22-146
Daniels-Feasel v. Forest Pharmaceuticals, Inc.

UNITED STATES COURT OF APPEALS
FOR THE SECOND CIRCUIT

SUMMARY ORDER

RULINGS BY SUMMARY ORDER DO NOT HAVE PRECEDENTIAL EFFECT. CITATION TO A SUMMARY ORDER FILED ON OR AFTER JANUARY 1, 2007, IS PERMITTED AND IS GOVERNED BY FEDERAL RULE OF APPELLATE PROCEDURE 32.1 AND THIS COURT'S LOCAL RULE 32.1.1. WHEN CITING A SUMMARY ORDER IN A DOCUMENT FILED WITH THIS COURT, A PARTY MUST CITE EITHER THE FEDERAL APPENDIX OR AN ELECTRONIC DATABASE (WITH THE NOTATION "SUMMARY ORDER"). A PARTY CITING A SUMMARY ORDER MUST SERVE A COPY OF IT ON ANY PARTY NOT REPRESENTED BY COUNSEL.

At a stated term of the United States Court of Appeals for the Second Circuit, held at the Thurgood Marshall United States Courthouse, 40 Foley Square, in the City of New York, on the 28th day of July, two thousand twenty-three.

Present:

WILLIAM J. NARDINI,
MYRNA PÉREZ,
MARIA ARAÚJO KAHN,
Circuit Judges.

NICHOLE DANIELS-FEASEL, individually and as parent and natural guardian of C.F., JESSICA ANGLIN, individually and as parent and natural guardian of J.A., GINGER EUGLEY, individually and as parent and natural guardian of D.E., CASEY HAYNER, individually and as parent and natural guardian of T.P., DEBORAH DIMEGLIO, Individually and as parent and natural guardian of L.D., REBECCA WARBERG, as parent and natural guardian of B.W.,

Plaintiffs-Appellants,

LANA RUTHART, individually and as parent and natural guardian of L.M.,

Plaintiff

v. 22-146

FOREST PHARMACEUTICALS, INC., FOREST LABORATORIES, LLC, FOREST

LABORATORIES INC., ALLERGAN PLC,

Defendants-Appellees.*

For Plaintiffs-Appellants:	BENJAMIN I. SIMINOU, Singleton Schreiber, LLP, San Diego, CA (Jason Rathod, Migliaccio & Rathod, LLP, Washington, DC; Christopher T. Nidel, Rockville, MD, *on the brief*).
For Defendants-Appellees:	BERT L. WOLFF, Dechert LLP, New York, NY (Lincoln Davis Wilson, Dechert LLP, New York, NY; Jonathan S. Tam, Dechert LLP, San Francisco, CA, *on the brief*).

Appeal from a judgment of the United States District Court for the Southern District of New York (Laura Taylor Swain, *Judge*).

UPON DUE CONSIDERATION, IT IS HEREBY ORDERED, ADJUDGED, AND DECREED that the judgment of the district court is **AFFIRMED.**

Plaintiffs-Appellants bring product liability claims under state law regarding the effects of Lexapro, a prescription antidepressant medication in the therapeutic class of selective serotonin reuptake inhibitors ("SSRIs"). SSRIs are molecules that affect the level and availability of the neurotransmitter serotonin in living tissue, and they play an established role in treating anxiety disorders and major depressive illnesses. Plaintiffs are a group of mothers who allege that they ingested Lexapro during pregnancy, and their minor children who allegedly developed autism spectrum disorder ("ASD") because of their mothers' prenatal use of the drug. Defendants-Appellants are pharmaceutical companies involved in the design, manufacturing, and/or marketing of Lexapro.

