# United States Court of Appeals
## For the First Circuit

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Nos. 11-1904, 11-2096

IN RE: NEURONTIN MARKETING AND SALES PRACTICES LITIGATION

KAISER FOUNDATION HEALTH PLAN, INC.; KAISER FOUNDATION HOSPITALS; KAISER FOUNDATION HEALTH PLAN OF COLORADO; KAISER FOUNDATION HEALTH PLAN OF GEORGIA, INC.; KAISER FOUNDATION HEALTH PLAN OF THE MID-ATLANTIC STATES, INC.; KAISER FOUNDATION HEALTH PLAN OF NORTHWEST; KAISER FOUNDATION HEALTH PLAN OF OHIO,

Plaintiffs, Appellees,

v.

PFIZER, INC.; WARNER-LAMBERT COMPANY, LLC,

Defendants, Appellants.

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APPEALS FROM THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

[Hon. Patti B. Saris, U.S. District Judge]

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Before

Lynch, Chief Judge,
Souter,[*] Associate Justice,
and Lipez, Circuit Judge.

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Kathleen Sullivan, with whom Mark S. Cheffo, Katherine A. Armstrong, Quinn Emanuel Urquhart Oliver & Hedges LLP, and Skadden, Arps, Slate, Meagher & Flom LLP were on brief, for appellants.

David C. Frederick, with whom Scott K. Attaway, W. Joss Nichols, Caitlin S. Hall, Linda P. Nussbaum, Kellogg, Huber,

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[*] Hon. David H. Souter, Associate Justice (Ret.) of the Supreme Court of the United States, sitting by designation.

Hansen, Todd, Evans & Figel, P.L.L.C. and Grant & Eisenhofer, P.A. were on brief, for appellees.

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April 3, 2013

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**LYNCH, Chief Judge**. This is an appeal from verdicts of over $140 million, reached by both a jury and a court, compensating Kaiser, a major health plan provider and insurer, for the injury Kaiser suffered by its payment for four categories of off-label Neurontin prescriptions which had been induced by a fraudulent scheme by Pfizer, the manufacturer of Neurontin. These verdicts followed a settlement that Warner-Lambert, a subdivision of Pfizer, had reached in a criminal case brought by the United States, in which Warner-Lambert pled guilty to two counts and agreed to pay a $240 million criminal fine concerning the off-label marketing of Neurontin; Pfizer agreed to pay an additional $190 million in civil fines. This is one of several related appeals regarding Neurontin, which result in separate opinions, of which this is the lead. We affirm the verdicts for Kaiser.

I.

On February 1, 2005, Kaiser Foundation Health Plan, Inc. and Kaiser Foundation Hospitals (together, "Kaiser"), Aetna, Inc. ("Aetna"), and The Guardian Life Insurance Company of America ("Guardian") filed a coordinated complaint in the U.S. District Court in Massachusetts against Pfizer, Inc. and Warner-Lambert Company (together, "Pfizer"), asserting injury from the fraudulent marketing of Neurontin for off-label uses. The coordinated plaintiffs asserted violations of, inter alia, the Racketeer Influenced and Corrupt Organizations Act ("RICO"), 18 U.S.C.

§ 1962, and the California Unfair Competition Law ("UCL"), Cal Bus. & Prof. Code § 17200. Ultimately, Kaiser prevailed, but Aetna and Guardian's claims were dismissed on summary judgment, and Aetna's dismissal is the subject of a separate appeal.

In a related case in which we issue a separate opinion, Harden Manufacturing Corporation ("Harden") filed a class action complaint on May 14, 2004, in the same court, against Pfizer and Parke-Davis (as a division of Warner-Lambert) on behalf of a broad purported class consisting of "[a]ll entities throughout the United States and its territories who, for purposes other than resale, purchased, reimbursed and/or paid for Neurontin for indications not approved by the FDA ('the Class') during the period from January 1, 1994 through the present ('the Class Period')." Harden asserted claims under RICO, as well as state-law claims for common law fraud, violation of consumer protection statutes, and unjust enrichment.

Both the class complaint and the coordinated complaint were part of a larger multidistrict litigation ("MDL") concerning the marketing and sale of Neurontin, which was consolidated in the District of Massachusetts in November 2004. In each case, the defendants moved for summary judgment. On January 8, 2010, on defendants' motion the district court dismissed the claims of Guardian and Aetna; the court denied summary judgment as to Kaiser's claims. See In re Neurontin Mktg. & Sales Practices

Litig. (Neurontin Coordinated SJ), 677 F. Supp. 2d 479 (D. Mass. 2010). On December 10, 2010, the court granted summary judgment against all of the Harden purported class plaintiffs except two, whose claims are not relevant to this appeal. See In re Neurontin Mktg. & Sales Practices Litig. (Neurontin Class SJ), 754 F. Supp. 2d 293, 311 & n.4 (D. Mass. 2010).

Beginning on February 22, 2010, the district court held a jury trial on Kaiser's RICO claims against the defendants. On March 25, 2010, after a five-week trial, the jury concluded that "Kaiser prove[d] that Pfizer violated RICO with respect to its promotion of Neurontin for" bipolar disorder, migraine, neuropathic pain,[1] and dosages exceeding 1800 mg per day, and that these "violation[s] of RICO cause[d] Kaiser injury." See In re Neurontin Mktg. & Sales Practices Litig. (Kaiser Findings), No. 04-cv-10739-PBS, 2011 WL 3852254, at *1 (D. Mass. Aug. 31, 2011). The jury awarded Kaiser damages in the amount of $47,363,092, which the court trebled to $142,089,276. Id. The jury also rendered an advisory verdict in favor of Kaiser on its state UCL claim, finding that Pfizer had engaged in fraudulent business acts or practices which caused Kaiser damages with respect to bipolar disorder,

[1] Neuropathic pain is pain caused by damage to the nerves, as opposed to nociceptive pain, which is pain caused by an injury. In re Neurontin Mktg. & Sales Practices Litig. (Kaiser Findings), No. 04-cv-10739-PBS, 2011 WL 3852254, at *38, *1 n.1 (D. Mass. Aug. 31, 2011).

migraine, neuropathic pain, and doses over 1800 mg, but no liability with respect to nociceptive pain.

On November 3, 2010, the district court found in Kaiser's favor on its claims under the UCL, issuing extensive findings of fact and conclusions of law. In re Neurontin Mktg. & Sales Practices Litig., 748 F. Supp. 2d 34 (D. Mass. 2010), amended and superseded by Kaiser Findings, 2011 WL 3852254. The district court ordered defendants to pay $95,286,518 in restitution, Kaiser Findings, 2011 WL 3852254, at *2, but because this figure reflected the same damage claims encompassed by the jury verdict on Kaiser's RICO claim, the court did not add it to the jury award, id. at *60 n.25. On February 22, 2011, the court entered judgment in favor of Kaiser on its RICO and UCL claims, and on July 27, 2011, the court denied Pfizer's motion for a new trial or, in the alternative, to alter or amend judgment.

On September 20, 2011, Pfizer filed a notice of appeal as to the court's entry of judgment in favor of Kaiser on its RICO and UCL claims, and as to the court's denial of Pfizer's motion for a new trial. This opinion concerns only that appeal.

II.

We review de novo defendants' contention that Kaiser's RICO and UCL claims failed as a matter of law, taking the evidence in the light most favorable to the verdict. Tuli v. Brigham & Women's Hosp., 656 F.3d 33, 38 (1st Cir. 2011). Where defendants

challenge the district court's findings of fact, we review these findings for clear error. Fed. R. Civ. P. 52(a)(6). We begin by setting out the district court's findings of fact and the jury's conclusions.

A. The Defendants' Fraudulent Marketing Campaign

Parke-Davis, an operating division of Warner-Lambert Company, developed Neurontin[2] during the 1980s and early 1990s as an anti-epileptic drug. Kaiser Findings, 2011 WL 3852254, at *5. To secure approval from the Food and Drug Administration ("FDA") for a drug for a particular indication, a drug manufacturer must submit two favorable double-blind randomized controlled trials ("DBRCTs"). Id. On December 30, 1993, the FDA approved Neurontin as an adjunctive therapy in the treatment of partial seizures in adults with epilepsy, setting the maximum dose at 1800 mg/day. Id. The FDA found that certain patients taking Neurontin experienced depressive side effects, and the FDA issued a warning to physicians in January 2008 to "[b]e aware of the possibility of the emergence or worsening of depression, suicidality, or any unusual changes in behavior" resulting from the use of anti-epileptic drugs including Neurontin. Id. (alteration in original) (internal quotation marks omitted). In 1996, Parke-Davis applied to the FDA for approval of Neurontin as a monotherapy for the treatment of seizures, and

[2] Neurontin's generic name is gabapentin. Kaiser Findings, 2011 WL 3852254, at *5.

sought an increase in Neurontin's effective dose range and maximum recommended dose; the FDA rejected this application. Id. at *6.

Pfizer acquired Warner-Lambert in 2000. Id. at *5. In 2001, Pfizer filed an application with the FDA seeking approval of Neurontin for the broad indication of neuropathic pain; after receiving negative feedback from the FDA and non-FDA experts, Pfizer withdrew its application. Id. at *10. The FDA did approve Neurontin for the treatment of post-herpetic neuralgia ("PHN"), a type of neuropathic pain associated with shingles, in 2002. Id.

In 1994, Parke-Davis had estimated that Neurontin would generate $500 million in profits over the duration of its patent. Id. at *6. In order to increase Neurontin's earning potential, Parke-Davis began in 1995 to develop strategies to market Neurontin for off-label conditions -- that is, conditions not included on the official label approved by the FDA. Id. As Parke-Davis was implementing these strategies, Pfizer acquired Warner-Lambert, and so, Parke-Davis. Id. at *5. These marketing strategies apparently worked; in the year 2003, Neurontin sales exceeded $2 billion. Id. at *6. Pfizer's Neurontin team estimated that only about ten percent of Neurontin prescriptions that year were for the FDA-approved on-label uses for epilepsy or PHN, and that more than a third of prescriptions were for the off-label uses of neuropathic pain, migraine or headache, or bipolar disorder.

