A SOCIALLY BENEFICIAL FALSE CLAIMS ACT?

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INTRODUCTION

Most people dislike gambling with their health. When a physician prescribes a patient a drug for an off-label use—that is, for a purpose for which the drug has not been formally approved by the Food and Drug Administration ("FDA")—they may be doing just that. Whether a consequence of the FDA's sluggish review pace or a strategic exploitation of sparse scientific data, off-label prescriptions have become an integral part of our current healthcare system. Almost 50% of cardiac therapy and anticonvulsant prescriptions and over 30% of anti-asthmatic, allergy therapy, and psychiatric therapy

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prescriptions are given for off-label uses.[1] Prescribers have considerable autonomy in using drugs off-label and are free to use their expertise to adopt and relinquish[2] off-label treatments.

Because the law affords providers so much freedom in prescribing off-label, it relies on them to accurately evaluate new information about off-label innovations, adopt beneficial innovations, and relinquish inappropriate[3] uses. The risk that an off-label use is unsafe or ineffective, however, is often ambiguous. As companies do not submit these uses for FDA approval, there is often little published evidence supporting such uses. In a survey of nationally-representative drug data, Radley, Finkelstein, and Stafford estimate that only 27% of off-label uses studied were supported by strong scientific evidence.[4]

Prescribing drugs with uncertain risks is not inherently bad; indeed, restricting access only to drugs with precisely-known risks can harm patients by depriving them of potentially helpful treatments.[5] Ambiguity is also not insurmountable—physicians can update their beliefs about ambiguously risky treatments based on new scientific information as it becomes available. Appropriate updating, however, depends on physicians using reliable information.

Whether physicians can distinguish between reliable and unreliable information is a legitimate concern. First, physicians receive a lot of information daily, making it difficult to analyze each new piece of information critically.[6] Second, physicians' reliance on one-on-one interactions with pharmaceutical representatives may

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1. David C. Radley et al., *Off-label Prescribing Among Office-Based Physicians*, 166 ARCHIVES INTERNAL MED. 1021, 1024 tbl.1 (2006).

2. For the purposes of this Article, relinquishment means the cessation of a treatment by providers.

3. This Article considers an off-label use "inappropriate" if it is ineffective, unsafe, or both.

4. Radley et al., *supra* note 1.

5. *See* Ryan Abbott & Ian Ayres, *Evidence and Extrapolation: Mechanisms for Regulating Off-label Uses of Drugs and Devices*, 64 DUKE L.J. 377, 389–91 (2014); *see also* W. Kip Viscusi & Richard J. Zeckhauser, *Regulating Ambiguous Risks: The Less than Rational Regulation of Pharmaceuticals*, 44 J. LEGAL STUD. S387, S395–96 (2015) (discussing "continuing limitations on access to experimental drugs for gravely ill patients").

6. *See, e.g.*, Aaron E. Carroll, *It's Hard for Doctors to Unlearn Things. That's Costly for All of Us*, N.Y. TIMES (Sept. 10, 2018) https://www.nytimes.com/2018/09/10/upshot/its-hard-for-doctors-to-unlearn-things-thats-costly-for-all-of-us.html.

outweigh their reliance on scientific studies.[7] The latter point is particularly troubling because pharmaceutical companies have substantial incentives to encourage off-label prescriptions: off-label sales are highly profitable because pharmaceutical companies are able to reach a larger market without incurring the cost of supplemental FDA approval. Given the overwhelming amount of information physicians receive along with their receptiveness to information from pharmaceutical representatives, do physicians learn when to adopt appropriate or relinquish inappropriate off-label treatments? If so, to what sources of information are physicians most responsive?

The importance of these questions is two-fold. First, insufficient relinquishment of inappropriate uses results in monetary waste: insurers end up paying for inappropriate treatments and passing those costs to their clients. Second, insufficient relinquishment increases the likelihood that patients receive suboptimal medical care. If physicians fail to relinquish inappropriate treatments, patients lose the opportunity to try more appropriate treatments.

The government has tried to penalize pharmaceutical companies for promoting off-label uses of their drugs through the use of False Claims Act ("FCA") lawsuits. The FCA prohibits fraudulent submission of claims to the government for reimbursement.[8] Originally passed in 1863 as a way to prevent profiteering during the Civil War,[9] the FCA has also been used to penalize off-label promotion by pharmaceutical companies. While the FCA has been a highly lucrative tool in compensating the government,[10] its application to penalize off-label promotion has been criticized as inappropriate.[11]

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7. *See* Howard Brody, *The Company We Keep: Why Physicians Should Refuse to See Pharmaceutical Representatives*, ANNALS FAM. MED., Jan.–Feb. 2005, at 82, 84.

8. 31 U.S.C. §§ 3729–3730 (2018); Kristin McCreary Eichel, *Focusing on Fraud: The Federal Government Expands Its Use of the False Claims Act to Police Off-label Pharmaceutical Promotion*, 8 IND. HEALTH L. REV. 399, 412 (2011).

9. Eichel, *supra* note 8.

10. *See, e.g.*, Judy Greenwald, *False Claims Act Settlements Reach $750M in 2019 First Half*, BUS. INS. (July 17, 2019), https://www.businessinsurance.com/article/20190717/NEWS06/912329659/False-Claims-Act-settlements-reach-$750M-in-2019-first-half.

11. *See* Steven Boranian, *Here Is Why the False Claims Act is an "Awkward Vehicle" in Pharma Cases*, DRUG & DEVICE L. BLOG (Nov. 9, 2017), https://www.druganddevicelawblog.com/2017/11/here-is-why-the-false-claims-act-is-an-awkward-vehicle-in-pharma-cases.html.

This Article argues that the FCA, while flawed, can perform a socially beneficial role by creating better information for physicians and third-party payers regarding the appropriateness of an off-label use. The FCA can create new information about a drug use's appropriateness in three ways: (1) by calling attention to public, but obscure, scientific information; (2) by publicizing internal information regarding a pharmaceutical company's fraudulent conduct; or (3) under certain conditions, by serving as a signal to the industry that the off-label use in question is less appropriate than initially thought.

This Article further argues that while the FCA can serve this social function, it also dampens incentives for the government to prospectively relinquish inappropriate off-label promotions. Because the government knows that it can recover monetary costs through suits, it could be less likely to invest resources into preventing inappropriate prescriptions from being written or reimbursed in the first place. This is not socially beneficial as it ignores the human cost of inappropriate off-label uses: patients receiving those drugs are unable to try more effective treatments. While developments in FCA jurisprudence that make settling or winning uniformly more difficult will incentivize the government to screen out inappropriate prescriptions in the first instance, they will also reduce the number of FCA suits generally, leading to less information creation. Instead, this Article argues that FCA legal standards should be structured to explicitly reward the government for engaging in screening. Such standards would preserve the potential informational value of FCA suits and also combat the moral hazard associated with allowing the government to recover for monetary costs of inappropriate reimbursements.

Against this theoretical backdrop, this Article presents an empirical case study of relinquishment of an inappropriate drug use: the use of Neurontin for the treatment of bipolar disorder. The case study demonstrates the informational content of the FCA claim and illustrates the differing reactions to such information by payer. Part I gives some background on the regulation of off-label uses and how the FCA is used in this context. Part II argues that although the purpose of the FCA is to compensate the government, certain features would allow it to achieve a more socially beneficial goal of improving patient care. Part III uses a case study of the FCA case against the manufacturers of Neurontin, one of the first off-label promotion FCA cases to settle, to illustrate the potential informational value of the FCA with a case study of Neurontin. The

study documents relinquishment in response to scientific and legal information shocks and finds heterogeneous responses by payer in response to these information shocks. Part IV discusses the implications of these results, and the final Part concludes.

I. THE CURRENT LANDSCAPE OF OFF-LABEL DRUG USE

The regulation of off-label uses of drugs is as important for patient care as it is complex. This Part defines and discusses the issues surrounding off-label usage as well as the mechanism that the government predominantly uses to regulate it, the FCA.

A. The Importance of Appropriate Off-label Usage

The FDA vets the safety and effectiveness of prescription drugs for specific diseases ("indications"), dosages, and populations through several phases of controlled study.[12] Not all drug uses go through this process. The practice of prescribing a drug for indications, dosages, and populations for which it has not undergone FDA approval is called prescribing "off-label."[13] Appropriate off-label drug use requires that physicians incorporate new scientific evidence about the safety and effectiveness of drugs into their prescription decisions. The FDA does not regulate physicians' off-label drug prescriptions but instead places restrictions on manufacturers' advertisements of off-label uses.[14] Pharmaceutical manufacturers that violate these restrictions often face FCA suits which can result in large monetary penalties. Examples of such offenders include Warner-Lambert, which illegally marketed Neurontin for the

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12. *See The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/drugs/resourcesforyou/consumers/ucm143534.htm (last updated Nov. 24, 2017).

13. Christopher M. Wittich et al., *Ten Common Questions (and Their Answers) About Off-label Drug Use*, 87 MAYO CLINIC PROC. 982, 982 (2012).

14. U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS ON UNAPPROVED NEW USES—RECOMMENDED PRACTICES 4 (2014) [hereinafter GUIDANCE FOR INDUSTRY]; Off. of the Comm'r, *Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/RegulatoryInformation/Guidances/ucm125126.htm (last updated Sept. 27, 2018) [hereinafter *Good Reprint Practices*].

treatment of bipolar disorder,[15] and Eli Lilly, which marketed Zyprexa for the treatment of dementia.[16]

In contrast, physicians have significant freedom to prescribe drugs for off-label uses. Prescription practices are limited by medical malpractice liability: physicians are liable for any deviations from the "acceptable and prevailing standard of practice" in prescribing drugs off-label just as they are for on-label drugs.[17] Physicians prescribing drugs off-label are not presumed to be negligent; in fact, several off-label drug uses are so prevalent that they are considered to be part of the standard of care (for example, aspirin for coronary disease prophylaxis).[18]

Because the FDA does not systematically assess off-label drug uses, these have a higher risk of being medically inappropriate. As noted earlier, Radley, Finkelstein, and Stafford find that only 27% of off-label uses are supported by strong scientific evidence.[19] The lack of publicly available scientific evidence, however, does not necessarily mean that off-label treatments are inappropriate. Suggestive scientific evidence can provide support for off-label treatments. If an off-label drug belongs to the same class as a drug already approved for the indication, physicians may expect the drug to perform similarly.[20] Similarly, if two indications have similar pathologic of physiologic features, physicians may expect a treatment for one indication to be effective for the other indication.[21] Such evidence is merely suggestive, however; without systematic study, physicians do not have any assurance of the appropriateness of a drug for an off-label use.

Even if such systematic studies were available, it is unclear how physicians would find such studies and how they would be

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15. *Warner-Lambert to Pay $430 Million to Resolve Criminal & Civil Health Care Liability Relating to Off-label Promotion*, U.S. DEP'T OF JUST. (May 13, 2004), http://www.justice.gov/opa/pr/2004/May/04_civ_322.htm.

16. Margaret Cronin Fisk et al., *Lilly Sold Drug for Dementia Knowing It Didn't Help, Files Show*, BLOOMBERG (June 12, 2009, 12:01 AM), https://www.bloomberg.com/news/articles/2009-06-12/lilly-sold-drug-for-dementia-knowing-it-didn-t-help-files-show.

17. James B. Riley, Jr., & P. Aaron Basilius, *Physicians' Liability for Off-label Prescriptions*, HEMATOLOGY & ONCOLOGY NEWS & ISSUES, May–June 2007, at 24, 27.

18. *See* Wittich et al., *supra* note 13, at 983.

19. Radley et al., *supra* note 1. Radley et al. clarify that "[a]n indication was considered to be scientifically supported if, according to DRUGDEX, its effectiveness has been shown in controlled trials or observed in clinical settings." *Id.* at 1022.

20. Randall S. Stafford, *Regulating Off-label Drug Use—Rethinking the Role of the FDA*, 358 NEW ENG. J. MED. 1427, 1427 (2008).

21. Wittich et al., *supra* note 13, at 982–83.

incorporated into choices. The literature on physicians' information needs and ability to find relevant information provides mixed evidence. Covell, Uman, and Manning surveyed physicians regarding their information needs and found that physicians cited insufficient time as the most frequently reported barrier to finding necessary information.[22] Ely et al. also found that insufficient time was a reason that physicians only looked for answers to about 55% of the questions that they had.[23] In a survey of physicians regarding their information needs, Williamson et al. found that physicians had difficulty locating appropriate studies to resolve questions of treatment choice.[24] Even if physicians located the study, 87% of the polled physicians assessed study validity by comparing the results to their own experiences rather than by evaluating the study's methodology.[25] A more recent study reported that surveyed physicians were largely able to distinguish between the scientific rigor of studies and generally discounted the probative value of studies funded by pharmaceutical companies.[26]

"Pharmaceutical detailing," where pharmaceutical representatives personally promote a drug to a physician, is another source of information for physicians' treatment decisions. A line of economics literature explores pharmaceutical detailing as a legitimate avenue of information dissemination even though legal promotion of off-label uses is limited and fraud is frequent.[27]

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22. David G. Covell et al., *Information Needs in Office Practice: Are They Being Met?*, 103 ANNALS INTERNAL MED. 596, 598 (1985).

