

# Second Training Workshop and Symposium MURIA Group 25 – 27 July 2016

# University of Botswana, Gaborone

# **Anti-Infective Abstracts**



UNIVERSITY BOTSWANA

Title of the abstract:	Efavirenz-Ugandan cross national study challenges and opportunities
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# Background:

The indications for efavirenz among HIV-infected individuals have expanded in recent years based on FDA/WHO/CDC recommendations. Efavirenz possess clinically relevant PK-PD challenges related to age, gender and genetics. There is a need for data regarding these factors. We are attempting to bridge this gap by conducting efavirenz-related research in African children and adults, including relevant drug-drug interactions. Collaborators include a Karolinska Institutet research group led by Lars Gustafsson, and three Ugandan Institutions (Makerere University, Baylor College and Mbarara University). The quest to acquire data doesn't go without challenges, including administrative complexities.

# **Objectives:**

We aim at providing evidence-based recommendations for better utilization of efavirenz in the treatment of HIV among young and adult Africans, including those co-treated for tuberculosis or neurological conditions, and include the impact of genetics. In addition, we are analyzing challenges attributable to cross-institutional and cross-national research, in order to create better collaborative environments.

# Methods:

Efavirenz research was initiated as general pharmacogenomics and pharmacodynamic studies among adult Ugandans with and without tuberculosis, in collaboration between Makerere and Karolinska Institutet. We are currently conducting a similar study in children, and forecast to study co-treatment of HIV and neurological conditions in children and adolescents. Challenges have been identified through friendly discussions or presentation.

#### Results:

Efavirenz pharmacokinetics were found to be highly influenced by genetics including among tuberculosis cotreated adults, and we therefore suggest reduced dosages for African populations. A similar pediatric study has enrolled 107 children (100 HIV treated + 7 TB/HIV co-treated). We are currently finalizing a protocol on combined treatments for HIV and neurological conditions, and hope to obtain data from long follow-up of the concluded pediatric study. Exploring the challenges has led to better and expanding collaborations.

#### **Conclusions:**

Our collaborative studies have resulted in important findings that would not have been achieved without collaborative efforts.



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Title of the abstract:	Management of URTIs in the Private Sector in Botswana
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# Background:

Inappropriate prescribing of antibiotics enhances the development of antimicrobial resistance (AMR) and increases subsequent morbidity, mortality, length of hospital stay as well as healthcare costs. Consequently, a growing concern world-wide. Increased resistance rates also increases the use of new more expensive antibiotics, exacerbating costs to patients and healthcare systems. Appropriate antibiotic use can decrease AMR rates. The management of upper respiratory tract infections (URTIs) are a particular concern in view of the over use of antibiotics worldwide for essentially a viral infection.

# **Objectives:**

Document the current use of antibiotics for the management of patients with URTIs among patients in two medical aid funds/schemes in Botswana (Botswana Public Officers' Medical Aid Scheme and The Pula Medical Aid) - covering approximately one fifth of the population. Assess prescribing against know quality indicators for antibiotics including (i) % penicillins vs. all antibiotics; (ii) % penicillin combinations vs. total penicillins and all antibiotics; (iii) % of 3rd and 4th generation cephalosporins as a % of all cephalosporins and (iv) % fluoroquinolones vs all antibiotics.

# Methods:

Retrospective cross over study based on all scheme patients treated from January 2012 to December 2015 by private GPs in Botswana with a diagnosis of URTIs. Exclusion criteria include (i) patient records having a diagnosis of bacterial co-infections other than URTI who needed antibiotic treatment and (ii) records with incomplete information.

Dataset researched include (i) Number of GP encounters for UTRIs per guarter (% of total encounters) - further divided into those ending up with a prescription, (ii) % of GP encounters for URTIs ending up with a prescription for an antibiotic - further divided into injectable and oral antibiotics; (iii) Dispensing point for prescriptions per quarter, e.g. pharmacy or general practitioner (iv) what antibiotics are prescribed/quarter broken down by DDDs and further divided by age group and against chosen quality indicators (above); (v) prescriptions broken down by patented vs. multiple sourced (prescriptions and DDDs) and associated costs.

# Results:

The results will be reported as the project progresses. The analysis will be fed back to private GPs to enhance the appropriate use of antibiotics in Botswana in the future. This may also involve educational initiatives among patients depending on the findings.





Title of the abstract:	Evolution of ESKAPE Organism Antibiotic Sensitivity over Time at a Private Hospital in Botswana
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Inappropriate prescription of antibiotics is a major driver of increasing antibiotic resistance, increased mortality, extended hospital stay and increased cost. As reported at the previous MURIA workshop held in February 2016, the Lenmed Bokamoso Private Hospital Infection Control Committee and the Drugs and Therapeutics Committees instigated a number of measures over the past 2 years with the objectives of optimization of treatment of bacterial infection, reduction of inappropriate antibiotic prescriptions, reduction of the incidence of hospital acquired infections and improvement of the sensitivity of common bacterial pathogens to available antibiotics. The efficacy of the interventions and their subsequent impact on patient outcomes needs to be assessed. Scrutiny of antibiograms over time could yield valuable information with regard to evolution of antibiotic resistance.

# Objectives:

To describe the evolution of antibiotic sensitivity patterns at LBPH between 2014 and 2016.

