Quality of Pharmaceutical Advertisements in Medical Journals: A Systematic Review

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Abstract

Background: Journal advertising is one of the main sources of medicines information to doctors. Despite the availability of regulations and controls of drug promotion worldwide, information on medicines provided in journal advertising has been criticized in several studies for being of poor quality. However, no attempt has been made to systematically summarise this body of research. We designed this systematic review to assess all studies that have examined the quality of pharmaceutical advertisements for prescription products in medical and pharmacy journals.

Methods and Findings: Studies were identified via searching electronic databases, web library, search engine and reviewing citations (1950 – February 2006). Only articles published in English and examined the quality of information included in pharmaceutical advertisements for prescription products in medical or pharmacy journals were included. For each eligible article, a researcher independently extracted the data on the study methodology and outcomes. The data were then reviewed by a second researcher. Any disagreements were resolved by consensus. The data were analysed descriptively. The final analysis included 24 articles. The studies reviewed advertisements from 26 countries. The number of journals surveyed in each study ranged from four to 24 journals. Several outcome measures were examined including references and claims provided in advertisements, availability of product information, adherence to codes or guidelines and presentation of risk results. The majority of studies employed a convenience-sampling method. Brand name, generic name and indications were usually provided. Journal articles were commonly cited to support pharmaceutical claims. Less than 67% of the claims were supported by a systematic review, a meta-analysis or a randomised control trial. Studies that assessed misleading claims had at least one advertisement with a misleading claim. Two studies found that less than 28% of claims were unambiguous clinical claims. Most advertisements with quantitative information provided risk results as relative risk reduction. Studies were conducted in 26 countries only and then the generalizability of the results is limited.

Conclusions: Evidence from this review indicates that low quality of journal advertising is a global issue. As information provided in journal advertising has the potential to change doctors’ prescribing behaviour, ongoing efforts to increase education about drug promotion are crucial. The results from our review suggest the need for a global pro-active and effective regulatory system to ensure that information provided in medical journal advertising is supporting the quality use of medicines.

Introduction

Advertising in medical journals is one of the techniques used by pharmaceutical companies to promote their products to medical doctors. During the first four years of a new medicine on the market, pharmaceutical companies may gain approximately US $2.43 for each dollar spent on medical journal advertisements for a medicine [1]. The return on investment has been reported to increase to more than US $4 after that period [1].

Doctors use advertising in medical journals as one of the main sources of information for newly marketed drugs [2,3,4,5]. Therefore, ideally, information provided in advertisements should be of high quality to support doctors to practice evidence-based medicine.

Internationally, two sets of guidelines have been developed for pharmaceutical advertising. In 1988, the World Health Organization (WHO) established the Ethical criteria for medicinal drug promotion [6]. These criteria constitute general principles for ethical standards that can be adapted by governments to national circumstances. The International Federation of Pharmaceutical Manufacturers Association (IFPMA) has adopted a Code of Pharmaceutical Marketing Practices, supplemented by member association and company codes, that sets standards for the ethical promotion of medicines [7]. It is a requirement of IFPMA membership that member associations adopt codes that meet local requirements but are consistent with, and as comprehensive as, the IFPMA Code. The IFPMA seeks to ensure that ethical
promotional practices are established worldwide. These guidelines provide recommendations on the type and quality of information that should be included in journal advertisements. In most countries, regulation of the quality of advertisements in medical journals is a responsibility of government agencies [9] and/or the pharmaceutical industry [9]. Pharmaceutical industry codes of conduct most often complement the requirements set in legislation by developing standards and investigating alleged breaches [9].

Despite the availability of regulations and controls of drug promotion worldwide, pharmaceutical advertising in medical journals has been criticized for being of poor quality [10,11,12,13,14,15,16,17,18,19,20,21,22]. Several studies have assessed the quality of pharmaceutical advertisements and examined a range of different outcome measures [10,11,12,14,17,18,20,22,23,24,25,26,27,28,29,30,31,32,33] such as availability of product information [14,29,30,31], type and truthfulness of marketing claims [20,24], quality and availability of references provided to support the claims [19,34], presentation of scientific results in terms of absolute or relative risk reductions [17,20], quality of graphs [12] and overall compliance with the national regulations or guidelines [10,11]. The overall results of these studies have never been synthesized. A systematic review would provide researchers and policy makers with information on the standards of pharmaceutical advertisements that may reflect the effectiveness of current guidelines and regulations.

We aimed to do a systematic review of all studies that have examined the quality of pharmaceutical advertisements for prescription products published in medical and pharmacy journals.

**Methods**

**Selection Criteria**

Studies were included in the review if they were published in English and examined the quality of information included in pharmaceutical advertisements for prescription products in medical or pharmacy journals. Studies were excluded from the review if they met one of the following conditions:

- only evaluated advertisements provided in pamphlets, brochures, leaflets and inserts. Unlike advertisements in medical journals, there is no repository of pamphlets, brochures and other things which makes it very difficult to collect appropriate and representative samples for a study,
- assessed advertisements for both prescription and non-prescription medicines without separating the results,
- assessed advertisements for both prescription medicines and medical devices without separating the results,
- only assessed gender, metaphors or race issues in advertisements,
- assessed outcomes that were not related to the quality of medical information such as the use of pharmaco-economic terms and patterns of advertising.

