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Point prevalence survey of antimicrobial consumption and resistance: 2015-2018 longitudinal survey results from Nigeria

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Abstract:

Background: Nigeria joined the global community in monitoring antimicrobial prescribing practices since 2015. Results of individual hospital Global Point Prevalence Survey (Global-PPS) have stimulated efforts at instituting hospital-based antimicrobial stewardship (AMS) programmes. We report the trends of antimicrobial prescribing rates and quality indicators for 3 surveillance periods; 2015, 2017 and 2018.

Methodology: The web-based Global-PPS for surveillance of antimicrobial use in hospitals (www.global-pps.com) was completed by each participating hospital site for all inpatients receiving antimicrobials on a selected day in 2015, 2017 and 2018. Data included details on antimicrobial agents, reasons and indications for treatment and a set of quality prescribing indicators. Data were validated by the web-based data management system of University of Antwerp, exported into Microsoft Excel and analyzed with EPI INFO version 7.2.

Results: Thirteen hospitals participated in the survey involving a total of 5,174 inpatients. Mean weighted overall antimicrobial prescribing prevalence was 70.7% which declined over the years from 71.7% in 2015 to 59.1% in 2018 ($p<0.001$). The rate of documentation of date for post prescription review improved from 27.9% in 2015 to 48.5% in 2018 ($p<0.001$) while the rates of targeted treatment declined from 12.0% in 2015 to 5.2% in 2018 ($p<0.001$). There was no significant change in the choice of parenteral drug administration (64.5% in 2015, 65.1% in 2017 and 62.6% in 2018; $p=0.6803$), and but there was significant increase in documentation of reasons for prescription in case notes (62.2% in 2015, 74.5% in 2017, and 70.9% in 2018; $p=0.008$). Overall, the main indications for therapeutic prescribing were skin and soft tissue infections (20.8%), sepsis (15.9%) and pneumonia (11.6%). The top three antibiotics for therapeutic use were ceftriaxone (18.2%), metronidazole (15.3%) and ciprofloxacin (10.4%).

Conclusions: The survey showed reduction in the overall antimicrobial prescribing rate especially in hospitals that had introduced AMS programmes. Among the quality prescribing indicators, documentation of post prescription review date showed improvement. The Global-PPS serves as a cost effective, flexible and user-friendly tool in instituting AMS programmes in hospitals.

Keywords: antimicrobial prescribing, hospital, global-point prevalence survey, quality indicators

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**Enquête ponctuelle de prévalence de la consommation et de la
résistance aux antimicrobiens: résultats de l'enquête
longitudinale 2015-2018 au Nigéria**

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Abstrait:

Contexte: Le Nigéria a rejoint la communauté mondiale pour surveiller les pratiques de prescription d'antimicrobiens depuis 2015. Les résultats de l'enquête sur la prévalence des antimicrobiens dans les hôpitaux individuels (Global-PPS) ont stimulé les efforts visant à instaurer des programmes de gestion des antimicrobiens dans les hôpitaux. Nous rapportons les tendances des taux de prescription d'antimicrobiens et des indicateurs de qualité pour 3 périodes de surveillance; 2015, 2017 et 2018.

Méthodologie: Le Global-PPS en ligne pour la surveillance de l'utilisation des antimicrobiens dans les hôpitaux (www.global-pps.com) a été complété par chaque site hospitalier participant pour tous les patients hospitalisés recevant des antimicrobiens un jour sélectionné en 2015, 2017 et 2018. Données incluses des détails sur les agents antimicrobiens, les raisons et les indications du traitement et un ensemble d'indicateurs de prescription de qualité. Les données ont été validées par le système de gestion de données en ligne de l'Université d'Anvers, exportées vers Microsoft Excel et analysées avec EPI INFO version 7.2.

