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MAJOR ARTICLE

HIV Testing Approaches to Optimize Prevention and Treatment for Key and Priority Populations in Malawi

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Background. Despite progress in improving antiretroviral therapy (ART) for people with HIV in Malawi, the burden of HIV infections and HIV treatment outcomes among key populations is suboptimal. Client-centered differentiated service delivery approaches may facilitate addressing HIV prevention and treatment needs of key populations in Malawi.

Methods. De-identified program data routinely collected as part of the LINKAGES project–Malawi were assembled from October 2017 to September 2019. HIV case finding was compared across different testing modalities for each population. Poisson regression was used to estimate the association between testing modalities and ART initiation.

Results. Of the 18 397 people included in analyses, 10 627 (58%) were female sex workers (FSWs), 2219 (12%) were men who have sex with men (MSM), and 4970 (27%) were clients of FSWs. HIV case finding varied by modality and population, with index testing and enhanced peer outreach demonstrating high yield despite reaching relatively few individuals. FSWs who tested positive through risk network referral testing were more likely to initiate ART within 30 days compared with those who tested positive through clinic-based testing (adjusted risk ratio [aRR], 1.50; 95% CI, 1.23–1.82). For MSM, index testing (aRR, 1.45; 95% CI, 1.06–2.00) and testing through a drop-in center (aRR, 1.82; 95% CI, 1.19–2.78) were associated with 30-day ART initiation.

Conclusions. These data suggest that differentiated HIV testing and outreach approaches tailored to the needs of different key populations may facilitate improved ART initiation in Malawi. Achieving 0 new infections by 2030 suggests the need to adapt treatment strategies given individual and structural barriers to treatment for key populations with HIV in high-prevalence settings.

Keywords. antiretroviral therapy; female sex worker; HIV testing; Malawi; sexual and gender minorities; vulnerable populations.

Significant decreases in HIV incidence have been reported in countries across Sub-Saharan Africa over the last decade, closing HIV prevention and treatment gaps and reducing HIV-associated morbidities and mortality [1]. In Malawi, prioritized scale-up of HIV testing and antiretroviral therapy (ART) programs has increased the availability of HIV-related services in geographic areas of high HIV prevalence [2]. Accordingly, national metrics report significant progress toward meeting UNAIDS 95-95-95 goals [3, 4]. In 2019, an estimated 93% of persons with HIV were estimated to know their HIV status, 80% of those with known status were reported to be on ART, and 92% of those on ART were virally suppressed [4].

HIV disproportionately affects key and priority populations in Malawi for whom HIV prevention and treatment services systematically remain out of reach, including female sex workers (FSWs) and their clients (CFSWs), gay men and other men who have sex with men (MSM), and transgender women (TGW). Structural barriers such as stigma, discrimination, and punitive legal policies perpetuate physical and sexual violence toward FSWs and other key populations (KPs), limiting their autonomy and power to negotiate safer sex and access sexual and reproductive health services [5, 6]. For MSM and TGW, intersecting social stigmas and criminalization of same-sex practices, coupled with a focus on reducing heterosexual and vertical transmissions, have limited provider knowledge for delivering comprehensive and affirming sexual health services [7–13]. Collectively, these challenges limit engagement in HIV prevention and treatment for KPs and sustain a high prevalence and incidence of infection [5, 8, 11, 14].

Differentiated client-centered approaches can provide customized high-quality services to meet the preferences and priorities of those who would otherwise be "left behind" and close existing HIV prevention, care, and treatment gaps [15–19]. Models include widening the geographic range of locations

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where services occur, tailoring the frequency and intensity of services to the needs of different KP groups (older vs younger KPs, virally suppressed vs unsuppressed), and engaging members of the KP community to deliver services to their peers [16, 20]. In Malawi, the Linkages across the Continuum of HIV Services for Key Populations Affected by HIV (LINKAGES) project provided differentiated HIV services by partnering with KP-led and KP-friendly community-based organizations [21–23]. Differentiated models implemented by LINKAGES included the establishment of KP safe spaces through drop-in centers (DICs), network-based approaches such as index testing, and community-based outreach such as enhanced peer outreach approach (EPOA) and peer navigation to reach KPs that may not readily engage in existing HIV services [21, 24–26]. Findings suggest that these service delivery models have improved access and uptake across the continuum of services [21, 27]. However, it remains unclear how testing and treatment success vary across different populations and service delivery modalities. We use routine program data collected by implementing partners of the LINKAGES project to identity differences in HIV testing uptake, HIV case finding, yield, and ART initiation for key and priority populations in Malawi.