Both the jury and the district court found that Parke-Davis, Warner-Lambert, and Pfizer had "engaged in the fraudulent marketing of Neurontin" for the treatment of bipolar disorder, beginning in July 1998, id. at *17; for the treatment of neuropathic pain, beginning in November 1997, id. at *23; for the treatment of migraines, beginning in April 1999, id. at *25; and for doses greater than 1800 mg/day, beginning in November 1997, id. at *28.[3] This fraudulent marketing included, but was not limited to, three strategies, each of which included subcomponents: (1) direct marketing (or "detailing") to doctors, which misrepresented Neurontin's effectiveness for off-label indications; (2) sponsoring misleading informational supplements and continuing medical education ("CME") programs; and (3) suppressing negative information about Neurontin while publishing articles in medical journals that reported positive information about Neurontin's off-label effectiveness. See id. at *12, *17, *18, *25, *28.

The defendants' fraudulent marketing campaign also targeted third-party payors ("TPPs"), including Kaiser, a non-profit healthcare provider which is also one of the largest health maintenance organizations ("HMOs") in the United States. Id. at *2. As to these targets, additional mechanisms were used to influence both formulary decisions and prescribing decisions. In

[3] The court and the jury found that Kaiser had not proven that Pfizer fraudulently marketed Neurontin for nociceptive pain. Kaiser Findings, 2011 WL 3852254, at *26.

1994, in a memo discussing the promotion of Neurontin as an anti-convulsant, Parke-Davis's marketing team listed Kaiser as second on its list of "Top 10 HMOs Targeted for Neurontin." Id. at *11. In 2004, Pfizer developed an "Operating Plan" for marketing a number of drugs, including Neurontin, to Kaiser; tellingly, the plan featured, as a strategy, "develop[ing] relationships with [decisionmakers affiliated with Kaiser] who are not considered whistle blowers." Id. (emphasis added) (internal quotation marks omitted). Pfizer also employed physicians associated with Kaiser to serve on speakers' bureaus and publish misleading articles about Neurontin. Id.

B. Kaiser's Management of Neurontin on Its Formularies

Kaiser is composed of two separate corporations: the Kaiser Foundation Health Plan, which owns six regional health plans and directly provides medical coverage to beneficiaries in California and Hawaii, providing medical insurance to about 8.6 million members; and Kaiser Foundation Hospitals, which operates health care facilities and pharmacies. Id. at *2. The Kaiser Foundation Health Plan and its subsidiaries do not employ physicians themselves, but have exclusive contractual relationships with regional Permanente Medical Groups ("PMGs"). Id. at *3.

Each PMG has its own Pharmacy and Therapeutics ("P & T") Committee which manages each PMG's formulary, or list of medications that treating physicians may prescribe. Id.

Representatives from both entities sit on the P & T Committees and participate in formulary management. Kaiser Foundation Hospitals has a Drug Information Service ("DIS") that researches and communicates information about drugs, including monographs about new drugs or new drug uses, to physicians and P & T Committees. Id. DIS monographs summarize available evidence -- including publicly available evidence and unpublished information obtained from pharmaceutical manufacturers -- on drug safety and efficacy, and P & T Committees rely heavily on these monographs in making formulary decisions. Id.

PMG formularies may list drugs (1) without restrictions; (2) with restrictions limiting prescribing to a particular group of physicians; or (3) with guidelines for appropriate prescribing. Id. at *4. Kaiser will pay for off-formulary prescriptions and no prior authorization is required for any prescription. Nonetheless, an internal Kaiser study found that 95% of prescriptions written by PMG physicians comply with formularies. Id.

After the FDA approved Neurontin for epilepsy in 1993, the P & T Committee of each regional PMG added Neurontin to its formulary, with one regional PMG -- Hawaii -- not adding Neurontin to its formulary until 2000. Id. The Southern California PMG initially restricted prescribing of Neurontin to neurologists. Id. In September of 1997, however, its P & T Committee permitted anesthesiologists to prescribe Neurontin for reflex sympathetic

dystrophy, a particular pain syndrome. Id. In June of 1999, the Committee removed prescribing restrictions on Neurontin and added guidelines reserving its use for neuropathic pain patients who were unresponsive to or intolerant of other treatments. Id. Then, in September of 1999, the P & T Committee removed all remaining formulary restrictions on Neurontin. Id. at *5. Prescriptions of Neurontin increased dramatically thereafter. Id. at *31.

The district court found that "Kaiser relied on Pfizer's misrepresentations and omissions during the development of drug monographs in both June and September 1999," id. at *29, and that Pfizer's misrepresentations "directly affected decisions about Neurontin's placement on formulary without restrictions," id. at *30.

C. Physicians' Prescribing Behavior as to Neurontin

The jury and court found that the prescribing of Neurontin had in fact been causally affected by the fraudulent marketing scheme, which included the sponsorship of CME events attended by physicians and direct marketing to physicians. Id. at *12. Defendants stress that no physician in this case, or in the Neurontin MDL as a whole, testified that he or she prescribed Neurontin because of defendants' fraudulent off-label marketing. Id. at *32. But Kaiser presented other evidence as to causation, and evidence as to why such individual testimony was unreliable.

The primary evidence was the expert testimony of Dr. Meredith Rosenthal, who holds a Ph.D. in health economics from Harvard University and is a professor at the Harvard School of Public Health. Id. Dr. Rosenthal "use[d] aggregate data and statistical approaches to link patterns in promotional spending[4] to patterns in prescribing for the drug." Id. (internal quotation mark omitted). Her regression analysis found a causal connection between the fraudulent marketing and the quantity of prescriptions written for off-label indications. She also testified as to why Pfizer's proposed physician-by-physician analysis of causation was not a scientifically valid approach to causation.

Dr. Rosenthal used "gold standard" national data on Neurontin prescriptions, and employed the assumptions that (1) "Kaiser's patient population and physician distribution are similar to the national mix," and (2) "promotional spending on off-label marketing was the same as the promotional spending on fraudulent off-label marketing." Id. at *32-33. The district court found both assumptions to be reasonable. Id. at *32-33.

As is customary for such experts, Dr. Rosenthal testified that she "assumed that the allegations in the complaint are true" for purposes of conducting her analysis, but offered no view as to

[4] Dr. Rosenthal's promotional spending data included "spending on detailing of doctors, advertisements in professional journals, and the retail value of samples." Kaiser Findings, 2011 WL 3852254, at *32 n.19.

whether or not there had been a fraudulent marketing scheme. She further explained that her assignment was only to calculate the percentage of prescriptions caused by Pfizer's fraudulent off-label marketing and not to convert that percentage into a damages number for Kaiser, which was the task of another expert witness, Dr. Raymond Hartman, Ph.D.

Dr. Rosenthal explained the difference between correlation and causation and stated that her analysis established causation by performing a regression analysis on sales information against promotional spending on detailing, professional journal advertising, and the retail value of samples, while controlling for other variables. Her analysis excluded the many off-label prescriptions by physicians who received legitimate on-label promotion. She concluded that the "percentage[s] of Neurontin prescriptions that were caused by Pfizer's fraudulent marketing of Neurontin" were, by off-label indication, as follows: 99.4% of prescriptions for bipolar disorder; 70% of prescriptions for neuropathic pain; 27.9% of prescriptions for migraine; and 37.5% of prescriptions for doses over 1800 mg/day. Id. at *33. Thus, three out of ten Neurontin prescriptions written by neurologists for migraine would not have been written or filled but for the alleged misconduct. As for Neurontin prescriptions written by psychiatrists for bipolar disorder between November 1995 and December 2004, 99.4% would not have been written had there been no

fraud. Dr. Rosenthal testified that it was her opinion "to a reasonable degree of scientific certainty that these calculations are the best way to estimate the number of prescriptions and the share of prescriptions that were affected by the alleged misconduct."[5]

Turning to Pfizer's insistence that only doctor-by-doctor evidence could prove causation, Dr. Rosenthal testified as to the well-recognized unreliability in the field of healthcare economics of asking doctors individually whether they were influenced by the many methods of off-label marketing. She said that self-reporting from physicians about patterns of practice that may be controversial shows both conscious reluctance and unconscious bias, which lead them to deny being influenced. As a result, it is preferable "[t]o examine objectively the causal association between promotion and sales using . . . econometric models." Dr. Rosenthal utilized the standard practice of using "aggregate data and . . . statistical approaches to link patterns in promotional spending to patterns in prescribing for the drug." Dr. Rosenthal testified that it was "neither standard nor appropriate to look physician by physician."

In opposition to Dr. Rosenthal's expert testimony, Pfizer introduced the expert testimony of Dr. Michael C. Keeley, Ph.D.,

[5] These calculations applied to Kaiser as well as to other payors across the country.

who testified as to alleged flaws in Dr. Rosenthal's methodology. Dr. Keeley testified that when he re-ran Dr. Rosenthal's regression analysis with different assumptions, he did not find a statistically significant relationship between Pfizer's promotion of Neurontin and prescriptions of Neurontin. Dr. Keeley did not present his own causation or damages model, however. The court rejected Dr. Keeley's criticisms and accepted Dr. Rosenthal's calculations. Id. at *58.

The court also found that subsidiary evidence tended to show a causal link. For example, PMG physicians attended conferences where Neurontin was promoted for off-label uses, and after one such conference, in May 1999, new starts of Neurontin increased by 62%. Id. at *30.

D. Criminal Proceedings and Related Proceedings Against the Defendants Concerning Neurontin

Dr. David Franklin was employed as a medical liaison at Parke-Davis for about five months in 1996; on August 13, 1996, he filed a sealed qui tam action against Parke-Davis under the False Claims Act ("FCA"), 31 U.S.C. §§ 3729-3733. United States ex rel. Franklin v. Parke-Davis, Div. of Warner-Lambert Co., 147 F. Supp. 2d 39, 43-44, 46 (D. Mass. 2001). Franklin alleged that Parke-Davis engaged in a fraudulent scheme to promote off-label uses of Neurontin, and that this campaign caused false claims to be submitted to the Veterans Administration and to the federal government for Medicaid reimbursement. Id. at 43. Franklin's suit

remained under seal for more than three years, as the government considered whether to intervene, and was then unsealed on December 21, 1999, with the government participating only as an amicus curiae. Id. at 46. On June 16, 2004, Franklin, Parke-Davis, Pfizer, and the United States entered into a stipulation of dismissal, under which Franklin received a relator's share of $24,640,000.

