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**Original Research Article**

# Evaluation of promotional drug literature using WHO guidelines: comparison between present and previous data

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## ABSTRACT

**Background:** Medical professionals get information about drugs from drug manufacturers through brochures, reminders, flip charts, pamphlets, visual aids and other forms of advertisements which together constitute promotional drug literature (PDL). The objectives of this study were to find out find out percentage of PDLs that adhere to the guidelines laid out by WHO and to compare data obtained from this study to that of a similar study conducted 13 years back to see if there has been any change in the quality and standard of PDLs over this time period.
**Method:** Total of 500 PDLs were collected from various OPDs of a tertiary care teaching hospital. These PDLs were evaluated against WHO ethical criteria for drug promotion, 1988. The results obtained were compared with a similar study conducted 13 years back (two authors from the previous study are co-investigators in present study) to check whether pharmaceutical companies adhere to WHO guidelines and whether there is any improvement in the quality and standard of PDLs over this time period.
**Results:** There is significant decrease in percentage of PDLs mentioning generic names, approved uses, regimen, references in the present study compared to the previous one. At the same time this study also revealed some positive outcomes like decrease in the number of irretrievable journal articles used as references, decrease in the number of pseudographs and increase in the number of valid references.
**Conclusion:** It is essential to consider the negative findings of this study and measures implemented to improve the same.

**Keywords:** Drug promotion, PDL, Drug advertisement

## INTRODUCTION

Promotional activities by pharmaceutical companies refers to all informative and persuasive activities by manufacturers and distributors, the effect of which is to induce the prescription, supply and purchase of medicinal drugs. PDL could be in the form of package inserts/brochures/pamphlets/reminder/advertisements/monographs etc.[1] Drug manufacturers spend billions of monies on promoting their drugs to increase sales. About one third of all sales earnings are spent on drug promotion which is nearly twice the amount spent on research and development.[2] PDL due to it's attractive and well-presented nature often remains physician's primary source of drug information. They can be highly informative but whether they present authentic and rational information is still a matter of concern. One of the well-known drugs promotional activities by the pharmaceutical industries is to produce advertising brochures which at times can contain inaccurate information and be of poor educational value.[3] In India promotional activities by industries are governed by organization of pharmaceutical producers of India (OPPI) self-regulatory code of pharmaceutical marketing practices, January (2007) and by National legislation.[4] Studies have repeatedly shown that pharmaceutical promotion influences physician

behaviour.[5] All promotion making claims concerning medicinal drugs should be reliable, accurate, truthful, informative, balanced, up-to-date, and capable of substantiation. They should not contain misleading or unverifiable statements or omissions likely to induce medically unjustifiable drug use or to give rise to undue risks.[6] Therefore, for the rational use of drugs, the WHO has laid down ethical criteria for medicinal drug promotion and has recommended pharmaceutical industries to implement these guidelines while developing PDLs.[7] We had conducted a study to evaluate the rationality of drug promotional literature as per WHO criteria for ethical medicinal drug promotion in 2010.[5] The present study was conducted with the objectives of evaluating the rationality of PDLs using WHO 1988 guidelines and to compare the results of this study with data from the study conducted in 2010 by the same authors to find out whether there have been any changes in the quality and standard of PDL during this time period.

## METHODS

This was an observational, descriptive study conducted in the outpatient department of a tertiary care teaching hospital in central India. The study was initiated after approval from the Institutional Ethics Committee. Five hundred PDLs were collected randomly from various OPDs. Medicine, Surgery, OBGY, Paediatrics, ENT, Ophthalmology, Skin, Orthopaedics and Psychiatry during June to August 2023. PDLs promoting up to four brands were included. PDLs containing the following were excluded. Literature promoting medical devices and equipment (e.g. insulin pump, orthopaedic braces, implants etc), ayurvedic medications, drug monographs and reminder advertisements, literature promoting more than four brands, each PDL collected was evaluated on the basis of WHO criteria according to which PDL should contain the following information. Names of the active ingredients using either international non-proprietary. Names (INN) or the approved generic names of the drug, brand name, content of active ingredient per dosage form or regimen, Name of other ingredients known to cause problems, i.e., adjuvant. Approved therapeutic uses, Dosage form or regimen, Side effects and major adverse drug reactions. Precautions, contraindications, and warnings. Major drug interactions. Name and address of the manufacturer or distributor. Reference to scientific literature as appropriate. Criteria six was evaluated separately as “dosage form” and details about “regimen” to look for completeness of therapeutic information given in the promotional brochures. In addition to this information, promotional materials made various claims about the medicinal products presented in it. Claims made in the promotional brochures were classified into following seven categories

