Enhancing tuberculosis (TB) diagnosis among hospitalized patients in KwaZulu-Natal, South Africa: a before-and-after study of a lay health worker-driven intervention

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Abstract

Background

Tuberculosis (TB) among hospitalized patients is underdiagnosed. This study assessed systematic TB-screening, followed by an enhanced TB-diagnostic package for hospitalized patientsimplemented by trained lay health workers in KwaZulu-Natal, South Africa.

Methods

In this before-and-after study we included patients ≥ 18 years. The intervention consisted of systematic clinical screening for TB, HIV and diabetes mellitus by lay health workers and provision of an enhanced TB-diagnostic package including sputum Xpert MTB/Rif Ultra, urine lateral-flow lipoarabinomannan assay (LF-LAM), chest x-ray, and sputum culture. We compared TB case findings with people hospitalized one year preceding the intervention.

Results

In the pre-intervention phase, 5217 people were hospitalized. Among 4913 (94.2%) people not on TB treatment, 367 (7.5%) were diagnosed with TB. In the intervention phase, 4015 eligible people were hospitalized. Among 3734 (93.0%) people not on TB treatment, 560 (15.0%) were diagnosed with TB. The proportion of patients diagnosed with TB was higher in the intervention phase (15.0% vs. 7.5%, $p < 0.001$). Overall in-hospital mortality was lower in the intervention phase [166/3734(4.5%) vs. 336/4913(6.8%), $p < 0.001$].

Conclusion

Lay health worker-led implementation of systematic TB-screening, coupled with provision of an enhanced TB-diagnostic package significantly improved TB case detection and mortality among hospitalized adults.

Background

Tuberculosis (TB) is a leading cause of global morbidity and mortality, with more than ten million people becoming sick with TB, of whom an estimated 1.3 million died in 2022 [1]. Studies show that even with newer TB diagnostic tools, up to one-third of people living withTB remain undiagnosed [1,2]. In hospitalized patients, TB diagnosis is often delayed, with as many as 50% of patients being “missed” despite being in ahealthcare setting [3–5].

Rapid improvement in TB case finding is necessary to achieve the global reduction targets in TB morbidity and mortality laid out inthe endTB strategy [6]. Achieving these goals will require more effective screening tools and more sensitive and specificpoint-of-care diagnostic tests. There is also a need for more effective implementationstrategies to deploy thesetools [7]. Especially the role of lay health workers (LHW) may play an essential role in improving TB screening.

A LHW is defined as any health worker carrying out functions related to health care delivery, who is trained in the context of the intervention, but who does not have formal professional training/certification [8]. LHWs have a long history of providing TB care services, but they are largely based in the community and involved in adherence support or patient tracing. The limited number of studies assessing LHWs based inhealth facilitiessuggest that their activities can significantly improve TB case detection [9]. Given the well-documented shortages in professional health worker cadres [10], LHWs may have a crucial role to play in TB diagnostic efforts, especially in improving TB screening.

In addition to screening, the impact of LHWs on TB diagnosis among hospitalized patients might be enhanced when combined with point-of-care TB tests that can be performed on easy to collect samples. One such existing test is the lateral-flow lipoarabinomannan assay (LF-LAM) recommended for all hospitalized people living with HIV (PLHIV) [11].The test can be done at the bedside using a urine sample and could thus be done by trained LHWs. Whenpoint-of-care diagnostic tools, such as the Xpert MTB/Rif Ultra and LF-LAM are coupled, TB diagnosis amongPLHIV increases by 17-25.9%; the addition of chest X-ray increases the diagnostic yield by an additional 10% [12,13].

In 2018, South Africa issued guidelines recommending the use of LF-LAM for critically ill hospitalized patients with HIV, but there was limited implementation. In 2023, South Africa updated their guidelines recommending MTB/Rif Ultra (Xpert) and LF-LAM for all hospitalized TB-symptomatic people living with HIV [14].

In addition to TB, other illnesses, especially Diabetes Mellitus, play a major role in morbidity and mortality in people living with HIV in South Africa [15]. Multimorbidity has been increasing, with significant comorbidity between HIV, TB and non-communicable diseases (NCDs) [16,17]. According to the latest WHO data, NCDs were estimated to account for over 50% of all deaths in the country in 2016 [18].

Systematic implementation of TB and NCD screening among hospitalized patients in high burden settings remains challenging. While there are a variety of reasons for this, one may be that existing facility staff are too overwhelmed to systematically screen all patients and to perform all available diagnostic TB tests among those who are eligible [19]. We explored an LHW-led intervention of systematic screening for TB, HIV and diabetes mellitus (DM), followed by the provision of an enhanced TB diagnostic package including urine LF-LAM, Xpert MTB/Rif Ultra, and chest X-ray for hospitalized patients in the high TB and HIV burden setting of KwaZulu-Natal, South Africa.

Methods

Methods

Setting

This study was conducted in two hospitals (Eshowe and Mbongolwane) in King Cetshwayo District, KwaZulu-Natal, South Africa. King Cetshwayo Districthas a high HIV prevalence, estimated at 26.4% of adults aged between 15–59 years in 2018 [20]. At the time the study started in 2018, the prevalence of TB was reported to be 717 per 100,000 people [21]. Médecins Sans Frontières (MSF) has run an HIV/TB project in this area since 2011 and supported both hospitals with HIV and TB care. Eshowe Hospital is a 460-bed district hospital located in a semi-urban area. Mbongolwane is a 196-bed hospital located in a rural area.The project area achieved the UNAIDS 90-90-90 targets in 2018 [22].

Study Design

This is abefore-and-after study. We compared the proportion of hospitalised people diagnosed with TB after the implementation ofthe intervention with a historical comparison group. The intervention period, which was from March 2019 to March 2020 in Eshowe Hospital and from April 2019 to April 2020 in Mbongolwane Hospital, is referred to as the “intervention phase”. The historical comparison was from March 2018 to February 2019, referred to as the “pre-intervention phase”.