23. John W. Ely et al., *Answering Physicians' Clinical Questions: Obstacles and Potential Solutions*, 12 J. AM. MED. INFORMATICS ASS'N 217, 220 (2005).

24. John W. Williamson et al., *Health Science Information Management and Continuing Education of Physicians: A Survey of U.S. Primary Care Practitioners and Their Opinion Leaders*, 110 ANNALS INTERNAL MED. 151, 158 (1989).

25. *Id.* at 151. Sandra Johnson provides an in-depth discussion of the issues regarding physician learning. Sandra H. Johnson, *Polluting Medical Judgment? False Assumptions in the Pursuit of False Claims Regarding Off-label Prescribing*, 9 MINN. J.L. SCI. & TECH. 61, 73–82 (2008).

26. Aaron S. Kesselheim et al., *A Randomized Study of How Physicians Interpret Research Funding Disclosures*, 367 NEW ENG. J. MED. 1119, 1122–23 (2012). Aaron Kesselheim and his coauthors gave 503 physicians three journal abstracts each and asked them to evaluate the methodological rigor of each. *Id.* at 1119. They also asked for the likelihood that, based on the evidence, physicians would prescribe a given drug. *Id.* at 1121. Two hundred and sixty-nine physicians responded, and most seemed able to assess the relative rigor of the studies. *Id.* at 1122. Moreover, physicians seemed to discount studies that received funding by pharmaceutical companies. *Id.*

27. *See, e.g.*, Tat Chan et al., *Treatment Effectiveness and Side Effects: A Model of Physician Learning,* 59 MGMT. SCI. 1309, 1309 & n.1 (2013); Pradeep K.

Pharmaceutical companies are frequently fined for distributing false or misleading evidence about off-label uses of their drugs.[28] It is unclear whether or not physicians anticipate this difference in information value.[29]

If physicians do encounter reliable new information on off-label drug use, the process by which they stop prescribing an inappropriate use is called "relinquishment."[30] Previous literature suggests that there is substantial heterogeneity in relinquishment. In a small study of an unsafe drug in the British market, Roy E. A. Mapes found that after journals published news of the drug's adverse effects, physicians did not reduce their prescriptions uniformly.[31] Physicians were less likely to relinquish if the physician attended fewer post-graduate medical courses.[32] Additionally, physicians who are more likely to consider a patient's social surroundings and environment continued to prescribe the drug.[33] In contrast, Majumdar et al. found that relinquishment is not different between generalists and specialists.[34]

This Article extends this relinquishment literature to off-label uses. Off-label drug uses may not experience the same pattern of

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Chintagunta et al., *New Drug Diffusion When Forward-Looking Physicians Learn from Patient Feedback and Detailing*, 49 J. MKTG. RSCH. 807, 807 (2012).

28. *See, e.g.*, Fisk et al., *supra* note 16; *Warner-Lambert to Pay $430 Million to Resolve Criminal & Civil Health Care Liability Relating to Off-label Promotion*, *supra* note 15. While pharmaceutical representatives were originally unable to promote off-label uses legally, the FDA has created "safe harbors" of activities that would not be considered illegal off-label promotion. GUIDANCE FOR INDUSTRY, *supra* note 14; *Good Reprint Practices*, *supra* note 14. Given the current First Amendment litigation over off-label promotion as protected commercial free speech, the realm of legal off-label promotion is undefined now but presumably larger. *See, e.g.*, Stephanie M. Greene, *After* Caronia*: First Amendment Concerns in Off-label Promotion*, 51 SAN DIEGO L. REV. 645, 655–56 (2014); Christopher Robertson, *When Truth Cannot Be Presumed: The Regulation of Drug Promotion Under an Expanding First Amendment*, 94 B.U. L. REV. 545, 546 (2014); Elissa Philip, Case Comment, United States v. Caronia*: How True Does "Truthful" Have to Be?*, 67 VAND. L. REV. EN BANC 157, 160 (2014).

29. *But see* Kesselheim, *supra* note 26 (suggesting that physicians trust trials funded by the National Institutes of Health over trials funded by the pharmaceutical industry).

30. Roy E. A. Mapes, *Physicians' Drug Innovation and Relinquishment*, 11 SOC. SCI. & MED. 619, 619 (1977).

31. *Id.* at 621–22.

32. *Id.* at 622.

33. *Id.*

34. Sumit R. Majumdar et al., *Influence of Physician Specialty on Adoption and Relinquishment of Calcium Channel Blockers and Other Treatments for Myocardial Infarction*, 16 J. GEN. INTERNAL MED. 351, 357 (2001).

relinquishment as on-label uses because the FDA does not issue industry-wide warnings or notices for off-label uses of drugs. This might suggest that another visible, quasi-regulatory notice—such as litigation—may be necessary. This Article discusses whether such a signal seems to be effective and under what circumstances such a signal might or might not be desirable.

B. Regulating Off-label Uses Through the False Claims Act

Given the potential for information regarding off-label uses to be unreliable, the government has sought to reduce the freedom with which pharmaceutical companies can promote off-label uses. This Section outlines the various tools the government has used to control off-label prescription, focusing on the ill-fitting and somewhat controversial use of the FCA.

Given the potential benefits of off-label usage, the FDA has long held that it does not regulate off-label prescription but considers it a practice of medicine outside of its mandate.[35] Despite this purported hands-off approach, the FDA has attempted to limit the way pharmaceutical companies can promote off-label uses of their drugs. The government first attempted to make off-label promotion illegal per se under the Food, Drug, and Cosmetic Act ("FDCA"), labeling it a misbranding violation.[36] Pharmaceutical companies have long chafed at this restriction, pushing back on the grounds of commercial free speech. The FDA responded by creating safe harbor provisions for the types of communications that would not be considered misbranding but stopped short of making these safe harbors binding.[37] The Supreme Court's commercial free speech jurisprudence broadened during the 2000's, eroding the FDA's ability to explicitly forbid pharmaceutical speech for off-label

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35. *See* 21 C.F.R. § 312.2(d) (2020) ("This part does not apply to the use in the practice of medicine for an unlabeled indication of a new drug product approved under part 314 or of a licensed biological product.").

36. 21 U.S.C. § 331(a)–(c) (2018) ("The following acts and the causing thereof are hereby prohibited: (a) The introduction or delivery for introduction into interstate commerce of any food, drug, device, tobacco product, or cosmetic that is adulterated or misbranded. (b) The adulteration or misbranding of any food, drug, device, tobacco product, or cosmetic in interstate commerce. (c) The receipt in interstate commerce of any food, drug, device, tobacco product, or cosmetic that is adulterated or misbranded, and the delivery or proffered delivery thereof for pay or otherwise.").

37. Washington Legal Found. v. Henney, 202 F.3d 331, 335–36 (D.C. Cir. 2000).

speech.[38] This tense stasis remained undisturbed until 2012, when the Second Circuit addressed the issue. In *United States v. Caronia*,[39] the Second Circuit held that truthful off-label promotion was protected as commercial free speech.[40] Critics have questioned whether the court was warranted in granting such protection without requiring pharmaceutical companies to prove that their speech was not false or misleading;[41] others acknowledge the potential pitfalls of having a broad truthfulness definition but suggest that requiring a significantly narrower definition indirectly through speech constraints might be too burdensome.[42] Others suggest that the government should specifically allege that off-label promotion is false or misleading.[43] In 2015, the Southern District of New York heard a similar case in which a pharmaceutical manufacturer alleged that the threatened misbranding action infringed its right to commercial free speech in *Amarin Pharma, Inc. v. U.S. Food & Drug Administration*.[44] The FDA tried to distinguish *Caronia* by saying that *Caronia* did not "preclude a misbranding action where the acts to promote off-label use consist solely of truthful and non-misleading speech, provided that the evidence also shows that the drug had been introduced into interstate commerce and that the FDA had not approved it as safe and effective for the off-label use."[45] The district court rejected this argument further suggesting that truthful speech alone cannot be used as a predicate action for misbranding.[46] While the state of this law is still in flux, the future use of misbranding to limit off-label promotion is uncertain.

The second major avenue for limiting off-label promotion has been through the FCA.[47] The FCA was enacted during the Civil War

38. *See* Sorrell v. IMS Health Inc., 564 U.S. 552, 557 (2011); Thompson v. W. States Med. Ctr., 535 U.S. 357, 360 (2002).

39. 703 F.3d 149, 152 (2d Cir. 2012).

40. *See id.*

41. Robertson, *supra* note 28, at 558.

42. Philip, *supra* note 28.

43. Greene, *supra* note 28, at 708.

44. 119 F. Supp. 3d 196 (2015); David C. Gibbons, *A Victory for Amarin Further Erodes FDA Regulation of Off-label Promotion*, FDA L. BLOG (Aug. 10, 2015), http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2015/08/a-victory-for-amarin-further-erodes-fda-regulation-of-off-label-promotion.html.

45. *Amarin Pharma*, 119 F. Supp. 3d at 224.

46. *Id.* at 226.

47. This Article focuses on the federal false claims act; however, many states have enacted state false claims acts as well. In 2005, the federal government provided additional incentives for state false claims acts to provide comparable

in order to enable the government to recover losses from fraud; recently, however, it has been used to punish promotion of off-label uses.[48] FCA liability is triggered in several ways. The two most relevant ways are as follows: someone (1) "knowingly presents, or causes to be presented, a false or fraudulent claim for payment or approval"; or (2) "knowingly makes, uses, or causes to be made or used, a false record or statement material to a false or fraudulent claim[.]"[49] The inclusion of parties to "cause[] [a false claim] to be made" or "presented" has allowed the government to go after pharmaceutical companies even though they do not actually submit any claims for reimbursement to the government.

There are at least two possible theories of liability. First, a pharmaceutical company can be liable for making a *false* claim about the safety and effectiveness of an off-label use, which induces the physician to submit the claim for reimbursement from the government.[50] Second, the *United States ex rel. Franklin v. Parke-Davis* court suggested that *truthful* information about an off-label use can also be the basis for FCA liability as long as the off-label promotion induces claims that are ineligible for reimbursement to be submitted to the government.[51]

The FCA is particularly unique in its *qui tam* provision, which allows a whistleblower with knowledge of fraud[52] to bring suit on behalf of the government.[53] The whistleblower in turn receives a percentage of the resulting penalty.[54] The *qui tam* provision results in two benefits. First, it reduces the resources the government has to spend on litigation as the government receives a cut of the award regardless of whether or not it chooses to intervene.[55] Second,

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protections as the federal federal false claims act. Deficit Reduction Act of 2005, Pub. L. No. 109–171, § 6031, 120 Stat. 4. (codified as amended at 42 U.S.C. § 1396h (2018)).

48. 31 U.S.C. §§ 3729–3730 (2018); Katherine A. Blair, *In Search of the Right Rx: Use of the Federal False Claims Act in Off-label Drug Promotion Litigation*, HEALTH LAW., Apr. 2011, at 44, 47.

49. 31 U.S.C. § 3729(a)(1)(A)–(B).

50. Eichel, *supra* note 8, at 415.

51. No. Civ.A. 96-11651PBS, 2003 WL 22048255, at *2 (D. Mass. Aug. 22, 2003); Eichel, *supra* note 8, at 415–16.

52. 31 U.S.C. § 3730(b).

53. Eichel, *supra* note 8, at 412–13.

54. *Id.* at 413.

55. 31 U.S.C. §§ 3729(a)(3), 3730b(1), (d)(2). Notably, there may be some difference between cases in which the government chooses to intervene or not. The differential effect of such cases might be interesting to explore in the future.

whistleblowers, especially employees or insiders, are able to provide internal information about fraud.[56]

Concerns over the appropriate scope of liability under the FCA have led to action by the Supreme Court and Congress. In an effort to narrow the scope of fraud targeted by the FCA, the Supreme Court in *Allison Engine Co. v. United States ex rel. Sanders* originally attempted to require proof that a false statement not only resulted in government payment of a false claim but that the statement was *intended* to induce the government to pay the false claim.[57] This would exclude subcontractors who submit false claims to prime contractors without intending the government to pay the false claim.[58] Despite the Supreme Court's attempt to limit the scope of the FCA, Congress passed the Fraud Enforcement and Recovery Act ("FERA") to remove this intent requirement.[59]

In addition to removing the intent requirement, FERA explicitly required materiality as an element of certain FCA claims, defining materiality as "having a natural tendency to influence, or be capable of influencing, the payment or receipt of money or property."[60] While this standard had been criticized for being too vague, with circuit courts applying the standard inconsistently,[61] the Supreme Court clarified the standard in 2016. In *Universal Health Services, Inc. v. United States*, the Supreme Court held that materiality looks through formalities of express conditions for payment and depends instead on the expected effect of a condition on payment.[62]

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56. Eichel, *supra* note 8, at 413.

