The prescribing of generic medicines in Nigeria: knowledge, perceptions and attitudes of physicians

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ABSTRACT

Background: Generic medicines have the same efficacy and safety as originators at lower prices. However, there are concerns with their utilization in Nigeria. Objectives: Evaluate physicians' understanding and perception of generics. Methods: Questionnaire among physicians working in tertiary healthcare facilities in four geo-political regions of Nigeria. Results: Response was 74.3% (191/257) among mainly males (85.9%). The mean knowledge score regarding generics was 5.3 (maximum of 9) with 36.6%, 36.1% and 27.2% having poor, average and good knowledge respectively. Cross-tabulation showed statistical significance (P = 0.047) with the duration of practice but not with position, subspecialty or sex. The majority did not agree that generic medicines are of lower quality than branded medicines. Therapeutic failure was a major concern in 82.7%, potentially discouraging prescribing of generics. Majority (63.9%) did not support generic substitution by pharmacists. Conclusion: Knowledge gaps were identified especially with the perception of generics. These need to be addressed.

INTRODUCTION

Generic medicines have the same quality, efficacy and safety properties as originator (branded) medicines while being available at more affordable prices (1-5). According to the United States Food and Drug Administration (FDA), a generic drug product is one that is comparable to an innovator drug product in dosage form, strength, route of administration, quality, performance characteristics and intended use. These are similar definitions in Europe (2, 6). As a result, published studies from these countries have shown similar effectiveness rates between generics and originators (brand name medicines) across a range of classes. These include medicines for infectious and cardiovascular diseases as well as mental health (7-13).

The increasing need for good quality low costs generic medicines has arisen with pharmaceutical expenditure growing by more than 50% in real terms among OECD (Organisation for Economic Co-

operation and Development) countries during the past decade (14), with expenditure on medicines accounting for up to 60% of total healthcare expenditure in some countries (15). This growth in pharmaceutical expenditure has been driven by well know factors. These include the increasing prevalence of non-communicable diseases, enhanced by growing elderly populations in a number of continents including Europe, and the continued launch of new higher priced medicines (16, 17). This has resulted in health authorities introducing measures to moderate pharmaceutical expenditure without compromising care (18, 19).This includes initiatives to increase the prescribing and dispensing of low cost generics versus originators (brand named medicines). Measures and initiatives include educational activities among physicians and patients, reference pricing in a class with patients covering the additional costs themselves for a more expensive molecule, financial incentives for physicians, compulsory generic substitution in pharmacies, substitution targets in pharmacies as well as compulsory International Nonproprietary name (INN) prescribing; alternatively education and other measures to ensure high voluntary INN prescribing (4, 18, 20-29). In their study, Cameron and colleagues believed up to 89% of the cost of medicines could be saved among developing countries from switching patients from originator brands to the lowest priced generics (5). Policies to enhance the prescribing and dispensing of generics in France led to annual savings estimated at €1bn in 2007, €0.905bn in 2008 and €1.01bn in 2009 (19). The use of generic medicines versus more expensive branded (originator) medicines has also been shown to positively impact on medication adherence, appreciably impacting on disease progression and the overall health of the population (30, 31).

There have also been initiatives across countries to increase the prescribing of low cost generics versus patented products in a class where all products in the class are seen as essentially similar at therapeutic doses. These classes include the proton pump inhibitors (PPIs), renin-angiotensin inhibitors and statins (17, 25, 32-36). Published studies have again shown that patient care is not compromised (32, 36-39), whilst moderating or even reducing pharmaceutical expenditure despite increasing utilisation (17, 25, 36, 40-42).

However, there are countries where the prescribing and dispensing of generics versus originators is suboptimal. The reasons for this include physicians' concerns with the safety, efficacy, and bioequivalence of generics versus originators, ease of remembering brand names as well as pharmaceutical company activities promoting concerns with generics (43-50). These differences in perceptions regarding generics have resulted in very different utilization rates for generics across countries. For instance, there is high acceptance of generics among physicians in the UK translating into very high voluntary INN prescribing rates apart from a limited number of situations including certain combination products, lithium, theophyllines and certain medicines to treat epilepsy (24, 25, 51-53).. A variety of educational and other initiatives in the UK have resulted in INN prescribing at 98% to 99% of medicines once they are available as generics across a range of classes where there are no issues with substitution (25). In Malaysia, 85.1% of physicians routinely prescribed generic drugs, although this figure was lower among physicians in private medical centers (43, 50). This contrasts with Italy where a survey conducted between January and March 2011 ascertained that 87% of pediatricians do not prescribe generics due to concerns (54).

Results from several studies in Nigeria have shown that only 42% to 50% of all medications were prescribed by their generic name (55-57). This low rate of generic medicine prescribing contradicts the National Standard Treatment Guidelines, which stipulates that medicines should be prescribed in their generic form, i.e. INN prescribing (58). In Nigeria, the National Agency for Food and Drug Administration (NAFDAC) is the main regulatory body for medicines including biologicals, responsible for marketing authorization of all medications – generics and branded medicines - in the country (59). At the same time, the healthcare sector in Nigeria is under-funded, accounting for less than 6% of the country's GDP between 2010 and 2012, while the proportion of federal government revenue expended on healthcare was 3.5% in 2010 (60, 61). Several studies have shown that out of pocket spending (OOP) in Nigeria constitutes the major form of healthcare expenditure among the population, which can be as high as 62% of total healthcare expenditure (61-64). This will impact on available choices of medicines to treat diseases as well as potential compliance, especially in patients with chronic diseases (65-67). The National Health Insurance Scheme (NHIS), which commenced operations in 2005, was introduced to address some of these issues and concerns; however, it's coverage has remained below 5% of the total population (68).

Increased prescribing of lower cost generic medicines could lead to a reduction in healthcare costs as well as OOP for patients. In addition, offering dispensers the freedom to choose from a wide variety of available generic medicines. However, there are barriers to address including concerns with their efficacy and safety.
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However, information regarding the knowledge, perception and attitude of Nigerian physicians towards generic medicines is lacking. This needs to be addressed in order to develop robust policies to overcome potential misinformation and misconceptions concerning generic medicines. Consequently, the primary objective of this study is to evaluate physicians' understanding of the concept of "generic medicines". Additional objectives include evaluating physicians' perception of generic medicines including their safety, efficacy and bioequivalence versus brand name (originator) medicines as well as assess physicians' prescribing of generic medicines. Subsequently, use the findings to suggest future activities in Nigeria to enhance the prescribing of generics.

METHODS

- Study design

This was a cross-sectional and questionnaire-based study conducted during the months of June to December, 2014.

- Study Sites

The study was conducted among medical doctors working in tertiary healthcare facilities located in four geo-political regions of Nigeria: south-west, south-east, north-central and north-west Nigeria.