**Search Strategy**

We searched Medline (from 1950), International Pharmaceutical Abstracts (from 1970), Current Contents (from 1998), Scopus, Sociological Abstracts (from 1952), PsychInfo (1950) and Business Source Complete (from 1950). We also searched the Drug promotion database [35], Google Scholar, Web of Science (from 1993), and the Healthy Skepticism web library [36]. The first 100 results returned by each search from the Google Scholar were scanned for relevant articles.

We searched the databases for all studies published up to February 2006. The following combinations of search terms were used: “pharmaceutical”, “advertising or advertisements”, “promotion”, “codes of conduct”, “medical journal”, “marketing”, “journals”, “physicians” and “quality” and “information”. One researcher carried out the search and scanned the title and abstracts of studies identified from this search. A copy of all articles potentially eligible was retrieved and screened by the same reviewer for the inclusion criteria. All bibliographies of selected papers were screened for additional relevant articles.

**Data Extraction**

Data extraction forms were developed to collect data on study design and study outcomes. For each eligible article, a researcher extracted the data. A second researcher then reviewed the data. All disagreements were resolved by consensus.

Information extracted on study design included: sampling methodology, total number of advertisements surveyed, total number of distinct advertisements surveyed, number of reviewers, consistency of reviewers, year of publication, period and country studied, type and number of journals evaluated.

The outcome measures examined included the availability of product information, the quality and availability of the references, the presentation of the risk results and the nature and quality of promotional claims.

**Availability of Product Information**

We extracted the proportion of advertisements that included information on brand name, generic name, indications, side effects, dosage, interactions, precautions and contraindications, warnings and treatment of overdose.

**References**

We examined information on references including the proportion of advertisements that used references, types of references provided to support marketing claims, quality of references, source of research funding of references and response from pharmaceutical companies to a requests for data on file.

**Claims**

We extracted information on number and type of claims, number of misleading claims and proportions of advertisements compliant with codes or guidelines.

**Risk Results**

We extracted proportions of advertisements mentioning relative risk reduction (RRR), absolute risk reduction (ARR) and number needed to treat (NNT).

**Data Analysis**

As studies calculated results differently either on the basis of the total number of advertisements or on the total number of distinct advertisements (similar advertisements may be repeated in journals), we recalculated the results based on the total number of distinct advertisements when the raw data were available.

Data were entered using Microsoft Office Excel 2003. Descriptive statistics were produced for each outcome. A narrative synthesis method was used to enable us to analyse a large and diverse evidence base.

**Results**

Fifty articles were identified and 24 were included in the systematic review (Table 1) [10,11,14,15,17,18,19,20,21,22,24,26,27,28,29,30,31,34,37,38,39,40,41,42]. Twenty-six studies [3,13,23,25,33,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63] were excluded after full review. The reasons for exclusion are detailed in the study flow diagram in Figure 1.
Characteristics of Studies Included

The studies reviewed advertisements from 26 countries predominantly the United Kingdom (UK) (7/24, 29%), Australia (5/24, 21%) and the United States (US) (4/24, 17%) (Table 1). Most studies (19/24, 79%) assessed the quality of advertisements in developed countries. All studies were cross-sectional studies.

All studies were published between 1975 and February 2006. Five studies (5/24, 21%) were published between 1975 and 1990.

### Table 1. General Characteristic of Studies.

| Study (First author) | Country surveyed | Year of publication | Number of journal examined | Period studied | Number of advertisements | Number of distinct advertisements | Sampling method |
|----------------------|------------------|---------------------|---------------------------|----------------|------------------------|-------------------------------|-----------------|
| Lexchin [24]         | Canada           | 1999                | 5                         | 1998           | 571                    | 130                           | Convenience sample |
| Lankinen [17]        | Finland          | 2004                | 4                         | 2002           | 1036                   | 245                           | Convenience sample |
| Carandang [10]       | Australia        | 1994                | 4                         | 1991 and 1992  | 127                    |                               | Convenience sample |
| Vlassov [31]         | Russia           | 2001                | 5                         | 1998           | 397                    | 207                           | Convenience sample |
| Chirac [11]          | French speaking African countries (West African and Maghreb) | 1993 | 6 | 1990 | 1311 | 141 | Convenience sample |
| Cooper [19]          | The US           | 2005                | 10                        | 1999           | Not reported           | 438                           | Convenience sample |
| Gilad [37]           | Israel           | 2005                | 24                        | 2000           | 779                    |                               | Convenience sample |
| Gitanjali [38]       | India and Britain| 1997                | 2                         | 1992 and 1993  | 203                    |                               | Convenience sample |
| Lal [39]             | India            | 1992                | 19                        | 1990–1991      | 903                    |                               | Convenience sample |
| Stimson [34]         | The UK           | 1976                | 19                        | 1974           | 1104                   | 89                            | Convenience sample |
| Moulds [28]          | Australia        | 1987                | 5 (results only given for 3) | 1986           | 274                    |                               | Convenience sample |
| Herxheimer [14]      | 18 countries. (Finland, Norway, Sweden, Denmark, Spain, France, Italy, Ireland, UK, Switzerland, Turkey, Indonesia, Nepal, Pakistan, Sri Lanka, Tanzania, Zimbabwe and Brazil) | 1993 | 23 | 1987 to 1988 | 6710 | No reported | Convenience sample |
| Mastroianni [30]     | Brazil           | 2003                | 4                         | 1985 to 2001   | Not reported           | 199                           | Convenience sample |
| Villanueva [22]      | Spain            | 2003                | 6                         | 1997           | 954                    | 287                           | Convenience sample |
| Stimson [42]         | The UK           | 1975                | 27                        | 1974           | 3895                   | 591                           | Convenience sample |
| Mould [26]           | Australia        | 1986                | 5                         | 1985           | Not reported           | 138                           | Convenience sample |
| Mindell [40]         | UK               | 1997                | 1                         | 1997           | Not reported           | 46                            | Convenience sample |
| Wilkes [15]          | The US           | 1992                | 10                        | 1990           | 143                    | 109                           | Convenience sample |
| Lal. [29]            | India, UK and the US | 1997 | Not reported | From July 1994 to June 1995 | Not reported | 762 | Random sample |
| Loke [20]            | Australia        | 2002                | 6                         | Oct to Dec 2000 | 1000 | 174 | Convenience sample |
| Gutknecht [21]       | The US           | 2001                | 4                         | 1999           | Not reported           | 187                           | Convenience sample |
| Lexchin [18]         | Canada           | 1994                | 1                         | 1990           | Not reported           | 22                            | Convenience sample |
| Moulds [27]          | Australia        | 1989                | 1                         | 1988           | 56                     | Not reported                  | Convenience sample |
| Smart [41]           | The UK           | 1997                | 1                         | 1996           | Not reported           | 81                            | Convenience sample |

