

## Research article

# Does provider-initiated counselling and testing (PITC) strengthen early diagnosis and treatment initiation? Results from an analysis of an urban cohort of HIV-positive patients in Lusaka, Zambia

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### Abstract

**Introduction:** Building on earlier works demonstrating the effectiveness and acceptability of provider-initiated counselling and testing (PITC) services in integrated outpatient departments of urban primary healthcare clinics (PHCs), this study seeks to understand the relative utility of PITC services for identifying clients with early-stage HIV-related disease compared to traditional voluntary testing and counselling (VCT) services. We additionally seek to determine whether there are any significant differences in the clinical and demographic profile of PITC and VCT clients.

**Methods:** Routinely collected, de-identified data were collated from two cohorts of HIV-positive patients referred for HIV treatment, either from PITC or VCT in seven urban-integrated PHCs. Univariate and multivariate analyses were conducted to compare the two cohorts across demographic and clinical characteristics at enrolment.

**Results:** Forty-five per cent of clients diagnosed via PITC had CD4 <200, and more than 70% (i.e. two thirds) had CD4 <350 at enrolment, with significantly lower CD4 counts than that of VCT clients ( $p < 0.001$ ). PITC clients were more likely to be male ( $p = 0.0005$ ) and less likely to have secondary or tertiary education ( $p < 0.0001$ ). Among those who were initiated on antiretroviral therapy (ART), PITC clients had lower odds of initiating treatment within four weeks of enrolment into HIV care (adjusted odds ratio, or AOR: 0.86; 95% confidence interval, or CI: 0.75–0.99;  $p = 0.035$ ) and significantly lower odds of retention in care at six months (AOR: 0.84; CI: 0.77–0.99;  $p = 0.004$ ).

**Conclusions:** In Lusaka, Zambia, large numbers of individuals with late-stage HIV are being incidentally diagnosed in outpatient settings. Our findings suggest that PITC in this setting does not facilitate more timely diagnosis and referral to care but rather act as a “safety net” for individuals who are unwilling or unable to seek testing independently. Further work is needed to document the way provision of clinic-based services can be strengthened and linked to community-based interventions and to address socio-cultural norms and socio-economic status that underpin healthcare-seeking behaviour.

**Keywords:** HIV; PITC; HIV testing; integration; early treatment.

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### Introduction

In sub-Saharan Africa (SSA), significant progress has been made in the past decade in providing access to antiretroviral therapy (ART) to persons living with HIV and diagnosed with AIDS. By 2010, almost 40% of those in need of ART in SSA were receiving care and treatment compared with just 2% in 2003. In addition, HIV-related deaths in SSA decreased by 18% between 2004 and 2009 from 740,000 to 610,000 annually [1]. Notwithstanding these improvements, SSA still has the world's greatest burden of HIV and AIDS. In 2009, for example, an estimated 22.5 million adults and children in the region were living with HIV and an estimated 1.3 million (72% of the global total) died from HIV-related diseases [2].

As the need for continued scale-up of effective HIV treatment programmes meets the need to consolidate and maintain the quality of existing programmes, policy makers and health programmers are faced with two major on-going

challenges. First, the high proportion of individuals ignorant of their HIV status. Second, the high proportion of HIV-positive individuals diagnosed late and presenting for treatment with advanced-stage HIV-related disease. Illustrating these issues, it was estimated that in 2009 only 30% of adults in SSA were aware of their disease status [2] and amongst those who accessed treatment in 2009, between 8% and 26% died during the first year of care [3–5].

Globally, strategies to reduce mortality, disease progression and transmission of HIV have included trialling the provision of different models of testing to strengthen access to testing, with generally positive outcomes [6–8]. Similarly, the revision of World Health Organization's (WHO) clinical guidelines to recommend initiation of ART for all HIV-positive individuals with a CD4 <350 cells/ $\mu$ L regardless of symptoms, and all tuberculosis (TB) patients regardless of CD4 count [9,10], were designed to ensure more timely

treatment. Such initiatives have been underscored by recent evidence demonstrating that earlier initiation of ART (i.e. initiation at a higher CD4 count) is associated with a 41% relative reduction in HIV-related clinical events (primarily extra-pulmonary TB) and a reduction of the incidence of HIV transmission amongst discordant heterosexual couples by up to 96% [11].

Because of the clinical and public health benefits of early treatment initiation, it is imperative to provide evidence not just of whether different models of testing increase access to testing, but also whether such models facilitate earlier diagnosis of HIV. While it is presumed that increased access to HIV testing combined with guidelines that fast-track treatment initiation will result in earlier treatment, this assumption has rarely been tested [12].

