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Abstract

Proof of causation in toxic torts has presented persistent problems for the legal system, because the probabilities that science can know fit poorly with the demands for particularistic proof imposed by the law's deterministic model of causation. Some scholars have hoped that genomic and molecular information will at last provide scientific certainty—definitive, individualized proof of toxic causation.

This Article argues that the opposite is true. Scientific research will increasingly elucidate the ways in which environmental exposures and human genes interact to produce disease, but this deeper knowledge will extend rather than resolve the problem of causal indeterminacy in toxic torts. Genomic and molecular understanding, instead of sounding the death knell for proposals to reform toxic tort causation law, will strengthen the argument for those reforms.

This Article proposes a probabilistic causal contribution model to replace the model of deterministic causation in toxic torts, building on earlier scholarly proposals and the creativity of

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a handful of courts. The Article explores how the model would work and argues that it is superior to present doctrine when assessed against the goals of the tort system.

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I. Introduction

Forty years after a jury first found that several asbestos product manufacturers each had caused someone's asbestosis and pleural mesothelioma,[1] sick people continue to come to court seeking compensation for illnesses that they allege were caused by exposure to various toxins. The defendants sued for making, selling, using, or disposing of the allegedly toxic products continue to protest that something else—dumb luck, bad genes, someone else's similar product, some entirely different toxin, or mother nature—is what really made the plaintiffs sick, and, more important, that the plaintiffs cannot prove otherwise.

Proof of toxic tort claims conforms poorly to the traditional deterministic legal model of but-for causation, because toxic injuries almost never involve an observable chain of physical events allowing easy inference of a causal relation between a particular defendant's conduct and a particular plaintiff's harm. Courts turn to science to replace causal intuition, but a disjunction remains between the probabilities that science can know and the determined result that the law wants proven. The resulting problem has produced hundreds of court opinions and numerous calls for doctrinal reforms in recognition of the difficulties that toxic causation presents. Yet, despite decades of thoughtful jurisprudence and scholarship, the core legal conception of toxic causation has hardly changed at all.

Science has changed, however, quickly and at an accelerating pace. The ability to peer into the genome heralds new insights into human susceptibility to toxic substances. Molecular technologies provide glimpses of previously inaccessible toxic mechanisms. Computing power allows this research to be conducted on a scale and at a rate never before possible.

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1. Borel v. Fibreboard Paper Prods. Corp., 493 F.2d 1076, 1094 (5th Cir. 1973) (holding that "the jury could find that each defendant was the cause in fact of some injury to Borel" although "it is impossible, as a practical matter, to determine with absolute certainty which particular exposure to asbestos dust resulted in injury"); *see* PAUL BRODEUR, OUTRAGEOUS MISCONDUCT 39–70 (1985) (describing the *Borel* trial); Joseph Sanders, *Risky Business: Causation in Asbestos Cancer Cases (and Beyond?)*, *in* PERSPECTIVES ON CAUSATION 11, 15–17 (Richard Goldberg ed., 2011) (describing the indivisible injury causation rationale of the *Borel* decision).

The law looks to this new science, hoping that its increased resolving power will at last build a bridge from probability to certainty. The dream is that genomic knowledge will lead to deterministic proof of the existence or absence of causal mechanism in individual cases. That "holy grail" of particularistic evidence would at last eliminate much of the indeterminacy that has plagued proof of specific causation in toxic tort claims;[2] it also could fatally undermine arguments for exceptional judicial treatment of toxic tort claims, restoring to tort law a universally applicable deterministic model of but-for causation.

This Article argues that the predominant reality is more likely to be exactly the opposite: at the highest magnifications, certainty will dissolve into probability. Scientific research will increasingly elucidate the ways in which environmental exposures and human genes interact to produce disease, but for the legal system, this deeper knowledge will extend rather than resolve the causal indeterminacy problem in toxic torts—and will therefore increase the justification for doctrinal adjustments to address that problem.[3]

Part II describes the traditional deterministic model of causation and how it fails in many toxic tort cases. Part III explains why it is likely that scientific success will exacerbate rather than solve that failure. Part IV proposes an alternative vision based on a probabilistic causal contribution model of causation. Part V assesses the proposal against goals of tort law.

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2. *See* Joseph Sanders, *Apportionment and Proof in Toxic Injury Cases*, 10 KAN. J.L. & PUB. POL'Y 200, 202 (2000) ("Specific causation evidence seems to be the holy grail of toxic torts."). "Specific causation" refers to causation of the individual plaintiff's case of disease, in contrast to the exposure-disease link that is often referred to as "general causation." *See infra* notes 20–25 and accompanying text.

3. This Article develops an argument and solution briefly suggested in an earlier Article, Steve C. Gold, *The More We Know, the Less Intelligent We Are?—How Genomic Information Should, and Should Not, Change Toxic Tort Causation Doctrine*, 34 HARV. ENVTL. L. REV. 369, 421–22 (2010).

II. The Persistent Problem: Toxic Injury and the Traditional, Deterministic Model of Causation

A. The Traditional, Deterministic Model of Causation

Some notion of causation inheres in the most elementary formulation of a tort claim. The claim that "defendant wronged plaintiff" implies a relation between the parties that is distinguishable from plaintiff's relation with persons other than the defendant. To further say that the wrong was more than abstract—that "defendant harmed plaintiff"—is to connect defendant's conduct and plaintiff's injury via a causal relation that is distinguishable from the vagaries of a universe in which people just get injured sometimes. The concept is so intuitive that torts casebooks typically apply it well before they get around to expressing it.[4] Yet articulating the meaning of causation is sufficiently difficult that the effort has long occupied philosophers, scientists, legal scholars, and judges.[5]

Part of that effort involved disentangling the factual from the normative in everyday assessments of causal responsibility. We have come a long way from the legal fiction that any given event has a single objective cause,[6] but the frank acknowledgment that the doctrine of proximate cause invokes policy choices did not extinguish the law's reliance on the idea that events have

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4. *See, e.g.*, MARC A. FRANKLIN ET AL., TORT LAW AND ALTERNATIVES: CASES AND MATERIALS 333 (9th ed. 2011) (introducing cause-in-fact by noting that "[f]rom the outset of the book we have implicitly accepted the notion that a defendant . . . should not have to compensate an injured plaintiff unless the plaintiff's injury is causally connected to the defendant's negligent conduct"); *cf.* Mark Kelman, *The Necessary Myth of Objective Causation in Liberal Political Theory*, 63 CHI.-KENT L. REV. 579, 587–88 (1987) (arguing that dissociating causation from standard of care is irrational under efficiency theories).

5. *See, e.g.*, H.L.A. HART & TONY HONORÉ, CAUSATION IN THE LAW (2d ed. 1985); Carl F. Cranor, *Genetic Causation*, *in* ARE GENES US? 125, 127–30 (Carl F. Cranor ed., 1994) (discussing common sense, scientific, and legal notions of causation, and noting that causal ascriptions depend on context and on interests of ascribing person); Richard W. Wright, *Causation, Responsibility, Risk, Probability, Naked Statistics, and Proof: Pruning the Bramble Bush by Clarifying the Concepts*, 73 IOWA L. REV. 1001, 1018–39 (1988).

6. *See* Morton J. Horowitz, *The Rise and Early Progressive Critique of Objective Causation*, *in* THE POLITICS OF LAW: A PROGRESSIVE CRITIQUE 471, 479–80 (David Kairys ed., 3d ed. 1998).

determinate factual causes.[7] Having shooed policy preferences into the back room of proximate cause, standard tort doctrine continues to insist that cause-in-fact reflects an objectively knowable reality—albeit knowable, ex post, only by counterfactual inference.

Causation-in-fact has traditionally been proven by persuading the fact finder that the familiar but-for test is satisfied: "Conduct is a factual cause of harm when the harm would not have occurred absent the conduct."[8] The first two restatements of the law of torts framed the required causal connection as a requirement that a cause be "a substantial factor in bringing about the harm."[9] They explained "substantial factor" as a limiting additional requirement distinguishing, from among all but-for causes, those that were legally cognizable.[10] The Third Restatement of Torts, opining that this use of "substantial factor" led to inchoate results, abandoned the term entirely,[11] completing

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7. *Id.* at 479–85 (describing the legal realist assault on the doctrine of objective causation and the rise of the distinction between "actual" and "legal" cause).

8. RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYSICAL & EMOTIONAL HARM § 26 (2010).

9. RESTATEMENT OF TORTS § 431 (1934); RESTATEMENT (SECOND) OF TORTS § 431 (1965).

10. RESTATEMENT OF TORTS § 431 cmt. a (1934) ("[T]hat the harm would not have occurred had the actor not been negligent . . . is necessary but . . . is not of itself sufficient [to establish that negligence was a legal cause of harm]."); RESTATEMENT (SECOND) OF TORTS § 431 cmt. a (1965) (same); *id.* § 433 (listing considerations important to determining whether an act is a "substantial factor"); *see* Mahoney v. Beatman, 147 A. 762, 766–67 (Conn. 1929) (adopting this view of "substantial factor"); *but see* RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYSICAL & EMOTIONAL HARM § 26 cmt. j & reporters' note (2010) (describing varied applications of "substantial factor"). Before publication of the First Restatement, some courts used "substantial factor" to justify the intuitively correct outcome in cases of multiple sufficient causes, in which a literal application of the "but-for" test would exonerate both causes. *See* Anderson v. Minneapolis, St. Paul & Sault Ste. Marie Ry. Co., 179 N.W. 45, 49 (Minn. 1920) (classic "two fires" case); RESTATEMENT (SECOND) OF TORTS § 432(2) (1965) (stating that in such circumstances "the actor's negligence may be found to be a substantial factor" in bringing about harm); Joseph Sanders et al., *The Insubstantiality of the "Substantial Factor" Test for Causation*, 73 MO. L. REV. 399, 416–17 (2008) (describing this use of "substantial factor").

11. *See* RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYSICAL & EMOTIONAL HARM § 26 cmt. j, reporters' note (2010) (noting that the term "substantial factor" seemed "to be doing scope-of-liability (proximate-cause) duty" in addition

(as asserted in the commentary) the conceptual separation of normatively driven proximate cause from (presumably objective) cause-in-fact.[12]

The Third Restatement modeled a but-for factual cause as any necessary element of a set of causes that, together, are sufficient to bring about the result.[13] This reflects an entirely deterministic conception of cause.[14] Its philosophic underpinning is the theory that causal laws connect fully specified sets of causes to effects in an invariant, rather than probabilistic, way. Take away a true cause, in this model, and the effect always disappears, unless the effect is overdetermined—that is, unless some other sufficient causal set exists that does not include this cause. Leave the cause in existence, and the effect is inevitable, unless some other necessary element of the causal set is removed. It may be impossible ever to fully specify a likely infinite set of causal antecedents, but this model of causation posits that we can nevertheless make generalizations about the element of a set of antecedents that is of interest, e.g., the one alleged to be the cause of harm in a given tort case.[15] Such a generalization reflects an experience-based imputation of a causal role ex ante that is applied ex post to make inferences about the antecedent's determined causal role in the actual event.

"to provid[ing] the standard for determining factual causation," and was sometimes used to stiffen and sometimes to relax causation standards).

12. *Id.* § 29 cmt. g. Although this separation is familiar to every American law student who has completed the first-year torts course, a distinguished British jurist recently questioned the use of cause-in-fact "as a kind of filter which you have to get through in order to qualify for the final round of being selected as legal causation." Lord Hoffmann, *Causation*, *in* PERSPECTIVES ON CAUSATION, *supra* note 1, at 3, 4–6 (2011).

13. RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYSICAL & EMOTIONAL HARM § 26 cmt. g (2010). As the Third Restatement explains, this model is generally consistent with the "NESS" (Necessary Element of a Sufficient Set) test. *Id.* § 26 cmt. c, reporters' note; *see also* Richard W. Wright, *Causation in Tort Law*, 73 CALIF. L. REV. 1735, 1788–1803 (1985) (explaining the NESS test). As Wright noted, however, but-for cause taken alone is not equivalent to the NESS test. Wright, *supra* note 5, at 1021–22 nn.109–11.

14. *See* RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYSICAL & EMOTIONAL HARM § 26 cmt. c (2010).

15. *See* Wright, *supra* note 5, at 1045.

This model also treats causation as a dichotomous, yes-or-no proposition: it either existed in a given case or it did not. Such treatment is not unique to causation, of course. In an adversarial truth-seeking system designed to choose between competing versions of events, many elements of claims or defenses are treated that way. But in today's doctrine some of these elements, dichotomous as they are, nevertheless are commonly aligned on a continuous quantitative scale rather than being limited to quantum values of zero or one. Many jurisdictions, for example, ask fact-finders to apportion fault or, more broadly, "responsibility."[16] Causation, however, has proven mostly resistant to treatment as a continuous variable.[17]

B. The Lack of Fit in Toxic Injury Cases

A toxic tort plaintiff claims that exposure to some chemical, radiological, or biological agent caused a disease. A fundamental difficulty in proving such a claim is that exposure and disease usually do not correlate perfectly: some people get sick without exposure, and some people receive exposure without getting sick.[18] In marked contrast to traumatic injury cases, the disease process itself is unobserved and unobservable as it occurs, and inscrutable afterward.[19] What evidence then will permit an

16. *See generally* RESTATEMENT (THIRD) OF TORTS: APPORTIONMENT OF LIAB. (2010) (describing comparative fault and comparative responsibility regimes).

17. *See id.* § 26 cmt. a (limiting apportionment based on causation to "separately caused" damages); *id.* § 26 cmt. c (prescribing that "the factfinder divides divisible damages into their indivisible component parts"); *id.* § 26 cmt. f (listing circumstances in which damages can be divided by causation); *see also, e.g.*, James v. Bessemer Processing Co., 714 A.2d 898, 909 (N.J. 1998) (noting that despite legal scholarship advocating reforms, "courts have been resistant to novel models of causation"); Waste Mgmt., Inc. v. S. Cent. Bell Tel. Co., 15 S.W.3d 425, 433 (Tenn. Ct. App. 1997) ("Causation in fact is an all-or-nothing proposition.").

18. If disease *only* appeared after exposure, causation might still be inferred, even if exposure frequently occurred without disease. Austin Bradford Hill, *The Environment and Disease: Association or Causation?*, 58 PROC. ROYAL SOC'Y MED. 295, 296 (1965) (giving examples).

19. *See* Richard W. Wright, *Proving Causation: Probability Versus Belief, in* PERSPECTIVES ON CAUSATION, *supra* note 1, at 195, 205–06 (distinguishing cases of alleged toxic injury from "bash-crash-slash" situations).

inference that a plaintiff's illness would not have occurred but for the exposure, to establish deterministically modeled causation-in-fact?

Courts initially demand proof of "general causation," asking whether the exposure in question is ever a *sine qua non* for the plaintiff's disease, or whether the existence of cases of disease after exposure is merely coincidental.[20] To prove general causation, plaintiffs have attempted to rely on toxicology studies (either *in vitro* or *in vivo* in experimental animals), evidence of toxins' biological mechanisms of action, simple inference from exposure dose and chronology, and epidemiologic studies (which investigate the relative risk of disease that is associated with exposure in samples of human populations). Many courts have insisted on the primacy of epidemiology for proof of general causation, in part because of situations in which many claims were brought despite large bodies of powerful epidemiologic studies that failed to find any association between the exposure and the disease the exposure allegedly caused.[21]

Even strong proof of general causation may be unavailing, however. The existence of disease without exposure leads courts to further demand proof of "specific causation," asking whether this plaintiff's case of disease is one that would not have occurred but for the exposure.[22] The difficulty lies in determining what if any additional proof a plaintiff must, may, or can adduce to prove specific causation.

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20. General causation is sometimes expressed as whether an agent "is capable of" causing a disease, but more than theoretical capability is implied. RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYSICAL & EMOTIONAL HARM § 28 cmt. c (2010); Henricksen v. ConocoPhillips Co., 605 F. Supp. 2d 1142, 1158 (E.D. Wash. 2009); *cf.* Joseph Sanders, *Proof of Individual Causation in Toxic Tort and Forensic Cases*, 75 BROOK. L. REV. 1367, 1375 (2010) ("The general causation question is whether a substance . . . has been shown to harm any individuals.").

21. *See, e.g.*, *In re* "Agent Orange" Prod. Liab. Litig., 611 F. Supp. 1223, 1231 (E.D.N.Y. 1985), *aff'd*, 818 F.2d 187 (2d Cir. 1987) ("[E]pidemiological studies . . . are the only useful studies having any bearing on causation."); Merrell Dow Pharm., Inc. v. Havner, 953 S.W.2d 706, 717–18 (Tex. 1997) (requiring a statistically significant epidemiologic result of relative risk greater than two).