### *Efficacy*

Statements about improved effectiveness of promoted drug as a disease outcome or a patient outcome solely or in comparison with other group of drugs for similar outcome (e.g., antihypertensive action of calcium channel blocker and β-blocker) or another brand of the same drug.

### *Safety*

Use of the word “safe” in the promotional text or the mention of reduction in adverse drug reaction and/or drug interaction and/or contraindication.

### *Cost*

Pointing out low price of promoted drug in absolute or relative terms or any description related to its better cost effectiveness.

### *Convenience*

Statements stating the comfort of patient, e.g., improved dose, low frequency of dosage, ease of administration, etc. with or without reasons to support the same

### *Pharmacokinetic property*

Properties of the drug related to its absorption, metabolism, half-life, etc

### *Pharmaceutical property*

New dosage formulations, different manufacturing procedures, excipients (e.g., cyclodextrin, sodium bicarbonate, etc.), storage facilities, etc.

### *Extravagant emotional claims*

Apart from all these claims, some PDLs also had some tall/unjust claims which gave exaggerated information which was not supported by any references. For e.g. some PDLs stated that the advertised drug had 95% efficacy without quoting any proof to support it.

References in the PDLs were classified as valid, partially valid, invalid or irretrievable based on their authenticity & completeness. Internet search was done to retrieve the references quoted in the PDL. A reference was considered as “irretrievable” if it was not possible to get a softcopy of the cited material in PubMed/Google scholar /other site in either full text or abstract form. The claim supported by the reference was further checked for its correctness to classify it as valid/ partially valid/ invalid. Some claims presented with support of references were as per the results mentioned in the cited material whereas few were manipulated away from the results of the quoted reference. The former references were classified as valid and the latter as partially valid/invalid.

References were further categorized as per their source. Journals, books, websites, data on file, others (vague description, departmental study, treatment guidelines, prescription information, conference proceedings, name of

author/institute, newspaper or magazine article, trial/surveillance). Journal articles were further classified according to their type: review article, meta-analysis, preclinical studies', RCT, observational studies, retrospective studies, case control studies, post marketing surveillance, case control studies, non-randomized trial, clinical trial, irretrievable, others (Letter to editor, Correspondence, Editorial, Case Report) PDLs were usually made informative by presenting various scientific graphs to prompt doctors to prescribe that drug. Scientific graphs were evaluated and categorized based on their type as follows: pseudographs (Graphical representation without proper axes, labelling legends or just arrows with numbering showing reduction or increase), tables, bar diagrams, cost comparison tables, pie chart, scatter diagram, line diagrams.

Data obtained from this study was compared to similar data of the previous study (as mentioned under introduction) to find out whether there have been any changes in the quality and standard of PDLs during this time period.

### *Statistical analysis*

Statistical analysis was carried out by applying Fischer's exact test using graph pad prism (version 10.0.1). All the results were expressed in numbers and percentages. P value less than 0.05 was considered statistically significant.

## RESULTS

### *Number of PDLs evaluated*

The study evaluated 500 PDLs whose data was compared to the previous study that evaluated 513 PDLs.

### *Fulfilment of WHO criteria*

In the present study none of the PDLs satisfied all the WHO criteria. Table 1 shows that the number of PDLs mentioning generic name, approved uses, regimen and references were statistically significantly lower in the present study compared to the previous study. However, brand name was mentioned in 100% PDLs in both the studies. Name and address of the manufacturer were mentioned in a statistically significantly higher number of PDLs in the present study.