## Methods

### Setting

In April 2004, a large-scale public sector HIV care and treatment programme was established in Lusaka by the Zambian Ministry of Health, with implementation assistance from the Centre for Infectious Disease Research in Zambia (CIDRZ) and funding from the President's Emergency Plan for AIDS Relief (PEPFAR). During initial scale up, HIV care and treatment departments were established at the primary care level, co-located but functionally separate from general outpatient services. Clients could enrol free of charge for treatment by presenting at any HIV care and treatment department with a test result or referral slip from an accredited HIV testing service. This included voluntary testing and counselling (VCT) services that operated within the primary care clinics themselves.

By 2008, 22 of Lusaka's 27 primary healthcare clinics (PHCs) had a co-located and stand-alone HIV care and treatment department. In the same year, partially as a response to concerns over siloed HIV service delivery, duplication of effort and treatment-related stigma, a model of integrated HIV and general outpatient healthcare services was piloted in two Lusaka clinics [7]. Under the integrated model, formerly stand-alone HIV care and treatment departments and general outpatient departments were integrated. All patients, regardless of HIV status, presented to the same clinic and were attended by the same staff. Patient flow, healthcare worker duties, medical record filing and pharmaceutical dispensing and storage were harmonized [7]. In addition, following WHO and Centers for Disease Control and Prevention (CDC) recommendations [13,14], the integrated departments introduced first-come first-serve provider-initiated counselling and testing (PITC) for any client without a recent (<6 months) HIV test result [15].

Newly introduced PITC services in the integrated clinics differed from the pre-existing VCT services in several key ways. Typically, clinic-based VCT services were staffed by nurses whose primary responsibility lay elsewhere but they provided VCT in a spare room during their free time. As a result, the service was only available on an ad hoc basis. The majority of VCT clients were self-initiated and counselling in VCT was conducted according to psycho-social principles without reference to clients' clinical condition. If a client

tested positive to HIV in VCT, he or she was issued with a referral slip and required to (self) present to the separate HIV care and treatment department for enrolment. Human resource shortages meant that when patients received a referral they were rarely, if ever, accompanied by a healthcare worker.

By contrast, PITC established in the newly integrated clinics was offered routinely on an "opt-out" basis to all clients attending the out-patient department (OPD) who had no knowledge of their HIV status. PITC was physically located within the OPD and formed part of a standardized patient flow, requiring no separate or additional queuing. Those who tested positive to HIV were able to enrol in HIV care and treatment department immediately or later and did so in the same building as all other outpatient services. Since PITC was offered by (trained and supervised) lay personnel who worked five-hour shifts from Monday to Friday [15], clients attending the clinic outside those hours or during particularly busy periods may not have been tested. However, if a client had an accompanying child, spouse or other adult, all present were offered (private) counselling and testing. Further details related to the programmatic features, including implementation, supervision and subsequent scale-up, have been previously published [7,15,16].

Both the integrated model as a whole and the incorporation of PITC specifically were designed to improve access to HIV testing and more timely referral for care and treatment. Since VCT services relied primarily on client self-referral (both to the testing services itself and subsequently to HIV care and treatment), it was anticipated that PITC would improve linkages to HIV care through provision of fully integrated, seamless service delivery [14,16–18]. Between 2009 and 2011, a further seven clinics (nine in total) were integrated and PITC was introduced. In 2011, the programmatic outcomes were published, including evidence of improved testing coverage, and high levels of acceptability [15]. However, initial work did not examine the clinical and demographic profile of those accessing PITC or address the question of whether PITC in fact facilitated earlier diagnosis and initiation of treatment.

### Objective

Building on earlier works, this study describes results from a cross-sectional study of a cohort of HIV-positive patients referred for ART in seven urban-integrated primary care clinics, via the recently established PITC services and pre-existing VCT services. The study aimed to a) understand the relative utility of PITC services for identifying clients with early-stage HIV-related disease compared to VCT services (using CD4 count as a proxy for disease stage) and b) determine whether there are any significant differences in the clinical and demographic characteristics of clients accessing PITC and VCT with regard to implications for scaling-up different types of testing models in the future.

### Site selection

Sites for this study were chosen purposively from a total sample of 13, based on at least six months of integrated status of their HIV care and treatment programme, the presence of PITC services and the presence of onsite data

entry of ART medical records into the national electronic medical database (SmartCare). Basic characteristics of each facility are reported in Table 1.

#### Data collection

Programmatic data from the national HIV care and treatment programme in Lusaka were analyzed. This programme is supported primarily by the Ministry of Health, with additional funding from the PEPFAR and the Global Fund for AIDS, Tuberculosis and Malaria (GFATM). Clinical care has been standardized according to national protocols. Clinical and demographic data are recorded on standardized forms by healthcare workers and subsequently entered into an electronic database (SmartCare) by dedicated, on-site data entry clerks.

