# **BMJ Open** Characterising persons diagnosed with HIV as either recent or long-term using a cross-sectional analysis of recent infection surveillance data collected in Malawi from September 2019 to March 2020

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**Objectives** In Malawi, a recent infection testing algorithm (RITA) is used to characterise infections of persons newly diagnosed with HIV as recent or long term. This paper shares results from recent HIV infection surveillance and describes distribution and predictors.

ABSTRACT

**Setting** Data from 155 health facilities in 11 districts in Malawi were pooled from September 2019 to March 2020.

**Participants** Eligible participants were  $\geq$ 13 years, and newly diagnosed with HIV. Clients had RITA recent infections if the rapid test for recent infection (RTRI) test result was recent and viral load (VL) ≥1000 copies/mL: if VL was <1000 copies/mL the RTRI result was reclassified as long-term. Results were stratified by age, sex, pregnancy/breastfeeding status and district. Results 13 838 persons consented to RTRI testing and 12 703 had valid RTRI test results and VL results after excluding clients not newly HIV-positive. RTRI negative or missing data (n=1135). A total of 12 365 of the 12 703 were included in the analysis after excluding those whose RTRI results were reclassified as long term (n=338/784 or 43.1%). The remainder, 446/12 703 or 3.5%, met the definition of RITA recent infection. The highest percentage of recent infections was among breastfeeding women (crude OR (COR) 3.2; 95% CI 2.0 to 5.0), young people aged 15-24 years (COR 1.6; 95% CI 1.3 to 1.9) and persons who reported a negative HIV test within the past 12 months (COR 3.3; 95% CI 2.6 to 4.2). Factors associated with recent infection in multivariable analysis included being a non-pregnant female (adjusted OR (AOR) 1.4; 95% CI 1.2 to 1.8), a breastfeeding female (AOR 2.2; 95% CI 1.4 to 3.5), aged 15-24 years (AOR 1.6; 95% Cl 1.3 to 1.9) and residents of Machinga (AOR 2.0; 95% Cl 1.2 to 3.5) and Mzimba (AOR 2.4; 95% Cl 1.3 to 4.5) districts.

**Conclusions** Malawi's recent HIV infection surveillance system demonstrated high uptake and identified

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This paper reports on HIV recent infections that are verified by viral load (VL); if the rapid test for recent infection (RTRI) test result is recent and VL ≥1000 copies/mL the RTRI recent result is considered valid and if VL is <1000 copies/mL the RTRI recent test result is reclassified as a long-term infection.
- ⇒ HIV recent infection surveillance in Malawi is integrated into HIV testing services so that all eligible persons who test HIV-positive, and provide consent, are tested with an RTRI.
- ⇒ When implementing HIV recent infection surveillance in Malawi, it is not possible to deduplicate HIV positive persons retesting for HIV because there are no unique national IDs at the moment that would allow deduplication.
- ⇒ Data reported in this paper include varying levels of implementation of HIV recent infection surveillance by district in Malawi and these differences in coverage could influence district-level HIV recent infection rates reported and the statistical significance of those findings.

sub-populations of new HIV diagnoses with a higher percentage of recent infections.

#### INTRODUCTION

The East and Southern Africa regions bear the highest burden of the global HIV/AIDS epidemic. In 2018, the number of people living with HIV (PLHIV) in these two regions was approximately 20.6 million, accounting for 47% of HIV infections worldwide.<sup>1</sup> In 2018, the HIV prevalence in Malawi was estimated at 9.2%, with almost one million PLHIV and 38 000 new HIV infections annually.<sup>2</sup> This prevalence is a considerable decline of almost 5% from 2005, when the prevalence was 14.1% and there were 66 000 new infections annually.<sup>2</sup>

Malawi has also made great progress in reaching the Joint United Nations Programme on HIV/AIDS (UNAIDS) 95-95-95 goals that were set in 2014. According to the 2020–2021, Malawi population-based HIV impact assessment (MPHIA), 88% of PLHIV knew their HIV status, 98% of PLHIV who knew their status were on treatment and 97% of those on treatment had achieved viral suppression.<sup>3</sup> Expanded access to HIV treatment has resulted in a substantial 55% decrease in AIDS-related deaths, from 29 000 in 2010 to 13 000 in 2018, with more PLHIV living healthy and longer lives on antiretroviral therapy (ART) than ever before.<sup>2</sup>

Although prevalence is a basic epidemiological measure in countries with generalised HIV epidemics, it is a poor indicator of changes in the epidemic. Since HIV is a lifelong infection, prevalence measures are cumulative, and do not differentiate between those who have been living with HIV for many years and recent transmission.<sup>4</sup> To better understand the epidemic and focus appropriate HIV-prevention programmes among specific populations and locations, it is important to identify patterns and trends of recent HIV infections.<sup>5</sup> Detecting locales with high amounts of ongoing HIV transmission and describing factors associated with recent infections can provide critical information for targeting HIV prevention strategies and measuring their impact.<sup>4 6-9</sup>

Antibody-based rapid tests for recent infection (RTRI) can distinguish recent HIV infection, that is, an infection that has likely occurred within the last 12 months, from long-term infection.<sup>10–12</sup> However, their interpretation is challenged by factors that can cause 'false-recent' results such as variable immune responses at the individual level, variable performance of the assay across diverse HIV-1 subtypes and across populations with naturally low viral loads (VLs), or current ARV use and advanced HIV disease.<sup>13</sup> To improve the accuracy of interpretation, recent infection testing algorithms (RITAs) incorporate the RTRI result with other markers of chronic infection (low VL, evidence of treatment).<sup>14</sup> In Malawi, use of RTRI at the point-of-care was first evaluated in a pilot study in four districts between November 2017 and June 2018.<sup>15</sup> Lessons learnt from this pilot study were used to establish a plan for a nationwide surveillance system for recent HIV infections starting in April 2019, using RTRI and RITA.<sup>16</sup>

This paper shares results from the Malawi recent HIV infection surveillance system, with the aim of describing the distribution and predictors of recent HIV infections among people newly diagnosed with HIV.