# Methods:

Calculation of antibiotic sensitivity percentages for ESKAPE organisms over the 6 month period January - June in each of 3 consecutive years - 2014-2016. Direct comparison of these cumulative antibiograms to assess if any appreciable change in antibiotic sensitivity has occurred.

# Results:

1. Comparison of antibiograms for Gram Negative Bacteria revealed either static or decreased antibiotic sensitivity in 2015 compared to 2014 .In contrast, the 2016 antibiograms appear to show small increases in antibiotic sensitivity across a range of bacteria and antibiotics - for example: Klebsiella - sensitivity to Amoxycillin/Clavulanic Acid 2014 - 100%, 2015 - 62%, 2016 - 75% : E coli - sensitivity to Amoxycillin- Clavulanic Acid 2014 - 82%, 2015 - 76%, 2016 - 84%.

2. Data available for gram positive bacteria organisms is not as extensive as our data for gram negative bacteria, but no particular trend is noted.

# Conclusions:

The use of bi annual antibiograms promises to encourage appropriate antibiotic use and hence reduce antimicrobial resistance at our institution. Preliminary results are encouraging. Completion of the study will occur on addition of data from May - June 2016. Final result will be communicated in early July 2016 to the MURIA Conference.





Title of the abstract	Lenmed Health Bokamoso Private Hospital Antibiotic Stewardship Programme
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Bokamoso Private Hospital is a private hospital with an open ICU. The specialists are self-employed and there is no particular restriction on their antibiotic prescribing for their patients in ICU. There has not been any follow up on antibiotic utilization in the ICU in the past.

#### Objectives:

To monitor antibiotic days for ICU admitted patients to determine how often doctors review patients on antibiotics, and to establish the extent of administration issues including: under-dosing, overdosing or missed doses. In essence, this would help towards optimizing antibiotic utilization at the hospital.

# Methods:

A pharmacist will visit ICU on daily basis with an antibiotic tracking form to record the number of days a patient is on a particular antibiotic, reasons for use of that particular antibiotic (being either, therapeutic, empiric or as prophylaxis), if any interaction was done with the doctor and the response to that. Renal dosing of antibiotics will also be monitored.

#### Results:

The result of the 6 weeks study up to the second week of July will be presented.

#### Conclusions:

The conclusion of such a study will be based on the results seen. An earlier study undertaken included not so much informative - hence the improvement on the form to be used.





Title of the abstract	Antimicrobial Stewardship Implementation In Gaborone Private Hospital
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# Background:

In recognition of the growing trend worldwide of the increase in antimicrobial resistance, and out breaks in some of the group hospitals, Life Healthcare Group of Hospitals decided on the drafting and Implementation of the Antimicrobial stewardship program in all its facilities. This study will focus on the implementation of the program at Life Gaborone Private hospital.

# **Objectives:**

The Objective of the Study was to determine the level of adherence to agreed antimicrobial bundle elements to determine where improvement is required.

# Methods:

This was a retrospective study looking at monthly interventions and the compliance to agreed bundle elements at Gaborone Private Hospital from July 2015 to June 2016. The following bundle elements were reviewed;

- 1. Microbiology requested for patients with an expected length of stay of more than 72 hours
- 2. Surgical prophylaxis stopped when patient out of theatre
- 3. Appropriate daily dose prescribed for patient
- 4. Antimicrobial spectrum duplication
- 5. Where appropriate step down from IV to oral antimicrobial was initiated
- 6. Treatment stopped or reviewed within seven days

The level of compliance was reviewed against the target of 85% agreed as the minimum to be reached for the process to be considered effective.

# Results:

A total of 353 patient interventions were done for the period of the study with a monthly average of 29 interventions. The average monthly compliance level for the study period was 77.4% against the agreed benchmark of 85%. Only one element of compliance (antimicrobial spectrum duplication) had an overall average above the benchmark and it stood at 88.02%. The lowest performing element was stoppage of surgical prophylaxis after patient left theatre at 40.42%, followed by request of microbiology at 65.8% and step down from IV to oral at 73.50%.

# Conclusions:

It is clear that adherence to the agreed bundle compliance for the antimicrobial stewardship program at Gaborone Private Hospital is still not at the desired level. Interventions are needed to ensure that this compliance is reached such that the level of antimicrobial resistance at the hospital is contained.





Title of the abstract	Point Prevalence Study on Antibiotic Utilization among Public Hospitals in Botswana
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**Background:** Increasing antimicrobial resistance is seen as one of the most critical problems challenging healthcare systems, increasing morbidity, mortality and costs due to inappropriate and indiscriminate antimicrobial use. The extent of antibiotic use and the adherence to antimicrobial use guidelines are largely unknown in Botswana. There is commitment in Botswana to enhance the appropriate use of antibiotics through development of national antimicrobial use guidelines and the recent introduction of antibiotic stewardship programmes in some hospitals.

**Objectives:** Undertake an antibiotic utilization study to understand the extent of current antibiotic use in hospitals and assess the capacities at hospitals to promote appropriate antibiotic use.

