Adherence to Antiretroviral Therapy and Associated Factors Among People Living With HIV Following the Introduction of Dolutegravir Based Regimens in Dar es Salaam, Tanzania

Mary Spicar Kilapilo, BPharm[1],
Raphael Zozimus Sangeda, BPharm, Mpharm, Msc, PhD[1] ⓘD,
George M Bwire, Bsc, Msc[1],
Godfrey Leonard Sambayi, BPharm, MPharm[2],
Idda Hubert Mosha, BA, MA, PhD[3], and Japhet Killewo, MD, MSc, PhD[4]

Abstract

Background: Adherence to antiretroviral therapy (ART) is the key determinant of virological suppression in people living with HIV (PLHIV). This study reports factors associated with non-adherence among PLHIV one year after introducing dolutegravir (DTG) based regimens in Tanzania. **Methods:** A hospital-based cross-sectional study was conducted in two health facilities in Dar es Salaam, Tanzania, in 2020. **Results:** A total of 406 PLHIV were recruited, where the majority (73.4%) were females, with 94.6% of patients being on DTG based regimens. Factors such as refill interval and sharing of antiretrovirals had significant effects on adherence. Multivariate analysis found that patients attending care and treatment center (CTC) at Temeke Regional Referral Hospital (RRH) were 4.3 times more likely to have non-adherence compared to those attending Amana RRH (aOR [adjusted odds ratio] 4.3, 95% CI [confidence interval]: 2.38 − 7.91, p-value < 0.0001). **Conclusions:** Sustainable adherence counseling is warranted to overcome non-adherence to ART.

Background

A non-adherence to antiretroviral therapy (ART) was revealed as an important factor contributing to virological failure[1] and the development of HIV drug resistance (HIVDR).[2] A study on the association between adherence to ART and HIVDR found that ART adherence of 70%–89% was strongly associated with the viral rebound with clinically significant HIVDR. It was also observed that participants who developed resistance had fewer refill visits than those who did not develop resistance had more visits to the refill centers.[3,4] Additionally, a transdisciplinary study on drivers for HIVDR identified various factors, of which adherence was among the leading factors.[5,6]

Adherence to ART not only reduces HIV-related deaths but also reduces incidence rates of HIV transmission.[1] Unlike developed

countries,[7] lower- and middle-income countries (LMICs), including Tanzania, have been struggling to achieve 90-90-90 goal;

[1] Department of Pharmaceutical Microbiology, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania
[2] Department of Pharmacognosy, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania
[3] Department of Behavioural Sciences, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania
[4] Department of Biostatistics and Epidemiology, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania

Corresponding Author:
Raphael Zozimus Sangeda, Department of Pharmaceutical Microbiology,
P. O. Box 65013, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania.
Email: sangeda@gmail.com

90% of people living with HIV (PLHIV) know their HIV status; 90% of PLHIV with diagnosed HIV infection receive sustained ART, and 90% of PLHIV on treatment with suppressed viral loads.[8] However, Tanzania has made considerable milestones towards achieving the Joint United Nations Programme of HIV/AIDS (UNAIDS) 90-90-90 targets. By 2018, 93.6% of adults aware of their HIV-positive status are on ART and 87.0% of adults on ART have suppressed viral loads.[9] To make this sustainable, ART's quality, safety, and efficacy are necessary to achieve the UNAIDS goal to end the HIV epidemic by 2030.[10]

In 2019, Tanzania introduced a dolutegravir (DTG) based regimen as the preferred first-line for managing HIV among adults.[11] DTG is an antiretroviral that belongs to the class of integrase strand transfer inhibitors[12] and is intended to treat HIV-1 infection.[13] However, tenofovir, lamivudine, and efavirenz regimens will remain an alternative to those who will not tolerate DTG and women of childbearing age, including those using effective long-term contraception.[11]

In two historic DTG trials named ADVANCE and NAMSAL performed in Sub-Saharan Africa, the role of non-adherence was evidently the contributing factor to delay virological suppression of HIV-1. However, HIVDR to DTG was not evident among ART-naive individuals in these trials.[14] The impact of adherence on virological outcome and HIVDR following the introduction of DTG based regimens in Tanzania has not been conducted. Therefore, this study assessed patients' adherence to ART and evaluated factors contributing to non-adherence to ART among PLHIV in Dar es Salaam, Tanzania.