22. *E.g.*, *Henricksen,* 605 F. Supp. 2d at 1155.

For some courts, epidemiology may—or must—serve that function, but only if the epidemiologic studies find that exposure more than doubles the risk of disease, which would imply that exposure accounted for more than one-half of the incidence of the disease. From this statistic based on the incidence of disease in exposed and unexposed populations, courts have reasoned that it is "more likely than not" that an individual plaintiff's disease is a case associated with the exposure.[23] Some commentators view this "doubling+" requirement[24] as too stringent. James Robins and Sander Greenland, for example, showed that if the inference of general causation is accepted, then in most circumstances the epidemiologic relative risk is a lower bound of the probability that a given individual who has both exposure and illness is a case of "true" causation.[25]

On the other hand, others have argued that because relative risk is undeniably a property of samples and populations, but specific causation is a property of an individual case, epidemiologic data cannot support inferences about specific causation at all.[26] Some courts have effectively demanded that a plaintiff produce particularistic evidence—proof of some fact that will distinguish a plaintiff's case of disease from the cases that would have occurred even absent exposure.[27] To try to satisfy

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23. *E.g.*, *In re* "Agent Orange" Prod. Liab. Litig., 597 F. Supp. 740, 781 (E.D.N.Y. 1984), *aff'd*, 818 F.2d 145 (2d Cir. 1987); Estate of George v. Vt. League of Cities & Towns, 993 A.2d 367, 375 (Vt. 2010).

24. Richard Wright seems to have coined this elegant shorthand for the "relative risk must exceed two" rule. Richard W. Wright, *Liability for Possible Wrongs: Causation, Statistical Probability, and the Burden of Proof*, 41 LOYOLA L.A. L. REV. 1295, 1318 (2008).

25. James M. Robins & Sander Greenland, *The Probability of Causation Under a Stochastic Model for Individual Risk*, 45 BIOMETRICS 1125, 1129–32 (1989); *see also* RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYSICAL & EMOTIONAL HARM § 28 cmt. c(4) (2010) ("[A]ny judicial requirement that plaintiffs must show a threshold increase in risk or a doubling in incidence in a group study in order to satisfy the burden of proof of specific causation is usually inappropriate.").

26. *See* Wright, *supra* note 5, at 1054 ("[P]articularistic evidence is necessary for causal explanation . . . ."); Wright, *supra* note 24, at 1318 (arguing that epidemiologic data provide no evidence that toxic exposure "actually caused" harm in individual case); Sienkiewicz v. Greif, [2011] UKSC 10, 157 (Lord Rodger), 170 (Lady Hale), 190–91 (Lord Mance).

27. *See, e.g.*, Henricksen v. ConocoPhillips Co., 605 F. Supp. 2d 1142, 1162–

such demands, some plaintiffs have turned to medical experts who try to rule out other plausible causes, a method called differential diagnosis or differential etiology. Some plaintiffs have tried to rely on epidemiologic studies coupled with analysis of the plaintiff's individual characteristics that put the plaintiff at a particularly heightened risk.[28]

The interaction of population-derived relative risk data and proof of specific causation under the traditional deterministic and dichotomous causation model received unusually explicit attention in two cases decided by the United States Court of Appeals for the Tenth Circuit. In each case, a group of plaintiffs alleged tortious exposure to radiation from uranium mining and milling.

In *June v. Union Carbide Corp.*,[29] twenty-seven former residents of Uravan, Colorado, alleged that radioactive contamination from uranium and vanadium mining and milling operations in the company town had caused their thyroid disease or non-thyroid cancer. General causation was not in dispute: the defendants had to concede that ionizing radiation in general is capable of causing cancer, and that products of uranium and vanadium radioactive decay, such as iodine-131, cause thyroid cancer in particular. In an attempt to prove specific causation, plaintiffs relied on experts who estimated each plaintiff's radiation dose and opined that such exposure was a "substantial factor" contributing to their various diseases.[30] The defendants argued, and the district and appellate courts agreed, that such testimony could not suffice to prove causation because it did not assert that any plaintiff's illness would not have occurred but for exposure to the Uravan radiation.

The Tenth Circuit panel analyzed the description of factual causation in both the Second Restatement of Torts, which used

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63, 1177 (E.D. Wash. 2009) (noting that plaintiff could not distinguish his case of leukemia from one that would have occurred without chemical exposure).

28. *See, e.g.*, *Estate of George*, 993 A.2d at 384 (Reiber, C.J., dissenting) (discussing the argument that a firefighter's individual risk of contracting lymphoma from inhaled chemicals was higher than the average risk reported in epidemiologic studies).

29. June v. Union Carbide Corp, 577 F.3d 1234 (10th Cir. 2009).

30. *Id.* at 1237.

the "substantial factor" formulation, and the Third Restatement, which consciously deleted reference to "substantial factor." The court concluded that despite the difference in language, the two restatements equivalently established but-for as the *sine qua non* for factual causation.[31] The restatements admitted only one exception—situations involving multiple sufficient causes—and the court reasoned that even in such situations, proof of causation requires a showing that the alleged cause would have been a but-for cause in the hypothetical absence of the other sufficient cause(s).

In support of that reasoning, the court cited several illustrations given in the Third Restatement, including "the one most pertinent to the case before us," a hypothetical product liability case in which a plaintiff whose daughter has a birth defect alleges that a drug manufacturer failed to warn of the drug's teratogenicity.[32] The plaintiff claims the drug caused the birth defect; the manufacturer claims that an independent genetic condition caused it. The Tenth Circuit noted that according to the Restatement, the plaintiff must show that the drug, acting alone, *would* have caused the birth defect, not merely that the drug *could* have caused the defect.[33] This formulation echoes the distinction typically made between general causation and specific causation.[34]

The majority held that the plaintiffs had "failed to present to the [district] court evidence, or even an argument" that radiation released by defendants constituted "either a but-for cause of . . .

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31. *Id.* at 1241.

32. *Id.* at 1244 (citing RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYSICAL & EMOTIONAL HARM § 27 cmt. e, illus. 2 (2010)).

33. *Id.* Actually, the illustration was not particularly pertinent to *June*, because it illustrated the rule for multiple sufficient causes and therefore necessarily *assumed* that both the parents and the drug company presented sufficient evidence that either the genetic condition or the drug alone *would* have caused the injury. *See* RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYSICAL & EMOTIONAL HARM § 27 (2010). The real question lurking in *June* is whether demanding such evidence can be realistic in a case like *June*, and how to respond if it is not.

34. Many courts have said that general causation requires proof that an exposure *can* cause the plaintiff's condition, and specific causation requires proof that the plaintiff's exposure *did* cause the plaintiff's individual case. *E.g.*, Kilpatrick v. Breg, Inc., 613 F.3d 1329, 1334 n.4 (11th Cir. 2010).

or . . . a necessary component of a causal set that would probably have caused" any of the plaintiffs' medical conditions.[35] Judge Holloway dissented in part, arguing that for those plaintiffs with thyroid disease, the testimony of one of plaintiff's experts created a material issue of disputed fact with respect to but-for causation.[36] Judge Holloway did not question the majority's explication of "but-for" as the sole test for causation.[37]

In *Wilcox v. Homestake Mining Co.*,[38] three plaintiffs alleged that their cancers had been caused by radiation exposure from another uranium mill in New Mexico. They submitted evidence similar to the plaintiffs' evidence in *June*,[39] but argued that New Mexico law, unlike Colorado law as interpreted in *June*, would permit a finding of causation based on the "substantial factor" test.[40] The district judge dismissed the action on summary judgment. A Tenth Circuit panel that included none of the *June* judges unanimously affirmed—but in three separate opinions.

Judges Lucero and McKay agreed—often verbatim—with *June*'s embrace of mechanistic "but-for" causation as the only valid interpretation of causation-in-fact. They held that New Mexico law allowed for substantial factor causation in lieu of but-for causation only in two exceptional cases. Regarding the first exception, multiple sufficient causes, the court followed *June*, holding that "[o]nly a substance that would have actually (that is, probably) caused the cancer can be a factual cause without being a but-for cause."[41] Regarding the second, alternative liability, the court saw no "basis for alternative liability where only one

35. *June*, 577 F.3d at 1245 (10th Cir. 2009).