Plaintiffs appeal from a December 29, 2021, judgment of the United States District Court

* The Clerk of Court is respectfully directed to amend the case caption as set forth above.

for the Southern District of New York (Laura Taylor Swain, *Judge*) granting summary judgment for Defendants. By opinion and order entered September 3, 2021, the district court granted Defendants' motion to exclude from evidence the testimony of Plaintiffs' expert witnesses, Dr. Lemuel Moyé, Dr. Laura Plunkett, and Dr. Patricia Whitaker-Azmitia, regarding the alleged causal relationship between Lexapro and ASD. By opinion and order entered December 29, 2021, the district court granted Defendants' motion for summary judgment on the ground that, following the exclusion of Plaintiffs' expert testimony, Plaintiffs were unable to prove general causation—that is, that prenatal exposure to Lexapro is capable of causing ASD in the general population.

On appeal, Plaintiffs argue that the district court erred by excluding the testimony of Dr. Moyé, Dr. Plunkett, and Dr. Whitaker-Azmitia. They further claim that, because the district court's order granting summary judgment for Defendants was derivative of its erroneous order excluding Plaintiffs' experts, it should be reversed. We assume the parties' familiarity with the case.

"We review a district court's decision to admit or exclude expert testimony under a highly deferential abuse of discretion standard." *In re Mirena IUS Levonorgestrel-Related Prods. Liab. Litig. (No. II)*, 982 F.3d 113, 122 (2d Cir. 2020) ("*Mirena II*") (internal quotation marks omitted). "A decision to admit or exclude expert scientific testimony is not an abuse of discretion unless it is manifestly erroneous." *Amorgianos v. Nat'l R.R. Passenger Corp.*, 303 F.3d 256, 265 (2d Cir. 2002) (internal quotation marks omitted). "Significantly, the abuse of discretion standard 'applies as much to the trial court's decisions about *how to determine reliability* as to its ultimate conclusion.'" *Id.* (quoting *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999)). Therefore, the district court has broad discretion in determining "what method is appropriate for evaluating reliability under the circumstances of each case." *Id.*

"We review a grant of summary judgment *de novo*, construing the facts in the light most favorable to the non-moving party and drawing all reasonable inferences in that party's favor." *Mirena II*, 982 F.3d at 122 (internal quotation marks omitted). "Summary judgment is appropriate only when 'the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law.'" *Kee v. City of New York*, 12 F.4th 150, 158 (2d Cir. 2021) (quoting Fed R. Civ. P. 56(a)). When we conclude that the district court acted within its discretion in excluding evidence "essential" to a party's claims, we "must also conclude that there [is] no triable issue of material fact" as to those claims. *See LaSalle Bank Nat. Ass'n v. Nomura Asset Cap. Corp.*, 424 F.3d 195, 212 (2d Cir. 2005).

We conclude that the district court acted within its discretion in excluding Dr. Moyé's testimony. Dr. Moyé's expert report determined that maternal use of SSRIs during gestation "is a cause of autism separate and apart from any relationship between maternal depression and autism." Joint App'x 1013. To reach this conclusion, Dr. Moyé synthesized literature examining prenatal SSRI use and ASD "using a weight of the evidence methodology and applying the standard Bradford-Hill criteria." *Id.* at 1010.

Dr. Moyé described the "weight of the evidence" analysis as the "process by which a body of evidence is examined component by component whereby each component is sifted and assessed using a transparent and standard method." *Id.* at 1061–62. "As this study-by-study evidentiary examination proceeds, contributions are made to the arguments for or against causality." *Id.*; *see also In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, 858 F.3d 787, 795 (3d Cir. 2017) ("*Zoloft II*") (cleaned up) ("The 'weight of the evidence' analysis involves a series of logical steps used to infer to the best explanation."). The Bradford Hill factors "form the generally accepted set of criteria by which, when reliably applied, modern practicing epidemiologists assign causality

to an association." Joint App'x 1062; *see also Zoloft II*, 858 F.3d at 795. Among others, the Bradford Hill factors include: (1) strength of association, which measures the degree of statistical association between cause and effect, (2) biological gradient, or "dose response," which assesses whether more exposure to the risk factor is related to greater damage from the disease, (3) biological plausibility, which pinpoints the mechanism by which the risk factor produces the disease, and (4) analogy, which asks whether the proposed cause-effect association is similar to some other known cause-effect association, Joint App'x. at 987 ("For example, the relationship between SSRIs and autism can be more clearly understood if it can be reconciled with the relationship between SSRIs and other birth defects . . . ."). *Id.* at 983–87. Dr. Moyé explains that epidemiologists using the "weight of the evidence" analysis apply the Bradford Hill criteria to "distill" the "peer review[ed] published papers, reflecting the universe of useful information about the state of the relationship between SSRIs and ASD." *Id.* at 1062.

