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Barriers and facilitators of adherence to antiretroviral treament at a public health facility in Ghana: a mixed method study

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Abstract

Background: HIV/AIDS is a disease of global public health concern with high morbidity and mortality rates. Poor adherence to antiretroviral therapy (ART) increases the risk of viral drug resistance and reduces treatment effectiveness towards viral suppression leading to disease progression, greater risk of death and increased risk of viral transmission. The study sought to assess current adherence levels to ART among patients in Ghana, exploring barriers and enablers of adherence to it, to provide future guidance to all key stakeholder groups.

Method: A mixed method approach was used comprising of a cross-sectional survey of patients followed by a focused group discussion with patients and an in-depth interview of four key health professionals working in the ART clinic of Atua Government Hospital, a primary care health facility in the Eastern Region of Ghana. A structured questionnaire was used to assess current adherence levels and their determinants among 231 randomly selected patients attending the clinic between July to September, 2019. Quantitative data were analysed using bivariate and multivariate methods while qualitative data were analysed using thematic framework approach.

Results: Adherence levels was found to be 42.9% among our study population. Lower adherence to ART was associated with patients' belief in herbal medicine (aOR =0.34 CI: 0.19-0.61). Other barriers identified from the qualitative analysis included low motivation arising from pill fatigue, forgetfulness, frequent stock out of medicines, long waiting times and worrying side-effects; while enablers, on the other hand, included measures that ensure improved assessment of adherence and health facility-related activities that improve patient satisfaction with ART services. **Conclusion:** Adherence to ART among patients living with HIV was sub-optimal in our study population. Understanding of the barriers and factors that enable adherence to ART is a key step to developing evidence-based adherence improvement strategies to enhance clinical outcomes.

1 Background

HIV/AIDS is a disease of global public health concern given its high prevalence rates and continued impact on morbidity and mortality (1). However, there have been appreciable improvements in life expectancy in recent years attributed mainly to the role of effective antiretroviral therapy (ART). As at 2020, about 37.7 million people globally were estimated to be living with HIV/AIDS, and as of 30th of June, 2021 28.2 million were accessing ART up from 7.8 million in 2010 (2, 3). While the incidence of new HIV infections have been reducing over the years, the number of people living with HIV (PLHIV) has remained high, attributed to the use of modern ART which is effective and contributes to longer, healthier lives (3).

One of the targets of the UNAIDS Fast Track approach to accelerate actions to end the AIDS epidemic is the 95-95-95 initiative, which seeks to achieve viral suppression in 95% of PLHIV taking ART (4). These targets are a revision of the 2014 90-90-90 targets which sought to ensure that by the end of that period, 90% of PLHIV know their status and 90% of PLHIV who their status are on ART, while 90% of those on therapy are virally suppressed

However, such a target of viral suppression among PLHIV requires a sustained high level of adherence (> 95%) to ART in managing HIV as a chronic disease, with the aim of ending the AIDS epidemic by 2030 (2, 5-9). UNAIDS data showed that Ghana's performance as at 2019 per the UNAID's target was 58-45-31, showing how far the country is towards achieving the goal of ending AIDS by 2030 (6). Studies have shown that poor adherence to ART increases the risk of viral drug resistance and reduces treatment effectiveness towards viral suppression.

As a result, leading to disease progression, greater risk of death and increased risk of viral transmission (9, 10).

We are aware though that adherence to ART is a complex process. Numerous studies conducted on this subject have identified a number of barriers to good adherence in both developed and developing countries (9-13). Firstly, the lifelong nature of treatment for HIV/ART makes adherence to ART challenging (11). Encouragingly, meta-analytsis studies have reported higher adherence rates to ART among Africans and Asians at approximately 70% compared with rates of 50-60% observed among Europeans and North Americans (8, 12). The WHO has also improved the opportunities to access to ART by removing the eligibility criteria limitation to ART for all populations, which includes pregnant women and children through the introduction of the 'Treat all' Policy (13). However, barriers to ART still remain among developing countries. Barriers include the socio-economic status of patients including unemployment, poverty, food insecurity, distance to clinics and transportation costs, human resource constraints, healthcare provider practices such as inadequate counselling sessions, abuse of patient confidentiality, stigma, depression and medicine stock-outs (7-10, 13-17). Other important factors affecting adherence to ART include ART-related factors such as a high pill burden, unacceptable side-effects and patient-related factors including forgetfulness, mistrust and myths about ART (7-9, 14, 16).

