BMJ Open  Interactions between physicians and the pharmaceutical industry generally and sales representatives specifically and their association with physicians’ attitudes and prescribing habits: a systematic review

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ABSTRACT
Objectives  The objective of this review is to explore interactions between physicians and the pharmaceutical industry including sales representatives and their impact on physicians’ attitude and prescribing habits.

Data sources  PubMed, Embase, Cochrane Library and Google scholar electronic databases were searched from 1992 to August 2016 using free-text words and medical subject headings relevant to the topic.

Study selection  Studies included cross-sectional studies, cohort studies, randomised trials and survey designs. Studies with narrative reviews, case reports, opinion polls and letters to the editor were excluded from data synthesis.

Data extraction  Two reviewers independently extracted the data. Data on study design, study year, country, participant characteristics, setting and number of participants were collected.

Data synthesis  Pharmaceutical industry and pharmaceutical sales representative (PSR) interactions influence physicians’ attitudes and prescribing behaviour and increase the number of formulary addition requests for the company’s drug.

Conclusion  Physician–pharmaceutical industry and its sales representative’s interactions and acceptance of gifts from the company’s PSRs have been found to affect physicians’ prescribing behaviour and are likely to contribute to irrational prescribing of the company’s drug. Therefore, intervention in the form of policy implementation and education about the implications of these interactions is needed.

INTRODUCTION
The relationship between physicians and the pharmaceutical industry has evoked heated debate for many decades.1 In 2012, the pharmaceutical industry spent $89.5 billion on physician–pharmaceutical sales representative (PSR) interactions that accounted for 60% of the global sales and marketing spending.2–8 Previous reports have demonstrated that PSRs may influence prescribing behaviour.9–16 However, the evidence determining whether pharmaceutical industry and PSRs interactions influence physicians is divided and contradictory. Studies have indicated that physicians may be unable to distinguish between promotional information and scientific evidence.17 18 Physicians, however, believe their colleagues are more susceptible to pharmaceutical industry marketing strategies than themselves.19–22 The majority of the physicians do not believe that they are affected by pharmaceutical industry and PSR interactions. Most medical and governmental institutions have installed guidelines and self-regulatory and legislative checks to regulate the relationship between physicians and the pharmaceutical industry and its representatives.5 15 16 23–26 However, while administrative proposals for deregulatory reforms...
that would remove some governmental authority over the industry are increasing, scientific evidence rigorously examining the extent of interactions between physicians and pharmaceutical industry and it PSRs is needed. This review evaluates critically and systemically the evidence on the impact of pharmaceutical industry and PSR interactions on physicians.

METHODOLOGY

Protocol
We followed a detailed methodology that we described in our review protocol, which is available on request to the corresponding author. Two independent reviewers assessed selected articles as per inclusion/exclusion criteria, shortlisted them for writing the review and cross-checked their decisions about inclusion/exclusion with each other. The review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (supplementary appendix 1).

Eligibility criteria
The eligibility criteria were:

- types of studies: observational study design, such as cross-sectional studies and cohort studies, but also (non-)randomised trials and survey designs comparing at least one facet that are mentioned below on the impact on behaviour and attitude;
- types of participants: physicians, pharmaceutical representatives and physicians in training/residents;
- types of exposure: any type of interaction between physicians and the pharmaceutical industry where there is direct interaction with the physician, such as meeting with drug representatives, participating in pharmaceutical-sponsored Continuing Medical Education (CME) events, receiving travel funding, free drug samples, industry-provided meals, gifts and presentations of industry-related information;
- types of outcome: knowledge, beliefs and/or attitudes of physicians regarding physician–industry interactions and (prescribing) behaviour of physicians;
- type of control: no interaction.

Exclusion criteria were: qualitative, ecological, econometric studies, editorials, letters to the editor, studies on other health professionals (eg, nurses and medical students), small samples sizes, studies assessing indirect interactions and research funding.

We did not exclude studies based on risk of bias. We took risk of bias into account when grading the quality of evidence using GRADE approach.

Search strategy
The search strategy included PubMed, Embase, Cochrane Library and Google Scholar electronic databases (January 1992 to August 2016). Databases were not searched.
before 1992, as these studies were already investigated in an earlier review. The search combined terms for physicians and pharmaceutical and included both free-text words and medical subject heading relevant to the topic. We did not use a search filter. The online supplementary information file provides the full details for one database. Additional search strategies included a search of the grey literature (theses and dissertations). Also, we reviewed the references lists of included and relevant papers.

