Evaluating Tuberculosis Case Detection via Real-Time Monitoring of Tuberculosis Diagnostic Services

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Rationale: **Tuberculosis case-detection rates are below internationally established targets in high-burden countries. Real-time monitoring and evaluation of adherence to widely endorsed standards of tuberculosis care might facilitate improved case finding.**

Objectives: **To monitor and evaluate the quality of tuberculosis case-detection and management services in a low-income country with a high incidence of tuberculosis.**

Methods: **We prospectively evaluated tuberculosis diagnostic services at five primary health-care facilities in Uganda for 1 year, after introducing a real-time, electronic performance-monitoring system. We collected data on every clinical encounter, and measured quality using indicators derived from the *International Standards of Tuberculosis Care*.**

Measurements and Main Results: **In 2009, there were 62,909 adult primary-care visits. During the first quarter of 2009, clinicians referred only 21% of patients with cough greater than or equal to 2 weeks for sputum smear microscopy and only 71% of patients with a positive sputum examination for tuberculosis treatment. These proportions increased to 53% and 84%, respectively, in the fourth quarter of 2009. The cumulative probability that a smear-positive patient with cough greater than or equal to 2 weeks would be appropriately evaluated and referred for treatment rose from 11% to 34% ($P = 0.005$). The quarterly number of tuberculosis cases identified and prescribed treatment also increased four-fold, from 5 to 21.**

Conclusions: **Poor adherence to internationally accepted standards of tuberculosis care improved after introduction of real-time performance monitoring and was associated with increased tuberculosis case detection. Real-time monitoring and evaluation can strengthen health systems in low-income countries and facilitate operational research on the effectiveness and sustainability of interventions to improve tuberculosis case detection.**

Keywords: tuberculosis; diagnosis; health care quality assurance; operations research; public health

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AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Tuberculosis case detection rates are far below internationally established targets in most high-burden countries. Little is known about the quality of case-detection services in relation to international standards of tuberculosis care.

What This Study Adds to the Field

We found poor baseline adherence to international standards of tuberculosis care in primary health clinics in a high-burden country. Improvements in adherence occurred after introduction of real-time performance monitoring and were associated with substantial increases in tuberculosis case detection.

In 2009, 5.8 million cases of tuberculosis (TB) were diagnosed worldwide, the most ever reported to the World Health Organization (1). However, the number of cases diagnosed and reported accounted for only 62% of the estimated 9.4 million annual incident cases of TB. This ratio of notified-to-incident cases, called the TB case-detection rate (2), remains far below the 84% target set by the Global Plan to Stop TB as part of efforts to eliminate TB worldwide by 2050 (3). Several explanations have been offered for the low case-detection rate, including poor access to and funding for primary health care; a shortage of qualified health-care personnel; and the low sensitivity of the standard diagnostic test for TB, sputum smear microscopy (4, 5). In sub-Saharan Africa, where high burdens of HIV and TB greatly exacerbate these factors and where 80% of global cases occur, the case-detection rate is only 50% (1).

Recent efforts to increase case detection have focused largely on developing more accurate and accessible diagnostic tests (5, 6) and on "active" case-finding strategies, in which mass screening targets high-risk communities (7, 8). However, few studies have described the quality of "passive" case-detection services in primary health clinics in relation to international guidelines (9, 10), even though quality-assured diagnosis is a core component of the World Health Organization's Stop TB Strategy (3). For passive case detection to be effective, health-care providers must first refer at-risk patients for TB testing, then ensure that referred patients complete testing, and finally make certain that patients with positive test results are notified as cases of TB and initiated on treatment (11). Thus, access to high-quality primary health-care services is the most important predictor of whether new diagnostic approaches can realize their promise for reducing global TB mortality (12, 13).