Adherence to ART can be determined by using both subjective and objective measurements (9, 10). Subjective measurements may involve methods such as self-reports while objective measurements may include pill counts, electronic monitoring and biochemical measures (18). The pill count method is acknowledged to be one of the simplest and most reliable adherence

measurement tools, and it is currently one of the main methods of determining adherence level among PLHIV in Ghana (19-22).

In Ghana, the National AIDS/STI Control Programme (NACP) of the Ghana Health Service, launched in 1987, is the technical lead agency charged with managing and coordinating the activities among the different sites in Ghana that provide ART services to PLHIV (19, 20).

A typical ambulatory ART centre in a typical district hospital in Ghana comprises a medical officer, pharmacist, nurse prescriber, and a data manager, who between them provide comprehensive services including HIV testing services, ART, adherence monitoring and follow-up, regular supply of medications, adverse event monitoring and drug resistance surveillance, as well as clinical, immunological and virologic monitoring to all PLHIV who come to receive any of their services (19). Ghana adopted in 2016 the WHO "treat all" policy, which was meant to scale up ART services by initiating ART in PLHV irrespective of patients' CD4 count as part of ongoing strategies to achieve the 95% viral suppression rates. Several strategies have now been adopted by NACP as means to achieve viral suppression. These include the use of treatment supporters, improving access to ART services through the introduction of the differentiated service delivery, and a shift to dolutegravir-based regimens (12, 23).

Considering the important role adherence plays in achieving viral suppression in patients with HIV/AIDS, this study was designed to assess current ART adherence levels and its determinants among patients in Ghana, including current barriers and enablers. The objective is to inform and design potential evidence-based strategies to accelerate the achievement of the UNAIDS milestones in resource poor settings such as primary care clinics in Ghana, putting the country on a trajectory to end the AIDS epidemic by 2030. This builds on previous

published studies in this area in Ghana including those assessing adherence rates (15-17, 24-26).

2 Method

2.1 Study Design

The study employed a mixed method approach. The quantitative design was a descriptive cross-sectional study using interviewer-administered/self-reported structured questionnaire among randomly sampled PLHIV of at least 18 years visiting the ART ambulatory clinic of Atua Government Hospital (AGH), who consented to participate in the study. This was followed by a qualitative design that involved the conduction of one Focus Group Discussion (FGD) comprising three male and three female PLHIV as well as in-depth interview among key informants comprising a medical officer, a pharmacist, a nurse prescriber, and a data manager, as these are the integral team of healthcare providers at each ART sites in Ghana.

2.2 Study Site

The study was conducted in the ART ambulatory clinic of AGH. AGH, located in the Lower Manya Krobo Municipality in the eastern region of Ghana, is the second of the 197 ART site established by the NACP in 2003 to provide highly active antiretroviral therapy as part of its comprehensive care to PLHIV living in and around the municipality (19). This ART ambulatory care centre was established due to the consistently high prevalence of HIV/AIDS in this part of the Eastern Region of Ghana. In 2019, the district prevalence of HIV/AIDS stood at 5.68% higher than the national prevalence of 2.0% (27).

The total population of the district in which AGH is located from the latest population and housing census was 89,246 representing 3.4% of the total population of the region, which is one of the 16 administrative regions in Ghana (28).

2.3 Sampling and sample size determination

The data collection for the survey was performed over a period of three months (July – September, 2019) among a targeted population of 900 PLHIV, who were eligible at the time of the study, i.e. at least 18 years, and had been exposed to ART regimen for at least 6 months as well as visiting the clinic within the study period. A sample size of 231 was determined using the standard formula from the 900 eligible PLHIV, using a prevalence rate of adherence of 77% (7, 29), a margin of error of 5%, a level of significance of 95% and a potential 10% non-response rate. Eligible participants who consented to participate using the structured questionnaire were randomly selected.

A convenient sampling approach was subsequently employed in the selection of participants who consented to participate in the FGD comprising three males and three females. A purpose sampling approach was used in the selection of the four key health care professionals for the in-depth interviews comprising of a medical officer, pharmacist, ART nurse and the data manager for the clinic. These professionals were selected to provide detailed information about the operation of the clinic as they represent the core team of staff in most ART sites in Ghana.