doi:10.1371/journal.pone.0006350.t001
eleven (11/24, 46%) between 1990 and 2000 and eight (8/24, 33%) between 2000 and 2005.

The studies were conducted with three main objectives. Four studies (4/24, 17%) compared the quality of advertisements in different countries. Sixteen studies (16/24, 67%) assessed the quality of advertisements in a single country. Five studies (5/24, 21%) compared advertisements published at different times [10,26,27,28,30]. Four of the five studies conducted in Australia used the same methodology and three of these were done by the same researchers enabling comparison overtime [10,26,27,28].

Twenty-three studies surveyed advertisements in medical journals and one study assessed advertisements in medical and paramedical journals. The number of journals surveyed in each study ranged from one to 24 journals. Eighteen studies (18/24, 75%) provided information on the total number of distinct advertisements analyzed. Nine studies (9/24, 38%) reported both the total number of advertisements and number of distinct advertisements examined in their studies. The total number of advertisements evaluated ranged from 56 to 6710 (median = 903) and the number of distinct advertisements ranged from 22 to 762 (median = 158).

Several types of outcome measures were examined (Table 2). Sixteen studies (16/24, 67%) assessed references provided in advertisements, nine studies (9/24, 38%) examined availability of product information and nine studies (9/24, 38%) assessed claims provided in advertisements. Four studies (4/24, 17%) evaluated presentation of risk results and seven studies (29%) assessed adherence to codes or guidelines.

Study Quality

Seventeen studies (17/24, 71%) provided data on the number of assessors. Three studies (3/24, 13%) used one assessor, eight studies (33.3%) used two assessors and five studies (2/24, 21%) used between three to five assessors. One multi-country study had different assessors per country [14] who may have applied different standards. Five studies (5/24, 21%) provided information on the consistency of assessors. Of the three studies (3/24, 12%) that reported kappa scores, good and excellent agreement was noted.

Twenty-three studies (23/24, 96%) used a convenience-sampling method. Six studies (6/24, 25%) selected journals based on readership [14,15,18,22,24,31]. One study (1/24, 4%) used random sampling but no information was given on how the randomization was conducted [29].
Availability of Product Information

Six of the eight studies (6/24, 25%) that recorded information on generic name found that generic names were mentioned in 83 to 100% of advertisements (median = 90%) (Table 3). A UK study in 1975 [42] and a Russian study in 2001 [31] found lower rates, 43% and 39% respectively.

Approved indications were mentioned in more than 70% (median = 94%) of advertisements in five studies [11,14, 29,30,39]. Lower rates were observed in a Russian study (45%) [31] and in some countries (Italy, 34%, Tanzania, 40%) in a multi-country study [14]. Six studies (6/24, 25%) that examined information on side effects reported mixed results [11,14,29,30,39,42]. Five studies (5/24, 21%) reported low rates, around 14% or less (median = 6%) in India [29,39], Finland [14], Switzerland [14] and in an 1975 UK study [42]. Two studies (2/24, 8%) published in 1993 and 1997 reported rates over 80% (median = 83%), namely in the US [29], Denmark [14], Spain [14], France [14] and the UK [14,29].

Studies that examined information on contraindications [11,14,29,30,31,39,42], warnings [14,29,30,31,39], precautions [14,29,30,39] reported variable findings. Six studies (6/24, 25%) that reported information on contraindications found that contraindications were mentioned in less than 74% (median = 35%). Two studies (2/24, 8%) reported that contraindications were mentioned in 82 to 93% (median = 88) of advertisements in Denmark [14], Spain [14], the UK [14,29] and the US [29]. Information on warnings was mentioned in less than 77% (median = 35%) of advertisements in five studies (5/24, 21%). One study reported that warnings were mentioned in 80 to 95% (median = 83%) of advertisements namely in Spain [14], France [14], and the UK [14]. Four studies that reported information on precautions found that precautions were mentioned in less than 65% (median = 32%). Two studies (2/24, 8%) reported that precautions were mentioned in 80 to 95% (median = 83) of advertisements in Spain [14], France [14], the UK [14,29] and the US [29].