On May 13, 2004, the U.S. Department of Justice filed a criminal information charging Warner-Lambert with illegal off-label promotion of Neurontin. Kaiser Findings, 2011 WL 3852254, at *11. Pfizer caused Warner-Lambert to plead guilty to two felony counts of marketing Neurontin for unapproved uses, with Warner-Lambert "expressly and unequivocally admit[ting]" that it promoted the sale and use of Neurontin for neuropathic pain, bipolar disorder, and migraine. Id. To be clear, this plea did not admit to fraudulent marketing. Warner-Lambert agreed to pay a $240 million criminal fine, and Pfizer paid $190 million in additional civil fines. Id. News of this action, plea, and settlement caused Kaiser to take certain steps, as described below.

E. Kaiser's Actions To Reduce Neurontin Prescriptions

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. Id. at *31. 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. Id.

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. Id. 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.

The P & T Committees did not remove Neurontin from their formularies or impose restrictions on its use after learning about the allegations of defendants' fraudulent off-label marketing of Neurontin. Favorable information about using Neurontin to treat neuropathic pain remained on Kaiser's website until the eve of trial. Id. at *30. The district court found, however, that Kaiser employees did not know about the full scope of defendants' fraud. Rather, they learned of the full scope of the fraud through (1) discovery in this suit, and (2) the publication, in November of

2009, of an article in the New England Journal of Medicine reporting defendants' use of scholarly publications to disseminate misleading information about Neurontin. Id. at *31, *7 & n.4.

F. Injury and Damages Sustained by Kaiser Due to Defendants' Fraud

The court and the jury found that Kaiser had suffered both injury and quantifiable damages as a result of defendants' actions.

After reviewing the evidence at trial -- including the results of DBRCTs and other clinical trials, anecdotal accounts of clinical success, regulatory approval in other countries, and expert opinions, id. at *34-45 -- the district court found that "there is no reliable scientific evidence that Neurontin is effective for bipolar disorder, migraine, or at high doses," and that although there was evidence that Neurontin was effective in treating some kinds of neuropathic pain, "there is no reliable scientific evidence to support a broad indication of neuropathic pain," id. at *34. The court also found that "PMG physicians would have almost certainly prescribed alternative medication to their patients had they not prescribed Neurontin." Id. at *33.

In addition to Dr. Rosenthal's expert testimony on causation and injury, Kaiser presented testimony by a second expert, Dr. Hartman, who provided evidence as to the damages

incurred by Kaiser. His analysis used a list[6] of alternative drugs that "were more appropriate for each off-label indication than Neurontin" in order to determine the average cost of the alternative medications that would have been prescribed in the absence of defendants' fraud. Id. Dr. Hartman then multiplied the quantity of affected prescriptions (as determined by Dr. Rosenthal) by the average excess cost of each Neurontin prescription as compared to alternative medications. Id. He concluded that Kaiser's damages from defendants' fraud totaled $62,457,082, with Kaiser sustaining the following damages from fraud-induced prescriptions for each off-label indication: $17,822,647 for bipolar disorder; $39,774,623 for neuropathic pain; $1,260,464 for migraine; and $3,599,348 for doses over 1800 mg/day. Id. at *34. In fact, the total awarded by the jury was less than this sum.

Dr. Keeley, Pfizer's expert, testified that Dr. Hartman's calculations were flawed because he did not have data that permitted him to determine which alternative drugs would have been prescribed in place of Neurontin. Dr. Keeley did not present his own estimate of Kaiser's damages, however.

Pfizer argued to the jury that Neurontin was effective for the off-label uses at issue, and that as a result, (1) Pfizer's promotional campaign involved no misrepresentations about

[6] This list had been developed by the chairperson of Kaiser's DIS, Dr. Marta Millares. Kaiser Findings, 2011 WL 3852254, at *33.

Neurontin's effectiveness; (2) even if Pfizer made misrepresentations, Kaiser doctors prescribed Neurontin for off-label uses because it was effective in their clinical experience, not because of Pfizer's misrepresentations; and (3) because Kaiser's damages theory was based on Neurontin's complete ineffectiveness for off-label uses, Kaiser's damages calculations were invalid if Neurontin was sometimes effective for these uses. The jury rejected Pfizer's arguments and awarded Kaiser $47,363,092 in damages, which the court trebled to $142,089,276. Id. at *1.

Pfizer argued to the district court that since doctors consider "multiple sources, types, and levels of scientific evidence" in making treatment decisions, and the effectiveness of a drug is a patient-specific inquiry, the court should not confine its analysis of Neurontin's effectiveness for off-label uses to whether DBRCTs demonstrated efficacy. Kaiser responded that DBRCTs were the "gold-standard for determining efficacy" and that "[l]ower-tier evidence is insufficient, especially in place of existing DBRCTs."

Pfizer further argued to the court that because Neurontin was not "completely and categorically ineffective" for off-label uses, Pfizer had not misled Kaiser about Neurontin's efficacy and Kaiser had not proved that it suffered economic injury. Pfizer also argued that Dr. Rosenthal's and Dr. Hartman's testimony was flawed and hence not probative of causation or damages. The court

rejected Pfizer's arguments and accepted Dr. Rosenthal's and Dr. Hartman's calculations as the basis for its own damages award of $95,286,518. Id. at *58-60.

III.

Pfizer seeks to vacate the court and jury findings of liability and damages on a number of theories. It argues that Kaiser's claims fail as a matter of law, that the evidence was insufficient, and that there were trial errors. At the heart of the appeal is the claim that, as a matter of law, Kaiser cannot meet the RICO or UCL causation requirements, and so Pfizer was entitled to a directed verdict. On appeal, Pfizer does not challenge the conclusions of the jury and district court that it engaged in a fraudulent scheme with respect to its promotion of Neurontin for off-label uses.[7]

A. RICO Causation

The civil damages provision of RICO provides that "[a]ny person injured in his business or property by reason of a violation of section 1962 of this chapter may sue therefor . . . and shall

[7] As noted, Pfizer argued to the jury and the district court that Neurontin was effective for off-label uses and that Pfizer therefore made no material misrepresentations. It does not make this argument on appeal. Instead, it argues on appeal only that Neurontin's effectiveness means Kaiser did not prove that it suffered economic injury from paying for off-label prescriptions of Neurontin. Pfizer does state on appeal, in passing, that Kaiser "presented no evidence of fraudulent detailing (sales calls) to PMG doctors," but it does not squarely challenge the district court's contrary finding and, in any event, makes this argument only to attack the "fit" of Kaiser's expert testimony.

recover threefold the damages he sustains and the cost of the suit, including a reasonable attorney's fee." 18 U.S.C. § 1964(c). In relevant part, section 1962 prohibits "any person employed by or associated with any enterprise engaged in, or the activities of which affect, interstate or foreign commerce" from "conduct[ing] or participat[ing], directly or indirectly, in the conduct of such enterprise's affairs through a pattern of racketeering activity." Id. § 1962(c). A "racketeering activity" can consist of a wide range of predicate offenses, including, as alleged in this case, mail and wire fraud, see id. § 1961(1), and a "pattern" of such activity requires at least two racketeering acts, id. § 1961(5).

Our RICO causation analysis is controlled by the Supreme Court's decisions in Holmes v. Securities Investor Protection Corp., 503 U.S. 258 (1992), and its progeny.[8] See Anza v. Ideal Steel Supply Corp., 547 U.S. 451 (2006); Bridge v. Phoenix Bond & Indem. Co., 128 S. Ct. 2131 (2008); Hemi Grp., LLC v. City of New York, 130 S. Ct. 983 (2010). In Holmes, the Supreme Court held that the civil RICO provision's "by reason of" language contains both but-for causation and proximate causation requirements. 503 U.S. at 268. In our view, these are two quite distinct questions. Here, the harm to Kaiser plainly was foreseeable, and foreseeability is needed for, but does not end the inquiry as to,

[8] The parties apply the same analysis on the proximate causation questions to both Kaiser's RICO claim and its UCL claim, so we proceed on the assumption that this approach is correct.

proximate causation. The proximate causation question in this appeal concerns whether the chain of events between Pfizer's misrepresentations and Kaiser's payment for the prescriptions is so attenuated that, for legal and policy reasons, Kaiser's claim for recovery should be denied. The but-for causation question, in contrast, is whether, absent Pfizer's fraud, Kaiser would have paid for fewer off-label Neurontin prescriptions.

Pfizer's primary argument is that, as a matter of law, there is no proximate causation in this case because there are too many steps in the causal chain connecting its misrepresentations to the injury to Kaiser, particularly because that injury rests on the actions of independent actors -- the prescribing doctors. As to but-for causation, Pfizer argues that its evidence at trial "falsified" Kaiser's theories of causation, and that some of the evidence Kaiser presented to prove but-for causation was inadmissible. We take these arguments in sequence.

B. Proximate Causation

In Holmes, the Supreme Court upheld entry of summary judgment for the defendant on RICO claims brought by a plaintiff who was subrogated to the rights of others, based on the plaintiff's failure to meet the proximate cause requirement. Id. at 262-64, 271-74. The Holmes plaintiff alleged that the defendant had engaged in an enterprise to manipulate the prices of certain stocks, id. at 261, and complained that this conduct caused the

plaintiff to have to pay the claims of customers of two broker-dealers that had become insolvent once the fraud was revealed, see id. at 262-63. The Court determined that, even if this plaintiff were allowed to stand in the shoes of a better-situated plaintiff (namely, the customers), the link was too remote between the alleged stock manipulation scheme and the harm to the customers, because that harm was itself contingent on the harm suffered by the broker-dealers who had purchased the manipulated stock. See id. at 271. The only connection between the RICO conduct and the claimed harm was the broker-dealers' insolvency. Id.

The Holmes Court stated that, "[a]t bottom, the notion of proximate cause reflects 'ideas of what justice demands, or of what is administratively possible and convenient.'" Id. at 268 (quoting W. Keeton, et al., Prosser & Keeton on Law of Torts § 41, at 264 (5th ed. 1984)). As a result, the Court explained, it was "us[ing] 'proximate cause' to label generically the judicial tools used to limit a person's responsibility for the consequences of that person's own acts." Id.

Because of "the infinite variety of claims that may arise" in which a court must analyze proximate causation, it is "virtually impossible to announce a black-letter rule that will dictate the result in every case." Id. at 272 n.20 (quoting Associated Gen. Contractors of Cal., Inc. v. Cal. State Council of Carpenters, 459 U.S. 519, 536 (1983)) (internal quotation marks

omitted). Instead, the Court set out certain principles, derived from the common law and from interpretations of analogous statutes, to govern the proximate cause inquiry under RICO.

