

**Original Article****Open Access****Roll out of a successful antimicrobial stewardship programme in Lagos University Teaching Hospital Nigeria using the Global-Point Prevalence Survey**

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**Abstract:**

**Background:** Antimicrobial resistance (AMR) has become a public health emergency with increasing rates and spread globally. Antimicrobial stewardship (AMS) has been advocated to reduce the burden of antimicrobial resistance, promote rational and appropriate use of antibiotics and improve clinical outcomes. Education and training are one of the AMS interventions to improve antimicrobial use. We present the roll out of a successful AMS programme with education and training using the Global-PPS as data collection tool to measure AMS interventions and impact.

**Methodology:** This was a cross sectional study on the implementation of an AMS programme at the Lagos University Teaching Hospital. Global PPS was conducted in 2015 to collect baseline data which was used to identify targets for quality improvement in AMS and was repeated in 2017 and 2018 to measure impact of AMS interventions. AMS interventions included education, feedback of Global-PPS result and writing of the hospital-wide antibiotic policy based on the baseline data.

**Results:** Out of the 746 inpatients surveyed, 476 (68.3%) had received at least one antimicrobial on the days of Global-PPS. The antimicrobial prescribing rates reduced significantly over the three time periods. In 2015, 82.5% were placed on antimicrobials, 65.5% in 2017 and 51.1% in 2018 ( $p < 0.00001$ ). The documentation of indication for treatment significantly improved from 53.4% in 2015 to 97.2% in 2018 ( $p < 0.0001$ ). Stop review date also significantly improved from 28.7% to 70.2% in 2018 ( $p < 0.00001$ ). Surgical prophylaxis for more than 24 hours reduced significantly from 93.3% in 2015 to 65.7% in 2018 ( $p = 0.002$ ) even though the prevalence was still high. The three most commonly administered antimicrobial groups were third generation cephalosporins, imidazole derivatives and quinolones. The most commonly prescribed antibiotics for surgical prophylaxis were ceftriaxone and metronidazole in 2015 and ceftriaxone in 2017.

**Conclusion:** The use of education and training as AMS intervention in a limited resource setting clearly made impact on antimicrobial prescribing patterns in the hospital. Global-PPS is useful to set quality improvement targets and for monitoring, evaluation and surveillance of an AMS programme.

**Keywords:** Antibiotic, Stewardship, Resistance, Education, Global-PPS

Received Feb 17, 2021; Revised Mar 4, 2021; Accepted Mar 17, 2021

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**Déploiement d'un programme réussi de gestion des antimicrobiens à l'hôpital universitaire de Lagos au Nigéria à l'aide de l'enquête sur la prévalence globale des points**

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## Abstrait:

**Contexte:** La résistance aux antimicrobiens (RAM) est devenue une urgence de santé publique avec des taux croissants et une propagation mondiale. La gestion des antimicrobiens (AMS) a été préconisée pour réduire le fardeau de la résistance aux antimicrobiens, promouvoir l'utilisation rationnelle et appropriée des antibiotiques et améliorer les résultats cliniques. L'éducation et la formation sont l'une des interventions AMS pour améliorer l'utilisation des antimicrobiens. Nous présentons le déploiement d'un programme AMS réussi avec éducation et formation en utilisant le Global-PPS comme outil de collecte de données pour mesurer les interventions et l'impact de l'AMS.

**Méthodologie:** Il s'agissait d'une étude transversale sur la mise en œuvre d'un programme AMS à l'hôpital universitaire de Lagos. Le PPS mondial a été mené en 2015 pour collecter des données de base qui ont été utilisées pour identifier les cibles d'amélioration de la qualité dans la MGS et ont été répétées en 2017 et 2018 pour mesurer l'impact des interventions de MGS. Les interventions d'AMS comprenaient l'éducation, le retour d'information sur les résultats de Global-PPS et la rédaction de la politique d'antibiotique à l'échelle de l'hôpital sur la base des données de base.

**Résultats:** Sur les 746 patients hospitalisés interrogés, 476 (68,3%) avaient reçu au moins un antimicrobien les jours de Global - PPS. Les taux de prescription d'antimicrobiens ont considérablement diminué au cours des trois périodes. En 2015, 82,5% étaient placés sous antimicrobiens, 65,5% en 2017 et 51,1% en 2018 ( $p < 0,00001$ ). La documentation de l'indication thérapeutique s'est significativement améliorée de 53,4% en 2015 à 97,2% en 2018 ( $p < 0,0001$ ). La date d'arrêt de l'examen s'est également considérablement améliorée, passant de 28,7% à 70,2% en 2018 ( $p < 0,00001$ ). La prophylaxie chirurgicale pendant plus de 24 heures a considérablement diminué, passant de 93,3% en 2015 à 65,7% en 2018 ( $p = 0,002$ ) même si la prévalence était encore élevée. Les trois groupes antimicrobiens les plus couramment administrés étaient les céphalosporines de troisième génération, les dérivés d'imidazole et les quinolones. Les antibiotiques les plus couramment prescrits pour la prophylaxie chirurgicale étaient la ceftriaxone et le métronidazole en 2015 et la ceftriaxone en 2017.

**Conclusion:** L'utilisation de l'éducation et de la formation comme intervention AMS dans un contexte de ressources limitées a clairement eu un impact sur les modèles de prescription d'antimicrobiens à l'hôpital. Global-Le PPS est utile pour fixer des objectifs d'amélioration de la qualité et pour le suivi, l'évaluation et la surveillance d'un programme AMS.

**Mots clés:** Antibiotique, intendance, résistance, éducation, mondial-PPS

## Introduction:

Antimicrobial resistance (AMR) has become a public health emergency with increasing rates and spread globally. In Nigeria, the rate of carbapenem resistant *Klebsiella pneumoniae* increased from 5.2% in 2010 to 17.5% in 2015 (1,2). The increasing rate of AMR worldwide has led to increased length of hospital stay, antibiotic use, cost of hospitalization, morbidity and mortality. The drivers of AMR include irrational antimicrobial use, easy access to purchase of antibiotics over-the-counter, self-medication, poor compliance to prescribed antibiotics, lack of access to appropriate care and lack of adequate laboratory infrastructure for proper diagnosis (3). The global point prevalence survey (Global-PPS) of antimicrobial consumption and resistance

showed high prevalence of antimicrobial use in teaching hospitals across Nigeria. In four teaching hospitals (in southwest, northcentral and northwest Nigeria), antimicrobial use was 76% (4), while in southeast Nigeria, it was 78.2% (5).