Assessment of risk of bias in included studies
Two reviewers assessed in duplicate and independently the risk of bias in each eligible study. Disagreements were resolved by discussion or adjudication by a third reviewer. We used the recommendations outlined in the Cochrane Handbook to assess the risk of bias in randomised studies. We graded each potential source of bias and rated the studies as high, low or unclear risk of bias.

Data analysis and synthesis
The information extracted from the selected studies included type of study, study design, type of pharmaceutical industry and PSR interaction and type of outcome. We did not conduct a meta-analysis due to the heterogeneity of study design, types of interventions, outcomes assessed and outcome measures used. Instead, we summarised the data narratively. We assessed the quality of evidence by outcome using the GRADE methodology.

RESULTS
We independently screened the titles and abstracts of the 2170 identified records for potential eligibility. Out of 2170, the full text of 49 eligible citations that matched the inclusion criteria were retrieved and used for qualitative assessment during the writing of the review (figure 1, table 1).

Characteristics of included studies
The identified studies were published between 1992 and August 2016. Most of the studies included were cross-sectional studies. Only two studies were cohort studies, three were randomised trials and one study was a case–control study.

Extent of interactions between physicians and the pharmaceutical industry
We found that PSR interactions are a regular feature in the daily lives of physicians across the world. Most of the attending physicians and residents have at least one interaction with industry representatives per month. The frequency of interactions or gifts offered and accepted varied with private versus public hospital setting and the position of the physicians in the medical hierarchy. Junior residents received twice as much free drug samples from PSR interactions than senior residents. PSR interactions were significantly higher at the beginning of residency. The majority of programme directors of internal medicine residencies in the USA allowed PSRs to meet with residents during working hours and permitted PSR sponsorship of conferences. Attending physicians and physician specialists had more PSR interactions and received higher numbers of medical samples and promotional material than residents. Participants working in private practice alone or in both sectors were more likely to receive gifts than physicians working in the public sector. Most common gifts received were medical samples, promotional material and free drug samples from industry representatives. Physicians perceived PSRs as important sources of education and funding, while some studies reporting sceptical attitudes about the contribution of PSRs towards teaching and education. Conference registration fees, informal luncheons, sponsorship of departmental journal clubs, anatomical models and free drug samples were considered as appropriate gifts, while other studies found that there was some extent of influence. In addition, physicians considered their colleagues more susceptible than themselves to PSR marketing strategies. There was a strong correlation between the amount of gifts and the belief that PSR interactions did not influence their prescribing behaviour.

Gifts
We found that better scores on knowledge and attitudes were significantly associated with fewer interactions with representatives and their gifts. Conference registration fees, informal luncheons, sponsorship of departmental journal clubs, anatomical models and free drug samples were considered as appropriate gifts. Most of the physicians considered themselves immune to the influence of gifts. Most common gifts received were medical samples, conference registration fees, informational luncheons, sponsorship of departmental journal clubs, anatomical models and free drug samples were considered as appropriate gifts. Most of the physicians considered themselves immune to the influence of gifts.

Drug samples
Most of the physicians who accepted drug samples had a positive attitude towards the pharmaceutical representatives. Accepting samples lead to higher branded drug prescription rather than generic prescribing.

Perspectives of physicians towards PSR interactions
We found that physicians have a positive attitude towards PSRs. Physicians perceived PSRs as important sources of education and funding, while some studies reporting sceptical attitudes about the contribution of PSRs towards teaching and education. Conference registration fees, informal luncheons, sponsorship of departmental journal clubs, anatomical models and free drug samples were considered as appropriate gifts, while other studies found that there was some extent of influence. In addition, physicians considered their colleagues more susceptible than themselves to PSR marketing strategies. There was a strong correlation between the amount of gifts and the belief that PSR interactions did not influence their prescribing behaviour.
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<td>Retrospective cohort</td>
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<td>Questionnaire of 93 physicians in a medical school</td>
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<td>Impact on prescribing, positive attitudes; most respondents thought it is proper to accept drug samples (92%), lunch (77%), an anatomical model (75%) or a well-paid consultantship (53%) from PSR</td>
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<td>25</td>
<td>Randall et al</td>
<td>USA</td>
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<td>Intervention group of physicians (n=18) that received education about PSR interaction and control group (n=14)</td>
<td>Controlled trial</td>
<td>Interaction with PSR</td>
<td>The majority of residents found the interactions and gifts useful. Compared with the comparison group, the intervention group significantly decreased the reported number of office supplies and non-educational gifts (p&lt;0.05)</td>
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<td>Most participants have contact with the pharmaceutical company; 24.6% of the participants thought gifts would influence their future prescribing behaviour, while 45.1% thought gifts would influence their classmates' future prescribing behaviour (p&lt;0.001)</td>
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<td>Workneh et al&lt;sup&gt;55&lt;/sup&gt;</td>
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<td>USA</td>
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<td>Survey</td>
<td>Interaction with PSR</td>
<td>Antidetailing policies reduced the prescription of off-label antidepressants and antipsychotics for children</td>
</tr>
</tbody>
</table>