Five studies (5/24, 21%) reported information on dosage (range: 14–100%, median = 80%) [11,29,30,39,42]. High results were noted in advertisements that appeared in the UK from July 1994 to June 1995 (97%) [29] and in West African and Maghreb in 1990 (87%) [11]. Variable findings were noted before and after the implementation of regulations on advertisements in a study conducted in Brazil in 2003 (range = 58–100%, median = 83%) [30]. Two Indian studies [29,39] conducted in different years revealed different results [30]. The study that was conducted in 1997 [29] found much lower (31%) information on dosage compared to the earlier study in 1992 (73%) [39].

References

References were provided in more than half of the advertisements (range 51–100%, median = 65%) in all studies that evaluated advertisements in developed countries [15,17,19,29,34,37,40,41] except a study published in Spain (13%) [22] (Table 4). References were more rarely provided (range 2–59%, median = 23%) in...
### Table 3. Availability of Product Information.

| Study (First author) | Results calculated based on | Brand name n (%) | Generic name n (%) | Indications n (%) | Contraindications n (%) | Interactions n (%) |
|----------------------|----------------------------|------------------|-------------------|---------------------|----------------------|------------------|
| Carandang 1994 [10]  | Distinct advertisements    | Not reported     | 115/127 (91)      | Not reported        | Not reported          | Not reported      |
| Chirac 1993 [11]     | Distinct advertisements    | Not reported     | 125/141 (89)      | 136/141 (96)        | 97/141 (69)           | Not reported      |
| Mastoianni 2003 [30]*| Distinct advertisements    | Not reported     | 34/39 (87), 29/31 (90) | 37/39 (95), 31/31 (100) | 20/39 (51), 20/31 (64) | 20/39 (51), 21/31 (68) |
|                      |                            | Not reported     | 17/19 (89), 18/19 (95) | 18/19 (95), 19/19 (100) | 10/19 (53), 12/19 (63) | 9/19 (47), 11/19 (58) |
|                      |                            | Not reported     | 51/60 (85), 34/34 (100) | 57/60 (95), 33/34 (97) | 22/60 (37), 25/34 (74) | 22/60 (37), 25/34 (73) |
| Stimson 1975 [42]    | Distinct advertisements    | 544/591 (92)     | 255/591 (43)      | Not reported        | 25/591 (4)           | Not reported      |
| Vlassov 2001 [31]    | Number of placements.      | 154/397(39)      | 177/397 (45)      | 42/397 (11)         | 21/397 (5)           |                  |

| Study (First author) | Results calculated based on | Brand name n (%) | Generic name n (%) | Indications n (%) | Contraindications n (%) | Interactions n (%) |
|----------------------|----------------------------|------------------|-------------------|---------------------|----------------------|------------------|
| Lal 1992 [39]        | No detail information was given | (100)           | (84)              | (80)                | (10)                 | (3)              |
| Henxheimer 1993 [14] (18 countries) | No detail information was given | Not reported | Not reported | 0.4(0.6),(0.94),(0.91),(0.97),(0.34), (0.93),(0.97),(0.91),(0.94), (0.84),(0.40),(0.97),(0.98), (1.67),(2.1),(0.88),(0.73),(0.35),(0.35), (0.93),(0.8),(0.33),(1),(0.35),(2),(0.24),(0.43) | Not reported |
| Lal 1997 [29]        | No detail information was given | (100),(100), (100) | (89), (98), (99) | (80), (92), (97) | (1.3),(0.82), (0.91) | (0.8),(0.63), (0.38) |

| Study (First author) | Dosage regimen n (%) | Drug overdose n (%) | Side effects n (%) | Warnings n (%) | Precautions n (%) |
|----------------------|----------------------|---------------------|-------------------|---------------|------------------|
| Carandang 1994 [10]  | Not reported         | Not reported        | Not reported      | Not reported  | Not reported      |
| Chirac 1993 [11]     | Not reported         | 99/141 (70)         | Not reported      | Not reported  | Not reported      |
| Mastoianni 2003 [30]*| Not reported         | 20/39 (51), 20/31 (64) | Not reported | 20/39 (51), 22/31 (71) | Not reported |
|                      | 10/19 (53), 12/19 (63) | Not reported        | Not reported      | 10/19 (53), 12/19 (63) | Not reported |
| Stimson 1975 [42]    | Not reported         | 22/60 (37), 25/34 (74) | Not reported | 21/60 (35), 26/34 (78) | Not reported |
| Vlassov 2001 [31]    | Not reported         | 23/591 (4)          | Not reported      | 44/591 (7)    | Not reported      |
| Gitanjali 1997 [38]  | Not reported         | Not reported        | Not reported      | Not reported  | Not reported      |

| Study (First author) | Dosage regimen n (%) | Drug overdose n (%) | Side effects n (%) | Warnings n (%) | Precautions n (%) |
|----------------------|----------------------|---------------------|-------------------|---------------|------------------|
| Lal 1992 [39]        | (73)                 | Not reported        | (9)               | (10)          | (10)             |
| Henxheimer 1993 [14] (18 countries) | Not reported | Not reported | (1), (71), (31), (92), (88), (81), (35), (35), (94), (61), (39), (18), Not Known, (32), (24), (16), (18),(65), (34), (48), (80), (83), (35), (35), (95), (7), (38), (17), (-), (31), (34), (24), (-), (40) | In this study warning and precaution is reported in the same group |

| Lal 1997 [29]        | (31),(77),(97)       | (2),(44), (23)      | (14), (83), (82)  | (9), (77), (60) | (12), (83), (80)  |
developing countries [29,30,31,39]. Three studies (3/24, 12%) [17,20,22] found that between 18 to 37% (median = 32%) of references supporting claims were irretrievable.