Methods

Study Design and Area

This hospital-based cross-sectional study was conducted in Temeke Regional Referral Hospital (RRH) and Amana RRH at the Care and Treatment Clinic (CTC) in Dar es Salaam, Tanzania. This survey was conducted for 31 days (between July and August 2020). The study aimed to investigate the factors contributing to non-adherence after the rollout of DTG based regimen rollout. Dar es Salaam is the largest city, business and the former capital of Tanzania, with an approximated population of more than five million people (almost 10% of the country population)[15] and projected to be seven million by 2021. In 2017, the Tanzania HIV impact survey found that more than 1.7 million people aged 15 years and older were living with HIV, while 4.7% of people living with HV live in the Dar es Salaam region.[9] Temeke RRH has a bed capacity of 304, while Amana RRH has a bed capacity of 250. These two hospitals were randomly selected out of three regional referral hospitals (tertiary hospitals) found in the Dar es Salaam region.[16]

Study Population and Sampling

A total of 406 PLHIV aged 18 years and above and on ART for ≥ 6months were included in this study to Temeke and Amana RRHs. This number was obtained using a cross-sectional study formula[17] and the assumed prevalence from the previous study.[18] Amana RRH CTC provides medical care to 8800 PLHIV, while Temeke RRH CTC provides medical care to 6500 PLHIV. A systematic approach was used during the recruitment of study participants. This was done by obtaining a sampling interval "n" (total number of patients on CTC divided by 200 and by the number of study days). Then a patient was recruited after every "n" interval by selecting the nth patient.

Data Collection Tool

After a comprehensive literature review, a semi-structured questionnaire was prepared. The questionnaire contained open and close-ended questions.[18–20] The English questionnaire was constructed, translated to Kiswahili (local language). The Kiswahili version was uploaded on REDCap (Research Electronic Data Capture). REDCap is an electronic data capture tool hosted at Muhimbili University of Health and Allied Sciences (MUHAS).[21,22] The questionnaire was tested on a pilot population of 30 patients (15 from each CTC). The necessary changes were made to create the updated version of the questionnaire.

The updated version of the Kiswahili questionnaire was then used to collect information on patients' demographics and factors related to pharmacy refill and adherence to ART. After translating to English, data was collected using tablets and coded in the REDcap.

Data Management and Analysis

REDCap data were downloaded, cleaned in Microsoft Excel (to remove incomplete records), then exported to statistical package for social sciences (SPSS software version 25, Chicago Inc., USA) for analysis. Descriptive statistics were summarized using frequencies and percentages. Self-reported adherence was estimated using a validated questionnaire from the Swiss HIV Cohort Study Adherence Questionnaire (SHCS-AQ).[18,23] PLHIV on ART who missed at least two consecutive doses per month were regarded to have poor adherence, while those who had not missed any doses per month were categorized under good adherence.[11] Association between categorical variables was analyzed using the Chi-square test. Factors associated with adherence were determined using a binary logistic regression test. All factors except with p-value <0.2 in univariate qualified for multivariate analysis as described elsewhere.[24] The p-value < 0.05 was considered statistically significant.

Ethical Approval and Informed Consent

Temeke RRH and Amana RRH permitted the study to be conducted on their respective premises. Ethical clearance was obtained from the MUHAS ethical review committee (Reference No. DA.C25/111/10/02/2021). All participants provided written informed consent prior to enrollment in the study. The consent includes information, the description of the study, data privacy/ confidentially and handling. Non-adherent patients were counseled on medication adherence. Due to the COVID-19 pandemic, researchers and participants were

required and reminded to observe all preventive measures such as regularly washing hands with soaps, physical distance (at least 2m apart) and cover of the faces with masks.