The Court noted that RICO's civil provision drew its language directly from the Clayton and Sherman Acts, which had for decades been interpreted as incorporating proximate cause requirements. Id. at 267-68; see Associated Gen. Contractors, 459 U.S. at 531-34. In the antitrust context, the Court had identified a number of factors that bear on the proximate cause question, including whether the injury was of the sort that the statutes sought to redress, Associated Gen. Contractors, 459 U.S. at 538; the "directness or indirectness of the asserted injury," including whether the "links" in the "chain of causation" were clear or were only "vaguely defined," id. at 540; the identity of the "immediate victims" of the antitrust conduct, id. at 541; whether the injuries complained of may have been caused by "independent factors," id. at 542; and whether the plaintiffs were part of "an identifiable class of persons whose self-interest would normally motivate them to vindicate the public interest in antitrust enforcement," id.

The Holmes Court used various phrases to define what it takes to meet RICO's proximate cause standard, such as "some direct relation between the injury asserted and the injurious conduct alleged," 503 U.S. at 268, and whether "the link is too remote" between the conduct and the harm suffered, id. at 271. The Court

noted that the proximate cause analysis at common law often included such a "demand for some direct relation"; that is, proximate cause would be lacking if, as in Holmes, the plaintiff "complained of harm flowing merely from the misfortunes visited upon a third person by the defendant's acts." Id. at 268. Later, in Anza v. Ideal Steel Supply Corp., 547 U.S. 451, the Court similarly found proximate cause lacking where the RICO conduct alleged had directly harmed a party other than the plaintiff and the plaintiff's alleged injury was only a collateral result of the direct harm. In that case, the defendant's scheme to underpay sales taxes had directly injured the state by depriving it of tax revenue, whereas the plaintiff's alleged harm related to the competitive effects of the defendant charging lower prices without sales tax. See id. at 458.

Importantly, the Holmes Court also provided three functional factors with which to assess whether proximate cause exists under RICO. First, the Court noted concerns about proof, reasoning that "the less direct an injury is, the more difficult it becomes to ascertain the amount of a plaintiff's damages attributable to the violation, as distinct from other, independent, factors." 503 U.S. at 269. Second were concerns about administrability and the avoidance of multiple recoveries: "[R]ecognizing claims of the indirectly injured would force courts to adopt complicated rules apportioning damages among plaintiffs

removed at different levels of injury from the violative acts, to obviate the risk of multiple recoveries." Id. Third, the Court focused on the societal interest in deterring illegal conduct and whether that interest would be served in a particular case: "[T]he need to grapple with [the previous two] problems [may be] simply unjustified by the general interest in deterring injurious conduct, since directly injured victims can generally be counted on to vindicate the law as private attorneys general, without any of the problems attendant upon suits by plaintiffs injured more remotely." Id. at 269-70.

Holmes makes it clear that both the directness concern and the three functional factors are part of the proximate cause inquiry. See id. at 271-74. Indeed, the Court warned that its "use of the term 'direct' should merely be understood as a reference to the proximate-cause enquiry that is informed by the concerns" of justice and administrability. Id. at 272 n.20; see id. at 268. Holmes and its successor, Anza, both found a lack of proximate cause when examining the attenuated relationship between the plaintiffs and the direct victim or victims of the alleged fraud.

In Bridge v. Phoenix Bond & Indemnity Co., 128 S. Ct. 2131, the Court considered the RICO claims of such direct victims. It also relatedly addressed the question of whether first-party

reliance on a defendant's misrepresentations is required under RICO, and answered that question "no."[9]

In Bridge, the plaintiffs alleged that the defendants had engaged in a scheme to make misrepresentations to county tax authorities in order to win more bids at tax lien auctions than they would have been able to win absent the fraud. See id. at 2135-36. The plaintiffs were other bidders at the auctions whose bids had tied with defendants' bids, and whose claimed injury was the deprivation of their fair share of winning bids. Id. at 2136.

A unanimous Court held that first-party reliance is not an element of proximate cause in a private RICO claim predicated on mail fraud. Id. at 2134. Thus, even where the plaintiffs did not receive the misrepresentations at issue -- the county was the party that had relied on the misrepresentations -- the plaintiffs had sufficiently alleged proximate causation under RICO. Id. at 2138,

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[9] We disagree with Pfizer's argument that "attempting to prove non-party doctors' reliance through inferences from aggregate sales data invokes the 'fraud on the market' doctrine." The fraud-on-the-market doctrine, utilized in securities law, "relieves the plaintiff of the burden of proving individualized reliance on a defendant's misstatement, by permitting a rebuttable presumption that the plaintiff relied on the 'integrity of the market price' which reflected that misstatement." In re PolyMedica Corp. Sec. Litig., 432 F.3d 1, 7 (1st Cir. 2005) (discussing Basic Inc. v. Levinson, 485 U.S. 224 (1988)). While reliance "is an essential element of the § 10(b) private cause of action," Amgen Inc. v. Conn. Retirement Plans & Trust Funds, ___ S. Ct. ___, 2013 WL 691001, at *4 (2013) (internal quotation marks omitted), first-party reliance is not an element of a private RICO claim predicated on mail fraud, Bridge, 128 S. Ct. at 2134, so the analogy is inapt.

2143-44. Here, like the defendants in Bridge, Pfizer argues that its supposed misrepresentations went to prescribing doctors, and so the causal link to Kaiser must have been broken. Even putting aside the evidence of Pfizer's direct communications to Kaiser, we think Bridge forecloses this argument. The Bridge Court rejected the attempt to impose a direct reliance requirement on top of the statutory language providing a private right of action under RICO, finding no support for it in the common law. See id. at 2139-41. We likewise find none here.

Bridge also supports the conclusion that Kaiser meets the proximate cause requirement for several additional reasons. First, Bridge held that the plaintiffs there "clearly were injured by [defendants'] scheme," as they lost valuable property they would not otherwise have lost. Id. at 2139. In so holding, the Court analogized to a business being harmed by misrepresentations made by a rival to its suppliers and competitors but not to the business itself. See id. The Court rejected the argument that no RICO injury could exist in such circumstances. In doing so, it commented on the fact that a business so injured would be "the primary and intended victim[] of the scheme to defraud." Id. Here, Kaiser was likewise a "primary and intended victim[] of [Pfizer's] scheme to defraud."[10] Its injury was a "foreseeable and

[10] In using this language, we do not suggest that a defendant can escape RICO liability to a foreseeably and actually injured plaintiff by saying it did not "intend" such a result. Pfizer

natural consequence" of Pfizer's scheme, id. at 2144 -- a scheme that was designed to fraudulently inflate the number of Neurontin prescriptions for which TPPs paid. The evidence that Pfizer had specifically targeted Kaiser for Neurontin sales in general supports the conclusion that Kaiser's injury was a natural consequence of Pfizer's fraudulent scheme, but such evidence was not required, given the mechanisms by which Pfizer's marketing plan operated. As Judge Posner stated in the Bridge case, after remand: "The doctrine of proximate cause . . . protects the ability of primary victims of wrongful conduct to obtain compensation . . . ." BCS Servs., Inc. v. Heartwood 88, LLC, 637 F.3d 750, 756 (7th Cir. 2011). Here Kaiser was a primary victim.

Further, the Bridge Court saw no risk of multiple recoveries or other policy reasons to limit recovery. See 128 S. Ct. at 2144 (citing Holmes, 530 U.S. 258; Anza, 547 U.S. 451). Nor did it see a "more immediate victim . . . better situated to sue." Id. So too here: none of the three functional problems that the Holmes test is meant to avoid are present in this case. To the contrary, the functional interests in justice and administrability work in Kaiser's favor. Because Kaiser was both the natural and foreseeable victim of the fraud and the intended victim of the fraud, there is no risk of duplicative recovery. See id. Neither the individual physicians, nor the DIS members, nor the P & T

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could not plausibly make such a claim here in any event.

Committee members -- the parties to whom Pfizer directly made its misrepresentations -- ever paid anything toward a Neurontin prescription, so there is no risk of multiple recoveries due to a suit by another of those actors.[11] See Holmes, 503 U.S. at 269. Kaiser is also in the best position to enforce the law because Kaiser is the party that directly suffered economic injury from Pfizer's scheme. See id. at 269-70. And, as we explain below, Kaiser was able to present sufficient evidence to ascertain the amount of its damages attributable to Pfizer's conduct. See id. at 269.

In our view, Kaiser has met both the direct relationship and functional tests articulated in Holmes and its progeny. We reject Pfizer's core defense that there are too many steps in the causal chain between its misrepresentations and Kaiser's alleged injury to meet the proximate cause "direct relation" requirement as a matter of law. Pfizer characterizes this causal relationship as involving at least four steps: Pfizer communicating tainted information about Neurontin to Kaiser's DIS; the DIS producing monographs that rely on the misrepresentations; those monographs

[11] There are, of course, other potential victims of Pfizer's scheme, such as uninsured individuals who paid for their own prescriptions. But any such injury would be different in kind from Kaiser's injury and could not be considered "multiple" in that respect. At oral argument, Pfizer raised the possibility that premium payers might also sue as victims of Pfizer's scheme, but the question of whether any injury to such payers was proximately caused by this scheme is not before us in this case.

influencing the PMGs in their formulary decisions; and the prescribing physicians (who exercise independent medical judgment) acting within the formulary to issue the prescriptions. We think this characterization misconstrues the way in which the Court has framed the direct relation test. Moreover, the adoption of Pfizer's view would undercut the core proximate causation principle of allowing compensation for those who are directly injured, whose injury was plainly foreseeable and was in fact foreseen, and who were the intended victims of a defendant's wrongful conduct.[12]

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[12] The Supreme Court's recent decision in Hemi Group, LLC v. City of New York, 130 S. Ct. 983, does not, as Pfizer argues, lead to a contrary conclusion. As an initial matter, that case produced a 4-1-3 decision with no majority on the proximate cause question. See id. at 995 (Ginsburg, J., concurring in part and concurring in the judgment) (providing fifth vote to overturn the decision below, "[w]ithout subscribing to the broader range of the Court's proximate cause analysis"). But in any event, the factual situation here is easily distinguished.