#### **METHODS**

This analysis includes persons enrolled in HIV recent infection surveillance between September 2019 and March 2020 at 155 health facilities in 11 districts of Malawi. Data from April 2019 to August 2019 were excluded from the analysis due to variability in facility data collection during the 5-month startup phase of the surveillance system. Surveillance was implemented over time, so not all facilities and districts were collecting data during this entire time period; for the time period reported on, recency surveillance had expanded to 11 of 28 districts and to 155 of an envisioned 251 facilities. The districts were prioritised for surveillance based on numbers of HIV-positive diagnoses in 2018.<sup>17</sup> All persons presenting for testing who reported being HIV negative or unknown (or having never tested HIV positive) and who were aged 13 years and older were eligible to consent to recent infection surveillance. Among those who provided consent, only those who were subsequently reactive for HIV using a rapid test were enrolled in recent infection surveillance. Persons were excluded from the analysis if they tested HIV-positive using self-testing, or were otherwise screened for HIV in the community and accessed the health facility only for HIV confirmatory testing.

All HIV testing was accompanied by pretest and posttest counselling and followed the national testing algorithm.<sup>18</sup> As noted, only persons who were (1) reactive on the first HIV rapid test in the national algorithm (Determine) and (2) had provided verbal consent (ie, eligible for recency testing) were subsequently tested with Asanté HIV Rapid Recency Assay (Sedia Biosciences, Portland, Oregon, USA) simultaneously with the HIV rapid test UniGold.<sup>19 20</sup> Verbal consent was the preferred consent format due to the low-risk nature of the surveillance and to better integrate recency testing into Government of Malawi-approved HIV testing guidelines. Persons under the age of 18 provided verbal consent to participate in recency testing, and assent was not used. Even though the Asanté assay is currently validated for persons 15 years and older,<sup>19</sup> ethics committees approved verbal consent for persons 13 years and older because this age is also allowed to consent to HIV testing per Malawi Government HIV testing services (HTS) guidelines. The protocol was approved by the National Health Sciences Research Committee in Malawi and by a U.S. Centres for Disease Control and Prevention institutional review board

Both the UniGold and Asanté HIV Rapid Recency Assay results were entered into the study database via a tablet. Persons testing negative with UniGold were dropped from all analyses. A dried blood spot specimen for VL testing was collected from persons who tested both HIV-positive and recent on the RTRI assay to assess recent infection per the RITA. HIV plasma RNA VL was quantified using Abbott m2000 Real Time HIV Viral Load Assay according to manufacturer instructions.<sup>21</sup>

Routinely collected HIV testing data, including demographics, self-reported HIV testing history, and RTRI results were recorded in a surveillance data register at each facility. We abstracted these data using ODK software<sup>22</sup> and sent them to a central data repository. Once VL results were available from the National HIV Reference Laboratory, these data were merged with the RTRI data using Stata V.13.0 (Stata). In the merged dataset, all persons with recent results on the RTRI assay and VL ≥1000 copies/mL were classified as RITA recent infections. All persons with long-term results on the RTRI assay were classified as long-term infections. Persons with an RTRI result indicating a recent infection and VL <1000 copies/mL were excluded from the analysis since viral suppression likely indicates current or recent ART use and, therefore, not a new diagnosis. The RTRI and RITA results were not returned to the clients (clients were aware when they provided consent) or clinicians but only used for surveillance. We were unable to identify people retesting for HIV or already on ART because the current system for HTS and ART does not use a unique identifier (eg, national identification number) that would allow deduplication.

We calculated percentages of people with newly diagnosed HIV infections classified as RITA recent by age, sex, and district of residence. We used  $\chi^2$  and the Kruskal-Wallis test to compare proportions and medians (IQR), respectively. We used logistic regression, with clusterbased robust standard errors<sup>23</sup> to account for clustering of individuals within health facilities, to model factors associated with recent infection. We calculated unadjusted and adjusted ORs (ORs and AORs, respectively) with 95% CIs to assess the associations between recent infection and demographic factors. The a priori variables chosen for inclusion in multivariable analysis were age and sex. Variables associated with recent infection at a significance level of p<0.05 in univariable analysis and those known to be risk factors for HIV infection or suspected confounders were included in the multivariable logistic regression model through the stepwise method. In multivariable logistic regression, we thus adjusted for age group and sex, urban/rural location of the participant's residence, and district of participant's residence. HIV testing history was not adjusted for in the multivariable analysis due to its clear role in mediating recent HIV infection. Statistical analyses were performed using Stata.

## Patient and public involvement

Our study involved the analysis of routinely collected Government of Malawi surveillance data and thus involvement from patient or members of the public in the design, conduct, reporting and dissemination plans for the study was not possible. Starting in late 2021, investigations of locales with higher rates of recent infections, and initiation of public health interventions based on the results, have included more patient and public involvement.

