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RESEARCH ARTICLE

REVISED **HIV treatment and monitoring patterns in routine practice: a multi-country retrospective chart review of patient care [version 3; referees: 1 approved, 2 approved with reservations]**

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Abstract

Background: A study of patient records in four HIV clinics in three sub-Saharan African countries examined routine clinical care patterns and variations.
Methods: Clinic characteristics were described, and patient data extracted from a sample of medical records. Data on treatment, CD4 count and viral load (VL) were obtained for the last visit in the records, dates mainly between 2015 and 2017, patient demographic data were obtained from the first clinic visit.
Results: Four clinics, two in Nigeria, one in Zambia and one in Uganda, all public facilities, using national HIV treatment guidelines were included. Numbers of patients and health professionals varied, with some variation in stated frequency of testing for CD4 count and VL. Clinical guidelines were available in each clinic, and most drugs were available free to patients. The proportion of patients with a CD4 count in the records varied from 84 to 100 percent, the latest median count varied from 269 to 593 between clinics. 35% had a record of a VL test, varying from 1% to 63% of patients. Lamivudine (3TC) was recorded for more than 90% of patients in each clinic, and although there was variation between clinics in the choice of antiretroviral therapy (ART), the majority were on first line drugs consistent with guidelines. Only about 2% of the patients were on second-line ARTs. In two clinics, 100% and 99% of patients were prescribed co-trimoxazole, compared with 7% and no patients in the two other clinics.
Conclusions: The wide variation in available clinic health work force, levels and frequency of CD4 counts, and VL assessment and treatment indicate sub-optimal adherence to current guidelines in routine clinical care. There is

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room for further work to understand the reasons for this variation, and to standardise record keeping and routine care of HIV positive patients.

Keywords

HIV, quality of care, variation, Public Health

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REVISED   **Amendments from Version 2**

This revision has specified the research questions in the Methods section which now contains information on the selection of study centres and the measurement of study factors. The Discussion section now also mentions information on what the study adds to the literature, and we have mentioned the missing data and sample size considerations in the study limitations paragraph.

See referee reports

Introduction

In addition to choice of appropriate drugs, best practice management of patients with HIV requires monitoring response to treatment and disease progression. This includes tracking clinical immunological, and virological data on patients at diagnosis and on follow-up. There is a rich literature guiding HIV treatment, and guidelines are developed and updated regularly as new evidence comes to light[1–5] (see http://www.who.int/hiv/pub/guidelines/en/ for an historic list of guidelines produced by the World Health Organisation). The implementation of standardized protocols for treatment and investigations may vary in resource constrained countries, with differences in resources available for such services. For example, the current guidelines for antiretroviral therapy (ART) requires all patients on ART to have viral load test at six months and 12 months[5], implementation might vary based on availability of resources to support viral load testing. While a number of reports of current treatment and testing practice are available from resource-limited settings, these are mainly in the context of patients enrolled in research centres or in research studies[6–8]. Such settings often have substantially more resources than routine clinical practices, and as such practice patterns may differ from routine practice, where issues such as clinic and patient resources or drug stock-outs can affect care. This study was designed to explore variation in the evaluation, treatment, care and follow-up among patients diagnosed with HIV in routine care settings in low- to middle-income countries.

Methods

Interest in participating in this study was sought among the Masters of Public Health Alumni of Peoples-uni[9]. There was no prior determination of the numbers of centres required or their geographical setting. A protocol was developed by those who responded (Supplementary File 1), which included the Research questions as follows: 1. Among a group of patients diagnosed with HIV by a health care facility newly diagnosed between 2 and 3 years previously, what proportion have standards of care in terms of the tests and treatments they receive and follow up to 2 years after diagnosis documented in their records? 2. Among the health care facilities in which the above patients are cared, what treatment, testing and referral facilities are available? 3. What is the extent of the variation in the above measures between facilities and countries, as well as in the availability of appropriate evidence based practice guidelines? A retrospective patient cohort was created via standardized record review, and clinic characteristics determined through an online survey form.

A data collection instrument was developed, based on previous research and publications and management guidelines[1–5]. A spreadsheet was created with coding instructions (Supplementary File 2). In addition, data on the characteristics of the setting for each facility were collected in early 2017 by each investigator in consultation with local clinic staff, and entered onto an online survey form (Supplementary File 3). This included country and city, hospital or other healthcare facility, number of patients seen, and what diagnostic, treatment, referral and follow-up facilities are available. Clinic and patient data were de-identified to maintain confidentiality. Four clinics from three countries in sub-Saharan Africa chose to participate in the study.

For clinic BA, a public hospital clinic in northern Nigeria, patients were selected in sequence of attendance as new patients, starting January 1, 2013 for whom records were also available over the next two years. Patient demographics were those obtained at the first visit, and CD4 count and ART treatments were recorded at each visit, with analysis relating to data recorded at the most recent visit.