36. *Id.* at 1253–54 (Holloway, J., dissenting). The majority refused on procedural grounds to consider the plaintiffs' arguments that persuaded Judge Holloway. *Id.*

37. *Id.* at 1252–54.

38. Wilcox v. Homestake Mining Co., 619 F.3d 1165 (10th Cir. 2010).

39. *See id.* at 1170–71 (Lucero, J., concurring) (describing testimony of plaintiffs' experts, including one who testified in *June*, regarding the "assigned share" of risk and the lack of other known significant risk factors).

40. *Id.* at 1167.

41. *Id.* at 1168 (quoting June v. Union Carbide Corp., 577 F.3d 1234, 1243 (10th Cir. 2009)).

potential wrongdoer has been identified and the injury may simply have resulted from natural causes."[42]

Judge Lucero nevertheless disagreed with Judge McKay's—and the *June* majority's—application of the but-for standard. Judge Lucero embraced Judge Holloway's partial dissent in *June*, but found the factual presentation in *Wilcox* insufficient to prove but-for causation, by contrast with *June*.[43]

Of the six judges on the two panels, only Judge Holmes seemed willing to contemplate the possibility that "the but-for standard of causation" ought not apply to cases like *June* and *Wilcox*.[44] But Judge Holmes did not decide that any other standard should or would apply, opining instead that plaintiffs had waived any argument for a different standard.[45] Judge Holmes agreed that the plaintiffs had failed to satisfy the but-for test.[46]

It is easy to understand the uneasiness reflected in the opinions of Judges Holloway, Lucero, and Holmes. In applying a deterministic model of causation, the Tenth Circuit effectively reinforced the specific causation requirement for toxic tort plaintiffs. The court demanded proof that each individual plaintiff would not have developed cancer absent exposure to the radiation released by the defendants in the respective cases. How could any plaintiff possibly do this?

The majorities, in very similar terms, denied that they had set the plaintiffs an impossible task.[47] They rooted their

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42. *Id.* at 1167. The court stated that alternative liability applies when "two or more defendants engage in simultaneous or nearly identical negligent acts but only one of these acts causes the injury complained of, thus making it difficult or impossible for the plaintiff to prove which defendant caused the harm" and distinguished asbestos cases in which "it is clear the plaintiff's injury was caused by asbestos" but the defendant that caused the harm could not be specified. *Id.*

43. *Id.* at 1170–73 (Lucero, J., concurring).

44. *Id.* at 1173 (Holmes, J., concurring).

45. *Id.*

46. *Id.*

47. *See id.* at 1169 ("[W]e are not persuaded this requirement is so insurmountable . . . ."); June v. Union Carbide Corp., 577 F.3d 1234, 1246 (10th Cir. 2009) (stating that in holding that plaintiffs did not attempt to prove but-for causation, the court was "not being hypertechnical").

explanations in the preponderance of the evidence standard: although a plaintiff must show that she or he "actually" would not have become ill absent a defendant's tortious exposure of the plaintiff to a toxic substance,[48] the plaintiff need not prove this to an "absolute certainty."[49] "Actually" actually means "probably"[50] or "likely,"[51] the majorities stated.

This question-begging explanation still leaves one to ponder what type of evidence might have satisfied the plaintiff's burden. How could a plaintiff show it was "likely" that the defendants' radiation releases "actually" caused his or her disease? Neither majority opinion says. Their discussions of but-for causation, however, are so mechanistic as to give the impression that only particularistic evidence—something about plaintiff's disease that betrayed its origin, like the ballistics marks on a bullet—could suffice. Perhaps—the opinions don't say—a sufficiently large population-based relative risk estimate derived from an epidemiologic study could also have satisfied the majorities. Neither of those options was available to the plaintiffs.

The plaintiffs in each of these cases did prove, however, that the defendants exposed them to radiation. The defendants did not deny that such exposure increased the likelihood that a person would develop the diseases from which the plaintiffs suffered. That increased risk is known partly because of an understanding of what ionizing radiation does to DNA, but also because of the observation that more disease is found in populations exposed to additional radiation than in populations not exposed.[52] Nevertheless, even though the defendants had exposed the

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48. *June*, 577 F.3d at 1243.

49. Wilcox v. Homestake Mining Co., 619 F.3d 1165, 1169 (10th Cir. 2010).

50. *June*, 577 F.3d at 1243.

51. *See Wilcox*, 619 F.3d at 1167 (characterizing plaintiffs' position as an argument that causation could be proven "without regard to whether the injuries would likely have occurred in the absence of defendant's action"); *id.* at 1169 (stating that a toxic tort plaintiff must demonstrate but-for causation "only to a reasonable degree of medical probability—not a certainty").

52. *See* Samuel D. Estep, *Radiation Injuries and Statistics: The Need for a New Approach to Injury Litigation*, 59 MICH. L. REV. 259, 266–67 (1960) (noting that the causal connection between radiation and cancer "can be measured only by a statistical increase in the incidence of the disease").

plaintiffs to known risk factors for their diseases, no plaintiff could obtain any recovery.

Ex hypothesi, the defendants' conduct was tortious—perhaps because reasonable precautions were available that would have avoided the haphazard broadcast of radionuclides in the community. The plaintiffs' evidence fairly supported the inference that someone got sick who, if the mine and mill operators had behaved differently, would not have been sick. Yet the deterministic concept of causation demands that this plaintiff show that he or she is the "someone" whose disease would not have occurred absent the defendants' wrongful conduct. In many cases, as in *June* and *Wilcox*, this will be impossible, resulting in denial of all recoveries against defendants who nevertheless wrongfully made people sick.

III. Solutions Illusory and Real: The False—and True—Promise of Genomics

The deterministic model of causation has performed poorly when confronted with the mechanistic opacity of toxic torts. That opacity is as intolerable to science and medicine as it is inconvenient for law. But science has developed tools to attack it. In just two decades, researchers have sequenced the human genome, developed information processing capacity to conduct statistical analysis of very large numbers of genetic variations, invented techniques to rapidly assay the effects of toxic substance exposure on highly variable genetic material, and learned new ways to detect disease-related changes at the sub-cellular or molecular level.

Observing all this biomedical research from the law school across campus, legal scholars understandably envision that one day the molecular impacts of carcinogens, mutagens, and other toxins will be as easy to detect and attribute as the impacts from wayward cricket balls, deformed automobile parts, and misdirected scalpels. If so, "an increasing number of people will have the tools necessary to prove *sine qua non* causation in toxic

tort litigation,"[53] making it easier for deserving plaintiffs to prevail and, by implication, allowing courts accurately to dismiss claims when those tools are available but do not provide the desired proof. At last, cause-in-fact in toxic torts will be as certain as in any other tort. Or will it?

A. A Bit of Genomics

The seed that grew into the Human Genome Project, interestingly, germinated in the soil of a toxic tort problem. In the early 1980s, veterans and their families demanded compensation for injuries allegedly resulting from service members' deliberate experimental exposure to radiation by the government during the Cold War; in response, Congress commissioned a study of the feasibility of detecting low-level damage to DNA caused by environmental exposures.[54] The researchers given the task realized that they would have to "scan many genomes' worth of DNA to pick up what were sure to be small alterations in the mutation rate."[55] A scientist at the Department of Energy conceived "a more manageable goal, that of sequencing the entire human genome once rather than many times," and the seed was planted.[56] It would be about a half-decade before the first federal appropriation for the Human Genome Project sprouted.[57]

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53. Andrew R. Klein, *Causation and Uncertainty: Making Connections in a Time of Change*, 49 JURIMETRICS J. 5, 35 (2008); *see also* Gary E. Marchant, *Genetic Data in Toxic Tort Litigation,* 14 J.L. & POL'Y 7, 8 (2006) ("New genetic methods and data have the potential to fill some of the scientific uncertainties and data gaps in toxic tort litigation, thus making toxic tort litigation more accurate and fair."); Sanders, *supra* note 20, at 1399 n.132 ("[T]he field of toxicogenomics offers the long run possibility that we will be able to ascertain causation at the level of the individual case, radically changing all specific causation testimony.").

54. CHRISTOPHER WILLS, EXONS, INTRONS, AND TALKING GENES 72 (1991). According to Wills, other significant compensation claims of the era, including those of Vietnam veterans exposed to Agent Orange and of people living near the damaged Three Mile Island nuclear plant, also contributed to the political impetus for the study. *Id.* at 71.

