Drug promotional activities in Nigeria: Impact on the prescribing patterns and practices of medical practitioners and the implications

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ABSTRACT

Objective: Pharmaceutical companies spend significant amount of resources on promotion influencing the prescribing behaviour of physicians. Drug promotion can negatively impact on rational prescribing, which may adversley affect the quality of patient care. However, little is know about these activities in Nigeria as the most populous country in Africa. We therefore aimed to explore the nature of encounters between Nigerian physicians and pharmaceutical sales representatives (PSRs) and how these encounters influence prescribing habits. Methodology: Cross-sectional questionnaire-based study conducted among practicing physicians working in tertiary hospitals in four regions of Nigeria. Results: 176 questionnaires were completed. 154 respondents (87.5%) had medicines promoted to them in the previous three months, with most encounters taking place in outpatients' clinics (60.2%), clinical meetings (46%) and new medicine launches (17.6%). Information about potential adverse effects and drug interactions was provided in 41.5%, and 27.3% of cases, respectively. Food, in the form of lunch or dinner, was the most common form of incentive (70.5%) given to physicians during promotional activities. 61% of physicians felt motivated to prescribe the drug promoted to them, with quality of information provided being the driving factor. Most physicians (64.8%) would agree to some form of regulation of this relationship between medical doctors and the pharmaceutical industry. Conclusion: Interaction between PSRs and physicians is a regular occurrence in Nigeria, influencing prescribing practices. Meals and cheap gifts were the most common items offered to physicians during their encounters with PSRs. The need for some form of regulation by professional organizations and the government was expressed by most respondents to address current concerns.

1. INTRODUCTION

In 2015, the pharmaceutical industry spent an estimated USD 69.2 billion on various forms of pharmaceutical promotion and advertising in 31 countries, 3.2% up from 2014[1]. Most of this spending was on detailing (61.2%), followed by providing drug samples (10.8%), meetings (10.5%), direct-to-consumer advertising (8%), digital (3.8%), mailing/others (3.1%), clinical trials (2.1%) and other forms advertising (0.5%).

The World Health Organization defines pharmaceutical promotion as "all informational and persuasive activities by manufacturers, the effect of which is to induce the prescription, supply, purchase and/or use of medicinal drugs"[2]. Typically, product detailing by pharmaceutical sales representatives (PSRs) is via hospital or clinic visits, drug launches, visits to conferences and through continuing medical education programmes[2-4]. During their visits, PSRs can offer gifts, invitations to luncheons/dinners and free samples[5]. Pharmaceutical companies also sponsor meetings and conferences, offer research grants and honorarium to physicians, and sponsor clinical trials[3,4,6,7]. However, there are increasing concerns among patients regarding such activities[8] due to their impact on prescribing and consumption of medicines.

Pharmaceutical promotion and other marketing activities can influence both prescribers[9-13] and users of promoted medicines, potentially negatively impacting on medicine utilization patterns[11,14,15]. In addition, potentially adding to costs; for example, the total costs of proton pump inhibitors in Ireland when adjusted for population size with limited counter actions to pharmaceutical company activities versus Sweden with extensive health authority activities promoting generics first line when available[16]. Spurling *et al* in their review found that in studies examining prescribing quality, five studies found an association between exposure to pharmaceutical company information and lower quality prescribing whilst four did not, and one study found associations with both lower and higher quality prescribing. 38 studies found associations between exposure to companies and a higher frequency of prescribing whilst 13 did not. Five studies also found evidence of higher costs following company interactions, whilst four studies found no association and one study found an association with lower costs[15]. Vancelik et al also found that pharmaceutical companies were highly influential in prescribing by ambulatory care physicians in Turkey[17]; similarly, Akande et al in Nigeria[18]. There are also concerns that information, especially around the risks and side-effects of medicines, are often missing from pharmaceutical company presentations, especially where they are the principle source of information as seen in a number of lower and middle income countries (LMICs)[18-20]. There are also concerns if only favourable findings are published and promoted by pharmaceutical companies[21,22], especially with less than 70% of studies undertaken actually published[23]. In addition, as mentioned, there are concerns with physician trust if patients believe physicians have been unduly influenced by pharmaceutical companies with gift relationships[8,24].

Consequently, we believe it is important to regulate the interaction between the pharmaceutical industry, health providers and patients, especially where there are currently limited regulations and limited continuous professional development post qualification, coupled with high co-payments, as seen in many LMICs including Nigeria[25,26]. Whilst most developed countries have national legislation regulating drug promotion involving voluntary codes among professional organisations, including those working in key positions in the industry[27,28], most of the day-to-day regulation is turned over to pharmaceutical companies which have their own codes of practice[27-29].

In Nigeria, the National Agency for Food and Drug Administration and Control (NAFDAC) has the mandate to regulate and control the advertisement of medicines[30]. However, it is unknown if any code of practice or guidelines are in place to address the promotion of prescription drugs promotion or direct to consumer advertisement in Nigeria. The Pharmaceutical Manufacturers Group of Manufacturers Association of Nigeria (PMG-MAN) is the umbrella of the Organization for Manufacturer of Pharmaceuticals and Allied Products in Nigeria, and currently PMG-MAN has no code for the marketing of prescription drugs. This is a concern as Nigeria is the most populous country in Africa with an estimated population of 185.9 million in 2016[31], with currently appreciable population growth. As a result, an appreciable opportunity to waste considerable resources for both the government and patients with inappropriate use of medicines.

We did not find any information on spending on pharmaceutical promotion in Africa, or the number of PSRs, in our review of the literature and the internet. However, we found an increased number of PSRs in the emerging markets of Asia Pacific (+3.7%) and Latin America (+0.3%), and their declining numbers in the established markets of North America (-0.9%), top 5 in Europe (-2.7%), other European countries (-2.7%) and Japan (0.9%) from 2014 to 2015[1]. These trends suggest that Africa is likely to be a region of intensified activities in the future, in particular its largest and likely most profitable markets such as Nigeria.

Currently, there is limited information available on the nature of the encounters with PSRs and their impact on prescribing in Africa despite publications showing an impact [18,32-40]. In Nigeria, only a few published studies have evaluated the interactions between Nigerian medical doctors and PSRs[39,40]. However, these studies did not address issues relating to physicians' attitude towards PSRs and typically covered only one geopolitical region.

Consequently, the objectives of this study were to explore the nature of current encounters between Nigerian physicians and PSRs, the types of medicines promoted and the extent to which these encounters influenced subsequent prescribing patterns. Subsequently, use these findings to provide guidance to Nigerian authorities and other relevant stakeholders on possible next steps to improve prescribing practices. This needs to be addressed to enhance the appropriate use of medicines and reduce out-of-pocket payments for patients in Nigeria. This is particularly important as Nigeria strives towards universal healthcare. Further, the findings and suggestions of this study can potentially guide other LMICs striving to control the influence of pharmaceutical promotion activities on their physician prescribing habits.

2. METHODOLOGY

2.1 Study design

This was a cross-sectional survey conducted among practicing physicians in tertiary health facilities in Nigeria.

2.2 Study Site(s)

Convenience sampling was used to select six tertiary health care facilities located in four out of the six geo-political zones of Nigeria: South-west, South-east, North-central and North-west. The rationale for selecting these facilities was the availability of personnel to carry out the study. We chose tertiary health care facilities for this study as they are the main training centres for physicians in Nigeria. As such, they play a very important role in establishing the prescribing habits of doctors and are therefore important targets for promotional activities by pharmaceutical companies.

2.3 Study Instrument

We developed 17-item structured questionnaire based on the literature on pharmaceutical promotion[3,16,25,26] . The questionnaire consisted of three parts. The first part collected information on the socio-demographic characteristics of the respondents, the second on drug promotional activities, and the third on the effect of promotional activities on doctors' prescribing practices (Appendix A). The survey was piloted among 10 physicians working in the general outpatient department of a tertiary healthcare facility in Lagos, Nigeria. Necessary amendments were then made based on responses received to enhance the clarity and the robustness of the subsequent findings.

