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# High yield of new HIV diagnoses during active case-finding for tuberculosis

**Walter Mchembere**[a], **Janet Agaya**[a], **Courtney M. Yuen**[b], **Douglas Okelloh**[a], **Millicent Achola**[c], **Joseph Opole**[a], **Jessica Cowden**[d], **Hellen Muttai**[e], **Charles M. Heilig**[f], **Martien W. Borgdorff**[e], **Kevin P. Cain**[e]

[a]Kenya Medical Research Institute, Kisumu, Kenya,

[b]Harvard Medical School, Boston, Massachusetts, USA,

[c]Kenya Medical Research Institute,

[d]US Army Medical Research Directorate – Kenya,

[e]Centers for Disease Control and Prevention, Kisumu, Kenya,

[f]Centers for Disease Control and Prevention, Atlanta, Georgia, USA.

## Abstract

**Objective:** To evaluate the utility of a broad and nonspecific symptom screen for identifying people with undiagnosed HIV infection.

**Design:** Secondary analysis of operational data collected during implementation of a cluster-randomized trial for tuberculosis case detection.

**Methods:** As part of the trial, adults reporting cough, fever, night sweats, weight loss, or difficulty breathing for any duration in the past month were identified in health facilities and community-based mobile screening units in western Kenya. Adults reporting any symptom were offered HIV testing. We analysed the HIV testing data from this study, using modified Poisson regression, to identify predictors of new HIV diagnoses among adults with symptoms and initially unknown HIV status.

**Results:** We identified 3818 symptomatic adults, referred 1424 (37%) for testing, of whom 1065 (75%) accepted, and 107 (10%) were newly diagnosed with HIV. The prevalence of new HIV diagnoses was 21% [95% confidence interval (CI) 17–25%] among those tested in health facilities and 5% (95% CI 4–7%) among those tested in mobile units. More men were diagnosed with HIV than women, despite fewer men being screened. People who reported 4–5 symptoms were over twice as likely to be diagnosed with HIV compared to those reporting 1–3 symptoms (adjusted

Correspondence to Kevin P. Cain, CDC Tanzania, 2448 Luthili Rd, NIMR Complex, Dar es Salaam, Tanzania. bvz1@cdc.gov.

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Conflicts of interest

The authors declare no conflicts of interest.

prevalence ratio in health facilities = 2.58, 95% CI 1.65–4.05; adjusted prevalence ratio in mobile units = 2.63, 95% CI 1.37–5.03).

**Conclusion:** We observed a high yield of new HIV diagnoses among adults identified by active application of a broad symptom screen. Use of integrated tuberculosis and HIV screening could help close the detection gap for both conditions.

### Keywords

Africa; health facilities; HIV; Kenya; tuberculosis

## Introduction

Globally in 2017, an estimated 25% of people living with HIV did not know their HIV status [1]. Sustained testing efforts are needed to close the HIV case-finding gap. However, in some settings, the yield of testing programs has dropped substantially [2], resulting in efforts to conduct more focused testing.

In settings with high burdens of both tuberculosis (TB) and HIV, integrated active case-finding is potentially efficient because symptoms of TB are general, and people with unexplained medical symptoms may have undiagnosed HIV. Undiagnosed HIV has frequently been observed among people undergoing TB evaluation [3–5] and the WHO recommends provider-initiated testing and counselling (PITC) for people with TB symptoms [6]. However, whereas 86% of TB patients in Africa had a documented HIV test in 2017 [7], limited numbers of people with TB symptoms benefit from PITC because TB programs commonly use a restrictive criterion of cough lasting more than 2 weeks as an indicator for TB evaluation. We sought to assess the utility of integrated TB and HIV case-finding with HIV testing focused on people identified through a broad symptom screen.

## Methods

We conducted a secondary analysis of HIV testing data collected during a cluster-randomized trial of programmatic TB screening interventions implemented during February 2015–June 2016 in parts of Kisumu and Siaya Counties in western Kenya – a region with high HIV prevalence (15% in 2012) [8] and a high TB burden [9]. The performance of the interventions for detecting TB has previously been reported [10]. The objectives of the present analysis were to describe the prevalence of undiagnosed HIV among people identified using a broad symptom screen, and to determine predictors of undiagnosed HIV in this population.

Screeners at 28 health facilities (combined catchment population ~300 000) and 25 community mobile screening units asked adults (≥15 years old) about cough, fever, weight loss, night sweats, or difficulty breathing in the past 4 weeks. Because this screening questionnaire was designed to be maximally sensitive, but poorly specific for TB, we refer to ‘symptoms’ rather than ‘TB symptoms’ in this study to avoid the connotation of specificity. People reporting any symptom were asked about their HIV status. Symptomatic adults who had never been tested or who reported a negative HIV test result more than 3 months ago

were referred for HIV testing at the health facility or tested at the mobile unit. Those with new HIV diagnoses were referred for antiretroviral therapy initiation. Symptomatic adults were evaluated for TB clinically and by Xpert MTB/RIF.

