xpert machines in a tuberculosis high-burden country: experiences from Nigeria. Pan Afr Med J. 2014; 18:1–5. DOI: 10.11604/pamj.2014.18.277.3906

18. Hanrahan CF, Selibas K, Deery CB, et al. Time to treatment and patient outcomes among TB suspects screened by a single point-of-care xpert MTB/RIF at a primary care clinic in Johannesburg, South Africa. PLoS One. 2013; 8(6):e65421.doi: 10.1371/journal.pone.0065421 [PubMed: 23762367]

19. Theron G, Zijenah L, Chanda D, et al. Feasibility, accuracy, and clinical effect of point-of-care Xpert MTB/RIF testing for tuberculosis in primary-care settings in Africa: A multicentre, randomised, controlled trial. Lancet. 2014; 383(9915):424–435. DOI: 10.1016/S0140-6736(13)62073-5 [PubMed: 24176144]

20. Churchyard GJ, Stevens WS, Mametja LD, et al. Xpert MTB/RIF versus sputum microscopy as the initial diagnostic test for tuberculosis: a cluster-randomised trial embedded in South African roll-out of Xpert MTB/RIF. Lancet Glob Heal. 2015; 3(8):450–457. DOI: 10.1016/s2214-109x(15)00100-x

21. Boehme CC, Nicol MP, Nabeta P, et al. Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance: A multicentre implementation study. Lancet. 2011; 377(9776):1495–1505. DOI: 10.1016/S0140-6736(11)60438-8 [PubMed: 21507477]

22. Hanrahan CF, Haguma P, Ochom E, et al. Implementation of Xpert MTB/RIF in Uganda: Missed opportunities to improve diagnosis of tuberculosis. Open Forum Infect Dis. 2016 In press.

23. Radelet, S.; Sachs, JD. Shipping costs, manufactured exports, and economic growth. 1998. http://academiccommons.columbia.edu/download/fedora_content/download/ac:124168/CONTENT/shipcost.pdf

24. FIND. [Accessed July 15, 2015] FIND - Negotiated prices for Xpert® MTB/RIF and FIND country list. http://www.finddiagnostics.org/about/what_we_do/successes/find-negotiated-prices/xpert_mtb_rif_with-warranty.html

25. Tan-Torres, Edejer T.; Baltussen, R.; Adam, T., et al. [Accessed July 23, 2015] Making Choices in Health: WHO Guide to Cost-Effectiveness Analysis. 2003. http://www.who.int/choice/publications/p_2003_generalised_cea.pdf

26. Chihota VN, Ginindza S, McCarthy K, Grant AD, Churchyard G, Fielding K. Missed Opportunities for TB Investigation in Primary Care Clinics in South Africa: Experience from the XTEND Trial. PLoS One. 2015; 10(9):e0138149.doi: 10.1371/journal.pone.0138149 [PubMed: 26383102]

27. Hermans S, Nasuuna E, van Leth F, et al. Implementation and effect of intensified case finding on diagnosis of tuberculosis in a large urban HIV clinic in Uganda: a retrospective cohort study. BMC Public Health. 2012; 12(1):674.doi: 10.1186/1471-2458-12-674 [PubMed: 22905704]

28. Sekandi JN, List J, Luzze H, et al. Yield of undetected tuberculosis and human immunodeficiency virus coinfection from active case finding in urban uganda. Int J Tuberc Lung Dis. 2014; 18(1):13–19. DOI: 10.5588/ijtld.13.0129 [PubMed: 24365547]
29. Salje H, Andrews JR, Deo S, et al. The Importance of Implementation Strategy in Scaling Up Xpert MTB/RIF for Diagnosis of Tuberculosis in the Indian Health-Care System: A Transmission Model. PLoS Med. 2014; 11(7)doi: 10.1371/journal.pmed.1001674
30. Pho MT, Deo S, Palamountain KM, Joloba ML, Bajunirwe F, Katamba A. Optimizing tuberculosis case detection through a novel diagnostic device placement model: The case of Uganda. PLoS One. 2015; 10(4):1–14. DOI: 10.1371/journal.pone.0122574
31. Cepheid. [Accessed February 4, 2016] GeneXpert Omni. http://www.cepheid.com/us/genexpert-omni. Published 2015
32. Alere. [Accessed March 1, 2016] Alere q. http://www.alere.com/en/home/products-services/brands/alere-q.html. Published 2016
33. World Health Organization. Automated Real-Time Nucleic Acid Amplification Technology for Rapid and Simultaneous Detection of Tuberculosis and Rifampicin Resistance: Xpert MTB/RIF Assay for the Diagnosis of Pulmonary and Extrapulmonary TB in Adults and Children. Policy Update. Geneva: 2013.
34. Pai M, Schito M. Tuberculosis Diagnostics in 2015: Landscape, Priorities, Needs, and Prospects. J Infect Dis. 2015; 211(suppl 2):S21–S28. DOI: 10.1093/infdis/jiu803 [PubMed: 25765103]

