

Drug promotion

what we know, what we have yet to learn

**Reviews of materials in the WHO/HAI
database on drug promotion**

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Contents

Executive summary	vii
Introduction	1
Background to the project	2
Development of the drug promotion database	3
Database entries	4
Potential data users.....	4
Reviews of database material.....	5
Methodology.....	6
Review 1. What attitudes do professional and lay people have to promotion?..	7
1.1 Attitudes do not necessarily match behaviour	7
1.2 Studies of the prevalence of different attitudes to promotion (excluding direct-to-consumer advertising)	8
1.3 Do trainers and trainees think that sales representatives should be banned during medical training?	9
1.4 Do doctors think they have enough training to deal with sales representatives?..	9
1.5 Do doctors think that sales representatives have a valuable role in medical education?	9
1.6 What do health professionals think about the quality of the information provided by sales representatives and advertisements about drugs?	10
1.7 What do other groups of people think of promotional information?	12
1.8 What are doctors' views of pharmaceutical company support of conferences and speakers?.....	12
1.9 Do trainee doctors plan to see sales representatives in their future practice?	12
1.10 What are professionals' and patients' attitudes to the appropriateness of gifts?.	13
1.11 Do health professionals feel that discussions with sales representatives affect prescribing?.....	14
1.12 Do people feel that accepting gifts influences prescribing?	15
1.13 Ethics and promotion.....	16
1.14 Attitudes to direct-to-consumer advertising of prescription drugs.....	17
1.15 Studies of differences in attitudes to promotion (excluding DTCA)	20
Summary of conclusions	22
Directions for future research	23
Review 2. What impact does pharmaceutical promotion have on attitudes and knowledge?	25
2.1 Reported use of promotion as a source of drug information.....	26
2.2 Reported use of promotion as a source of information in adopting new medicines	27
2.3 Impact of promotion on self-reported attitudes and knowledge	28
2.4 Research designs that aim to avoid the limitations of self-report data	30
Summary of conclusions.....	31
Directions for future research.....	32

Review 3. What impact does pharmaceutical promotion have on behaviour? .	33
3.1 Impact of promotion on individual prescribing practices.....	33
3.2 Self-reported reasons for prescribing changes.....	34
3.3 Prescribing by those who rely on commercial information	36
3.4 Prescribing and exposure to promotion	38
3.5 Exploring the impact of samples on prescribing	41
Summary	41
3.6 Impact of promotion on overall sales.....	42
3.7 Impact of promotion and industry funding on requests for formulary additions	45
3.8 DTCA and consumers' decisions.....	46
3.9 Impact of sponsorship on content of continuing medical education courses.....	48
3.10 Impact of industry funding on research	48
3.11 Does funding affect the research agenda?	54
3.12 Do authors reveal funding sources?.....	54
Summary of conclusions.....	54
Review 4. What interventions have been tried to counter promotional activities, and with what results?.....	57
4.1 Guidelines, codes and regulations for printed and broadcast material	57
4.2 The 'Fair balance' requirement	61
4.3 Guidelines for sales representatives.....	62
4.4 Guidelines for post-marketing surveillance	63
4.5 Guidelines on conflict of interest in research	64
4.6 Guidelines for package inserts and compendia.....	64
4.7 Guidelines about gifts	65
4.8 Guidelines for trainee doctors and for hospitals	66
4.9 Knowledge of these guidelines and their effect on attitudes.....	67
4.10 Education about promotion.....	68
4.11 Monitoring/countering promotion.....	70
4.12 Research as an intervention.....	71
Summary of conclusions.....	72
Directions for future research.....	73
Final conclusions.....	73
References.....	75

Executive summary

Pharmaceutical manufacturers spend vast sums of money on promotion, including sales representatives, samples, advertisements in broadcast and print media, and sponsorship of educational events and conferences. In the USA alone, almost US\$21 billion was spent on promotion in 2002. In developing countries sales representatives are frequently the only source of drug information.

This report is part of a project on drug promotion being carried out by WHO and HAI Europe. This stage of the project involved collecting and analysing existing information on promotion. A database (<http://www.drugpromo.info>) including over 2700 journal articles, books and other material has been developed. Research studies from the database were analysed and these form the basis of this report.

What attitudes do professional and lay people have to promotion?

Research suggests that doctors' attitudes to promotion vary, and do not necessarily match their behaviour. Their opinions differ on the value of sales representatives, on whether they should be banned during medical training, and on whether doctors are adequately trained to interact with them. Most doctors think information from pharmaceutical companies is biased, but many think it is useful. Health professionals find small gifts from drug companies acceptable. Doctors who report relying on promotion tend to be older, and more likely to be general practitioners. Opinions about direct-to-consumer advertising of prescription medicines (DTCA) are mixed. Most companies, the advertising industry and the media favour it, while doctors generally oppose it. Consumers and patients are divided on the issue.

Studies on people's attitudes to promotion rely too much on quantitative surveys, on the use of convenient, accessible samples, and on describing the prevalence of attitudes rather than relationships between attitudes and other characteristics. Qualitative studies are needed in this area.

What impact does pharmaceutical promotion have on attitudes and knowledge?

Doctors themselves report that they often use promotion as a source of information about new drugs. Doctors in private practice, or who graduated long ago report the highest use of promotion as a source of drug information. Promotion influences attitudes more than doctors realise.

There is no research in the database on the impact of promotion on the attitudes of other groups, such as consumers, pharmacists, nurses or drug-store staff, all of whom are important decision-makers about medicines. Such research would be useful for developing interventions for these groups.

What impact does pharmaceutical promotion have on behaviour?

This is the most important and most difficult area to research. People may not be aware how much promotion influences them, and/or they may be unwilling to report this.

Research clearly shows that doctors who report relying more on promotion tend to prescribe less appropriately, prescribe more often and adopt new drugs more quickly. Samples appear to influence prescribing, but more research is needed on this issue. Studies which look at the impact of promotion on overall sales usually show increased sales after promotional activities. Pharmaceutical funding for doctors, such as research funding, increases request for medicines made by these companies to be added to hospital formularies. DTCA is associated with increased requests from patients for advertised medicines. Sponsorship may affect the content of continuing medical education.

The pharmaceutical industry has become a much more significant source of funding for academic research. Industry funding tends to be associated with influence over the choice of topic, secrecy, delayed publication and conflicts of interest. Pharmaceutical company funded research is more likely to show results favourable to the product being studied than research funded from other sources.

More research is needed on the public health consequences of drug promotion. For example, this might explore causal relationships between promotion and prescribing of drugs which have little or no place in rational prescribing, or which have serious adverse consequences when over-prescribed, such as antibiotics. More research is needed on the effect of promotion in developing countries.

What interventions have been tried to counter promotional activities, and with what results?

This report does not describe the whole range of interventions that have been used, only those which have been the subject of evaluative research.

Many studies show that printed advertisements do not meet regulations and guidelines in force in various countries. Neither self-regulatory systems nor review by journal editors provide effective control on drug advertising. Studies of promotion by drug company representatives suggest that the guidelines and regulations that should control them are ineffective. The only reported regulatory system for post-marketing surveillance that has been studied has not been successful. Many organizations lack adequate policies for dealing with conflicts of interest. Guidelines for regulating contacts between companies and medical

trainees vary greatly between institutions. There is conflicting evidence about whether these affect the attitudes of trainee doctors, and if so whether these effects persist over time. Education about promotion appears to change attitudes and can improve skills. Its impact on prescribing has not yet been tested. Publication of descriptions of deceptive promotion can lead manufacturers to improve their promotional practices.

Interventions need to be designed using the current evidence base about drug promotion, and these need to be evaluated and published. Research comparing the effect of different regulatory frameworks is urgently needed.

Conclusions

There is a wide range of evidence on different topics, using a range of different designs, suggesting that promotion affects attitudes and behaviour. However there are gaps in the evidence, and more high-quality studies are needed to establish causal relationships between promotion and attitudes and behaviour of doctors and others, to provide more nuanced information about people's attitudes to promotion, and to investigate the impact of interventions to regulate or counter the effect of promotion.

Introduction

It is increasingly important to understand the effects that drug promotion has on prescribing and the use of medication given the growing amounts of money companies are devoting to this activity. In 2002, almost US\$21 billion was spent on promotion in the USA, including over US\$2.6 billion on direct-to-consumer advertising (DCTA)ⁱ. These amounts are at least 30 times what national governments spend on drug information (for example, in Italy: US\$4475/doctor by the pharmaceutical industry versus US\$180/doctor by the government)ⁱⁱ. In Canada in 2000 there were over 3.4 million visits by sales representatives to doctors, leaving behind 21.5 million drug samplesⁱⁱⁱ and in the USA companies organized over 300 000 events for doctors^{iv}. Sales representatives are frequently the only source of information about medicines in developing countries where there may be as many as one representative for every five doctors^v.

Attempts to control promotion have largely relied on a combination of voluntary codes adopted by industry associations and medical organizations. On the surface, voluntary self-regulatory codes from the pharmaceutical industry may look like a sensible approach to controlling the promotional activities of companies; lacking government-industry adversariness, they have the potential to be a more flexible and cost-effective option. In a highly competitive industry, the desire of individual companies to prevent competitors from gaining an edge could be harnessed to serve the public interest through a regime of voluntary self-regulation run by a trade association. However, like many theories this one proves to be unsupported by the evidence. The mission of trade associations, such as Pharmaceutical Research and Manufacturers of America (PhRMA), is primarily to increase sales and profit. From the business perspective, self-regulation is mostly concerned with the control of anti-competitive practices. Therefore, when industrial associations draw up their codes of practice they deliberately make them vague or do not cover certain features of promotion to allow companies a wide latitude. Many misleading advertising tactics are good for business. As a result voluntary codes tend to be reactive, they lack transparency, they omit large areas of concern, and they lack effective sanctions.

ⁱ Canadian Medical Association Journal 2003;169:699.

ⁱⁱ Centro Studi Farindustria, Indicatori farmaceutici, Farindustria, Rome, 1998, p. 186.

ⁱⁱⁱ CBC Disclosure, Targeting doctors. Graph: top 50 drugs by total promotional dollars. Available at: www.cbc.ca/disclosure/archives/0103_pharm/resources.html

^{iv} Scott-Levin. Rx's and RSVP's: pharmaceutical companies holding more physician meetings and events. July 9, 2001. Available at: http://www.quintiles.com/products_and_services/informatics/scott_levin/press_releases/press_release/1,1254,244,00.html.

^v Lexchin J. Deception by design: pharmaceutical promotion in the third world. Penang: Consumers International, 1995.

Codes from medical associations may have stronger provisions but they are unenforceable and rely on moral suasion for their power. In the few countries where promotion is directly controlled by government, resource limitations mean that only a small fraction of activities can be monitored^{vi}.

If promotion leads to better prescribing, more rational use of medications or improved cost-effectiveness then there would be no concern. While the evidence is not conclusive, what there is all points in the direction of a strong association between reliance on promotion and less appropriate overall use of prescription drugs^{vii}. Heavy promotion of new drugs leads to widespread prescribing and use before the safety profile of these products is fully understood. Newer, more expensive medicines displace older, less costly ones without any evidence of an improvement in therapeutic outcomes^{viii}.

Background to the project

The impetus for a major project on pharmaceutical promotion originated at the May 1999 meeting of the WHO/Public-Interest Nongovernmental Organizations Roundtable on Pharmaceuticals. Unethical and inappropriate drug promotion has been a continuing concern of both NGOs and the WHO. At the 1997 Roundtable on WHO's Ethical Criteria for Medicinal Drug Promotion there was firm agreement that inappropriate promotion of medicinal drugs remains a problem both in developing and developed countries.

Although there is an abundance of information about drug promotion it had never been fully documented and as such organizations, governments, individuals and others were restricted in their ability to access the breadth of knowledge that had been accumulated, to analyse it, to learn from it and to expand on it. Therefore, the first phase of the promotion project was to collect, analyse and make publicly accessible as wide a range of material as possible that described, analysed, reported or commented on any aspect of pharmaceutical promotion.

This drug promotion project is a collaboration between the WHO Department of Essential Drugs and Medicines Policy (EDM) and Health Action International (HAI) Europe.

^{vi} Lexchin J, Kawachi I. Voluntary codes of pharmaceutical marketing: controlling promotion or licensing deception. In: Davis P ed. *Contested ground: public purpose and private interest in the regulation of prescription drugs*. New York: Oxford University Press, 1996:221-235.

^{vii} Wazana A. Physicians and the pharmaceutical industry: is a gift ever just a gift? *JAMA* 2000;283:373-380.

^{viii} Lexchin J. Should doctors prescribe new drugs? *International Journal of Risk and Safety in Medicine* 2002;15:213-22.

Development of the drug promotion database

In October 2002 the drug promotion web site was freely accessible online at <http://www.drugpromo.info>. The main feature, the database of drug promotion material, currently contains approximately 2700 entries.

For this project, promotion was broadly defined using the WHO definition: “all informational and persuasive activities by manufacturers, the effect of which is to induce the prescription, supply, purchase and/or use of medicinal drugs.” Material on promotion was sought from books, journal articles, magazine and newspaper stories, articles from drug bulletins/newsletters, videos, radio and television transcripts, and guidelines from organizations and professional bodies.

Material for inclusion in the database was identified primarily from a MEDLINE search going back to 1 January 1970. Dr Joel Lexchin, a drug promotion expert from Toronto, was the principal investigator and compiled the entries. Melissa Raven, a public health specialist from Flinders University, South Australia, has been updating the database since mid-2002.

Additional material was found by scanning the list of references in the items found through the MEDLINE search, through contacts in the E-Drug discussion group and from other experts in drug promotion. Material was only included if it was currently possible to obtain the item and was excluded if it came from sources such as unpublished articles where there was no contact address available, or articles from magazines that had gone out of production, etc. All material that fitted these criteria was included regardless of who produced it, i.e., government, industry, NGOs, etc. Note - advertisements for drugs were not included unless there was a commentary on the advertisement, either positive or negative. Only material in English has been included but there are plans to expand the database to cover material in French and German.

While WHO and HAI believe the present database is a valuable resource on what is known about drug promotion, it needs to evolve with use and experience. We welcome comments by users. We also need to broaden involvement, for example, through pharmaceutical companies providing their research on the influence of drug promotion (currently not usually accessible outside of the company). That way, the database would give a more complete picture of what is known and not known about drug promotion.

Database entries

Depending on the source of the material, each entry has been catalogued in some or all of the following fields:

- Author
- Title
- Source (address, e-mail address etc of group/organization producing the material)
- Web site addresses where available, including sites where journal articles that are available online can be obtained
- Abstract
- Keywords
- Date material produced (for journal entries complete identifying data e.g. year, journal volume and page numbers).

Entries on studies that generated new data and/or reported specific methodological designs include notes on strengths or potential weaknesses in how the study was carried out and the limitation in the generalizability of the results.

Entry content is described in two ways: through keywords and also by putting each entry into one or more 'groups'. These groups are an additional method of broadly describing the main topics covered by the entry. A step-by-step demonstration of searching the database is included on the web site to assist users.

Potential data users

- **Health professionals**
Doctors, pharmacists and other health care workers will be able to see what promotional techniques the pharmaceutical industry uses, and how promotion influences the choice of drugs and the appropriateness of prescribing.
- **Health professional associations**
These groups can use the database to see what guidelines other groups have adopted for interaction between health professionals and the pharmaceutical industry to help them formulate policies.

- **Governments and other regulatory bodies**
The database will enable regulators to see what methods have been tried to control promotion and their successes and failures.
- **Academic researchers**
The database enables researchers to see which promotional issues have been investigated, the methodology others have used and what areas are priorities for further research. In addition, they can look at trends in promotion over a 30-year period.
- **Educators**
The database will be a valuable source of information for those who teach medical and pharmacy students, nurses and other health science students about the influence of drug promotion.
- **Consumer organizations**
These groups can use the database to help them lobby for effective control over pharmaceutical promotion and to help educate consumers and patients about the influence that promotion has over the choices that health professionals make. They can also use the material to become better acquainted with emerging issues.
- **Pharmaceutical industry**
Pharmaceutical companies will be able to see what criticisms have been made about their promotion in order to help them develop better internal controls. The database will also help pharmaceutical industry associations to strengthen their voluntary codes.
- **Public and private sector payers, and providers of development aid.**
These groups can see how promotion affects drug use and, therefore, drug costs.

Reviews of database material

As part of the project, four reviews were produced based on some of the database material. These reviews were written to provide an overview of what is and is not known in four key areas:

Review 1. *What attitudes do people (professional and lay) have to promotion?*

Issues covered include attitudes to pharmaceutical company sales representatives, gifts and sponsorship of conferences. Attitudes of doctors, consumers and others to direct-to-consumer drug advertising are also reviewed. In addition, there are reviews of differences in doctors' attitudes to promotion and whether they think that promotion affects their prescribing.

Review 2. *What impact does pharmaceutical promotion have on attitudes and knowledge?*

In addition to studies on the effect of promotion on attitudes and knowledge, this review looks at how much doctors report using promotion as a source of information (either for all drugs, or particularly for new drugs).

Review 3. *What impact does pharmaceutical promotion have on behaviour?*

This review looks at the evidence for several different possible effects of promotion on behaviour. These are the impact of promotion on individual prescribing behaviour, on overall drug sales, and on requests for formulary additions; the effect of direct-to-consumer drug advertising on consumers' decisions, the effect of promotion on the content of continuing medical education (CME) courses, and the impact of industry funding on research outcomes.

Review 4. *What interventions have been tried to counter promotional activities, and with what results?*

This review reports on research on interventions to control or counter promotion, and the effects of such interventions. It is not a comprehensive review of interventions, because there are many descriptive reports on these in the database.

The purpose of the reviews was to allow users of the database to understand the research that has been done on promotion, the strengths and weaknesses of that research, and to suggest directions for future research. The reviews were lodged on the web site in mid-2003.

Methodology

The reviews summarise the research evidence and, therefore, they do not include all of the material contained in the database. Only entries based on original research, systematic reviews or meta-analyses are included. Such entries all had written methodological notes. They were identified and extracted from the database by searching all entries that included a methodological note. This search took place in November 2001. Studies that were purely descriptive of promotion were excluded, and all studies which touched in some way on the four review questions were then included. The reviews were drafted, and in July 2002 a further group of relevant newer studies were added to the reviews. It is intended that the reviews will be updated periodically as the database grows.

Review 1.

What attitudes do professional and lay people have to promotion?

Finding out what people think about promotion, and what effect they think it has on them, is important because it can help us to develop relevant interventions. However, research on this topic cannot provide evidence about the actual effects of promotion. Promotion may affect people in ways that they do not know about, or are reluctant to tell others about.

This review describes studies that examine what people think about promotion. Studies about how people use promotion and other sources of drug information are not included here; these can be found in Review 2.

Research on attitudes to promotion relies heavily on survey methods. It tends to provide estimates of how many people agree with or disagree with certain statements, mostly about the appropriateness and effect of various forms of promotion. There are some more complex studies, which attempt to explore other variables associated with different attitudes to promotion. These try to find out what kinds of people have different opinions on promotion. Such studies are more useful.

There is little qualitative research on people's attitudes to promotion, and this is a major gap. In order to understand people's perspectives and values more clearly, in-depth interviews are needed. People should be express themselves in their own way about what they think about promotion and how it affects them. Ethnographic research, in which the researcher spends time with doctors and tries to understand how promotion fits into their working lives, would also be useful.

1.1 Attitudes do not necessarily match behaviour

Several studies show that finding out what people think about promotion may not be a good way to predict their behaviour. For example, Peay and Peay's 1984 paper¹ suggests a doctor's view of the worthiness of an information source may not be reflected in how often s/he uses it. Sales representatives and other commercial sources were not evaluated highly, but sales representatives were the most frequent source of first information about medicines, and were one of the most frequently mentioned sources of information needed to prescribe. Other commercial sources were also often mentioned as sources of first information about a drug. Similarly, Gambrill and Bridges-Webb found that 56% of the

Australian doctors in their study reported that they used sales representatives as a regular source of information, but only 17% ranked them as the most useful². McCue et al.³ surveyed general practitioners (GPs), internists and surgeons in North Carolina, about their attitudes towards and use of different sources of information about new drugs. Although only 27.7% of the respondents viewed drug sales representatives as accurate and accessible sources of information about new drugs, they were used more frequently than other sources. This study had a low response rate.