Data relevant to this study included the number of patients counselled, tested and identified as HIV-positive in PITC services in the seven clinics between July 2008 and June 2011. Data were collated monthly from clinic registers, entered manually into an electronic database and cleaned by a project coordinator from the CIDRZ. A cohort of PITC clients who had enrolled for HIV care was subsequently identified by cross-referencing the unique patient identifiers of HIV-positive PITC clients with the national electronic medical database, SmartCare. The cohort included all those who were matched in SmartCare for the period from the start of integrated service delivery for each clinic up to our study freeze date (1 July 2011). Likewise, the VCT cohort of clients was extracted from the SmartCare database, based on two criteria: i) having enrolled in HIV care in any of the seven clinics during the same period of integrated service delivery and ii) documented as having being referred by any VCT service. Because of unlinked patient identification numbers in VCT, data on the *rates* of counselling, testing and successful referral to care were not available for the VCT cohort [15].

#### Analysis

De-identified demographic and clinical characteristics at enrolment, including age, CD4 cell count (cells/ $\mu$ L), body mass index (BMI; kg/m<sup>2</sup>), haemoglobin (Hgb; g/dL) levels, as

well as education level, and partner's HIV status, were extracted from SmartCare for both cohorts. We investigated five programmatic outcomes: (i) ever initiated ART, if eligible; ii) initiated ART within four weeks of HIV care; iii) retention in HIV care at six months; iv) early mortality (within 90 days of enrolment); and v) medication possession ratio (MPR) at six months post-ART initiation. According to the Zambian national guidelines, during the period of analysis, patients were defined as eligible for ART if they were documented as having CD4 count <200 cells/ $\mu$ L or WHO Stage III or IV disease. For retention in care, only patients with a minimum of six months between their HIV care enrolment date and the study freeze date were evaluated. Retention at six months was defined as having a pharmacy or clinical visit date within a 60-day window in six months' time, post-enrolment date [19]. For patients initiated on ART at least six months prior to the study freeze date, MPR at six months was calculated by dividing the number of days beyond designated pharmacy refills by total days on therapy and then subtracting that percentage from 100. Patients were classified as optimally adherent ( $\geq 95\%$ ), sub-optimally adherent (80–94%) or poorly adherent (<80%) [20].

We used Pearson's Chi-square test for categorical variables and non-parametric Wilcoxon rank-sum tests for continuous variables to compare demographic and clinical characteristics between PITC and VCT patients. Crude odds ratios (ORs) and 95% confidence intervals (95% CIs) were computed using logistic regression models to assess the relationship between testing group and the five programmatic outcomes. AORs and their corresponding 95% CIs were generated using generalized estimating equations to account for clustering by site. Age, sex, CD4 cell count, BMI, HGB, TB status at enrolment, education level and partner HIV status were included in the multivariate models.

Analyses were performed using SAS Version 9.1 (Cary, North Carolina), and the protocol was approved by the institutional review boards of the University of Zambia, Protocol # 003-02-08 (Lusaka, Zambia), and the University of Alabama at Birmingham, Protocol # X080403013 (Birmingham, Alabama, USA), and received clearance from the Zambian Ministry of Health.

**Table 1. Clinic characteristics of nine integrated urban primary health care facilities**

Integrated Clinics	ART Introduced to clinic	ART Integrated in clinic	Catchment population (2010)	Approx. daily outpatient attendance	Ever enrolled (b/f 1 July 2011)*	PITC** cohort	VCT** cohort
Clinic 1	Jan 2005	Nov 2008	52,549	100	3,822	337	1014
Clinic 2	Feb 2009	Feb 2009	18,050	45	1,907	263	1364
Clinic 3	Aug 2004	Apr 2010	74,116	180	13,032	92	1,339
Clinic 4	May 2008	Oct 2009	47,904	95	3,987	489	1,370
Clinic 5	Mar 2007	Jun 2010	28,979	60	4,896	51	1,038
Clinic 6	Jul 2006	Apr 2009	70,219	120	7,057	546	1,928
Clinic 7	Mar 2007	Jul 2008	31,872	80	3,802	461	1,677
TOTAL	–	–	323,689	680	38,503	2239	9730

\* Includes clients referred from TB Department and Maternal & Child Health Department; b/f = before.

\*\* VCT and PITC cohort numbers represent those enrolled from the date of integration at each clinic through to 1 July 2011. Only clients newly enrolled from the date that ART was integrated in each clinic were included; clients enrolled before this date are automatically excluded.

