Original Article

Readability of Medication Package Inserts Accompanying Prescription Drugs and Conformity of the Package Inserts Information with Regulatory Requirements

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ABSTRACT

Background: Medication package inserts (MPIs) provides patients with appropriate information on the rational use of drugs. This study evaluated the level of conformity of MPIs with the regulatory drug labelling requirements and determined the readability of selected prescription MPIs. **Methods:** One hundred and fifty-six MPIs of commonly used and prescribed antilipidemics, anticonvulsants, anti-diabetes, antiarthritis and antihypertensives in Nigeria were retrieved from four pharmacies. The MPIs were evaluated on the availability of 20 items drug labelling requirements for prescription drugs by the National Agency for Food and Drug Administration and Control (NAFDAC). The readability of 31 randomly selected MPIs was assessed with seven readability measures. Primary outcomes were percentage conformity with the labelling requirements and reading grade level of the MPIs. Secondary outcomes were the MPIs sentence characteristics. **Results:** The percentage conformity with NAFDAC drug requirements of the MPIs ranged from 82.9% to 89.6%. All the MPIs included information on active ingredient(s), adverse drug reactions, and indications. Few MPIs, 46.8% had section on product net content and 53 (34.0%) omitted information on overdose. The reading grade level for the MPIs was 14.55 ± 1.71 (undergraduate level). Most of the MPIs, 25 (80.6%), were very difficult to read. **Conclusion:** The percentage conformity of the MPIs with NAFDAC drug labelling requirements was high though few vital information were missing in some MPIs. Majority of the MPIs were very difficult to read. The regulatory authority may need to optimize MPIs readability and conformity of content with drug labelling requirements prior to marketing.

Keywords: Medication package inserts, Drug labelling, Readability assessment, SMOG readability assessment, Reading grade level, Nigeria.

INTRODUCTION

Medication package inserts (MPIs) are essential health education and information tool for both patients and health care professionals. The World Health Organization's Ethical Criteria for Medical Drug Promotion advocated the inclusion of patient MPIs in all medicinal products,[1] a shift from the more technical drug literature inserts. Medication package inserts are written by pharmaceutical companies but regulated by national bodies such as the U.S Food and Drug Administration, European Medicine Agency, and in Nigeria by the National Agency for Food and Drug Administration and Control (NAFDAC). The new ethical criteria for medical drug promotion recommended that information in MPIs should reflect only those approved by the country's drug regulatory authority.[1] In line with this, NAFDAC regulation for product registration stated that *"All prescription only drugs shall be accompanied by a package insert with relevant information as required in these Regulations and any other information as may be required by the Agency"*.[2]

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Well written information in MPIs should encourage adherence to medications, improve patient knowledge of the disease, and understanding of the treatment goals.[3] To achieve these, MPIs must first conform with the requirements of the nation's drug regulatory guideline on the content of MPIs. The information in the MPIs should be clear, readable, understandable, and written in layman›s language. Because of the brevity of the time patients spend with the physician and pharmacist during consultation and counselling, respectively; vital drug information for the patient may be missed.[4-5] In such situation the MPIs then becomes a ready source of drug information for the patients. Information missed by the health professionals should be accessible in MPIs by the patients, however, several studies have shown that MPIs are froth with omission of vital information for the patients.[6-8] A study conducted in East Africa reported that some of the medication package inserts circulating in the East African Community Partner States market did not conform to regulatory requirement and lack some vital information for the patient.[7]