1.2 Studies of the prevalence of different attitudes to promotion (excluding direct-to-consumer advertising)

These are studies that simply assess percentages of people who report certain attitudes or beliefs about promotion. Some do start to explore differences within their samples, but this is not their main objective. Many of these studies look at the attitudes of medical students, doctors in training programmes, their trainers, or patients. Few studies look at practicing doctors, or at the public in general. Studies are often based at one or two institutions (usually in the USA and/or Canada), or are written questionnaires sent to directors of training programmes around the USA and/or Canada. Most studies focus on doctors in training or their trainers, examining and discussing what is an appropriate relationship between promotion and training.

Surveys of the prevalence of different attitudes include: Hodges⁴ who looked at psychiatry residents, interns and clerks in seven Canadian hospitals; Sergeant et al.⁵ who looked at family medicine residents in Ontario; Aldir et al.'s⁶ survey of practicing and resident doctors in Northeastern Ohio, USA, about their views of promotion; Barnes and Holcenberg's⁷ survey of medical and pharmacy students at the University of Washington in 1970; Blake and Early's⁸ survey of Missouri patients about their attitudes to gifts given by pharmaceutical companies to doctors; Madhavan et al.⁹, who surveyed West Virginia doctors about their attitude to gifts from the industry; and Keim's¹⁰ survey of directors of emergency medicine programmes, and residents in these programmes, about their attitude to interactions with the pharmaceutical industry. Others include: Mainous et al.¹¹, who surveyed 649 adults in Kentucky about their attitudes to doctors accepting gifts from the pharmaceutical industry; Reeder et al.¹², who surveyed all chiefs of US emergency medicine residency programmes; Strang et al.¹³ who surveyed Canadian doctors; Lichstein et al.¹⁴ who surveyed directors of internal medicine residency programmes; and Dunn et al.¹⁵ who surveyed Ontario physicians.

CONCLUSION: These studies do not suggest any clear patterns in attitudes to promotion. Further research would be required to determine if variations in the findings depend on the population surveyed, and on the way questions were asked, who asked the questions, and in what context.

1.3 Do trainers and trainees think that sales representatives should be banned during medical training?

Most (71%) psychiatry trainees surveyed by Hodges disagreed that sales representatives should be banned from making presentations in their training programme⁴. Most directors of internal medicine residency programmes (67%) felt that the benefits of sales representatives outweighed the negative effects. Forty-two per cent felt that curtailing sales representative interactions with residents would jeopardise company sponsorship of other departmental activities¹⁴. Of the internal medicine faculty and residents surveyed by McKinney et al.¹⁶, 52% of faculty and 66% of residents agreed that presentations by sales representatives should be banned at their institutions.

CONCLUSION: Only three studies in the database address this question: some trainers and trainees do, others do not think that sales representatives should be banned, and qualitative studies would be needed to discover their reasons.

1.4 Do doctors think they have enough training to deal with sales representatives?

Seventy per cent of psychiatry trainees did not feel they had had sufficient training about interacting with sales representatives⁴. Only 10% of internal medicine faculty and residents surveyed by McKinney et al.¹⁶ felt they had had enough training for professional interviews with sales representatives. On the other hand, 90% of the practicing doctors and 87% of the residents in Aldir et al.'s study felt that they had had sufficient training to critically understand information from companies⁶.

CONCLUSION: Only three studies in the database addressed this question. In two studies the vast majority indicated that they did not have adequate training to interact with representatives. However, in another study the vast majority said that they had sufficient training to critically understand information from pharmaceutical companies. This discrepancy may arise from differences in the framing of the questions, for example, locating the deficiency in the training as opposed to in the individual.

1.5 Do doctors think that sales representatives have a valuable role in medical education?

Twenty-nine per cent of psychiatry trainees agreed that sales representatives have an important teaching role (although in the text this is described as 'more than 40%')⁴. Eighty per cent of the US emergency medicine chief residents thought that their residency programme benefited from interactions with sales representatives. Only six chief residents indicated very strong opposition to

allowing residents to interact with sales representatives¹². In Bucci and Frey's study¹⁷ of US family practice residency programmes, 48.3% of programme directors felt that sales representatives were a valuable drug information resource for residents, and 55.1% felt they were valuable for practicing doctors.

In Dunn's study of Ontario physicians, about 10% of doctors rated 'pharmaceutical handouts' as an important or very important continuing medical education resource (10.9% of primary care doctors and 12.2% of hospital-based specialists)¹⁵. Hayes et al.¹⁸ surveyed general practitioners in the UK about their involvement in and attitudes towards industry involvement in continuing medical education. They found that most GPs (90%) had had meetings at their practice for which pharmaceutical companies organized the educational content. The characteristic of these which was most disliked, particularly by trainers and those in practice for more than eight years, was the promotional aspect.

CONCLUSION: The studies reported here all ask quite different (and relatively useless) questions. Opinions about the value of sales representatives are mixed; again differences may have resulted from the way in which the question was framed, and more research would be needed to clarify this.

1.6 What do health professionals think about the quality of the information provided by sales representatives and advertisements about drugs?

Thirty-two per cent of the psychiatry trainees surveyed by Hodges agreed that sales representatives provide useful and accurate information on new drugs (25% for established drugs)⁴. Fifty-eight per cent of family medicine residents in Sergeant et al.'s study⁵ felt that the literature provided by sales representatives was useful.

Ninety-two per cent of the Canadian doctors surveyed by Strang et al.¹³ felt that sales representatives had product promotion as their major goal, and 80% felt they overemphasised medicines' effectiveness. Forty-seven per cent of the doctors in Eaton and Parish's study¹⁹ felt that they were not able to obtain an unbiased assessment of a newly introduced drug. Most of them felt that most drug information was too commercial and therefore biased.

In a New Zealand study, Thomson et al.²⁰ found that 58 out of a sample of 67 doctors saw sales representatives. In response to an open-ended question about why, 56 of them gave a reason related to learning about new or existing products. The director of the Pharmaceutical Manufacturers' Association of New Zealand described a survey of doctors, in a letter to the editor of the *New Zealand Medical Journal*²¹. Without giving methodological details, he claimed that most New Zealand doctors felt that sales representatives are a good source of information about drugs and recognise practitioners' information needs, but are over-biased towards their own products.

In contrast, only 16% of UK GPs surveyed by Hayes et al. found visits by sales representatives to be educationally valuable¹⁸. University and community practice doctors surveyed by Shearer et al.²² rated direct mail, journal advertising and detailers as the three least reliable sources of drug information. Doctors in community hospitals ranked the representatives they saw higher than university hospital doctors ranked those reps whom they saw. Whelan et al.²³ report that staff members in a family medicine residency training programme in Canada did not rate sales representatives as a very useful source of information in response to drug information questions. They rated them poorly on all aspects: frequency of use, availability, ease of use, understandability, helpfulness, extensiveness, and how much confidence they had in them. Among Cockerill and Williams' Ontario pharmacists²⁴, a minority of the respondents (25%) said sales representatives were an important source of information, while only 17% thought advertisements and promotional literature were. Drug sales representatives were never mentioned as sources of information for the complex clinical case studies used by Boerkamp et al.²⁵. The majority of psychiatrists shown advertisements for psychotropics by Lion et al.²⁶ did not find them attractive or informative.

Sixty-eight per cent of doctors working in a Turkish city surveyed by Güldal and Semin²⁷ thought the information provided by representatives was unreliable. Ninety-four per cent felt a reliable source of information about drugs, other than pharmaceutical companies, was needed.

Benseman²⁸ found that the 45 New Zealand doctors he surveyed expressed varying degrees of anger and frustration at the waste involved in the material they were sent by drug companies. Almost all felt that company material was biased and should not be taken at face value. However they preferred drug company sponsored journals to academic journals, because they found them more relevant to general practice.

Mackowiak et al.²⁹ surveyed a small convenience sample of US community pharmacists and a small sample of pharmacy students about advertisements for over-the-counter drugs in pharmacy journals. In the USA, advertisements for over-the-counter medicines are regulated by the Federal Trade Commission. They must be truthful and not misleading. This is a lower standard than that enforced for prescription drugs. Around half the pharmacists, and students, surveyed by Mackowiak regarded the advertisements they were shown as misleading and not truthful. However they also reported high levels of reliance on them. Most respondents (90% of pharmacists and 81% of students) thought regulations for over-the-counter products should be the same as prescription products.

In a study of health care providers in Africa³⁰, commissioned by the International Federation of Pharmaceutical Manufacturers Associations and the US Pharmaceutical Manufacturers' Association, 95% of those who received company-provided information reported finding it helpful. The design of this study is not well described.

CONCLUSION: Doctors' opinions on the usefulness of information from drug companies vary but most believe that such information is biased.

1.7 What do other groups of people think of promotional information?

Journalists who wrote about medicines claimed to be critical of material from the drug industry in a study by van Trigt et al.³¹. Companies were not considered important sources for drug information in general, but the manufacturer was seen as a major source of information when a new drug was registered or became available.

CONCLUSION: Only one study in the database addresses this question. More research is needed.

1.8 What are doctors' views of pharmaceutical company support of conferences and speakers?

Most of the psychiatry trainees surveyed by Hodges⁴ (77%) agreed that sales representatives support important conferences and speakers. Most family medicine residents surveyed by Sergeant et al.⁵ agreed that the content of continuing medical education activities should be set by the doctors organizing them, rather than the company sponsoring them.

CONCLUSION: Only two studies in the database address this question. More research is needed.

1.9 Do trainee doctors plan to see sales representatives in their future practice?

Most (76%) family medicine residents in one Canadian centre surveyed by Sergeant et al. planned to see representatives in their future practice⁵. A significant minority (42%) of the Canadian psychiatry trainees surveyed by Hodges⁴ said they would not maintain the same degree of contact with sales representatives if no gifts were distributed.

CONCLUSION: Only two Canadian studies from 1994 and 1996 address this question. Data from recent graduates would be useful.

1.10 What are professionals' and patients' attitudes to the appropriateness of gifts?

Most (55%) of the family medicine residents surveyed by Sergeant et al. said that they would attend a private dinner with a sales representative paid for by a company. Thirty-six per cent felt that gifts from sales representatives to doctors resulted in higher drug costs for patients⁵. The doctors surveyed by Aldir et al. felt that smaller gifts were more appropriate than more valuable ones⁶. Of the Canadian doctors surveyed by Strang et al.¹³ 85% agreed that sales representatives should be able to offer free samples, but 74% felt they should not be able to offer all-expenses-paid trips to meetings organized by companies.

More than half of the residents surveyed by Keim et al.¹⁰, reported accepting gifts such as textbooks because they needed financial assistance with their education. Seventy-eight per cent of programme directors and 92% of students believed it was appropriate to accept textbooks from drug sales representatives. Keim et al. found that those who were more sensitive to bioethical issues in general were less willing to accept non-educational gifts. Twenty-five per cent of resident doctors in Virginia surveyed by Sigworth et al.³² said they would not want patients to know that they had received gifts and awards from drug companies and would try to hide this.

In a simple but clever research design, Palmisano and Edelstein³³ asked 100 medical students and 100 family planning nurses about the propriety of various people accepting gifts. Of the 50 medical students who were asked, 85.4% felt it was improper for a government official to accept a US\$50 gift from someone who wanted to gain a contract. Of the other 50 students, 46% felt it was improper for a medical student to accept a US\$50 gift from a drug company. The nurses were divided into three groups and asked different versions of the question. Of those who were asked, 97% felt it was improper for the government official to accept the gift, 64% felt it was improper for a resident doctor to accept the gift, but only 30% felt it was improper for a nurse practitioner to accept the gift. Amongst the Turkish doctors surveyed by Güldal and Semin²⁷ 33% felt that gifts were not ethical, 36% felt they were not ethical in some respects, and 21% felt that gifts were ethical.

Sixty-four per cent of the patients surveyed by Blake and Early⁸ believed that gifts would increase the costs of medicines. They approved more of doctors accepting some gifts, like drug samples, medical books, ballpoint pens and conference expenses, than others, such as dinners, baby formula and golf tournaments. Men, older people and those with tertiary education were more likely to disapprove of gifts. They were more likely to disapprove of gifts (except free samples) if they felt that these influenced prescribing and increased cost. One limitation of this study was that many patients were unaware that such gifts were given, so had little time to consider their opinion of them while completing

the questionnaire. In Mainous et al.'s Kentucky study¹¹ many more people (82%) were aware that doctors received office-based gifts than personal gifts (32%). This study used a population-based sample, rather than a practice-based sample. Substantial minorities of people felt that gifts had a negative effect on health care costs (42% for personal and 26% for office gifts) and health care quality (23% for personal and 13% for office gifts). These beliefs were more common amongst respondents with higher levels of education.

Gibbons et al.³⁴ asked doctors and patients about the same list of 10 gifts, and found that patients rated the gifts as less appropriate and more likely to influence prescribing than doctors did. Those with higher levels of education (i.e. those who had completed high school) were more likely to think that the cost of gifts was passed on to patients. Before the survey about half of the patients (54%) were aware that doctors accepted such gifts. Of those who were previously unaware of this, 24% said that learning about them had changed their perception of the medical profession.

CONCLUSION: Seven studies in the database address the question of professionals' attitudes to gifts. The studies available suggest that there is a range of views about gifts but a tendency for gifts that were smaller or more relevant to helping patients to be regarded as more acceptable. There is evidence that professionals believe that their acceptance of gifts goes below community standards and their own standards for other people in positions of responsibility.

Three studies in the database address the question of lay peoples' attitudes to gifts. The studies available suggest that only a minority are aware that doctors receive personal gifts, so only a minority disapprove, but people with higher levels of education were more likely to disapprove.

1.11 Do health professionals feel that discussions with sales representatives affect prescribing?

Thirty-five per cent of the psychiatry trainees in Hodges' study⁴ agreed that discussions with sales representatives did not influence their prescribing behaviour. This attitude was less prevalent among more senior trainees. Among the Canadian family medicine residents in the Sergeant et al.⁵ study, 34% agreed and 43% disagreed that sales representatives influenced their prescribing habits. In emergency medicine, Keim et al.¹⁰ found that 75% of programme directors, but only 49% of residents, believed that marketing techniques affect residents' prescribing practices. Seventy per cent of the Canadian doctors surveyed by Strang et al.¹³ agreed that sales representatives affected physicians' prescribing habits. Thirty-one per cent of the internal medicine residency programme directors surveyed by Lichstein et al. were concerned, and 13% were very concerned, about the impact of sales representatives on the attitudes and prescribing behaviours of their residents¹⁴. Most directors of family practice residency programmes in the USA (56%) felt that the information and resources

provided by sales representatives affected the prescribing of residents and practicing doctors¹⁷.

Bansinath et al.³⁵ state that only 5-6% of Indian cardiologists report that medical sales representatives had played a role in their decisions to prescribe brand or generic drugs. Sixty-three per cent of doctors in a Turkish city surveyed by Güldal and Semin²⁷ felt that information from sales representatives did not influence their prescribing. Those who found information from sales representatives reliable tended to report that this information had more influence on them.

American general practitioners surveyed by Pitt and Nel³⁶ rated sales representatives as the third most important influence on their prescribing decisions, advertisements as fifth and gifts as sixth. However, this study had a low response rate and excluded journal articles in the list of possible influences. Clinical pharmacists involved in family medicine residency programmes, surveyed by Hume and Shaughnessy³⁷, rated sales representatives, along with journal articles, as the third most important source of drug information influencing the prescribing of family medicine residents.

In Sigworth et al.'s³² study of resident doctors in Virginia in 2000, 91% reported that sales representatives had some effect on their prescribing. The authors suggest that this high rate could be the result of recent publicity and discussion on these issues, although the residents had not had formal educational sessions on drug promotion.

CONCLUSION: Many doctors denied that they were influenced by drug representatives: in three studies of residents 34, 49 and 91% believed they were affected, in three groups of programme directors 75, 31 and 56% did so. The available data suggest that doctors may be more willing to say that other doctors are influenced than they are themselves, but this remains a hypothesis.

1.12 Do people feel that accepting gifts influences prescribing?

Most (56%) of the psychiatry trainees surveyed by Hodges felt that accepting gifts did not influence their prescribing⁴. In the Aldir et al. study⁶ few doctors thought that a gift of a textbook influenced prescribing habits (less than 6%). Similarly, they felt that lunches or dinners provided by the industry had little influence on them, although they did feel that free samples affected their prescribing. In Barnes and Holcenberg's study, 60% of medical students and 75% of pharmacy students felt that promotional practices influenced prescribing⁷. Patients surveyed by Blake and Early⁸ also felt that gifts from the pharmaceutical industry to doctors were likely to influence prescribing (6% said it never did, 18% said rarely, 43% sometimes, and 16% frequently). They were more likely to disapprove of gifts (except free samples) if they felt that they influenced prescribing and increased cost. One limitation of this study was that many

patients were unaware that such gifts were given, so had little time to consider their opinion of them while completing the questionnaire.

Eighteen per cent of the Turkish doctors in Güldal and Semin's study²⁷ felt that gifts strongly affected prescribing, 12% felt they had a medium effect, 44% low, and 27% felt that they had no effect on prescribing.

Madhavan et al.⁹, found that physicians were more likely to think that other doctors' prescribing was influenced by gifts, than that their own was. They also found doctors with more patients were less likely to agree that most doctors are influenced by gifts and less likely to think it is inappropriate to accept gifts. Banks and Mainous³⁸ surveyed medical school faculty at the University of Kentucky, USA. Of a list of gifts given by sales representatives, none were seen as influencing prescribing by more than half of the respondents, although personal relationships with sales representatives were seen as influencing prescribing by 66% of faculty. PhD staff were more likely than MD staff to think that gifts influenced prescribing, and to oppose the acceptance of gifts. Most internal medicine faculty and residents surveyed by McKinney et al.¹⁶ felt that doctors could be compromised by accepting gifts (67% and 77%). However some (23% of faculty members and 15% of residents) believed that doctors could not be compromised regardless of the value of the gift received. In Cockerill and Williams'²⁴ survey of Ontario pharmacists, 50% felt there was a conflict of interest in accepting benefits from the drug industry. Those licensed after 1980 were less likely to think so.

CONCLUSION: In most studies most doctors denied that they were influenced by gifts. The available data suggest that doctors may be more willing to say that other doctors are influenced than they are themselves but this hypothesis merits more research. The only study on patients' attitudes found they were more likely to disapprove of gifts (except free samples) if they felt that they influenced prescribing.

1.13 Ethics and promotion

Seventy-four per cent of the emergency medicine residents surveyed by Keim et al.¹⁰ felt that sales representatives sometimes crossed ethical boundaries by giving gifts. Fourteen per cent of internal medicine residency programme directors reported observing unethical activities by sales representatives¹⁰. These included detailing in clinical areas, making false claims, giving monetary gifts, and conducting unauthorised studies.

A study by Poirier et al.³⁹ of people who make decisions about formularies in US private hospitals, found that most (93%) felt that providing non-monetary benefits to doctors to influence formulary decisions or product use was unethical. The respondents included chairs of pharmacology and therapeutics committees, directors of pharmacy, and pharmacists involved in evaluating drugs for

inclusion in formularies. More pharmacists than doctors rated providing meals to influence decisions as unethical (22% versus 12%).

A US study by La Puma et al.⁴⁰ examined payments to doctors to participate in post-marketing research on new medicines. Most of the doctors they surveyed (64%) felt it was acceptable to be paid a fee for each patient enrolled in post-marketing research. Most patients (56%) felt that this was unacceptable. Fewer doctors than patients felt that patients should be informed if the doctor was being paid a fee per patient enrolled (75% versus 86%).

CONCLUSION: Only four studies have addressed this issue and each of them looked at different aspects of the question, making it hard to draw any conclusions. From one study it appears that doctors think that it is more ethical to accept fees for enrolling patients in clinical trials than do patients.

