IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND

UNITED STATES OF AMERICA ex rel. H. Edmund Pigott,	§	
	§	Civil Action No. _____
STATE OF ARKANSAS ex rel. H. Edmund Pigott, Relator,	§	
	§	JURY TRIAL DEMAND
STATE OF CALIFORNIA ex rel. H. Edmund Pigott, Relator,	§	
	§	**FILED IN CAMERA AND UNDER SEAL PURSUANT TO 31 U.S.C. § 3730**
STATE OF COLORADO ex rel. H. Edmund Pigott, Relator,	§	
STATE OF CONNECTICUT ex rel. H. Edmund Pigott, Relator,	§	**DO NOT ENTER INTO PACER**
	§	**DO NOT ENTER INTO CM/ECF**
STATE OF DELAWARE ex rel. H. Edmund Pigott, Relator,	§	**DO NOT PLACE IN PRESS BOX**
DISTRICT OF COLUMBIA ex rel. H. Edmund Pigott, Relator,	§	
STATE OF FLORIDA ex rel. H. Edmund Pigott, Relator,	§	
STATE OF GEORGIA ex rel. H. Edmund Pigott, Relator,	§	
STATE OF HAWAII ex rel. H. Edmund Pigott, Relator,	§	
STATE OF ILLINOIS ex rel. H. Edmund Pigott, Relator,	§	
STATE OF INDIANA ex rel. H. Edmund Pigott, Relator,	§	
STATE OF LOUISIANA ex rel. H. Edmund Pigott, Relator,	§	
STATE OF MASSACHUSETTS ex rel. H. Edmund Pigott, Relator,	§	
STATE OF MICHIGAN ex rel. H.	§	

Edmund Pigott, Relator,	§
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STATE OF MINNESOTA ex rel. H. Edmund Pigott, Relator,	§
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STATE OF MONTANA ex rel. H. Edmund Pigott, Relator,	§
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STATE OF NEVADA ex rel. H. Edmund Pigott, Relator,	§
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STATE OF NEW HAMPSHIRE ex rel. H. Edmund Pigott, Relator,	§
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STATE OF NEW JERSEY ex rel. H. Edmund Pigott, Relator,	§
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STATE OF NEW MEXICO ex rel. H. Edmund Pigott, Relator,	§
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STATE OF NEW YORK ex rel. H. Edmund Pigott, Relator,	§
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STATE OF NORTH CAROLINA ex rel. H. Edmund Pigott, Relator,	§
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STATE OF OKLAHOMA ex rel. H. Edmund Pigott, Relator,	§
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STATE OF RHODE ISLAND ex rel. H. Edmund Pigott, Relator,	§
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STATE OF TENNESSEE ex rel. H. Edmund Pigott, Relator,	§
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STATE OF TEXAS ex rel. H. Edmund Pigott, Relator,	§
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STATE OF VIRGINIA ex rel. H. Edmund Pigott, Relator,	§
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STATE OF WISCONSIN ex rel. H. Edmund Pigott,	§
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Relator,	§
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	§

FILED UNDER SEAL

vs. §
§
FOREST PHARMACEUTICALS, INC., §
§
Defendant. §
§

FALSE CLAIMS ACT COMPLAINT

PRELIMINARY STATEMENT

1. This is an action brought by H. Edmund Pigott ("Relator") to recover damages and civil penalties on behalf of the United States of America and individual states for false and/or fraudulent claims made, used, and caused to be made, used, or presented, by Forest Pharmaceuticals, Inc., ("Forest") in violation of the False Claims Act ("FCA"), 31 U.S.C. § 3729, *et seq.* and comparable state statutes.

2. The central allegation of this Complaint is that the largest antidepressant drug study ever conducted, the STAR*D study[1] funded by the National Institute of Mental Health, was biased in favor of Forest's antidepressant drug Celexa, a fact that the Relator has demonstrated in peer-reviewed journal articles. Relator here alleges upon information and belief that the demonstrated bias in the STAR*D study, which cannot be explained on any other reasonable basis, was the result of kickbacks, bribes and other improper financial inducements paid by Forest to John Rush, M.D., the project's principal investigator, and one or more of the project's other investigators.

3. Relator believes and therefore alleges that conflicts of interest and improper financial arrangements between Forest and Dr. Rush and other investigators not only caused the selection of Forest's drug Celexa to be used as the only antidepressant employed in the first leg of the study, a significant advantage by itself, but also caused falsification and overstatement of the effectiveness of

[1] STAR*D stands for Sequenced Treatment to Relieve Depression.

Celexa in the published reports of the study. The end result was a significant increase in sales of Celexa (and its second-generation version, Lexapro) to patients covered by federal and state healthcare programs.

JURISDICTION AND VENUE

4. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. § 1331 and 31 U.S.C. § 3732, the latter of which specifically confers jurisdiction on this Court for actions brought pursuant to 31 U.S.C. §§ 3729 and 3730. Under 31 U.S.C. § 3730(e), there has been no relevant public disclosure of the "allegations or transactions" in this Complaint.

5. This Court has personal jurisdiction over Defendant pursuant to 31 U.S.C. § 3732(a) because Defendant can be found in, resides or transacts, or has transacted business nationally and specifically within the District of Maryland.

6. Venue is proper in this District pursuant to 31 U.S.C. § 3732(a) and 28 U.S.C. §§1391(b) and (c) because Defendant has transacted business in the District of Maryland.

7. The causes of action alleged herein are timely brought because of, among other things, efforts by the Defendant to conceal from the United States wrongdoing in connection with the allegations made herein.

PARTIES

8. Relator H. Edmund Pigott, is a Ph.D. psychologist who resides in Clarksville, Maryland. Relator has reported bias in the STAR*D study in at least one scholarly publication, but has not previously reported the allegations made here that kickbacks and other improper financial ties caused the bias in the STAR*D study. If there have been any public disclosures of the particular allegations and transactions set forth in this Complaint, Relator is the original source of those disclosures as he conducted the investigation that revealed the bias in the study, he is the source of allegation that improper financial

arrangements with Forest caused that bias, and he has voluntarily provided the information to the United States Attorney before filing of this Complaint.

9. Defendant Forest is a wholly owned subsidiary of Forest Laboratories, Inc. Defendant Forest has its principal place of business in St. Louis, Missouri. Forest manufactures, distributes, and sells prescription drug products in the United States. Forest Laboratories, Inc. has a license from H. Lundbeck A/S ("Lundbeck"), a Danish company, to promote and sell Celexa in the United States.

ALLEGATIONS

10. The STAR*D study was the largest antidepressant effectiveness study ever conducted. It was funded by the National Institute of Mental Health ("NIMH") at a cost of $35 million. STAR*D enrolled 4,041 depressed patients and provided them with free acute and 12 months of continuing antidepressant care to maximize their likelihood of achieving and maintaining remission.

11. Patients were first prescribed Defendant Forest's antidepressant drug Celexa, a Selective Seratonin Reuptake Inhibitors ("SSRI"), similar to but chemically distinct from Prozac, Zoloft, Paxil and other popular antidepressants that work by preventing the body's reuptake or removal of a naturally-occurring neurotransmitter that is believed to have a positive impact upon mood.

12. Those who failed to get adequate relief from Celexa were provided with up to three additional trials of pharmacologically distinct drug treatments, only one of which was an SSRI (Zoloft) that is sold in competition with Celexa. In contrast though to Zoloft, whose effectiveness was compared in the second leg of the study to two other antidepressants that were not SSRIs, Celexas was not compared to any other antidepressants in the first leg of the study and was identified as being an appropriate "first step" antidepressant for this largest depression study ever conducted. In effect, Forest was provided an opportunity to demonstrate the superiority of its branded SSRI without a side-to-side or sequential comparison of the effectiveness of Celexa to other such as Prozac, Zoloft and Paxil.

13. NIMH initially entered into a contract with the University of Texas' Southwest Medical Center

in September 1999, with John Rush, M.D. serving as the study's principal investigator ("P.I."). The first phase of the contract was to develop an agreed-upon research protocol which was finalized on June 28, 2002.

14. Celexa was recommended by Dr. Rush to be the antidepressant given first to all 4,041 patients, supposedly because in June of 2002, it had the lowest market share of the SSRIs with a depression indication. Because of its lower market share, the research protocol determined that Celexa would facilitate participant recruitment given the lower likelihood of prior exposure. Celexa was also chosen because, supposedly, there would be minimal discontinuation symptoms so that the tolerability of the switch to other pharmacological agents at level 2 would not be confounded by the emergence of significant discontinuation reactions. Finally, the research protocol also suggested that Celexa had minimal risk of drug-drug interactions, thereby reducing the complications due to its use in medically ill participants who are on concomitant medications.

15. Relator believes and therefore alleges that it is questionable that Celexa has a scientifically established superiority over other SSRIs such as Prosac, Zoloft, and Paxil with respect to discontinuation syndrome and drug-to-drug interactions. If Celexa were known to be superior on these grounds, and to be equally effective, then it surely would not have been the least-prescribed SSRI. It seems more likely that Celexa was less popular with doctors because it was less effective or had greater risk of discontinuation syndrome or drug-to-drug interactions.

16. Selecting a drug to be the sole antidepressant used in the first leg of a publicly-funded study on the ground that fewer patients would have been exposed to it because it was not as popular as other SSRIs has the hallmarks of a choice made to increase the drug's market share, not a choice based upon scientific principles.

17. Being selected as the step-1 antidepressant in the STAR*D study was highly advantageous to Defendant for numerous reasons including the fact that with the STAR*D study being the largest and

most prestigious antidepressant study ever conducted, Celexa's selection as the initial drug could be pointed to in Forest's marketing efforts as an indication of the drug's superiority over other SSRIs. Also, because the first leg of the study, for which Celexa was used, did not involve a comparison of Celexa to other SSRIs or any other control condition such as a placebo, there was really no way for Defendant to not benefit as long as the success rates were the same or better than previously documented.

18. Relator believes and therefore alleges that the decision to use Celexa was influenced by kickbacks, bribes and other financial remuneration provided by Forest to Dr. Rush. If NIMH personnel went along with Dr. Rush's choice, then it is likely that they did so because Dr. Rush misrepresented to them the real reasons for his recommendation of Celexa. Relator believes and therefore alleges that any of the other popular SSRIs[2] could have been substituted for Celexa and that the stated grounds for the selection of Celexa were a rationalization of a choice that was dictated more than anything else by financial ties between the principal investigator and Defendant Forest.

19. STAR*D was supposedly designed as a comparative effectiveness study of different treatment options for people with major depression and included 12 pre-specified research outcome measures and a detailed analytic plan for evaluating the effectiveness and cost-efficiency of 11 pharmacologically distinct drug treatments for depressed patients who failed to improve from their first antidepressant.

20. After the protocol for the study was approved, the recruitment and treatment of depressed patients began in 41 clinics associated with various leading universities (e.g., UT, University of Pittsburgh, Harvard, UC San Diego, and Columbia University) and continued through mid-2005. The STAR*D investigators began publishing their main findings in seven articles beginning in January 2006 concluding with their summary article published in November 2006.

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[2] SSRI stands for Selective Seratonin Reuptake Inhibitor.

21. Despite the passage of four years since the publication of STAR*D's major summary article and the publication of over 70 peer-reviewed articles on the STAR*D findings, none of the articles published by the STAR*D authors have reported the outcomes for any of the 12 pre-specified measures nor reported any findings in a manner consistent with the study's analytic plan as presented in STAR*D's research protocol, including not discussing the main purpose of the study which was to evaluate the cost-effectiveness of the various antidepressant treatments.

22. In contrast to STAR*D's report of positive findings supporting the effectiveness of antidepressants, Relator, with others, in 2010 published a paper attached as Appendix A documenting that only 108 of STAR*D's 4,041 patients (2.7%) had an acute-care remission and neither relapsed nor dropped out during the 12 months of continuing care that followed. This paper also documented how STAR*D changed its research outcome measures and analyses resulting in an inflation of STAR*D's reported acute-care remission rates.

23. Relator has also determined, through an examination of the STAR*D protocols and reported data, that the remission rate for Celexa was inflated by 44.9%. That and related findings will soon be published in the article attached as Appendix B.

24. Ten of the STAR*D authors, including Dr. Rush, have disclosed in journal articles that they have received unspecified sums of money from Forest. In the summer of 2008, about the time that U.S. Senator Grassley identified failures on Dr. Rush's part to fully disclose conflicts of interest related to NIH grants he received, Dr. Rush left the University of Texas, moved to Singapore and was removed as the PI for STAR*D.

25. Relator has concluded, and therefore alleges, that the only reasonable explanation for the false and biased reporting of the study results is that Dr. Rush received significant financial remuneration from Forest which Forest paid to him for the purpose of influencing his actions.

THE LAW

26. The federal Anti-Kickback statute ("AKS") makes it a felony punishable by imprisonment of up to five years and a fine of up to $25,000 to "offer or pay remuneration (including any kickback, bribe, or rebate)" to any person to "induce such person . . . to . . . *recommend* purchasing, leasing, or ordering any good, facility, service or item for which payment may be made in whole or in part under a Federal health care program . . . ." 42 U.S.C. 1320a-7b(b)(2) (emphasis added).

27. The AKS is violated if one purpose of the remuneration is to induce future referrals of business reimbursable under federal health care programs. *United States v. Shaw*, 106 F. Supp. 2d 103,121 (D. Mass. 2000), citing *United States v. Greber*, 760 F.2d 68 (3rd Cir. 1985) and *United States v. Kats*, 871 F.2d 105 (9th Cir. 1989). "The gravamen of Medicare Fraud [under the AKS] is inducement . . . ." Id at 121, citing *United States v. Bay State Ambulance and Hospital Rental Service*, 874 F.2d 20 (1st Cir. 1989).

28. The FCA provides that any person who or entity which knowingly submits, or causes the submission of, a false or fraudulent claim to the United States government for payment or approval, is liable for a civil penalty of up to $11,000 for each such claim, plus three times the amount of the damages sustained by the government. 31 U.S.C. 3729(a)(1)(A). The FCA defines "knowingly" to include acts committed with "actual knowledge," as well as acts committed "in deliberate ignorance" or in "reckless disregard" of their truth or falsity. Liability attaches when a defendant fraudulently seeks, or causes others to seek, payment that is unwarranted from the government, or otherwise retains payments from the government which should have never been paid at all. The FCA allows any person having information about a false or fraudulent claim against the government to bring an action for him or herself and the government, and to share in any recovery.

29. Likewise, section 31 U.S.C. 3729(a)(1)(B) states that any person who knowingly makes, uses, or causes to be made or used, a false record or statement material to a false or fraudulent claim is liable to

the United States government. Anyone who conspires to commit a violation under the Federal False Claims Act will also be held liable pursuant to section 31 U.S.C. 3729(a)(1)(C).

30. The false claims acts of the individual states are largely patterned based upon the Federal False Claims Act.

COUNT I

ANTI-KICKBACK VIOLATIONS OF FEDERAL AND STATE FALSE CLAIMS ACTS

31. Relator re-alleges the allegations of paragraphs 1 through 30 of this Complaint as if fully set forth herein.

32. At least one purpose of the remuneration paid to Dr. Rush by Forest was to induce him to recommend use of Celexa as the first-stage antidepressant in the STAR*D study and to recommend through scholarly publications the use of Celexa (and its substitute Lexapro) for treatment of depression by overstating the effectiveness of Celexa in the published reports of the STAR*D study. Forest is therefore guilty of violations of the AKS.

33. Compliance with the AKS is both a condition of participation and a condition of payment under government healthcare programs and is material to the decisions of state and federal programs to reimburse for prescriptions of Celexa and Lexapro. Through violations of the AKS, Forest knowingly caused doctors to prescribe and pharmacies to fill prescriptions for Celexa and Lexapro that it knew would be submitted for reimbursement to state and federal healthcare programs.

34. Forest has therefore caused the submission of false or fraudulent claims for payment or approval in violation of 31 U.S.C. § 3729 (a)(1)(A).

35. The United States has been damaged.

COUNT II

FALSE STATEMENT VIOLATIONS OF FEDERAL AND STATE FALSE CLAIMS ACTS

36. Relator re-alleges and incorporates herein by reference the preceding paragraphs, 1 – 35 of this Complaint as if fully set forth herein.

37. Published reports of the STAR*D study that overstated the effectiveness of Celexa were false reports or statements knowingly made or used by Forest or caused to be made or used by Forest that were material to false or fraudulent claims submitted by pharmacies for the reimbursement of prescriptions for Celexa and Lexapro in violation of 31 U.S.C. §3729(a)(1)(B).

38. The United States has been damaged.

PRAYER FOR RELIEF UNDER THE FEDERAL FALSE CLAIMS ACT

Relator respectfully requests this Court to enter judgment against Defendant, as follows:

(a) That the United States be awarded damages in the amount of three times the damages sustained by them because of the false and fraudulent claims alleged within this Complaint;

(b) That civil penalties of $11,000 be imposed for each and every false claim that Defendant presented to the United States;

(c) That pre- and post-judgment interest be awarded, along with reasonable attorneys' fees, costs, and expenses which the Relator necessarily incurred in bringing and pressing this case;

(d) That Relator be awarded the maximum percentage of any recovery allowed to him pursuant the False Claims Act and its state law counterparts and

(e) That this Court award such other and further relief as it deems proper.

COUNT THREE

VIOLATION OF THE ARKANSAS MEDICAID FRAUD FALSE CLAIMS ACT

39. Relator re-alleges and incorporates the allegations in paragraphs 1 - 38 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of Arkansas. Upon information and belief, Defendant's actions described herein occurred in the State of Arkansas as well.

40. This is a qui tam action brought by Relator and the State of Arkansas to recover treble damages and civil penalties under the Arkansas Medicaid Fraud False Claims Act, A.C.A. §§ 20-77-901 *et seq*.

41. The Arkansas Medicaid Fraud False Claims Act § 20-77-902 provides liability for any person who:

> Knowingly makes or causes to be made any false statement or representation of a material fact in any application for any benefit or payment under the Arkansas Medicaid program;
>
> At any time knowingly makes or causes to be made any false statement or representation of a material fact for use in determining rights to a benefit or payment;

42. In addition, A.C.A. § 20-77-902(7)(A) prohibits soliciting, accepting, or agreeing to accept any type of remuneration for the following:

Recommending the purchase, lease, or order of any good, facility, service, or item for which payment may be made under the Arkansas Medicaid program.

43. Defendant violated the Arkansas Medicaid Fraud False Claims Act § 20-77-902(1) (2) & (7)(A) by continuously engaging in the fraudulent and illegal conduct described herein.

44. Defendant furthermore violated Arkansas Medicaid Fraud False Claims Act § 20-77-902(1) & (2) and knowingly caused thousands of false claims to be made, used, and presented to Arkansas by their continuous violation of federal and state laws, including A.C.A. § 20-77-902(7)(A) and the AKS, as

described herein.

45. Arkansas, by and through the Arkansas Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

46. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to Arkansas in connection with Defendant's fraudulent and illegal conduct.

47. Had Arkansas known that defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

48. As a result of Defendant's violations of A.C.A. § 20-77-902(1) (2) & (7)(A), the State of Arkansas has been damaged in an amount far in excess of millions of dollars exclusive of interest.

49. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to A.C.A. § 20-77-911(a) on behalf of himself and the State of Arkansas.

50. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of Arkansas in the operation of its Medicaid program.

51. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against defendant:

To the STATE OF ARKANSAS:

Three times the amount of actual damages which the State of Arkansas has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $5,000 and not more than $10,000 for each false claim which defendant caused to be presented to the State of Arkansas;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to A.C.A. § 20-77-911(a) and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this court deems equitable and just.

COUNT FOUR

VIOLATON OF THE CALIFORNIA FALSE CLAIMS ACT

52. Relator re-alleges and incorporates the allegations in paragraphs 1 - 51 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of California. Upon information and belief, Defendant's actions described herein occurred in the State of California as well.

53. This is a qui tam action brought by Relator and the State of California to recover treble damages and civil penalties under the California False Claims Act, Cal. Gov't. Code §§ 12650 *et seq*.

54. Cal. Gov't Code § 12651(a) provides liability for any person who:

Knowingly presents, or causes to be presented, to an officer or employee of the state of any political division thereof, a false claim for payment or approval;

Knowingly makes, uses, or causes to be made or used a false record of statement to get a false claim paid or approved by the state or by any political subdivision;

Conspires to defraud the state or any political subdivision by getting a false claim allowed or paid by the state of by any political subdivision.

Is a beneficiary of an inadvertent submission of a false claim to the state or a political subdivision, subsequently discovers the falsity of the claim, and fails to disclose the false claim to the state or the political subdivision within a reasonable time after discovery of the false claim.

55. In addition, the payment or receipt of bribes or kickbacks is prohibited under Cal. Bus. & Prof. Code §§ 650 & 650.1, and is also specifically prohibited in treatment of medical patients pursuant to Cal. Welf. & Inst. Code § 14107.2.

56. Defendant violated Cal. Gov't Code § 12651(a), Cal Bus. & Prof. Code §§ 650 & 650.1, and Cal. Welf. & Inst. Code § 14107.2 by continuously engaging in the fraudulent and illegal conduct described herein.

57. Defendant furthermore violated Cal. Gov't Code § 12651(a) and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of California by their continuous violation of federal and state laws, including Cal. Bus. & Prof. Code §§ 650, 650.1, Cal. Welf. & Inst. Code § 14107.2, and the AKS, as described herein.

58. The State of California, by and through the California Medi-Cal program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

59. Compliance with applicable Medicare, Medicaid, Medi-Cal, and the various other federal and state laws cited herein was implied, and upon information and belief, also an express condition of payment of claims submitted to the State of California in connection with Defendant's fraudulent and illegal conduct.

60. Had the State of California known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

61. As a result of Defendant's continuous violations of Cal. Gov't Code § 12651(a), the State of California has been damaged in an amount far in excess of millions of dollars exclusive of interest.

62. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to Cal. Gov't Code § 12652(c) on behalf of himself and the State of California.

63. This Court is requested to accept supplemental jurisdiction over this related state claim as it is predicated upon the same exact facts as the federal claim and merely asserts separate damages to the State of California in the operation of its Medicaid program.

64. WHERFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF CALIFORNIA:

Three times the amount of actual damages which the State of California has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of up to $10,000 for each false claim which Defendant presented or caused to be presented to the State of California;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to Cal. Gov't Code § 12652 and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT FIVE

VIOLATION OF THE COLORADO MEDICAID FALSE CLAIMS ACT

65. Relator re-alleges and incorporates the allegations in paragraphs 1 - 64 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of Colorado. Upon information and belief, Defendant's actions described herein occurred in Colorado as well.

66. This is a qui tam action brought by Relator and the State of Colorado to recover treble damages and civil penalties under the Colorado Act, Co. St. §§ 25.5-4-304 to 25.5-4-310 *et seq*.

67. Co. St. § 25.5-4-305 provides liability in relevant part, to any person who:

> (a) Knowingly presents, or causes to be presented, to an officer or employee of the state a false or fraudulent claim for payment or approval;
>
> (b) Knowingly makes, uses, or causes to be made or used a false record or statement material to a false or fraudulent claim;
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> ***
>
> (f) Knowingly makes, uses, or causes to be made or used, a false record or statement material to an obligation to pay or transmit money or property to the state in connection with the "Colorado Medical Assistance Act," or knowingly conceals or knowingly and improperly avoids or decreases an obligation to pay or transmit money or property to the state in connection with the "Colorado Medical Assistance Act;"
>
> (g) Conspires to commit a violation of paragraphs (a) to (f) of this subsection (1).

68. Defendant violated Co. St. § 25.5-4-305 by continuously engaging in the fraudulent and illegal conduct described herein.

69. Defendant furthermore violated Co. St. § 25.5-4-305 and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of Colorado by its continuous violation of federal and state laws, including the AKS, as described herein.

70. The State of Colorado, by and through the Colorado Medicaid Program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

71. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Colorado in connection with Defendant's fraudulent and illegal conduct.

72. Had Colorado known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

73. As a result of Defendant's continuous violations of Co. St. §§ 25.5-4-304 to 25.5-4-310 *et seq.*, the State of Colorado has been damaged in an amount far in excess of millions of dollars exclusive of interest.

74. Defendant did not, within thirty days after they first obtained information as to such violations, furnish such information to officials of the State responsible for investigating false claims violations, did not otherwise fully cooperate with any investigation of the violations, and have not otherwise furnished information to the State regarding the claims for reimbursement at issue.

75. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to Co. St. § 25.5-4-306 on behalf of himself and the State of Colorado.

76. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of Colorado in the operation of its Medicaid program.

77. WHERFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF COLORADO:

Three times the amount of actual damages which the State of Colorado has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of up to $10,000 for each false claim which Defendant presented or caused to be presented to the State of Colorado;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to Co. St. § 25.5-4-305 and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT SIX

VIOLATION OF THE CONNECTICUT FALSE CLAIMS ACT

78. Relator re-alleges and incorporates the allegations in paragraphs 1 - 77 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of Connecticut. Upon information and belief, Defendant's actions described herein occurred in Connecticut as well.

