Promotion, Professional Practice and Patient Trust

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This chapter describes the wider context of promotion: the effects on discriminatory prescribing, on the health of patients individually and collectively and on the relationship between a clinician and a patient.

At the heart of this manual is the patient. Patients have a right to good care and providing it should be the aim and the responsibility of all health-care practitioners. This begins with the individual sitting with a clinician in a consultation – the patient is often worried, sometimes frightened, but almost always trusting that the health professional will provide advice based on the best available information. Above all, patients expect to be protected from unnecessary harm. Good care entails giving advice that is informed by both science and wisdom, which requires seeking out sources of good science on the harmful as well as the beneficial effects of the treatments available.

Prescribing and dispensing decisions must always balance the potential for benefit against the possibility of harm. It is important that in our desire to help patients who are suffering we do not add to their burden by inflicting the harms of medicines unnecessarily on them. It is easy to confuse the practice of medicine with the giving of medicines. However, good care also requires considering the effect of not doing anything or of using non-pharmacological treatments. Sometimes giving a medicine is not the wisest choice and the best course is to use other treatment options, or no intervention at all. Where effective treatments are not available, good care includes giving patients information and a sense of competence in coping or adjusting to illness so that life remains worth living. The giving of hope, appreciation of context, trust and reassurance are fundamental components of this interaction with patients. While patients should and do take an active role in their own care, and in deciding whether or not to take a professional's advice, good care also means not always giving patients what they request – particularly if their expectation is generated by misleading advertising.

Discriminatory prescribing

Giving a medicine is one of the riskiest things you will do for patients. Promotion, whether

direct or indirect, is aimed at increasing the use of newer, patented medicines. Being an early adopter of new medicines is not necessarily in patients' best interests, considering the often relatively small benefits and how little is known about unknown rare and long-term harms of newly introduced medicines. In minimising potential harm, adopting a 'precautionary prescribing' approach is safer.

Another key concept is that of discriminatory prescribing. The good prescriber is one who is discriminatory – who knows when to suggest a particular medicine, but most importantly when *not* to. Phillipe Pinel, a psychiatrist in 18th-century Paris, one of the earliest exponents of an evidence base to medicine, understood the concept of discriminatory prescribing well: *"It is an art of no little importance to administer medicines properly: but, it is an art of much greater and more difficult acquisition to know when to suspend or altogether to omit them."* (Pinel, 1809).

Not prescribing is often the best decision, for example, where the natural history of the illness is more acceptable than the hazards of treatment or where the effect of the medicine is so modest that it is clinically insignificant. Similarly, pharmacists and other dispensers need to know when and when not to recommend pharmaceutical treatment in response to patients' requests for advice, particularly in environments where prescription-only status is poorly enforced.

Misleading promotion: a note of caution

Why is developing a strategy for dealing with promotion important? The difficulty for physicians and pharmacists is that sources of independent evidence that should form the basis for good care are overwhelmed by the volume of promotional material. In the UK, for example, the pharmaceutical industry has a marketing budget of £1.65 billion – 300 times more than the UK National Health Service spends on independent information to health professionals (House of Commons Health Committee, 2005). To use medicines in a rational way requires access to sources of independent evidence on the effects of medicines, an understanding of the commercial biases that occur during the generation of that evidence and the ability to recognise and take account of the effects of misleading promotional material and activities.

The 'benefits' of indiscriminate prescribing and dispensing resulting from misleading promotion go directly to pharmaceutical companies and health professionals, but it is patients who bear the risks. Sometimes, they will be mortal ones. The case study of the Cox-2 inhibitor rofecoxib described in this manual is a stark, recent example of this – the risks of this medicine were known for four of the five years that it was promoted.