Study population

In the pre-intervention phase, we included all patients aged 18 years and above admitted to the medical and infectious disease wards in Eshowe Hospital and Mbongolwane Hospital. In the intervention phase, we included patients aged 18 years and above admitted to these wards if they provided informed consent.

Interventions and procedures

Our team recruited and trained six LHWs to provide systematic screening for TB, HIV and DM for patients in the intervention phase. These LHWswere trainedin TB screening and testing andworked in the hospitals' inpatient wards. They were supported by the physicians and nurses working in the hospital. The screening and diagnostic algorithm is depicted in Fig. 1. For DM screening, LHWs were trained to measure random blood sugar (RBS) for all patients and assess for symptoms or history of DM. HbA1c or fasting blood sugar was done for those with RBS ≥ 11.1mmol/L. HbA1c was measured for patients known to have DM before admission to determine their glycemic control. The Society for Endocrinology, Metabolism, and Diabetes of South Africa guidelines were followed for the diagnosis of DM [23].

Figure 1: Diagnostic algorithm for hospitalised patients.

We systematically assessed the HIV status of the patients through clinical history and medical file review. LHW performed HIV testing for those with unknown status. South African national HIV counseling and testing policy guideline was followed for HIV testing [24].

LHW provided TB health education, including an explanation of TB screening questions. They then screened for the presence of TB symptoms, including cough of any duration, fever of any duration, weight loss in the last one month, or night sweats. They showed a video on how to produce quality sputum samples for all patients with HIV, DM, or those patients who reported at least one TB symptom. They collected sputum for the Xpert test. All procedures were conducted by the LHWs in the wards where the patients were admitted, supervised by the DoH ward nurse. Sputum sample processing and quality assurance were performed according to the standards of the South African National Health Laboratory Service [25].

Patients who had at least one TB symptom, HIV, or DM also had a posterior-anterior chest X-ray (CXR). The attending medical officers read the CXRs. If there was ambiguity about the CXR findings, telemedicine radiology support was provided by MSF.

Patients who were known or newly diagnosed HIV-positive underwent bedside urine LF-LAM testing irrespective of CD4 count or symptoms. LF-LAM diagnostic procedure was done by the LHW according to the manufacturer's recommendation and South African guidelines [14,26].

TB culture was done as described in Fig. 1. Genotypic testing for resistance to isoniazid, rifampicin, fluoroquinolones, and the injectable class of medications was done using line-probe assay testing in all persons found to have rifampicin resistant (RR)-TB on Xpert test.

Table 1 summarizes the screening and diagnostic tests done in the pre-intervention and intervention phases. In the pre-intervention phase, practice differed from the South African guidelines in that symptom-based screening was not systematically done, and LF-LAM wasn't done despite the introduction of a policy to do LF-LAM for selected patients in 2017 [14]. Task-shifting to LHWs was done in the intervention phase, while pre-intervention, nurses were assigned these tasks.

Table 1
Comparison of screening strategy and diagnostic tests between pre-intervention and intervention phases of the study.

	Pre-intervention phase		Intervention phase	
	Activity	Cadre responsible	Activity	Cadre responsible
DM screening	RBS was clinically prompted	MO to decide when RBS was needed, nurse to take the sample	Systematic DM screening and RBS, with HbA1c or FBS for those with RBS > 11.1mmol	LHW to screen RBS Nurse to do HbA1c/ FBS
HIV testing	HIV testing for all TB patients	Nurse	Systematic HIV testing for those with unknown status[a] regardless of TB status	LHW
TB screening and diagnosis	Symptom screening not systematically done	Nurse	Systematic symptom screening after TB education	LHW
	CXR was done for presumptive TB patients and interpreted by medical officers	CXR requested by nurse, done by hospital radiographer MO to interpret CXR	Systematic CXR for HIV-positive, DM, or presumptive TB patients CXR interpretation	CXR requested by nurse, done by hospital radiographer MO / expert telemedicine radiologist advice
	No use of urine LF-LAM	NA	Systematic urine LF-LAM for HIV-positive patients regardless of symptoms or CD4 count	LHW
	Xpert if a clinical presumption of TB	Nurse to collect sputum sample	Systematic Xpert for HIV-positive, DM or presumptive TB patients	LHW explains how to produce a good sputum sample and collects the sample. Nurse to process the sample and send it for testing to the lab.
	TB Culture if Xpert negative and other conditions are met	MO to decide need for culture	Depending on screening results we considered: - Suggestive CXR - First-line TB treatment failing - Clinical presumption of TB - Positive LF-LAM	MO to decide need for culture

DM, diabetes mellitus; **RBS**, random blood sugar; **HbA1c**, hemoglobin A1; **FBS**, fasting blood sugar; **TB**, tuberculosis; **CXR**, chest x-ray; **LF-LAM**, lateral flow lipoarabinomannan assay; **Xpert**, Xpert MTB/RIF ultra; **LHW**, lay health worker; **MO**, medical officer;

[a] **unknown HIV status**, never tested before or does not have a documented HIV negative test in the last 3 months

TB diagnosis was determined, and treatment was started by the attending medical officers. TB was classified based on the method of diagnosis, site of TB, and rifampin sensitivity. TB was considered to be bacteriologically confirmed if at least one of the following were positive: 1) Xpert; 2) culture for *M. tuberculosis*; 3) LF-LAM. TB was considered to be radiologically confirmed if the CXR showed findings suggestive of TB. Patients were considered to be clinically diagnosed if they had clinical findings suggestive of TB and the treating physician decided to initiate TB treatment, and neither the Xpert, culture,

CXR, nor LF-LAM were positive. TB treatment was provided based on the South African national guidelines [27]. Patients who were discharged before release of culture results were traced by phone and linked to care. Patients diagnosed with DM or HIV were also linked to care for their HIV and DM treatment.

Data collection and analysis

For the pre-intervention phase, we retrospectively collected data on demographic characteristics, TB diagnosis, and discharge outcomes from hospital admission and discharge registers. For patients who had evidence of a diagnosis of TB in admission and discharge registers, additional information on the date of diagnosis, type of TB, TB site, methods of TB diagnosis, date of TB treatment initiation, HIV status, CD4 count, and DM status was collected from the South African electronic patient management system (TIER.Net) or patient files. In the intervention phase, we used a pretested case report form to collect the patients' socio-demographic and clinical data prospectively.

