Causality and Collateral Estoppel: Process and Content of Recent SSRI Litigation

Paul D. Whitehead, MD

In *Tobin v. SmithKline Beecham Pharmaceuticals* a jury in the U.S. District Court for the District of Wyoming found that the medication Paxil "can cause some individuals to commit homicide and/or suicide," and that it was a legal cause of the deaths in this case. A motion was recently put before the United States District Court for the District of Utah to adopt the findings of the *Tobin* case—via the application of collateral estoppel—to a case involving an individual's suicide while prescribed Paxil. This article summarizes these two cases, as reflected in court documents, and comments on limitations of common causality assertions.

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Tobin v. SmithKline Beecham Pharmaceuticals (SKB)[1] is the first paroxetine, wrongful death/suicide case to go to a jury trial in the United States. The following facts were stipulated by both parties.

On February 13, 1998, Donald Schell, a 60-year-old man living in Gillette, Wyoming, shot and killed his 55-year-old wife, 31-year-old daughter, 9-month-old granddaughter, and then himself. When discovered the following day, the victims had multiple large- and small-caliber gunshot wounds to their heads and shoulders. Mr. Schell had a large wound to his head and a .357 revolver near his hand. The coroner estimated that the deaths had occurred in the early morning. Mr. Schell had been married since 1961. He had a history of depression and had been treated at times with psychotherapy, fluoxetine, trazodone, lorazepam, and imipramine. After becoming depressed again, he saw his physician on February 10, 1998, to obtain sleeping pills. He received a diagnosis of depression and was prescribed zolpidem for sleep and paroxetine (Paxil) for the depression. Two paroxetine and two zolpidem pills were not accounted for at the time of his death, and toxicology reports indicated 13 ng/mL of paroxetine and 11 ng/mL of zolpidem in his blood.

Dr. Whitehead is a Forensic Psychiatrist and Clinical Director, Forensic Acute Unit, Utah State Hospital, Provo, UT. Address correspondence to: Paul D. Whitehead, MD, 1300 E. Center Street, Provo, UT 84603. E-mail: pwhitehe@utah.gov

Collateral information[2] indicates Mr. Schell had experienced five prior episodes of depression that were serious enough to keep him out of work. He had a history of not following treatment recommendations given by multiple psychiatrists, problems at work involving a threatened lawsuit, and other stressors.

The estate of the family brought suit against SKB, alleging that Mr. Schell's actions were the result of Paxil. SKB initially filed a motion for summary judgment, contending that the "learned intermediary doctrine," in which physicians have the duty to be informed of the characteristics of the prescribed medication in light of patient susceptibilities, shielded it from liability. The court denied the motion based on the prescribing physician's deposition that warnings might have changed his prescribing decision (in contrast to *Woulfe v. Eli Lilly & Co.*,[3] and *Motus v. Pfizer, Inc.*,[4] where summary judgments were granted based on the treating physician's testimony that a warning regarding suicide risk with selective serotonin reuptake inhibitors (SSRIs) would not have altered the prescribing decision.)

At trial, there were 46 jury instructions. According to Jury Instruction 22, plaintiffs sought to recover damages on two theories: a negligence theory for failure to test, and a claim of inadequate warnings. SKB contended the homicides/suicide were a result of Mr. Schell's depression, not the two ingested Paxil pills. Jury Instruction 25 stated that the burden was on the

plaintiffs to establish by a preponderance of evidence the following: (1) that Paxil can cause some individuals to commit homicide and/or suicide; (2) that Paxil was a proximate cause of Donald Schell's committing the homicides and suicide; (3) that SKB knew, or should have known, that Paxil can cause some individuals to commit homicide and/or suicide and that the defendant failed to make such tests as are reasonably necessary to determine the presence of any defects that render Paxil unsafe for its intended use or for any reasonably foreseeable uses; and (4) that the negligent failure to test was a proximate cause of the homicides and suicide in this litigation.