1.14 Attitudes to direct-to-consumer advertising of prescription drugs

Since the introduction of direct-to-consumer advertising of prescription medicines (DTCA) in the USA in the 1980s, there have been phenomenal increases in spending on it. One estimate was that in 1999, US\$1.6 billion was spent on DTCA⁴¹.

Doctors

Petroshius et al.⁴² describe the results of a questionnaire delivered to doctors (general practitioners, family practitioners, internists and dermatologists) by sales representatives as part of their normal visits. They found older doctors and internists to be less supportive of advertising of drugs and cosmetic drugs than other doctors. This was especially the case with DTCA. Those aged over 50 had a negative response to DTCA (mean response was 2.84 on a scale from 1 for strongly agree, to 5 for strongly disagree). The authors found that doctors' attitudes towards DTCA were good predictors of whether they paid attention to such advertisements, and how they said they would respond to patient enquiries and requests for advertised drugs. This study obviously excluded doctors who do not receive sales representatives.

Cutrer and Pleil found largely negative attitudes towards DTCA of prescription medicines among the Texas doctors they surveyed⁴³. However their response rate was very low (17%). Doctors felt that DTCA would increase the demand for drugs, and increase questioning by patients.

Lipsky and Taylor⁴⁴ surveyed a 2% sample of active members of the American Academy of Family Physicians about their attitudes to DTCA. Doctors reported an average of 6.9 patients in the previous six months who requested a specific prescription drug, although the article is not explicit about whether doctors were asked specifically about requests that resulted from DTCA. Eighty per cent of those surveyed were opposed to print DTCA and 84% opposed to broadcast

DTCA. While there was some agreement about possible positive outcomes of DTCA (56% agreed that it encourages patients to seek medical advice for conditions that may otherwise go untreated, and 73% that it alerts patients to new products), there was also consensus about possible negative outcomes (89% disagreed that DTCA enhances the doctor-patient relationship, 71% agreed that DTCA pressures doctors to use drugs they might not ordinarily use, and 72% felt DTCA discourages the use of generics).

CONCLUSION: Doctors are largely opposed to DTCA.

Consumers

Lipton, a public relations executive from the USA, reports on a survey of consumers' attitudes to DTCA⁴⁵. The methodology of the study is not described. Half of the people thought that DTCA would provide them with more information about prescription drugs. Those who were better educated, younger, and those with higher incomes were less likely to feel that DTCA would increase their knowledge about specific drugs.

Bell, Kravitz and Wilkes⁴⁶ surveyed 329 adults in Sacramento, California, about their awareness, knowledge and attitudes to DTCA. They asked whether people remembered advertisements for 10 different drugs, and found recognition varied between 8% and 72% for different drugs. Men reported seeing fewer advertisements than women. There was greater awareness of advertisements amongst sufferers of the conditions treated by the advertised medicines. More positive attitudes to DTCA were correlated with greater awareness of DTC advertisements. The authors found significant public misconceptions about the regulatory framework for DTCA. Fifty per cent of respondents believed that DTC advertisements had to be submitted to the government for prior approval, 43% thought that only completely safe prescription drugs could be advertised to consumers, 21% thought that only extremely effective drugs could be advertised to consumers, and 22% thought the advertising of prescription drugs with serious side-effects was banned. None of these beliefs are true. People from minority ethnic groups were more misinformed than whites. Positive attitudes towards DTCA were positively correlated with these misconceptions.

Prevention magazine carries out regular surveys which include consumers' knowledge or and attitudes to DTCA. Telephone interviews with a representative sample of 1,222 adults in the USA were described in the 2000/2001 report⁴¹. Lower levels of awareness of DTCA advertising (i.e., reporting ever having seen a DTC advertisement) were found amongst ethnic minorities, low-income consumers, and those not taking prescription medicines. Ninety-one per cent of respondents reported having seen an advertisement for at least one of 10 highly advertised medicines (such as Claritin, Xenical). Fifty-seven per cent of consumers thought DTCA gave them the necessary information to ask their doctors about the risks of the medicines (62% for asking about benefits).

Magazine Publishers of America⁴⁷ surveyed allergy sufferers in the USA. In their sample, 34% had seen advertisements for allergy medicines in magazines, while 36% had seen such advertisements on TV. Nineteen per cent were able to identify the brand for advertisements in each medium. Since less is spent on magazine advertising than TV advertising, the authors argue that advertising in magazines is more cost-effective. They also report that the perceived believability of advertisements for medicines has declined since restrictions on DTCA were relaxed in 1997.

Maddox and Katsanis⁴⁸ surveyed consumers in a Canadian city that was exposed to DTCA advertising from the USA. They constructed two scenarios involving a fictitious drug. Patients who were given the scenario where they heard about the drug through DTCA, asked their doctor for it, and received a prescription, were more confident in their doctors than those whose scenario was that they heard about the medicine from their doctor first. This study had a rather low response rate, and the discussion and conclusions include assertions that do not appear to be justified by the findings.

Rockwell describes the attitudes of a sample of viewers of a US cable TV channel⁴⁹. He is the president of this channel, which shows programmes intended for and advertised to health professionals. Advertisements for prescription drugs have been shown during these programmes since 1983. The programmes proved to be popular with the general public who subscribed to this channel. A survey of the non-professional viewers of these programmes found that 95% of them thought DTCA would make patients aware that useful treatments exist. Rockwell suggests that negative public attitudes to DTCA found in other studies are a result of fear of the unknown, but those who have been exposed to DTCA are positive towards it. However it seems untenable to assume that people who watch programmes intended for health professionals are representative of the general population.

Alperstein and Peyrot⁵⁰ surveyed 440 people in Baltimore, USA. They found a moderate level of awareness of DTCA. Thirty-five per cent of people had heard of prescription drug advertising, and given a prompt, 42% were aware of advertisements for Seldane (an antihistamine). Most respondents felt that DTCA could help educate consumers (70%), while a minority agreed with possible objections to DTCA. Twenty-eight per cent felt it would confuse consumers, 21% that asking for an advertised product would upset a doctor, and 12% that DTCA would weaken the doctor-patient relationship. Respondents of higher socio-economic status were more aware of DTCA advertising. Those who were more aware of the advertisements were less likely to believe that the doctor should be the sole source of information about drugs, that DTCA would confuse consumers, and that it would weaken the doctor-patient relationship.

CONCLUSION: Most of the available studies report mostly positive attitudes to DTCA amongst consumers. The apparent positive attitudes could have resulted from the ways the questions were framed or the population were sampled or

who undertook the studies. Social and educational differences seem to influence acceptance of DTCA: the less educated may accept it more readily.

Others

Mintzes and colleagues⁵¹ conducted a mail survey of experts in New Zealand, the USA and Canada, on their views of DTCA, and the evidence that supported these views. (DTCA is allowed in the USA and New Zealand, and Canadians are exposed to significant cross-border broadcast DTCA). The experts included people from health professional organizations, NGOs, government, the pharmaceutical industry, advertising and the media. Opinions about DTCA were divided by sector. Those from the pharmaceutical and advertising industries were overwhelmingly positive, patient representatives showed a lesser degree of support, and other experts had negative opinions of DTCA. Most respondents felt that the information DTCA provided about drug risks and benefits was poor. Respondents felt DTCA increased expenditure on medicines, but beliefs about the impact on doctor-patient communication varied according to sector.

In another study, most of the 97 Canadian Drug Directorate personnel surveyed⁵² believed that more prescription drug information was needed for consumers, but only a quarter of these thought advertising was an appropriate mechanism for this.

Amonkar and Lively⁵³ mailed a survey to pharmacists in one Ohio county. Their study achieved a low response rate. Forty-two per cent of respondents did not think DTCA on television was beneficial to consumers. Although most (75%) thought that advertising may inform patients about available treatments, and some (32%) thought it may improve patient-pharmacist contact, most (90%) felt there should be prior review of advertisements by an independent panel, and most (87%) felt advertising would probably lead patients to pressure doctors to prescribe advertised drugs.

CONCLUSION: Surveys of experts' beliefs about DTCA suggest that the beliefs expressed depend on what sector the expert belongs to, with industry experts expressing positive beliefs, patient advocates having mixed beliefs and medical experts having negative beliefs.

1.15 Studies of differences in attitudes to promotion (excluding DTCA)

Peay and Peay's 1984 study¹ found two reasonably clear patterns amongst doctors. Those who reported using journals as important information sources evaluated journals more highly and commercial sources lower than other doctors. Those doctors who reported using commercial sources rated these more highly and journals lower than other doctors. There was a group of about 15% of doctors who consistently and exclusively relied on commercial sources of drug information. Those who cited sales representatives as providing information

needed to prescribe medicines were older, and those who cited journals were younger.

Although Linn and Davis's study⁵⁴ was done in 1969-70, there is no reason to believe that the findings are not still relevant. Linn and Davis found that doctors who preferred to use medical journals as a source of advice had more conservative attitudes in other areas than those who preferred sales representatives or other doctors. The former were less positive about the use of non-medical sources of advice (such as friends and family), and the use of medicines in response to daily social stress.

Amongst the New Zealand doctors surveyed by Thomson et al.²⁰ those who reported peer advice being less readily available reported seeing more sales representatives. Cockerill and Williams²⁴ surveyed Ontario pharmacists and found that 60% of them placed no restrictions on visits from sales representatives. However those who became licensed after 1980 were more likely to have restrictions. Andaleeb and Tallman⁵⁵ surveyed doctors in four teaching hospitals in Pennsylvania and found that doctors who treated a higher volume of patients were more positive towards sales representatives. They were also more likely to think that they provided informational and educational support. This study had a low response rate. Stinson and Mueller⁵⁶ carried out a survey of Alabama health professionals, which included 309 doctors as well as other health professionals. They found that doctors with more years of professional experience reported using sales representatives and unsolicited medical literature more often than others, and that general or family practitioners reported using them more than other specialists.

Evans and Beltramini⁵⁷ found in their survey that respondent GPs were more likely to solicit information about prescription drugs from sales representatives than specialists were, and that older doctors were more likely to use sales representatives for information than younger doctors. Overall the doctors they surveyed preferred non-industry sources of prescription drug information. This study had a low response rate, and response bias was not assessed.

County doctors in Oppenheim et al.'s study⁵⁸ tended to rely more on sales representatives as a source of information on prices, compared to other doctors; county physicians and faculty members had limited knowledge of medicine prices and tended to overestimate them. Miller and Blum also found that doctors had limited knowledge of the price of advertised prescription medicines⁵⁹. This study of doctors attending a continuing medical education event had a low response rate.

Santell et al.⁶⁰ surveyed hospital pharmacy directors and sales directors of pharmaceutical manufacturing firms about the role of sales representatives in hospitals. The response rate was low, particularly for the sales directors. Most sales directors thought that sales representatives met the needs of hospital pharmacists more than 80% of the time, but most hospital pharmacy directors

thought they were met less than 61% of the time. There was disagreement both about what services were important and how often they were provided.

Hull and Marshall⁶¹ report on an international study of GPs' sources of drug information. They claim that sales representatives are seen as very important in Sweden, Finland and Yugoslavia (now Serbia and Montenegro) and not important in the UK and Belgium. There are very low numbers in the study, and no details are given about the selection process, so the results should be viewed with a great deal of caution. However, the study raises the important issue of potentially large national differences in attitudes to promotion, which should be taken into account when designing interventions.

CONCLUSION: Doctors appear to fall into different groups with regard to the most used sources of drug information. The available evidence suggests that those who rely more on information from industry tend to be older, less conservative, see more patients, are generalists rather than specialists, have less access to peer support and more positive attitudes to the use of drugs. The finding that older doctors and general practitioners rely more heavily on commercial sources of information comes from multiple sources but other observations about differences between those using non-industry versus industry sources lack confirmatory evidence from more than one study.

Summary of conclusions

Doctors' attitudes to promotion vary, and do not necessarily match their behaviour. Their opinions differ on the value of sales representatives, on whether they should be banned during medical training and on whether doctors are adequately trained to interact with them.

Most doctors think information from pharmaceutical companies is biased, but many think it is useful. Health professionals find small gifts from drug companies acceptable. Most believe that drug representatives or gifts do not influence them personally, but do influence many colleagues. Few patients know that doctors receive promotional gifts, and so few disapprove.

Doctors who rely on promotion tend to be older, less conservative, see more patients, are general practitioners rather than specialists, have less access to peers and have a more positive attitude towards medicines.

Opinions about DTCA are mixed. Most companies, the advertising industry and the media favour it, while doctors and others (e.g. government, NGOs and health professional organizations) generally oppose it. Consumers and patients are divided: some, especially the less educated, would welcome more information from whatever source, while others distrust commercial bias.

Directions for future research

This review presents evidence about people's attitudes to promotion, including whether doctors believe that promotion affects their prescribing. Some studies consider this as evidence of the impact of promotion⁶, but this is incorrect. The evidence in the review could be useful in designing interventions, but should not be used to describe the effects of the different forms of promotion on prescribing behaviour.

The main limitations of the studies presented here are an over-reliance on survey methods, on the use of convenience and accessible samples, and on describing the prevalence of attitudes rather than exploring their inter-relationship or relationships between attitudes and other characteristics. Qualitative studies are needed in this area.

Survey methods are extremely useful in finding out factual information about a group of people but are of less use in understanding how people think about issues, such as drug promotion. Many of the studies in this review seem to rely on participants who are easily accessible to researchers, rather than being guided by research questions. This has led to an over-emphasis on the views of trainee doctors, and their trainers, as opposed to practicing doctors; and the inclusion of patients more often than the general public. Some authors suggest that it is important to study doctors in training because this is where their attitudes are formed. However it seems more likely that this emphasis results simply from convenience. In addition, the studies described here tend to rely on small samples, and many studies have been conducted in one or two institutions. These are unlikely to represent doctors and patients in general. Some of this research also suffers from low response rates^{9,57}.

Qualitative research, exploring in more depth people's feelings and beliefs about medicines promotion would be an important step forward. We need to move beyond simple surveys of attitudes to more sophisticated understandings of how people react to promotion, and how they understand their own reactions. Cognitive and social psychology may be able to make important contributions in this area. For example, some studies suggest that doctors are more likely to think that 'doctors in general' are influenced by promotion than they are themselves. This may be similar to other situations in which individuals sometimes regard themselves as less vulnerable to a hazard (such as HIV) than other members of a similar group. Research is needed to explore this further: why and in what ways do doctors think that they are invulnerable to promotion, how do they explain their own and others' vulnerability or lack of it? This points to a general need for research on promotion to learn from other disciplines and research on other topics. Attitudes to promotion should be seen as a specific case of other more general phenomena.

Qualitative research could also help to explore what survey respondents mean when they say that they or others are 'influenced' by promotion. Do they include informed (i.e. a positive meaning) or do they interpret the question to mean 'unduly' or 'negatively' influenced?

Ethnographic research, which examines medical sub-cultures, would also be extremely helpful in exploring attitudes to promotion. It appears that doctors vary substantially in their views of, and use of, promotion. How do these differences come about? What underlies them? Do they reflect overall different political and social views? Are they reflected in different social organizations (such as professional organizations, social networks, etc)? What brings about changes in these values? Do doctors move between them during their working lives? What factors enhance or impede this movement?

Review 2.

What impact does pharmaceutical promotion have on attitudes and knowledge?

Many descriptive studies clearly show that much promotional material contains inaccuracies, or at least presents very selective accounts of the evidence about the drug presented^{62,63,64}. The question this review addresses is whether and how far promotion (including these inaccuracies and biases) affects the attitudes and knowledge of those who are exposed to it.

Very little research has looked specifically at the effect of promotion on attitudes, much more has examined the effect of promotion on knowledge. The studies here are part of a field of research into the determinants of prescribing – how doctors learn about drugs, and how they come to prescribe new products.

Most of the studies discussed in this review are really about how much doctors report using promotion as a source of information (either for all drugs, or particularly for new drugs) rather than about effects of promotion on attitudes or knowledge. They are included because they provide information relevant to the question of whether promotion affects prescribers' knowledge.

Some studies look directly at the impact of promotion on attitudes and knowledge, by using an experimental approach⁶⁵, by interviewing people about previous exposure⁶⁶, or by following up participants in a promotional event⁶⁷. Others approach the question in a more sophisticated or indirect way. Ziegler et al.⁶² look at whether doctors notice and remember errors in promotion. Sansgiry et al.⁶⁸ look at whether consumers are aware of information missing from advertisements. Others^{63,64} look at doctors' attitudes or knowledge in areas where there is disagreement between commercial and scientific information and infer the impact of promotion from this. Ferry et al.⁶⁹ directly assessed knowledge of prescribing for the elderly and looked at it in relation to self-assessed reliance on promotion.

The methods that have been used in this area are not capable of producing certainty about causal relationships. Firstly both exposure to promotion, and knowledge and attitudes about drugs, are often assessed using self-report data. Secondly the relationship between them is often also assessed using self-report. That is, doctors are asked how much their prescribing is influenced by promotion. Self-report can be misleading when doctors' beliefs are inaccurate (e.g., they may believe that they are exposed less often than they are), or when

their answers to questions are biased towards being more socially acceptable than what they really believe.

2.1 Reported use of promotion as a source of drug information

In a 1974 FDA survey in the USA, 64% of all doctors, and 80% of GPs and paediatricians reported using materials from sales representatives as a source of drug information. Fifty per cent of doctors reported using journal advertisements⁷⁰. Christensen and Wertheimer⁷¹ found that sales representatives were reported to be the first source of information for one of the two drugs they studied. Advertisements in journals were the third source for the other drugs. This small study (29 doctors) is now very old (1975-6).

Two studies found doctors in developing countries relied very heavily on industry-based sources of information. Ahmad and Bhutta⁷² found 95% of the doctors they interviewed in Karachi relied upon industry promotional material as their main source of information about drugs. They also found extremely high levels of irrational prescribing and dispensing for children. Similarly, Tomson and Angunawela⁷³ describe heavy reliance on industry sources of information, and much polypharmacy in a peripheral clinic in Sri Lanka. In contrast, in Osio's two Nigerian studies^{74,75} health professionals and health professional faculty members reported low use of commercial information.

Some differences have been described between different kinds of drug information, and over time. In Hatton et al.'s study sales representatives were used more as a source of general information about drugs rather than pregnancy related information⁷⁶. Williams and Hensel⁷⁷ claim from their review of studies on sources of information about drugs, that commercial sources of information had declined in importance over time. They do not describe the search methods that they used to locate the articles included in their review. The studies included in this review were all surveys and social acceptability bias could be the cause of the results, i.e. over time it may have become less acceptable to claim reliance on commercial sources of information.

Some studies have explored differences between doctors in how far they say they rely on commercial sources of drug information. In McCue et al.'s study³ doctors who had been practicing more than 15 years used drug sales representatives as a source of information about new drugs more frequently than other doctors did. In Abate et al.'s study⁷⁸ academic medicine physicians used drug industry sources for their drug information questions less than private practice physicians did. Drug sales representatives were rated the most important source of information about advances in anti-rheumatic drugs by doctors who qualified in the 1950s, the second most important by those who qualified in or after 1960 in Murray-Lyon's study of GPs in Scotland⁷⁹. Gaither et al.⁸⁰ found that, among the 108 Michigan Health Maintenance Organization (HMO) doctors they surveyed, those who were not Board certified were more likely to intend to use sales

representatives and literature from the pharmaceutical industry than others, for information about a fictitious new drug. Also those with more than five colleagues at their work site were less likely to use industry literature.

CONCLUSION: Doctors' own reports suggest that promotion is often used as a source of drug information, less so by doctors who qualified more recently or who practice in an academic rather than a private setting.

2.2 Reported use of promotion as a source of information in adopting new medicines

Hibberd and Meadows⁸¹ found 85% of the UK doctors they interviewed said they used MIMS (a commercial source) to learn about new drugs, but most used non-commercial sources to find out about efficacy. Similarly, the British doctors in Eaton and Parish's study⁸² reported using sales representatives as a source of information about new medicines, but relying on them less to establish whether a medicine was useful and should be prescribed.