Patient information for both study phases was entered in a study database designed in Epi-InfoTM 7 (CDC, Atlanta). Data analysis was done using STATA version 15 (StataCorp, College Station, TX). Descriptive statistics were carried out. For comparison of the two phases, we used the Wilcoxon rank-sum test for nonparametric data and the chi-square test for categorical variables.

Ethics

The study was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, South Africa (BFC/109/18) and the MSF Ethics Review Board (Geneva, Switzerland) (ID: 1833). All methods were performed in accordance with the relevant guidelines and regulations.

All patients in the intervention phase were explained the purpose of the study by the study staff and written informed consent was sought. For patients who were, due to their medical condition, unable to provide consent, informed consent from the next of kin was sought. This related mainly to patients with psychiatric illnesses or patients with decreased consciousness and this was attested by their treating physician. Informed consent and participant information forms were available in English and isiZulu.

Results

Study population

A total of 10,159 eligible patients were admitted to both hospitals during the study period (Fig. 2). In the pre-intervention phase, 5217 eligible patients were admitted, of which 304 (5.8%) were excluded because they were already on TB treatment. A total of 4913 patients [median age 50 years (IQR: 32–67); 56.6% females] were included. Out of these, 367 (7.5%) patients were diagnosed with TB. We have no information on overall HIV positivity rate or patients with diabetes in the pre-intervention phase. In the intervention phase, 4942 eligible patients were admitted, among whom 4015 (81.2%) provided informed consent; 281 (7.0%) were excluded because they were already on TB treatment; 3734 patients [median age 51 years (IQR: 33–68); 62.0% females] were included. Out of these, 560 (15.0%) patients were diagnosed with TB. The age distribution of people included in the study was similar between the intervention and non-intervention phase (median age 50 years, IQR 32–67 vs. median age 51 years, IQR 33–68 respectively ($p = 0.053$), but the proportion of females included in the intervention phase was higher than the pre-intervention phase (62.0% vs. 56.6%, $p < 0.001$).

Figure 2: Study population flow diagram by study phase.

Diagnosis

Compared with the pre-intervention phase, the proportion of patients newly diagnosed with TB during hospitalization in the intervention group was higher [367/4913 (7.5%) vs. 560/3734 (15.0%), $p < 0.001$]. The description of people diagnosed with TB during hospitalization is shown in Table 2.

Table 2
Characteristics of patients diagnosed with TB during hospitalization by study phase.

	Pre-intervention (n %)	Intervention (n %)	*P-value*
Total	367	560	
Female	141(38.4)	244(43.6)	*0.12*
Median Age years (IQR)	40(30–53)	43(32–57)	*0.004*
Site of TB Disease			
PTB	306(83.4)	448(80.0)	0.197
EPTB	61(16.6)	112(20.0)	
Type of TB			
DSTB	353(96.2)	548(97.9)	*0.132*
RRTB	14(3.8)	12(2.1)	
HIV status			
Negative	88(24.0)	152(27.1)	*0.666*
Positive	249(67.8)	402(71.8)	
Unknown	30(8.2)	6(1.1)	
Median CD4 count (IQR)*	136(42–323)	183(45–432)	*0.145*
Diabetes Mellitus			
No	283(77.1)	511(91.2)	0.105
Yes	17(4.6)	49(8.8)	
Unknown	67(18.3)	0(0.0)	

TB, tuberculosis; **IQR**, interquartile range; **PTB**, pulmonary TB; **EPTB** extra-pulmonary TB; **DSTB**, drug sensitive TB; **RRTB** rifampin-resistant TB

* CD4 test was done for 134 patients in pre-intervention and 400 patients in intervention phase.

In the pre-intervention period, TB was mainly diagnosed based on radiography (CXR), bacteriology (Xpert MTB/RIF) and on clinical grounds. In the intervention period there was an increase in the number of people who had bacteriologically confirmed TB or radiologic diagnosis of TB (Fig. 3), with fewer people diagnosed on clinical grounds alone (94(25.6%) vs. 49(8.8%); $p < 0.001$). Out of those diagnosed clinically, 26 (27.7%) in the pre-intervention group and 38 (77.6%) in the intervention group were diagnosed with EPTB.

Figure 3: Methods of TB diagnosis among patients diagnosed with TB, n (%). A) Pre-intervention (n = 367) and B) Intervention (n = 560)

Comorbidities

The overlap of TB, HIV, and DM in the intervention phase is depicted in Fig. 4. Out of the 3734 patients included in the intervention, 1346 (36.0%) were HIV-positive, 706 (18.9%) had diabetes, and 560 (15.0%) were newly diagnosed with TB during this admission. Among patients with TB, 402 (71.8%) were HIV-positive, and 49 (8.8%) had DM; among the HIV-positive, 402 (29.9%) were newly diagnosed with TB and 114 (8.5%) had DM; and among those with DM, 114 (16.1%) had HIV and 49 (6.9%) were diagnosed with TB.

Figure 4: Overlap of HIV, DM, and TB among patients in intervention phase

(total number = 3734), n (% total participants)

Outcomes

Among those diagnosed, 361 (98.4%) in the pre-intervention and 556 (99.3%) in the intervention group were initiated on TB treatment during hospitalization. The median time from admission to TB treatment initiation was two days (IQR: 0–5) in the pre-intervention phase and 2 days (IQR: 0–4) in the intervention phase. Most of the patients enrolled in the study started TB treatment within 30 days of admission [369 (99.2%) in the pre-intervention phase (min-max 0–44 days), and 557 (99.5%) in the intervention phase (min-max 0–62 days)].

The overall in-hospital mortality of the patients included in the study was significantly lower in the intervention phase compared with the pre-intervention phase [166/3734(4.4%) vs. 336/4913(6.8%), $p < 0.001$].