79. This is a qui tam action brought by Relator and the State of Connecticut to recover treble damages and civil penalties under the Connecticut False Claims Act, C.G.S.A. §§ 17b-301 *et seq.*

80. C.G.S.A. § 17b-301a provides for liability for any persons who:

> (1) Knowingly present, or cause to be presented, to an officer or employee of the state a false or fraudulent claim for payment or approval under a medical assistance program administered by the Department of Social Services;

> (2) Knowingly make, use or cause to be made or used, a false record or statement to secure the payment or approval by the state of a false or fraudulent claim under a medical assistance program administered by the Department of Social Services;
>
> (3) Conspire to defraud the state by securing the allowance or payment of a false or fraudulent claim under a medical assistance program administered by the Department of Social Services;
>
> ***
>
> (7) Knowingly make, use or cause to be made or used, a false record or statement to conceal, avoid or decrease an obligation to pay or transmit money or property to the state under a medical assistance program administered by the Department of Social Services.

81. Defendant violated C.G.S.A. § 17b-301a by continuously engaging in the fraudulent and illegal conduct described herein.

82. Defendant furthermore violated C.G.S.A. § 17b-301a and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of Connecticut in continuous violation of federal and state laws, including the AKS, as described herein.

83. The State of Connecticut, by and through the Connecticut Medicaid Program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

84. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Connecticut in connection with Defendant's fraudulent and illegal conduct.

85. Had Connecticut known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

86. As a result of Defendant's violations of C.G.S.A. § 17b-301, the State of Connecticut has been damaged in an amount far in excess of millions of dollars exclusive of interest.

87. Defendant did not, within thirty days after they first obtained information as to such violations, furnish such information to officials of the State responsible for investigating false claims violations, did not otherwise fully cooperate with any investigation of the violations, and have not otherwise furnished information to the State regarding the claims for reimbursement at issue.

88. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to C.G.S.A. § 17b-301 on behalf of himself and the State of Connecticut.

89. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of Connecticut in the operation of its Medicaid program.

90. WHERFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF CONNECTICUT:

Three times the amount of actual damages which the State of Connecticut has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of up to $10,000 for each false claim which Defendant presented or caused to be presented to the State of Connecticut;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to C.G.S.A. 17b-301b and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT SEVEN

VIOLATION OF THE DELAWARE FALSE CLAIMS ACT

91. Relator re-alleges and incorporates the allegations in paragraphs 1 - 90 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of Delaware. Upon information and belief, Forest's actions described herein occurred in Delaware as well.

92. This is a qui tam action brought by Relator and the State of Delaware to recover treble damages and civil penalties under the Delaware Medicaid False Claims Act, 6 Del. C. §§ 1201 *et seq*.

93. 6 Del. C. § 1201 provides liability for any person who:

> Knowingly presents, or causes to be presented, directly or indirectly, to an officer or employee of the Government a false or fraudulent claim for payment or approval;
>
> Knowingly makes, uses or causes to be made or used, directly or indirectly, a false record or statement to get a false or fraudulent claim paid or approved;
>
> Conspires to defraud the Government by getting a false or fraudulent claim allowed or paid;
>
> Knowingly makes, uses, or causes to be made or used a false record or statement to conceal, avoid, increase or decrease an obligation to pay or transmit money or property to or from the Government.

94. Further, 31 Del. C. § 1005 provides that:

It shall be unlawful for any person to offer or pay any remuneration (including any kickback, bribe or rebate) directly or indirectly, in cash or in kind to induce any other person . . . [t]o purchase, lease, order or arrange for or recommend purchasing, leasing or ordering any property, facility, service, or item of medical care or medical assistance for which payment may be made in whole or in part under any

public assistance program.

95. Defendant violated 6 Del. C. § 1201 & 31 Del. C. § 1005 by continuously engaging in the fraudulent and illegal conduct described herein

96. Defendant furthermore violated 6 Del. C. § 1201 and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of Delaware by their continuous violation of federal and state laws, including 31 Del. C. § 1005 and the AKS, as described herein.

97. The State of Delaware, by and through the Delaware Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

98. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Delaware in connection with Defendant's fraudulent and illegal conduct.

99. Had the State of Delaware known that Defendant was violating the federal and state laws cited herein, it wound not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

100. As a result of Defendant continuing violations of 6 Del C. § 1201(a), the State of Delaware has been damaged in an amount far in excess of millions of dollars exclusive of interest.

101. Defendant did not, within 30 days after they first obtained information as to such violations, furnish such information to officials of the State responsible for investigating false claims violations, did not otherwise fully cooperate with any investigation of the violations, and have not otherwise furnished information to the State regarding the claims for reimbursement at issue.

102. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to 6 Del. C. § 1203(b) on behalf of himself and the State of Delaware.

103. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of Delaware in the operation of its Medicaid program.

104. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties against Defendant:

To the STATE OF DELAWARE:

Three times the amount of actual damages which the State of Delaware has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty on not less than $5,500 and not more than $11,000 for each false claim which Defendant caused to be presented to the State of Delaware;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to 6 Del C. § 1205, and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT EIGHT

VIOLATION OF THE DISTRICT OF COLUMBIA PROCUREMENT REFORM AMENDMENT ACT

105. Relator re-alleges and incorporates the allegations in paragraphs 1 - 104 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the District of Columbia. Upon information and belief, Defendant's actions described herein occurred in the District of Columbia as well.

106. This is a qui tam action brought by Relator and the District of Columbia to recover treble damages and civil penalties under the District of Columbia Procurement Reform Amendment Act, D.C. §§ 2-308.13 *et seq*.

107. D.C. Code § 2-30814(a) provides liability for any person who:

> Knowingly presents, or causes to be presented, to an officer or employee of the District a false claim for payment or approval;
>
> Knowingly makes, uses or causes to be made or used, a false record or statement to get a false claim paid or approved by the District;
>
> Conspires to defraud the District by getting a false claim allowed or paid by the District;
>
> Is the beneficiary of an inadvertent submission of a false claim to the District, subsequently discovers the falsity of the claim, and fails to disclose the false claim to the District.

108. In addition, D.C. Code §§ 4-802(c) & 2-30814(a) prohibits soliciting, accepting, or agreeing to accept any type of remuneration for the following:

> Referring a recipient to a particular provider of any item or service or for which payment may be made under the District of Columbia Medicaid program;
>
> Recommending the purchase, lease, or order of any good, facility, service, or item for which payment may be made under the District of Columbia Medicaid Program.

109. Defendant violated D.C. Code §§ 2-30814(a), 4-802(c), & 2-30814(a) by continuously engaging in the fraudulent and illegal conduct described herein.

110. Defendant furthermore violated D. C. Code § 2-30814(a) and knowingly caused thousands of false claims to be made, used, and presented to the District of Columbia by their continuing violation of federal and state laws, including D. C. Code §§ 4-802(c) & 2-30814(a) and the AKS, as described herein.

111. The District of Columbia, by and through the District of Columbia Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

112. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the District of Columbia is connection with Defendant's fraudulent and illegal conduct.

113. Had the District of Columbia known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

114. As a result of Defendant violations of D.C. Code § 2-308.14(a), the District of Columbia has been damaged in an amount far in excess of millions of dollars exclusive of interest.

115. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to D.C. Code § 2-308.15(b) on behalf of himself and the District of Columbia.

116. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the District of Columbia in the operation of its Medicaid program.

117. WHEREFORE, Relator respectfully request this Court to award the following damages to the following parties and against Defendant:

To the DISTRICT OF COLUMBIA:

Three times the amount of actual damages which the District of Columbia has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $5,000 and not more than $10,000 for each false claim which Defendant caused to be presented to the District of Columbia;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to D. C. Code § 2-308.15(f) and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this court deems equitable and just.

COUNT NINE

VIOLATION OF THE FLORIDA FALSE CLAIMS ACT

118. Relator re-alleges and incorporates the allegations in paragraphs 1 - 117 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of Florida. Upon information and belief, Defendant's actions described herein occurred in the State of Florida as well.

119. This is a qui tam action brought by Relator and the State of Florida to recover treble damages and civil penalties under the Florida False Claims Act, West's F.S.A. §§ 68.081 *et seq*.

120. West's F.S.A. § 68.082 provides liability for any person who:

Knowingly presents or causes to be presented to an officer or employee of an agency a false claim for payment or approval;

Knowingly makes, uses, or causes to be made or used a false record or statement to get a false or fraudulent claim paid or approved by an agency;

Conspires to submit a false claim to an agency or to deceive an agency for the purpose of getting a false or fraudulent claim allowed or paid.

121. Defendant violated West's F.S.A. § 68.082 by continuously engaging in the fraudulent and illegal conduct described herein.

122. Defendant furthermore violated West's F.S.A. § 68.082 and knowingly caused thousands of false claims to be made, used, and presented to the State of Florida by their continuous violation of federal and state laws, including the AKS, as described herein.

123. The State of Florida, by and through the State of Florida Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

124. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Florida in connection with Defendant's fraudulent and illegal conduct.

125. Had the State of Florida known that defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

126. As a result of Defendant's violations of West's F.S.A. § 68.082, the State of Florida has been damaged in an amount far in excess of millions of dollars exclusive of interest.

127. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to West's F.S.A. § 68.083(2) on behalf of himself and the State of Florida.

128. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of Florida in the operation of its Medicaid program.

129. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF FLORIDA:

Three times the amount of actual damages which the State of Florida has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $5,000 and not more than $10,000 for each false claim which Defendant caused to be presented to the State of Florida;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to West's F.S.A. § 68.085 and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this court deems equitable and just.

COUNT TEN

VIOLATION OF THE GEORGIA STATE FALSE MEDICAID CLAIMS ACT

130. Relator re-alleges and incorporates the allegations in paragraphs 1 - 129 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of Georgia. Upon information and belief, Defendant's actions described herein occurred in Georgia as well.

131. This is a qui tam action brought by Relator and the State of Georgia to recover treble damages and civil penalties under the Georgia State False Medicaid Claims Act, Ga. Code Ann. §§ 49-4-168 *et seq*.

132. Ga. Code Ann. §§ 49-4-168.1 *et seq*. provides liability for any person who:

> Knowingly presents or causes to be presented to the Georgia Medicaid program a false or fraudulent claim for payment or approval;
>
> Knowingly makes, uses, or causes to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the Georgia Medicaid program;
>
> Conspires to defraud the Georgia Medicaid program by getting a false or fraudulent claim allowed or paid;
>
> Knowingly makes, uses, or causes to be made or used, a false record or statement to conceal, avoid, or decrease an obligation to pay, repay or transmit money or property to the State of Georgia.

133. Defendant violated Ga. Code Ann. § 49-4-168.1 by continuously engaging in the fraudulent and illegal conduct described herein.

134. Defendant furthermore violated Ga. Code Ann. § 49-4-168.1 and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of Georgia by its continuous violation of federal and state laws, including the AKS, as described herein.

135. The State of Georgia, by and through the Georgia Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

136. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Georgia in connection with Defendant's fraudulent and illegal conduct.

137. Had the State of Georgia known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with Defendant's fraudulent and illegal conduct.

138. As a result of Defendant's violations of Ga. Code Ann. § 49-4-168.1, the State of Georgia has been damaged in an amount far in excess of millions of dollars exclusive of interest.

139. Defendant did not, within 30 days after first obtaining information as to such violations, furnish such information to officials of the State responsible for investigating false claims violations, did not otherwise fully cooperate with any investigation of the violations, and have not otherwise furnished information to the State regarding the claims for reimbursement at issue.

140. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to Ga. Code Ann. § 49-4-168.2(b) on behalf of himself and the State of Georgia.

141. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of Georgia in the operation of its Medicaid program.

142. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties against Defendant:

To the STATE OF GEORGIA:

Three times the amount of actual damages which the State of Georgia has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty on not less than $5,500 and not more than $11,000 for each false claim which Defendant caused to be presented to the State of Georgia;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to Ga. Code Ann. § 49-4-168.2(i), and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT ELEVEN

VIOLATION OF THE HAWAII FALSE CLAIMS ACT

143. Relator re-alleges and incorporates the allegations in paragraphs 1 - 142 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of Hawaii. Upon information and belief, Defendant's actions described herein occurred in Hawaii as well.

144. This is a qui tam action brought by Relator and the State of Hawaii to recover treble damages and civil penalties under the Hawaii False Claims Act, Haw. Rev. Stat. §§ 661.21 *et seq.*

145. Haw. Rev. Stat. § 661-21(a) provides liability for any person who:

Knowingly presents, or causes to be presented, to an officer or employee of the state a false or fraudulent claim for payment or approval;

Knowingly makes, uses, or causes to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the state;

Conspires to defraud the state by getting a false or fraudulent claim allowed or paid;

Is a beneficiary of an inadvertent submission of a false claim to the State, who subsequently discovers the falsity of the claim, and fails to disclose the false claim to the State within a reasonable time after discovery of the false claim.

146. Defendant violated Haw. Rev. Stat. § 661-21(a) by continuously engaging in the fraudulent and illegal conduct described herein.

147. Defendant furthermore violated Haw. Rev. Stat. § 661.21(a) and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of Hawaii by their continuous violation of federal and state laws, including the AKS, as described herein.

148. The State of Hawaii, by and through the Hawaii Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

149. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Hawaii in connection with Defendant's fraudulent and illegal conduct.

150. Had the State of Hawaii known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

151. As a result of Defendant's violations of Haw. Rev. Stat. § 661-21(a), the State of Hawaii has been damaged in an amount far in excess of millions of dollars exclusive of interest.

152. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to Haw. Rev. Stat. § 661-25(a) on behalf of himself and the State of Hawaii.

153. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of Hawaii in the operation of its Medicaid program.

154. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF HAWAII:

Three times the amount of actual damages which the State of Hawaii has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $5,000 and not more than $10,000 for each false claim which Defendant caused to be presented to the State of Hawaii;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to Haw. Rev. Stat. § 661-27 and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT TWELVE

VIOLATION OF THE ILLINOIS WHISTLEBLOWER REWARD AND PROTECTION ACT

155. Relator re-alleges and incorporates the allegations in paragraphs 1 - 154 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of Illinois. Upon information and belief, Defendant's actions described herein occurred in Illinois as well.

156. This is a qui tam action brought by Relator and the State of Illinois to recover treble damages and civil penalties under the Illinois Whistleblower Reward and Protection Act, 740 ILCS 175 *et seq.*

157. 740 ILCS 175/3(a) provides liability for any person who:

Knowingly presents, or causes to be presented, to an officer or employee of the State of a member of the Guard a false or fraudulent claim for payment or approval;

Knowingly makes, uses, of causes to be made or used, a false record or statement to get a

false or fraudulent claim paid or approved by the State;

Conspires to defraud the State by getting a false or fraudulent claim allowed or paid.

158. In addition, 305 ILCS 5/8A-3(b) of the Illinois Public Aid Code (Vendor Fraud and Kickbacks) prohibits the solicitation or receipt of any remuneration, including any kickback, bribe or rebate, directly or indirectly, overtly or covertly, in cash or in kind in return for furnishing any item of service for which payment may be made in whole or in part under the Illinois Medicaid program.

159. Defendant violated 740 ILCS 175/3(a) & 305 ILCS 5/8A-3(b) by continuously engaging in the fraudulent and illegal conduct described herein.

160. Defendant furthermore violated 740 ILCS 175/3(a) and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of by its continuous violation of federal and state laws, including 305 ILCS 5/8A-3(b) and the AKS, as described herein.

161. The State of Illinois, by and through the Illinois Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

162. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Illinois in connection with Defendant's fraudulent and illegal conduct.

163. Had the State of Illinois known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

164. As a result of Defendant's violations of 740 ILCS 175/3(a), the State of Illinois has been damaged in an amount far in excess of millions of dollars exclusive of interest.

165. Relator is a private person with direct and independent knowledge of the allegation in this Complaint, who has brought this action pursuant to 740 ILCS 175/3(b) on behalf of himself and the State of Illinois.

166. This court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of Illinois in the operation of its Medicaid program.

167. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF ILLINOIS:

Three times the amount of actual damages which the State of Illinois has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $5,000 and not more than $10,000 for each false claim which Defendant caused to be presented to the State of Illinois;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to 740 ILCS/4(d) and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT THIRTEEN

VIOLATION OF THE INDIANA FALSE CLAIMS AND WHISTLEBLOWER PROTECTION ACT

168. Relator re-alleges and incorporates the allegations in paragraphs 1 - 167 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of Indiana. Upon information and belief, Defendant's actions described herein occurred in Indiana as well.

169. This is a qui tam action brought by Relator and the State of Indiana to recover treble damages and civil penalties under the Indiana False Claims and Whistleblower Protection Act, IC 5-11-5.5 *et seq.*

170. IC 5-11-5.5-2 provides liability for any person who:

> (1) Presents a false claim to the state for payment or approval;
>
> (2) Makes or uses a false record or statement to obtain payment or approval of a false claim from the state;
>
> (3) With intent to defraud the state, delivers less money or property to the state than the amount recorded on the certificate or receipt the person receives from the state;
>
> (4) With intent to defraud the state, authorizes issuance of a receipt without knowing that the information on the receipt is true;
>
> (5) Receives public property as a pledge of an obligation on a debt from an employee who is not lawfully authorized to sell or pledge the property;
>
> (6) Makes or uses a false record or statement to avoid an obligation to pay or transmit property to the state;
>
> (7) Conspires with another person to perform an act described in subdivisions (1) through (6);
>
> (8) Causes or induces another person to perform an act described in subdivisions (1) through (6).

171. In addition, IC 12-15-24-1 & IC 12-15-24-2 prohibits the provision of a kickback or bribe in connection with the furnishing of items or services or the making or receipt of the payment under the Indiana Medicaid program.

172. Defendant violated IC 5-11-5.5-2, IC 12-15-24-1 & IC 12-15-24-2 by continuously engaging in the fraudulent and illegal conduct described herein.

173. Defendant furthermore violated IC 5-11-5.5-2 and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of Indiana their continuous violation of federal and state laws, including IC 12-15-24-1 & IC 12-15-24-2, and the AKS, as described herein.

174. The State of Indiana, by and through the Indiana Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

175. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein is an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Indiana in connection with Defendant's fraudulent and illegal conduct.

176. Had the State of Indiana known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

177. As a result of Defendant's violations of IC 5-11-5.5-2, the State of Indiana has been damaged in an amount far in excess of millions of dollars exclusive of interest.

178. Relator is a private person with direct and independent knowledge of the allegation in this Complaint, who has brought this action pursuant to IC 5-11-5.5-4 on behalf of himself and the State of Indiana.

179. This court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of Indiana in the operation of its Medicaid program.

180. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF INDIANA:

Three times the amount of actual damages which the State of Indiana has sustained as a result of Defendant's fraudulent and illegal conduct;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to IC 5-11-5.5-6 and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT FOURTEEN

VIOLATION OF THE LOUISIANA MEDICAL ASSISTANCE PROGRAMS INTEGRITY LAW

181. Relator re-alleges and incorporates the allegations in paragraphs 1 - 180 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of Louisiana. Upon information and belief, Defendant's actions described herein occurred in Louisiana as well.

182. This is a qui tam action brought by Relator and the State of Louisiana to recover treble damages and civil penalties under the Louisiana medical Assistance Programs Integrity Law, La Rev. Stat. Ann §§ 437.1 *et seq*.

183. La. Rev. Stat. Ann. § 438.3 provides:

No person shall knowingly present or cause to be presented a false or fraudulent claim;

> No person shall knowingly engage in misrepresentation to obtain, or attempt to obtain, payment from medical assistance programs funds;
>
> No person shall conspire to defraud, or attempt to defraud, the medical assistance programs through misrepresentation or by obtaining, or attempting to obtain, payment for a false or fraudulent claim;

184. In addition, La. Rev. Stat. Ann.§ 438.2(A) prohibits the solicitation, receipt, offering or payment of any financial inducements, including kickbacks, bribes, rebates, etc., directly or indirectly, overtly or covertly, in cash or in kind, for furnishing health care goods or services paid for in whole or in part by the Louisiana medical assistance programs.

185. Defendant violated La. Rev. Stat. Ann. §§ 438.3 & 438.2(A) by continuously engaging in the fraudulent and illegal conduct described herein.

186. Defendant furthermore violated La. Rev. Stat. Ann. § 438.3 and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of Louisiana by their continuous violation of federal and state laws, including La. Rev. Stat. Ann. § 438.2(A) and the AKS, as described herein.

187. The State of Louisiana, by and through the Louisiana Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

188. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Louisiana in connection with Defendant's fraudulent and illegal conduct.

189. Had the State of Louisiana known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

190. As a result of Defendant's violations of La. Rev. Stat. Ann. § 438.3, the State of Louisiana has been damaged in an amount far in excess of millions of dollars exclusive of interest.

191. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to La. Rev. Stat. Ann. § 439.1(A) on behalf of himself and the State of Louisiana.

192. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of Louisiana in the operation of its Medicaid program.

193. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF LOUISIANA:

Three times the amount of actual damages which the State of Louisiana has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $5,000 and not more than $10,000 for each false claim which Defendant caused to be presented to the State of Louisiana;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to La. Rev. Stat. § 439.4(A) and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award or reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT FIFTEEN

VIOLATION OF THE MASSACHUSETTS FALSE CLAIMS ACT

194. Relator re-alleges and incorporates the allegations in paragraphs 1 – 193 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the Commonwealth of Massachusetts. Defendant's actions described herein occurred in Massachusetts as well.

195. This is a qui tam action brought by Relator and State of Massachusetts for treble damages and penalties under Massachusetts False Claims Act, Mass. Gen. Laws Ann. Chap 12 §§ 5(A) *et seq.*

196. Mass. Gen. Laws Ann. Chap 12 § 5B provides liability for any person who:

> Knowingly presents, or causes to be presented, a false or fraudulent claim for payment or approval;
>
> Knowingly makes, uses, or causes to be made or used, a false record or statement to obtain payment or approval of a claim by the commonwealth or any political subdivision thereof;
>
> Conspires to defraud the commonwealth or any political subdivision thereof through the allowance or payment of a fraudulent claim;
>
> Is a beneficiary of an inadvertent submission of a false claim to the common wealth or political subdivision thereof, subsequently discovers the falsity of the claim, and fails to disclose the false claim to the commonwealth or political subdivision within a reason able time after discovery of the false claim.

197. In addition, Mass. Gen. Laws Ann. Chap. 118E § 41 prohibits the solicitation, receipt or offering of any remuneration, including any bribe ore rebate, directly or indirectly, overtly or covertly, in cash or in kind in return for furnishing any good, service, or item for which payment may be made in whole or in part under the Massachusetts Medicaid program.

198. Defendant violated Mass. Gen. Laws Ann. Chap. 118E § 41 & Mass. Gen. Laws Ann. Chap. 12 § 5B by continuously engaging in the fraudulent and illegal conduct described herein.

199. Defendant furthermore violated Mass. Gen. Laws Ann. Chap 12 § 5B and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of Massachusetts by their continuous violation of federal and state laws, including Mass. Gen. Laws Ann. Chap. 118E § 41 and the AKS, as described herein.

200. The State of Massachusetts, by and through the Massachusetts Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

201. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Massachusetts in connection with Forest's fraudulent and illegal conduct.

202. Had the State of Massachusetts known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

203. As a result of Defendant's violations of Mass. Gen. Laws Ann. Chap. 12 § 5B, the State of Massachusetts has been damaged in an amount far in excess of millions of dollars exclusive of interest.

204. Relator is a private person with direct and independent knowledge of the allegations in this Compliant, who has brought this action pursuant to Mass. Gen. Laws Ann Chap. 12 § 5(c)(2) on behalf of himself and the State of Massachusetts.

205. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon that exact same facts as the federal claim, and merely asserts separate damage to the State of Massachusetts in the operation of its Medicaid program.

206. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF MASSACHUSETTS:

Three times the amount of actual damages which that State of Massachusetts has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $5,000 and not more than $10,000 for each false claim which Defendant caused to be presented to the State of Massachusetts;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to Mass. Gen. Laws Ann. Chap. 12 § 5F and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT SIXTEEN

VIOLATION OF THE MICHIGAN MEDICAID FALSE CLAIM ACT

207. Relator re-alleges and incorporates the allegations in paragraphs 1 - 206 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in Michigan. Upon information and belief, Defendant's actions described herein occurred in Michigan as well.

208. This is a qui tam action brought by Relator and State of Michigan for treble damages and penalties under Michigan Medicaid False Claim Act, M.C.L.A. 400.601 *et seq*.

