Interpreting evidence in general practice

Bias and conflicts of interest

CPD

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Background
Sponsorship of research and education occurs commonly in the pharmaceutical, medical device, and food and drink industries. This sponsorship is a conflict of interest, creating a situation where there may be bias in favour of the sponsors' interests. General practitioners (GPs) need to be aware of potential conflicts of interest in industry-sponsored research and education.

Objectives
The aim of this article is to alert GPs to the risk of bias in research and education funded by for-profit organisations, and to provide strategies to avoid being influenced by information that may be biased.

Discussion
Types of bias known to be associated with industry sponsorship include: methodological bias, where there is a systematic error in the design, conduct or analysis of the study such that it deviates from the truth; agenda bias, where study topics align with increased use of industry products; publication and reporting bias, where unfavourable studies or results are suppressed or omitted; and marketing bias, where supportive evidence is preferentially disseminated and sympathetic opinion leaders are given a broad platform. Industry influence can be reduced by seeking out independent reviews and avoiding industry-funded educational events.

GENERAL PRACTITIONERS (GPs) are likely to use evidence from a variety of sources to assist their daily practice. These sources might include published scientific studies, systematic reviews, clinical guidelines, educational seminars and conferences, discussions with colleagues, health news in the lay press, advertisements in professional journals and visits from sales representatives. Industry sponsorship of sources of evidence, including research and education, creates a conflict of interest, resulting in a risk of bias in related information.[1–6] Biased evidence may exaggerate benefits and downplay adverse effects of a sponsor's drug, leading doctors to prescribe treatments that are ineffective and/or harmful. Biased evidence may also aim to create a need for a sponsor's product, which facilitates overdiagnosis and over-treatment.[7] This can lead to unnecessary prescriptions in situations where detection and management of conditions does not provide any benefit to the patient.[8]

Conflicts of interest are defined as a set of circumstances that create a risk that professional judgements or actions regarding a primary interest will be unduly influenced by a secondary interest.[9] Industry sponsorship in the form of money, food, travel costs or other gifts is a conflict of interest in medical research or education because it constitutes a situation where there is a risk that primary professional interests (which should include research integrity, medical education and/or patient welfare) will be unduly influenced by secondary interests (eg money). Industry sponsorship can result in bias in the way that evidence is created, disseminated and discussed in such a way as to preferentially align with the interests of the funding entity. Key concepts around bias and conflicts of interest in evidence are summarised in Box 1.

Industry sponsorship is not the only source for conflict of interest, and a conflict of interest does not necessarily lead to bias. However, in the context of generating and disseminating evidence in health and medicine, the links between industry sponsorship and bias are strong. This is particularly the case in relation to the pharmaceutical industry[1] and the tobacco industry,[10] and it is increasingly recognised in food and drink industries.[11] Every GP should be aware of the risk of bias when industry sponsorship is involved and have the means to avoid its influence.

Bias in evidence used by general practitioners

Most clinicians are familiar with the concept of methodological bias – a systematic error or deviation from the truth in results or inferences.[12] Methodological bias within individual studies can be difficult to detect and may sometimes go unnoticed by peer reviewers of academic articles. Examples of methodological bias include the following:

- Study populations differ in material ways – for example, the study population may have a younger average age than the control population. This can occur through non-random recruitment and allocation of participants (selection bias; eg if randomisation is not blinded)

or unequal dropout (attrition bias) – for example, if the dropout rate is higher among young patients in the control group).
- Some study variables are more relevant than others (performance bias) – for example, the control group may be given a subclinical dose of the control drug, while the study group receives a clinical dose of the trial drug.
- Data collection is flawed (detection bias) – for example, a non-blinded study for reporting and recording of subjective data such as pain or nausea, or a data collection period that is too short to pick up important late outcomes.
- Data analysis is faulty (reporting bias) – for example, selected results or analyses are excluded.

Individual study publications may also contain bias due to misleading presentation or discussion of results – for example, non-significant results may be described as a promising trend; significant secondary outcome results may be highlighted in the abstract while non-significant primary outcomes are omitted; an observational study may be inappropriately interpreted as indicating causality.[13] This kind of bias is sometimes called 'spin'.

Other sources of bias are less frequently talked about and harder to detect within individual studies but may become apparent across a body of evidence. These kinds of bias are increasingly understood to be associated with industry sponsorship. For example, a recent Cochrane review found that studies sponsored by drug or device companies are more likely to report results and conclusions favourable to the sponsor than studies not receiving industry sponsorship, even when studies are equally well designed and free from detectable methodological bias.[1]

Box 1. Key concepts in bias and conflicts of interest

Sources of bias in evidence

Agenda bias: bias due to patterns in the topics selected for study, review or clinical guidance

Methodological bias: a systematic error or deviation from the truth in results or inferences[12]

Spin: misleading presentation or discussion of results

Publication and reporting bias: entire studies or selected results go unpublished

Marketing bias: selected publications or results are highlighted, for example, in commentaries, media reports, seminars or conversations

Conflicts of interest are circumstances that create a risk that professional judgements or actions regarding a primary interest will be unduly influenced by a secondary interest.[9] For example, industry sponsorship of research or education is a conflict of interest because it creates a risk that research integrity, medical education and/or patient welfare will be unduly influenced by industry.