## Results

Between July 2008 and January 2011, 2239 clients were matched with our enrolment records after testing HIV-positive in PITC. A comparison cohort of 9730 clients enrolled via VCT at the same clinics during the same period (Table 2). The larger number of client enrolments via VCT during this period is primarily due to a larger number of VCT referral services. These include VCT services at each of the integrated

clinics, VCT services at other government clinics and stand-alone private and non-profit testing services, all of which may refer HIV-positive clients to public HIV care and treatment services. In addition, VCT services were operating prior to the period of analysis, with the possibility of clients who tested positive any time in the past presenting at the clinics for enrolment during the period of analysis. By comparison, the PITC cohort could include only those who tested in the

**Table 2. Baseline demographic and clinical characteristics for clients accessing HIV treatment in nine integrated clinics via PITC and VCT**

Characteristics	PITC* median (IQR) or N (%)	VCT** median (IQR) or N (%)	p
Age	N = 2239	N = 9730	
At enrolment	32.0 (26.0–39.0)	32.0 (26.0–38.0)	0.5429 <sup>^</sup>
≤15	225 (10.0%)	719 (7.4%)	<0.0001 <sup>^^</sup>
16–35	1193 (53.3%)	5617 (57.7%)	.
36+	821 (36.7%)	3394 (34.9%)	.
Sex	N = 2239	N = 9730	
Female	1261 (56.3%)	5868 (60.0%)	0.0005 <sup>^^</sup>
Male	978 (43.7%)	3862 (40.0%)	.
CD4 (cells/μL) at enrolment	N = 1998	N = 8506	
≤50	224 (110.0–387.0)	264 (137.0–427.0)	<0.0001 <sup>^</sup>
51–199	223 (11.2%)	701 (8.3%)	<0.0001 <sup>^^</sup>
200–349	676 (33.8%)	2561 (30.1%)	.
≥350	514 (25.7%)	2195 (25.8%)	.
BMI (kg/m <sup>2</sup> ) at enrolment	N = 1932	N = 8602	
<18.5	20.0 (18.1–22.2)	20.4 (18.4–22.8)	<0.0001 <sup>^</sup>
18.5–24.99	559 (28.9%)	2196 (25.5%)	<0.001 <sup>^^</sup>
≥25	1180 (61.1%)	5357 (62.3%)	.
HBG (g/dL) at enrolment	N = 1951	N = 8339	
≤8	11.2 (9.7–12.6)	11.7 (10.1–13.2)	<0.0001 <sup>^</sup>
8.1–9.9	163 (8.4%)	539 (6.5%)	<0.0001 <sup>^^</sup>
≥10	388 (19.9%)	1420 (17.0%)	.
Active TB at enrolment	N = 2239	N = 9730	
Yes	113 (5.0%)	99 (1.0%)	<0.0001 <sup>^^</sup>
No	2126 (95.0%)	9631 (99.0%)	.
Education	N = 2234	N = 9092	
None	809 (36.2%)	2503 (27.5%)	<0.0001 <sup>^^</sup>
Primary	674 (30.2%)	2919 (32.1%)	.
Secondary and tertiary	751 (33.6%)	3670 (40.4%)	.
Partner HIV status	N = 2239	N = 9730	
Negative	93 (4.2%)	500 (5.1%)	<0.0001 <sup>^^</sup>
Positive	376 (16.8%)	2611 (26.8%)	.
Unknown/missing	1770 (79.1%)	6619 (68.0%)	.

\*PITC = Clients who tested positive to HIV in provider-initiated testing services available in an integrated clinic and subsequently enrolled in HIV care up to study cut-off date.

\*\*VCT = Clients who tested positive to HIV in any (on-site or off-site) voluntary HIV testing services and enrolled in HIV care in an integrated clinic, up to study cut-off date.

<sup>^</sup> Wilcoxon rank-sum tests.

<sup>^^</sup> Pearson's Chi-square test.

outpatient departments of the nine integrated clinics following the introduction of PITC (maximum of 24 months).

### Clinical and demographic characteristics

In the PITC cohort, the median age was 32 years, median CD4 = 224 cells/ $\mu$ L and median BMI = 20.0 (Table 2). Children (under 15 years) constituted 10% ( $n=225$ ) of the cohort and males made up 43.7%. Approximately 45% of the PITC cohort had a CD4  $\leq$  200 cells/ $\mu$ L, whereas 70% had a CD4  $\leq$  350. Just under a third of the cohort (29%) had BMI below the normal range ( $<18.0$ ). In the same cohort, 36% were reported as having no formal education, 30% as having some primary education and 34% as having some secondary or tertiary education. The majority (79%) of PITC clients either did not know or did not report their partner's HIV status and 5% had active TB at the time of enrolment into HIV care. Disaggregating the PITC cohort by gender, men had more advanced HIV-related disease than women as evidenced by lower median CD4 cell counts (268 vs. 302 cells/ $\mu$ L;  $p=0.004$ ) and lower median BMI (19.5 vs. 21.3 kg/m<sup>2</sup>;  $p<0.0001$ ).