METHODS

LINKAGES Project

With support from USAID and PEPFAR, LINKAGES was implemented in collaboration with the Department of HIV and AIDS and the National AIDS Commission of the Malawi Ministry of Health, and in partnership with 4 local civil society organizations, including the Pakachere Institute of Health and Development Communication, the Center for the Development of People, Youth Net and Counseling Organization, and Family Planning Association of Malawi. From 2015 through 2019, LINKAGES delivered a package of comprehensive HIV prevention and treatment services for key and other priority populations, including FSWs, MSM, TGW, adolescent girls and young women (AGYW), clients, and male sex workers. Services were designed to increase uptake of HIV testing while ensuring efficient HIV case finding and to improve engagement in HIV treatment for persons with HIV (PWH). Participants enrolled into the program were tested using multiple modalities including standard clinic-based HIV testing (provider- or client-initiated HIV testing at facilities) and peer-led approaches including community-based testing (HIV testing through routine mobile outreach), index testing, and through community-led drop-in centers providing dedicated services for KPs. Additional approaches included an EPOA, a coupon-based referral network approach that incorporates performance-based incentives to access hard-to-reach KP networks using peer mobilizers [28], and risk network referral testing for FSWs [26], whereby FSWs refer social network contacts—including sexual or injecting partners, for testing. Full procedures for recruitment and enrollment have been previously described [27–29]. Once enrolled in the program, participants were eligible to access additional services through the drop-in centers. Services initially included repeat HIV testing and counseling for those who previously tested negative with subsequent referrals for ART at hybrid facilities, but were expanded over time to include ART provision, postexposure prophylaxis, and screening for sexually transmitted infections (STIs), family planning, and gender-based violence. For KPs that were newly diagnosed with HIV as well as those previously diagnosed but not initiated on treatment, peer navigators provided support for ART initiation and adherence. Program implementation occurred across 6 districts in Malawi and included major cities and urban centers where HIV prevalence was generally higher than the national average (Figure 1).

Analytic Cohort

Data were restricted to those participants who accessed services through the LINKAGES program between November 28, 2017, and September 30, 2019 (FYs 2018–2019). Date restrictions were selected based upon the routinization and availability of individual-level program data for the full cadre of program services, which were implemented beginning in FY 2018. All participants accessing services through a LINKAGES implementing partner were assigned a unique alphanumeric code. These codes were used to link individuals across multiple services over time using a web-based DHIS2 tracker database that facilitated the merging of records across different data collection forms. Forms included the standard LINKAGES enrollment form, which collected demographic information—including age, gender, and self-identified population membership, and selected measures of sexual behavior. A clinical visit form captured results from HIV testing, along with other clinical examinations including STI screening. For participants with HIV, an additional form (PWH form) documented routine ART outcomes including the dates of HIV diagnosis and ART initiation. Viral load data, interruptions in treatment, mortality, and clinic transfer were captured for a limited number of participants and were thus not reported in this analysis. Records were merged across these 3 forms to create an analytic cohort comprising up to 2 years of prospective follow-up for all participants diagnosed with HIV through the program. To ensure acceptable quality of the program data, LINKAGES country office and stakeholders conducted data quality assessments every quarter where data captured in the DHIS2 tracker were compared with data in physical reporting forms based in drop-in centers and public health facilities. Data were then updated in the DHIS2 tracker wherever significant variations within forms (±5%) were observed.