Medication package inserts should contain all necessary drug information needed by patients for optimal use of their medications. This drug information should however be provided in low literacy level for easy patient understanding and usability. According to the 2018 Nigeria Demographic and Health Survey report, 47% of women and 28% of men are illiterate, meaning they cannot read.[9] The recommended readability level for health-related materials vary from one country to another. In Nigeria there are four levels of education which comprises kindergarten, primary, secondary and tertiary education.[10] The primary education is completed in six years from age 5 -10 years. Thus primary 1 to 6 represents 1st grade to the 6th grade. The secondary education comprises of three years junior secondary school (JSS 1, JSS2, JSS3) and another three years of senior secondary school (SSS1, SSS2, SSS3). The classes in the junior secondary school are equivalent to 7th, 8th, and 9th grade while the three senior secondary school classes are equivalent to the 10th, 11th and 12th grade.[10-11] The age of students in the secondary school is from 11 to 16 years. Also, in Nigeria students spend a minimum of 4 years in the University from age 17 to 20 years and this represents the 13th to 16th grade. The National Institute of Health (NIH) recommended that health education material should be written at 6th – 7th grade level.[12] Several studies have reported a higher reading level (> 10th grade) for most MPIs.[13-14] There is no national guideline for minimum literacy level in Nigeria. Few studies in Nigeria have however examined the readability of MPIs vis-à-vis font size,[6,15] and usability.[6] Despite several efforts to optimize MPIs for a more patient-friendly tool,[16] patients still face challenges understanding the complexity of some MPIs.[17] Bernardini *et al.*[18] reported that Italian patients find their MPIs incompressible while a survey of German MPIs showed that sections on interactions and the maximum dose required were missing and more than 22% of the MPIs surveyed had more than 2000 words.[19]

Patients with chronic diseases require more drug information to sustain long-term management of their disease. Sometimes these patients are on multiple medications and need that their drug information as contained in MPIs and given by health professionals be simplified for easy understanding and utilization. In the light of this, coupled with the fact that in some MPIs there is lack of or inadequate vital information; this study evaluated the content of MPIs of drugs used for five selected chronic diseases (hypertension, diabetes, hyperlipidaemia, arthritis and seizures) for its readability and conformity of the information contained in the MPIs with the drug labelling requirements.

MATERIALS AND METHODS

Study Site and Period

This cross-sectional study was carried out in Ibadan, a city in southwest Nigeria from September 2019 to January 2020. Medication package inserts of commonly used and frequently prescribed drugs for five selected chronic diseases; diabetes, hypertension, arthritis, hyperlipidaemia, and seizure were collected.

Sampling of Package Inserts

There were 25 brands of antilipidemics, 31 of anticonvulsants, 50 of antidiabetics, 88 of antiarthritis and 110 of antihypertensives registered in Nigeria according to Emdex,[20] an official drug compendium in Nigeria. The MPIs of these products were retrieved from three major pharmacies in Ibadan and from the General out-patient Pharmacy Department of the University College Hospital, Ibadan. Permission to collect product MPIs were obtained from the owners of the pharmacies and the Departmental Head in the University College Hospital Pharmacy. Purposive sampling method was used to select commonly used and frequently prescribed drugs whether generics or brands in these classes of drugs. All available brands in each class of drugs were selected from the four pharmacy sites. Branded products were chosen because they are more common than generic drugs in Nigerian market. The MPIs were retrieved from each selected product. Brand duplicates of same drug and strength were not allowed and where such occurred inadvertently, the duplicate was discarded.

Medication Package Inserts Guideline Conformity Assessment

An excel data collection sheet was developed to collect information on the presence or absence of the following 20 items from each MPI: Brand name, Generic name, Dosage form, Dosage strength, Net content, and Name of manufacturer. Others include Address of manufacturer, Clinical pharmacology, Indication, Contraindication, Drug interaction, Warnings, Precautions, Adverse reactions, Dosage and Administration, Overdose, Drug abuse and dependence, Presentation, Storage, and List of active ingredients(s). These items are required in MPIs of prescription drugs according to the NAFDAC drug labelling requirement as part of drug registration in Nigeria.[2] Each item present in a MPI is assigned a score of "1" and items not mentioned in a MPI is assigned a score of "0". Maximum obtainable conformity score for each MPI is 20 and the minimum is 0. Percentage conformity (% Conformity) was calculated as (100 x mean score) / (maximum score). It was further categorised similar to Silo *et al.* description[7] as Very high conformity (91 - 100%), High conformity (81 - 90%), Moderately high conformity (71 - 80%), Moderate conformity (61 - 70%), Fairly moderate conformity (51 - 60), and Low conformity (≤ 50%). All the MPIs retrieved from each of the selected five drug classes for chronic diseases were assessed.