### *Types of references*

Table 2 shows that the percentage of PDLs quoting journal articles as references were significantly lower in the present study (P<0.0001) compared to the previous study whereas the number of PDLs quoting websites and data on file were significantly higher in the present study (P value 0.0024 and <0.0001 respectively)

### *Types of journal articles*

There was a significant increase in percentage of PDLs that quoted review articles and observational studies as references in the present study compared to the previous study. There was a significant decrease in percentage of PDLs that quoted case control studies, non-randomized trial and clinical trial as references in the present study when compared with the previous study. There was also a significant decrease in percentage of irretrievable references quoted as journal articles in the present study. Table 3 shows that the number of PDLs quoting review articles (P value <0.0001) and observational studies (P value <0.0001) were significantly higher in the present study. There is also a significant decrease in number of PDLs quoting irretrievable references (p<0.0001) in the present study.

### *Validity of references*

Table 4 shows that the number of PDLs quoting valid references were significantly higher in the present study (p value<0.0001). There is also a significant decrease in number of PDLs quoting invalid references in the present study compared to the previous study (p value <0.0001)

### *Types of graphical representation*

Figure 1 shows that there was statistically significant decrease in number of PDLs with pseudographs in the present study compared with the previous one, while there was statistically significant increase in the use of tables.

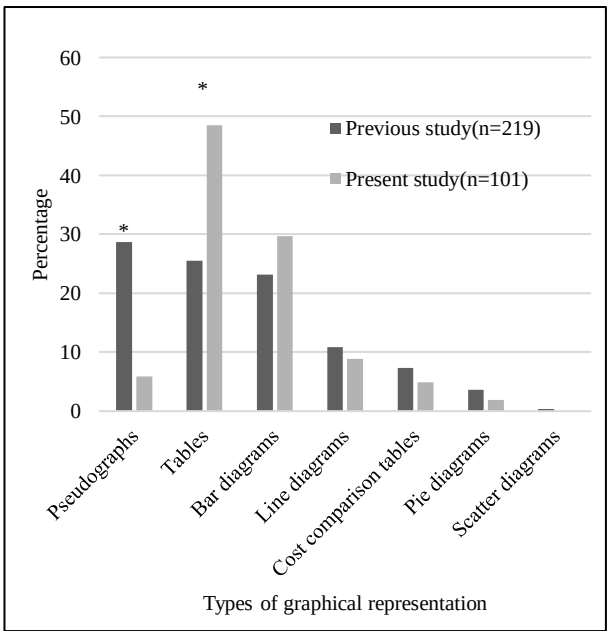


**Figure 1: Comparison of graphical representation in PDLs.**

'*' indicates P value <0.05, Data analysed by Fischer's exact test.

**Table 1: Evaluation of promotional drug literature as per WHO criteria: comparison between two studies.**

| | Previous study (n=513) | | Present study (n=500) | | P value |
|---|---|---|---|---|---|
| | Mentioned | Not mentioned | Mentioned | Not mentioned | |
| **INN[a]** | 492 (95.9) | 21 (4.1) | 413 (82.6) | 87 (17.4) | <0.0001 |
| **Brand name** | 513 (100) | 0 (0) | 500 (100) | 0 (0) | >0.9999 |
| **Content[b]** | 408 (79.5) | 105 (20.5) | 381 (76.2) | 119 (23.8) | 0.2257 |
| **Adjuvants** | 10 (1.9) | 503 (98.1) | 6 (1.2) | 494 (98.8) | 0.4515 |
| **Uses[c]** | 443 (86.3) | 70 (13.7) | 343 (68.6) | 157 (31.4) | <0.0001 |
| **Dosage form** | 447 (87.1) | 66 (12.9) | 455 (91) | 45 (9) | 0.0558 |
| **Regimen[d]** | 165 (32.1) | 348 (67.9) | 63 (12.6) | 437 (87.4) | 0.0001 |
| **Safety information** | 45 (8.7) | 468 (91.3) | 38 (7.6) | 462 (92.4) | 0.567 |
| **Name and address[e]** | 362 (70.5) | 151 (29.5) | 453 (90.6) | 47 (9.4) | <0.0001 |
| **References** | 316 (61.5) | 197 (38.5) | 178 (35.6) | 322 (64.4) | <0.001 |

[a]International non-proprietary name, [b]active drug per dosage form, [c]Drug use as per Central Drugs Standard Control Organization (CDSCO), [d]Drug dose, frequency and duration of administration, [e]Name and address of the manufacturer. Figures indicate number of PDLs. Figures in parentheses indicate percentage. Data analysed by Fischer's exact test.