Methods: A modified and adapted Point Prevalence Study [PPS] study design that is similar to the Global Point Prevalence Study used by the European Centre for Disease Prevention and Control would be used. The study settings include 10 public hospitals covering widely all geographical regions of Botswana. The study received the Ethical approval for the Ministry of Health. The study population will include all in-patients remain admitted at the hospital at 7am who are on antibiotic therapy that have consented to access data from their medical records. The study that began in a hospital would end in a day but expected to complete the data collection from the entire hospitals on different dates. There will be no direct questioning of patients. Patients that do not consent, A & E and outpatients will be excluded from the study. The survey will include descriptive variables of the hospital, ward and patient level data to describe the extent of current antibiotic use in hospitals and assess the healthcare systems capacities to promote appropriate antibiotic use. The forms will be tested in a pilot and potentially adapted before use among both public and private hospitals. The study population will include all in-patients (at 7am, i.e. admitted at least the day before) within a hospital - especially patients who are on antibiotic therapy that have consented to have their information access from their medical records. There will be no direct questioning of patients. Different wards may be assessed on different days - but each ward will be completed within a day. Excluded patients include A & E and day case patients. Key data sets include (i) Whether laboratory facilities and sensitivity discs routinely available; (ii) antibiotic resistance patterns for common antibiotics within the hospitals; (iii) extent of treatment guidelines/DTCs within the hospitals to guide antibiotic prescribing; (iv) characteristics of the patients prescribed antibiotics during their hospital stay including diagnosis, whether sensitivity analyses requested and the extent of switching between antibiotics if first/ second line chosen antibiotics are failing to achieve desired outcomes; (v) dose, route of administration, length of treatment and costs (pharmacy costs) of all antibiotics prescribed during the patient's hospital stay; (vi) extent of switching from IV to oral antibiotics. It is envisaged that ten public hospitals will take part - Nyangabgwe Hospital, Francistown; Princess Marina Hospital, Gaborone; Scottish Livingston Hospital, Molepolole; Mahalapaye District Hospital, Serowe; Letsholathebe-II memorial Hospital, Maun: Goodhope Primary Hospital, Goodhope: Deborah Retif Hospital, Mochudi: Bobonong Primary Hospital, Bobonong; Lethlakane Primary Hospital, Lethlakane and Gweta Primary Hospital, Gweta.

Results: The current status and preliminary results will be discussed during the conference





Title of the abstract:	Comparison of selected prescribing indicators measured before and after the implementation of standard treatment guidelines in Swaziland
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In 2012, Swaziland launched its first standard treatment guidelines (STGs) to improve care and treatment outcomes of common conditions.

# **Objectives:**

The aim of this study is compare pre and post STG implementation prescribing patterns.

# Methods:

Simple cross-sectional survey of out-patient prescriptions assessing prescribing patterns using WHO/INRUD prescribing indicators was carried out at 33 health facilities prior to launching the STGs in 2012. Two years after the launch of the STGs, a follow up study was carried out at the same facilities, geographically conveniently selected from all 4 regions of Swaziland, reflective of facility type (e.g. hospitals, clinics) and sector (e.g. private, public). Prescriptions for STIs, HIV and immunisations were excluded in the analysis to reduce bias. Data was analysed using Wilcoxon Signed Rank Test and Mann-Whitney U-Test using R.

# Results:

The average number of medicines per encounter improved from 3.33 to 3.19 medicines per encounter. Percentage of encounters with an antibiotic prescribed improved from 59% to 52%. However both of these remain undesirably above the WHO recommendations of 1.7 and 23% respectively. Percentage of facilities with STGs improved from 60% to 100%. Percentage of encounters with an injection prescribed improved from 19% to 15%, within WHO standards.

# **Conclusions:**

The implementation of the STG in Swaziland has had an overall positive impact on prescribing patterns, with small improvements in the extensive poly pharmacy and antimicrobial prescribing observed at pre-implementation. Patient education, training, supervision and mentorship on STG use and further studies into prescriber motivations and beliefs are recommended





Title of the abstract:	An analysis of policies for cotrimoxazole , amoxicillin and azithromycin use in Namibia's public sector: findings and therapeutic implications
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Despite Namibia's robust medicine use systems and policies, antibiotic use indicators in public health facilities remain suboptimal. Recent medicine use surveys and ABC analyses rank cotrimoxazole, amoxicillin and azithromycin (CAA) among the most used medicines. The WHO identifies antibiotic overuse as the main driver of antimicrobial resistance. In addition, the Namibia Institute of Pathology antibiograms depict a rising resistance to CAA (55.9% - 96.7%); limited studies have evaluated antibiotic policies.

# Objectives:

To evaluate therapeutic policies guiding the use of CAA by disease and health facility level.

# Methods:

We reviewed pharmaceutical policy documents for recommended indications for CAA use, by type of health facility. Indications for CAA that were abstracted from treatment guidelines, essential medicine list, Medicines Act and Pharmacy Act were entered in SPSS v21 for quantitative analysis. Main outcome variable was the frequency of policy recommendations for CAA use by disease condition, and health facility level.

# Results:

Out of seven policy documents reviewed, only the draft National Medicines Policy 1/7 (14.2%) has a policy statement on antibiotic use. Out of the 59 listed indications for all antibiotics, the CAA antibiotics are indicated for the prophylaxis or treatment of 34 (57.6%) conditions at all levels of healthcare. The majority of the conditions (45/59 or 76%) are treatable at the primary health care (PHC) level than hospital OR 35.75(95% CI; 4.21–303.42), p < 0.001. Most policies recommend amoxicillin 23(38.9%) and azithromycin 24 (40.7%) for acute infections, particularly in acute respiratory infections 22(37.2%).

