Adriane Fugh-Berman, MD
U.S. Senate Homeland Security and Governmental Affairs Committee
Roundtable on opioids sales and marketing practice
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Since the 1990s, pharmaceutical companies have stealthily distorted the perceptions of consumers and health care providers about pain and opioids. Opioid manufacturers used drug reps, physicians, consumer groups, medical groups, accreditation and licensing bodies, legislators, medical boards, and the Federal government to advance marketing goals to sell more opioids. This aggressive marketing push has resulted in hundreds of thousands of deaths from the overprescribing of opioids.

Drug Reps

Drug reps, selected for their presentability and outgoing natures, are trained to assess physicians' personalities, practice styles, and preferences, and to use this knowledge to influence prescribing. Reps may be genuinely friendly, but they are not genuine friends. Physicians are overworked, overwhelmed with information, buried in paperwork, and feel underappreciated. Cheerful and charming, drug reps provide food, appreciation, and information. Unfortunately, the information they provide is innately unreliable because the role of the drug rep is to sell a drug, not to educate the physician.[1]

Reciprocity is a strong guiding principle of human interaction.[2] Drug reps provide flattery, food, and “friendship”; physicians respond by writing more prescriptions for targeted drugs. Pharmaceutical companies influence healthcare providers’ attitudes and therapeutic choices through financial incentives that include research grants, educational grants, consulting fees, speaking fees, gifts, and meals. Any gift, no matter the size, has a powerful effect on human relationships. Even a small gift (pizza, for example) fosters a subconscious obligation to reciprocate through changes in prescribing practices.[3] A meal worth less than $20 has been shown to increase the prescribing of cardiovascular drugs and antidepressants.[4] Studies show that promotion increases the number of prescriptions;[5] industry gifts are also associated with more expensive prescriptions for Medicare patients.[6]

Ironically, physicians often do not recognize their vulnerability to commercial information. Studies have also consistently shown that physicians do not believe that promotion affects their

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[1] Fugh-Berman A, Ahari S. Following the script: How drug reps make friends and influence doctors. PLoS Medicine. 2007;4(4):e150-0625.
[2] Mather C. The pipeline and the porcupine: Alternate metaphors of the physician–industry relationship. Soc Sci Med. 2005;60:1323-34. Sah S. Conflicts of interest and your physician: psychological processes that cause unexpected changes in behavior. J Law Med Ethics. 2012;40(3):482-7. Fugh-Berman A, Ahari S. Following the script: How drug reps make friends and influence doctors. PLoS Medicine. 2007;4(4):e150-0625.
[3] Sah S. Conflicts of interest and your physician: psychological processes that cause unexpected changes in behavior. J Law Med Ethics. 2012;40(3):482-7.
[4] DeJong C, Aguilar T, Tseng CW, Lin GA, Boscardin WJ, Dudley RA. Pharmaceutical Industry-Sponsored Meals and Physician Prescribing Patterns for Medicare Beneficiaries. JAMA internal medicine. 2016;176(8):1114-10.
[5] Chren MM, Landefeld CS. Physicians’ behavior and their interactions with drug companies: A controlled study of physicians who requested additions to a hospital drug formulary. JAMA. 1994;271(9):684-9. Wazana A. Physicians and the pharmaceutical industry: is a gift ever just a gift? JAMA. 2000;283(3):373-80. Yeh JS, Franklin JM, Avorn J, Landon J, Kesselheim AS. Association of Industry Payments to Physicians With the Prescribing of Brand-name Statins in Massachusetts. JAMA internal medicine. 2016;176(6):763-8.
[6] Perlis RH, Perlis CS. Physician Payments from Industry Are Associated with Greater Medicare Part D Prescribing Costs. PLoS One. 2016;11(5):e0155474.

own prescribing.[7] (PharmedOut's educational modules are the only modules shown to change physician's attitudes about their own vulnerability to pharmaceutical marketing.)[8] Drug reps stop visiting prescribers they cannot influence. It is good news that in the last five years, the number of physicians who refuse to see drug reps has risen steadily. Currently, 40% of the physicians in the U.S. do not see drug reps.[9]

Changing the Culture of Medicine

Besides drug reps, industry has many other modes of influence, including seeding misleading articles into medical journals,[10] creating misleading educational modules,[11] and paying "key opinion leaders" to address their peers at meetings and events.[12] These tactics persuade health care providers to prescribe more opioids to more patients, precipitating the epidemic we have today.