In a study of British GPs, by Strickland-Hodge and Jepson⁸³, three commercial sources were rated in the top five sources used to alert respondents of new medicines, but five professional sources were the most popular for providing information to evaluate medicines. GPs who worked alone cited sales representatives as a source of information for evaluating drugs more often than GPs who worked in group practices.

In Peay and Peay's 1994 paper⁸⁴ about specialists and high-risk medicines, they found that commercial sources of information played little or no role in the adoption of drugs in the doctor's primary area of expertise, but suggest that these sources may provide information about new drugs outside this area of expertise.

Manning and Denson⁸⁵ looked at how US internal medicine specialists first learnt about cimetidine. Their study was performed soon after cimetidine was launched in the USA in 1977. Sales representatives were rated as the sixth or seventh most commonly mentioned source in each stage of learning about cimetidine. However advertisements declined in importance. They were the eighth most common source for first knowledge of the drug, tenth for learning principles of using it, and thirteenth for providing update information.

Parboosingh et al.⁸⁶ in Canada interviewed specialists attending annual scientific meetings and asked them to identify two or three changes they had made in their clinical practice in the last two years, and the factors involved in these changes. Eighty-one of the 192 changes made were changes in prescribing. Sales representatives were noted as initial sources of information for less than 20% of the changes, and very infrequently noted as precipitating the changes. Like other studies, this suggests that commercial information may be more important in

alerting doctors to drugs, and less important in later stages of decisions to adopt new medicines.

Williamson⁸⁷ draws on literature on risk assessment to examine GP prescribing of new drugs. He concludes that the level of risk which a doctor perceives determines how much external validation he or she requires in order to prescribe the drug. From a small survey, Kleinman claims to show that doctors' preferred information sources vary with the perceived riskiness of medicines. He argues that sales representatives are the most important source for low-risk drugs, but are less important for higher risk drugs. Both studies are too limited to provide conclusive evidence but their theory deserves more testing and their approach of drawing on other social science literature is one that other researchers should follow.

A US survey of 680 doctors⁸⁸ found that 9% of doctors rarely or never met with sales representatives. The study suggested that documented evidence of a product's efficacy and applications was the major factor in doctors' decisions to switch or increase the frequency of a particular medication. The report of the survey in *Pharmaceutical Executive* provides no detail about the methods used so the study is hard to evaluate.

In one of the few qualitative studies on promotion, Jones et al.⁸⁹ interviewed 38 consultants in Birmingham hospitals in the UK, and 56 GPs who regularly referred patients to the teaching hospital. They also monitored the prescribing of specific drugs by the GPs, and in the hospital. They reported that sales representatives were an important source of information for both GPs and specialists. Jones et al. suggest that prescribers were not consistent in their definition of 'prescribing a new drug'. They were unsure whether this meant adding this drug to their regular prescribing repertoire, or whether it could involve prescribing it only a few times. In addition, GPs were unsure whether to include new medicines that they were prescribing because the hospital had started a patient on them. This suggests definitions need to be very clear in quantitative studies in this area, so that results are consistent.

CONCLUSION: Self reports indicate that promotion is often used as a source of information about new drugs, especially for indications for which the doctor has less expertise.

2.3 Impact of promotion on self-reported attitudes and knowledge

Engle⁶⁵ carried out a large study on the effect of a single-advertiser publication on doctors' attitudes and expected prescribing behaviour. Four first-edition hardcover books, about 100 pages long were mailed, one at a time, to 19,200 doctors. These were on topics related to medicine but were mostly non-technical and enjoyable to read. The books each included 18 pages of advertising for a broad-spectrum antibiotic. Questionnaires were sent to random selections of 1200

of the doctors 45 days before the first book was sent, and about one month after each of the other books was sent. Engle compared the attitudes and expected prescribing of readers (those who had read at least one book, those who had read at least two books) with non-readers (baseline and those who had not received the books). Readers were significantly more positive toward the company that sent the books than non-readers, but not more positive toward other companies. Readers were more likely to expect their frequency of prescribing the company's product to increase. This was statistically significant and seemed to affect only the sponsor's product. Engle suggests that the campaign may have been successful because the books were probably read cover to cover, unlike technical journals. This large and ambitious study provides before and after study evidence that a promotional campaign can significantly affect prescribers' attitudes. The study design could have been improved by including a randomly selected control group.

Sandberg et al.⁶⁶ present evidence that students given textbooks by pharmaceutical sales representatives are unlikely to remember the name of the company or its products. They interviewed 205 fourth year medical students, of whom 90% had received one or more textbooks from companies. Most could remember the title of the book, but only 25% could remember the company or a product associated with the gift. Most of the students were interviewed during their personal interview for admission to a residency. This seems a far from ideal interview situation. Students may have been very nervous and this may have affected their recall, and they are likely to have had a strong desire to give the answer that they thought the interviewer wanted. More importantly, this study did not explore one of the key points about giving gifts to students. It is likely that the effects of gifts on students include establishing habits, e.g. a willingness to receive gifts and the development of positive attitudes towards drug companies. Because prescribing cannot be influenced immediately, the memory of the link between a gift and a specific product or company is less important.

Spingarn et al.⁶⁷ found that house staff who had attended a Grand Round on Lyme disease, presented by a drug company, were more likely than non-attenders to prefer the use of the expensive parenteral drug made by the speaker's company. They reported that they would choose this drug for Lyme disease, even in mild cases where it would not be the best choice. This was in spite of the fact that the speaker did not recommend this style of treatment. The authors speculate that the effect may have come about because the speaker devoted extra time to the late complications of Lyme disease. These cases are infrequent but require the more expensive treatment. They note that this may also occur in non-commercial presentations. In addition, most of those who were present claimed that they did not know at the time that the speaker was from a drug company, even though he was introduced in this way.

CONCLUSION: Promotion influences attitudes despite some evidence that the details are not always remembered.

2.4 Research designs that aim to avoid the limitations of self-report data

Research by Ziegler, Lew and Singer⁶² suggests that doctors may not be very critical of verbal promotional information. They found 12 inaccurate statements (i.e. statements which contradicted the *Physicians' Desk Reference* or literature quoted by or handed out by the sales representative) in brief presentations given by sales representatives at industry-sponsored lunches. When they later surveyed 27 doctors who attended these presentations only seven recalled hearing the representative make a claim that they knew to be false.

Similarly, Sansgiry et al.⁶⁸ in the USA found that consumers may not be very critical of advertisements. They compared consumers' (students in non-health related subjects) assessments of 14 advertisements for over-the-counter medicines with those of experts (clinical pharmacists). Each advertisement was viewed by nine participants. The consumers rated the advertisements as more factual, good and complete than the experts, even though information on contraindications and side-effects was missing. Consumers were not able to identify misleading and inaccurate information. Only 20% of consumers identified side-effects correctly and 14% contraindications.

A 1982 study by Avorn, Chen and Hartley is very commonly quoted as evidence of the negative impact of promotion⁶³. They surveyed doctors about two drugs about which there was significant disagreement between scientific and commercial sources of information. There was no scientific evidence of benefit from cerebral vasodilators and evidence of minimal efficacy for propoxyphene. However promotional material presented them as efficacious and reliable. Avorn et al. argued that by looking at which of these beliefs doctors held they could see which type of information source doctors were really influenced by. Most of the 85 Boston doctors they surveyed said that they relied mainly on academic sources of information, and that advertising, sales representatives and patient preference were minimal influences on their prescribing. However their beliefs about cerebral vasodilators and propoxyphene tended to be more consistent with the commercial literature than with the scientific consensus. Nearly half (48%) of the doctors who supported the use of vasodilators stated that they were more influenced by scientific rather than commercial sources of information. Avorn et al. say that this discrepancy between where the doctors' beliefs seemed to come from, and their statements about what influenced them could be because doctors are unaware of how commercial sources influence them, or it could be because doctors are unwilling to admit this influence.

The Avorn et al. study is particularly important because it is very widely quoted. Therefore it is important to analyse it critically, and to suggest how further research might explore its findings. The study was simple, presumably inexpensive, yet cleverly designed. However it could be criticised in several ways. Avorn et al. focus on two sources of influence: 'scientific' and 'commercial'. However more doctors in the study rated their own 'training and clinical experience' as a very important influence on their prescribing than rated

either scientific or commercial sources in this way. At the time of the study there was a clear disagreement between the scientific and commercial views of the medicines studied, but the authors suggest incidentally that this had not previously been the case (e.g. the link between cerebral blood flow and senile dementia is “a concept now abandoned”). Doctors holding the ‘commercial’ belief could be holding on to a view taught in medical school or learnt from other doctors in the past and/or reinforced by the placebo effect in practice (their ‘clinical experience’). Avorn et al. do not convincingly demonstrate that the doctors’ ideas came from commercial sources. They may instead have resulted from their training and beliefs that ‘clinical experience’ is more valuable than scientific evidence-based medicine. It may be hard for doctors to exclude medicines from their prescribing repertoires if they learnt about them in medical school and they seem to work in practice.

Greenwood’s study⁶⁴ included a sub-study that repeated Avorn et al.’s method. He surveyed 332 GPs, in one area of England, about the use of four medicines on which scientific and commercial views conflict. The commercial view was held by 77% of doctors for one drug, and by 55%, 28% and 13% for the others. This study was a PhD thesis, and is difficult to obtain. Summaries are published in *HAI News*, No 48, August 1989⁹⁰ and in Lexchin⁹¹.

Similarly, in Peru, Cardenas and Isenrich⁹² found that while doctors said that they relied mostly on medical literature for their drug information, in fact their self-reported prescribing decisions were clearly not based on this.

Ferry et al.⁶⁹ found that doctors who reported relying on advertising as a source of information achieved lower scores on a test of knowledge about prescribing for the elderly. Only 25% of the doctors who received this mailed survey responded to it.

CONCLUSION: Doctors’ attitudes are influenced by promotion much more than they think.

Summary of conclusions

Promotion influences doctors’ attitudes much more than they realise. They often use it as a source of information about new medicines, and for medicines used outside their usual therapeutic field. Doctors in private practice, or who graduated long ago, report the highest use of promotion as a source of drug information.

Directions for future research

There is no literature in the database on the impact of promotion on the attitudes and knowledge of other people, such as consumers, pharmacists, nurses, or drug-store staff, all of whom may be important decision-makers about medicines. Future studies could include these groups. That the effects of promotion are likely to be great is suggested by long experience with promotion of breast-milk substitutes throughout the world⁹³. Publications in this area are of course outside the scope of this database.

Promising research designs, such as that pioneered by Avorn et al., seem worth pursuing further. One possible approach would be to examine a treatment for which there is substantial scientific support, but little advertising, such as oral rehydration solution (ORS). If such a study also found that doctors claimed to be influenced more by scientific rather than commercial information, but tended not to prescribe ORS (because there is little or no commercial information about its benefits), Avorn et al.'s conclusions would be much strengthened. Such a study would also avoid the difficulty of excluding a drug from one's prescribing repertoire: because in this case a treatment is being added rather than deleted. One of the advantages of this type of study is that it is relatively cheap: essentially it involved a telephone survey of 85 doctors.

Review 3.

What impact does pharmaceutical promotion have on behaviour?

This is both the most difficult area to research and the most important. Doctors may not be aware of how much promotion they are exposed to. Therefore, as much as possible, research on the effect of promotion on behaviour should avoid relying on self-report data to show causal relationships. Self-report data are appropriate for finding out what people think is happening, or how they want to present themselves to others, but in this area, that may be far from the reality.

This review looks at the evidence for several different possible effects of promotion on behaviour. These are the impact of promotion on individual prescribing behaviour, on overall drug sales, and on requests for formulary additions; the effect of DTCA on consumers' decisions, the effect of promotion on the content of continuing medical education courses, and the impact of industry funding on research outcomes.

3.1 Impact of promotion on individual prescribing practices

The ideal study would use data on actual prescribing before and after documented exposure to promotion whilst keeping other influences on prescribing constant. This situation is very difficult to create in real life. Instead researchers have often relied on self-assessments of exposure to or reliance on promotion, and self-reported prescribing. They have also found it hard to measure changes over time, and have often used data on different practitioners to guess at such changes. This has serious limitations.

This section examines various approaches to the question of how promotion affects individual prescribing. The first approach uses self-reported reasons for changes in prescribing, and investigates whether promotion is one of these self-reported reasons⁹⁴⁻⁹⁸. The prescribing changes might be measured (i.e. externally verified) or they might be self-reported. Ideally there are specific changes in prescribing particular drugs. It is inherent in this approach that the exposure to, and relative influence of promotion is self-assessed. Consequently, with this approach it is difficult to do more than give practitioners opportunities to present researchers with their self-image as people who are, or are not, influenced by promotion.

Stronger evidence for some kind of association between promotion and individual prescribing decisions comes from studies that look for associations between variations in prescribing decisions and variations in reliance on promotion. In these studies doctors are asked general questions like how reliable or useful promotional information is, and/or whether it is important in their prescribing decisions. Prescribing by those who give more positive assessments of promotion is then compared with prescribing by those who are more sceptical. Prescribing data are either self-assessed, elicited in response to hypothetical situations, or real prescribing data are used. There is strong consensus from these studies that doctors who rely more on promotion are heavier or less rational prescribers, or adopt new medicines earlier than those who rely less on promotion⁹⁹⁻¹⁰⁸. However, this kind of research cannot show a causal connection between promotion and prescribing. The results may be confounded by other factors, such as the practice setting or method of payment. Furthermore, these studies cannot establish a temporal relationship between use of promotion and inappropriate prescribing: doctors who are already poorer prescribers may be the ones who rely on promotion, or a reliance on promotion may lead to poorer prescribing. Therefore, this body of research does not prove that if these doctors relied less on promotion their prescribing would improve.

A third group of studies looks at different levels of exposure to promotion (between doctors or over time), and prescribing. These studies look at specific drugs, and the promotion related to them. These are the best kind of evidence that promotion actually causes changes in individual prescribing behaviour. The studies described by Peay and Peay¹⁰⁹, Orłowski and Wateska¹¹⁰ and Gönül et al.¹¹¹ are rather convincing, and worth replicating in other situations and with other drugs. This would considerably strengthen the argument that exposure to promotion causes prescribing changes. Other studies of this kind are also somewhat suggestive, but have methodological shortcomings such as the possibility of a recall bias, uncertainty about generalizability, and reliance on self-reporting of prescription, or do not give enough methodological details, such as the method of selecting doctors to be surveyed, to allow evaluation¹¹²⁻¹¹⁶.

This section ends with a discussion of the effect of samples on prescribing. This is discussed separately because it presents different methodological challenges, so different approaches have been used.

3.2 Self-reported reasons for prescribing changes

Taylor and Bond used real prescribing data⁹⁴. They asked 201 doctors in Scotland to fill out duplicate prescriptions, which included details about perceived influences on prescribing. Of the 161 266 prescriptions most were either repeat prescriptions or drugs that the prescribers had prescribed in the past. New drugs formed a median of 3.5% of the prescription items per doctor. Sales representatives were mentioned as influences for 20% of new drugs added to doctors' prescribing repertoires during the research period. Sales representatives

were more likely to be listed as an influence on the prescribing of drugs used short-term. It is difficult to know how generalizable these findings might be. They may depend on the type of drugs that are being heavily marketed at the time, and other influences on prescribing at the time (Taylor and Bond note the concurrent introduction of a 'limited list').

Dasta et al.⁹⁵ also had objective evidence of prescribing. Their study, partly supported by Abbott Laboratories, looked at sources of doctors' information about clarithromycin, a new antibiotic. The study was carried out in one inpatient and several outpatient medical care facilities. In the hospital, doctors who placed an order for clarithromycin were contacted by phone, and in the outpatient facilities doctors were sent a questionnaire when a prescription for clarithromycin, written by them, was presented at the pharmacy. In the hospital 65% of the doctors who prescribed clarithromycin reported not having had contact with a sales representative, and had never received or used samples of the drug at the time of the first interview. Eighteen per cent of outpatient prescribers had first heard about clarithromycin from a commercial source.

Peay and Peay⁹⁶ looked at the role of different information sources in specialists' decisions to adopt new drugs. Each specialist was asked about his or her general drug adoption practices and also about one of eight target drugs. The results suggest that commercial sources of information are relatively unimportant to specialists, with only 4.7% of respondents naming any commercial source as the most influential in their decision to first prescribe the target drug.

These studies are better at identifying the influence of promotion than those that ask for a general self-assessment of the influence of promotion, because they isolate particular prescribing decisions. But they cannot be taken at face value because they rely on doctors' own assessments of what has influenced their decisions.

Two studies, by Curry & Putnam⁹⁷ and Lurie et al.⁹⁸, relied entirely on self-assessments of reasons for prescribing changes. The former found that only 0.3% of their respondents (practicing doctors in Maritime Canada) reported changing their practice in the last year because of discussions with sales representatives. The latter surveyed faculty at seven university teaching hospitals in the USA and house staff in two of the teaching programmes, about their interactions with pharmaceutical representatives. Twenty-five per cent of the faculty and 32% of the residents reported that they had changed their practice at least once in the last year as a result of a discussion with a sales representative.

CONCLUSION: Doctors rarely acknowledge that promotion has influenced them to make specific prescribing changes. Specialists tend to report that promotion has less effect on them.

3.3 Prescribing by those who rely on commercial information

One study found no link between prescribing characteristics and self-reported reliance on promotion. Hemminki¹¹⁷ found no differences in observed frequency of prescribing psychotropic drugs between doctors who chose journals, textbooks or commercial sources as their main information source.

However most studies have found links. Mapes⁹⁹ found that doctors who reported relying on pharmaceutical industry literature were more likely to prescribe three or more drugs that frequently cause side-effects. Conservative doctors, who did not endorse the industry as a source of post-graduate knowledge, prescribed drugs that were newer, more effective and safer. This study used prescribing data routinely collected by the Department of Health in the UK. Bower and Burkett¹⁰⁰ found that family physicians who reported relying less on sales representatives for information were likely to prescribe more generic medicines, as were residency trained doctors, and regular readers of the *New England Journal of Medicine*. The self-assessed ability to recognise generic drug names was also highest amongst these doctors, those who relied least on journal advertising, and regular readers of the *Medical Letter*. Caudill et al.¹⁰¹ found, among primary care doctors in Kentucky, USA, that those who rated information provided by sales representatives highly (as credible, available, and applicable) and reported using it more, chose more expensive prescribing options in response to three clinical vignettes. This study had a low response rate. The study reported in Becker et al.¹⁰² and Stolley et al.¹⁰³ used self-report data on attitudes to and reliance on promotion; expert ratings of responses to questions about prescribing for certain conditions, and knowledge about certain drugs; and analysis of actual prescribing of chloramphenicol (an antibiotic that should not be widely used). They found that doctors who relied on journal articles and tended to be disdainful of journal advertisements, sales representatives and retail pharmacists as sources of information received higher ratings from the experts and prescribed less chloramphenicol. Better prescribers were more positive about generics, and gave other indications of a less positive attitude towards the industry and promotion than other doctors. A single question, about whether sales representatives were good sources of prescribing information about new medicines, produced the highest correlation with prescribing appropriateness. Berings et al.¹¹⁸ found that Belgian doctors in their study who felt that commercial sources of information were more important, prescribed more benzodiazepines than those who rated these sources as less important. Their prescribing was observed through the use of special prescription forms provided by the researchers.

In the Netherlands, Haayer¹⁰⁴ presented eight case studies of hypothetical patients to GPs and asked them if they would prescribe medication for this patient, and if so, what they would prescribe. An expert panel assessed the rationality of their prescriptions. The GPs were later interviewed and asked about their use of different sources of information about medicines. Less than half (48%) of the prescribing decisions made were rated as 'entirely rational'.

Differences between doctors accounted for more variance than differences between cases: that is, doctors seem to be more or less rational prescribers, over a range of different conditions. Haayer found that reliance on information provided by the pharmaceutical industry was negatively associated with prescribing rationality. That is, doctors who relied on promotional information wrote less rational prescriptions for the case studies than those who reported relying less on promotion.

