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Evaluation of trimoxazole availability for preventive therapy in adolescents and adults patients living with HIV/AIDS in pepfar supported antiretroviral treatment sites in Akwa Ibom State, Nigeria. Time-series analysis: July 2016 – April 2017

Urama BO[1], Agusiobo AN[2] , Idang B[3], Iwheye-Adie BG[4], Babatunji Odelola[5] and Obioma UM[6]

Abstract

Background: Cotrimoxazole preventive therapy (CPT) is a cheap, suitable and well-tolerated means of using cotrimoxazole intervention for patients living with HIV/AIDS to decrease mortalities and morbidities related to HIV/AIDS. The aim of this study was to ascertain the level of availability and stock out of Cotrimoxazole in antiretroviral treatment sites supported by U.S President's Emergency Plan for AIDS Relief (PEPFAR) in Akwa Ibom State. This research will show the number of health facilities with a zero or positive stock on hand data for adult cotrimoxazole at the health facilities.

Methods and Findings: Quantitative data were collected from health facilities focal persons in a cluster review meeting between July 2016 and May 2017. The data (stock on hand and consumption) were extracted from the Inventory Control Cards and adult pharmacy daily worksheet respectively using Combined Report and Receipt Form (CRRF). The data were entered and analyzed in an MS Excel worksheet. Charts depicting the extent of stock availability were generated and transferred to an MS Word. The findings revealed that stock out of CTX was not common in PEPFAR supported antiretroviral treatment sites in Akwa Ibom State. CTX availability was lower in Government owned Primary Health Center providing antiretroviral treatment services than in General Hospitals and private/mission hospitals.

Limitations of the study: The evaluation was limited to antiretroviral treatment sites supported by PEPFAR.

Conclusions: The data demonstrate adequate CTX availability and may be an indication of a strong supply chain system for PEPFAR HIV/AIDS program in the state.

Key words: Cotrimoxazole, consumption, combined report and requisition Form (CRRF), human immunodeficiency virus type 1 (HIV-1), logistics management coordination unit (LMCU), Stock on hand

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INTRODUCTION

Co-trimoxazole (CTX) is a fixed-dose combination of sulfamethoxazole and trimethoprim, and a broad-spectrum antimicrobial agent that targets a series of aerobic gram-positive and gram-negative organisms, fungi and protozoa (Polyak et al., 2016; WHO, 2016). It was prescribed commonly in the past for several infection but for severe allergic skin reactions linked with it, other newer antibiotics are now preferred to treat simple infections (Polyak et al., 2016). Because of demonstrated efficacy in the prevention of infections such as pneumocystis pneumonia and toxoplasmosis in immunocompromised individuals, the joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) in 2000 recommended co-trimoxazole as an integral component of the HIV chronic care package as it is key to pre-antiretroviral therapy (ART) care.

Co-trimoxazole is a simple, well-tolerated, off-patent and low-priced antibiotic (Nersesian, Andrew, & Melissa, 2011). When used regularly as prophylaxis, CTX has shown to decrease mortality, morbidity, and hospitalizations among HIV-infected adults (Badri, Ehrlich, Wood, & Maartens, 2011; Suthar, Granich, Mermin, & Van Rie, 2012), primarily by decreasing rates of malaria, pneumonia, and diarrhea,

[1] *USAID Global Health Supply Chain - Procurement and Supply Management Project, Nigeria*
[2] *USAID Global Health Supply Chain - Procurement and Supply Management Project, Nigeria*
[3] *Ministry of Health, Uyo, Nigeria*
[4] *USAID Global Health Supply Chain - Procurement and Supply Management Project, Nigeria*
[5] *United State Agency for International Development*
[6] *Catholic Relief Services*

as well as severe bacterial infections, even in settings with high prevalence of CTX resistance (Anglaret et al., 1999; Wiktor et al., 1999; Mermin et al., 2006; Bwakura-Dangarembizi et al., 2014; Campbell et al., 2012).