2.4 Study outcomes and data collection

Adherence to the ART was measured by analysing the pill count method (22, 30). Using this methodology, adherence levels are estimated by subtracting the total remaining pills at the current visit from the estimated total pills provided (with an allowance of 5 pills since patients were counselled to return to ART clinic before their last 5 pills were used up) at the last visit (numerator); subsequently dividing this by total number of pills given at the last visit

(denominator). Patients with an adherence level of <95% was considered as non-adherent because this cut-off point is well documented in the literature for ART (8, 22).

A structured questionnaire for the quantitative assessment, adapted from previous studies (29–34), was administered by a trained pharmacist (FM) with the support of pharmacy technicians to the participants in their local dialect (Twi and Krobo) to collect patient socio-demographic details and potential healthcare related characteristics that may influence their adherence to ART. All interviews were audiotaped, transcribed verbatim in their local dialect with the help of NVivo version 7 (©QSR International Pty and then translated into english to reduce data loss. The transcripts were cross-checked by the principal investigator (IAS) for accuracy before using it to fill the questionnaire with the approproiate responses.

The FGD was conducted using a semi-structured questionnaire to explore patient's experience with the use of ART concerning potential barriers to ART uptake and retention. The discussion which was undertaken in their local dialect, which lasted for about an hour and was led by the principal investigators (IAS and FM). The discussions were audiotaped and the process of transcription and translation of responeses as stated above were followed.

The in-depth interviews among the four key ART clinic staff were conducted with open-ended structured questions lasting between 30 to 45 minutes in english, which was audiotaped and participants' responses were transcribed. The interview questions were adapted from previous studies and the questionnaire comprised of issues on provider knowledge about ART treatment guidelines, opinion about the documented factors influencing adherence and health managers' strategies to improve adherence level among their patients (31-34).

2.5 Data Analysis

2.5.1 Quantitative Data Analysis

Survey data collected from the sampled patients using the interviewer-administered questionnaire were entered into Microsoft Excel and then imported into STATA version 14 for analysis. Number and proportions of participant who were classified as adherent (≥95%) and non-adherent (<95%) were estimated. Bivariate analysis (using cross-tabulation, Chi-square test and Fischer exact test) were conducted to assess crude association of adherence with the study covariates.

Multivariate logistic regression was then conducted to assess the independent association of the study covariates with the adherence status. Results were presented as adjusted odd ratios (aOR) and 95% confidence intervals. The co-variates included in the model were reduced with a stepwise backward model using a cut-off p-value of at most 0.1.

2.5.2 Qualitative Data Analysis

The transcribed data from both in-depth interviews and FGD were individually analysed using the thematic framework approach to identify major themes related to the facilitators and barriers for adherence to ART as well as potential strategies to enhance future patient adherence (8, 35, 36).

2.6 Ethical considerations

Ethical approval (GHS-ERC 033/06/19) for the study was obtained from Ghana Health Service Ethical Review Committee. Administrative permission was also sought from the authorities of AGH before data were collected. Informed consents were obtained from all respondents in the study. Participants' confidentiality and privacy of the data collected were safeguarded by

keeping them under lock and key with the Principal Investigator. Data entered were stored on password-protected computers.

3. Results

3.1 Results from quantitative analysis

3.1.1 Demographic characteristics

Out of a total of 231 participants, 65.4% were female and 68.0% were less than 45 years. Over 80% of patients had at least basic education and 66.7% were employed.

3.1.2 Adherence level and factors influencing adherence to antiretroviral therapy

Overall, only 42.9% (n=99/231) of the study participants were adherent to their ART (Table 1).

The bivariate analysis showed statistically significant association between ART adherence by PLHIV and their perception of ART importance (p-value =0.032) as well as their belief in the efficacy of herbal medicine (p-value =0.044) shown in Table 1.

The multiple logistic regression results showed patients' belief in herbal medicine as the only co-variate that was significantly associated with PLHIV adherence level to ART (p-value = 0.000) (Table 2).