# Conclusions:

Pharmaceutical policies in Namibia promote the wide access and use of CAA by disease indication and health facility level. This calls for more judicious use of these antibiotics, given the rising antimicrobial resistance patterns to CAA in Namibia. Treatment guidelines should be regularly updated to be in tandem with antimicrobial resistance patterns.





Title of the abstract:	Prevalence and practice of non-prescription sale and dispensing of antibiotics in selected community retail pharmacies in Lusaka district of Zambia
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In Zambia, like most parts of the world, antibiotics are categorized as prescription-only medicines. Global estimates reveal that over 50% of antibiotics are purchased privately without a prescription from pharmacies, unlicensed drug stores or informal vendors. Left unchecked, continued irrational use of antibiotics poses huge consequences on public health.

# **Objectives**:

To conduct a situational analysis of the prevalence and practice of non-prescription sale and dispensing of antibiotics in community retail pharmacies of Lusaka district, Zambia. Methods:

A descriptive cross-sectional survey undertaken in 73 randomly selected registered community retail pharmacies in Lusaka district. A structured interviewer-administered questionnaire was used to collect quantitative data. One pharmacy person at each selected retail pharmacy was spot-interviewed after obtaining informed consent. Data was analyzed using SPSS version 20 software. Ethical approval was granted by University of Zambia, School of Medicine Research Ethics Committee (IRB00001131 of IORG0000774).

# Results:

From the 73 registered community pharmacies surveyed, pharmacy personnel interviewed included 56% male, 44% female out of which 55% were pharmacy technologists, 33% were pharmacists, and 11% were non-pharmaceutical personnel. 34 had <5 years work experience, 29 had worked 5 to 10 years, whereas only 10 had >10 years work experience in pharmacy. Majority (97%) indicated that customers frequently requested to purchase antibiotics without a prescription. All respondents (100%) dispensed some antibiotics without a prescription. Commonly dispensed antibiotics included: Amoxicillin (52%), Cotrimoxazole (25%) and Metronidazole (23%). Pharmacy personnel usually asked clients the indication for using the antibiotic (94%), counselled clients on dosing instructions (96%), and would suggest changes to customers' antibiotic choice (97%).

# Conclusions:

Findings of this study strongly suggest that non-prescription sale and dispensing of antibiotics in community retail pharmacies in Lusaka is a common and frequent practice. Concerted public education on the risks and stronger regulatory enforcement on dispensing antibiotics is urgently required.





Title of the abstract:	EVALUATION OF CEFTRIAXONE USE AT THE GHANA POLICE HOSPITAL
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Widespread empiric use of antibiotics such as ceftriaxone exist especially in developing countries. This has raised concerns of rational use due to increasing bacterial resistance.

#### **Objectives**:

This study sought to evaluate ceftriaxone utilization at the Ghana Police Hospital.

#### Methods:

This cross-sectional study evaluated the appropriateness of prescribed ceftriaxone of 251 patient medication records presented at the Pharmacy Department of the Ghana Police Hospital between January and June 2015. Data was obtained using the pharmacy department's drug evaluation form. Assessment of data was done using a modified WHO drug utilization evaluation criteria, with reference to the national standard treatment guidelines and ceftriaxone package insert (Roche).

# Results:

The top six conditions for which ceftriaxone was prescribed were comorbid malaria with bacterial infections, urinary tract infections, sepsis, gastroenteritis, upper respiratory tract infections and appendicitis. Appropriateness of indication for which ceftriaxone was prescribed was 53 % (n = 218), and most prescribed doses were 1 gm (41.4 %) and 2 gms (39.4 %). Stat dose and once daily dosage regimen constituted 51.4 % and 84.5 %, respectively. Common duration of treatment were 1 (51.4%) and 2 days (35.1%). Inappropriate prescribing of ceftriaxone was observed with respect to duration, indication, possible drug-drug interaction and complementary antibiotic therapy. However, overall actual threshold for all prescribing indicators assessed was 94.1 %, as against expected threshold of 98.1 %.

# **Conclusions**:

Appropriateness of ceftriaxone prescribed was less than expected threshold, therefore, continual education of prescribers at the hospital is required to improve antibiotic use.