Results

Participants' Socio-Demographic Characteristics

A total of 406 PLHIV were recruited, 205 PLHIV from Amana RRH, and 201 PLHIV were from Temeke RRH. The mean age (standard deviation) years of the participants was 42.41 (11.7) years, with the majority 202 (50%) having the age between 25–44 years. Of the 406 participants, 298 (73.4%) were females, whereas the majority of the respondents, 151 (38.2%), had used ART for 7 to 12 years. Most of the participants, 382 (94.6%), were on a DTG based regimen, with the majority of PLHIV, 373 (91.6%) being on the tenofovir + lamivudine + DTG (TLD) regimen. Married participants were the largest group, 171 (42%). The majority, 215 (52.8%), had a refill interval of three months, whereas 204 (56.8%), where the general cost for a single hospital visit was less than 2000 TZS (equivalent to 0.865 USD) for the majority of the participants, 283(69.9%). Most of the participants, 137 (33.8%), responded that the waiting time at CTC was between 30min and one hour, whereas 188 (46.3%) of PLHIV used 30 min to 1 hour to reach CTC from their homes (Table 1).

Pharmacy Refill and Self-Reported Adherence

Of 406 PLHIV, 15% reported missing one or more doses of ARV per year, while the weekly self-reported adherence found almost 70 (17.3%) PLHIV missed one or more than one dose of ARV. The assessment of monthly adherence found that 286 (70.6%) did not skip any dose, while 16 (4.0%) missed more than three doses in a month (Table 2).

Pharmacy Refill and a Self-Reported non-Adherence

The majority of participants, 389 (95.8%), reported that they did not encounter out-of-stock for the past three years, while 376 (93.1%) of PLHIV reported that family roles did not affect medication adherence. Almost 52 (19.9%) of PLHIV recruited were on long-term medication other than ARV, whereas 161 (39%) experienced side effects while using ARV. Of 161 PLHIV who reported side effects, 14 (9.3%) discontinued taking ARV for some time. Most of the participants, 317 (78.1%),

Table 1. Participants Social Demographic Characteristics.

Variable	Category	Frequency (%)
Gender	Female	298 (73.2)
	Male	108 (26.5)
Age	18 – 24	33 (8.2)
	25 – 44	202 (50.0)
	45 – 54	108 (26.7)
	55 – 64	48 (11.9)
	≥ 65	13 (3.2)
Hospital facility	Amana RRH	205 (50.4)
	Temeke RRH	201 (49.4)
Start of ARV (years)	≤ 2	80 (20.3)
	3–6	103 (26.1)
	7–12	151 (38.2)
	≥ 13	61 (15.4)
Marital status	Married	171 (42.0)
	Single	106 (26.0)
	Divorced	79 (19.4)
	Widowed	46 (11.3)
On DTG based regimen	Yes	382 (94.6)
	No	22 (5.4)
Specific regimen	TLD	373 (91.6)
	*Others	33 (8.4)
Refill interval (months)	1	83 (20.4)
	2	7 (1.7)
	3	215 (52.8)
	6	101 (24.8)
Monthly income (TZS)	< 100,000	9 (2.5)
	100, 000–500,000	204 (56.8)
	> 500,000	146 (40.6)
Cost for a single hospital visit (TZS)	< 2000	283 (69.9)
	≥ 2000	87 (21.4)
	No cost	35 (8.6)
Waiting time at CTC (hours)	< 0.5	51 (12.6)
	0.5 - 1	137 (33.8)
	1.1 – 2	128 (31.6)
	> 2	89 (22)
Travelling time from home to CTC (hours)	< 0.5	105 (25.9)
	0.5 - 1	188 (46.3)
	1.1 - 2	91 (22.4)
	> 2	22 (5.3)

RRH: Regional Referral Hospital; TDF: Tenofovir; 3TC: Lamivudine; DTG: Dolutegravir; ABC: Abacavir; AZT: Zidovudine; FTC: Emtricitabine; ATV/r: Atazanavir/ ritonavir; TLD: TDF + 3TC + DTG.
*Others: **ABC + 3TC + DTG, TDF + 3TC + EFV, TDF + FTC + ATV/r, ABC + 3TC + ATV/r, AZT + 3TC + ATV/r, AZT + 3TC + DTG, TDF + FTC + DTG, TDF + FTC + EFV.**

Table 2. Pharmacy Refill and Self-Reported Adherence (N = 406).