2.4 Sampling

2.4.1 Sample size calculation

The sampling frame consisted of an estimated 1110 physicians working in the six selected tertiary health care facilities located in four geo-political zones of Nigeria. Using the Raosoft® software[41], we calculated a sample size of 167 participants under the assumption of a 50% response rate, at 7% margin error and 95% confidence interval. Assuming a non-response rate of 5% from the piloted study, we obtained a final corrected minimum sample size of 175. However, a larger sample size of 250 physicians was used to allow adequate power of the study.

2.4.2 Participant Selection
Physicians working in the selected tertiary health care facilities were chosen through stratified random sampling. The number of questionnaires sent to each of the participating tertiary health care facilities was proportional to their physician population. With each hospital, questionnaires were distributed between different departments based on the number of physicians working in each department.

The names of all physicians (including medical interns) working in the clinical departments of selected hospitals were compiled from departmental staff lists and participants chosen using a random number interval. The selected physicians were approached during regular departmental meetings in each hospital and invited to participate in the study.

2.4.3 Data collection
The questionnaire was then administered by designated doctors in each of the participating centres for a period of approximately 30 minutes to those who agreed to take part in the study. Information was collected on promotional encounters between doctors and PSRs in the three months prior the survey. Data collection took place during the first two weeks of February 2016. There was no financial reward for taking part in the study.

2.5 Ethical consideration
The questionnaires were completed anonymously to ensure confidentiality. The acceptance of the doctors to complete the questionnaire was taken as explicit consent. A waiver for ethical approval was given as the study did not involve patients and sought only information about habits/clinical practice.

2.6 Statistical Analysis
The information obtained from the questionnaire was coded, entered and analyzed using IBM SPSS version 19. Univariate and multivariate analyses were conducted to test for the association between prescription of promoted medicines and the following variables: drug information provided during the promotional encounter, cost and efficacy of the drug, personality of the PSR, quality of the drug presentation and demographics of the participants. Pearson Chi-square or Fisher's exact test and the Mann-Whitney test were used in the univariate analysis and binary logistic regression was used for the multivariate analysis. A p- value of <0.05 was considered significant.

3. RESULTS

3.1 Descriptive analysis
Of the 250 questionnaires distributed to participants, 210 were returned, giving a response rate of 84%. However, 34 of which were incomplete and consequently were excluded. A total of 176 duly filled questionnaires were subsequently analysed for this study. The highest proportion of respondents were male doctors (80.7%), residents (50%%) and internal medicine residents (35.8%) (Table 1).

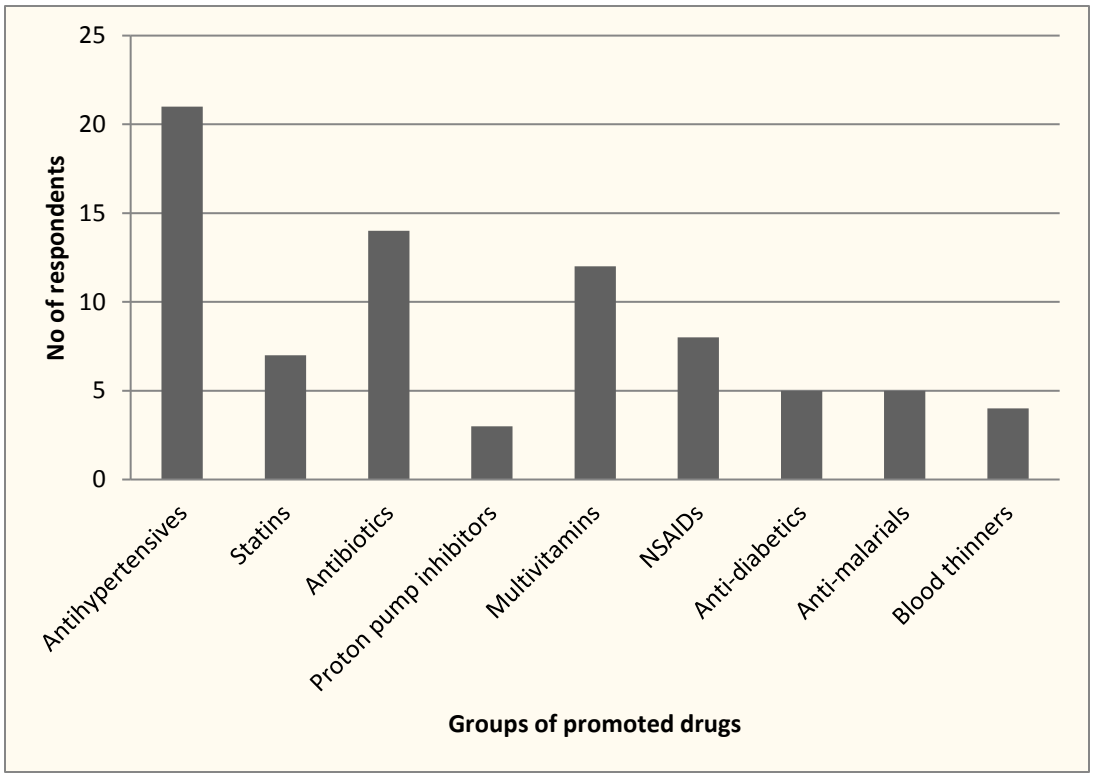
Table 1: Distribution of the respondents according to their demographic and professional characteristics

Parameters	**Median**	**N (%)**
General characteristics *Age(yrs)* *Years of practice* *Gender* *Male* *Female*	 32 yrs 4.0 yrs	 142 (80.7) 34 (19.3)
Physician's cadre in hierarchical order		
Interns (House Officers)		61 (34.7)
Medical Officers		16 (9.1)
Residents		88 (50)
Consultants		11 (6.2)
Specialty		
Internal Medicine		63 (35.8)
Family Medicine/General Practice		43 (24.5)
Obstetrics and Gynaecology		25 (14.2)
Surgery		22 (12.5)
Paediatrics		12 (6.8)
Others		11 (6.2)

The median age of the respondents was 32 years, with a mean age of 32.5±6.9 years. The median number of years of practice was 4 (IQR – 1-5). Overall, 68% of the physicians had been practicing for five years or less, 21% had been practicing between six and ten years and 11% had been practicing for more than ten years.

One hundred and fifty-four respondents (87.5%) had medicines promoted to them in the previous three months. In the majority of cases (86.4%), this happened over the course of one to five encounters with PSRs. Outpatients' clinics (60.2%), clinical meetings (46%), drug launches (17.6%), medical conferences (11.9%) and other organized events (8.5%) were the main points of drug promotion. The most commonly promoted medicines where indicated were anti-hypertensives (n=21), antimicrobials (n=14), multivitamins (n=12) and anti-lipidemic medicines (n=7) (Figure 1).