To understand the quality and limitations of current practices for evaluating patients suspected of having TB in low-income countries, we collaborated with the Uganda Ministry of Health Management Information Services and the Uganda National TB and Leprosy Control Program to implement an electronic, real-time performance monitoring system at five primary health-care facilities in five districts of Uganda. Our aims were to describe adherence to international guidelines for TB suspect evaluation and TB case detection during a 1-year period after the introduction of the monitoring and evaluation system.

METHODS

Study Sites and Participants

All adults (age ⩾15 yr) undergoing evaluation for any reason at five widely distributed Uganda Ministry of Health Level IV Health Centres between January and December 2009 contributed data to the analysis (*see* Figure E1 in the online supplement). Level IV Health Centres have a catchment population of approximately 100,000 people and at full capacity are staffed by one medical officer, two clinical officers, five nurses, one laboratory technician, one laboratory assistant, one dispenser, one records officer, one health educator, and one health assistant. All sites have a simple diagnostic laboratory that provides basic testing, including sputum smear microscopy for acid-fast bacilli. The Government of Uganda provides all health-care services in these facilities free of charge.

The national TB program oversees routine monitoring and evaluation of TB services at these sites, which include quarterly visits by the District TB and Leprosy Supervisor to deliver laboratory supplies for sputum smear microscopy, to collect microscopy slides for external quality review at the National TB Reference Laboratory, and to examine the laboratory and treatment registers to assess adherence to Uganda national TB management guidelines. Published national guidelines in 2009 were consistent with the *International Standards of Tuberculosis Care* (9) and recommended collection of three sputum specimens (including at least one early morning specimen) for smear microscopy from all patients suspected of TB; treatment of any patient with greater than or equal to one acid-fast bacillus per slide as a case of TB; and HIV testing of all cases of TB. During the period of this study, the program did not use TB suspect registers to capture the number of patients with symptoms suggestive of TB.

We chose study sites based on their participation in the Uganda Malaria Surveillance Project, an electronic disease surveillance network established in 2006 through a collaboration involving Makerere University, the University of California San Francisco, and the Uganda Ministry of Health. The surveillance project provides an infrastructure for local providers to capture demographic and clinical information from every patient encounter through a one-page clinical encounter form that facilitates patient care and electronic data collection. The form prompts staff to inquire about and record presenting symptoms, laboratory tests ordered, laboratory test results, clinician diagnoses, and drug prescriptions (*see* Figure E2). In October 2008, the surveillance team modified the form to allow collection of TB-related data, including the presence or absence of cough greater than or equal to 2 weeks; the ordering, completion, and results of sputum acid-fast bacilli examination; and the prescription of treatment for TB. To track patients instructed to return after initial sputum collection, laboratory staff retained a carbon copy of the encounter form, where results of smear examination could also be recorded.

The surveillance project employs one full-time data assistant at each site in addition to the regular clinic staff to enter data from the clinical encounter forms into a customized electronic database (Epi Info; Centers for Disease Control and Prevention, Atlanta, GA). In addition, during the study period, a medical officer, a data officer, and a laboratory technician employed by the surveillance project visited each health facility approximately once every 2 months to encourage local staff to follow the TB suspect evaluation practices recommended by national guidelines and the *International Standards of Tuberculosis Care* (9, 10), and to remind them to document these practices on the clinical encounter form. After a 4-month run-in period to orient staff to collecting TB data on the new form, formal TB data collection began in January 2009. In addition, research personnel reviewed TB laboratory and treatment registers at each site for the entire 2009 year to identify sputum examinations and TB treatments that might have been omitted from the clinical encounter form and entered them into the surveillance database.

