Interactions between physicians and the pharmaceutical industry: What does the literature say?

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Objective: To determine the effect of three types of interaction between physicians and the pharmaceutical industry — company-funded clinical trials, company-sponsored continuing medical education (CME) and information for physicians supplied by pharmaceutical detailers — on orientation and quality of clinical trials, content of CME courses and physicians' prescribing behaviour.


Study selection: A total of 227 papers from the MEDLINE and HEALTH searches and about 2000 items from the author's library were initially reviewed. The following selection criteria were used: studies conducted in Australia, Canada, New Zealand, Britain and the United States; studies conducted after 1977; quantitative surveys containing details of the survey methods; studies on the orientation and quality of company-funded clinical trials and on the content of CME courses giving explicit criteria used in the evaluation; and reports on the outcome of interactions stating how the outcomes were assessed. Thirty-six studies met these criteria.

Data extraction: Information was extracted on five topics: physicians' attitudes toward drug industry interactions, frequency with which physicians participate in the interactions, orientation and quality of company-funded clinical trials, content of company-sponsored CME courses and changes in physicians' prescribing behaviour as a result of an interaction.

Data synthesis: Although most physicians participate only occasionally in company-sponsored clinical trials, most see detailers and attend company-sponsored CME courses. However, physicians do not have a very high opinion of the information from detailers or of company-sponsored CME events. Many doctors regard pharmaceutical companies as an important source of funding for clinical trials, but they also have concerns about accepting money from this source. Company funding of clinical trials may affect the quality of the trials and the types of research that physicians undertake. Company-sponsored CME courses may have a commercial bias even if conducted under guidelines designed to ensure the independence of the event. All three types of interactions affect physicians' prescribing behaviour and, in the case of obtaining information from detailers, physicians' prescribing practices are less appropriate as a result of the interaction.

Conclusions: Physicians are affected by their interactions with the pharmaceutical industry. Further research needs to be done in most cases to determine whether such interactions lead to more or less appropriate prescribing practices. The CMA's guidelines on this topic should be evaluated to see whether they are effective in controlling physician-industry interactions. Further measures may be necessary if the guidelines fail to prevent negative effects on prescribing practices.
**Objectif** : Déterminer l’effet sur l’orientation et la qualité des essais cliniques, le contenu des cours de formation médicale continue (FMC) et le comportement des médecins lorsqu’ils prescrivent de trois types d’interaction entre les médecins et l’industrie pharmaceutique — essais cliniques financés par les sociétés pharmaceutiques, FMC financée par les sociétés et renseignements aux médecins par les délégués à l’information médicale des sociétés pharmaceutiques.

**Sources de données** : Recherche d’articles publiés en anglais de 1978 à 1993 dans MEDLINE et HEALTH, complétée par des documents provenant de la collection personnelle de l’auteur.

**Sélection d’études** : Pour commencer, on a examiné au total 227 articles provenant des recherches effectuées dans MEDLINE et HEALTH et environ 2 000 documents provenant de la bibliothèque de l’auteur. Les critères de sélection suivants ont été utilisés : études menées en Australie, au Canada, en Nouvelle-Zélande, en Grande-Bretagne ou aux États-Unis ; études menées après 1977 ; enquêtes quantitatives détaillant les méthodes d’enquête ; études sur l’orientation et la qualité des essais cliniques financés par les sociétés et sur le contenu des cours de FMC ; utilisant des critères explicites pour évaluer les résultats. Rapports sur les conséquences des interactions spécifiant comment on a évalué ces conséquences. Trente-six études satisfaisaient à ces critères.

**Extraction de données** : Les renseignements extrait touchent cinq sujets : les attitudes des médecins envers les interactions avec l’industrie pharmaceutique, la fréquence de leur participation à ces interactions, l’orientation et la qualité des essais cliniques financés par les sociétés, le contenu des cours de FMC financés par les sociétés et les changements de comportement des médecins lorsqu’ils prescrivent suite à une interaction.