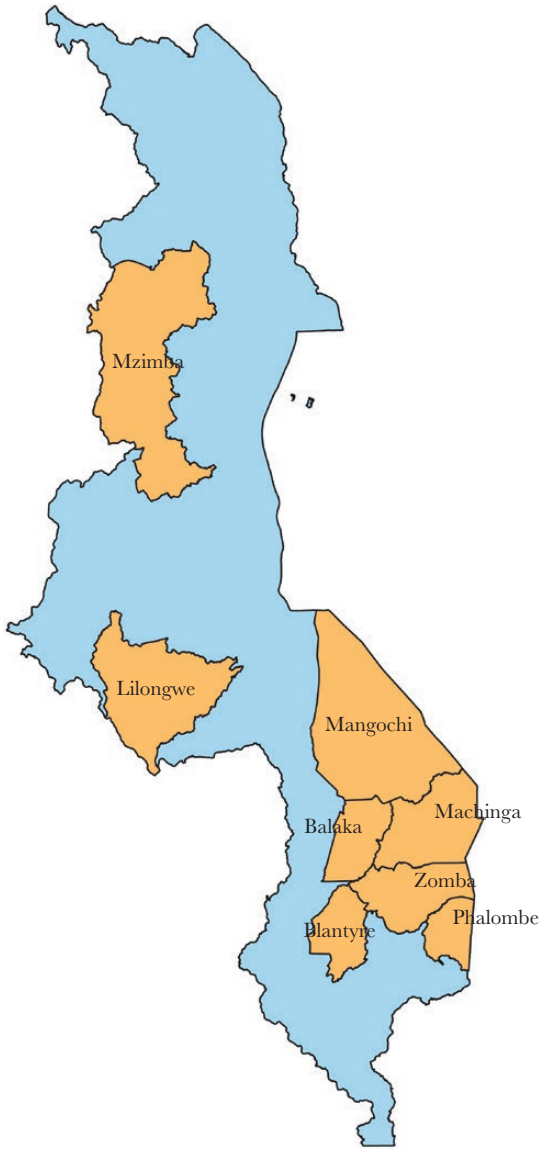

Figure 1. LINKAGES project districts in Malawi, 2018–2019. Abbreviation: LINKAGES, Linkages across the Continuum of HIV Services for Key Populations Affected by HIV.

Outcome Definitions

This analysis assessed HIV testing uptake by KPs and by modality, as well as the number and proportion of positive cases per tests conducted (yield). Additionally, ART initiation was compared across HIV testing modalities for positive cases. ART initiation was defined as documented ART initiation within 30 days of HIV diagnosis through LINKAGES (yes/no), per program standards.

Statistical Analysis

Program participants were described overall and by self-identified population membership upon entry into the program. HIV testing approaches and the number and proportion of HIV-positive tests resulting from each approach were summarized overall and for all populations. Fisher exact tests were used to test differences in proportions (alpha = 0.05). The proportion of participants who initiated ART within 30 days for each approach was calculated overall and by population.

To estimate the association between modality and ART initiation, we prospectively followed all HIV-positive participants beginning at their date of diagnosis to determine if they initiated ART within 30 days. Unadjusted and adjusted modified Poisson regression models were fit to estimate risk ratios (RRs) and 95% CIs, with standard clinic-based testing considered the referent for all comparisons. Adjusted models were conditioned on district; in sensitivity analyses, models were stratified by program year and further adjusted for age and prior engagement in HIV testing services.

All statistical analyses were performed using Stata (version 15; College Station, TX, USA) and SAS statistical software (version 9.4; Cary, NC, USA).

Patient Consent

This study was reviewed by the FHI 360 Protection of Human Subjects Committee and classified as nonhuman subjects research as data did not contain individual identifiers.

RESULTS

Between October 2017 and September 2019, 28 415 individuals representing 44 155 person-visits received services through LINKAGES implementing partners in Malawi. Of these individuals, 18 397 (64.7%) were tested for HIV at least once and were included in further analyses; the remaining 10 018 were those who had previously been diagnosed with HIV, had refused HIV testing, or those that were reached with other nonclinical services (Supplementary Table 1). More than half (58%) of the 18 397 individuals identified as FSWs, and 21% were MSM (Table 1). Clients of FSWs comprised 27% of participants, with AGYW, TGW, and male sex workers each accounting for <2% of the sample. Participant characteristics including median age and service district representation varied by population.

Among the 18 397 participants included in analyses, 2961 (16.1%) had HIV.

Nearly half (1421, 47.9%) had no recorded PWH form. Given an established relationship between the LINKAGES program and local ART clinics, including standardized reporting procedures for all persons initiating ART, these individuals were assumed to not have initiated ART within 30 days of diagnosis. The same assumption was made for 88 (3.0%) individuals whose ART initiation dates were missing or >30 days after HIV detection.

HIV Testing Modalities, HIV Case Finding, and Yield

HIV testing modalities differed in frequency across all populations engaged in LINKAGES services (Figure 2). Community-based peer testing was the most common entry point into the

Table 1. Sample Characteristics by Key Population, 2018–2019[a]

	Overall	FSWs	MSM	TGW	AGYW	Clients	MSW
	n = 18397	n = 10627	n = 2219	n = 240	n = 289	n = 4970	n = 52
Age, median (IQR), y	24 (21–30)	23 (20–28)	27 (24–32)	25 (21–29)	16 (15–18)	27 (21–34)	26 (22–33)
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
District							
Blantyre	3589 (19.5)	2875 (27.1)	624 (28.1)	74 (30.8)	-	-	16 (30.8)
Lilongwe	2369 (12.9)	1784 (16.8)	489 (22.0)	69 (28.8)	1 (0.4)	18 (0.4)	8 (15.4)
Machinga	2040 (11.1)	893 (8.4)	2 (0.09)	-	11 (3.8)	1134 (22.8)	-
Mangochi	5149 (28.0)	2666 (25.1)	455 (20.5)	46 (19.2)	264 (91.4)	1708 (34.4)	10 (19.2)
Mzuzu	1924 (10.5)	1209 (11.4)	649 (29.3)	51 (21.3)	-	-	15 (28.9)
Zomba	3326 (18.1)	1200 (11.3)	-	-	13 (4.5)	2110 (42.5)	3 (5.7)
Program year							
FY18	3307 (18.0)	2914 (27.4)	376 (16.9)	17 (7.1)	-	-	-
FY19	15090 (82.0)	7713 (72.6)	1843 (83.1)	223 (92.9)	289 (100)	4970 (100)	52 (100)