Résultats: Treize hôpitaux ont participé à l'enquête portant sur un total de 5174 patients hospitalisés. La prévalence moyenne pondérée globale des prescriptions d'antimicrobiens était de 70,7%, ce qui a diminué au fil des ans, passant de 71,7% en 2015 à 59,1% en 2018 ($p<0,001$). Le taux de documentation de la date pour le réexamen post-prescription est passé de 27,9% en 2015 à 48,5% en 2018 ($p<0,001$) tandis que les taux de traitement ciblé sont passés de 12,0% en 2015 à 5,2% en 2018 ($p<0,001$). Il n'y a pas eu de changement significatif dans le choix de l'administration parentérale du médicament (64,5% en 2015, 65,1% en 2017 et 62,6% en 2018; $p=0,6803$), mais il y a eu une augmentation significative de la documentation des motifs de prescription dans les notes de cas (62,2 % en 2015, 74,5% en 2017 et 70,9% en 2018; $p=0,008$). Dans l'ensemble, les principales indications de prescription thérapeutique étaient les infections de la peau et des tissus mous (20,8%), la septicémie (15,9%) et la pneumonie (11,6%). Les trois principaux antibiotiques à usage thérapeutique étaient la ceftriaxone (18,2%), le métronidazole (15,3%) et la ciprofloxacine (10,4%).

Conclusions: L'enquête a montré une réduction du taux global de prescription d'antimicrobiens, en particulier dans les hôpitaux qui avaient mis en place des programmes AMS. Parmi les indicateurs de qualité de prescription, la documentation de la date de revue post-prescription a montré une amélioration. Le Global-PPS est un outil rentable, flexible et convivial pour la mise en place de programmes AMS dans les hôpitaux.

Mots clés: prescription d'antimicrobiens, hôpital, enquête de prévalence globale, indicateurs de qualité

Introduction:

Uncontrolled use of antibiotics has been attributed to be one of the main factors contributing to the development of antimicrobial resistance (AMR). The challenge of AMR is rapidly reversing the gains and the advances made in medical practice in past decades. The cause of AMR is multifactorial, and the control is of great public health importance. Previously susceptible organisms have developed multidrug resistance (MDR) to broad spectrum antibiotics thus limiting their clinical efficacy. AMR is associated with higher cost of treatment, increased morbidity and mortality (1–3).

Some intervention methods such as prospective audit with intervention and feedbacks have been found to be effective in reducing irrational use of antimicrobials by improving antimicrobial prescribing practices. Similarly, antimicrobial stewardship (AMS) programme combined with educational interventions have resulted in improved rational use of antimicrobials and resulted in lower rates of resistance, improved clinical outcome and reduced costs of care (4-7). However, these cannot be sustained without continuous surveillance on the pattern of antimicrobial use (AMU) and the resistance profiles of microorganisms.

Nigeria joined the global community

in monitoring antimicrobial prescribing practice using the Global-PPS in 2015. Since then, the number of hospitals participating in the G-PPS has increased, thus creating awareness and providing data to guide decision making. Some hospitals have established AMS programmes after they started monitoring the pattern of antimicrobial prescription and use in their facilities. Most of these surveys have been on single hospital (8–11) or two hospitals (12), and have reported varying frequencies of AMU in the individual hospitals. These individual hospital reports have stimulated the interest of more hospitals in establishing the baseline pattern of AMU and resistance. These findings were to guide the planning of interventions in the respective hospitals but there are still gaps on the pattern of AMU in the country.

In 2017, Nigeria joined the World Health Organization (WHO) Global Antimicrobial Resistance Surveillance System (GLASS), and commenced reporting to the global platform. Nigeria has also developed the national action plan on AMR (13), however, there is paucity of data to present a

representative picture of AMU, AMR and trends in the country. In this study, we present the reports of antimicrobial prescribing trends and quality indicators in 2015, 2017 and 2018 from 13 hospitals across Nigeria. It is our belief that this information will help to bridge the data gap on AMU and AMR situations in the country.

Materials and method:

Study area

The study involved 13 (12 tertiary and 1 secondary level) participating hospitals across the geographical regions of Nigeria. The Nigeria health system is three-tiered involving the primary, secondary and tertiary levels of care. The tertiary level provides training and research in addition to advanced curative and rehabilitative services to the populace. Nigeria first joined the Global-PPS survey in 2015 with 4 participating hospitals, and the number increased to 13 in 2018. The hospitals were distributed across 5 of the 6 geopolitical regions, thus providing a good representative coverage of Nigeria (Fig 1).