Measurements and Statistical Analysis

According to Piot's "onion" model (14), "the operational efficiency of [delivering TB management] services can be expressed in terms of … the probabilities of coverage achieved by each successive 'operation'… [to identify which parameters] exert the greatest influence over the total efficiency of the system." Applied to individual clinics, the onion model suggests that the operational efficiency of evaluating patients suspected of TB can be calculated by determining the cumulative loss of patients at each layer of evaluation. Using this concept, we defined a series of performance indicators, each measuring an important step in the diagnostic pathway, as set out in the *International Standards of Tuberculosis Care* (Table 1) (9, 10). Among those with cough greater than or equal to 2 weeks, the three key indicators included the proportion of patients referred for sputum examination; the proportion of referred patients completing sputum examination, defined as having at least one positive or at least two negative specimens examined; and the proportion of patients with a positive sputum examination prescribed TB treatment. In addition, to quantify the operational efficiency of the diagnostic process, we estimated the cumulative conditional probability that a smear-positive patient with cough greater than or equal to 2 weeks would be evaluated and treated appropriately (i.e., be referred for sputum examination, complete sputum examination, and initiate treatment). For this estimate, we assumed that both smear-positive and smear-negative patients with cough greater than or equal to 2 weeks had equal probabilities of being referred for testing and completing testing. We used logistic regression models with robust standard errors and accounted for clustering by site to obtain quarterly point estimates and 95% confidence intervals (CI) for each indicator. We evaluated changes in each indicator over time using chi-squared tests for heterogeneity and trend. We used bootstrap resampling by site to obtain conservative 95% CIs for the summary proportions. All analyses were performed using STATA 11.0 (Stata Corporation, College Station, TX).

Waiver of Informed Consent

The Makerere University Faculty of Medicine Research and Ethics Committee, the University of California San Francisco Committee on Human Research, and the Uganda National Council for Science and Technology approved the electronic performance monitoring and evaluation system, and waived the requirement for informed consent.

RESULTS

Between January and December 2009, a total of 62,909 adults visited the five health centers, with the number seen per site ranging from 6,426 to 20,612. The median age of patients across all encounters was 29 years (interquartile range, 21–40). Women accounted for 44,217 (70%) patient visits, a sex predominance most pronounced in the child-bearing years and consistent with the role of primary health centers in providing obstetric services. The proportion of data uniquely captured by review of the laboratory or treatment registers and not by the monitoring system was 20–33% in quarter 1, decreasing to 15–21% in quarter 2, and to less than 10% in both quarter 3 and quarter 4 (*see* Table E1).

Screening for Cough

A high proportion of patients were screened for cough, with missing data on cough peaking at 4% in the second quarter of 2009, and decreasing to less than 0.5% by the fourth quarter ($P = 0.064$; chi-squared test for trend). Cough greater than or equal to 2 weeks was documented in 1,288 (2.1%) clinical encounters, and varied from 1.8–3.6% ($P < 0.001$) across sites.

TABLE 1. TUBERCULOSIS SUSPECT EVALUATION PERFORMANCE INDICATORS BASED ON SELECTED STANDARDS FROM THE *INTERNATIONAL STANDARDS OF TUBERCULOSIS CARE*

International Standards of Tuberculosis Care	TB Suspect Evaluation Performance Indicators
Standard 1. All persons with otherwise unexplained productive cough lasting 2–3 weeks or more should be evaluated for tuberculosis	**Indicator 1.** Proportion of patients with cough ⩾2 weeks who were referred for sputum examination
Standard 2. All patients who are capable of producing sputum suspected of having pulmonary tuberculosis should have at least two sputum specimens submitted for microscopic examination in a quality-assured laboratory	**Indicator 2.** Proportion of patients with cough ⩾2 weeks referred for sputum examination who completed sputum examination*
Standard 8. All patients diagnosed with tuberculosis should receive an internationally accepted first-line treatment regimen	**Indicator 3.** Proportion of patients with cough ⩾2 weeks with positive sputum examination who were prescribed treatment

* The 2nd edition of the *International Standards* (November, 2009) made slight changes in the definition of Standard 2. In the 1st edition, which was the edition available throughout most of the study, Standard 2 stated that patients "...suspected of having pulmonary tuberculosis should have at least two, and preferably three, sputum specimens obtained for microscopic examination," and that "[w]hen possible, at least one early morning specimen should be obtained." Because the recommendations for collecting three sputum specimens instead of two and for including at least one early morning specimen in the collection were conditionally phrased ("preferably" and "when possible") and subsequently rescinded in the 2nd edition, we have defined Indicator 2 based on the 2nd edition.