3.2 Results from the qualitative analysis

3.2.1 Adherence barriers

3.2.1.2 Patient-related barriers

A number of patient-related factors as a barrier to adherence were identified during the FGD and the in-depth interview of key informants. Some of the barriers identified were age, gender, education, forgetfulness, pill fatigue and distance of participant's residence from the treatment center (Table 3 and 4).

One participant recounting his experience with the use of ART during the FGD said that:

"Sometimes I forget to take my medications but I take the next dose anytime I remember especially when am in a hurry for a programme or going to work".

One of the key health professionals who asked to share from his experience barriers to adherence during interview mentioned that:

"Because it (ART) is lifelong therapy, those who start at a younger age get fed up along the way".

3.2.1.2 Socio-economic barrier

Some socio-economic barriers such as poor social support, inadequate meals to support drug uptake and cost of transportation to the treatment center were identified as barriers to adherence (Table 3 and 4).

One participant recounted to the interviewer during the FGD that:

"I sometimes struggle to get money for my transportation even though the drugs are for free".

3.2.1.3 Therapy-related barriers

Pill fatigue, high pill burden and drug side-effects were identified from both the interview of key health professionals and the FGD as reasons for poor adherence to ART (Table 3 and 4).

One health professional interviewed reported that:

"Some patients default when the side effects are intolerable rather than report for possible change in regimen".

This was supported by one participant during the FGD who admitted this by saying that:

"*I stopped taking my medications when I was having severe side effect but I came to complain and the doctor changed the regimen for me".*

3.2.1.4 Health system barriers

Several health system barriers were also identified as barriers to ART adherence and they included lack of essential logistics, stock of ART, long waiting time for pharmacy service and discrimination by service providers (Table 3 and 4).

One participant complaining about the challenge of ART availability mentioning that:

"Sometimes I travel all the way from Accra only to be told my medicine is not available. How will you feel if it were to be you?".

Another participant also complained about the delay in service provision and mentioned that:

"I know I will spend the whole day at the hospital so I psyche myself up and when I feel they are delaying, I boldly go to the pharmacist to complain for him to serve me".

One participant giving his experience of provider's favouritism said that:

"There seem to be some form of favouritism at the records unit since they give protocol to some people. You will be the first person to bring your card but they will bypass you".

3.2.2 Adherence enhancers

3.2.2.1 Patient-related factors

Self-motivation from peers and early disclosure of HIV status to the partner were identified as patient-related factors as enhancers of adherence (Table 3).

"We have to motivate ourselves to take the medications since the healthcare providers have done their part".

3.2.2.2 Adherence assessment tools

The key informants' interviews identified adherence assessment using periodic and routine monitoring of viral load, pill count during refill, electronic tracker system to monitor appointment and follow up visits as enhancers of patients' adherence to ART (Table 3).

3.2.2.3 Health System Related Factors

Some of the health system-related factors that were identified as enhancers to adherence were patient satisfaction with the service provided, improved infrastructure of the clinic, routine adherence counselling and social support such as food provision by the facility (Table 3).

This is what one participant mentioned during the FGD:

The counselling is very helpful since I am able to remember what I have been told (to do) when am taking my medications".

Another participant commenting the positive influence of social support said this:

"The facility sometimes provides us with food items and it is helpful".

4.0 Discussion

The level of adherence to ART recorded among the study participants was 42.9%. This is a concern as this observed adherence rate is appreciably below the globally accepted adherence rate of 95% needed to maintain viral suppression (5, 6). As a result, this may lead to poor treatment outcomes than desired including progression to AIDS and death, drug resistance development and increased costs of health delivery despite the availability of effective ART (9, 37, 38). Our findings are also below rates seen in previous studies conducted in Ghana (25, 26, 39).

This difference in adherence rates may be attributed to the different methods used for their assessment and the different cut off points for adherence levels making comparison difficult. This study employed the pill count methodology for adherence assessment as it has shown to be inexpensive and has close sensitivity and reliability with more objective methods including medication event monitoring system, which is currently considered the gold standard measurement tool compared to the self-reported tools (40, 41). The pill count methodology is also known to be one of the mostly widely used methods for adherence assessment in Ghana (19). Its accuracy can however be improved by combining this method with other patient self-reported method and assay of patient blood level of the chemical compound of interest.