Among people tested for HIV, we estimated the prevalence of undiagnosed HIV, and the sensitivity and specificity of different symptom criteria, treating each screening site as a cluster. We then assessed bivariate and multivariable associations between characteristics of screened individuals and new HIV diagnosis. For this analysis of predictors, we included all people with an unknown HIV status at the time of screening, defined as those who had never been tested or who reported a negative test result more than 3 months ago; we did not exclude people who refused HIV testing, therefore identifying predictors of new HIV diagnoses among all those with initial unknown HIV status. To assess how HIV test refusal may have affected these associations, we conducted a sensitivity analysis restricted to those who were tested, and we assessed predictors of test refusal.

We estimated prevalence ratios using modified Poisson regression with generalized estimating equations and robust variance estimates to account for clustering among people screened at a single site. Because people at health facilities might differ from those attending mobile units, we assessed the statistical significance of pair-wise interaction terms between screening venue and each predictor to determine whether to present different models for the two venues. All variables were included in multivariable analyses. We interpreted P values less than 0.05 as statistically significant. Analyses were performed in SAS, version 9.4 (SAS Institute Inc., Cary, North Carolina, USA).

The parent study was approved by KEMRI Scientific and Ethics Review Unit (SERU). The Centers for Disease Control and Prevention relied on the review and oversight of KEMRI SERU. The Walter Reed Army Institute for Research determined that their engagement did not constitute human subjects research. A waiver of informed consent was received for participation in the study.

## Results

In health facilities and mobile units, 2394 and 1424 adults, respectively, reported any symptom in the past month. Women comprised 1273 (53%) of symptomatic adults in health facilities and 965 (68%) in mobile units.

In health facilities, 1840 (77%) symptomatic adults knew their HIV status, the majority of whom were HIV-positive (Fig. 1). Of 554 who did not know their HIV status, 68 (12%) tested HIV-positive, 254 (46%) tested HIV-negative, and 232 (42%) refused HIV testing. The prevalence of undiagnosed HIV among those tested was 21% [95% confidence interval (CI) 17–25%]. One new HIV diagnosis was made for every 35 symptomatic adults, including those with known as well as unknown HIV status at the initial screening. In total, 45 HIV diagnoses were made among 1121 symptomatic men, versus 23 HIV diagnoses among 1273 symptomatic women.

At mobile units, 870 (61%) symptomatic adults did not know their HIV status at the time of evaluation, of whom 39 (4%) tested HIV-positive, 704 (81%) tested HIV-negative, and

127 (15%) refused HIV testing (Fig. 1). The prevalence of undiagnosed HIV among those tested was 5% (95% CI 4–7%). One new HIV diagnosis was made for every 37 symptomatic adults, including those with known as well as unknown HIV status at the initial screening. In total, 18 HIV diagnoses were made among 459 symptomatic men, versus 21 HIV diagnoses among 965 symptomatic women.

Between the health facilities and mobile units, 107 people were newly diagnosed with HIV. Of these, 26 (24%) were also diagnosed with TB, whereas 81 (76%) had TB ruled out. Among symptomatic adults tested for HIV, the criterion of 4–5 symptoms had a sensitivity of 73% (95% CI 65–80%) and a specificity of 55% (95% CI 51–60%) for detecting undiagnosed HIV. Weight loss had a sensitivity of 79% (95% CI 73–85%) and a specificity of 52% (95% CI 49–56%). Other individual symptoms had substantially lower specificity.

Among symptomatic adults with initially unknown HIV status, male sex, age 35–54 years, being screened in a health facility, being screened in an urban location, and having 4–5 symptoms were each associated with increased risk of new HIV diagnosis in bivariate analysis (Table 1). Screening location modified the associations between new HIV diagnosis, and both age ($P = 0.001$) and number of symptoms ($P = 0.046$). Therefore, separate multivariable models were assessed for health facilities and mobile units (Table 1). In health facilities, people 34–54 years old were at significantly higher risk for new HIV diagnosis [adjusted prevalence ratio (aPR) 2.32, 95% CI 1.55–3.48]; this age group was not a significant predictor of new HIV diagnosis in mobile units. People aged at least 55 years were at significantly lower risk for new HIV diagnosis in both venues (aPR in health facilities 0.28, 95% CI 0.08–0.94; aPR in mobile units 0.29, 95% CI 0.10–0.80). In both venues, people with 4–5 symptoms were at significantly higher risk of new HIV diagnosis than people with 1–3 symptoms (aPR in health facilities 2.58, 95% CI 1.65–4.05; aPR in mobile units 2.63, 95% CI 1.37–5.03).