Medication Package Inserts Readability Assessment

The readability assessment was conducted on randomly selected MPIs from each class of drugs under study. The number of MPIs collected for antilipidemics, anticonvulsants, antidiabetics, antiarthritis and antihypertensives were 11, 14, 25, 39, and 67, respectively. From these, a total of 31 MPIs comprising: 5 MPIs each from antilipidemics and anticonvulsants, 6 MPIs each from antidiabetics and antiarthritis and 9 MPIs from antihypertensives were selected using computer generated random numbers. The number of MPIs selected was based on a simple ratio of the MPIs retrieved for the classes of drugs.

The text from each of the 31 MPIs was accurately typed out omitting titles, headers, symbols, logos, hyperlinks, abbreviations, footers, chemical formulae, web links, item numbers, bullets, text in non-English language and contact information which may impact on the readability of the text. Free online readability calculator[21] was used to evaluate the reading level of each MPI. The calculator had been employed by several studies in determining the readability level of online material, books and MPIs.[22-26] The readability calculator used seven readability measures which include Flesch Reading Ease formula, Flesch-Kincaid Grade Level, Fog Scale (Gunning FOG Formula), Simple Measure of Gobbledygook - SMOG Index, Coleman-Liau Index, Automated Readability Index, and Linsear Write Formula. These readability formulas provided in Table 1, considered the number of words, syllables, characters, and sentences in a text to generate the reading and grade levels of the text. The free online readability calculator uses the output of the seven readability formulas to calculate a readability consensus which provided three key information on the text: average

Table 1: Description of readability indices and formula used on the free online readability calculator.

S.No	Readability index	Formula	Description of variables
1	Flesch Reading Ease formula	$RE = 206.835 - (1.015 \times ASL) - 84.6 \times ASW$	RE = readability Ease ASL – Average Sentence Length (number of words divided by the number of sentences) ASW – Average number of Syllables per Word (number of syllables divided by the number of words) PHW – Percentage of Hard Words (words with 3 or more syllables) FKRA – Flesch-Kincard Reading Age CL - Coleman-Liau ACW – Average Characters per Word (number of characters divided by number of words) ARI - Automated Readability Index AVL – Average number of Letters per word AVW – Average number of words in sentences LW - Linsear Write SMOG - Simple Measure of Gobbledygook
2	Flesch-Kincaid Grade Level	$FKRA = (0.39 \times ASL) + (11.8 \times ASW) - 15.59$	
3	Fog Scale (Gunning FOG Formula),	$\text{Grade Level} = 0.4(ASL + PHW)$	
4	SMOG Index	$SMOG\ grade = 3 + \sqrt{\text{Polysyllable count}}$	
5	Coleman-Liau Index	$CL\ grade = \frac{5.89 \times ACN - 0.3 \times \text{Sentences}}{(100 \times \text{words}) - 15.8}$	
6	Automated Readability Index	$ARI = (AVL \times 4.71) + (AVW \times 0.5) - 21.43$	
7	Linsear Write Formula	Select a 100-word sample: Add 1 point to words with 2 syllables or less. Add 3 points to words with 3 syllables or more. Divide the points by the number of sentences in the 100-word sample. Adjust the provisional result r: If r > 20, LW = r / 2. If r ≤ 20, LW = r / 2 - 1.	

grade level, reading level and reading age. A maximum of 3000 words is analysable on the website. Text with more than 3000 words were truncated.

Data Analysis

Mean and standard deviation, median and proportions were used in interpreting the data. One-way analysis of variance (ANOVA) with Tukey *post hoc* test was used to evaluate the difference in the mean conformity of the MPIs to each of the 20 items in the drug labelling requirements among the five selected drug classes. One-way ANOVA was also used to assess the mean differences in the readability scores of the seven readability measures, number of words, sentences and syllable characteristics among the five classes of drugs. The analysis was performed with Statistical Package for Social Sciences Windows version 25 (IBM Corp, New York, U.S.A.). The level of significance was set at $p<0.05$.