209. M.C.L.A. 400.607 provides liability for any person who, among other things:

> Causes to be made or presented to an employee or officer of this state a claim under the social welfare act, Act No. 280 of the Public Acts of 1939, as amended, being sections 400.1 to 400.121 of the Michigan Compiled Laws, upon or against the state, knowing the claim to be false;
>
> Presents or causes to be made or presented a claim under the social welfare act, Act No. 280 of the Public Acts of 1939, which he or she knows falsely represents that the goods or services for which the claim is made were medically necessary in accordance with professionally accepted standards.

210. In addition, M.C.L.A. 400.604 prohibits the solicitation, receipt, or offering of a kickback or bribe in connection with the furnishing of goods or services for which payment is or may be made in whole or in part pursuant to the Michigan Medicaid program.

211. Defendant violated M.C.L.A. 400.607 & 400.604 by continuously engaging in the fraudulent and illegal conduct described herein.

212. Defendant furthermore violated M.C.L.A. 400.607 and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of Michigan by their continuous violation of federal and state laws, including M.C.L.A. 400.604 and the AKS, as described herein.

213. The State of Michigan, by and through the Michigan Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

214. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Michigan in connection with Defendant's fraudulent and illegal conduct.

215. Had the State of Michigan known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

216. As a result of Forest's violations of M.C.L.A. 400.607, the State of Michigan has been damaged in an amount far in excess of millions of dollars exclusive of interest.

217. Relator is a private person with direct and independent knowledge of the allegations in this Compliant, who has brought this action pursuant to M.C.L.A. 400.610a on behalf of himself and the State of Michigan.

218. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon that exact same facts as the federal claim, and merely asserts separate damage to the State of Michigan in the operation of its Medicaid program.

219. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF MICHIGAN:

All damages to which the State of Michigan is entitled pursuant to M.C.L.A. 400.612;

Civil penalties for each false claim which Defendant caused to be presented to the State of Michigan;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to M.C.L.A. 400.610a(9) and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT SEVENTEEN

VIOLATION OF THE MINNESOTA FALSE CLAIMS ACT

220. Relator re-alleges and incorporates the allegations in paragraphs 1 - 219 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in Minnesota. Upon information and belief, Defendant's actions described herein occurred in Minnesota as well.

221. This is a qui tam action brought by Relator and State of Minnesota for treble damages and penalties under Montana False Claims Act, M.S.A. §§ 15C.02 *et seq*.

222. M.S.A. § 15C.02a provides liability for any person who:

> (1) knowingly presents, or causes to be presented, to an officer or employee of the state or a political subdivision a false or fraudulent claim for payment or approval;
>
> (2) knowingly makes or uses, or causes to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the state or a political subdivision;
> (3) knowingly conspires to either present a false or fraudulent claim to the state or a political subdivision for payment or approval or makes, uses, or causes to be made or used a false record or statement to obtain payment or approval of a false or fraudulent claim;
>
> (4) has possession, custody, or control of public property or money used, or to be used, by the state or a political subdivision and knowingly delivers or causes to be delivered to the state or a political subdivision less money or property than the amount for which the person receives a receipt;
>
> (5) is authorized to prepare or deliver a receipt for money or property used, or to be used, by the state or a political subdivision and knowingly prepares or delivers a receipt that falsely represents the money or property;
>
> (6) knowingly buys, or receives as a pledge of an obligation or debt, public property from an officer or employee of the state or a political subdivision who lawfully may not sell or pledge the property;
>
> (7) knowingly makes or uses, or causes to be made or used, a false record or statement to conceal, avoid, or decrease an obligation to pay or transmit money or property to the state or a political subdivision.

223. Defendant violated M.S.A. § 15C.02a by continuously engaging in the fraudulent and illegal conduct described herein.

224. Defendant furthermore violated M.S.A. § 15C.02a and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of Minnesota by their continuous violation of federal and state laws, including the AKS, as described herein.

225. The State of Minnesota, by and through the Minnesota Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

226. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Minnesota in connection with Defendant's fraudulent and illegal conduct.

227. Defendant did not, within 30 days after first obtaining information as to such violations, furnish such information to officials of the State responsible for investigating false claims violations, did not otherwise fully cooperate with any investigation of the violations, and have not otherwise furnished information to the State regarding the claims for reimbursement at issue.

228. Had the State of Minnesota known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

229. As a result of Defendant's violations of M.S.A. § 15C.02a, the State of Minnesota has been damaged in an amount far in excess of millions of dollars exclusive of interest.

230. Relator is a private person with direct and independent knowledge of the allegations in this Compliant, who has brought this action pursuant to M.S.A. § 15C.02a on behalf of himself and the State of Minnesota.

231. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon that exact same facts as the federal claim, and merely asserts separate damage to the State of Minnesota in the operation of its Medicaid program.

232. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF MINNESOTA:

All damages to which the State of Minnesota is entitled pursuant to M.S.A. §§ 15C.02 *et seq.*;

Civil penalties for each false claim which Defendant caused to be presented to the State of Minnesota;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to M.S.A. § 15C.02a and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT EIGHTEEN

VIOLATION OF THE MONTANA FALSE CLAIMS ACT

233. Relator re-alleges and incorporates the allegations in paragraphs 1 - 233 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a

nationwide, continuous practice of Defendant. Forest conducts business in Montana. Upon information and belief, Defendant's actions described herein occurred in Montana as well.

234. This is a qui tam action brought by Relator and State of Montana for treble damages and penalties under Montana False Claims Act, MT ST 17-8-401 *et seq*.

235. MT ST 17-8-403 provides liability for any person who:

> Knowingly presenting or causing to be presented to an officer or employee of the governmental entity a false claim for payment or approval;
>
> Knowingly making, using, or causing to be made or used a false record or statement to get a false claim paid or approved by the governmental entity;
>
> Conspiring to defraud the governmental entity by getting a false claim allowed or paid by the governmental entity.

236. In addition, MT ST 45-6-313 prohibits the solicitation, receipt or offering any remuneration, including but not limited to a kickback, bribe, or rebate, other than an amount legally payable under the medical assistance program, for furnishing services or items for which payment may be made under the Montana Medicaid program.

237. Defendant violated MT ST 17-8-403 & MT ST 45-6-313 by continuously engaging in the fraudulent and illegal conduct described herein.

238. Defendant furthermore violated MT ST 17-8-403 and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of Montana by their continuous violation of federal and state laws, including MT ST 45-6-313 and the AKS, as described herein.

239. The State of Montana, by and through the Montana Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

240. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Montana in connection with Defendant's fraudulent and illegal conduct.

241. Had the State of Montana known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

242. As a result of Defendant's violations of MT ST 17-8-403, the State of Montana has been damaged in an amount far in excess of millions of dollars exclusive of interest.

243. Relator is a private person with direct and independent knowledge of the allegations in this Compliant, who has brought this action pursuant to MT ST 17-8-406 on behalf of himself and the State of Montana.

244. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon that exact same facts as the federal claim, and merely asserts separate damage to the State of Montana in the operation of its Medicaid program.

245. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF MONTANA:

Three times the amount of actual damages which that State of Montana has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of $10,000 for each false claim which Defendant caused to be presented to the State of Montana;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to MT ST 17-8-410 and/or any other applicable

provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT NINETEEN

VIOLATION OF THE NEVADA FALSE CLAIMS ACT

246. Relator re-alleges and incorporates the allegations in paragraphs 1 - 245 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Defendant. Forest conducts business in the State of Nevada. As set forth above, Defendant's actions described herein occurred in Nevada as well.

247. This is a qui tam action brought by Relator and the State of Nevada to recover treble damages and civil penalties under the Nevada False Claims Act, N.R.S. §§ 357.010 *et seq*.

248. N.R.S. § 357.040(1) provides liability for any person who:

Knowingly presents or causes to be presented a false claim for payment or approval;

Knowingly makes or uses, or causes to be made or used, a false record or statement to obtain payment or approval of a false claim;

Conspires to defraud by obtaining allowance or payment of a false claim;

Is a beneficiary of an inadvertent submission of a false claim and, after discovering the falsity of the claim, fails to disclose the falsity to the state or political subdivision within a reasonable time.

249. In addition, N.R.S. § 422.560 prohibits the solicitation, acceptance or receipt of anything of value in connection with the provision of medical goods or services for which payment may be made in whole or in part under the Nevada Medicaid program.

250. Defendant violated N.R.S. §§ 357.040(1) & 422.560 by continuously engaging in the fraudulent and illegal conduct described herein.

251. Defendant furthermore violated N.R.S. § 357.040(1) and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of Nevada by their continuous violation of federal and state laws, including N.R.S. § 422.560 and the AKS, as described herein.

252. The State of Nevada, by and through the Nevada Medicaid program and other health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

253. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Nevada in connection with Defendant's fraudulent and illegal conduct.

254. Had the State of Nevada known that Forest were violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

255. As a result of Defendant's violations of N.R.S. § 357.040(1), the State of Nevada has been damaged in an amount far in excess or millions of dollars exclusive of interest.

256. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to N.R.S. § 357.080(1) on behalf of himself and the State of Nevada.

257. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of Nevada in the operation of its Medicaid program.

258. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF NEVADA:

Three times the amount of actual damages which the State of Nevada has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $2,000 and not more than $10,000 for each false claim which Defendant caused to be presented to the State of Nevada;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to N.R.S § 357.210 and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT TWENTY

VIOLATION OF THE NEW HAMPSHIRE FALSE CLAIMS ACT

259. Relator re-alleges and incorporates the allegations in paragraphs 1 - 258 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the New Hampshire. Upon information and belief, Defendant's actions described herein occurred in New Hampshire as well.

260. This is a qui tam action brought by Relator and State of New Hampshire for treble damages and penalties under New Hampshire False Claims Act, N.H. Rev. Stat. §§ 167:61-b *et seq*.

261. N.H. Rev. Stat. § 167:61-b provides liability for any person who:

> Knowingly presents, or causes to be presented, to an officer or employee of the department, a false or fraudulent claim for payment or approval;
>
> Knowingly makes, uses, or causes to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the department;
>
> Conspires to defraud the department by getting a false or fraudulent claim allowed or paid.

262. Defendant violated N.H. Rev. Stat. § 167:61-b by continuously engaging in the fraudulent and illegal conduct described herein.

263. Defendant furthermore violated N.H. Rev. Stat. § 167:61-b and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of New Hampshire their continuous violation of federal and state laws, including the AKS, as described herein.

264. The State of New Hampshire, by and through the New Hampshire Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

265. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of New Hampshire in connection with Defendant fraudulent and illegal conduct.

266. Had the State of New Hampshire known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

267. As a result of Defendant's violations of N.H. Rev. Stat. § 167:61-b, the State of New Hampshire has been damaged in an amount far in excess of millions of dollars exclusive of interest.

268. Relator is a private person with direct and independent knowledge of the allegations in this Compliant, who has brought this action pursuant to N.H. Rev. Stat. § 167:61-c on behalf of himself and the State of New Hampshire.

269. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon that exact same facts as the federal claim, and merely asserts separate damage to the State of New Hampshire in the operation of its Medicaid program.

270. WHEREFORE, Relator respectfully request this Court to award the following damages to the following parties and against Defendant:

To the STATE OF NEW HAMPSHIRE:

Three times the amount of actual damages which that State of New Hampshire has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $5,000 and not more than $10,000 for each false claim which Defendant caused to be presented to the State of New Hampshire;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to N.H. Rev. Stat. § 167:61-e and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT TWENTY-ONE

VIOLATION OF THE NEW JERSEY FALSE CLAIMS ACT

271. Relator re-alleges and incorporates the allegations in paragraphs 1 - 270 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a

nationwide, continuous practice of Defendant. Forest conduct business in New Jersey. Upon information and belief, Forest's actions described herein occurred in New Jersey as well.

272. This is a qui tam action brought by Relator and State of New Jersey for treble damages and penalties under New Jersey False Claims Act, N.J.S.A. 2A:32C-1 *et seq*.

273. N.J.S.A. 2A:32C-3 provides liability for any person who:

> Knowingly presents or causes to be presented to an employee, officer or agent of the State, or to any contractor, grantee, or other recipient of State funds, a false or fraudulent claim for payment or approval;
>
> Knowingly makes, uses, or causes to be made or used a false record or statement to get a false or fraudulent claim paid or approved by the State;
>
> Conspires to defraud the State by getting a false or fraudulent claim allowed or paid by the State.

274. In addition, N.J.S.A. 30:4D-17 prohibits solicitation, offers, or receipt of any kickback, rebate, or bribe in connection with the furnishing of items or services for which payment is or may be made in whole or in part under the New Jersey Medicaid program, or the furnishing of items or services whose cost is or may be reported in whole or in part in order to obtain benefits or payments under New Jersey Medicaid.

275. Defendant violated N.J.S.A. 2A:32C-3 & N.J.S.A. 30:4D-17 by continuously engaging in the fraudulent and illegal conduct described herein.

276. Defendant furthermore violated N.J.S.A. 2A:32C-3 and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of New Jersey by their continuous violation of federal and state laws, including N.J.S.A. 2A:32C-3 and the AKS, as described herein.

277. The State of New Jersey, by and through the New Jersey Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

278. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of New Jersey in connection with Defendant's fraudulent and illegal conduct.

279. Had the State of New Jersey known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

280. As a result of Defendant's violations of N.J.S.A. 2A:32C-3, the State of New Jersey has been damaged in an amount far in excess of millions of dollars exclusive of interest.

281. Relator is a private person with direct and independent knowledge of the allegations in this Compliant, who has brought this action pursuant to N.J.S.A. 2A:32C-5 on behalf of himself and the State of New Jersey.

282. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon that exact same facts as the federal claim, and merely asserts separate damage to the State of New Jersey in the operation of its Medicaid program.

283. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF NEW JERSEY:

Three times the amount of actual damages which that State of New Jersey has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $5,000 and not more than $10,000 for each false claim which Defendant caused to be presented to the State of New Jersey;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to N.J.S.A. 2A:32C-7and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT TWENTY-TWO

VIOLATION OF THE NEW MEXICO MEDICAID FALSE CLAIMS ACT AND THE FRAUD AGAINST TAXPAYERS ACT

284. Relator re-alleges and incorporates the allegations in paragraphs 1 - 283 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of New Mexico. Upon information and belief, Forest's actions described herein occurred in the State of New Mexico as well.

285. This is a qui tam action brought by Relator and the State of New Mexico to recover treble damages and civil penalties under the New Mexico Medicaid False Claims Act, N. M. S. A. 1978, § 27-14-1 *et seq.* and the New Mexico Fraud Against Taxpayers Act, N. M. S. A. 1978, § 44-9-1 *et seq.*

286. N. M. S. A. 1978, § 27-14-4 provides liability for any person who:

Presents, or causes to be presented, to the state a claim for payment under the Medicaid program knowing that the person receiving a Medicaid benefit or payment is not authorized or is not eligible for a benefit under the Medicaid program;

Makes, uses, or causes to be made or used a record or statement to obtain a false or fraudulent claim under the Medicaid program paid for or approved by the state knowing such record or statement is false;

Conspires to defraud the state by getting a claim allowed or paid under the Medicaid program knowing that such claim is false or fraudulent.

287. N.M.S.A. 1978, § 44-9-3 provides liability for any person who:

Knowingly presents, or causes to be presented, to an employee, officer or agent of the state or to a contractor, grantee or other recipient of state funds a false or fraudulent claim for payment or approval;

Knowingly makes or uses, or causes to be made or used, a false, misleading or fraudulent record or statement to obtain or support the approval of or the payment on a false or fraudulent claim;

Conspires to defraud the state by obtaining approval or payment on a false or fraudulent claim;

Conspires to make, use or cause to be made or used, a false, misleading or fraudulent record or statement to conceal, avoid or decrease an obligation to pay or transmit money or property to the state.

288. Defendant violated N. M. S. A. 1978, §§ 27-14-4 & 44-9-3 by continuously engaging in the fraudulent and illegal conduct described herein.

289. Defendant furthermore violated N. M. S. A. 1978, §§ 27-14-4 & 44-9-3 and knowingly caused thousands of false claims to be made, used, and presented to the State of New Mexico by their continuous violation of federal and state laws, including the AKS, as described herein.

290. The State of New Mexico, by and through the State of New Mexico Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

291. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of New Mexico in connection with W Defendant fraudulent and illegal conduct.

292. Had the State of New Mexico known that Forest were violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

293. As a result of Defendant's continuous violations of N. M. S. A. 1978, §§ 27-14-4 & 44-9-3, the State of New Mexico has been damaged in an amount far in excess of millions of dollars exclusive of interest.

294. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to N. M. S. A. 1978, §§ 27-14-7 & 44-9-5 on behalf of himself and the State of New Mexico.

295. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of New Mexico in the operation of its Medicaid program.

296. WHEREFORE, Relator respectfully request this Court to award the following damages to the following parties and against Defendant:

To the STATE OF NEW MEXICO:

Three times the amount of actual damages which the State of New Mexico has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $5,000 and not more than $10,000 for each false claim which Defendant caused to be presented to the State of New Mexico;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to N. M. S. A. 1978, §§ 27-14-9 & 44-9-7 and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this court deems equitable and just.

COUNT TWENTY-THREE

VIOLATION OF THE NEW YORK FALSE CLAIMS ACT

297. Relator re-alleges and incorporates the allegations in paragraphs 1 - 296 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Defendant. Forest conducts business in the New York. As set forth above, Defendant's actions described herein occurred in New York as well.

298. This is a qui tam action brought by Relator and State of New York for treble damages and penalties under New York False Claims Act, McKinney's State Finance Law § 187 *et seq.*

299. McKinney's State Finance Law § 189 provides liability for any person who:

> Knowingly presents, or causes to be presented, to any employee, officer or agent of the state or a local government, a false or fraudulent claim for payment or approval;
>
> Knowingly makes, uses, or causes to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the state or a local government;
>
> Conspires to defraud the state or a local government by getting a false or fraudulent claim allowed or paid.

300. Defendant violated McKinney's State Finance Law § 189 continuously engaging in the fraudulent and illegal conduct described herein.

301. Defendant furthermore violated McKinney's State Finance Law § 189 and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of New York by their continuous violation of federal and state laws, including the AKS, as described herein.

302. The State of New York, by and through the New York Medicaid program and other state health care programs, and unaware of Defendant fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

303. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment

of claims submitted to the State of New York in connection with Defendant's fraudulent and illegal conduct.

304. Had the State of New York known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

305. As a result of Defendant's violations of McKinney's State Finance Law § 189, the State of New York has been damaged in an amount far in excess of millions of dollars exclusive of interest.

306. Relator is a private person with direct and independent knowledge of the allegations in this Compliant, who has brought this action pursuant to McKinney's State Finance Law § 190(2) on behalf of himself and the State of New York.

307. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon that exact same facts as the federal claim, and merely asserts separate damage to the State of New York in the operation of its Medicaid program.

308. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Forest:

To the STATE OF NEW YORK:

Three times the amount of actual damages which that State of New York has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $6,000 and not more than $12,000 for each false claim which Defendant caused to be presented to the State of New York;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to McKinney's State Finance Law § 190(6) and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT TWENTY-FOUR

VIOLATION OF THE NORTH CAROLINA FALSE CLAIMS ACT

309. Relator re-alleges and incorporates the allegations in paragraphs 1 - 308 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of North Carolina. Upon information and belief, Defendant's actions described herein occurred in the State of North Carolina as well.

310. This is a qui tam action brought by Relator and the State of North Carolina to recover treble damages and civil penalties under the North Carolina False Claims Act, NC ST §§ 1-605 *et seq*.

311. NC ST § 1-607(a) provides liability in relevant part, for any person who:

> (1) Knowingly presents or causes to be presented a false or fraudulent claim for payment or approval;
>
> (2) Knowingly makes, uses, or causes to be made or used, a false record or statement material to a false or fraudulent claim;
>
> (3) Conspires to commit a violation of subdivision (1), (2), (4), (5), (6), or (7) of this section;
>
> ***
>
> (7) Knowingly makes, uses, or causes to be made or used, a false record or statement material to an obligation to pay or transmit money or property to the State, or knowingly conceals or knowingly and improperly avoids or decreases an obligation to pay or transmit money or property to the State.

312. Defendant violated NC ST § 1-607(a) by continuously engaging in the fraudulent and illegal conduct described herein.

313. Defendant furthermore violated NC ST § 1-607(a) and knowingly caused thousands of false claims to be made, used, and presented to the State of North Carolina by their continuous violation of federal and state laws, including NC ST § 1-607(a) and the AKS, as described herein.

314. The State of North Carolina, by and through the State of North Carolina Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

315. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of North Carolina in connection with Defendant's fraudulent and illegal conduct.

316. Had the State of North Carolina known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

317. As a result of Defendant's violations of NC ST § 1-607(a), the State of North Carolina has been damaged in an amount far in excess of millions of dollars exclusive of interest.

318. Defendant did not, within 30 days after they first obtained information as to such violations, furnish such information to officials of the State responsible for investigating false claims violations, did not otherwise fully cooperate with any investigation of the violations, and have not otherwise furnished information to the State regarding the claims for reimbursement at issue.

319. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to NC ST § 1-607(a) on behalf of himself and the State of North Carolina.

320. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of North Carolina in the operation of its Medicaid program.

321. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF NORTH CAROLINA:

Three times the amount of actual damages which the State of North Carolina has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $5,000 and not more than $11,000 for each false claim which Defendant caused to be presented to the State of North Carolina;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant NC ST § 1-610 and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this court deems equitable and just.

COUNT TWENTY-FIVE

VIOLATION OF THE OKLAHOMA MEDICAID FALSE CLAIMS ACT

322. Relator re-alleges and incorporates the allegations in paragraphs 1-321 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of Oklahoma. Upon information and belief, Defendant actions described herein occurred in the State of Oklahoma as well.

323. This is a qui tam action brought by Relator and the State of Oklahoma to recover treble damages and civil penalties under the Oklahoma Medicaid False Claims Act, 63 Okl. St. Ann. § 5053 *et seq.*

324. 63 Okl. St. Ann. § 5053.1 provides liability for any person who:

> Knowingly presents, or causes to be presented, to an officer or employee of the State of Oklahoma, a false or fraudulent claim for payment or approval;
>
> Knowingly makes, uses, or causes to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the state;
>
> Conspires to defraud the state by getting a false or fraudulent claim allowed or paid.

325. In addition, 56 Okl. St. Ann. § 1005 prohibits solicitation or acceptance of a benefit, pecuniary benefit, or kickback in connection with goods or services paid or claimed by a provider to be payable by the Oklahoma Medicaid Program.

326. Defendant violated 63 Okl. St. Ann. § 5053.1 & 56 Okl. St. Ann. § 1005 by continuously engaging in the fraudulent and illegal conduct described herein.

327. Defendant furthermore violated 63 Okl. St. Ann. § 5053.1 and knowingly caused thousands of false claims to be made, used, and presented to the State of Oklahoma by their continuous violation of federal and state laws, including 56 Okl. St. Ann. § 1005 and the AKS, as described herein.

328. The State of Oklahoma, by and through the State of Oklahoma Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

329. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Oklahoma in connection with Defendant's fraudulent and illegal conduct.

330. Had the State of Oklahoma known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

331. As a result of Defendant's violations of 63 Okl. St. Ann. § 5053.1, the State of Oklahoma has been damaged in an amount far in excess of millions of dollars exclusive of interest.

332. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to 63 Okl. St. Ann. § 5053.2(B) on behalf of himself and the State of Oklahoma.

333. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of Oklahoma in the operation of its Medicaid program.

334. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF OKLAHOMA:

Three times the amount of actual damages which the State of Oklahoma has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $5,000 and not more than $10,000 for each false claim which Defendant caused to be presented to the State of Oklahoma;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant 63 Okl. St. Ann. § 5053.4 and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this court deems equitable and just.

COUNT TWENTY-SIX

VIOLATION OF THE RHODE ISLAND FALSE CLAIMS ACT

335. Relator re-alleges and incorporates the allegations in paragraphs 1 - 334 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of Rhode Island. Upon information and belief, Defendant's actions described herein occurred in the State of Rhode Island as well.

336. This is a qui tam action brought by Relator and the State of Rhode Island to recover treble damages and civil penalties under the Rhode Island False Claims Act, Gen. Laws 1956, §§ 9-1.1-1 *et seq*.

337. Gen. Laws 1956, § 9-1.1-3 provides liability for any person who:

> Knowingly presents, or causes to be presented, to an officer or employee of the state or a member of the guard a false or fraudulent claim for payment or approval;
>
> Knowingly makes, uses, or causes to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the state;
>
> Conspires to defraud the state by getting a false or fraudulent claim allowed or paid.

338. In addition, Gen. Laws 1956, § 40-8.2-3 prohibits the solicitation, receipt, offer, or payment of any remuneration, including any kickback, bribe, or rebate, directly or indirectly, in cash or in kind, to induce referrals from or to any person in return for furnishing of services or merchandise or in return for referring an individual to a person for the furnishing of any services or merchandise for which payment may be made, in whole or in part, under the Rhode Island Medicaid program.

