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EDITOR'S CHOICE

Secrecy does not serve us well

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A slow moving, desert dwelling lizard that eats only a few times a year inspired a whole new class of diabetes drugs. Glucagon-like peptide-1 (GLP-1) agonists, developed initially from a peptide extracted from the Gila monster's saliva, are now taken by millions of people around the world. Together with DPP-4 inhibitors, their apparent ability to reduce hyperglycaemia without causing weight gain is an important advance on older off-patent diabetes drugs, and has created a huge new market for the drug industry.

But have clinicians and patients been adequately informed about safety concerns—specifically about possible increases in the risk of pancreatitis and pancreatic cancer? A *BMJ* investigation and linked editorials published this week suggest that they haven't (doi:10.1136/bmj.f3680).

After reviewing thousands of pages of regulatory and other documents obtained through freedom of information requests, Deborah Cohen has found that the drug manufacturers and regulators have had in their hands ample warning signs and chances to resolve some of the controversies. But the regulators have been slow to pursue safety concerns. Rather than insist on further independent research, they have allowed themselves to be reassured by the drugs' manufacturers.

Cohen has unearthed unpublished data from animal and human studies that point to pathological changes in the pancreas. These changes are consistent with the drugs' mechanism of action, suggesting that unwanted proliferative effects could have been anticipated and properly investigated at an early stage. She has also uncovered attempts by drug companies to suppress scientific debate through pressure on academics and medical journals.

As Thorvardur Halfdanarson and Rahul Pannala emphasise in their accompanying commentary (doi:10.1136/bmj.f3750), the observational studies available so far do not prove causality. Adverse event databases that rely on voluntary reporting are limited by the potential for reporting bias. Because of this, manufacturers and others say we should wait for the outcome of further clinical trials. But trials will have to be enormous to exclude an increased risk of pancreatic cancer, and unless the rules on openness of clinical trial data have changed radically by the time they are reported, most of the data will remain hidden from independent scrutiny. Meanwhile, as Sonal Singh asks in Cohen's piece, "who bears the burden of the passage of time while these debates are settled?"

So what should doctors and patients do? Victor Montori concludes that after careful reflection most patients and clinicians may opt to avoid using GLP-1 based drugs at all, or to avoid them early in the disease or for long periods (doi:10.1136/bmj.f3692).

Edwin Gale concludes that the drugs' fate has yet to be determined, but that, once again the current regulatory procedures have been shown to be inadequate, especially for so called shotgun drugs—those, like the GLP-1 based drugs, that act on many targets. "Similar scenarios will play out again while secrecy rules and companies control access to the data" (doi:10.1136/bmj.f3617).

Science thrives on open challenge and objective debate. Patients will not receive safe and effective care in an environment characterised by commercial secrecy, bullying of academics and journal editors, or reliance on overstretched regulators.

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