RESULTS

A total of 156 package inserts were retrieved comprising of 44.0% (11/25) from registered: antilipidemics, 45.2% (14/31) anticonvulsants, 50.0% (25/50) antidiabetics, 44.3% (39/88) antiarthritis, and 60.9% (67/110) antihypertensives. All the MPIs evaluated conformed with the drug labelling requirements of including sections on the list of active ingredients, adverse drug reactions, and indications. Seventy-three MPIs, 46.8%, did not include information on the product net content and 34.0% (53/156) omitted information on overdose. The percentage conformity of antidiabetic MPIs, 60.0% (15/25), with the inclusion of generic names significantly lower ($p<0.001$) than antilipidemics - 100.0% (11/11), anticonvulsants - 100.0% (14/14), antiarthritis - 69.2% (27/39), and antihypertensives - 92.5% (62/67). There were less than 100% conformity of 17 items with the drug labelling requirements in some of the MPIs from the classes of drugs (Table 2). Significant differences in percentage conformity of MPIs with the drug labelling requirement in the five selected classes of drugs are shown in Table 2. From Table 3, the MPIs of antilipidemics had the highest percentage conformity, (89.6%), while anticonvulsant MPIs had the lowest percentage conformity of 82.6% with the NAFDAC drug labelling requirements.

The overall average reading grade level for the MPIs was 14.55 ± 1.71 (undergraduate level). Twenty-five (80.6%) of the MPIs were very difficult to read. The reader's age was University graduate for 17 (54.8%) of the MPIs, Undergraduate level for 8 (25.8%) of the MPIs, 10th - 11th grader (SSS1 to SSS2) for 2 (6.5%) MPIs, 12th grader (SSS3) for 2 (6.5%) MPIs, and University entry level for 2 (6.5%) MPIs. The readability score for MPIs from each class of drugs were similar except for the Automated Readability Index and Linsear Write Formula where the mean readability score for MPIs from Antiarthritis was significantly higher than the mean readability scores for MPIs from other four classes of drugs ($p < 0.05$, Table 4).

The average number of words per MPIs was 1165.74 ± 860.71. This contains 61.16 ± 43.13 sentences with an average of 18.58 ± 2.91 words per sentence. The average number of difficult words in the MPIs was 306.90 ± 210.64 constituting 27.6% of the MPI content (Table 5). Antiarthritis MPIs had significantly higher number of words per sentence 22.50 ± 3.21 ($p = 0.003$) compared with the MPIs of Antilipidemics - 18.00 ± 2.12, Anticonvulsants - 17.40 ± 3.05, Antidiabetics - 17.50 ± 1.52, and Antihypertensives - 17.67 ± 1.58.

DISCUSSION

All the MPIs of the antilipidemics, anticonvulsants, antidiabetics, antiarthritis and antihypertensives evaluated in this study had high conformity to the drug labelling requirements by the regulatory authority, NAFDAC. All the MPIs included sections on the list of active ingredients, indications, and adverse drug reactions (ADRs) but only 34.0% of the MPIs had information on overdose. Most patients often check the MPIs of their drugs for indications, doses, side effects and ADRs. Inclusion of these items in the MPIs sometimes reassures the patient that the correct medication for the ailment had been given. Patient may modify the dose of the medication or stop taking the drug based on the information in the MPIs on dose and ADRs, respectively. Pharmacists and other health professionals also consult the MPIs on doses, indications, and side effects during consultation and counselling.[27] According to a study conducted in Jos Nigeria by Joseph *et al.*[6] 46% of the 66 MPIs for chronic diseases omitted information on overdose. Another study from three East African Community Partner States: Kenya, Tanzania and Uganda, reported omission of overdose information in 47.5% of the 99 MPIs evaluated.[7] Though, the information on overdose is critical for drugs with narrow therapeutic indices, they are equally important for all drugs. The absence of it may encourage irrational prescribing and dispensing and may negatively affect treatment outcomes. As reported in this study, some of the missing items in some of the MPIs included contents like clinical pharmacology, and precautions. These items were also reported missing in some MPIs in Joseph *et al.* and Sillo *et al.* studies.[6-7] Strict compliance with the

Table 2: Conformity and differences in conformity of information in medication package inserts with NAFDAC drug labelling guidelines among five selected classes of drugs used for chronic diseases.