55. *Id.* at 74.

56. *Id.* at 75.

57. *Id.* at 81.

Remarkably, it took only a bit more than twice that time to harvest the crop: a highly accurate sequential listing, coordinated with physical locations on the chromosomes, of about three billion nucleotide base pairs that constitute human nuclear DNA.[58] The success of the Human Genome Project spawned a slew of other "omics" projects pursuing comprehensive indices of classes of human biochemicals.[59] Some of this research promises better understanding of the genetic and environmental components of disease etiology, and thus may be directly relevant to the causation issue in toxic torts.[60]

1. Genes and Disease

A gene is a segment of DNA that encodes information, which may be translated into a sequence of amino acids. The amino acid chain can then be formed into all or part of a protein. Biologists did not need to sequence the entire human genome to understand that a person's inherited genotype could affect the phenotype—

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58. Press Release, Nat'l Human Genome Research Inst., International Consortium Completes Human Genome Project (Apr. 14, 2003), *available at* http://www.genome.gov/11006929; *see also* Int'l Human Genome Sequencing Consortium, *Initial Sequencing and Analysis of the Human Genome*, 409 NATURE 860, 873, 875 (2001) (estimating the total number of bases in the genome). A nucleotide or "base" is one of the four different molecules that bond together to form a strand of DNA. ISRAEL ROSENFIELD ET AL., DNA 73 (2011). In the double helix of the DNA molecule, each base is "paired" with its complementary nucleotide. *Id.*

59. *See* Mirsolava Janković, *Glycans as Biomarkers: Status and Perspectives*, 30 J. MED. BIOCHEMISTRY 213, 213–14, 219 (2011) (describing glycomics, study of sugar-protein molecules); Paolo Vineis & Frederica Perera, *Molecular Epidemiology and Biomarkers in Etiologic Cancer Research: The New in Light of the Old*, 16 CANCER EPIDEMIOLOGY, BIOMARKERS & PREVENTION 1954, 1955 (2007) ("[N]ew technologies/markers, such as proteomics, metabonomics, and epigenomics, will become highly relevant . . . .").

60. Two examples are the Environmental Genome Project and HuGENet (Human Genome Epidemiology Network). *See generally* Samuel H. Wilson & Kenneth Olden, *The Environmental Genome Project: Phase I and Beyond*, 4 MOLECULAR INTERVENTIONS 147 (2004) (describing Environmental Genome Project); Wei Yu et al., *HugeWatch: Tracking Trends and Patterns of Published Studies of Genetic Association and Human Genome Epidemiology in Near-real Time*, 16 EUR. J. HUMAN GENETICS 1155 (2008) (describing HuGENet and related projects).

the person's observable traits—in important health-related ways. The most straightforward situations involve an inherited allele, a specific variation in a given gene, which changes the coded protein in a way that produces a particular disease or condition.[61]

The story of a genetic disease can be considerably more complicated, however, even for diseases caused by changes in a single protein coded by a single gene. Cystic fibrosis is a case in point. In 1989, researchers announced the sequencing of "the cystic fibrosis gene," which codes for a protein involved in transporting molecules across cell membranes.[62] A person who inherits from each parent a copy of a variant allele that results in the omission of one amino acid from the protein will have cystic fibrosis.[63] But since that discovery, researchers have identified more than 1,600 different mutations that can produce cystic fibrosis.[64] The mutations, located in various parts of the gene, affect the protein in various ways that produce disease of varying severity.[65]

Genes also relate to diseases in even more complex ways. For example, people with a particular variation of a gene called *APOE* are dramatically more likely to develop Alzheimer's disease than people without that allele: ten times more likely if they inherited two copies of the variant gene, four times if they inherited one copy.[66] But other genes also appear to play roles in

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61. For example, alteration of one DNA nucleotide in a gene that codes for hemoglobin yields a substitution of one amino acid in that protein, which changes the molecule's shape—producing the sickle-cell phenotype—and reduces its ability to carry oxygen. Muin J. Khoury & Janice S. Dorman, *Genetic Disease*, *in* MOLECULAR EPIDEMIOLOGY 365, 370 (Paul A. Schulte & Frederica P. Perera eds., 1993).

62. Sherman Elias et al., *Carrier Screening for Cystic Fibrosis: A Case Study in Setting Standards of Medical Practice*, *in* GENE MAPPING 186, 187 (George J. Annas & Sherman Elias eds., 1992).

63. *Id.* at 188; Steven M. Rowe et al., *A Breath of Fresh Air*, SCI. AM., Aug. 2011, at 69, 71.

64. Rowe et al., *supra* note 63, at 72; *see also* WILLS, *supra* note 54, at 210 (stating that in initial experiments fewer than 70% of cystic fibrosis patients' genes tested displayed the variation that deleted one amino acid).

65. Rowe et al., *supra* note 63, at 72; *see also* WILLS, *supra* note 54, at 212–13 ("[M]utations are found all over the gene.").

66. Gina Kolata, *Vast Gene Study Yields Insights on Alzheimer's*, N.Y. TIMES, Apr. 4, 2011, at A1.

Alzheimer's disease, albeit much smaller roles.[67] There is no one "Alzheimer's disease gene."

The Alzheimer's pattern is not unusual. Susceptibility alleles, rare variants of the *BRCA1* and *BRCA2* genes, significantly increase a woman's risk of developing breast cancer.[68] But genome-wide association studies—which examine large numbers of genes in persons with and without a disease to determine if particular DNA variations are statistically associated with higher disease incidence—identified half a dozen new susceptibility alleles; these occur relatively frequently in the population, but individually confer small increments of risk ranging from seven to twenty-six percent.[69] Thus, the degree to which disease or other phenotypic change results from variation in a gene, which biologists call "penetrance," varies from gene to gene.[70] Sometimes, the risk conferred by a variation in a

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67. Pooled data from numerous studies revealed associations between five genes and the incidence of Alzheimer's disease; each of these alleles is associated with an increase in risk of 10 to 15%. *Id.*

68. *See, e.g.*, Athina Christopoulou & John Spiliotis, *The Role of BRCA1 and BRCA2 in Hereditary Breast Cancer*, 10 GENE THERAPY & MOLECULAR BIOLOGY 95, 96 (2006), http://www.gtmb.org/pages/Vol10A/PDF/09. Christop&Spiliot,95-100.pdf (noting that women carrying mutations have a 40% to 85% lifetime risk, versus 12.5% in general population).

69. Paul D.P. Pharoah et al., *Polygenes, Risk Prediction, and Targeted Prevention of Breast Cancer*, 358 NEW ENG. J. MED. 2796, 2797–99 (2008).

70. *See* Eleanor Raffan & Robert K. Semple, *Next Generation Sequencing—Implications for Clinical Practice*, 99 BRIT. MED. BULL. 53, 62–63 (2011) (defining variable penetrance as "the variable tendency of genetic mutations to translate into clinical disease;" noting that "every genome sequenced" includes numerous alleles implicated in disease); *see also* Elisabeth A. Lloyd, *Normality and Variation: The Human Genome Project and the Ideal Human Type*, *in* ARE GENES US?, *supra* note 5, at 99, 100 (noting that most identified genetic differences are risk factors for, or provide a vulnerability to, development of a specific disease, rather than determinants of disease); Evgeny N. Imyanitov et al., *Searching for Cancer-Associated Gene Polymorphisms: Promises and Obstacles*, 204 CANCER LETTERS 3, 8 (2004) ("[L]ow penetrance is often exemplified as something like 1.5-fold risk elevation."); *see generally* SUZANNE H. REUBEN, PRESIDENT'S CANCER PANEL, REDUCING ENVIRONMENTAL CANCER RISK: WHAT WE CAN DO NOW 1 (2010) ("Single-gene inherited cancer syndromes are believed to account for less than 5 percent of malignancies in the United States.").

particular gene may depend on a person's genotype at other genes or on the action of other biochemical constituents.[71]

2. Toxic Exposure and Disease—and Genes

Biologists also did not need to sequence the entire human genome to understand that different people may respond to the same dose of the same toxin in different ways. Even for acutely lethal poisons, although there may be a dose above which no person (or research animal) can survive, toxicologists typically determine what dose is lethal for half of the organisms. Because the toxin and dose are the same for all the exposed organisms, something—a variation from organism to organism, a variation in the environment from organism to organism, or pure random chance—must explain why the toxin is lethal to some but not to others.[72]