There are many other examples. In 1997 a new medicine, troglitazone, was introduced for the treatment of Type 2 diabetes and was promoted to the US public. It was quickly linked to severe liver damage and, by the end of 1997, was implicated in 6 deaths and 135 cases of severe liver toxicity. This led to its withdrawal from the UK market by the UK Medicines Control Agency at the end of 1997, just six weeks after it was made available. Despite this, it continued to be advertised to consumers and health professionals in the US. By the time it

was finally withdrawn from the US market, troglitazone was named as the probable cause of 391 deaths, 63 from liver failure. (Meek, 2001; Gale, 2001). Troglitazone had not been proven to save lives or reduce the complications of Type 2 diabetes. At the time of approval, the pharmaceutical company's chief executive was quoted as telling investors he saw the medicine as a "billion dollar blockbuster". This was correct. Rezulin (troglitazone) generated sales totalling US$2.1 billion for the company in its first three years on the US market (Willman, 2000). Since then, two newer forms of the glitazone medicines have been introduced – rosiglitazone and pioglitazone. Despite lowering glycated haemoglobin, there is no evidence that this drug group extends lives or reduces the complications of Type 2 diabetes. One of the main aims of diabetes treatment is preventing myocardial infarction (MI, better known as heart attack). Recent evidence indicates that rosiglitazone increases the risk of myocardial infarction (RR 1.42 95% C I 1.06 to 1.91) and doubles the risk of heart failure (RR 2.1 95% CI 1.5 to 2.9) (Singh et al., 2007). It is estimated that in 2006 there were 3.5 million users of rosiglitazone in the US alone, and that at a conservative estimate, this would result in 4,000 excess myocardial infarctions and 9,000 excess heart failure events (Singh et al., 2007). At the time of publication, rosiglitazone was still licensed for treatment.

Chronic conditions such as diabetes represent a large potential market for pharmaceutical companies, and long-term exposure to medicines for patients. Direct-to-consumer and associated direct-to-physician advertising are largely focused on a small number of medicines for chronic conditions (General Accounting Office, 2002). These medicines are new and still under patent (General Accounting Office, 2002). When prescribing and dispensing a long-term medicine for a chronic condition, there should be reasonable certainty that, on balance, it will relieve the burden of disease, not add to it. Similarly, when changing a medicine, there has to be clear evidence of clinical advantage for the patient, particularly if the medicine is newer and therefore more expensive while having less long-term safety data available. This is especially important for prescribing and dispensing of medicines for chronic conditions. Promotional pressure often exists to provide newer, more expensive medicines when patents expire on medicines a patient is currently taking. There are a number of examples where such promotion has led to widespread use of more costly medicines that are clinically identical to the parent medicine from which they were derived. This is illustrated in the case study of omeprazole and esomeprazole (Nexium) in Chapter 2. Other examples include citalopram and escitalopram, loratadine and des-loratadine. These are all single enantiomers of the racemic medicine that they have replaced. (An isomer has the same chemical formula, but only one specific configuration in space.) While there are instances in which new single enantiomers may bring improvements, in many cases, effects on the body are identical (Therapeutics Initiative, 2002).

Clinical decision-making carries an additional responsibility when introducing preventive treatments. There is an ethical difference between offering treatments when patients seek help for relief of their symptoms and making recommendations for treatments for prevention of future illness in people who currently think of themselves as well. When offering treatment to relieve symptoms we rely on the best available evidence with an awareness of its gaps, biases and uncertainties and some guidance from the patient's individual response to that treatment. For preventive treatments, a greater burden of proof

is needed that the treatment has a high likelihood of altering the natural history of that disease and that any improvement to the future health and well-being of the person in front of us is meaningful to them. It is important here to be aware of the role of promotion in constructing not only how we understand the effects of medicines, but also our understanding of disease and risk. For example, rating scales that have little meaning in health terms are often used to evaluate disease outcomes. Sometimes natural physiological processes, such as a gradual decrease in bone density as people age, are misrepresented as diseases. The phrase 'disease mongering' is used to describe this process of medicalisation (see Chapter 5).