Contents	Total	Antilipidemics *n*=11	Anticonvulsants *n*= 14	Antidiabetics *n*= 25	Antiarthritis *n*= 39	Antihypertensives *n*= 67	*p*-value*
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
Brand name	148 (94.9)	11(100.0)	14 (100.0)	24 (96.0)	39 (100.0)	60 (89.6)	0.116
Generic name	129 (82.7)	11 (100.0)	14 (100.0)	15 (60.0)	27 (68.2)	62 (92.5)	<0.001
Dosage form	153 (98.1)	11 (100.0)	13 (92.9)	24 (96.0)	39 (100.0)	66 (98.5)	0.464
Dosage strength	154 (98.7)	11 (100.0)	13 (92.9)	24 (96.0)	39 (100.0)	67 (100.0)	0.150
Net content	83 (53.2)	9 (81.8)	9 (64.3)	11 (44.0)	23 (59.0)	31 (46.3)	0.138
Name of manufacturer	154 (98.7)	11 (100.0)	13 (92.9)	25 (100.0)	39 (100.0)	66 (98.5)	0.314
Address of manufacturer	153 (98.1)	11 (100.0)	13 (92.9)	25 (100.0)	39 (100.0)	65 (97.0)	0.428
Clinical pharmacology	128 (82.1)	11 (100.0)	9 (64.3)	19 (76.0)	32 (82.1)	57 (85.1)	0.170
Indication	156 (100)	11 (100.0)	14 (100.0)	25 (100.0)	39 (100.0)	67 (100.0)	ND
Contraindication	147 (94.2)	10 (90.9)	13 (92.9)	22 (88.0)	36 (92.3)	66 (98.5)	0.340
Drug interaction	125 (80.1)	11 (100.0)	8 (57.1)	24 (96.0)	28 (71.8)	54 (80.5)	0.010
Warnings	149 (95.5)	10 (90.9)	14 (100.0)	24 (96.0)	35 (89.7)	66 (98.5)	0.231
Precautions	149 (95.5)	10 (90.9)	14 (100.0)	24 (96.0)	35 (89.7)	66 (98.5)	0.231
Adverse reaction	156 (100)	11 (100.0)	14 (100.0)	25 (100.0)	39 (100.0)	67 (100.0)	ND
Dosage and Administration	147 (94.2)	10 (90.9)	13 (92.9)	23 (92.0)	37 (94.9)	64 (95.5)	0.949
Overdose symptoms and treatment	103 (66.0)	8 (72.7)	7 (50.0)	18 (72.0)	19 (48.7)	51 (76.1)	0.032
Drug abuse and dependence#	5 (3.2)	0 (0.0)	3 (21.4)	0 (0.0)	0 (0.0)	2 (3.0)	0.001
Presentation	128 (82.1)	8 (72.7)	9 (64.3)	19 76.0)	32 (82.1)	60 (89.6)	0.147
Storage	147 (94.2)	11 (100.0)	11 (78.6)	25 (100.0)	38 (97.4)	62 (92.5)	0.046
List of active ingredients(s)	156 (100.0)	11 (100.0)	14 (100.0)	25 (100.0)	39 (100.0)	67 (100.0)	ND

NAFDAC – National Agency for Food and Drugs Administration and Control, *ANOVA with Tukey post hoc test. P<0.05 is significant. ND – Not determined.
#Not all product is expected to include this section in the medication package insert, N – total number of medication package inserts collected per class of drugs, n – number of medication package inserts with required drug labelling requirement.

Table 3: Level of conformity of selected classes of drugs for chronic diseases with NAFDAC labelling guidelines.