Title of the abstract	Infant Cotrimoxazole Prophylaxis Associated with Commensal Gut Flora Resistance
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for HIV-exposed infants until the risk of HI antiretroviral treatment (ART), postpartum and the risks and benefits of extended infa <b>Methods</b> : The Mpepu Clinical Trial, condu- either CTX or placebo between 14 and 34 months. In 2014-2015, stools were collect (mos), and stored at -70°C prior to culture susceptibility testing by Kirby Bauer method 10µg) in Mueller Hinton agar. Disc diffusion classified as resistant to the antibiotic and organism. Fisher's exact testing was used (CTX/placebo) by study visit, occurrence of Division of AIDS (DAIDS) grade 3 or 4 def <b>Results</b> : A total of 380 stool samples from months, and 112 at 6 months; 446 organis Klebsiella spp; consisting of K. pneumonia spp was common at the randomization vis CTX-randomized infants were more likely (p<0.001 for both), and E coli isolates were pattern similar at 6 mos. 86 infants were from their 3 and/or 6 mos specimen. Amore resistance at 3 and/or 6 mos. Compared sensitive to CTX, there was no difference DAIDS grade 3 or 4 diarrheal illness (3 vs <b>Conclusions</b> : Infant CTX prophylaxis incu- gastrointestinal bacteria, without apparent	rganization recommends Cotrimoxazole (CTX) prophylaxis V transmission ends. However, with scale-up of maternal mother-to-child HIV transmission is on the decline globally, ant CTX prophylaxis need to be re-evaluated in this context. Ucted in Botswana, randomized HIV-exposed infants to days of life and continued the intervention through 15 ted from infants at randomization and at 3 and 6 months a. In specimens that grew E coli or Klebsiella spp, antibiotic od was done for CTX (CTX 25µg) and Amoxicillin (Amox on of < =10mm for CTX and $\leq$ 13 mm for Amox were $\geq$ 16 mm for CTX and $\geq$ 17 mm for Amox as sensitive to the d to compare resistance by randomization arm of diarrheal illness or pneumonia after randomization using finitions, and death in the first 12 months. In 221 infants were analyzed: 116 at randomization, 152 at 3 sms grew, including 206 (46%) E. coli and 135 (31%) ae and K. oxytoca. Resistance to both E coli and Klebsiella sit but did not differ by study arm (See Figure). At 3 months, to have E coli and Klebsiella spp resistance to CTX re also more likely to have Amox resistance (p= 0.02). This randomized to CTX with E coli and/or Klebsiella spp with CTX-randomized infants with E coli and Klebsiella spp in prevalence of death (1 vs 0; p = 1.0), or episodes of 0; p = 1.0) or pneumonia (1 vs 0; p = 1.0) through 12 mos. reased both CTX- and Amox-resistant commensal t clinical consequences. Further research is needed to iologic, and public health impact of extended CTX





Title of the abstract:	Effect of changing from first- to Second- Line Antiretroviral Therapy on Renal Function
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Tenofovir disoproxil fumarate (TDF) and lopinavir/ritonavir (LPV/r) can cause renal impairment with this combination co-administered during second-line combination antiretroviral therapy (cART). Consequently, potentially associated with a greater risk of nephrotoxicity.

# **Objectives:**

Assess the effects of second-line cART on renal function among patients receiving cART at the HIV clinic at the Katutura Intermediate Hospital (KIH), Namibia.

# Methods:

Retrospective longitudinal study among patients receiving cART. A list of patients on second-line cART was generated from the electronic Dispensing Tool (EDT - The EDT is a computerised database that stores cART dispensing records for all patients receiving ART in the public sector in Namibia).

# **Results:**

71 patients received TDF, zidovudine or stavudine, each combined with 3TC (TDF/lamivudine)/NVP (Nevirapine) or 3TC/ EFV (Efavirenz). Before second-line cART, 46.5% had abnormal kidney function. First-line cART had no relationship with the calculated creatinine clearance (CrCl). During second-line cART, more males than females had abnormal renal function and more females experienced increases in CrCl. Calculated CrCl during second-line cART related strongly with CrCl during first-line cART; time spent on cART had a weak relationship with CrCl.

# **Conclusions:**

Patients on first-line cART for several years without renal impairment may experience new onset impairment during cART. Patients with pre-existing renal impairment just before switching to second-line cART may experience a further decline in their renal function.



Title of the abstract:	The Impact of a Change in the CD4 Threshold on HIV Treatment in Rwanda: Interrupted Time Series Analysis
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# Background:

In recent years, many countries have increased the threshold beyond which HIV+ individuals receive access to antiretroviral therapy (ART). Concerns have been raised, however, about the cost implications of such changes.

# **Objectives:**

We studied the impact of such a change in Rwanda, one of the first countries to move from ART initiation at CD4 <500.

# Methods:

We studied monthly data from the TRACNET system to study the impact of Rwanda's 2014 change in treatment initiation at CD4 counts <350 to <500. Using interrupted time series, we analyzed changes in the number of individuals initiating ART, the total number receiving ART, and loss to follow-up.

# **Results:**

We found the change in CD4 threshold led to an immediate increase of 743 people initiating treatment each month (51% increase, 95% CI: 487 to 1000, p<0.001), but a decrease in trend meant this returned to the baseline level within 2 years. Overall, this increase in starters equated to a less than 1% change in the total number of people receiving ART treatment. The number of patients lost to follow-up decreased by 248 per month immediately following the change, and this lower rate persisted (40% decrease, 95% CI: -337 to -154, p<0.001).

# **Conclusions:**

Rwanda's change in the threshold for ART initiation led to a sharp short-term increase in the number of people initiating treatment, but this increase was short-lived and did not translate into a substantial increase in overall treatment utilization. It is likely that current moves to treatment upon diagnosis will have a similar impact.





Title of the abstract	Effect of Renal Function Assessment Methods on Tenofovir Disoproxil Fumarate's Safety Reports: Pharmacovigilance
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In Namibia, the Cockcroft-Gault (CG) method is recommended for monitoring renal function in HIV patients receiving Tenofovir Disoproxil Fumarate (TDF)-containing antiretroviral therapy (ART).

#### **Objectives:**

We set out to find out if the CG method would potentially increase the number of adverse reaction reports for TDF.