Abbreviations: AGYW, adolescent girls and young women; FSWs, female sex workers; FY, fiscal year; IQR, interquartile range; LINKAGES, Linkages across the Continuum of HIV Services for Key Populations Affected by HIV; MSM, men who have sex with men; MSW, male sex workers; TGW, transgender women.

[a]Comprises all persons who were tested at least once through the LINKAGES program between 2018 and 2019.

program for all populations (MSM: 44.3%, 1316/2971; TGW: 46.5%, 138/297; AGYW: 71.4%, 217/304; CFSWs: 35.3%, 1808/5122; male sex workers: 31.3%, 21/67), with the exception of FSWs, for whom the greatest proportion (41.9% of all FSWs, 5359/12791) were initially engaged through drop-in centers. A high proportion of clinic-based HIV testing was also reported among MSM (34.9%, 1037/2971), TGW (36.0%, 107/297), and FSW clients (31.2%, 1598/5122). Across all populations, the proportion of participants recruited through EPOA or index testing was generally low relative to other approaches. Characteristics of participants who engaged with each testing modality are reported in Supplementary Tables 2 and 3.

HIV case finding and yield varied by approach, with index testing and EPOA generally resulting in the largest proportion of persons testing positive for HIV, although the numbers of individuals reached by these methods was much lower (Table 2, Figure 2). For FSWs, clinic-based HIV testing resulted in

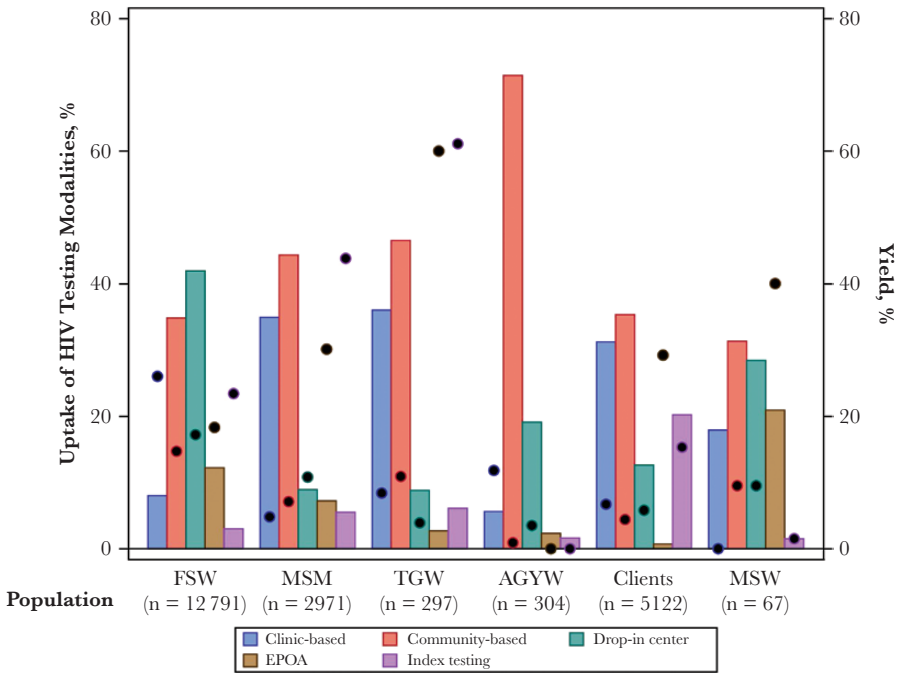

Figure 2. HIV testing modality and yield by population, 2018–2019. Bars represent the proportion of all HIV tests for each population performed through a given modality; for each population, proportions sum to 100%. Dots correspond to the proportion of HIV tests that were positive for each testing modality. FSWs were recruited through a risk network referral strategy and not traditional index testing. Abbreviations: AGYW, adolescent girls and young women; EPOA, enhanced peer outreach approach; FSWs, female sex workers; MSW, male sex worker; MSM, men who have sex with men; TGW, transgender women.