To combat this rise in AMR, the World Health Organization (WHO) advocates the adoption of antimicrobial stewardship (AMS) by health-care providers to check and reduce the burden of antibiotic resistance (6). This strategy involves the application of objective interventions to influence prescribing practices, thereby promoting rationale and appropriate antimicrobial use (6). Although AMS has been adopted and practiced in many high-income countries, there are challenges with the implementation of AMS in low-and-middle-income-countries (LMIC). In Africa, some hos-

pitals in South Africa, Kenya and Tanzania have implemented AMS programmes which has shown an overall reduction in antibiotic use (7), and reduction in surgical site infection for those who implemented interventions targeted at surgical antibiotic prophylaxis (8).

In Nigeria, there is a national action plan on AMR but no national AMS programme. A few healthcare facilities have instituted AMS interventions. The challenges identified in AMS in tertiary hospitals in Nigeria include lack of funding, poor awareness of the usefulness of AMS by staff, lack of information technology (IT) infrastructure and lack of leadership support (9). In two surveys of AMS among tertiary health care facilities in Nigeria, only 30-35% of hospitals have AMS committees in place (9,10). The success of AMS depends largely on support from the hospital leadership, however none of the hospitals in a survey of AMS in tertiary healthcare facilities had leadership support for AMS (10).

With respect to the AMS interventions commonly used in the country, a study found that 24% of hospitals had facility specific antibiotic treatment guide- lines (10) while another study found only 5% (9); 12% of hospitals use formulary restriction with pre- authorisation and 18% of hospitals use post prescription review and 5% used education and training (9,10). Monitoring and evaluation of AMS programmes can be done using the Global-PPS (11). In Nigeria, there are 19 hospitals conducting the Global-PPS and reporting data to the global network.

The aim of this study was to present the roll out of a successful AMS programme with education and training and use of antibiotic policy using the Global-PPS to design AMS interventions and measure impact at the Lagos University Teaching Hospital, Nigeria.

## Materials and method:

### Study location

The study was conducted at the Lagos University Teaching Hospital (LUTH), a tertiary care hospital with 761 beds and 10,600 admissions annually. It comprises of adult medical and surgical wards, adult intensive care unit, paediatric medical and surgical wards and neonatal wards.

### Study design

This was a cross sectional study of audit of antimicrobial prescribing practices and resistance using the Global-PPS protocol (11). There was implementation of AMS programme and the Global-PPS conducted in 2015 was used to make a baseline assessment of antimicrobial prescribing practices to identify targets to improve quality of antimicrobial prescribing, design stewardship intervention to promote rational use of antimicrobials. The Global-PPS was repeated in 2017 and 2018 to

monitor rates of antimicrobial prescribing in adults and children and measure the impact of the AMS interventions. Fig 1 outlines the steps for implementation of AMS programme at the Lagos University Teaching Hospital

### **Step 1: Formation of antimicrobial stewardship committee**

In 2012, an AMS programme was set up in LUTH. A multidisciplinary AMS committee was formed and inaugurated by the Chief Medical Director with clear terms of reference. The committee consist of physicians, surgeons, paediatricians, gynaecologists, dentists, dental surgeons, epidemiologists, pharmacists, nurses, infection prevention and control specialists, clinical microbiologists, and staff from hospital administration. The committee has a physician leader who is a clinical microbiologist. A subcommittee was formed to develop a proposal to obtain baseline information on the burden of infection and antimicrobial use in the hospital but did not make any meaningful progress for three years due to lack of funds. The committee held meetings monthly. There was a 24-hour service clinical microbiology laboratory, infection prevention and control team and committee and department of pharmacy, with strong cooperation amongst members.

### **Step 2: Baseline data**

In 2015, there was a call for Global-PPS which was open to all hospitals around the world. LUTH participated in the Global-PPS and obtained baseline data to start the AMS programme.

### **Step 3: Intervention (Education and feedback with use of antibiotic policy)**

In 2016, a hospital grand round was held to present the result of the Global-PPS to the prescribers, pharmacists, nurses and other healthcare workers. This was an opportunity to educate the healthcare workers on rational antibiotic use and introduce them to the principles of antimicrobial stewardship. Education and awareness were done by the AMS team. More interventions were planned which included writing a hospital antibiotic policy and the requirement for each of the four major clinical departments (Medicine, Paediatrics, Surgery and Obstetrics and Gynaecology) to write their departmental antibiotic guidelines.

The AMS team visited each department to educate the prescribers and other healthcare workers on prudent antibiotic use, how to write guideline, and starting AMS. Each department was encouraged to write their guidelines which were to be ratified by the AMS committee and also to choose an AMS strategy. A hospital-wide antibiotic policy was formulated based on the hospital Global-PPS results which was distributed to all stakeholders (Appendix 1).