#### Methods:

This was a retrospective longitudinal study. The population was patients on 2<sup>nd</sup>-line ART, at Katutura Intermediate Hospital. Renal function was assessed using CG and Chronic Kidney Disease-Epidemiology (CKD-EPI) methods. We used Pearson correlation; Cohen's Kappa; and linear-regression coefficients; and Bland-Altman plots to assess relationship and agreement between CG and CKD-EPI. We set the confidence level at 95%, and statistical significance at a p-value <0.05.

# **Results:**

71 patients were included in this study: 57.7% were female. The majority (62%) received TDFcontaining 1<sup>st</sup> line ART. All patients received 2<sup>nd</sup>-line ART containing TDF/ lamivudine (3TC)/ zidovudine (AZT) and LPV/r. The patients had spent a mean of  $5.2\pm2.7$  and  $1.8\pm0.5$  years on 1<sup>st</sup>- and 2<sup>nd</sup>- line ART, respectively. Before switching to 2<sup>nd</sup>-line ART 40.8% (n=29) and 8.5% (n=6) had an abnormal eGFR according to CG and CKD-EPI methods, respectively. During 2<sup>nd</sup>-line ART, 47.9% (n=34) and 7% (n=5) patients had an abnormal eGFR, by CG and CKD-EPI methods, respectively. According to CG and CKD-EPI methods, 10 and 2 patients experienced decline in eGFR respectively. Pearson correlation showed a strong relationship between eGFR measurements during 1<sup>st</sup>- and 2<sup>nd</sup>line regimen: r=0.803 and r=0.749; p=0.000. However, Cohen's kappa revealed a lack of agreement between CG and CKD-EPI methods: *k*=0.224 (p=0.003) and *k*=0.110 (p =0.042). The Bland-Altman plots and linear regression analysis confirmed this: -0.191 (p=0.001), and -0.336 (p=0.001).

# **Conclusion:**

The CG method has the potential to report more cases of TDF-associated renal impairment, compared with CKD-EPI; however, the reports may not be true clinical events of renal impairment. Confirmatory studies are required before CG can be relegated.





Title of the abstract	Adverse drug reactions to antiretroviral therapy in Kenya
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There are 41.7% adults on antiretroviral drugs (ARVs) in Kenya. Despite these drugs reducing morbidity and mortality, they also cause adverse drug reactions (ADRs) which affect patients' adherence. The Pharmacy and Poisons Board (PPB) in Kenya collects Individual Case Safety Reports (ICSRs) generated from ADR cases by a spontaneous reporting system.

#### **Objectives:**

To analyse the ICSRs for severity, outcomes and risk factors associated with ADRs due to antiretroviral therapy (ART) from the spontaneous reporting database in Kenya from January 2014 to December 2014.

# Methods:

A retrospective cross-sectional study collected 850 ICSRs on ART-related ADRs reported between January and December 2014 from the National Pharmacovigilance System at the PPB in Kenya. The 729 ICSRs included in the study were analysed using IBM SPSS statistics version 21 software.

#### Results:

There were more females (63.4%) cases. The mean age of the cases was 40 (SD + 14) years. Lipodystrophy was the most commonly reported ADR (42.1%). Stavudine was suspected in most of the ADRs at 44.7% of all the cases. Most of the ADRs reported were mild (44.4%) with 85.5% of the cases having the offending drug withdrawn. Complete recovery was reported in 11.9% of the cases while four died due to an ADR. Allergies and Stevens Johnson Syndrome (SJS) were independent predictors of severity. Older age, being male and having more than one ADR increased the risk of having an undesirable outcome or no recovery.

# **Conclusions:**

Most of the patients were on stavudine (D4T) based regimens explaining why lipodystrophy was the most common ADR. Concomitant cotrimoxazole was an independent predictor of skin rashes and SJS. The findings in this study emphasize the need for close monitoring and follow up of all patients on ART and concomitant cotrimoxazole.





Title of the abstract:	Antimalarial drugs treatment pattern among pregnant women attending antenatal care clinics in Anambra state, South East Nigeria
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Prompt and effective treatment of malaria in pregnancy in line with recommended guidelines is essential for preventing adverse events of malaria in pregnancy. Regular review of treatment practices has been recommended for identifying opportunities for promoting and improving the rational and effective use of antimalarial (AM) drugs in pregnancy.

# **Objectives:**

The study aimed to determine the extent to which the use of antimalarial drugs in pregnancy conforms to policy guidelines in selected communities of Anambra state, south east Nigeria

# Methods:

Prescription records of pregnant women treated for malaria in selected primary and secondary health facilities in the state were reviewed to assess the pattern of prescription of AM drugs over a six-month period. Data were collected for drugs prescribed for prevention and treatment at each trimester of pregnancy and analysed to determine conformity to recommended guidelines for malaria treatment in pregnancy

# Results:

Among a total of 859 antenatal care records reviewed, majority, 715 (83.2%) of cases occurred in the 2<sup>nd</sup> and 3<sup>rd</sup> trimesters. ACTs, 40.9% (351/859) were the most prescribed AM drugs for both treatment and prophylaxis in all trimesters. Overall, only 68.5% (588/859) of prescriptions conformed to recommendations while 31.5% was prescribed contrary to policy. The first trimester was the most violated period in which the use of currently recommended AM drugs occurred only in 11.8% (17/144) of cases. In the 2<sup>nd</sup> and 3<sup>rd</sup> trimesters, up to 79.8% of pregnant women received appropriate drugs for both treatment and prevention. Artemether-lumefantrine (AL) was the most prescribed AM drug regimen

# **Conclusions:**

Current practice indicates significant use of non-recommended antimalarial drugs contrary to policy guidelines for malaria treatment in pregnancy. This has implications for the safety of the unborn child and increased burden of malaria in pregnant women. Policy strategies are needed to improve adherence to malaria treatment guidelines in pregnancy to ensure the safety of the unborn child and the pregnant mother.