A sensitivity analysis excluding people who refused testing did not substantially change the magnitude or significance of the associations with new HIV diagnoses. Independent predictors of test refusal were being screened at a health facility (aPR 3.77, 95% CI 2.76–5.14), age at least 55 years (aPR 1.54, 95% CI 1.23–1.93), and urban screening location (aPR 0.67, 95% CI 0.52–0.84). Neither sex nor number of symptoms was significantly associated with test refusal.

## Discussion

We found that symptom screening using a broad five-symptom screen identified a population with a high prevalence of undiagnosed HIV. In both health facilities and communities, people with more symptoms were more likely to have new HIV diagnoses. As many new HIV diagnoses were made in men as women, despite fewer men being identified with symptoms. Our results suggest that actively screening for a broad range of symptoms and offering both HIV testing and TB evaluation could improve detection of both conditions.

Although other health facility-based studies have shown high prevalences (10–40%) of undiagnosed HIV among people with presumptive TB, these have typically used more

restrictive symptom criteria (e.g. cough lasting ≥2 weeks) to define presumptive TB [3,4,11]. Our study adds to existing knowledge by showing that the yield of new HIV diagnoses is high even when using a less restrictive symptom screen, which captures a larger population that is overall less likely to have TB. Our study also suggests a role for community-based HIV testing of symptomatic adults, despite a lower prevalence of HIV among those tested in community settings as opposed to health facilities. Most symptomatic adults who attended the mobile units did not know their HIV status, and HIV testing uptake was high, leading to a comparable number of new HIV diagnoses made per number of people with symptoms assessed between the two venues.

More cases were diagnosed among men than women, despite more symptomatic women being screened. Although HIV prevalence is higher among women than men in sub-Saharan Africa [12], the case detection gap is larger in men [13]. Men in sub-Saharan Africa are less likely than women to have been tested recently [14], and are less likely to know their HIV status [13]. Test refusal did not differ by sex in our intervention. The strategy of offering HIV testing to men with symptoms may thus be a particularly useful strategy for closing the case detection gap among men. Our study had several limitations. HIV test refusal was common among health facility attendees. Although our findings suggest that test refusal did not bias the evaluation of predictors of new HIV diagnoses, it limited our ability to assess the prevalence of undiagnosed HIVamong those with unknown HIV status. In addition, we do not have data on HIV testing in people who lack symptoms. Thus, our study demonstrates that having more of the symptoms we evaluated is an important predictor of HIV infection, not that symptoms are the only predictor.

We found a high prevalence of undiagnosed HIV among people identified by actively applying a broad and nonspecific symptom screen in health facility and community settings. This strategy could complement other strategies for focused HIV testing in healthcare settings, such as testing emergency department attendees [15] or patients with a range of ‘indicator’ conditions such as sexually transmitted infections [16]. Moreover, integrated HIVand TB screening could increase the impact of mobile screening units, as we found little overlap between the people newly diagnosed with HIVand those diagnosed with TB. Thus, integrated screening could help countries with high HIV and TB burdens achieve the UNAIDS target of diagnosing 90% of people living with HIV, while simultaneously improving TB case detection.