The proportion with cough did not vary substantially over time, measuring 2.5% (95% CI, 0.87–4.1) in the first quarter; 2% (95% CI, 1.1–2.9) in the second quarter; 2.1% (95% CI, 1.2–2.9) in the third quarter; and 1.8% (95% CI, 0.96–2.7) in the fourth quarter ($P = 0.27$; chi-squared test for trend) (Figure 1). A low but increasing proportion of those reporting cough greater than or equal to 2 weeks were evaluated for HIV, ranging from 16% (95% CI, 1–31) in the first quarter to 27% (95% CI, 15–39) in the fourth quarter ($P = 0.066$; chi-squared test for trend). Among the 298 patients who reported cough greater than or equal to 2 weeks and were evaluated for HIV, 105 (35%; 95% CI, 30–41) were seropositive.

Referral for Sputum Examination

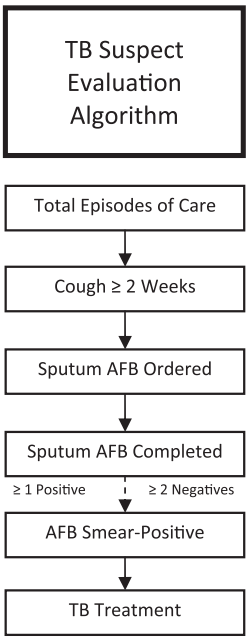
The proportion of patients with cough greater than or equal to 2 weeks who were referred for sputum examination increased from 21% (95% CI, 8.3–33) in the first quarter to 40% (95% CI, 18–61) in the second quarter and 60% (95% CI, 47–74) in the third quarter, before stabilizing at 53% (95% CI, 25–81) in the fourth quarter of 2009 ($P = 0.014$; chi-squared test for trend) (Figures 1 and 2).

Completion of Sputum Examination

The proportion of referred patients who completed sputum examination did not change substantially, from 73% (95% CI, 57–90) in the first quarter to 81% (95% CI, 70–92) in the second quarter, to 80% (95% CI, 64–96) in the third quarter, and to 77% (95% CI, 55–99) in the fourth quarter ($P = 0.85$; chi-squared test for trend).

Treatment Initiation

The proportion of patients with positive sputum examinations who were prescribed appropriate anti-TB therapy initially remained flat from 71% (95% CI, 28–100) in the first quarter to 68% (95% CI, 48–89) in the second quarter, before increasing to 77% (95% CI, 67–86) in the third quarter and 84% (95% CI, 64–100) in the fourth quarter ($P = 0.016$; chi-squared test for trend).



Indicator	Numbers, by Quarter				Proportions*, by Quarter				p-Value
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	
	14,852	14,652	17,369	16,036	--	--	--	--	--
	365	280	349	294	2.5%	2.0%	2.1%	1.8%	0.27
1	75	111	211	155	21%	40%	60%	53%	0.014
2	55	90	168	119	73%	81%	80%	77%	0.85
	7	19	30	25	13%	21%	18%	21%	0.25
3	5	13	23	21	71%	68%	77%	84%	0.016
Cumulative Probability of Being Diagnosed with and Treated for TB†					11%	22%	37%	34%	0.005

Figure 1. Tuberculosis (TB) suspect evaluation algorithm with performance indicators presented as absolute numbers and site-adjusted quarterly proportions, 2009. *Proportions account for clustering by site, and therefore differ from the proportions that would be calculated directly from the numbers displayed in the left side of the table. †Assuming the presenting patient had a detectable case of TB, defined as having cough greater than or equal to 2 weeks and a positive sputum smear examination. AFB = acid-fast bacilli. Q1 = Quarter 1 (January-March); Q2 = Quarter 2 (April-June); Q3 = Quarter 3 (July-September); Q4 = Quarter 4 (October-December).