More extreme variations typify the chronic or latent toxicity ordinarily involved in toxic tort cases. Consider tobacco smoke,

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71. *See* Raffan & Semple, *supra* note 70, at 63 (stating that variable penetrance "is usually ascribed either to environmental factors or to unspecified 'genetic modifiers'"); Marc A. Schaub et al., *Linking Disease Associations with Regulatory Information in the Human Genome*, 22 GENOME RES. 1748, 1748 (2012) (noting that for the vast majority of DNA variations found to be associated with disease, "it is likely that the underlying mechanism linking them to the phenotype is regulatory" rather than a change in coded protein sequence). The effects of the breast cancer susceptibility alleles, for example, are modified by other genes that alter the body's response to environmental insults such as radiation. Logan C. Walker et al., *Use of Expression Data and the CGEMS Genome-Wide Breast Cancer Association Study to Identify Genes that May Modify Risk in BRCA1/2 Mutation Carriers*, 112 BREAST CANCER RES. & TREATMENT 229, 229, 233 (2008). Cystic fibrosis is another example: some people have symptoms worse than would be suggested by the change in the protein coded by the "cystic fibrosis gene" because a group of several hundred helper proteins recognize the altered protein as defective and destroy it before it can be put into position to do its job. Rowe et al., *supra* note 63, at 72. *See generally* James R. Griesemer, *Tools for Talking: Human Nature, Weismannism, and the Interpretation of Genetic Information*, *in* ARE GENES US?, *supra* note 5, at 69, 82 (observing that genes "cause" inherited somatic characteristics but "[t]he body is a cause in inheritance . . . . Proteins and other cell components are causally responsible for the events of cell division and DNA replication").

72. FRANK C. LU, BASIC TOXICOLOGY 102 (1985).

which is almost universally acknowledged to cause lung cancer.[73] Many people with lung cancer seem to have acquired the disease by smoking.[74] But some people smoke to a ripe old age,[75] and only a small fraction of even the heaviest smokers ever contract lung cancer.[76] On the other hand, though lung cancer was very rare before smoking became common, some people who never smoked did—and do—get lung cancer.[77] What explains the differences?

The search for explanations commonly distinguishes extrinsic from intrinsic potential sources of inter-individual difference: environment versus genetics.[78] Perhaps exposure to something other than tobacco smoke—say, diesel exhaust—causes lung cancer in some non-smokers, while another factor—say, a diet rich in just the right antioxidants—inhibits

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73. As recently as 2005, however, Britain's Imperial Tobacco successfully defended a tort claim by disputing that it had been "scientifically established" that cigarette smoking causes lung cancer. *See* McTear v. Imperial Tobacco Ltd., [2005] C.S.O.H. 69, 5.694–5.695, 6.149–6.17, 9.9 (stating that the burden of proof on causation was not satisfied); *id.* 9.10 (finding that epidemiologic data failed to prove individual causation).

74. *See* Graham G. Giles & Peter Boyle, *Smoking and Lung Cancer*, *in* TOBACCO AND PUBLIC HEALTH 485, 486 (Peter Boyle et al., eds. 2004) (estimating that 83% to 92% of lung cancer deaths in five developed countries are attributable to smoking).

75. *See, e.g.*, George Davey Smith, *Epidemiology, Epigenetics and the "Gloomy Prospect": Embracing Randomness in Population Health Research and Practice*, 40 INT'L J. EPIDEMIOLOGY 537, 537–38 (2011) (describing a healthy centenarian believed to have smoked 170,000 cigarettes).

76. *See, e.g.*, Adrian Cassidy et al., *Lung Cancer Risk Prediction: A Tool for Early Detection*, 120 INT'L J. CANCER 1, 1 (2006) (noting that eighty-five percent of heavy smokers will not develop lung cancer).

77. *See* Asta Scesnaite et al., *Similar DNA Methylation Pattern in Lung Tumours from Smokers and Never-smokers with Second-hand Tobacco Smoke Exposure,* 27 MUTAGENESIS 423, 423 (2012) (acknowledging that 10% to 15% of lung cancer deaths occur in people who never smoked). Exposure to environmental tobacco smoke may explain some of those cases. *See* Giles & Boyle, *supra* note 74, at 495.

78. *See generally* Jennifer E. Below, *Factors that Impact Susceptibility to Fiber-Induced Health Effects*, 14 J. TOXICOLOGY ENVTL. HEALTH 246 (2011) (noting that only five percent of people exposed to asbestos develop mesothelioma and discussing genetic, nutritional, and other environmental factors that may affect susceptibility to the disease); Davey Smith, *supra* note 75, at 539 (describing studies that partition contributions to health outcomes from genetics, shared environment, and non-shared environment).

carcinogenesis in the lungs of some smokers.[79] Or perhaps a fortunate genetic endowment protects some lifelong smokers from lung cancer, while a genetic mischance induces lung cancer in some non-smokers.[80] Both environmental and genetic differences between individuals appear responsible for at least some of the variation in individuals' responses to toxic exposures.[81] For the most part, it has been impossible (or at least impractical) to identify, quantify, and tease apart these possibilities using the investigatory tools of toxicology, environmental epidemiology, conventional biochemistry, and classical genetics.[82]

3. The Tools of Toxicogenomics

Technologies developed during and after the Human Genome Project provide new tools of vast potential power. DNA microarrays and even more powerful next-generation sequencing technologies allow assays of many genes at once and make it

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79. *See, e.g.*, Cassidy, *supra* note 76, at 2 (identifying dietary and other environmental factors that affect lung cancer risk); Giles & Boyle, *supra* note 74, at 487 (listing other environmental causes of lung cancer); Elizabeth A. Ward et al., *Research Recommendations for Selected IARC-Classified Agents*, 118 ENVTL. HEALTH PERSP. 1355, 1358 (2010) (describing meta-analyses showing diesel exhaust associated with slightly elevated risk of lung cancer (relative risks 1.33 (95% confidence interval 1.24–1.44) and 1.47 (1.29–1.67)).

80. *See* Ping Zhan et al., *CYP1A1 MspI and exon7 Gene Polymorphisms And Lung Cancer Risk: An Updated Meta-Analysis and Review*, 30 J. EXPERIMENTAL CLINICAL CANCER RES. 99, *15 (2011) (explaining that variations of two genes are associated with increased risk of lung cancer, and some variations particularly increase risk in smokers).

81. For example, the authors of a study that observed "[m]arked inter-individual variation in response to the same level of exposure" to air pollution concluded "that susceptibility might be due to genetic factors." Shuang Wang et al., *Methods for Detecting Interactions Between Genetic Polymorphisms and Prenatal Environment With a Mother-Child Design*, 34 GENETIC EPIDEMIOLOGY 125, 131 (2010).

82. *See* David Altshuler et al., *Genetic Mapping in Human Disease*, 322 SCI. 881, 881 (2008) (describing limitations of classical genetics); Michael D. Waters et al., *Toxicogenomic Approach for Assessing Toxicant-Related Disease*, 544 MUTATION RES. 415, 415 (2003) (describing the potential of toxicogenomics to address previously "intractable" problems).

practicable to sequence an individual's entire genome.[83] The young but rapidly developing science of toxicogenomics marries the experimental techniques of toxicology to the analytical techniques of genomics.[84] Using laboratory animals or cells or tissues cultured *in vitro*, researchers can expose genetic material containing many variations of many genes to a suspected toxin and observe any variations in response, or they can compare exposed and non-exposed genetic material and observe any differences.[85] New technologies allow detection not only of variations (polymorphisms) in the DNA sequence of particular genes, but also rearrangements and other variations of the structure of genes along a chromosome.[86]

Alternatively, researchers can study the genes of samples of actual human populations and determine whether observable genetic differences are associated with differential exposure to toxins or with differential toxic effects among those exposed.[87]

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83. Raffan & Semple, *supra* note 70, at 55; *see also, e.g.*, S. Le Scouarnec & S.M. Gribble, *Characterising Chromosome Rearrangements: Recent Technical Advances in Molecular Cytogenetics*, 108 HEREDITY 75, 79 (2012) (describing how the Human Genome Project took more than a decade, but a whole human genome now can be sequenced in a few days); D.A. Wheeler et al., *The Complete Genome of an Individual by Massively Parallel DNA Sequencing*, 452 NATURE 872, 872 (2008) (reporting first sequencing of a human's genome using "massively parallel" next-generation technology).