Cormack and Howells¹⁰⁵ surveyed GPs in the UK before and after they attended a course on benzodiazepine prescribing. Their prescribing, adjusted by their number of patients ('list size') and the number over 65 years of age, was also analysed using Prescription Pricing Authority data. This produced a very wide range of scores. Doctors were classified as high or low prescribers of benzodiazepines. In interviews low prescribers rated information from pharmaceutical companies more sceptically than high prescribers.

Williams and Cockerill¹⁰⁶ in Ontario found that doctors who reported writing higher numbers of prescriptions per week had more contact with the industry (i.e. interacting with sales representatives, receiving benefits such as meals or conference fees) and were more likely than others to rate sales representatives and industry-sponsored seminars as important sources of drug information. The first result may have been partly due to higher prescribers being likely to spend more time in medical practice per week than lower prescribers. However Williams et al. note that high volume prescribers reported writing more prescriptions per patient, which adds weight to the idea that these are doctors who prescribe heavily. Another possible explanation for these findings is that sales representatives selectively target doctors who are already known to be heavier prescribers. These results are also presented in Williams, Cockerill and Lowy¹¹⁹.

There is also evidence that those who rely more on promotion may be older, and are earlier adopters of new drugs. Stross¹⁰⁷ investigated the reasons for changes in the management of chronic airways obstruction between 1978 and 1983 in small community hospitals. Using chart audits he identified a significant change in management of the condition during this period. He interviewed doctors who had treated patients at these hospitals in the study years. Older doctors reported relying more on sales representatives as a source of information for changing patient management. Stross looked at decisions to adopt three types of medicines (single-agent bronchodilators, beta-sympathomimetic agents and corticosteroid aerosols). For the last two, around 35% of doctors said sales representatives were their most important source of information in decisions to adopt the drugs. Early adopters of the changes were more likely than late adopters to list sales representatives as a major source of information. This study is useful in that it relies on significant observed changes in prescribing, which the researcher identified.

Strickland-Hodge and Jepson¹⁰⁸ compared the characteristics of the first and last 100 doctors to prescribe cimetidine in one area in the UK. Although their response rate was only 50%, they found that earlier prescribers rated commercial sources of information (sales representatives, advertisements in medical journals, direct mail, MIMS and controlled circulation journals) significantly higher as information sources than late prescribers. Early prescribers reported reading more of their direct mail than late prescribers and reading fewer journals.

Together these studies provide convincing evidence that doctors who regard promotion more highly, and report relying on it more as a source of information about drugs, prescribe more drugs, prescribe less rationally and prescribe new drugs earlier than other doctors. However they can only provide circumstantial evidence for a causal link between promotion and individual prescribing. Other doctor characteristics, such as attitudes to risk, beliefs about clinical experience and evidence, views of new technologies, and academic inclination or ability may be behind these results. For example, doctors who believe that their clinical experience is more important than scientific evidence may be less likely to respond to evidence presented in journals, therefore be more dependent on other sources of information such as promotion, and less likely to prescribe rationally (i.e., according to the evidence). Alternatively less academically inclined doctors may not read journals, may rely on advertising because it is very accessible, and may also prescribe in less than optimal ways. The main problem with these studies is that they cannot show that doctors who report relying on promotion would prescribe differently or more rationally, if they did not rely on promotion.

CONCLUSION: Doctors who report relying more on promotion prescribe less appropriately, prescribe more often, or adopt new drugs more quickly.

3.4 Prescribing and exposure to promotion

Peay and Peay in 1988¹⁰⁹ clearly showed a relationship between seeing sales representatives and prescribing one new drug, and are often quoted by others. They interviewed 124 doctors in private practice, about their perceptions and use of temazepam, a benzodiazepine hypnotic, and their sources of information about it. The study was done in 1981, approximately a year after temazepam was introduced in Australia. They found that contact with a sales representative about temazepam most consistently predicted a favourable reception of temazepam at various points in the adoption process. Doctors who had seen a sales representative reported earlier awareness of temazepam, prescribed it earlier, were more likely to rate it as a moderate (rather than minor) advance over other drugs, were more likely to have prescribed it, reported prescribing it earlier, and were more likely to prescribe it routinely in preference to other alternatives. Compared to those who saw sales representatives less frequently, those who saw representatives more than once a week were aware of temazepam earlier, prescribed it earlier, and (amongst GPs) were more likely to prescribe it than other alternatives. Peay and Peay found no relationship between doctors'

professional involvement, or involvement in the medical community, and beliefs about temazepam. The study has considerable advantages over those described above. It does not ask doctors to assess themselves whether promotion has affected their decisions. It does not ask them to rate their own level of reliance on commercial information. The question “have you seen a sales representative regarding temazepam?” requests one simple fact that is likely to be easier for doctors to recall than the number of journal advertisements seen, etc. The group of GPs who had seen sales representatives about temazepam may have included more of the commercial information oriented doctors described above, but this is unlikely to account completely for Peay and Peay’s results.

In another important study Orłowski and Wateska¹¹⁰ analysed the effect on prescribing of drug company funded, all-expenses paid trips to educational symposia in resort locations. Using the hospital pharmacy inventory, they tracked the use of two drugs within one institution 22 months before and 17 months after each symposium about them. They also collected data on the national usage of these drugs, and informally interviewed the doctors who had gone to the symposia. Most of the doctors said that the symposia would not influence their prescribing, but some said that they might make them think of the drug more and the symposium might convince them of the benefits of the drug. Orłowski and Wateska found a dramatic and statistically highly significant increase in the use of the drugs in the hospital after the relevant symposia. These increases were not reflected in national data, and they did not seem to affect the hospital’s use of alternative drugs. This study provides evidence firstly, that exposure to promotion increases prescribing, and secondly that it can do so whether or not those exposed consider themselves vulnerable to such influence.

A useful study by Gönül et al.¹¹¹ explored the impact of visits by sales representatives and samples, on prescribing. They used data from Scott-Levin Inc. (a company which describes itself as a leading pharmaceutical consulting firm) derived from survey sheets filled in by doctors. These included prescribing, minutes of detailing received for different drugs, and number of samples received, for a ‘typical’ week in each month, from January 1989 to December 1994. Gönül et al. looked at one condition and seven drugs used to treat it. Throughout the article it is unclear whether these were different drugs, or different brands of the same drug, and this is a major weakness of the study. Using a multinomial logit model, it appears that exposure to personal selling related to a medicine (visits from sales representatives and samples) increased the probability of that medicine being prescribed (other things being equal). However, the study also showed that excessive detailing or samples did not increase sales further, and that doctors who saw a high proportion of Medicare or Health Maintenance Organization patients were less influenced by promotion. The authors are from marketing schools, and they conclude that the study provides no evidence that personal selling has negative social consequences. There seems little evidence for this in the study. Part of the difficulty in evaluating the conclusion is that it is unclear whether the study examined seven brands of one drug, or seven drugs. The health consequences of changing drug

therapy in response to marketing are likely to differ from those of changes in brand.

Research by Walton, a pharmacist and advertising executive, suggests that recall of print advertisements is associated with prescribing^{112,113}. In one study published in 1980¹¹² results are presented from a study of 1000 doctors in private practice who were shown print advertisements with drug and company names and logos blacked out. They were asked whether they had seen each advertisement before, and were then read a list of the advertised products and asked if they had prescribed or recommended these in the last month. For 95% of the advertisements the percentage of doctors who prescribed them was greater for those aware of the advertisements than for those not aware of them. However the effect of specialty was not controlled for. That is, doctors may be both more likely to notice and recall, and to prescribe, drugs relevant to their specialty. A similar study by Walton¹¹³ appears to be a smaller version or subset of this study.

Matalia¹²⁰ reviews a range of advertising industry-related studies that claim to show the effectiveness of print advertising¹¹⁴⁻¹¹⁶. In the first, family practitioners and internists evaluated advertisements. 'Prescribing data' were also collected but it is unclear whether these are self-assessments of willingness to prescribe, or actual prescription data. Matalia claims that as non-prescribers became more familiar with the advertisements their willingness to write trial prescriptions increased. It seems from his earlier description that this study assessed correlations between attitudes and familiarity with advertisements, so he seems to be extrapolating from data collected at one point in time from a range of people, to trends over time. The account of the second study¹¹⁵ is somewhat more convincing, but again the methods and analysis are not described well enough for proper evaluation. The study was an experiment where different groups of doctors (who had prescribed similar numbers and value of prescriptions in the previous six months) were sent identical journals but with varying numbers of advertisements for a mature cardiovascular drug (i.e. one that had been on the market for some time). Those in the group who received the most advertising increasingly prescribed the drug. After 12 months the manufacturers market share was 4% higher in the high intensity and 2.3% higher in the medium intensity group, than in the lower group. The third study was also a kind of experiment. Companies stopped all promotion for four products from nine months before the study. Four advertisements were designed for the study and placed in half the copies of eight journals. Doctors were interviewed, and those who had received the advertisements were more likely to recall the products than those who had not. However, prescribing was not analysed: the outcome variable was simply recall of the products.

CONCLUSION: Exposure to promotion influences prescribing more than some doctors realise.

3.5 Exploring the impact of samples on prescribing

There is little literature on the effect of samples on prescribing. Backer et al.¹²¹ report an ethnographic study of 18 medical practices. At least four weeks of fieldwork were done in each practice. Samples were used in 19.8% of the 1588 patient encounters observed. This varied widely between practices (range 4% to 39%) and also between doctors within each practice. Reasons given for using samples included, to test for efficacy and tolerability, to offer temporary relief or convenience, and/or to reduce costs to patients.

In Morelli and Koenigsberg's study¹²² samples which were dispensed as new medication for chronic problems were accompanied by a prescription for the same brand 48% of the time. This finding is hard to interpret, but it may suggest that the availability of a sample influences the choice of brand prescribed. This area needs further investigation.

Chew et al.¹²³ used three hypothetical case studies and asked their respondents (131 general medicine and family physicians) which medicine they would prescribe. They were then given a list of samples available and asked whether they would prescribe their drug of choice, or give a sample of another drug. For a patient with hypertension (and no health insurance) almost all respondents (92%) ideally chose a diuretic or beta-blocker (consistent with practice guidelines). However when samples were available, 27% (35 doctors) said they would dispense a sample. In almost all of these cases the sample was a different class of drug (e.g. ACE inhibitor or calcium channel blocker). Almost all of those who would give a sample (97%) said avoiding cost to the patient was an important or very important reason for their choice. A follow-up scenario in which the patient returns, with their hypertension well controlled on the sample drug, and now with health insurance, was presented. Of the 35 doctors who had said they would dispense a sample, 24 would now write a prescription for the sample drug, to avoid switching the patient. If this reflects real behaviour, it suggests that in some circumstances drug samples may strongly influence prescribing.

CONCLUSION: Samples appear to influence prescribing but more research is required on this issue.

Summary

Doctors' own assessments of whether promotion affects their prescribing are of limited value in establishing whether this is the case. The research clearly shows that doctors who report relying more on commercial information, prescribe more heavily, less rationally, and adopt new medicines more quickly. Some researchers have interpreted this finding as showing that 'relying on pharmaceutical company information increases prescribing'. This interpretation is not justified by evidence from these studies. The studies cannot show whether doctors would prescribe differently if their level of reliance on promotion were to

change. Some doctors may have characteristics (such as attitudes, skills) that lead to both reliance on promotion, and heavy or irrational prescribing.

The studies that look at different levels of exposure to promotion (between prescribers or over time) and prescribing provide more convincing evidence that promotion changes behaviour. Further research using this kind of approach would be valuable. Simply replicating the Peay and Peay study in another place, using another drug, would strengthen the evidence considerably: similar findings would add substantial weight to the argument that contact with sales representatives does change prescribing behaviour. In addition, other studies that look at prescribing changes after exposure to promotion would be very useful. Cormack and Howells¹⁰⁵ and Strickland-Hodge and Jepson¹⁰⁸ used prescribing data from the Prescription Pricing Authority in the UK. Such data could be utilised further to observe prescribing changes, for example, before and after visits by sales representatives. Other countries where all or most prescriptions are subsidised by the government, such as Australia and New Zealand, have similar data available.

Samples appear to influence prescribing, but this has received little attention and needs further study. Other literature^{122,124,125} has highlighted the widespread misuse of samples by health professionals, sales representatives and others, but ironically less is known about their use for patients.

Marketing literature tends to assume that evidence of behaviour changes is a good outcome: it shows investment in advertising is worthwhile. The public health and medical based literature tends to assume that higher prescribing levels of what is judged to be a sub-optimal medicine will lead to worse health outcomes. Some of the research suggesting that doctors who rely heavily on promotion prescribe differently does explicitly look at the quality of the prescribing (e.g., Haayer's¹⁰⁴ use of an expert panel, or the extent of chloramphenicol prescribing in the study by Becker et al.¹⁰²). Such measures of appropriateness need to be used more.

3.6 Impact of promotion on overall sales

Some studies have investigated whether promotion affects overall consumption or sales of medicines. There are several ways to do this. Some studies have simply observed changes that occurred before, during or after promotional activities^{96,126-129}. These studies are relatively simple and inexpensive but can provide quite convincing evidence if appropriate study periods are chosen and sales or consumption data are available. Other studies have used econometric modelling to investigate the relationship between promotion and sales over time¹³⁰⁻¹³². These methods are so complex and sophisticated that it is hard for non-econometricians to judge whether the models are appropriate. Some studies in this area look at levels of promotion and sales of a range of drugs¹³³⁻¹³⁴. These cannot separate effects of promotion on sales from effects of sales on promotion.

That is, they ignore the fact that companies may heavily promote their most popular drugs because the robust sales have enabled them to pay for more promotion. In theory it is more likely that the relationship between promotion and sales is not a one-way causation link but a two-way negative feedback loop - more promotion leads to higher sales which leads to more promotion.

Cleary's small study¹²⁶ looked at what happened when the level of promotion varied naturally over time, when a sales representative was away on a sales training course. He examined trends in numbers of new prescriptions for three third-generation antibiotics in one hospital. He found that when the sales representative was away the numbers of new prescriptions for this product dropped. This did not happen to the other products studied, and there was no correlation between the pattern in this hospital or regional or national sales. This study has the advantage of avoiding any effect of sales on promotion: i.e., the change in level of promotion was not a result of changes in the level of sales. Similarly Dieperink and Drogemuller¹²⁷ report their investigation of the reasons for a dramatic increase in the use of an atypical antipsychotic agent in their Minneapolis hospital. The most plausible explanation for this was a Grand Rounds presentation sponsored by the manufacturer of the product.

A small study reported in a letter to the *Lancet* by Suresh et al.¹³⁵, suggests that useful medicines may be relatively underutilised if they are not promoted. They describe the under-use of adenosine, an effective first-line treatment for supraventricular tachycardia, until it started to be marketed commercially in 1991. The medicine was available and cheap, and there was good evidence of its usefulness, but it was underused until an advertising campaign was carried out.

Stern¹²⁸ examined the number of visit to doctors where topical tretinoin was prescribed, and the number of articles in the popular press and medical publications discussing its use. In 1988 a highly publicised study suggest that topical tretinoin improved the appearance of aged skin, and it was prescribed at an increasing number of consultations in the USA after this. Most of these prescriptions were probably for the unlabelled unapproved use of tretinoin to treat the effects of aging. Stern's time series data are sporadic but, like Cleary's and Suresh's work, the paper suggests a link between promotion and overall sales.

Eichner and Maronick¹²⁹ analysed correlations between sales, expenditure on DTCA and patient visits to doctors for four groups of medicines between 1996 and 1998. They concluded that DTCA campaigns had variable success, and that factors other than DTCA (such as product characteristics and other marketing efforts) were important in determining sales levels. However, that DTCA did seem to increase patient visits to doctors for advertised conditions.

Mackowiak and Gagnon¹³⁰ used econometric modelling to investigate the relationship between promotion and demand for medicines. They looked at diuretics and benzodiazepines from 1977 to 1981, to investigate how overall

expenditure on promotion, and individual company promotional expenditure affected demand for a group of medicines (i.e. overall market size), and how individual company promotional expenditure affected demand for a particular drug (i.e. market share). They used IMS data on the extent of sales representative activity and the extent of journal advertising, and converted these into estimates of expenditure. Advertising agency fees were not included and this seems a significant omission. IMS also provided data on the number of new prescriptions for the products studied. Using ARIMA (Auto Regression Integrated Moving Average) modelling, they could find no relationships between promotional expenditure and demand in any of the three areas outlined above. They suggest that this may be due to limitations of the methodology, or it could suggest that companies are spending so much on advertising that they are getting little marginal return for extra dollars spent. Although this study clearly has methodological limitations (such as the choice of two drugs whose markets were not very dynamic in the period studied), it seems to make a minimum of unwarranted assumptions.

In another econometric study, Basara¹³¹ looked at the impact of a campaign of DTCA on sales of a new medicine. She used a quasi-experimental, interrupted time-series research design, comparing the number of new prescriptions before, during and after a real-life DTCA campaign. The paper includes a very long description of the complex analytical method used. Basara concluded that the campaign significantly increased the number of new prescriptions for the product. This effect appeared immediately and then tapered off over the campaign. The number of new prescriptions decreased after the campaign ended. Basara is an employee of Rhone-Poulenc Rorer Pharmaceuticals.

Similarly, using data on expenditure on advertising (from Competitive Media Reporting) and prescribing (from the National Ambulatory Medical Care Survey), Zachry et al.¹³² found positive correlations for some medicines and classes, but not for others. They based quasi-experimental time-series techniques. There were significant positive relationships between advertising expenditure and the number of prescriptions written for Zocor and Claritin, but a negative relationship between advertising for acid-peptic disorder medications and prescriptions for Zantac.

Krupka and Vener¹³³ compared advertising in the *New England Journal of Medicine* and the *Journal of the American Medical Association* (JAMA) in 1972, 1977 and 1982, with the number of prescriptions filled for the 15 most advertised drugs in 1972, 73, 77, 78, and 82. They found that about a fifth of the 15 most advertised drugs were also one of the leading 15 drugs in terms of the number of prescriptions filled for the five years analysed. Ten of the 15 most advertised drugs in 1972 had advanced their ranking in terms of prescription numbers between 1972 and 1973, and two were in the same position. Dajda¹³⁴ plotted the number of advertisements received in three GP practices in Swansea by therapeutic group, and the number of prescriptions written for drugs in these groups. He found a high correlation.

The ideal way to investigate this area would be, as Mackowiak and Gagnon suggest¹³⁰, to ask manufacturers to experimentally vary promotion over regions and times, monitor the effect of this and publish the results. It is possible that pharmaceutical companies have done many such studies but not published them. In the absence of such data, the published studies do provide considerable circumstantial evidence for a positive, but not always consistent, association between promotion and overall sales.

CONCLUSION: Increased promotion is usually associated with increased sales.

3.7 Impact of promotion and industry funding on requests for formulary additions

Two studies in the database address this topic. One relies on self-report and is not very useful. The other is an important and useful study that independently assessed relationships with industry and requests for formulary additions.

Lurie's study⁹⁸ of faculty at seven university teaching hospitals in the USA, and house staff in two of the teaching programmes, found that 20% of faculty and 4% of residents reported recommending additions to hospital formularies at least once in the last year at the suggestion of a sales representative. However, the number of staff who recommended additions for other reasons is unknown.

Chren and Landefeld¹³⁶ showed that doctors who requested that medicines should be added to a hospital formulary were more likely to have received funding from companies than other doctors. They independently observed requests for formulary additions at a university hospital between January 1989 and October 1990. The 40 doctors who made these requests, plus 80 randomly selected doctors who acted as controls, were sent a survey asking about their demographic characteristics and their relationships with the pharmaceutical industry, such as acceptance of money to go to educational symposia, speaking at symposia, and receipt of research funding. They found that doctors who interacted with a company were between nine and 21 times more likely than other doctors to have requested that a medicine made by that company be added to the formulary. The relationship between funding from companies and requests for formulary additions was strong and consistent, and independent of many confounding factors. Chren and Landefeld note that they did not establish causality: and that it could be that doctors learn of a new drug, request its addition to the formulary and then interact with the company. However they suggest that this scenario is unlikely because most requested medicine represented little or no therapeutic advantage over others already on the formulary.