Pharmaceutical companies convinced health care providers that they were "opiophobic" and causing suffering by denying opioids to patients with back pain or arthritis. They persuaded prescribers that patients with pain were somehow immune to addiction. Even when addiction was suspected, physicians were taught that it might be "pseudoaddiction"[13] – an invented condition – treated by increasing opioid dosages.

Industry created the American Pain Foundation[14] and other sham groups, co-opted medical organizations, and changed state laws to eliminate curbs on opioid prescribing. Between 2006 and 2015, pharmaceutical companies and the advocacy groups they controlled employed 1,350 lobbyists a year in legislative hubs.[15] Industry-influenced regulations and policies ensured that hospitalized patients were (and are) berated constantly about their level of pain and overmedicated for that pain. Even a week of opioids can lead patients into addiction,[16] so many patients are discharged from hospitals already dependent on opioids.

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[7] Sigworth SK, Nettleman MD, Cohen GM. Pharmaceutical branding of resident physicians. JAMA. 2001;286(9):1024-5. McKinney WP, Schiedermayer DL, Lurie N, Simpson DE, Goodman JL, Rich EC. Attitudes of internal medicine faculty and residents toward professional interaction with pharmaceutical sales representatives. JAMA. 1990;264(13):1693-7. Steinman MA, Shlipak MG, McPhee SJ. Of principles and pens: Attitudes and practices of medicine housestaff toward pharmaceutical industry promotions. Am J Med. 2001;110(7):551-7. Dana J, Loewenstein G. A social science perspective on gifts to physicians from industry. JAMA. 2003;290(2):252-5.

[8] Fugh-Berman A, Scialli A, Bell AM. Why lunch matters: Assessing physician's perceptions about industry relationships. J Cont Ed Health Professions. 2010 (Summer); 30(3): 197-204.

[9] SK&A Info. Commercial access to physicians: Medical Industry Sales Reps Accessibility to U.S. physicians. QuintilesIMS. 2017 Sep. Available: http://www.skainfo.com/reports/access-to-physicians.

[10] Porter J, Jick H. Addiction rare in patients treated with narcotics. NEJM. 1980;302(2):123. Portenoy RK, Foley KM. Chronic use of opioid analgesics in non-malignant pain: Report of 38 cases. Pain. 1986;25:171-86. Weissman DE, Haddox JD. Opioid pseudoaddiction – an iatrogenic syndrome. Pain. 1989;36(3):363-6.

[11] Government Accountability Office (formerly General Accounting Office). Prescription Drugs, OxyContin Abuse and Diversion and Efforts to Address the Problem. 2003 Dec. Available: http://www.gao.gov/new.items/d04110.pdf

[12] *Id.*

[13] Porter J, Jick H. Addiction rare in patients treated with narcotics. NEJM. 1980;302(2):123. Portenoy RK, Foley KM. Chronic use of opioid analgesics in non-malignant pain: Report of 38 cases. Pain. 1986;25:171-86. Weissman DE, Haddox JD. Opioid pseudoaddiction – an iatrogenic syndrome. Pain. 1989;36(3):363-6. Weissman DE, Haddox JD. Opioid pseudoaddiction – an iatrogenic syndrome. Pain. 1989;36(3):363-6.

[14] Government Accountability Office (formerly General Accounting Office). Prescription Drugs, OxyContin Abuse and Diversion and Efforts to Address the Problem. 2003 Dec. Available: http://www.gao.gov/new.items/d04110.pdf

[15] Essley Whyte L. Politics of pain: Drugmakers fought state opioid limits amid crisis. The Center for Public Integrity. 2016 Sep 8. Available: https://www.publicintegrity.org/2016/09/18/20200/politics-pain-drugmakers-fought-state-opioid-limits-amid-crisis

[16] Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain – United States, 2016. JAMA. 2016;315(15):1624-45. doi: 10.1001/jama.2016.1464.

Pharmaceutical companies changed the culture of medicine regarding pain and opioids in a way that addicted – and continues to addict – many patients. It is a misperception to think that most opioid deaths are caused by misuse of opioids. In fact, many deaths occur when people are using drugs in exactly the way they were prescribed.[17] Misuse isn't the problem; use is the problem.

