Important New Evidence Service

In Partnership with The Centre for Medicines Optimisation at Keele University

ScriptSwitch™ Rapid Update 1 – October 2017

Are drugs approved on the basis of surrogate outcomes promoted appropriately by pharmaceutical representatives?

A new study has investigated unwarranted claims of clinical efficacy for drugs by pharmaceutical sales representatives to primary care doctors in the US, France and Canada. Claims of significant morbidity or mortality benefits for drugs approved on the basis of surrogate outcomes were reported to have been made in nearly half of all promotional visits. Many doctors may consider themselves to be immune from influence by the pharmaceutical industry; however, promotional visits from pharmaceutical representatives have been shown to impact the prescribing patterns of doctors. While the results of this new study cannot necessarily be generalised to the present day situation in the UK, this study highlights that such promotional activities do occur and that prescribers should be aware of this.

Reference: Habibi R, Lexchin J, Mintzes B *et al.* Unwarranted claims of drug efficacy in pharmaceutical sales visits: are drugs approved on the basis of surrogate outcomes promoted appropriately? Br J Clin Pharmacol. 2017 Jun 29. doi: 10.1111/bcp.13360.

What do we know already?

- Visits from pharmaceutical representatives are one of the factors shown to influence the prescribing behaviour of doctors (Lieb and Scheurich, 2014). While it is possible that promotional activity may sometimes improve prescribing, several systematic reviews have found that most studies investigating prescribers' interactions with pharmaceutical companies and their clinical actions reported associations with higher prescribing frequency, higher prescribing costs, or lower prescribing quality (Spurling *et al*, 2010; Brax H *et al*, 2017). Paradoxically, surveys suggest that many doctors consider themselves to be immune to pharmaceutical marketing (Rutledge *et al*, 2003; Morgan *et al*, 2006; Gross *et al*, 2011;).
- Inappropriate promotional activities include inflated claims of drug efficacy. One example of inappropriate promotion is claiming that a drug has a benefit on a clinically important, patient-oriented outcome (such as protection from a cardiovascular event or a reduction in the risk of mortality) when that drug that has only been approved based on an evaluation of surrogate, disease-oriented outcomes (for example, reductions in biomarkers, such as HbA1c).
- The use of surrogate endpoints is often accepted by regulatory agencies to support drug approvals, with proponents arguing that market access is expedited. However, effects on surrogate outcomes may not always translate into benefits in clinical outcomes. For example, rosiglitazone was a drug approved on the basis of surrogate outcomes but which was found to increase, and not decrease, cardiovascular risks.

What does this evidence add?

- This study analysed doctors' recall of visits from pharmaceutical representatives to promote brand-name drugs used in the treatment of hypertension, hypercholesterolaemia or diabetes, focusing on unwarranted claims of serious morbidity or mortality benefit – an aspect of inappropriate promotion that the authors suggest has been the subject of little investigation.
- Claims of clinically meaningful benefit were reported in 42% of visits concerning drugs that had only been approved on the basis of surrogate outcomes. Furthermore, doctors indicated they were nearly twice as likely to be 'somewhat or very likely' to prescribe a 'surrogate outcome' drug if a claim of serious morbidity or mortality benefit was reported during the promotional visit.
- In the UK, the Association of the British Pharmaceutical Industry (ABPI) Code of Practice regulates the advertising of medicines for prescription to healthcare professionals. It also covers the information about prescription-only medicines that is made available to the general public. The Prescription Medicines Code of Practice Authority (PMCPA) is responsible for administering the ABPI code for the pharmaceutical industry.

- This particular study relates to pharmaceutical representative visits to doctors in the US, France and Canada in 2009 and 2010, thus it is uncertain how applicable these findings are to today's ABPI-regulated interactions between the pharmaceutical industry and prescribers in the UK. Based on the cases currently under investigation by the PMCPA, code breaches relating to inappropriate promotional claims by representatives appear uncommon in the UK. For healthcare professionals who have any concerns about materials or activities in relation to the ABPI Code, the PMCPA can be contacted at complaints@pmcpa.org.uk.

Study details

Study Design:

- The study was a pre-planned subgroup analysis of a prospective cohort study of pharmaceutical sales representative visits to primary care physicians in Montreal and Vancouver (Canada), Sacramento (United States) and Toulouse (France).
- Between 2009 and 2010, primary care physicians were included if they met with sales representatives in their regular practice, worked at least 20 hours per week and served a greater than 50% primary care population. Member of advocacy groups, including Healthy Skepticism and No Free Lunch, were excluded.
- Physicians saw sales representatives as per their usual practice and recorded information about the subsequent eight consecutive promotions for diabetes, hypertension or hypercholesterolaemia drugs. This information was captured using a questionnaire adapted from previous observational studies undertaken in France, Australia and Malaysia and subsequently pilot-tested by 15 physicians and 41 promotions in British Columbia.
- Comparisons were made between how frequently physicians reported that sales representatives made claims of serious morbidity or mortality benefit i.e. a claim of a clinically meaningful patient-oriented outcome for drugs approved on the basis of surrogate outcomes versus drugs approved on the basis of clinical outcomes.
- The researchers also examined the physicians' intent to prescribe a surrogate outcome drug after a claimed effect on serious morbidity or mortality was made, versus a promotion where no such claim was made. 'Intent to prescribe' was rated on a 4-point scale in which physicians rated themselves as 'somewhat likely', 'very likely', 'somewhat unlikely' or 'very unlikely' to prescribe. Responses were then combined into two categories: 'somewhat or very likely to prescribe' and 'somewhat or very unlikely to prescribe'.

Results:

- 448 promotions for 58 brand-name drugs were made to 196 physicians (92 in Canada, 57 in France and 47 in the U.S.).
- Physicians received a median of 2 promotions (range 1 – 7) and the majority of promotions (77%) were for drugs approved on the basis of surrogate outcomes.
- 83% of promotions occurred during one-to-one visits. In 76% of promotions, the drug had previously been promoted to the same physician and in 67% of promotions, the physician had previously prescribed the drug. 67% of promotions were longer than 5 minutes.
- Claims of clinically meaningful benefit were reported in 156 (45%) of the 347 promotions for 'surrogate outcome' drugs.
- For drugs that had been approved on the basis of clinically important outcomes, claims of clinical importance were reported to be made in 72 of the 101 promotions (71%).
- Physicians were nearly twice as likely to report being 'somewhat or very likely' to prescribe a surrogate outcome drug if a claim of serious morbidity or mortality benefit was reported during the promotion (Odds Ratio = 1.9; 95% Confidence Interval 1.1 to 3.9, p = 0.01).

Level of evidence:
Level 3 (other evidence) according to the SORT criteria.

Study funding:
Funded by Michael Smith Foundation for Health Research and Institute of Health Services and Policy Research.