Figure 1: Groups of promoted medicines



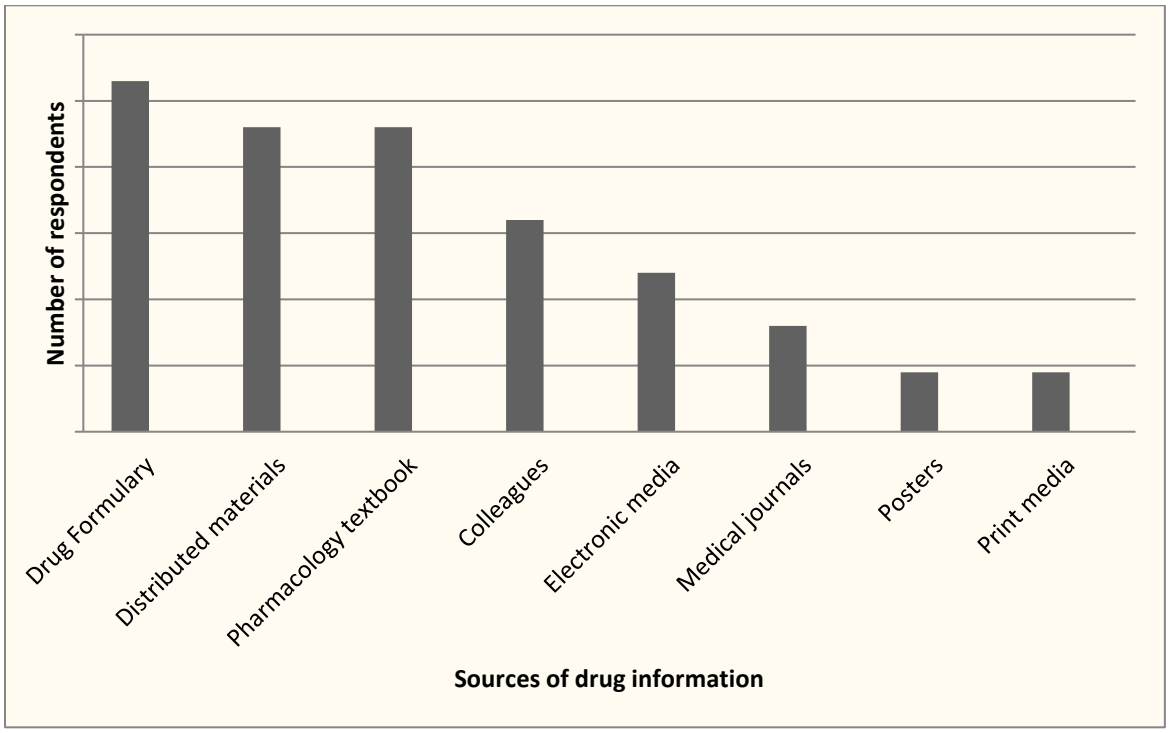
The information provided during the promotional encounters included the generic name of medicines (n=137, 77.8%), brand names (n=140, 79.5%), clinical indications (n=142, 80.7%), contra-indications (n=96, 54.5%), the pharmacological effects of drugs (n=114, 64.8%) and dosing information (n=124, 70.5%). Information about potential adverse effects, drug interactions and storage conditions was provided in 73(41.5%), 48(27.3%) and 18(10.2%) of the cases, respectively. The majority of the respondents (68.2%) had received some gifts or incentives during their encounters with PSRs. Food, in the form of lunch or dinner, was the most common incentive offered (n=124, 70.5%), followed by gift items such as ward coats, pen and calendars with the names of the medicine/company branded on them (n=121, 68.8%), cash (n=7, 4%), conference sponsorship (n=6, 3.4%) and free drug samples (n=4, 2.3%).

Over half of the respondents (60.8%) felt motivated to prescribe the promoted medicines. The factors that may influence this included the perceived quality of information provided (63.6%), cost and efficacy of the presented medicine (51.1%), the reputation of the pharmaceutical company (28.4%), the quality of the presentation (18.2%), the personality of the PSR (9.1%) and the nature of the gifts/incentives (4.5%). Thirty-five percent of the physicians who were motivated to prescribe the promoted medicines would do so using the brand names, while 55.1% would use both brand and generic (INN – International non-proprietary name) names.

More than half of the respondents (53.4%) would consult additional sources of information before considering to prescribe the promoted medicines. The sources of medicine information included the internet (39.2%), formularies such as the British National Formulary (BNF) and the Monthly Index of Medical Specialities (MIMS, a commercial prescribing guide), (30.1%), (Figure 2). Other factors influencing prescribing habits included their residual knowledge of pharmacology from medical school (79.5%), knowledge obtained during the medical internship (79.5%), influence of more senior colleagues (57.4%), availability of such medicines at the hospital pharmacy or nearby pharmacies (75%), whether the medicine would be affordable for the patient (75.6%) and patients' requests (21.6%). Finally, 60% and

50.2% of interns and residents mentioned that their prescribing choices were influenced by the opinion of senior colleagues.

Figure 2: Alternative sources of information for prescribing



Most doctors (n=114, 64.8%) agreed that the relationship between doctors and pharmaceutical medical representatives should be regulated. The Nigerian Medical Association (NMA), the Pharmaceutical Society of Nigeria (PSN) and NAFDAC were the identified organizations that could regulate this relationship. The forms of control suggested were outright prohibition of gifts and incentives from the pharmaceutical representatives (n=36, 20.5%), allowing physicians to receive only low-priced gift items (n=47, 28.7%), declaration of monetary/expensive gifts and stoppage of industry sponsored conferences/CME (n=2, 1.1%).

In the univariate analysis (Table 2), more years of medical practice, the perceived quality of the information provided, the cost and efficacy of the medicine, the personality of the PSR, the receipt of gifts and expected rewards from the pharmaceutical company were significantly correlated with motivation to prescribe the promoted medicines.

Table 2: Demographics, cadre, and promotional drug variables compared for participants that are motivated or not motivated to prescribed promotional drugs

Characteristics	**Motivated (n= 109)**	**Not motivated (n= 70)**	*P* value
	Frequency (%)* or median (IQR)**		
Demographics			
Median (IQR) age of the participants (years)	32 (28-34)	31 (28-34)	0.309
Median (IQR) years of practice	4 (2-7)	2 (1-6)	0.030*
Specialty			
Family medicine	12	5	0.127
Obstetrics and gynecology	17	8	
Surgery	11	11	
Paediatrics	7	5	
General Practice	18	8	
Others	10	1	
Gender			
Male	86	56	0.897
Female	21	13	
Cadre/ Level			
Interns	29	32	0.051
Medical officers	11	5	
Residents	61	27	
Consultants	6	5	
Promotional drug variables			
Adequate information provided during promotion	112	64	0.000
Reputation of the drug marketing company	50	126	0.055
Quality of the presentation	32	144	0.026
Cost-benefit ratio of the drug	*90*	86	0.000
Personality of presenter	*16*	*160*	0.022
Gifts	*8*	*168*	0.020
Future benefits from company	*6*	*170*	0.045

Table 3 shows the results of the multivariate analysis of variables potentially associated with motivation to prescribe promotional medicines. The odds of the motivation to prescribe the promoted medicines were significantly lower with the reputation of the pharmaceutical company (adjusted odds ratio: 0.24, 95% CI: 0.08- 0.74) but higher with the quality of presentation (adjusted odds ratio: 27.09, 95% CI: 8.43-87.11) and the cost-benefit ratio (10.90, 95% CI: 8.43- 28.48) of the promoted medicines.

Table 3: Multivariate analysis of predictors that motivated the participants to prescribe promoted drugs

Variable	OR (95% CI)	
	Unadjusted	Adjusted┘
Adequate information provided during promotion	0.55 (0.15 – 2.44)	0.61 (0.19 – 2.04)
Reputation of the pharmceutical company	0.20 (0.07- 0.65)	0.24 (0.08- 0.74)
Quality of the presentation	29.16 (9.32 – 88.21)	27.09 (8.43 – 87.11)
Cost-benefit ratio of the drug	12.80 (6.10 -30.36)	10.90 (4.18 -28.48)
Personality of the pharmaceutical sales representative	5.35 (0.76 -22.35)	3.37 (0.56 -20.28)
Age of the physicians	1.02 (0.82- 1.09)	1.02 (0.91- 1.14)
Specialty of the physician	0.70 (0.55- 1.00)	0.80 (0.64- 1.00)
Year of practice	0.89 (0.78 – 1.02)	0.95 (0.84 – 1.08)

┘ Adjusted for 8 covariates (age, specialty and year of practice of the physician, adequate information provided during promotion, reputation of the drug company, quality of the presentation, etc), OR= odds ratio, CI= confidence interval.