This study provides good evidence that association with a pharmaceutical company – such as receiving research funds – leads to requests for formulary additions. This finding is important because formularies determine the medicines

available in a hospital and are therefore likely to affect other doctors' prescribing habits both in the hospital and when doctors in training leave the hospital and set up an independent practice.

CONCLUSION: Funding for doctors from pharmaceutical companies increases requests for medicines made by these companies to be added to hospital formularies.

3.8 DTCA and consumers' decisions

For a good review of published and unpublished evidence about the impact of DTCA see Mintzes et al., Volume II¹³⁷.

Everett¹³⁸ asked 238 people in Denver, USA to respond to a hypothetical situation in which they had back pain and saw an advertisement for a prescription-only muscle pain reliever. About one-third of the sample said they would ask their doctor for the drug and about 5% said they would change doctor if s/he did not prescribe it. Those who were less educated were more likely to say they would tell the doctor they had seen the advertisement and ask her/him to prescribe the drug. Bell et al.¹³⁹ report on a survey of Sacramento adults' anticipated responses to a hypothetical situation in which a doctor denies their request for an advertised drug. Nearly half the sample (46%) said they would be disappointed, 25% would attempt to persuade the doctor to prescribe the drug, 24% would seek the prescription elsewhere, and 15% would consider leaving the doctor. Nearly half the sample (47%) said they would not be disappointed, and would take no action. Those who would take action were more likely to rate their doctors' communication skills as poor, be more positive about DTCA and more (unduly) confident about government regulation of DTCA. These studies rely completely on self-report, in response to hypothetical situations. It is very difficult to know if consumers would respond in this way in reality, especially since important contextual factors, such as the doctors' explanation of why s/he would not prescribe the drug, are excluded.

In a somewhat more realistic study, Perri and Dickson¹⁴⁰ sent fake advertisements for fictitious prescription medicines through the mail to 200 patients who had scheduled regular appointments with their doctors. They used the advertisements developed by Morris^{141,142}, which he had found to produce the highest knowledge and recall scores. The four doctors treating the patients in the study knew about the advertisements, acted as if the medicines were real, and recorded patient behaviour. One hundred and fifty-five patients were observed by doctors. Thirteen made general comments or asked general questions about the medicines, but none made requests for the medicine. Ninety-four patients also completed questionnaires, which showed that those with chronic medical conditions were more receptive to the advertisements and had more favourable attitudes. The four doctors in the study felt that the advertisements had had no negative effect on their relationships with the patients. However this result may

have been different if patients had requested or demanded the drugs. The key advantage of this study is that it observes actual patient behaviour in response to the advertisements rather than reported attitudes or behaviour. Using fictitious drugs also means that it is clear that the effect came from the mailed advertisements because there was no other advertising for these medicines.

Three studies used different ways of measuring real responses to real DTC advertisements. In *Prevention* magazine's survey of consumers [2000-2001 edition⁴¹] 32% of consumers who had seen a DTC advertisement had talked to their doctor about an advertised medicine. Twenty-six per cent of these had asked for a prescription for the advertised medicine. Of these, 71% received a prescription for it, and 10% received a prescription for another medicine. In Bell et al.'s study of Sacramento adults⁴⁶ 19% reported having asked for a prescription, and 35% having asked a doctor for more information, as a result of a DTC advertisement. One difficulty with this kind of study is that it is unclear how much DTCA has brought about this situation. For example, even without DTCA some patients ask their doctors for medicines they have heard about from friends etc, and some of the prescriptions which were reported in the *Prevention* magazine study might have been written with or without DTCA.

Mintzes et al.¹⁴³ analysed a sample of 1431 visits to primary care physicians in one Canadian and one US city. They found patients requested prescriptions in 12% of visits, and 42% of these requests were for products advertised to consumers. The 50 drugs with the highest US advertising budgets, plus those noted as advertised to the public in a Canadian medical journal were defined as 'advertised'. The authors found that patients who requested a prescription were more likely to receive one than those who did not (after controlling for health status, socio-economic status, demographics and doctor characteristics). Doctors were ambivalent about the choice of treatment in 50% of cases where the patient requested an advertised drug versus 12% of the time when no request was made. Although this study suggests links between advertising, consumer demand and suboptimal care, it is by no means conclusive. It is unclear how many of the patient requests were prompted by advertising. Advertised medicines may differ from unadvertised medicines in other ways (e.g., they may be for more common conditions, or be newer) and this could make patients more likely to request them.

Further research is needed to monitor the impact of DTCA, particularly on overall consumption of advertised drugs, non-advertised drugs, and non-drug treatments for health problems.

CONCLUSION: DTCA is associated with increased requests from patients for drugs, and some evidence suggests that when doctors respond positively to these requests they are ambivalent about the product they are prescribing.

3.9 Impact of sponsorship on content of continuing medical education courses

Bowman¹⁴⁴ analysed the content of two continuing medical education sessions on calcium channel blockers, funded by different companies, and taught by faculty members. In one of the courses the funding company's drug was mentioned many more times than other medicines. In both courses the clinical effect ascribed to the funding company's drug were more positive. There were few comparative statements made, but most favoured the funding company's drug. This bias was in spite of university policies being instituted between the courses that required the institution rather than the company to control the course content. Bowman and Pearle¹⁴⁵ then examined self-reported changes in prescribing patterns related to three company-funded continuing medical education courses. The method they used is not very satisfactory. They attempted to ask course participants before, and six months after each course, about their prescribing of the group of drugs covered in the course. For two courses there was no matching of responses from individuals pre and post the course, and the response rates were not high. Bowman and Pearle conclude that in all three courses the sponsoring company's drug had the greatest increase in absolute terms. However, some increases occurred in prescribing of other company's drugs. This study is limited by its reliance on self-report instead of prescribing data. Participants may have wanted to please the authors by saying that they prescribe more of the drug that was presented as the best at the course, if the authors were also the course organizers (this is unclear in the papers).

CONCLUSION: Sponsorship may affect the content of continuing medical education. More research is needed to examine this.

3.10 Impact of industry funding on research

a. Extent of industry funding

Many authors document considerable reliance on industry funding for medical research. This also appears to be increasing. Massie and Rothenburg¹⁴⁶ surveyed authors of papers on the medical treatment of angina. Sixty-nine per cent of the studies were funded by the pharmaceutical industry and 45% of the authors would have done the study without industry funding. Anderson et al.¹⁴⁷ found that, over time, it has become increasingly common for clinical trials of second-line agents for rheumatoid arthritis to be supported by the pharmaceutical industry. In 1945-1969 they found no published studies that were fully funded by the industry, but by 1980-89, 61% of studies were. Kunin¹⁴⁸ found 39% of his respondents (members of the Infectious Diseases Society of America) had obtained research funds from pharmaceutical companies. This sum accounted for 34% of the funding reported. About half the researchers felt that they needed industry support for their work. Dorman et al.¹⁴⁹ found that the proportion of

published trials on acute stroke that were apparently supported by the industry increased substantially from 1955 to 1995, from 0 to 54%. They also concluded that descriptions of the nature and extent of industry involvement were poor, and consequently 54% could underestimate the real level of industry involvement.

Blumenthal and colleagues have documented extensive relationships between industry and university life sciences faculty in the US. They have also shown that such links lead to more secrecy around research findings. In 1986 they surveyed faculty members involved in biotechnology in 40 major universities in the USA¹⁵⁰. Those who had received industry funding for their work were found to publish more, patent more, participate in administration and professional activities more, and to earn more. They were also four times as likely to report that their work had resulted in trade secrets, and four times as likely to say that commercial considerations had influenced their choice of research projects, as biotech faculty members without industrial support. Most faculty, with or without industry support, agreed that relationships between industry and universities led to a risk of shifting too much emphasis towards applied research¹⁵⁰.

Similarly, Krinsky et al.¹⁵¹ describe extensive relationships between academic scientists and biotechnology companies. They developed a database of 889 US and Canadian biotechnology companies, and 832 scientists with whom they had formal ties. They found that at least 37% of members of the National Academy of Sciences (a group that provides advice to Congress and other government bodies) had formal ties with biotechnology companies.

In 1994 the Blumenthal group surveyed both faculty about relationships with industry, and industry about their relationships with universities. In their work 'industry' refers not only to the pharmaceutical industry, but to other life-science related sectors, such as agriculture. In one study¹⁵² the group describe the survey of agricultural, chemical and pharmaceutical companies in the US about their links with academic institutions. More than 90% of the 210 companies they surveyed had some relationship with academia. The most common was the use of faculty members as consultants. From these results the authors estimated that these industries as a whole supported 6000 research projects at a cost of US\$1.5 billion. Of the respondents, 34% of companies reported disputes with their academic partners over intellectual property, 82% sometimes required academics to keep information secret until a patent application was filed, and 47% occasionally required secrecy longer. The Blumenthal group also reported results of their survey of over 2000 faculty members from the 50 US universities that received the most National Institutes of Health funding in 1993¹⁵³⁻¹⁵⁵. The group found that nearly 20% of the scientists reported having delayed publication of their results for more than six months for a commercial reason, and 8.9% had refused to share results with other university scientists¹⁵³. Those who had received industry funding were more likely to report having delayed publication for commercial reasons, but those who relied more on industry (i.e. obtained a

higher proportion of their funding from industry) were less likely to report having refused to share results. The group also reported that 28% of the faculty surveyed had received research funding from industry, that the receipt of industry support was more common in clinical than non-clinical departments, and that industry had supplied 8.9% of all research funds (excluding overheads)¹⁵⁴. Those who had received industry funding for their research published more, participated more in administrative activities and were more commercially active than others. But those receiving more than two-thirds of their research support from industry were less academically productive than those receiving lower levels of support.

In 1998, Campbell and colleagues from the Blumenthal group¹⁵⁵ described the extent of research-related gifts given to academic life scientists by companies. Twenty-four per cent of respondents had been given biomaterials, 15% discretionary funds, 11% equipment, and 11% travel to professional meetings. Thirty-two per cent of respondents thought that the donors expected to review reports and articles before publication, as a consequence of the gift.

Choudhry et al.¹⁵⁶ investigated relationships between authors of clinical practice guidelines and the pharmaceutical industry. They looked at 44 guidelines endorsed by European or North American professional societies. Eighty-seven per cent of the authors they contacted had some relationship with industry, 59% had relationships with companies whose products were considered or included in guidelines, and almost all of these pre-dated the guidelines. In 42 of the 44 guidelines no declarations were made about potential conflicts of interest.

CONCLUSION: The percentage of research studies funded by pharmaceutical companies has increased over the past 50 years. Funding of research by these companies is associated with influence over choice of topic, secrecy, delayed publication for commercial reasons and conflict of interest problems for authors of guidelines.

b. The effect of industry funding on published results

Several studies explore this area. Some suggest different mechanisms by which the published evidence on drugs is likely to over-estimate their benefits¹⁵⁷⁻¹⁶². One of these¹⁵⁷ also suggests that company funded research is less likely to be published than non-company funded research. Many studies show that funded studies are more likely to present positive results about the study drug¹⁶³⁻¹⁷⁶. One study¹⁷⁷ examines the effect of company research sponsorship on what kind of research is done.

c. Is there an association between funding source and publication status?

Several studies have looked at whether the source of funding for studies affects their publication status. If company-funded studies with negative results are less likely to be published this could lead to an over-estimate of treatment effects or

risk-factor associations in published work, and in meta-analyses that rely only on published work.

Easterbrook et al.¹⁵⁷ attempted to follow up studies that had been approved by the Oxford Regional Ethics Committee, in the UK. They found that drug company-sponsored clinical trials were significantly less likely to be published or presented than unfunded studies. Stern and Simes¹⁵⁸ successfully followed up 520 studies out of 748 submitted to a Sydney hospital ethics committee in 1979-1988. In their study, pharmaceutical industry funding was not a statistically significant predictor of time to publication. Ioannidis¹⁵⁹ looked at Phase 2 and Phase 3 trials related to HIV treatments and did not find that the source of funding affected the time it took the results to appear in peer reviewed literature. Dickersin et al.¹⁶⁰ followed up studies approved by institutional review boards at two centres. The publication rate at one of the two was considerably higher for studies funded by the National Institutes of Health than for pharmaceutical industry-funded studies, but there was no evidence that the tendency to publish important results differed.

d. Multiple publication

Huston and Moher¹⁶¹ report that trials can be published in different forms, with different authors, which can make it seem that there is more evidence favouring a treatment than there actually is. They recount trying to untangle the genealogy of a risperidone trial funded by its manufacturer. Similarly, Johansen and Gotzsche¹⁶² describe the difficulties they encountered trying to carry out a meta-analysis on trials of anti-fungal agents. It was often unclear whether data in multi-centre trials were also published separately, and when contacted, many authors did not respond, or said they no longer had access to the data because it was with the manufacturing company or their previous employer. Tramer et al.¹⁷⁸ reviewed 84 trials investigating the use of ondansetron for post-operative emesis to quantify the impact of duplicate data on estimates of efficacy. They found that 17% of published full reports and 28% of patient data were duplicated, concluding that trials reporting greater treatment effect were significantly more likely to be duplicated, and that inclusion of duplicated data in meta-analysis led to a 23% overestimation of ondansetron's antiemetic efficacy.

CONCLUSION: The evidence that trials sponsored by a drug company are less likely to be published is contradictory. Some major company-funded trials have been published in multiple papers that make them appear to be separate studies, and this can distort the findings of systematic reviews or meta-analyses.

e. Is there an association between industry funding and published results?

Stelfox et al.¹⁶³ examined links between financial relationships with pharmaceutical manufacturers and doctors' published positions on calcium channel antagonists. They found 70 articles about calcium channel antagonists, and classified them, and their authors as either 'supportive', 'neutral' or 'critical'

about the use of these medicines. They then contacted the authors and asked them about their financial relationships with manufacturers of calcium channel antagonists and/or competing products. They found that authors who supported the use of calcium channel antagonists were more likely than others to have financial relationships with manufacturers of these products. Unexpectedly they found that authors who criticised the use of calcium channel antagonists were less likely than other authors to have financial relationships with manufacturers of competing products. The timing of the authors' position on calcium channel antagonists and their financial relationships were not explored. It is possible that authors supportive of calcium channel antagonists were sought out by companies, rather than company sponsorship leading to more positive positions on calcium channel antagonists. The authors note that only two of the 70 articles disclosed potential conflicts of interest.

In their meta-analysis of third generation oral contraceptives and the risk of venous thromboembolism, Kemmeren et al.¹⁶⁴ found odds ratios of 1.3 (1.0-1.7) in industry funded studies, and 2.3 (1.7-3.2) in other studies. On the same topic, in a letter to the editor of the *British Medical Journal*, Vandenbroucke et al.¹⁶⁵ report that of nine unsponsored studies, eight found relative risks of 1.5 to 4.0, while four sponsored studies found relative risks of 0.8 to 1.5. Similarly, Mandelkern wrote to the *Journal of Clinical Psychiatry*¹⁶⁶ that in 1997 all 16 industry-supported studies in the journal were favourable to the manufacturer's drug, while all six unsupported studies were not favourable to the study drug.

Wahlbeck and Adams, in a letter to the editor of the *British Medical Journal* outline their findings that industry-funded trials on clozapine reported more positive results than non-industry sponsored trials¹⁶⁷. Similarly, Cho and Bero found that articles that acknowledged support from the industry were more likely to present results which favoured the drug of interest¹⁶⁸. Rochon et al.¹⁶⁹ analysed 56 published trials of NSAIDs that they defined as 'manufacturer associated', including studies where the manufacturer had only provided study drugs. They found that the manufacturer's drug was always reported as comparable to (71%) or superior to (29%) the comparison drug. This was usually justified by the results. In 22 trials one drug was claimed to be less toxic, and in 19 of these this was the manufacturer-associated drug. This claim was justified by a test of statistical significance only 54% of the time. Liebeskind et al.¹⁷⁰, in a poster presentation, outlined a study of controlled clinical trials in acute ischaemic stroke from 1957 to 1997. They suggest there is under-reporting of trials showing adverse effects of experimental agents, and that the time from the start of enrolment to publication is longer for trials with negative outcomes than positive outcomes, and that this difference is greater for trials with corporate sponsorship.

Azimi and Welch¹⁷¹ looked at cost-effectiveness analyses in journals most visible to clinicians and found that funding source significantly affected the authors' conclusions about whether therapies requiring additional expenditure were justified, regardless of the quantitative conclusions of the study. Nine out of 10 articles that acknowledged industry funding supported additional expenditure,

while 15 of the 34 with no industry funding did. Authors of articles supported by the industry supported the use of new technologies at higher costs than other authors.

Friedberg et al.¹⁷² looked at studies on the cost or cost-effectiveness of new oncology drugs. They found that industry sponsored studies were less likely to report unfavourable qualitative conclusions than studies funded by non-profit organizations. Eighty-nine per cent of the studies they looked at used a retrospective design, which Friedberg et al. say allows the sponsor to look at the results of clinical trials and fund economic studies based on those most likely to give favourable economic results. Knox et al.¹⁷⁹ used the same trials as Friedberg et al., and concluded that industry-funded studies provided less information about the generalizability of their findings. They tended to highlight specific settings where the drug was most likely to be cost-effective.

Davidson¹⁷³ analysed all trials with concurrent or cross-over control groups published in 1984 in five major medical journals. He classified them according to whether they favoured a new therapy or intervention, or favoured traditional management. He also recorded whether the authors acknowledged industry funding or not. Provision of the study drugs or placebos was not counted as industry support. Davidson found a statistically significant association between industry support and whether studies favoured new therapies. Only four industry supported studies favoured traditional therapies. In two of these the manufacturer who supported the study did not make either medicine, and in one they made both medicines. Davidson speculates on the mechanism for the relationship between funding and published results. He suggests that industry funding may allow researchers to include large sample sizes which increases their ability to detect statistically significant differences and therefore to publish in a major journal. He also suggests companies may select drugs for study that have already been shown to be efficacious, that they may discontinue studies if the results are appearing to be negative, and that they may pressure investigators not to submit negative results.

Jadad et al.¹⁷⁴ looked at meta-analyses and systematic reviews of treatments for asthma. The six industry-funded reviews were of low quality and the conclusions of all but one favoured the intervention associated with the sponsoring company. The one exception examined the effect of Vitamin C, which was not a new proprietary compound.

Djulgovic et al.^{175,176} argue that randomised controlled trials should only be done if there is substantial uncertainty about which treatment is best. Therefore over time, roughly half of the trials should favour standard treatments, and half should favour experimental treatments. However, when looking at 126 published randomised trials on one disease, those supported by commercial organizations mostly (74%) supported new treatments over standard treatments. This was not due to low quality of commercially-supported trials. Kjaergard et al.¹⁸⁰ also found

industry-funded trials to be higher quality than some others (those not receiving external funding).

Freemantle et al.¹⁸¹ found that sponsored trials were likely to show greater efficacy of the sponsors' drugs, but this result was not statistically significant.

CONCLUSION: Pharmaceutical company funded research is more likely to show results favourable to the product being studied than research funded from other sources. There is an association between the opinions of investigators about products and their source of funding but causality has not been established.

3.11 Does funding affect the research agenda?

Tallon, Chard and Dieppe¹⁷⁷ report that of 930 controlled trials of treatment for osteoarthritis of the knee, 59% were drug trials, and 26% trials of surgery. They suggest that many of these address questions of little relevance to current management of the disease. They used focus groups and a postal survey to investigate the views and priorities of research consumers. They found that although groups wanted research into areas such as education, self-help, physiotherapy and exercise, most of the commercial funding was going into trials of drug therapy. Dieppe et al.¹⁸² present a subset of these data. In another study, Chard, Tallon and Dieppe¹⁸³ show that research on oral drugs produced positive results more often than research on other interventions, and that commercially funded studies were more likely to show positive results than non commercially-funded studies.

CONCLUSION: Pharmaceutical company funding of research influences the topics studied and the outcome of research.

3.12 Do authors reveal funding sources?

Wilkes and Kravitz¹⁸⁴ surveyed 221 North American medical journal editors and found that only 26% required authors to reveal their funding sources. Sacristan et al.¹⁸⁵ report that in a large number of pharmaco-economic studies funding sources are not specified. Moynihan et al.¹⁸⁶ found that ties between researchers and industry were often omitted from media reports about drugs.