339. Defendant violated Gen. Laws 1956, §§ 9-1.1-3 & 40-8.2-3 by continuously engaging in the fraudulent and illegal conduct described herein.

340. Defendant furthermore violated Gen. Laws 1956, § 9-1.1-3 and knowingly caused thousands of false claims to be made, used, and presented to the State of Rhode Island by their continuous violation of federal and state laws, including Gen. Laws 1956, § 40-8.2-3 and the AKS, as described herein.

341. The State of Rhode Island, by and through the State of Rhode Island Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

342. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Rhode Island in connection with Defendant's fraudulent and illegal conduct.

343. Had the State of Rhode Island known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

344. As a result of Defendant's violations of Gen. Laws 1956, § 9-1.1-3, the State of Rhode Island has been damaged in an amount far in excess of millions of dollars exclusive of interest.

345. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to Gen. Laws 1956, § 9-1.1-4(b) on behalf of himself and the State of Rhode Island.

346. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of Rhode Island in the operation of its Medicaid program.

347. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF RHODE ISLAND:

Three times the amount of actual damages which the State of Rhode Island has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $5,000 and not more than $10,000 for each false claim which Defendant caused to be presented to the State of Rhode Island;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant Gen. Laws 1956, § 9-1.1-4(d) and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this court deems equitable and just.

COUNT TWENTY-SEVEN

VIOLATION OF THE TENNESSEE FALSE CLAIMS ACT

348. Relator re-alleges and incorporates the allegations in paragraphs 1 - 347 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of Tennessee. Upon information and belief, Defendant's actions described herein occurred in Tennessee as well.

349. This is a qui tam action brought by Relator and the State of Tennessee to recover treble damages and civil penalties under the Tennessee Medicaid False Claims Act, Tenn. Code Ann. §§ 71-5-181 *et seq*.

350. Section 71-5-182(a)(1) provides liability for any person who:

Presents, or causes to be presented to the state, a claim for payment under the Medicaid program knowing such claim is false or fraudulent;

> Makes or uses, or causes to be made or used, a record or statement to get a false or fraudulent claim under the Medicaid program paid for a approved by the state knowing such record or statement is false;
>
> Conspires to defraud the State by getting a claim allowed or paid under the Medicaid program knowing such claim is false or fraudulent.

351. Defendant violated Tenn. Code Ann. § 71-5-182(a)(1) from at least 2001 to the present by continuously engaging in the fraudulent and illegal conduct described herein.

352. Defendant furthermore violated Tenn. Code Ann. § 71-5-182(a)(1) and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of Tennessee from at least 2001 to the present by their continuous violation of federal and state laws, including the AKS, as described herein.

353. The State of Tennessee, by and through the Tennessee Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

354. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Tennessee in connection with Defendant's fraudulent and illegal conduct.

355. Had the State of Tennessee known that Defendant violated the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

356. As a result of Defendant's violations of Tenn. Code Ann. § 71-5-182(a)(1), the State of Tennessee has been damaged in an amount far in excess of millions of dollars exclusive of interest.

357. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to Tenn. Code Ann. § 71-5-183(a)(1) on behalf of himself and the State of Tennessee.

358. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of Tennessee in the operation of its Medicaid program.

359. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF TENNESSEE:

Three times the amount of actual damages which the State of Tennessee has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $5,000 and not more than $10,000 for each false claim which Defendant caused to be presented to the State of Tennessee;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed to Tenn. Code Ann. §71-5-183(c) and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this Court deems equitable and just.

COUNT TWENTY-EIGHT

VIOLATION OF THE TEXAS MEDICAID FALSE CLAIMS ACT

360. Relator re-alleges and incorporates the allegations in paragraphs 1 - 359 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of Texas. Defendant's actions described herein occurred in Texas as well.

361. This is a qui tam action brought by Relator and the State of Texas to recover double damages and civil penalties under the Texas False Claims Act, V.T.C.A. Hum. Res. Code § 36.001 *et seq*.

362. V.T.C.A. Hum. Res. Code § 36.002, in relevant part, provides liability for any person who:

> (1) Knowingly makes or causes to be made a false statement or misrepresentation of a material fact to permit a person to receive a benefit or payment under the Medicaid program that is not authorized or that is greater than the benefit or payment that is authorized;
>
> (2) Knowingly conceals or fails to disclose information that permits a person to receive a benefit or payment under the Medicaid program that is not authorized or that is greater than the benefit or payment that is authorized;
>
> (3) Knowingly applies for and receives a benefit or payment on behalf of another person under the Medicaid program and converts any part of the benefit or payment to a use other than for the benefit of the person on whose behalf it was received
> (5) Except as authorized under the Medicaid program, knowingly pays, charges, solicits, accepts, or receives, in addition to an amount paid under the Medicaid program, a gift, money, a donation, or other consideration as a condition to the provision of a service or product or the continued provision of a service or product if the cost of the service or product is paid for, in whole or in part, under the Medicaid program;
>
> * * *
> (5) Except as authorized under the Medicaid program, knowingly pays, charges, solicits, accepts, or receives, in addition to an amount paid under the Medicaid program, a gift, money, a donation, or other consideration as a condition to the provision of a service or product or the continued provision of a service or product if the cost of the service or product is paid for, in whole or in part, under the Medicaid program;
>
> * * *
> (9) Knowingly enters into an agreement, combination, or conspiracy to defraud the state by obtaining or aiding another person in obtaining an unauthorized payment or benefit from the Medicaid program or a fiscal agent;

* * *

(12) Knowingly makes, uses, or causes the making or use of a false record or statement to conceal, avoid, or decrease an obligation to pay or transmit money or property to this state under the Medicaid program.

363. Defendant violated V.T.C.A. Hum. Res. Code § 36.002, as referenced in part above, by continuously engaging in the fraudulent and illegal conduct described herein.

364. Defendant furthermore violated V.T.C.A. Hum. Res. Code § 36.002 and knowingly caused hundreds of thousands of false claims to be made, used, and presented to the State of Texas by their continuous violation of federal and state laws, including, the AKS, as described herein.

365. The State of Texas, by and through the Texas Medicaid program and other state healthcare programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

366. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Texas in connection with Defendant's fraudulent and illegal conduct.

367. Had the State of Texas known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

368. As a result of Defendant;' violations of V.T.C.A. Hum. Res. Code § 36.002, the State of Texas has been damaged in an amount far in excess of millions of dollars exclusive of interest.

369. Defendant did not, within 30 days after they first obtained information as to such violations, furnish such information to officials of the State responsible for investigating false claims violations, did not otherwise fully cooperate with any investigation of the violations, and have not otherwise furnished information to the State regarding the claims for reimbursement at issue.

370. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to V.T.C.A. Hum. Res. Code § 36.101 on behalf of himself and the State of Texas.

371. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of Texas in the operation of its Medicaid program.

372. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF TEXAS:

Damages at two times the value of any payment or monetary or in-kind benefit provided under the Medicaid program, directly or indirectly, as a result of the unlawful acts set forth above, as provided by the Texas Human Resources Code § 36.052(a)(1) & (4);

Civil penalties of $15,000 for each and every unlawful act set forth above that resulted in injury to a person younger than 18 years of age, as provided by the Texas Human Resources Code § 36.052(3)(A);

Pre- and post-judgment interest, Tex. Hum. Res. Code § 36.052(a)(2).

To RELATOR:

The maximum amount allowed pursuant to V.T.C.A. Hum Res. Code § 36.110(a), and/or any other applicable provision of law;

Reimbursement for reasonable expenses and costs which Relator incurred in connection with this action, Tex Hum Res. Code §§ 36.007 & 36.110(c);

Reasonable attorneys' fees which the Relator necessarily incurred in bringing and pressing this case, Tex Hum Res. Code §§ 36.007 & 36.110(c); and

Such further relief as this Court deems equitable and just.

COUNT TWENTY-NINE

VIOLATION OF THE VIRGINIA FRAUD AGAINST TAXPAYERS ACT

373. Relator re-alleges and incorporates the allegations in paragraphs 1 - 372 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the Commonwealth of Virginia. Upon information and belief, Defendant's actions described herein occurred in the Commonwealth of Virginia as well.

374. This is a qui tam action brought by Relator and the Commonwealth of Virginia to recover treble damages and civil penalties under the Virginia Fraud Against Taxpayers Act, Va. Code Ann. §§ 8.01-216.1 *et seq*.

375. Va. Code Ann. § 8.01-216.3 provides liability for any person who:

> Knowingly presents, or causes to be presented, to an officer or employee of the Commonwealth a false or fraudulent claim for payment or approval;
>
> Knowingly makes, uses, or causes to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the Commonwealth;
>
> Conspires to defraud the Commonwealth by getting a false or fraudulent claim allowed or paid.

376. Defendant violated Va. Code Ann. § 8.01-216.3 by continuously engaging in the fraudulent and illegal conduct described herein.

377. Defendant furthermore violated Va. Code Ann. § 8.01-216.3 and knowingly caused thousands of false claims to be made, used, and presented to the Commonwealth of Virginia by their continuous violation of federal and state laws, including the AKS, as described herein.

378. The Commonwealth of Virginia, by and through the Commonwealth of Virginia Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

379. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment

of claims submitted to the Commonwealth of Virginia is connection with Defendant's fraudulent and illegal conduct.

380. Had the Commonwealth of Virginia known that Forest were violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

381. As a result of Defendant's violations of Va. Code Ann. § 8.01-216.3, the Commonwealth of Virginia has been damaged in an amount far in excess of millions of dollars exclusive of interest.

382. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to Va. Code Ann. § 8.01-216.5(A) on behalf of himself and the Commonwealth of Virginia.

383. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the Commonwealth of Virginia in the operation of its Medicaid program.

384. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the COMMONWEALTH OF VIRGINIA:

Three times the amount of actual damages which the Commonwealth of Virginia has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $5,000 and not more than $10,000 for each false claim which Defendant caused to be presented to the Commonwealth of Virginia;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant to Va. Code Ann. § 8.01-216.7 and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this court deems equitable and just.

COUNT THIRTY

VIOLATION OF THE WISCONSIN FALSE CLAIMS FOR MEDICAL ASSISTANCE ACT

385. Relator re-alleges and incorporates the allegations in paragraphs 1 - 384 as if fully set forth herein. Additionally, Relator states that the course of conduct described in this Complaint was a nationwide, continuous practice of Forest. Forest conducts business in the State of Wisconsin. Upon information and belief, Defendant's actions described herein occurred in the State of Wisconsin as well.

386. This is a qui tam action brought by Relator and the State of Wisconsin to recover treble damages and civil penalties under the Wisconsin False Claims for medical Assistance Act, W.S.A. 20.931 *et seq*.

387. W.S.A. 20.931(2) provides liability for any person who:

> Knowingly presents or causes to be presented to any officer, employee, or agent of this state a false claim for medical assistance;
>
> Knowingly makes, uses, or causes to be made or used a false record or statement to obtain approval or payment of a false claim for medical assistance;
>
> Conspires to defraud this state by obtaining allowance or payment of a false claim for medical assistance, or by knowingly making or using, or causing to be made or used, a false record or statement to conceal, avoid, or decrease an obligation to pay or transmit money or property to the medical Assistance program.

388. In addition, W.S.A. 49.49(2) prohibits solicitation or receipt of any remuneration, including any kickback, bribe, or rebate, directly or indirectly, overtly or covertly, in cash or in kind, in return for referring an individual to a person for the furnishing or arranging for the furnishing of any item or service for which payment may be made in whole or in part under any Wisconsin medical assistance program.

389. Defendant violated W.S.A. 20.931(2) & W.S.A. 49.49(2) by continuously engaging in the fraudulent and illegal conduct described herein.

390. Defendant furthermore violated W.S.A. 20.931(2) and knowingly caused thousands of false claims to be made, used, and presented to the State of Wisconsin by their continuous violation of federal and state laws, including W.S.A. 49.49(2) and the AKS, as described herein.

391. The State of Wisconsin, by and through the State of Wisconsin Medicaid program and other state health care programs, and unaware of Defendant's fraudulent and illegal conduct, paid the claims submitted by pharmacists in connection therewith.

392. Compliance with applicable Medicare, Medicaid, and the various other federal and state laws cited herein was an implied, and upon information and belief, also an express condition of payment of claims submitted to the State of Wisconsin in connection with Defendant's fraudulent and illegal conduct.

393. Had the State of Wisconsin known that Defendant was violating the federal and state laws cited herein, it would not have paid the claims submitted by pharmacists in connection with such fraudulent and illegal conduct.

394. As a result of Defendant violations of W.S.A. 20.931(2), the State of Wisconsin has been damaged in an amount far in excess of millions of dollars exclusive of interest.

395. Relator is a private person with direct and independent knowledge of the allegations in this Complaint, who has brought this action pursuant to W.S.A. 20.931(5) on behalf of himself and the State of Wisconsin.

396. This Court is requested to accept supplemental jurisdiction of this related state claim as it is predicated upon the exact same facts as the federal claim, and merely asserts separate damage to the State of Wisconsin in the operation of its Medicaid program.

397. WHEREFORE, Relator respectfully requests this Court to award the following damages to the following parties and against Defendant:

To the STATE OF WISCONSIN:

Three times the amount of actual damages which the State of Wisconsin has sustained as a result of Defendant's fraudulent and illegal conduct;

A civil penalty of not less than $5,000 and not more than $10,000 for each false claim which Defendant caused to be presented to the State of Wisconsin;

Prejudgment interest; and

All costs incurred in bringing this action.

To RELATOR:

The maximum amount allowed pursuant W.S.A. 20.931(11) and/or any other applicable provision of law;

Reimbursement for reasonable expenses which Relator incurred in connection with this action;

An award of reasonable attorneys' fees and costs; and

Such further relief as this court deems equitable and just.

DEMAND FOR JURY TRIAL

398. Relator hereby demands a jury trial.

Dated: March 17, 2011

UNITED STATES OF AMERICA ex rel.
H. EDMOND PIGOTT

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Appendix A

Special Article

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Efficacy and Effectiveness of Antidepressants: Current Status of Research

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Key Words

Antidepressant-resistant depression · Antidepressive agents · Depression relapse · Depressive disorder · Maintenance · Placebo treatment · Treatment continuation · Treatment-resistant depression

Abstract

Background: This paper examines the current status of research on the efficacy and effectiveness of antidepressants. ***Methods:*** This paper reviews four meta-analyses of efficacy trials submitted to America's Food and Drug Administration (FDA) and analyzes STAR*D (Sequenced Treatment Alternatives to Relieve Depression), the largest antidepressant effectiveness trial ever conducted. ***Results:*** Meta-analyses of FDA trials suggest that antidepressants are only marginally efficacious compared to placebos and document profound publication bias that inflates their apparent efficacy. These meta-analyses also document a second form of bias in which researchers fail to report the negative results for the prespecified primary outcome measure submitted to the FDA, while highlighting in published studies positive results from a secondary or even a new measure as though it was their primary measure of interest. The STAR*D analysis found that the effectiveness of antidepressant therapies was probably even lower than the modest one reported by the study authors with an apparent progressively increasing dropout rate across each study phase. ***Conclusions:*** The reviewed findings argue for a reappraisal of the current recommended standard of care of depression.

Introduction

When medications are evaluated to determine their applicability to evidence-based clinical practice, it is important to assess their efficacy in randomized, double-blind, placebo-controlled trials (RCT) in addition to determining their effectiveness in treating real-world patients under conditions that simulate real-world practice.

Efficacy

Due to long-held concerns about publication bias inflating perceived efficacy [1–4] and the resulting adverse impact on evidence-based care, public-minded researchers have long argued for a comprehensive registration data repository providing full access to drug trial protocols and results [1, 5, 6]. Though by no means complete, America's Food and Drug Administration (FDA)

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maintains a large repository of RCT trials as part of its new drug application process. Prior to conducting new drug application trials, drug companies must register them with the FDA, which includes pre-specifying the primary and secondary outcome measures and means of analysis. Pre-specification is essential to ensure the integrity of a trial and enables the discovery of when investigators selectively publish the measures that show the outcome the sponsors prefer following data collection and analysis, a form of researcher bias known as HARKing [7] or *'hypothesizing after the results are known'*.

Rising et al. [8] recently published a meta-analysis of all efficacy trials for new drugs approved by the FDA from 2001 to 2002 and the subsequent publication status of these trials 5 years later. Key findings were:

- New drug application studies with favorable outcomes were almost five times more likely to be published as those with unfavorable ones.
- 26.5% of pre-specified primary outcome measures were omitted from journal articles of new drug trials.
- Of the 43 primary measures not supporting efficacy, 20 (47%) were not included in the published results.
- 17 measures were only presented in the published studies and 15 of these showed positive effects for the new drug.

The analysis of Rising et al. [8] documents significant publication bias that inflates the apparent efficacy of new drugs. In addition to selective publication of positive trials, more disturbingly researchers at times fail to report the negative results of pre-specified primary outcome measures while highlighting in published studies positive results from a secondary or even a new measure as though it was their primary measure of interest. Besides casting doubt on the accurate reporting of individual drug trials in journal articles, their findings also directly challenge the validity of meta-analyses covering specific drugs and drug classes when limited to published studies.

Several antidepressant meta-analyses have been conducted using the FDA data repository to avoid the inflationary effects of publication bias. In 2008, Turner et al. [9] reviewed 74 trials of 12 antidepressants to assess subsequent publication bias and its influence on apparent efficacy.

In their meta-analysis, antidepressant studies with favorable outcomes were 16 times more likely to be published as those with unfavorable ones. According to the FDA scientific reviews though, only 38 trials (51%) found positive drug/placebo differences and 37 were subsequently published. The FDA judged the remaining 36 studies to be either negative (24 studies) or questionable (12 studies) – that is, no difference on the primary outcome but significant findings on a secondary measure. Only 3 (8%) were published reporting negative results, while the remaining 33 were either not published (22 studies) or published as though they were positive (11 studies) in contradiction to the FDA conclusions. Similar to Rising et al. [8], Turner et al. [9] report that in these 11 studies the authors did not report their negative results for the pre-specified primary outcome measure and instead highlighted positive results from a different measure as though it was their primary measure of interest.

Turner et al. [9] next compared the effect size derived from the FDA repository to that from the 51 published studies. This analysis found that the weighted mean effect size in the FDA data set was a modest 0.31 (95% confidence interval, 0.27–0.35) versus 0.41 (95% confidence interval, 0.36–0.45) in the published studies indicating a 32% inflation of the apparent efficacy of antidepressants. Their findings are similar to those of Kirsch et al. [10] in 2002 in a meta-analysis of 47 trials of 6 FDA-approved antidepressants. Though statistically significant due to the large combined number (n = 6,944), they found that the weighted mean difference between groups on the 17-item Hamilton Rating Scale for Depression (HRSD) was only 1.8 points and 57% of the trials found no significant drug/placebo differences [11].

Kirsch et al. [10] and Kirsch and Antonuccio [12] also examined patients' response as a function of dosing strength and time. These analyses found no advantage for higher antidepressant dosing. Regarding the common belief that drug effects are more enduring than placebo effects, they found that while patients' initial positive responses to both decrease over time, the correlation was higher for antidepressants ($r = -0.84$) than placebos ($r = -0.62$), suggesting that the effects of antidepressants diminish more rapidly than those of placebo.

In 2008, Kirsch et al. [13] examined the relationship between depression severity and efficacy in all 35 trials (n = 5,133) of four new-generation antidepressants. This analysis found no clinically significant difference (defined as a drug/placebo difference of ≥ 3 on the HRSD) between antidepressants and placebos as a function of severity except for the most severely depressed patients (i.e. those with a ≥ 29 HRSD score). However, even this difference was due to a decreased placebo response in more severely depressed patients, not an increased response to antidepressants.

Also in 2008, Barbui et al. [14] analyzed 40 paroxetine studies (29 published/11 unpublished; n = 6,391) using early trial termination for any reason (i.e. dropout) as the

primary outcome assessing it as the best available *'hard measure of treatment effectiveness and acceptability'* [14, p. 296]. Their analysis found no drug/placebo difference on this measure in contrast to a secondary one that paroxetine was clinically superior to placebo in patients' likelihood of achieving a ≥50% reduction in depressive symptoms. They also found that significantly more paroxetine patients dropped out due to side effects and increased suicidal tendencies. In a subsequent analysis though of these same studies, the apparent clinical superiority of paroxetine disappeared after statistically controlling for the differences in drug/placebo side effects [15, cited in 16, p. 19]. This finding is similar to that of Greenberg et al. [17] of an exceptionally high correlation between side effects and improvement in fluoxetine/placebo trials and suggests that when it does occur, the apparent superiority of antidepressants may be due to unblinding among study patients (and raters) given the greater frequency of side effects in active drug groups and patients' education about said effects as part of informed consent [18, 19]. Kirsch [16, pp 7–22] and Kirsch and Sapirstein [20], among others [18, 19, 21], argue that side effects enhance the placebo effects of antidepressants by confirming to patients that they are taking the active medication and thereby increasing their expectation of improvement. Given the often small drug/placebo differences in these studies, it would not take much such unblinding to account for positive results when they do occur. On the other hand, the fact that many RCTs fail despite significant drug/placebo side effect differences suggests that said effects alone are not sufficient to consistently result in greater improvement even if they do contribute to unblinding.

The analyses performed by Rising et al. [8] and Turner et al. [9] document that readers should be wary when researchers replace their pre-specified primary outcome measure with a new one. This concern is reinforced by recent analyses documenting widespread selective outcome reporting in industry-sponsored research and the inflationary effect that often occurs when the pre-specified primary outcome measure is not used to report findings [22, 23]. Perhaps the most troubling implications of the Rising-Turner-Kirsch-Barbui findings are that journal readers, seeking articles to guide evidence-based practice, may have been misled by meta-analyses and reviews based on biased published articles on antidepressant efficacy.

However, some explain only marginal superiority of antidepressants by the fact that subjects enrolled in RCTs do not necessarily present with adequate illness severity. Lieberman et al. [24] observed that early RCTs often enrolled hospitalized patients who were less responsive to placebo, whereas more recent trials typically enroll highly selected outpatients, contacted through mass media advertisements, who may be less severely depressed. In a meta-analysis of 75 RCTs published between 1981 and 2000, Walsh et al. [25] showed that the response to both antidepressants and placebos has increased over time with a significant positive correlation between year of publication and response. Parker [26] argues that this progressively increasing response to both compromises the ability to differentiate truly efficacious antidepressants from placebos, particularly among less severe patients.

Fava et al. [27] notes that the analysis of Walsh et al. [25] likely understates placebo response rates since most failed trials go unpublished; they estimate that the true rate is 35–45%. They then explore various potential causes for failed trial findings (e.g. measurement errors or diagnostic heterogeneity) and propose a new study design that might reduce placebo rates and thereby the number required to differentiate efficacious antidepressants from placebos. Both Fava et al. [27] and Otto and Nierenberg [28] observe that only two RCTs showing drug superiority are required for FDA approval regardless of how many were conducted, and both cite the example of paroxetine that took nine trials to get the two necessary to *'win'* approval [29]. The apparent lack of significant adverse consequences to drug companies from failed trials (other than added costs and delayed time to market) may have fostered a production-oriented mindset favoring trial quantity over quality (since it takes only two to win, and losses are not counted) too often resulting in flawed science and thereby the ensuing vigorous debate over methodology and interpretation while furthering the disconnect between trial findings and their application to clinical practice.

In an analysis of psychiatric outpatients with major depressive disorder (MDD), Zimmerman et al. [30] found that RCTs would have excluded 86% due to their having a comorbid anxiety or substance use disorder, insufficient depressive symptoms, and/or current suicidal ideation. Similarly, a post hoc analysis of STAR*D (Sequenced Treatment Alternatives to Relieve Depression) patients, the largest antidepressant effectiveness study ever conducted, found that 77.8% would have been excluded from RCTs due to having a baseline HRSD score ≤19, more than one concurrent medical condition, more than one comorbid psychiatric disorder, and/or a current depressive episode lasting >2 years [31]. This analysis

found that STAR*D patients who met RCT inclusion criteria had greater likelihood of remission than those more representative of the vast majority seeking care (34.4 vs. 24.7% remission rate). As Wisniewski et al. [31] note, by enrolling more representative patients RCT results would better estimate the benefit of an antidepressant in practice and may also reduce placebo response rates and the associated risk of failed trials. Likewise, Parker [26, p. 2] argues that the apparent limited efficacy of antidepressants may not be related to the modest effects of these compounds but rather to RCT design and methodological issues, *'whereby the "apples" assessed in such studies do not correspond to the "oranges" of clinical practice'*.