Our study showed an association between ART adherence and patients' belief in herbal medicine (aOR =0.34 CI: 0.19-0.61). Herbal medicines are widely used in Ghana and are

believed to be natural with little serious adverse effects, making them a preferred option for chronic diseases (42-45). Consequently clinicians must always undertake a detailed assessment of patient medication history and counsel them on the dangers of combining ART to herbal meidines and the need to avoid the temptation to stop taking thier ART all together when immediate improvement in symptoms of opportunistic infections is observed. Herbal medicines are perceived to be more efficacious and easy to access compared to their orthodox counterparts (46). Patients may also opt for herbal medicines when they start experiencing worrying ART-related adverse drug reactions as herbal medicines are perceived to be natural with minimal adverse effects (45). Belief in herbal medicines has though been observed to be a barrier to adherence to prescription medicines due to their perceived easy accessibility, efficacy and affordability (47, 48). We have also seen an increase in the use of herbal medicines to treat patients with actual or suspected COVID-19 (49, 50). Such practices should be avoided where possible as this could be harmful to patients (49, 51, 52). Consequently, such practices need to be addressed especially in resource poor settings as part of measures to achieving the Fast Track targets of ending AIDS epidemic by 2030 and avoiding unnecessary harm to patients. We will be monitoring this in the future in these clinics.

Other adherence barriers assessed from the qualitative data included patient factors such as forgetfulness, low motivation from pill fatigue; socio-economic factors including transportation costs to treatment center; health facility related factors such as stock out of ART, long client waiting times at the pharmacy when picking up refills and long distances between residence and treatment centers as well as therapy-related factors including worrying side-effects. These findings are consistent with previous studies that have shown association between adherence and several patient medication taking behaviours (23, 26, 29, 33, 34, 37, 40). Consequently, strategies to address patients' adherence to ART to achieve viral load

suppression, prevent the development of drug resistance, and improve patient outcomes including health-related quality-of-life (53), must target these underlying barriers while assessing individual patients for their specific barriers to adherence to ensure effective targeted counselling. We will be using our findings to help address key issues in this clinic in Ghana to improve future outcomes.

The study also identified a number of enablers of adherence to ART. These included improved assessment of adherence by healthcare professionals using routine and periodic monitoring of patients viral loads, pill counting during refills, e-tracker system to monitor patient visit times and health system-related factors such as food provision to poor and needy patients, integration of ART services with other ambulatory care services, patient satisfaction activities including ART availability, and improved physical infrastructure of the clinic. These identified factors support previous studies that have demonstrated these as promoters of patient retention on treatment and consequently viral suppression in resource-limited settings (19, 26, 32, 38).

We are aware there are a number of limitations with our study. This includes the fact that this study was limited by the cross sectional nature, and therefore lacking the ability to establish a temporal association. Assessment of adherence using the pill count method could be less accurate as this method depends on the number of tablets patient declared as the leftover of what was dispensed to patients at their last visit to the clinic without an ability to check this. Information bias could also have been introduced during data collection as the questionnaires were not validated. However, they were adapted from previous studies. In addition, we are aware that this study was conducted in only one ART centre in a public health facility in Ghana. Alongside this, whilst our study found an association between patients' adherence levels and their belief in herbal medicines, we failed to assess whether they use such medicines.

However despite these concerns, we are confident that our study will serve as useful baseline information for more rigorous studies on potential barriers and enablers of adherence to ART towards the achievement of the UNAIDS target of 95-95-95. We also believe our findings would be useful to improve patient care in this clinic and possibly clinics in other poor healthcare resource settings.

5 Conclusion and recommendations

Adherence to ART among PLHIV was sub-optimal in our study population. Adherence to ART was observed to be hindered by multiple barriers including patient belief in herbal medicine, low motivation arising from pill fatigue, forgetfulness, transportation cost to treatment clinic, stock out of drugs, long waiting time and worrying side effects. We also identified adherence enabling factors such as measures that ensure improved assessment of adherence and health facility-related activities that improve patient satisfaction with ART services. Understanding of these barriers and factors that enable adherence to ART is a key step to developing impact-driven strategies to achieving viral suppression, which we have started to implement in our clinic.

References

1. Gona PN, Gona CM, Ballout S, Rao SR, Kimokoti R, Mapoma CC, et al. Burden and changes in HIV/AIDS morbidity and mortality in Southern Africa Development Community Countries, 1990–2017. BMC public health. 2020;20(1):867.