Variable	Categories	Frequency (n)
Number of Refills Missed per Year.	1–2	59 (14.6)
	3–6	1 (0.2)
	> 6	3 (0.7)
	None	342 (84.4)
Number of Doses Missed per Week	1	42 (10.4)
	2	15 (3.7)
	3	4 (1.0)
	> 3	9 (2.2)
	None	334 (82.7)
Number of Doses Missed per Month	1	64 (15.8)
	2	30 (7.4)
	3	9 (2.2)
	> 3	16 (4.0)
	None	286 (70.6)

reported taking medication on time, while 50 (12.3%) reported forgetting to take medication. About 20% of PLHIV reported being affected (be minor to severely affected) by the COVID-19 pandemic in their refill and adherence. (Table 3).

Comparing Factors Associated with Adherence

Using Chi-square analysis, it was found that Temeke RRH had 92 (46%) non-adhering patients, as compared to Amana RRH, which had 27 (13.2%), p-value < 0.0001. PLWHIV who did not share medication 218 (76.8%) were more adherent (p-value < 0.01) as compared to their counterpart. Response after disclosing the status also had a significant effect were

Table 3. Responses to Questions on ART Pharmacy Refill and non-Adherence.

Variable	Categories	Frequency (%)
Adherence affected by family duties	No	376 (92.3)
	Yes	27 (6.7)
Out of stock out at CTC in the past three years	None	389 (95.8)
	1–3	15 (3.7)
	4–8	2 (0.5)
Had chronic comorbidity	No	361 (89.4%)
	Yes	46 (10.6)
Long term medication other than ARV	No	323 (80.1)
	Yes	52 (19.9)
Did you experience any side effects?	No	245 (60.3)
	Yes	161 (39.7)
Response after experiencing side effects	Continued with their medication	137 (90.7)
	I stopped medication for some days	14 (9.3)
Effect of COVID-19 on refill and adherence?	Negligibly affected	326 (80.9)
	Minorly affected	62 (15.4)
	Moderately affected	12 (3.0)
	Severely affected	3 (0.7)
Reason for non-adherence	They take their medication on time	317 (78.1)
	Forgetting to take medication	50 (12.3)
	Traveling away from home	37 (9.1)
	Scheduling conflicts with work	35 (8.6)
	Lack of regular food and water	8 (2.0)
	Misplacing the medication	4 (1.0)
	No money to go to refills	2 (0.5)
Checking ARV medication expire date	They do check	225 (55.6)
	They do not regularly check	119 (29.4)
	They do not know how to check	61 (15.1)
Used expired medication	Yes	16 (3.9)
	No	259 (63.8)
	They do not know	131 (32.3)

those who were encouraged to take medication 251 (71.5%) were adherent (p-value < 0.05), those who reported taking their medication on time 235 (75%) were more adherent, p-value < 0.01 (Table 4).

Regression Analysis of Factors Associated with non-Adherence

On univariate analysis, factors such as refill interval and sharing of antiretrovirals had significant effects on adherence. Multivariate analysis found that patients attending CTC at Temeke RRH were 4.3 times more likely to have non-adherence compared to those attending the clinic at Amana (aOR [adjusted odds ratio] 4.3, 95% CI [confidence interval]: 2.38 – 7.91, p-value < 0.0001) (Table 5).

Discussion

This study aimed to assess the adherence to ART and the associated factors among patients attending CTC at Regional Referral Hospitals in Dar es Salaam, region. The study was conducted one year after introducing the introduction of the DTG based regimen as the preferred first-line for managing HIV among adults in Tanzania.[11] DTG is preferred because of its high genetic barrier to resistance.[14] However, there was a need to understand how adherence and other demographic factors may impact the virological outcome in patients taking DTG in Tanzania.

Most of the respondents were females, which is close to the current demographics data of patients currently receiving HIV/ AIDS care and treatment in Tanzania.[9] Young adults (sexually active group) aged between 25 and 44 years were the most affected group by more than half of all studied PLHIV, reflecting globalized statistics that HIV highly affects young adults.[25] These findings were consistent with the study done in Botswana in 2010 by Do et al.[26] Factors such as early marriage among females and women having older partners than men were associated with higher susceptibility of women to HIV infection than males.[27]

The majority of the participants took their medication on time and had no reasons for missing their medications. These results are consistent with other studies done in Dar es Salaam, Tanzania, where most reported taking medicines on time, while about one-third reported simply forgetting.[28]

Regarding failure to refill due to stock out at CTC, the majority of participants stated that none of the days had a stock out. This result contrasts with another study done in DRC in 2018, which indicated that more than half of ART stockout cases and patients did not receive any medicines. In some cases, patients were switched to different ART formulations or regimens.[29] The small sample size used in the Congolese study and differences in the health system could contribute to these differences.