# UNIVERSITY BOTSWANA

# Second Training Workshop and Symposium MURIA Group 25 – 27 July 2016 University of Botswana, Gaborone

Title of the abstract:	Adherence to antiretroviral treatment amongst patients at a clinic in South East District, Botswana
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# Background:

Strict adherence (≥95%) to antiretroviral therapy (ART) is essential for individual and programmatic treatment success. Sub-optimal adherence has serious public health consequences, necessitating continuous monitoring.

# **Objectives:**

To determine adherence to ART amongst patients at Lesetlhana Clinic, Botswana, using pill counts, two self-report measures and a composite measure; to identify possible factors contributing to non-adherence.

# Methods:

A quantitative descriptive study was conducted amongst 304 adult patients. Three months' retrospective pill count data were collected from clinic records and mean adherence percentage calculated. Self-reported adherence using two measures (set of four questions; rating scale) and factors contributing to non-adherence were collected in an interview with a structured questionnaire. Proportions of adherent (≥95%) patients were calculated according to each measure, and for a composite score based on all three measures. Ethical clearance and written informed consent were obtained.

# **Results:**

Of the 304 participants, females predominated (66.1%) and the mean age was 40.4 (SD:9.3) years. Mean duration on ART was 52.5 (SD:33.94) months. Distance travelled to the clinic was an average of 5.9 (SD:10.5) km. Although mean pill count adherence (3 months) was 98.0% (SD:2.2), 88.2% of patients were categorised as  $\geq$ 95% adherent with the pill count, 80.6% with the self-report questions and 78.9% with the rating scale. Adherence with the composite measure was significantly lower (60.86%; p<0.001). Challenges with adherence as reported by 87 patients, included arriving home late (33.3%), forgetfulness (23.0%), visiting or attending functions (19.5%), alcohol (18.4%) and medication side-effects (16.1%).

# **Conclusions:**

Mean pill count adherence was higher compared to the percentage of patients categorised as ≥95% adherent. Three individual adherence measures yielded different results and all significantly higher than a composite measure. Adherence challenges were identified despite high mean pill count adherence. Results illustrated the importance of adherence monitoring and using a combination of adherence measures.





Title of the abstract	Incidence of neuropsychiatric side effects of efavirenz in HIV-positive treatment-naïve patients in public-sector clinics in the Eastern Cape
Name of the submitting author	Razia Gaida
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Details of other co-authors including their organizations/ affiliations	<ul> <li>Ilse Truter, Professor – Nelson Mandela Metropolitan University</li> <li>Christoffel Grobler, Professor – Nelson Mandela Metropolitan University</li> </ul>

# Background:

It is acknowledged that almost half of patients initiated on efavirenz will experience at least one neuropsychiatric side effect.

#### **Objectives:**

The aim was to determine the incidence and severity of neuropsychiatric side effects associated with efavirenz use in five public-sector primary healthcare clinics in the Eastern Cape.

#### Methods:

The study was a prospective drug utilisation study. A total of 126 medical records were reviewed to obtain the required information. After baseline assessment, follow-up reviews were conducted at 4, 12 and 24 weeks in 2014 to 2015.

#### **Results:**

The participant group was 74.60% female (n=94) and the average age was  $37.57\pm10.60$  years. There were no neuropsychiatric side effects recorded for any patient. After the full follow-up period, there were a total of 49 non-adherent patients and one patient had demised. A non-adherent patient was defined as a patient who did not return to the clinic for follow-up assessment and medication refills 30 days or more after the appointed date. Some patients (n=11) had sent a third party to the clinic to collect their ART. The clinic pharmacy would at times dispense a two month's supply of medication resulting in the patient presenting only every two months.

# **Conclusions:**

Further pharmacovigilance studies need to be conducted to determine the true incidence of these side effects. Healthcare staff must be encouraged to keep complete records to ensure meaningful patient assessments. Patients being initiated on ART need to personally attend the clinic monthly for at least the first six months of treatment. Clinic staff should receive regular training concerning ART including changes made to guidelines as well as reminders of side effects experienced.





Title of the abstract	Antimalarial prescribing patterns in South Africa
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Email address of the submitting author	ilse.truter@nmmu.ac.za
Details of other co-authors including their organizations	Johan Lamprecht, Department of Clinical Pharmacy, King Khalid University, Abha, Kingdom of Saudi Arabia

# Background:

Malaria is endemic in certain areas of South Africa, yet little is known about the prescribing patterns of antimalarials.

# **Objectives:**

The primary aim of the study was to determine the dispensing patterns of antimalarial products in a community pharmacy patient population in South Africa.

# Methods:

A retrospective, cross-sectional drug utilisation study was conducted on a 2013 pharmacy database. Both medicines reimbursed by private medical aid schemes and private purchases were included. Records for antiprotozoals (ATC group P01) were extracted, with the focus on antimalarials.