**Type of References**

Eight studies (8/24, 33%) assessed the type of references provided in pharmaceutical advertisements. Overall, the references most commonly cited were journal articles (range = 55 to 90%, median = 73%). Other types of evidence were data on file (range = 15–19%, median = 17%) [10,14,19], meeting abstract and presentations (range = 5–23%, median = 15%) [19,22,40], books or monographs (range = 5–18%, median = 8%), marketing reports (5%) [19], prescribing information (range = 6–20%, median = 13%) [19,40], government documents (4%) [19], and other evidence (1%).

**References - Source of Research Funding**

Three studies (3/24, 12%) examined the funding of studies used in references (range = 39–58%, median = 40%) [19,22,34]. A study that was conducted in the US determined that the majority (58%) of the original research cited in the pharmaceutical advertisements was sponsored by or had an author affiliated with the product’s manufacturer [19]. A Spanish study [22] found that 41 studies (40%) had been financed by the pharmaceutical industry. Similar findings were noted in a UK study of which 39% of references were sponsored by the industry [34].

**Response to Request for Data on File**

Three studies (3/24, 12%) investigated how companies responded to request for data on file [18,19,39]. The response rates were 42%[19], 37% [39] and 60% [18].

**Quality of References**

Of seven studies (7/24, 29%) [17,18,20,22,34,40,41] that examined the quality of references, four studies (4/24, 17%) [17,20,22,41] assessed the level of evidence of the references cited to support marketing claims (Table 5). One to twelve percent of references (median = 2%) were supported by a systematic review or meta-analysis. More randomised control trials were cited in a Spanish study (67%) compared to studies published in the UK (30%), Finland (9%) and Australia (35%).

Three studies (3/24, 12%) examined other aspects of the quality of the references [18,34,40]. A UK study [40] found that only two fifths of advertisements cited were published, peer reviewed references. A Canadian study found that the mean methodological quality score (58%, 95% CI 51–65%) and the mean relevance score (76%, 95% CI 72–80%) of the references were significantly lower than the acceptable score of 80% (p<0.05) [18]. The poor rating for methodological quality was primarily because of the citation of references to low-quality review articles and “other” sources [18]. A UK study [34] assessed whether the claims were supported by adequate references. Of 49 references cited to substantiate the claims, 14 (29%) were judged adequate on the basis of predetermined criteria including presence of adequate controls, randomisation of treatments, objective assessment and statistical analysis of results.

**Type of Claims**

One study in Australia (2002) [20] and one in Finland (2004) [17] (2/24, 8%) used the same system to classify the claims provided in advertisements. Nine to 28% of the claims were about an unambiguous clinical outcome, 29 to 37% provided a vague clinical outcome, 20 to 31% an emotive or immeasurable outcome and 23% a non-clinical outcome.

**Validity of Claims**

Seven (7/24, 29%) studies examined the validity of promotional claims [10,14,15,26,27,28,38]. Four Australian studies in 1986 [26,1987 [26], 1989 [27] and 1994 [10] examined the proportion of misleading claims in Australian advertisements. Thirty-one percent of the claims were about an unambiguous clinical outcome, 29 to 37% provided a vague clinical outcome, 20 to 31% an emotive or immeasurable outcome and 23% a non-clinical outcome.

### Table 4. Availability of References.

| Study (First author) | Number of advertisements with references n (%) |
|----------------------|-----------------------------------------------|
| Mindell 1997 [40]    | 31/46 (67)                                   |
| Lankinen 2004 [17]   | 245/245 (100)                                |
| Cooper 2005 [19]     | 312/438 (71)                                 |
| Stimson 1976 [34]    | 89/89 (100)                                  |
| Smart 1997 [41]      | 41/81 (51)                                   |
| Mastroianni 2003 [30] | 6/39 (15), 7/31 (23)                       |
| Lankinen 2004 [17]   | 8/19 (42), 9/19 (47)                         |
| Villanueva 2003 [22] | 33/60 (55), 20/34 (59)                       |
| Wilkes 1992 [15]     | 38/287 (13)                                  |
| Smart et al, 1997 [41]| 69/109 (63)                                  |

*Advertisements published before and after 3 regulation were established.*

doi:10.1371/journal.pone.0006350.t004

### Table 5. Level of evidence.

| Study (First author) | Level of evidence n (%) |
|----------------------|-------------------------|
|                      | Systematic review or Meta analysis | Randomized control trial | Other evidence |
| Smart et al, 1997 [41]| 2/139 (1) | 41/139 (30) | 96/139 (69) |
| Lankinen et al, 2004 [17] | 9/381 (2) | 33/381 (9) | 135/381 (38) |
| Loke et al, 2002 [20] | 99/855 (12) | 297/855 (35) | 75/855 (9) |
| Villanueva et al, 2003 [22] | - | 84/125 (67) | 18/125 (14) |

doi:10.1371/journal.pone.0006350.t005
same methods but a different principal investigator classified 8% of advertisements as misleading [10].

In a study [30] conducted in India, ten randomly selected advertisements from the Indian edition of British Medical Journal were sent to three experts. They found that all the advertisements were misleading or made unsubstantiated claims [30]. One multicountry study with a different evaluator in each country [14] found that relatively few (no detailed information provided) advertisements provided misleading information except in Brazil (25%), Finland (50%), Italy (30%) and Pakistan (38%). However, no definition of misleading information was given [14].