Sarah Fuller's case is a good example. The fact that an Insys drug rep was in her doctor's office counseling her to use Subsys for an unapproved use[18] is outrageous. This Committee's report showing that Insys employees misled pharmacy benefit managers to facilitate payment approvals for Subsys reveals the company's efforts to maximize profits no matter what the cost was to human health.

Opioids are appropriate for end-of-life care and for a few days following surgery or trauma. For most people, long-term opioid use is a bad idea. Opioids often lose effectiveness over time; ironically, they can cause hyperalgesia, or increased sensitivity to pain (withdrawal symptoms can also include pain). And while patients may need higher and higher doses over time to treat pain, higher doses cause more adverse effects. Unfortunately, tolerance to painkilling effects does not correlate with tolerance of adverse effects (especially respiratory depression); [19] in other words, a patient could still be in pain and die from too much opioids.

New Marketing Strategies

Promotion of opioids is not in the past. Between 2013 and 2015, one in 12 physicians took money from opioid manufacturers – a total of more than $46 million.[20] Industry-friendly messages that pharmaceutical companies are currently perpetuating reassure physicians that prescribing opioids is safe as long as patients do not have a history of substance misuse or mental illness.

Astoundingly, the same industry that created the addiction epidemic is arguing that it can save us from this epidemic with more pills. New opioid formulations are touted as the answer, although they are not less addictive. The term "abuse-deterrent formulation" is dangerously misleading because the patients and providers may assume that these formulations are less addictive if taken as prescribed.

In fact, "abuse-deterrent" opioids are just as likely to cause addiction as conventional preparations. These formulations may be slightly harder to turn into an injectable form, but even that's not very important. The most common way people misuse opioids is by swallowing them or putting them under the tongue.

Industry-Free Continuing Education is Necessary

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[17] Johnson EM, Lanier WA, Merrill RM, et al. Unintentional prescription opioid-related overdose deaths: Description of descents by next of kin or best contact, Utah, 2008-2009. J Gen Intern Med. 2013;28(4):522-9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3599020/

[18] Armstrong, D. A potent painkiller, and the drug maker's marketing, are faulted in a woman's death. Stat. September 30, 2016. Available: https://www.statnews.com/2016/09/30/fentanyl-opioid-insys-subsys/

[19] Dahan A, Yassen A, Bijl H, et al. Comparison of the respiratory effects of intravenous buprenorphine and fentanyl in humans and rats. Br J Anaesth. 2005;94(6)L825-34.

[20] Hadland SE, Krieger MS, Marshall BDL. Industry Payments to Physicians for Opioid Products, 2013–2015. American Journal of Public Health 2017; 107 (9):1493-1495. Available: http://ajph.aphapublications.org/doi/10.2105/AJPH.2017.303982

The opioid addiction epidemic will not end as long as new people are addicted through bad prescribing practices. Prescribers must be educated on the true benefits and harms of opioids through objective sources of information. For example, the District of Columbia Center for Rational Prescribing (DCRx),[21] funded by the Washington D.C. Department of Health, provides industry-free continuing education for prescribers and pharmacists on opioids and many other topics, and should be a model for the rest of the nation.

The White House Commission on Combating Drug Addiction and the Opioid Crisis recommends mandatory education for providers before they receive a DEA license. This recommendation is fatally flawed because the Commission did not specify that these educational modules must be free of pharmaceutical company influence.[22] Industry-funded education of physicians is what created this problem in the first place. As long as prescribers are being educated by companies that market drugs fueling the problem, the body count will continue to rise.

Conflict of interest statement
Dr. Fugh-Berman directs PharmedOut, a research and education project at Georgetown University Medical Center that examines inappropriate pharmaceutical marketing practices and promotes rational prescribing. Dr. Fugh-Berman receives some salary support from the District of Columbia Center for Rational Prescribing (DCRx), a joint project of the DC Department of Health, the George Washington Milken Institute School of Public Health, and Georgetown University Medical Center. Dr. Fugh-Berman is also a paid expert witness at the request of plaintiffs in litigation regarding pharmaceutical marketing practices.

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[21] DCRx: The DC Center for Rational Prescribing. Washington DC Department of Health. Available: https://doh.dc.gov/service/dcrx.
[22] White House Commission on Combating Drug Addiction and the Opioid Crisis. White House Commission on Combating Drug Addiction and the Opioid Crisis – Draft Interim Report. 2017. Accessed: 2017 Sep 7. Available: https://www.whitehouse.gov/ondcp/presidents-commission/meetings.