

wake up during the night or interrupt their day to take their pain medication; patients could instead have a restful night, without the need to wake and take their medication⁶. But, in the process of marketing and promoting OxyContin, Purdue Pharma used many false claims about the drug's window of pain relief, superiority to other treatments, and risk of addiction.

The subsequent sections present Purdue Pharma's claims, and the evidence refuting their claim.

12 Hours of Pain Relief – Too Good to be True

The 12-hour-relief claim presented a great vision where patients would only need to take two pills a day for pain relief. But, in many circumstances, the 12-hour-relief claim did not hold true. In Purdue Pharma's own clinical trials, conducted in accordance with an eventual drug application to the US Food & Drug Administration (FDA) for approval, they reported that many patients given OxyContin were asking for more pain medication before their next dose scheduled 12 hours later. Many patients were either shifted to an 8-hour dosage of OxyContin, or took supplemental painkillers between the two OxyContin doses.

Despite this knowledge that the 12-hour-relief claim was not true for many patients, Purdue Pharma still marched forward to obtain FDA approval for OxyContin as an analgesic which provides 12 hours of relief, and then produced multiple-page advertisements in medical journals to unequivocally state that effective pain relief in patients can be accomplished by a 12-hour dosage regimen. In a 2004 letter to the FDA, Purdue Pharma lawyers even admitted that 8-hour dosages could optimize treatment for patients, but that their 12-hour-relief claim was simply better for business, in that it framed OxyContin in a better light than other treatments⁶.

OxyContin Is Not Superior to Pre-Existing Treatments

In advertising material for OxyContin, Purdue Pharma noted that OxyContin is superior to some existing treatments, such as the combination treatment of hydrocodone and acetaminophen⁷. But, clinical trials only proved OxyContin to be equivalent to pre-existing treatments, rather than superior. Randomized controlled trials comparing the new "wonder drug" with extended-release formula to the pre-existing immediate-release oxycodone, which is administered 4 times a day, reported similar efficacy and safety between the two treatments^{8,9}. OxyContin was likewise compared to morphine in randomized controlled trials, and documented to have equivalent efficacy and safety profiles^{10,11}.

Despite the published literature reporting on OxyContin's similar analgesic profile to other treatments, Purdue Pharma marketed OxyContin to be more effective than some existing treatments, leading to the FDA issuing written warnings to Purdue Pharma about misleading marketing claims⁷.

The Risk of Addiction

Purdue Pharma misrepresented the risk of addiction to be low, writing in their promotional material that the risk of addiction to OxyContin was small¹², and training their sales representatives to advertise that the risk of addiction was less than 1%¹³. In reality, however, the risk of addiction among Purdue Pharma's target population of patients with chronic non-cancer-related pain, can be as high as 50%¹⁴, with many studies reporting prescription drug abuse in 20-40% of patients¹⁵⁻¹⁸.

In 2007, Purdue Pharma pled guilty to criminal charges of misbranding OxyContin to be less addictive than it is and less likely to be abused compared to other opioids, and paid over \$600 million in fines¹².

The Aggressive Yet Successful Marketing Tactics

Despite the false claims and published evidence that OxyContin is no better than other treatments, OxyContin's revenues skyrocketed from \$48 million in 1996 to \$1.1 billion in 2000 to \$3 billion in 2010^{6,12}. The magnitude of success even shocked executives of Purdue Pharma⁶, with the revenue from OxyContin prescriptions registering over tenfold greater than Purdue Pharma's previous top-selling drug, MS Contin⁶.

The successful commercialization of OxyContin is attributed to Purdue Pharma's aggressive promotion and marketing campaigns, where they spent hundreds of millions of dollars¹⁹⁻²⁴. Their marketing expense was many times larger than what they previously spent on MS Contin, and also many times larger than marketing expenditures by OxyContin's competitors such as Janssen Pharmaceutical's Duragesic¹². With their much-larger budget, they undertook large-scale and unprecedented marketing directed primarily to clinicians, to increase the rate of OxyContin prescriptions²⁵.

When OxyContin launched, Purdue Pharma doubled their sales force to over 600 sales representatives, spending over \$200 million in the expansion⁶. Purdue Pharma then trained their sales representatives to convince general practitioners to use OxyContin for many common pain conditions and falsely claim to physicians about the low risk of addiction¹². To maximize the impact of their large sales force, Purdue Pharma then leveraged prescribing profiles of individual physicians to identify physicians who are the highest prescribers for opioids, and deploy their sales representatives to convince those physicians to prescribe OxyContin²⁶.

Additionally, Purdue Pharma provided in-kind benefits to clinicians, subliminally influencing their prescription practice. They hosted dozens of pain management symposiums across the nation, and sponsored all-expenses-paid trips to these symposiums for thousands of physicians, pharmacists and nurses²⁷; these sponsored trips have been reported to favourably influence clinicians' prescribing towards OxyContin²⁸. Sales representatives also distributed OxyContin-branded swag, ranging from fishing hats to plush toys to luggage tags, serving as a reminder for clinicians about OxyContin²⁹.