The majority reported that they did not experience any side effects with ART medications. In contrast, more than one-third experienced side effects, of whom the majority reported

Table 4. Comparing Factors Associated with Non-Adherence (N = 406).

Variable	Category	Total	Adherent N (%)	Non-adherent N (%)	P-value
Hospital facility	Amana RHH	205	178 (86.8)	27 (13.2)	< 0.0001
	Temeke RRH	200	108 (54)	92 (46)	
Sharing of the ARV	Do not share	284	218 (76.8)	66 (23.2)	< 0.0001
	Do share	119	66 (55.5)	53 (44.5)	
Response after disclosing the status	They encouraged me to take medication	351	251 (71.5)	100 (28.5)	0.014
	They supported me financially and socially	111	73 (65.8)	38 (34.2)	
	They stigmatized me	15	7 (46.7)	8 (53.3)	
	They left me to deal with it	12	5 (41.7)	7 (58.3)	
Reasons for non-adherence	They take their medication on time	317	235 (75)	79 (25)	< 0.0001
	Forgetting to take Medication	50	30 (60)	20 (40)	
	Traveling away from home	37	17 (46)	20 (54)	
	Scheduling conflicts with work	35	15 (43)	20 (57)	
	Lack of regular food and water	8	2 (25)	6 (75)	
	Misplacing the medication	4	1 (25)	3 (75)	
	No money to go to refills	2	0	2 (100)	

ARV: Antiretroviral; RRH: Regional Referral Hospital.

continuing with their medication when they experienced side effects. This is congruent with the study by Ammassari et al.[30] This is the area of concern to the Tanzanian policymakers, especially where the refilling intervals are one month for unstable patients and three months for stable patients. During a qualitative interview with PLHIV in Dar es Salaam, Tanzania (unpublished), they mentioned a need for patients to have health insurance cover. This will help patients have a close follow-up on their health status, including reporting side effects rather than waiting after 1or 3 months during the refill or clinic. However, most PLHIV are trained to continue with medication if severe adverse drug reaction occurs.[11] Additionally, they have to report the side effect to a health care worker to determine if the medicine has to be changed to another combination.[31]

PLHIV who did not share their ART medication were more adherent than those who shared their medication. This finding is in line with other studies done in Mozambique by Groh et al. 2011, which indicated that sharing medications with family members was a barrier to ART adherence success.[32]

Similarly, patients disclosing their HIV status were significantly encouraged to take medication and thus became adherent to ART. This result is consistent with another study done by Bemelmans M et al. 2014 in sub-Saharan Africa, which indicated that encouraging community-based peer support ensures that PLHIV adheres to their medication.[33]

Furthermore, hospital facility was also a significant factor where Amana RRH had more adherent participants than Temeke RRH. This result is similar to another study done in Kenya where the difference in how care and support to the patient affect the patient's adherence. Both patient and healthcare providers at CTC in Amana RRH reported having more intensive pre-and post-testing, treatment, and adherence counseling compared to Temeke RRH. The latter only provided routine adherence counseling compared to the former facility.[34]

Multivariate analysis showed a significant association between pharmacy refill and sharing of ART and non-adherence. Patients with three-month refill intervals were more likely to have non-adherence as compared to those who refill after every month. In Tanzania, stable patients (virological

Table 5. Univariate and Multivariate Regression Analysis of Factors with non-Adherence.