While the relative efficacy of antidepressants is not settled, progress will only come as RCTs enroll representative MDD samples for which the medication is intended under conditions that simulate real-world practice. Such trials should follow Gaudiano and Herbert's [19] recommendations for distinguishing between specific and nonspecific treatment effects, the first one being having an active placebo arm to reduce the likelihood of unblinding and thereby control the potential role of side effects in enhancing patients' expectation of improvement.

Real-World Effectiveness of Antidepressants

In conformity with this goal of enrolling more representative MDD patients, the NIMH-funded STAR*D study [32–38]:

- enrolled 4,041 real patients seeking care versus persons responding to advertisements for depressed subjects;
- included patients with comorbid medical and psychiatric conditions as well as those whose current MDD episode was >2 years;
- included patients currently undergoing antidepressant treatment provided that there was not a history of nonresponse or intolerance to either step-1 or step-2 protocol antidepressants;
- used *'remission'* versus *'response'* as the primary criterion of successful treatment which is a higher clinical standard than used in prior effectiveness studies;
- provided 12 months of continuing care while monitoring the durability of treatment effects versus only reporting acute-care improvement.

STAR*D provided a very high quality of free acute and continuing care to maximize the likelihood that MDD patients would achieve remission and maintain it. Table 1 describes in detail the high quality of treatment and the extensive efforts of STAR*D to retain patients. The treatment protocol included state-of-the-art acute care to achieve remission followed by 1 year of continuing care for all patients who achieved a satisfactory clinical response. The goal of continuing care was to maintain remission and prevent relapse [39, p. 15].

The continuing-care phase of STAR*D also provided a real-world test of the practice guideline of the American Psychiatric Association (APA) that *'following remission, patients who have been treated with antidepressant medications in the acute phase should be maintained on these agents to prevent relapse'* [40, p. 15]. This guideline received the highest confidence rating of the expert panel.

STAR*D was designed to provide guidance in selecting the best *'next-step'* treatment for the many patients who fail to get adequate relief from their initial selective serotonin reuptake inhibitors (SSRI) trial by evaluating the relative efficacy of eleven pharmacologically distinct treatments [41]. Cognitive therapy (CT) was also an option in step 2, but too few patients included it as an acceptable treatment resulting in only 101 contributing data after randomization [33]. CT was therefore excluded from the primary step-2 switch and augmentation articles [33, 34]. Possible reasons so few patients found CT acceptable included: (1) biased self-selection since all patients started on citalopram in step 1; (2) the added costs of CT which STAR*D did not cover whereas it covered all medication and physician visit costs, and (3) CT patients had to go to another site to see a new non-physician professional [42, pp 748–749]. Despite these impediments, in a subsequent article STAR*D reported that the 101 step-2 patients who received CT *'(either alone or in combination with citalopram) had similar response and remission rates to those assigned to medication strategies'* [42, p. 739].

The conclusion section of the research design article of STAR*D states: *'STAR*D uses a randomized, controlled design to evaluate both the theoretical principles and clinical beliefs that currently guide the management of treatment-resistant depression in terms of symptoms, function, satisfaction, side-effect burden, and health care utilization and cost estimates. Given the dearth of controlled data, results should have substantial public health and scientific significance, since they are obtained in representative participant groups/settings, using clinical management tools that can easily be applied in daily practice'* [43, p. 136].

Given the *'substantial public health and scientific significance'* of STAR*D in evaluating the effectiveness of antidepressants when optimally delivered to real-world patients, it is critical that the methodology and findings of STAR*D are presented accurately.

Table 1. Highest quality of acute and continuing care to maximize remissions while minimizing relapse and dropouts

Descriptor	Explanation
Optimized sustained study participation to minimize dropouts [41, pp 473–474]	– Promoted patients' study affiliation via STAR*D-branded brochures, bimonthly newsletters, and an informational video emphasizing the public health significance of STAR*D and the critical role played by patients; – educated patients and families about depression and its treatment using a multistep educational package; – used a letter reminder system to alert patients before appointments in those clinics without such systems who had a >15% rate of missed appointments; – ensured timely follow-up and rescheduling of missed appointments by calling patients on the day of the missed appointment, and again within 24 h, if there was no response; the patient's physician sent a letter within 48 h if contact was not established; – used a letter reminder system for all research outcome assessment calls during acute and continuing care; – in every clinic visit, the clinical research coordinator discussed the research outcomes in phone calls with the patient to ensure that the calls were completed on schedule and worked to resolve any problematic issues regarding said calls [39, p. 75]; – paid patients USD 25.00 for participating in each telephonic research outcome assessment; – permitted patients to re-enter acute and/or continuing care within 4 weeks after having dropped out [39, p. 80]; – recommended 1 year of continuing care for all patients who achieved a satisfactory clinical response with the essential goal of preventing relapse [39, p. 15]; – permitted continuing-care patients to remain in the study if they moved from the area [39, p. 81]; – provided all medical and pharmacological treatment care-free to patients.
Acute-care visits	Physicians met with patients on entry into each new step to initiate drug treatment with follow-up visits scheduled on weeks 2, 4, 6, 9, and 12, with an optional week 14 visit.
Measurement-based care	Conducted structured evaluations of symptoms and side effects at each visit and included a centralized treatment monitoring and physician feedback system to ensure consistent implementation of optimal care across research sites.
Aggressive medication dosing	Provided aggressive medication dosing with a fully adequate dose for a sufficient duration to *'ensure that the likelihood of achieving remission was maximized and that those who did not reach remission were truly resistant to the medication'* [32, p. 30].
Liberal prescribing of non-study medications	Physicians had great leeway in prescribing non-study medications to treat comorbid symptoms resulting in: – 17.2% taking trazodone for sleep; – 11.9% taking an anti-anxiety medication; – 16.7% taking either a sedative or hypnotic medication; – an undisclosed percentage taking medications to address side effects [33, table 2].
Continuing-care visits	Patients saw their physician every 2 months and continued taking their treatment medication(s) at the same doses, but their physicians were allowed to make any psychotherapy, medication, and/or medication dose changes to maximize the likelihood of maintaining patients' remission status [38, p. 1908]; additional continuing-care visits were scheduled when patients began to experience a return of depressive symptoms and/or intolerable side effects [39, p. 78].
Clinical research coordinator (CRC)	Each site had a clinical research coordinator who [32, p. 30]: – saw patients before each visit administering multiple measures to them including the QIDS-SR during each acute-care visit; – assisted physicians in protocol implementation; – provided patients with support and encouragement in protocol implementation.
Treatment designed to enhance subject retention	Treatment was designed to minimize dropouts and/or non-compliance including: – open-label prescribing during acute and continuing care with no placebo control condition during any study phase; – patients chose their acceptable treatment assignments for steps 2 and 3 to eliminate any concerns they might have about receiving an unacceptable assignment; this resulted in only 21 of 1439 (1.5%) step-2 patients making themselves available for random assignment to all treatment options [33, p. 1235] while only 29 of 377 (7.7%) did so in step 3 [36, p. 1521]; – during each step, patients could enroll immediately into the next step if they had intolerable side effects or had maximized the dosing of their current medication(s) without achieving a remission; – during any step, patients could enter continuing care directly on their current medication(s) if they were treatment responders even if they had not achieved remission; this was done to minimize responders from dropping out in order to avoid having to discontinue their current medication(s) and start a new drug regimen.

Change in One of the Outcome Measures

As designed, the HRSD was the pre-specified primary measure of STAR*D and the Inventory of Depressive Symptomatology-Clinician-Rated (IDS-C30) the secondary one for identifying *'remitted'* (i.e. those with a score ≤7 HRSD) and *'responder'* (i.e. those with a ≥50% reduction in depressive symptoms) patients [41, p. 476, 43, p. 123]. These measures were obtained by research outcome assessors (ROAs) blind to treatment assignment at entry into and exit from each treatment level, and every 3 months during continuing care. Additional measures assessing symptoms, level of functioning, satisfaction, quality of life, side effect burden, and health care utilization were obtained by an interactive voice response (IVR) telephone system on the same schedule as the HRSD and IDS-C30 [43, p. 129] (table 2).

As mentioned earlier, STAR*D was designed to identify the best next-step treatment for the many patients who fail to get adequate relief from their initial SSRI trial. Due to

Table 2. Survival analysis by treatment step of patients who entered continuing care in remission

Step	n[1]	0–3 months[2]	3–6 months[3]	6–9 months[4]	9–12 months[5]
1	1,085	628	431	290	84
2	383	199	133	79	20
3	35	16	11	8	2
4	15	8	5	5	2
Total	1,518	851	580	382	108
Relapse and/or dropout rate by quarter[6]		43.9%	61.8%	74.8%	92.9%

[1] Number of patients entering continuing care with a QIDS-SR-defined remission [38, table 5, column 2].

[2] Number of patients who called in at least once into the STAR*D IVR system during months 0–3 and did not relapse scoring in the moderate/severe depression range on the QIDS-SR [38, fig. 3, table, row 2].

[3] Number of patients who called in at least once during months 3–6 and did not relapse scoring in the moderate/severe depression range on the QIDS-SR during this or any prior assessment in months 0–3 [38, fig. 3, table, row 3].

[4] Number of patients who called in at least once during months 6–9 and did not relapse scoring in the moderate/severe depression range on the QIDS-SR during this or any prior assessment in months 0–6 [38, fig. 3, table, row 4].

[5] Number of patients who called in at least once during months 9–12 and did not relapse scoring in the moderate/severe depression range on the QIDS-SR during this or any prior assessment in months 0–9 [38, fig. 3, table, row 5].

[6] The percent of STAR*D remitted patients who relapsed and/or dropped out during continuing care.

the high study dropout rate in STAR*D which frequently resulted in missing exit IDS-C30 and HRSD assessments (and thereby the required imputation level made these assessments relatively uninformative), the statistical analytical plan was revised with input from the Data Safety and Monitoring Board prior to data lock and unblinding.

The revised statistical analytical plan of STAR*D dropped the IDS-C30 and replaced it with the Quick Inventory of Depressive Symptomatology-Self-Report (QIDS-SR), a tool developed by the principal investigators of STAR*D that is highly correlated with the HRSD (the primary measure) since it was administered at every visit [44–46]. In the step-1 to step-4 studies, the QIDS-SR was the secondary measure for identifying remissions and sole measure for identifying responders while the HRSD was the primary measure for identifying remitted patients [32–37].

As originally planned, STAR*D used the QIDS-SR in two ways. The research version was IVR administered on the same schedule as the other measures during steps 1–4 and as an *'interim'* monthly measure during continuing care [39, p. 120, table 3].

Patients also completed a paper-and-pencil QIDS-SR at the beginning of each clinic visit along with two self-rated side effect measures and a medication adherence questionnaire. These four self-assessments were overseen by non-blinded clinical research coordinators who reviewed the results to make certain that all items were completed and then saw the patient to administer the QIDS-C (the clinician-administered version with the identical 16 questions and response options as the QIDS-SR), the Clinical Global Impression Improvement Scale, and discuss with the patient any symptoms and side effects that he/she was experiencing as well as present patient education materials [39, p. 75].

The clinical research coordinators then recorded the six measures on the clinical record form for the treating physician's review before he/she saw the patient *'to provide consistent information to the clinicians who use this information in the protocol'* [43, p. 128]. In this way, the paper-and-pencil QIDS-SR was one of the *'clinical management tools that can easily be applied in daily practice'* [43, p. 136] of STAR*D and used as such in the *'measurement-based'* system of care of STAR*D as STAR*D states: *'To enhance the quality and consistency of care, physicians used the clinical decision support system that relied on the measurement of symptoms (QIDS-C and QIDS-SR), side-effects (ratings of frequency, intensity, and burden), medication adherence (self-report), and clinical judgment based on patient progress'* [32, p. 30]. This distinction between

Table 3. Remission and discontinuance rates in STAR*D by treatment step

Treatment	Remission rate[1]	Discontinuance rate[2]
Step 1	25.4% 790 out of 3,110	26.6%[3] 826 out of 3,110
Step 2	25.1% 324 out of 1,292	30.1%[4] 389 out of 1,292
Step 3	17.8% 67 out of 377	44.8%[4] 169 out of 377
Step 4	10.1% 11 out of 109	60.1%[4] 66 out of 109

[1] Calculated by combining all HRSD-defined remissions in each of steps 1–4 of the published study divided by each combined n of the study [32–37]. Step 1 includes the 234 patients who met the original ≥14 HRSD baseline admission criterion and were started on citalopram but then dropped out without a follow-up visit [32, fig. 1].

[2] The number of patients who dropped out for any reason including intolerance, lack of adequate response, declining to enter the next-step treatment phase, or declining to enter continuing care despite having a positive response during the current treatment phase.

[3] Calculated from figure 1 in the step 1 study.

[4] Calculated from figure 1 in the final report.

the originally intended use of the QIDS-SR as a clinical tool versus research measure is made explicit in both tables of the design article (tables 2, 3) [43, pp 128–129] and the Clinical Procedure Manual of STAR*D (tables 2, 4) [39, pp 119, 121].

The revised statistical analytical plan did not change any of the next-step comparison results of STAR*D, as both the QIDS-SR and HRSD found no significant group differences between treatments in all five comparisons. However, this decision appears to have inflated the reported remission and response rates of STAR*D. As stated in the step-1 article: *'Higher remission rates were found with the QIDS-SR than with the HRSD because our primary analyses classified patients with missing exit HRSD as nonremitters a priori. Of the 690 patients with missing exit HRSD scores, 152 (22.1%) achieved QIDS-SR remission at the last treatment visit'* [32, p. 34]. In the six step-1 to step-4 studies, there were 1,192 HRSD-identified remissions versus 1,398 QIDS-SR ones, an increase of 17.3% (table 4), and the major summary article of STAR*D only used the QIDS-SR to report its step-by-step acute and continuing-care findings [38].

Table 4. HRSD and QIDS-SR remission rates

Medication step study	HRSD	QIDS-SR	References
Step-1 citalopram	790	943	[32, table 4, row 1]
Step-2 switch	155	186	[33, table 3, rows 2 and 3]
Step-2 augmentation	169	202	[34, table 3, rows 2 and 3]
Step-3 switch	38	24	[35, table 4, rows 1 and 3]
Step-3 augmentation	29	27	[36, table 4, rows 13 and 14]
Step-4	11	16	[37, table 3, rows 3 and 4]
Total	1,192	1,398	

Change in Eligibility for Analysis Criteria

The step-1 article of STAR*D states that eligible patients *'had a non-psychotic major depressive disorder determined by a baseline HRSD score ≥14'* [32, p. 29]. This is a modest symptom severity threshold (see Davidson et al. [47] with a ≥20 HRSD inclusion threshold for example) though similar to many MDD patients seeking treatment [30].

Of the 4,790 patients administered the screening HRSD (completion time: 15 min [39, p. 118]), 4,041 were started on citalopram in their baseline visit [39, p. 17, 48]. Of these patients, 3,110 scored ≥14 on the more thorough and blinded ROA-administered HRSD (completion time: 20–25 min [39, p. 118]), 234 of whom failed to return for a follow-up visit. For the resulting 2,876 step-1 patients eligible for analysis [32, fig. 1], their baseline HRSD scores averaged 21.8 [32, table 1, row 2]. There were also 607 patients reportedly excluded (but later included – see discussion below) because their score <14 signified only mild depression and 324 patients were reportedly excluded (but later included) because they lacked a baseline ROA-administered HRSD [32, fig. 1].

The subsequent step-2 to step-4 articles of STAR*D continued to state that all patients had *'non-psychotic major depressive disorder'* and did not clarify a deviation from eligibility of step 1 for analysis criteria [32–37]. Specifically, the 607 patients who scored <14 in their baseline ROA assessment along with the 324 patients with no such assessment received citalopram in step 1, progressed to subsequent acute and continuing-care treatments, and were included in step-2 to step-4 articles and also in the summary article. Thus, 931 of the 4,041 STAR*D patients (23%) did not have a ROA-administered HRSD ≥14 when enrolled into the study.

The effect of including these patients' data was to lower the average step-1 HRSD from 21.8 to 19.9 [38, table 2, row 2]. STAR*D also included these 931 patients to recalculate the step-1 remission rate of citalopram in its summary article. In so doing, the step-1 remission rate was inflated to 36.8% from the original 32.8% of the step-1 article both based on the lenient QIDS-SR determination.

Perhaps a more serious problem is trying to determine the effect of these 931 patients in changing the relapse rate during continuing care. Initial symptom severity is a powerful predictor of relapse – with less depressed patients far less likely to relapse. For patients who entered the study with a HRSD <14, there is a special conundrum because STAR*D defined relapse as a HRSD ≥14. This means that 607 patients, in order to be counted as relapsed, had to score worse during continuing care than when they first entered the study.

In addition, a failure to consider dropout permitted STAR*D to assert a 67% *'cumulative'* remission rate after up to four medication steps [38, p. 1910]. STAR*D authors arrived at this figure simply by adding together its inflated QIDS-SR remissions in steps 1–4. STAR*D acknowledges that this assertion assumes no dropouts and the same remission rate for persisting patients as those who exited. These assumptions though are not true in the real world and were certainly not true in STAR*D since more patients dropped out from the study in each step than had a remission (table 3). Furthermore, comparing persisting patients' remission rates to dropouts is not possible since dropouts do not provide data.

Table 3 presents the HRSD-determined remission and dropout rates of STAR*D for steps 1–4. These data are quite important for a clinical understanding of the effectiveness of antidepressants in real-world patients receiving *'measurement-based'* state-of-the-art treatment:

- in step 1, 25.4% of patients had a remission while 26.6% dropped out [49];
- in step 2, 25.1% of patients had a remission while 30.1% dropped out;
- in step 3, 17.8% of patients had a remission while 44.8% dropped out;
- in step 4, 10.1% of patients had a remission while 60.1% dropped out.

Continuing-Care Findings

One of the most important questions in evaluating antidepressants is how durable are the remissions. A major STAR*D contribution was to provide 12 months of follow-up data on remitted and improved patients' continued treatment. Patients who achieved remission during acute care were strongly encouraged to enter continuing care. In addition, responder patients who failed to attain remission and did not want to continue to the next acute-care step were encouraged to enter continuing care.

The protocol of continuing care *'strongly recommended that participants continue the previously effective acute treatment medication(s) at the doses used in acute treatment'* [38, p. 1908]. This recommendation is consistent with the APA continuation phase guideline that *'following remission, patients who have been treated with antidepressant medications in the acute phase should be maintained on these agents to prevent relapse'* [40, p. 15]. However, the STAR*D protocol was more naturalistic than the APA guideline in that physicians were allowed to make *'any psychotherapy, medication, or medication dose change'* [38, p. 1908] they deemed necessary to maximize patients' likelihood of sustaining remission. This included scheduling additional visits if depressive symptoms returned and/or intolerable side effects emerged [39, p. 78].

STAR*D made strong efforts to maximize retention and collect follow-up data. These efforts included continued use of all acute-care patient retention strategies during continuing care, prompting patients prior to all research outcome assessment phone calls, and paying patients USD 25.00 for taking said assessments as well as permitting patients to remain in the study if they moved from the area (table 1). Furthermore, informed consent was re-obtained for all patients entering continuing care to ensure their understanding of its treatment and outcome assessment procedures and expectations [39, p. 68].

For evaluating the outcome of continuing care, STAR*D authors decided to use the IVR-administered QIDS-SR that was originally intended as only an interim monthly measure during continuing care [39, p. 120, table 3], not the pre-specified HRSD and IDS-C30. If the patient called in and scored ≥11 on the QIDS-SR, relapse was declared; that score (said to correspond to a HRSD ≥14) indicated moderate-to-more-severe depression. Given this, it is important to note that STAR*D was not reporting the rate that remitted patients sustained remission, only the rate at which they relapsed while remaining in continuing care.

In calculating relapse, STAR*D authors decided not to use intent-to-treat procedures in which dropouts would count as continuing-care failures (despite the separate informed consent process) but instead use the data from patients who called into the IVR system once (or more)

during the 12 months. The calculated relapse rate was the proportion of patients relapsing of those who made at least one such call and reported a ≥11 QIDS-SR [38, table 5, column 6, footnote d).

By this relapse definition, the continuing-care patients who dropped out early and never called in, or the many patients who called in once or more without scoring ≥11 and then dropped out, could never meet the relapse criterion. Because the likelihood of relapse increases with time in follow-up, this definition is biased toward underestimating relapse rates. It is common for patients to lose hope when depressive symptoms return thereby increasing their likelihood of discontinuing a treatment that is no longer effective for them. This is particularly true for the 75% of STAR*D patients diagnosed with *'recurrent depression'* [38, table 2]. Given that most STAR*D patients had *'reoccurring'* depression and *'loss of hope'* is one of the most common symptoms of depression, it is reasonable to expect that many continuing-care dropouts relapsed.

The summary report of STAR*D identifies 1,854 remitted patients in steps 1–4 [38, table 3, row 8] yet only 1,518 consented to continuing care [38, table 5, column 2] while the other 336 dropped out. Many of these patients achieved their remission based on the paper-and-pencil QIDS-SR in their last clinic visit but then discontinued treatment without taking the HRSD despite the USD 25.00 payment for taking said measure (e.g. the step-1 article states, *'Of the 690 patients with missing exit HRSD scores, 152 (22.1%) achieved QIDS-SR remission at the last treatment visit'* [32, p. 34]. An additional 344 patients consented to continuing care but then dropped out during the 1st month without ever calling into the IVR system [38, table 5, column 5]. This indicates that 670 of 1,854 remitted patients (36.7%) of STAR*D dropped out within 1 month of their QIDS-SR remission. Due to its open-label prescribing though, the ultimate outcome for these patients (and all dropouts during any phase) is unclear since patients could continue their treatment without staying in STAR*D by paying for their medications and physician services that heretofore had been free. Given that such a decision required assuming this new cost which could be substantial, particularly for the one third who lacked insurance coverage [38, table 1], it is unlikely that many STAR*D dropouts continued their treatment on antidepressant medication(s).

The weighted mean relapse rate of STAR*D for remitted patients that called at least once into its IVR system was 37.4% (range: from 33.5% for step-1 to 50% for step-4 patients) and 64.4% for improved patients who entered continuing care not in remission (range: from 58.6% for step-1 to 83.3% for step-4 patients) [38, table 5, column 6]. Table 2 presents the survival analysis for the 1,518 patients who entered continuing care in remission. The numbers in table 2 represent the remitted patients who *'survived'*, i.e. did not relapse or dropout. Relapses of course represent unsuccessfully treated patients. Dropouts represent unsuccessfully treated patients as well, viewed from the intent-to-treat perspective. STAR*D authors highlighted their findings that *'relapse rates were higher for those who entered follow-up after more treatment steps ($p < 0.0001$)'* [38, p. 1911] and *'remission at entry into follow-up was associated with a better prognosis than was simple improvement without remission'* [38, p. 1912]. While both statements are statistically accurate, they do not address the fact that STAR*D patients' had extraordinarily high relapse and/or dropout rates during continuing care regardless of the treatment step their remission occurred nor their extent of acute-care improvement prior to entering continuing care.

These findings call into question continuation phase guideline of APA that *'following remission, patients who have been treated with antidepressant medications in the acute phase should be maintained on these agents to prevent relapse'* despite this recommendation having received the highest *'clinical confidence'* rating of the expert panel [40, p. 15].

Discussion

Given its 35 million dollar cost and thoughtful design, STAR*D provides a rare opportunity to evaluate the effectiveness of antidepressants with real-world patients and therefore warrants analysis from multiple perspectives independent of those of its authors. While similar to the analysis of Fava et al. [50] documenting decreasing step-by-step remission rates with increasing rates of relapse and drug intolerance, our analysis found that the results of STAR*D appear even worse than previously realized. Even with the extraordinary care of STAR*D, only about one fourth of patients achieved remission in step 1. The study dropout rate was slightly larger than the success rate. The success rate of step 2 was slightly less than that of step 1 and the dropout rate was larger. The success rates in step 3 (17.8%) and step 4 (10.1%) were even more modest with still larger dropout rates (44.8 and 60.1%, respectively).

Of the 4,041 patients started on citalopram, 370 (9.2%) dropped out within 2 weeks. After up to four trials, each provided with vigorous medication dosing *'to ensure that*

the likelihood of achieving remission was maximized and that those who did not reach remission were truly resistant to the medication' [32, p. 30], only 1,854 patients (45.9%) obtained remission using the lenient QIDS-SR criteria. In each step, more patients dropped out than were remitted and this dropout rate steadily increased throughout the study. Of the 1,854 remitted patients, 670 (36.7%) dropped out within 1 month of their remission and only 108 (5.8%) survived continuing care and took the final assessment without relapsing and/or dropping out. Even for these 108 patients, it is unclear how many were one of the 607 whose baseline HRSD <14 signified only mild symptoms when first started on citalopram in step 1 and therefore had to score worse during continuing care than when they first entered the study to be counted as relapsed.