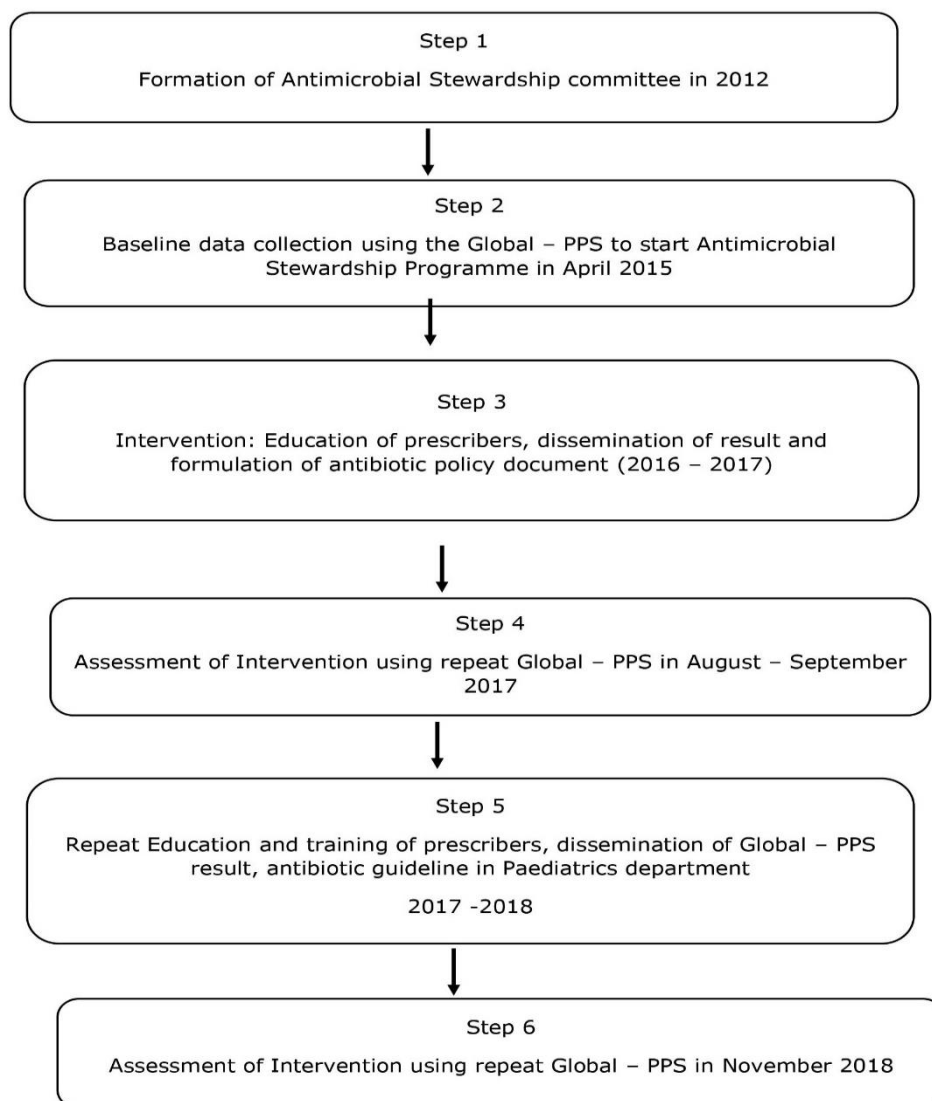


Fig 1: Steps for implementation of Antimicrobial Stewardship Programme at the Lagos University Teaching Hospital

Education involved presentation of the following topics at the hospital grand round; (i) Antimicrobial stewardship: choosing a strategy for LUTH; (ii) Feedback of the result of the Global-PPS in 2015; and (iii) Antibiotic policy/guideline and surveillance of multi-drug resistant organisms (MDRO). Education at the departments focused on; (i) the Global-PPS of antimicrobial consumption and resistance; (ii) results of antimicrobial prescribing in LUTH; (iii) antibiotic consumption in LUTH paediatric patients: trends in the last 3 years; (iv) antibiotic resistance pattern in LUTH in the last 2 years; and (v) management of infectious diseases: rational for antibiotic use.

Awareness was through celebration of the antibiotic awareness week in November each year. An antibiotic awareness week was celebrated in 2018, where some heads of departments were made antibiotic champions

and took oath to protect the use of antibiotics in their sphere of influence.

#### **Step 4: Assessment of effectiveness of intervention**

In 2017, the second round of Global-PPS was called and LUTH participated in April 2017. The repeat PPS provided a means to assess the effectiveness of the intervention (education and awareness). The result of the 2017 Global-PPS was disseminated to each of the four clinical departments to give feedback on the monitoring of the antimicrobial prescribing pattern in the hospital. The department of paediatrics formed an antibiotic management team consisting of doctors, pharmacists and nurses. The antibiotic management team wrote an antibiotic guideline and chose prospective audit with feedback as their AMS strategy. The challenges noted were limited

staff to implement the strategy, healthcare workers resisting change, lack of information technology resources and lack of funds. The department of surgery has also formed an antibiotic management team but is still working on the development of their local antibiotic guidelines. In 2018, the third Global-PPS was done and the results were also disseminated to the prescribers. The department of Paediatrics has since started using prospective audit and feedback as an AMS strategy.

#### Data collection

Data was collected by resident doctors in clinical microbiology in 2015, 2017 and 2018 using the Global-PPS protocol. All wards in the hospital were included for all surveys which was conducted on a single day in order to calculate correctly the denominator (number of admitted patients). On the day of the survey, all inpatients admitted and stayed overnight on a ward at 8 o'clock in the morning on the day of survey were counted in the denominator. All inpatients "on antimicrobial agents" at 8 o'clock in the morning on the day of survey were included in the numerator (i.e., a patient form is to be filled in for these patients only).

Exclusion criteria were; (i) day hospitalizations and outpatients. These were defined as ambulatory care patients, therefore, data from "day" surgery and "day" hospital units were excluded from the survey; and (ii) patients admitted after 8 o'clock on the day of the survey (even though these would be present by the time the survey is carried out). All patients/wards in the exclusion criteria were excluded from both the numerator and denominator data.

Data were collected using two forms, the ward form to collect denominator data and the patient form to collect numerator data. Data collected on the ward form included the date of survey, name of ward, ward type, ward activity, total number of admitted patients at 8am, total number of beds. Data collected on the patient form included hospital number, age, weight, ward activity, ward name, gender, treatment based on biomarker, whether culture was sent to the clinical microbiology laboratory.

The antimicrobial data included name of antimicrobial, dose, frequency, and route of administration. The others were diagnosis, reason in notes, stop/review date, type of indication, compliance to guidelines and information about empirical or targeted therapy. If therapy was based on microbiology data, then data was collected on targeted multidrug resistant organisms. The antimicrobials classification system used was the World Health

Organization's (WHO) Anatomic Therapeutic Chemical (ATC) classification ([www.whocc.no/atc\\_ddd\\_index](http://www.whocc.no/atc_ddd_index)). Antibiotics were further classified as 'Access', 'Watch', 'Reserve' or 'Not recommended' using the 2019 WHO AWaRe classification list (12). Antibiotics not listed in the AWaRe classification were listed as 'Unclassified'.

#### Data analysis

A web-based application was used for data-entry, validation and reporting as designed by the University of Antwerp (<https://www.global-pps.com>) (11) and exported as Microsoft Excel file. The prevalence of antibiotic prescription was calculated by dividing the number of patients treated with an antibiotic over the total number of inpatients surveyed. The prevalence of healthcare associated infection (HAI) was calculated by dividing the number of treated patients on at least one HAI over the number of inpatients surveyed. Data was analysed using the SPSS version 20 software. Data were presented as percentages or proportions. The Chi square test for trend was used to assess differences in the prevalence of antibiotic prescription and differences in quality indicators over the three PPS. The level of statistical significance was set at  $p < 0.05$ .

#### Results:

The total number of eligible inpatients surveyed in the three time periods (2015, 2017 and 2018) was 746 of which 573 were admitted on adult wards and 173 on paediatric or neonatal wards. Table 1 provides the general patient characteristics, antimicrobial use and HAI prevalence for the three time periods.

The antimicrobial prescribing rates reduced significantly over the three time periods (82.5% in 2015, 65.5% in 2017 and 51.1% in 2018 ( $p < 0.00001$ )). Fig 2 provides the antimicrobial prescribing rates for adults and paediatric/neonatal wards which also reduced significantly over time ( $p < 0.00001$ ). Overall, the proportion of patients treated with combination of (multiple) antimicrobials was 65.6% in 2015, 55% in 2017 and 69.9% in 2018, with a combination of two antimicrobials accounting for 42.4%, 35.5% and 58.3% respectively in 2015, 2017 and 2018 and three or more antimicrobial combination accounting for 23.2%, 19.5% and 11.6% in 2015, 2017 and 2018 respectively. A total of 19 (10.4%), 36 (14%) and 20 (6.6%) patients in 2015, 2017 and 2018 respectively were treated with at least one antimicrobial for HAIs. The prevalence of HAIs was higher among children and neonates (Table 1).