"To ensure that the Bradford Hill/weight of the evidence criteria is truly a methodology, rather than a mere conclusion-oriented selection process[,] there must be a scientific method of weighting that is used and explained." *Zoloft II*, 858 F.3d at 796 (cleaned up). Although an expert could "theoretically assign the most weight to only a few factors, or draw conclusions about one factor based on a particular combination of evidence[,]" "the assessment or weighing of that evidence must not be arbitrary." *Id.* In "deciding whether . . . an expert's analysis is unreliable, the district court should undertake a *rigorous examination* of the facts on which the expert relies, the method by which the expert draws an opinion from those facts, and how the expert applies the facts and methods to the case at hand." *Mirena II*, 982 F.3d at 123.

The district court excluded Dr. Moyé's testimony because, among other things, Dr. Moyé cherry-picked only favorable studies to support his causal conclusion and did not rigorously

explain the weight he attached to each Bradford Hill factor. These determinations were not manifestly erroneous.

First, there was sufficient support for the district court's conclusion that Dr. Moyé cherry-picked only favorable studies. For example, Dr. Moyé opined that the strength-of-association Bradford Hill factor weighed in favor of causation because "[t]here is substantial evidence demonstrating an increase in the incidence of autism associated with SSRI." Joint App'x 1010. He premised this conclusion on three studies showing statistically significant associations between SSRI use in pregnant women and ASD in children. *Id.* Yet, "despite their number," *id.*, he deemed the studies showing *no* statistically significant association (called null or low-association studies) as "unworthy of consideration," *id.*, because they assumed that "a prescription is *prima facie* evidence that the pregnant woman actually" complied and ingested the pill, *id.* at 999–1000, 1009. But, as the district court observed, the problem that pregnant women prescribed SSRIs may not actually be taking them—known as lack of compliance validation—was also present in some of the studies Dr. Moyé cited for the existence of a statistically significant association.

Even though at least one null study acknowledged that "ascertainment bias with respect to exposure . . . add[ed] to the imprecision of [its] estimates," *id.* at 1104, there is no indication that the studies Dr. Moyé disregarded identified a lack of compliance validation as a "critical weakness[]" that fully invalidated their findings, *id.* at 1010. Moreover, although he (1) generally discussed the "unpopularity" of using SSRIs during pregnancy, *id.* at 1058, and (2) cited a separate study for the principle that "the prevalence of SSRI . . . use [during pregnancy in Europe] varied by country" and "in some countries is quite low," *id.*, Dr. Moyé did not discuss precisely why lack of compliance validation in the studies he ignored was a big enough flaw to render them irrelevant.

Therefore, even accepting Plaintiffs' argument that lack of compliance validation operates to understate the relationship between SSRIs and ASD, thus "call[ing] the results of null or low-association studies into doubt," the district court's determination that Dr. Moyé failed to consider contrary evidence was not manifestly erroneous *See* Pl. Br. 69–70.

Another example of cherry-picking is Dr. Moyé's categorical disregard of meta-analyses, several of which suggest that maternal mental illness is a confounding factor in the association between prenatal SSRI use and ASD in children. "When epidemiologists hypothesize that there is a 'true' association which individual studies are underpowered to detect at a statistically significant level, the widely accepted approach to combining data from multiple studies—thus increasing the power to detect an association—is to conduct a systematic meta-analysis." *In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, 26 F. Supp. 3d 449, 457 (E.D. Pa. 2014). Dr. Moyé testified that he gave meta-analyses no weight because, among other reasons, the individual studies they analyze "were not designed, collected, or intended to be combined with data from other studies." Joint App'x 1064. But protocols exist for using pre-specified criteria to ensure that meta-analyses are conducted properly, and meta-analyses are often an integral part of documenting a robust association. Therefore, the district court was not manifestly erroneous in concluding that Dr. Moyé's wholesale omission of meta-analyses was concerning.