In STAR*D, failed trials had negative consequences for patients beyond not obtaining remission. Such failures decreased patients' likelihood for obtaining remission in subsequent trials while increasing their likelihood for drug intolerance, relapse, and/or dropping out. These negative effects lend support to the observation of Fava et al. [50, p. 262] that successive pharmacological manipulations *'may propel depressive illness into a refractory phase'* by fostering oppositional tolerance in which the antidepressant sensitizes some patients to depression. Chouinard and Chouinard [51, p. 75] document similar risks with atypical antipsychotics and estimate that 50% of treatment-resistant schizophrenia cases are related to supersensitivity psychosis. The following issue remains to be determined: the extent that diminishing outcomes of STAR*D are due to a subset developing such oppositional tolerance, patients' natural diminished expectations of improvement following each failure (i.e. a step-by-step diminishing placebo effect), other unknown factors, and/or some combination thereof.

Most importantly to clinicians, STAR*D results show that antidepressants were only minimally effective with real-world patients when provided consistent with *'the theoretical principles and clinical beliefs that currently guide the management of treatment-resistant depression'* [43, p. 136]. This admittedly harsh assessment is most evident when using study completion rates as the best *'hard measure of treatment effectiveness and acceptability'* [14, p. 296].

Turner et al. [9] demonstrates how publication bias inflates the perceived efficacy of antidepressants thereby promoting the widespread acceptance of this treatment. The separate analyses of Turner et al. [9] and Kirsch et al. [10] suggest that antidepressants are only marginally efficacious compared to inert placebos, though the findings in these trials may be due to the under-representation of less symptomatic patients with greater comorbidity (particularly anxiety disorders that have been found to lower antidepressant response rates [52]) and long-standing depressive illness who better characterize the majority seeking care. The analysis of Barbui et al. [15, cited in 16, p. 19] demonstrates how the apparent clinical superiority of paroxetine over placebo disappeared after statistically controlling for differences in drug/placebo side effects suggesting that side effects contribute to unblinding in RCTs and thereby enhance patients' expectation of improvement since they often guess correctly that they are getting the *'real'* drug and therefore anticipate improvement. Similar analyses are needed of antipsychotic/placebo antidepressant augmentation trials for *'treatment-resistant depression'* due to significant side effect profiles of antipsychotics and the role these might play in unblinding. Such analyses are crucial to evaluate properly Nelson and Papakostas' [53] recent meta-analysis finding that atypical antipsychotics were superior to placebo as augmentation agents since this analysis did not control for said differences in drug/placebo side effects and the fact that this apparent *'superiority'* was exceptionally modest, with 9 being the number needed to treat to have one additional remission in trials lasting only 6–8 weeks.

What more can we learn from STAR*D and the reviewed articles? First, even with exemplary pharmaceutical efforts it is difficult to achieve sustained recovery for patients reflecting the range of illness severity of STAR*D. Second, the results from efficacy trials (whether for medication, an evidence-based psychotherapy, or any other treatment) are limited in their ability to estimate a treatment benefit to the extent that the *'the "apples" assessed in such studies do not correspond to the "oranges" of clinical practice'* [26]. The analyses of Zimmerman et al. [30] and Wisniewski et al. [31] further highlight this fundamental disconnect between RCT patients and those most often presenting in real-world clinical practice. Third, the fact that the effectiveness rate in step-2 CTs was no better than antidepressants underscores that MDD – *with its common co-morbidities and recurrent nature* – is a serious, complex, and difficult-to-treat disorder whose treatment often results in fewer positive outcomes than would be expected from efficacy trials of its two most extensively researched interventions.

Fourth, it is worth considering whether or not the measurement-based system of STAR*D with its focus on measuring side effects and symptoms in every visit until *'remission'* was achieved hindered or helped patient care.

STAR*D authors clearly believed that it helped and even equated *'high quality care'* with their system stating: *'Finally, high quality of care was delivered (measurement-based care) with additional support from the clinical research coordinator. Consequently, the outcomes in this report may exceed those that are presently obtained in daily practice wherein neither symptoms nor side-effects are consistently measured and wherein practitioners vary greatly in the timing and level of dosing'* [38, p. 1914]. STAR*D encouraged all patients who did not achieve remission based on a number to enter the next trial despite the failure of QIDS/HRSD to differentially weight core depressive symptoms (e.g. mood, guilt, suicidal ideation, or anhedonia) and accessory ones (e.g. appetite, insomnia, or agitation) [54, 55] and patients' self-assessments of the relative importance of each. In the absence of a meaningful therapeutic alliance between the patient and doctor, relying instead on patients' recitation of side effects and symptomatic change to guide treatment, STAR*D may have failed to capitalize on a crucial ingredient necessary for patient improvement. In contrast, psychosomatic methods would likely have improved patient retention and outcomes given its use of more clinically-rich clinimetric assessment procedures, collaborative decision-making, and its focus on enhancing patients' self-efficacy by teaching them the self-management skills that are likely essential to sustain recovery from MDD [56]. Such psychosomatic methods are at their core *'psychotherapeutic'* and would likely enhance outcomes from any intervention, be it an antidepressant, a placebo, or some other strategy; particularly when applied to treating depressed – *often initially helpless and hopeless* – patients and their commonly occurring comorbid conditions.

Fifth, the continuation and maintenance phase guidelines of APA which essentially encourage open-ended use of antidepressants at *'the same full antidepressant medication doses'* as used in acute treatment appear misguided [40, p. 15]. While the guidelines of APA are consistent with the meta-analyses performed by Geddes et al. [57] and Papakostas et al. [58] reporting large effect sizes for antidepressants in preventing relapse, these analyses do not control for publication bias [59, 60] nor selective outcome reporting [22, 23], both of which may significantly inflate the findings from meta-analyses that fail to control for these common forms of researcher bias. For now, prospective naturalistic studies are likely a better guide to estimate real-world outcomes. In STAR*D, even for the 1,085 remitted patients in step 1 who consented to continuing-care and therefore had the highest likelihood of sustained recovery, only 84 (7.7%) did not relapse and/or dropout by the 12th month of continuing care. STAR*D results are similar to findings of Bockting et al. [61] that only 42% used antidepressants continuously during maintenance phase treatment, of whom 60.4% relapsed, whereas patients who stopped using antidepressants experienced less relapse, with only 8% of those who received preventive CT relapsing. These naturalistic continuation phase studies support Fava's [62, 63] hypothesis that long-term antidepressant use may worsen the course of depression. Besides these studies, failure to find any apparent benefit from continued antidepressant treatment, the recent finding that long-term use of SSRIs at moderate/high daily doses doubles the risk of diabetes [64], and the uncertain risk of oppositional tolerance, provides additional reasons for reexamining this all too common practice.

Finally, in light of the meager results of STAR*D, it is worth reconsidering the term *'treatment-resistant depression'* when referring to patients who do not respond favorably to drug treatment. Should we not direct our attention to what is wrong with our treatment rather than classifying some patients as having an exotic form of depression because they fail to respond? Our understanding is hampered by using language that wrongly implies that there is an exceptional subgroup of patients who are refractory to an otherwise effective treatment. The inescapable conclusion from STAR*D results is that we need to explore more seriously other forms of treatment (and combinations thereof) that may be more effective. This effort will require developing new service delivery models to ensure that as such treatments are identified, they are widely implemented [65, 66].

Despite the pervasive belief regarding the effectiveness of antidepressants and cognitive therapy (CT) among physicians and society at large, STAR*D shows that antidepressants and CT fail to result in sustained positive effects for the majority of people who receive them. STAR*D authors noted at the outset of the study that the *'results should have substantial public health and scientific significance'*. As healthcare professionals and in line with what STAR*D authors themselves recommend, we should take notice of what this largest antidepressant effectiveness trial ever conducted is telling us and reassess the role of antidepressant medications and CT in the evidence-based treatment for depression.

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Conflicts of Interest

H. Edmund Pigott, PhD, and Gregory S. Alter, PhD, are founders of NeuroAdvantage, LLC, a for-profit neurotherapy company. During the past 3 years, Dr. Pigott has consulted for CNS Response, Midwest Center for Stress and Anxiety, and SmartBrain Technologies.

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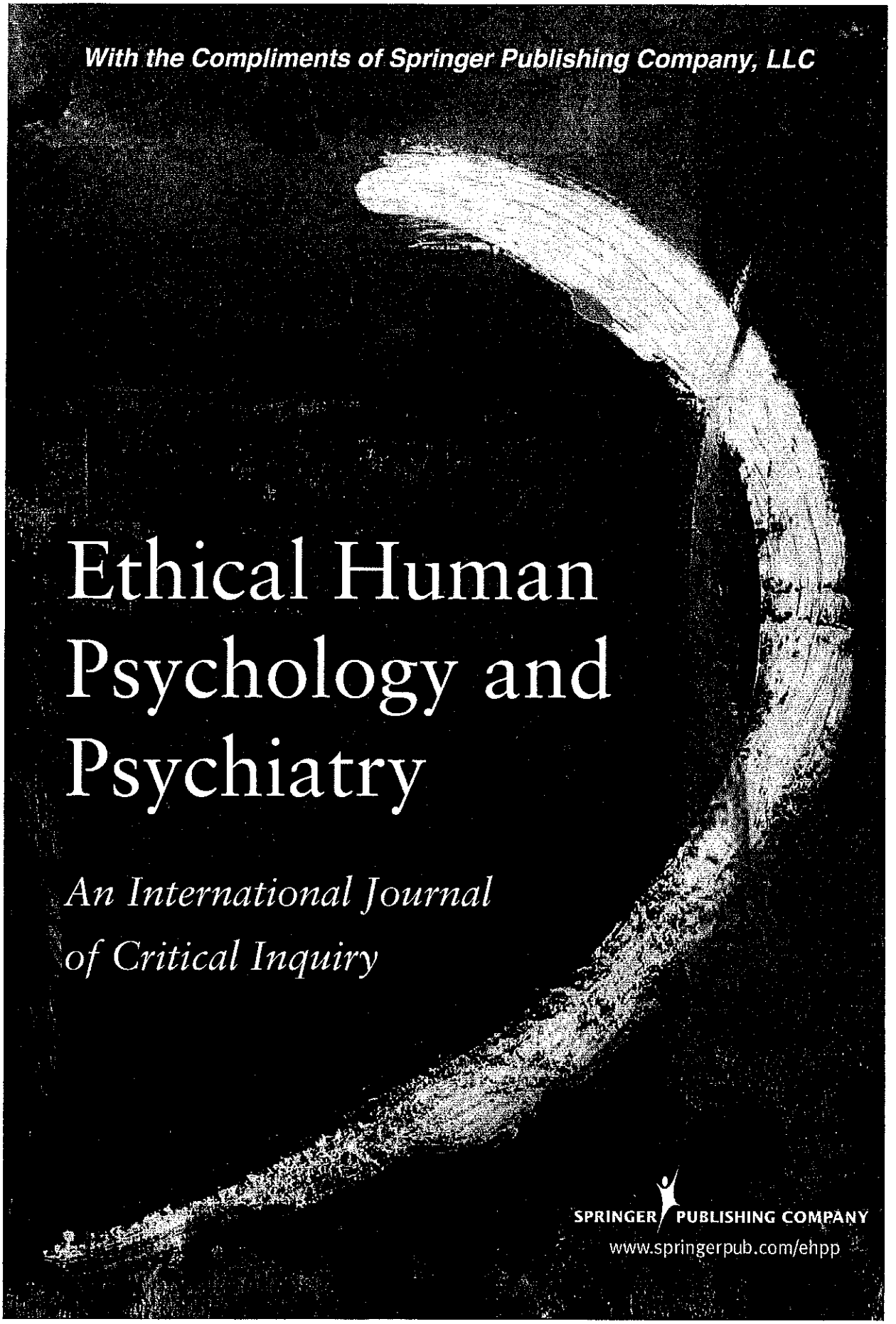
Appendix B



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STAR*D: A Tale and Trail of Bias

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The 35-million-dollar Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study is the largest antidepressant effectiveness study ever conducted. STAR*D enrolled 4,041 depressed patients and provided them with exemplary free acute and continuing antidepressant care to maximize their likelihood of achieving and maintaining remission. Patients who failed to get adequate relief from their first antidepressant were provided with up to three additional trials of pharmacologically distinct treatments. This article identifies numerous instances of apparent bias in the conduct and reporting of outcomes from this study. In contrast to STAR*D's report of positive findings supporting antidepressants' effectiveness, only 108 of its 4,041 patients (2.7%) had an acute-care remission, and during the 12 months of continuing care, these patients neither relapsed nor dropped out. This article also discusses the roles of the *American Journal of Psychiatry* (AJP) and the National Institute of Mental Health (NIMH) in promoting the biased reporting of STAR*D's results.

Keywords: major depression; antidepressants; researcher bias; STAR*D

In the controlled clinical trials article describing STAR*D's methods, research design, and purpose, its authors state:

> STAR*D uses a randomized, controlled design to evaluate both the theoretical principles and clinical beliefs that currently guide the management of treatment-resistant depression in terms of symptoms, function, satisfaction, side-effect burden, and health care utilization and cost estimates. Given the dearth of controlled data, results should have substantial public health and scientific significance, since they are obtained in representative participant groups/settings, using clinical management tools that can easily be applied in daily practice. (Rush, Fava, et al., 2004, p. 136)

To accomplish these objectives, STAR*D:

- Enrolled 4,041 real patients seeking care versus people responding to advertisements for depressed subjects as is common in industry-sponsored research.
- Included patients meeting a lower depression severity threshold than common in efficacy trials by requiring only a baseline Hamilton Rating Scale of Depression (HRSD) score of ≥ 14 versus ≥ 20 (e.g., see Davidson et al., 2002). This low symptom threshold, though, is similar to the many patients who are only mildly depressed when first prescribed antidepressants in routine clinical practice (Zimmerman, Mattia, & Posternak, 2002).
- Included depressed patients with comorbid medical and psychiatric conditions while only excluding those with a primary diagnosis of bipolar, psychotic, obsessive-compulsive, or eating disorders.

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- Used "remission" versus "response" as the primary criterion of successful treatment.
- Provided 12 months of continuing care while monitoring the durability of treatment gains versus only reporting acute-care improvement.

STAR*D provided these 4,041 "real-world" depressed patients with exemplary free acute and continuing-care drug treatment while making extensive efforts to keep patients in treatment and maximize their likelihood of achieving and maintaining remission in a manner consistent with "the theoretical principles and clinical beliefs that currently guide the management of treatment-resistant depression." These efforts included:

- Providing a multistep educational program for patients and families throughout acute-care based on the neurochemical imbalance theory of depression that included "a glossy visual representation of the brain and neurotransmitters," consistently emphasizing that "depression is a disease, like diabetes or high blood pressure, and has not been caused by something the patient has or has not done. (Depression is an illness, *not* a personal weakness or character flaw.) The educator should emphasize that depression can be treated as effectively as other illnesses," and "explaining the basic principles of mechanism of action" for the patient's current antidepressant drug (O'Neal & Biggs, 2001, pp. 4–7).
- Providing "measurement-based care" that involved measuring symptoms and side effects at each clinic visit to guide aggressive medication dosing during each trial with a fully adequate dose for a sufficient duration to "ensure that the likelihood of achieving remission was maximized and that those who did not reach remission were truly resistant to the medication" (Trivedi, Rush, et al., 2006, p. 30). These "clinical management tools" were administered by each site's clinical research coordinator (CRC) who also provided the patient education.
- Allowing patients to select acceptable treatment options in steps 2–4 if their initial drug trial was not successful "to empower patients, strengthen the therapeutic alliance, optimize treatment adherence, and improve outcome" (Fava, Rush, et al., 2003, p. 483).
- Allowing liberal prescribing of nonstudy medications during every treatment phase (Trivedi, Rush, et al., 2006, p. 31).
- Open-label prescribing of all study medications with no placebo-control condition during any treatment phase.
- Using marketing strategies to promote patients' study affiliation via STAR*D-branded brochures, bimonthly newsletters (*The STAR*D Gram*), and an informational video emphasizing STAR*D's public health significance and the critical role played by patients (Fava, Rush, et al., 2003, p. 473).
- Using a reminder system to alert patients before appointments and calling patients on the day of any missed appointments to reschedule, and again within 24 hours, if there was no response, as well as having the patient's physician send a letter within 48 hours if contact had still not been established urging the patient to reschedule (Fava, Rush, et al., 2003, p. 474).
- Using a reminder system for all research outcome assessment phone calls and paying patients $25 for participating in said assessments (Fava, Rush, et al., 2003, p. 474).
- Permitting patients to reenter the study within 4 weeks after having dropped out (Trivedi, Stegman, Rush, Wisniewski, & Nierenberg, 2002, p. 80).
- Allowing physicians to make any therapeutic change necessary during continuing care to maximize patients' likelihood of sustaining remission, including scheduling additional visits if depressive symptoms returned and/or intolerable side effects emerged (Trivedi et al., 2002, p. 78).

In light of these "best practice" efforts, STAR*D's results should be viewed as reflecting antidepressants' optimal level of effectiveness when care is delivered in such a way to maximize patients' likelihood of achieving and maintaining remission by taking these drugs.

STAR*D's primary objective was to evaluate the relative efficacy of 11 pharmacologically distinct "next-step" treatments in up to three additional drug trials for the many patients who failed to get adequate relief from their first antidepressant. Table 1 describes each step's compared drugs. Cognitive therapy was also a treatment option in step 2, but too few patients accepted this form of treatment and it was therefore excluded from the primary step-2 switch and augmentation analyses (Rush, Trivedi, Wisniewski, Stewart, et al., 2006; Trivedi, Fava, et al., 2006).

TABLE 1. Compared Drug Treatment Strategies

Treatment Step	Compared Drug(s)
Step 1	Citalopram (Celexa) was the first-line SSRI treatment because of: • Absence of discontinuation symptoms; • Demonstrated safety in elderly and medically fragile patients; • Easy once-a-day dosing with few dose adjustment steps; and • Favorable drug–drug interaction profile (Trivedi et al., 2006b, p. 30).
Step 2 Switch study	• Sertraline (Zoloft), an SSRI with the same pharmacological profile as citalopram (Celexa); • Extended-release venlafaxine (Effexor), a "dual-action" agent that inhibits the reuptake of both serotonin and norepinephrine; and • Sustained-release bupropion (Wellbutrin SR), an "out-of-class" agent whose neurochemical action mechanisms are unknown; other than that, it does not inhibit serotonin reuptake and is believed to produce antidepressant effects by blocking the reuptake of dopamine and norepinephrine (Rush, Trivedi, Wisniewski, Stewart, et al., 2006, p. 1232).
Step 2 Citalopram (Celexa) augmentation study	• Buspirone (Buspar), a partial agonist at the postsynaptic 5-hydroxytryptamine 1A (5-HT1A) receptor that is believed to enhance the activity of SSRIs through the 5HT1A receptors; and • Sustained-release bupropion (Wellbutrin SR) whose neurochemical action mechanisms are unknown but is believed to produce antidepressant effects by blocking the reuptake of dopamine and norepinephrine (Trivedi et al., 2006a, p. 1244).
Step 3 Switch study	• Nortriptyline (Pamelor), a tricyclic antidepressant; and • Mirtazapine (Remeron), a tetracyclic antidepressant that blocks inhibitory α2-adrenoceptors on norepinephrine and serotonin neurons to enhance both norepinephrine and serotonin neurotransmission (Fava et al., 2006, p. 1169).
Step 3 Augmentation study of step 2's drug(s)	• Lithium; and • Triiodothyronine (Cytomel), a thyroid hormone.
Step 4 Switch study	• Tranylcypromine (Parnate), a monoamine oxidase inhibitor; and • Coadministered venlafaxine (Effexor) and mirtazapine (Remeron) to inhibit the reuptake of both serotonin and norepinephrine and block inhibitory α2-adrenoceptors on both norepinephrine and serotonin neurons to enhance both norepinephrine and serotonin neurotransmission.

EVIDENCE OF APPARENT BIAS IN PIGOTT ET AL. ARTICLE

Pigott, Leventhal, Alter, and Boren (2010) recently published an article on the status of antidepressants' efficacy and effectiveness research. This article's effectiveness section focused on a detailed reanalysis of STAR*D and discovered evidence suggestive of bias, which inflated STAR*D's reported acute-care remission rates while not reporting forthrightly its rate of relapse and/or dropout during the 12 months of continuing care. Specifically, Pigott et al. documented that:

- STAR*D changed its outcome measures following data collection. As designed, STAR*D's prespecified primary measure was the HRSD and the Inventory of Depressive Symptomatology—Clinician-Rated (IDS-C30), the secondary one for identifying "remitted" (i.e., those with a ≤7 HSRD score) and "responder" (i.e., those with a ≥50% reduction in depressive symptoms) patients. These measures were obtained in interviews by research outcome assessors (ROAs) blind to treatment assignment at entry into and exit from each trial and every 3 months during the 12 months of continuing care.
- STAR*D dropped the IDS-C30 and replaced it with the Quick Inventory of Depressive Symptomatology–Self-Report (QIDS-SR), a proprietary tool developed by STAR*D's principal investigators. The QIDS-SR was not a prespecified research measure, but rather one of STAR*D's "clinical management tools" that was used to guide care during every treatment visit. In the Pigott et al. paper's peer-review process, a reviewer wrote that the National Institute of Mental Health's (NIMH) Data Safety and Monitoring Board (DSMB) authorized the use of the QIDS-SR prior to "data lock and unblinding" because of STAR*D's high study dropout rate, which frequently resulted in missing exit IDS-C30 and HRSD assessments. Pigott et al. made this change in the paper, even though it could not be documented in the published literature. Subsequently, this author learned that no such DSMB authorization occurred (see the succeeding discussion).
- STAR*D changed its eligibility for analysis criteria in the steps 2–4 and summary articles without making this change explicit to readers. This change resulted in 607 patients who were initially reported as excluded because their <14 score on the ROA-administered baseline HRSD signified at most only mild depressive symptoms when starting on citalopram (Celexa) in step 1 subsequently being included. Similarly, an additional 324 patients who were initially reported as excluded because they lacked a baseline ROA-administered HRSD in step 1 were subsequently included. Thus, 931 of STAR*D's 4,041 patients (23% of all subjects) did not meet its step-1 eligibility for analysis criteria but were included in the steps 2–4 and summary articles' analyses.
- STAR*D failed to disclose that all 4,041 patients were started on citalopram (Celexa) in their initial baseline visit and that they excluded from analysis the 370 patients who dropped out without any subsequent visits, although the step-1 article states, "our primary analyses classified patients with missing exit HRSD scores as nonremitters a priori" (Trivedi, Rush, et al., 2006, p. 34). These early dropout patients did not take the exit HRSD and therefore should have been counted as treatment failures as prespecified.
- STAR*D did not disclose how to interpret the quarter-by-quarter survival data for continuing-care patients and thereby obscured from readers their startling finding that only 108 of the 1,518 remitted patients (7.1%) had not relapsed and/or dropped out by continuing-care's 12th month (see Table 2).

The cumulative effect of these decisions inflated STAR*D's reported findings, giving a false impression of antidepressants' optimal effectiveness with patients commonly prescribed these drugs. For example, STAR*D's major summary article reports a 36.8% remission rate in step 1 based on the QIDS-SR (Rush, Trivedi, Wisniewski, Nierenberg, et al., 2006, p. 1905).

TABLE 2. Survival Analysis by Treatment Step for Remitted and All Remitted/Responder Patients Who Consented to Continuing Care

Treatment Step and Status on Entry Into Continuing Care	N[a]	0–3 Months[b]	3–6 Months[b]	6–9 Months[b]	9–12 Months[b]
Step-1 remitted patients	1,085	628 (57.9%)	431 (39.7%)	290 (26.7%)	84 (7.7%)
Step-2 remitted patients	383	199 (52%)	133 (34.7%)	79 (20.6%)	20 (5.2%)
Step-3 remitted patients	35	16 (45.7%)	11 (31.4%)	8 (22.9%)	2 (5.7%)
Step-4 remitted patients	15	8 (53.3%)	5 (33.3%)	5 (33.3%)	2 (13.3%)
Survival Rate by Quarter for All Remitted Patients	1,518	851 (56.1%)	580 (38.2%)	382 (25.2%)	108 (7.1%)
Step-1 remitted/responder patients	1,475	803 (54.4%)	529 (35.7%)	347 (23.5%)	98 (6.6%)
Step-2 remitted/responder patients	622	300 (48.2%)	190 (30.5%)	115 (18.5%)	29 (4.7%)
Step-3 remitted/responder patients	102	37 (36.3%)	22 (21.6%)	15 (14.7%)	3 (2.9%)
Step-4 remitted/responder patients	49	20 (40.8%)	12 (24.5%)	9 (18.4%)	2 (4.1%)
Survival Rate by Quarter for All Patients Who Entered Continuing Care	2,248	1,160 (51.6%)	753 (33.5%)	486 (21.6%)	132 (5.9%)

[a]Number of patients entering continuing care (Rush, Trivedi, Wisniewski, Nierenberg, et al., 2006, Figures 2 and 3).