Discussion

In this study, LHWs led an enhanced screening and TB diagnostic package at hospital admission that was associated with a significant increase in patients newly diagnosed with TB. Over half of hospital admissions had HIV, DM, TB, or a combination of the three diseases. Two-thirds of patients with TB were HIV-positive, which is consistent with previous reports from the province [28], and one-third of those living with HIV were newly diagnosed with TB, highlighting the importance of providing integrated HIV and TB care. Another important finding from our study is that the overall in-hospital mortality in the intervention phase was significantly lower than in the pre-intervention phase. This result is consistent with modelling studies, in which enhanced techniques of TB diagnosis were estimated to reduce mortality [29]. Although our study design limits our ability to make causal inferences, the decreased mortality rate suggests a notable benefit for patients that should be further assessed.

Although not statistically significant, there was a trend towards a higher median CD4 count in the intervention phase, which is in line with higher ART coverage in the area and results in decreased mortality as seen in this study. While this is expected to contribute to decreased TB, the number ofpeople diagnosed with TB in the intervention phase was significantly higher than in the pre-intervention phase. This is likely due to the systematic screening and diagnostic interventions that were implemented by the LHWs. The improvement in TB diagnosis in our study is consistent with the result of the STAMP trial in which the addition of LF-LAM to the TB diagnostic algorithm in HIV-positive patients in South Africa and Malawi improved TBcase-finding [30]. However, our study differs from the STAMP trial in thatour study is an implementation study and LHW delivered the interventions.

Compared with the pre-intervention group, a lower proportion of patients in the intervention group were diagnosed on clinical grounds alone. Of note, most of the patients diagnosed clinically in the intervention group had EPTB. Similar results have also been reported in other studies in which the certainty of diagnosis of TB improved when the TB diagnostic algorithm included the use of urinary LF-LAM, particularly insputum-scarce patients [31,32]. Increased certainty in TB diagnosis might have downstream positive effects for patients, as studies with other diseases show that the certainty of diagnosis may improve adherence [33,34]. Although this would need to be formally assessed in persons living with TB, it represents another compelling reason to increase access to improved TB tests.

Our study utilized trained, supervised, and paid LHWs to delivermuch of the screening and point-of-care testing in the intervention period. They also facilitated the sample collection and logistics for the other TB diagnostic tests, working in partnership with nurses and medical officers. The presence of this cadre of healthcare workers was likely an important part of the success of the overall intervention. Other studies have shown the effectiveness of LHWs in inpatient settings, but these are largely from the era before the use of LF-LAM and Xpert MTB/Rif Ultra [35,36]. Our study also expanded the role of LHWs beyond what is sometimes described in the literature as “cough officers” focused only on symptom screening or sample

collection [37]. The range of activities LHWs can take on, can increase for HIV and TB [38], and our findings support expanding their work to inpatient settings and NCD screening as part of overall health systems strengthening. Healthsystem weaknesses in the diagnostic approach to TB, including shortages of physicians and nurses enhance the importance to task-shift work to LHWs [39,40]. The LHWs were a key part of this intervention, however, facility LHW are not existing cadres within the Department of Health system, so their positions were not maintained after the study. There is need for professionalizing and formalizingthis important cadre of healthcare paraprofessionals.

This study has several limitations. Improvements in care over the study period might have contributed to improvement in TB diagnosis and mortality as we used a historical comparison group. Data in the pre-intervention phase was collected retrospectively. TB, HIV and DM screening were not done systematically and as such, screening information was often missing in the pre-intervention phase, which might introduce bias. In the intervention phase, 12.8% of the patients were not able to give informed consent, and 6% declined to participate. This was because of the high number of patients with psychiatric conditions admitted to the medical wards during the study period. It may be that these groups of patients were fundamentally different from those included, and they could have had both higher or lower rates of TB.Furthermore, by implementing a comprehensive package, it is difficult to determine which components of the intervention might have been more effective in improving TB case detection.

Conclusion

The implementation of LHW-supported, systematic screening for TB, HIV, and DM with the provision of an enhanced package of diagnostic tests, including LF-LAM, Xpert, CXR, and/or TB culture for patients with TB symptoms, DM, or HIV, improved TB case finding among hospitalized patients. Task shifting of a major part of the screening and testing package to LHWs sets this intervention apart and turns the implementation of an enhanced TB diagnostic package into a success without overburdening medical staff, offering a potential solution to improve widespread implementation of enhanced TB screening.

Abbreviations

ART Anti-Retroviral Therapy

CXR Chest X-ray

DM Diabetes mellitus

DoH Department of Health

DSTB Drug sensitive tuberculosis

EPTB Extrapulmonary tuberculosis

FBS Fasting blood sugar

HBA1C Glycated haemoglobin

IQR Interquartile range

LF-LAM lateral flow urine lipoarabinomannan assay

LHW Lay Health Worker

MO Medical Officer

MSF Médecins sans Frontières

NCD Non-communicable disease

PLHIV People living with HIV

PTB Pulmonary tuberculosis

RBS Random blood sugar

RR-TB Rifampicine-resistant tuberculosis

TB Tuberculosis

WHO World Health Organization

Xpert ultra Xpert MTB/RIF Ultra

Declarations

Author Contribution

Conceived the study and wrote the protocol: AS, GVC, SJS, CL, JF, PI, LOCollected the data: ABB, Performed the analysis: ABB, AYD, AS, CLWrote the main manuscript: ABB, JF, PI, LOreviewed the manuscript: ABB, AYD, AS, GVC, SJS, MSB, MM, CL, JF, PI, LO