In the VCT cohort, the median age was 32 years, median CD4 = 264 cells/ $\mu$ L and median BMI = 20.4 (Table 2). Children under 15 years constituted 7.4% of the cohort and males made up 39.7%. Approximately 38% of the VCT cohort had a CD4  $\leq$  200 cells/ $\mu$ L, whereas 64% had a CD4  $\leq$  350 cells/ $\mu$ L, and just under a third (28.9%) had BMI below the normal range ( $<18.5$ ). In the same cohort, 25.7% were reported as having no formal education, 30% as having some primary education and 37.7% as having some secondary or tertiary education. Some 68% of VCT clients either did not know, or did not report their partner's HIV status and 1% ( $n=99$ ) had active TB at the time of enrolment into HIV care.

By comparison to the VCT cohort, more PITC clients were men (43.7% vs. 39.7%,  $p<0.0005$ ). Age distribution also differed significantly ( $p<0.0001$ ) with the PITC cohort having more children under 15 years (10% vs. 7.4%) and more adults over 35 years (36.7% vs. 34.9%), but fewer adults in the high-risk age group of 16–35 (53.3% vs. 57.7%). Median baseline CD4 for PITC patients was 224 cells/ $\mu$ L versus 264 cells/ $\mu$ L in the VCT cohort ( $p<0.0001$ ). At enrolment, more PITC clients were underweight (BMI  $<18.5$ ) (28.9% vs. 25.5%;  $p<0.0001$ ) and had low HGB ( $\leq 8$  g/dL) (8.4% vs. 6.5%;  $p<0.0001$ ) by comparison to the VCT cohort. The PITC cohort was also found to have significantly more active TB at enrolment (5.0% vs. 1.0%;  $p<0.0001$ ).

Differences were also identified in the educational status and knowledge of partners' HIV status (Tables 2 and 3). PITC clients were more likely to be uneducated (36.2% vs. 27.5%) and less likely to have a primary (30.2% vs. 42.1%) or secondary (33.6% vs. 40.4%) education ( $p<0.0001$ ). Similarly, fewer PITC clients were able report their partner's HIV status (21.0% vs. 31.9%;  $p<0.0001$ ). Amongst both PITC and VCT clients, a greater proportion of men compared to women had primary and/or secondary education and also knew their partner's HIV status (Table 3). More men than women had active TB at enrolment in the PITC cohort, whereas in the VCT

**Table 3. Education level, partner serostatus and active TB among male and female PITC and VCT Clients**

Sex	Education status	*PITC (%)	**VCT (%)	$p^{\wedge}$
Male	No education	330 (34%)	922 (26%)	<0.0001
	Primary	268 (27%)	977 (27%)	
	Secondary	378 (39%)	1701 (47%)	
Female	No education	479 (38%)	1581 (29%)	<0.0001
	Primary	406 (32%)	1942 (35%)	
	Secondary	373 (30%)	1969 (36%)	
Partner HIV status		PITC (%)	VCT (%)	
Male	Negative	61 (6%)	284 (7%)	<0.0001
	Positive	203 (21%)	1293 (33%)	
	Unknown or missing	714 (73%)	2285 (59%)	
Female	Negative	32 (3%)	216 (4%)	<0.0001
	Positive	173 (14%)	1318 (22%)	
	Unknown or missing	1056 (84%)	4334 (74%)	
Active TB at enrolment		PITC (%)	VCT (%)	
Male	No TB	914 (93%)	3821 (99%)	<0.0001
	Active TB	64 (7%)	41 (1%)	
Female	No TB	1212 (96%)	5810 (99%)	<0.0001
	Active TB	49 (4%)	58 (1%)	

\*PITC = Clients who tested positive to HIV in provider-initiated testing services available in an integrated clinic and subsequently enrolled in HIV care up to study cut-off date.

\*\*VCT = Clients who tested positive to HIV in any (on-site or off-site) voluntary HIV testing services and enrolled in HIV care in an integrated clinic, up to study cut-off date.

$\wedge$  Pearson's Chi-square test.

cohort, TB at enrolment was found in equal proportions among men and women.

### Programmatic outcomes

Table 4 reports the results of five analyses, exploring the association between testing group and five programmatic outcomes. Multivariate analyses are adjusted for age, sex, enrolment CD4 cell count, BMI, HGB and TB status. Adjusted analysis showed a marginal association between the testing cohort and the outcome "Dead in 90 Days" (AOR: 1.36; CI: 0.94–1.96;  $p=0.10$ ). The odds of being "Initiated on ART if eligible" were lower for PITC patients than for VCT patients (AOR: 0.9; 95% CI: 0.82–0.97;  $p=0.01$ ). Among those who initiated ART, PITC patients had lower odds of initiating within four weeks' of enrolment for HIV care (AOR: 0.86; 95% CI: 0.75–0.99;  $p=0.035$ ). PITC clients also had reduced odds of being retained in care at six months (AOR: 0.84; 95% CI 0.74–0.95;  $p=0.004$ ). No difference was found in the MPR between the two cohorts ( $p=0.982$ ).