- Study Instrument

The questionnaire, comprising four sections, was adapted from a previous study (69). It comprised sections on the general characteristics of the participants, assessment of physicians' understanding of the concept of generic medicines, their perception of their safety and efficacy as well as attitudes towards their prescribing.

The section on physicians' knowledge consisted of 9 statements regarding the concept of generic medicines to which three questions had three options - Yes, No and Don't Know. Each correct (Yes) response was scored 1 whilst "No" and "Don't know" were scored 0, making the total available score of 9. Physicians' knowledge (knowledge level) was subsequently classified into poor (score <5), average (score 5-6) and good (score 7-9). The questionnaire was pilot- tested among ten medical doctors from a secondary level healthcare facility and necessary adjustments made to achieve the objectives before it being administered to the study participants. The internal consistency of the three parts of the questionnaire was calculated (Cronbach's alpha) with the knowledge, perception/attitude and practice aspects scoring 0.70, 0.62 and 0.76 respectively.

We have divided medicines into brand name (originator) medicines and generics. We accept that branded generics are common in a number of countries. However, we wanted to avoid any confusion. We have made this distinction in a number of previous studies involving some of the co-authors when researching the utilization of generics, originators and patented products in a class (34, 42, 70-72). In addition, this was the definition of Cameron and colleagues from the WHO in their recent paper (5).

- Sample size calculation

The estimated sample size was 233 from a population of 1200 physicians from the four geo-political regions. Ten percent of the calculated sample size was added to cater for possible non – responders and poorly completed questionnaires, making a total of 257. The sample size was calculated using the online statistical software from Raosoft Incorporated (73) .

- Sample Population/Selection

Random sampling was used to select respondents among medical doctors working in tertiary healthcare facilities in the selected geo-political regions of Nigeria. The names of all doctors (excluding medical interns) working in the hospitals were compiled from departmental duty rosters and participants were selected using a random technique – dice rolling. Medical interns were excluded because of their lack of experience with prescribing. The selected medical doctors were approached during a departmental seminar in their different units and invited to participate in the study. Written informed consent was then obtained from those who agreed to participate in the study. The questionnaire was subsequently administered to those who agreed to take part and they were given approximately 30 minutes to complete it. The distribution and collection of the questionnaires was coordinated by a co-investigator and one research assistant in each of the participating centers.

- Ethical consideration

Ethical approval was obtained from relevant hospital authorities before commencement of the study. Confidentiality was maintained as respondents were advised not to disclose their identities in their completed questionnaires.

The study was funded through contributions from all co-investigators

- Statistical Analysis

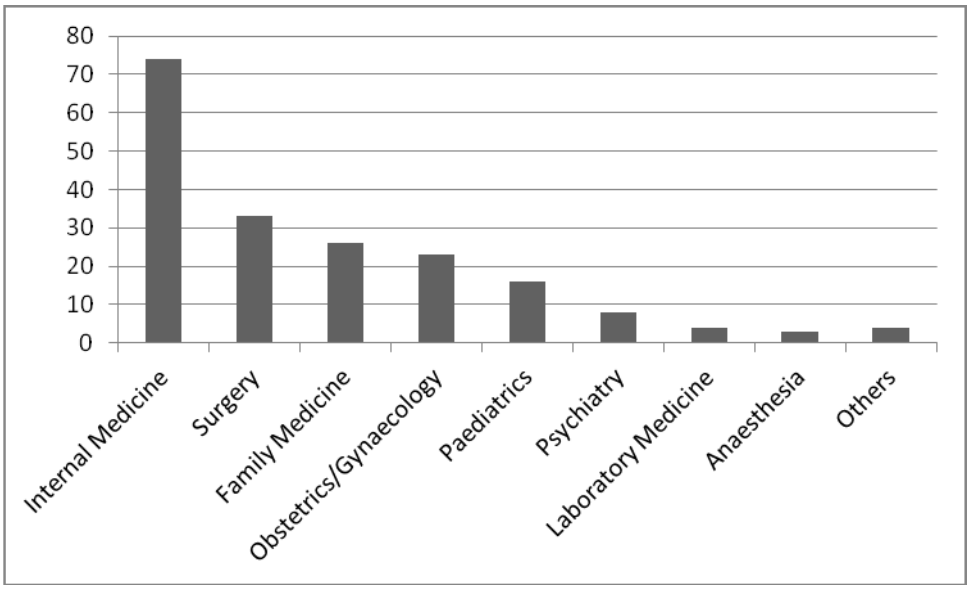
The information obtained from the questionnaire was coded, entered and analyzed using IBM compatible SPSS version 19. Analysis was undertaken using descriptive statistics to obtain the general characteristics of the study participants. Chi square was used to determine the level of significance of the groups of categorical variables. P values <0.05 were considered significant.

RESULTS

- General characteristics of respondents

The response rate was 74.3% (191/257) with a preponderance of males (164/85.9%). Respondents comprised medical registrars (98/51.5%), medical officers (53/27.7%), senior registrars (27/14.1%) and consultants (13/6.7%). Most respondents worked in Internal medicine, followed by Surgery and Family Medicine (Figure 1).

Figure 1: Frequency distribution of respondents (actual numbers) according to their medical specialty



The median duration of work experience (time since obtaining their medical degree) was 4 years with 119 (62.3%), 50 (26.2%) and 22 (11.5%) having 1 to 5yrs, 6 to 10yrs and >10yrs work experience respectively.

- Knowledge about generic medicines

Generic medicines were recognized as copies of brand name (originator) medicines by only 44% of the respondents, whilst 47.1% were aware that generic medicines are interchangeable with brand name medicines (Table 1). The fact that generic medicines are therapeutically equivalent to brand name medicines was known by 97 (50.8%) of respondents. Sixty-seven respondents (35.1%) did not know that generic medicines must be in the same dosage form as its' corresponding brand name medicines, with only 74 (38.7%) respondents aware of the time frame for licensing of generic medicines (Table 1).