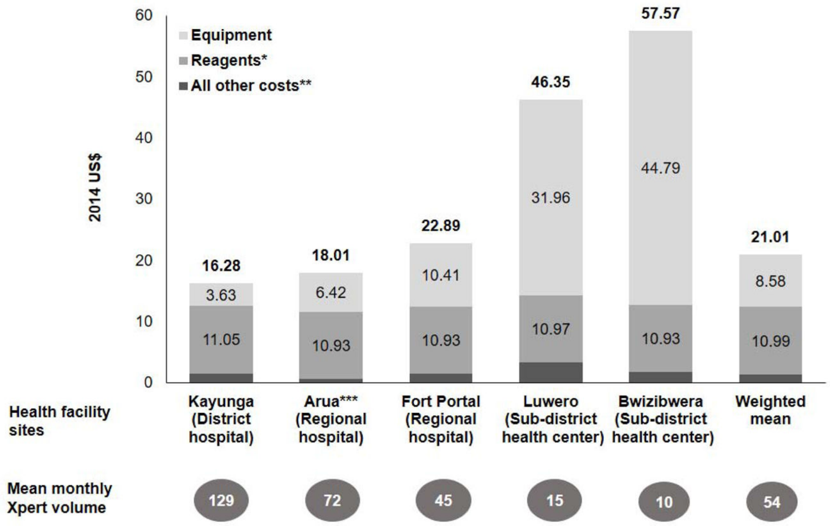

Figure 1. Unit cost of Xpert test by input type at each site

The height of each column (in bold above each column) represents the mean unit cost of Xpert at each of five sites in Uganda; the corresponding observed monthly Xpert volume is indicated in circles below each column. Different shades within each bar represent components of the unit cost. Note that Kayunga, as a district hospital, is at a lower level of the Uganda healthcare system than Arua and Fort Portal regional hospitals, but had a greater volume of tests. *The cost of reagents includes the Xpert cartridge. **Includes costs of overheads, building space, staff time, and consumables. ***Because time-motion data for Xpert testing was not collected at Arua, allocation of resources not directly related to Xpert (i.e., all but GeneXpert system and Xpert cartridge) was based on time-motion studies in Fort Portal; these resources accounted for 9% of costs per Xpert test in Fort Portal.

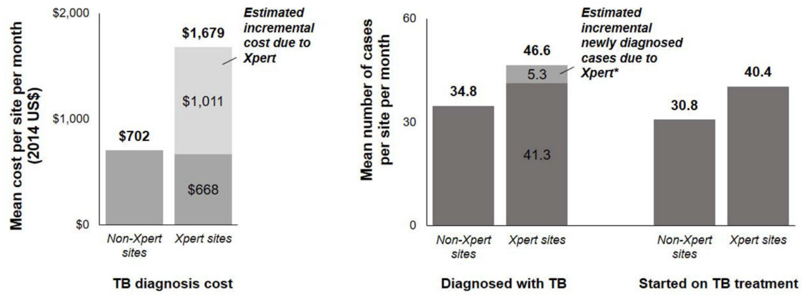

Figure 2. Incremental costs and associated diagnostic and treatment impact of Xpert implementation

The left graph shows costs of diagnosis from the healthcare setting in sites without and with on-site Xpert testing, while the right graph shows corresponding outcomes: the number of cases diagnosed and number of cases started on treatment. Incremental newly diagnosed cases due to Xpert (in light blue) were estimated by applying the observed proportion of newly diagnosed cases with a preceding positive Xpert result (Table 2) to the mean number of new TB diagnoses diagnosed by Xpert per month in sites with on-site Xpert testing available. The remaining TB cases at Xpert sites were either detected by smear microscopy or started on treatment before a positive Xpert result.