For clinic EV, a public hospital clinic also in Nigeria, all existing patients were re-tested with an ELISA method in 2013/14, and patients were randomly selected for this study among those who tested positive at that time. CD4 count and treatments recorded were those at the latest visit, and patient demographics were those in the records from their first visit.

For clinic MW, a public community-based clinic in Zambia, patients were randomly selected from those present on the patient registry in 2015/16. At that time, patients were reviewed for the need to start on highly active antiretroviral therapy (HAART) based on CD4 count, and the ART regime recorded was that started as a result of that review at that time. Data on patient demographics were those present in the records, often this would be prior to the date of entry to this study.

For clinic AM, a public hospital based clinic in Uganda, the sampling frame was the register of all clients on active ART, and every third patient file was retrieved from files ordered according to clinic appointment date. The CD4 counts and ART regimes recorded were for the most recent measures in the records, and patient demographics were those in the records from their first visit.

Measurement of study factors

Data on individual patients were extracted from medical records, including age, gender, and baseline clinical data at diagnosis and follow-up. Clinical information included clinical, immunological and virological information on patients at diagnosis and on follow-up, prescription of ART and other drug choices. Potentially important co-infections and/or co-morbidities, identified from the literature, were coded as indicated in Supplementary File 2.

Measurement of outcome factors

Details of the tests ordered and their results, and treatments ordered were extracted from medical records. Individual patients were not contacted. Data were obtained from the records, and no attempt was made to validate the information. Missing data were recorded as missing, and not explored further.

A pilot study tested the feasibility of the data collection and the method of recording on to a spreadsheet. Data were collected by a research assistant in each setting, using the spreadsheet, from examination of individual records.

Ethics requirements
As a retrospective patient records study, consent was not requested from individual patients. Ethics approval was sought and obtained in each setting from the appropriate authority (see Ethical approval and consent section). Considerable care was taken not to reveal the identity of any individual and all data were de-identified. The spreadsheet for the recording of data only had an identification number, and the key to the identity of each patient was kept separately to maintain confidentiality. To further this, the clinics names and exact locations have been removed.

Sample size considerations
Each centre was asked to obtain information from at least 100 patients.

Data analysis
Descriptive statistics were used to characterise the study population. Data distributions were assessed, checking for skewness and kurtosis. Data summary statistics were generated. Categorical variables were summarized using proportions while continuous variables were summarized using medians and interquartile ranges. Due to differences in data extraction across sites, no statistical analyses comparing across sites was conducted. All analyses were conducted in Stata 14.1 (StataCorp, College Station, X) and R version 3.3.0 (The R Foundation for Statistical Computing).

Results
Ten alumni expressed interest in participating, three centres were able to pilot the data collection instrument and four centres in three countries participated in the data collection for the study. Overall, data were abstracted for 600 patients.

Table 1 shows the characteristics of the 4 clinics. The number of patients seen per month varied from 500 to 4200, and the number of doctors, nurses, and allied health professionals available at the clinics varied from 1 to 50, 10 to 65, and 6 to 45 respectively. There was some variation in the stated frequency of testing for CD4 count (either every three or six months) and for measurement of viral load. Each clinic had availability of clinical guidelines, and most drugs were available free of charge to patients. All clinics have access to ART and co-trimoxazole.

Table 2 shows the patient characteristics and test results. Age, gender and body mass index (BMI) were similar between clinics, with overall median age of 31 years, 62% were female and median BMI was 20. The proportion of patients with a CD4 count in the records varied from 84 to 100 percent, and the latest median count varied from 269 to 593 between the clinics. 209 (35%) had a record of a viral load test with 81% of then having a viral load of less than 50 copies/µL. Only 23 (19%) of 119 patients had records of AIDS defining illnesses. Figure 1 shows the variation in the distribution of the CD4 counts in each of the four clinics. As reported in the records, 58% of the latest CD4 counts were from 2016 or 2017, 27% from 2015, and the remaining 15% earlier; 95% of the viral load tests were from 2016 or 2017. There was no information about the timing of the reports being given to the patients themselves.

Table 1. Characteristics of the 4 participating clinics.

	Nigeria 1 [BA]	Nigeria 2 [EV]	Zambia [MW]	Uganda [AM]
Hospital or community	Hospital	Hospital	Community	Hospital
Public or private	Public	Public	Public	Public
HIV screening	Separate clinic	In clinic	In clinic	In clinic
Number of patients per month	500	4200	1200	1200
Number of doctors	6	50	1	2
Number of nurses	10	65	15	10
Number of allied health professionals	21	45	6	6
Access to HIV clinical guidelines	Yes, National, Electronic	Yes, National, Electronic and paper	Yes, National, Paper	Yes, National, Electronic and paper
CD4 count	Yes, each 3 months	Yes, each 3 months	In central lab, each 6 months	Yes, transported to lab, each 6 months
Viral load	Yes, each year	Yes, on referral, occasionally	Yes, on referral, when indicated	Yes, each 6 months for adolescents, yearly for adults
Drugs available free	All ART, Co-trimoxazole	All	All (IDV and ATV not free)	All
CD4 to start treatment	<350	<350	<350	<350
Referral	Yes, TB	Yes, complicated eg multi-drug resistance	Yes, if fail treatment	Yes, patients with other medical conditions

ART antiretroviral therapy

IDV indinavir

ATV atazanavir

Table 2. Patient characteristics.