## Discussion

### Clinical outcomes

Previous work has demonstrated that access to, and uptake of, HIV testing in Lusaka can be strengthened by incorporating routine PITC into integrated primary care services [15]. Until now, the critical question of whether or not such



**Table 4. Outcomes for PITC and VCT clients across four clinical management indicators**

Programmatic outcomes <sup>1</sup>	Number of clients	Crude odds ratio <sup>7</sup>	<i>p</i>	Adjusted odds ratio <sup>8</sup>	<i>p</i>
Dead in 90 days <sup>2</sup>					
VCT <sup>3</sup>	155/8680 (1.8%)	Referent		Referent	
PITC <sup>4</sup>	75/2239 (3.3%)	1.91 (1.44–2.52)	<.001	1.36 (0.94–1.96)	0.100
Initiated on ART if eligible <sup>5</sup>					
VCT	4523/6520 (69.4%)	Referent		Referent	
PITC	1187/1655 (71.7%)	1.12 (0.99–1.26)	0.063	0.90 (0.82–0.97)	0.010
Time to ART initiation < 4 weeks (among those who initiated)					
VCT	2828/4523 (62.5%)	Referent		Referent	
PITC	665/1187 (56.0%)	0.76 (0.67–0.87)	<.001	0.86 (0.75–0.99)	0.035
Retained in care at 6 months					
VCT	3765/6079 (61.9%)	Referent		Referent	
PITC	1105/1929 (57.3%)	0.82 (0.74–0.91)	<.001	0.84 (0.74–0.95)	0.004
MPR <sup>6</sup> >95 after 6 months on ART					
VCT	1604/2880 (55.7%)	Referent		Referent	
PITC	543/933 (58.2%)	1.11 (0.95–1.29)	0.180	1.00 (0.79–1.27)	0.982

<sup>1</sup> Denominator for those included in programmatic outcome includes those with sufficient follow-up time and those with data available in the electronic medical record. For example, MPR <95 after six months on ART was assessed amongst those initiated on ART for at least six months within the time parameters. Additionally, since the study relied on routinely collected data some clients had missing data excluding them from analysis.

<sup>2</sup> Dead in 90 Days = clients recorded as dead within 90 days of enrolling in HIV care and treatment.

<sup>3</sup> VCT = Clients who tested positive to HIV in any (on-site or off-site) voluntary HIV testing services and enrolled in HIV care in an integrated clinic, up to study cut-off date.

<sup>4</sup> PITC = Clients who tested positive to HIV in provider-initiated testing services available in an integrated clinic and subsequently enrolled in HIV care up to study cut-off date.

<sup>5</sup> Initiated on ART if eligible = clients enrolled in HIV care and treatment and initiated on antiretroviral therapy if eligible according to Zambian national guidelines.

<sup>6</sup> MPR = Medication possession ratio, an estimation of client adherence to individual antiretroviral drug regime.

<sup>7</sup> Crude odds ratios (ORs) and 95% confidence intervals (95% CIs) computed using logistic regression models to assess the relationship between testing group and the five programmatic outcomes.

<sup>8</sup> Adjusted odds ratios (AORs) and their corresponding 95% CIs generated using generalized estimating equations to account for clustering by site; adjusted for age, sex, CD4 cell count, BMI, HGB, TB status at enrolment, education level and partner HIV status.

routine PITC improves the timeliness of that HIV treatment has remained unanswered. In this large urban cohort, we found 45% of HIV-positive clients diagnosed via PITC had CD4 <200 cells/ $\mu$ L, and more than two-thirds (70%) had CD4 <350 cells/ $\mu$ L at enrolment. Compared to clients enrolled from VCT, PITC clients had significantly higher rates of late-stage disease and active TB at enrolment. Our results demonstrate that majority of clients accessing HIV care via PITC services have advanced immune-suppression, resulting in less timely treatment according to current WHO and Zambian national standards.

Delayed diagnosis of HIV and later initiation on ART is associated with poor clinical outcomes. Recent studies demonstrate that initiating ART at CD4 levels *higher* than 200 or 250 cells/ $\mu$ L reduces mortality rates in asymptomatic, ART-naive, HIV-positive people [21]. Sterne and colleagues found that deferring combination therapy until CD4 = 251–350 cells/ $\mu$ L was associated with higher rates of AIDS and mortality than starting therapy in the range 351–450 cells/ $\mu$ L (HR: 1.28, 95% CI 1.04–1.57), and that the adverse effect of deferring treatment increased with decreasing CD4 cell count threshold [22]. Delayed initiation on ART also has implications for population health, with the HIV Prevention Trials

Network (HPTN) 052 trial [11] demonstrating a 96% relative reduction in HIV transmission between sero-discordant couples who initiated ART earlier (CD4 350–550 cells/ $\mu$ L).