## RESULTS

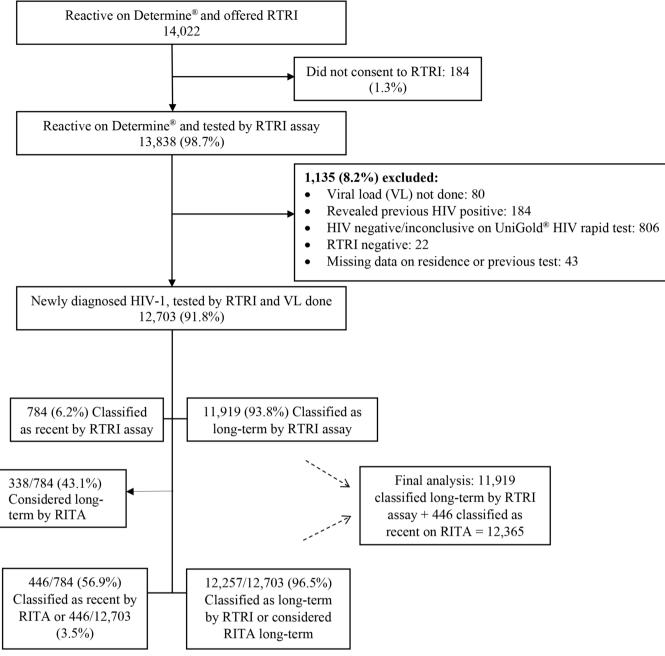
Between September 2019 and March 2020, 14 022 eligible persons aged  $\geq 13$  were asked to participate in recency testing. Of these, 13 838/14 022 (98.7%) consented to recent HIV infection surveillance and were then tested using the RTRI assay (figure 1). Of these, a total of 1135/13 838 (8.2%) were excluded for the following reasons: an HIV-negative or invalid UniGold result (n=806), disclosure of a previous HIV-positive diagnosis during post-test counselling (n=184), missing VL results (n=80), missing data on previous HIV test (n=43) or a negative (or invalid) result on the RTRI assay (n=22) (figure 1). Of the 12 703 participants included in the analysis after these exclusions, 784/12 703 were RTRI recent (6.2%) and 11 919/12 703 were RTRI long term (93.8%). Of the 784 RTRI recent participants, 446/784 (56.9%) met the definition of RITA recent infection and 338/784 (43.1%) met the definition of RITA long-term infection. This corresponds to an overall RITA-recent rate of 3.5% (446/12 703) and a RITA long-term rate of 96.5% $(12 \ 257/12 \ 704)$ . The final analysis thus included 446 RITA-recent cases and 11 919 long-term infection cases (as classified by RTRI) or a total of 12 365 participants. The final analysis did not include RITA long-term cases since technically these cases could not be reclassified as RTRI long-term (338) (figure 1).

## **Characteristics of surveillance participants**

Females accounted for 60.5% (n=7481) of the participants included in the analysis (table 1) and, among those of reproductive age, 70.2% were not pregnant (n=4974), 26.7% were pregnant (n=1893) and 3.1% were breast feeding (n=220). The overall median age for all participants was 31 years (IQR: 25-39 years), with the most common age group being 25-34 years (38.2%, n=4722). Participants were split almost equally between urban and rural settings. A large proportion of recent infection surveillance participants were from Blantyre district (47.3%, n=5851), followed by Zomba district (14.6%, n=1800), Lilongwe district (7.7%, n=949) and Machinga (7.6%, n=941). The proportion of participants who reported an HIV test within the previous 12 months (40.9%, n=5055) vs more than 12 months ago (40.7%, n=5030) were similar, while a lower proportion reported never having tested before (18.4%, n=2280; table 1).

## **Characteristics of persons with recent HIV infection**

Breastfeeding women (crude OR, COR 3.2; 95% CI 2.0 to 5.0) had the highest proportion of recent infections, which was significantly higher than that of pregnant (COR 1.6; 95% CI 1.2 to 2.1) and non-pregnant women (COR 1.7; 95% CI 1.4 to 2.1) (table 2). By age group, recent HIV infections were highest in females (6.0%) and males (4.7%) aged 15–24 years (figure 2) and highest in the 15-24 age group overall (COR 1.6; 95% CI 1.3 to 1.9) (table 2). A larger percentage of recent infection among people with new HIV diagnoses was found in persons from rural settings (COR 1.3; 95% CI 1.0 to 1.8) compared with urban settings, although this was not statistically significant. Residents of Mzimba (COR 2.3; 95% CI 1.3 to 4.0), Machinga (COR 2.1; 95% CI 1.2 to 3.5), Balaka (COR 1.7; 95% CI 0.7 to 4.1), Lilongwe (COR 1.6; 95% CI 1.0 to 2.6) and Chikwawa (COR 1.6; 95% CI 1.0 to 2.6) districts had the highest proportions of recent infections, although not statistically significant in



**Figure 1** Flow chart of persons included in the analysis of HIV recency surveillance data in Malawi, from September 2019 to March 2020. RITA, recent infection testing algorithm; RTRI, rapid test for recent infection; VL, viral load.

Balaka, Lilongwe and Chikwawa. By HIV testing history, the highest percentage of recent infections (COR 3.3; 95% CI 2.6 to 4.2) was among persons who self-reported having had a negative HIV test within the 12 months prior (table 2). For a description of persons with long-term infections (n=338), please see additional online supplemental appendix.

## Factors associated with recent HIV infection

After adjusting for age group and sex, urban/rural location of the participant's residence, and district of participant's residence, factors significantly associated with recent infection among newly diagnosed PLHIV included living in Mzimba (AOR 2.4; 95% CI 1.3 to 4.5) or Machinga (AOR 2.0; 95% CI 1.2 to 3.5) districts compared with Zomba district and being aged 15–24 years (AOR 1.6; 95% CI 1.3 to 1.9) compared with being aged 25–34 years. Women who were not pregnant (AOR 1.4; 95% CI 1.2 to 1.8) and women who were breastfeeding (AOR 2.2; 95% CI 1.4 to 3.5) compared with males were also at higher risk of recent infection (table 2).