**Synthèse des données** : Bien que la plupart des médecins ne participent qu’à l’occasion aux essais cliniques financés par les sociétés, la plupart reçoivent les délégués à l’information médicale et assistent à des interactions en faveur des sociétés. Cependant, ils n’ont pas une très haute opinion de l’information provenant des délégués ou des activités de FMC financées par les sociétés. Beaucoup de médecins pensent que les sociétés pharmaceutiques comme source importante de financement pour les essais cliniques, tout en manifestant des réticences lorsqu’il s’agit d’accepter de l’argent de cette source. Le financement des essais cliniques par les sociétés peuvent affecter la qualité des essais et le type de recherche que les médecins peuvent prêter. Les cours de FMC financés par les sociétés peuvent comporter un biais commercial même s’ils sont menés en fonction de lignes directrices conçues pour garantir l’indépendance de l’activité. Les trois types d’interaction affectent le comportement des médecins lorsqu’ils prêter et, lorsqu’il s’agit d’obtenir des renseignements des délégués, les pratiques de prescription des médecins deviennent moins opportunes à la suite de l’interaction.

**Conclusions** : Les médecins sont affectés par les interactions avec l’industrie pharmaceutique. Dans la plupart des cas, il faudrait approfondir les recherches pour déterminer si des telles interactions conduisent à des pratiques de prescription plus ou moins opportunes. Il faudrait évaluer les lignes directrices de l’AMC à ce sujet pour vérifier si elles réussissent à contrôler les interactions entre les médecins et l’industrie. D’autres mesures pourraient être nécessaires si les lignes directrices ne réussissent pas à prévenir les effets négatifs sur les pratiques de prescription.

In the past few years at least four medical organizations in Canada and the United States have released discussion papers and policy statements, including guidelines for physicians, on the relationship between the medical profession and the pharmaceutical industry. The rationale is to ensure that the interactions do not lead to inappropriate prescribing behaviour.

To date, debate on the effect of interactions between physicians and pharmaceutical companies has mainly taken the form of personal observations or opinions. Although this type of debate serves to alert physicians to the issues, there has been little objective research into physician–industry interactions. The purpose of this review is to identify and summarize the literature and set forth a research agenda.

**Methods**

In this review I examined and summarized studies dealing with three types of interactions — company-funded clinical trials, company-sponsored continuing medical education (CME) and information for physicians supplied by pharmaceutical detailers — to answer the following questions:

- How frequently do physician–industry interactions take place?
- What are physicians’ attitudes toward the interactions?
• Does the source of funding affect the orientation of clinical trials or their quality?
• Does the source of funding affect the content of CME?
• Do these interactions affect doctors’ prescribing behaviour?

MEDLINE and HEALTH databases were searched for English-language articles published from 1978 to 1993 with various combinations of the following terms: clinical investigators, continuing medical education, continuing pharmaceutical education, knowledge/attitudes/practice, pharmaceutical industry, physicians’ practice patterns, prescriptions/drugs, promotion and research support. Articles identified were scanned for references and potentially relevant papers retrieved, in some instances through direct communication with the author or authors. The articles found through the computer searches were supplemented by a manual search of my personal holdings.

A total of 227 papers from the MEDLINE and HEALTH searches and about 2000 items from my library were initially reviewed. The following selection criteria were used:

• Canadian studies or those undertaken in countries with medical systems roughly similar to Canada’s — Australia, New Zealand, Britain and the United States.
• Studies conducted after 1977.
• Quantitative surveys documenting the frequency of interactions and physicians’ attitudes toward them and containing details of the survey methods.
• Studies on the orientation and quality of company-funded clinical trials and the content of CME giving explicit criteria used in the evaluation.
• Reports on the outcome of interactions that state how the outcomes were assessed.

Results

A total of 36 studies fit the criteria: 24 dealt with physicians’ attitudes toward the interactions, 12 with the frequency of the interactions, 4 with the quality or content of the interaction and 7 with the outcome of the interaction. (Some studies reported on more than one topic.)

Frequency of physician–industry interactions

Participation in industry-funded clinical trials does not appear to be widespread. A survey of 842 randomly selected Ontario physicians found that they had, on average, participated in company-sponsored drug trials about once in the previous 2 years.15 These same doctors had attended, on average, 5.2 drug-company-sponsored symposia in the previous 2 years, as compared with 1.9 CME courses.15 Seventy-six percent of general practitioners in Wales had attended company-funded CME courses in the previous year.16

About 85% to 90% of doctors in Canada,15,17 New Zealand,18 Britain19 and the United States20 see pharmaceutical detailers. On average, Canadian15 and US19 doctors are visited about once every 2 weeks. Canadian22 and British19 general practitioners ranked detailers as either the first or second most frequently used information source in recent surveys. (Specialists in Canada22 and Australia20 reported less frequent use of detailers.)