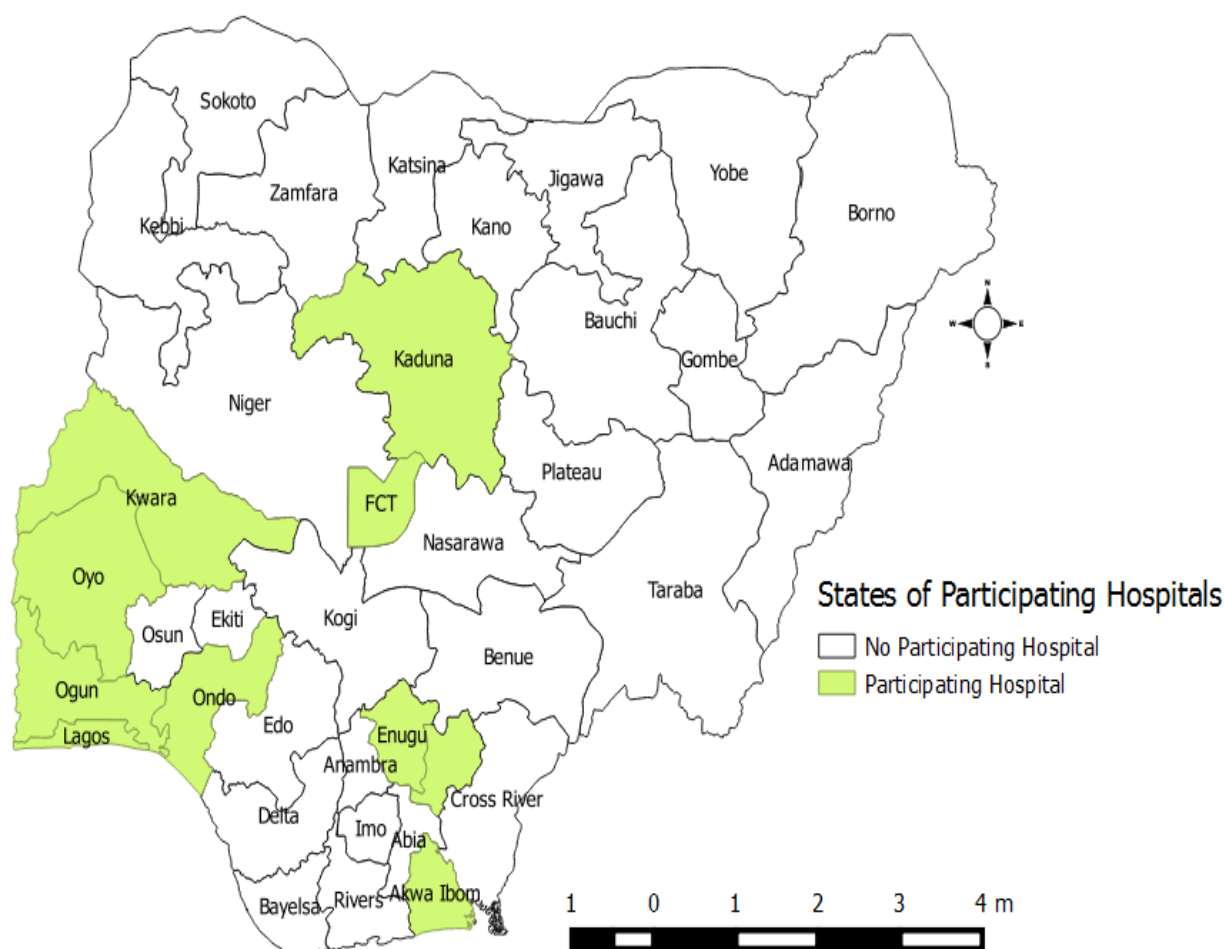


Fig 1: Map of Nigeria showing the states of participating hospitals

Study design, population and sampling

A longitudinal survey was conducted involving the total population of inpatients in each hospital at the time of the surveys. We included all inpatients admitted into any of the hospital wards before 08.00hrs on the day of the survey but surgical wards were not surveyed on Mondays and Fridays, and all patients admitted after 08.00hrs were excluded from the survey. All inpatients formed the denominator while all inpatients that had any antimicrobial treatment at the time of the survey formed the numerator.