## DISCUSSION

Our results demonstrate an association of recency with plausible risks such as younger age (<25 years) and sex (women vs men), confirming successful implementation

Table 1Characteristics of recent HIV infection surveillanceamong determine reactive participants in Malawi, fromSeptember 2019 to March 2020 (n=12 365)

Characteristic	Total % (n)	
Sex		
Male	39.5 (4884)	
Female	60.5 (7481)	
Pregnancy and breast feeding*		
Not pregnant	70.2 (4974)	
Pregnant	26.7 (1893)	
Breast feeding	3.1 (220)	
Age, years		
13–14	0.6 (68)	
15–24	22.2 (2748)	
25–34	38.2 (4722)	
35–44	26.0 (3210)	
45–49	6.2 (770)	
≥50	6.9 (847)	
Median (IQR)	31 (25–39)	
Residence		
Urban	48.5 (5992)	
Rural	51.5 (7373)	
District of residence		
Balaka	2.3 (283)	
Blantyre	47.3 (5851)	
Chikwawa	6.2 (763)	
Lilongwe	7.7 (949)	
Machinga	7.6 (941)	
Mangochi	6.5 (806)	
Mzimba	1.7 (214)	
Zomba	14.6 (1800)	
Other	6.1 (758)	
Previous HIV test†		
≤12 months	40.9 (5055)	
>12 months	40.7 (5030)	
Never tested	18.4 (2280)	

\*Data for all females in the reproductive age group (15–49 years).  $\pm 12$  months and >12 months represent client's last self-reported HIV-negative test.

of recency surveillance in Malawi. In addition, recency testing identified breastfeeding women and residents of certain districts as persons at higher risk of ongoing HIV transmission. In multivariable regression, factors that remained associated with recent infection included younger age and district of residence.

The proportion of recent infections found in this study, using RITA, was 3.5%. There have been no other nationallevel recent infection studies in Malawi to compare these

findings to. A study in Kenva using similar methods, though with a much smaller sample size and using a laboratory-based recency test, reported a recent infection per cent of 8.6% in Nairobi<sup>24</sup> and another recency study in Zimbabwe reported a recent infection percent of 10.5% among female sex workers.<sup>25</sup> Our study likely has a comparatively lower recent infection rate given the large, national sample that constitutes the recent infection surveillance system in Malawi. For example, a larger surveillance study recently completed in Cambodia found a RITA recent rate of 5.0% and surveillance of 27 792 newly HIV-diagnosed individuals in Nigeria found an RITA recent rate of 2.4%.<sup>26 27</sup> Furthermore, recency surveillance in Eswatini found an overall RITA recent rate of 3.1% and surveillance in DRC found an overall RITA recent rate of 5.0%.<sup>28 29</sup> All of these surveillance studies were aided by the use of clinical information such as VL, history of prior HIV diagnosis, and ART-exposure to confirm that a recent infection was truly recently acquired and not a long-term infection. The validity of our recent infection rate in Malawi is also aided by the inclusion of VL testing to rule out long-term infections-without the VL testing, the percent HIV recent would have been 6.2%.

The percentage of recent infections among newly diagnosed females aged 15–24 years, or adolescent girls and young women (AGYW), in this study was lower than that found in previous studies in Malawi<sup>30</sup> and in nearby countries.<sup>4 31 32</sup> The differences in percentages may be attributed to factors such as the case definition of recent infection. For example, Kim *et al*, in Kenya, the case definition for recent infection included testing recent on LAg and having no evidence of ART use.<sup>4</sup> This case definition for recent infection is different from what is used in this analysis, which used a point-of-care test and did not use ART use as an eligibility criterion.

The multivariable analysis indicating a risk of recent HIV infection among younger persons may be partly because older persons are less likely to have had a history of HIV testing.<sup>33</sup> Higher percentages of recent infection in women can also be partly explained by data showing higher HIV testing rates in women compared with men.<sup>33 34</sup> The 2015–2016 MPHI survey estimated that 5.1% of women had never tested for HIV or received an HIV test result compared with 12.4% of men.<sup>35</sup> This is especially true in antenatal care (ANC) settings, which are accessed by 95% of pregnant women in Malawi,<sup>36</sup> compared with studies that show that as few as 35% of the male partners of pregnant women are tested for HIV.<sup>37 38</sup> Women may be offered HIV testing both during maternal health visits (ANC, labour and delivery, and postnatal) and during paediatric services for their children. Therefore, women may have multiple opportunities for routine HIV testing, increasing the likelihood of being diagnosed with HIV early.<sup>39</sup>

The higher proportion of women currently breast feeding who tested recent for HIV may similarly be explained by HIV testing practices in Malawi for pregnant and breastfeeding women. Women who test positive during Table 2Prevalence of RITA recent HIV infections by participant characteristic and factors associated with RITA recent HIVinfection in persons with new HIV diagnoses among surveillance participants in Malawi, from September 2019 to March 2020(n=12 365)