	BA (N=100)	EV (N=100)	MW (N=100)	AM (N=300)	Overall (N=600)
Age (median, IQR)	32 (28 to 40)	28 (21 to 37)	33 (29 to 39)	31 (23.5 to 38)	31 (24 to 38)
Female sex	57 (57%)	62 (62%)	55 (55%)	197 (66%)	371 (62%)
BMI at presentation[1]	22.8 (19.5 to 31.2)	No data	19.5 (17.9 to 21.8)	20.0 (18.3 to 22.2)	20.0 (18.2 to 22.3)
Number of patients w/CD4 count data	100	94 (94%)	84 (84%)	279 (93%)	558 (93%)
Latest CD4 Count (median, IQR)	269 (177 to 461)	593 (390 to 880)	307 (169 to 471)	499 (321 to 691)	436 (267 to 471)
Proportion of patients w/viral load	14 (14%)	6 (6%)	1 (1%)	188 (63%)	209 (35%)
Latest viral load <50 50-9,999 10,000-99,999 >99,999	6 (43%) 1 (7%) 3 (21%) 4 (29%)	2 (33%) 4 (67%) 0 0	1 (100%) 0 0 0	160 (85%) 0 28 (15%) 0	169 (81%) 5 (2%) 31 (15%) 4 (2%)
AIDS defining illness	2/2(100%)	7/21(33%)	14/96(15%)	No data	23/119(19%)

[1]Missing BMI data: AM: 3/300, BA: 81/100, EV: 100/100, MW: 14/100 (total 198/600)
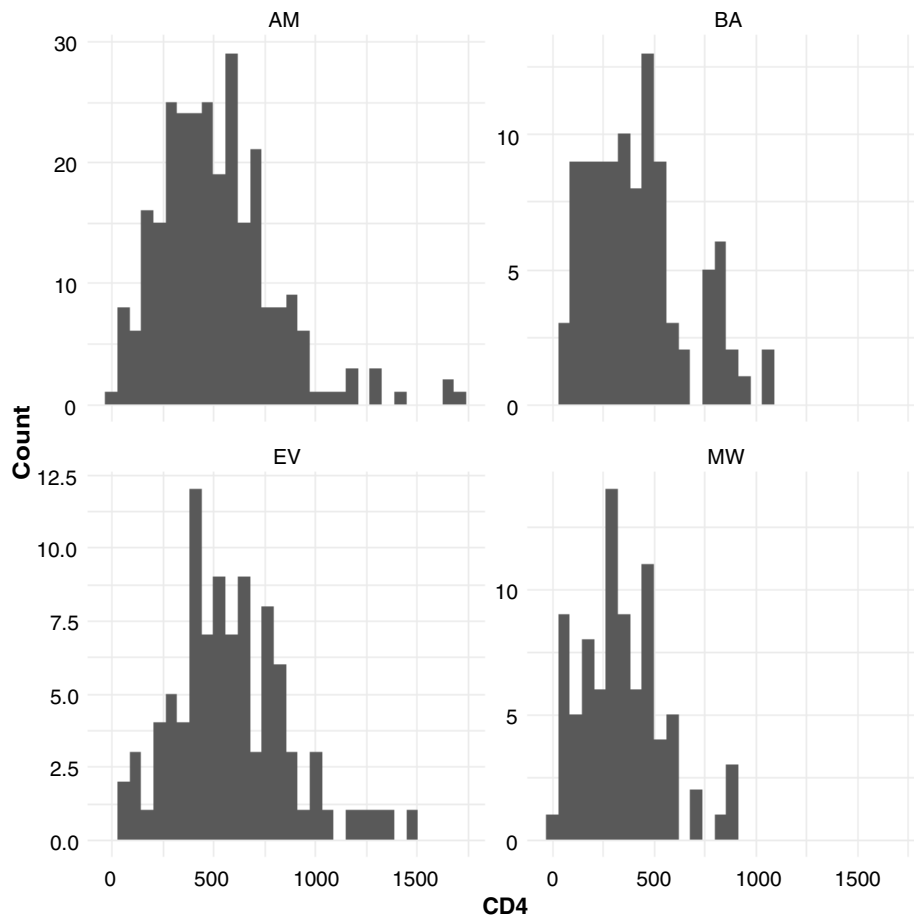

Figure 1. Distribution of CD4 counts in each of the four clinics.

Table 3 shows the treatment regimes. Lamivudine (3TC) was recorded for more than 90% of patients in each clinic, but otherwise there was considerable variation between clinics in the choice of ART. Tenofovir disoproxil fumarate (TDF) was prescribed for 317 (53.9%) of studied patients. Efavirenz (EFV) was prescribed for 326 (55%) of the patients, making combination of TDF/3TC/EFV the most common ART combination used by studied patients. In two clinics, 100% and 99% of patients were prescribed co-trimoxazole prophlaxis, compared with 7% and no patients in the two other clinics. There were 6 patients on lopinavir and 8 on atazanavir (second line treatment choices).