References

1. World Health Organization. Global Tuberculosis Report. *WHO* https://iris.who.int/bitstream/handle/10665/373828/9789240083851-eng.pdf?sequence=1 (2023).
2. Walzl, G. *et al.* Tuberculosis: advances and challenges in development of new diagnostics and biomarkers. *Lancet Infect. Dis.* **18**, e199–e210 (2018).
3. Carol Metcalf, Debbie Bradshaw & Victoria Pillay-Van Wyk. *Cause of Death Statistics for South Africa: Challenges and Possibilities for Improvement*. (Burden of Disease research Unit, 2010).
4. Cohen, T. *et al.* The prevalence and drug sensitivity of tuberculosis among patients dying in hospital in KwaZulu-Natal, South Africa: a postmortem study. *PLoS Med.* **7**, e1000296 (2010).
5. Wong, E. B. *et al.* Causes of death on antiretroviral therapy: a post-mortem study from South Africa. *PloS One* **7**, e47542 (2012).
6. *Implementing the End TB Strategy: The Essentials - 2022 Update*. (World Health Organization, Geneva, 2022).
7. Vesga, J. F. *et al.* Assessing tuberculosis control priorities in high-burden settings: a modelling approach. *Lancet Glob. Health* **7**, e585–e595 (2019).
8. Lewin, S. A. *et al.* Lay health workers in primary and community health care. *Cochrane Database Syst. Rev.* CD004015 (2005) doi:10.1002/14651858.CD004015.pub2.
9. José, B. *et al.* Using community health workers for facility and community based TB case finding: An evaluation in central Mozambique. *PLOS ONE* **15**, e0236262 (2020).
10. National Department of Health, SA. 2030 Human Resources for Health strategy: Investing in the Health Workforce for Universal Health Coverage. https://www.spotlightnsp.co.za/wp-content/uploads/2020/08/2030-HRH-strategy-19-3-2020.pdf (2020).
11. World Health Organization (WHO). WHO updates policy for the use of lateral flow urine lipoarabinomannan assay (LF-LAM) for diagnosing active tuberculosis in people living with HIV. https://www.who.int/news/item/04-11-2019-who-updates-policy-for-the-use-of-lateral-flow-urine-lipoarabinomannan-assay-(lf-lam).

12. Broger, T. *et al.* Diagnostic yield of urine lipoarabinomannan and sputum tuberculosis tests in people living with HIV: a systematic review and meta-analysis of individual participant data. *Lancet Glob. Health* **11**, e903–e916 (2023).
13. Huerga, H. *et al.* Incremental Yield of Including Determine-TB LAM Assay in Diagnostic Algorithms for Hospitalized and Ambulatory HIV-Positive Patients in Kenya. *PLoS ONE* **12**, e0170976 (2017).
14. National Department of Health, SA. Guidance on the use of Lateral Flow Urine Lipoarabinomannan (LF-LAM) assay for the diagnosis of tuberculosis in people living with HIV. (2018).
15. Rajagopaul, A. & Naidoo, M. Prevalence of diabetes mellitus and hypertension amongst the HIV-positive population at a district hospital in eThekwini, South Africa. *Afr. J. Prim. Health Care Fam. Med.* **13**, e1–e6 (2021).
16. Weimann, A., Dai, D. & Oni, T. A cross-sectional and spatial analysis of the prevalence of multimorbidity and its association with socioeconomic disadvantage in South Africa: A comparison between 2008 and 2012. *Soc. Sci. Med. 1982* **163**, 144–156 (2016).
17. Roomaney, R. A., van Wyk, B., Turawa, E. B. & Pillay-van Wyk, V. Multimorbidity in South Africa: a systematic review of prevalence studies. *BMJ Open* **11**, e048676 (2021).
18. Non-communicable diseases - country profile south Africa.
19. Salifu, R. S. & Hlongwana, K. W. Barriers and facilitators to bidirectional screening of TB-DM in Ghana: Healthcare workers' perspectives. *PLoS ONE* **15**, e0235914 (2020).
20. Nolwenn Conan. Mbongolwane and Eshowe HIV Impact in population Survey (2nd survey) 2018. (2019).
21. Nolwenn Conan. Mbongolwane and Eshowe HIV Impact in Population Survey (2nd Survey) and tuberculosis symptom screening results. (2020).
22. Conan, N. *et al.* Increase in HIV viral suppression in KwaZulu-Natal, South Africa: Community-based cross sectional surveys 2018 and 2013. What remains to be done? *PLOS ONE* **17**, e0265488 (2022).
23. SEMDSA Type 2 Diabetes Guidelines Expert Committee. The 2017 SEMDSA Guideline for the Management of Type 2 Diabetes. https://www.kznhealth.gov.za/family/SEMDS-2017-Guidelines.pdf (2017).
24. National Department of Health, SA. National HIV Counselling and Testing Policy Guidelines. https://www.nicd.ac.za/assets/files/HCT-Guidelines-2015.pdf (2015).
25. *Primary Healthcare Laboratory Handbook, a Step-by-Step Guide*. (South African Department of health, Pretoria, South Africa, 2018).
26. Alere. Alere Determine TB-LAM Ag insertion package. (2013).
27. National Department of Health, SA. National Tuberculosis Management Guidelines 2014. https://www.tbonline.info/media/uploads/documents/national_tuberculosis_management_guidelines_%282014%29.pdf (2014).
28. National Department of Health, SA. Strategic Plan 2015 - 2019. https://www.kznhealth.gov.za/Strategic-Plan-2015-2019.pdf (2015).
29. Dowdy, D. W., Chaisson, R. E., Moulton, L. H. & Dorman, S. E. The potential impact of enhanced diagnostic techniques for tuberculosis driven by HIV: a mathematical model. *AIDS Lond. Engl.* **20**, 751–762 (2006).
30. Gupta-Wright, A. *et al.* Rapid urine-based screening for tuberculosis in HIV-positive patients admitted to hospital in Africa (STAMP): a pragmatic, multicentre, parallel-group, double-blind, randomised controlled trial. *Lancet Lond. Engl.* **392**, 292–301 (2018).
31. Lawn, S. D. *et al.* Diagnostic accuracy, incremental yield and prognostic value of Determine TB-LAM for routine diagnostic testing for tuberculosis in HIV-infected patients requiring acute hospital admission in South Africa: a prospective cohort. *BMC Med.* **15**, 67 (2017).
32. Sabur, N. F., Esmail, A., Brar, M. S. & Dheda, K. Diagnosing tuberculosis in hospitalized HIV-infected individuals who cannot produce sputum: is urine lipoarabinomannan testing the answer? *BMC Infect. Dis.* **17**, 803 (2017).