[b]Number of patients who called in at least once into the IVR system during this time period and did not score has having relapsed in this or a prior time period (Rush, Trivedi, Wisniewski, Nierenberg, et al., 2006, Figures 2 and 3).

Actually, though, only 790 of the 3,110 patients (25.4%) who had a baseline ≥14 HRSD score met the prespecified remission criterion. STAR*D's reported 36.8% step-1 remission rate for citalopram (Celexa) inflates this drug's actual rate by 44.9%.

Numerous recent meta-analyses and systematic reviews have found that selective outcome reporting bias, in which researchers fail to report the negative results for the prespecified primary measure and instead highlight positive results from a new measure as though it was their primary measure of interest, plagues industry-sponsored research and significantly inflates the reported outcomes (Mathieu, Boutron, Moher, Altman, & Ravaud, 2009; Rising, Bacchetti, & Bero, 2008; Turner, Matthews, Linardatos, Tell, & Rosenthal, 2008; Vedula, Bero, Scherer, & Dickersin, 2009). Reporting outcomes, as prespecified, is essential to ensure the integrity of clinical research because it guards against investigators selectively publishing results that merely reinforce their original expectations and beliefs by changing the prespecified measures and planned analyses

following data collection and analysis—a form of researcher bias known as *HARKing*, an acronym for "hypothesizing after the results are known" (Kerr, 1998). Although such HARKing is most commonly associated with industry-sponsored research, Chan, Krleza-Jerić, Schmid, and Altman (2004) document its occurrence in publicly funded research as well. Such was the case in STAR*D.

ADDITIONAL EVIDENCE SUGGESTIVE OF BIAS BEYOND THE SCOPE OF PIGOTT ET AL.

Deception in Justifying the Use of the QIDS-SR

As stated previously, in the Pigott et al. peer-review process, a reviewer claimed that STAR*D's DSMB had authorized using the QIDS-SR as an outcome measure prior to "data lock and unblinding." To better understand what took place in this study, the author filed a Freedom of Information Act (FOIA) request for STAR*D's contract, the contract's research protocol, its statistical analytic plan, the minutes from all DSMB meetings, and the quarterly and annual progress reports submitted by the investigators to NIMH (Pigott, 2010a). The author received from NIMH the contract and research protocol, which included the analytic plan but not the DSMB meeting minutes or any quarterly or annual progress reports. The author was informed that these later documents could not be located and may have been destroyed (NIMH, 2010b). Despite not receiving all that was requested, the contract, research protocol, and analytic plan were very helpful in providing additional information in understanding STAR*D's original purpose, measures, methods, and planned analyses (NIMH, 2002).

In its published reports, STAR*D's authors never inform readers that the QIDS-SR was explicitly NOT intended to be used as a research measure. Instead, when stating the reasons for dropping the HRSD and using only the QIDS-SR to report the step-by-step acute and continuing-care remission and relapse rates in the summary article, its authors' state:

> We used the QIDS-SR as the primary measure to define outcomes for acute and follow-up phases because 1) QIDS-SR ratings were available for all participants at each acute treatment clinic visit, 2) QIDS-SR and HRSD outcomes are highly related, 3) the QIDS-SR was not used to make treatment decisions, which minimizes the potential for clinician bias, and 4) the QIDS-SR scores obtained from the interactive voice response system, the main follow-up outcome measure, and the paper-and-pencil QIDS-SR are virtually interchangeable, which allows us to use a similar metric to summarize the acute and follow-up phase results. (Rush, Trivedi, Wisniewski, Nierenberg, et al., 2006, p. 1908)

STAR*D authors' assertion that "the QIDS-SR was not used to make treatment decisions" is a half-truth at best. Although the QIDS-SR was not the sole or final measure for making treatment decisions, it was clearly part of STAR*D's 'clinical decision support system' as the authors themselves state in their step-1 article:

> To enhance the quality and consistency of care, physicians used the clinical decision support system that relied on the measurement of symptoms (QIDS-C and QIDS-SR), side-effects (ratings of frequency, intensity, and burden), medication adherence (self-report), and clinical judgment based on patient progress. (Trivedi, Rush, et al., 2006, p. 30)

Also in the controlled clinical trials article, the QIDS-SR is identified as one of several measures used "to provide consistent information to the clinicians who use this information in the protocol" (Rush, Fava, et al., 2004, p. 128). Furthermore, on pages 32 and 47 of the research protocol, the researchers explicitly distinguish between the research outcomes assessments that were conducted by ROAs blind to what treatment(s) the patient had received and the nonblinded assessments, such as the QIDS-SR that were collected at every clinic visit and used to guide care, stating, "The latter are designed to collect information that guides clinicians in the implementation of the treatment protocol. Research outcomes assessments are not collected at the clinic visits. They are not collected by either clinicians or CRCs" (pp. 47–48). STAR*D authors' assertion that "the QIDS-SR was not used to make treatment decisions" is highly deceptive since by their own admission it was part of STAR*D's clinical decision support system and *not* a research measure.

Second, although STAR*D's authors report that the "QIDS-SR and HRSD outcomes are highly related," the question is: Were patients' last-administered QIDS-SR "highly related" to the HRSD for those who dropped out and did not take the HRSD? STAR*D's claim is based on their research correlating the QIDS-SR and HRSD assessments in patients continuing in active treatment at the end of step 1 (Rush, Bernstein, et al., 2006). STAR*D provides no research supporting its use of the nonblinded QIDS-SR in the last visit to determine the remission status for those patients who dropped out without taking the blinded HRSD. STAR*D states that the reason for dropping out was not obtained for the "vast majority" of such patients (Rush, Trivedi, Wisniewski, Nierenberg, et al., 2006, p. 1908) and 24% (690 of 2,876) dropped out without taking the exit HRSD in step 1 alone.

Patients dropping out are by definition different from patients continuing in treatment in their estimation of the value of the free care that they are receiving. This is particularly true in STAR*D because the QIDS-SR was overseen by the CRC who also administered in every visit a clinician-interview version of this same tool (the QIDS-C) that had the identical 16 questions and response options as the QIDS-SR (in education, this practice would be considered an extreme example of teaching to the test). Furthermore, given that the CRC also provided patient education ensuring that patients understood the basic "mechanism of action" for their current antidepressant and educating the patient that "depression is a disease, like diabetes or high blood pressure" and "can be treated as effectively as other illnesses," the demand characteristics for patients to answer the QIDS-SR in a manner more consistent with the CRC's patient education than their actual experience was likely high for many patients who dropped out without informing the CRC of their plans to do so. STAR*D's authors were well aware of these demand characteristics and their potential to bias results in this open-label study, which is why in the research protocol, they emphasized, "Research outcomes assessments are not collected at the clinic visits. They are *not* collected by either clinicians or CRCs."

Finally, STAR*D states that the "QIDS-SR scores obtained from the IVR-system, the main follow-up outcome measure, and the paper-and-pencil QIDS-SR are virtually interchangeable, which allows us to use a similar metric to summarize the acute and follow-up phase results" (Rush, Trivedi, Wisniewski, Nierenberg, et al., 2006, p. 1908). Just as the QIDS-SR was NOT a research measure, the interactive voice response (IVR) version was NOT STAR*D's "main follow-up outcome measure." Although STAR*D's objective to use "a similar metric to summarize the acute and follow-up phase results" is admirable, such outcome metrics had already been both prespecified and collected—the blindly

administered HRSD and IDS-C30. STAR*D's authors chose not to report to readers its results as prespecified nor inform readers that they were not doing so. Instead, they resorted to deception to justify their use of the QIDS-SR, a sham measure, to report outcomes.

Bias by Omission

STAR*D lacked a control group in every phase despite its authors being fully aware that it was common for antidepressants to not differentiate from placebos in controlled trials. In an editorial, STAR*D researcher Michael Thase (2007) acknowledges that drug/placebo differences are often nonexistent in antidepressant drug trials, whereas Maurizio Fava estimated that placebo's true response rate in antidepressant trials was 35%–45% since most failed trials go unpublished (Fava, Evins, Dorer, & Schoenfeld, 2003). By not including a placebo in any phase, STAR*D's researchers and NIMH avoided the difficulty of explaining the likelihood that many of the compared drugs would not differentiate from placebo.

The research protocol states in its opening abstract using capital letters that STAR*D was a comparative EFFECTIVENESS study of different treatment options for people with major depression. In this regard, STAR*D was a well-designed study that had 12 prespecified research outcome measures and a detailed analytic plan for evaluating the effectiveness and cost-efficiency of 11 pharmacologically distinct drug treatments (along with cognitive psychotherapy) for depressed patients who failed to improve from their first antidepressant trial. These measures included preassessment/postassessment of depressive symptoms, level of functioning, patient satisfaction, quality of life, side-effect burden, health care utilization and cost of care, health status, work productivity, and personal income (NIMH, revised 2002 pages 48–51; Rush, Fava, et al., 2004, p. 127–131; Fava, et al., 2003, 476–479) as well as reassessing remitted patients every 3 months on these same measures during 12 months of free continuing care.

Despite it being 5 years since the completion of STAR*D's data collection and its authors having published more than 70 peer-reviewed articles on its findings, none of these articles have reported the pre/post mean change scores for any of the 12 prespecified measures nor reported its findings in a manner consistent with the analytic plan as presented in STAR*D's research protocol (e.g., see pp. 55–62 that describe STAR*D's plan for comparing the cost-effectiveness of the antidepressant treatments, including their impact on overall health care utilization and cost of care) and background articles (Fava, et al., 2003, 476–479; Rush, Fava, et al., 2004, p. 127–131, 135–136).

STAR*D's raison d'être was to compare treatments in their ability to both relieve depressive symptoms and improve patients' health status, functioning, and quality of life while also assessing the offsets to the cost of providing such drug care through reductions in healthcare utilization and costs.

Given the "substantial public health and scientific significance" of this information, it is deeply troubling that STAR*D's researchers have still not published these findings despite it being 4 years since the publication of the summary article and having ample funding to complete this effort. Instead, out of the more than 70 articles STAR*D's authors have published (NIMH, 2009), the vast majority have little relevance from either a treatment or health care policy perspective, and such studies' trivial nature is evidenced by their not being included in the analytic plan. This triviality is exemplified in STAR*D's most recently published study, this one on insomnia, that concludes "insomnia symptoms are very common, undertreated, and indicative of a more severe depression" (Sunderajan

et al., 2010, p. 394). This article fails to report any outcomes, not even the effectiveness of adding trazodone or a sedative to insomniac patients' antidepressant, which frequently occurred in this study (e.g., Rush, Trivedi, Wisniewski, Stewart, et al., 2006, Table 2). Therefore, $35 million later, we still do not know even if the common practice of adding one drug to another drug for depressed insomniac patients improves any outcome, only that insomnia is "indicative of a more severe depression."

STAR*D's failure to publish its findings as prespecified is highly suggestive that antidepressant drug care failed to deliver the wide range of positive outcomes and offsetting costs its authors and NIMH expected so they chose not to publish this damning data.

The author therefore filed a second FOIA request for all data analytic reports provided by STAR*D's investigators to NIMH as specified in the contract as well as any correspondence regarding modifications to the contract authorizing the investigators to deviate from the analytic plan (Pigott, 2010b). This request resulted in a conference call with George Niederehe, the government program officer responsible for overseeing all aspects of STAR*D, and Stephen Wisniewski, STAR*D's chief biostatistician. When asked for these analyses, the author was told that to their knowledge, they were never performed. Niederehe also stated that the publication of STAR*D's results constituted the investigators' fulfillment to NIMH of the contract's data analytic reporting requirements, and if such analyses have not been published, they were likely never conducted (Pigott, 2010c). Both then stated that STAR*D's dataset is now available to researchers to perform such analyses as well as any others deemed warranted (NIMH, 2010a). Additional highlights from this call include:

- Both denied that STAR*D's DSMB authorized using the QIDS-SR prior to "data lock and unblinding" as Pigott et al. had been informed by the reviewer. Instead, they stated that this decision occurred in the Communications Committee meetings for which notes were not taken as they were for the DSMB meetings.
- Wisniewski acknowledged that the QIDS-SR was not a prespecified research measure but stated that the reason this was not disclosed in the steps 1–4 and summary articles was that "there was not enough journal space" and noted that they did report the HRSD remission rates as the primary outcome in the steps 1–4 articles. Wisniewski's justification for not using the HRSD in the summary article was that it was not part of the main study, only a secondary analysis; therefore, it was not necessary to use the HRSD to report outcomes in this article.
- At the call's conclusion, Niederehe explained that in government research contracts such as STAR*D, it was common for changes to be made without documentation.

After the call, the author reread the contract and found additional contractually required reports from the contractor and therefore has filed a third FOIA requesting them (Pigott, 2010d).

Biased Interpretation of Results

Besides documenting antidepressant drugs' general lack of effectiveness even when optimally administered, STAR*D's findings failed to support its neurochemical imbalance theory of depression. STAR*D's hypothesis was that patients who failed to respond adequately during the prior step did so because the drug(s) did not produce the "right" neurochemical change. Therefore, "switching" to a new drug, or combination of new drugs, with a different neurochemical "mechanism of action," or "augmenting" the current

drug(s) with a new drug that has a different neurochemical action, might trigger the "right" change resulting in remission (Boren, 2007).

To develop the science necessary to guide such "next-step" decision-making, STAR*D carefully selected each new drug and drug combinations to be evaluated based on those found most promising in prior research while ensuring that each step's compared drugs had distinct pharmacological profiles (see Table 1). Surprisingly, there were no significant differences in the five next-step comparisons of 11 pharmacologically distinct drug treatments, even though the *N* per each specific treatment ranged from 51 to 286 patients and was therefore more than sufficient to identify meaningful differences if any existed.

Despite the lack of significant differences in all five comparisons and this fact's logical meaning, STAR*D's authors assert, "These results also have provocative theoretical implications. The findings are suggestive that major depressive disorder is biologically heterogeneous such that different treatments differ in the likelihood of achieving remission in different patients" and then go on to make the obligatory observation, "However, without a placebo control at each step and without substantial differences in remission rates among treatments in the same step, such a notion remains to be fully established" (Rush, Trivedi, Wisniewski, Nierenberg, et al., 2006, p. 1913).

Fundamentally, STAR*D's findings suggest no such "biologically heterogeneous" theory in which "different treatments differ in the likelihood of achieving remission in different patients." What is "provocative" is STAR*D's authors ignoring the obvious. Because of the similar remission rates in all five comparisons, the most parsimonious explanation is that it did not matter what drugs were prescribed because every compared drug or drug combination yielded about the same effect as every other drug or drug combination. To reconcile STAR*D's theory with their findings requires that in every comparison:

- Each class of biologically needed change was equally dispersed across treatments (a reasonable assumption given random assignment); and
- Each class's size was always essentially equivalent, allowing no statistically significant separation in outcomes between them (a highly dubious assumption).

For instance, it requires in step 2's switch comparison where the three drugs triggered an indistinguishable remission rate averaging 21.2% that:

- Those patients needing a selective serotonin reuptake inhibitor (SSRI) versus "dual-action" versus "out-of-class" agent were equally dispersed into the three compared strategies; and
- Each of the three compared groups' *N* was always approximately 21% of the total *N*, with an additional 37% needing an as-of-yet untested neurochemically derived change.

For STAR*D's theory to remain plausible, this scenario would have to then be repeated in all four other comparisons.

Second, step 2's switch comparison also contradicts this theory. In this comparison, sertraline (Zoloft), an SSRI neurochemically similar to step 1's SSRI citalopram (Celexa), was no different in effectiveness and tolerability as bupropion (Wellbutrin) and venlafaxine (Effexor), even though 56% of step 2's "switch" patients were found intolerant to citalopram (Celexa) in step 1 (Trivedi, Fava, et al., 2006, p. 1240).

Since patients who failed to gain a step-1 remission were by STAR*D's definition "SSRI medication resistant" (Trivedi, Rush, et al., 2006, p. 30), and 56% of step 2's switch patients were "citalopram intolerant," why was a similar SSRI as effective and tolerable in

step 2 for such highly "SSRI resistant and intolerant" patients as were bupropion (Wellbutrin) and venlafaxine (Effexor) with their different pharmacological profiles? This finding directly contradicts STAR*D's theory, yet was not even discussed in step 2's switch article nor the summary article.

Third, the fact that STAR*D allowed liberal prescribing of nonstudy drugs during every step precludes its authors' ability to assert anything regarding different drug treatments "achieving remission in different patients" because it is impossible to disentangle what were the unique effects of the compared drugs versus their coadministration with other nonstudy drugs. For example, in step 2's switch comparison, 17.1% of patients were also prescribed trazodone, 16.5% a sedative or hypnotic drug, and 11.8% an anxiolytic (Rush, Trivedi, Wisniewski, Stewart, et al., 2006, Table 2). Given this, the only "provocative" observation STAR*D's authors should have made is that even with such polypharmacy efforts, their outcomes were far less than expected.

A final fact contradicting STAR*D's theory is its staggering relapse rate such that by follow-up's 12-month conclusion, 94.2% of all "remitted" patients had relapsed and/or dropped out. If "different treatments differ in the likelihood of achieving remission in different patients," why the loss of efficacy for so many patients so quickly while continuing to take the same drug(s) that allegedly were the bases for their remissions? Again, STAR*D's authors never address this, or any of the other glaring inconsistencies to their "biologically heterogeneous" theory, yet instead claim support for that which their results disprove.

Small Biases Reflecting BIG BIAS

STAR*D's authors demonstrate a pattern of rounding up their findings, thereby inflating the reported remission and response rates. In the step-2 switch study in which the combined HRSD remission rate for the three switch medications was 21.2%, the authors state in the abstract's conclusion section that "approximately one in four patients had a remission of symptoms after switching to another antidepressant" (Rush, Trivedi, Wisniewski, Stewart, et al., 2006, p. 1231). Evidently, STAR*D's authors failed to realize that 21.2% is closer to "one in five" than "one in four" patients.

STAR*D's summary article's "Acute Treatment Outcomes by Treatment Step" Table 3 has rounding "errors" in steps 1–3 each time inflating STAR*D's reported remission and response rates by 0.1 to 0.2 points (Rush, Trivedi, Wisniewski, Nierenberg, et al., 2006, p. 1910). In step 1, STAR*D reports that 1,346 of 3,671 patients had a QIDS-defined remission, and STAR*D then reports this as a 36.8% remission rate. Actually, 1,346 divided by 3,671 is equal to 0.36665; therefore, STAR*D should have rounded it up to only 36.7% versus 36.8%. Similar rounding-up "errors" occurred in calculating steps 2 and 3's remission rates.

This same pattern occurs in STAR*D's reported response rates. In step 1, 1,776 of 3,671 patients had a QIDS-defined response, and STAR*D reports this as a 48.6% response rate when actually 1,776 divided by 3,671 is equal to 0.48379; therefore, it should have been rounded up to only 48.4% versus 48.6%. Again, similar rounding-up "errors" occurred in steps 2 and 3's reported response rates.

In this same table, STAR*D also calculated the step-by-step rates of intolerable side effects in the row immediately below those for remission and response. There were no rounding errors in these four calculations. Therefore, out of 12 calculations—8 of whom

reported antidepressants' remission and response rates—STAR*D had rounding-up errors in 75% (6 of 8) of those reporting its already inflated QIDS-SR rates and none in those reporting the intolerable side-effect rates. Although the inflationary effect of these rounding UP "errors" was trivial, the pattern's consistency speaks volumes.

In the summary article's result section, STAR*D's authors calculated a theoretical cumulative remission rate of 67% based on the inflated QIDS-SR whose findings they inflated further. In this article's discussion section, they assert that "the overall cumulative remission rate would approach 70% after four steps (if needed)" (Rush, Trivedi, Wisniewski, Nierenberg, et al., 2006, p. 1912). In an article published in the *Cleveland Clinic Journal of Medicine* targeting primary care physicians (PCPs), STAR*D's authors' final "Key Point" states, "With persistent and vigorous treatment, most patients will enter remission: about 33% after one step, 50% after two steps, 60% after three steps, and 70% after four steps (assuming patients stay in treatment)" (Gaynes et al., 2008, p. 57).

When it comes to reporting remission rates, STAR*D's progression is always UP. The highly inflated 67% becomes "approach 70%" and finally "70% after four steps," with no acknowledgment in the Cleveland Clinic article that this theoretical rate is based on the assumption that dropouts would have had the same remission rate as those who did not dropout nor acknowledge the often short-lived duration of said "remissions" nor acknowledge that this alleged "cumulative" rate was based on a sham measure.

Inflating the Extent of Improvement From Antidepressant Drug Treatment

STAR*D's authors inflated the extent of improvement that patients obtained from achieving remission. In the Cleveland Clinic article's "Key Points" section, the first point states, "Remission (i.e., complete relief from a depressive episode) rather than response (merely substantial improvement) should be the goal of treatment, as it is associated with a better prognosis and better function" (Gaynes et al., 2008, p. 57). This description of remission is similar to STAR*D's statement in its controlled clinical trials article that describes remission as "the complete absence of depressive symptoms" and then defined remission as a score of ≤ 7 on the HRSD (Rush, Fava, et al., 2004, p. 121).

Although an HRSD ≤ 7 score is a common criterion for classifying remission in depression research, such a score is by no means synonymous with "complete relief from a depressive episode" or "the complete absence of depressive symptoms" because patients could have up to seven HRSD symptoms mildly expressed and still met this criterion. For example, on the HRSD suicide question, "feels like life is not worth living" is scored as 1; "recurrent thoughts or wishes about death of self" is scored as 2; "active suicidal thoughts, threats, gestures" is scored as 3; and a recent "serious suicide attempt" is scored as 4. Similar progressions in severity are found on all of the questions such that for the guilt and delusions question, "feels he/she has let people down" is scored as 1; for the work and interest question, "feels incapable, listless, less efficient" is scored as 1; and for the libido question, "has decreased sexual drive and satisfaction" is scored as 1. A patient scoring 1 on just these four HRSD questions would be counted as remitted with three "mild" symptoms to spare, yet few would describe such a patient as experiencing "complete relief" from his or her depressive episode because each of these symptoms is used in diagnosing major depression.

As should be obvious, in the absence of STAR*D reporting on the quality of life, level of functioning, and side-effect burden research measures that they collected, no reader can

judge the extent of improvement that the drug treatments actually bought about for the "remitted" patients. We do know though that it was certainly not "complete relief" and a return to euthymia because patients could have up to seven depressive symptoms and still be counted as having obtained remission.

Apparent Bias by the *American Journal of Psychiatry*

The *American Journal of Psychiatry* (AJP) published five of STAR*D's seven outcome articles. Many of the apparent biases indentified in this paper should have been corrected through competent peer review. Examples include:

- Insisting that STAR*D's authors disclose the fact that all 4,041 patients were started on citalopram (Celexa) in their baseline visit. Even with careful reading, this fact is not disclosed in either the step-1 or the summary articles. Instead, the summary article's patient flowchart misleads readers into believing that only 3,671 patients were in the step-1 citalopram (Celexa) trial. This is because in the patient flowchart's top level is a box stating "Enrolled (N=4,041)," followed by a box to the side with "No postbaseline visit (N=370)," and the figure's "Level 1" treatment box stating "Citalopram (N=3,671)" (Rush, Trivedi, Wisniewski, Nierenberg, et al., 2006, Figure 1), leading to the false assumption by many that the citalopram (Celexa) trial consisted of only 3,671 patients. In evaluating antidepressants use with real-world patients under optimal conditions, it is critical for readers to know that 9.2% of depressed patients who consented to antidepressant care, had started STAR*D's multistep "depression-as-disease" model educational program, and begun free SSRI treatment dropped out without a follow-up visit.
- Insisting that STAR*D report its acute and continuing-care remission and relapse rates using the HRSD. The HRSD was identified as STAR*D's primary outcome measure in the steps 1–4 articles. By dropping the HRSD in its summary article, STAR*D significantly inflated its acute-care remission rates with unknown effects on its purported relapse rate. AJP reviewers should not have allowed this switch because simply reading the steps 1–4 abstracts stating the HRSD and QIDS-SR remission rates would have alerted them to its inflationary effects.
- Not allowing STAR*D's authors to falsely assert that "the QIDS-SR was not used to make treatment decisions" as justification for using it as the sole measure to report its summary findings. Again, simply reading AJP's step-1 article makes explicit that the QIDS-SR was part of STAR*D's "clinical decision support system."
- Insisting that STAR*D's authors exclude the 931 patients who were enrolled into the study without a ROA-administered baseline ≥14 HRSD or, at a minimum, disclosing these patients' enrollment in a straightforward manner. Instead, this disclosure was dispersed over three pages in the summary article. Again, simply comparing the step-1 AJP article's QIDS-SR remission rate of 32.8% to the step-1 QIDS-SR remission rate of 36.8% as reported in the summary article demonstrates the inflationary effects of this decision.
- Insisting that STAR*D's authors report in the summary article how to interpret the three survival analysis tables and discuss the survival analyses' astonishing findings that out of the 1,518 remitted patients, only 108 (7.1%) survived continuing care without relapsing and/or dropping out.