Dataset 1. De-identified data collected from clinical records used to create Tables 2 and 3 and Figure 1

http://dx.doi.org/10.5256/f1000research.15169.d206333

Scheme used to code the data is available as Supplementary File 2

Discussion
Data were collected according to the standardised data collection instrument (Supplementary File 2), with data on treatment regimes and CD4 counts relating to the latest information in the records (dates mainly between 2015 and 2017). While we initially planned to collect data on a cohort of patients enrolled two years before data collection in each clinic, this did not prove feasible and patients had presented to the clinics at variable times.

This study found modest documentation of clinical activities, with a wide variation in available clinic health work force, frequency of CD4 counts and levels and viral load assessment. The two clinics in Nigeria had markedly different caseloads. The centre with the high caseload is one of the oldest in Nigeria and provides incentives to this population of patients (free medical care to family members, distribution of food supplements and sometimes fares, etc.), Differences in case load may reflect population distribution and heterogeneity in HIV prevalence, or that patients may seek care far away from their base to avoid

stigmatization. Variation in case load can lead to differences in efficiency and quality of care, and potentially could have implications for care outcomes. However determining its impact on outcome would a require a properly powered longitudinal study.

While most patients had a CD4 count in the records, there was a wide spread of latest CD4 counts, with both within- and between-centre variation in the CD4 counts. Only one in three patients had a record of viral load at any time during the course of treatment, and most of these had an undetectable level (<50 copies/μL). Some of the absence of viral load might be poor record keeping, and the high proportion of undetectable results might reflect an absent rather than a low test result, and hence not an indicator of treatment success. Over the years the CD4 threshold for commencing ART had been lowered, as can be seen in Table 4, with the most current guideline requiring a "test and treat approach" ie eliminating CD4 threshold as a prerequisite for commencement of ART[5]. While this guideline is based on sound evidence, it adds an unanticipated number of potential eligible patients for ART care, with attendant strain on countries with an already fragile economy. The low frequency of viral load test results might also reflect resource limitations.

Most patients were on TDF/3TC/EFV drug regimen, which is consistent with current guideline advice for first line treatment. Only 2% of the patients were on second-line ART, varying from 9% to less than 1% between clinics. It is likely that most of the studied patients are still on a potent first line ART judging by the low second-line ART usage. Use of a regimen with a low pill burden would enhance therapy adherence and might lead to reduced need for switching patients to second line ART[10]. TDF/3TC/EFV drug regimens have a low pill burden, and may contribute to the low usage of second-line ART regimens.

The variation in the use of co-trimoxazole, from almost universal in two clinics, to negligible in the other two clinics, is an extreme example of the variation we identified. The reason for

Table 3. Antiretroviral therapy (ART) Regimens.

ART regimen contains	BA (N=100)	EVT (N=94)	MW (N=99)	AM (N=295)	Overall (N=588)
AZT zidovudine	28 (28.0%)	87 (92.6%)	0	113 (38.3%)	228 (38.8%)
TDF tenofovir disoproxil fumarate	70 (70.0%)	3 (3.2%)	90 (90.9%)	154 (52.2%)	317 (53.9%)
FTC emtricitabine	10 (10.0%)	0	5 (5.2%)	0	15 (2.6%)
3TC lamivudine	90 (90.0%)	94 (100%)	94 (95.0%)	276 (93.6%)	554 (94.2%)
NVP nevirapine	24 (24.0%)	91 (96.8%)	0	111 (37.6%)	226 (38.4%)
IDV indinavir	0	0	0	0	0
RTV ritonavir	0	0	0	0	0
d4T stavudine	0	0	6 (6.4%)	0	6 (1.0%)
ABC abacavir	2 (2.0%)	0	9 (9.1%)	9 (3.1%)	20 (3.4%)
LPV lopinavir	3 (3.0%)	0	3 (3.0%)	0	6 (1.0%)
ATV atazanavir	6 (6.0%)	1 (1.1%)	0	1 (0.3%)	8 (1.4%)
EFV efavirenz	69 (69.0%)	2 (2.1%)	93 (93.9%)	162 (54.9%)	326 (55.4%)
Co-trimoxazole	100(100%)	7 (7.5%)	0	292 (98.9%)	399 (66.6%)

Table 4. Summary of key features of World Health Organisation guidelines.