57. 553 U.S. 662, 668–69 (2008); Eichel, *supra* note 8, at 425.

58. *Allison Engine Co.*, 553 U.S. at 671–72.

59. Eichel, *supra* note 8, at 427–28.

60. 31 U.S.C. § 3729(b)(4). Some argue, however, that FERA made requirements less rigorous insofar as courts largely interpreted materiality as an implicit requirement for all FCA claims and FERA explicitly added it only to certain ones. *2009 Amendments to False Claims Act Pose New Challenges for Health Care Industry*, AKIN GUMP STRAUSS HAUER & FELD, LLP (June 2, 2009), https://www.akingump.com/en/news-insights/2009-amendments-to-false-claims-act-pose-new-challenges-for-health-care-industry.html.

61. Megan L. Hoffman, *The Substantial Weight Test: A Proposal to Resolve the Circuits' Disparate Interpretations of Materiality Under the False Claims Act*, 58 U. KAN. L. REV. 181, 182 (2009).

62. 136 S. Ct. 1989, 2002–03 (2016) ("The materiality standard is demanding. . . . A misrepresentation cannot be deemed material merely because the [g]overnment designates compliance with a particular statutory, regulatory, or contractual requirement as a condition of payment. Nor is it sufficient for a finding of materiality that the [g]overnment would have the option to decline to pay if it knew of the defendant's noncompliance.").

Finally, coming full circle, the ramifications of *Caronia* may create new problems for at least one FCA theory. Given that truthful off-label promotion is protected by the First Amendment, courts have questioned *United States ex rel. Franklin v. Parke-Davis*'s conclusion that truthful off-label promotion can serve as the basis for a FCA claim. Lars Noah also questioned whether the *Caronia* decision will affect FCA prosecutions as "whistleblowers have repeatedly pointed to off-label promotion as a basis for triggering prosecution even where the FDA later approved some of these uses."[63] The government has contended that these two areas are distinct. Rogoff, Mayell, and Ramer note that the government filed a Statement of Interest in *United States ex rel. Cestra v. Cephalon, Inc.*, distinguishing it based on the fact that the FCA "prohibits any conduct that causes the submission of false claims to the government . . . ."[64] Rogoff, Mavell, and Ramer note that "[a]ccording to the government, even if that conduct is carried out through truthful speech—the same speech that Caronia holds may be constitutionally protected under the FDCA—FCA liability could still attach."[65] It is unclear how persuasive this argument actually is. Indeed, at least one district court has suggested that for the purposes of pleading standards merely alleging that a company promoted a product for off-label uses—without alleging any false or misleading statements—"[did] not meet the *Twombly*/*Iqbal* plausibility standard because truthful and non-misleading promotions fall within the protection of the First Amendment . . . ."[66] It remains to be seen whether other courts are so persuaded.

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63. Stephanie M. Greene & Lars Noah, Debate, *Off-label Drug Promotion and the First Amendment*, 162 U. PA. L. REV. ONLINE 239, 265 (2014); *see also* Joan H. Krause, *Truth, Falsity, and Fraud: Off-label Drug Settlements and the Future of the Civil False Claims Act*, 71 FOOD & DRUG L.J. 401, 432–34 (2016) (discussing the potential disconnect between truthfulness and liability under the FCA).

64. Michael Rogoff et al., *The Aftermath of* Caronia *in Pursuing Off-label Cases*, INSIDECOUNSEL (Mar. 10, 2014), http://www.insidecounsel.com/2014/03/10/the-aftermath-of-cronia-in-pursuing-off-label [http://perma.cc/92QE-AHPR].

65. *Id.*

66. United States *ex rel.* Sullivan v. Atrium Med. Corp., No. SA-13-CA-244-OLG, 2015 WL 13799885, at *13 (W.D. Tex. Nov. 20, 2015). Moreover, the 21st Century Cures Act allows for more latitude for the dissemination of healthcare economic information outside of approved indications to formularies and reimbursement committees. *See* Sam F. Halabi, *Off-label Marketing's Audiences: The 21st Century Cures Act and the Relaxation of Standards for Evidence-Based Therapeutic and Cost-Comparative Claims*, 44 AM. J.L. & MED. 181, 188–94 (2018).

In light of its lucrative past, the following Part focuses on the FCA and explores how its requirements impact its ability to be more than just a revenue-raising tool for the government.

II. A SOCIALLY BENEFICIAL FALSE CLAIMS ACT?

It is uncontested that the FCA is a powerful tool in raising money for the government. However, insofar as society is interested in using the FCA not only to fill government coffers but to provide a public service to other patients, payers, and providers, two characteristics are essential. First, the FCA suit should create new information about the appropriateness of an off-label use. Second, the legal incentives must prompt earlier relinquishment of inappropriate uses even for patients of public payers. This Article addresses each of these characteristics in turn.

A. A More Informative FCA

The current non-regulation of off-label use results in potentially inappropriate prescription due to insufficient information.[67] Interventions that raise the visibility of existing information or that create new information about the efficacy of off-label uses can result in more appropriate prescriptions.

1. The Trial Can Publicize New Information

In some ways, the FCA is well-positioned to fulfill the goal of bringing new information about off-label uses into the public sphere. The details of its execution, however, affect how helpful this information creation may be in aiding prescribers in appropriate off-label prescription.

In particular, the FCA's *qui tam* provision is designed to incentivize the revelation of internal information. Indeed, whistleblowers cannot bring a claim "if substantially the same allegations or transactions . . . were publicly disclosed in a [f]ederal criminal, civil, or administrative hearing in which the [g]overnment or its agent is a party; in a congressional, [g]overnment Accountability Office, or other [f]ederal report, hearing, audit, or investigation; or from the news media . . . ."[68]

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67. *See supra* Part I.
68. 31 U.S.C. 3730 (e)(4)(A) (2018).

Accordingly, whistleblowers who publicize internal information about the appropriateness of a drug use can identify types of fraud and publication bias that are otherwise near impossible to detect. Such fraudulent conduct can include falsification of data, suppression of studies, and private information about safety risks, all of which would be relevant for prescribers.

While all whistleblowers must allege non-public information in order to bring the FCA claim, if the new information is related solely to technical violations of the FCA rather than new information about the appropriateness of a drug use, the informational value created by the suit will be low. Indeed, an FCA suit that solely rebroadcasts publicly-available scientific information about a use's medical appropriateness might constitute a wasteful exercise.

This is not to suggest that rebroadcasting public results is not an important goal: indeed, it might even be necessary given the prevalence of publication bias. As insurance companies have accused pharmaceutical companies of burying negative studies in lower-circulating journals,[69] physicians may not be aware of the negative studies due to this practice. More benignly, the publication of scientific studies alone might be insufficient to trigger relinquishment merely due to the sheer volume of studies published daily.

There are, however, more efficient ways to consolidate and publicize existing studies. A lawsuit is an expensive signal for what should be purely scientific information. Ideally, some government entity would publish a drug digest synthesizing all studies done on each use and assigning a recommendation regarding the appropriateness of the use.[70] But this would only address the practice of burying negative results in low circulating journals (rather than more insidious forms of publication bias).

While either information-creating function—revelation of new scientific information or republication of obscure but public scientific

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69. *See In re* Neurontin Mktg. & Sales Pracs. Litig., No. 04-cv-10739-PBS, 2011 WL 3852254, at *8 (D. Mass. Aug. 31, 2011), *aff'd*, 712 F.3d 21 (1st Cir. 2013) ("Another type of publication bias described by Dr. Dickersin is 'location bias' or 'gray literature bias' where a company publishes a negative trial in a journal that has a smaller circulation than more well-known medical journals.").

70. There are private drug digests, but some wonder about whether the publications are truly unbiased. David Armstrong, *How Drug Directory Helps Raise Tabs for Medicaid and Insurers*, WALL ST. J. (Oct. 23, 2003, 12:01 AM), http://online.wsj.com/article/0,,SB106685564225943200,00.html. Even with appropriate drug digests, such consolidated information will still need to be contemporaneously incorporated into physicians' decisions.

information—can be beneficial to providers, the latter might be more effectively achieved by a separate mechanism.

2. Signal Value of Suit Resolution

In addition to actually creating new substantive information at trial, the resolution of a FCA suit in either a verdict or settlement can serve as a signal that a drug use's value is suspect. In order for this to be the case, more discretion must be exercised in which cases to target. Bringing FCA suits against both inappropriate and appropriate off-label uses dilutes the signal value of suit resolution.

Given that the FCA is concerned with the reimbursement status of a claim, there is an important distance between the social goal of policing of false information and the FCA's goal of policing of reimbursements. Non-reimbursable claims and medically inappropriate claims are not necessarily identical. This is no clearer than when courts have allowed a truthful statement to serve as the basis of a suit as long as the statement resulted in the submission of claims that were not reimbursable by the government. As noted above, the future of this sort of claim is uncertain, particularly in light of developing commercial free speech jurisprudence. Even if this theory is still viable—and to the extent that this was never a bar to FCA suit in the past—allowing suit for truthful off-label promotion dampens the signal value of an FCA suit. If the government is allowed to bring an FCA suit against a manufacturer for truthful promotion of an off-label use, this likely allows FCA suits to be brought for appropriate uses in addition to inappropriate uses.[71] Accordingly, the fact that the government brings such a suit sheds little information on whether the use at issue is inappropriate.[72]

In addition to the issues surrounding truthful promotion of off-label uses, mass settlement presents a danger to signal value. Given the sizable penalties available through the FCA, a pharmaceutical company may be more likely to settle rather than risk the high penalties in court even if the case only has a slight chance of being

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71. Indeed, while truthful promotion does not necessary imply that the underlying use is medically appropriate, it seems likely that false claims are more prevalently made about medically inappropriate uses.

72. Presumably, physicians would catch on to this weakening signal if off-label uses that they know are well-established or successful to become subject to the FCA. Pharmaceutical companies could also build this narrative by focusing on technical violations of the FCA and suggesting that the government is simply greedy.

meritorious.[73] While settlements serve an important function within our legal system, other scholars have pointed out that mass settlement of claims prevents the formal development of FCA jurisprudence.[74] For our purposes, an additional danger is that mass settlement—specifically settlement insensitive to appropriateness of suit—muddies the signal value of an FCA settlement.

Given this basis, developments in FCA jurisprudence that limit the government's ability to recover for truthful claims about a drug will only move us closer to a socially beneficial FCA. Conversely, developments that merely increase the potential damages associated with each claim or make legal standards too lenient[75] can lead to inefficient settlement and accordingly lower the signal value of suit.

B. Incentives to Preemptively Screen Inappropriate Uses

While FCA suits potentially provide information to other providers about the appropriateness of a drug use, they also reduce the government's incentive to prevent inappropriate prescriptions in the first instance. As noted above, the cost of inappropriate off-label prescription is both monetary and human. Accordingly, society should be concerned about monetary waste associated with inappropriate off-label uses and also patients' lost opportunities to consume more beneficial treatments. While the government may be able to recoup its monetary losses from erroneously reimbursing inappropriate uses, patients cannot get back the time they spent on an ineffective drug. Accordingly, an optimal fraud statute would incentivize the government to not only update its reimbursement list in accordance with new scientific evidence (to exclude medically inappropriate prescriptions) but also to aid in preventing inappropriate prescriptions.

As a practical matter, the government could prospectively prevent inappropriate prescriptions in at least three ways. First, the government could publicize broadly the uses it reimburses and which it does not. Physicians who know that their patients will be covered by Medicare or Medicaid will then incorporate this restriction into their prescription choice. Second, the government

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73. Joan H. Krause, *Reflections on Certification, Interpretation, and the Quest for Fraud that Counts Under the False Claims Act*, 2017 U. ILL. L. REV. 1811, 1844 (2017).