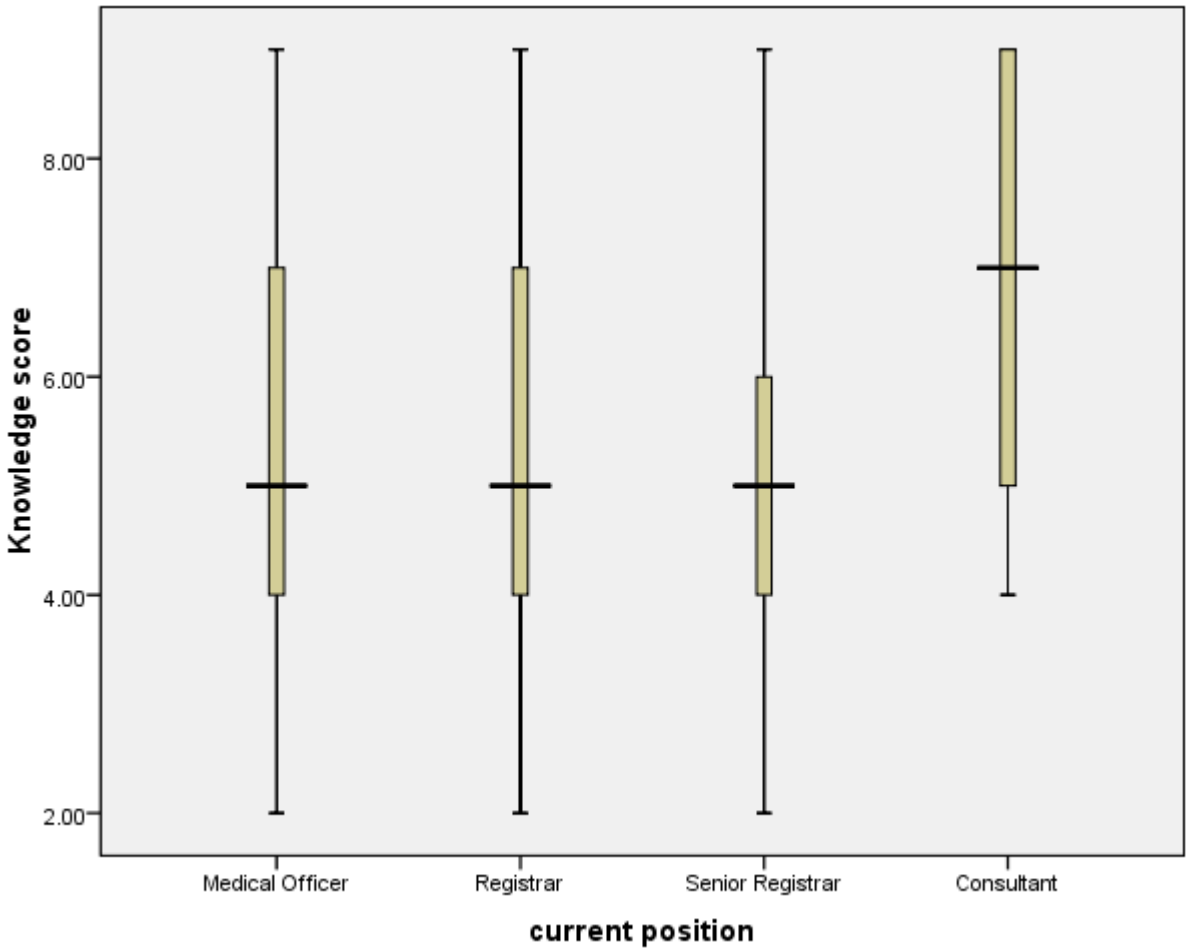
Table 1: The association of physicians' knowledge about generic medicines and some categorical variables

Statements	Yes (%)	No (%)	Don't know (%)	Position X^2 (P-value)	Sex X^2 (P-value	Duration X^2 (P-value
Generic medicines are copy of brand name (originator) medicines	84(44)	88(46.1)	19(9.9)	0.29	0.17	0.18
Generic medicines are interchangeable with brand name (originator) medicines	90(47.1)	86(45.0)	15(7.9)	0.001*	0.94	0.02*
Generic medicines are therapeutically equivalent to brand name medicines	97(50.8)	76(39.8)	18(9.4)	0.008*	0.92	0.40
Generic medicines must be in the same dosage form (such as tablet, capsule) as brand name (originator) medicines	124(64.9)	49(25.7)	18(9.4)	0.72	0.15	0.63
Generic medicines are less safe than brand name (originator) medicines	29(15.2)	139(72.8)	23(12.0)	0.05*	0.18	0.28
Generic medicines are available in the market of Nigeria	147(77.0)	27(14.1)	17(8.9)	0.56	0.35	0.22
Generic medicines are manufactured after the expiration of the patent of the originator/innovator	74(38.7)	67(35.1)	50(26.2)	0.02*	0.17	0.01*
Brand name medicines are of better quality compared with generic medicines	68(35.6)	109(57.1)	14(7.3)	0.045*	0.22	0.17
Brand name (originator) medicines produce lesser side effects than generic medicines	33(17.3)	132(69.1)	26(13.6)	0.83	0.01*	0.31

NB: * denotes P value less than 0.05 (Statistical significance)

The mean knowledge score recorded was 5.3 (SD 1.8) out of the total obtainable score of 9, with 70 (36.6%), 69 (36.1%) and 52 (27.2%) of respondents having poor, average and good knowledge respectively. A comparison of the mean knowledge score among various categories (current position and duration of practice) showed significant statistical significance (P value of 0.02 and 0.01 respectively). A box plot comparing the means of various cadres of respondents is shown in Figure 2.

Figure 2: Comparison of the mean knowledge score of various cadre of physicians



The association of respondents' knowledge, perception and practice with their positions, duration of practice and sex is shown in Tables 1 to 3.

Table 2: The physicians' perception of generic medicines with respect to categorical variables

Statement	Agree (%)	Don't Agree (%)	No opinion (%)	Position X^2 (P value)	Sex X^2 (P value)	Duration X^2 (P value)
Generic medicines are of low quality compared with brand name (originator) medicines	41(21.5)	137(71.7)	13(6.8)	0.02*	0.51	0.67
Generic medicines produce more adverse effects than brand name (originator) medicines	29(15.2)	142(74.3)	20(10.5)	0.03*	0.14	0.28
Low-priced medicines are as safe as high-priced medicines	90(47.1)	72(37.7)	28(18.4)	0.99	0.08	0.84
Drugs from multinational companies are of better quality than medicines produced by local companies	90(47.1)	82(42.9)	19(9.9)	0.001*	0.31	0.09
I believe that not all the local companies in Nigeria are following Good Manufacturing Practices (GMP) guidelines as multinationals	139(72.8)	31(16.2)	21(11.0)	0.83	0.65	0.83
Few local companies are reputable generic medicine manufacturers	134(70.2)	30(15.7)	27(14.1)	0.09	0.28	0.24
My prescribing decision is influenced by medical representatives	39(20.4)	137(71.7)	15(7.9)	0.02*	0.31	0.19
Doctors should be educated more about prices of medicines	169(88.5)	11(5.8)	11(5.8)	0.23	0.09	0.87
Doctors should be given incentives to write generic names	34(17.8)	137(71.7)	20(10.5)	0.31	0.02*	0.95
I think that confidence should be conveyed to the patient about the low-cost medicines	136(71.2)	27(14.1)	28(14.7)	0.81	0.15	0.85
I believe that it is easier to remember a brand name (originator) medicine than a generic	94(49.2)	85(44.5)	12(6.3)	0.78	0.53	0.93

NB: * denotes P value less than 0.05 (Statistical significance)

Table 3: The physicians' attitude/practice of generic medicine prescribing with respect to categorical variables (continued)