Second, the district court acted within its discretion when it determined that Dr. Moyé failed to thoroughly explain how he weighted the Bradford Hill factors he considered. As the district court observed, Dr. Moyé's expert report does not explicitly identify exactly which factors he believes support a causal relationship between maternal use of SSRIs and ASD in children. As examples, he merely suggests that there is "some evidence" in support of the dose-response factor, "[m]echanistic studies point to the effect of SSRIs in the developing fetus" under the biological

plausibility factor, and "[m]any examples of birth defects related to perinatal exposure are available" under the analogy factor. *Id.* at 1010–13. Dr. Moyé's failure to explain whether each factor weighs in favor of general causation significantly hinders the replication and validation of Dr. Moyé's analysis. It is unclear, for instance, whether Dr. Moyé's causal conclusion would still stand if any one of the Bradford Hill factors he discusses were found to weigh against that result. Accordingly, the district court did not err by holding that Dr. Moyé's Bradford Hill analysis departed from rigorous methodology. In sum, the district court properly undertook a careful review of Dr. Moyé's testimony and, based on that review, reasonably found that his methods were not sufficiently reliable. Therefore, the district court did not abuse its discretion in excluding his opinions.

Without Dr. Moyé's testimony, Plaintiffs cannot prove general causation, and summary judgment for Defendants is appropriate. "State law controls on the question of what evidence is necessary to prove an element of a state law claim, such as general causation." *Mirena II*, 982 F.3d at 124. Plaintiffs do not dispute that in cases like this one, "involving complex products liability (or medical) issues," there is a general causation requirement across all fifty states. *Id.*; *see also C.W. ex rel. Wood v. Textron, Inc.*, 807 F.3d 827, 838 (7th Cir. 2015) ("With no experts to prove causation . . . the appellants cannot prove their toxic-tort case. . . . [and] summary judgment in this case was proper."); *Wells v. SmithKline Beecham Corp.*, 601 F.3d 375, 378 (5th Cir. 2010) ("Without the predicate proof of general causation, the [failure to warn] tort claim fails.").

Neither Dr. Plunkett nor Dr. Whitaker-Azmitia purported to offer a full general causation opinion; instead, each focused on biological plausibility. Dr. Plunkett concluded that there is a "biologically plausible relationship that exists" between *in utero* exposure to SSRIs during

pregnancy and an increased risk of neurodevelopmental disorders, Joint App'x 1175, and she disclaimed offering an opinion on general causation, *id.* at 1244. Similarly, Plaintiffs acknowledge that Dr. Whitaker-Azmitia's role was to address biological plausibility by providing an opinion about the hyperserotonemia model: "the biological mechanism by which prenatal [SSRIs] lead to behavioral and neurochemical changes linked to autism." *Id.* at 1314. Even assuming *arguendo* that the opinions of Dr. Plunkett and Dr. Whitaker-Azmitia were admissible, biological possibility alone is not enough to overcome Plaintiffs' general causation hurdle. *See* Pl.'s Br. at 11 (explaining that the three experts "created a mosaic of general causation" "when considered collectively"). Therefore, the district court's exclusion of Dr. Moyé is dispositive of Defendants' motion for summary judgment.

In sum, we conclude that the district court did not abuse its discretion in excluding Dr. Moyé's testimony, the opinions of Dr. Plunkett and Dr. Whitaker-Azmitia go only to biological plausibility, and Plaintiffs are accordingly unable to prove general causation, which is an essential element to their claims. Thus, there is no triable issue of material fact as to Plaintiffs' claims, and we agree with the district court's decision to grant Defendants' motion for summary judgment.

* * *

We have considered all of Plaintiffs' remaining arguments and find them unpersuasive. Accordingly, we **AFFIRM** the judgment of the district court.

FOR THE COURT:
Catherine O'Hagan Wolfe,
Clerk of Court