Physicians’ attitudes toward interactions

Physicians who undertake clinical trials regard the drug industry as an important source of funding. In the United States over half of the membership of the Infectious Disease Society of America who were engaged in chemotherapeutic studies felt that industry support was necessary for their research.25 Although nearly all investigators into antianginal therapy performed their trials because of interest in the topic, only 45% would have conducted their trials without funding from the pharmaceutical industry.26

A recent survey of 40 Canadian “key informants” (e.g., deans of medical schools, researchers from CME departments and clinical investigators) showed that nearly all were grateful for the clinical research funding provided by industry.7 At the same time, 90% saw a likely conflict of interest, 65% said that there was a potential for undermining standards, and 40% were worried about a potential delay in publication of unfavourable results.

In general, physicians ranked company-sponsored CME lower than objective sources, such as journal articles, as sources of credible prescribing information.22,28,29 Forty-one percent of Ontario doctors said that company-sponsored seminars were not an important source of information about drugs, as opposed to 25% who said that they were.19 In Wales 63% of general practitioners said that they found educational events organized by companies to be of little or no value.16

Detailers were rated as less influential and less credible than journals, colleagues and scientific meetings.15,22-24,28-40 In two other studies, most doctors said that they received little value from detailers’ visits.16,41 These rankings are influenced by how much risk doctors attach to the use of a particular drug,30 whether physicians are “early” or “late” prescribers of a new medication42 and whether physicians are generalists or specialists.24,38,39

Effect of source of funding on orientation or quality of clinical trials

Waller and associates43 looked at company-sponsored postmarketing surveillance studies undertaken in Britain since 1987, when voluntary guidelines for the conduct of these studies were introduced.44 Of 31 studies only 9 were controlled, 5 achieved at least 75% of the projected sample size, and 11 were abandoned because
of recruitment problems. The authors did not attribute the weak study designs to industry funding.

Davidson\(^6\) reviewed all 107 clinical trials that included a concurrent or cross-over control group and that were published in 1984 in one of the following journals: *New England Journal of Medicine*, *Annals of Internal Medicine*, *American Journal of Medicine*, *Archives of Internal Medicine* and *Lancet*. Of the studies 71% favoured new therapies; 43% of them were funded by pharmaceutical firms. Of the 31 trials favouring traditional therapy, only 4 (13%) were supported by a pharmaceutical firm. There was a statistically significant association between the source of funding and the outcome of the study. The author offered three nonmutually exclusive hypotheses to explain his results: industry selects drugs likely to prove efficacious, study results are flawed because of type II errors (sample not large enough) and researchers fear discontinuation of funding should studies show that the drug being investigated is no better than, or inferior to, traditional therapy.

Dieppe, Frankel and Toth\(^6\) identified 151 clinical trials on osteoarthritis therapy published between 1985 and 1992: 148 compared one nonsteroidal anti-inflammatory drug (NSAID) with another. 1 compared acetaminophen with placebo and the remaining 2 compared an NSAID with a pure analgesic drug. The authors of this review felt that one of the main reasons for the paucity of studies comparing analgesics with NSAIDs is the vested interests of the pharmaceutical industry.

### Effect of source of funding on content of CME

Bowman\(^4\) analysed the content of CME events in relation to their source of funding. She looked at two courses on calcium channel blockers funded by different drug companies. Both courses were given at a university that had policy guidelines on CME, although these had not been approved at the time of the first course. These guidelines required the course content to be controlled by the institution, generic drug names to be used during the course and alternate therapies to be appropriately identified and addressed. Despite these requirements Bowman reported a bias in favour of the sponsoring company’s drug in both courses, although the nature of the bias differed. In the second course the sponsoring company’s drug was mentioned much more often than either of two competing drugs. For both courses, positive clinical effects were attributed to the sponsoring company’s drug more often than to other drugs. In the first course clinical effects attributed to competing drugs were more likely to be negative.