Categories of inserts	Mean score ± Standard deviation	95% Confidence interval	% Conformity	Level of conformity
Anti-lipidemics (*n* = 11)	17.91±1.05	17.21; 18.61	89.55	High
Anti-convulsants (*n* = 14)	16.57±2.38	15.20; 17.94	82.85	High
Anti-diabetics (*n* = 25)	16.84±1.84	16.07; 17.60	84.20	High
Anti-arthritis (*n* = 39)	16.77±1.74	16.21; 17.33	87.00	High
Anti-hypertensives (*n* = 67)	17.12±1.76	16.84; 17.40	85.60	High

NAFDAC – National Agency for Food and Drugs Administration and Control
% Conformity = [mean score / maximum score] x 100
91- 100 = Very high conformity
81- 90 = High conformity
71- 80 = Moderately high conformity
61- 70 = Moderate conformity
51-60 = Fairly moderate conformity
≤ 50 = Low conformity

Table 4: Readability scores and consensus for medication package inserts from five selected classes of drugs used for chronic diseases.

	Readability indices and scores								Reliability consensus	
Classes of drugs	**FRE**	**FKG**	**G-F**	**SMOG**	**C-LI**	**ARI**	**LWF**	**Grade level**	**Reading level****	**Reader's age****
Antilipidemic; Mean ± SD	19.68 ± 14.45	14.98 ± 1.88	16.38 ± 1.32	12.50 ± 1.10	15.00 ± 2.00	13.94 ± 1.27	13.72 ± 1.66	14.00 ± 1.23	Very difficult to read 4 (80.0%)	Undergraduate level, 2 (40.0%) University graduate, 2 (40.0%)
Anticonvulsants; Mean ± SD	23.56 ± 9.89	14.62 ± 2.58	17.30 ± 2.77	12.78 ± 1.81	15.40 ± 2.30	13.68 ± 2.82	13.42 ± 3.29	14.00 ± 2.55	Very difficult to read; 3 (60.0%)	Undergraduate level - 2 (40.0%);
Antidiabetics; Mean ± SD	16.00 ± 6.77	15.37 ± 0.91	18.43 ± 0.46	13.18 ± 0.31	16.83 ± 1.60	15.00 ± 1.18	13.92 ± 0.88	14.82 ± 0.75	Very difficult to read 6 (100.0%)	University graduate – 4 (66.0%)
Anti-Arthritis; Mean ± SD	18.65 ± 11.18	16.23 ± 1.54	19.10 ± 1.81	13.93 ± 1.29	16.00 ± 2.19	16.63 ± 1.54	17.08 ± 2.21	16.17 ± 1.47	Very difficult to read; 5 (83.3%)	University graduate – 5 (83.3%)
Antihypertensives; Mean ± SD	24.36 ± 13.47	14.14 ± 2.07	16.89 ± 2.36	12.44 ± 1.54	15.33 ± 1.73	13.81 ± 1.73	13.51 ± 1.74	13.89 ± 1.54	Very difficult to read; 7 (77.8%)	University graduate – 5 (55.6%)
***p*-value**	0.668	0.322	0.130	0.274	0.525	0.035*	0.019*	0.083		
Overall Mean ± SD	20.75 ± 11.34	15.00 ± 1.90	17.60 ± 2.08	12.94 ± 1.36	15.71 ± 1.92	14.59 ± 1.99	14.39 ± 2.35	14.55 ± 1.71	Very difficult to read; 25 (80.6%)	University graduate; 17 (54.8) Undergraduate level; 8 (25.8%)

FRE - Flesch Reading Ease; FKG - Flesch Kincaid Grade; G-F - Gunning Fog; SMOG - Simple Measure of Gobbledygook; C-LI - Coleman-Liau Index; ARI - Automated Readability Index; LWF - Linsear Write Formula; *p<0.05, **Categories with the highest proportion recorded.

Table 5: Words, sentences, and syllable statistics of medication package inserts from five selected classes of drugs used for chronic diseases.