Characteristic	Total	Recent infections %	Crude OR (95% CI)	Adjusted* OR (95% CI)
Sex				
Male	4884	2.5	1	1
Female not pregnant	5362	4.3	1.7 (1.4 to 2.1)	1.4 (1.2 to 1.8)
Female pregnant	1898	4.0	1.6 (1.2 to 2.1)	1.1 (0.8 to 1.5)
Female breast feeding	221	7.7	3.2 (2.0 to 5.0)	2.2 (1.4 to 3.5)
Age, years				
13–14	68	1.5	0.4 (0.1 to 2.7)	0.4 (0.1 to 2.6)
15–24	2748	5.8	1.6 (1.3 to 1.9)	1.6 (1.3 to 1.9)
25–34	4722	3.7	1	1
35–44	3210	2.7	0.7 (0.6 to 0.9)	0.8 (0.6 to 0.9)
45–49	770	1.7	0.5 (0.3 to 0.8)	0.5 (0.3 to 0.9)
≥50	847	1.5	0.4 (0.2 to 0.7)	0.4 (0.2 to 0.7)
Residence				
Urban	5992	3.1	1	1
Rural	6373	4.1	1.3 (1.0 to 1.8)	1.0 (0.7 to 1.5)
District of residence				
Balaka	283	5.7	1.7 (0.7 to 4.1)	1.7 (0.7 to 4.0)
Blantyre	5851	2.6	0.8 (0.5 to 1.2)	0.8 (0.5 to 1.2)
Chikwawa	763	5.2	1.6 (1.0 to 2.6)	1.5 (0.9 to 2.4)
Lilongwe	949	5.5	1.6 (1.0 to 2.6)	1.7 (1.0 to 2.8)
Machinga	941	6.8	2.1 (1.2 to 3.5)	2.0 (1.2 to 3.5)
Mangochi	806	3.5	1.0 (0.6 to 1.8)	1.0 (0.6 to 1.8)
Mzimba	214	7.5	2.3 (1.3 to 4.0)	2.4 (1.3 to 4.5)
Zomba	1800	3.4	1	1
Other	758	2.5	0.7 (0.4 to 1.2)	0.7 (0.4 to 1.2)
†Previous HIV test				
≤12 months	5055	6.1	3.3 (2.6 to 4.2)	
>12 months	5030	1.9	1	
Never tested	2280	2.0	1.1 (0.7 to 1.5)	

\*Adjusted for age group, sex, urban/rural location of the participant's residence and district of participant's residence.

RITA, recent infection testing algorithm.

breastfeeding may have tested negative during pregnancy but seroconverted either later in the pregnancy or postpartum after becoming sexually exposed to HIV. Others might not have had their HIV status ascertained during pregnancy but tested positive during the breastfeeding period.<sup>40</sup> The smaller number of women breastfeeding compared with women who were not pregnant or breast feeding, or were currently pregnant, may have influenced the results and explain why this variable did not remain strongly significant in the multivariable model, though it does border on significance. Chagomerana *et al* conclude in their ANC cohort study in Malawi that mother-tochild-transmission (MTCT) occurred disproportionately among women with a last positive HIV test during breastfeeding. This means that testing delayed until the postpartum period may lead to higher MTCT and that prevention of MTCT programmes should focus on early ART initiation and providing targeted testing, prevention, treatment and support to breastfeeding women.<sup>40</sup> Because breastfeeding women do not routinely attend health facilities after the first set of infant vaccinations, the Malawi 2022 HIV testing guidelines has added HIV

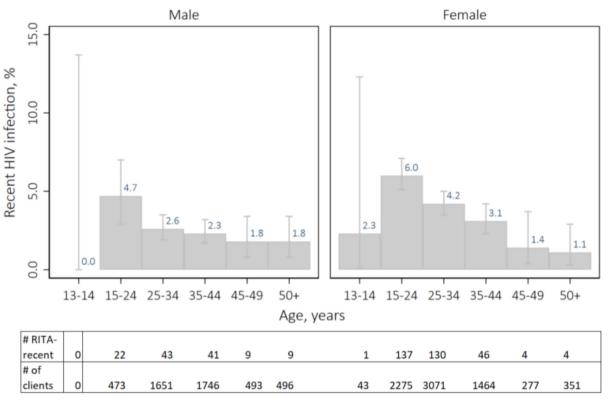


Figure 2 Number and percentage of recent HIV infections, per RITA, by age group among men and women included in HIV recency surveillance in Malawi, from September 2019 to March 2020. RITA, recent infection testing algorithm.

testing of mothers at the measles vaccination visit (9–12 months) to increase the chances of finding incident infected mothers.<sup>41</sup>

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There is a clear association in our survey between a history of HIV testing within the last 12 months and recent HIV infection. This finding is consistent with other studies that demonstrate a higher rate of HIV testing history among newly HIV-positive individuals, with as much as 70% of newly diagnosed individuals reporting previously testing either positive (meaning they were not truly newly diagnosed) or negative.<sup>42</sup> Since recent infection assays are designed to detect HIV infections that have occurred during the previous 12 months, it seems reasonable that persons who tested positive with a recent infection during our surveillance were more likely to have perceived themselves at risk and sought HIV testing sometime during the previous 12 months when compared with those persons who had not, or who reported having never been tested for HIV. Also, people newly diagnosed with HIV and with a recent history of testing negative for HIV are likely to have seroconverted since their last test and thus are more likely to be recently infected. More needs to be done to enhance the quality of HIV prevention counselling, such as initiation of pre-exposure prophylaxis and a thorough assessment of factors that may have influenced the person to seek a test.

There are several implications from our findings. The high percentage of long-term infections among newly diagnosed PLHIV found in the surveillance is alarming given that these late diagnoses mean that a significant

proportion of the population is unaware of their HIV status and likely transmitting infection.<sup>43 44</sup> In addition, when these persons with long-term infections are then linked to treatment programmes, they are more likely to experience poor health outcomes, including in the younger age groups.<sup>45–47</sup> This finding underscores the continued need for expanding HIV testing, as well as testing strategies that are narrowly focused on specific populations. Still, many of the long-term infections identified may be due to persons who reported testing negative on their last test but in truth were previously diagnosed with HIV and possibly had a history of ART use, as shown by the many people who tested RTRI recent but were subsequently reclassified as long-term when their VL test indicated they had a controlled VL.<sup>48 49</sup> Given the high rate of retesting and rediagnosis in Malawi<sup>50</sup> more research is needed to better understand stigma and misconceptions associated with revealing a history of testing positive, reasons why those who test positive will often retest even after starting treatment and how a person's retesting history, including the length of time between tests, may influence HIV outcomes.<sup>41</sup> Our study also points to the need for a unique identifier in Malawi that can be used during HTS to quickly identify and quantify HIV-positive retesters. This is increasingly important given that across sub-Saharan Africa, approximately 84% of people have knowledge of their HIV status.<sup>49</sup>