Many people can be described as 'at risk' of chronic diseases so the potential for market expansion for pharmaceutical companies promoting treatments for prevention is enormous. The promotion of statins in populations who do not stand to benefit has resulted in the unnecessary exposure of large numbers of people to the potential harms of these medicines. There is no evidence that statins used for primary prevention protect women against non-fatal myocardial infarction or fatal heart disease, yet these medicines are promoted indiscriminately for both men and women (Eisenberg & Wells, 2008). Evidence for primary prevention with statins in the elderly is also lacking, yet these medicines are used indiscriminately in this group and are recommended for use in the elderly in treatment guidelines (Mangin et al., 2007). In addition, using these medicines for prevention in the population over 75 has other ethical implications. It appears that introducing this preventive intervention beyond the average lifespan, even in groups that do show cardiovascular benefit, has unintended effects on their health and lives. Looking at the balance of overall benefits and harms, we may be simply changing a patient's cause of death with medicines rather than improving or extending his or her life. An elderly person who is told that a medicine will "*reduce the risk of heart attack and stroke by…*" may make a different decision when the rider is added "*however you will not extend your years of life and you will increase your risk of being diagnosed with and dying of cancer by the same amount.*" The potential harms are not just those related to the medicines themselves or to patients with chronic disease. Preserving health also means avoiding unnecessary medical care and medicalisation among the healthy.

These examples show how promotion influences the landscape you work in and how it may compromise good care, discriminatory prescribing and dispensing and the ethical practice of medicine.

Promotion and clinical practice

Promotion of pharmaceuticals is designed to drive prescribing decisions in order to stimulate sales. This manual describes examples of a range of promotional techniques used by pharmaceutical companies to influence the prescriptions you write and dispense for your patients. The description includes the carefully constructed links in the chain of commercial influence on clinical practice that begins with control of research design and interpretation as well as publication decisions and the development of treatment guidelines based upon that research. A study published in the *Journal of the American Medical Association* (2002) showed that four out of five experts responsible for clinical practice guidelines have

financial relationships with pharmaceutical companies, and the majority of these experts "had relationships with companies whose drugs were considered in the guideline they authored." (Choudhry, 2002). This is compounded by the level to which opinion influences these guidelines. A recent review of the American Heart Association and the American Cardiology Association guidelines showed that of 2,711 recommendations, half were based on level C (expert opinion) evidence while only 1 in 10 was based on strong (level A) evidence (Tricoci, 2009). Promotion continues with attempts to directly influence your clinical practice through advertising and sales representative visits and indirect marketing techniques. Added to this is the effect of promotion on the beliefs and desires of all of us, both doctors and patients, through direct and disguised direct-to-patient advertising.

Pharmaceutical companies' primary responsibility is quite appropriately to maximise profits for shareholders. The purpose of regulation is to ensure that these interests do not override the values of good clinical care and the interests of individuals and society. Regulation to protect patients from harmful products and misleading claims has failed to control the negative influence of promotion on patients and on the credibility of the medical profession. This is because adequate regulatory frameworks either do not exist, are inadequately monitored and enforced or are compromised by conflict of interest or because promotional activities are not recognised as such. This is most obvious in the case of heavily-promoted medicines with a greater potential for harm than benefit. However, much more commonly, a medicine does have some useful effects in a particular group of patients, but promotion creates adverse effects by extending treatment into populations in which pharmaceutical treatment is not indicated, or in which benefits do not outweigh harm for this particular medicine.

The responsibility of health professionals

Pharmaceutical companies are simply fulfilling their role as commercial businesses in trying to sell more medicines to more people in order to increase profits for shareholders. They have some products that are helpful in life-transforming ways for some people, but pharmaceutical companies, through their marketing departments, are fundamentally traders trying to increase profit rather than being altruistic organisations trying to improve health. It is our failure as health professionals to recognise this fact and respond appropriately to promotion and poor science that results in harm to patients. Some potential ethical 'red flags' have been highlighted in this manual to help you see when you or those who might influence you, are in situations likely to lead to a direct conflict of interest. The challenge for you now is how you will deal with this in order to provide the best possible care for your patients. All of us are vulnerable to conflicts of interest and the influence of promotion – they are designed to act through our own most basic desires and sense of entitlement, altruism, obligation and reciprocity. This is well understood by the pharmaceutical marketing industry.