Plaintiffs relied on the testimony of two experts, both of whom have testified in similar SSRI cases. The first, David Healy, MD, PhD, opined that Paxil can cause murder/suicide by inducing either extreme anguish, akathisia, or agitation; psychotic decompensation; or emotional blunting. He "generally suggested that all SSRIs can produce a state of affairs which make an individual who may not have been likely to commit suicide before taking the pill, more likely to do so while on a course of treatment" (Ref. 5, p 3) His testimony was offered regarding general causation—that Paxil can induce suicidal ideation in a vulnerable subset of people. His opinion was based on his research and experience, several self-authored supporting studies, and "an extensive literature on SSRIs in respect to these possibilities." The plaintiffs' second expert, a psychiatrist and psychoanalyst, performed a psychological autopsy and testified regarding specific causation—that Mr. Schell's ingestion of Paxil led to the fatal results. According to his expert report, quoted in a court order (*sic*):

> [I]t is generally understood by most psychiatrists that a certain number of patients, perhaps five percent, will develop restlessness and anxiety when prescribed selective serotonin uptake inhibitor drugs (SSRIs). . . . Furthermore, a certain number of depressed patients are known to "switch" in to hypomanic states when treated with antidepressant drugs. When a patient has a hypomanic history (Mr. Schell appears to have had none) or already exhibits akathisic symptoms (Mr. Schell did), SSRI compounds should not be prescribed because they have the potential to make the anxiety much worse, indeed, to make it unbearable. There are credible reports of patients becoming suicidal and homicidal when thrown into intolerable states of anguish by prescription of these drugs. . . . Further, we know that depressed patients given SSRI drugs are more likely to harm themselves than are those who are given tricyclic antidepressants. . . . Already anxious, his mind speeding, and sleepless, when given an SSRI in 1998, he quickly became violent and killed his family and himself. . . . In this case I can identify only one factor which triggered the murders and subsequent suicide—Paxil. . . . Though we lack details of what exactly Mr. Schell's mental state was on that fatal night, it is clear to me that it was Paxil that drove him out of control [Ref. 5, p 4].

Prior to trial, SKB filed a motion to limit or exclude the testimony of plaintiffs' causality experts based primarily on methodologies supporting their opinions. Plaintiffs countered that their methodologies and opinions were based on the best scientific evidence and that the study by Donovan *et al.*[6] provided significant support for them. The data in this study was proffered by plaintiffs to claim that the frequency of "deliberate self-harm" for people taking SSRIs is five and one-half times higher than individuals taking tricyclic antidepressants. The court denied defendant's motion, finding that the causality opinions were sufficiently grounded in reliable methodology—such as being consistent with Koch's Postulates—to establish causation. The court added that the causality experts' reliance on the Donovan study—"which represents at least one clear study demonstrating that significantly more self-harm occurred following prescription of an SSRI than that of a tricyclic-antidepressant" (Ref. 5, p 22)—as well as their own analysis and experience, provided a sufficiently reliable foundation for their opinions regarding Paxil and suicide, and that Dr. Healy's opinions had attained sufficient general acceptance in the scientific community. Fifteen days after the trial began, the jury returned a unanimous verdict in favor of the plaintiffs. SKB then moved for a new trial, arguing that the verdict was not supported by reliable scientific evidence and that the general causation expert inappropriately testified to specific causation as well. The court denied the motion and emphasized that Dr. Healy, although "impassioned and overresponsive," presented evidence supporting the jury's conclusion that Paxil can induce a state of heightened agitation that would eventually cause a person to become homicidal or suicidal and that warnings to this effect might have changed the prescribing decision. The jury awarded in excess of $6 million to the plaintiffs. *Tobin v. SKB* was initially appealed to the Tenth Circuit Court of Appeals but was subsequently settled and dismissed.