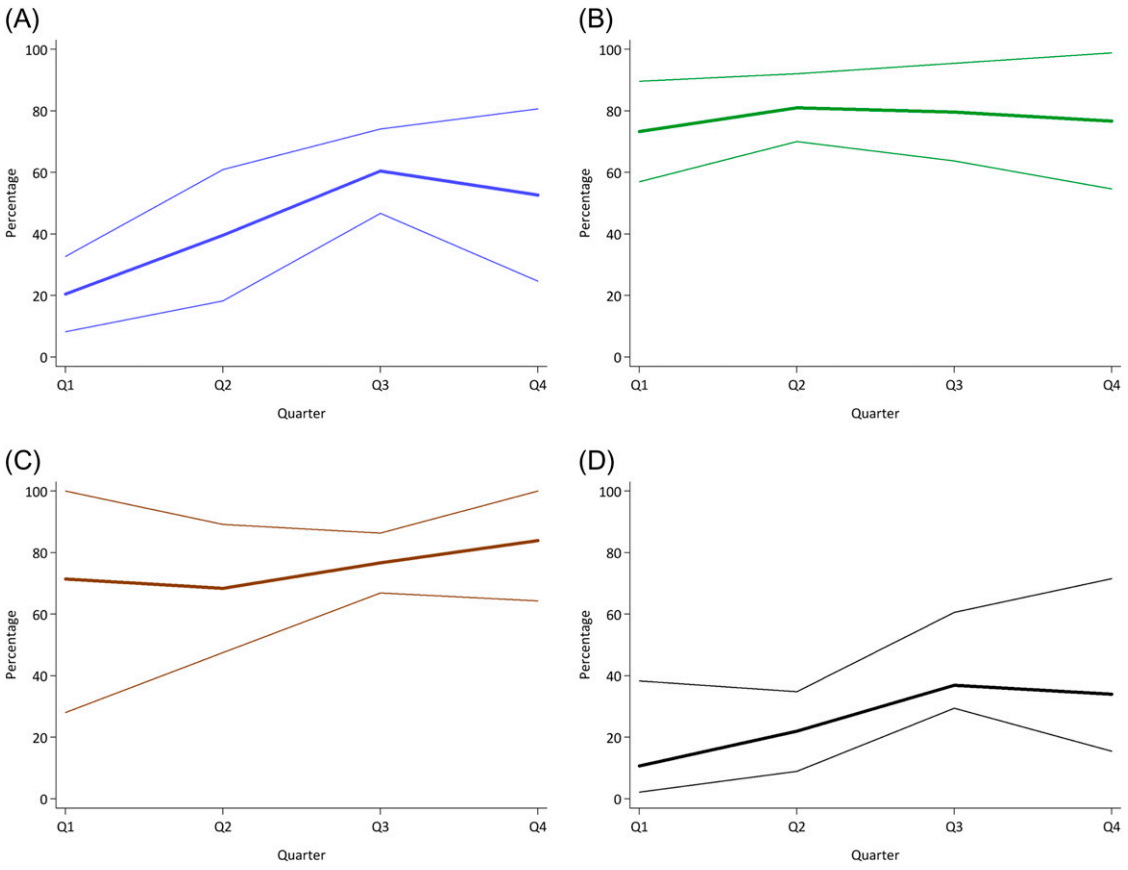


Figure 2. Tuberculosis suspect evaluation performance indicators, 2009, as site-adjusted quarterly proportions with 95% confidence intervals. The *thick lines* represent the estimates of the effects specified below; the *thin lines* represent the upper and lower bounds of the 95% confidence intervals. (*A*) Indicator 1, proportion of patients with cough greater than or equal to 2 weeks referred for sputum smear examination over time. (*B*) Indicator 2, proportion of patients with cough greater than or equal to 2 weeks referred for sputum smear examination who completed sputum smear examination over time. (*C*) Indicator 3, proportion of patients with cough greater than or equal to 2 weeks with positive sputum smear examination who were prescribed treatment over time. (*D*) Summary Indicator, cumulative conditional probability that a patient with cough greater than or equal to 2 weeks and positive sputum smear examination would have been successfully diagnosed and prescribed treatment over time.