Recommendations for the use of sulfamethoxazole and trimethoprim (CTX) in adults patients with HIV-1 vary by location. In Nigeria, CTX is recommended as a standard for HIV-1-infected adults with severe immunosuppression (WHO stage 3 or 4) and or with CD4+ cell count ≤ 500 cells/mm3) to prevent Pneumocystis jiroveci pneumonia and toxoplasmosis (FMOH, 2016; Kaplan et al., 2009; WHO, 2016). However, due to high prevalence of malaria and severe bacterial infections, CTX is initiated in all immunocompromised patients regardless of the CD+ cell count with priority given to adult (including pregnant women) with severe immunosuppression (WHO stage 3 or 4) and or with CD4 count < 500 cells/mm3) (FMOH, 2016; WHO, 2016). Routine CTX is also recommended for immunocompromised patients with active Tuberculosis regardless of the C4 count (FMOH, 2016; WHO, 2016).

Following antiretroviral therapy (ART), CTX can be discontinued once immune recovery and viral suppression is documented (Mocroft, 2010; Furrer, 1999; FMOH, 2016; Kaplan et al., 2009; WHO, 2016), but, due to high prevalence of malaria and bacterial infection in Nigeria, it is suggested that CTX should be continued in immunocompromised patients regardless of the $CD4^+$ cell count or WHO clinical stage (FMOH, 2016; WHO, 2016). Although this recommendation is provisional and with low to moderate-quality evidence, possible benefits of cessation of CTX include lower risk of drug toxicity or drug–drug interactions, reduced risk of antimicrobial resistance, decreased costs of care, and lower pill burdens for patients (Polyak et al., 2016).

The recommended dose of CTX for adult and adolescent patients living with HIV is two single strength tablets of CTX (tablets of 80 mg Trimethoprim and 400 mg Sulphamethoxazole) or one double strength tablet (1 tablet of 160 mg Trimethoprim and 800 mg sulfamethoxazole) daily or three times per week (WHO, 2016). Two studies have established that daily CTX 480mg is not inferior to daily CTX 960mg with regards to reducing death, pneumocystis jiroveci pneumonia, toxoplasmosis, malaria, pneumonia, and diarrhea in immunocompromised patients. But, the trails were unable to confirm consistent lessening in treatment limiting adverse events with CTX 480mg (Boeree, Sauvageot, Banda, Harries, & Zijlstra, 2005; Schneider et al., 1995). Both strengths are available in Nigeria and are interchangeable.

With the scale-up of HIV care and treatment programs, PEPFAR has committed substantial funding to guarantee an uninterrupted supply of co-trimoxazole for people living with HIV (PLWH), but access to this cotrimoxazole remains inconsistent. Stock assessment of HIV/AIDS and malaria commodities in Akwa Ibom State of Nigeria by Agusiobo et al (2014) established that both cotrimoxazole 480 mg and 960 mg were well below the recommended minimum level of inventory. Subjective evidence suggests some of the product provided through PEPFAR donation is being used in out-patient's clinics, but this is hard to validate given the fact that government health logistics systems do not track products. However, concern about leakage of donated co-trimoxazole into out-patient's clinic is necessary when people living with HIV lack access because the product provided by donors for HIV programs is out of stock.

It is in recognizing that judicious use of cotrimoxazole will bring success not only to HIV/AIDS program in Akwa Ibom State but also to the socio-economic development, and against the background of the study by Agusiobo et al that this evaluation was conducted, with the purpose of ascertaining the availability and stock-out of CTX required for preventive therapy in people with HIV infection in PEPFAR supported antiretroviral treatment sites in Akwa Ibom State.

METHODOLOGY

The design of this assessment was a cluster review involving collection of quantitative data from pharmacy adult daily worksheet and inventory control cards. The evaluation was conducted between July 2016 and May 2017 among 63 antiretroviral treatment sites supported by PEPFAR in the three-senatorial district of Akwa Ibom State. The assessment targeted focal persons in charge of drugs for the HIV/AIDS program in the subject facilities. All selected health facilities were approached for participation by the State Logistics Management Coordination Unit (LMCU) of the Ministry of Health (although some sites were private and mission facilities, they were contacted by the Ministry through the

LMCU). The health facilities were stratified into three groups in line with senatorial district arrangement of the country. The focal persons managing CTX from the health facilities in the three strata were invited to bimonthly cluster meetings at a central location in Uyo, Eket and Ikot Ekpene (the central locations of the strata).