Table 1: General characteristics of patients, antimicrobial use and prevalence of healthcare associated infection

Characteristic	Year (%)		
	2015	2017	2018
Number of inpatients	183	258	305
Adults	144 (78.7)	209 (81.0)	220 (72.1)
Children and neonates	39 (21.3)	49 (19)	85 (27.9)
Patients treated with at least one antimicrobial	151(82.5)	169(65.5)	156(51.1)
Gender*			
Male	85 (56.3)	87 (51.5)	87 (55.8)
Female	66 (43.7)	82 (48.5)	69 (44.2)
Adults treated with at least one HAI	14 (9.7)	27 (12.9)	5 (2.3)
Children and neonates treated with at least one HAI	5 (12.8)	9 (18.4)	15 (17.6)

\*Defined for patients treated with at least one antimicrobial

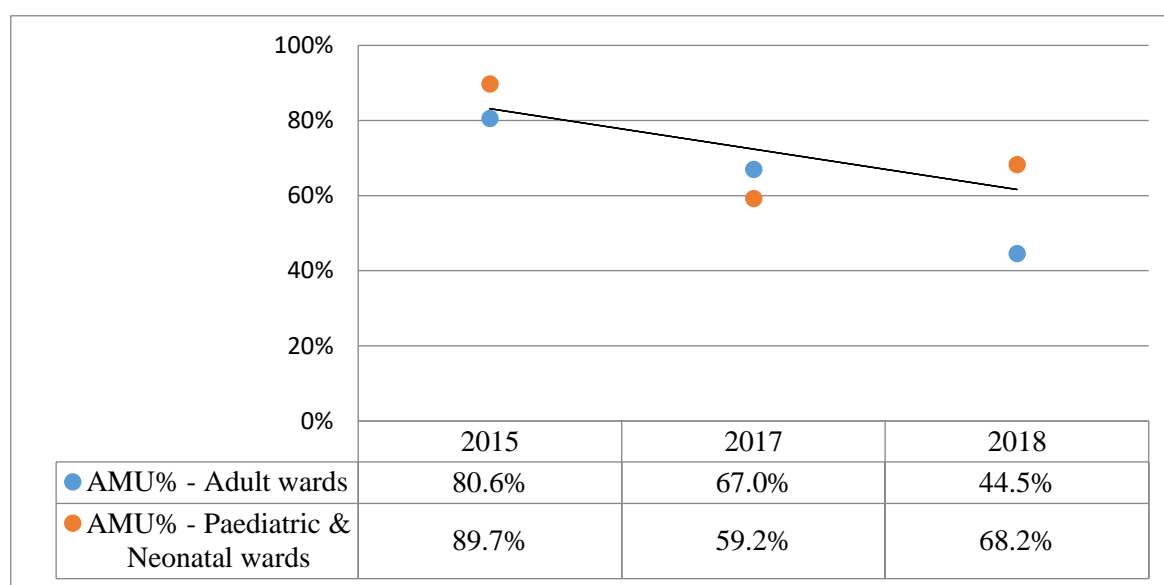


Fig 2: Antimicrobial use prevalence in adult and Paediatric/Neonatal wards (2015 – 2018)  
AMU – Antimicrobial use

A total number of 895 antimicrobials were administered for the three time periods, 307 in 2015, 303 in 2017 and 285 in 2018. Parenteral use accounted for 70% in 2015, 76.9% in 2017 and 76.8% in 2018. Table 2 provides the indication for antimicrobial prescribing over time. Most of the antimicrobials were administered for community acquired infections. Antimicrobial prescribing for HAI was highest in 2017 (20.4%). Antimicrobial prescription for surgical prophylaxis significantly increased steadily. For medical prophylaxis, antimicrobial prescription was highest in 2015 (16%).

Table 3 shows the antimicrobial agents prescribed during the three time periods of Global-PPS. Antibacterials for systemic use accounted for most of the antimicrobial prescriptions. The three most commonly administered antimicrobials during the three time periods were third generation cephalo-

sporins, imidazole derivatives and fluoroquinolones. The prescription of penicillins with extended spectrum, antimycobacterials and nitroimidazole derivatives (oral metronidazole) decreased over time, while the prescription of antimalarials and antivirals for systemic use increased over time.

The most commonly prescribed antibiotic for surgical prophylaxis were ceftriaxone and metronidazole in 2015 and 2018 (both represented 31.7% and 35.8% of prescriptions respectively) and ceftriaxone alone in 2017 (33.7%) (Fig 3). The ten most common diagnoses for which therapeutic antimicrobials were given are shown in Table 4. The most common diagnosis was skin and soft tissue infections. The proportion of antimicrobial prescription for sepsis and tuberculosis decreased over time while that of pneumonia and bone and joint infections increased over time from 2015 to 2018 (Table 4).

Table 2: Indications for antimicrobial use at three time periods (2015, 2017 and 2018)

Indication	Year (%)		
	2015 (n=307 AMP)	2017 (n=303 AMP)	2018 (n=285 AMP)
Community acquired infection	141 (45.9)	116 (38.3)	150 (52.6)
Health-care associated infection	30 (9.8)	62 (20.4)	33 (11.7)
Medical prophylaxis	49 (16)	24 (7.9)	28 (9.8)
Surgical prophylaxis	60 (19.5)	61 (20.1)	67 (23.5)
Other	0	7 (2.3)	7 (2.5)
Unknown	27 (8.8)	33 (10.9)	0

AMP = Antimicrobial prescriptions

Table 3: Antimicrobial agents prescribed during the three time periods (2015, 2017 2018)

ATC	Antimicrobial	Year (%)		
		2015(n=307)	2017 (n=303)	2018 (n=285)
<b>J01</b>	Antibacterials for systemic use	262 (85.3)	276 (91.1)	254 (89.1)
J01AA	Tetracycline	0	1 (0.3)	0
J01CA	Penicillins with extended spectrum	14 (4.6)	10 (3.3)	0
J01CE	Beta-lactamase sensitive penicillins	1 (0.3)	1 (0.3)	0
J01CF	Beta-lactamase resistant penicillins	2 (0.7)	2 (0.7)	2 (0.7)
J01CR	Combination of penicillins including beta-lactamase inhibitors	10 (3.3)	21 (6.9)	19 (6.7)
J01DC	Second generation cephalosporins	16 (5.2)	17 (5.6)	14 (4.9)
J01DD	Third generation cephalosporins	86 (28)	75 (24.8)	81 (28.4)
J01DE	Fourth generation cephalosporins	0	3 (1.0)	1 (0.4)
J01DH	Carbapenems	11 (3.6)	10 (3.3)	11 (3.9)
J01EE	Combination of sulphonamides and trimethoprim	3 (1.0)	1 (0.3)	1 (0.4)
J01FA	Macrolides	2 (0.7)	4 (1.3)	2 (0.7)
J01FF	Lincosamides	5 (1.6)	6 (2)	3 (1.1)
J01GB	Other aminoglycosides	25 (8.1)	13 (4.3)	32 (11.2)
J01MA	Fluoroquinolones	38 (12.4)	45 (14.9)	31 (10.9)
J01RA	Combination of antibacterials	2 (0.7)	0	1 (0.4)
J01XA	Glycopeptide antibacterials	6 (2.0)	2 (0.7)	3 (1.1)
J01XD	Imidazole derivatives	40 (13)	64 (21.1)	52 (18.2)
J01XE	Nitrofurantoin derivatives	1 (0.3)	1 (0.3)	1 (0.4)
<b>J02</b>	Antimycotics	7 (2.3)	8 (2.6)	3 (1.1)
<b>J04</b>	Antimycobacterials	16 (5.2)	8 (2.6)	4 (1.4)
<b>J05</b>	Antivirals	0	0	6 (2.1)
<b>P01B</b>	Antimalarial	7 (2.3)	0	9 (3.2)
<b>P01AB</b>	Nitroimidazole derivatives	15 (4.9)	11 (3.6)	9 (3.2)