CONCLUSION: Funding from pharmaceutical companies is often not disclosed.

Summary of conclusions

Increased promotion is associated with increased medicines sales, promotion influences prescribing more than doctors realise, and doctors rarely acknowledge that promotion has influenced their prescribing. Doctors who report relying

more on promotion prescribe less appropriately, prescribe more often, and adopt new drugs more quickly.

Samples stimulate prescribing.

Doctors who receive drug company funds tend to request additions to hospital formularies. Drug company sponsorship influences the choice of topics for continuing medical education and the choice of research topics and the outcome of research. It leads to secrecy, delay in publication for commercial reasons, and conflict of interest problems for contributors to guidelines. Researchers often do not disclose funding from drug companies.

DTCA leads to increased requests from patients for medicines. Doctors who prescribe a requested drug are often ambivalent about the medicine.

Directions for future research

There are major gaps and weaknesses in the evidence. One important gap is the lack of evidence about public health outcomes of behaviour changes: does promotion lead to appropriate levels of use of medicines? The evidence that shows conclusively that doctors who rely more on promotion are poorer prescribers suggests that it does not. However, because these results could be due to other underlying doctor characteristics, this argument is somewhat weak. More work is needed to establish causal relationships between promotion and prescribing of drugs which have little or no place in rational prescribing, or which have serious adverse consequences when over-prescribed, such as antibiotics.

Other gaps include the lack of evidence from developing countries. All of the studies presented in this review are from developed countries. It is very difficult to untangle the effect of promotion from other inadequacies in systems of medicines distribution in developing countries. In addition there is less funding available for sophisticated studies. However the Cleary study¹²⁶ shows how a small, low budget project can provide quite convincing evidence.

Weaknesses include lack of clarity about what studies can and cannot prove. Some researchers do not seem appropriately sceptical about self-report data, and many infer causality from data which simply show associations. There is also some laxity in use of concepts, and in describing previous research. For example, in their survey Lurie et al.⁹⁸ asked about 'changes in practice' but in their discussion they discuss 'changes in prescribing habits'. These are not equivalent. A change in practice could be one small change and may not be related to prescribing, while a change in habit suggests an ongoing and substantial change. Inaccurate descriptions of previous studies are sometimes found in literature reviews at the beginning of articles, particularly inaccurate claims about the conclusions that can be drawn from these studies. Future research needs greater methodological rigour in order to yield more definitive answers to the questions being posed.

Review 4.

What interventions have been tried to counter promotional activities, and with what results?

This review reports on research on interventions to control or counter promotion, and the effects of such interventions. It is not a comprehensive review of interventions, because there are many descriptive reports on these in the database, which are not included here. These reviews only describe research into the effects of interventions, not descriptions of methods to control promotion, such as guidelines, that do not report any quantitative or qualitative data.

4.1 Guidelines, codes and regulations for printed and broadcast material

This is by far the most commonly researched intervention.

Few studies describe regulations and guidelines about printed and broadcast promotional material and how they are monitored in different countries. Lexchin describes the situation in the UK, Australia and Canada. He suggests that in most industrialised countries the day to day control of promotion rests with voluntary national industry associations¹⁸⁷. He examines the enforcement of the four codes (there are two in Canada) according to five critical aspects. These are mechanisms for recognising violations, the composition of monitoring committees, sanctions for violation, the quality and quantity of information in reports issued about complaints and violations, and the circulation of these reports. He argues that codes that rely on complaints are inadequate because too many violations are missed. Instead he recommends proactive monitoring of a random sample of promotional activities. Lexchin also suggests that the majority of members of committees should be from outside the industry, that sanctions should be raised so that they deter companies from misleading promotion, that offenders should be required to correct false information, and that information about the enforcement of the code should be publicly available¹⁸⁷. His analysis is particularly clear and useful.

Herxheimer and Collier described the situation in the UK¹⁸⁸, where the Association of the British Pharmaceutical Industry (ABPI) introduced a Code of Practice for the promotion of prescription medicines in 1958. This is administered by a code of practice committee consisting of one independent barrister, 12 representatives from member companies, and two independent doctors (and now also a representative of a patients' organization). The ABPI secretariat examines advertisements in a random selection of journals to see if they comply

with the code, and since 1985 a medical consultant also makes an independent scrutiny of a random selection of advertisements. Possible breaches of the code are pursued by informal correspondence with the company which placed the advertisements. The code of practice committee deals with cases not resolved by this informal correspondence, plus all complaints originating outside the ABPI. This process was largely secret until 1982. Herxheimer and Collier argue that the evidence suggests that the code has failed to deter promotional excesses. The ABPI's wish to secure compliance with the code seems weaker than its wish to pre-empt outside criticism and action: its self regulation seems to be a service to itself rather than to the public. They suggested that the code of practice committee should become publicly accountable, that the majority of its members should represent the health professions and the public, and that effective sanctions were needed.

Some journals also have policies about pharmaceutical advertisements. Wilkes and Kravitz¹⁸⁴ surveyed 221 editors of medical journals in North America. Twelve per cent acknowledged occasional conflicts of interest between editorial decisions and the wishes of advertisers. Most journals published pharmaceutical advertisements (67%) and 41% of the editors of these journals reported having a great deal of control over advertisements. However only eight journals had required advertisers to make a change to an advertisement in the last five years. Forty per cent of the editors thought that journal advertisements should be subject to the same peer review process as scientific articles.

CONCLUSION: Neither the self regulatory systems that have been studied nor review by journal editors provide effective controls on drug advertising.

Many studies show that printed advertisements do not meet regulations and guidelines in force in various countries.

In the UK, Morgan et al.¹⁸⁹ suggested in 1976 that the ABPI guidelines were "not being observed strictly". Herxheimer and Collier¹⁸⁸ reviewed 302 cases considered by the ABPI code of practice committee between January 1983 and December 1988, and found that the ABPI code was commonly broken. Breaches were identified in 192 of the complaints from competing companies, doctors and pharmacists. In total there were 379 breaches, of which 270 were also possible breaches of the Medicines Act. Misleading claims or comparisons, and misleading or unsubstantiated information were the most common breaches. Herxheimer and Collier argued that the code had no obvious deterrent effect. The code of practice committee had no power to require retraction or correction of misleading statements and gave no adverse publicity to those responsible for breaches. Although they required an undertaking from offenders that the breach would not be repeated, this was not always honoured. The authors noted that there was no consumer input into the code, and complainants had no opportunity to respond to defendants' arguments.

In developing countries, frequent breaches of codes have also been found. In French-speaking West Africa, Chirac et al.¹⁹⁰ found that 13.5% of the advertisements they studied did not meet even the most liberal interpretation of the IFPMA code. Dikshit and Dikshit¹⁹¹ found that the Indian issue of the *Monthly Index of Medical Specialities* (MIMS) did not seem to follow the code of the IFPMA, which it is covered by. Vo-Kyung and Ok Kim¹⁹² report a high level of violations of South Korean regulations on the advertising of medicines. Lal et al.¹⁹³ found that only 2% of the 585 advertisements in their study cited adequate references, and therefore conformed with the WHO Ethical Criteria for Medicinal Drug Promotion. These advertisements were supplied by sales representatives to clinical departments of an Indian hospital. Both the IFPMA and the WHO Ethical Criteria for Medicinal Drug Promotion include the concept of 'reminder' ads, which do not need to contain full prescribing information. Tomson and Weerasuriya¹⁹⁴ analysed advertisements in the *Sri Lanka Medical Journal* and found that only a quarter contained information on adverse effects and a quarter on contraindications. However they suggest that 68% would pass both the IFPMA and the WHO codes if they were classified as reminder advertisements.

In the USA, Roth¹⁹⁵ found that 65% of the newspaper and magazine DTCA advertisements reviewed by two pharmacists presented a 'fair balance' of information, as required by the FDA. Stryer and Bero concluded that 42% of the 482 items received by an internal medicine residency programme, an HMO and a private internist's office, did not meet the FDA's requirements. Others failed to adequately meet the requirements for 'fair balance', or instructions for use, or included unapproved uses. However the article does not clearly outline how they operationalised the FDA requirement for 'fair balance'. In a similar study Rothermich et al.¹⁹⁶ suggested that 42% of the advertisements they reviewed from medical journals in 1984, 1988 and 1992 did not appear to comply with FDA requirements. In Wilkes et al.'s very thorough study^{197,198} advertisements were reviewed by experts in relevant fields of medicine and by clinical pharmacists, and 40% of advertisements were considered by at least two reviewers to be not balanced.

In Canada, Lexchin and Holbrook¹⁹⁹ found problems with the methodological quality of studies referenced in drug advertisements, despite the existence of guidelines.

In Australia, Moulds et al., in a letter to the *Medical Journal of Australia* reported that a review by clinical pharmacologists of advertisements in Australian journals found only 53% of the advertisements to be acceptable. Technical breaches of the Australian Pharmaceutical Manufacturers' Association Voluntary Code of Conduct were found in 22% of the advertisements²⁰⁰. Carandang and Moulds²⁰¹ assessed 127 advertisements found in four issues of Australian medical journals against the Association's code. Forty per cent were judged to be technical breaches, and these had increased since previous surveys. Seven per cent of the advertisements made unacceptable claims, fewer than in previous

surveys, but the difference could have arisen from use of different judges rather than being the result of a real difference over time.

In New Zealand, Lexchin²⁰², in a letter to the editor, reports that only around half of the non-reminder advertisements in four 1987 issues of the *New Zealand Medical Journal* contained each of the kinds of information required by the Pharmaceutical Manufacturers Association (PMA) Code of Practice. In a small study Peacock²⁰³ found that many advertisements did not comply with the voluntary code of the Researched Medicines Industry (formerly the PMA) or the Medicines Regulations.

These studies all show high levels of non-compliance with codes of practice and guidelines about promotional material, indicating that these are poor ways of controlling promotion. However they did not study the impact of changing codes or regulations, nor do they provide evidence (from different countries or different medicines) of the advantages or disadvantages of different forms of regulation. Three studies that do this are Sencan and Üstell²⁰⁴, Najman et al.²⁰⁵ and the Canadian Drugs Directorate⁵².

Sencan and Üstell²⁰⁴ examined the introduction of Turkish regulations that required advertisers to include basic information about medicines in advertisements. They found a considerable increase in the percentage of advertisements in a Turkish medical journal that contained basic information, after the introduction of the regulations. In 1990, the year before the regulations were introduced, only 41% of advertisements included adverse effects, while in 1991, 60% did. The figures for contraindications were 37% and 57%, for contraindications 26% and 51%, and for price 1% and 46%. The proportion of advertisements from foreign countries increased significantly (58% to 89%).

A particularly useful study by Najman et al.²⁰⁵ investigated the impact of legislative or voluntary codes of practice on advertisements in three countries. In the US, legislative requirements have been in place since 1961, while in the UK and Australia pharmaceutical manufacturers have voluntary codes of practice. Comparing advertisements in the major medical journals of those three countries for 1961, 1967, 1973 and 1977 Najman et al. found it hard to see evidence of the impact of the voluntary codes. Advertisements in the USA outlined the dangers of medicines much more than those in the UK and Australia. Fisherow²⁰⁶ notes that the FDA has considerable power in its interactions with companies over advertising, because it is also the regulatory body which decides whether to allow medicines onto the American market.

A Canadian report⁵² looked at how often magazine advertisements for non-prescription drugs complied with regulatory requirements. This is interesting because these advertisements are not subject to mandatory pre-publication clearance, and are monitored by a complaints-only system. The study found an extremely high level of non-compliance with the requirements. Of the 51 advertisements only 37% complied fully, and 39% contained major violations.

CONCLUSION: Government regulation of advertising can be more effective than voluntary regulation.

4.2. The 'Fair Balance' requirement

In the USA the Kefauver-Harris Amendment of 1962 required that prescription drug advertisements contained a fair balance of both negative and positive information. This resulted in the inclusion of a 'brief summary' of side-effects, warnings and contraindications. For a good history of the regulation of DTCA in the US, see Wilkes et al.²⁰⁷. There is a surprisingly large amount of research on the possible effect of the 'fair balance' requirement, of which the high quality work was done by Louis Morris from the FDA²⁰⁸. Some of the research on this topic looks at advertisements for consumers, some at advertisements for doctors.

In three articles, Morris and different co-authors look at ways of conveying risk information to consumers in DTCA. This type of analysis is important for working out how best to regulate DTCA, what kind of risk information should be presented and how. These papers describe aspects of a study that experimented with different forms of presenting risk information in mock DTCA advertisements for two fictitious prescription drugs. Morris et al.¹⁴¹ focused on TV advertisements in which the amount of information, the content (either general or specific), the format (video, audio) and the placement of information about risks were varied. Six hundred and seventy six people, (of whom 50% had one or more of the conditions that the drugs treated), viewed the advertisements. They found that more risk messages were recalled if more were included in the advertisement, if these were more specific, if they were both written and spoken, and if they were spread out throughout the advertisement. When people remembered high levels of risk information they tended to have less knowledge and awareness of the benefits of the medicines. Morris et al.¹⁴² outlined results from both the TV advertisements and magazine advertisements. Presenting the entire patient package insert in magazine advertisements led to lower knowledge of risks than advertisements that included the information in other forms. Morris et al.²⁰⁸ also described the results related to both TV and magazine advertisements, and looked at differences among the sample. For example, older people were more positive about both the medicine and the advertisement.

Similarly, but in a much smaller and less rigorous study, Larson et al.²⁰⁹ tested a small number of doctors' assessments of the believability of mock advertisements which included or did not include brief summaries. They also looked at whether the country in which the advertisement was found (USA or Mexico) affected believability, and found that it did not. Although the inclusion of brief summaries led to statistically significant increases in believability, this was relatively unimportant in explaining the variance in believability. They use attribution theory to explain their results. Larson and Smith²⁰⁹ appear to describe the same study. Hurd²¹¹ described a small study where pharmacy students were asked to rate the credibility and honesty of a sales representative, and whether

they would purchase the product, in a series of hypothetical situations. Including negative information about the product did not affect their preference for the product, but they rated the sales representative's honesty more highly.

Cady and Larson²¹² attempted to find out whether the inclusion of a brief summary made ads more believable. They used advertisements for two mock products and asked students to rate their believability with and without the brief summary. The major claim in one advertisement was more believable in the version with the brief summary, but the results were somewhat equivocal overall. Schommer et al.²¹³ assessed what patients had learnt after viewing an DTCA advertisement which included both positive and negative information about an antihistamine. The study used patients waiting for appointments at a clinic, and only 34% of those approached agreed to participate. The participants were confused by the claim that the antihistamine gave 'non-drowsy' relief, and the statement that about one in a hundred people experience drowsiness. The authors suggest that it may be confusing to have both risk and benefit information in the same advertisement. (However these claims do seem to be contradictory and the viewers' confusion seems entirely appropriate). Tucker and Smith²¹⁴ asked 192 people in a shopping mall to view four different versions of an advertisement for a fictional influenza vaccine. Those which included risk information were rated as more 'appealing' than those without, but those with no warning or a general warning (all medicines have side-effects, please consult your doctor), were rated as providing more 'security'.

It is hard to interpret the practical significance of these studies. While Morris et al. usefully explore different formats for conveying risk information, many of the other studies simply compare advertisements with and without risk information.

CONCLUSION: Communicating risk information to achieve "fair balance" requires great care and testing.

4.3 Guidelines for sales representatives

There is surprisingly little discussion in the literature about attempts to regulate the behaviour of sales representatives. This suggests that, compared to print and broadcast advertisements, sales representatives' activities are more difficult to document and study. That also makes them more difficult to regulate.

In Australia, the Australian Pharmaceutical Manufacturers Association has a code of conduct covering sales representatives. Roughead et al.²¹⁵ looked at whether sales representatives in Australia conform to this. Although the code does not state what kind of information sales representatives must provide, it does insist that their presentations be current, accurate and balanced. Roughead et al. recorded and analysed meetings between sixteen sales representatives and seven GPs. These included 33 presentations of prescription medicines. They found that omission of risk information was common, and that adverse reactions

and interactions were mentioned only in statements that minimised the risk of the product being detailed. Thirteen of the 16 presentations included at least one inaccuracy, and four mentioned unapproved indications. This is a really useful study and a simplified version of the method could form the basis of a system for routine monitoring of the quality of representatives' presentation. A fuller account of the study is available²¹⁶.

In France, a network of volunteer GPs and specialists monitor the activities of sales representatives. After s/he is visited by a sales representative, each doctor completes a questionnaire on whether the indications and dose regimen given by the sales representative matched the Summary of Product Characteristics (as they are required to); whether contraindications, precautions for use, interactions and adverse effects were mentioned by sales representatives; and the arguments and incentives used. The completed questionnaires are analysed and a summary published in *La revue Prescrire. Prescrire International*^{217,218} has discussed these findings and is in English. This is discussed further below (in Monitoring/countering promotion).

At the practice level, Becker et al.'s ethnographic study¹⁰² found that practices with policies and guidelines about when sales representatives could visit appeared to find interactions with them more useful and less intrusive.

CONCLUSION: Studies of promotion by drug company representatives suggest that the guidelines and regulations that should control them are not effective.

4.4 Guidelines for post-marketing surveillance

In the UK, in 1988 the Committee on Safety of Medicines, the Association of the British Pharmaceutical Industry, the British Medical Association, and the Royal College of General Practitioners agreed voluntary guidelines on post-marketing surveillance. These relate to observational cohort studies, in which doctors prescribe drugs under normal conditions. Under the guidelines, information about these studies, and the results, must be submitted to the Medicines Control Agency. Waller et al.²¹⁹ reviewed the studies that had been carried out under these guidelines. They found that studies were characterised by weak designs and had considerable difficulties in recruiting participants, and suggest that they could make only a limited contribution to assessing the safety of new medicines. Others have suggested that in reality these studies are a promotional tool^{220,221}.

CONCLUSION: The only reported regulatory system for post-marketing surveillance that has been studied has not been successful.

4.5 Guidelines on conflict of interest in research

The previous review described a number of studies that showed that published studies that are funded by manufacturers are likely to support the manufacturers' drugs. Published work does not always disclose relationships between manufacturers and researchers. Two studies have looked at research institutions' policies about conflict of interest.

Lo et al.²²² looked at 10 medical schools that received the largest amounts of National Institutes of Health funding in the US. They found wide variation and significant limitations in policies about conflict of interest in clinical trials. Five universities required disclosure of all possibly conflicting financial interests, independent of value. Universities varied in whether their policies covered non-faculty research staff. The authors recommend that university-based investigators and research staff be prohibited from holding stock, stock options, or decision-making positions in a company that may reasonably appear to be affected by the results of their clinical research.

McCrary et al.²²³ surveyed medical schools and other research institutions that received over US\$5 million annually from the National Institutes of Health or the National Science Foundation, 48 journals and 17 federal agencies. They found five medical schools and 10 other research institutions had no policy on conflicts of interest. There was marked variation amongst the rest. Less than half of the journals (43%) had policies requiring disclosure of conflict of interest. The management of conflicts and penalties for non-disclosure were almost always totally discretionary. Only three institutions required financial interests to be disclosed to research subjects.

Many authors have called for researchers to explain clearly sponsoring company involvement in clinical trials¹⁴⁹. There have also been calls for a prospective register of all trials to be set up, before the results are known. This would reduce the problems of bias in published findings. Stern and Simes point out that this should not be difficult in countries where ethical approval is required for trials, because the register could be added on to this process¹⁵⁸.

CONCLUSION: many organizations, including many medical schools, research institutions and medical journals lack adequate policies for dealing with conflicts of interest. There is a strong case for all trials to be listed on a public register at the time they are set up.

4.6 Guidelines for package inserts and compendia

It seems that in the USA, FDA control over the content of *Physicians' Desk Reference* (PDR, the commonly used compendium of prescribing information) leads to greater inclusion of important information. Alloza and Lasagna found that compared to compendia in Spain, Brazil and Mexico, the PDR included three

times as many precautions as the mean for the other three countries, and four times the number of adverse effects. Their study focused on anti-inflammatory drugs marketed in the four countries²²⁴.