Statement	Agree (%)	Disagree (%)	Neutral (%)	Position X^2 (P value)	Sex X^2 (P value)	Duration X^2 (P value)
I am concerned about the therapeutic failures that are associated with some locally manufactured medicines	158(82.7)	13(6.8)	20(10.5)	0.22	0.62	0.98
I am hesitant to prescribe low-priced medicines in some specific therapeutic classes in my practice	143(74.9)	29(15.2)	19(9.9)	0.41	0.01*	0.96
The socioeconomic condition of my patient sometimes influence the prescription given	170(89)	13(6.8)	8(4.2)	0.76	0.08	0.56
I am comfortable prescribing products from local manufacturers	79(41.4)	51(26.7)	61(31.9)	0.96	0.09	0.09
My personal experience with medicines influence my prescribing decisions	165(86.4)	12(6.3)	14(7.3)	0.91	0.09	0.77
I feel that patient's demand of certain medicines influence my prescription	43(22.5)	129(67.5)	19(9.9)	0.22	0.12	0.78
Medical representatives are good sources of information for me	85(44.5)	62(32.5)	44(23)	0.13	0.008*	0.86
Pharmaceutical companies' premium offers (gifts) influence my prescribing behaviour	23(12.0)	135(70.7)	33(17.3)	0.54	0.01*	0.64
I am comfortable if the brand name (originator) medicine in prescription is substituted by the pharmacist	34(17.8)	122(63.9)	35(18.3)	0.03*	0.51	0.52
I usually prescribe generic medicines for my patients	117(61.3)	37(19.4)	37(19.4)	0.55	0.008*	0.32

NB: * denotes P value less than 0.05 (Statistical significance)

Cross-tabulation of the knowledge level of respondents showed significant statistical significance (P = 0.047) with duration of practice but not with position, subspecialty and sex (Table 4).

Table 4: knowledge level of respondents according to some categorical variables

Categorical variable	Poor knowledge	Average knowledge	Good knowledge	X^2 (P value)
Position				
Medical Officer	20 (37.7)	19 (35.9)	14 (26.4)	
Registrar	38 (38.8)	34 (34.7)	26 (26.5)	
Senior Registrar	10 (37.1)	12 (44.4)	5 (18.5)	
Consultants	2 (15.4)	4 (30.8)	7 (53.8)	0.361
Duration (post qualification)				
1-5 years	45 (37.8)	46 (38.7)	28 (23.5)	
6 – 10 years	19 (38.0)	19 (38.0)	12 (24.0)	
>10 years	6 (27.3)	4 (18.2)	12 (54.5)	0.047*
Sex				
Male	58 (35.4)	60 (36.6)	46 (28.1)	
Female	12(44.5)	9 (33.3)	6 (22.2)	0.65

NB: *Indicates P value less than 0.05 (Statistical significance)

- Perception of doctors towards generic medicines

The majority (71.7%) of respondents did not agree that generic medicines are of lower quality than branded medicines (Table 2). Only 29 (15.2%) respondents agreed that generic medicines produced more side-effects than brand name medicines while 90 (47.1%) felt that low-priced generic medicines are as safe as the expensive branded ones (Table 2).

Regarding the quality of generic medicines produced by local drug manufacturers, 90 (47.1%) of respondents were of the opinion that they were of lower quality than those produced by multi-national pharmaceutical companies (Table 2). On the issue of Good Manufacturing Practice (GMP), 139 (72.8%) respondents believe that few local companies observe GMP, hence only 30 (15.7%) view local manufacturers as reputable producers of generic drugs. On whether doctors should be given incentives to prescribe generic medicines, the majority (71.7%) disagreed with this suggestion; whilst71.2% felt that patients should be educated about generic medicines to boost their confidence (Table 2).

- Attitude/Practice of doctors towards prescribing generic medicines

On the issue of therapeutic failures occurring with generic medicines, 158 (82.7%) respondents were seriously concerned discouraging them from prescribing low-priced generic medicines (Table 3). In fact, 74.9% stated their reluctance to prescribe generic medicines from some specific therapeutic classes based on these concerns (Table 3). Many (89%) of the respondents were also influenced by the socio-economic class of the patients and personal experience with the medicines (86.4%) when prescribing (Table 3).

Eighty-five respondents (44.5%) believed that medical representatives are good sources of information regarding medicines whilst only 23 (12%) believed they are influenced by gifts from pharmaceutical companies (Table 3).

Finally, most of the physicians (63.9%) would not be comfortable if there was generic substitution of brand name (originator) medicines by pharmacists (Table 3).

DISCUSSION

This cross-national study is one of the few studies to date in Nigeria evaluating the knowledge, perception and attitude of medical doctors towards generic medicines. It has identified significant gaps in the knowledge and perception among physicians in Nigeria that may hamper the prescribing of generic medicines.

Overall, we had a response rate to the questionnaire at close to 75%. This is close to 80% obtained in a similar study among Greek physicians (74). However, appreciably higher than a 36% response rate obtained in a questionnaire study to ascertain private physicians' perception of generic medicines in Malaysia (50). It was also noticed that more junior medical doctors participated in our study. This though reflects the current distribution of medical doctors in many tertiary healthcare facilities in Nigeria. Results from surveys conducted among physicians have identified lack of time as the main reason for non-response (75, 76).

We will first comment on the findings before suggesting potential ways forward in Nigeria to enhance the prescribing of generics.

- Knowledge about generic medicines

In this study, less than half of the respondents were aware of the definition of generic medicines as copy of the original brand and being interchangeable with it (Table 1). This was higher than some published studies but lower than others. Jamshed et al in their study among general practitioners in Pakistan found that 71.8% of respondents had the correct definition (69). However, Fabianio et al in their study found only 32.6% and 37.2% of Italian pediatricians were seen to have sufficient and good knowledge of generic medicines respectively (54). In addition, only 2.3% to 4.6% of physicians in Malaysia correctly identified bioequivalence standards for generic medicines in recent studies (43, 50).

In this study, 63.7% of respondents had at least average knowledge about the concept of generic medicine, with those with more than 10 years post-graduation experience having a higher mean score. This finding is suggestive of a positive influence of post-graduate education and experience on physicians' knowledge about the concept of generic medicines. This was in contrast to the study by Awaisu et *al* among community pharmacists in Qatar, who found that work experience did not positively influence the knowledge of their respondents about generic medicines (77). The different findings may not be surprising as our study was conducted in tertiary healthcare facilities where the majority of respondents were involved with post-graduate medical education. The pharmacist studied by Awaisu *et al* might not be undergoing similar continual education.

- Perception of doctors towards generic medicines

As mentioned, most of the concerns regarding generic medicines revolve around their safety and efficacy versus originators (brand name medicines). This was a common finding in a recent systematic review regarding attitudes towards generics among physicians from low and middle income countries (78).