4. DISCUSSION

We were encouraged by the high response rate in our study (84%), which was appreciably higher than that seen by Pinto et al (25.5%)[42]. This study revealed that the majority (87.5%) of respondents had recent encounters with PSRs and received various forms of gifts/incentives from them. A study published in 2007 on medicines' promotion in a teaching hospital in Ilorin, Nigeria, found that 89% of the doctors had encounters with PSRs in the preceding 6 months and more than two-thirds reported that their prescribing habits were affected by the promotional drug material received [18]. This can be a concern if this leads to inappropriate prescribing especially if there is bias in the promotion materials[16,21,22]. However, as mentioned, Spurling et al found a variable association between exposure to pharmaceutical company information and lower quality prescribing, a higher frequency of prescribing and higher costs[15], with Vancelik et al finding pharmaceutical companies were highly influential in the prescribing practices of ambulatory care physicians similar to Godman et al Akande et al8[16-17]. On the other hand, the importance of physician-PSR interactions as an efficient and convenient source of drug information has been noted in a number of studies[26,32], and the adoption of structured educational programmes for young physicians and medical students on the interaction with PSRs can help improve their ability to maximise on the benefits of such interactions[33,34,43].

Among the medicines promoted to physicians were antihypertensives, antimicrobials and cholesterol-lowering agents. The branded forms of these medicines can be expensive for individuals paying out-of-pocket in a resource poor country, hence the need for generics. A concern is that almost a third of those motivated to prescribe the medicines being promoted would do so by brand name only. Studies have shown that prescribing by generic names could reduce the cost of medicines by as much as 90% or more, reducing overall medicine cost for the class as well as overall healthcare costs [44-47] . This is especially important for Nigeria where the majority of health care expenditure is still currently out-of-pocket, with medicines being responsible for a substantial part of healthcare costs [48-50]. This is being addressed in other African countries with pharmaceutical companies offering medicines for as little as 1US$/patient/ month as part of improved access programmes[51]. There is now little controversy surrounding the prescribing of good quality generics with a number of meta analyses and other studies showing no difference in outcomes between generics and originators across a range of medicines and disease areas[52-60], although recognizing there are some medicines which should not be prescribed by INN such as lithium and certain anti-epileptic medicines[61-63], with generic immunosuppressants now less of an issue[64]. However, there are still concerns with the quality of generics in Nigeria, which needs to be addressed to enhance their use[50]. There are also concerns if interactions with PSRs increases empiric treatment with antibiotics enhancing potential antimicrobial resistance (AMR). Ethical drug promotion in developing countries has been identified as a means of containing AMR[65].

It can be argued that the majority of encounters between doctors and PSRs in our study were reasonable such as an offer of a lunch or dinner as an incentive for doctors to take time out of their schedules to listen to information provided about by pharmaceutical companies or offers gifts. While this may hold for doctors in high income countries, the case may differ for those in resource poor countries[35,42,66-68]. A previous study in South East Nigeria indicated that 60% of the surveyed doctors felt influenced after receiving gratifications in the form stickers, food and souvenirs to prescribe promoted medicines[40].

Among the predictors to be motivated to prescribe promoted medicines, the odds of motivation were lower with greater years of practice. Similarly, the odds were lower when the pharmacological information of the medicine provided during the promotion activities were inadequate compared to when adequate information was provided. These findings are appropriate as they were expected since clinical and prescribing experiences are known to improve with years of practice of a doctor. Previous studies evaluating prescribing patterns of doctors in Nigeria have shown that junior doctors perpetrate the most prescribing errors and inappropriate prescribing[69]. Adequate pharmacological information of promoted medicine is essential for rational and appropriate prescribing[70,71]. By contrast, the odds of the motivation

to prescribe the promoted medicines were higher when the quality of the presentation was good compared to a poor quality presentation. Similarly, the odds of motivation were higher with a high cost-benefit ratio of the promoted medicine compared to those medicines with a low cost-benefit ratio. Rational and appropriate prescribing entails cost-benefit considerations, which is particularly important in LMICs where the cost of medication is typically borne by the patient[72].

In this study, two thirds of respondents felt there should be some form of regulation between doctors and pharmaceutical companies and it was felt that this should be provided by the NMA in conjunction with the PSN and the NAFDAC. Regulatory measures suggested by the respondents was either stopping the PSRs from offering gifts or offering only gifts with a low monetary value. In an international cross-sectional survey on educational initiatives for medical and pharmacy students about drug promotion, the majority of the respondents admitted that many countries do not have a functioning drug regulatory agency or other national private or public sector organizations responsible for overseeing drug promotion[43]. This may have informed the suggestion of most respondents in the current survey that drug promotion should be regulated by the two major associations for healthcare providers and NAFDAC, which is in keeping with the findings in high income countries[42,73]. The American Medical Association[42] and the FDA[73] are known to have played prominent roles in containing greater interactions between doctors and pharmaceutical companies in the US.

Following increasing concern among health authorities and civil society in other countries, national legislations regulating the advertising and promotion of medicines have been developed in many developed countries with the United Kingdom and Australia as example[67,68] . The pharmaceutical industry themselves have also developed voluntary codes of conduct to address concerns, outlining ethical principles that should guide the promotion of medicines, and the interactions between pharmaceutical companies and the health care community, across countries[29] . For example, these principles and rules outline the kind of interactions PSRs can have with health care professionals and what claims can be made about the prescription medicines being promoted, as well as other areas of interaction with the health care community such as clinicals trials and interactions with patient representatives[28] .

There are a number of examples of such codes including the 2012 International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) Code of Practice, the 2009 Code on Interactions with Healthcare Professionals of the Pharmaceutical Research and Manufacturers of America (PhRMA) and the 2014 Code of Conduct of the European Association of Researching Pharmaceutical Industries (EFPIA)[74-76] . Such industry self-regulatory codes have also been developed in emerging economies such as India, China and South Africa[77-79]. However, evidence from Sweden and the United Kingdom shows that industry self-regulation does not always work [80]. This is due to four main inherent challenges. Firstly, self-regulation by pharmaceutical companies can be perceived as a conflict of interest as the codes are developed and implemented by the party with financial motivations; secondly, they are voluntary. Thirdly, due to general lack of pre-vetting and reactive monitoring, breaches are typically brought to light, and sanctions only administered, once the campaigns have already affected health professionals and consumers. Fourthly, financial penalties can be too low to be really effective[81].

In Nigeria, while there is some regulation for the advertising of pharmaceutical products by NAFDAC[30], there is currently no regulation by the Government on pharmaceutical company promotion and there is no body monitoring unethical promotional practices. Consequently, this research highlights a need for the Nigerian government to develop a code of conduct that will address some of the raised concerns. In view of our findings, we recommend the development of a legal provision on all pharmaceutical promotion, which is currently missing as the existing legislation only covers the advertising of medicinal products. There could for instance be financial and other consequences for pharmaceutical companies that violate the laws, if and when established, similar to other countries[82, 83]. However, getting the necessary manpower to enforce any developed code of conduct as well as obtaining the resources to address identified problems are potential challenges in resource limited countries such as Nigeria.

Limited information was also given to physicians regarding adverse drug affects, potential drug-drug interactions and storage conditions of promoted medicines, by PSRs during their interactions with physicians, which is similar to other countries[20]. This has been a consistent problem, and is a short-

sighted approach, as the lack of key information could potentially lead to serious adverse reactions for patients or even withdrawals if vital information is not disclosed[84,85] .