Data extraction tool

We used pretested questionnaires (ward and patient forms) to extract information from the patients' folders. The ward form captured information on total number of inpatients, bed capacity of ward, category of ward (medical, surgical, or mixed), and date of the survey. The patient form captured information on the demographics of patients (gender, age, and weight), indication for treatment, antimicrobial agents (name, unit, dose, frequency and strength), prescribing quality indicators (stop/review date, adherence to guideline, route of administration, documented reason for antimicrobial use), type of antimicrobial biomarkers use and antimicrobial resistance type.

Data management and statistical analysis

The data were entered into the web-based data management system designed by University of Antwerp. The system has in-built data validation rules that ensure uniformity in data collection and other elements of data quality. After validation, the dataset was exported into Microsoft Excel and analyzed with EPI INFO version 7.2.

We estimated the mean weighted antimicrobial prevalence rate for the participating hospitals over the period. The annual antimicrobial prevalence was calculated for each year to appreciate changes over the period. The proportion of the prescriptions that met the quality prescribing indicators (record of stop/review dates, adherence to guideline, targeted treatment and route of administration) was estimated and the trend of antimicrobial use in the various wards over the years was also described in a chart.

Ethical consideration

Ethical clearance for the conduct of the study was obtained from the various local research and ethics committees of the participating hospitals. There was no direct contact with patients, and no identifiers such as name, phone number and address were

used. The hospital number was collected on the patient form but not on the online platform, the online platform automatically assigned a survey number to each participant.

Results:

Thirteen hospitals participated in the 2018 Global-PPS, of which 7 had participated at least twice since 2015 (4 in 2015, 10 in 2017 and 7 in 2018). There were 5,174 inpatients overall. The mean weighted antimicrobial prescribing prevalence over the period was 70.7%. This figure declined over the years from 71.7% in 2015 to 59.1% in 2018 ($p < 0.001$). A high variation in prescribing practices among and within the hospitals was observed. While there were increased prescribing rates in some hospitals over the years, rates reduced in two hospitals that had initiated AMS programmes (Fig 2).

Generally, the antimicrobial prevalence rate was on the decline among the adult inpatients (medical and surgical inpatients) but not in paediatric and intensive care patients. However, the prevalence rate increased among haemato-oncology patients over the years (Fig 3). The main indications for therapeutic prescribing were skin and soft tissue infections (20.8%), sepsis (15.9%) and pneumonia (11.6%). Overall top three antibiotics for therapeutic use were ceftriaxone (18.2%), metronidazole (15.3%) and ciprofloxacin (10.4%).

With respect to quality of antimicrobial prescription, documentation of the stop/review date showed some improvement over the three-year period, rising from 27.9% in 2015 to 48.5% in 2018, ($p < 0.001$), however, it remained below 50% average. There was no change in documentation of switch from parenteral to oral route of administration through the three-year period (2015: 64.5%; 2017: 65.1%; 2018: 62.6%, $p = 0.6803$) and slight change in documentation of reasons for antimicrobial prescription in notes at the start of the prescription (2015: 62.2%; 2017: 74.5%; 2018: 70.9%; $p = 0.008$).

The use of laboratory services to guide antibiotic prescription was poor. The best observed targeted prescription was 12% in 2015 (Table 1) and declined over the three years period (2015: 12.0%; 2017: 2.9%; 2018: 5.2%; $p < 0.001$). Metronidazole, ceftriaxone and ciprofloxacin were the most commonly used antibiotics among the inpatients in the participating hospitals (Table 2). Others were cefuroxime, amoxicillin with enzyme inhibitor, and levofloxacin (Table 2).

