

# Drug Watch

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## Reporting bias in randomised controlled trials

A study published 15 February 2010 has examined the prevalence of outcome reporting bias and its impact on Cochrane reviews. The authors found selective publication of only part of the results in many reviews.

More than half [157/283 (55%)] the reviews did not include full data. The median amount of data missing for any reason was 10%, whereas 50% or more of the potential data were missing in 70 (25%) reviews. A third of Cochrane reviews [96/283 (34%)] contained at least one trial with high suspicion of outcome reporting bias for the review primary outcome. In a sensitivity analysis undertaken for 81 reviews, the treatment effect estimate was reduced by 20% or more in 19 (23%). Of the 42 meta-analyses with a statistically significant result, eight (19%) became non-significant after adjustment for outcome reporting bias and 11 (26%) would have overestimated the treatment effect by 20% or more.

Outcome reporting bias is an under-recognised problem that affects the conclusions in a substantial proportion of Cochrane reviews. Individuals conducting systematic reviews need to address explicitly the issue of missing outcome data for their review to be considered a reliable source of evidence.

BMJ. 2010;340:c365.

## Prescribing safeguards for ESAs

The FDA and Amgen have notified healthcare professionals and patients that all Erythropoiesis-Stimulating Agents [ESAs – darbepoetin (Aranesp), Epoetin (Epogen), erythropoietin (Procrit)] must from now on be prescribed under a risk management programme to ensure their safe use.

The warning is based on studies which have shown an increased risk of tumour growth and shortened survival in patients who use these drugs for cancer, and an increased risk of heart attack, heart failure, stroke or blood clots in patients who use these drugs for other conditions.

As part of the risk evaluation and mitigation strategy, a Medication Guide explaining the risks and benefits of ESAs must be provided to all patients receiving ESAs. In addition to the Guide, Amgen was required to develop the ESA APPRISE Oncology programme for healthcare professionals who prescribe ESAs to patients with cancer.

Under this programme, Amgen will ensure that only those hospitals and healthcare professionals who have enrolled and completed training in the programme will prescribe and dispense ESAs to patients with cancer. Amgen is also required to oversee and monitor the programme to ensure that hospitals and healthcare professionals are fully compliant with it.

[www.fda.gov/Drugs/search/ESAs](http://www.fda.gov/Drugs/search/ESAs)

## Voltage-gated sodium channels as therapeutic targets

An article published in *The Lancet*, April 2010, discusses the possibility that voltage-gated sodium channels (VGSCs) are key mediators of intrinsic neuronal and muscle excitability in the brain.

Abnormal VGSC activity is central to the pathophysiology of epileptic seizures, and many of the most widely used antiepileptic drugs, including phenytoin, carbamazepine and lamotrigine, are inhibitors of VGSC function. These antiepileptic drugs might also be efficacious in the treatment of other nervous system disorders, such as migraine, multiple sclerosis, neurodegenerative diseases, and neuropathic pain. In this review, the authors summarise the structure and function of VGSCs and their involvement in the pathophysiology of several neurological disorders. They also describe the biophysical and molecular bases for the mechanisms of action of antiepileptic VGSC blockers and discuss the efficacy of these drugs in the treatment of epileptic and non-epileptic disorders. Overall, clinical and experimental data indicate that these drugs are efficacious for a range of diseases, and that the development of drugs with enhanced selectivity for specific VGSC isoforms might be an effective and novel approach for the treatment of several neurological diseases.

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## Meta-analysis: statins and risk of incident diabetes

There is controversy about the risk of development of diabetes in patients treated with statins. However a meta-analysis published early online 17 February 2010 by *The Lancet* found that although statin therapy is associated with a slightly increased risk of incident diabetes, the benefits of statin therapy in the reduction in coronary events outweigh the risk.

The authors searched Medline, Embase, and the Cochrane Central Register of Controlled Trials from 1994 to 2009 for randomised controlled endpoint trials of statins with more than 1,000 patients, with identical follow-up in both groups and duration of more than one year. The authors concluded that the benefit in preventing total vascular events to the risk of diabetes is a ratio of about 9:1 in favour of the cardiovascular benefit - the benefit clearly outweighs the risk.

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