### Effect of interactions on doctors’ prescribing behaviour

Results of several studies suggest that the source of funding affects decision-making by recipients. Research support from pharmaceutical companies was an independent predictor of requests for formulary additions from internal medicine faculty members at seven midwest US teaching hospitals.\(^2\) Another study compared physicians who requested formulary additions with a random sample of other staff doctors.\(^4\) All physicians were surveyed about their interactions with drug companies over the previous year. Of those who requested additions 19% had received research funding or honoraria from the company making the drug in question, as compared with only 3% of physicians not making such requests.

Bowman and Pearle\(^4\) investigated the effects of company-funded CME on subsequent prescribing behaviour. Physicians were surveyed before and 6 months after their attendance at three separate CME events conducted under the guidelines outlined in the previous section. In each case there was a greater increase in prescriptions for the drug made by the sponsoring company than for other drugs in the same class.

The acceptance of “all-expenses-paid” trips to attend symposia sponsored by pharmaceutical companies can also influence physicians’ prescribing behaviour.\(^5\) Of 20 physicians interviewed before they went to conferences none felt that their prescribing behaviour would be affected. However, after the conferences the physicians demonstrated a significant increase in prescribing the drugs that had been the subjects of the symposia.

There is little doubt that detailers are effective in changing physicians’ prescribing behaviour. In one study 25% of internal medicine faculty members and 32% of residents reported that they had changed their practice at least once in the preceding year based on a discussion with a detailer.\(^2\) In another study the more contact that Australian doctors had with detailers promoting temazepam the more quickly they began prescribing that drug and the more rapidly it became their hypnotic drug of choice.\(^3\) Physicians who requested formulary additions were much more likely than other doctors in the same hospital to have seen detailers from the manufacturers of the drugs in question.\(^3\)

Although these studies did not comment on the appropriateness of the changes in prescribing, others suggested that physicians’ use of detailers leads to inappropriate prescribing behaviour. Family physicians most likely to prescribe generic drugs were the ones who relied least on detailers as a source of information on new drugs.\(^3\)

Greenwood\(^4\) surveyed 332 general practitioners in one area in England about the use of certain medications in therapeutic contexts in which medical and commercial opinion conflict. He concluded that detailers may have a significant effect on physicians’ attitudes. In the case of one product, some 77% of physicians favoured the commercial view of a product rather than the scientific view; the commercial views of three other products were favoured by 55%, 28% and 13% of doctors.
Discussion and conclusion

Although most physicians participate in company-sponsored clinical trials only occasionally, the majority of doctors see detailers and attend company-sponsored CME courses. However, physicians do not have a very high opinion of the information that they receive from either of these sources. Although many doctors regard company funding for clinical trials as important the survey of 40 key Canadian informants\(^3\) suggests that they also have concerns about accepting money from this source. Since this survey used a convenience sample the results may not be applicable to Canadian researchers in general.

The orientation and quality of clinical trials may be adversely affected by the source of funding, but this conclusion is tentative. Waller and associates\(^4\) did not state whether the postmarketing trials they evaluated were conducted by the companies involved or by independent researchers. Davidson's findings\(^5\) on the outcome of comparative clinical trials are subject to a number of interpretations. Similarly, there is no objective evidence to support the assertion of Dieppe, Frankel and Toth\(^6\) that the interests of the pharmaceutical industry have resulted in a bias in comparative NSAID studies.

Company-sponsored CME courses, even those conducted under guidelines designed to eliminate bias, may favour the company providing the funding, but only one study has addressed this issue.\(^7\)

Finally, there is strong evidence that all three types of interaction considered here influence the prescribing behaviour of physicians. The direction of that influence on company funding of clinical trials and CME is uncertain. Lurie and colleagues\(^8\) and Chen and Landefeld\(^9\) studied requests for formulary additions and found that they correlated with the receipt of research funding; however, these studies did not assess the appropriateness of the requested addition.