Generic name	Total number of words	Average number of words per sentence	Total number of sentences	Total number of words with single syllables	Percent of single syllables in text	Total number of words with double syllables	Percent of double syllables in text	Total number of words with 3+ syllables	Percent of 3+ syllables in text
Antilipidemic; Mean ± SD	1627.00 ± 1058.34	18.00 ± 2.12	89.20 ± 58.29	890.00 ± 600.43	53.60 ± 4.39	324.40 ± 213.21	20.00 ± 0.71	412.60 ± 273.02	26.40 ± 4.83
Anticonvulsants; Mean ± SD	1013.00 ± 1129.99	17.40 ± 3.05	52.20 ± 51.26	528.60 ± 617.59	51.60 ± 3.21	201.80 ± 227.16	20.00 ± 1.41	282.60 ± 289.93	28.60 ± 4.34
Antidiabetics; Mean ± SD	824.50 ± 594.65	17.50 ± 1.52	45.67 ± 27.78	402.00 ± 297.69	48.00 ± 3.10	185.67 ± 157.26	21.83 ± 2.79	236.83 ± 142.10	30.17 ± 2.99
Anti-Arthritis; Mean ± SD	1536.17 ± 725.26	22.50 ± 3.21	68.83 ± 33.14	790.50 ± 390.46	51.00 ± 4.14	339.33 ± 147.89	23.00 ± 2.45	406.33 ± 216.66	26.50 ± 4.81
Antihypertensives; Mean ± SD	974.89 ± 806.87	17.67 ± 1.58	55.78 ± 44.69	512.44 ± 460.00	52.00 ± 4.80	224.33 ± 221.61	21.33 ± 2.41	242.11 ± 148.18	26.56 ± 5.34
***P*-value**	0.412	0.003*	0.512	0.391	0.247	0.564	0.184	0.400	0.535
Overall Mean ± SD	1165.74 ± 860.71	18.58 ± 2.91	61.16 ± 43.13	608.39 ± 477.20	51.23 ± 4.22	251.61 ± 194.25	21.32 ± 2.41	306.90 ± 210.64	27.55 ± 4.57

*p < 0.05

drug labelling requirements of the content of MPIs should be ensured by all drug regulatory authorities, in particular NAFDAC, at the product registration stage before marketing and intermittent post-marketing survey may also help reduce the level of non-compliance.

The readability of the MPIs was above the 10th grade level (Senior Secondary School 1 Level), mostly at the undergraduate grade level and very difficult to read. This is comparable with two studies in Nigeria. One reported a readability level of university graduates for MPIs of drugs used for chronic diseases[6] while the other reported a readability of 13th grade level (fresh undergraduates) for antimalaria MPIs.[8] Similarly, analysis of 158 MPIs in Iran with Flesch–Dayani readability showed the average reading level to be 10th - 11th grade (senior secondary school).[28] The low readability (> 6th grade reading level, that is, primary 6 reading level in Nigeria) seems to be common not only with MPIs but also with most online patient education materials or resources,[14,29] Since the recommended reading level by NIH[12] is 6-7th grade level (primary 6 to junior secondary school year 1), the MPIs of antilipidemics, anticonvulsants, antidiabetics, antiarthritis and antihypertensives available in Nigeria may not be readable by an average patient. This is also buttressed by a study which reported that 30–50% of English speaking patients in Spain had challenges reading patient information materials written at the 10th grade level.[30] Another study showed that the level of understanding and comprehension of patients is 3-5 levels below self-reported educational level. This supports the fact that the patient's ability to read contrasts with MPIs readability level and the level of education of patients may not necessarily translate to proficiency.[31] Nonetheless, optimization of MPIs by regulatory authorities to a more patient-friendly and readable material will encourage its uptake and impart positively in educating patients.