**Table 1 Continued**
### Pharmaceutical representative speakers

Sponsored lectures/symposia of pharmaceutical companies influenced behaviour of the attendees leading to the attendees prescribing more drugs from the sponsoring companies without sufficient evidence supporting superiority of those drugs. The majority of attending physicians failed to identify inaccurate information about the company drug.

### Honoraria and research funding

Physicians who received money to attend pharmaceutical symposia or to perform research requested formulary addition of the company’s drug more often than other physicians. This association was independent of many confounding factors (table 2). Brief encounters with PSRs and receipt of honoraria or research support were predictors of faculty requested change in hospital formulary.

### Conference travel

Pharmaceutical company-sponsored conference travels to touristic locations have quantifiable impact on the prescribing rational of attendees. A significant increase (three times) in the prescribing rate of two company drugs was observed after the physicians attended a company-sponsored symposium with all their expenses covered. Despite this significant difference in the prescribing patterns, physicians insisted there was no impact on their prescribing behaviour.

### Industry-paid lunches

Most physicians received invitations for dinners and free lunches. Clerks, interns and junior residents attended more company-sponsored lunches than senior residents. Pharmaceutical companies also sponsored departmental lunches during journal clubs. There was no significant association between attending industry-paid lunches and dinners and formulary request for that company’s drug (table 2).

### CME sponsorship

Physicians who attended company-sponsored CME events had more positive attitudes towards and inclination to prescribe the branded drugs. We found that physicians who refused CME sponsorship were seen to prescribe higher proportion of generics and lower expenditure medicines when compared with physicians who attended CMEs.

### Discussion

We report that there is widespread interaction between the pharmaceutical industry and physicians. Interactions are in the form of personal communications, free gifts such as drug samples, sponsored meals, sponsored conference travel, funding for research and CMEs and honoraria. The frequency of these interactions is comparable between residents and physicians. However, the amount and type of gifts vary with the position...
Table 2  Impact of physician–pharmaceutical industry interaction on physician

<table>
<thead>
<tr>
<th>#</th>
<th>Attitudes</th>
<th>Prescribing behaviour</th>
<th>Knowledge</th>
<th>Formulary requests</th>
<th>Quality of evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gifts</td>
<td>Receiving higher number of gifts associated with belief that PSR (pharmaceutical representative) have no impact on their prescribing behaviour&lt;sup&gt;14 30&lt;/sup&gt;</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Moderate</td>
</tr>
<tr>
<td>Drug samples</td>
<td>Positive attitude towards the drug industry and the representatives&lt;sup&gt;11 21 34&lt;/sup&gt;</td>
<td>Higher prescription of the company drug&lt;sup&gt;21 41&lt;/sup&gt;</td>
<td>–</td>
<td>–</td>
<td>High</td>
</tr>
<tr>
<td>Pharmaceutical representative speakers</td>
<td>–</td>
<td>Irrational prescribing&lt;sup&gt;16 18 34&lt;/sup&gt;</td>
<td>Inability to identify false claims&lt;sup&gt;16&lt;/sup&gt;</td>
<td>Increased prescription of sponsor’s drug&lt;sup&gt;36&lt;/sup&gt;</td>
<td>High</td>
</tr>
<tr>
<td>Honoraria and research funding</td>
<td>Positive attitude towards sponsor’s drug&lt;sup&gt;50&lt;/sup&gt;</td>
<td>–</td>
<td>–</td>
<td>Increased prescription of sponsor’s drug&lt;sup&gt;36&lt;/sup&gt;</td>
<td>Low</td>
</tr>
<tr>
<td>Conference travel</td>
<td>–</td>
<td>Significant increase in prescribing of sponsor drug&lt;sup&gt;18&lt;/sup&gt;</td>
<td>–</td>
<td>Increased prescription of sponsor’s drug&lt;sup&gt;36&lt;/sup&gt;</td>
<td>Low</td>
</tr>
<tr>
<td>Industry-paid lunches</td>
<td>Positive attitude towards sponsor’s drug&lt;sup&gt;14 34&lt;/sup&gt;</td>
<td>Significant increase in prescribing of sponsor drug&lt;sup&gt;12&lt;/sup&gt;</td>
<td>–</td>
<td>Increased formulary request for company drug&lt;sup&gt;1 21&lt;/sup&gt;</td>
<td>High</td>
</tr>
<tr>
<td>CME sponsorship</td>
<td>Positive attitude towards sponsor’s drug&lt;sup&gt;3 4 5 6&lt;/sup&gt;</td>
<td>Avoidance of industry-sponsored CME associated with more rational prescribing habits&lt;sup&gt;23&lt;/sup&gt;</td>
<td>–</td>
<td></td>
<td>Moderate</td>
</tr>
<tr>
<td>Interaction with PSR</td>
<td>Positive attitude towards PSR drugs&lt;sup&gt;1 1 1 4 6 8&lt;/sup&gt;</td>
<td>Higher prescription of the company drug&lt;sup&gt;24&lt;/sup&gt;</td>
<td>Positive correlation between the physicians’ prescribing cost and the information provided by the drug representative during the interaction&lt;sup&gt;36&lt;/sup&gt;</td>
<td>Increased prescription of sponsor’s drug&lt;sup&gt;39&lt;/sup&gt;</td>
<td>High</td>
</tr>
</tbody>
</table>