In this study, 39.8% of respondents believed generic medicines were not therapeutically equivalent to brand named medicines and 35.6% believed brand named medicines were of better quality (Table 1). However, 69.1% did not believe brand named (originator) medicines produce less side-effects and only 15.2% of respondents believed generic medicines are less safe (Tables 1 and 2). This was lower than 41.3% of respondents in the study by Jamshed (69) and 42.2% of private physicians in Malaysia, who believed generic medicines produce more side-effects than brand named medicines (50). In addition, lower than Zaoui et *al* in their study conducted in Morocco found that 68% of respondents believed generic drugs were not always effective (79).

The possibility of therapeutic failure is a major concern among physicians when prescribing generic medicines. In this study, 82.7% of respondents were worried about the possibility of treatment failure and 74.9% would hesitate to prescribe generics from certain therapeutic classes (Table 3). The issue of therapeutic failure is directly related to that of bioequivalence (80, 81). In the study by Zaoui in Morocco, 70% of respondents would prescribe generic drugs if bioequivalence to branded medicines is ascertained (79). In the study among community pharmacists in Qatar, the lack of proven bioequivalence to branded medicines is a major hindrance to the prescribing of generic medicines (77).

The view of majority of respondents in this study (70.2% - Table 2) that only a few local companies are reputable manufacturers of generic drugs is a cause for concern. Building trust and capacity in the local manufacture of generics will help to lower costs and enable the manufacturers in Nigeria to compete globally.

- Attitude/Practice of doctors towards prescribing generic medicines

The relationship between the pharmaceutical industry and medical practitioners has attracted considerable debate globally (82-88).

In our study, 12.0% of respondents admitted their prescribing practices are influenced by gifts from pharmaceutical companies and 44.5% believed medical representatives were a good source of information regarding medicines (Table 3). This is similar to the study by Kersnik et al among pharmacists and prescribers in Slovenia, who found only 15.5% of prescribers considered their prescribing was influenced by pharmaceutical representatives (89). However, lower than the study by Riaz et al in Pakistan who found that 68% to 86% of the physicians surveyed obtained their knowledge of medicines from medical representatives (90).

The importance of knowing the costs of medications being prescribed cannot be over-emphasized as it contributes to rational use of medications. In this study, 88.5% of respondents agreed that medical doctors should be educated about the costs of medicine (Table 2). Toklu et *al* in their study conducted in Turkey also reported that 92% of prescribers took cost of medicines into consideration when prescribing (91).

- Future suggestions and initiatives

This study identified a number of gaps especially in the areas of perception and practice of generic medicines and their prescribing by physicians in Nigeria.

The perception of poor quality of generic medicines by respondents in this study resonates with the widespread problems of sub-standard medication that has attracted a lot of attention in recent times (92, 93). The role of the World Health Organization (WHO) and other international donor agencies in ensuring the provision of quality generic medicines for diseases such as malaria, TB and HIV has positively impacted patients' outcomes (94). Expanding this pre-qualification process to other essential medicines, especially for non-communicable diseases like hypertension and diabetes mellitus, would most likely have a similar effect. Also, strict regulations including proven bioequivalence of medicines would promote physicians' confidence in prescribing generics (95).

The findings suggest there is an urgent need in Nigeria to build up the trust of prescribers in generic medicines to save costs for patients and the health service. This can be achieved through instigating mandatory quality assurance programmes among local generic manufacturers, as well as the statutory provision of the bioequivalence data and standards, given that 72.8% had concerns with local manufacturers (Table 2). This mirrors practices in the US and Europe (2). Such measures should enhance physician trust regarding local generic manufacturers, and enhance their potential for export across Africa and more widely.

The findings also suggest there is a need to instigate measures to enhance the prescribing of generics versus brand named (originator) medicines in line with the National Standard Treatment Guidelines in Nigeria (58). Measures could include routine encouragement of INN prescribing apart from a limited number of situations, starting with training in medical school similar to the UK (25). This

includes educating physicians on issues such as bioequivalence for generics to address misconceptions (2). In addition, emphasizing that the prescribing of good quality generics should not compromise care as seen by published studies across a range of disease areas (7-13).

Generic substitution has also been one of the measures adopted by many countries to enhance the use of generic medicines (1). However, the majority (63.9%) of respondents in this study did not support generic substitution by the pharmacists (Table 3). This is similar to other findings depending on the faith physicians have in their regulatory system as well as other factors. 68% of prescribers in a study conducted in Morocco rejected generic substitution because it infringed on their prescribing freedom whilst 35.6% of patients in a Nigerian study rejected generic substitution at some time (79, 96). In a study conducted among drug retailers and community pharmacists in India, 80% of respondents rejected generic substitution(97). However, Awaisu et al found that 72% of community pharmacists supported generic substitution (77). Generic substitution is also generally supported by key stakeholder groups in Sweden to help conserve costs (26, 98, 99). These differences in opinion may be due to inter-professional conflicts between physicians and pharmacists, the practice environment (country), perceived differences between generic products and brand named products as well as personal experience with generic and brand named (originator) products.

There also needs to be an increase in continual professional development activities among physicians in Nigeria, including education from Drugs and Therapeutics Committees, to reduce the reliance on the pharmaceutical industry for education about medicines (Table 3).

We are aware that there are limitations with this study. We acknowledge that this study was conducted mainly among physicians working in tertiary healthcare facilities in Nigeria and its findings may not be completely generalized to physicians in other care settings. However we believe our findings may partly reflect the prescribing behaviour and understanding of generic medicines among doctors in other settings as more than 10% of the participating physician worked in general medical/family medicine specialty. We are also aware there was a greater proportion of male physicians taking part in our study at 86% of respondents compared with the normal situation of 75% in hospitals. We also accept that using the default option in allocating equal weights to the questions in the “knowledge” domain might be associated with some problems. Finally, whilst there are difficulties in estimating the actual number of medical doctors working in different geo-political regions of Nigeria to add further depth to our analysis, data from the Nigerian Medical Association revealed that approximately 70% of medical doctors practice in urban areas where most tertiary healthcare institutions (including those where some of the study participants practice) are located (100).

However, the sample size, multi-centered nature of the study and the use of previously validated instrument in previous studies with good internal constituency are strengths that add robustness to the study results and the implications. In addition, the ability to compare findings across countries. Consequently, we are confident in the findings and their implications.

We are also aware that cost differences between generics and brand named (originator medicines) was not addressed in this study with previous published studies in Nigeria showing the importance of the cost of medicines on prescribing choices (65). There is however ample evidence of significant cost differences between these two groups of medicines. In the study conducted by Cameron et *al* in Nigeria and 35 other developing and middle income countries (101), the ratio of the cost of originator (branded) to generic medicines for amoxicillin, ciprofloxacin and glibenclamide was 10, 14 and 9 respectively (101).In addition, this will be the subject of future papers with recent findings showing prices of originator atorvastatin were four times higher in Nigeria than the generic (Onyinye Akunne personal communication). Prices of generic simvastatin in Nigeria were also considerably higher than those seen in the Netherlands, Sweden or the UK where multiple measures have resulted in generic simvastatin (20 and 40mg) costing only US$2 to US$5 per month (25, 102, 103).