33. Backer, V., Stensen, L., Sverrild, A., Wedge, E. & Porsbjerg, C. Objective confirmation of asthma diagnosis improves medication adherence. *J. Asthma Off. J. Assoc. Care Asthma* **55**, 1262–1268 (2018).
34. Aarestrup, L. K., Hermansen, M. N., Prahl, J., Hansen, K. S. & Chawes, B. L. Objective confirmation of asthma diagnosis, treatment adherence and patient outcomes in children and adolescents. *Acta Paediatr. Oslo Nor. 1992* **111**, 1220–1229 (2022).
35. Cardarelli, R. *et al.* Reducing 30-day readmission rates in a high-risk population using a lay-health worker model in Appalachia Kentucky. *Health Educ. Res.* **33**, 73–80 (2018).
36. Basnight, R. *et al.* Evaluation of lay health workers on quality of care in the inpatient setting. *PLOS ONE* **18**, e0293068 (2023).
37. Lin, C.-H. *et al.* 'Cough officer screening' improves detection of pulmonary tuberculosis in hospital in-patients. *BMC Public Health* **10**, 238 (2010).
38. Ndlovu, Z. & Ellman, T. Lay testing cadres and point-of-care diagnostic tests for HIV and other diseases: An essential combination in health service delivery. *PLoS Med.* **18**, e1003867 (2021).
39. World Health Organization (WHO). *Systematic Screening for Active Tuberculosis: Principles and Recommendations*. (World Health Organization, Geneva, 2013).
40. Ahmad Khan, F. *et al.* Performance of symptom-based tuberculosis screening among people living with HIV: not as great as hoped. *AIDS Lond. Engl.* **28**, 1463–1472 (2014).

Figures

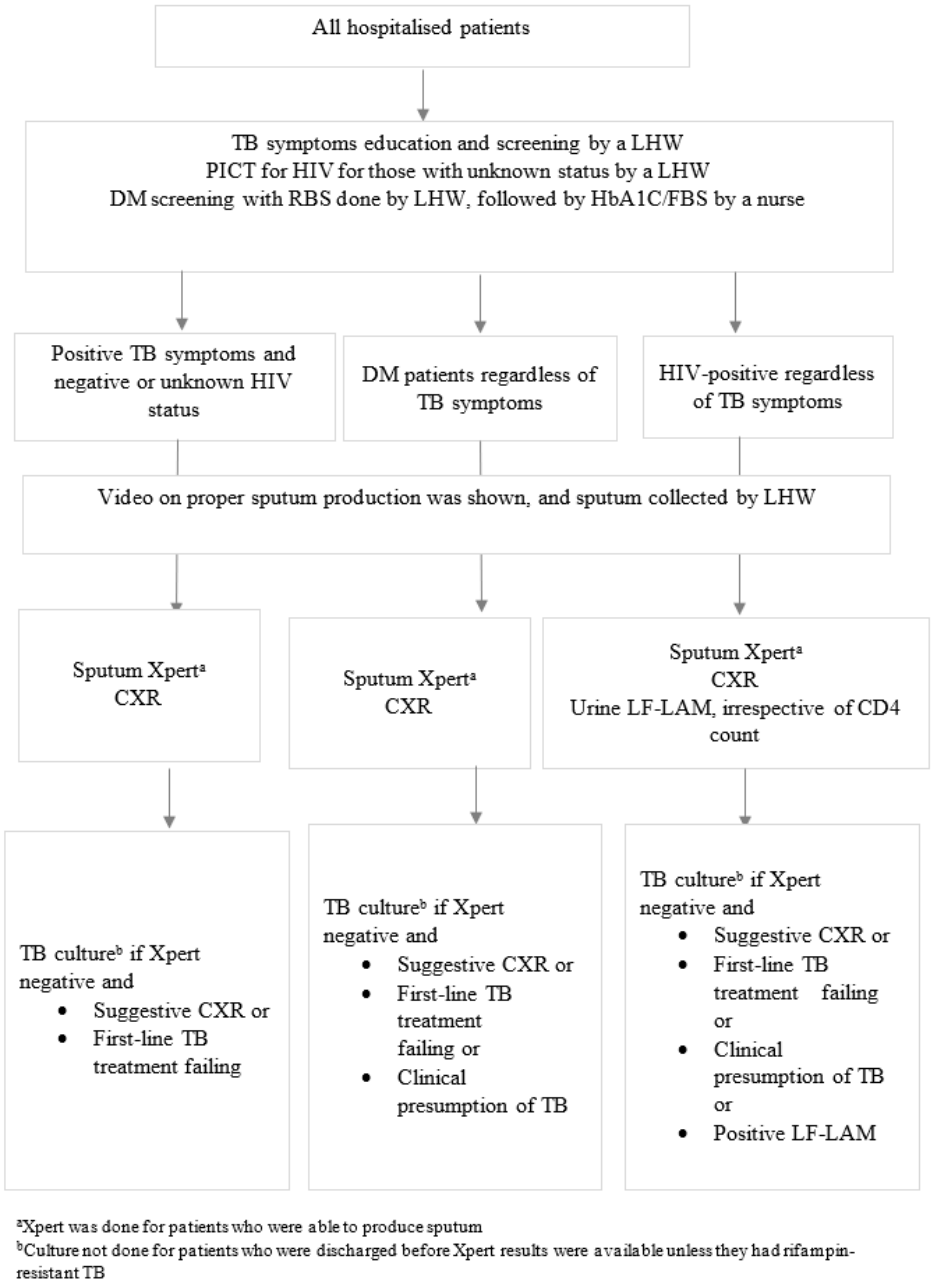

Figure 1

Diagnostic algorithm for hospitalised patients.