74. *Id.*

75. The specifics of this restriction are discussed in Part II.0

could try to disseminate information about drug use appropriateness directly to physicians in order to prevent inappropriate prescriptions. This would provide an educational function outside of the mere reimbursement status mechanism. Finally, in cases in which false statements are alleged to have changed the reimbursement status of a drug use, a government can demonstrate that it updates its reimbursement status in response to new information.[76]

Notably, any modification that makes recovery less likely will incentivize the government to preemptively prevent inappropriate prescriptions. Because of the relative ease with which an FCA claim can be brought—and generally settled—the government may be less sensitive to new information on off-label appropriateness, knowing it can recoup any monetary losses through suit. In contrast, other payers may put more effort into screening out inappropriate uses as avenues for reimbursement are less certain.[77] A government confident of recouping losses through the FCA (either under a verdict or settlement) has less incentive to undertake any effort to make these standards or new information well known. Indeed, particularly given the high stakes, a government may even be confident that pharmaceutical companies may settle even if when it is unclear where the drug was reimbursable.[78] Conversely, if the government believes that recouping its lost reimbursements is uncertain or unlikely, it will invest more resources into ensuring

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76. For Medicare Part D and Part B, reimbursement for off-label uses is pegged to drug compendia and peer-reviewed studies, respectively. *CMA Report: Medicare Coverage for Off-label Drug Use*, CTR. FOR MEDICARE ADVOC. (Sept. 16, 2010), http://www.medicareadvocacy.org/cma-report-medicare-coverage-for-off-label-drug-use/#_edn11. Insofar as the compendia—and whatever review of studies is given—update consistently with new data, this is appropriate. However, the focal public communication of these changes would be necessary to prevent inappropriate prescriptions in the first place. Medicaid reimburses some off-label treatments but not others; though, states have some discretion in this decision. Krause, *supra* note 63, at 423–24. Accordingly, Medicaid coverage decisions are more detached from the federal government. However, given the fact that many states have passed comparable state false claims act statutes, analogous arguments can be made for state governments' behavior in bringing suit under their own statutes.

77. For example, private insurance companies have had a harder time recovering for fraudulently induced reimbursements under the Racketeer Influenced and Corrupt Organizations Act. *See, e.g.*, United Food & Com. Workers Unions & Emps. Midwest Health Benefits Fund. v. Walgreen Co., 719 F.3d 849, 850, 856–57 (7th Cir. 2013).

78. Again, this is especially true when some states reimburse the use and others do not.

that it does not reimburse inappropriate prescriptions in the first place.

Because the FCA also performs an information-creating function,[79] we may prefer that the screening function be incentivized by standards that actually reward screening behavior rather than standards that uniformly reduce the likelihood of success at trial. While lenient standards that lead to uniform mass settlement ruins both the signal value of suit and government incentives to relinquish inappropriate uses, uniformly *stringent* standards lead (eventually) to no FCA suits. While this does increase government incentives for preemptive relinquishment, it also limits the informational content that could be generated through the FCA suit. In order to maximize both functions, legal standards should reward the government for putting effort into communicating their reimbursement choices—and the evidentiary reasons underlying such choices—as this prospectively prevents inappropriate prescriptions.

Given that the basis of an FCA suit is fraudulent reimbursement not inappropriate prescription, it may seem like a stretch to expect FCA requirements to affect prospective prescriptions. However, given the connection between reimbursement status and prescription, even the transparent listing of reimbursement status for each use has a potential effect on prescription of that use. Accordingly, in cases alleging that false statements by pharmaceutical companies caused a change in reimbursement status, a screening standard may require that the government prove that it would have prominently updated the use's reimbursement status or provided guidance on disfavored drugs in order to claim that a false statement caused fraudulent reimbursements. These requirements relate purely to communications on reimbursement status but would have the accompanying effect of affecting prescriptions in the first instance.

In contrast, other standards may decrease the likelihood of recovery at trial but not otherwise incentivize the government to prevent inappropriate prescriptions. For example, the disconnect between the necessary specificity in identifying erroneous reimbursements and the type of evidence available to relators has been a bar to recovery.[80] Courts have noted that relators must show

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79. *See supra* Part II.II.A.

80. Robert Salcido, *False Claims Act – Year in Review: Five Decisions that Will Affect the Future of FCA Litigation – The Salcido Report: False Claims Act Public*

that "the defendant caused a false claim to be presented to the government, because liability under the Act attaches only to a claim actually presented to the government for payment, not to the underlying fraudulent scheme."[81] However, while relators have access to companies' promotion campaigns and the information distributed, they do not have access to patient records or reimbursement claims.[82] With an overly stringent application of this pleading standard, which penalizes relators for not having access to reimbursement data, the government's incentives to screen stem from a reduced expectation of winning—not from anticipated rewards from screening.

Given that the legal standards characterizing the execution of FCA claims affect its potential informational value and incentives to preemptively screen uses, the strength of these effects given current standards is an empirical question. To demonstrate the potential value of the FCA, the next Part focuses on the case of Neurontin. The FCA suit against Warner-Lambert, Pfizer's subsidiary, was one of the first off-label FCA cases to settle. The strength of considering this case, however, is that it concerns an objectively inappropriate off-label use: the use of Neurontin for the treatment of bipolar disorder. Accordingly, the socially beneficial outcome is unambiguously the relinquishment of this treatment as early as possible.

Based on the arguments from this Part, two hypotheses follow. First, an FCA claim should trigger the relinquishment of inappropriate off-label uses. Second, to the extent that the FCA differently incentivizes public and private payers to preemptively relinquish inappropriate off-label uses earlier, this Article hypothesizes that relinquishment should differ by payer. Specifically, government payers should be less likely to preemptively relinquish inappropriate uses, confident of recovering damages

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Disclosure Alert, JDSUPRA (Jan. 28, 2020), https://www.jdsupra.com/legalnews/false-claims-act-year-in-review-five-32970/.

81. United States *ex rel.* Nathan v. Takeda Pharm. N. Am., Inc., 707 F.3d 451, 456 (4th Cir. 2013); *see also* United States *ex rel.* Booker v. Pfizer, Inc., 847 F.3d 52, 58 (1st Cir. 2017) ("This court has made clear that where relators offer only 'aggregate expenditure data by the government for' the drug at issue, 'with[out] identify[ing] specific entities who submitted claims . . . much less times, amounts, and circumstances,' their claim falls 'far short.'" (alterations in original)).

82. Courts acknowledge this difficulty but reason that this is required by pleading requirements. *Takeda Pharm.*, 707 F.3d at 458.

through FCA suit.[83] Private payers, on the other hand, might engage in more preemptive screening[84] given that recovery through suit is substantially more difficult. The remainder of this Article empirically tests these hypotheses.

III. NEURONTIN: A CASE STUDY

This Part examines a focal off-label promotion case, that of Neurontin. Neurontin was marketed for many off-label uses, one of the most important being for bipolar disorder. Neurontin was not found to be effective for the treatment of bipolar disorder in a study conducted by its own manufacturer, Warner-Lambert.[85] This Part studies prescriptions of Neurontin for the treatment of bipolar disorder to cleanly measure relinquishment of an "inappropriate" off-label treatment. A few studies have studied Neurontin prescription patterns for publicly-funded programs[86]; this Article expands this analysis to allow for heterogeneity by payer.

Using data from the National Ambulatory Medical Care Survey ("NAMCS"), this Part measures the responsiveness of physicians to news of Neurontin's ineffectiveness in treating bipolar disorder. The results suggest that physicians do not uniformly relinquish the drug after scholarly news of its ineffectiveness. Instead, this Article finds that a patient's payment method affects the likelihood of whether

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83. As will be discussed below, however, this may be a weaker effect because this suit largely considered Medicaid suits and the federal government has less control over such coverage decisions. Non-coverage interventions, however, are possible.

84. Payers can prospectively screen off-label uses and influence treatment decisions in two ways: (1) they can refuse to reimburse a treatment (or as a less extreme option, can place the drug on a more expensive tier in their formulary); or (2) they can influence treatment by constructing guidelines regarding "preferred" treatments. The former can affect the treatment decision by making the treatment marginally more expensive and less attractive. The former can also serve as a signal from the payer that they do not value a particular use. The latter serves as a source of information for physicians, persuading physicians that a use is inappropriate through research conducted by its pharmacy benefit manager.

85. Atul C. Pande et al., *Gabapentin in Bipolar Disorder: A Placebo-Controlled Trial of Adjunctive Therapy*, 2 BIPOLAR DISORDERS 249, 252 (2000).

86. *See* Aaron S. Kesselheim et al., *False Claims Act Prosecution Did Not Deter Off-label Drug Use in the Case of Neurontin*, 30 HEALTH AFFS. 2318, 2320 (2011); *see also* Catherine A. Fullerton et al., *The Rise and Fall of Gabapentin for Bipolar Disorder: A Case Study on Off-label Pharmaceutical Diffusion*, 48 MED. CARE 372, 372 (2010) (studying the roles of marketing, clinical evidence, and off-label use of the drug gabapentin).

the patient is prescribed the disfavored drug. Patients with private insurance and Medicaid were less likely to receive Neurontin after 2002. These results suggest that prescriptions may not be as sensitive to scientific data as society might like and that some payers relinquish treatment earlier than others.

A. Testing the Relinquishment Hypotheses

Patient-level records from the NAMCS 1998–2008 are used to estimate the determinants of bipolar treatment choices. Each year, the NAMCS sample includes around 3,000 physicians and samples the eligible physicians' patient records.[87] The survey encompasses non-federally employed physician offices engaged in "office-based patient care."[88] All patient records that list bipolar disorder as one of the three possible diagnoses for the visit are included.

1. Dependent Variable: Choice of Drug

Physicians have several options for bipolar disorder treatment. In the 1970s, lithium was discovered to be an effective mood stabilizer.[89] Anticonvulsant drugs are also generally effective mood stabilizers. In particular, Depakote was FDA-approved for the treatment of bipolar in 1995.[90] Several other anticonvulsant drugs used off-label for bipolar were used as mood stabilizers and later approved by the FDA for the treatment of bipolar disorder. Lamictal was approved for bipolar disorder on June 20, 2003,[91] Equetro on December 10, 2004,[92] and Stavzor on July 29, 2008.[93]

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87. CTR. FOR DISEASE CONTROL & PREVENTION, 2008 NAMCS MICRO-DATA FILE DOCUMENTATION 2, 6 (2008); *see* Denys T. Lau et al*., Toward a More Complete Picture of Outpatient, Office-Based Health Care in the US*, 51 AM. J. PREVENTATIVE MED. 403–09 (2016).

88. Lau et al., *supra* note 87. In 2006, a sample of community health centers was added to the survey. *Id*. at 403.

89. Edward Shorter, *The History of Lithium Therapy*, CAN. INSTS. HEALTH RSCH., June 2009, at 4, 4–9.

90. *Depakote*, LUCIDA TREATMENT: ADDICTION BLOG (Mar. 12, 2012), https://www.lucidatreatment.com/addiction-blog/depakote/.

91. *See* Letter from Russell Katz, Dir. of the Div. of Neuropharmacological Drug Prods., Food & Drug Admin., to Eric B. Benson, Senior Dir. of Regul. Affs., SmithKline Beecham Corp. (June 20, 2003).

92. *See* Letter from Russell Katz, Dir. of the Div. of Neuropharmacological Drug Prods., Food & Drug Admin., to Zohra Lomri, Senior Manager, Shire Dev., Inc. 1 (Dec. 10, 2004).

The following analysis will focus on the prescription of Neurontin; while Neurontin is an anticonvulsant, it was not found to be effective as a mood stabilizer. The dependent variable in this analysis is whether a patient is prescribed Neurontin for bipolar disorder. *Neurontin* takes the value of one if Neurontin (or its generic version) is prescribed during the visit, the reason for the visit is not related to convulsions, and none of the diagnoses are for epilepsy. These exclusions ensure that these drugs are prescribed for the bipolar disorder rather than a concurrent epilepsy problem.

2. Information Shocks

There are three major information shocks in the Neurontin scandal. Some are scientific, and some are legal. Each information shock is represented by an indicator variable that takes the value of zero prior to the shock and the value of one after the shock.[94] The first shock involved a journal article regarding Neurontin's ineffectiveness for bipolar disorder that was published in 2000 by Warner-Lambert itself. In 1998, Warner-Lambert conducted a study (the "Pande Study"),[95] which found that Neurontin was less effective for bipolar disorder than a placebo, but the company did not publish the study until 2000.[96] Because the study was conducted by the manufacturer and still reported a negative finding, it should have had a large, negative effect on physicians' prescriptions of Neurontin. Moreover, this study was more rigorous than previous studies—it was one of the first randomized controlled trials ("RCT") to be conducted.[97] Another RCT was published later in 2000 (the "Frye Study").[98] While several RCTs were subsequently published—

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93. *See* Letter from Russell Katz, Dir. of the Div. of Neuropharmacological Drug Prods., Food & Drug Admin., to Dana S. Toops, Dir. of Regul. Affs., Banner Pharmacaps, Inc. 1 (July 29, 2008).

94. For example, *Post2000* takes the value of one after 2000 and *Post2002* takes the value of one after 2002. These overlapping variables allows for the interpretation described below.