In Hemi Group, the defendant's alleged RICO conduct was using the mails to violate the federal Jenkins Act, which requires out-of-state cigarette vendors to report customer information to the customers' states of residence. See id. at 987 (plurality opinion). Thus, if the defendant's scheme could even be said to have a foreseen or intended victim, it was New York State (to whom Hemi Group owed the Jenkins Act reports), not the plaintiff New York City. Cf. id. at 990 (identifying the state as a "better situated" plaintiff).

Further, Hemi Group raised a policy problem not at issue here: in that case, allowing the city to bring what was essentially a Jenkins Act claim under the rubric of RICO would have risked "turning RICO into a tax collection statute." Id. at 993 n.2; see id. at 995 (Ginsburg, J., concurring in part and concurring in the judgment) (stating that Justice Ginsburg would have rejected the city's claim because it was an attempt to make an "end-run" around the scope of the Jenkins Act). Kaiser's case involves no such unusual policy risk. If anything, the risk cuts in the other direction: accepting Pfizer's argument on proximate cause as a matter of law would effectively preclude TPPs from bringing suit

In fact, the causal chain in this case is anything but attenuated. Pfizer has always known that, because of the structure of the American health care system, physicians would not be the ones paying for the drugs they prescribed. Pfizer's fraudulent marketing plan, meant to increase its revenues and profits, only became successful once Pfizer received payments for the additional Neurontin prescriptions it induced. Those payments came from Kaiser and other TPPs. See Bridge, 128 S. Ct. at 2144 (noting that other auction bidders, not the county officials who immediately relied on defendants' misrepresentations, were the intended victims of defendants' RICO conduct); BCS Servs., 637 F.3d at 756. Kaiser sought only economic recovery in this case, and its economic injury occurred when it paid for fraudulently induced Neurontin prescriptions.[13]

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under RICO as the primary victims of fraudulent off-label drug marketing, and from recovering for their economic injuries. That could mean that no viable plaintiffs would remain to "vindicate the law as private attorneys general." Holmes, 503 U.S. at 269-70. Given the high costs imposed by fraud in our health care system, and Kaiser's status as a primary victim, this result would not be in the service of either justice or accountability.

[13] While first-party reliance was not needed, the evidence as to Kaiser's reliance on Pfizer's misrepresentations was particularly strong, and it came directly from Pfizer itself. Pfizer had specifically identified Kaiser as a potential target for increased Neurontin sales and had developed a five-point plan for promoting Neurontin to Kaiser. That plan included making contact with members of the DIS and the P & T Committees. Kaiser Findings, 2011 WL 3852254, at *11. This strategy shows that Pfizer did not view the various arms within Kaiser as "third and even fourth parties," Hemi Grp., 130 S. Ct. at 992 (plurality opinion); rather, it viewed the Kaiser organization as a single entity to which

With respect to the mechanisms by which Pfizer marketed Neurontin to PMG doctors through detailing and educational programs, Pfizer fraudulently marketed to physicians with the intent that those physicians would write prescriptions paid for by Kaiser. The fraudulent scheme worked as intended, inducing a huge increase in Neurontin prescriptions for off-label uses. Pfizer now argues that because doctors exercise independent medical judgment in making decisions about prescriptions, the actions of these doctors are independent intervening causes. But Pfizer's scheme relied on the expectation that physicians would base their prescribing decisions in part on Pfizer's fraudulent marketing. The fact that some physicians may have considered factors other than Pfizer's detailing materials in making their prescribing decisions does not add such attenuation to the causal chain as to eliminate proximate cause. Rather than showing a lack of proximate causation, this argument presents a question of proof regarding the total number of prescriptions that were attributable to Pfizer's actions. This is a damages question. Cf. Anza, 547 U.S. at 466 (Thomas, J., concurring in part and dissenting in part) ("Proximate cause and certainty of damages, while both related to the plaintiff's responsibility to prove that the amount of damages he

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Pfizer could pitch Neurontin in order to create effects that would reach prescribing physicians.

seeks is fairly attributable to the defendant, are distinct requirements for recovery in tort.").

The doctrine of proximate cause, as Judge Posner has noted, "does its work" in situations where

> too many unexpected things had to happen between the defendant's wrongdoing and the plaintiff's injury, in order for the injury to occur -- so many unexpected things that the defendant couldn't have foreseen the effect of his wrongdoing and therefore couldn't have been influenced, in deciding how much care to employ in the activity that produced the wrongful act, by the prospect of inflicting such an injury as occurred.

BCS Servs., 637 F.3d at 754. That is not the situation here. Holding Pfizer liable will have an effect in deterring wrongful conduct. And the effect of that wrongful conduct was clear in foresight, not hindsight. See id. at 755. Upholding the finding of proximate cause here will "protect[] the ability of primary victims of wrongful conduct to obtain compensation; simplif[y] litigation; recognize[] the limitations of deterrence . . . and eliminate[] some actual or possible but probably minor causes as grounds of legal liability." Id. at 756. The district court correctly concluded that Kaiser met the proximate causation requirement.

C. But-For Causation

Kaiser introduced several categories of evidence at trial which clearly demonstrated but-for causation. It produced evidence that (1) its employees directly relied on Pfizer's

misrepresentations in preparing monographs and formularies, which, in turn, influenced doctors' prescribing decisions; and (2) Pfizer's fraudulent off-label marketing directed to physicians caused PMG doctors to issue more Neurontin prescriptions than they would have absent such marketing. The latter type of evidence came from Dr. Rosenthal's report[14] as well as inferences from other data. Pfizer has argued both that the direct reliance evidence was insufficient and that Dr. Rosenthal's aggregate evidence was inadmissible and insufficient. Pfizer's insufficiency claims rest on the argument that certain evidence, introduced at trial and considered by the jury and district court, "falsified" Kaiser's theories of causation. We reject both of Pfizer's arguments.

1. But-For Reliance Evidence

Kaiser presented ample evidence of the ways in which its reliance on Pfizer's misrepresentations regarding the effectiveness

[14] Kaiser has argued that the district court did not actually use the Rosenthal report as evidence of causation, but rather used it only to quantify damages. The district court's findings are not clear on this point. Compare Kaiser Findings, 2011 WL 3852254, at *32 ("To meet its burden of proving causation, plaintiffs offered the testimony of Professor Meredith Rosenthal . . . ."), with id. at *54 (describing causation question as "what misrepresentations and omissions Kaiser and DIS relied on[,] . . . whether that reliance caused Kaiser to suffer injury[, and] . . . whether or not PMG physicians would have nonetheless prescribed Neurontin to their patients if DIS had not published monographs recommending Neurontin or if the P & T Committees had added guidelines or restrictions to Neurontin's formulary status"). The jury charge on causation and damages did not mention the aggregate evidence one way or another. We will proceed on the understanding that the aggregate evidence both went to causation and set the basis for damages.

of Neurontin for the four relevant off-label uses met the but-for causation requirement. Kaiser received Pfizer's misrepresentations through Pfizer's contacts with Kaiser's DIS, which disseminated information throughout the Kaiser organization. See Kaiser Findings, 2011 WL 3852254, at *3-4. The DIS also relied on publicly available information about Neurontin, id. at *3, which, because of Pfizer's publication strategy, omitted important information about negative study results, see id. at *7-8. A reasonable factfinder could readily conclude that misinformation received by the DIS would be widely disseminated, utilized, and relied upon throughout the Kaiser organization to cause but-for injury.

Kaiser specifically presented evidence that the DIS shared with all regions at least two monographs that recommended Neurontin for bipolar disorder and that recommended removal of any formulary restrictions on Neurontin. See id. at *28-29. These monographs were compiled without Pfizer having disclosed certain adverse material information. Id. "In making formulary decisions, P & T Committees rely heavily on DIS's monographs," id. at *3, and PMG physicians comply with the formulary at a 95 percent rate, id. at *4.

There was also evidence that PMG physicians received and acted upon Pfizer's misrepresentations, both through information sent through the DIS and information provided to them at Pfizer-

sponsored events. For one, when DIS answered physicians' questions through its inquiry service, DIS relied on half-truths communicated to it by Pfizer. See id. at *29. Second, after PMG physicians attended a medical education conference in May 1999, new Neurontin prescriptions increased by 62 percent. Id. at *30. And significantly, when Kaiser conducted the DRUG and DUAT campaigns to reduce Neurontin usage after the negative information about Neurontin came to light, new prescriptions of Neurontin fell by about 33 percent. At the same time, such prescriptions continued to rise nationally. Id. at *31.

From this evidence, the district court concluded that

> [t]he publication strategies and the other communications between Pfizer and Kaiser directly affected decisions about Neurontin's placement on formulary without restrictions. In addition, the direct communications to PMG physicians caused Kaiser injury because it reimbursed for Neurontin rather than less costly alternatives. Because Kaiser has a 95% compliance rate with its formulary, formulary restrictions necessarily affect the number of prescriptions written for any given drug. I find that Kaiser was injured as a result of its reliance on Pfizer's intentional misrepresentations and omissions.

Id. at *30. This finding was not clearly erroneous. Further, a reasonable jury could have reached the same conclusion.

Pfizer argues that Kaiser's DRUG and DUAT campaigns to reduce prescriptions of Neurontin were not evidence of but-for causation because they were motivated by the desire to contain costs, not by concerns about Neurontin's efficacy for off-label

uses. Pfizer also argues that once evidence of the DRUG and DUAT campaigns is properly discounted, there is no evidence that the Kaiser PMGs took steps to restrict Neurontin on their formularies, which "falsifies" Kaiser's causal theory of direct reliance.

Pfizer did present evidence that Kaiser continued to permit and even recommend the prescription of Neurontin for certain off-label uses after it became aware of Pfizer's fraud, as well as evidence that Kaiser's efforts to limit Neurontin prescriptions were driven in part by its cost. But Kaiser presented evidence that it did not learn the full scope of Pfizer's fraud until November 2009, Kaiser Findings, 2011 WL 3852254, at *31, and that its efforts to limit Neurontin prescriptions were motivated by concerns about its efficacy for off-label uses. It was within the factfinder's province to weigh this evidence. Pfizer's evidence did not, as a matter of law or of evidence, "falsify" Kaiser's theory of reliance upon Pfizer's misrepresentations.