On the implementation side, drug and therapeutic committees (DTCs) should be key players in hospitals in the training of physicians in the appropriate use of medicines along with clinical pharmacologists and clinical pharmacists. We are already seeing such activities grow across Europe to enhance appropriate use of medicines in hospitals given increasing pressures for funding new medicines[70,71,86,87], providing examples to Nigeria. There are also ongoing programmes among public hospitals in South Africa to improve the functioning of DTCs and the reporting of adverse drug reaction in hospitals to enhance the appropriate use of medicines as well as reduce the need and influence of PSRs[88-91] .

There are various reports that regulation of interaction between medical students, interns, residents and PSRs influences their future relationship and practice[92,93]. In the nearest future, medical students, interns, and residents who have interacted with PSRs are not willing to further interact with the industry once they started to practice[43,92,93]. This underscores the importance of education of physician in training on how to critically evaluate the adequacy of pharmacological information of promoted drugs before prescribing. Such educational training has been recognized by the WHO and Health Action International (HAI) and contained in a practical guide handbook on understanding and responding to pharmaceutical promotion[43].

Consequently, the next stage of our research will be to document further current DTC activities in Nigeria and the implications, building on the recent findings from a pilot study[94]. Furthermore, we will start promoting the fact that the university curricula of medical doctors, nurses, and pharmacists in Nigeria should now include education about pharmaceutical promotion, the need for regulations and the existing regulatory framework in the country, alongside general education about the appropriate use of medicines.

Efforts should also be geared towards encouraging all professionals in Nigeria to use the WHO and HAI practical handbook to guide their understanding and response to pharmaceutical promotion[43]. Educational activities continue as part of continuous professional development once physicians are qualified along with activities to potentially strengthen DTCs in hospitals as learning organisations. Finally, independent information on efficacy and safety of medicines should be made available to health professionals and patients. In countries with developing health care systems, limited availability of this information is often the reason for physicians to rely on promotional material[19] to the detriment of patients and the healthcare system.

4.1 STUDY LIMITATIONS

This study was conducted among physicians working in tertiary health care facilities in Nigeria, almost all of which are located in urban centres and managed by the government. As such, our findings may not be applicable to physicians working in other care settings (e.g. private and faith-based health facilities). The majority of the respondents were also young (< 40 years) with limited years of practice (average of 4 years) suggesting they were junior doctors. This may not represent the majority of doctors in Nigeria as only a limited number of consultants participated in the survey. Previous questionnaire-based studies involving doctors in Nigeria though have also shown that consultants very rarely participate in such surveys[95,96]. It is to be hoped that future studies would address this problem. Nonetheless, we believe our data is representative of doctors in Nigeria since the population of residents and interns at any point in a year is far more than those of the consultants in all teaching hospitals in Nigeria. In addition, given the sensitivity of the topic, some respondents may not have been fully honest in their responses.

However, we believe these limitations are offset by the multi-centered nature of the study, the focus on teaching hospitals where future physicians are trained and the anonymity of completed questionnaires. As a result, we believe our findings provide important insights regarding the current extent and impact of pharmaceutical promotion among teaching hospitals in Nigeria. Such findings can be used to inform interventions and policy changes aimed at improving pharmaceutical promotion practices in line with international best practices to enhance the quality of future prescribing. Future studies will be conducted among a larger selection of hospitals in Nigeria with opportunities for interventions, and post-intervention analyses, based on recommended changes.

5. CONCLUSION

Our findings on the impact of pharmaceutical promotion in Nigeria on prescribing habits are a concern as this may negatively impact on the quality of prescribing and the cost of treating both communicable and non-communicable diseases in Nigeria. Enhancing the quality and efficiency of prescribing is key to improving patient outcomes, reducing out-of-pocket expenditure on medicines for patients, and reducing expenditure for health care systems. Greater efforts, not just in regulating, but most importantly in ensuring that regulations are implemented, are needed. Rigorous studies on the impact of pharmaceutical promotion can make an evidence-based case for this need. Strengthening the implementation of regulations of pharmaceutical promotion requires monitoring and evaluation of regulatory effectiveness in Nigeria. This will help in reducing inefficiencies in prescribing and the use of medicines, especially as African countries are striving for universal access. Practical steps towards reducing the impact of drug promotion on inappropriate physician prescribing in Nigeria would include enforcement of generic prescribing in healthcare facilities providing their quality can be assured as well as the establishment of functioning DTCs to guide future medicine use including the uptake of new medicines into the healthcare system.

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AUTHORS' CONTRIBUTIONS
JOF, KAO and OOO were responsible for the conception and design of the study and initial draft of the manuscript. OOD, AA, TAS and OOE participated in the acquisition of data and critical review of the manuscript for intellectual content. JOF, KAO, OOD, AB and BG participated in data analysis and interpretation. AB, AF, AS and BG critically reviewed the manuscript for intellectual content and updated successive drafts. All co-authors gave their final approval of the manuscript to be published.

References
1. QuintilesIMS. An annual review of pharmaceutical sales force and marketing channel performance [Internet]. 2016. Available at URL: http://www.imshealth.com/files/web/Market%20Insights/Channel%20Dynamics/QIMS_ChannelDynamics_Global_Reference.pdf.
2. Norris P HA, Lexchin J, Mansfield P. Drug promotion - what we know, what we have yet to learn. Reviews of materials in the WHO/HAI database on drug promotion. Available at URL: http://apps.who.int/iris/bitstream/10665/69177/1/WHO_EDM_PAR_2004.3_eng.pdf

3. Lexchin J. Interactions between physicians and the pharmaceutical industry: what does the literature say? CMAJ. 1993;149(10):1401-7.
4. Wazana A. Physicians and the pharmaceutical industry: is a gift ever just a gift? Jama. 2000;283(3):373-80.
5. DeJong C, Aguilar T, Tseng CW, Lin GA, Boscardin WJ, Dudley RA. Pharmaceutical Industry-Sponsored Meals and Physician Prescribing Patterns for Medicare Beneficiaries. JAMA Intern Med. 2016;176(8):1114-10.
6. Civaner M. Sale strategies of pharmaceutical companies in a "pharmerging" country: the problems will not improve if the gaps remain. Health policy. 2012;106(3):225-32.
7. Campbell EG, Gruen RL, Mountford J, Miller LG, Cleary PD, Blumenthal D. A national survey of physician-industry relationships. NEJM. 2007;356(17):1742-50.
8. Holbrook A, Lexchin J, Pullenayegum E, Campbell C, Marlow B, Troyan S, et al. What do Canadians think about physician-pharmaceutical industry interactions? Health policy. 2013;112(3):255-63.
9. King M, Essick C. The geography of antidepressant, antipsychotic, and stimulant utilization in the United States. Health & place. 2013;20:32-8.