Probability of Appropriate Evaluation

The operational efficiency of TB diagnostic services provided at these clinics (i.e., the cumulative conditional probability that a sputum smear-positive patient with cough ⩾2 weeks entering the diagnostic pathway would be evaluated and treated in accordance with the *International Standards of TB Care*) rose steadily from 11% (95% CI, 2.2–38) in the first quarter to 22% (95% CI, 9–35) in the second quarter to 37% (95% CI, 29–61) in the third quarter, before stabilizing at 34% (95% CI, 16–72) in the fourth quarter ($P = 0.005$; chi-squared test for trend).

TB Case Detection

The absolute number of smear-positive cases of TB detected and referred for treatment also increased steadily from 5 patients in the first quarter to 13 in the second quarter to 23 in the third quarter, before stabilizing at 21 patients in the fourth quarter. Among patients referred for and completing sputum examination, the proportion of smear-positive cases of TB identified increased initially from 13% (95% CI, 7–18) to 21% (95% CI, 17–26) ($P < 0.001$), before stabilizing at 18% (95% CI, 11–25) in the third quarter, and 21% (95% CI, 13–29) in the fourth quarter ($P = 0.25$; chi-squared test for trend).

Between-Site Differences

All sites improved at one or more aspects of case detection and treatment referral, although there were differences between sites and some departures from the overall upward trend. In addition, one site performed better than other sites on all indicators. At this site, when performance was averaged over the 12-month study period, 81% (95% CI, 74–87) of patients with cough greater than or equal to 2 weeks were referred for sputum examination, compared with 28–45% at the other sites; 96% (95% CI, 93–100) of referred patients completed sputum examination, compared with 55–91% elsewhere; and 87% (95% CI, 73–100) of smear-positive patients were prescribed treatment, compared with 61–84% at the other sites. The yield of smear microscopy among TB suspects who completed the sputum examination process was high at all sites, with the average proportion testing positive ranging from 15–24%.

DISCUSSION

Tools for electronic data collection, including mobile telephone–based applications, are becoming readily available and can facilitate real-time monitoring and evaluation of TB care at the level of individual clinics. In this operational research study examining the quality of routine diagnostic services for patients suspected of TB attending primary health clinics in rural Uganda, we found that baseline adherence to widely accepted standards of TB suspect evaluation and case management was low but improved modestly during the 12-month study period. Even as the number of patients referred to the laboratory more than doubled, the yield of sputum examination, as defined by the proportion of patients found sputum smear-positive, remained high, and even increased from 13% to 21%. Our findings suggest that improvements in the quality of TB diagnostic services could substantially boost TB case detection and treatment rates in primary health clinics in low-income, high TB-burden countries.

To our knowledge, this is the first study to evaluate TB suspect evaluation practices using objective indicators derived from the *International Standards for Tuberculosis Care*. A striking finding was that at baseline the most readily detectable cases of TB (smear-positive patients who had been coughing for ⩾2 weeks or more) had only an 11% probability of being evaluated and treated in accordance with the *International Standards*. The principal points in the diagnostic pathway at which these cases were lost were referral for testing (only 21% of all patients with cough ⩾2 weeks had sputum smear examination ordered) and referral for treatment (only 71% of those with positive sputum smear examinations were prescribed TB treatment). However, between the first and fourth quarters of 2009, we observed a three-fold increase (from 11% to 34%) in the probability that smear-positive patients with cough greater than or equal to 2 weeks would be evaluated and treated appropriately. These process improvements were associated with a large and statistically significant increase in TB case detection, from 5 to 21 cases. Of note, the four-fold increase in case detection that we observed as evaluation practices improved is greater than the two-fold increase in case detection one would expect if a new test with 100% sensitivity were introduced to replace sputum smear microscopy (assuming the sensitivity of smear microscopy is ~50% in routine settings) (15).