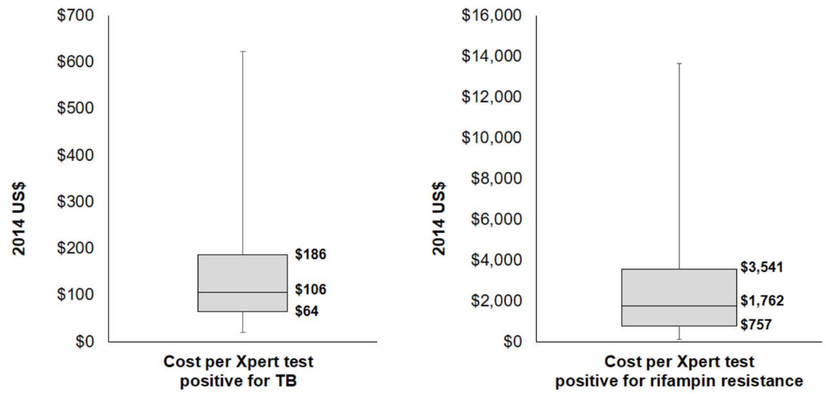

Figure 3. Distribution of cost per positive Xpert test across 10,000 probabilistic simulations

Boxplots represent the distributions of cost-effectiveness estimates in probabilistic sensitivity analyses considering the cost per Xpert test positive for TB (left panel) or rifampin resistance (right panel). Boxes represent interquartile ranges; whiskers represent the 5th and 95th percentiles (not including simulations for which Xpert did not increase the number of positive tests [17% of simulations] or lead to any individuals being diagnosed with rifampin resistance [13% of simulations]).

Table 1

Unit cost of Xpert test by monthly volume

	Weighted mean cost of Xpert test (2014 US$)*		
Input Type	**At minimum monthly volume**	**At median monthly volume**	**At maximum monthly volume**
Overhead	0.03	0.03	0.03
Building space	1.79	1.35	0.15
Equipment	50.94	9.44	4.33
Staff	0.40	0.40	0.37
Reagents	10.97	10.98	10.99
Consumables	0.67	0.72	0.75
TOTAL	64.80	22.92	16.62

*Calculated by adding variable monthly costs of building space and equipment with constant monthly costs of all other input types as would be required to attain the minimum, median, or maximum volume observed in each site. These total unit costs were then weighted according to the site volume observed in each scenario:

Minimum monthly volume - Kayunga: 15, Arua: 17, Fort Portal: 8, Luwero: 4, Bwizibwera: 1

Median monthly volume - Kayunga: 109, Arua: 68, Fort Portal: 46, Luwero: 16, Bwizibwera: 9

Maximum monthly volume - Kayunga: 275, Arua: 132, Fort Portal: 83, Luwero: 23, Bwizibwera: 28

Table 2

Total costs and associated diagnostic impact of Xpert implementation at each site

		Cost	Associated diagnostic impact			Cost per diagnosis made	
Health facility site	**Health facility level**	**Total diagnostic cost of Xpert program per month (2014 US $)**	**Mean number of Xpert tests run per month**	**Mean number of new TB positive Xpert tests per month***	**Mean number of RIF positive Xpert tests per month†**	**Diagnostic cost per new TB positive Xpert test (2014 US$)**	**Diagnostic cost per RIF positive Xpert test (2014 US$)**
Arua	Regional hospital	1291	71.7	14.0	1.1	92	1191
Fort Portal	Regional hospital	1021	44.6	5.7	0.7	180	1531
Kayunga	District hospital	2098	128.9	26.2	0.0	80	n/a
Luwero	Sub-district health center	672	14.5	1.3	0.8	538	896
Bwizibwera	Sub-district health center	590	10.3	0.7	0.1	885	7081
MEAN‡	n/a	1134	54.0	9.6	0.5	119	1383

*Excludes TB positive results of Xpert tests run on individuals already diagnosed with TB, but includes those where the reason for testing is not recorded

†Includes RIF positive results of Xpert tests run on individuals already diagnosed with TB, and RIF positive results where the reason for testing is not recorded

‡Weighted mean used in cost calculations, where each site's data was weighted by number of patients diagnosed