ATC = Anatomical Therapeutic Chemical

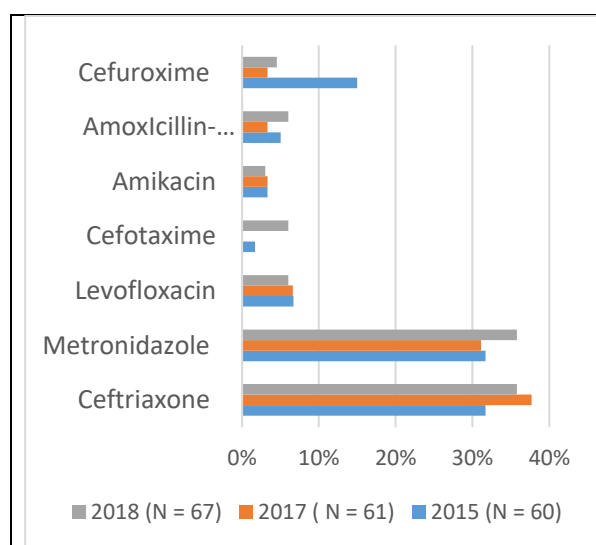


Fig 3a: Most frequently prescribed antibiotics for surgical prophylaxis

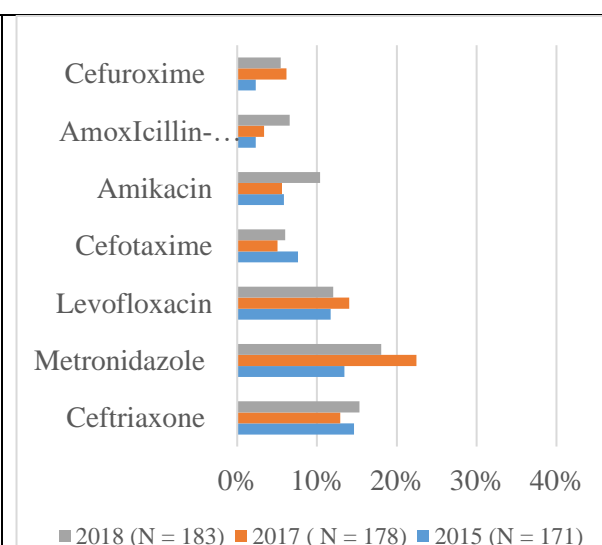


Figure 3b: Most frequently prescribed antibiotics for therapeutic use (community acquired infections and healthcare associated infections)

There was a general trend in favour of improvement in the quality indicators both for adult and paediatric/neonatal wards. The documentation of the reason for antimicrobial prescription (from 53.4% in 2015 to 97.2% in 2018) and stop-review date (from 28.7% to 70.2% in 2018) both significantly improved over time ( $p < 0.0001$ ) (Figs 4a & 4b). Prolonged surgical prophylaxis (for more than 24 hours) reduced significantly over time (from 93.3% in 2015 to 65.7% in 2018,  $p = 0.002$ ) mainly in the paediatric wards (Fig 4c). In the vast majority of cases, anti-microbials were administered empirically. Targeted therapy increased from 11% in 2015 to 13.1% in 2018 and the increase was mainly among paediatric and neonatal wards ( $p = 0.0003$ ) (Fig 4d). The

use of procalcitonin as a biomarker was only observed in 2018 on the paediatric/neonatal wards and was used to guide treatment in only 2.6% of inpatients prescribed at least one antimicrobial. There was no antibiotic guideline available in 2015 and 2017. An antibiotic guideline was available in the department of Paediatrics in 2018. The overall Access/Watch ratio increased from 0.62 in 2015, 0.72 in 2017 to 0.77 in 2018. Fig 4e provides the proportion of total antibiotic use according to the AwaRe classification. There was no antibiotic prescribed belonging to the reserve list. Only a few 'not recommended' ( $n = 6$ ) and one 'unclassified' antibiotic were prescribed for the three survey periods.

Table 4: Ten most common diagnoses treated with at least one therapeutic antimicrobial

Diagnosis	Year (%)		
	2015 (n=84)	2017 (n=96)	2018 (n= 100)
SST	18 (21.4)	23 (24)	19 (19.0)
Intraabdominal	6 (7.1)	17 (17.7)	12 (12.0)
Sepsis	16 (9.8)	16 (16.7)	14 (14.0)
BJ	5 (19.0)	11 (11.5)	14 (14.0)
Pneu	6 (7.1)	10 (10.4)	9 (9.0)
CNS	7 (8.3)	5 (5.2)	13 (13.0)
Upper UTI	6 (7.1)	3 (3.1)	3 (3.0)
Cystitis	0	3 (3.1)	2 (2.0)
OBYG	0	3 (3.1)	0
TB	4 (4.8)	3 (3.1)	2 (2.0)

CNS=Infection of central nervous system; Pneu=Pneumonia or lower respiratory tract infection; TB=tuberculosis; SST= Skin & Soft Tissue: Cellulitis, wound including surgical site infection, deep soft tissue not involving bone e.g., infected pressure or diabetic ulcer, abscess; BJ= Bone joint Infection: Septic arthritis (including prosthetic joint), osteomyelitis; Cys=lower urinary tract infection; Upper UTI=upper urinary tract infection including catheter related urinary tract infection, pyelonephritis;; OBYG=obstetric/gynaecological infections; Intra-abdominal= Intraabdominal sepsis including hepatobiliary, intra-abdominal abscess etc; Sepsis= sepsis, sepsis syndrome or septic shock with no clear anatomic site;