Table 2. Proportion Testing Positive, by HIV Testing Modality and Population, 2018–2019[a]

	FSWs	MSM	TGW	AGYW	Clients	MSWs
	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)
HIV testing modality						
Clinic-based	262/1023 (25.6)	93/1316 (7.1)	16/138 (11.6)	2/217 (0.9)	80/1811 (4.4)	2/21 (9.5)
Community-based	655/4455 (14.7)	50/1038 (4.8)	8/107 (7.5)	2/17 (11.8)	106/1597 (6.6)	-
Drop-in center	923/5634 (17.2)	26/240 (10.8)	1/26 (3.9)	2/58 (3.4)	37/643 (5.8)	2/19 (10.5)
EPOA	281/1562 (17.9)	63/215 (29.3)	6/8 (75.0)	-	10/37 (27.0)	4/14 (28.6)
Index testing[b]	90/387 (23.3)	71/162 (43.8)	11/18 (61.1)	-	158/1034 (15.3)	-
P value	<.001	<.001	<.001	.001	<.001	.419

Abbreviations: AGYW, adolescent girls and young women; FSWs, female sex workers; MSM, men who have sex with men; MSWs, male sex workers; TGW, transgender women.

[a]Comprises all persons that were tested at least once through the LINKAGES program between 2018 and 2019.

[b]FSW were recruited through a risk network referral strategy and not traditional index testing.

the highest yield (25.6%, 262/1023) despite accounting for a small proportion of total tests performed (8.0%, 1023/12 791), and testing conducted at the drop-in centers resulted in the highest number of new diagnoses. For MSM, community-based testing produced the smallest yield (4.8%, 50/1038), and index testing and EPOA resulted in the highest yield (43.8%, 71/162, and 29.3%, 63/215, respectively). Index testing and EPOA also produced the highest yield for TGW (61.1%, 11/18, and 75.0%, 6/8, respectively), although across both these approaches only 17 PWH were identified. For clients of FSWs, EPOA resulted in the highest yield (27.0%, 10/37), while index testing resulting in the highest number of identified cases. Few cases were identified for both AGYW and male sex workers, precluding a more nuanced assessment of yield and HIV case finding.

ART Initiation by HIV Testing Modality

ART initiation within 30 days of diagnosis occurred for half (49.0%, 1452/2961) of all persons testing HIV positive. Among all PWH identified through index testing, nearly 80% (260/330) initiated ART within 30 days. The proportion initiating ART among those reached through community-based peer testing was 38.3% (324/846). ART initiation within 30 days was most common for clients of FSW (67.0%, 262/391) and TGW (71.4%, 30/42), although overall numbers were small (Table 3). More than half (55.5%, 168/303) of MSM initiated ART within 30 days, and ART initiation for FSW was 44.7% (989/2211). Few AGYW and male sex workers initiated ART, although the small number of identified cases among these populations was generally insufficient to evaluate meaningful differences in ART initiation by modality.

Table 3. HIV Testing Modalities and Associations With Program ART Initiation Among Population Members With HIV, 2018–2019[a]

	Incidence of ART Initiation Within 30 Days, No. (%)	Unadjusted RR	Adjusted RR[b]
FSWs			
Clinic-based	108 (40.9)	1 (ref)	1 (ref)
Community-based	239 (36.5)	0.89 (0.75–1.06)	0.74 (0.63–0.88)
Drop-in center	406 (44.0)	1.08 (0.92–1.27)	1.03 (0.88–1.21)
EPOA	166 (59.3)	1.45 (1.22–1.73)	1.06 (0.89–1.26)
Risk network referral testing	70 (77.8)	1.90 (1.58–2.28)	1.50 (1.23–1.82)
MSM			
Clinic-based	25 (50.0)	1 (ref)	1 (ref)
Community-based	48 (51.1)	1.02 (0.73–1.44)	1.02 (0.73–1.44)
Drop-in center	18 (72.0)	1.44 (0.99–2.09)	1.82 (1.19–2.78)
EPOA	28 (44.4)	0.89 (0.60–1.32)	1.12 (0.74–1.69)
Index testing	49 (69.0)	1.38 (1.00–1.90)	1.45 (1.06–2.00)
Clients			
Clinic-based	89 (83.2)	1 (ref)	1 (ref)
Community-based	24 (30.4)	0.37 (0.26–0.52)	0.63 (0.45–0.88)
Drop-in center	14 (37.8)	0.45 (0.30–0.69)	0.65 (0.43–0.99)
EPOA	3 (30.0)	0.36 (0.14–0.93)	0.61 (0.28–1.33)
Index testing	132 (83.5)	1.00 (0.90–1.12)	1.02 (0.92–1.14)

Abbreviations: ART, antiretroviral treatment; EPOA, enhanced peer outreach approach; FSWs, female sex workers; LINKAGES, Linkages across the Continuum of HIV Services for Key Populations Affected by HIV; MSM, men who have sex with men; RR, risk ratio.