95. Pande et al., *supra* note 85, at 252–53.

96. Jeanne Lenzer, *Pfizer Pleads Guilty, but Drug Sales Continue to Soar*, 328 BMJ 1217, 1217 (2004).

97. *See* John W. Williams, Jr. et al., *How Reviews Covered the Unfolding Scientific Story of Gabapentin for Bipolar Disorder*, 31 GEN. HOSP. PSYCHIATRY 279, 285 (2009).

98. Mark A. Frye et al., *A Placebo-Controlled Study of Lamotrigine and Gabapentin Monotherapy in Refractory Mood Disorders*, 20 J. CLINICAL PSYCHOPHARMACOLOGY 607, 607 (2000).

one in 2002 (the "Obrocea Study")[99] and one in 2006 (the "Vieta Study"),[100] this study should be most probative because of its novelty, authorship, and scientific rigor.

Litigation provides the next two information shocks. The media began to report on the suit in 2002.[101] Several NPR pieces and other media outlets carried this news.[102] During litigation, various internal documents showed Warner-Lambert's efforts at promoting Neurontin despite no evidence of effectiveness.[103]

The final information shock occurred in 2004 when the litigation settled. Pfizer paid $430 million to settle its civil FCA and criminal FDCA charges for illegal and fraudulent promotion of off-label uses of Neurontin.[104] This is a very visible landmark as Neurontin was one of the first FCA cases based on off-label promotion.

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99. Gabriela V. Obrocea et al., *Clinical Predictors of Response to Lamotrigine and Gabapentin Monotherapy in Refractory Affective Disorders*, 51 BIOLOGICAL PSYCHIATRY 253, 253 (2002).

100. Eduard Vieta et al., *A Double-Blind, Randomized, Placebo-Controlled, Prophylaxis Study of Adjunctive Gabapentin for Bipolar Disorder*, 67 J. CLINICAL PSYCHIATRY 473, 473 (2006).

101. The lawsuit was not filed at this time but had been kept under seal until 1999. United States *ex rel.* Franklin v. Parke-Davis, Div. of Warner-Lambert Co., 147 F. Supp. 2d 39, 46 (D. Mass. 2001). The first opinion did not come out until mid-2001, but the news began reporting on the suit in 2002. In October 2002, the District of Massachusetts allowed the media to see nonprivileged documents produced in discovery. United States *ex rel.* Franklin v. Parke-Davis, 210 F.R.D. 257, 257–58 (D. Mass. 2002).

102. Snigdha Prakash, *Court Files Yield New Information in Suit Against Drugmaker*, NPR (Nov. 2, 2002, 12:00 AM), https://www.npr.org/templates/story/story.php?storyId=829633; Snigdha Prakash, *Neurontin Lawsuit*, NPR (June 18, 2002, 12:00 AM), https://www.npr.org/templates/story/story.php?storyId=1145205; Marcia Purse, *Neurontin and Its Off-label Use in Bipolar Disorder*, VERYWELLMIND, https://www.verywellmind.com/neurontin-and-off-label-use-bipolar-disorder-380400 (last updated Feb. 25, 2020).

103. *Warner-Lambert to Pay $430 Million to Resolve Criminal & Civil Health Care Liability Relating to Off-label Promotion*, *supra* note 15. This litigation was accompanied by another suit, a class action suit, filed against Pfizer in 2002 alleging that the company engaged in off-label promotion and sham patent litigation to retain market exclusivity. Andrew Longstreth, *Pfizer Agrees to $190 Million Settlement over Generic Neurontin*, REUTERS (Apr. 21, 2014, 4:57 PM), https://www.reuters.com/article/us-usa-antitrust-pfizer/pfizer-agrees-to-190-million-settlement-over-generic-neurontin-idUKBREA3K17420140421. Though this is a separate suit, the allegation of off-label promotion is the same as the allegation in the FCA suit, and the patent litigation should not affect physician decisions if price does not actually change.

104. *Warner-Lambert to Pay $430 Million to Resolve Criminal & Civil Health Care Liability Relating to Off-label Promotion*, *supra* note 15 (noting that in addition to the FCA claims, the settlement involved guilty pleas to misbranding under the FDCA and civil liability to states for losses to state Medicaid programs). Another

These information "shocks" are not without complications. Because they are mostly identified by year, this Article lists possible concurrent events that might influence relinquishment. One concurrent event that complicates the analysis is that, as previously noted, the Obrocea Study in 2002 found that Neurontin use alone did not outperform a placebo in treating bipolar disorder.[105] The author was unable to control for this because it also occurred in 2002. It is possible that this was the extra information necessary to catch physicians' attention. However, this seems unlikely for several reasons. First, the Obrocea Study does not seem to be cited by review studies—of the seven review studies published between 2003–2005 (after the third RCT and before the fourth RCT was published), each cited the two RCTs published in 2000 but not the Obrocea Study.[106] This suggests that the study was not very influential at all and likely did not drive the results. Second, the Obrocea Study was no more negative than the previous two studies. While noting that Neurontin performed no better than the placebo, the study noted that it was most effective in young people and people with lower baseline weight.[107] Second, nothing about its authorship or novelty should have struck physicians as more probative than the Pfizer study. Third, this was not the only other study published confirming Pfizer's study—a second RCT, the Frye Study, was published two months after Pfizer's study confirming the results.[108]

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information shock regarding Neurontin in general occurred in 2005. On April 22, 2005, Pfizer and the FDA issued a voluntary recall from the manufacturer for 40,000 bottles of capsules distributed in October and November of 2004 because an error in production resulted in empty or partially filled capsules. *Gabapentin FDA Alerts*, DRUGS.COM, https://www.drugs.com/fda-alerts/1147-0.html (last updated Dec. 19, 2019). Because this date is so close to the litigation date and this is a national alert, it is difficult to disentangle the effect of the litigation and the recall. It is possible that physicians prescribing Neurontin for bipolar disorder were sensitive to this information shock. One could argue that the recall shook physicians' trust in Warner-Lambert so that they decrease their prescriptions. However, physicians are more likely to distrust a manufacturer more for its fraudulent promotion than for a mechanical error. The former would seem to breed more lasting fears and actually change prescribing behavior long term.

105. Obrocea et al., *supra* note 99, at 256–57.

106. This study in 2009 briefly mentioned the date of the Obrocea Study but did not include a summary of its findings in its table detailing summaries of past studies. *See* Williams, Jr. et al., *supra* note 97, at 282–85 tbl.1 & fig.2. One study lists the second RCT in its citations but only discusses the Pande and Frye Studies. Carrie L. Ernst & Joseph F. Goldberg, *Antidepressant Properties of Anticonvulsant Drugs for Bipolar Disorder*, 23 J. CLINICAL PSYCHOPHARMACOLOGY 182, 188 (2003).

107. Obrocea et al., *supra* note 99, at 256–57.

108. *See* Frye et al., *supra* note 98, at 607–14.

The second concurrent event is that the American Psychiatric Association issued a new practice guideline for patients with bipolar disorder in 2002,[109] which incorporated the 2000 negative study by Warner-Lambert as well as the Frye Study.[110] Thus, it is unclear whether a drop in 2002 for psychiatrists would be due to the litigation or the revised bulletin. To account for this, only patients seeing psychiatrists (around 80% of the sample) are considered because they are equally likely to have seen the guidelines in 2002. While this does not eliminate the concurrent event, it does place all patients on the same footing.

3. Third-party Payer Behavior

Indicators for payment type included Medicare, Medicaid, private insurance, "other" or no insurance,[111] and Medicaid.[112] The residual category is self-payment. The first issue is that the expected payer for the visit may be different from the person who pays for the prescription, which this Article does not observe. For several of these categories, there is a high likelihood that these two payers will be the same, particularly private insurance, Medicaid, and self-payment.[113] For Medicare, however, this is different: there may be a difference in the expected payment for prescription drugs and the expected payment for the visit. Medicare patients did not have

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109. ROBERT M.A. HIRSCHFELD ET AL., AM. PSYCHIATRIC ASS'N, PRACTICE GUIDELINE FOR THE TREATMENT OF PATIENTS WITH BIPOLAR DISORDER 5–6 (2d ed. 2002).

110. *Id.* at 39, 43, 73; *see also* Fullerton et al., *supra* note 86, at 372–79 (describing how the two studies in 2000 failed to show the benefits of gabapentin).

111. This category is included as a control but not discussed.

112. The process by which expected payer is coded in NAMCS data changes in 2005. Previously, they collected "primary" expected source of payment; in 2005 they collected multiple sources and imposed the following hierarchy: Medicaid, Medicare, private, worker's compensation, self-pay, no charge, other, and unknown. In 2007 they reversed this hierarchy, making Medicare dominant over Medicaid. If there is a concern that the relinquishment in 2002 for private payers was driven by the imposition of the hierarchy in general, running the model on 1998–2004 produces the same *Post2002* results. Additionally, insofar as the change after 2004 categorized Medicare above private in contrast to previous coding procedure, an additional robustness check recoded the hierarchy with private first. Whenever "paypriv," a dummy indicating that private insurance was expected to pay, the recode indicates that payment was from private insurance even if the hierarchy would have listed Medicare or Medicaid. The results using this recoding seem qualitatively unchanged.

113. Of course, this will not always be true, but there is no reason to believe the error will vary by payer.

Medicare coverage for outpatient drugs until Medicare Part D[114] was implemented in 2006. Thus, these patients may have paid for their drugs in a number of ways: self-payment, supplemental private coverage, or dual coverage under Medicaid. If the drug was administered inpatient, it may have been covered by another Medicare Part though this is less likely. The Medicare category is retained in the analysis, but caution should be taken in interpreting these coefficients, and this Article does not focus on these results. However, this takes into account possible treatment differences when the patient's total visit is characterized predominantly as being covered by Medicare.

The variables of interest are the sensitivities of each payer to these information shocks. As mentioned above, a payer can influence treatment in two possible ways: a payer can refuse to cover a particular treatment or can use persuasive measures to spread information about a use's appropriateness. Each of these measures is discussed below.

The first way a payer can influence treatment is by refusing to cover a particular treatment. Refusal to reimburse results in two effects. First, if a physician maximizes expected patient benefit, changes in reimbursement make a treatment relatively more expensive for a patient. This should make physicians less likely to prescribe the drug. Private payers seem to cover Neurontin's off-label uses to varying degrees. Public payers are more complicated: the *Parke-Davis* court struggled with whether government programs actually allowed reimbursement of Neurontin's off-label uses.[115] While Neurontin was not supported by a medical compendium, Parke-Davis argued that a majority of state Medicaid programs allowed coverage of non-compendium off-label uses.[116] The government in turn argued that Medicaid was confined to uses listed in the designated compendia.[117] The court did not resolve this issue

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114. Medicare Part D covers prescription drugs that are approved by one of three compendia in order to be reimbursable. The three compendia include American Hospital Formulary Service – Drug Information (AHFS-DI), United States Pharmacopeia – National Formulary (USP-NF), and DRUGDEX. *CMA Report: Medicare Coverage for Off-label Drug Use*, *supra* note 76. DRUGDEX, the most inclusive of the compendia, was approved as an official compendium in 1997. Armstrong, *supra* note 70.

115. *United States ex rel. Franklin v. Parke-Davis*, No. Civ.A. 96-11651PBS, 2003 WL 22048255, at *3 (D. Mass. Aug. 22, 2003).

116. *Id.* at *2.

117. *Id.* at *3. This arises from an interpretation of the Medicaid statute which stated that "[a] State may exclude or otherwise restrict coverage of a covered

but noted that if a state Medicaid program did cover Neurontin, the reimbursements could not constitute a false claim.[118] Second, refusal to reimburse may function as a signal to the physician that the payer does not think the drug use is appropriate.

The second way a payer can influence treatment decisions is by implementing drug utilization reviews to examine how a drug is prescribed and to make suggestions to its physicians. Private payers often do this through their Pharmacy Benefit Managers.[119] The Medicaid statute also provides for a drug use review program in order to "educate physicians and pharmacists to identify and reduce the frequency of patterns of fraud, abuse, gross overuse, or inappropriate or medically unnecessary care . . . ."[120] At least one private insurance company seemed to influence treatment not through refusing reimbursement but through the persuasive means. Kaiser campaigned to reduce its Neurontin prescriptions after it was alerted to Pfizer's fraudulent conduct; however, Kaiser did not reduce its prescriptions by refusing to reimburse Neurontin.[121] Instead, it retained its open formulary in which it would even reimburse prescriptions not on the formulary. Kaiser issued reports about preferred effective drugs through its Drug Information Service.[122] Its physicians relied on these reports to such an extent that, although they were permitted to prescribe off-formulary, 95% of Kaiser physicians' prescriptions were on-formulary.[123] Upon receiving news of Neurontin's ineffectiveness, Kaiser's campaign against Neurontin prescriptions reduced new prescriptions by about

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outpatient drug if . . . the prescribed use is not for a medically accepted indication [as defined in subsection (k)(6) of this section]." Stephanie Greene, *False Claims Act Liability for Off-label Promotion of Pharmaceutical Products*, 110 PENN ST. L. REV. 41, 62 (2005) (first alteration in original) (citing 42 U.S.C. § 1396r-8(d)(1)(B) (2000)). Some suggest that this negative framing means that Medicaid can reimburse uses not in the designated compendia: American Hospital Formulary Service – Drug Information (AHFS-DI), United States Pharmacopeia – National Formulary (USP-NF), and DRUGDEX. *See, e.g.*, Benjamin S. Martin, Assoc., Arnold & Porter LLP, Presentation at the Pharmaceutical Compliance Congress: Medicaid Coverage for Drugs for Off-label Uses 4 (Nov. 15, 2004) (presentation slides available at http://www.ehcca.com/presentations/pharmacongress5/martin_2.pdf); *CMA Report: Medicare Coverage for Off-label Drug Use*, *supra* note 76.