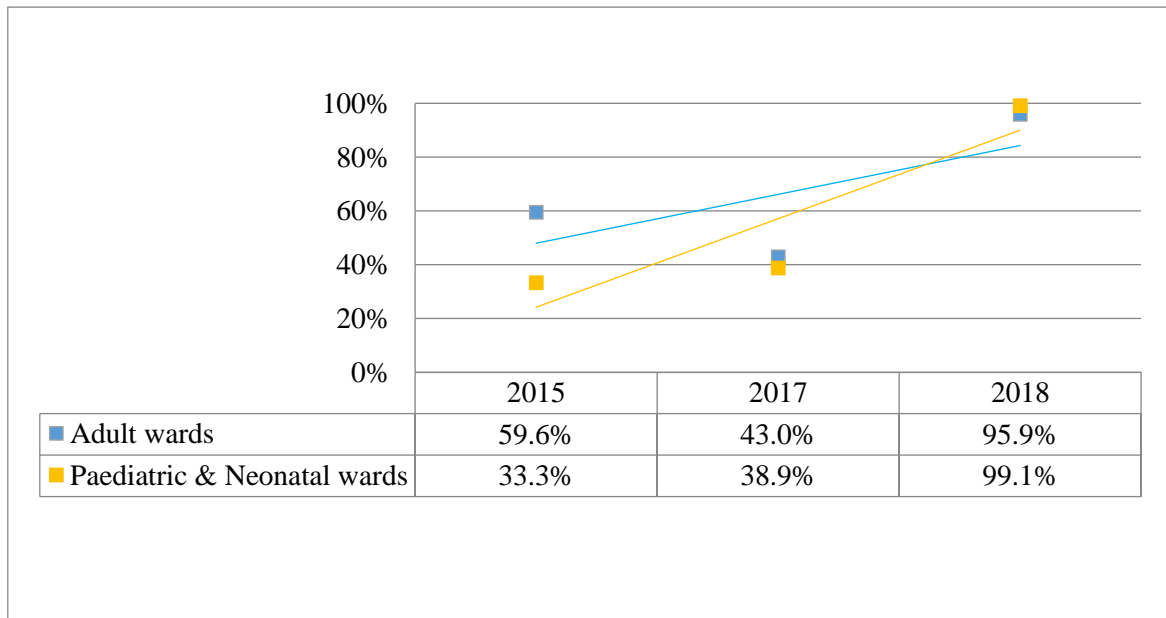


Fig 4a: Indication or reason documented in the notes



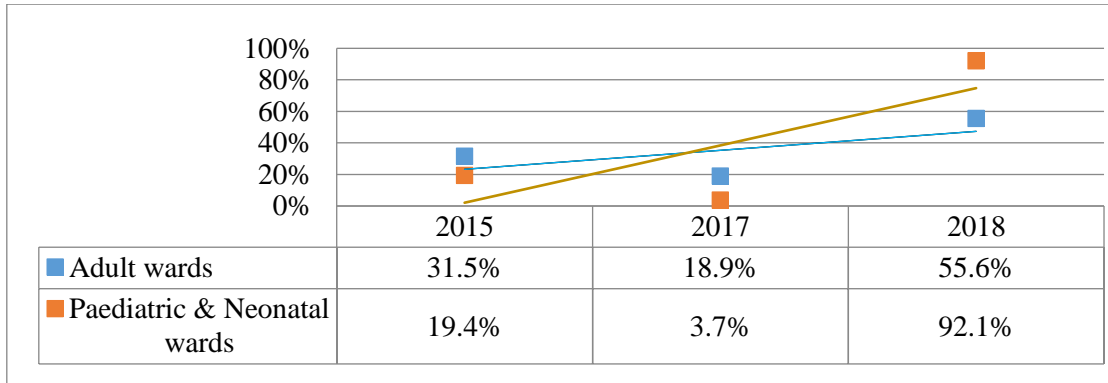


Fig 4b: Stop or review date documented in the notes

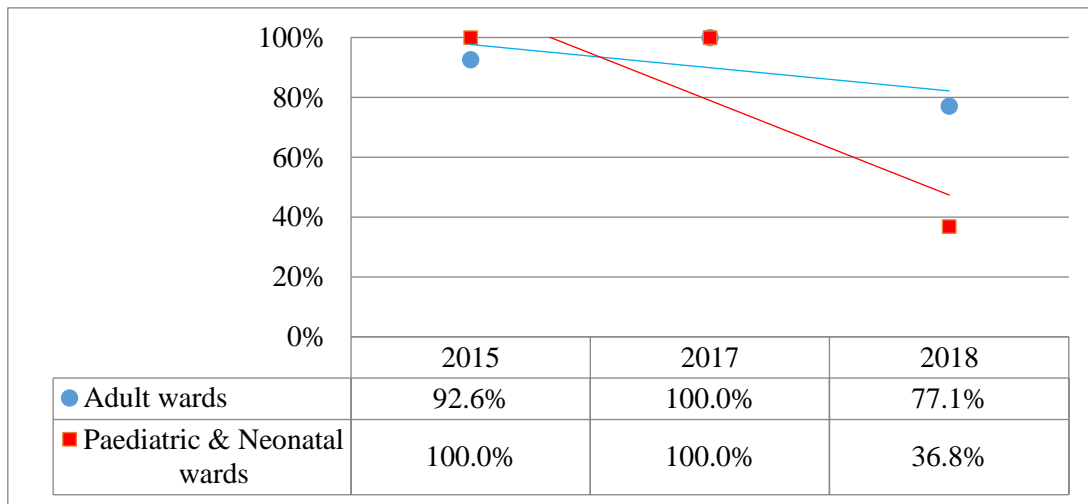


Fig 4c: Prolonged surgical prophylaxis (>24hrs)