TB, tuberculosis; **LHW**, lay health workers; **PICT**, provider-initiated HIV counseling and testing; **DM**, diabetes mellitus; **RBS**, random blood sugar; **HbA1C**, hemoglobin A1C; **FBS**, fasting blood sugar; **Xpert**, Xpert MTB/RIF Ultra; **CXR**, Chest X-ray; **LF-LAM**, lateral flow urine lipoarabinomannan assay

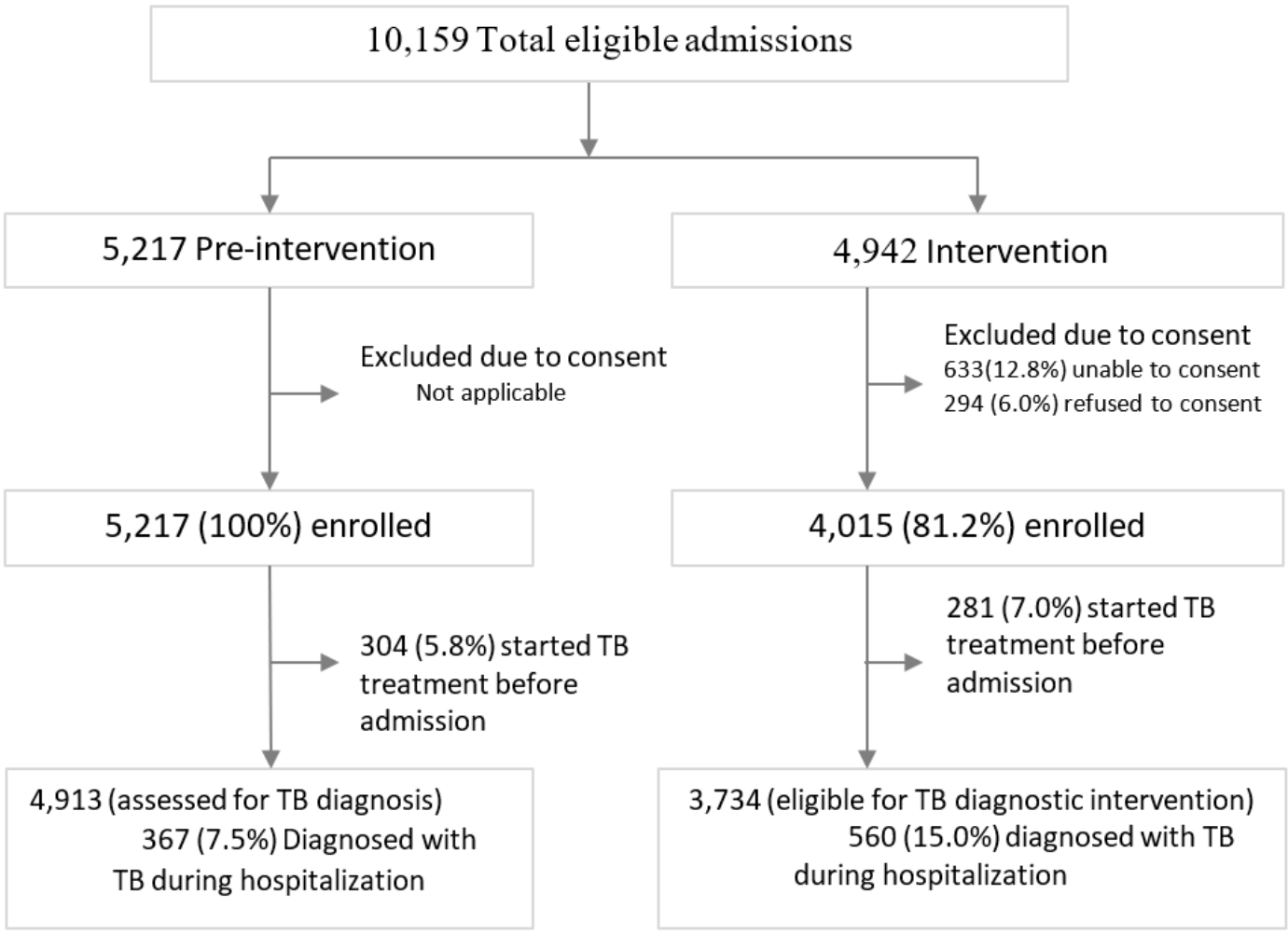

Figure 2

Study population flow diagram by study phase.