According to plaintiffs' causality expert reports in *Coburn v. SmithKline Beecham* (GSK),[7,8] George Coburn was a 56-year-old man who lived in Utah and had 13 children. He had a history of depression treated with nortriptyline in the early 1990s, and

there was evidence of past suicidal ideation in the 1980s. Twice in 1994 he was treated with antidepressants for a recurrence of depression. He was reported as "not tolerating" sertraline well—although medical records were not detailed in this respect. In 1996 he visited his physician, who diagnosed severe depression and prescribed 10 mg paroxetine daily with instruction to increase to 20 mg after 10 days. According to several family members, he had difficulty sleeping, reported the "medicine is making me feel worse" and had "the shakes." He did not report suicidal ideation or plan to his family or doctor. He died of carbon monoxide poisoning, two days after beginning the 20-mg dose. He worked until the weekend before his death. He had an alcoholic father, a sister with bipolar disorder and schizophrenia who had killed her two children and herself, a grandson who had died in an accidental fall at home two months before Coburn's suicide, a brother who died in a car accident, a daughter who had suicidal ideation, a wife who was afflicted with lupus, a niece who suffered from depression, and another daughter who attempted suicide by ingestion of lye subsequent to Coburn's death. He had financial pressures and a $10,000 loan payment due the month of his death. He had no medical problems other than sexual impotence, which according to a plaintiff's expert was probably first caused by sertraline and later aggravated by paroxetine.

The *Coburn* plaintiffs' submitted reports by three experts, including again, Dr. Healy. In addition to data including healthy volunteer studies conducted by SKB, he utilized information from interviewing senior figures in psychopharmacology, nonpublished studies, and published literature related to the level of ghost-writing in articles sponsored by the pharmaceutical industry, to support the identical general causation opinion as that in *Tobin.* According to the plaintiffs' second causality expert, a PhD psychologist specializing in suicidology, the proximate causes of the suicide were both depression and paroxetine. He noted that prior to prescription of paroxetine, Mr. Coburn had signs and symptoms of depression and thoughts of death and suicide for at least two weeks and opined that paroxetine can make depressed patients worse through the above-described mechanisms. The expert believed it was unclear whether Mr. Coburn actually had akathisia based on conflicting reports from family members, but by virtue of his past inability to tolerate sertraline and poor response to nortriptyline, inferred that Mr. Coburn had physical reactions to all of his antidepressants—"whether this reaction was emotional blunting and/or akathisia is difficult to determine. He certainly became withdrawn, restless, anxious, and 'vibrated' or shook" (Ref. 8, p 12). The expert believed that paroxetine was a proximate cause of the suicide by Mr. Coburn entering a "suicide zone" due to adverse reactions, that apart from taking paroxetine, he was only "moderately suicidal," and that it was more likely than not that had he not taken paroxetine, he would not have committed suicide. The third expert, board certified in internal medicine, wrote that he intended to testify that SKB acted in an unreasonable manner by marketing paroxetine without adequate warnings about the risks of suicide and homicide, in view of the evidence of a strong causal relationship and that both Dr. Healy's expert report in the *Tobin* case and his articles confirmed his opinion.

Plaintiffs, represented by the same attorney as the *Tobin* plaintiffs, then filed a motion for partial summary judgment based on the doctrine of offensive, nonmutual collateral estoppel. This motion urged the Utah court to adopt two findings of fact from the *Tobin* case: that paroxetine can cause some individuals to commit homicide and/or suicide, and that SKB is at "fault" for its failure to warn either prescribing physicians or patients about this risk. Granting the motion would preclude pretrial challenges to the causality experts' qualifications to render opinions on these issues, would eliminate the need for any proof regarding these findings at trial, and would compel the court to instruct the jury that it must accept these findings. Plaintiffs argued that application of collateral estoppel would be consistent with the underlying policies of the doctrine[9] (i.e., to economize judicial resources and lessen the burdens of relitigating an issue "identical" to one that has already been decided) and that the requisite four factors required in the Tenth Circuit,[10] enumerated in a case involving negligent dispersion of radioactive waste, were satisfied.