Agenda bias

Bias can arise in a body of evidence through patterns in the topics and questions that are selected for study, review or clinical guidance. For example, research sponsored by the pharmaceutical and medical device industries is likely to focus on pharmaceutical or device management for an illness rather than non-pharmaceutical strategies.[14] Food industries are likely to study specific nutrients rather than whole food groups or dietary patterns, because specific nutrients are more amenable to manipulation within industry products.[15] Industries that produce products found to be harmful to the public's health are likely to pursue research agendas that deflect from the harms. For example, the sugar industry has been found to pursue a research agenda focused on reducing the impact of sugar on dental caries rather than ways to reduce sucrose intake.[11] Similarly, tobacco industry research focuses on air pollutants other than secondhand tobacco smoke, distracting from tobacco smoke as a hazard.[10]

Publication and reporting bias

Study results may be suppressed if they are not favourable to the sponsor. This may mean that selected results within a study are omitted from final publications, or that entire research studies remain unpublished or are published only after a significant time lag.[16] For example, internal company documents relating to industry promotion of the Pfizer drug Neurontin (gabapentin) clearly state that trials on the benefit of Neurontin for neuropathic pain would, if positive, be published and publicised in medical meetings. Those with negative findings were not to be published.[2]

Well-conducted systematic reviews should include an assessment of methodological bias, but they may be also affected by agenda bias or publication and reporting bias. Guidelines may perpetuate biases from individual studies and systematic reviews, and the recommendations of guideline authors may be biased because of financial conflicts of interest such as payments from industry for consulting, advisory roles or speakers' bureaus.[17]

Marketing bias

Research is often used as a marketing tool by the pharmaceutical industry. Industry discussion and distribution of research literature occurs, for example, during personal drug representative visits and sponsored educational events. Published research distributed during face-to-face visits and events and cited in journal advertisements may be carefully selected for items that are favourable to the sponsor, while unfavourable items are omitted. This perpetuates and amplifies biases in original studies, leading to an inaccurate impression of the true events.[2]

Similarly, key opinion leaders speaking at industry-funded educational events may be carefully selected spokespersons, known to be sympathetic to industry products and capable of influencing large numbers of medical colleagues. Prominent clinicians who are critical or questioning of industry products are likely to receive fewer invitations to speak at industry-funded events and less airtime in general. The pharmaceutical industry has well-developed strategies to identify sympathetic, high-profile clinicians and give them opportunities to speak favourably about particular medications.[18,19] Industries may release biased media reports, leading to unrealistic patient expectations and requests to GPs for inappropriate medications.[20]

How to detect and avoid bias

There are a number of strategies that GPs can use to detect biased evidence and avoid its use in guiding their practice.

Published research and guidelines

- When reading published literature (including original studies, systematic reviews and guidelines), check for signs of industry sponsorship. For example, always read research funding and conflicts of interest statements and recognise that industry funding of a study or individual authors confers a risk of bias.
- Where possible, rely on high-quality systematic reviews and meta-analyses. Rigorous reviews (such as Cochrane reviews) do not cherry pick the literature – they do a thorough search, and they assess and take into account biases in the included studies. Even systematic reviews, however, may not report on agenda or publication bias.
- When reading an original study, always read the methods section carefully and check for signs of methodological bias. Look for hints that there could be publication bias, such as lack of a clear protocol in the study design. Compare published outcomes with planned outcomes in clinical trial registries. Read from reputable, peer-reviewed journals. Do not rely on the news or reported versions.[6,21]
- Seek out independent sources of information likely to be free from industry sponsorship, such as the Cochrane Library collection[22] and NPS MedicineWise.[23]

Educational events

- When considering educational events, always check who has sponsored the event. If possible, attend events that are independent of industry funding. If industry sponsors are present (eg at large conferences), avoid sponsored content.
- Decline invitations to industry-sponsored talks by key opinion leaders.

Marketing materials and activities

- Refuse offers of free meals, gifts, paid travel, free drug samples and visits from sales representatives. Studies have repeatedly shown that clinicians are not immune to influence.[24] For example, a recent study of doctors in the US found a significant association between the consumption of small amounts of 'free food' (generally at less than $US20 per meal) from the pharmaceutical industry and prescription of the promoted drug.[25]

Conclusions

GPs should be aware of the potential for bias in evidence and information arising from industry-sponsored work. Industry sponsorship creates a substantial risk of bias in research and educational events directed at GPs. It would be beneficial for GPs to adopt a suite of strategies to minimise their exposure to potentially biased information.

Key points

GPs who rely heavily on evidence from people who have financial ties with industry may be receiving biased information. This may influence their clinical practice and be detrimental to patient outcomes. The following is a daily guide to using evidence in general practice.

- Read the section pertaining to conflict of interest in published literature, including reviews and guidelines, and be sceptical about those written by professionals who receive industry sponsorship.
- Read independent systematic reviews of evidence and use independent clinical practice guidelines.
- Be aware of agenda bias, even in independent reviews, and actively seek information about non-pharmaceutical interventions.
- Educate yourself about conditions that are prone to overdiagnosis and overtreatment.
- Take particular care to model professional independence from industry to your junior trainees.
- Refuse the offer of gifts, even low-cost meals and drug samples, from industry sales representatives.
- Do not rely on industry-funded educational events for continuing professional development.

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