When to start ART in adults		
TIME	**REFERENCE**	**RECOMMENDATION**
2002	Scaling up antiretroviral therapy in resource-limited settings: guidelines for a public health approach[1] http://www.who.int/hiv/pub/guidelines/pub18/en/	ART treatment if: • CD4 <200 cells/mm3 WHO stage I, II, or III OR • WHO Stage IV AIDS-defining illness, irrespective of CD4 count • First line therapy ZDV/3TC/EFZ or ZDV/3TC/NVP
2006	<u>Antiretroviral therapy for HIV infection in adults and adolescents</u>. Recommendations for a public health approach (2006 revision)[2] http://www.who.int/hiv/pub/arv/adult/en/	• All adolescents and adults including pregnant women with HIV infection and CD4 counts of ≤200 cells/mm3, should start ART, • First line treatment NRTI AZT or TDF combined with either 3TC or FTC; NNRTI, either EFV or NVP, should be added
2010	<u>Antiretroviral therapy for HIV infection in adults and adolescents</u>. Recommendations for a public health approach: 2010 revision[3] http://www.who.int/hiv/pub/arv/adult2010/en/	• All adolescents and adults including pregnant women with HIV infection and CD4 counts of ≤350 cells/mm3, should start ART, • First-line therapy should consist of an NNRTI + two NRTIs, one of which should be AZT or TDF • Second-line ART should consist of a ritonavir-boosted protease inhibitor (PI) plus two NRTIs, one of which should be AZT or TDF • Irrespective of CD4 cell counts, patients coinfected with HIV and TB should be started on ART • Irrespective of CD4 cell counts or WHO clinical stage, patients who require treatment for HBV infection should start ART.
2013	Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach[4] http://www.who.int/hiv/pub/guidelines/arv2013/download/en/	• As a priority, ART should be initiated in all individuals with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and individuals with CD4 count ≤350 cells/mm3 • ART should be initiated in all individuals with HIV with CD4 count >350 cells/mm3 and ≤500 cells/mm3 regardless of WHO clinical stage • ART should be initiated in all individuals with HIV regardless of WHO clinical stage or CD4 cell count in the following situations: • Individuals with HIV and active TB disease (strong recommendation, low-quality evidence). • Individuals coinfected with HIV and HBV with evidence of severe chronic liver disease • Partners with HIV in serodiscordant couples should be offered ART to reduce HIV transmission to uninfected partners (strong
2015/6	Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - Second edition[5]. http://www.who.int/hiv/pub/arv/arv-2016/en/	• Retesting prior to enrollment in care ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count • As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with a CD4 count ≤350 cells/mm3 • ART should be started in all TB patients living with HIV regardless of CD4 count • Preferred first line ART regimen TDF + 3TC (or FTC) + EFV • Combinations of ATV and LPV are the preferred boosted PI options for second-line ART • Routine viral load monitoring can be carried out at 6 months, at 12 months and then every 12 months thereafter if the patient is stable on ART to synchronize with routine monitoring and evaluation reporting • CD4 count every 6 months until in settings where routine viral load monitoring is available, until are stable on ART • Viral load is recommended as the preferred monitoring approach to diagnose and confirm treatment failure

ART antiretroviral therapy

AZT zidovudine : ZDV retrovir

3TC lamivudine

EFV (EFZ) efavirenz

NVP nevirapine

NRTI Nucleotide analog reverse transcriptase inhibitor

TDF tenofovir disoproxil fumarate

FTC emtricitabine

NNRTI Non-nucleoside reverse transcriptase inhibitor

HBV Hepatitis B virus

LPV lopinavir

this variation despite the guideline recommendation is not clear, but it is possible that it is a result of local clinic policy settings, possibly related to concerns about increasing antibiotic resistance. Variation in the use of co-trimoxazole has been found in other resource-limited settings, while efforts are being made to improve the rates of use[11].

While each clinic reported having access to treatment guidelines, those current at the time of the data collection do not appear to have been universally followed. The guidelines also do change regularly, as shown in Table 4. For example in relation to the frequency of CD4 count monitoring and the CD4 count threshold at which treatment should be started have changed since the time relating to the study data - new guidelines recommend starting treatment regardless of the CD4 count[5,12]. Some discrepancy between WHO guidelines and actual implementation in practice may arise from the time it takes to implement new guidelines, or due to lack of resources to immediately initiate all patients with HIV on ART. We see considerable between-clinic variation in a number of key management strategies reported by the clinics, from the recording of CD4 counts, median CD4 counts on treatment, and treatments used. This variation is consistent with a previous survey of stated management practices in 6 sub-Saharan countries[13,14].

The management of patients in routine clinical care has been shown to differ from that seen in clinical trials[15], as well as to lead to worse clinical outcomes, although it is beyond the scope of our study to explore outcomes. Findings of variation from standard management practice has previously been reported from routine care settings in other parts of sub-Saharan Africa including Ethiopia[16], Uganda[17] and Tanzania[18], mostly in single isolated centres. Here we present combined data on health system related measures across multiple sub-Saharan African HIV treatment sites. Hence, this study adds to the literature a current examination of the routine care provided to patients with HIV, rather than that in the context of a clinical trial. The study adds information from a number of centres in multiple countries, using a common protocol, of both the characteristics of the clinics and of the care given in these clinics.

In the absence of standardised record keeping systems, it is difficult to make clear comparisons of management and outcome in routine clinical care. Our findings suggest that there is room for further work to understand the reasons for these record gaps, and to standardise the record keeping in routine care of HIV positive patients[19–21]. The potential of electronic medical records to improve records could be explored[22].