10. Fleischman W, Agrawal S, King M, Venkatesh AK, Krumholz HM, McKee D, et al. Association between payments from manufacturers of pharmaceuticals to physicians and regional prescribing: cross sectional ecological study. BMJ. 2016;354:i4189.
11. Wall LL, Brown D. The high cost of free lunch. Obstetrics and gynecology. 2007;110(1):169-73.
12. Salmasi S, Ming LC, Khan TM. Interaction and medical inducement between pharmaceutical representatives and physicians: a meta-synthesis. Journal of Pharmaceutical Policy and Practice. 2016;9:37.
13. Datta A, Dave D. Effects of Physician-directed Pharmaceutical Promotion on Prescription Behaviors: Longitudinal Evidence. Health economics. 2017;26(4):450-68.
14. Lexchin J. Models for financing the regulation of pharmaceutical promotion. Global Health. 2012;8:24.
15. Spurling GK, Mansfield PR, Montgomery BD, Lexchin J, Doust J, Othman N, et al. Information from pharmaceutical companies and the quality, quantity, and cost of physicians' prescribing: a systematic review. PLoS medicine. 2010;7(10):e1000352
16. Godman B, Shrank W, Andersen M et al. Comparing policies to enhance prescribing efficiency in Europe through increasing generic utilisation: changes seen and global implications. Expert Rev. Pharmacoeconomics Outcomes Res 2010; 10: 707–722
17. Vancelik S, Beyhun NE, Acemoglu H, Calikoglu O. Impact of pharmaceutical promotion on prescribing decisions of general practitioners in Eastern Turkey. BMC public health. 2007;7:122.
18. Akande TM, Aderibigbe SA. Influence of drug promotion on prescribing habits of doctors in a teaching hospital. African journal of medicine and medical sciences. 2007;36(3):207-11
19. Riaz H, Godman B, Hussain S, Malik F, Mahmood S, Shami A, Bashir S. Prescribing of bisphosphonates and antibiotics in Pakistan: challenges and opportunities for the future. JPHSR 2015;6:111-21.
20. Othman N, Vitry AI, Roughead EE, Ismail SB, Omar K. Medicines information provided by pharmaceutical representatives: a comparative study in Australia and Malaysia. BMC public health. 2010;10:743
21. Marra LP, Araújo VE, Silva TBC, Diniz LM, Guerra Junior AA, Acurcio FA, et al. Clinical Effectiveness and Safety of Analog Glargine in Type 1 Diabetes: A Systematic Review and Meta-Analysis. Diabetes Ther. 2016 Jun;7(2):241–58
22. Heres S, Davis J, Maino K, Jetzinger E, Kissling W, Leucht S. Why olanzapine beats risperidone, risperidone beats quetiapine, and quetiapine beats olanzapine: an exploratory analysis of head-to-head comparison studies of second-generation antipsychotics. The American journal of psychiatry. 2006;163(2):185-94
23. Ross JS, Tse T, Zarin DA, Xu H, Zhou L, Krumholz HM. Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis. BMJ. 2012;344(d7292):1–10
24. Grande D, Shea JA, Armstrong K. Pharmaceutical Industry Gifts to Physicians: Patient Beliefs and Trust in Physicians and the Health Care System. Journal of General Internal Medicine. 2012;27(3):274-9
25. Workneh BD, Gebrehiwot MG, Bayo TA, Gidey MT, Belay YB, Tesfaye DM, et al. Influence of Medical Representatives on Prescribing Practices in Mekelle, Northern Ethiopia. PLoS One. 2016;11(6):e0156795.
26. Saito S, Mukohara K, Bito S. Japanese practicing physicians' relationships with pharmaceutical representatives: a national survey. PLoS One. 2010;5(8):e12193.
27. Grande D. Limiting the Influence of Pharmaceutical Industry Gifts on Physicians: Self-Regulation or Government Intervention? Journal of General Internal Medicine. 2010;25(1):79-83
28. Dubois DJ, Jurczynska A, Kerpel-Fronius S, Kesselring G, Imamura K, Nell G, et al. Fostering Competence in Medicines Development: The IFAPP Perspective. Frontiers in pharmacology. 2016;7:377.
29. Francer J, Izquierdo JZ, Music T, Narsai K, Nikidis C, Simmonds H, et al. Ethical pharmaceutical promotion and communications worldwide: codes and regulations. Philosophy, Ethics, and Humanities in Medicine. 2014;9(1):7
30. NAFDAC. Guidelines for advertisement of regulated products in Nigeria. Available from URL: http://www.nafdac.gov.ng/index.php/regulation/draft-regulations/item/248-guidelines-for-advertisement-of-regulated-products-in-nigeria
31. World Bank Open Data. Available from: http://data.worldbank.org.
32. Salmasi S, Ming LC, Khan TM. Interaction and medical inducement between pharmaceutical representatives and physicians: a meta-synthesis. Journal of pharmaceutical policy and practice. 2016;9.

33. Wofford JL, Ohl CA. Teaching appropriate interactions with pharmaceutical company representatives: the impact of an innovative workshop on student attitudes. BMC medical education. 2005;5(1):5.
34. Kelcher S, Brownoff R, Meadows LM. Structured approach to pharmaceutical representatives. Family medicine residency program. Canadian Family Physician. 1998;44:1053-60.
35 Alssageer MA, Kowalski SR. What do Libyan doctors perceive as the benefits, ethical issues and influences of their interactions with pharmaceutical company representatives? The Pan African medical journal. 2013;14:132.
36. Alssageer MA, Kowalski SR. A survey of pharmaceutical company representative interactions with doctors in Libya. The Libyan journal of medicine. 2012;7.
37. Alssageer MA, Kowalski SR. Doctors' opinions of information provided by Libyan pharmaceutical company representatives. The Libyan journal of medicine. 2012;7.
38. Workneh BD, Gebrehiwot MG, Bayo TA, et al. Influence of Medical Representatives on Prescribing Practices in Mekelle, Northern Ethiopia. PLoS One. 2016;11(6):e0156795.
39. Oshikoya KA, Oreagba I, Adeyemi O. Sources of drug information and their influence on the prescribing behaviour of doctors in a teaching hospital in Ibadan, Nigeria. Pan Afr Med J. 2011;9:13.
40. Ijoma U OI, Onodugo O, Aguwa E, Ejim E, Onyedum C et al. Effect of Promotional Strategies of Pharmaceutical Companies on Doctors' Prescription Pattern in South East Nigeria. TAF Prev Med Bull. 2010;9(1). Available at URL: http://www.scopemed.org/?mno=758.
41. Raosoft®. Raosoft® sample size calculator. Available at URL: http://www.raosoft.com/samplesize.html
42. Pinto SL, Lipowski E, Segal R, Kimberlin C, Algina J. Physicians' intent to comply with the American Medical Association's guidelines on gifts from the pharmaceutical industry. Journal of medical ethics. 2007;33(6):313-9
43. Mintzes B. World Health Organization. Educational initiatives for medical and pharmacy students about drug promotion: an international cross-sectional survey. 2005. Available atURL: http://apps.who.int/medicinedocs/pdf/s8110e/s8110e.pdf
44. Woerkom M, Piepenbrink H, Godman B, Metz J, Campbell S, Bennie M, et al. Ongoing measures to enhance the efficiency of prescribing of proton pump inhibitors and statins in The Netherlands: influence and future implications. Journal of comparative effectiveness research. 2012;1(6):527-38.
45. Bennie M, Godman B, Bishop I, Campbell S. Multiple initiatives continue to enhance the prescribing efficiency for the proton pump inhibitors and statins in Scotland. Expert review of pharmacoeconomics & outcomes research. 2012;12(1):125-30.
46. Godman B, Wettermark B, van Woerkom M, Fraeyman J, Alvarez-Madrazo S, Berg C, et al. Multiple policies to enhance prescribing efficiency for established medicines in Europe with a particular focus on demand-side measures: findings and future implications. Frontiers in pharmacology. 2014;5:106.
47. Cameron A, Laing R. Cost savings of switching private sector consumption from originator brand medicines to generic equivalents. Available at URL: http://www.who.int/healthsystems/topics/financing/healthreport/35MedicineCostSavings.pdf
48. Fadare JO, Adeoti AO, Aina F, Solomon OA, Ijalana JO. The influence of health insurance scheme on the drug prescribing pattern in a Nigerian tertiary healthcare facility. Nigerian medical journal : journal of the Nigeria Medical Association. 2015;56(5):344-8.
49. Olakunde BO. Public health care financing in Nigeria: Which way forward? Annals of Nigerian Medicine. 2012;6(1):4.
50. Fadare JO, Adeoti AO, Desalu OO, Enwere OO, Makusidi AM, Ogunleye O, et al. The prescribing of generic medicines in Nigeria: knowledge, perceptions and attitudes of physicians. Expert review of pharmacoeconomics & outcomes research. 2015:1-12.
51. Mbui JM, Oluka MN, Guantai EM, Sinei KA, Achieng L, Baker A, et al. Prescription patterns and adequacy of blood pressure control among adult hypertensive patients in Kenya; findings and implications. Expert review of clinical pharmacology. 2017;10(11):1263-71
52. Kesselheim AS, Misono AS, Lee JL, Stedman MR, Brookhart MA, Choudhry NK, et al. Clinical equivalence of generic and brand-name drugs used in cardiovascular disease: a systematic review and meta-analysis. Jama. 2008;300(21):2514-26.
53. Gagne JJ, Choudhry NK, Kesselheim AS, Polinski JM, Hutchins D, Matlin OS, et al. Comparative effectiveness of generic and brand-name statins on patient outcomes: a cohort study. Annals of internal medicine. 2014;161(6):400-7.