Variable	Category	Univariate analysis			Multivariate analysis		
		cOR	95%CI	P-value	aOR	95%CI	P-value
Hospital	Temeke RRH	5.62	3.44-9.18	< 0.0001	4.3	2.38-7.91	<0.0001
	Amana RRH	Ref					
Refill interval	One month	2.36	1.12-4.94	0.024	1.3	0.60-3.0	0.477
	Two month	1.02	0.11-9.16	0.983	0.31	0.03-2.92	0.305
	Three month	3.71	1.98-6.96	<0.0001	0.16	0.81-3.39	0.164
	Six month	Ref					
Sharing of ARV	No	0.38	0.24-0.60	<0.0001	0.78	0.46-1.34	0.369
	Yes	Ref					

Ref: reference category (non-adherence), cOR: crude odds ratio; aOR: adjusted odds ratio; CI: confidence interval, P values<0.05 are shown in bold, RRH: regional referral hospital.

suppression) refill their medications after every three months, while unstable patients (viral load rebound) refill their ART after each month.[11] This calls for measures such as a close follow-up, especially for stable patients, to keep using their ART appropriately even after suppressing their viral load to prevent virus rebound and HIVDR.[35,36] More education is also needed for patients who are willing to share their ART refills with family members to avoid the risk of incomplete viral suppression.

Study Limitations

Findings from this study may be limited to self-reported bias. Self-reported data had several potential sources of bias that include recall bias, social desirability and lie bias. However, bias was controlled through a comprehensive description of the study aim before enrolling the participant. Two different study settings were included to minimize the chance of site bias. However, a better approach would be to have multiple sites for comparability. Also, patients were requested to leave blank on the section(s) they do not remember rather than guessing the responses.

Conclusions

The majority of adults living with HIV currently use DTG based regimes as their first line for treatment of HIV. Self-reported non-adherence appeared to be influenced by both medical and behavioral factors. Factors such as refill time interval, care facility and sharing of antiretrovirals were associated with non-adherence to ART among people living with HIV in Dar es Salaam, Tanzania. Education provision on adherence should be sustainably provided to health care professionals, patients and the community.

Authors' Contributions

MK and RZS participated in conceptualization, design, data collection, analysis, and manuscript drafting. IHM & GS participated in study design and analysis. GB participated in data analysis and manuscript revisions. RS participated in conceptualization, study design, data analysis and manuscript revision. All authors have read and approved the final version of the manuscript.

Consent to Publish

Not applicable.

Availability of Data and Materials

Data sets used to draw a conclusion of this study are available from the corresponding author on reasonable request.

ORCID iD

Raphael Zozimus Sangeda https://orcid.org/0000-0002-6574-5308

References

1. Bulage L, Ssewanyana I, Nankabirwa V, et al. Factors associated with virological Non- suppression among HIV-positive patients on antiretroviral therapy in Uganda, August 2014 – July 2015. *BMC Infect Dis.* 2017;17(1):326. doi:10.1186/s12879-017-2428-3

2. Masikini P, Mpondo BCT. HIVdrug resistance mutations following poor adherence in HIV -infected patient: a case report. *Clin Case Reports.* 2015;3(6):353–356. doi:10.1002/ccr3.254

3. Sethi AK, Celentano DD, Gange SJ, Moore RD, Gallant JE. Association between adherence to antiretroviral therapy and human immunodeficiency virus drug resistance. *Clin Infect Dis.* 2003;37(8):1112–1118. doi:10.1086/378301

4. Sangeda RZ, Mosha F, Prosperi M, et al. Pharmacy refill adherence outperforms self-reported methods in predicting HIV therapy outcome in resource-limited settings. *BMC Public Health.* 2014;14(1):1035. doi:10.1186/1471-2458-14-1035

5. Herrmann J, Lushaba J, Michielsen L, et al. HIV-positive men as a key population for fighting HIVDR in Africa. *Transdiscipl Insights.* 2018;2(1):78–91. doi:10.11116/tdi2018.2.3

6. Kiekens A, Mosha IH, Zlatić L, et al. Factors associated with HIV drug resistance in Dar es Salaam, Tanzania: analysis of a complex adaptive system. *Pathogens.* 2021;10(12):1535. doi:10.3390/pathogens10121535

7. Lima VD, St-jean M, Rozada I, et al. Progress towards the United Nations 90-90-90 and 95-95-95 targets : the experience in British Columbia, Canada. *J Int AIDS Soc.* 2017;20(3):e25011. doi:10.1002/jia2.25011