In 1992, an American study [15] reviewed 109 advertisements published in 10 medical journals and noted that headlines were found to mislead the reader about efficacy in 32% of advertisements. In 44% of cases, reviewers felt that the advertisement would lead to improper prescribing if the physician had no other information about the drug other than the advertisement [15].

A Spanish study [22] found that 44% of claims with citations were not supported by the reference, most frequently because it would lead to improper prescribing if the physician had no other information about the drug other than the advertisement [15].

In a study [38] conducted in India, ten randomly selected advertisements were sent to three experts. They found that all the advertisements provided misleading information except in Brazil (25%), Finland (50%), Italy (30%) and Pakistan (38%). However, no definition of misleading information was given [14].

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Presentation of Risk Results

Four studies (4/24, 17%) reported information on how benefit and harm were presented in advertisements that reported changes in clinical outcomes (Table 6) [17,20,21,24]. Between 7 and 22% (median = 7%) of advertisements provided information on risk results [20,24]. In a Canadian study [24], half of the 22 advertisements that reported changes in clinical outcomes reported the RRR, none reported the ARR or NNT, but 41% provided data that would enable readers to calculate those figures if they knew how. In an Australian study [20], none of the claims explicitly reporting quantitative outcomes provided ARR or NNT. In two other studies, none of the advertisements provided NNTs [17,21].

Table 6. Risk Results’ Information.

| Study (First author) | Advertisements with n (%) | Relative risk reduction | Absolute risk reduction | Number needed to treat | Original data permitting calculation by readers |
|----------------------|--------------------------|------------------------|------------------------|------------------------|-----------------------------------------------|
| Lexchin 1999 [24]    | 29/130 (22)              | 0 (0)                  | 0 (0)                  | 9/130 (7)              |
| Lankinen 2004 [17]   | No reported              | 1/245 (0.4)            | 0/245 (0)              | Not reported           |
| Loke 2002 [20]       | 13/174 (7)               | 0 (0)                  | 0 (0)                  | 2/174 (1)             |
| Gutknecht 2001 [21]  | Not reported             | Not reported           | 0 (0)                  | Not reported           |

doi:10.1371/journal.pone.0006350.t006
recipient to form his or her own opinion of the therapeutic value of the pharmaceutical product concerned. Promotional information should be based on an up-to-date evaluation of all relevant evidence and reflect that evidence clearly. It should not mislead by distortion, exaggeration, undue emphasis, omission or in any other way. Every effort should be made to avoid ambiguity”.

The code does not provide any detailed requirements on how quantitative results should be presented. This limitation highlights the need for IFPMA to amend its code with regards to the presentation of statistical information in journal advertising in order to support the quality use of medicines.

Information on medicines is essential to help doctors ensure the optimal use of medicines. However, studies show that doctors who use journal advertisements as a source of information may prescribe less appropriately [68,69]. In addition, reliance on journal advertising for information is associated with increased costs of prescribing [70,71]. Even doctors who think that they obtain their knowledge from the scientific literature can be influenced by promotional sources without being aware of it [72]. As information provided in journal advertising has the potential to change doctors’ prescribing behaviour, our review indicates that ongoing efforts including complaints and recommendations by researchers, health professionals and policy makers to improve the quality of advertisements in medical journals are crucial.

The Ethical Criteria for Medicinal Drug Promotion developed by the World Health Organization (WHO) [6] recommend a minimum set of medicines information for journal advertising. However, this review found that safety information was still missing in studies undertaken after the publication of the WHO Ethical Criteria. Since 1988, the WHO has not reviewed the ethical criteria concerning advertising in medical journals [6]. Since the criteria lay the foundation for behaviour concerning the pharmaceutical promotion, it may be necessary for WHO to be proactive in updating the requirements for these activities.

Journal advertising is typically governed through self-regulatory codes administered by industry associations. In most countries, the recognition of breaches is based on a complaints mechanism. Complaints of violations can only be made after advertisements have already been circulated. The current system is limited by retrospective detection of code breaches and has no prevention focus. Furthermore, there is evidence that many violations of marketing codes go unreported [73,74] and only a small portion of promotional materials voluntarily submitted for comment before submission are reviewed [75]. The poor quality of information found in this review suggests that the current system may be unable to regulate journal advertisements effectively. This limitation highlights the need for governments and pharmaceutical industry to be jointly responsible for regulating journal advertising. Governments may need to take more proactive action such as engaging independent experts to help in designing regulation for journal advertising where self-regulatory codes are limited. In addition to that, effective regulatory system may complement pharmaceutical promotion to ensure accuracy and reliability of information in journal advertising [76].

Most medical journals rely on advertising for part of their revenue. Dependence on revenue from the industry may minimize the independence of the medical journals [77,78]. A survey in North American survey found that 21% of journals editors claimed that they did not review advertisements provided by the industry before their appearance in the journals [79]. The low quality of information provided in journal advertising noted by this review highlight the need of journal editors and publishers to consider regulatory controls for advertising in their publications. Introduction of journal own codes is expensive. Journals obviously need to have independent financial resources to remove the conflict of interest with pharmaceutical companies. The Public Library of Science (PLOs) [80], a non-profit scientific and medical publisher has provided a good model which can be copied by other journals. Sources of revenue for PLoS includes donations from individual, paid individual memberships, support from foundations, from institutional memberships, and from asking research funders to pay a publication charge for accepted research papers. In addition to that, medical journals’ financial resources could be relied on the advertising of products other than those supplied by pharmaceutical companies [77].

