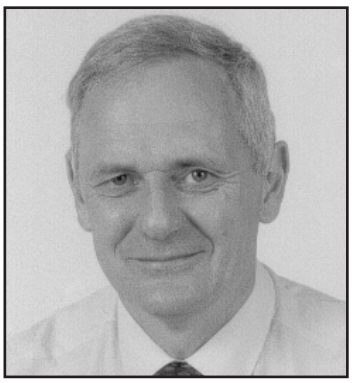
Lessons from the troglitazone story: don't believe everything you hear



Edwin Gale

Can I say that reading a paper about diabetes has changed my life? Not without some exaggeration, or revealing myself as rather a sad individual. Certainly not when compared to the life-changing effect of attending a summer camp for children with diabetes. My life event resulted from trying to write a paper. It began with a phoned request to review glitazones at the 2000 meeting of the European Association for the Study of Diabetes. I reeled off the names of people who were more qualified to do the job. 'We're looking for someone who is not in the pocket of the companies', came the response. Ridiculous, I thought. My own sponsored presentations for other companies had not biased my opinions in any way. But – on reflection – had my true beliefs been fully and frankly explored? Possibly not. A worm of doubt began to squirm.

As in any new area, the first task was to assemble the papers and review the evidence. It was disconcerting to realise the lack of published evidence supporting the use of drugs to which around 3 million people had already been exposed. Lesson one: big pharmaceutical companies see clinical studies as a means of satisfying the regulators and promoting sales, not of providing information. Published reports are not designed to help clinicians use the new agent effectively; they are selected and slanted in such a way as to persuade us to use the new agent. Hence the huge amount of junk literature of irrelevant and badly reported studies with misleadingly optimistic titles.

Next time the representative comes to see you with a heap of glossies, ask him or her how many trials conform to CONSORT reporting standards? The pile will dwindle. Ask how many relevant studies in the summary of product characteristics (SPC) are fully published? Where it says 'data on file', ask to see them – you have the right to do so. When the representative provides a clinical review by a leading authority in the field, turn immediately to the conflict of interest statement. If it says 'none', yet the author has done sponsored studies on the agent (often cited in the same review) and performed on the platform of symposia, the author is a self-confessed liar. Are you going to believe the rest of what they tell you?

Harmless enough, you might think. After all none of us, myself included, is in a position to cast the first stone. And yet, it is not harmless. No-one will ever know how many people were killed by troglitazone, perhaps somewhere between 200–1000, and yet the culture of secrecy protected the industry (which had a $2.1 billion turnover) from full and timely disclosure of the mounting evidence of risk. No adequate head-to-head comparison with metformin was ever performed. Not one physician stood up to say that the evidence base was inadequate and that no drug for diabetes is worth dying for. It was, in fact, internal rebellion at the FDA and the work of an investigative journalist at the *Los Angeles Times* (who won a Pulitzer Prize for doing so) that helped to get it off the market. One year before it was finally withdrawn in the US (21 March, 2000) the American Endocrine Association officially condemned the work of a public interest group fighting to get the drug withdrawn. Every claim made by the interest group was subsequently confirmed. Our profession did absolutely nothing to protect the public. No-one wants to remember troglitazone. It is treated as an unfortunate aberration of the system. It was not. It was a consequence of the system. Finding that out certainly changed my life.

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Gale EAM (2001) Lessons from the glitazones: a story of drug development. *Lancet* **357**:1870–75

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