118. *Parke-Davis*, 2003 WL 22048255, at *3–4.

119. Peter D. Fox, *Prescription Drug Benefits: Cost Management Issues for Medicare*, HEALTH CARE FIN. REV., Winter 2003, at 7, 7–10.

120. 42 U.S.C. § 1396r-8(g)(1)(A) (2018).

121. *In re* Neurontin Mktg. & Sales Pracs. Litig., 712 F.3d 21, 29 (1st Cir. 2013).

122. *Id.*

123. *Id.*

33%.[124] This demonstrated screening process helped Kaiser win its Racketeer Influenced and Corrupt Organizations Act ("RICO") claim against Pfizer, proving that it would not have reimbursed Neurontin prescriptions but for the fraudulent information.

Given that payers can theoretically influence treatment in these two ways, one interesting comparison is between third-party payers and self-payers. For this reason, the omitted payment category—the category which provides the baseline for all other payment effects—is "self-pay." Self-pay patients arguably are not influenced by payers through either mechanism: they are not subject to reimbursement changes, and they presumably do not receive any persuasive literature. Treatment for self-pay patients may be influenced by persuasive techniques used by payers of patients with the same doctor. The study attempts to account for this by clustering errors by physician code and year.[125] Examining the other payers relative to self-pay patients provides an interesting comparison.

As Medicaid claims were the basis for the FCA suit, another important comparison is how patients with Medicaid were treated relative to patients with private insurance. The federal government sought reimbursement for Medicaid claims under the FCA, while private insurance companies had to seek compensation elsewhere.

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124. The opinion notes:

> Neurontin prescriptions written by PMG physicians increased dramatically after September 1999 (the fraudulent marketing campaign began in 1997). This notable increase led some Kaiser regions to "examine their members' use of Neurontin" and make efforts to limit it. By the spring of 2002, the Northern California PMG had barred Pfizer drug representatives from detailing its physicians regarding Neurontin, and the same PMG's Drug Utilization Group ("DRUG") began a campaign to promote only the appropriate use of Neurontin, which other regional PMGs joined. In late 2002, Kaiser learned about Franklin's qui tam action and escalated its efforts to limit prescribing of Neurontin for neuropathic pain, bipolar disorder, migraine, and nociceptive pain. Kaiser shared materials about Neurontin produced by DRUG and the Southern California PMG's Drug Utilization Action Team ("DUAT") with all regional PMGs. The district court found that though Neurontin use continued to increase nationally, Kaiser's efforts to limit its use "result[ed] in a 33–34% decrease in new starts of Neurontin."

Id. at 31–32 (citations omitted).

125. Physician codes indicate when the same physician treats multiple patients within a given year.

Private insurance companies have had a harder time recovering their reimbursements and might apply more pressure on physicians to police prescriptions more carefully. Kaiser's success can be attributed at least in part to its proactive relinquishment of Neurontin, such as barring pharmaceutical representatives from detailing their physicians and launching their own campaigns for appropriate drug promotion.[126]

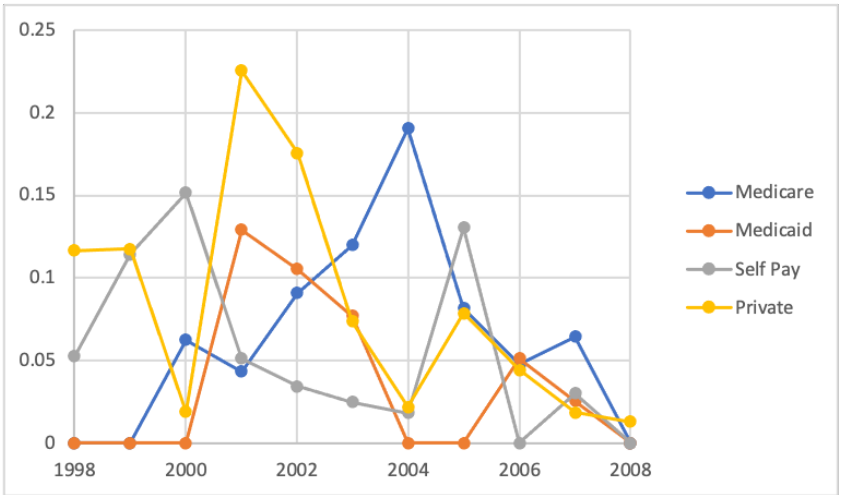
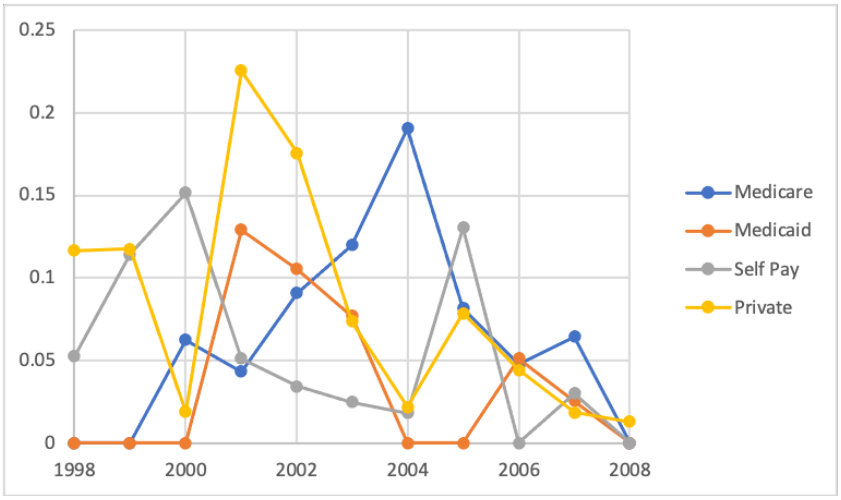


Figure 1. Percent of Neurontin Prescriptions by Payer and Year



126. *See In re Neurontin Mktg.*, 712 F.3d at 31–32.

Figure 1 plots the percent of Neurontin prescriptions in the sample by payer and year.

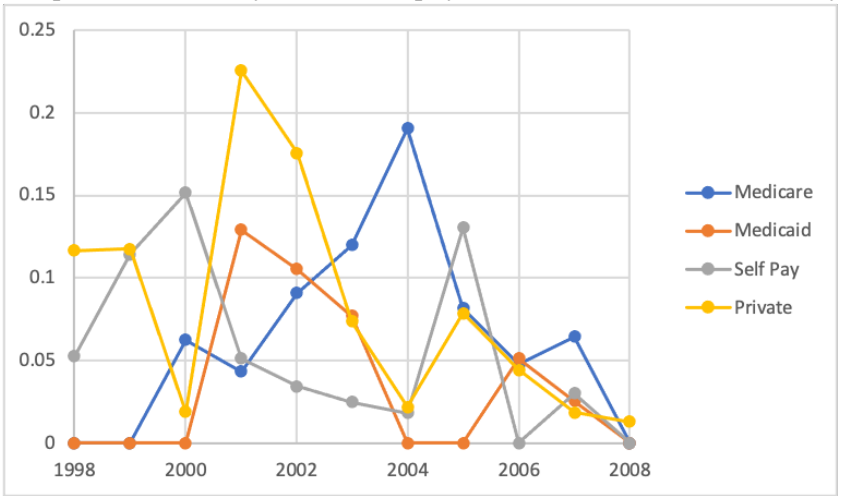


Figure 1 shows that there is considerable heterogeneity in adoption and relinquishment by payer. Self-pay patients seem to increase their prescriptions until 2000, after which they decline until 2005. Private insurance patients experience a big increase in prescriptions after 2000 and then a sharp decline after 2002. Medicaid prescriptions increase after 2001 and gradually decline after 2002. Medicare patient prescriptions continue increasing until 2004, after which they decline.

4. Other Control Variables

Finally, in order to account for differences in medical treatment by physical difference, this Article includes a number of patient-level controls, including sex and age. Because the data does not have detailed information about patient health, smoking status is used as a proxy for patient health.[127] Patient-level controls also include measures of bipolar severity. Diagnosis codes found in NAMCS are

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127. Because smoking is correlated with heart disease, stroke, and various cancers, it can be used as a rough measure of patient general health. *See generally* BORIS D. LUSHNIAK, U.S. DEP'T OF HEALTH & HUM. SERVS., THE HEALTH CONSEQUENCES OF SMOKING—50 YEARS OF PROGRESS (2014). Current smoking status is indicated for years 1994–1996 and 2001–2010 for NAMCS. For the missing years, smoking status is assigned if the record indicated that the patient received counseling for smoking cessation. The results are robust to the exclusion of this measure.

used as a measure for this.[128] Bipolar severity should be positively correlated with the prescription of a nontraditional treatment such as Neurontin or other anticonvulsants because people with severe bipolar might not respond to traditional treatment. Similarly, the presence of comorbidities such as psychotic behavior presents complexity for which physicians might seek innovative treatments. To measure comorbidities, an indicator variable measures whether a patient displays psychotic symptoms. A patient is categorized as having psychotic symptoms if the diagnosis code indicates psychotic behavior.

To capture the effect of accumulating scientific evidence outside of the main information shocks, this Article includes a cumulative measure of the number of review studies that either made positive or negative conclusions about Neurontin's effectiveness for bipolar disorder.[129]

Finally, previous research emphasizes the role of pharmaceutical detailing on physician learning.[130] Unfortunately, NAMCS does not include a measure for detailing patterns. To not account for pharmaceutical detailing would result in omitted variable bias, so as a crude indicator, the four region controls provided by NAMCS are included. These region controls attempt to account for different pharmaceutical representative territories, different CME programs, and region-specific prescription idiosyncrasies.

B. Empirical Analysis

This Section tests whether there is heterogeneity in relinquishment by payer. Importantly, this Article measures relative relinquishment, the comparative change in a payers' prescriptions in response to an information shock relative to the corresponding change for self-pay payers. Relative relinquishment does not necessarily mean that nominal prescriptions declined or that the

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128. There are two diagnosis codes designated as severe—one indicating that the diagnosis is severe with psychotic behavior and the other indicating that the diagnosis is severe without psychotic behavior. The author used both diagnosis codes for the severity measure.

129. This measure is from one of the earlier listed studies which documents review studies that evaluated the use of Neurontin for the treatment of bipolar disorder. This data only covers 1998–2006, so the cumulative measure does not increase after 2006. Williams, Jr. et al., *supra* note 97, at 282–86 tbl.1, fig.2 & fig.3.

130. *See generally* Ram Bala et al., *Offering Pharmaceutical Samples: The Role of Physician Learning and Patient Payment Ability*, 32 MKTG. SCI. 365 (2013).

total nominal decline is significant. However, this is an informative measure as comparing behavior relative to self-pay patients provides a baseline of consumer behavior in the absence of third-party intervention. This Section tests for heterogeneity in relinquishment.

The likelihood of being prescribed a particular drug is estimated using a statistical technique called a linear probability model. Specifically, these linear probability models measure the propensity of physicians to prescribe Neurontin. The data are not longitudinal, and the model treats each observation as a separate draw.

The linear probability model disentangles the effect of each of the enumerated factors on the probability of prescribing Neurontin. This Section will not focus on the effect of the patient characteristics as these are largely included as controls.[131] The variables of interest are the main effects of the information shocks and the different payers as well as the interactions between the two.