84. *See generally* Gerald T. Ankley et al., *Toxicogenomics in Regulatory Ecotoxicology*, 40 ENVTL. SCI. TECH. 4055, 4056 (2006) (documenting increasing numbers of toxicogenomics publications in each of the next five years following the first such publication, in 2000); Syril Pettit et al., *Current and Future Applications of Toxicogenomics: Results Summary of a Survey from the HESI Genomics State of Science Subcommittee*, 118 ENVTL. HEALTH PERSP. 992, 995 (2010) (reporting that toxicogenomics has improved understanding of biological mechanisms of toxicity but biological understanding of toxicogenomic data remains limited).

85. *See* Jamie A. Grodsky, *Genetics and Environmental Law: Redefining Public Health*, 93 CALIF. L. REV. 171, 190 (2005) ("DNA microarrays . . . permit thousands of genes to be monitored simultaneously to determine whether they have been activated or deactivated as a result of chemical exposure."); *see also* Le Scouarnec & Gribble, *supra* note 83, at 76 (explaining how microarrays work).

86. Le Scouarnec & Gribble, *supra* note 83, at 75.

87. *See e.g.*, Peter Soderkvist & Olav Axelson, *On the Use of Molecular Biology Data in Occupational and Environmental Epidemiology*, 37 J. OCCUPATIONAL ENVTL. MED. 84, 84–86 (1995) (describing study models); Wang et al, *supra* note 81, at 131 (discussing results of study of gene-environment

This extension of epidemiologic methods marks the field of molecular epidemiology.[88]

A goal of toxicogenomic and molecular epidemiologic studies is to identify biomarkers—biochemical characteristics that reveal a toxic relation of interest. A biomarker of exposure is an observable change that occurs with exposure but is otherwise absent. A biomarker of effect is an observable, medically significant, harmful change that occurs with exposure but is otherwise absent. A biomarker of susceptibility, by contrast, is an observable genetic variation that alters the extent to which an exposure causes toxic harm.[89] Researchers have begun to find markers of each type.

For example, as stem cells divide and differentiate into various types of white blood cells, metabolites of benzene interact with DNA to cause errors during the copying of chromosomes.[90] Research has revealed that blood cells of individuals occupationally exposed to benzene are more likely to have particular chromosomal aberrations associated with the development of certain forms of a group of cancers called acute myelogenous leukemia (AML).[91] The observation suggests a biological mechanism of benzene carcinogenicity, tending to confirm classical epidemiologic studies that detected an association between exposure to benzene and incidence of AML. It also could provide a marker of benzene exposure or effect.[92]

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interaction in variable health effects of air pollution).

88. *See* Margaret R. Spitz & Melissa L. Bondy, *The Evolving Discipline of Molecular Epidemiology of Cancer*, 31 CARCINOGENESIS 127, 127 (2010) (explaining that molecular epidemiology is an extension of classical epidemiology using biomarkers); Vineis & Perera, *supra* note 59, at 1954 (defining molecular epidemiology).

89. *See* Grodsky, *supra* note 85, at 181–87.

90. *See* Milward v. Acuity Specialty Prods. Grp., Inc., 664 F. Supp. 2d 137, 143–46 (D. Mass. 2009), *rev'd*, 639 F.3d 11 (1st Cir. 2011) (describing testimony about chromosome aberrations associated with benzene exposure).

91. *See* Luoping Zhang et al., *The Nature of Chromosomal Aberrations Detected in Humans Exposed to Benzene*, 32 CRITICAL REV. TOXICOLOGY 1, 4–12 (2002) (reviewing published research).

92. *See id.*; *see also* Luoping Zhang et al., *Nonrandom Aneuploidy of Chromosomes 1, 5, 6, 7, 8, 9, 11, 12, and 21 Induced by the Benzene Metabolites Hydroquinone and Benzenetriol*, 45 ENVTL. MOLECULAR MUTAGENESIS 388, 394–95 (2005) (finding that preliminary work in exposed humans shows benzene

Other studies have found potential biomarkers of susceptibility. For instance, epidemiologic studies strongly linked mesothelioma incidence to asbestos exposure, but estimates of relative risks varied.[93] In a region of Turkey with high environmental exposure to a form of asbestos, researchers found that mesothelioma was not randomly distributed but rather clustered in certain families, suggesting that susceptibility to asbestos-induced mesothelioma has a genetic component.[94] Although the full picture is far from clear, one study of asbestos-exposed people found higher susceptibility in those with certain variations in a gene that codes for an enzyme that catalyzes production of antioxidant molecules.[95]

Another example involves the suspected link between tobacco smoke and breast cancer, which eluded conventional epidemiologic investigation.[96] Genomic investigations observed that variations in a gene that codes a carcinogen-neutralizing enzyme dramatically influenced the breast cancer danger from smoking. Women whose genes coded for the most protective form

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selectively affects certain chromosomes).

93. *See* J. Corbett McDonald, *Epidemiology of Malignant Mesothelioma—An Outline*, 54 ANN. OCCUP. HYG. 851, 852 (2010) (listing studies).

94. R.M. Rudd, *Malignant Mesothelioma*, 93 BRIT. MED. BULL. 105, 108 (2010); *see also* Below, *supra* note 78, at 254 (suggesting that genome-wide association studies (GWAS) would likely reveal genetic susceptibility factors). Other factors, including random sampling error, could account for some of the variation in relative risk results as well. *See* Michael D. Green, *Second Thoughts About Apportionment in Asbestos Litigation*, 37 SW. L. REV. 531, 538 (2008) (describing gaps in knowledge of mesothelioma causation); *see also* McDonald, *supra* note 93, at 852–55 (discussing possible differences in forms of asbestos that study subjects were exposed to).

95. Aki Murakami et al., *Heme Oxygenase-1 Promoter Polymorphism is Associated with Risk of Malignant Mesothelioma*, 1 LUNG 333 (2012); *see also* Joseph R. Testa et al., *Germline* BAP1 *Mutations Predispose to Malignant Mesothelioma*, 43 NATURE GENETICS 1022, 1022, 1025 (2011) (reporting that mutations in a gene that codes for a tumor suppressor protein may be associated with heightened risk of several cancers even without asbestos exposure, but predominantly mesothelioma if asbestos exposure is present).

96. *See* David H. Phillips & Seymour Garte, *Smoking and Breast Cancer: Is There Really a Link?*, 17 CANCER EPIDEMIOLOGY BIOMARKERS & PREVENTION 1, 1 (2008) (explaining that epidemiologic associations are lacking despite evidence from rodent studies and presence of activating enzymes and DNA adducts in human breast tissue).

of the enzyme had no increased risk of breast cancer even if they smoked, but women smokers with less protective forms of the gene were eight times more likely to get breast cancer than were women with the same genotype who did not smoke.[97] The gene variations thus could act as biomarkers of susceptibility.

These examples show the potential of toxicogenomics and molecular epidemiology but should not obscure the difficulties facing these sciences. Biologists did not need, or should not have needed, to sequence the entire human genome to understand that sequencing the genome alone would not tell the entire story of disease or of toxicity.[98] The links between genes, toxic substances, and disease form a web far more complex than previously imagined.

Genome-scale studies test vast numbers of genes and alleles[99]—so many that random chance would produce large numbers of coincidental associations between gene and disease (or between gene and toxicity). Although genomic researchers abide by a statistical significance convention orders of magnitude more stringent than the typical 95% level used in most scientific

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97. Rick Weiss, *What's Your Cancer Profile?, Scientists Focus on an Overlooked Class of Genes that May Determine Your Odds*, WASH. POST, Sept. 19, 1995, at Z12. The gene in question is distinct from the so-called "breast cancer genes" *BRCA1* and *BRCA2. See* Christine B. Ambrosone et al., *Cigarette Smoking, N-Acetyltransferase 2 Genotypes, and Breast Cancer Risk: Pooled Analysis and Meta-analysis,* 17 CANCER EPIDEMIOLOGY BIOMARKERS & PREVENTION 15, 25 (2008) (explaining that "cigarette smoking is associated with an increase in breast cancer risk among women with NAT2 slow acetylator genotypes").