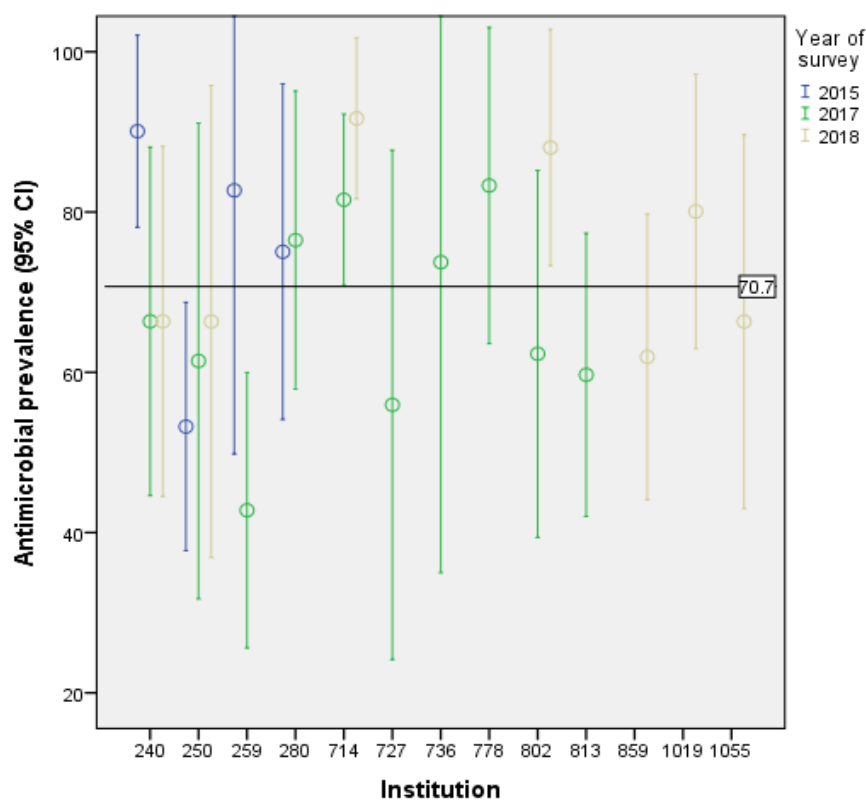


Fig 2: Variation of antimicrobial prevalence in participating Nigerian hospitals (2015, 2017 and/or 2018)