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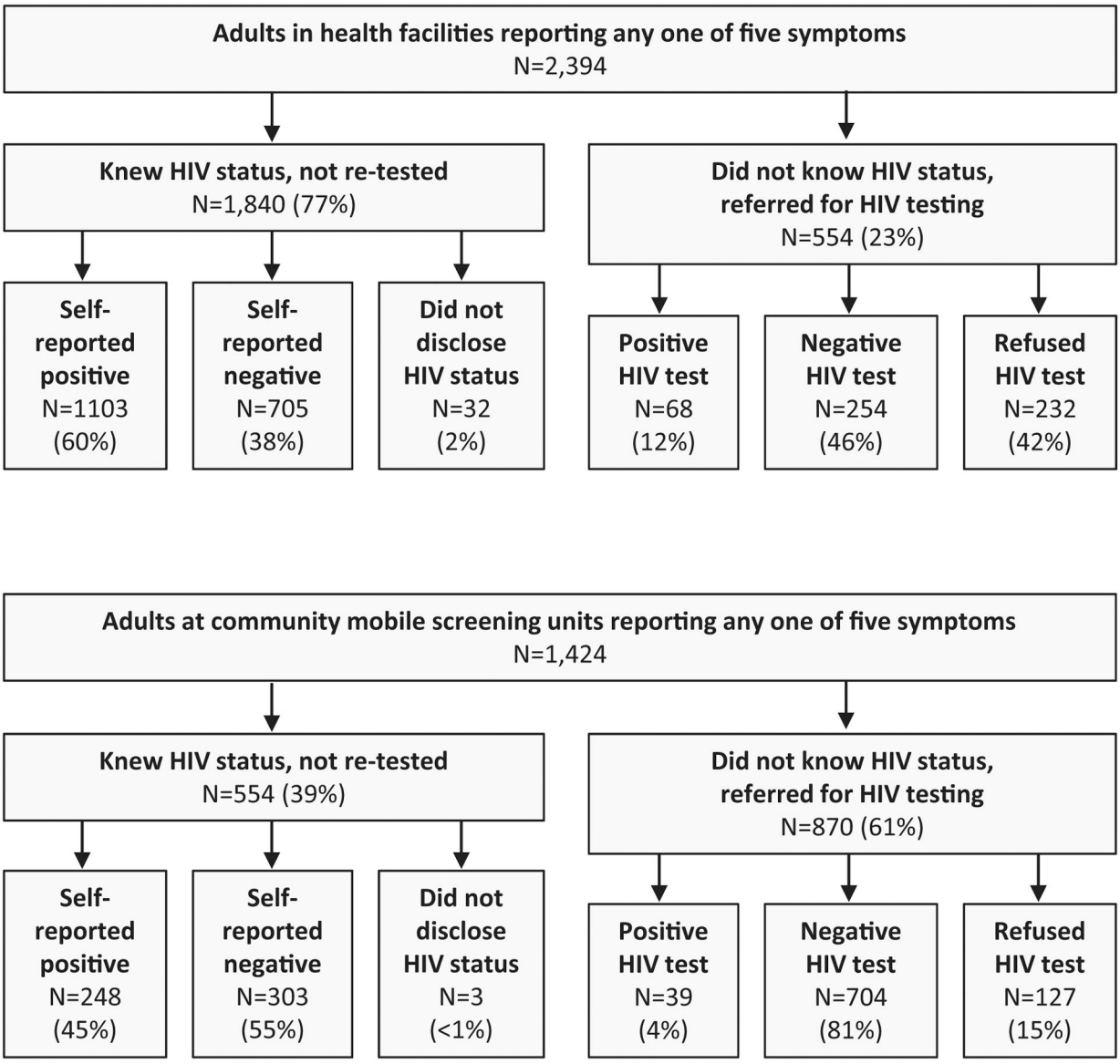


**Fig. 1. Yield of HIV testing among adults in health facilities (*n* = 2394) and mobile units (*n* = 1424) who reported any cough, fever, weight loss, night sweats, or difficulty breathing in the past 4 weeks.**

People who reported never having been HIV tested or a negative HIV test result more than 3 months ago were considered not to know their HIV status and offered HIV testing.

**Table 1.**

Bivariate predictors of new HIV diagnoses among symptomatic adults with initially unknown HIV status ($n = 1424$), and separate multivariable analyses for those with initially unknown HIV status screened in health facilities ($n = 554$) and mobile units ($n = 870$).

| | New HIV diagnoses/number with unknown HIV status (%) | PR (95% CI) | aPR for health facilities (95% CI) | aPR for mobile units (95% CI) |
|---|---|---|---|---|
| Sex | | | | |
| Male | 63 / 595 (11) | **1.67 (1.06–2.61)** | 1.24 (0.68–2.29) | 1.67 (0.93–3.03) |
| Female | 44 / 829 (5) | Reference | Reference | Reference |
| Age, years | | | | |
| 15–34 | 43 / 477 (9) | Reference | Reference | Reference |
| 35–54 | 53 / 407 (13) | **1.69 (1.07–2.67)** | **2.32 (1.55–3.48)** | 0.96 (0.49–1.88) |
| 55+ | 12 / 540 (2) | **0.33 (0.16–0.67)** | **0.28 (0.08–0.94)** | **0.29 (0.10–0.80)** |
| Screening location | | | | |
| Health facility | 68 / 554 (12) | **2.38 (1.48–3.84)** | Not included | Not included |
| Mobile unit | 39 / 870 (4) | Reference | Not included | Not included |
| Rural or urban | | | | |
| Rural | 43 / 845 (5) | Reference | Reference | Reference |
| Urban | 64 / 579 (11) | **1.95 (1.09–3.48)** | 1.53 (0.74–3.19) | 1.08 (0.62–1.88) |
| Number of symptoms | | | | |
| 1–3 | 29 / 708 (4) | Reference | Reference | Reference |
| 4–5 | 78 / 716 (11) | **2.52 (1.72–3.68)** | **2.58 (1.65–4.05)** | **2.63 (1.37–5.03)** |

Bold text indicates statistical significance. aPR, adjusted prevalence ratio; CI, confidence interval; PR, prevalence ratio.