2. Global HIV and AIDS statistics Fact Sheet. Accessed on the 19th of January, 2022 via https://www.unaids.org/en/resources/fact-sheet on https://www.unAIDS.org/sites/default/files/media_asset/Global_AIDS_update_2017_en.pdf

3. Mbuagbaw L, Mertz D, Lawson DO, Smieja M, Benoit AC, Alvarez E, et al. Strategies to improve adherence to antiretroviral therapy and retention in care for people living with HIV in high-income countries: a protocol for an overview of systematic reviews. BMJ open. 2018;8(9):e022982.

4. UNAIDS. Understanding fast-track: accelerating action to end the AIDS epidemic by 2030. 2015. Available at URL: https://www.unAIDS.org/sites/default/files/media_asset/201506_JC2743_Understanding_FastTrack_en.pdf. .

5. UNAIDS. The Aids Epidemic Can Be Ended By 2030 With Your Help. 2016. Available at URL: https://www.unAIDS.org/sites/default/files/media_asset/UNAIDS_with-your-help_en.pdf.

6. UNAIDS. UNAIDS Data 2020. 2020. Available at URL: https://www.unAIDS.org/sites/default/files/media_asset/2020_AIDS-data-book_en.pdf.

7. Mai HT, Le GM, Tran BX, Do HN, Latkin CA, Nguyen LT, et al. Adherence to antiretroviral therapy among HIV/ AIDS patients in the context of early treatment initiation in Vietnam. Patient preference and adherence. 2018;12:2131-7.

8. Azia IN, Mukumbang FC, van Wyk B. Barriers to adherence to antiretroviral treatment in a regional hospital in Vredenburg, Western Cape, South Africa. South Afr J HIV Med. 2016;17(1):476.

9. Kim SH, Gerver SM, Fidler S, Ward H. Adherence to antiretroviral therapy in adolescents living with HIV: systematic review and meta-analysis. AIDS. 2014;28(13):1945-56.

10. Ankrah DN, Koster ES, Mantel-Teeuwisse AK, Arhinful DK, Agyepong IA, Lartey M. Facilitators and barriers to antiretroviral therapy adherence among adolescents in Ghana. Patient preference and adherence. 2016;10:329-37.

11. Spaan P, van Luenen S, Garnefski N, Kraaij V. Psychosocial interventions enhance HIV medication adherence: A systematic review and meta-analysis. J Health Psychol. 2020;25(10-11):1326-40.

12. Scanlon ML, Vreeman RC. Current strategies for improving access and adherence to antiretroviral therapies in resource-limited settings. HIV/AIDS (Auckland, NZ). 2013;5:1-17.

13. Chaiyachati KH, Ogbuoji O, Price M, Suthar AB, Negussie EK, Bärnighausen T. Interventions to improve adherence to antiretroviral therapy: a rapid systematic review. AIDS. 2014;28 Suppl 2:S187-204.

14. Merten S, Kenter E, McKenzie O, Musheke M, Ntalasha H, Martin-Hilber A. Patient-reported barriers and drivers of adherence to antiretrovirals in sub-Saharan Africa: a meta-ethnography. Trop Med Int Health. 2010;15 Suppl 1:16-33.

15. Adjetey V, Obiri-Yeboah D, Dornoo B. Differentiated service delivery: a qualitative study of people living with HIV and accessing care in a tertiary facility in Ghana. BMC health services research. 2019;19(1):95.

16. Dzansi G, Tornu E, Chipps J. Promoters and inhibitors of treatment adherence among HIV/AIDS patients receiving antiretroviral therapy in Ghana: Narratives from an underserved population. PloS one. 2020;15(3):e0230159.

17. Poku RA, Owusu AY, Mullen PD, Markham C, McCurdy SA. Antiretroviral therapy maintenance among HIV-positive women in Ghana: the influence of poverty. AIDS care. 2020;32(6):779-84.

18. Campbell JI, Eyal N, Musiimenta A, Burns B, Natukunda S, Musinguzi N, et al. Ugandan Study Participants Experience Electronic Monitoring of Antiretroviral Therapy Adherence as Welcomed Pressure to Adhere. AIDS and behavior. 2018;22(10):3363-72.