**Table 2: Type of references used in PDLs.**

| Type of reference | Number of references | | P value |
|---|---|---|---|
| | Previous study (n=1003) | Present study (n=451) | |
| **Journal articles** | 847 (84.4) | 312 (69.1) | <0.0001 |
| **Books** | 32 (3.2) | 11 (2.4) | 0.0056 |
| **Websites** | 30 (3) | 30 (6.6) | 0.0024 |
| **Data on file** | 14 (1.4) | 45 (10) | <0.0001 |
| **Others[a]** | 80 (8.1) | 53 (11.7) | 0.0237 |

[a]Others include vague description, departmental study, treatment guidelines, prescription information, report, conference proceedings, name of author/institute, newspaper or magazine article, trial or surveillance data. Figures indicate number of PDLs. Figures in parentheses indicate percentage. Data analysed by Fischer's exact test.

**Table 3: Classification of journal articles as per type of study: Comparison between two studies.**

| Type of journal articles | Previous study (n=847 ) | Present study (n=312 ) | P value |
|---|---|---|---|
| **Review** | 178 (17.7) | 131 (41.9) | <0.0001 |
| **Meta analysis** | 28 (2.8) | 4 (1.2) | 0.0692 |
| **Pre clinical studies** | 77 (7.7) | 14 (4.4) | 0.0094 |
| **RCT[1]** | 234 (27.6) | 81 (25.9) | 0.6027 |
| **Observational studies** | 56 (5.6) | 47 (15) | <0.0001 |
| **Retrospective studies** | 14 (1.4) | 7 (2.2) | 0.4671 |
| **Case control studies** | 8 (0.9) | 0 | 0.1173 |
| **Post marketing surveillance** | 3 (0.3) | 2 (0.6) | 0.6155 |
| **NRT[2]** | 32 (3.2) | 0 | <0.0001 |
| **Clinical trial[3]** | 41 (4) | 0 | <0.0001 |
| **Others[4]** | 17 (1.7) | 6 (1.9) | >0.9999 |
| **Irretrievable** | 159 (15.8) | 20 (6.4) | <0.0001 |
| **Total** | 847 (84.4%) | 312 (69.1%) | |

[1]Randomized controlled trial, [2]Non Randomized trial, [3]Clinical trial without details of design, [4]Others: vague description, departmental study, treatment guidelines, prescription information, report, conference proceedings, name of author/institute, newspaper or magazine article, trial or surveillance data. Figures indicate number of PDLs. Figures in parentheses indicate percentage. Data analysed by Fischer's exact test.

**Table 4: Classification of references based on validity: Comparison between two studies.**

| Status of reference | Previous study (n=1003) | Present study (n=451) | P value |
|---|---|---|---|
| **Valid** | 495 (49.3) | 296 (65.6) | <0.0001 |
| **Partially valid** | 64 (6.4) | 38 (8.4) | 0.1824 |

Continued.

| Status of reference | Previous study (n=1003) | Present study (n=451) | P value |
|---|---|---|---|
| **Invalid** | 224 (22.3) | 29 (6.4) | <0.0001 |
| **Not retrievable** | 220 (21.9) | 88 (19.5) | 0.3314 |

Figures indicate number of PDLs. Figures in parentheses indicate percentage. Data analyzed by Fischer's exact test.

**Table 5: Types of claims made in the PDLsa.**

| Type of claims | Number of PDLs | | P value |
|---|---|---|---|
| | Previous study (n=1170) | Present study (n=671) | |
| **Efficacy** | 472 (92) | 404 (81) | <0.0001 |
| **Safety** | 194 (37.8) | 35 (7) | <0.0001 |
| **Cost effectiveness** | 91 (17.7) | 22 (4.4) | <0.0001 |
| **Pharmacokinetic property** | 86 (16.7) | 21 (4.2) | <0.0001 |
| **Convenience** | 84 (16.4) | 22 (4.4) | <0.0001 |
| **Pharmaceutical property** | 151 (29.6) | 35 (7) | <0.0001 |
| **Tall/Unjust** | 92 (17.9) | 132 (26.4) | <0.0014 |

[a]Promotional Drug literature. Figures indicate the number of references. Figures in parentheses indicate percentages. Data analysed by Fischer's exact test.