Our study has a number of limitations. First, this study was an analysis of data extracted from existing medical records, which are prone to error including missing data. We have found missing data where it should ordinarily not be missing. We cannot comment on other factors that may have contributed to missing data, such as whether tests were not done or if they were not recorded. A future study should perform an audit of the medical records to determine the reason for missing data and hence the potential effect on the study findings. Second, some of the variation between centres may be due to differences in patient populations which we were unable to capture, even though we selected clinics involved in routine clinical care. Third, since this is a descriptive study and not hypothesis testing, it was not feasible to determine sample size in advance. A pragmatic approach was adopted, with each centre expected to obtain information from the first 100 patients presenting over a 6-month period, or from at least 100 patients. Fourth, participation in the study was restricted to few countries, and to individual clinics, which may not be representative of the national picture in these countries. A prospective cohort study on representative samples would provide a more robust study design with more detailed quantitative data to delineate care dynamics and to provide longitudinal data to better understand how clinical practice in these settings is linked to patient outcomes.

Conclusions

We demonstrate a wide variability in compliance with HIV treatment guidelines in four routine care settings in sub-Saharan Africa, as well as gaps in the records available. The findings of this study may provide an explanation for heterogeneous HIV treatment outcomes across sub-Saharan Africa. In spite of the limitations, these data underscore the need for an in-depth study to address compliance with HIV treatment guidelines and best practice. While electronic medical record implementation might be a challenge for many HIV care points in sub-Saharan Africa, our findings emphasize the need for more robust interim paper-based medical record keeping.

Ethics approval and consent

Ethics approval was sought in each setting from the appropriate authority. For two of the centres, research ethics committees gave approval. In two of the centres, the ethics committees stated that they did not require formal approval from them, however approval to access records was obtained from the relevant District Health Office/r. Details for each clinic as follows:

Clinic BA: Ethics approval obtained from Aminu Kano Teaching Hospital Research Ethics Committee.

Clinic EV: Ethics approval obtained from Research and Ethics Committee of State House Medical Centre, Abuja.

Clinic MW: University of Zambia Biomedical Research Ethics Committee contacted and advised to notify the Lusaka District Health Office (LDHO) who gave approval.

Clinic AM: Eastern Uganda AIDS Support Organization (TASO) contacted who recommended no need for an approval but rather write to the Amuria District Health Officer (DHO) for permission to have access to the hospital records, which was given.

Informed consent was not obtained from individual patients since this was a records study with appropriate institutional approval,

strict confidentiality arrangements, and no patient contact, as stated in the manuscript.

Data availability

Dataset 1. De-identified data collected from clinical records used to create Table 2 and Table 3 and Figure 1. Scheme used to code the data is available as Supplementary File 2. 10.5256/ f1000research.15169.d206333[23]

All data underlying the survey responses from clinic informants for Table 1 are available as part of the article.

Supplementary material

Supplementary File 1 – Study protocol

Click here to access the data.

Supplementary File 2 – Data coding scheme

Click here to access the data.

Supplementary File 3 – Written from of online survey

Click here to access the data.

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Open Peer Review

Current Referee Status: ? ✔ ?

Version 2

Referee Report 31 December 2018

? **Samuel A. Olowookere** 🆔

Department of Community Health, Obafemi Awolowo University, Ile-Ife, Nigeria

1. Methods: Kindly include the research question being answered. Study design needs to be made clearer in this section.

2. Measurement of study factors: Kindly specify important co-infections and co-morbidities.

3. Sample size consideration/selection: how were the centres selected? It is not clear how the size of 100 patients was arrived at. If the sample size and record selection was arbitrary this should be stated as a limitation of the study. What is standardised data collection? If this study is looking for variations, what of the similarities? The method section should give more background information on the centres chosen. This will include the health care worker/patient ratio, patient load and type of care provided to the patients.

4. What are the effects of missing values on the study findings? Efforts should be made by the authors to highlight reasons for missing values. A statement on the best way to address the missing values should be stated. What is the new information that this study added to the literature?

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

Referee Expertise: Family Medicine, Infectious diseases including HIV/AIDS

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 02 Jan 2019

Richard Heller, People's Open Access Education Initiative (Peoples-uni), Australia

Comments from Referee 3, and how we have responded and made changes (*Referee comments in italics*).

Methods: Kindly include the research question being answered. Study design needs to be made clearer in this section.
Response: Paragraph 1 in the Methods section has been revised as follows: "Interest in participating in this study was sought among the Masters of Public Health Alumni of Peoples-uni. A protocol was developed by those who responded (Supplementary File 1) which included the Research questions as follows: 1. Among a group of patients diagnosed with HIV by a health care facility newly diagnosed between 2 and 3 years previously, what proportion have standards of care in terms of the tests and treatments they receive and follow up to 2 years after diagnosis documented in their records? 2. Among the health care facilities in which the above patients are cared, what treatment, testing and referral facilities are available? 3. What is the extent of the variation in the above measures between facilities and countries, as well as in the availability of appropriate evidence based practice guidelines? A retrospective patient cohort was created via standardized record review, and clinic characteristics determined through an online survey form."

