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Insight into how pharma manipulates research evidence: a case study

Here Jon Jureidini explains what he encountered while examining internal documents as an expert witness in a case against a pharmaceutical

company.

It's well known that academic literature on medication in psychiatry is distorted by selective publication – failing to publish studies with negative results or selectively publishing only positive results from studies with mixed outcomes.

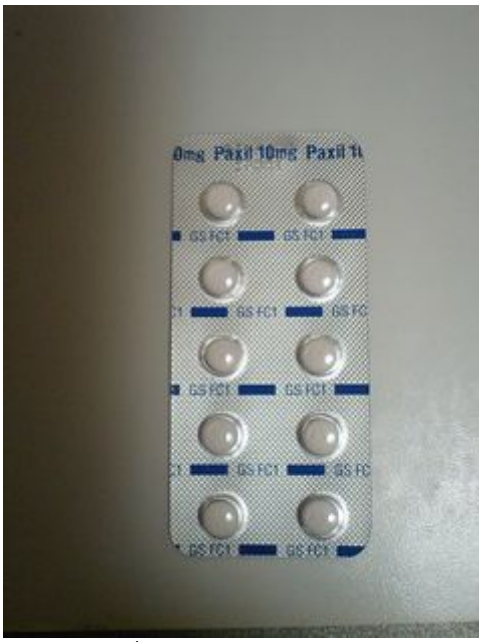
I had the unusual opportunity to see inside the process of how the marketing department of a pharmaceutical company controls and distorts information in the medical literature. This chance arose when I was provided with access to a huge number of internal documents because I acted as an expert witness for a US law firm.

Between 1993 and 1998, SmithKline Beecham (SKB, subsequently GlaxoSmithKline) provided **$5 million** to various academic institutions to fund research into paroxetine (also known as Aropax, Paxil (GSK) or Seroxat), led by **Martin Keller**. Keller was from Brown University and received $800,000 for participation in the project.

The results were published in 2001 by Keller et al. in the **journal article**, "Efficacy of paroxetine in the treatment of adolescent major depression: a randomized, controlled trial", in the **Journal of the American Academy of Child & Adolescent Psychiatry (JAACAP)**. The article concluded that "paroxetine is generally well tolerated and effective for major depression in adolescents".

This was a serious misrepresentation of both the effectiveness and safety of the drug. In fact, when

SKB set out **their methodology** for their proposed study protocol, they had specified two primary and six secondary outcome measures. All eight proved negative, that is, on none of those measures did children on paroxetine do better than those on placebo.



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The published article misrepresented one of the primary outcomes so that it appeared positive, and deleted all six pre-specified secondary outcomes, replacing them with more favourable measures.

SKB papers also revealed that at least eight adolescents in the paroxetine group had self-harmed or reported emergent suicidal ideas compared to only one in the placebo group. But these adverse events were not properly reported in the published paper. Instead, some were described

as “emotional liability” while others were left out altogether.

Although published in Keller’s name, the article was ghostwritten by agents of SKB, and the company maintained tight control of the article’s content throughout its development.

GlaxoSmithKline’s **internal documents**, disclosed in litigation, show that company staff were aware that the study didn’t support the claim of efficacy but decided it would be “unacceptable commercially” to reveal that.

According to a company position paper, the data were selectively reported in Keller et al.’s article, in order to **“effectively manage the dissemination of these data in order to minimise any potential negative commercial impact”**.

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As it turns out, the Keller et al. article was used by GlaxoSmithKline to ward off potential damage to the profile of paroxetine and to promote off-label prescribing to children and adolescents.

While problems with the study and the Keller et al paper have been thoroughly exposed in legal actions, the bioethical and **medical literature**, a **book**, and a BBC Panorama **documentary**, the paper continues to be **cited uncritically** as evidence of the efficacy of paroxetine for treatment of adolescent depression.

Repeated **attempts** to get JAACAP to retract the offending paper have been unsuccessful.

For paroxetine, the concern is that adolescents are being harmed because well-intentioned physicians have been misled about its safety and effectiveness.

But more broadly, the case raises questions about how widespread such dubious practice is in the academic community, and in the editorial practices of “scientific” journals.