AGYW continue to face the highest risk of HIV in Malawi. More needs to be done to expand HIV testing among AGYW in Malawi beyond traditional facility-based testing to modalities that are preferred by adolescents.<sup>5152</sup> In a recent HIV testing study in Kenya, most AGYW participants (77.5%) chose staff-aided testing either at home or at a mobile event; (22.4%) chose self-testing; and only 2 (.2%) chose facility referral.<sup>53</sup> Even with the elevated risk that AGYW face, young men aged 15–24 in our surveillance also had high rates of new infections, and in multivariable analysis only young age remained significant, clearly indicating a need for renewed focus on HIV prevention in all youth aged 15–24 in Malawi.

The prevalence of recent infection was highest in four districts: Mzimba (in the northern region), Machinga and Chikwawa (in the southern region), and Lilongwe (in the central region). These findings provide new information to complement prevalence data from MPHIA studies that have found that southern districts had higher HIV prevalence compared with central and northern districts (even though the MPHIA was not powered to provide districtlevel prevalence estimates).<sup>3</sup> Since recent HIV surveillance can generate a disaggregated summary of where recent HIV infections occur at more granular geographic sub-units, such as district and health facilities,<sup>16</sup> the rapid identification of such HIV transmission clusters is the next important step in using the recent infection surveillance data in Malawi. This in fact has begun with a geospatial transmission 'hotspot' analysis using Malawi recency data.<sup>54</sup> Continuing such analyses, and following them up with local facility-based investigations, may help explain our district-level recent infection findings more fully and can provide the basis for using recent infection surveillance to identify gaps in HIV prevention and care services.4 5 55 56

The strength of this study includes the large sample of persons with new HIV diagnoses from districts in Malawi with high HIV prevalence. Since RITA was integrated into the national HTS model with high acceptability, these data are likely a good representation of the general characteristics of persons newly diagnosed with HIV seeking healthcare from health facilities in Malawi and similar settings. The study had some limitations. First, since the initial phase of the recent HIV infection surveillance system was focused on integrating recent HIV infection testing into routine HTS, additional data were not collected that may have helped identify factors associated with recent infection, such as marital status, cultural beliefs and socioeconomic status. Future surveillance may benefit from linking information generated from recent HIV infection testing data with other sociodemographic factors and triangulating additional factors such as clinical history that may be related to recent HIV infection.

Participation in this investigation relied on selfreported history of HIV testing among eligible persons. Hence, as noted above, it is possible that participants were reluctant to disclose a previous HIV-positive diagnosis and were inadvertently included as a new HIV diagnosis. Indeed, UNAIDS/WHO estimates that approximately up to 50% of people testing positive in Malawi are re-diagnoses.<sup>50</sup> This would result in an underestimation of the

proportion of recent infections. An overestimation of the proportion of recent infections would result from our exclusion from the analysis of persons screening HIV-positive with a self-test or visiting the facility for confirmatory testing (and testing HIV-positive). Another limitation is that the included districts, and therefore participants, are likely not representative of all of Malawi especially since districts were prioritised for HIV recency surveillance based on the number of newly reported HIV cases the year before. In addition, during the time period reported additional districts and facilities were continuing to be added to the surveillance system and so these results cannot be generalised to all of Malawi. Finally, some validation studies of recency assays indicate a tendency to produce false-recent results, particularly for those individuals on ART,<sup>10-12</sup> which would result in an overestimation of the proportion of recent infections. However, efforts have been made to reduce false-recent results through the addition of RITAs<sup>13</sup> such as was used in this study.

## CONCLUSION

Recent HIV infection surveillance can help to identify sociodemographic, clinical and geographical factors associated with recent HIV infection. Given that recent infection surveillance in Malawi confirms the high risk of HIV faced by AGYW, youth-focused programmes that aim to limit HIV acquisition and transmission among young people, especially young women, should remain a priority and be strengthened to sustain the gains made towards HIV epidemic control in Malawi. More data derived from triangulation and modelling with other data sources, as well as recent infection cluster analyses, are needed to allow for the targeting of HIV interventions at the district level in the country. The higher percentage of long-term infections than recent infections among newly diagnosed PLHIV underscores the continuing need for innovative ways to expand targeted HIV testing to ensure early diagnosis and treatment, especially among hard-to-reach populations.