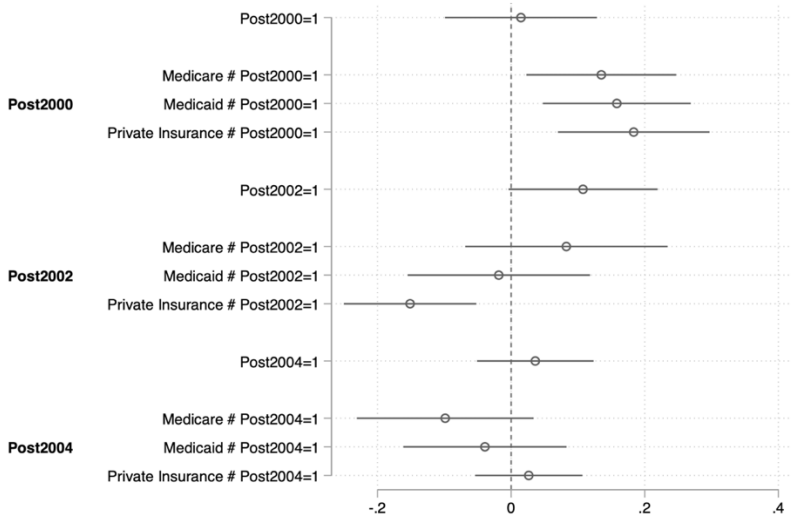

Figure 2. Marginal Effects on Likelihood of Prescribing Neurontin

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ders. in

Figure 2 correspond to column (2) of Appendix Table 1.

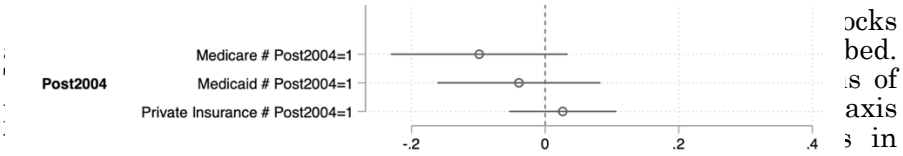

Figure 2 indicate the magnitude of each effect, and the lines indicate the accuracy of these estimates. If the line does not touch the zero line, the estimates are significantly different than zero (i.e., the estimate is sufficiently precise that the 95% confidence interval does not include zero). The information shock interactions are the main variables of interest. The main effect of each period (information shock) can be interpreted as the incremental change from the previous information shock for self-pay patients. For example, *Post2002* should be interpreted as the change in likelihood for self-pay patients after 2002 relative to after 2000. The information shock–payment interactions should be interpreted as the incremental change for a particular payer due to the information shock relative to the corresponding change for self-pay patients. These symbolize the marginal changes in likelihood of prescription for patients with a given payer after each information shock. For example, *Post2002*Private Insurance* should be interpreted as the relative change for private insurance patients after 2002 (relative to after 2000) compared to the corresponding change for self-pay patients.

Given that the negative scientific study was published in 2000, *Post2000* and its subsequent interactions were hypothesized to be negative as the negative scientific study on Neurontin should have reduced the number of Neurontin prescriptions for bipolar disorder. This variable is insignificant for self-pay patients. *Private Insurance*Post2000*, *Medicaid*Post2000*, *and Medicare*Post2000* are positive and significant, suggesting that the publication of the article did not correspond to decreased likelihood of being prescribed Neurontin for private insurance, Medicaid, or Medicare patients relative to the changes in likelihood for self-pay patients. Instead, relative to self-pay patients, the above patients were more likely to receive Neurontin after this time. A possible reason for this relative increase is found in Kaiser's RICO lawsuit against Pfizer. Kaiser claims that Pfizer's "misrepresentations and omissions during the

development of drug monographs" led them to remove any restrictions on the prescription of Neurontin in late 1999.[132]

Post2002 is barely insignificant at the 5% level. Relative to this, the likelihood that private insurance patients are prescribed Neurontin significantly declines by around 14–15%. This is consistent with private insurance company Kaiser's claims that they intensified their campaign to decrease the prescriptions of Neurontin after hearing about the FCA litigation.[133] The likelihood of prescription for Medicaid patients also declines but not significantly. The difference between *Post2002*Medicaid* and *Post2002*Private* is significant at the 10% level.[134] This differential response is intriguing and suggests that anticipated payment is a strong influence on a physician's prescription patterns.

Post2004 main terms and interactions for Medicaid and private insurance are largely insignificant.

C. Discussion

While causal inference is challenging within the confines of the data, it is clear that any relative decrease in Neurontin prescriptions does not occur directly after publication of the 2000 study for patients with third-party payers. It is possible that relinquishment is indeed caused by the scientific study but that it was merely a delayed reaction. However, the observed trend seems more consistent with delayed relinquishment than gradual relinquishment because prescriptions seem to increase after 2000. Kaiser's account of removing restrictions on Neurontin suggests that the availability of unrestricted reimbursement might have caused physicians to continue prescribing Neurontin. For self-pay payers, in contrast, it is possible that the negative study was sufficient to cast doubt on the appropriateness of the drug such that physicians did not want to impose an expensive drug on their patients without insurance. This might suggest that physicians focus less on medical opportunity cost of a drug if the monetary cost is low.

For third-party payers, relinquishment is spurred more only after 2002. The results indicate that patients with private insurance

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132. *In re* Neurontin Mktg. & Sales Pracs. Litig., 712 F.3d 21, 29 (1st Cir. 2013).

133. *See id.* at 31–32; *supra* note 124.

134. For Appendix Table 1, Column (2), the difference between *Post2002*Medicaid* and *Post2002*Private* has an F-statistic of 3.10 (prob > F=0.0786).

became less likely to be prescribed Neurontin after 2002 relative to the change in likelihood for self-pay patients. Patients with Medicaid similarly experienced relinquishment after 2002 although this effect is significantly different than the effect for private insurance patients. Attributing the decline after 2002 to litigation is not without challenges: it is possible that any effect from 2002 was driven by the updated APA guidelines. However, even if the APA guidelines were a driver of this result, this would still undercut the assumptions of the current off-label regime: scientific studies alone would not lead to relinquishment for some patients without a mechanism to rebroadcast the results. There is, however, anecdotal evidence that FCA litigation was a nontrivial driver of this decline, at least for private physicians: Kaiser claimed that after learning about the FCA lawsuit in 2002, it started an aggressive campaign to get its physicians to stop prescribing Neurontin to treat bipolar disorder.[135]

One concern might be that these results are actually driven by the differing costs of Neurontin over time. Neurontin was set to go off patent around 2001,[136] which might have made the drug cheaper for patients.[137] The increase in prescriptions after 2000 might be caused by physicians simply finding Neurontin sufficiently cheap to prescribe even if they knew about the study. However, this argument is problematic for two reasons. First, this does not explain the decline in Neurontin prescriptions after 2002. If physicians knew about the drug ineffectiveness in 2000 and simply prescribed Neurontin because of the lower price, the 2002 litigation would produce no new information and should not affect the prescription decision—because the price would remain at off-patent levels between 2000 and 2002, there should be no decline in 2002. Second, it is unclear whether the price of Neurontin actually dropped during this period. Before the patent expired, Pfizer obtained a production patent to extend protection until 2014; though generic companies contested this patent,[138] it was upheld in 2007.[139]

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135. *See In re Neurontin Mktg.*, 712 F.3d at 31–32; *supra* note 124.

136. Patricia J. Neafsey, *Lyrica (Pregabalin): Neurontin Replacement?*, 23 HOME HEALTHCARE NURSE 563, 563 (2005).

137. It is not clear that prices would have necessarily dropped post-patent. Post-patent price changes are dependent on many different variables not discussed in this Article.

138. Some sources suggest that a generic launch was attempted in 2004. Press Release, Pfizer, Court Rules for Pfizer in Patent Infringement Case on Neurontin (Sept. 21, 2007), https://www.pfizer.com/news/press-release/press-release-

Another potential explanation is that the changes in prescriptions were due to underlying changes in pharmaceutical detailing effort. Although the data only include a crude measure of pharmaceutical detailing, anecdotal evidence suggests that this was not the case. In its announcement of settlement, the DOJ notes that the Pfizer settlement included agreeing to a corporate compliance program "which will ensure that the changes Pfizer Inc[.] made after acquiring Warner-Lambert in June 2000, are effective in training and supervising its marketing and sales staff . . . ."[140] This suggests that Pfizer might have tried to curb some detailing after buying the company. Additionally, the DOJ asserts that the "charged conduct" occurred before Pfizer bought Warner-Lambert in 2000.[141] Finally, the original FCA claim was unsealed in 1999,[142] suggesting that Pfizer was under greater federal scrutiny during this period. Arguably then, pharmaceutical detailing should have begun to decline by 1999 or 2000, which would not explain the continued increase through 2000 and the decline after 2002.

The evidence presented in this Part suggests that some types of information are more influential in spurring relinquishment. Moreover, such relinquishment seems heterogeneous by payer. The implications of these findings, particularly regarding the ability of the FCA to function as a socially beneficial tool, are discussed below.

IV. CONSEQUENCES OF THE FALSE CLAIMS ACT

This Article argues that under certain circumstances, the FCA can not only reimburse the government for fraudulent expenditures but also provide information to other payers and providers and incentivize the government to work to prospectively screen out ineffective off-label uses for reimbursement. Part III studies one

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detail/court_rules_for_pfizer_in_patent_infringement_case_on_neurontin. This would have resulted in lower-priced Neurontin; however, it is unclear how large or successful this launch was. Additionally, this launch should have increased the number of Neurontin prescriptions after 2004 if cost is relevant, but there is little evidence of this. *See also* Neafsey, *supra* note 136 (noting that generic manufacturers were contesting the extended patent).

139. *Court Rules for Pfizer in Patent Infringement Case on Neurontin*, *supra* note 138.

140. *Warner-Lambert to Pay $430 Million to Resolve Criminal & Civil Health Care Liability Relating to Off-label Promotion*, *supra* note 15.

141. *Id.*

142. *See* United States *ex rel.* Franklin v. Parke-Davis, Div. of Warner-Lambert Co., 147 F. Supp. 2d 39, 46 (D. Mass. 2001).

inappropriate off-label use of one drug and examines important deadlines in the drug's timeline, including FCA settlement. While attributing the relinquishment in Part III to FCA suit is not without difficulty, there are at least two clear takeaways. First, there seems to be a significant effect of FCA settlements on relinquishment of off-label uses. Second, there are differences in relinquishment by expected payer. The likelihood that patients received Neurontin decreased after news of the FCA suit in 2002 more for patients with private insurance, and to a lesser extent Medicaid, relative to the change for self-pay patients. These two findings will be discussed separately below.

A. FCA as an Informational Learning Mechanism

Part III demonstrates that relative to traditional sources of relinquishment, such as the publication of influential articles, the FCA claim seems to be a visible event that spurs relinquishment. Indeed, even the clearest signal of ineffectiveness—a randomized study by the manufacturer finding a placebo outperformed the drug[143]—spurred relinquishment for third-party payers only afterward, seemingly in response to the FCA suit and discovery. Publication alone of this very probative study seems insufficient to get physicians to change their treatment patterns. This unfortunately undermines the assumption that physicians are able to incorporate new information into their treatment pattern unaided.

Turning to the FCA, the results do suggest that the FCA performs some sort of informative role. As previously discussed, there are at least two reasons for this phenomenon. First, an FCA suit can act as an industry-wide signal, bringing to light obscure scientific publications. Second, an FCA suit can bring new knowledge to light by exposing internal documents or suppressed studies.

For Neurontin, the FCA suit seems to have merely republicized existing scientific evidence. The FCA suit did alert private insurance companies to the existence of contradictory public scientific evidence. While the suit uncovered the fact that the company was promoting such uses despite knowledge of its ineffectiveness,[144] this should not

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143. *See* Pande et al., *supra* note 85, at 251–54.

144. *See In re* Neurontin Mktg. & Sales Pracs. Litig., 712 F.3d 21, 33 (1st Cir. 2013).

add any relevant information to the prescription decision. Insofar as the reports of the trial alluded to further private scientific evidence on the inappropriateness of Neurontin for bipolar disorder,[145] this might be evidence of the second mechanism.

As noted above, the first mechanism seems better performed by other policy interventions. Digests that summarize evidence on given treatments would be more cost-effective ways to disseminate new information on appropriateness. Indeed, we might even expect that such methodical coverage, presumably by scientific and medical experts, would be a more consistent source of information. In contrast, lawsuits are often prohibitively expensive to bring and would vary based on how lucrative the potential reward would be for the relator. Moreover, insofar as the lawsuit simply provides color to the scientific information (i.e., by showing that a company was profiting greatly from their off-label marketing), this may even result in a biased use of scientific information. Prescribers should only prescribe the treatment if there is evidence that it could be helpful; separate issues of corporate greed are often irrelevant to whether treatment was appropriate.

Indeed, even if the FCA creates new public knowledge relevant to prescription decisions, physicians' reliance on such knowledge undermines the assumption underlying the off-label regulatory scheme. If internal documents are necessary to ascertain a drug's effectiveness, the assumption underlying off-label uses—that physicians will make appropriate decisions based on current public scientific literature—might be flawed.

B. Implications of Heterogeneity in Relinquishment by Payment

Part III presents evidence of different relative relinquishment patterns among patients with different payers. This Section discusses both the hypothesized reasons behind the current findings and possible future effects.