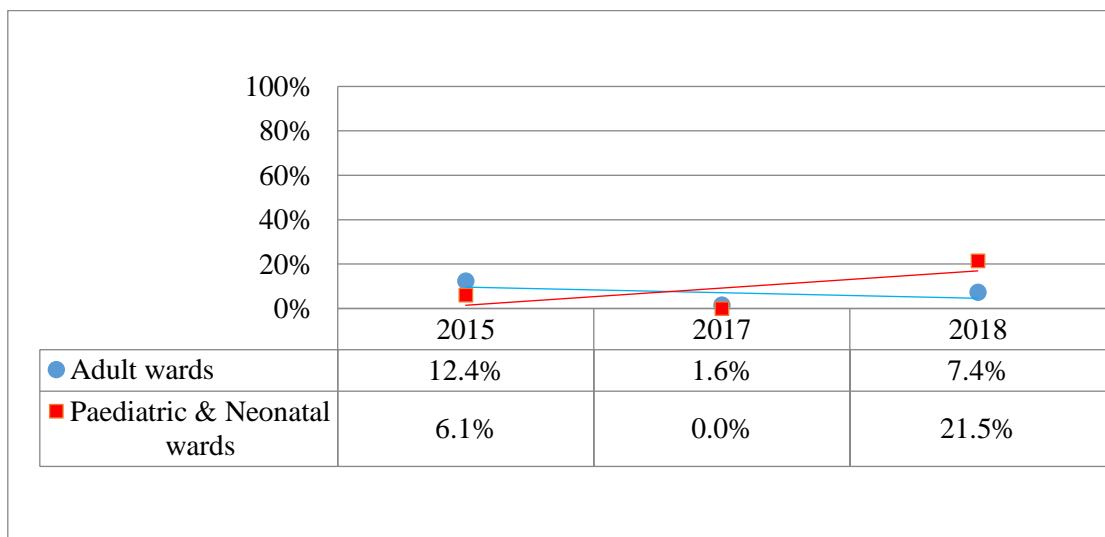


Fig 4d: Targeted prescribing of antibiotics (J01 (prophylactic prescribing is excluded)) following a microbiological result for Adult and Paediatric/Neonatal wards.

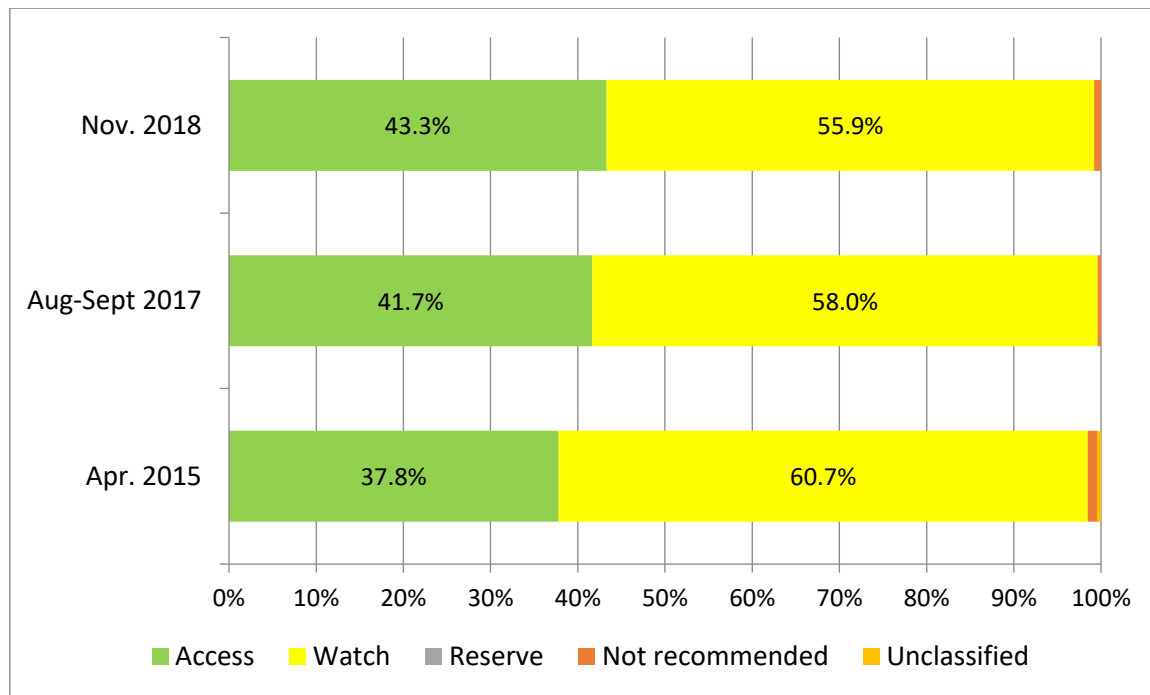


Fig 4e: Proportion of total antibiotic (ATC J01) use according to the AWaRe classification

## Discussion:

We successfully rolled out AMS interventions and evaluated their effectiveness on antimicrobial prescribing patterns and quality indicators using the Global-PPS. The Global-PPS enabled us to collect data at three time periods (2015, 2017 and 2018) and served as an inexpensive and convenient monitoring and evaluation system rather than a robust, expensive system that requires substantial financial, human and IT resources. The AMS interventions included dedicated education and training, use of hospital antibiotic policy with feedback of result of Global-PPS to all clinical departments in the hospital.

There was a significant overall improvement in the prevalence of antimicrobial use with a reduction from baseline of 82.5% in 2015 to 51.1% in 2018 based on the implemented AMS interventions using education and training of prescribers and other healthcare workers. A study showed reduction in antibiotic use as an impact of education on AMS programme (13). The rate of antimicrobial use was very high at baseline comparable to most other teaching hospitals that have been surveyed in the Nigeria (4,5) and hospitals in Pakistan (14). The rate of 51.1% in 2018 is higher than 37.7% in South African hospitals (15), and 37.2% in Northern Ireland hospitals (16) and similar to the 50% among African hospitals taking part in the Global-PPS (17) and 52.2% in Brazil (18). The reason for the high rate of antimicrobial use may be due to non-availability of antibiotic treatment guidelines, reliance on empiric therapy, poor

utilisation of the medical microbiology laboratory for the diagnosis of infections and in general, inappropriate antibiotic use.

We observed a reduction in the HAI rates from 10.4% in 2015 to 6.6% in 2018. The reduction was more significant in the adult wards. These HAI rates are in line with the main HAI prevalence found in Europe (17). Strikingly however, we observed much higher HAI prevalence in the children and neonatal wards with up to 18% of children/neonates been treated for at least one HAI in 2017 and 2018. These high rates in 2017 were mainly related to post-operative surgical site infections and in 2018, more children with an infection from another hospital were admitted (results not presented). More research needs to be done to further decrease these high HAI rates along with sustained infection prevention and control measures.

Most of the patients were placed on multiple antimicrobial therapy (55%-69.9%) while there was a significant decrease in the proportion of those placed on 3 or more antimicrobials from 23.2% in 2015 to 11.6% in 2018. Use of combination therapy was also high in studies from other parts of Nigeria (4,5), and lower in Pakistan (50%) (14) and Brazil (43.2%) (18). High rates of multiple antimicrobial therapy may lead to increased antimicrobial resistance and adverse drug events. Most of the antimicrobials were used for therapeutic purpose (56.7%-67.7%) similar to what has also been reported by other studies in Nigeria (4,5) and 66.9% among Africans taking part in Global-PPS (17). The proportion of antimicrobials used for

medical prophylaxis decreased over the time period from 16% in 2015 to 9.8% in 2018. This may have contributed to the reduction in overall antibiotic use in the hospital over the period. This is similar to reduction of proportion of medical prophylaxis over a 3-year period in Russian hospitals (19).