#### Programmatic outcomes

The PITC and VCT cohorts received care contemporaneously and within the same facilities. Despite this, we found that in comparison to VCT clients, PITC clients had reduced odds of being initiated on ART within four weeks (of being identified as eligible) and significantly higher rates of loss-to-follow-up (LTFU), especially during the first 180 days of enrolment in HIV care and treatment. Higher rates of LTFU in the PITC cohort may be partially explained by higher rates of unrecorded mortality. Evidence from previous modelling studies suggests that unrecorded deaths may be responsible for up to 30% of early LTFU [23], and PITC clients in this cohort had significantly higher risk of being severely immunosuppressed by comparison to VCT clients. Another contributing factor could be that PITC clients with active TB refused, were advised against or defaulted from HIV care and treatment while still on anti-TB therapy due to fear or misconceptions regarding TB/HIV co-treatment [24].

PITC patients may also be less psychologically prepared for HIV care and treatment contributing to a higher rate of LTFU.

#### **Gender and socio-economic indicators**

Social determinants are well recognized to affect health status and healthcare-seeking behaviour [25], and our analysis suggests that late presentation for testing and LTFU amongst HIV-positive clients in this setting is no exception. After comparing a number of socio-demographic characteristics, we found HIV-positive clients enrolled via PITC were significantly more likely to be male, illiterate, unaware of their partner's HIV status, and children aged under 15 years.

A lower level of education impedes both understanding of, and access to, information about HIV and the treatment options available. Clients with less education may thus be less informed or ill-informed about the nature of HIV and HIV treatment. Lower educational attainment is also associated with a less empowered population, who may be susceptible to myths and misconceptions and less confident to seek outside care and support until late in their disease progression when all other options have been exhausted. This explanation meshes with an outpatient population that receives HIV testing co-incidentally (as part of a routine opt-out service) after presenting sick to a general outpatient department. Such clients may similarly be more susceptible to abandoning ART, where clinical improvement or "feeling-well" is (mis-)interpreted as being "cured".

Although the PITC cohort had proportionally more adult males and children compared to VCT, women constituted the majority. Critically, our findings demonstrated that women in the PITC cohort were less educated and more immunosuppressed compared to both men in the same PITC cohort and women in the VCT cohort. Gender norms that subjugate women and girls in Zambia both influence and are influenced by low educational status and women and girls' social and financial dependence on fathers, brothers and husbands [26]. In a setting where HIV-positive individuals risk discrimination, abandonment and dispossession, women are less likely to prioritize their health [27]. These findings potentially reflect the nexus of gender and socio-cultural norms and economic dependence that make seeking HIV testing and treatment (particularly during the early non-symptomatic disease stages) a lower priority for women compared to issues of financial security and social acceptance.

Children under 15 years represented a significantly larger proportion of the PITC versus VCT cohort. As with women, children in Zambia are less likely to be empowered to make a decision to actively seek HIV testing and treatment, typically relying on parents or older family members to help them. Parents, particularly mothers, may actively avoid testing their children, with previous work in the region documenting a variety of reasons, including the perceived futility of knowing a child's status [28–30], poor caregiver knowledge of paediatric HIV infection and available healthcare services [31], a fear of spousal abandonment when a mother's HIV-positive status is inferred from her child's [32] and fear of children's negative reactions and of inability to answer their questions [33–35].

Compared to VCT, there were a significantly higher proportion of men in the PITC cohort. Several factors may have contributed to this. In SSA, cultural norms and stigma proscribe seeking medical care other than for acute illnesses [36–41], a critical factor in relation to HIV, which can frequently be asymptomatic until its advanced stages. Similarly, men in SSA are less likely to seek healthcare voluntarily, especially where it involves long waiting times that clash with formal or informal employment [25,40,42–45]. Due in part to the association of PHCs with maternal and child health, these facilities are commonly perceived to be a "female" domain, potentially contributing to a reticence by men to independently seek out services. Men may also be less likely to perceive themselves as "at risk" of being HIV positive [46]. Such factors may lead men to present for outpatient care only when they are symptomatic, rather than specifically testing for HIV. Further supporting this hypothesis is the finding that men in the PITC cohort had proportionally more active TB than any other group.

#### **Alternative models**

In view of the clinical capacity to reduce mortality and disease progression and prevent HIV transmission through earlier care and treatment, greater attention must be paid to ways to improve timely diagnosis and subsequent care. Although PITC has been shown to improve access to testing and provide an additional route to HIV care and treatment in many settings including Zambia, the findings presented here suggest that, in Zambia, these services by themselves are insufficient to improve the timeliness of that care.