54. Gagne JJ, Kesselheim AS, Choudhry NK, Polinski JM, Hutchins D, Matlin OS, et al. Comparative effectiveness of generic versus brand-name antiepileptic medications. Epilepsy & behavior. 2015;52(Pt A):14-8.
55. Corrao G, Soranna D, Arfe A, Casula M, Tragni E, Merlino L, et al. Are generic and brand-name statins clinically equivalent? Evidence from a real data-base. European journal of internal medicine. 2014;25(8):745-50.
56. Corrao G, Soranna D, La Vecchia C, Catapano A, Agabiti-Rosei E, Gensini G, et al. Medication persistence and the use of generic and brand-name blood pressure-lowering agents. Journal of hypertension. 2014;32(5):1146-53
57. Corrao G, Soranna D, Merlino L, Mancia G. Similarity between generic and brand-name antihypertensive drugs for primary prevention of cardiovascular disease: evidence from a large population-based study. European journal of clinical investigation. 2014;44(10):933-9.
58. Lessing C, Ashton T, Davis PB. The impact on health outcome measures of switching to generic medicines consequent to reference pricing: the case of olanzapine in New Zealand. Journal of primary health care. 2015;7(2):94-101.
59. Paton C. Generic clozapine: outcomes after switching formulations. The British journal of psychiatry. 2006;189:184-5.
60. Veronin M. Should we have concerns with generic versus brand antimicrobial drugs? A review of issues. JPHSR 2011;2:135-50.
61. Ferner RE, Lenney W, Marriott JF. Controversy over generic substitution. BMJ. 2010;340:c2548.
62. Duerden MG, Hughes DA. Generic and therapeutic substitutions in the UK: are they a good thing? British journal of clinical pharmacology. 2010;70(3):335-41.
63. MHRA. Antiepileptic drugs: new advice on switching between different manufacturers' products for a particular drug. Available at URL: https://www.gov.uk/drug-safety-update/antiepileptic-drugs-new-advice-on-switching-between-different-manufacturers-products-for-a-particular-drug
64. Godman B, Baumgartel C. Are generic immunosuppressants safe and effective? BMJ. 2015;350:h3248
65. Olivier C, Williams-Jones B, Doize B, Ozdemir V. Containing global antibiotic resistance: ethical drug promotion in the developing world. Antimicrobial Resistance in Developing Countries: Springer; 2010. p. 505-24.
66. De Ferrari A, Gentille C, Davalos L, Huayanay L, Malaga G. Attitudes and relationship between physicians and the pharmaceutical industry in a public general hospital in Lima, Peru. PLoS One. 2014;9(6):e100114.
67. MHRA. The Blue Guide. Advertising and promotion of medicines in the UK [Internet]. Medicines and Healthcare products Regulatory Agency; 2014. Available at URL: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/376398/Blue_Guide.pdf.
68. Medicines Australia: Code of conduct. Available at URL: http://medicinesaustralia.com.au/code-of-conduct
69. Oshikoya KA, Senbanjo IO, Amole OO. Interns' knowledge of clinical pharmacology and therapeutics after undergraduate and on-going internship training in Nigeria: a pilot study. BMC medical education. 2009;9:50.
70. Bjorkhem-Bergman L, Andersen-Karlsson E, Laing R, Diogene E, Melien O, Jirlow M, et al. Interface management of pharmacotherapy. Joint hospital and primary care drug recommendations. European journal of clinical pharmacology. 2013;69 Suppl 1:73-8.
71. Gustafsson LL, Wettermark B, Godman B, Andersen-Karlsson E, Bergman U, Hasselstrom J, et al. The 'wise list'- a comprehensive concept to select, communicate and achieve adherence to recommendations of essential drugs in ambulatory care in Stockholm. Basic & clinical pharmacology & toxicology. 2011;108(4):224-33.
72. Ofori-Asenso R, Agyeman AA. Irrational Use of Medicines—A Summary of Key Concepts. Pharmacy 2016;4, 35
73. Kessler DA, Pines WL. The federal regulation of prescription drug advertising and promotion. Jama. 1990;264(18):2409-15.
74. PhRMA. Code on interactions with healthcare professionals. Available at URL: http://www.phrma.org/codes-and-guidelines/code-on-interactions-with-health-care-professionals. Washington DC: PhRMA; 2009.

75. IFPMA. IFPMA Code of Practice. 2012. Available at URL: https://www.ifpma.org/wp-content/uploads/2016/01/IFPMA_Code_of_Practice_2012_new_logo.pdf. Available from: http://www.ifpma.org/about-ifpma/members/associations.html.
76. EFPIA. EFPIA code on the promotion of prescription-only medicines to, and interactions with, healthcare professionals [Internet]. European Federation of Pharmaceutical Industries and Associations; 2014. Available at URL: https://www.efpia.eu/media/24302/3a_efpia-hcp-code-2014.pdf.
77. OPPI. Organisation of Pharmaceutical Producers of India. Code of Pharmaceutical Practices. 2012Availavle at URL: https://www.indiaoppi.com/sites/all/themes/oppi/images/OPPI-Code-of-Pharmaceutical-Practices-2012.pdf.
78. MCA. Marketing Code Authority. SA CODE OF MARKETING PRACTICE. 2014. Available at URL: http://www.marketingcode.co.za/images/SACodeMarketingPractice.pdf.
79. RDPAC. China Association of Enterprises with Foreign Investment. R&D-based Pharmaceutical Association Committee. Ethic Promotion-Code of conduct - Ensuring Ethical Promotion of Pharmaceutical Products. Available at URL: http://www.rdpac.org/ChannelShow.aspx?cha=3&mod=3&cla=20&lan=en&con=0
80. Zetterqvist AV, Merlo J, Mulinari S. Complaints, complainants, and rulings regarding drug promotion in the United Kingdom and Sweden 2004-2012: a quantitative and qualitative study of pharmaceutical industry self-regulation. PLoS Med. 2015;12(2):e1001785.
81. HAI. Health Action International. Fact or fiction? What healthcare professionals need to know about pharmaceutical marketing in the European Union [Internet]. 2016. Available at URL: http://haiweb.org/wp-content/uploads/2016/10/Fact-or-Fiction-1.pdf.
82. Yu SY, Yang BM, Kim JH. New anti-rebate legislation in South Korea. Applied health economics and health policy. 2013;11(4):311-8.
83. Brkicic LS, Godman B, Voncina L, Sovic S, Relja M. Initiatives to improve prescribing efficiency for drugs to treat Parkinson's disease in Croatia: influence and future directions. Expert review of pharmacoeconomics & outcomes research. 2012;12(3):373-84.
84. Cohen D. Dabigatran: how the drug company withheld important analyses. BMJ. 2014;349:g4670.
85. Malmstrom RE, Godman BB, Diogene E, Baumgartel C, Bennie M, Bishop I, et al. Dabigatran - a case history demonstrating the need for comprehensive approaches to optimize the use of new drugs. Frontiers in pharmacology. 2013;4:39.
86. Hoffmann M. The right drug, but from whose perspective? A framework for analysing the structure and activities of drug and therapeutics committees. European journal of clinical pharmacology. 2013;69 Suppl 1:79-87.
87. Eriksen J, Gustafsson LL, Ateva K, Bastholm-Rahmner P, Ovesjo ML, Jirlow M, et al. High adherence to the 'Wise List' treatment recommendations in Stockholm: a 15-year retrospective review of a multifaceted approach promoting rational use of medicines. BMJ open. 2017;7(4):e014345
88. South African National Department of Health. National Policy for the Establishment and Functioning of Pharmaceutical and Therapeutics Committees in South Africa. 2015. Available at URL: http://www.health.gov.za/index.php/pharmaceutical-and-therapeutics-committees
89. Matlala M, Gous AG, Godman B, Meyer JC. Structure and activities of pharmacy and therapeutics committees among public hospitals in South Africa; findings and implications. Expert review of clinical pharmacology. 2017:1-8.
90. Terblanche A, Meyer JC, Godman B, Summers RS. Knowledge, attitudes and perspective on adverse drug reaction reporting in a public sector hospital in South Africa: baseline analysis. Hospital practice (1995). 2017;45(5):238-45.
91. Meyer JC, Schellack N, Stokes J, Lancaster R, Zeeman H, Defty D, et al. Ongoing Initiatives to Improve the Quality and Efficiency of Medicine Use within the Public Healthcare System in South Africa; A Preliminary Study. Frontiers in pharmacology. 2017;8:751
92. King M, Essick C, Bearman P, Ross JS. Medical school gift restriction policies and physician prescribing of newly marketed psychotropic medications: difference-in-differences analysis. BMJ. 2013;346:f264.
93. McCormick BB, Tomlinson G, Brill-Edwards P, Detsky AS. Effect of restricting contact between pharmaceutical company representatives and internal medicine residents on posttraining attitudes and behavior. Jama. 2001;286(16):1994-9.