2. Regression Analysis Aggregate Evidence

Pfizer relies heavily on its argument that the aggregate statistical evidence presented by Dr. Rosenthal was also insufficient to show causation (or injury) as a matter of law, and was inadmissible as well.

a. Admissibility of Rosenthal Testimony

We review a district court's ruling on the admissibility of an expert witness's testimony for abuse of discretion. In re

Pharm. Indus. Average Wholesale Price Litig. (AWP), 582 F.3d 156, 198 (1st Cir. 2009). Under Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993), expert testimony must have a "reasoning or methodology" that is "scientifically valid," id. at 592-93, and that methodology must also have a "valid scientific connection to the pertinent inquiry" -- that is, a proper "fit" with the facts of the case, id. at 591-92. Admissibility does not turn on a determination by the trial court of "which of several competing scientific theories has the best provenance," nor does it turn on convincing the trial court that the proffered expert is correct. Milward v. Acuity Specialty Prods. Grp., Inc., 639 F.3d 11, 15 (1st Cir. 2011) (quoting Ruiz-Troche v. Pepsi Cola of P.R. Bottling Co., 161 F.3d 77, 85 (1st Cir. 1998)) (internal quotation mark omitted).

It is clear that Dr. Rosenthal's evidence met several requirements of Federal Rule of Evidence 702. Dr. Rosenthal is a witness with the requisite "knowledge, skill, experience, training, or education," Fed. R. Evid. 702, and her opinion would assist the trier of fact to understand the evidence or to determine a fact in issue, Fed. R. Evid. 702(a). Yet Pfizer argues that Dr. Rosenthal's testimony should have been excluded, attacking both the methodology and the "fit" of the Rosenthal report.

As to the methodology, regression analysis is a well recognized and scientifically valid approach to understanding statistical data, and courts have long permitted parties to use

statistical data to establish causal relationships. See, e.g., Wards Cove Packing Co., Inc. v. Atonio, 490 U.S. 642, 657-58 (1989) (holding that under Title VII of the Civil Rights Act of 1964, "specific causation" is shown and a "prima facie case" is "establish[ed]" when plaintiff identifies a specific employment practice linked to a statistical disparity); Watson v. Fort Worth Bank & Trust, 487 U.S. 977, 994 (1988) (opinion of O'Connor, J.) (explaining that, to establish a prima facie case under Title VII, "[o]nce the employment practice at issue has been identified, causation must be proved; that is, the plaintiff must offer statistical evidence of a kind and degree sufficient to show that the practice in question has caused the exclusion of applicants for jobs or promotions because of their membership in a protected group"); Duren v. Missouri, 439 U.S. 357, 366-67 (1979) (permitting petitioner to establish prima facie violation of fair cross-section requirement of Sixth and Fourteenth Amendments by using "statistics and other evidence" to show that "the underrepresentation of women, generally and on his venire, was due to their systematic exclusion in the jury-selection process"); Times-Picayune Pub. Co. v. United States, 345 U.S. 594, 621 (1953) (in antitrust case, looking to "economic statistics" to determine whether "demonstrably deleterious effects on competition may be inferred"); In re High Fructose Corn Syrup Antitrust Litig., 295 F.3d 651, 660-61 (7th Cir. 2002) (permitting use of regression analysis to show causation

in antitrust case); Conwood Co., L.P. v. U.S. Tobacco Co., 290 F.3d 768, 794 (6th Cir. 2002) (finding regression analysis "to be admissible on the issue of causation" in antitrust case (emphasis omitted) (quoting Jahn v. Equine Servs., PSC, 233 F.3d 382, 390 (6th Cir. 2000))).

Pfizer argues that Dr. Rosenthal's analysis is nonetheless unreliable in this instance because it did not account for other factors that may have led a doctor to prescribe Neurontin for off-label use, particularly because the model did not include a "time trend."[15] Pfizer also argues that the methodology must be unsound because the data contradict the results of Dr. Rosenthal's regression in three ways: (1) gabapentin prescriptions continued to grow after October 2004, when marketing spending plummeted as Neurontin lost patent protection; (2) the model improperly controlled for a spike in promotional spending in 2003, when Neurontin prescriptions remained relatively flat; and (3) the model attributed 85% of Neurontin prescriptions for nociceptive pain to alleged fraudulent marketing, but the factfinders found that there was no fraudulent marketing for that indication.

The district court acted well within its discretion in concluding that Dr. Rosenthal's methods met the scientific validity

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[15] Dr. Rosenthal described a "time trend" as a variable that is "introduced to capture some conglomeration of variables believed to have a pattern over time . . . . [I]t's a hypothetical based on the idea that there are some things [other than promotional spending] over time that drive sales."

standard under Rule 702. "So long as an expert's scientific testimony rests upon 'good grounds, based on what is known,' it should be tested by the adversarial process, rather than excluded for fear that jurors will not be able to handle the scientific complexities." Milward, 639 F.3d at 15 (citation omitted) (quoting Daubert, 509 U.S. at 590). Pfizer's own expert witness admitted that peer-reviewed, published studies do not always contain time trends. Moreover, Dr. Rosenthal explained her reason for declining to use a time trend: because the case involved only a single drug (as opposed to other studies involving multiple drugs), the time trend would likely be a confounding variable, because its inclusion would produce results showing that promotional spending had no statistically significant effect on prescriptions -- a conclusion that would not comport with basic economics. Indeed, Pfizer's own documents and testimony show that it expected and believed that off-label marketing of Neurontin would increase off-label prescriptions, and that its marketing had that result. The choice not to use a time trend did not make Dr. Rosenthal's methodology unreliable.

Pfizer's objections regarding data that allegedly contradict the reliability of the model also do not show that the district court abused its discretion. These objections presented a question for the jury. The post-October 2004 increase in gabapentin prescriptions does not render the regression analysis

inadmissible. Indeed, the increase can be explained by the fact that gabapentin became a generic drug at that time, and the generic's lower price would be expected to increase gabapentin sales even though marketing efforts for Neurontin had ceased. This change in circumstances does not negate the causal relationship between marketing and prescriptions that the model revealed for the pre-October 2004 period.

There was also nothing methodologically suspect about Dr. Rosenthal's controlling for a spike in promotional spending in 2003, because that spike was likely the result of "strategic interaction" between the marketing efforts for Neurontin and for Pfizer's launch of a new anti-epileptic drug, Lyrica. As Dr. Rosenthal explained, this was the most plausible reason why promotional spending for Neurontin would increase even as it neared the end of its patent life.

Finally, Pfizer's argument about the 85% figure for nociceptive pain misunderstands the structure of the model. In conducting her analysis, Dr. Rosenthal assumed -- at the plaintiffs' direction -- that all off-label marketing was fraudulent,[16] then analyzed the relationship between marketing and prescriptions. Such an approach to proving injury from an underlying assumption of unlawful behavior (to be proven to the fact-finder) is well accepted in the antitrust context from which

[16] Her analysis excluded the marketing for on-label uses.

RICO has drawn many of its causation principles. See, e.g., Associated Gen. Contractors, 459 U.S. at 528, 535-46 (noting that appellate court had "properly assumed" that defendant's alleged conduct "might violate the antitrust laws," id. at 528, then going on to separately evaluate whether plaintiff had sufficiently alleged antitrust injury). Ultimately, Pfizer's attacks on Dr. Rosenthal's methodology were all grist for the trier of fact; they warranted "test[ing] by the adversarial process, rather than exclu[sion]." Milward, 639 F.3d at 15.

As to the "fit" between Dr. Rosenthal's model and the facts at issue in the case, Pfizer objects that: (1) Dr. Rosenthal did not analyze the effect of the distorted studies or educational events on prescriptions, but rather the effect of promotional spending on prescriptions; (2) she did not analyze the effect of formulary expansion on the number of prescriptions written; (3) the analysis used national drug utilization data, as opposed to drug utilization data of Kaiser; (4) the analysis assumes all off-label marketing expenditures for Neurontin were for fraudulent marketing; and (5) the diagnostic codes used to determine what condition the drug was prescribed for indicate a patient's primary condition, so Neurontin could have been prescribed for an on-label use, but appear to be off-label. The basic thrust of Pfizer's argument is that Dr. Rosenthal's analysis does not provide insight into the

quantity of prescriptions written as a result of Pfizer's alleged fraudulent marketing.

None of these arguments demonstrate that the district court abused its discretion under the "fit" criterion in admitting Dr. Rosenthal's testimony. The use of promotional spending as a variable was a reasonable "fit" to represent Pfizer's fraud because Pfizer targeted its promotional activities toward PMG physicians and toward Kaiser itself, and the money it spent on promotion helped to implement its fraudulent publication strategy. See Kaiser Findings, 2011 WL 3852254, at *11-28. The analysis did not require Kaiser to quantify the "publication strategy" as distinct from other promotional activities in order to effectively model the causal relationship. In fact, if publications and CME events did exert an effect independent of detailing (for instance, an effect on decisions about the formulary), the model would have underestimated the impact of the fraud.

Next, the use of national drug data was reasonable, and the district court did not abuse its discretion in so holding. See id. at *32. Dr. Rosenthal used data that was prepared by independent consulting companies, and this type of data is used by Pfizer itself in its own strategic planning and marketing efforts. Kaiser did not independently keep track of the usage for which each prescription was written, so Dr. Rosenthal used what she considered the best alternative, derived from national databases that the

district court described as the "gold standard." Id. Pfizer does not challenge the district court's determination that it was reasonable to assume that Kaiser's patient population and physician distribution are similar to the national mix. See id. The district court also permissibly found a "fit" in Dr. Rosenthal's use of the databases' diagnostic codes (particularly with respect to bipolar disorder) to determine the percentage of prescriptions written for each indication. Indeed, Pfizer's own estimate was that bipolar disorder accounted for 14.7 percent of Neurontin prescriptions, which is "quite close" to Dr. Rosenthal's estimate of 16 percent. See id. at *32 n.20.

Finally, that Dr. Rosenthal's report assumed all of Pfizer's off-label marketing was fraudulent marketing is not a basis to find that the district court erred in admitting the report. Pfizer is incorrect that this assumption means that Dr. Rosenthal was "assum[ing] the very conclusion she was attempting to prove." Dr. Rosenthal's analysis sought to determine whether Pfizer's marketing had a causal effect on prescribing behaviors, not whether the marketing was in fact fraudulent. Pfizer's objection does not go to the question of whether Dr. Rosenthal's regression had a close enough "fit" to satisfy Daubert; rather, it is a question of damages.

b. Sufficiency of Aggregate Evidence

Having found that Dr. Rosenthal's testimony was admissible, we turn to Pfizer's argument that it was insufficient evidence to support the jury's and district court's findings of causation. We reject the argument, while pointing out that her testimony was not the only evidence of but-for causation.