Key points

- The prescribing of good quality generics saves considerable resources for patients and health care systems without compromising care. This is especially important in Nigeria where the healthcare sector is underfunded and there are considerable out-of-pocket payments

- However, there have been low rates of generic prescribing in Nigeria contradicting the National Standard Treatment Guidelines
- A cross-sectional questionnaire among physicians in Nigeria ascertained that only 27% had good knowledge concerning generics versus 36% with average knowledge and 37% with poor knowledge. There was though statistical significance with the duration of medical practice but not with physicians' position, subspecialty or sex
- The majority of physicians (72% and 69% respectively) did not agree that generic medicines were of lower quality than branded (originator) medicines and are associated with greater side-effects. In addition, only 15.2% believed generic medicines are less safe than brand (originator) medicines
- An appreciable proportion of physicians believed (44.5%) pharmaceutical companies were a good source of information regarding medicines although only 12% admitted being influenced by gifts from pharmaceutical companies
- There is an urgent need to address physician trust in the generics from local manufacturers as well as enhance INN prescribing generally. This will benefit local manufacturers as well as patients and the healthcare system

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References

1. Hassali MA, Alrasheedy AA, McLachlan A, Nguyen TA, Al-Tamimi SK, Ibrahim MI, et al. The experiences of implementing generic medicine policy in eight countries: A review and recommendations for a successful promotion of generic medicine use. Saudi pharmaceutical journal : SPJ : the official publication of the Saudi Pharmaceutical Society. 2014;22(6):491-503.
2. Baumgartel C. Myths, questions, facts about generic drugs in the EU. Generics and Biosimilars Initiative Journal (GaBI). 2012;1(1):34-8.
3. Dylst P, Vulto A, Godman B, Simoens S. Generic medicines: solutions for a sustainable drug market? Applied health economics and health policy. 2013;11(5):437-43.
4. Vogler S. The impact of pharmaceutical pricing and reimbursement policies on generics uptake: implementation of policy options on generics in 29 European countries–an overview. Biosimilars Initiative Journal (GaBI Journal). 2012;1(2):93-100.
5. Cameron A, Mantel-Teeuwisse AK, Leufkens HG, Laing RO. Switching from originator brand medicines to generic equivalents in selected developing countries: how much could be saved? Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2012;15(5):664-73.
6. U.S. Food and Drug Administration. Abbreviated New Drug Application (ANDA): Generics.
7. 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 : the journal of the American Medical Association. 2008;300(21):2514-26.
8. Kesselheim AS, Stedman MR, Bubrick EJ, Gagne JJ, Misono AS, Lee JL, et al. Seizure outcomes following the use of generic versus brand-name antiepileptic drugs: a systematic review and meta-analysis. Drugs. 2010;70(5):605-21.
9. 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.
10. 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.
11. 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; discussion 53.
12. Veronin M. Should we have concerns with generic versus brand antimicrobial drugs? A review of issues. JPHSR 2011;2:135-50.
13. Paton C. Generic clozapine: outcomes after switching formulations. The British journal of psychiatry : the journal of mental science. 2006;189:184-5.
14. OECD. OECD, Health at a Glance 2011: OECD Indicators. Pharmaceutical expenditure OECD Publishing. Available at URL:http://www.oecd.org/els/health-systems/49105858.pdf

15. Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. Lancet. 2009;373(9659):240-9.
16. Kaplan W, Wirtz V, Mantel-Teeuwisse A, Stolk P, Duthey B, Laing R. Priority Medicines for Europe and the World 2013 Update Report. Available at URL::http://www.who.int/medicines/areas/priority_medicines/MasterDocJune28_FINAL_Web.pdf?ua=1.
17. 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.
18. Dylst P, Vulto A, Simoens S. Demand-side policies to encourage the use of generic medicines: an overview. Expert review of pharmacoeconomics & outcomes research. 2013;13(1):59-72.
19. Godman B, Abuelkhair M, Vitry A, Abdu S, Bennie M, Bishop I et al. Payers endorse generics to enhance prescribing efficiency; impact and future implications, a case history approach. GaBI. 2012;1(2):21-35.
20. Vogler S, Zimmermann N. How do regional sickness funds encourage more rational use of medicines, including the increase of generic uptake? A case study from Austria. . Generics and Biosimilars Initiative Journal (GaBI Journal). 2013;2(2):65-75.
21. Poluzzi E, Veronese G, Piccinni C, Raschi E, Koci A, Pagano P, et al. Switching among Equivalents in Chronic Cardiovascular Therapies: 'Real World' Data from Italy. Basic & clinical pharmacology & toxicology. 2015.
22. Sermet C, Andrieu V, Godman B, Van Ganse E, Haycox A, Reynier JP. Ongoing pharmaceutical reforms in France: implications for key stakeholder groups. Applied health economics and health policy. 2010;8(1):7-24.
23. Garuoliene K, Godman B, Gulbinovic J, Wettermark B, Haycox A. European countries with small populations can obtain low prices for drugs: Lithuania as a case history. Expert review of pharmacoeconomics & outcomes research. 2011;11(3):343-9.
24. 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.
25. Godman B, Bishop I, Finlayson AE, Campbell S, Kwon HY, Bennie M. Reforms and initiatives in Scotland in recent years to encourage the prescribing of generic drugs, their influence and implications for other countries. Expert review of pharmacoeconomics & outcomes research. 2013;13(4):469-82.
26. Andersson KA, Petzold MG, Allebeck P, Carlsten A. Influence of mandatory generic substitution on pharmaceutical sales patterns: a national study over five years. BMC health services research. 2008;8:50.
27. Moe-Byrne T, Chambers D, Harden M, McDaid C. Behaviour change interventions to promote prescribing of generic drugs: a rapid evidence synthesis and systematic review. BMJ open. 2014;4(5):e004623.
28. Kjoenniksen I, Lindbaek M, Granas AG. Patients' attitudes towards and experiences of generic drug substitution in Norway. Pharmacy world & science : PWS. 2006;28(5):284-9.
29. Godman B, Bishop I, Campbell SM, Malmstrom RE, Truter I. Quality and efficiency of statin prescribing across countries with a special focus on South Africa; findings and future implications. Expert review of pharmacoeconomics & outcomes research. 2015;15(2):323-30.
30. Bao Y, Ryan AM, Shao H, Pincus HA, Donohue JM. Generic initiation and antidepressant therapy adherence under Medicare Part D. Am J Manag Care. 2013;19(12):989-98.
31. Briesacher BA, Andrade SE, Fouayzi H, Chan KA. Medication adherence and use of generic drug therapies. The American journal of managed care. 2009;15(7):450-6.
32. Sakshaug S, Furu K, Karlstad O, Ronning M, Skurtveit S. Switching statins in Norway after new reimbursement policy: a nationwide prescription study. British journal of clinical pharmacology. 2007;64(4):476-81.
33. Martikainen JE, Saastamoinen LK, Korhonen MJ, Enlund H, Helin-Salmivaara A. Impact of restricted reimbursement on the use of statins in Finland: a register-based study. Medical care. 2010;48(9):761-6.
34. Moon J, Godman B, Petzold M, Alvarez-Madrazo S, Bennett K, Bishop I, Bucsics A, Hesse U, Martin A, Simoens S, Zara C, Malmstrom RE. Different initiatives across Europe to enhance losartan utilisation post generics: impact and implications Frontiers in pharmacology. 2014;5(Article 219):1-10.
35. Heinze G, Hronsky M, Reichardt B, Baumgartel C, Mullner M, Bucsics A, et al. Potential Savings in Prescription Drug Costs for Hypertension, Hyperlipidemia, and Diabetes Mellitus by Equivalent Drug Substitution in Austria: A Nationwide Cohort Study. Applied health economics and health policy. 2014.
36. Usher-Smith J, Ramsbottom T, Pearmain H, Kirby M. Evaluation of the clinical outcomes of switching patients from atorvastatin to simvastatin and losartan to candesartan in a primary care setting: 2 years on. International journal of clinical practice. 2008;62(3):480-4.
37. 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.
38. Martin A, Godman B, Miranda J, Tilstone J, Saleem N, Olsson E, et al. Measures to improve angiotensin receptor blocker prescribing efficiency in the UK: findings and implications. Journal of comparative effectiveness research. 2014;3(1):41-51.
39. Norman C, Zarrinkoub R, Hasselstrom J, Godman B, Granath F, Wettermark B. Potential savings without compromising the quality of care. International journal of clinical practice. 2009;63(9):1320-6.
40. King DR, Kanavos P. Encouraging the use of generic medicines: implications for transition economies. Croat Med J. 2002;43(4):462-9.