19. Ayisi Addo S, Abdulai M, Yawson A, Baddoo AN, Zhao J, Workneh N, et al. Availability of HIV services along the continuum of HIV testing, care and treatment in Ghana. BMC health services research. 2018;18(1):739.

20. Biritwum RB. HIV in Ghana. Postgraduate Medical Journal of Ghana. 2014;3(2):71-2.

21. Baisley K, Baeten JM, Hughes JP, Donnell DJ, Wang J, Hayes R, et al. Summary measures of adherence using pill counts in two HIV prevention trials: the need for standardisation in reporting. AIDS and behavior. 2013;17(9):3108-19.

22. Achieng L, Musangi H, Billingsley K, Onguit S, Ombegoh E, Bryant L, et al. The use of pill counts as a facilitator of adherence with antiretroviral therapy in resource limited settings. PloS one. 2013;8(12):e67259.

23. Ghana Health Service. Differentiated Service Delivery for HIV in Ghana - An Operational Manual NACP. 2017. Available at URL:

https://www.differentiatedservicedelivery.org/Portals/0/adam/Content/nD4Qpp8C6Ei7R-TPPAKeLw/File/DSD%20for%20HIV%20in%20Ghana_FINAL.pdf.

24. Adam A, Fusheini A, Ayanore MA, Amuna N, Agbozo F, Kugbey N, et al. HIV Stigma and Status Disclosure in Three Municipalities in Ghana. Ann Glob Health. 2021;87(1):49.

25. Okotah AN, Korbuvi J. Adherence to Antiretroviral Therapy (Art) Among Adult Hiv Positive Patients in Volta Regional Hospital, Ghana. Value in health. 2014;17(7):A329.

26. Obirikorang C, Selleh PK, Abledu JK, Fofie CO. Predictors of Adherence to Antiretroviral Therapy among HIV/AIDS Patients in the Upper West Region of Ghana. Isrn AIDS. 2013;2013:873939.

27. Ghana AIDS Commission - Ghana HIV Fact Sheet. 2019. Available at URL: https://www.ghanAIDS.gov.gh/mcadmin/Uploads/2019%20FACT%20SHEET%2022%2006%202020%20revised(1).pdf

28. Ghana Statistical Service. 2010 Population and Housing Census: Summary report of final results. Available at URL: https://www2.statsghana.gov.gh/pop_stats.html.

29. Neupane S, Dhungana GP, Ghimire HC. Adherence to antiretroviral treatment and associated factors among people living with HIV and AIDS in CHITWAN, Nepal. BMC public health. 2019;19(1):720.

30. Ndubuka NO, Ehlers VJ. Adult patients' adherence to anti-retroviral treatment: a survey correlating pharmacy refill records and pill counts with immunological and virological indices. Int J Nurs Stud. 2011;48(11):1323-9.

31. Moomba K, Van Wyk B. Social and economic barriers to adherence among patients at Livingstone General Hospital in Zambia. Afr J Prim Health Care Fam Med. 2019;11(1):e1-e6.

32. Shubber Z, Mills EJ, Nachega JB, Vreeman R, Freitas M, Bock P, et al. Patient-Reported Barriers to Adherence to Antiretroviral Therapy: A Systematic Review and Meta-Analysis. PLoS medicine. 2016;13(11):e1002183-e.

33. Becker N, Cordeiro LS, Poudel KC, Sibiya TE, Sayer AG, Sibeko LN. Individual, household, and community level barriers to ART adherence among women in rural Eswatini. PloS one. 2020;15(4):e0231952.

34. Adeoti AO, Dada M, Elebiyo T, Fadare J, Ojo O. Survey of antiretroviral therapy adherence and predictors of poor adherence among HIV patients in a tertiary institution in Nigeria. Pan Afr Med J. 2019;33:277.

35. Zakumumpa H, Rujumba J, Kwiringira J, Katureebe C, Spicer N. Understanding implementation barriers in the national scale-up of differentiated ART delivery in Uganda. BMC health services research. 2020;20(1):222.

36. Engler K, Lènàrt A, Lessard D, Toupin I, Lebouché B. Barriers to antiretroviral therapy adherence in developed countries: a qualitative synthesis to develop a conceptual framework for a new patient-reported outcome measure. AIDS care. 2018;30(sup1):17-28.