Purdue Pharma's aggressive marketing tactics were ultimately successful due to a highly motivated sales force, who had much to gain from a lucrative bonus system based on volume of sales. Sales representatives were rewarded bonuses if a larger percentage of their prescribers administered high doses of OxyContin, hence motivating sales representatives to advocate for greater dose strengths³⁰. In the end, many sales representatives made more money via bonuses than their annual salary; in 2001, for example, the average annual salary was \$55,000 for sales representatives, but \$71,500 for the average annual bonuses¹².

OxyContin's commercial success and high revenue was ultimately born from Purdue Pharma's aggressive marketing program, skyrocketing it to the most frequently prescribed brand-name opioid in the US for treating moderate to severe pain in the early 2000s.

The Societal Consequences

While OxyContin became a commercial success for Purdue Pharma, it became a public health disaster for the rest of the nation. The downstream effects of Purdue Pharma's aggressive marketing tactics were that OxyContin were prescribed in much larger quantities and higher doses than required, as clinicians prescribed OxyContin more readily. This overprescription placed patients at a higher risk to developing tolerance and addiction, and abusing opioids. Excess leftover OxyContin pills may have been consumed for intents of drug abuse rather than pain management³¹. Additionally, higher doses within OxyContin tablets allowed for more oxycodone to be extracted from a crushed tablet, so that it can be swallowed, inhaled or injected to achieve a morphinelike high¹².

The addiction to OxyContin of patients and discovery that it can be abused to obtain a morphinelike high by drug abusers ultimately led to the first wave of the ongoing opioid crisis, claiming the lives of hundreds of thousands in the US population.

Lessons Learned

Regulation of Pharmaceutical Companies

The perpetuation of false claims in marketing material blossomed due to both a failure of the existing infrastructure, and also an inadequate infrastructure. The Food, Drug and Cosmetics Acts entrusts the FDA with the authority to regulate advertising and promotion of prescription drugs, and to ensure that prescription drug advertising and promotion are truthful. But, during Purdue Pharma's marketing campaign, the FDA and their 39 staff members were submerged in their revision of 34,000 promotional packages; it was extremely difficult for the FDA's limited staff to meticulously review each promotional package in a timely manner and protect the public from false claims. In fact, Purdue Pharma submitted a video advertisement of OxyContin to the FDA, which the FDA never reviewed until

one year later when it was probed by the General Accounting Office²⁷; only then did the FDA identify that there were false claims and issued letters to inform Purdue Pharma. In other words, the overstretched FDA failed to carry out their mandate from the Food, Drug and Cosmetics Acts, and needed an inquiry from the General Accounting Office to institute much-delayed action.

At the same time, the marketing approval system was more akin to a post-marketing notification to the FDA rather than a pre-market approval system; the infrastructure was inadequate to prevent the propagation of Purdue Pharma's false claims. Regulation only required that promotional material be submitted to the FDA for review when the material was initially submitted, rather than prior to its use. As a result, even if the FDA can review marketing material in a timely manner, the marketing material would still have been circulated to clinicians and the community prior to the FDA instituting any action to prevent future marketing¹².

To prevent future tragedies rooted in false claims, a pre-market approval system can be implemented. Under this system, the FDA would review all marketing material prior to their use, hence preventing any spread of false claims. However, in order to review material in a timely manner, the FDA would likely need more staff and funding.

Regulation of Clinicians

Aside from false claims, Purdue Pharma's marketing campaign proved successful and lethal to public health due to its intimate and influential relationships with clinicians. In particular, the in-kind gifts to clinicians created biased judgement in care of patients, perhaps due to lack of regulation in this respect. While professional associations such as the American Medical Association have made steps in the right direction to advise physicians not to accept significant gifts from the pharmaceutical industry³², the advisory nature is not as robust as a regulatory system. A regulatory system could be designed and implemented such that clinicians are required to disclose any relationship to the pharmaceutical industry to their governing/licensing body, and need to receive approval prior to engaging with the pharmaceutical industry. As with the proposal to change the FDA to a pre-market notification system, this will likely require significant funding and employees.

Both these recommendations for new regulatory systems may be viewed as expensive or too authoritarian. But, upfront investment in setting up and maintaining a regulatory system could potentially prevent another drug crisis. The proposed system would also come at the cost of a laissez-faire pharmaceutical and medical professional community; reflection will be needed to determine whether preventing a future drug crisis is worth the lost in operational freedom for pharmaceutical companies and medical professionals.

Conclusion

Purdue Pharma's successful commercialization and marketing campaign of OxyContin led to the boom of opioid prescriptions. Unfortunately, this came at the expense of public health – over the past several decades, nearly half a million American lives have been claimed by drug overdoses from the opioid crisis. Future crises could potentially be prevented, if we overhaul the regulatory system for pharmaceutical companies and implemented a regulatory system for clinicians. However, these changes would require significant funding and resources, and come at the cost of operational freedom; careful reflection will be needed to assess whether the costs are worth the benefits.

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