Measurement of study factors: Kindly specify important co-infections and co-morbidities.
Response: We have changed the sentence in the section of Measurement of study factors from 'Clinical information included clinical, immunological and virological information on patients at diagnosis and on follow-up, prescription of ART and other drug choices, important co-infections and/or co-morbidities.' to the following: "Clinical information included clinical, immunological and virological information on patients at diagnosis and on follow-up, prescription of ART and other drug choices. Potentially important co-infections and/or co-morbidities, identified from the literature, were coded as indicated in Supplementary File 2," The list is long and since the file is easily accessible to the reader we think that this is a reasonable way to meet the request of the Referee while not adding too much to the size of the paper.

Sample size consideration/selection: how were the centres selected? It is not clear how the size of 100 patients was arrived at. If the sample size and record selection was arbitrary this should be stated as a limitation of the study. What is standardised data collection? If this study is looking for variations, what of the similarities? The method section should give more background information

on the centres chosen. This will include the health care worker/patient ratio, patient load and type of care provided to the patients.

Response: As indicated in the paper (Methods) 'Interest in participating in this study was sought among the Masters of Public Health Alumni of Peoples-uni' and (Results) 'Ten alumni expressed interest in participating, three centres were able to pilot the data collection instrument and four centres in three countries participated in the data collection for the study.' We have added to the sentence in the Methods section as follows: "Interest in participating in this study was sought among the Masters of Public Health Alumni of Peoples-uni. There was no prior determination of the numbers of centres required or their geographical setting." We have added to the section on study limitations as follows: "Since this is a descriptive study and not hypothesis testing, it was not feasible to determine sample size in advance. A pragmatic approach was adopted, with each centre expected to obtain information from the first 100 patients presenting over a 6-month period, or from at least 100 patients."

We have changed the first sentence in the Discussion to the following: "Data were collected according to the standardised data collection instrument (Supplementary File 2), with data on treatment regimes and CD4 counts relating to the latest information in the records (dates mainly between 2015 and 2017)."

We believe that the background information that the Referee requires on the centres chosen is fully reported in Table 1 in the Results section.

What are the effects of missing values on the study findings? Efforts should be made by the authors to highlight reasons for missing values. A statement on the best way to address the missing values should be stated. What is the new information that this study added to the literature?

Response: Unfortunately, we do not have information on whether missing values are due to the tests not having been performed, or the information not having been recorded. As we have mentioned in the Discussion section 'Some of the absence of viral load might be poor record keeping, and the high proportion of undetectable results might reflect an absent rather than a low test result, and hence not an indicator of treatment success.' and in the section on study limitations 'We have found missing data where it should ordinarily not be missing. We cannot comment on other factors that may have contributed to missing data, such as whether tests were not done or if they were not recorded.' We have added the following in the study limitations section in response to the Referee's request: "A future study should perform an audit of the medical records to determine the reason for missing data and hence the potential effect on the study findings."

In response to the Referee's request to identify the new information added by our study, we have added the following sentences to the Discussion section (paragraph 7) to follow our original sentence 'Here we present combined data on health system related measures across multiple sub-Saharan African HIV treatment sites.' the additional sentences read: "Hence, this study adds to the literature a current examination of the routine care provided to patients with HIV, rather than that in the context of a clinical trial. The study adds information from a number of centres in multiple countries, using a common protocol, of both the characteristics of the clinics and of the care given in these clinics."

Competing Interests: No competing interests were disclosed.

Referee Report 12 October 2018

? **Thomas Crellen** (iD)

Mahidol Oxford Tropical Medicine Research Unit (MORU), Bangkok, Thailand

The authors have corrected minor issues in the article, though I retain my reservations around the study design and the lack of a research question.

Competing Interests: No competing interests were disclosed.

Referee Expertise: Epidemiology, regression modelling, pathogen genomics

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

> Author Response 12 Oct 2018
> **Richard Heller**, People's Open Access Education Initiative (Peoples-uni), Australia
>
> I am sorry that you did not make your reservations clear in your first report. With regard to the research question, we stated in the Introduction "This study was designed to explore variation in the evaluation, treatment, care and follow-up among patients diagnosed with HIV in routine care settings in low- to middle-income countries". With regard to the study design, we stated in the Discussion "Data were collected in a standardised way, with data on treatment regimes and CD4 counts relating to the latest information in the records (dates mainly between 2015 and 2017). While we initially planned to collect data on a cohort of patients enrolled two years before data collection in each clinic, this did not prove feasible and patients had presented to the clinics at variable times."
>
> *Competing Interests:* No competing interests were disclosed.

Referee Report 11 October 2018

✓ **Sehlulekile Gumede-Moyo** (iD)

Department of Population Health, Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK

There has been some improvements in the current draft and most of the issues raised have been addressed. However l was wondering whether it's possible for the authors to comment to the patient doctor ratio with regards to co-trimoxazole distribution.