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## REFERENCES

- 1 Global HIV and AIDS statistics [Internet]. Brighton (UK): Avert.org, 2021. Available: https://www.avert.org/global-hiv-and-aids-statistics
- 2 Malawi country data [Internet]. Geneva (Switzerland): UNAIDS, 2021. Available: https://www.unaids.org/en/regionscountries/countries/ malawi
- 3 Ministry of Health, Malawi. Malawi population-based HIV impact assessment (MPHIA) 2020-2021: summary sheet. Lilongwe, Ministry of health, 2022. https://phia.icap.columbia.edu/wp-content/uploads/ 2022/03/110322\_MPHIA\_Summary-sheet-English.pdf
- 4 Kim AA, Parekh BS, Umuro M, *et al.* Identifying risk factors for recent HIV infection in Kenya using a recent infection testing algorithm: results from a nationally representative population-based survey. *PLoS One* 2016;11:e0155498.
- 5 Chen M, Ma Y, Chen H, et al. Demographic characteristics and spatial clusters of recent HIV-1 infections among newly diagnosed HIV-1 cases in Yunnan, China, 2015. BMC Public Health 2019;19:1507.
- 6 Oster AM, France AM, Panneer N, et al. Identifying clusters of recent and rapid HIV transmission through analysis of molecular surveillance data. J Acquir Immune Defic Syndr 2018;79:543–50.
- 7 Janssen RS, Satten GA, Stramer SL, *et al.* New testing strategy to detect early HIV-1 infection for use in incidence estimates and for clinical and prevention purposes. *JAMA* 1998;280:42–8.
- 8 Brookmeyer R, Quinn TC. Estimation of current human immunodeficiency virus incidence rates from a crosssectional survey using early diagnostic tests. *Am J Epidemiol* 1995;141:166–72.
- 9 UNAIDS/WHO Working Group on Global HIV/AIDS/STI Surveillance, WHO Technical Working Group on HIV Incidence Assays. *When and*

how to use assays for recent infection to estimate HIV incidence at a population level. Geneva (Switzerland: World Health Organization, Department of HIV/AIDS, 2011.

- 10 Duong YT, Qiu M, De AK, et al. Detection of recent HIV-1 infection using a new limiting-antigen avidity assay: potential for HIV-1 incidence estimates and avidity maturation studies. *PLoS One* 2012;7:e33328.
- 11 Kassanjee R, Pilcher CD, Keating SM, et al. Independent assessment of candidate HIV incidence assays on specimens in the CEPHIA Repository. AIDS 2014;28:2439–49.
- 12 Barin F, Meyer L, Lancar R, et al. Development and validation of an immunoassay for identification of recent human immunodeficiency virus type 1 infections and its use on dried serum spots. J Clin Microbiol 2005;43:4441–7.
- 13 Kassanjee R, Pilcher CD, Busch MP. Consortium for the evaluation and performance of HIV incidence assays (CEPHIA). viral load criteria and threshold optimization to improve HIV incidence assay characteristics. AIDS 2016;30:2361–71.
- 14 World Health Organization (WHO). UNAIDS/WHO Working group on global HIV/AIDS and STI surveillance: when and how to use assays for recent infection to estimate HIV incidence at a population level, 2011.
- 15 Agyemang EA, Kim AA, Dobbs T, et al. Performance of a novel rapid test for recent HIV infection among newly-diagnosed pregnant adolescent girls and young women in four high-HIV-prevalence districts-Malawi, 2017-2018. PLoS One 2022;17:e0262071.
- 16 Kim AA, Behel S, Northbrook S, *et al.* Tracking with recency assays to control the epidemic: real-time HIV surveillance and public health response. *AIDS* 2019;33:1527–9.
- 17 Integrated HIV Program Report October-December. Lilongwe (Malawi): Ministry of health, government of Malawi, 2018.
- 18 Malawi comprehensive HIV testing and counselling training. *Lilongwe* (*Malawi*): *Ministry of health, government of Malawi*, 2013.
- 19 Asanté<sup>™</sup> HIV-1 Rapid Recency® Assay [Internet]. Beaverton (Oregon, US): Sedia biosciences Corporation, 2021. https://www. sediabio.com/asante-hiv-1-rapid-recency/
- 20 Yufenyuy EL, Detorio M, Dobbs T, et al. Performance evaluation of the Asante rapid Recency assay for verification of HIV diagnosis and detection of recent HIV-1 infections: implications for epidemic control. PLOS Glob Public Health 2022;2:e0000316.
- 21 Tang N, Pahalawatta V, Frank A, et al. Hiv-1 viral load measurement in venous blood and fingerprick blood using Abbott RealTime HIV-1 DBS assay. J Clin Virol 2017;92:56–61.
- 22 Hartung C, Lerer A, Anokwa Y. Open data kit: tools to build information services for developing regions. In: *Proceedings of* the 4th ACM/IEEE International Conference on Information and Communication Technologies and Development (ICTD '10. 18th ed. New York, NY, USA: Association for Computing Machinery, 2010: 1–12.
- 23 Colin Cameron A, Miller DL. A Practitioner's Guide to Cluster-Robust Inference. *J Hum Resour* 2015;50:317–72.
- 24 Welty S, Motoku J, Muriithi C, et al. Brief report: recent HIV infection surveillance in routine HIV testing in Nairobi, Kenya: a feasibility study. J Acquir Immune Defic Syndr 2020;84:5–9.
- 25 Rice BD, de Wit M, Welty S, et al. Can HIV recent infection surveillance help us better understand where primary prevention efforts should be targeted? results of three pilots integrating a recent infection testing algorithm into routine programme activities in Kenya and Zimbabwe. J Int AIDS Soc. In Press 2020;23 Suppl 3:e25513.
- 26 Ouk V, Soch K, Ngauv B. Recent HIV infection surveillance and partner testing outcomes in Cambodia from March 2020 through September 2021, In suggession.
- 27 Abate S, Poirot E, Steiner C. Correlates of recent infection among persons newly diagnosed with HIV in Nigeria. *Paper presented at: INTEREST 2022* 2022.
- 28 Poirot E, Reid G, Irabona JC. Trends in recent HIV-1 infection among new diagnoses in Eswatini and Rwanda, 2019–2021, 2022.
- 29 Saito S. Detecting recent infections in outpatient departments: A multi-country analysis.. In: *Trace: tracking with Recency assays to control the epidemic*, 2022. https://trace-recency.org/wp-content/uploads/2022/03/CROI-2022-Slides-SaitoPOC2320022.pdf
- 30 Ministry of Health, Malawi.. Estimating HIV Incidence and Detecting Recent Infection among Pregnant Adolescent Girls and Young Women in Malawi, 2017-18: Final Report.. In: *Lilongwe (Malawi): Ministry of health*, 2019..
- 31 Bernasconi D, Tavoschi L, Regine V, *et al.* Identification of recent HIV infections and of factors associated with virus acquisition among pregnant women in 2004 and 2006 in Swaziland. *J Clin Virol* 2010;48:180–3.
- 32 Mermin J, Musinguzi J, Opio A, *et al*. Risk factors for recent HIV infection in Uganda. *JAMA* 2008;300:540.