In that AJP published most of the STAR*D outcome studies, Pigott et al. submitted their paper to AJP and only after rejection to Psychotherapy and Psychosomatics. This submission included a detailed letter to Robert Freedman, the journal's editor, documenting multiple instances of bias in the AJP-published STAR*D articles that warranted correction to better inform readers. The letter highlighted how an unbiased presentation of STAR*D's findings discredits the American Psychiatric Association's (APA) continuation

phase guideline that "following remission, patients who have been treated with antidepressant medications in the acute phase should be maintained on these agents to prevent relapse" despite this recommendation having received its expert panel's highest "clinical confidence" rating (APA, 2000, p. 15).

The letter also offered to send Freedman the author's July 2008 e-mail exchanges with Wisniewski confirming the accuracy of the paper's analysis so that this information could be provided to AJP peer reviewers. Freedman never requested the Wisniewski e-mail exchanges. Pigott et al.'s AJP submission resulted in a form-letter rejection with no comment on the paper's substance or indication that it was sent out for peer review. AJP's refusal to allow an examination of apparent bias in its STAR*D publications combined with incompetent peer review suggests a disregard for open and honest science on its leadership's part.

Clear Bias by NIMH

STAR*D was an NIMH-initiated research contract starting in September 1999 and continuing for 7 years with additional follow-on studies that are still in progress today—not a mere research grant award in response to a request for proposals. NIMH was therefore intimately involved in STAR*D's oversight because of its expense and public health significance. This involvement included three NIMH employees being coauthors on four or more of the steps 1–4 and summary articles; two being research branch chiefs, Barry Lebowitz and George Niederehe who was also STAR*D's government program officer with ultimate oversight responsibility for the study. Louise Ritz, the third NIMH employee/coauthor, was also STAR*D's program officer with day-to-day oversight responsibilities.

It is troubling, with glaring conflicts of interest, when those charged with oversight in taxpayer-funded research are also included in the spoils of publication. These spoils in STAR*D were not inconsequential. Through their oversight roles, both Niederehe and Ritz became coauthors of articles in the *New England Journal of Medicine* (NEJM) and AJP; Niederehe coauthored one article in NEJM and six in AJP and Ritz coauthored two articles for each journal. Who was watching out for the public interest by ensuring the scientific integrity and proper reporting of findings in this study? Was it John Rush, STAR*D's principal investigator, who disclosed 19 conflicts of interests, the vast majority of which were with pharmaceutical companies, OR was it the federal employees included in prestigious publications? Who? Evidently not the other coauthors who averaged 9.8 disclosed conflicts each; ten of whom report receiving money from Forest Pharmaceuticals, the maker of citalopram/Celexa based on their conflict of interest disclosures in the steps 2-4 and summary articles. As noted previously, the summary article inflated this drug's remission rate by 44.9%.

NIMH was fully complicit in the biased reporting of STAR*D's results as evidenced by the contract provision that none of the study findings could be "released, presented at meetings, or published" without the prior "review and approval" of the Government Program Officer (NIMH STAR*D Contract, 1999, p. 21). This provision is similar to those commonly found in pharmaceutical-industry sponsored studies and renders meaningless the statement that "The content of this article does not necessarily reflect the views or policies of the Department of Health and Human Services" which appears at the end of each STAR*D article.

Rather than insisting on forthright and honest reporting in peer-reviewed articles, NIMH issued STAR*D press releases that are highly misleading to both professionals and

people with depression on the likely benefits from antidepressant drug care. Examples of this bias include:

- The title of NIMH's press release and web page summarizing the step-2 results published in NEJM is: "New Strategies Help Depressed Patients Become Symptom-Free" and includes a quote from NIMH's Director Thomas Insel stating:

  > If the first treatment attempt fails, patients should not give up. By remaining in treatment, and working closely with clinicians to tailor the most appropriate next steps, many patients may find the best single or combination *[drug]* treatment that will enable them to become symptom-free. (NIMH, 2006a, para. 5)

- The step-2 NIMH press release refers eight times to remitted patients becoming "symptom-free" and includes a quote from STAR*D author Madhukar Trivedi stating, "Augmenting the first medication may be an effective way for people with depression to become symptom-free" (NIMH, 2006a, para. 11).
- NIMH's press releases summarizing the step-3 and step-4 results continue to state that remitted patients became "symptom-free," repeating this false claim four times in the step-3 press release (NIMH, 2006d) and five more times in the step-4 press release (NIMH, 2006b). In the step-4 press release, NIMH adds to the misrepresentation by stating, "Over the course of all four levels, about 70 percent of those who did not withdraw from the study became symptom-free." (para. 4)
- NIMH's (2006c) summary results' press release states in the opening paragraph, "In STAR*D, the outcome measure was a 'remission' of depressive symptoms—becoming symptom-free" ("5. What were the results?" para. 1) and then repeats this false "symptom-free" claim 17 more times.

Both NIMH and STAR*D's authors were well aware that remitted patients' HRSD ≤ 7 score was not synonymous with them becoming "symptom-free," given the severity of symptoms such as "feels like life is not worth living" and "feels incapable, listless, less efficient" that are scored as only 1 on this measure. NIMH leadership's decision to repeatedly state in its press releases and Internet website that "almost 70%" of those patients who persisted through STAR*D's various drug trials became "symptom-free" makes medical claims for antidepressant drugs' level of effectiveness that are simply not true and suggests a profound pro-drug bias within this taxpayer-funded agency.

Additional evidence of NIMH's pro-drug bias is that instead of insisting that STAR*D's results be published as prespecified, NIMH rewarded STAR*D's lead investigators with new taxpayer funding to conduct the *Combining Medication to Enhance Outcomes of Depression* (CO-MED) study, evaluating polypharmacy drug treatments of depression (ScienceDaily, 2008b). Furthermore, these investigators secured an additional 1.2 million taxpayer dollars from the Agency for Healthcare Research and Quality to develop and evaluate a computerized version of their proprietary "measurement-based system" for ensuring "high-quality" antidepressant drug care (ScienceDaily, 2008a). Both of these taxpayer funded initiatives appear designed to foster further a drug-centric approach to treating depression.

DISCUSSION

This article identifies numerous instances of apparent bias by STAR*D's authors as well as AJP's and NIMH's leadership. This bias significantly inflated the alleged benefits of

antidepressant drug treatment while not disclosing the staggering relapse and/or dropout rate that occurred in those patients who initially responded favorably.

In contrast to the STAR*D authors' and NIMH's false representations Pigott et al.'s analysis found that of the 4,041 patients initially started on citalopram (Celexa), only 1,518 patients (37.6%) obtained remission after up to four medication trials and entered STAR*D's free continuing care. In every drug trial, more patients dropped out than were remitted and this dropout rate increased throughout the study. Of these 1,518 remitted patients, only 108 (7.1%) survived continuing care without relapsing and/or dropping out. Moreover, it is not known how many of these few patients were one of the 607 patients whose baseline <14 HRSD signified at most only mild symptoms when first started on citalopram (Celexa) and therefore had to score worse during continuing care than when they first entered the study to be counted as relapsed, nor how many actually remained "in remission" during continuing care. This reality directly counters NIMH leaderhip's false claim that "about 70 percent of those who did not withdraw from the study became symptom-free."

In a 2009 article, Insel acknowledges the severe inadequacy of the neurochemical imbalance theory of mental disorders to advance treatment outcomes and later states that there is "no evidence that the morbidity or mortality of mental disorders has dropped substantially in the past decades" despite the increased use of second-generation antidepressant and antipsychotic drugs to treat them with these drugs having "a combined market of $25 billion" in 2007 in the United States alone (Insel, 2009, pp. 701, 703). Rather than not "substantially" dropping though, the morbidity and chronicity of mental disorders appears to be increasing with a twofold to threefold increase between 1987 and 2007 in the number of Americans receiving disability payments for such disorders (Whitaker, 2005, 2010). Although there are certainly multiple factors affecting this increased disability rate, the fact that this dramatic increase has occurred during the same time as the dramatic increased use of second-generation psychotropic drugs to treat these disorders—combined with the emergence of APA's continuation phase treatment guidelines calling for essentially the open-ended use of same—demands serious investigation and not simply dismissing Whitaker's investigative journalism out of hand because it is counter to accepted wisdom.

In the same article, Insel observes that in every large comparative effectiveness study of second-generation drugs for depression, schizophrenia, and bipolar disorder, these drugs have repeatedly been found to be no better than their first-generation cousins from the 1950s, 1960s, and 1970s despite their added costs (and this reality is despite the tens of billions spent over decades in public and private research efforts to make improvements in said drugs). In this same section, Insel also acknowledges that even "after 14 weeks of optimal treatment with the second-generation medication citalopram," STAR*D's step-1 success rate was no different from that commonly found by placebos in controlled trials. Insel then goes on to state, "The unfortunate reality is that current medications help too few people to get better and very few people to get well" (Insel, 2009, pp. 703–704).

Insel's belated acknowledgment of the dismal outcomes from psychotropic drug care is a far cry from his 2006 claims regarding STAR*D's results. This author searched in vain on NIMH's website to find anything indicative of this more sober assessment of psychotropic drugs effectiveness, yet instead found information more in common with the pharmaceutical industry's marketing efforts than an unbiased taxpayer-funded research institute committed to fostering sound science to advance the treatment of mental disorders.

By failing to insist on an accurate reporting in 2006 of STAR*D's comparative effectiveness findings as specified in this 35-million-dollar contract—and instead repeatedly making false claims of the alleged "symptom-free" benefits achieved through try-try-try-and-try-again drug care—NIMH's leadership subverted and delayed an honest reappraisal of antidepressant drugs' appropriate role in the treatment of depression.

NIMH's long-standing pro-drug bias as documented by Whitaker has had profound public health consequences (Whitaker, 2010). Each year, major depression disorder affects approximately 6.7% of American adults (Kessler, Chiu, Demler, & Walters, 2005), with costs exceeding $80 billion per year, two thirds of which are caused by the disability and workplace-related costs that are associated with it (Greenberg et al., 2003; Kessler, et al., 2006). This reality is not caused by a lack of pharmaceutical efforts. Between 1996 and 2005, Americans' prescribed antidepressant drugs almost doubled, increasing from 5.8% to 10.1% of all those 6 years of age or older, with a concurrent significant increase in the average number of antidepressant drug prescriptions filled per patient/per year from 5.6 to 6.93 (Olfson & Marcus, 2009). During this same period, psychiatrists significantly increased their use of polypharmacy such that outpatient visits resulting in two or more prescribed psychotropic drugs increased from 42.6% in 1996 to 59.8% in 2005 and psychiatry visits resulting in three or more such drugs being prescribed doubled, increasing from 16.9% to 33.2% (Mojtabai & Olfson, 2010). This increased polypharmacy has occurred despite the fact that meta-analyses of antidepressant drug augmentation strategies have found significant increased risk of adverse events with only exceptionally modest (if any) added benefit from such polypharmacy efforts whether the augmentation be with another antidepressant or an atypical antipsychotic drug (Nelson & Papakostas, 2009; Yury, Fisher, Antonuccio, Valenstein, & Matuszak, 2009).

Antidepressant drugs' failure to promote sustained recovery is not something newly discovered by Pigott et al.'s STAR*D reanalysis. As Pigott et al. noted, although APA's continuation phase guideline recommending open-ended use of antidepressant drugs is consistent with meta-analyses reporting large effect sizes for them in preventing relapse (e.g., Geddes et al., 2003), these analyses do not control for publication bias nor selective outcome reporting, both of whom significantly inflate the report of positive findings.

Instead, despite the APA's highest "clinical confidence" rating for this guideline, prospective studies have documented excessively high relapse and/or dropout rates resulting from the continued use of these drugs. For example, Rush, Trivedi, et al. (2004) found a sustained remission rate of only 5.1% over 12 months in 118 depressed patients treated by following a decision "algorithm" to guide drug treatment and providing patient/family education teaching the importance of these drugs to treat depression. Even this 5.1% rate though is an overestimation because the study used last observation carried forward (LOCF) analysis such that patients who dropped out before study completion, but had not scored as relapsed in their last assessment, were counted as having achieved a sustained remission; evidently, LOCF enthusiasts are unaware that depressed patients commonly discontinue drug treatment when their once helpful drug stops working and their depression returns. In 2008, Bockting et al. reported the results of 172 patients with recurrent depression and found that only 42% used antidepressants continuously during 2 years of continuation phase treatment of which 60.4% relapsed while taking these drugs, whereas patients who stopped using them experienced significantly less relapse, with only 8% of those who received preventive cognitive therapy relapsing. In STAR*D, even for step 1's 1,085 remitted patients,

only 84 (7.7%) did not relapse and/or dropout during continuing care (see Table 2), and these few patients had the greatest likelihood of achieving a sustained remission.

The concept that continuation phase antidepressant drug treatment may increase versus decrease depression's chronicity and likelihood of relapse is not new. While endorsing the use of antidepressants during acute-care treatment for major depressive disorder, in 1994, Giovanni Fava proposed that long-term use of antidepressant and antianxiety drugs increases the neurobiological vulnerability of some patients to affective disorders while decreasing the likelihood of positive response to new drug treatments when symptoms reemerge (Fava, 1994). In a 2003 systematic review, Fava found evidence suggesting very poor long-term outcomes from continuation phase antidepressant drug treatment and that in some patients, such continued drug use appears to foster changes that counter the drug's initial beneficial effects resulting in (1) loss of efficacy with symptom worsening, (2) increased risk of relapse during drug withdrawal, (3) drug-induced switching to mania and rapid mood cycling in bipolar patients, and (4) diminished responsiveness to subsequent drug treatment (Fava, 2003). Fava termed this hypothesized phenomena *oppositional tolerance*. In an updated 2010 systematic review, Fava and Offidani found additional support for this hypothesis and conclude by stating

> When we prolong treatment over 6–9 months we may recruit processes that oppose the initial acute effects of antidepressant drugs (loss of clinical effects). We may also propel the illness to a malignant and treatment-unresponsive course that may take the form of resistance or episode acceleration. When drug treatment ends, these processes may be unopposed and yield withdrawal symptoms and increased vulnerability to relapse. Such processes are not necessarily reversible. The more we switch or potentiate antidepressant drugs the more likely is oppositional tolerance to take place. (Fava & Offidani, 2010)

Fava's oppositional tolerance hypothesis is supported by both the dismal continuing-care findings from antidepressant drug–effectiveness studies and the apparent 1987-to-2007 increase in disability caused by mental disorders that is correlated with the increased usage of these drugs. Viewed from the perspective of oppositional tolerance, there is little wonder why STAR*D's "try-try-try-and-try-again" approach to care yielded such poor "real-world" results and highlights the folly of relying on drug efficacy trials to guide practice because of the selective publication and outcome reporting biases that plague this body of research.

In addition to the risk of oppositional tolerance from continued care on these drugs, STAR*D found that 8.6% of step-1 patients reported increased suicidal ideation while taking citalopram (Celexa) during acute phase treatment (Perlis et al., 2007). Furthermore, in another article STAR*D reported that 71.3% of those who had a remission during acute-care treatment reported increased weight gain while taking citalopram (Celexa) and 71.7% reported residual symptoms of sleep disturbance despite having achieved "remission" status (Nierenberg et al., 2010). The increased weight gain during acute-care SSRI drug treatment is of particular significance because a recent study of 165,958 depressed patients found that long-term treatment with SSRIs doubled their risk of developing diabetes (Andersohn, Schade, Suissa, & Garbe, 2009).

In light of the modest to no drug/placebo advantage for antidepressants in the now five meta-analyses free from publication bias, combined with the substantial adverse risks from using these drugs, it is hard to find any reason for their first-line "come-one-come-all" use to treat depression other than convention, ease to prescribe for physicians, and the success of pharmaceutical

companies' relentless marketing efforts (Barbui, Furukawa, & Cipriani, 2008; Eyding et al., 2010; Kirsch, Moore, Scoboria, & Nicholls, 2002; Kirsch et al., 2008; Turner et al., 2008).

As emphasized in Pigott et al., APA's continuation phase guideline is profoundly misguided because there is no apparent benefit for most patients from continued antidepressant drug treatment, yet this "evidence-based" practice unnecessarily exposes such patients to significant adverse risks.

Unfortunately, APA's depression guidelines have been widely adopted by American health plans, and the National Committee for Quality Assurance (NCQA) has incorporated APA's acute and continuation phase guidelines into its measurement system to use in determining each plan's accreditation by tracking the percentage of newly diagnosed depressed adults who are treated with an antidepressant drug and remain on an antidepressant drug for at least 6 months (NCQA, 2009). To gain (and maintain) NCQA accreditation, health insurance plans are evaluated on their success in keeping depressed patients taking their antidepressant drugs, with such plans, in turn, increasingly using this same metric to evaluate and grade physicians.

Furthermore, under the Affordable Care Act all health insurance policies must begin providing 100% reimbursement for depression screening by PCPs with no co-pay required by patients as part of this act's mandated preventative services (Affordable Care Act, 2010). Although, in theory, more widespread identification of depressed patients may be beneficial, in practice, PCPs already prescribe most antidepressant drugs and this will only increase further, thereby channeling even more patients into open-ended drug treatment because of NCQA's accreditation requirements. The potential adverse public health consequences from the act's mandatory depression screening coverage are significant because of the very low depression threshold that is commonly applied when prescribing antidepressants (Zimmerman et al., 2002) particularly in the prescribing of these drugs by PCPs (Mojtabai & Olfson, 2008).

"First, do no harm" has become an abandoned concept when treating depression because of the APA and NIMH leaderships' long-standing pro-drug biases. These biases have resulted in misguided public health policy as evidenced by NCQA's Orwellian-like metric and now the U.S. government's depression screening coverage mandate.

Until such misguided efforts and pro-drug biases are corrected, America will likely see continuing increases in the chronicity and disability caused by depression and other mental disorders. It is far past time for an honest reappraisal of antidepressant drugs' role in the treatment of depression. Critical to this reappraisal is an analysis of STAR*D's comparative effectiveness dataset by independent researchers according to STAR*D's prespecified outcome measures and analytic plan. People with depression and their families, the public interest, and honest science deserve no less because of STAR*D's "substantial public health and scientific significance" once its findings are accurately analyzed and reported.

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Conflicts of Interest. H. Edmund Pigott is a partner in NeuroAdvantage, LLC, a neurotherapy company. In 2010, Ed Pigott has consulted for Amen Clinics, Brain Resources, CNS Response, EEG Spectrum International, International Society of Neurofeedback and Research, and Neuronetics.

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JS 44 (Rev. 12/07)

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The JS 44 civil cover sheet and the information contained herein neither replace nor supplement the filing and service of pleadings or other papers as required by law, except as provided by local rules of court. This form, approved by the Judicial Conference of the United States in September 1974, is required for the use of the Clerk of Court for the purpose of initiating the civil docket sheet. (SEE INSTRUCTIONS ON THE REVERSE OF THE FORM.)

DISTRICT COURT DISTRICT OF MARYLAND

I. (a) PLAINTIFFS

U.S. et al. EX REL. H Edmund Pigott

(b) County of Residence of First Listed Plaintiff _____
(EXCEPT IN U.S. PLAINTIFF CASES)

(c) Attorney's (Firm Name, Address, and Telephone Number)

Waters & Kraus, LLP. 315 North Charles Street, Baltimore, MD, 21201. (410) 528-1153

DEFENDANTS

Forest Pharmaceuticals, Inc.

2011 MAR 17 P 3:46

AT BALTIMORE

County of Residence of First Listed Defendant St. Louis County, MO
(IN U.S. PLAINTIFF CASES ONLY)

NOTE: IN LAND CONDEMNATION CASES, USE THE LOCATION OF THE LAND INVOLVED.

BY _____ DEPUTY

Attorneys (If Known)

WMN11CV 717

II. BASIS OF JURISDICTION (Place an "X" in One Box Only)

- ☒ 1 U.S. Government Plaintiff
- ☐ 3 Federal Question (U.S. Government Not a Party)
- ☐ 2 U.S. Government Defendant
- ☐ 4 Diversity (Indicate Citizenship of Parties in Item III)

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- ☐ 130 Miller Act
- ☐ 140 Negotiable Instrument
- ☐ 150 Recovery of Overpayment & Enforcement of Judgment
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- ☐ 152 Recovery of Defaulted Student Loans (Excl. Veterans)
- ☐ 153 Recovery of Overpayment of Veteran's Benefits
- ☐ 160 Stockholders' Suits
- ☐ 190 Other Contract
- ☐ 195 Contract Product Liability
- ☐ 196 Franchise

REAL PROPERTY
- ☐ 210 Land Condemnation
- ☐ 220 Foreclosure
- ☐ 230 Rent Lease & Ejectment
- ☐ 240 Torts to Land
- ☐ 245 Tort Product Liability
- ☐ 290 All Other Real Property

TORTS

PERSONAL INJURY
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- ☐ 315 Airplane Product Liability
- ☐ 320 Assault, Libel & Slander
- ☐ 330 Federal Employers' Liability
- ☐ 340 Marine
- ☐ 345 Marine Product Liability
- ☐ 350 Motor Vehicle
- ☐ 355 Motor Vehicle Product Liability
- ☐ 360 Other Personal Injury

PERSONAL INJURY
- ☐ 362 Personal Injury - Med. Malpractice
- ☐ 365 Personal Injury - Product Liability
- ☐ 368 Asbestos Personal Injury Product Liability

PERSONAL PROPERTY
- ☒ 370 Other Fraud
- ☐ 371 Truth in Lending
- ☐ 380 Other Personal Property Damage
- ☐ 385 Property Damage Product Liability

CIVIL RIGHTS
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- ☐ 442 Employment
- ☐ 443 Housing/ Accommodations
- ☐ 444 Welfare
- ☐ 445 Amer. w/Disabilities - Employment
- ☐ 446 Amer. w/Disabilities - Other
- ☐ 440 Other Civil Rights

PRISONER PETITIONS
- ☐ 510 Motions to Vacate Sentence

Habeas Corpus:
- ☐ 530 General
- ☐ 535 Death Penalty
- ☐ 540 Mandamus & Other
- ☐ 550 Civil Rights
- ☐ 555 Prison Condition

FORFEITURE/PENALTY
- ☐ 610 Agriculture
- ☐ 620 Other Food & Drug
- ☐ 625 Drug Related Seizure of Property 21 USC 881
- ☐ 630 Liquor Laws
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- ☐ 650 Airline Regs.
- ☐ 660 Occupational Safety/Health
- ☐ 690 Other

LABOR
- ☐ 710 Fair Labor Standards Act
- ☐ 720 Labor/Mgmt. Relations
- ☐ 730 Labor/Mgmt.Reporting & Disclosure Act
- ☐ 740 Railway Labor Act
- ☐ 790 Other Labor Litigation
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IMMIGRATION
- ☐ 462 Naturalization Application
- ☐ 463 Habeas Corpus - Alien Detainee
- ☐ 465 Other Immigration Actions

BANKRUPTCY
- ☐ 422 Appeal 28 USC 158
- ☐ 423 Withdrawal 28 USC 157

PROPERTY RIGHTS
- ☐ 820 Copyrights
- ☐ 830 Patent
- ☐ 840 Trademark

SOCIAL SECURITY
- ☐ 861 HIA (1395ff)
- ☐ 862 Black Lung (923)
- ☐ 863 DIWG/DIWW (405(g))
- ☐ 864 SSID Title XVI
- ☐ 865 RSI (405(g))

FEDERAL TAX SUITS
- ☐ 870 Taxes (U.S. Plaintiff or Defendant)
- ☐ 871 IRS—Third Party 26 USC 7609

OTHER STATUTES
- ☐ 400 State Reapportionment
- ☐ 410 Antitrust
- ☐ 430 Banks and Banking
- ☐ 450 Commerce
- ☐ 460 Deportation
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- ☐ 875 Customer Challenge 12 USC 3410
- ☐ 890 Other Statutory Actions
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- ☐ 900Appeal of Fee Determination Under Equal Access to Justice
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V. ORIGIN (Place an "X" in One Box Only)

☒ 1 Original Proceeding ☐ 2 Removed from State Court ☐ 3 Remanded from Appellate Court ☐ 4 Reinstated or Reopened ☐ 5 Transferred from another district (specify) ☐ 6 Multidistrict Litigation ☐ 7 Appeal to District Judge from Magistrate Judgment

VI. CAUSE OF ACTION

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Brief description of cause:
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DEMAND $

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03/17/2011

SIGNATURE OF ATTORNEY OF RECORD
George Tarbutt, III

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