Our review found that the low quality of journal advertising was a global issue. Poor quality advertising has been observed in developing countries and post-Soviet Russia where controls might be weak and limited as well as in developed countries which have stricter regulations [91]. IFPMA states that the industry has an obligation and responsibility to establish a clear understanding of the appropriate use of prescription medicines. Based on the results of this review, stronger enforcement mechanisms would appear necessary to encourage pharmaceutical companies to provide reliable information which is essential for the rational prescribing of promoted products as recommended by the code. This is particularly the case in developing countries and post-Soviet Russia where independent sources of information on medicines are limited and where doctors rely on industry for most medicine information [92,93].

This systematic review provides the current body of evidence on the quality of advertising in medical journals which will assist researchers in designing future studies. However, the variability in outcomes utilised in assessing the quality of information in the studies made collation of results difficult. There appears to be no consensus among researchers on the most appropriate outcomes. Most studies assessed references, availability of product information and adherence to codes or guidelines as indicators for information quality. Pharmaceutical companies may provide advertisements adhering to guidelines and with complete information supported by strong research based evidence. However, this does not mean that the advertisements are supporting rational prescribing. There is a need for developing more appropriate indicators to assess the quality of information in advertisements. This effort will minimize the heterogeneity of data and will allow direct comparison between studies.

Limitations

This review was limited to studies that had been published in English language. Excluding studies in other languages may have led to the omission of some studies that provide evidence about the quality of information in journal advertising.

No attempt was made to define what was meant by quality of information. Rather than entering into discussion regarding the definition of the quality, we decided to define it based on presence or absence of information, availability and level of evidence of references, type and number of misleading claim and proportion of advertisements compliant with code or guidelines and the presentation of risk results.

Only one of the 24 studies included in this review selected advertisements randomly and the report of that study did not specify the random selection procedure. Also the countries studied are not representative of all countries. Consequently extrapolation of the average findings of this review to the average for all advertisements around the world may not be accurate. The number of studies is too small and their methods and quality are too variable to allow confident overall conclusions about changes over time or differences between countries.
Future Work

This review has noted several outcomes measures that have not been adequately investigated in research during the review period. Firstly, only one study assessed whether claims were supported by references [22]. Additional research on the use the references to support claims in journal advertising is needed. Secondly, the majority of studies that examined misleading claims were not well reported [10,14,26,27,28,30]. Although it is difficult to judge misleading claims, this review demonstrates the need for development of a widely accepted definition of a misleading claim and development of well described methods that can be used in different countries and years to enable comparisons. Thirdly, all multinational studies that measured content of journal advertising were published before 1998. Since then, codes of conducts and regulations on pharmaceutical advertising have been updated. It will be useful to conduct a comparative international study to provide recent comparative data on journal advertising. The study should be conducted to compare the effects of different regulatory frameworks. The study would provide policy makers with recent evidence of the strengths and weaknesses of different systems. This information is crucial for improving standards and regulations for pharmaceutical promotion.

Most pharmaceutical markets are dominated by international companies. These companies have their own marketing standards which are often based on the standards set forth in the IFPMA code of conduct [84,85]. According to the codes that are publicly available promotional materials should encourage the appropriate use of medicines by presenting information accurately, without exaggeration and must follow all relevant local laws and companies policies and procedures [84,85]. This review noted that no independent study has been conducted to evaluate whether companies are implementing their codes in a uniform way across countries. It would be useful to conduct a study to compare how advertisements for the same medicines are presented in different countries. The study would provide the first data pertaining the adherence of pharmaceutical companies to their own ethical codes and local standards in the provision of medicines information in journal advertising for international marketing communications.

Journal advertising is one among various promotional practices. However, it has been reported that pharmaceutical companies are cutting back print media to promote medicines and increase their promotional activities on internet marketing [86,87] and continuing medical education [88,89]. Therefore it would be beneficial to conduct a review to examine the quality of medicines information in internet marketing and continuing medical education.

Conclusion

Globally, pharmaceutical advertising in medical journals often provides poor quality information. The impact of this problem on doctors’ prescribing behaviour might be even greater in developing countries and post-Soviet Russia where access to industry-free medicine information is limited. The results from our review suggest the need for a global pro-active and effective regulatory system to ensure that information provided in medical journal advertising is supporting the quality use of medicines.

Author Contributions

Conceived and designed the experiments: NO AV ER. Performed the experiments: NO AV. Analyzed the data: NO. Contributed reagents/materials/analysis tools: NO. Wrote the paper: NO AV ER.