Readability of MPIs is a modifiable factor which can improve patient care and disease outcomes.[32] Patients are sometimes faced with the challenges of understanding and remembering the information in MPIs especially due to the verbosity of the text and usage of technical terms.[33] The average number of words per MPI in this study was 1100. This is comparable with the finding of Joseph *et al.*[6] in Jos Nigeria where the 66 MPIs evaluated had mean word count > 900, but different from the average of 2000 words per MPI reported for German MPIs with a mean of 114.1 difficult words.[19] This may mean that Nigerian MPIs are less wordy than German MPIs. However, the average number of difficult words in the MPIs we evaluated was 306 constituting about 27.6% of the MPI content. This is higher than the German MPIs. Difficult words are words with more than three syllables and are due in part to complex words, sentence length and medical jargons. Raynor *et al.*[34] stated that complex words in MPIs are a source of concern to patients. Arguably, medical jargons or disease related terminologies have increased syllables when assessed for readability. Removing medical terminologies or replacing them with simpler words appreciably reduced the grade level but not below the 5th - 6th grade.[35] Once the medical jargons are defined, it is easier for patients to understand it if used continuously in the text. This may improve comprehensibility but not readability.[36] Medical jargons may be difficult to avoid but related or descriptive phrases can be used to improve readability. Likewise, wordiness can be avoided by using common words to replace longer words[37] for example the word "endeavour" can be replaced with "try" using the PLAIN website suggestions.[38]

In optimizing MPIs several factors have been considered such as using or developing a patient-friendly format different from the more technical MPIs, involving the end users of the MPIs who are the target patients or clients in the design and evaluation of the readability and understanding of the contents. This has been tested in some countries and found to improve the uptake of MPIs among targeted patients and clients, and the development of patient-friendly and easily understandable MPIs resulting from patients or client's input[17]

Strength and Limitations of the Study

Medication package insert is a veritable patient education tool and contributes indirectly to patients' disease management. This study highlights the incomplete conformity to drug labelling requirements and poor readability (> 6th grade level) of MPIs of drugs used for five major chronic diseases in Nigeria. However, there are limitations peculiar to this type of studies. One of the limitations of this study is the over-reliance of the readability measures used on number of words and the length of a sentence. Readability formulas do not consider the readers familiarity with terminology used in diseases and their motivation to read the MPIs. Also, not all the registered brands were encountered during the collection of the MPIs. This affected the number of MPIs collected from each class of drugs.

CONCLUSION

The selected medication package inserts of commonly used antilipidemics, anticonvulsants, antidiabetics, antiarthritis and antihypertensives in Nigeria showed high conformity with the drug labelling requirements

on the content of the package inserts. However, conformity of the package inserts with the inclusion of net content, clinical pharmacology, precautions, dose and administration, and overdose information was low. The package inserts were written at undergraduate student level and very difficult to read. Patients who use these classes of drugs may benefit from medication package inserts written at lower grade level such as primary 6 level. Hence, policy makers and the drug regulatory body, NAFDAC, should make concerted effort to include in the drug registration guideline modalities for ensuring that medication package inserts are written at lower grade level for patient understanding. Efforts should also be made to optimize the readability of medication package inserts.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

MPIs: Medication package inserts; **NAFDAC:** National Agency for Food and Drug Administration and Control; **JSS:** Junior secondary school; **SSS:** Senior secondary school; **SMOG Index:** Simple Measure of Gobbledygook; **ANOVA:** One-way analysis of variance; **ADRs:** Adverse drug reactions; **NIH:** National Institute of Health.

SUMMARY

Medication package inserts are useful to patients in understanding the medication profile such as indication, contraindication, safety and adverse drug reactions. However, many medication package inserts omit vital information and are difficult to read and understand by average patient. Thus, the need to evaluate the conformity of Nigeria medication package inserts to the drug labelling requirements and the readability of the medication package inserts became pertinent. Though there was high conformity of the selected medication package inserts of antilipidemics, anticonvulsants, anti-diabetes, antiarthritis and antihypertensives with the drug labelling requirements, some vital information like net product content and overdose were missing in some medication package inserts. Overall, the selected medication package inserts were very difficult to read as they were written at the $\geq 10^{th}$ grade level equivalent to senior secondary school in Nigeria.

Ethics Approval

Ethical approval was secured from the University of Ibadan/University College Hospital ethics review committee with approval number UI/EC/19/0409.

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