37. Bezabhe WM, Chalmers L, Bereznicki LR, Peterson GM. Adherence to Antiretroviral Therapy and Virologic Failure: A Meta-Analysis. Medicine. 2016;95(15):e3361.

38. Heestermans T, Browne JL, Aitken SC, Vervoort SC, Klipstein-Grobusch K. Determinants of adherence to antiretroviral therapy among HIV-positive adults in sub-Saharan Africa: a systematic review. BMJ global health. 2016;1(4):e000125.

39. Prah J, Hayfron-Benjamin A, Abdulai M, Lasim O, Nartey Y. Factors affecting adherence to antiretroviral therapy among HIV/AIDS patients in cape coast metropolis. Ghana J HIV AIDS. 2018; 4(1).

40. van den Boogaard J, Lyimo RA, Boeree MJ, Kibiki GS, Aarnoutse RE. Electronic monitoring of treatment adherence and validation of alternative adherence measures in tuberculosis patients: a pilot study. Bull World Health Organ. 2011;89(9):632-9.

41. El Alili M, Vrijens B, Demonceau J, Evers SM, Hiligsmann M. A scoping review of studies comparing the medication event monitoring system (MEMS) with alternative methods for measuring medication adherence. British journal of clinical pharmacology. 2016;82(1):268-79.

42. Boateng MA, Danso-Appiah A, Turkson BK, Tersbøl BP. Integrating biomedical and herbal medicine in Ghana - experiences from the Kumasi South Hospital: a qualitative study. BMC Complement Altern Med. 2016;16:189.

43. van Andel T, Myren B, van Onselen S. Ghana's herbal market. Journal of ethnopharmacology. 2012;140(2):368-78.

44. Ameade EP, Amalba A, Helegbe GK, Mohammed BS. Medical students' knowledge and attitude towards complementary and alternative medicine - A survey in Ghana. Journal of traditional and complementary medicine. 2016;6(3):230-6.

45. Aziato L, Antwi HO. Facilitators and barriers of herbal medicine use in Accra, Ghana: an inductive exploratory study. BMC Complement Altern Med. 2016;16:142.

46. Laar A, Amoah Ampah E, Fernandez Y, Senyo Amevinya G, Nortey P, Benyah F, et al. 'What the herbal medicine can do for me in a week, the orthodox does in a year': Perceived efficacy of local alternative therapies influences medication adherence in patients with atherosclerotic cardiovascular disease. Health Expect. 2021;24(2):444-55.

47. Atinga RA, Yarney L, Gavu NM. Factors influencing long-term medication non-adherence among diabetes and hypertensive patients in Ghana: A qualitative investigation. PloS one. 2018;13(3):e0193995.

48. Dhar L, Dantas J, Ali M. A Systematic Review of Factors Influencing Medication Adherence to Hypertension Treatment in Developing Countries. Open Journal of Epidemiology. 2017;07:211-50.

49. Sefah I, Essah D, Haque M, Opanga S, Kumar S, Chikowe I, et al. COVID-19, health care and self-medication issues in resource-limited settings: Findings and implications based on experiences in Ghana. Advances in Human Biology. 2021;11(3):224-33.

50. Sefah I, Ogunleye O, Essah D, Opanga S, Rizvi N, Wamaitha A, et al. Rapid assessment of the potential paucity and price increases for suggested medicines and protection equipment for COVID-19 across developing countries with a particular focus on Africa and the implications. Frontiers in pharmacology. 2021;11(2055).

51. Yang Y. Use of herbal drugs to treat COVID-19 should be with caution. Lancet (London, England). 2020;395(10238):1689-90.

52. Nkeck JR, Tsafack EE, Ndoadoumgue AL, Endomba FT. An alert on the incautious use of herbal medicines by sub-Saharan African populations to fight against the COVID-19. PAMJ 2020; 35 (2): 26. 10.11604/pamj.supp.2020.35.2.23161.

53. Vagiri RV, Meyer JC, Godman B, Gous AGS. Relationship between adherence and health-related quality of life among HIV-patients in South Africa: findings and implications. Journal of AIDS and HIV Research. 2018; 10(8): 121-32.