# Results:

A total of 140 132 antiprotozoal products were dispensed. Most products (67.28%) were for agents against amoebiasis and other protozoal diseases, followed by antimalarials (31.54% of products). A total of 19 121 patients (52.72% females) were prescribed 44 191 antimalarial products. The average age of these patients was 49.81 (SD=15.64) years. Half of all the antimalarial products dispensed were for chloroquine (49.39%), followed by mefloquine (19.32%), the combination of atovaquone and proguanil (19.21%) and quinine (11.09%). Other active ingredients were artemether in combination with lumefantrine (386 products), the combination of sulfadoxine and pyrimethamine, halofantrine hydrochloride and pyrimethamine. Most products were prescription-only medicines. There was an increase in the number of products dispensed from July to December, that is, towards the warmer months of the year in South Africa. The northern provinces of South Africa (North-West, Gauteng, Mpumalanga and Limpopo) had the highest number of products dispensed. Chloroquine accounted for half of antimalarial medicines. However, chloroquine has dual usage for malaria and rheumatoid arthritis, and the high chloroquine prescribing rate may therefore not only reflect malaria prescriptions. It confirms the importance of capturing diagnoses in databases. Nearly all antimalarials were prescription-only medicine.

# **Conclusions:**

Pharmacists, together with other health care practitioners, have an important role in malaria prevention.





Title of the abstract:	Adherence to Antiretroviral Therapy in HIV- Infected Children and Adolescents Attending Sekou Toure Care and Treatment Clinic in Mwanza, Tanzania
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# Introduction:

Patients who are infected with human immunodeficiency virus (HIV) have to use a combination of drugs throughout their life time. The HIV mutates continuously and the mutants may be resistant to any of the prescribed drugs and hence the necessity for the combination therapy. Compliance to the prescribed antiretroviral drugs (ARVs) is a key factor in the success of antiretroviral therapy (ART).

# **Objectives:**

This study aimed at examining the extent at which children below 18 years complied with the prescribed drugs. The study also looked for some of the factors which could have been the cause of non-adherence to the prescribed medicines.

# Material and Methods:

Children (aged between 8 and 18 years) who were selected to participate in the study were among those attending the Care and Treatment Center (CTC) at Sekou Toure Referral Hospital. After parents/guardians had given informed consent, 185 children were recruited into the study. A cross-sectional study design using questionnaires and pill counting was carried out to determine non-adherence to ART and the factors which could be associated with it.

# Results:

Based on self-report adherence method, about 70% of the children showed 100% adherence to ARV therapy. The pill counting method revealed that only 22.2% of the participants were more than 95% adherent. Friendly interaction between the drug dispensers and the children, employed parent/ guardian and age of the child showed a positive association with adherence to ART. Forgetfulness on the part of parent/ guardian and child was the main reason for non-compliance.

# **Conclusions:**

There was a big discrepancy between the self-reporting and pill counting results (70% versus 22% respectively). It is possible there were false positives in self-reporting and similarly dispensing errors could produce false negatives. Cordial relationship between the drug dispensers and parent/guardian/child, age of the child and unemployed parent/guardian had positive effects on adherence to therapy.





Title of the abstract	The effect of health education intervention on the level of knowledge of HIV/AIDS among factory workers in Matsapha, Swaziland
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# Background:

HIV/AIDS has remained a health risk/challenge all over the world. Knowledge about HIV/AIDS in Swaziland and specifically amongst factory workers requires serious/ urgent attention. *Objectives: To* assess the effect of health education intervention on the level of knowledge about HIV/AIDS among factory workers in Matsapha, Swaziland

# Methods:

Quasi-experimental study was done among workers at the Texray Garment factory in March 2016. Factory workers (n=80) meeting the eligibility criteria were randomly assigned to either the experimental group or control group using systematic sampling techniques. Paired-samples t-test was used to assess any difference between pre-test/the post-test results of both groups. Independent ttest was also used. Chi-square used for analyzing nominal data. Statistical significance was set at  $p \le 0.05$ 

# Results:

All (100%) study participants had poor knowledge at pre-test. For the experimental group at post-test, 27.5% (n=11) had good knowledge and 72.5% (n=29) had average knowledge. For the control group at post-test, all (100%; n=40) still had poor knowledge. There was a statistically significant increase in knowledge scores in the experimental group from Time 1 (pre-test) [M=12.6, SD=5.19] to Time 2 (post-test) [M=33.15, SD=5.88, t(39)= -18.024,  $p \le 0.05$ ]. The eta squared statistic (0.89) indicated a large effect size. A paired-samples t-test showed that there was no statistically significant increase in knowledge scores in the control group from Time 1 (pre-test) [M=12.75, SD=7.94] to Time 2 [M=12.68, SD=8.07, p>0.05]. An independent-samples t-test showed a significant difference in the post-test scores for the experimental group (M=33.15, SD=5.88) compared to the control group [M=12.68, SD=8.07; t(78)=12.966, p=0.0001]. The magnitude of the differences in the means was large (eta squared=0.68).

# **Conclusions:**

Health education intervention improved factory workers' knowledge about HIV/AIDS. As a result, I suggest concerted educational efforts and initiatives by both governmental and Non-governmental organizations to reduce the incidence of HIV/ AIDS in the future.