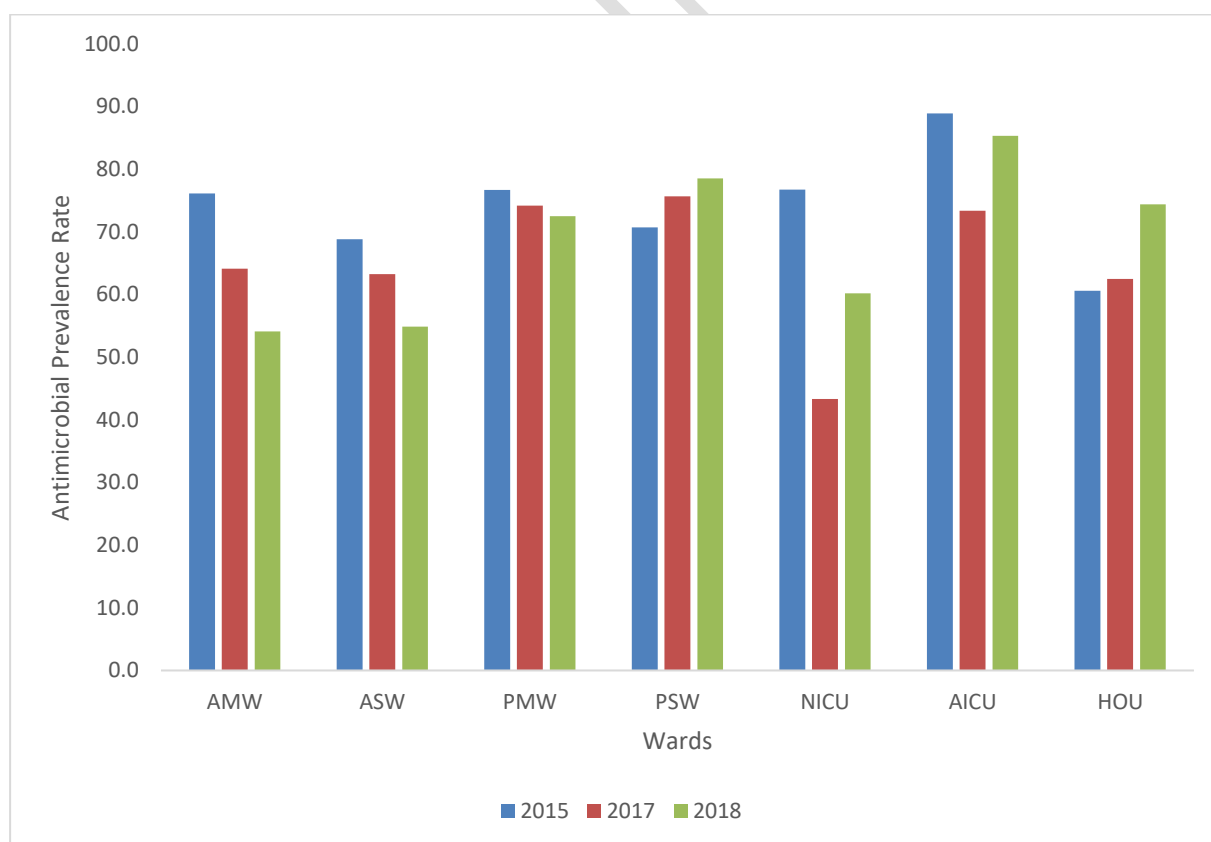


Fig 3: Antimicrobial prevalence rate in the different wards disaggregated by year of survey

AMW= adult medical ward, ASW=adult surgical ward, PMW= Paediatric Medical Ward, PSW = Paediatric Surgical Ward, NICU= Neonatal Intensive Care Unit, AICU = Adult Intensive Care unit, HOU = Haemato-Oncology Unit

Table 1: The antimicrobial prescription quality indicators in Nigerian hospitals 2015 – 2018

Variable	2015 (n=1085)		2017 (n=2500)		2018 (n=2612)	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Reason in notes						
Yes	675	62.2	1863	74.5	1851	70.9
No	410	37.8	637	25.5	761	29.1
Documented Stop/review date						
Yes	303	27.9	823	32.9	1266	48.5
No	783	72.1	1677	67.1	1344	51.5
Treatment						
Empirical	955	88.0	2427	97.1	2458	94.8
Targeted	130	12.0	73	2.9	136	5.2
Route of administration						
Oral	385	35.5	873	34.8	976	37.4
Parenteral	700	64.5	1627	65.1	1636	62.6
Guideline compliance						
Yes	128	11.8	152	6.1	341	13.0
No	179	16.5	170	6.8	104	4.0
NA/NI	778	71.7	2178	87.1	2167	83.0

NA/NI = Guidelines were either not available or could not be accessible to make judgement to assess; n = no of inpatients

Table 2: Class of antimicrobials used in Nigerian hospitals (2015 – 2018)

Antimicrobial	AWaRe Class	2015 n (%)	2017 n (%)	2018 n (%)
Metronidazole	Access	241 (22.2)	583 (23.3)	579 (22.2)
Ceftriaxone	Watch	199 (18.3)	367 (14.7)	435 (16.7)
Ciprofloxacin	Watch	104 (9.6)	242 (9.7)	237 (9.1)
Cefuroxime	Watch	98 (9.0)	235 (9.4)	114 (4.4)
Amoxicillin and enzyme inhibitor	Access	31 (2.9)	155 (6.2)	118 (4.5)
Levofloxacin	Watch	41 (3.8)	95 (3.8)	124 (4.8)
Gentamicin	Access	35 (3.2)	131 (5.2)	104 (4.0)
Total		1085	2500	2612

n = no of inpatients; AWaRe = Access Watch and Reserve group of antibiotics according to the World Health Organization classification

Discussion:

Starting with four hospitals in 2015, we were able to enlarge and maintain a network, allowing sharing of experiences and knowledge to combat AMR issues in Nigeria. We found that the prevalence of antimicrobial use (AMU) declined especially among the hospitals that had commenced AMS programmes. These hospitals had formed AMS committees with the support of their hospital management. They had shared their findings and commenced sensitization of the physicians on the need to avoid irrational use of antimicrobial agents and the potential consequences of AMR in patients' management. In one of the hospitals, the development of departmental level antibiotic guideline had commenced with the technical support of the AMS committee.