The presence of a third-party payer seems to make a difference in adoption and relinquishment patterns. From the raw data alone, self-pay patients seem less likely to receive Neurontin after 2000 while Medicaid patients adopted Neurontin and then relinquished it after 2002. Private patients were more liberal in their adoption; however, their relinquishment effect was also strong. Through the regression analysis, patients with private insurance were less likely

145. *See id.* at 42.

to receive Neurontin after 2002 relative to the change in likelihood experienced by self-pay patients. Medicaid patients also experienced a decline after 2002 relative to self-pay patients although significantly different than the decline for private insurance patients.

These results provide some evidence of heterogeneity within third-party payers and can have implications for the broader question of heterogeneity between public and private third-party payers. There may be two reasons for such heterogeneity: varying ability and different incentives[146] of each payer to relinquish early.

The first concern may be that there is a significant difference in the ability of Medicaid and Medicare to refuse to reimburse a particular use and subsequently to prevent it from being prescribed relative to private payers. The Medicaid statute does allow for requiring prior authorization or even exclusion of "a covered outpatient drug if . . . the prescribed use is not for a medically accepted indication . . . ."[147] As soon as a compendium updates its recommendation based on the new negative information (or immediately if there was no preexisting compendia evidence and Medicaid was exercising its discretion in covering the use), Medicaid can refuse to reimburse. Moreover, through its drug utilization review,[148] it may be able to issue recommendations against such uses as Kaiser did.

Medicare Part D might pose a different set of challenges. While Medicare Part D was not a big player in the Neurontin case, going forward, Medicare Part D will play a larger role in FCA suits. Medicare Part D likely sets a more uniform reimbursement standard compared to Medicaid, relying strongly on uses listed in three compendia.[149] There are also additional requirements to cover all

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146. Notably, the Neurontin case was among the first off-label promotion cases in which a lot of the FCA jurisprudence was developed; thus, it is unclear whether the differences in legal obligations were fully exploited in this case. Future work might examine whether these effects get stronger as more off-label FCA suits are brought.

147. 42 U.S.C. § 1396r-8(d)(1)(B)(i) (2018).

148. While, according to the District Court of Massachusetts, Medicaid does not gather information on indication in their reimbursement forms, which would make monitoring usage more difficult, this is theoretically something the government could require. *See* United States *ex rel.* Franklin v. Parke-Davis, Div. of Warner-Lambert Co., No. Civ.A. 96-11651PBS, 2003 WL 22048255, at *4 (D. Mass. Aug. 22, 2003).

149. *CMA Report: Medicare Coverage for Off-label Drug Use*, *supra* note 76.

drugs falling within "protected classes."[150] Finally, depending on the level of communication between private insurance companies managing the Part D program and the parts of Medicare outlining medical care, Medicare may not have sufficient tools to monitor appropriate usage.

The second possible reason for heterogeneity between public and private payers is that the broad standards of the FCA reduce incentives for Medicare and Medicaid to exercise persuasive power to relinquish inappropriate treatments. The FCA standards are rather lenient and may have become increasingly so after FERA.[151] Thus, the government program might invest less time in disseminating information on inappropriate uses than a payer who has a harder time recovering through a fraud statute.

Although the court in *Parke-Davis* side-stepped the question of heterogeneity in reimbursement status in state Medicaid,[152] this might be a concern for future cases.[153] If a state allows for the reimbursement of off-label non-compendia uses, those prescriptions cannot serve as false claims. The government would have to prove that the particular use was still nonreimbursable in a given state. In the Neurontin case, this did not matter as at least eight states did not allow reimbursement, providing sufficient basis for the case to go forward; the issue only was relevant in terms of damages (and the case subsequently settled).[154]

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150. Thomas Barker & Ross Margulies, *Centers for Medicare & Medicaid Services Proposes Changes to Six Protected Class Rule Under Medicare Part D*, FOLEY HOAG LLP (Jan. 10, 2014), http://www.foleyhoag.com/publications/alerts-and-updates/2014/january/cms-proposes-changes-to-six-protected-class-rule-under-medicare-part-d.

151. *See supra* Part I.B.

152. Greene, *supra* note 117.

153. Martin, *supra* note 117, at 7.

154. United States *ex rel.* Franklin v. Parke-Davis, Div. of Warner-Lambert Co., No. Civ.A. 96-11651PBS, 2003 WL 22048255, at *3 (D. Mass. Aug. 22, 2003). This type of rationale was used to defend against a motion to dismiss in a more recent case. *See* United States *ex rel.* Booker v. Pfizer, Inc., 9 F. Supp. 3d 34, 51–52 (D. Mass. 2014); *see also* United States *ex rel.* Banigan v. Organon USA Inc., 883 F. Supp. 2d 277, 294 (D. Mass. 2012) ("Organon contends that if a state Medicaid program chooses to reimburse a claim for a drug prescribed for off-label use, then that claim is not 'false or fraudulent,' and liability cannot therefore attach for reimbursement. The court agrees."). State control over Medicaid coverage may limit the federal government's strategic role. Analogously, however, state governments' behavior in state false claims act suits would be interesting to study in tandem with coverage decisions.

These results have interesting implications for future work. Given that the data from Part III is largely from the pre-FERA period, it is not clear how subsequent jurisprudence affects the difference in behavior by payer type. Similarly, it will be interesting to see whether cases based on Medicare Part D reimbursements display the relinquishment behavior that this Article hypothesizes a purely federal payer would exhibit. Alternatively, Medicare patients' behavior may mimic that of private insurance patients given that private insurance companies manage Medicare Part D.

Kaiser's RICO victory in 2013 might provide a blueprint for private payers to recover if they show evidence of effective prospective screening of off-label uses. The Supreme Court denied certiorari for Pfizer's appeal of this RICO judgment against it in 2018. Some speculate that this denial will lead to the filing of more RICO claims.[155] While this response is not necessarily obvious—as the First Circuit holding seems to be a minority position and a denial of certiorari is not a very strong signal—this issue is likely to be in controversy in the future. Insofar as it does spur other private companies to polices their reimbursements, the gap between private and public payer reactions might widen in the future. The results of this Article indicate that this line of inquiry is important and should be further pursued.

CONCLUSION

While off-label uses have the potential to deliver innovative treatment to patients most in need, the lack of direct governmental regulation makes inappropriate use of off-label treatments a real danger. Because inappropriate off-label usage incurs both monetary costs and opportunity costs of receiving a more appropriate treatment, earlier relinquishment of unsafe or ineffective therapies is preferred. This Article examined the possibility that the FCA can not only serve a compensatory function for the government but be socially beneficial. This can occur in two ways.

First, a socially beneficial FCA can create new information about the appropriateness of a drug use through relator disclosures and

155. Notably, in 2018, the Supreme Court denied certiorari to Pfizer's appeal from the First Circuit's judgment against it, prompting some to speculate that more such cases could go forward. Thomas Sullivan, *Supreme Court Rejection of Pfizer's Request for RICO Off Label Review: Could Open Floodgate of Cases*, POL'Y & MED., https://www.policymed.com/2014/01/supreme-court-rejection-of-pfizers-request-for-rico-off-label-review-could-open-floodgate-of-cases.html (last updated May 6, 2018).

curated signal value. False Claim Act suits can function as a source of information for physicians and third-party payers regarding the appropriateness of off-label uses. The informational value of the FCA depends on whether it merely rebroadcasts already-public information or if it creates new public information regarding drug use appropriateness. Given the difficulties the government faces in regulating off-label uses, and the amount of private information pharmaceutical companies often have regarding the safety and efficacy of their drugs, the FCA's potential to create new public information is important. Part III presents evidence of such an informational role for the FCA suit concerning Neurontin. In that case, the informational content seemed to be mostly to make other payers aware of existing literature about the inappropriateness of Neurontin's use to control bipolar disorder. Similarly, evidence of false dealings led private payers in particular to reexamine the scientific evidence and persuade their physicians to stop prescribing the drug.

Secondly, a socially beneficial FCA would reduce the moral hazard associated with the generous fraud statute. Because the FCA is primarily a compensation tool for the government, and insofar as most parties settle, public payers may have less incentive to preemptively screen their reimbursement. A socially beneficial FCA would explicitly reward the government for policing its reimbursements in a way that incentivizes it to prevent inappropriate prescriptions in the first place. This Article provided evidence consistent with differential sensitivity of payers to various landmarks within the FCA suit process.

As these results reflect an early period in FCA off-label jurisprudence, future study should examine the change in responses in subsequent periods. The prescription decisions for Part D patients might be a particularly informative comparison to those for private patients. Similarly, the RICO win for one private third-party payer may result in greater differences in payer response. Conversely, insofar as future FCA jurisprudence becomes more limited, the government may become less optimistic about its ability to recoup its losses through FCA suits. This will lead the government to invest more resources into preventing inappropriate prescriptions in the first place. As this Article notes, uniformly difficult legal standards might just lead to relators not bringing FCA suits generally. While this would incentivize screening, it would also deny society of the information created by FCA suits. Instead, this Article argues that creating legal standards that reward government screening can

accomplish both goals. Whether this ideal will ever be reached, however, remains to be seen.

DATA APPENDIX

This following data appendix details the empirical specification for interested readers. The details listed therein are simply meant to supplement—not substitute—the text in the relevant sections.

The results displayed in this Article are results of a linear probability model. The basic model is in equation (1).

(1) $Neurontin = X'\beta_1 + J'\beta_1 + I'\beta_1 + Z'\beta_1 + Z * I'\beta_1 + \varepsilon$,

Where *Neurontin* takes a value of one if Neurontin is prescribed (and zero otherwise), X is a vector of patient characteristics that measure differences in medical benefits based on physical differences, J contains information like journal articles on Neurontin, I is a vector of the aforementioned information shock time periods, Z is a vector of payment characteristics, and $Z*I$ is a series of interaction terms between time shocks and payment characteristics. Because the time shocks are a list of often overlapping indicator variables, the interpretation of these coefficients is the marginal effect relative to the previous time shock rather than the base period.

The full results of the linear probability models are listed below in Appendix Table 1.

Appendix Table 1: Likelihood of Prescribing Neurontin, Linear Probability Models, 1998–2008

	(1)	**(2)**
Patient age	0.000	0.000
	(0.000)	(0.000)
Male patient	-0.027**	-0.027**
	(0.012)	(0.012)
Severe bipolar diagnosis	0.108*	0.105
	(0.065)	(0.065)
Use tobacco	0.000	-0.000
	(0.019)	(0.019)
Psychotic behavior	-0.009	-0.006
	(0.096)	(0.095)
Medicare	-0.116***	-0.113***
	(0.038)	(0.038)
Medicaid	-0.111***	-0.103**
	(0.041)	(0.043)
Private Insurance	-0.032	-0.035
	(0.047)	(0.046)
Post2000	-0.066	0.015
	(0.040)	(0.058)
Post2000*Payment		

Medicare	0.135**	0.135**
	(0.056)	(0.057)
Medicaid	0.166***	0.158***
	(0.055)	(0.056)
Private Insurance	0.182***	0.183***
	(0.060)	(0.058)
Post2002 = 1	-0.005	0.108*
	(0.038)	(0.057)
Post2002*Payment		
Medicare	0.085	0.083
	(0.077)	(0.077)
Medicaid	-0.018	-0.019
	(0.070)	(0.069)
Private Insurance	-0.152***	-0.151***
	(0.051)	(0.051)
Post2004 = 1	-0.030	0.036
	(0.036)	(0.044)
Post2004*Payment		
Medicare	-0.089	-0.099
	(0.067)	(0.067)
Medicaid	-0.037	-0.039
	(0.062)	(0.062)
Private Insurance	0.032	0.026
	(0.041)	(0.041)
Positive Studies		0.001
		(0.020)
Negative Studies		-0.025***
		(0.009)
Constant	0.125***	0.149
	(0.041)	(0.116)
Observations	2,142	2,142
R-squared	0.061	0.066

*** p<0.01, ** p<0.05, * p<0.1. Variables included but not shown include indicators for region and the main effects/interactions for "other payment." The regressions are separate linear probability models that are weighted by patient weight and include standard errors clustered by physician code-year pairs.

Columns (1) and (2) run weighted linear probability models for comparison. Column (1) only includes information shocks while Column (2) also includes a cumulative measure of positive and negative review articles on Neurontin for the treatment of bipolar disorder. The patient demographics are significant. Males are less likely to receive Neurontin. Patients with a "severe" bipolar diagnosis are more likely to receive Neurontin than those without such designation, suggesting that Neurontin might have been more

of a "last-resort" treatment. The payment indicator variables are also interesting: relative to self-pay patients, patients with Medicare and Medicaid were less likely to receive Neurontin. As predicted, "negative" studies, studies implying that Neurontin would be inappropriate for the treatment of bipolar disorder, reduce the likelihood that Neurontin is prescribed. The remainder of the analysis is discussed in the body of this Article.