[a]Program ART initiation was defined as ART initiation with 30 days of a reported positive test through the LINKAGES program.

[b]Models were adjusted for district.

ART initiation was associated with HIV testing modality for FSW, with those who tested positive through risk network referral testing being more likely to initiate within 30 days compared with those who tested positive through clinic-based testing (adjusted risk ratio [aRR], 1.50; 95% CI, 1.23–1.82) (Table 3).

Conversely, FSW who tested positive through community-based peer testing were less likely to initiate ART compared with those who were diagnosed through clinic-based testing (aRR, 0.74; 95% CI, 0.63–0.88). For MSM, those who tested positive through a drop-in center and those who tested positive through index testing were more likely to initiate within 30 days compared with those who tested positive in-clinic (DIC: aRR, 1.82; 95% CI, 1.19–2.78; index testing: aRR, 1.45; 95% CI, 1.06–2.00). Clinic-based testing appeared the most successful for initiating clients of FSW on ART; clients who were diagnosed through community-based peer testing and through the drop-in center were less likely to initiate ART when compared with those who were diagnosed through the clinic (community-based peer testing: aRR, 0.63; 95% CI, 0.45–0.88; DIC: aRR, 0.65; 95% CI, 0.43–0.99). Similar associations were observed when analyses were restricted to FY 2019 data and when models were further adjusted for district, age, and prior HIV testing (Supplementary Table 4). Sparse data precluded comparative analyses for TGW, AGYW, and male sex workers.

DISCUSSION

We assessed differences in HIV testing and treatment outcomes for key and priority populations across standard and differentiated approaches using routinely collected and de-identified individual-level program data in Malawi. We found that HIV case finding varied by approach for each KP, with intensive approaches including index testing and EPOA demonstrating a high yield despite reaching few individuals overall. Further, ART initiation among PWH also differed by approach, suggesting that treatment uptake may be a function of how KPs are initially engaged by programs. Given the limited availability of prospectively collected data for KPs, our findings demonstrate the utility of data collected by routine community-based HIV programs to inform optimization of the local HIV response.

Differences in HIV testing uptake and case finding were evident across all testing modalities and populations. For MSM and TGW, community-based and clinic-based testing strategies accounted for the majority of reported HIV tests. Consistent with findings from other studies in the region, these were low-yield approaches [30], likely resulting from saturation within existing networks and difficulties in identifying those KP who are at the highest risk of HIV acquisition [31]. EPOA and index testing accounted for a smaller proportion of tests performed, in part because EPOA was implemented only intermittently when program efforts were needed to increase HIV case finding. However, both modalities produced substantially higher yields, demonstrating the potential utility of these approaches in recruiting and engaging MSM and TGW who have HIV but have yet to be linked to services [28, 29, 32–34].

For FSWs, the majority of new diagnoses were identified through the community-led drop-in centers, reflecting the already high levels of community engagement at these centers even before HIV service provision. In Malawi, FSWs have reported their preferences for receiving HIV prevention services, including PrEP, at drop-in centers [35]. These centers provide clinically competent services where FSWs may avoid the anticipated or enacted stigmas by providers and staff often associated with health care facilities [36, 37]. We similarly observed high attendance at the drop-in centers among AGYW, suggesting that drop-in centers can also provide supportive sexual and reproductive health services for vulnerable young women including those who are too young to legally be considered sex workers [38]. Of note, case finding was high among the small number of FSWs and AGYW program participants receiving facility-based HIV testing, in part reflecting referrals from the drop-in centers for women who required more intensive clinical services, immediate ART initiation, or further medical reasons requiring linkage to specific clinics.

Strategies for HIV testing also affected ART initiation, suggesting that testing modalities and approaches by which KPs are initially engaged by programs can impact treatment uptake. MSM who tested through the drop-in centers were nearly twice as likely to initiate ART compared with those who received clinic-based testing, affirming that peer-based approaches and early support at diagnosis may provide men the structure they need to start and potentially maintain ART [39]. Moreover, when paired with innovative recruitment strategies such as social media–based interventions [40], drop-in centers can function as an offline physical space where MSM can safely access regular care and treatment. Along with mobile clinics run by the outreach team, the drop-in centers also offered index testing for the sexual partners of MSM, resulting in a high frequency of ART initiation within 30 days for elicited contacts who had HIV. Index testing has previously been found to increase both linkage to care and ART initiation [41, 42], although evidence for improved engagement among MSM specifically has been mixed [42].