The overall weighted antimicrobial prevalence rate remained high with wide variations existing within and among the participating hospitals. A closer look at the trend of the AMU by ward over the period showed that while the adult medical and surgical wards, and the paediatric medical ward had shown decline, this was the case for high dependency wards or intensive care units. The high prevalence of AMU reported

among these Nigerian hospitals is similar to the high rates reported in other studies in Nigeria and other tropical countries (12,14, 15). This could be as a result of the generally low awareness on appropriate antibiotic use and AMR, high over-the-counter use of antibiotics, low level of implementation of AMS programmes such as awareness campaigns in the regions and lack of stringent guidelines and policy for AMU. The high level of infectious diseases as the major cause of hospitalization could also be contributory.

Community acquired infections (CAIs) were the most common indications for AMU over the period. This high prevalence of CAIs may not be unconnected with the high level of infectious diseases in the tropics due to poor personal hygiene, low environmental sanitation and poor housing. However, the low level of targeted treatment of these infections is a great concern. Most of the participating hospitals were tertiary level specialized hospitals with adequate laboratory support. One would have expected that CAIs could be promptly diagnosed on presentation and the treatment guided by the antimicrobial sensitivity patterns of prevalent microorganisms in the region. Alternatively, where the antibiogram of the community has been mapped out, a locally formulated anti-

microbial guideline could serve as guide for empirical treatment of some infections and syndromes common in those localities. Our findings however, revealed that AMU among Nigerian hospitals was neither based on antimicrobial guidelines nor laboratory diagnosis.

There was generally poor documentation in the patients' case note of the reasons for AMU and stop/review dates. Lack of documentation of reasons for AMU could encourage unnecessary use of these agents. Similarly, lack of documentation of the stop or review date of antimicrobial agents could lead to prolonged use of antimicrobials and increased risk of developing resistance. These practices varied widely across the participating hospitals, some had earlier reported improved documentation of reason for antimicrobial use (8,9). There is need for immediate intervention to enlighten the prescribers on the need to clearly indicate the reason for any antimicrobial use.

We observed a preference for broad spectrum antibiotics belonging to the Watch group of the WHO AWaRe classification such as the third generation cephalosporins (ceftriaxone) and fluoroquinolones. These antimicrobials have a higher risk of selecting for resistance and should therefore be monitored and prioritized in AMS programmes. There was also a preference for parenteral route of administration over oral route among the prescribers. Although, these prescribing practices may have some immediate advantage for the prescribers especially in absence of microbiological culture and sensitivity, they could expose these newer agents to high selection pressure for resistance. The prescribers preference for use of broad spectrum antimicrobials has been reported earlier (16).

This study to our knowledge, represents the largest collections of longitudinal data collection on AMU from multiple hospitals across regions in Nigeria over a three-year period. However, no hospital in the northeast region of the country participated in the survey, which implied that the unique antimicrobial prescribing practices in the region were not captured.

Conclusion:

We conclude that the level of AMU in Nigeria public hospitals remained high. There are poor documentations on reasons for the AMU and the stop/review date, as well as a suboptimal use of the available laboratory services. There is high prescribers' preference for broad-spectrum antibiotics and parenteral route of administration, and general lack of antibiotic guidelines among the hospitals. There is therefore urgent need for targeted

interventions to reverse these trends. There is also the need to encourage the establishment of AMS programmes and the development of antibiotic guidelines in Nigerian hospitals.

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Conflict of interest:

Authors declare no conflict of interest

Source of funding:

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Previous publication

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 26th and 27th November 2020, and the abstract has been published in the conference program.

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