94. Fadare J OO, Enato E, Godman B, Gustafsson LL. Presence and Functionality of Drug and Therapeutics Committees (DTC) in Selected Nigerian Hospitals – Results of a Pilot Study MURIA Conference PV NCD DU Studies. 2016: 2. Available at URL: http://muria.nmmu.ac.za/2nd-MURIA-Training-Workshop-and-Symposium,-25-27-J.

APPENDIX A

SURVEY OF IMPACTS OF DRUG PROMOTIONAL ACTIVITIES ON THE PRESCRIBING PATTERNS AND PRACTICES OF DOCTORS IN SOME SELECTED TERTIARY HEALTH FACILITIES

Introduction:
Dear Sir/Madam,
This study is being carried out among doctors in tertiary health institutions in some Nigerian cities to gain insight into the impact of drug promotional activities on their practices. The purpose of this study is not to indict you or any organization. It is a self- sponsored research for academic purposes only. Your honest response is therefore important and will be greatly appreciated. You are to respond on the basis of anonymity and your responses will be given the utmost confidentiality required. Thank you.
SERIAL NUMBER: ……
SECTION A (DEMOGRAPHY AND PROFESSION)
Age last birthday ----------

Sex , Male = 1, Female = 2

Number of year/s of Practice ----------

Professional status
House officer = 1, Medical officer=2, Senior medical officer and above=3, Registrar=4, Senior Registrar=5, Consultant =6.
Area of Practice
General Practice = 1, Family Medicine=2, Internal Medicine = 3, Surgery = 4,
Pediatrics = 5, Obstetrics & Gynecology = 6, Psychiatry = 7, Ophthalmology = 8, Ear Nose andThroat (ENT) = 9, Dentistry =10,
Others = 11, pls specify…….
SECTION B (DRUG PROMOTIONAL ACTIVITIES)
How many times have you had drug/s promoted to you in the last 3 months……

In which of the settings below did such activities/interactions take place?

	Settings	Mark X	Frequency in last 3 months
a	Outpatient clinic visit		
b	Statutory Clinical meetings		
c	Organized outdoor events		
d	Drug launch		
e	Conferences		
f	Others, pleases specify……		

Multiple responses allowed.

Can you please list the names of drugs promoted to you in the last 3 months
…….
…….
…….

Please indicate the information provided during the promotional events you have had?

	Information	Yes	No
a	Generic name of the drug		
b	Brand name of the drug		
c	Clinical indications		
d	Contraindications/Cautions		

e	Pharmacological effects of the drug		
f	Mode of action		
g	Pharmacokinetics		
h	Dosing information		
i	Potential adverse effects		
j	Average duration of treatment recommended		
k	Potential drug interactions		
l	Available dosage forms		
m	Product and package descriptions		
n	Route of administrations		
o	Drug additives used		
p	Storage conditions		
q	Expiration dates/shelf life		
r	Name/Address of manufacturers		
s	Alternate sources of information about the drug		
t	Drug local registration information/NAFDAC no		
u	Name/address of the drug marketer		
v	Reference materials/ Relevant Publications		
w	Cost of the drug		
x	Others, pls specify……..		

Were gifts or incentives distributed at such fora
Yes = 1, No =2 ☐

Kindly indicate the type/s of gifts/incentives you have once received from a pharmaceutical organisation

	Items	Mark X
a	Food items (launch/dinner/snacks/drinks)	
b	Souvenirs (e.g. pen, writing pads, mug, keys holders, wallets, clock, organizers, ward coats)	
c	Cash	
d	Sponsorship to conferences	
e	Others,pls specify …….	

SECTION C (PRESCRIBING HABITS)

Have you in any way being motivated by the promotional activity/ies to prescribe a drug?
Yes = 1, No = 2 ☐

What contributed to your being motivated to prescribe such drug/s?

	Factor/s	Mark X
a	Information provided during the promotion encounter	
b	Reputation of the organization	
c	Personality of the pharmaceutical sales representative	
d	The gifts/motivational items received	
e	Perceived future benefits from the company	
f	The quality of the presentation	
g	The cost and efficacy of the product	
h	Others, please specify ……	

☐

If yes to 12 above, in what form is/are the drug/s prescribed?
Generic name only = 1, Brand name only =2, Both brand and generic names = 3, Acronyms = 4

Apart from the drug promotional forum/a, did you source for more information about such drugs before prescribing?
Yes =1, No = 2. ☐

If yes to 15 above, what was/were the source/s of such additional information sort?

	Source	Mark X
a	Print materials received at presentation	
b	Drug formulary/ies (e.g. BNF, MIMS)	
c	Posters and bill boards	
d	Peer reviewed journals	
e	Print medias	
f	Electronic medias	
g	Pharmacology textbooks	
h	Colleagues	
i	Internet resources	
j	Other, please specify ……	

Other than drug promotional activities, which of the following factors has influenced your prescribing practices?

	Factors	Yes	No
a	Knowledge acquired from medical school		
b	Knowledge acquired during internship		
c	Knowledge acquired during postgraduate training		
d	Senior colleagues influences and preferences		
e	Drug availability		
f	Common practice in medical community		
g	Personal experience with the drug		
h	Affordability to patients		
i	Patient's priority		
j	Out of curiosity		
k	Others, pls specify……		

Do you agree that the relationship between doctors and pharmaceutical medical representatives should be regulated? Yes =1, No = 2.

If yes, in what form should the regulation be

	Regulation	
A	Stopping all kinds of gifts	
B	Allowing only souvenirs/gift with small monetary value	
C	Declaration of monetary value of expensive gifts/ sponsorships	
D	Stopping industry sponsorship of conferences/CME	
E	Others…..	

Thank you.