Competing Interests: No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 02 Jan 2019

Richard Heller, People's Open Access Education Initiative (Peoples-uni), Australia

Thank you for your comments. We could not demonstrate an obvious relationship between the doctor/patient ratio and use of co-trimoxazole, although it is an intriguing suggestion. A study including a larger sample of clinics might be able to explore this further.

Competing Interests: No competing interests were disclosed.

Version 1

Referee Report 17 September 2018

https://doi.org/10.5256/f1000research.16524.r37307

? **Sehlulekile Gumede-Moyo** (iD)

Department of Population Health, Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK

The paper is well written, however in some instances the authors have used outdated references. In the case of Nigeria where there are 2 health facilities with different caseloads per month, the authors could also enlighten us on the impact of having a high and low case load as presented.

The authors should also enlighten us on whether the records indicate the dates when the CD4 count and viral load tests were taken and when they were reported back. I suppose this of great importance since, there are reports of patients who have their blood samples taken and never receive results.

1) Is The study design appropriate and is the work technically sound?
The study design wand the work is technically, as the authors endeavoured to analyse multi-country settings

2. Are sufficient details of methods and analysis provided to allow replication by others?
The methods and analysis were sufficient, however in the case of Nigeria where there are 2 health facilities with different case loads per month; the authors could also enlighten us on the impact of having a high and low case load as presented.

3. If applicable, is the statistical analysis and its interpretation appropriate?
The statistical analysis was appropriate, although the authors should also enlighten us on whether the records indicate the dates when the CD4 count and viral load tests were taken and when they were reported back. I suppose this of great importance since, there are reports of patients who have their blood samples taken and never receive results.

4. Are the conclusions drawn adequately supported by the results?
The authors however need to address the issues that have been raised above.

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
No source data required

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

> Author Response 22 Sep 2018
> **Richard Heller**, People's Open Access Education Initiative (Peoples-uni), Australia
>
> Thank you for your generally positive comments. In the revised version submitted, we have added four recent references, and given further details on the dates of CD4 counts and viral load tests (although we have no data on the time that the results were reported to the patients). We have also discussed the reasons that the two Nigerian clinics might have different caseloads and the potential impact of this.
>
> *Competing Interests:* No competing interests were disclosed.

Referee Report 03 September 2018

https://doi.org/10.5256/f1000research.16524.r37430

? **Thomas Crellen**

Mahidol Oxford Tropical Medicine Research Unit (MORU), Bangkok, Thailand

This article by Musa and colleagues uses a snapshot of patient records from four HIV clinics in Nigeria, Zambia and Uganda to describe the variability in a number of patient measures. Data are not reported longitudinally and all analysis is descriptive.

The most useful part of this report is to show that ordinary clinics in countries with some of the highest HIV burdens globally do not confirm with WHO guidelines. For instance, only commencing ART when CD4 cells <350/ul. Further, the high amount of missing data in viral loads suggest there are logistical or cost

challenges to routine testing.

It is perhaps unsurprising that clinics in different countries vary in their patient characteristics and levels of reporting. The variability in CD4 counts is not particularly informative as it is not linked to length of time under ART. No research questions are addressed.

Table 2 should be amended as some percentage values are missing and figures are presented to different numbers of significant figures.

Despite the descriptive nature of the study, the authors are to be commended on presenting hard to access data from routine health care settings in sub-Saharan Africa. I hope that they will be able to take longitudinal data in the future and better understand how clinical practice in these settings is linked to patient outcomes.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Not applicable

Are all the source data underlying the results available to ensure full reproducibility?
No

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Referee Expertise: Epidemiology, regression modelling, pathogen genomics

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 22 Sep 2018

Richard Heller, People's Open Access Education Initiative (Peoples-uni), Australia

Thank you for your positive comments on the paper. In the revised version submitted, we have tried to emphasise the points you make, and have amended Table 2 as requested.

Competing Interests: No competing interests were disclosed.

Author Response 02 Jan 2019

Richard Heller, People's Open Access Education Initiative (Peoples-uni), Australia

In a later revision of the paper, paragraph 1 in the Methods section has been revised as follows to include the research question: "Interest in participating in this study was sought among the Masters of Public Health Alumni of Peoples-uni. A protocol was developed by those who responded (Supplementary File 1) which included the Research questions as follows: 1. Among a group of patients diagnosed with HIV by a health care facility newly diagnosed between 2 and 3 years previously, what proportion have standards of care in terms of the tests and treatments they receive and follow up to 2 years after diagnosis documented in their records? 2. Among the health care facilities in which the above patients are cared, what treatment, testing and referral facilities are available? 3. What is the extent of the variation in the above measures between facilities and countries, as well as in the availability of appropriate evidence based practice guidelines? A retrospective patient cohort was created via standardized record review, and clinic characteristics determined through an online survey form."

Competing Interests: No competing interests were disclosed.

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