41. Paris V. Pharmaceutical regulation in France 1980-2003. Int J Health Plann Manage. 2005;20(4):307-28.
42. Godman B, Shrank W, Andersen M, Berg C, Bishop I, Burkhardt T, et al. Comparing policies to enhance prescribing efficiency in Europe through increasing generic utilization: changes seen and global implications. Expert review of pharmacoeconomics & outcomes research. 2010;10(6):707-22.
43. Chua GN, Hassali MA, Shafie AA, Awaisu A. A survey exploring knowledge and perceptions of general practitioners towards the use of generic medicines in the northern state of Malaysia. Health Policy. 2010;95(2-3):229-35.
44. Theodorou M, Tsiantou V, Pavlakis A, Maniadakis N, Fragoulakis V, Pavi E, et al. Factors influencing prescribing behaviour of physicians in Greece and Cyprus: results from a questionnaire based survey. BMC Health Serv Res. 2009;9:150.
45. Al-Jazairi AS, Bhareth S, Eqtefan IS, Al-Suwayeh SA. Brand and generic medications: are they interchangeable? Ann Saudi Med. 2008;28(1):33-41.
46. Babar ZU, Grover P, Stewart J, Hogg M, Short L, Seo HG, et al. Evaluating pharmacists' views, knowledge, and perception regarding generic medicines in New Zealand. Res Social Adm Pharm. 2011;7(3):294-305.
47. Dylst P, Vulto A, Simoens S. Analysis of French generic medicines retail market: why the use of generic medicines is limited. Expert review of pharmacoeconomics & outcomes research. 2014;14(6):795-803.
48. Editorial. Generic bashing: effective but illegal. PRESCRIRE INTERNATIONAL 2013;22(144):307.
49. Baumgärtel C, Godman B, Malmström R, Andersen M et al. What lessons can be learned from the launch of generic clopidogrel? GaBI Journal. 2012;1(2):58-68.
50. Kumar R, Hassali MA, Saleem F, Alrasheedy AA, Kaur N, Wong ZY, et al. Knowledge and perceptions of physicians from private medical centres towards generic medicines: a nationwide survey from Malaysia. Journal of pharmaceutical policy and practice. 2015;8(1):11.
51. Ferner RE, Lenney W, Marriott JF. Controversy over generic substitution. BMJ (Clinical research ed). 2010;340:c2548.
52. MHRA. Antiepileptic drugs: new advice on switching between different manufacturers' products for a particular drug. Available from URL: http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON3367162013.
53. Godman B, Baumgartel C. Are generic immunosuppressants safe and effective? BMJ (Clinical research ed). 2015;350:h3248.
54. Fabiano V, Mameli C, Cattaneo D, Delle Fave A, Preziosa A, Mele G, et al. Perceptions and patterns of use of generic drugs among Italian family pediatricians: first round results of a web survey. Health Policy. 2012;104(3):247-52.
55. Adebayo ET, Hussain NA. Pattern of prescription drug use in Nigerian army hospitals. Ann Afr Med. 2010;9(3):152-8.
56. Enwere OO, Falade CO, Salako BL. Drug prescribing pattern at the medical outpatient clinic of a tertiary hospital in southwestern Nigeria. Pharmacoepidemiology and drug safety. 2007;16(11):1244-9.
57. Tamuno I, Fadare JO. Drug prescription pattern in a Nigerian tertiary hospital. Tropical Journal of Pharmaceutical Research. 2012;11(1):146-52.
58. Federal Ministry of Health. Standard Treatment Guidelines,. Abuja, Nigeria2008.
59. National Agency for Food and Drug Administration and Control (NAFDAC). GUIDELINES FOR REGISTRATION OF DRUGS AND RELATED PRODUCTS

MANUFACTURED IN NIGERIA. 2014.
60. Health Expenditure, total (% of GDP) [Internet]. [cited 7th March, 2015]. Available from: www.worldbank.org.
61. Onah MN, Govender V. Out-of-Pocket payments, health care access and utilisation in South-Eastern Nigeria: A gender perspective. PLoS One. 2014;9(4):e93887.
62. Onwujekwe O, Hanson K, Ichoku H, Uzochukwu B. Financing incidence analysis of household out-of-pocket spending for healthcare: getting more health for money in Nigeria? Int J Health Plann Manage. 2014;29(2):e174-85.
63. Ewelukwa O, Onoka C, Onwujekwe O. Viewing health expenditures, payment and coping mechanisms with an equity lens in Nigeria. BMC Health Serv Res. 2013;13:87.
64. Odeyemi IA, Nixon J. Assessing equity in health care through the national health insurance schemes of Nigeria and Ghana: a review-based comparative analysis. Int J Equity Health. 2013;12:9.
65. Ezenduka C, UbochiV, Ogbonna B. The Utilization Pattern and Costs Analysis of Psychotropic Drugs at a Neuropsychiatric Hospital in Nigeria. British Journal of Pharmaceutical Research. 2014;4(3):325-37.
66. Barbui C, Conti V. Adherence to generic v. brand antidepressant treatment and the key role of health system factors. Epidemiology and psychiatric sciences. 2014:1-4.
67. Shrank WH, Hoang T, Ettner SL, Glassman PA, Nair K, DeLapp D, et al. The implications of choice: prescribing generic or preferred pharmaceuticals improves medication adherence for chronic conditions. Archives of internal medicine. 2006;166(3):332-7.
68. Onwujekwe OE, Uzochukwu BS, Obikeze EN, Okoronkwo I, Ochonma OG, Onoka CA, et al. Investigating determinants of out-of-pocket spending and strategies for coping with payments for healthcare in southeast Nigeria. BMC Health Serv Res. 2010;10:67.