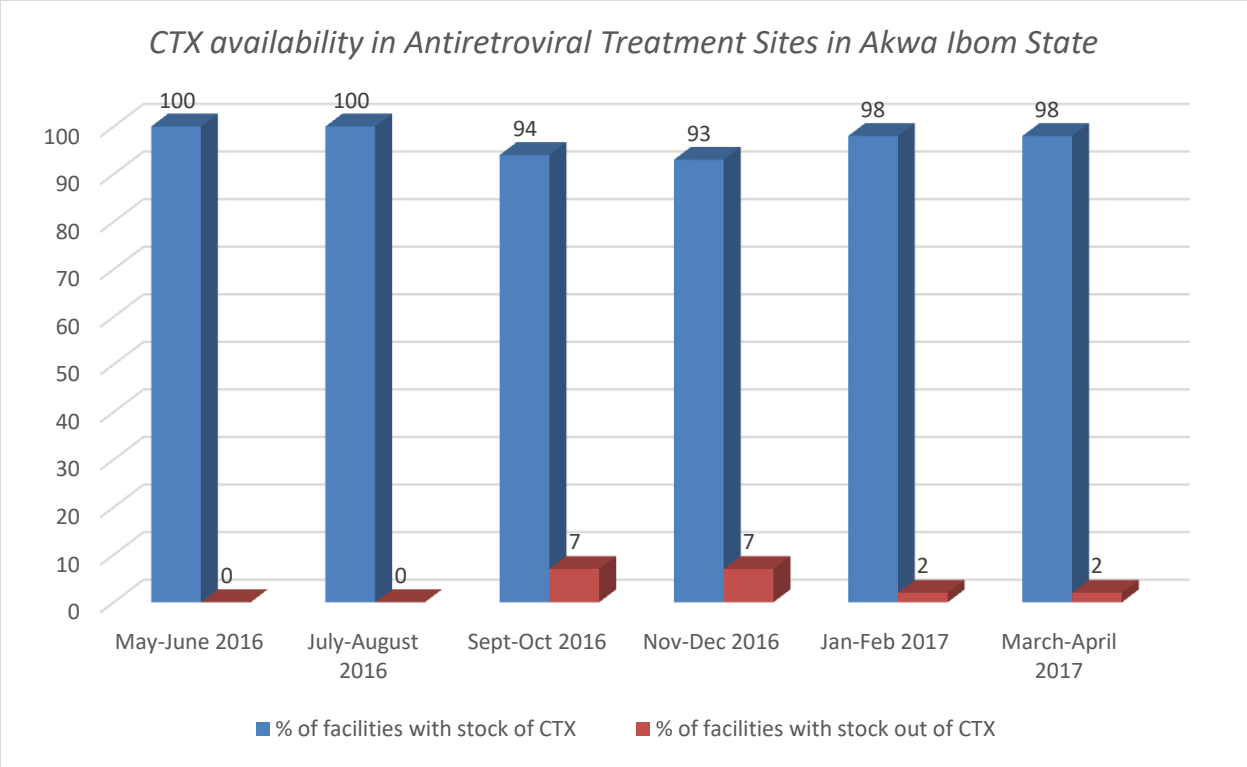
Three Pharmacists participated in the cluster review meetings to complete the data collection, with facility data being obtained from facility staff on the day of the meeting. A six review periods data were taken from pharmacy daily worksheet and Inventory control cards to see the pattern of CTX consumption and stock status in the health facilities. The data was collected using paper based Combined Report and Requisition Form (CRRF) for ARVs and medicine for opportunistic infections. The CRRF is a national bi-monthly reporting tool used by the health facilities to generate request for resupply of commodities. Data collected were recorded on two identical CRRF sheets and one copy was left with the facility while the second copy was transferred to the State LMCU office immediately following collection. Data from each cluster was swapped amongst the pharmacists and was double-checked for validity, completeness and consistencies. Data were entered in a spreadsheet database (Microsoft® Excel™) and reviewed for data entry error. Data entry error were identified using consistency and logical check. In case of obscure data, the staff were called to get the missing data. Data clean-up was conducted by crosschecking original manuscript with observed outliers. Data was analyzed using pivot table.

In evaluating availability, CTX was documented to be available in health facilities with viable stock of either CTX 480mg or 960mg considering that both strengths are used interchangeably. Deliberate manipulation of recording was observed in few instances with health facilities mutilating the inventory control cards with corrections fluid and altering the stock on hand records. Nonetheless, no stock of CTX was recorded to have expired on the health facilities inventory control cards.