The Utah district court denied the collateral estoppel motion, based on ambiguity around what the jury had actually decided in *Tobin*, as several nonspecific theories had been offered on how Paxil could cause some people to commit homicide and/or suicide and any "vulnerable subpopulation" was undefined and undefinable based on the verdict. The court noted that even if the elements of collateral

estoppel had been satisfied, it would still deny this motion under its broad discretion to determine when it is appropriately applied and that to preclude SKB from litigating general causation and fault issues would be fundamentally unfair. For instance, the jury could not merely be told that paroxetine "can cause some people to commit homicide and/or suicide," without some guidance as to the probability of such. The court declined to "enshrine a jury verdict in a way that could trump the FDA's determination of safety and effectiveness and jeopardize the availability of a product that is beneficial to many people" (Ref. 7, p 15). The court highlighted that the *Tobin* jury's verdict was necessarily based on experts whose testimony has not been found to be consistently reliable—such as another SSRI case in the District of Kansas, *Miller v. Pfizer*,[11] where the *Daubert* hearing on this issue was pending (see Comment). The specific causation expert from *Tobin* was noted to have had his testimony rejected by another court.[12] *Coburn v. SKB* was ultimately settled out of court.

Comment

Primarily at issue in SSRI-litigation is the infrequent extent to which medication side effects become problematic or exacerbation of psychiatric conditions occur, with consequent possibility of violence. In *State of Connecticut v. DeAngelo*,[13] an individual was adjudicated not guilty by reason of insanity in significant part because of behavioral sequelae of SSRI-induced mania; although touted by the defense attorney and accompanying press as a straightforward "Prozac defense," multiple confounding and comorbid variables were also present to the degree that, even absent SSRI use and risk of concomitant mania, an involuntary commitment of up to 10 years was ordered by the court. This comment does not address various controversies involving this type of litigation but focuses instead on limitations of common causality assertions.

Proponents of the theory of SSRI-induced homicide/suicide argue that the pharmaceutical industry has fraudulently marketed products and co-opted psychiatric research to obfuscate suicide/homicide risks, in a manner similar to tobacco companies with cancer risks. Some suggest that there is a "profile" for SSRI-induced violence, such as mass murder, school violence, adolescent suicide, or deaths in a manner purportedly atypical for people with depression (e.g., violent death without previous mention of suicide or leaving behind a suicide note).[14–16] Proponents appear to rely characteristically and disproportionately on a limited pool of data to support causality conclusions: their own publications, those of similar causality experts, several studies from the early 1990s, and alleged unpublished data of pharmaceutical companies.

Substituting for any actual psychiatric examination by causality experts are nonspecific descriptors to explain behaviors of a decedent. Implicit in this practice are obvious limitations: terms such as "agitation," "emotional indifference," or "anguish," have little meaning absent a specific and applicable contextual matrix. Some would be known *a priori* to have accompanied any fatal event independent of either SSRI use or nexus to mental illness. Their use runs the risk of taking on special meaning when amplified by public myths and fears[17] regarding people with mental illness. Nonspecificity of these terms is arguably demonstrated by the frequency of "agitation" as a possible side effect in over 16 percent of all medications listed in the Physicians' Desk Reference.[18]

Little information is typically provided by causality expert reports regarding the specific factual backdrop of each case. In *Coburn*, for instance, reports embark on statistical inferences on data allegedly distorted by pharmaceutical companies. Little emphasis is given to the timing of the doctor appointment or the context in which it was made and the medications prescribed—often in the wake of accelerating symptoms and events. Reductionistic expressions of causality appear to be applied independent of events involved in the incident. This is troubling, given the extent that SSRIs are prescribed in high risk populations. Little is offered by causality experts to frame appropriately possible side effects such as akathisia (e.g., its frequency and relative treatability, in what context it might be more or less of a risk, its nonspecificity to SSRIs, the frequency of similar complaints even before SSRI use, or the capacity of most patients to bring this complaint to professional attention). The safeguarding role of regulatory agencies that disagree with causality experts' conclusions is claimed to be tainted by distorted data. The magnitude of independent research that has established the relative safety of these medications is generally ignored, and the widespread and standard-of-care use of these medications in forensic and correctional settings by

patients with an already demonstrated capacity to kill is not mentioned.