TB, tuberculosis

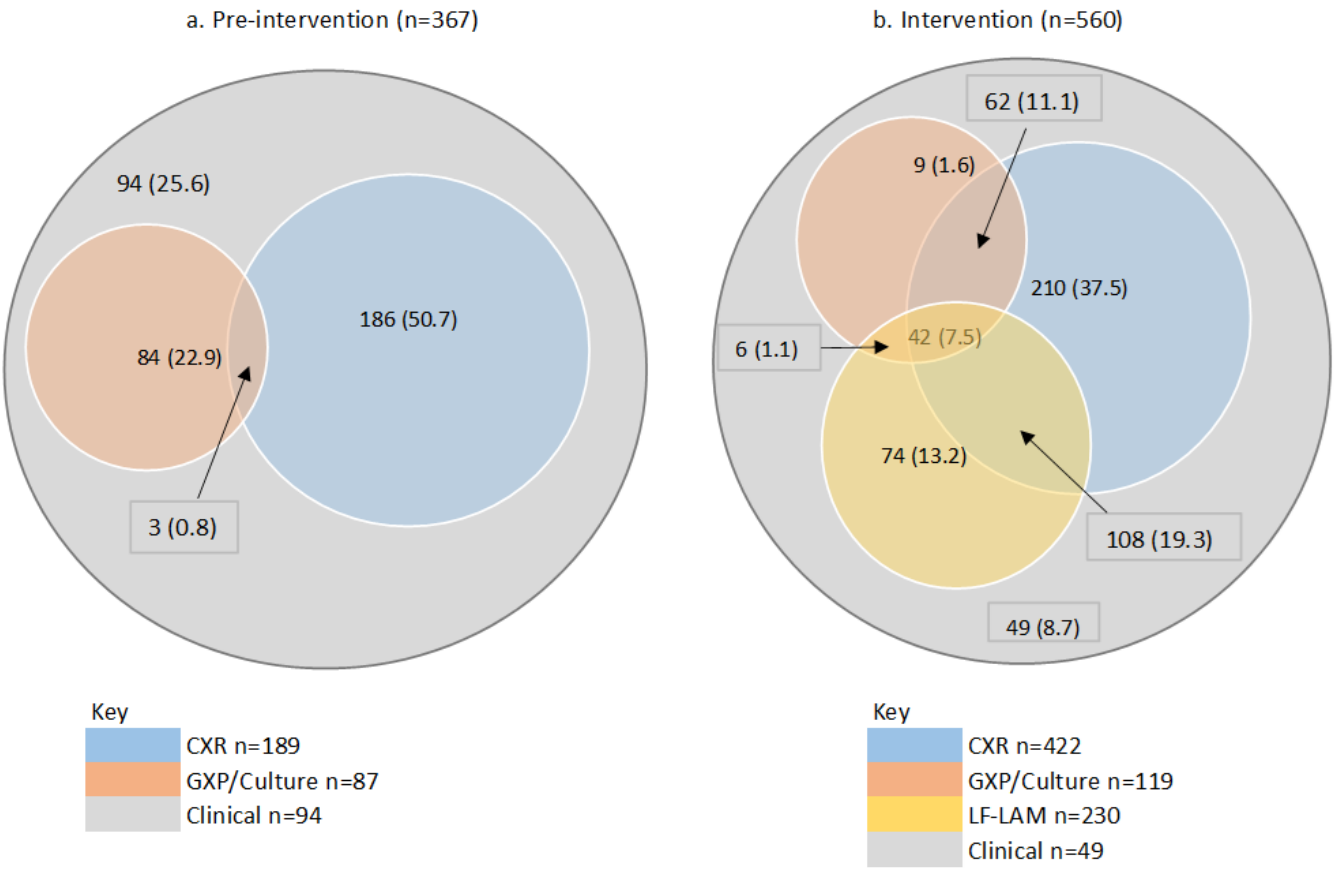

Figure 3

Methods of TB diagnosis among patients diagnosed with TB, n (%). A) Pre-intervention (n=367) and B) Intervention (n=560)

CXR, Chest X-ray; **GXP**, Xpert MTB/RIF Ultra; **LF-LAM**, lateral flow urine lipoarabinomannan assay

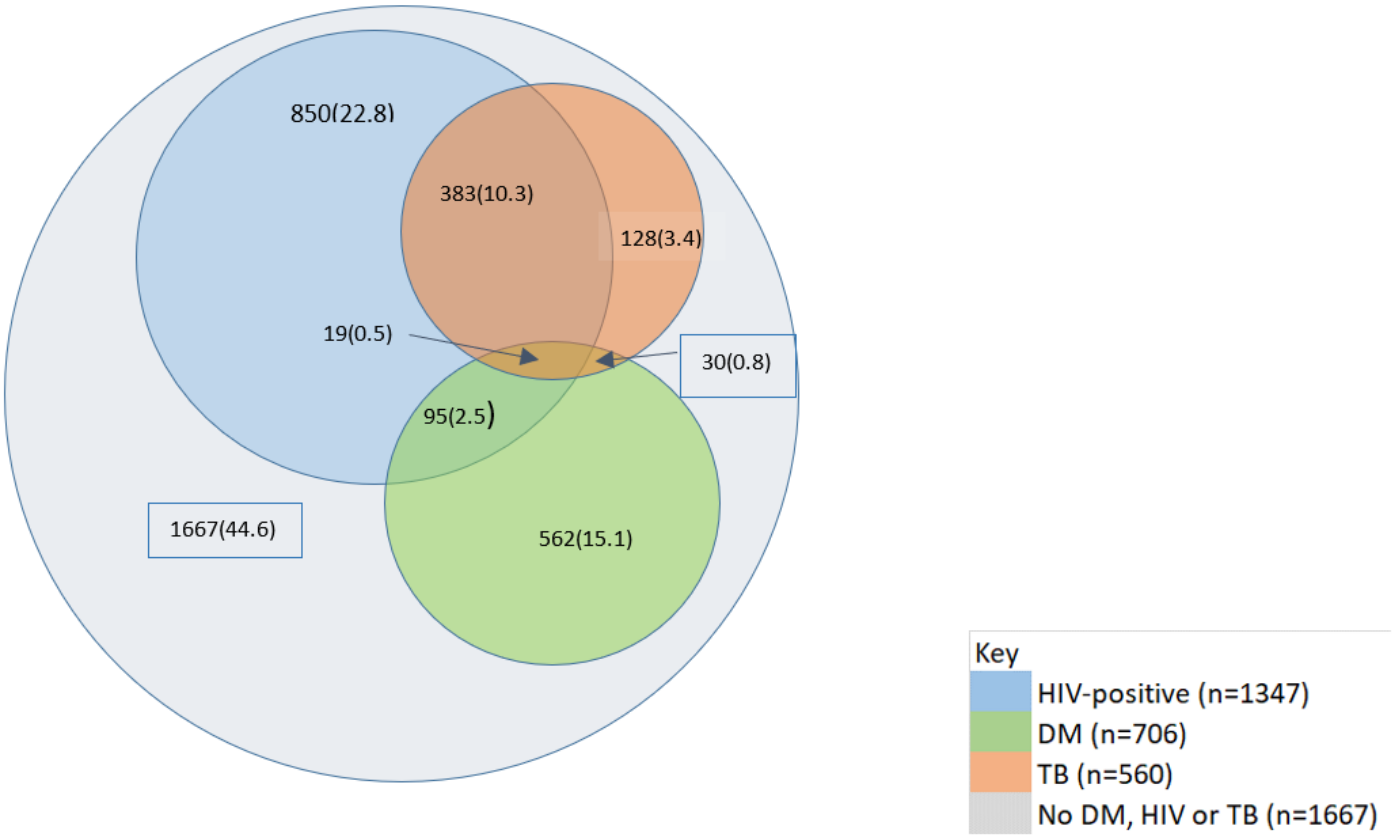

Figure 4

Overlap of HIV, DM, and TB among patients in intervention phase (total number =3734), n (% total participants)

DM. diabetes mellitus; **TB**, tuberculosis