9

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- 33 Staveteig S, Wang S, Head SK. *Demographic patterns of HIV testing uptake in sub-Saharan Africa*. Calverton, MD: ICF International, 2013.
- 34 Yeatman S, Chamberlin S, Dovel K. Women's (health) work: a population-based, cross-sectional study of gender differences in time spent seeking health care in Malawi. *PLoS One* 2018;13:e0209586.
- 35 Malawi Population-based HIV Impact Assessment (MPHIA) 2015-16: first report. *Lilongwe (Malawi): Ministry of health, government of Malawi*, 2017.
- 36 National Statistical Office (NSO) [Malawi] and ICF. Malawi demographic and health survey 2015-16. Zomba, Malawi, and Rockville, Maryland, USA. NSO and ICF, 2017.
- 37 Choko AT, Fielding K, Stallard N, *et al.* Investigating interventions to increase uptake of HIV testing and linkage into care or prevention for male partners of pregnant women in antenatal clinics in Blantyre, Malawi: study protocol for a cluster randomised trial. *Trials* 2017;18:349.
- 38 Hensen B, Taoka S, Lewis JJ, et al. Systematic review of strategies to increase men's HIV-testing in sub-Saharan Africa. AIDS 2014;28:2133–45.
- 39 Maheu-Giroux M, Jahn A, Kalua T, et al. Hiv surveillance based on routine testing data from antenatal clinics in Malawi (2011-2018): measuring and adjusting for bias from imperfect testing coverage. AIDS 2019;33 Suppl 3:S295–302.
- 40 Chagomerana MB, Edwards JK, Zalla LC, *et al.* Timing of HIV testing among pregnant and breastfeeding women and risk of mother-tochild HIV transmission in Malawi: a sampling-based cohort study. *J Int AIDS Soc* 2021;24:e25687.
- 41 Ministry of Health, Malawi.. Integrated HIV, Syphilis, and Viral Hepatitis Testing Guidelines. In: *Lilongwe: Ministry of health*. 1st ed, 2022.
- 42 De Anda S, Njoroge A, Njuguna I, et al. Predictors of first-time and repeat HIV testing among HIV-positive individuals in Kenya. J Acquir Immune Defic Syndr 2020;85:399–407.
- 43 Girardi E, Sabin CA, Monforte Antonella D'Arminio. Late diagnosis of HIV infection: epidemiological features, consequences and strategies to encourage earlier testing. *J Acquir Immune Defic Syndr* 2007;46 Suppl 1:S3–8.
- 44 Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 2011;365:493–505.

- 45 Hocking JS, Rodger AJ, Rhodes DG, *et al.* Late presentation of HIV infection associated with prolonged survival following AIDS diagnosis--characteristics of individuals. *Int J STD AIDS* 2000;11:503–8.
- 46 Fleishman JA, Yehia BR, Moore RD, *et al.* The economic burden of late entry into medical care for patients with HIV infection. *Med Care* 2010;48:1071–9.
- 47 Cooney N, Hiransuthikul N, Lertmaharit S. Hiv in young people: characteristics and predictors for late diagnosis of HIV. *AIDS Care* 2015;27:561–9.
- 48 Ministry of Health. *Malawi population-based HIV impact assessment*. Lilongwe, Malawi: MOH, 2018.
- 49 Giguere K, Eaton JW, Marsh K, et al. Trends in knowledge of HIV status and efficiency of HIV testing services in sub-Saharan Africa, 2000-20: a modelling study using survey and HIV testing programme data. Lancet HIV 2021;8:e284–93.
- 50 UNAIDS/WHO. *Hiv testing services Dashboard*. Geneva (Switzerland: World Health Organization, Department of HIV/AIDS, 2021. https:// whohts.web.app/MWI
- 51 Pilgrim N, Mwapasa V, Chipeta E. Project SOAR Final Report. In: Evidence to support HIV prevention for adolescent girls and young women (AGYW) & their male partners: results from Malawi DREAMS studies with AGYW, male partners of AGYW, men living with HIV, and program implementing partners. USAID | Project SOAR: Washington, DC, 2020.
- 52 Harrison A, Colvin CJ, Kuo C, *et al*. Sustained high HIV incidence in young women in southern Africa: social, behavioral, and structural factors and emerging intervention approaches. *Curr HIV/AIDS Rep* 2015;12:207–15.
- 53 Inwani I, Chhun N, Agot K, *et al.* Preferred HIV testing modalities among adolescent girls and young women in Kenya. *J Adolesc Health* 2021;68:497–507.
- 54 Telford CT, Tessema Z, Msukwa M, et al. Geospatial Transmission Hotspots of Recent HIV Infection - Malawi, October 2019-March 2020. MMWR Morb Mortal Wkly Rep 2022;71:329–34.
- 55 Recency Response Tools [Internet]. *Trace: tracking with Recency assays to control the epidemic*, 2020. https://trace-recency.org/ response-tools/
- 56 Wand H, Ramjee G. Targeting the hotspots: investigating spatial and demographic variations in HIV infection in small communities in South Africa. *J Int AIDS Soc* 2010;13:41.