Decentralized treatment models can help overcome barriers to ART initiation and engagement for PWH and optimize sustained treatment outcomes for KPs [43, 44]. Occupational barriers to ART initiation for KPs include work-related migration among FSWs and limited or inconvenient clinic hours [45]. Additionally, perceived discrimination from providers, along with concerns around privacy and disclosure, may similarly limit engagement in care [46–50]. Importantly, and with the support of the Malawi government, LINKAGES was able to integrate on-site ART distribution at the drop-in centers, serving

as an essential community-based service delivery point that potentially closed treatment gaps among KPs with HIV. This model functioned with the support of both public and private health facilities, which supplied ART and provided clinicians and nurses to deliver core services on specific days of the week, and likely contributed to the high proportion of KPs initiating ART through the drop-in centers reported in this analysis. Leveraging this model in other settings, along with strategies such as peer navigation, can help close the remaining gaps by ensuring that KPs are promptly and consistently connected to ART.

All data presented here were collected during delivery of routine services for KPs in Malawi through the LINKAGES program. With funding for large epidemiologic studies becoming more and more scarce in the context of more people needing ART [51, 52], program data offer a relatively untapped resource to evaluate effective HIV-related interventions and implementation strategies to better serve KPs. As programs continue to roll out differentiated services for KPs, and as data collection systems are strengthened, program data may be quickly leveraged to assess performance and guide adaptations to better meet the diverse and dynamic needs of KPs, thus providing for a more nuanced and ultimately more efficient HIV pandemic response [53].

Consistent with the use of program data, there were some limitations to this study. First, data were merged across multiple forms over ~2 years, and inconsistencies associated with data collection or data entry may have resulted in missing or incorrectly combined data for specific individuals. We also assumed that PWH without program documentation of ART initiation did not initiate ART within 30 days. This assumption was grounded in formative work conducted by the program suggesting that before LINKAGES, KPs were not previously comfortable accessing HIV-related services at public ART facilities. The program's model specifically aimed to address this gap by developing community-based sites that were offshoots of public ART clinics or "mother" facilities. These sites were not designed to operate as standalone sites, and thus maintained a strong connection to the larger public ART facilities. While clients of LINKAGES have expressed their preferences for receiving services at LINKAGES-affiliated sites, it is possible that PWH were able to start treatment at other facilities not affiliated with the LINKAGES program. In the case that this was common for approaches that did not offer ART on-site (eg, community outreach during early 2018), our effect estimates may be slightly attenuated. Additionally, outcomes including CD4 count and viral load were largely missing, precluding further analysis of how disease progression may have impacted program engagement and subsequent ART initiation.

CONCLUSIONS

Findings from this analysis demonstrate the need to implement a mix of differentiated testing modalities for KPs to optimize HIV case finding and treatment outcomes. Such approaches include those described here, as well as HIV self-testing, peer navigation, and other client-centered efforts that have previously been successful in increasing testing and treatment for KPs. Further, in settings such as Malawi where 95-95-95 targets are within reach, differentiated approaches tailored to the needs of those who remain underserved and most at risk can help accelerate efforts to close "last mile" gaps. Finally, strengthening routine data monitoring and evaluation systems remains critical and can help facilitate and guide the application of targeted HIV prevention and treatment approaches for KPs in Malawi, ultimately improving the efficiency of these efforts moving forward.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Dovato
dolutegravir/lamivudine

EVIDENCE SUPPORTS THE HIGH BARRIER TO RESISTANCE OF DOVATO UP TO 5 YEARS[1-3]

CONFIDENCE IN DOVATO ACROSS TREATMENT SETTINGS[4–9]

Treatment-naïve resistance rates, with up to **3 years of evidence**[5–7]

0% (n=0/1,885)*,[4] **REAL-WORLD EVIDENCE**

0.1% (n=1/953)**,†,‡,§,5–7 **RANDOMISED CONTROLLED TRIALS**

Treatment-experienced resistance rates, with up to **5 years of evidence**[1–3]

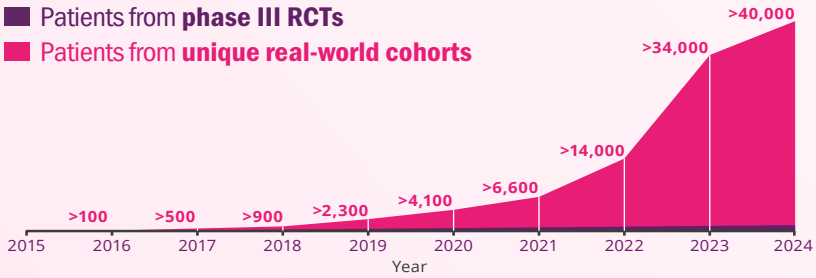
0.03% (n=10/35,888)*,[4] **REAL-WORLD EVIDENCE**

0% (n=0/615)||,¶,#,8,9 **RANDOMISED CONTROLLED TRIALS**

>300,000 PEOPLE LIVING WITH HIV HAVE BEEN TREATED WITH DOVATO GLOBALLY[10]

DOVATO is supported by a wealth of evidence, with the outcomes of **>40,000** people living with HIV captured within clinical trials and real-world evidence, including those with:[4–9,11,12]

- **NO PRIOR TREATMENT EXPERIENCE**[13]
- **NO BASELINE RESISTANCE TESTING**[13]
- **HIGH BASELINE VIRAL LOAD** (>100,000 copies/mL and even >1M copies/mL)[6,13]
- **LOW CD4 + COUNT** (≤200 cells/mm³)[13]



IS IT TIME TO RECONSIDER THE VALUE OF THE 2ND NRTI?