However, there was a significant association between attending industry-paid lunches and increased prescription of branded drugs.<sup>52 63 72</sup>
of the physician in medical hierarchy, specialisation and location of practice. In general, trainees (residents and interns) are treated with more drug samples, stationery items and free meals than senior physicians. Senior physicians usually avail of sponsored conferences/trips, research funding, honoraria and CME events. The extent of these interactions varies with academic versus non-academic institutions: non-academic hospitals record more interactions than others. The majority of the physicians do not believe that they are affected by PSR interactions. However, a sizeable percentage in various surveys responded in the affirmative when asked whether they thought that their peers are vulnerable.

Future implications

Pharmaceutical industry and PSR interactions compromise the objectivity of the physicians. Educating physicians and increasing regulation of pharmaceutical industry and PSR interactions may lower the likelihood of prescribing non-superior industry drugs and irrational prescription behaviour. Further studies are required to evaluate the impact of pharmaceutical industry and PSR interactions on physicians over time and the benefits of various intervention-based education programmes on the clinical and ethical behaviour of the physicians.

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Data sharing statement Any data relevant to a published article will be made available alongside the article when published.

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Policies and educational intervention

The relationship of physicians with patients is of a fiduciary nature. Hence, activities that might affect that relationship by altering physicians’ clinical behaviour are not acceptable. Physician–pharmaceutical industry and PSR interactions may put the trust of patients in physicians at risk. Interaction with pharmaceutical industry and PSRs begins early in the physicians’ career. Trainees are exposed to pharmaceutical industry marketing and promotional techniques from the initial years of their medical education, which impact their prescribing behaviour in future. Overall, trainees, that is, residents and interns, are more vulnerable to pharmaceutical industry and PSR interactions than senior physicians. Physicians are susceptible to pharmaceutical industry and PSR interactions, which influences their clinical decision making leading to greater prescriptions of branded drugs over low-cost generic medicines and increasing healthcare costs. Therefore, there is need to institute and implement stringent policies curtailing physician-pharmaceutical industry and PSR relationships, as well as educational programmes to increase awareness. Previous reports have indicated that implementing policies and conducting educational programmes are effective in increasing awareness of physician’s attitudes towards pharmaceutical industry and PSR interactions.

Strengths and limitations of the study

A major strength of this study is that it is a large, up-to-date systematic review of studies exploring the effects of physician and pharmaceutical industry representative interactions and residents in different settings (eg, academic and primary care). Another strength of this study is the use of Cochrane and GRADE methodologies for conducting a review and assessing the quality of the studies. Moreover, we performed an extensive search in three databases and the grey literature. Some of the limitations of this review are related to the included studies, as some did not provide evidence for the significance of their findings or had varying study designs and outcomes, which made it impossible to conduct a meta-analysis. Also, the included studies were subject to risk of bias related to the lack of validity of outcome measurement and inadequate handling of significant potential confounders.


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