Pfizer insists that Dr. Rosenthal's testimony cannot be credited because it does not take into account the patient-specific, idiosyncratic decisions of individual prescribing physicians. Thus, according to Pfizer, the report was legally insufficient proof of causation. Indeed, Pfizer purports to find support for its position in the district court's rulings entering summary judgment against Aetna and Harden. See Neurontin Class SJ, 754 F. Supp. 2d at 310-11; Neurontin Coordinated SJ, 677 F. Supp. 2d at 485, 494-95.

A tort plaintiff need not "prove a series of negatives; he doesn't have to 'offer evidence which positively exclude[s] every other possible cause of the accident.'" BCS Servs., 637 F.3d at 757 (alteration in original) (quoting Carlson v. Chisholm-Moore Hoist Corp., 281 F.2d 766, 770 (2d Cir. 1960) (Friendly, J.)). "Once a plaintiff presents evidence that he suffered the sort of injury that would be the expected consequence of the defendant's wrongful conduct," the burden shifts to the defendant to rebut this causal inference. Id. at 758.

Pfizer's argument is a repetition of its assertion that there is an intervening cause -- individual physicians' independent medical judgment -- which precludes a finding of causation based on aggregate evidence. But "the burden of proving an 'intervening cause' -- something which snaps the 'causal chain' (that is, operates as a 'superseding cause,' wiping out the defendant's liability) that connects the wrongful act to the defendant's injury -- is on the defendant." Id. at 757 (citation omitted). Pfizer did offer the testimony of doctors who said that their decisions to prescribe Neurontin were not influenced by Pfizer's fraudulent marketing, and the jury and district court, within their powers, rejected the argument.

Pfizer also argues that its testimony from doctors who stated that they prescribed Neurontin for off-label uses without relying on Pfizer's misrepresentations "falsified" Kaiser's statistical analysis. Not so. The existence of some doctors who purportedly were not influenced by Pfizer's misinformation would not defeat the inference that this misinformation had a significant influence on prescribing decisions which injured Kaiser. Indeed, Dr. Rosenthal noted the scientific invalidity of looking to physician-by-physician accounts of their prescribing decisions. Weighing the individual testimony presented by Pfizer against the aggregate evidence presented by Kaiser was a task for the jury and district court.

Pfizer next argues that the Rosenthal report merely demonstrated "correlation" and not "causation." But if Pfizer's information could not be expected to affect a single doctor's decisionmaking, the company's choice to undertake the marketing campaign would be inexplicable. Cf. id. at 758 ("The object of [the defendants'] conspiracies was to obtain liens that would otherwise go to [the plaintiffs and other] bidders -- there could be no other reason for wanting to pack the room in violation of the County's rule. . . . How likely is it that [plaintiffs] lost no bids to bidders who had 13 arms in the room but should have had only three?").

More generally, Pfizer argues that Kaiser's use of aggregate evidence is precluded by the decisions of other courts in pharmaceutical marketing RICO fraud cases. Pfizer relies on a series of cases that it argues have rejected evidence like Kaiser's. See, e.g., In re Schering Plough Corp. Intron/Temodar Consumer Class Action, 678 F.3d 235 (3d Cir. 2012); Ironworkers Local Union 68 v. AstraZeneca Pharm., LP, 634 F.3d 1352 (11th Cir. 2011); UFCW Local 1776 v. Eli Lilly & Co., 620 F.3d 121 (2d Cir. 2010); Se. Laborers Health & Welfare Fund v. Bayer Corp., 655 F. Supp. 2d 1270 (S.D. Fla. 2009). But we disagree with Pfizer's characterization of these cases and find them either supportive of our result or inapposite. We see no split in authority.

In particular, Pfizer leans heavily on the Second Circuit's decision in UFCW Local 1776 v. Eli Lilly & Co., 620 F.3d 121, which reversed a district court's certification of a class of TPP plaintiffs who claimed that Eli Lilly's fraudulent marketing of Zyprexa caused them to pay an inflated price for that drug and to pay for prescriptions that would not have otherwise been written. Id. at 123, 137. To begin, the district court in Eli Lilly granted class certification on the former (excess pricing) claim, and the Second Circuit reversed on that basis. See id. at 133. By contrast, the claimed injury to Kaiser resembles the latter (excess quantity) theory. The Second Circuit found a lack of but-for causation only on the excess pricing theory, because doctors do not generally consider the price of a drug when they make prescribing decisions. Id. at 133-34. On the other hand, doctors would certainly consider information about the efficacy of a drug when deciding whether to prescribe it for their patients.

As to the excess quantity theory, the Second Circuit described the plaintiffs' aggregate evidence of causation as involving only an extrapolation from the fact that the number of off-label prescriptions for Zyprexa fell after Eli Lilly's fraud became known. See id. at 135. This does not come close to resembling Dr. Rosenthal's evidence, which examined contemporaneous data that reflected what was actually happening with regard to spending and prescriptions while Pfizer's fraud was ongoing.

Finally, the Second Circuit specifically noted that, "while [the excess quantity] theory cannot support class certification, it is not clear that the theory is not viable with respect to individual claims by some TPPs." Id. at 136. Kaiser's case, of course, is just such an individual claim by a TPP.

The other cases on which Pfizer relies are distinguishable. The Eleventh Circuit, addressing alleged fraudulent marketing claims involving the drug Seroquel, specifically declined to decide the case on causation grounds. Ironworkers, 634 F.3d at 1359-60. Instead, that court held that the TPP plaintiffs had failed to show economic injury because the prescriptions at issue were merely less cost-effective than the alternatives, rather than being "medically unnecessary or inappropriate."[17] Ironworkers, 634 F.3d at 1360. Kaiser, in contrast, staked much of its case on proving that Neurontin was ineffective for the promoted off-label uses, and the district court so found. See Kaiser Findings, 2011 WL 3852254, at *34-45.

The Third Circuit addressed the causation question as a matter of Article III standing rather than RICO doctrine. In re Schering Plough, 678 F.3d at 246. It also did not address the use

[17] The Eleventh Circuit also decided that the TPPs had assumed the risk of paying for all prescriptions of covered drugs, even those induced by fraud, through the process of setting and collecting premiums. Ironworkers, 634 F.3d at 1364. Without commenting on such a theory, we note that neither party in this litigation has raised it.

of aggregate evidence at all, finding merely that the TPP plaintiff in that case had not connected the pharmaceutical company's alleged fraudulent marketing scheme as to two drugs to the TPP's payment for a third drug owned by the same company. Id. at 247-48. The Ninth Circuit, in an unpublished decision, did not mention aggregate evidence. United Food & Commercial Workers Cent. Pa. & Reg'l Health & Welfare Fund v. Amgen, Inc., 400 F. App'x 255, 257-58 (9th Cir. 2010).[18]

Courts' treatment of aggregate evidence is not as Pfizer represents. Earlier we cited to the use of such aggregate evidence to show causation under several causes of action. We see no reason to reach a different conclusion for the specific subset of RICO claims based on fraudulent marketing.

IV.

At trial, Pfizer argued that it had not committed fraud because Neurontin was effective for the off-label uses at issue. The jury and court rejected the argument, and on appeal Pfizer does not contest the finding of fraud. Nonetheless, it uses the

[18] Further, some courts appear to have conflated the proximate and but-for causation inquiries in evaluating aggregate evidence and the role of doctors' medical judgments. See, e.g., Se. Laborers, 655 F. Supp. 2d at 1280-81 (stating that court was performing proximate cause inquiry, but proceeding to analyze but-for cause question of whether doctors would have prescribed drug at issue in the absence of misrepresentations). And to the extent that some district courts may have endorsed Pfizer's position that aggregate evidence is legally insufficient to prove but-for causation, we disagree, at least on the facts of this case.

question of Neurontin's effectiveness to argue that Kaiser failed to prove that it suffered economic injury. Pfizer contends that because Neurontin was actually effective for the off-label uses at issue, Kaiser suffered no economic injury from paying for prescriptions for these uses. Pfizer claims that the court applied an erroneous burden of proof and an erroneous medical standard in making its findings as to Neurontin's effectiveness.[19] We disagree.

Pfizer asserts that the district court erroneously shifted the burden of proof to it when the court allowed Kaiser to prove its economic injury by showing that "there is no reliable scientific evidence that Neurontin is effective" for the conditions at issue, Kaiser Findings, 2011 WL 3852254, at *34, rather than requiring Kaiser to show that Neurontin was actually ineffective for these conditions in all cases.[20] See, e.g., In re Schering

[19] Pfizer also advances a somewhat confusing argument about the lack of jury instructions on efficacy. Because we decide that, for the purpose of proving injury, Kaiser adequately proved Neurontin's inefficacy for the relevant indications, we need not determine exactly what standard the jury may have used.

[20] Pfizer also argues, briefly, that Kaiser presented another theory of injury: that cheaper, alternative drugs could have been used even if Neurontin was effective. Pfizer asserts that this theory has been rejected by numerous courts, citing, for example, Ironworkers, 634 F.3d at 1360; and Dist. 1199P Health & Welfare Plan v. Janssen, L.P., 784 F. Supp. 2d 508, 520 (D.N.J. 2011). Kaiser does not explicitly defend the cheaper alternative drug theory in any detail, devoting only one footnote in its brief to the theory and relying on only one case, Desiano v. Warner-Lambert Co., 326 F.3d 339 (2d Cir. 2003), without delving into the trial evidence. Because neither party has properly briefed the issue, and because we can dispose of the damages question on the fully briefed effectiveness theory instead, we do not pass on the

Plough Corp. Intron/Temodar Consumer Class Action, No. 2:06-cv-5774, 2010 WL 2346624, at *4 (D.N.J. June 9, 2010) ("[A] lack of data or evidence affirmatively proving that a Subject Drug was effective in treating a condition [is] not the same as the actual ineffectiveness of the Subject Drug.").

The district court did not place the burden on Pfizer to show that Neurontin was effective. Kaiser produced expert witnesses and evidence showing that Neurontin was no more effective than placebo for the indications at issue -- i.e., that it was ineffective. See Kaiser Findings, 2011 WL 3852254, at *35-45 (reviewing such evidence). Pfizer then produced its own evidence to attempt to rebut Kaiser's evidence.