***Types of claims***

Table 5 shows that over the extended time period the claims made in the PDLs decreased significantly. But there was a significant increase in the number of tall/unjust claims in the present study. Previous study PDLs had more claims promoting safety, cost effectiveness, pharmacokinetic and pharmaceutical property and convenience compared to the present study.

## DISCUSSION

PDLs influence the prescribing habits of physicians.[8] This study intended to analyse PDLs according to WHO criteria and to compare data obtained from this study with that of a previous study. Even though there were several similar studies in the past, none of them has compared the results with a previous study to see the change in quality and standard of PDLs over a period of time.[9-14]

By analysing the PDLs as per WHO criteria, it was noted that there was a decrease in percentage of PDLs mentioning generic names, approved uses, regimen, references in the present study compared to the previous one. These being the crux of any PDL is a matter of serious concern which indicates deterioration in the quality of PDLs over this time period. This reflects the fact that, though there exist guidelines for framing of PDLs, there is lack of monitoring by regulatory authorities due to which such irrational PDLs are rampantly available. In more recently published studies, generic name was mentioned in 100% PDLs.[15,16] Generic name not being mentioned in a significant number of PDLs in the present study is very surprising. At the same time brand name was mentioned in 100% PDLs in both the studies. This is as expected because promoting the brand is the basic objective of PDLs. In both the studies that were compared in the article, safety information was mentioned in very few PDLs (8.7% and 6.7% respectively). This is in contrast to some of the recently published studies in which safety information was mentioned in 31.93% and 79.6% of the PDLs.[15,16] Safety of a drug is a major parameter in addition to efficacy on the basis of which a clinician can choose a drug. Decrease in safety information mentioned in a PDL indicates that safety profile of a drug may not be clearly evident and a false sense of superiority of the drug in terms of safety may prevail.

In our analysis it was found that the present study had a significant decrease in percentage of journal articles quoted as references compared to the previous study. Though we did not analyse the type of journal, but journal articles are usually considered reliable sources and decrease in their use as references quoted in the PDLs is an indication of declining standard. In another recently published study, similar percentage of PDLs had used journal articles as references. There was increase in the percentage of 'Websites' and 'Data on file' used as references in the present study. It is not incorrect to use 'Data on file' or 'websites' as references but it is important to check the authenticity of such sources before quoting them as references.

On a positive note, the number of irretrievable journal articles quoted as references were reduced significantly in the present study. One of the reasons for this might be the availability of powerful search engines which have made literature search easier. But this also indicates that use of fake references in PDLs has reduced in this study compared to the previous one. Another positive outcome of this study is the increased percentage of PDLs having valid references. This also is an encouraging finding as validity of references is an important criterion to ensure reliability and authenticity of the references.

Analysing the graphical representations, the percentage of PDLs that use pseudographs has significantly decreased in the present study. This change can also be considered noteworthy as it is not possible to draw any conclusion from a pseudograph, so the use of such type of graphs should be totally discouraged.

Considering the claims made in the PDLs, majority of claims were aimed at promoting the efficacy of drugs in both the studies. This is as expected as drug companies' major purpose is to promote efficacy of their drugs through PDLs. But there also is a significant decrease in the number of safety claims in the present study which is a matter of concern. The present study also showed increase in the number of tall/exaggerated claims. Such claims are unreliable and unauthentic and should not find a place in any PDL. We did not come across any study which analysed the validity of references, type of claims, type of journal articles used as references, type of graphical presentation. So, we do not have data for comparison.

## CONCLUSION

Decrease in percentage of PDLs mentioning generic names, approved uses, regimen, references in the present study compared to the previous one is a matter of concern and reflects deteriorating standards of PDLs over a period of time. At the same time this study also revealed some positive outcomes like decrease in the number of irretrievable journal articles used as references, decrease in the number of pseudographs and increase in the number of valid references. It is essential to consider the negative findings of this study and measures implemented to improve the same.

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