69. Jamshed SQ, Ibrahim MI, Hassali MA, Masood I, Low BY, Shafie AA, et al. Perception and attitude of general practitioners regarding generic medicines in Karachi, Pakistan: A questionnaire based study. Southern med review. 2012;5(1):22-30.
70. Godman B, Shrank W, Andersen M, Berg C, Bishop I, Burkhardt T, et al. Policies to enhance prescribing efficiency in europe: findings and future implications. Frontiers in pharmacology. 2010;1:141.
71. Godman B, Petzold M, Bennett K, Bennie M, Bucsics A, Finlayson AE, et al. Can authorities appreciably enhance the prescribing of oral generic risperidone to conserve resources?: Findings from across Europe and their implications. BMC medicine. 2014;12(1):98.
72. Voncina L, Strizrep T, Godman B, Bennie M, Bishop I, Campbell S, et al. Influence of demand-side measures to enhance renin-angiotensin prescribing efficiency in Europe: implications for the future. Expert review of pharmacoeconomics & outcomes research. 2011;11(4):469-79.
73. Raosoft Inc. Raosoft Sample Size Calculator Seattle, USA2004 [cited 2015 May 15]. Available from: http://www.raosoft.com/samplesize.html.
74. Labiris G, Fanariotis M, Kastanioti C, Alexias G, Protopapas A, Karampitsakos T, et al. Greek Physicians' Perceptions on Generic Drugs in the Era of Austerity. Scientifica (Cairo). 2015;2015:251792.
75. Key C, Layton D, Shakir SA. Results of a postal survey of the reasons for non-response by doctors in a Prescription Event Monitoring study of drug safety. Pharmacoepidemiol Drug Saf. 2002;11(2):143-8.
76. Fischer S, Miccinesi G, Hornung R, Bosshard G, Deliens L, van der Heide A, et al. Responders and non-responders in a study on medical end-of-life decisions in Denmark, the Netherlands, Sweden and Switzerland. Soz Praventivmed. 2006;51(1):24-33.
77. Awaisu A, Kheir N, Ibrahim MI, El-Hajj M, Hazi H, Khudair N, et al. Knowledge, attitudes, and practices of community pharmacists on generic medicines in Qatar. Int J Clin Pharm. 2014;36(2):394-404.
78. Hassali MA, Wong ZY, Alrasheedy AA, Saleem F, Mohamad Yahaya AH, Aljadhey H. Perspectives of physicians practicing in low and middle income countries towards generic medicines: a narrative review. Health Policy. 2014;117(3):297-310.
79. Zaoui S, Hakkou F, Filali H. [Generic drugs in morocco: survey of physicians]. Therapie. 2011;66(6):499-506.
80. Borgheini G. The bioequivalence and therapeutic efficacy of generic versus brand-name psychoactive drugs. Clin Ther. 2003;25(6):1578-92.
81. Le Corre P. [Bioequivalence and generics of index drugs with narrow therapeutic margins]. Presse Med. 2010;39(2):169-76.
82. 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.
83. Yu SY, Yang BM, Kim JH. New anti-rebate legislation in South Korea. Applied health economics and health policy. 2013;11(4):311-8.
84. Roehr B. Drug companies will have to report all payments to US doctors from March 2014. BMJ. 2013;346:f826.
85. Davis C, Abraham J. Is there a cure for corporate crime in the drug industry? BMJ. 2013;346:f755.
86. Voncina L, Strizrep T. Croatia: 2009/2010 pharmaceutical pricing and reimbursement reform. Eurohealth. 2011;16(4):20-2.
87. 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.
88. 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.
89. Kersnik J, Peklar J. Attitudes of Slovene general practitioners towards generic drug prescribing and comparison with international studies. J Clin Pharm Ther. 2006;31(6):577-83.
90. 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. Journal of Pharmaceutical Health Services Research. 2015;6:111-21.
91. Toklu HZ, Dulger GA, Hidiroglu S, Akici A, Yetim A, Gannemoglu HM, et al. Knowledge and attitudes of the pharmacists, prescribers and patients towards generic drug use in Istanbul - Turkey. Pharm Pract (Granada). 2012;10(4):199-206.
92. Newton PN, Amin AA, Bird C, Passmore P, Dukes G, Tomson G, et al. The primacy of public health considerations in defining poor quality medicines. PLoS Med. 2011;8(12):e1001139.
93. Johnston A, Holt DW. Substandard drugs: a potential crisis for public health. Br J Clin Pharmacol. 2014;78(2):218-43.
94. t Hoen EF, Hogerzeil HV, Quick JD, Sillo HB. A quiet revolution in global public health: The World Health Organization's Prequalification of Medicines Programme. J Public Health Policy. 2014;35(2):137-61.
95. Wang YR. The Chinese pharmaceutical market at the crossroads: pro-competition solutions to improve access, quality and affordability. Appl Health Econ Health Policy. 2005;4(3):147-51.
96. Oyetunde OO, Aina BA, Tayo F. Impact of generic substitution practice on care of diabetic patients. Int J Clin Pharm. 2014;36(3):623-9.
97. Basak SC, Sathyanarayana D. Exploring knowledge and perceptions of generic medicines among drug retailers and community pharmacists. Indian J Pharm Sci. 2012;74(6):571-5.

98. Andersson K, Sonesson C, Petzold M, Carlsten A, Lonnroth K. What are the obstacles to generic substitution? An assessment of the behaviour of prescribers, patients and pharmacies during the first year of generic substitution in Sweden. Pharmacoepidemiology and drug safety. 2005;14(5):341-8.
99. Andersson K, Jorgensen T, Carlsten A. Physicians' opinions and experiences of the Pharmaceutical Benefits Reform. Scandinavian journal of public health. 2006;34(6):654-9.
100. Nigerian Medical Association. Available from: http://nationalnma.org/.
101. Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. The Lancet.373(9659):240-9.
102. 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.
103. Godman B, Wettermark B, Hoffmann M, Andersson K, Haycox A, Gustafsson LL. Multifaceted national and regional drug reforms and initiatives in ambulatory care in Sweden: global relevance. Expert review of pharmacoeconomics & outcomes research. 2009;9(1):65-83.