Improving clinic-based services, including a reduction in clinic waiting times, more intensive pre- and post-test HIV counselling and adherence support for those initiating ART, presents a starting point. For these services, an increasingly strong evidence-base is emerging regarding the critical role played by clinic-based lay counsellors and peer educators. However, moving beyond the clinic, home-based HIV counselling and testing (HBHCT) and home-based care (HBC), particularly those models supported by community health workers providing door-to-door services to consenting community members [12], present a strong alternative. HBHCT has been shown to increase uptake of HIV testing, improve access to testing, as well as limiting travel costs and reducing the likelihood of stigma [8,12,13]. Evidence from Kenya and Uganda demonstrates that HBC for people living with HIV and AIDS can produce equally good clinical outcomes as compared to clinic-based care, at a lesser cost to both clients and providers [47,48]. Unfortunately, HBHCT and HBC models tested to date have had limited coverage and there is insufficient evidence linking such services to more timely testing and treatment on a larger scale [49,50].

Ultimately, further work is needed to document the possibilities inherent in more holistic community-based interventions that are better able to account for the way cultural taboos, gender inequity, educational status and economic dependence shape health-related decision making.

## Limitations

Despite this study including a large number of HIV-positive patients, it may not be representative of Zambians at-large as the patients were drawn from an urban population. The study relied on routinely collected data, making it susceptible to the limitations of operational research, including missing data that may have skewed results. Importantly, the database used was not primarily designed to assess access to testing or delayed diagnosis and results should therefore be interpreted with caution. The scope of this study, which focuses on clients' clinical and demographic characteristics and uses routinely collected data, did not allow us to collect detailed information on clinic-based factors, such as staffing or other supply-side factors that may have influenced client behaviour. Finally, whether accessing HIV or general clinic services, PITC and VCT clients are by definition self-selecting. Those who access PITC via primary healthcare outpatient departments were likely to be more ill as they were presumably seeking medical care; however, we cannot eliminate the possibility of some clients presenting in the outpatient departments to receive testing. In addition, our programmatic data did not allow us to distinguish between VCT clients referred from services located on PHC premises versus those located external to the clinic (e.g. NGO-run). Further and more rigorous work in this area is required to answer important questions, including whether community-based testing and treatment models (already known to improve access) also improve the rates of early diagnosis and facilitate retention in care in high-prevalence settings, and how established clinic-based services can better address the socio-cultural barriers to testing and care-seeking that continue to inhibit uptake of care and retention in clinic-based care and treatment.

## Conclusions

Our findings indicate that large numbers of HIV-positive individuals with late-stage disease (particularly those with less education) are being "incidentally" identified in outpatient settings. Contrary to expectation then, PITC in this high-prevalence setting does not appear to be facilitating more timely diagnosis and referral to care. Rather, in Lusaka, Zambia, PITC is acting as a "safety net" for individuals who are unwilling or unable to voluntarily seek testing. Although PITC services are designed, in part, to facilitate linkage to care for those who may not independently seek HIV testing or treatment, it remains a concern that in a setting with such a relatively mature HIV treatment programme, so many with such late-stage disease are being incidentally identified. Our results constitute further evidence that care-seeking behaviours in Zambia, as elsewhere, are influenced by a range of social determinants that must be concurrently addressed to improve timely uptake and retention in essential clinical services.

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### Competing interests

The authors declare they have no competing interests.

### Authors' contributions

All authors have read and approved the final version. SMT conceived of and designed the study, helped collate the data, assisted with analysis and wrote the first draft; MSL led analysis and provided substantive edits; JMC led data collection for the PITC cohort and provided critical edits; MMC provided programme oversight for LDHMT and provided critical edits; EM assisted with data collection and provided critical edits; CBM provided programme oversight and critical edits to the manuscript; SER was involved in drafting the manuscript and revising it critically for important intellectual content.

### Abbreviations

AOR, adjusted odds ratio; ART, antiretroviral therapy; BMI, body mass index; CDC, Centers for Disease Control and Prevention; CIDRZ, Centre for Infectious Disease Research in Zambia; CI, confidence interval; GFATM, Global Fund for AIDS Tuberculosis and Malaria; HBC, home-based care; HBHCT, home-based HIV counselling and testing; HGB, haemoglobin; HPTN, HIV Prevention Trials Network; OR, odds ratios; PEPFAR, President's Emergency Plan for AIDS Relief; PHCs, primary healthcare clinics; PITC, provider-initiated counselling and testing; SSA, sub-Saharan Africa; TB, tuberculosis; VCT, voluntary testing and counselling; WHO, World Health Organization.

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