The top three prescribed antibiotics over the period were third generation cephalosporins mainly ceftriaxone (24.8% - 28.4%), followed by metronidazole and then the fluoroquinolones. This is similar to studies in Nigeria (4,5) Kenya, Brazil, Pakistan and Russia where ceftriaxone was the most frequently prescribed antibiotics (14,18-20). The increased use of third generation cephalosporins may be responsible for the high rate of endemic extended spectrum beta lactamase (ESBL) producing Enterobacteriaceae seen in different parts of Nigeria and Africa. Metronidazole is also found to be second most commonly used in other parts of Nigeria (4,5) and Ghana (21). It is important to note that the high use of metronidazole may be due to inappropriate use as most times it may not be for treatment of anaerobic bacterial infections and as part of redundant combination antibiotic coverage.

Ceftriaxone and metronidazole were the two most common antibiotic use for surgical prophylaxis and both are used in combination in about 90% of the time in the study. Ceftriaxone was the most commonly prescribed antibiotic for surgical prophylaxis in Eastern Europe, Southern Europe and Africa in the Global-PPS in 53 countries (17) and in Pakistan hospitals (14). It is very interesting to note that the high use of ceftriaxone and metronidazole is also driven by surgical prophylaxis; 32.7% - 44.4% of the total number ceftriaxone used and 25.3%-39.3% of the total metronidazole used were for surgical prophylaxis over the 3 time periods.

To our satisfaction however, we observed a decrease in prescription of antibiotics belonging to the Watch group (from 60.7% in 2015 to 55.9% in 2018) in favour of the Access group; a direct result of the educational training sessions to various prescribers. Strict follow up monitoring however will be needed if we want to continue to increase the proportion of the Access group. The Global-PPS allows for the analysis of additional quality indicators of antimicrobial use which can be set as targets for quality improvement in AMS programmes (11). The educational training sessions and use of antibiotic policy resulted in a significant improvement in most of the quality indicators of antimicrobial use. The documentation of the indication for antimicrobial prescription in notes improved significantly from 53.4% in 2015 to 97.2% in 2018 and this helps to ensure the communication of diagnosis and treatment among clinicians and other healthcare workers

(17). The documentation of stop/review date also improved significantly with an increase from 28.7% in 2015 to 70.2% in 2018. Documenting the stop/review date helps the clinician to review continued use of antibiotics (with opportunities to deescalate, escalate, change or stop antibiotic use), reduce unnecessary prolonged duration of antibiotic use and adverse drug effects.

Furthermore, there was a significant reduction in surgical prophylaxis > 24 hours from 93.3% in 2015 to 65.7% in 2018. It is important to appreciate that though there was significant improvement, 65.6% is still high and targeting surgical prophylaxis as low hanging fruit in AMS will help to further reduce this figure. The proportion of 65.6% for prolonged prophylaxis is higher than rates in Europe (16,23). Evidence shows that surgical prophylaxis > 24 hours has no benefit in reducing surgical site infection (SSI) compared to single dose of antibiotic prophylaxis (24,25). Prolonged prophylaxis increases the likelihood of antimicrobial resistance and adverse drug effects. Prolonged surgical prophylaxis is often given out of fear of the implications of poor infection prevention and control practices in the operating room and surgical wards of hospitals. Therefore, AMS programmes should be strengthened with a strong infection prevention and control programme.

The use of parenteral antimicrobial therapy was very high (>70%) in all time periods and no significant change was noticed. This is similar to the result from studies in Nigeria (4,5), East and South Asia, North America and Africa from the Global-PPS study (17). An AMS intervention using intravenous (IV) to oral antibiotic switch may be a low hanging fruit to consider in our hospital to reduce the high rate of parenteral therapy. The IV to oral switch can help to reduce length of hospital stay, cost of healthcare, staff workload and risk of catheter associated infections (26-28).

Targeted antimicrobial therapy was very low in this study even though there was an improvement from 11% in 2015 to 13.1% in 2018. The low rate is similar to the 14.6% in Africa, Northern Europe and West and Central Asia from Global-PPS data (17). This means that clinical specimens for diagnosis of infections were not collected before antimicrobial therapy. A recent study showed that there is poor utilisation of medical microbiology laboratory by clinicians for the diagnosis of infections in Nigeria with only 15.9% of them always using the laboratory for diagnosis when treating suspected infections and infectious diseases (29). The reasons for the suboptimal use were perceptions that clinical diagnosis is sufficient, delay in getting the laboratory report and poor access to the

microbiology laboratory (29). The implication of a lack of targeted therapy is prolonged duration of empiric broad spectrum antibiotics with no opportunity to deescalate based on culture and antibiotic susceptibility test result leading to increased antimicrobial resistance and killing of the normal flora.

There was limited information on multidrug resistant organisms (MDRO) in the study because of the poor use of the microbiology laboratory. There was also very low use of biomarkers like procalcitonin and C-reactive protein though procalcitonin was observed in 2018 on the paediatric/neonatal wards and was used to guide treatment in only 2.6% of inpatients prescribed at least one antimicrobial. There was no antibiotic guideline for adult inpatients throughout the study period, however, an antibiotic guideline was available for children during the 2018 Global-PPS. Use of local antibiotic guidelines for empiric antibiotic therapy help to improve clinical outcomes like mortality, length of hospitalization, duration of treatment (30,31).

The limitations are inherent to a cross sectional survey showing a snapshot of antimicrobial prescription. There was no information on the duration of therapy, whether the antimicrobial prescription was justified, correction for comorbidity and other patient characteristics that may act as confounders.

## Conclusion:

The study shows the usefulness and advantages of using the Global-PPS to set quality improvement targets and for monitoring, evaluation and surveillance of an AMS programme. The use of education and training and development of an antibiotic policy as AMS interventions in a limited resource setting clearly made an impact on antimicrobial prescribing patterns in terms of quantity and quality of antibiotic prescription in the hospital.

Further efforts are needed to increase the utilisation of the medical microbiology laboratory in order to increase targeted antimicrobial therapy. Identified low hanging fruit in AMS include IV to oral switch of antimicrobials, surgical prophylaxis along with improved infection prevention and control measures. With the successful roll out of the AMS programme, there will be need to consolidate the progress by identifying and implementing a core AMS strategy and other supplemental strategy by engaging the hospital leadership for support in terms of financial, human and information technology resources.

## Acknowledgements:

The authors acknowledge the hospital management and the participating clinical departments in the hospital for their support to the AMS programme.

## Conflict of interest:

Authors declared no conflict of interest

## Source of funding:

bioMérieux is the sole private sponsor (funder) of the Global Point Prevalence Survey. However, the hospital did not receive any funding support directly for the surveys. The data analysis and interpretation of results were done by the researchers.

## Oral presentation:

Oral presentation of this paper was made at the virtual conference of the Clinical Microbiology and Infectious Diseases Society of Nigeria (CLIMIDSON) via Zoom on 27<sup>th</sup> November 2020.

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