Health professionals usually believe that while others are influenced by promotion they personally are not. This is an illusion. "*To do the bigger scams you need the victims to trust their own capabilities and experience*," a fraud expert said, commenting on the particular vulnerability of doctors to being misled because they thought they were doing good

(Malvern, 2008).

As you have read, this attempt to influence your behaviour begins during your student years, with direct as well as indirect promotion using sales representatives, sponsored education, gifts and modelling from your colleagues and teachers. Until now, there has been little help within the medical and pharmacy curriculum to assist students in dealing with this 'hidden curriculum'. The aim of this manual has been to improve your understanding and awareness of the ways in which you will be influenced. If you think that after using this manual you are immune to this influence then it has failed in its intent. We will all experience situations that create conflicts of interest. We are all subject to the effects of conflicts of interest and promotion. The important thing is how to ensure that the care and the trust of our patients is not compromised. This involves personal approaches to mitigate the effects of promotion as much as possible and to understand the ways in which we are influenced. It also involves thinking proactively about the potential for conflicts of interest and how to manage them while being open and honest about their influence.

The characteristics that define a profession are clearly described (Downie, 1990). One of these has direct relevance to promotion: a credible profession should be independent of the influence of the state or commerce (Downie, 1990). While it is not possible to escape influence, the current entanglement between health professionals and pharmaceutical companies has been and continues to be deeply corrosive to the practice of medicine. More money is spent by pharmaceutical companies on promotion than on research and development, so much of the cost of medicines to patients, health-care agencies and governments goes towards paying for this promotion (General Accounting Office, 2002). The rise of the corporate model of health care may have helped promote entanglement and validate the passage of large sums of money as well as other ties between pharmaceutical companies and health professionals. These ties are increasingly coming under public scrutiny. There are calls to mitigate the effects of promotion with disentanglement and increased transparency in research and development of guidelines as well as disentanglement of professionals from pharmaceutical company promotional activities. This requires social change and improvements in research transparency, regulatory oversight and institutional policies, as well as individual responses. These will not work unless individual prescribers and dispensers act from early in their training to make sure these principles are incorporated into the framework of professional practice. Students groups such as the American Medical Students Association are becoming increasingly active in this area.

Society aims to improve each individual's experience of life by minimising the burden of suffering due to ill health. Clinicians can contribute to this by providing the highest quality individual health care, but this on its own will be overwhelmed if the system within which such care is provided is flawed. It is equally important to advocate as professional groups for ongoing improvement in the systems within which this care is provided – structural therapeutics. This advocacy is an important part of physicians' role in not just 'doing no harm' but in ensuring that the promise of the benefits of improved medical care and advances in science are realised.

Student exercises

1.Dealing with promotion and conflicts of interest

There are a range of options for engaging with the pharmaceutical industry and dealing with promotion. The aim of this final section is to help you to begin thinking about the approaches you will take in recognising and dealing with the effects of different promotional strategies and ethical dilemmas in your professional life. This exercise will give you the basis of a personal approach to promotion.

- Compile a list of promotional strategies and ethical conflicts you are likely to encounter once you are in professional practice;
- Think about the risks and benefits you perceive from each for you and for your patients;
- Assess whether there are alternative ways of achieving these benefits; and
- Plan your strategy for dealing with each one.

Fill in the table below about five key promotional strategies.

Promotional strategy / conflict of interest	**Risks and benefits for you and your patients**	**Alternative way of getting the same benefits**	**Your personal strategy**
1.			
2.			
3.			
4.			
5.			

2. Independent information

An important step in minimising the harmful effects of promotion is the development of positive strategies to improve prescribing. What resources are available in your country? Where can you get independent, unbiased, comparative information about medicines? Are there similar resources available for patients?

Discuss this with your professors, fellow students, librarians and others who you believe may know what resources are available. Access the suggested resources and list the three you believe will be the most useful, either for you or your patients.

1. What are the positive characteristics that made you choose them?
2. How do you think you might use each of them (or already use them)?
3. Are there any drawbacks or gaps in information?

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