Bowman and Pearle's study on the effects of attendance at company-sponsored CME\(^10\) did not include a control group of physicians, so it is unclear whether the authors' results reflect the influence of the courses or other factors. Without knowing the context in which the drugs were prescribed one cannot say whether the increased prescribing was appropriate. Although Orlowski and Wateska\(^11\) felt that the prescribing behaviour of the physicians who attended the all-expenses-paid trips was adversely affected, they did not directly assess prescribing practices after attendance.

The evidence is stronger that interactions between detailers and physicians lead to less appropriate prescribing behaviour. Greenwood's finding that interactions with detailers can lead doctors to adopt commercial views about drugs\(^12\) echoes conclusions reached by Avorn, Chen and Hartley\(^13\) a decade earlier.

The main limitation of this review is that an unknown volume of relevant literature may have been overlooked. Material in many sociology or business publications is not included in the MEDLINE and HEALTH databases, and some surveys conducted for private clients are not available or cannot be identified through standard search procedures. The available literature on company-sponsored CME and on detailers was fairly consistent. However, in assessing the orientation and quality of clinical trials, the content of CME courses and the effects of both of these types of interaction on prescribing behaviour, there was only a small volume of material. Additional studies would have been useful.

Future research in this field could explore a number of issues. Attitudinal surveys of clinical researchers would help to determine to what extent industry funding determines the research agenda. A register of clinical trials and their funding sources would help to distinguish among the possible explanations for Davidson's findings of a statistically significant association between source of funding and clinical trial outcome.\(^14\) Funding sources for trials that are discontinued or unpublished could be identified and analysed. To determine whether pharmaceutical company funding introduces bias in clinical trials or the attendance at CME courses, prospective controlled studies and evaluations of resulting changes in prescribing patterns are needed.

The adequacy of the CMA guidelines also requires further study. Bowman's finding of a bias in the content of CME courses\(^15\) is disturbing since the courses she monitored were operating under guidelines similar to those recommended by the CMA.\(^4\) If further studies confirm Bowman's work, then guidelines may not be enough to prevent bias in this area. In addition, there is convincing evidence that physicians' prescribing behaviour is negatively affected by physician-detailer interactions; however, the current version of the CMA guidelines does not mention detailers. The guidelines state that "the industry should not pay for travel or lodging costs or for other personal expenses of physicians attending a CME event."\(^16\) Some CMA members had suggested altering this prohibition,\(^16\) but General Council defeated a recent motion to water down the guideline.\(^15\)

Further, dissemination of the guidelines through publication in CMAJ may not be sufficient to change physicians' practices, as experiences with guidelines in other areas have shown.\(^17\) An evaluation of the guidelines is needed. Physicians could be surveyed about their awareness of the guidelines and their contents. CME events could be monitored to determine how closely they comply with the guidelines. Studies could be conducted before and after revisions to the guidelines to see whether their effectiveness was altered. In some locations the guidelines could be actively promoted through seminars and public forums to see whether awareness and effectiveness are improved.

The results of the research I am proposing will help to determine whether any further measures need to be taken in dealing with physician–industry interactions. In
the past, individual medical schools have instituted courses on evaluating drug company promotion.55-58 Such an approach could also be tried at the postgraduate level. Other initiatives are already under way. The internal medicine residency training program at McMaster University, Hamilton, Ont., has adopted guidelines that require detailers to submit educational materials to the clinical teaching unit directors, that prohibit residents from receiving nondonedural benefits (including “drug lunches”) and that exclude detailers from residency educational events.59 The US Food and Drug Administration is looking at ways to ensure that the providers of CME will be solely responsible for the conduct of the programs, through a mandatory written agreement between meeting sponsors and providers and through monitoring by major accrediting organizations such as the Accreditation Council for Continuing Medical Education.60 All of these actions should be critically evaluated to see whether they produce the desired results.

The existing studies show that despite doctors’ negative attitudes toward physician–industry interactions they readily participate in them and are being influenced by them. Still unclear, in most cases, is the direction of that influence. I hope that the research I am proposing will help to resolve that question. If physician–industry interactions are shown to lead to inappropriate prescribing behaviour, then the issue becomes whether guidelines are a sufficient solution to the problem. If they are not, other measures will be necessary.

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Apr. 18–21, 1994: T-Cell Receptor Use in Human Autoimmune Diseases (cosponsored by the Arthritis Foundation)
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