8. Bain LE, Nkoke C, Noubiap JJN. UNAIDS 90–90–90 targets to end the AIDS epidemic by 2020 are not realistic: comment on "Can the UNAIDS 90–90–90 target be achieved? A systematic analysis of national HIV treatment cascades." *BMJ Glob Heal.* 2017;2(2):e000227. doi:10.1136/bmjgh-2016-000227

9. United Republic of Tanzania. Tanzania HIV Impact Survey (THIS) 2016-2017. Published 2018. Accessed January 12, 2022. https://phia.icap.columbia.edu/wp-content/uploads/2019/06/FINAL_THIS-2016-2017_Final-Report__06.21.19_for-web_TS.pdf.

10. Cooper V, Clatworthy J, Harding R, Whetham J. Measuring quality of life among people living with HIV: a systematic review of reviews. *Health Qual Life Outcomes.* 2017;15(1):220. doi:10.1186/s12955-017-0778-6

11. United Republic of Tanzania. National Guidelines for the management of HIV and AIDS in Tanzania. Published 2019. Accessed January 12, 2021. http://www.nacp.go.tz/download/national-guidelines-for-the-management-of-hiv-and-aids/.

12. Seatla KK, Avalos A, Moyo S, et al. Four-class drug-resistant HIV-1 subtype C in a treatment experienced individual on dolutegravir-based antiretroviral therapy in Botswana. *AIDS*. 2018;32(13):1899–1902. doi:10.1097/QAD.0000000000001920. Four-class

13. Rhyne DN, Byrd ES, Klibanov OM. Dolutegravir (tivicay) for HIV infection. *Nurse Pract*. 2014;39(6):11–15. doi:10.1097/01. NPR.0000444657.88872.7f

14. McCluskey SM, Pepperrell T, Hill A, Venter WDF, Gupta RK, Siedner MJ. Adherence, resistance, and viral suppression on dolutegravir in sub-saharan Africa: implications for the TLD era. *AIDS*. 2021;35(Supplement 2):S127–S135. doi:10.1097/QAD. 0000000000003082

15. National Bureau of Statistics. Report of 2012 Population and Housing census, The United Republic of Tanzania. Published 2013. Accessed January 12, 2022. https://www.nbs.go.tz/nbs/takwimu/census2012/Basic_Demographic_and_Socio-Economic_Profile_PopularVersion-KeyFindings_2012_PHC_EnglishVersion. pdf.

16. Ishijima H, Suzuki S, Masaule F, Mlay V, John R. Measuring hospital performances of regional referral hospitals in Tanzania. *J Hosp Adm*. 2021;10(2):1. doi:10.5430/jha.v10n2p1

17. Pourhoseingholi MA, Vahedi M, Rahimzadeh M. Sample size calculation in medical studies. *Gastroenterol Hepatol from bed to bench*. 2013;6(1):14–17.

18. Sangeda RZ, Mosha F, Aboud S, et al. Predictors of non adherence to antiretroviral therapy at an urban HIV care and treatment center in Tanzania. *Drug Healthc Patient Saf*. 2018;10:79–88. doi:10.2147/DHPS.S143178

19. Dehens J, de Hemptinne M, Galouchka M, et al. Exploring the value and acceptability of peer support in the process of improving adherence to HIV antiretroviral drugs in Tanzania. *Dar-es-Salaam. Transdiscipl Insights*. 2017;1(1):9–32. doi:10.11116/TDI2017.1.2

20. Mosha F, Ledwaba J, Ndugulile F, et al. Clinical and virological response to antiretroviral drugs among HIV patients on first-line treatment in Dar-es-salaam, Tanzania. *J Infect Dev Ctries*. 2014;8(7):845–852. doi:10.3855/jidc.3879

21. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: building an international community of software platform partners. *J Biomed Inform*. 2019;95:103208. doi:10.1016/j.jbi.2019. 103208

22. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377–381. doi:10.1016/j.jbi.2008.08.010

23. Deschamps AE, De Geest S, Vandamme A-M, Bobbaers H, Peetermans WE, Van WE. Diagnostic value of different adherence measures using electronic monitoring and virologic failure as reference standards. *AIDS Patient Care STDS*. 2008;22(9):735–743. doi:10.1089/apc.2007.0229

24. Kilipamwambu A, Bwire GM, Myemba DT, Njiro BJ, Majigo M V. WHO/INRUD core prescribing indicators and antibiotic utilization patterns among primary health care facilities in ilala district. *Tanzania. JAC-Antimicrobial Resist*. 2021;3(2):1–7. doi:10.1093/jacamr/dlab049

25. UN Joint Programme on HIV/AIDS (UNAIDS). Global HIV statistics. Published 2020. Accessed January 12, 2022. https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf.