RESULTS

Table 1: CTX availability in Antiretroviral Treatments Sites in Akwa Ibom State

Review Periods	**Number of LMIS reports collected**	**Number of facilities with stock of CTX**	**Number of facilities with stock out of CTX**	**% of facilities with stock of CTX**	**% of facilities with stock out of CTX**
May-June 2016	51	51	0	100	0
July-August 2016	50	50	0	100	0
Sept-Oct 2016	63	59	4	94	7
Nov-Dec 2016	58	54	4	93	7
Jan-Feb 2017	58	57	1	98	2
March-April 2017	59	58	1	98	2



DISCUSSION

This assessment has tried to assess the level of availability and stock-out of CTX required for preventive therapy in people with HIV infection in PEPFAR supported antiretroviral treatment sites in Akwa Ibom State. CTX stock out was not experienced during the period May to August 2016 among the health facilities that took part in the evaluation. This will increase the ability of facility staff to manage symptoms and to adhere to basic care protocols. Stock out of CTX was reported in 4 (7%) of the health facilities that participated in the study in Sept-Oct 2016 review period. The same result was obtained with health facilities that participated in the study during Nov-Dec 2016 review period. Among the 58 (98%) health facilities that participated in the study in Jan-Feb 2017 review period, 1 (2%) reported stock-outs of cotrimoxazole, while 1 (2%) out of the 59 (94%) health facilities that participated in the study in March-April 2017 review period experienced stock-outs of CTX. Data review also shows that the stock outs were particularly observed from the primary health centers (PHC) providing antiretroviral treatment. The focal persons revealed that communication was usually made with the GHSC-PSM team in event of stock-outs of CTX for possible local sharing through redistribution. Decreasing the ordered quantity of CTX by the supplier was mentioned as a main reason for the stock out. PHC's are often the first health system contact for many HIV patients in rural areas, yet these findings suggest that some of the PHC's surveyed were unable to dispense the drugs for the most common symptoms and conditions. When CTX are unavailable, patients are less likely to buy, thus increasing the risk of death and disease progression (Sethi, Celentano, Gange, Moore, & Gallant, 2003; Nischal, Khopkar, & Saple, 2005; Wood et al., 2003). The study also found that it was much more common for facilities to suffer stock-outs than to have expired CTX in stock. This suggests that facilities were more likely to have too few expired CTX, rather than too many in the future.

Strengths and limitations

Data were collected directly from health facilities source documents by professionals, so the results were not based on facility staff reports and are likely to reflect the situation in the health facilities. Since the

study was conducted by people from different organization with distinct funding support, inventory records and the pharmacy review were not influenced, thereby avoiding data bias.
To simplify the study data collection and reporting, data on different strength of the product (CTX 480mg and CTX 960mg) were not collected separately but, as an aggregated single unit of CTX adult formulation. This limits the depth to which the data can be analyzed. The reporting rates of the first two review periods (May-June and July-August 2016) were below nationally approved bench mark of 90%.

CONCLUSIONS

Ensuring availability of CTX is important to the success of HIV/AIDS program in Nigeria, as this will encourage implementation of cotrimoxazole preventive therapy thereby reducing AIDS related morbidities and mortalities. The study demonstrated that stock-out of CTX was not common in the health facilities that were studied. It was beyond the scope of this study to discover drug supply chain issues that may explain the stock out situations in the PHC's. Further study may be required to understand why stock-outs are experienced in health facilities that apply min-max inventory control system. If government is interested in decentralizing HIV treatment and care services to the PHC's, greater effort is needed to understand the challenges with CTX availability at rural health facilities.
Disclaimer: The findings and conclusions in this paper are those of the authors and do not necessarily represent the official position of the USAID or GHSC-PSM.

Competing interests

The authors of this manuscript declare that they have no competing interests.

Authors' contribution

Agusiobo AN, Iwheye-Adie BG and Urama BO conceived and designed the study. Agusiobo AN, Idang B, and Obioma UM conducted the data collection and performed the data entry while Urama BO completed the analysis and drafted the manuscript. Agusiobo AN and Iwheye-Adie BG reviewed and corrected the manuscript. All authors read and approved the final manuscript.
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