References

1. Lieberman M. Listen up, publishers say - journal advertising sells! Medical Marketing & Media 35(5): 89–94.
2. McGettigan P, Golden J, Fryer J, Chan R, Feely J (2001) Prescribers prefer people: The sources of information used by doctors for prescribing suggest that the medium is more important than the message. British Journal of Clinical Pharmacology 51: 184–189.
3. Rohra DK, Gilani AH, Memon IK, Perven G, Khan MT, et al. (2006) Critical evaluation of the claims made by pharmaceutical companies in drug promotional material in Pakistan. Journal of Pharmacy and Pharmaceutical Sciences 9: 50–59.
4. The Association of Medical Media. The case for medical journal advertising. Available: http://www.ammonline.org/AMMTool.aspx. Accessed Mar 12, 2009.
5. Prosser H, Almond S, Walley T (2003) Influences on GPs’ decision to prescribe new drugs - the importance of who says what. Family Practice 20: 61–63.
6. World Health Organization. Ethical criteria for medical drug promotion. Available: http://www.who.int/medicinedocs. Accessed Aug 3, 2008.
7. International Federation of Pharmaceutical Manufacturers Associations (IFPMA). Code of Pharmaceutical Marketing. Available: http://www.ifpma.org/pdf/ IFPMA-TheCode-FinalVersion-30May2006-EN.pdf. Accessed Sep 3, 2008.
8. Morris LA, Pines WL (2000) Regulation of pharmaceutical promotion in the medium is more important than the message. British Journal of Clinical Pharmacology 51: 184–189.
9. The Organisation for Professionals in Regulatory Affairs. Worldwide survey on national controls of pharmaceutical advertising and promotion. Available: http://www.topra.org/files/2005N11_Focus_02.pdf. Accessed Mar 11, 2009.
10. Carandang ED, Moulds RFW (1994) Pharmaceutical Advertisements in Australian Medical Publications - Have They Improved. Medical Journal of Australia 159: 410–411.
11. Gutknecht DR (2001) Evidence-based advertising? A survey of four major journals. J Am Board Fam Pract 14: 197–200.
12. Villanueva P, Peiro S, Librero J, Pereiro I (2003) Accuracy of pharmaceutical advertisements in British medical journals. Journal of the American Medical Association 289: 779–785.
Mastroianni PdC, Galduroz JCF, Carlini EA (2003) Influence of the legislation on the advertisement of psychoactive medications in Brazil. Revista Brasileira De Psiquiatria (São Paulo, Brazil: 1999) 25: 146–155.

Vlassov V, Mansfield P, Leuschin J, Vlassova A (2001) Do drug advertisements in Russian medical journals provide essential information for safe prescribing? Western Journal of Medicine 174: 391–394.

Cooper RJ, Schirger DL, Tashman DA (2001) An evaluation of the graphical literacy of Annals of Emergency Medicine. Annals of Emergency Medicine 37: 13–17.

Rothermich EA, Smerak DA (1996) Health-related quality-of-life claims in prescription drug advertisements. American Journal of Health-System Pharmacy 53: 1565–1569.

Stimson GV (1976) The use of references in drug advertisements. Journal of the Royal College of General Practitioners 26 Suppl 1: 76–80.

Department of Essential Drugs and Medicine Policy. Drug Promotion Database. Available: http://www.drugpromoto.info/. Accessed Dec 26, 2008.

Healthy skepticism. Available: http://healthyskepticism.org/harm.php. Accessed Dec 22, 2008.

Glad J, Moran L, Schlaffer F, Borer A (2005) Antibiotic drug advertising in medical journals. Scandinavian Journal of Infectious Diseases 37: 910–912.

Girmajali B, Shashidharan GH, Tripathi J, Sethuraman KR (1997) Are drug advertisements in Indian edition of BMJ unethical? BMJ 313.

Lal A, Sharma ML (1992) Drug advertisements in Indian medical journals. Indian Journal Of Physiology And Pharmacology 36: 139–140.

Mindej J (1997) Evidence based advertising? Only two fifths of advertisements cited published, peer reviewed references. British Medical Journal 315: 1622–1622.

Smart S, Williams C (1997) Evidence based advertising - Half of drug advertisements in BMJ over six months cited no supporting evidence. British Medical Journal 315: 1622–1623.

Stimson GV (1975) Information contained in drug advertisements. British Medical Journal 4: 508–509.

Stahly C, Westerholm B (1987) Are drug advertisements of any informative value? Analysis of drug advertisements in the Swedish Medical Journal (Lakartidningen) and the Norwegian Medical Journal (Tidsskrift for Den norske lægeforening) during the first half of 1986. Tidsskrift for Den Norske Lægeforening 107: 1573–1577.

Hansen JF, Osborne D (1995) Portrayal of Women and Elderly Patients in Psychotropic-Drug Advertisements. Women & Therapy 16: 129–141.

Lvdahl U, Rika E (2000) The construction of gender and mental health in Nordic psychotropic-drug advertising. International Journal of Health Services 30: 395–406.

Munce SEPB, Robertson EKP, Sansom SNMA, Stewart DEMDF. Who Is Portrayed in Psychotropic Drug Advertisements? [Article]. Journal of Nervous & Mental Disease April 2004; 192(4): 204–208.

Riska E, Haaglund U (1991) Advertising for Psychotropic-Drugs in the Nordic Countries - Metaphors, Gender and Life Situations. Social Science & Medicine 32: 465–471.

Smith MC, Griffin L (1977) Rationality of appeals used in the promotion of psychotropic drugs. A comparison of male and female models. Social Science & Medicine 16(7): 409–414.

Trigo Hervas MM, Garcia Lopez JA, Garcia Lopez MA (1995) Advertising of pharmaceutical products in professional pharmaceutical journals. Farmacia Clinica 12: 703–713.

Madridepaz R, Cabezas C, Flor F (1996) Drug advertising in medical journals. Publicidad de medicamentos en las revistas medicas 17: Farmacia Clinica 12: 703–713.

Spigset O (1998) Are advertisements for pharmaceuticals reliable? [Kan man v$this text is truncated...