26. Do NT, Phiri K, Bussmann H, et al. Psychosocial factors affecting medication adherence among HIV-1 infected adults receiving combination antiretroviral therapy (cART) in Botswana. *AIDS Res Hum Retroviruses*. 2010;26(6):685–691. doi:10.1089/aid. 2009.0222

27. Glynn JR, Caraël M, Auvert B, et al. Why do young women have a much higher prevalence of HIV than young men? A study in Kisumu, Kenya and Ndola, Zambia. *AIDS*. 2001;15(Suppl 4): S51–S60. doi:10.1097/00002030-200108004-00006

28. Kiekens A, Dehens J, de Hemptinne M, et al. HIV-related Peer support in Dar es Salaam: a pilot questionnaire inquiry. *Transdiscipl Insights*. 2019;3(1):1–18. doi:10.11116/TDI2019.3.1

29. Gils T, Bossard C, Verdonck K, et al. Stockouts of HIV commodities in public health facilities in Kinshasa: barriers to end HIV. Bochenek T, ed. *PLoS One*. 2018;13(1):e0191294. doi:10.1371/journal.pone.0191294

30. Ammassari A, Murri R, Pezzotti P, et al. Self-reported symptoms and medication side effects influence adherence to highly active antiretroviral therapy in persons with HIV infection. *J Acquir Immune Defic Syndr*. 2001;28(5):445–449. doi:10.1097/00042560-200112150-00006

31. USAID. Understanding and Challenging HIV Stigma toward Entertainment Workers. Published 2007. Accessed August 19, 2021. https://www.icrw.org/wp-content/uploads/2016/10/Understanding-and-Challenging-HIV-Stigma-toward-Entertainment-Workers-Toolkit-for-Action.pdf.

32. Groh K, Audet CM, Baptista A, et al. Barriers to antiretroviral therapy adherence in rural Mozambique. *BMC Public Health*. 2011;11:650. doi:10.1186/1471-2458-11-650

33. Bemelmans M, Baert S, Goemaere E, et al. Community-supported models of care for people on HIV treatment in sub-Saharan Africa. *Trop Med Int Health*. 2014;19(8):968–977. doi:10.1111/tmi. 12332

34. Talam NC, Gatongi P, Rotich J, Kimaiyo S. Factors affecting antiretroviral drug adherence among HIV/AIDS adult patients attending HIV/AIDS clinic at Moi teaching and referral hospital, eldoret, Kenya. *East Afr J Public Health*. 2008;5(2):74–78.

35. Been SK, Yildiz E, Nieuwkerk PT, Pogány K, van de Vijver DAMC, Verbon A. Self-reported adherence and pharmacy refill adherence are both predictive for an undetectable viral load among HIV-infected migrants receiving cART. Ceccherini-silberstein F, ed. *PLoS One*. 2017;12(11):e0186912. doi:10.1371/journal.pone.0186912

36. Sangeda RZ, Gómes P, Rhee S-Y, et al. Development of HIV drug resistance in a cohort of adults on first-line antiretroviral therapy in Tanzania during the stavudine Era. *Microbiol Res (Pavia*. 2021;12[4]:847–861. doi:10.3390/microbiolres12040062

List of Abbreviations

3TC	Lamivudine
ABC	Abacavir

ARV	Antiretroviral	FTC	Emtricitabine
AZT	Zidovudine	PLHIV	People living with HIV
COVID-19	Coronavirus disease – 2019	RRH	Referral regional hospital
CTC	Care and treatment Center	TDF	Tenofovir
DTG	Dolutegravir	TLD	TDF + 3TC + DTG