From 1976 the Nigerian Government required pharmaceutical manufacturers to produce leaflets and package information to be included with medicines. These were to be inspected before medicines were registered. Osifo²²⁵ compared the content of package inserts found in 28 prescription drugs obtained from pharmacies in Benin City with the American PDR. Those for the four products from American firms were the same or similar to the PDR entries. Those from foreign subsidiaries and affiliates of US firms included more indications and fewer precautions. Osifo suggests that the Nigerian health authorities have failed to adequately enforce the drug labelling controls.

A major study by the Office of Technology Assessment of the US Congress²²⁶ in 1993 found that the label and package inserts for at least half of a sample of 241 products sold by US-based companies in four countries - Brazil, Kenya, Panama and Thailand - failed to provide sufficient information for doctors to use the drugs safely and effectively.

CONCLUSION: Product inserts tend to be more informative in the USA than in other countries.

4.7 Guidelines about gifts

In the USA, the American Medical Association has guidelines about gifts from the pharmaceutical industry incorporated in its Code of Ethics. These suggest that gifts to doctors should primarily benefit patients and should not be of substantial value. The American College of Physicians also suggests that a useful criterion for determining acceptability is whether doctors would "be willing to have these arrangements generally known".

In Gibbons et al.'s study of attitudes to gifts from the pharmaceutical industry to doctors, only 62% of doctors were aware of any guideline about accepting gifts³⁴. Awareness of a guideline was the only predictor of doctors reporting that gifts were not appropriate. However these are self report data, so those who knew about guidelines may have felt more social pressure to say that gifts were unacceptable.

Drug samples, although not intended as gifts to doctors, may in fact be used in this way. Westfall, McCabe and Nicholas¹²⁴ found that in their family practice residency almost all staff, including medical practitioners, office staff etc had used samples provided by sales representatives for their personal or family use. The total retail cost of these was over US\$10,000. As a result of their findings they instituted new controls over access to the medicine samples.

CONCLUSION: Not enough is known about the impact of guidelines for gifts to reach any conclusions.

4.8 Guidelines for trainee doctors and for hospitals

As noted before, much North American research has been on trainee doctors. Many studies have looked at codes of practice that regulate the contact between trainee doctors and the industry.

Mahood et al.²²⁷ surveyed all 16 Canadian family medicine training programmes about their policies and practices about contact with the pharmaceutical industry, and what they taught in their curriculum about relationships with the industry. Four programmes had formal policies about interaction with the industry, and one had a policy on research involvement only. Thirteen of the programmes taught critical appraisal of industry products and claims. One programme did not allow sales representatives in training units, and one only allowed contact with sales representatives if faculty members or pharmacists were present. All programmes had some degree of industry sponsorship. Keim et al.¹⁰ surveyed 80 directors of US emergency medicine training programmes. They found 61% of programmes had specific guidelines to limit interaction between trainees and students. In 34% such interaction was not allowed in the clinical department. Only 17% of programmes allowed unrestricted group presentations by sales representatives to students. Bucci and Frey¹⁷ surveyed directors of family practice residency programmes in the US in 1989. They found 20.5% of their respondents included methods to evaluate material provided by sales representatives in their curricula, 79% limited contact between sales representatives and faculty and residents, and about 30% had printed guidelines for sales representatives. In 1991, US family medicine residency programmes were again surveyed, by Brotzman and Mark²²⁸. They examined a range of promotional activities and found that for each, most programmes allowed it within informal guidelines. Fifty-eight per cent of programmes had a written policy about at least one aspect of promotion. They concluded that programmes were more concerned with regulating access to and information from sales representatives, rather than gifts.

In two articles^{229,330} Thomas describes a survey of pharmacy directors from 446 US hospitals about their hospitals' policies towards drug sales representatives. Sixty-seven per cent of hospitals had written policies about drug representatives. Policies included the need for representatives to make appointments, to sign in at each visit, limitations on the areas in which they could detail their products and controls on samples. Some hospitals used fines or loss of exhibit privileges as penalties for those who broke guidelines. Between late 1983 and 1986 about a fifth of hospitals increased their restrictions and many anticipated more restrictions. Most appeared to be motivated by a desire to contain costs. Small hospitals were less likely to have increased their restrictions, but changes were planned across all sizes and types of hospitals. These were most often restrictions

on the products which sales representatives could detail and sample, and the people who they could have business contact with.

Jewesson and Herer²³¹ describe the Vancouver Hospital and Health Science Centre's (VHHSC) policy to restrict and monitor the activities of sales representatives at the hospital. Representatives are required to register on arrival and departure, wear an identification badge throughout their visit; and record the purpose of their visit, who they will contact at the hospital, which company they represent, and copies of any literature they distribute.

CONCLUSION: Guidelines for regulating contacts between companies and medical trainees vary greatly between institutions. Further research into this area would be relatively straightforward to do when changes are instituted.

4.9 Knowledge of these guidelines and their effect on attitudes

Only 23% of family medicine registrars surveyed by Sergeant et al.⁵ had read the Canadian Medical Association's (CMA) guidelines on appropriate interactions between doctors and representatives. Although six of the seven training centres had policies or referred to guidelines, only 26% of residents thought that their institution did. Although accepting a private dinner provided by a company contravenes the CMA guidelines, residents who knew about the guidelines, or were aware that their training centre had a policy about this, were no less likely to say they would accept such a dinner. However at one centre where company-sponsored lunches were not allowed, and where there was a teaching session on interacting with industry representatives, residents were less likely to see the literature from sales representatives as useful, and were less likely to say they would accept the private dinner or see representatives when they were practicing.

Brotzman and Mark²³² also looked at whether residency programmes' policies on drug sales representatives affected the attitudes of residents in the programmes. They randomly selected 14 US family medicine residency programmes, of which seven had written policies and at least one restriction on the activities of sales representatives. Residents in programmes with no policy were four times as likely to see detailing as a helpful source of information, and twice as likely to see journal advertisements as helpful, as residents in programmes with policies (the latter difference was not statistically significant). Those in programmes without policies felt gifts were more acceptable, and had more interactions with sales representatives. Brotzman and Mark note several possible reasons for this association between policies and residents' attitudes. Residents may interpret the absence of a policy as approval by the programme directors of promotional activities; programmes may differ in their culture regarding promotion; residents in programmes without policies may be exposed to more promotion, be more used to it and therefore more accepting. In addition programmes with policies may also include other interventions which shape residents' attitudes. However,

when Brotzman and Mark removed from the analysis the three programmes with an explicit curriculum in this area, the results remained the same.

Ferguson et al.²³³ asked practicing internists (internal medicine specialists) in the US whether they had trained in an institution with an enforced policy about sales representatives, and whether they now saw sales representatives and accepted samples. They found no differences in whether doctors now saw sales representatives and accepted samples between those who had trained in an institution with an enforced policy and others. This suggests that any impact of policies during training may not persist over time.

McCormick et al.²³⁴ reached different conclusions. They compared doctors who had trained at a Canadian medical school which did not have a policy restricting sales representatives' access to residents, with those who trained at another medical school which did have such a policy. They also compared doctors who had trained at the second school before the policy had been introduced. Those who trained while the policy was in force were less likely to find information from sales representatives beneficial in guiding their practice than other doctors several years after they graduated. The authors speculate that this could be due to the educational environment, to strong faculty opinions, or the doctors never having learnt to interact in a constructive way with sales representatives.

CONCLUSION: There is conflicting evidence about whether guidelines affect the attitudes of trainee doctors and if so whether any effects persist over time. Guidelines alone seem to have no strong influence on the attitudes of trainee doctors, but can be effective together with active faculty support in an academic setting.

4.10 Education about promotion

Several authors describe programmes to teach health professionals how to interact with sales representatives and interpret promotional information. Palmisano and Edelstein³³ briefly describe a seminar programme used for a range of health professionals. This included a simulation of a sales representative's sales pitch. Anastasio and Little²³⁵ describe a programme for family practice residents which aimed to improve their ability to obtain useful information from sales representatives. Over three hours, students were taught skills for controlling interactions with sales representatives, and for critically analysing promotion, and they discussed ethical issues. Students had two appointments with sales representatives to practice their skills, and these were watched and evaluated by others. Students rated themselves as more confident in their skills after the course.

Kelcher et al.²³⁶ describe a programme to provide family medicine residents with a structured approach to dealing with sales representatives. This consisted of a one-hour educational seminar, and five visits from sales representatives. The

sales representatives were asked to give their presentations according to a structured plan, and during their presentations the residents completed evaluation forms and discussed the advertising techniques used. These were followed by discussions with preceptors where the residents discussed what they had learnt about the drugs. According to questionnaires most of the small number of residents (15) who had completed the programme thought it should continue. The authors argue that this approach is better than restricting residents' access to sales representatives. The project was funded by two pharmaceutical companies.

Hopper et al.²³⁷ measured the effect of a 40 minute lecture and discussion session about pharmaceutical promotion, on primary care and internal medicine-paediatric residents. Surveys were completed three weeks before and four weeks after the teaching session. Very small numbers of people were involved. After the intervention residents were more likely to believe that sales representatives may use unethical marketing practices, that gifts with no patient benefit may be inappropriate, and that other doctors' prescribing habits may be negatively influenced by accepting gifts. This study suffers from very small numbers of participants. It is also unclear whether these reported attitude changes are likely to persist over time.

Suryawati and Santoso²³⁸ described the effect of a teaching module for medical students in Indonesia. This consisted of a one-hour lecture on commercial and non-commercial sources of drug information, the WHO Ethical Criteria for Medicinal Drug Promotion, and examples of misleading promotion. This was followed by a two hour workshop in which participants critically assessed advertisements from local medical journals. Participants in the course, and two control groups, completed tests that involved assessing 10 different advertisements. The intervention group significantly improved after the course and this effect was still apparent after 12 months. One control group, who were part of the same class, improved somewhat after 12 months, probably due to cross-contamination, and the other control group performed poorly in the test 12 months after the course.

Shaughnessy et al.²³⁹ reported on an educational intervention for resident doctors in the USA. This centred around a Pharmaceutical Representative Evaluation Form which residents used to evaluate presentations by sales representatives. The form included the completeness of the presented information, the techniques of persuasion used, and the use of rational and irrational appeals. Using a modified version of the questionnaire developed by McKinney et al.¹⁶ the authors found that a year after the programme residents were more likely to disagree that sales representatives and gifts have no impact on prescribing. Similarly, Vinson et al.²⁴⁰ found a change in students' attitudes after a lecture on concerns about pharmaceutical marketing practices to second year medical students. However this change was measured by questionnaire only seven weeks after the lecture.

Wilkes and Hoffman²⁴¹ describe an educational programme in which university pharmacists portrayed pharmaceutical company representatives to model a promotional presentation, that they designed to generate critical thinking among third-year medical students about the influence of pharmaceutical representatives on physicians' prescribing practices. The authors found that the programme increased the uncertainty many students felt about the accuracy and ethics of standard drug "detailing." Compared to questionnaire responses that students provided before the exercise, the attitudes they expressed in course assessments completed 12 weeks after the session revealed much more uncertainty about the ethics and value of interactions with representatives, and the number who stated that they wanted to interact with representatives during their residency fell from 86% to 61%. This is potentially a valuable approach for inoculating medical students against some of the worst potential consequences of biased drug detailing presentations.

In some of these studies it is difficult to determine whether any reported changes in attitudes after educational sessions are due to actual changes in attitudes, or to participants perceiving it to be less socially appropriate to express their original attitudes. However this is less of a problem in the Suryawati and Santoso study, because they tested participants' skills at assessing advertisements, rather than their attitudes. This study provides a useful model and convincing evidence of its effects.

CONCLUSION: Education about promotion appears to change attitudes and can improve skills. The impact of education about promotion on prescribing has not yet been tested.

4.11 Monitoring/countering promotion

The Medical Lobby for Appropriate Marketing (MaLAM), based in Australia, asked people around the world to send complaints about medicines advertisements. MaLAM chose particularly serious complaints, and prepared a letter to the advertiser, quoting the advertisement, summarising the literature and asking the company to provide their best evidence to support the claims made in the advertisement. A copy of the letter was then sent to MaLAM's subscribers (over 700 in 1991) and they were invited to sign and send it to the company. Most, but by no means all MaLAM subscribers were doctors²⁴². From 1998, MaLAM produced a series of newsletters called *Healthy Skepticism* for New Zealand GPs²⁴³⁻²⁴⁵. Each issue critically appraised advertising for one therapeutic group, by looking at the possible interpretations of the advertisements and marking these as unjustified, borderline, or justified by the evidence. The newsletter was funded by PHARMAC (Pharmaceuticals Management Agency). PHARMAC is the New Zealand government's drug purchasing agency. It negotiates subsidies for medicines, and is now also involved in attempting to improve medicines use. MaLAM has now changed its name to Healthy Skepticism, and it no longer sends letters critiquing specific advertisements.

Two papers report on the success of MaLAM's letters to companies requesting evidence to support claims made in advertisements^{246,247}. Wade et al.²⁴⁶ report on January 1988 to June 1989. In this time 10 companies were contacted about seventeen products, and fifteen replies were received. In four cases the advertising was changed, and in one the marketing of the product in developing countries was discontinued. Mansfield²⁴⁷ reports on the July 1989 to June 1990 period. Eight companies were contacted regarding nine drugs. No response was received from two companies, two said they would withdraw the claims, one that they would withdraw the indication, one that they would reformulate the product, and two that they would withdraw the products. In May 1995, MaLAM reports²⁴⁸ on Hoechst's discontinuation of Baralgin, presumably in response to a 1994 MaLAM letter. MaLAM operated on a very small budget, but seemed to be very effective in lobbying companies to change the worst examples of their advertising.

The Prescrire Network (described above) is also an attempt to monitor promotion. They have found that the legal requirements for sales representatives in France (that Summaries of Product Characteristics, and Transparency Commission reports be given to doctors) are frequently not met²¹⁸. The Prescrire network has identified many problems in presentations given by sales representatives to individual doctors, but there is no evaluation of the impact of the network itself.

Berings et al.¹¹⁸ report on an intervention to improve the prescribing of benzodiazepines by providing industry-independent information. They randomly allocated the 128 doctors in the study to three groups. One received no information, one received a pamphlet on rational prescribing of benzodiazepines that was similar in format to pharmaceutical company brochures, and one received the pamphlet and oral information from a visiting GP. Throughout the study, benzodiazepine prescriptions were recorded on specially designed prescription forms. During the four week follow-up period the groups which received both written and oral information prescribed 24% less benzodiazepines, those who received written information only prescribed 14% less, and the control group prescribed 3% less. There was no significant increase in the use of other psychotropics: in fact in the experimental group these also decreased. Forty of the 44 doctors who received the visit said that they would like more of these in the future.

4.12 Research as an intervention

Several authors, notably Milton Silverman, Philip Lee and Mia Lydecker have published descriptions and analyses of promotion and its effects, which appear to have been instrumental in improving the quality of promotional material.

In 1976 the Silverman team published *The Drugging of the Americas*, which compared promotion of 40 products by 12 companies in the US and Latin America. Looking at standard, widely used drug compendia, they found that promotional claims were exaggerated, and warnings were limited, minimised or entirely ignored. The findings were summarised in an article published in 1977²⁴⁹ which also notes the enormous media coverage the book received around the world. In 1982, *Prescriptions for Death*²⁵⁰, reported similar research in a wider range of countries: the USA, the UK, African countries, Indonesia, Malaysia, Singapore, Philippines and Latin America. Similar results were found. The groups' 1982 article²⁵¹ reports no readily apparent differences between US and other multinationals, multinationals and other domestic firms, brand and generic companies, or companies from the capitalist or the socialist block. Fieldwork for the third study was carried out in 1984, published in book form in 1986 and summarised in ²⁵². This involved 63 drugs, 1069 different products, 303 companies and 30 countries. They found noticeable differences between the results of their earlier work and the situation in 1983. Companies showed more restraint in describing the value of medicines and more willingness to disclose potential hazards. However, problems still existed, particularly in Latin American countries. The 1992 book *Bad Medicine*²⁵³ presents a more positive picture. Fieldwork for this was done in 1987/8, and included 40 drugs, 1500 products, 400 companies, in the US, UK and 74 developing countries. The authors concluded that most multinationals had improved considerably by the late 1980s. Local and domestic firms were now mainly responsible for inaccurate promotion. Silverman et al.'s books show a clear improvement over time in promotion in developing countries, and it is likely that the books themselves, by drawing international attention to the topic, have been at least partly responsible for this improvement.

CONCLUSION: Publication of descriptions of deceptive promotion can lead to improvements.

Summary of conclusions

Effective:

Government regulation of promotion is more effective than industry self-regulation

Educating doctors about drug promotion influences attitudes and can improve skills

Publicising deceptive promotion leads to improvements

Ineffective:

Industry self-regulation

Review by journal editors

Guidelines/regulations for sales representatives or for advertisements

Government control of post-marketing surveillance

Requiring research:

Which methods of educating doctors on drug promotion can change their behaviour

The influence of guidelines on the acceptance of gifts

The influence of guidelines on managing conflicts of interest in commercially-funded research.

Directions for future research

There is a need for greater linkage between research, interventions and evaluation is needed. Those planning interventions need to draw on previous research for designing and targeting their programmes. For example, previous reviews have suggested that some doctors rely heavily on promotion, and that their prescribing is also sometimes irrational. Interventions targeted at these doctors are likely to have a greater impact than those targeted at doctors in general, or particularly interventions which include volunteers only (likely to be those who are already sympathetic to rational prescribing messages). Interventions also need to be evaluated, and these evaluations need to be published so that others can learn from them. Reasonable follow-up times are needed, to show whether the effects of interventions persist over time.

Studies are also urgently needed comparing the effect of different regulatory frameworks. Najman et al.'s study²⁰⁵ was the only one included here which did this. Governments and others introducing policies to regulate promotional activities need good evidence of the advantages and drawbacks of different systems.

Final conclusions

Drug promotion strongly influences prescribing behaviour, but doctors underestimate this influence. Company funding of doctors, of educational events and of research are important elements in this influence.

Of various interventions to control or counter the influences of promotion, the only ones that have been found effective are government regulation, training of students (both before and after graduation), media exposure of abusive promotion, and free and abundant provision of reliable non-commercial therapeutic information to professionals and the public.

Research and policy questions to be addressed include the development of effective methods of educating doctors about drug promotion, the impact of guidelines on promotional gifts, and the development of effective guidelines for managing conflicts of interest in research. The effects of different regulatory frameworks also urgently need to be compared. Governments and other

organizations that introduce policies to regulate promotional activities need good evidence of the advantages and drawbacks of different systems.

Some promising research designs, such as that pioneered by Avorn et al. to determine how far prescribers' beliefs are influenced by promotional information, should be applied in different contexts. It could be used to examine a treatment for which there is strong scientific support, but little advertising, such as oral rehydration solution (ORS). If such a study also found that doctors claimed to be influenced more by scientific rather than commercial information, but tended not to prescribe ORS (because there is little or no commercial information about its benefits), Avorn et al.'s conclusions would be much strengthened. Such a study, using a modest telephone survey, would be relatively cheap. Research should also study actual prescribing patterns rather than relying on self reports. Studies should utilize a time series analysis to examine prescribing before and after visits by sales representatives looking for changes associated with these visits. It would be especially useful to explore prescribing in areas where there is a strong consensus about first-line therapy, for example strep throat and hypotension, to see if prescribing for these problems is influenced by representatives.

Finally, qualitative studies are essential to provide an understanding of prescribers' and patients' behaviour and their attitudes to commercial and non-commercial information. These would involve using focus groups from each population in multiple settings, for example, developed and developing countries, specialists and general practitioners, male and female doctors and patients. They should be done through semi-structured face-to-face interviews so that different trains of thought could be explored in sufficient detail to gain an in-depth understanding of behaviour and attitudes.

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Note: the availability of unpublished reference material (often a student thesis) is listed in the database entry (go to www.drugpromo.info, then the review article, and click on the entry number in the review article).

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