Pfizer's second argument asserts that the district court rested its conclusion on the FDA approval standard -- two positive DBRCTs showing efficacy -- to determine whether Neurontin was effective, and that this meant the court's conclusion was fatally flawed. Pfizer argues that the proper standard was the standard governing the practice of medicine, not the standard for FDA approval.[21] In clinical practice, Pfizer argues, FDA-type trials are not dispositive; instead, physicians rely on their own experience, other doctors' positive clinical experiences, and other

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"cheaper alternatives" theory.

[21] We acknowledge the brief of amicus curiae Pharmaceutical Research and Manufacturers of America on this issue.

evidence. Relatedly, Pfizer argues that Kaiser's use of "negative" studies to show ineffectiveness was not legally sufficient because such studies do not "establish the drug's inefficacy for treating the condition in all other patients and circumstances."

Kaiser responds that the district court did not frame the issue of ineffectiveness only in terms of DBRCTs, but rather considered a number of different types of evidence, including clinical trials that did not meet the DBRCT requirements and reports of clinical judgments such as case studies. The court was aware of Pfizer's critique of DBRCTs; it was also aware that, due to the placebo effect, some patients would report improvements regardless of whether the drug was scientifically effective for their conditions, making non-DBRCT evidence less probative of effectiveness. Kaiser argues that the court properly chose the weight to give each type of medical evidence. Kaiser's is the more accurate description of the record. We conclude that the totality of the evidence supported the district court's ultimate conclusion that Kaiser met its burden of showing that Neurontin was ineffective for the four off-label indications.

Randomized controlled studies like DBRCTs are widely accepted as "ideally suited" for showing causation and as a "good measure of the treatment effect." D. Kaye & D. Freedman, Reference Guide on Statistics, in Federal Judicial Center, Reference Manual on Scientific Evidence 211, 218, 220 (3d ed. 2011). Where, as

here, numerous DBRCTs indicate that a drug is ineffective, that provides powerful scientific evidence of inefficacy, particularly as compared to anecdotal experiences, which can be tainted by the placebo effect. As one witness in this trial testified, "the default position [in medical decisionmaking] is that a drug is ineffective unless it's proven otherwise." Experiments start with a null hypothesis that the drug is no more effective than placebo. In this case, DBRCTs repeatedly showed that there was not enough evidence to reject the null hypothesis for the indications at issue. See Kaiser Findings, 2011 WL 3852254, at *35-45. Pfizer's claimed evidence of Neurontin's efficacy came from less convincing sources.

Thus, the totality of the evidence strongly supports a conclusion that Neurontin was not effective for the four off-label conditions as to which the district court and jury found liability. We need not address what the standard for efficacy would be if there were no DBRCTs in existence, or if the results of DBRCTs were equivocal, or if there were a different mix of DBRCT and non-DBRCT evidence.

V.

Because Kaiser met both causation requirements with legally sufficient evidence and proved that it suffered economic injury from Pfizer's fraudulent scheme, we move to the separate challenges to the amount of damages awarded. "On that phase of the

case the plaintiff has a more relaxed burden of proof . . . , especially if as in this case the defendants' conduct has made it difficult for the plaintiff to prove the precise extent of his damages." BCS Servs., 637 F.3d at 759; see also Thermo Electron Corp. v. Schiavone Constr. Co., 958 F.2d 1158, 1166 (1st Cir. 1992). Under such circumstances, damages do not need to be proven "with mathematical certainty, provided an award has a rational basis in the evidence." Thermo Electron, 958 F.2d at 1166 (quoting Jay Edwards, Inc. v. New Eng. Toyota Distrib., Inc., 708 F.2d 814, 819 (1st Cir. 1983)) (internal quotation mark omitted); see Restatement (Second) of Torts § 912 cmt. a. "Otherwise 'the more grievous the wrong done, the less likelihood there would be of a recovery.'" BCS Servs., 637 F.3d at 759 (quoting Bigelow v. RKO Radio Pictures, Inc., 327 U.S. 251, 265 (1946)).

Pfizer argues that the district court erred in its calculation of damages, primarily because Dr. Hartman used a list of alternatives to Neurontin created by Dr. Millares (the chairman of the DIS) but no expert testified that the drugs on the list were at least as effective or as well tolerated as Neurontin. Moreover, Pfizer argues, there was no evidence that PMG doctors would have prescribed those lower-cost alternative drugs but for Pfizer's conduct; indeed, those doctors may have prescribed more expensive drugs instead of Neurontin. Pfizer claims that these assumptions made the estimation of damages too speculative. See Irvine v.

Murad Skin Research Labs, Inc., 194 F.3d 313, 320 (1st Cir. 1999). Our review of the district court's admission of Dr. Hartman's testimony is for abuse of discretion, AWP, 582 F.3d at 197, and there was none here.

The burden of proof as to damages is lower than that for causation, and the factfinder is afforded a greater deal of freedom to estimate damages where the defendant, as here, has created the risk of uncertainty. See Ocean Spray Cranberries, Inc. v. PepsiCo, Inc., 160 F.3d 58, 63 (1st Cir. 1998). The damages inquiry does not allow a defendant to benefit from the scope of its wrongdoing; this is why "[e]ven 'speculation has its place in estimating damages, and doubts should be resolved against the wrongdoer.'" BCS Servs., 637 F.3d at 759 (quoting Mid-Am. Tablewares, Inc. v. Mogi Trading Co., 100 F.3d 1353, 1365 (7th Cir. 1996)).

The district court did not err in accepting Dr. Hartman's methodology for calculating damages. In fact, Pfizer never offered an alternative: it did not provide its own list of substitute drugs, nor did it offer testimony about the Kaiser list's exclusion of lamotrigine (the only drug Pfizer names on appeal as improperly excluded).

VI.

Pfizer raises two other issues on appeal, concerning the district court's denial of Pfizer's motion to transfer venue before trial and its denial of Pfizer's motion for a new trial.

A. Denial of Pfizer's Motion to Transfer Venue

The coordinated plaintiffs filed their complaint in the Massachusetts district court on February 1, 2005. More than four years later, on December 4, 2009, Pfizer filed a motion to transfer venue to California pursuant to 28 U.S.C. § 1404.

Pfizer's motion followed more than two months of discussions among the coordinated plaintiffs, the defendants, and the Massachusetts district court regarding the possibility of holding a bellwether trial as to one TPP's claims against the defendants. The court stated on September 18, 2009, that it favored holding a trial on Kaiser's claims, a view joined by plaintiffs on October 2, 2009.[22] Defendants opposed, saying that any bellwether trial should not be on Kaiser's claims because "Kaiser is the most atypical of the named TPPs." During none of these discussions did Pfizer suggest that venue should be transferred to California.

On November 12, 2009, the district court ordered that "[t]he trial in the action brought by coordinated plaintiff Kaiser will begin [before it] on February 22, 2010." About a month later, Pfizer moved to transfer venue pursuant to 28 U.S.C. § 1404, arguing for the first time that transfer was favored by (1) Kaiser's residence in California, (2) California's greater interest

[22] While the coordinated plaintiffs represented that they would prefer to all proceed to trial at one time, they agreed that if the court were to initially hold only one trial, it should be Kaiser's.

in the litigation, (3) the greater familiarity of California federal courts with the California UCL, and (4) the convenience of witnesses. The district court, with years of experience in the case, denied this motion, explaining that (1) Kaiser did not wish to transfer venue; (2) transfer would result in considerable delay as any transferee judge familiarized herself with the case; and (3) defendants would not be prejudiced, since they had access to videotaped deposition testimony of non-party witnesses. Kaiser Findings, 2011 WL 3852254, at *11 n.6.

On appeal, Pfizer argues that this was error because it violated the MDL transfer requirements pursuant to 28 U.S.C. § 1407(a) and the rule of Lexecon Inc. v. Milberg Weiss Bershad Hynes & Lerach, 523 U.S. 26 (1998), and because it was an abuse of discretion, in any event, under 28 U.S.C. § 1404.

Pfizer is wrong on the law. Section 1407(a) provides that an action "transferred to any district for coordinated or consolidated pretrial proceedings . . . shall be remanded by the panel at or before the conclusion of such pretrial proceedings to the district from which it was transferred unless it shall have been previously terminated." The Court held in Lexecon that a district court conducting such pretrial proceedings could not "invoke § 1404(a) to assign a transferred case to itself for trial." 523 U.S. at 28. The coordinated plaintiffs filed their complaint in the District of Massachusetts; it was not transferred

to this district for pretrial proceedings, and so § 1407(a) and Lexecon do not govern here.

There was no abuse of discretion as to § 1404. See Coady v. Ashcraft & Gerel, 223 F.3d 1, 11 (1st Cir. 2000). Kaiser opposed defendants' motion to transfer, and coordinated plaintiffs Aetna and Guardian were domiciled in New York and Connecticut, respectively. The Massachusetts district court had considerable experience with complex claims against defendants arising out of the fraudulent marketing of Neurontin, and coordinated plaintiffs' claims were national in scope, not localized to California.

B. Denial of Pfizer's Motion for New Trial Based on Purportedly New Evidence Regarding the Cochrane Review of Neuropathic Pain

There was no abuse of discretion in the district court's denial of defendants' March 22, 2011 motion for new trial. At trial, Pfizer had presented expert testimony that Neurontin was effective for the broad treatment of neuropathic pain, which relied in part on a 2005 review by the Cochrane Collaboration, an independent organization, that concluded that adequate evidence supported Neurontin's efficacy for neuropathic pain. Kaiser Findings, 2011 WL 3852254, at *42. The district court discounted this testimony because the 2005 Cochrane Review was based on incomplete information, given defendants' suppression of negative information about Neurontin's efficacy for the broad treatment of neuropathic pain. Id. at *42-43.

In 2011, the Cochrane Collaboration published another review of the effects of gabapentin in treating chronic neuropathic pain. This revised review was "updated with the inclusion of unpublished information made available through litigation" and concluded that "[g]abapentin provides pain relief of a high level in about a third of people who take [it] for painful neuropathic pain."

The district court denied defendants' motion for a new trial, explaining that a credible meta-analysis from the Cochrane Collaboration based on the entirety of the scientific evidence concerning Neurontin's use in treating broad neuropathic pain was unavailable to defendants at the time of trial only because "Pfizer itself did not provide the Cochrane Group with all available studies prior to the trial because it fraudulently suppressed these studies." That reason was sufficient.

VII.

The judgment of the district court is affirmed.