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DOVATO is indicated for the treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection in adults and adolescents above 12 years of age weighing at least 40 kg, with no known or suspected resistance to the integrase inhibitor class, or lamivudine.[13]

Adverse events should be reported. Reporting forms and information can be found at **https://yellowcard.mhra.gov.uk/** or search for MHRA Yellowcard in the Google Play or Apple App store. Adverse events should also be reported to GSK on 0800 221441

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ABBREVIATIONS

3TC, lamivudine; **CD4,** cluster of differentiation 4; **DTG,** dolutegravir; **FDA,** United States Food and Drug Administration; **FTC,** emtricitabine; **HIV,** human immunodeficiency virus; **ITT-E,** intention-to-treat exposed; **NRTI,** nucleoside/nucleotide reverse transcriptase inhibitor; **RCT,** randomised controlled trial; **RNA,** ribonucleic acid; **TAF,** tenofovir alafenamide fumarate; **TDF,** tenofovir disoproxil fumarate; **XTC,** emtricitabine.

FOOTNOTES

*Data extracted from a systematic literature review of DTG+3TC real-world evidence. Overlap between cohorts cannot be fully excluded.

**The reported rate reflects the sum-total of resistance cases calculated from GEMINI I and II (n=1/716, through 144 weeks), STAT (n=0/131, through 52 weeks), and D2ARLING (n=0/106, through 24 weeks).[5–7]

†GEMINI I and II are two identical 148-week, phase III, randomised, double-blind, multicentre, parallel-group, non-inferiority, controlled clinical trials testing the efficacy of DTG/3TC in treatment-naïve patients. Participants with screening HIV-1 RNA ≤500,000 copies/mL were randomised 1:1 to once-daily DTG/3TC (n=716, pooled) or DTG + TDF/FTC (n=717, pooled). The primary endpoint of each GEMINI study was the proportion of participants with plasma HIV-1 RNA <50 copies/mL at Week 48 (ITT-E population, snapshot algorithm).[13]

‡STAT is a phase IIIb, open-label, 48-week, single-arm pilot study evaluating the feasibility, efficacy, and safety of DTG/3TC in 131 newly diagnosed HIV-1 infected adults as a first line regimen. The primary endpoint was the proportion of participants with plasma HIV-1 RNA <50 copies/mL at Week 24.[6]

§D2ARLING is a randomised, open-label, phase IV study designed to assess the efficacy and safety of DTG/3TC in treatment-naïve people with HIV with no available baseline HIV-1 resistance testing. Participants were randomised in a 1:1 ratio to receive DTG/3TC (n=106) or DTG + TDF/XTC (n=108). The primary endpoint was the proportion of participants with plasma HIV-1 RNA <50 copies/mL at Week 48.[7] Results at week 24 of the study.

||The reported rate reflects the sum-total of resistance cases calculated from TANGO (n=0/369, through 196 weeks) and SALSA (n=0/246, through 48 weeks).[8,9]

¶TANGO is a randomised, open-label, trial testing the efficacy of DOVATO in virologically suppressed patients. Participants were randomised in a 1:1 ratio to receive DOVATO (n=369) or continue with TAF-containing regimens (n=372) for up to 200 weeks. At Week 148, 298 of those on TAF-based regimens switched to DOVATO. The primary efficacy endpoint was the proportion of subjects with plasma HIV-1 RNA ≥50 copies/mL (virologic non-response) as per the FDA Snapshot category at Week 48 (adjusted for randomisation stratification factor).[8,13]

#SALSA is a phase III, randomised, open-label, non-inferiority clinical trial evaluating the efficacy and safety of switching to DTG/3TC compared with continuing current antiretroviral regimens in virologically suppressed adults with HIV. Eligible participants were randomised 1:1 to switch to once-daily DTG/3TC (n=246) or continue current antiretroviral regimens (n=247). The primary endpoint was the proportion of subjects with plasma HIV-1 RNA ≥50 copies/mL at Week 48 (ITT-E population, snapshot algorithm).[9]

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