In *Miller v. Pfizer*, the presiding judge appointed two independent physician-scientists from academic centers to review Dr. Healy's methodology regarding sertraline-induced suicide at issue in that case. Essentially none of Dr. Healy's asserted claims withstood dispassionate and detailed scientific scrutiny: methodology was generally thought not to be reliable and not to have been accepted in the scientific community, and calculations of relative risks were neither reproducible nor subjected to peer review.[19] For example, Dr. Healy's published articles addressing the association between sertraline and suicide—used as a foundation for his opinions and mentioned as a factor by the *Tobin* court in the *Daubert* finding—were noted by the independent reviewers to comprise a "thought piece" of possible mechanisms by which suicide could happen, and a trial of two agents given to 20 patients with a component of qualitative analysis: "neither article formally proposes new or modified methods to establish causality, and their publication does not endorse (via the editors or reviewers) such methodology" (Ref. 19, pp 1, 2). Also noted was an off-point citing of the *American Psychiatric Press Textbook of Psychiatry*[20] to support causality arguments (Ref 19, p 6). The *Miller* court's finding on the *Daubert* factors ultimately excluded Dr. Healy's testimony due to "flaws in methodology. . .that are glaring, overwhelming, and unexplained."[21,22] His specific causation conclusion was also found to fall short of admissibility standards, because of his failure to take into account highly relevant and undisputed evidence.

Contrary to the usual scientific process regarding causality inferences,[23] competing theories and confounding variables appear minimally explored by causality experts. One example is the possible role of alcohol. When alcohol or illicit substances are detected subsequent to violent behavior while the individual was taking an SSRI, some causality experts and plaintiffs argue that the ingestion was either caused by the SSRI (the *DeAngelo* case) or occurred after the violent act (Ref. 15, see *Omdahl v. Pfizer, Inc.*) Superimposed are assertions that appear to minimize risks inherent in major depressive disorder, such as Dr. Healy's claims that lifetime rates of suicide in primary care mood disorders are "very low," and suicide rates among 13-year-olds are "vanishingly low" (Ref. 19, p 6).

The Donovan study was cited in the *Tobin* court's *Daubert* findings. Among other critics of this study who comment that it is "open to grave misinterpretation,"[24] are its own authors, who highlight the study's specific limitations and admonish against extrapolating causality from it. Also significant is the suggestion fostered by causality experts, and seemingly adopted by the *Tobin* court, that "deliberate self-harm" is synonymous with "suicide." The *Tobin* court's *Daubert* findings recently resonated in a case in the Western District of Pennsylvania—*Cassidy v. Eli Lilly & Co.*,[25] where the court cited data presented there by Dr. Healy to accept that his theory had attained general acceptance in the scientific community; the Donovan study was again cited as significant to that opinion. In sum, process and content of recent SSRI litigation reflect an unsettling sequence: self-authored and methodologically limited data, by virtue of having been peer reviewed and published, are equated with mainstream scientific consensus. Then, application of collateral estoppel is attempted (and probably will continue to be attempted) to fuse the data into dogma shielded from further scientific scrutiny.

The 1990s Decade of the Brain inadvertently underscored terms such as "chemical imbalances" to explain mental illness.[26,27] During the Leopold and Loeb trial of 1924, psychiatric experts invoked social and psychological determinism to explain the vagaries of human behavior.[28] Arguably, *Tobin* experts set an opposite but equally dogmatic benchmark for biochemical reductionism. Reductionistic emphasis on biochemistry as cause of behavior, combined with controversial experts, confusing jargon, suggestions of corporate malfeasance, and widespread myths about mental illness, present challenges to courts navigating these issues. Independent of rebutting experts, several processes have been helpful in this respect: court-appointed scientific experts were useful in *Miller v. Pfizer*, and during the *DeAngelo* commitment proceedings, a psychiatric consultant to the state's attorney aided in illuminating what the court ultimately construed as an opinion lacking objectivity by the psychiatrist-author of *Toxic Psychiatry*.[29] There is a place for SSRI litigation and a need to monitor symptoms and side effects. Ultimately, the process and content of recent SSRI litigation add weight to the potential value of peer review and formalized study of expert testimony[30] and run the risk

of further stigmatizing mental illness and promulgating fear in people seeking treatment.

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