Our findings echo a fundamental principle of TB control espoused by Piot (14) more than 40 years ago: a substantial proportion of cases of TB occur among individuals who fail to access high-quality diagnostic and treatment services. Our data support the extension of this concept to patients who access primary health services but fail to receive appropriate referrals for TB diagnostic testing. Smear-positive case detection can increase substantially if, at a minimum, all patients with chronic cough are referred for TB testing. Although additional cases are potentially identifiable if more sensitive screening algorithms are used, this could place additional demands on already overburdened clinicians and laboratory staff (16).

About one-quarter of all patients failed to complete smear examination after referral, a proportion that did not change substantially during the study period. This is consistent with the proportions previously reported in other studies from sub-Saharan Africa (17–20). The failure of this indicator to improve is not surprising, because high patient costs associated with returning to the clinic on a second day influence this indicator more than provider behavior (20, 21). The fact that some patients fail to return after the initial visit may also explain the surprisingly low proportion of smear-positive patients prescribed treatment. Novel diagnostic algorithms, such as same-day microscopy and reporting, may improve these indicators (22, 23). Shortages of HIV testing kits, along with the location of HIV testing services in separate HIV clinics at some sites, may explain the low proportion of suspects with TB referred for HIV testing. Monitoring systems that also track essential supply inputs, and improved integration of TB and HIV services may prevent such barriers to improving diagnostic processes from arising.

Our data suggest a role for real-time, clinic-level monitoring of TB suspect evaluation practices to increase detection of TB cases. This approach has a number of advantages over existing monitoring and evaluation systems. First, the system captures individual data on symptoms of TB from every patient evaluated in primary health clinics, permitting direct calculation of the numbers at risk for and suspected of TB, and longitudinal measurement of the quality of TB evaluation services for an individual clinic or provider. Second, electronic data collection decreases the burden that hand-written registers place on busy staff in primary health clinics, and also decreases the likelihood of loss, transcription errors, and delays in transmitting data to central public health authorities. Third, a real-time monitoring system allows evaluation of the real-world effectiveness of new interventions and technologies for increasing case detection.

The main limitation of our study is that a new monitoring and evaluation system may underestimate the quality of services provided if data are captured incompletely. However, the system that we used has been successfully collecting data on malaria services at these sites since 2006 (24). Furthermore, auxiliary data collection from existing handwritten TB laboratory and treatment registers added only a small proportion of patients to the number captured by the real-time performance monitoring and evaluation system, and this added proportion disappeared over the course of the study. Second, because of the temporal design of our study, we cannot exclude the possibility that unmeasured secular factors contributed to the improvements we observed in both TB suspect evaluation practices and case detection. However, the magnitude and consistency of these advances over multiple time periods and across multiple sites make secular trends alone an unlikely explanation (25).

In summary, routine evaluation practices for patients suspected of TB in primary health clinics in Uganda fell far short of standards recommended in national and international guidelines. Electronic monitoring and evaluation proved to be feasible, and demonstrated that modest improvements in individual clinic performance in assessing patients suspected of TB were associated with increases in TB case detection. Strategies for future evaluation include interventions using proven techniques to effect and sustain behavioral change, and expansion of the data collection system to include longitudinal capture of individual patient information for measuring treatment outcomes. Quality improvement initiatives coupled with real-time monitoring and evaluation could substantially increase case-detection rates, and the absolute number of cases diagnosed, notified, and treated in low-income countries with a high burden of TB.

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