98. RICHARD C. LEWONTIN, THE TRIPLE HELIX 16–17, 80–82 (2000).

99. So far, at least 16 million single nucleotide polymorphisms (SNPs)—variations that change one DNA base pair—have been identified. Simon N. Stacey et al., *A Germline Variant in the* TP53 *Polyadenylation Signal Confers Cancer Susceptibility*, 43 NATURE GENETICS 1098, 1099 (2011). That number is rapidly increasing. *See* Altshuler et al., *supra* note 82, at 833 (discussing how the number of known SNPs rose from 1.4 million in late 1990s to more than 10 million by 2008). At least two million variations involving small insertions or deletions of DNA have been found as well. Julienne M. Mullaney et al, *Small Insertions and Deletions (InDels) in Human Genomes*, 19 HUM. MOLECULAR GENETICS R131, R133 (2010). Some researchers suggest that these and other structural variations in DNA may be even more important than SNPs. Yingrui Li et al., *Structural Variation in Two Human Genomes Mapped at Single-Nucleotide Resolution by Whole Genome de Novo Assembly*, 29 NATURE BIOTECHNOLOGY 723, 723, 728 (2011).

investigation, false positive results are easy to obtain and difficult to exclude.[100] Associations must be investigated to assess their biological reality.[101] And the effect of a given allele on toxic susceptibility may not be a fixed value; it may vary depending on the alleles found at other genes or on other environmental factors.[102]

Furthermore, a gene's base sequence is not its only biologically relevant feature. All of a person's cells have the same DNA, except for mutations acquired in individual cells during life,[103] but they do many different things.[104] Whether a gene is expressed or not, and to what extent—that is, whether its DNA is actively being transcribed into RNA and translated into assembled proteins—is critical to the proper functioning of cells, tissues, and organs.[105] Deviations from normal gene expression

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100. *See* Ian P.M. Tomlinson et al., *Investigation of the Effects of DNA Repair Gene Polymorphisms on the Risk of Colorectal Cancer*, 27 MUTAGENESIS 219, 219 (2012) (describing a study that failed to support previously reported gene-disease associations); Samuel P. Dickson et al., *Rare Variants Create Synthetic Genome-Wide Associations,* PLOS BIOLOGY, Jan. 2010, at 1, 5–7.

101. Spitz & Bondy, *supra* note 88, at 130; *see also* Inês Barroso, *Non-Coding but Functional*, 489 NATURE 54, 54 (2012) ("[A]ssociation is not causality, and identifying those variants which are causally linked to a given disease or trait . . . has been difficult.").

102. *See* Camille Limoges, *Errare Humanum Est: Do Genetic Errors Have a Future*, *in* ARE GENES US?, *supra* note 5, at 113, 121 (noting that even in Mendelian disorders caused by changes in a single gene, phenotype is often subject to modification by other genes and environmental factors); Christopher A. Maxwell et al., *Genetic Interactions: The Missing Links for a Better Understanding of Cancer Susceptibility, Progression and Treatment*, 7 MOLECULAR CANCER 4, *8 (2008), http://www.molecular-cancer.com/content/pdf/1476-4598-7-4.pdf ("The detection of these [gene-gene] interactions will be invaluable to our understanding of cancer risk."); Leonardo A. Pinto et al., *Impact of Genetics in Childhood Asthma*, 84 JORNAL DE PEDIATRIA S68, S68, S72 (2008) (noting that asthma involves many genes and results from interaction of genetic and environmental factors); Christopher P. Wild, *Environmental Exposure Measurement in Cancer Epidemiology,* 24 MUTAGENESIS 117, 117 (2009) ("[P]recise contribution of specific risk factors and their interaction, both with each other and with genotype, continues to be difficult to elucidate.").

103. *See generally* WILLS, *supra* note 54, at 91 (explaining that about one DNA base per 500,000 is mutated during a lifetime). The gametes (sperm and egg cells), of course, do not contain the same DNA as other body cells. *Id.*

104. *See* ROSENFIELD ET AL., *supra* note 58, at 108–13.

105. *Id.* at 95–101, 108–13.

are important to many disease processes.[106] Gene expression is controlled in part by regulatory genes[107] and in part by an epigenome of other biochemical constituents that provides instructions that influence gene activity.[108] The epigenome is easily altered by environmental factors, sometimes in ways that echo long after the exposure and sometimes in ways that (unlike a change to a gene) cannot be detected later.[109]

All this complexity has implications for the genetic study of disease as well as for the study of toxicogenomics. Both the power and the limits of toxicogenomics will affect proof of specific causation in toxic torts.

B. The False Promise

A number of commentators have eagerly anticipated the day when science exposes the presumed deterministic mechanism of toxic causation for all to see.[110] The hope is that biomarkers will

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106. *See generally* Altshuler et al., *supra* note 82, at 881.

107. Raffan & Semple, *supra* note 70, at 14; *see also* Joseph R. Ecker, *Serving Up a Genome Feast*, 489 NATURE 52, 52 (2012) ("[T]he space between genes is filled with enhancers (regulatory DNA elements), promoters (the sites at which DNA's transcription into RNA is initiated) and numerous previously overlooked regions that encode RNA transcripts that are not translated into proteins but might have regulatory roles.").

108. Constituents of the epigenome include methyl groups that may be attached to DNA bases, histone proteins associated with DNA, non-coding DNA sequences, RNA sequences that interfere with or otherwise regulate the translation of DNA into protein, and other aspects of a cell's biochemistry. *See* Mark A. Rothstein et al., *The Ghost in Our Genes: Legal and Ethical Implications of Epigenetics*, 19 HEALTH MATRIX 1, 5–8 (2009) (describing composition and function of epigenome); Ward et al., *supra* note 79, at 1356 (describing epigenetic effects).

109. *See* Kathryn Z. Guyton et al., *Improving Prediction of Chemical Carcinogenicity by Considering Multiple Mechanisms and Applying Toxicogenomic Approaches*, 681 MUTATION RES. 230, 235 (2009) (noting that epigenetic effects are important "especially during critical developmental windows").

110. *E.g.,* Jamie A. Grodsky, *Genomics and Toxic Torts: Dismantling the Risk-Injury Divide*, 59 STAN. L. REV. 1671, 1723 (2007); Klein, *supra* note 53, at 6–8; Albert C. Lin, *Beyond Tort: Compensating Victims of Environmental Toxic Injury*, 78 S. CAL. L. REV. 1439, 1441–42 (2005); Gary E. Marchant, *Genetic Susceptibility and Biomarkers in Toxic Injury Litigation,* 41 JURIMETRICS 67 (2000).

mark the truth or falsity of an individual plaintiff's causal allegation or a defendant's suggested alternate cause. The image one gets is of tiny molecular flags waving from damaged DNA or proteins: red for benzene, green for X-rays, blue and yellow for polycyclic aromatic hydrocarbons in tobacco smoke, etc. At the dawn of the genomic era, it was easy for both scientists and law professors to anticipate the discovery of those flags.[111] Deeper knowledge, however, has brought reason for doubt.

Scientists searching for biomarkers are concerned to ensure that the biomarkers are valid.[112] Biomarker validity, from the scientific perspective, entails a number of technical requirements related to the marker's intended use.[113] Despite the large amount of research into potential biomarkers, validation of new markers remains frustrating.[114]

To fulfill the hopes of tort scholars seeking relief from the puzzle of toxic causation, biomarkers must be valid both in a general sense and in a very particular way. In a general sense, the markers must be analytically valid so the results of a search for them can be trusted.[115] With respect to the legal system's needs, however, markers can only eliminate the indeterminacy of toxic causation claims if they can reliably distinguish between "true" and "false" causation claims in ill people. This implies, on the one hand, that a marker's presence demonstrates the

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111. For an example from medical research literature, see Soderkvist & Axelson, *supra* note 87, at 85 (suggesting that different patterns of DNA and protein adducts may be detected for different carcinogens). For an example from legal scholarship, by an author who is both a lawyer and a scientist, see Marchant, *supra* note 110, at 109 (suggesting that biomarkers will help resolve "vexing causation issues").

112. *See generally* Paul A. Schulte & Frederica P. Perera, *Validation*, *in* MOLECULAR EPIDEMIOLOGY, *supra* note 61, at 79.

113. *See* Nada Majkic-Singh, *Biomarkers: From Standardization to Performance*, 30 J. MED. BIOCHEM. 183, 183 (2011) (stating that a valid biomarker must be sufficiently sensitive, accurate, precise, specific, and reproducible for its intended use).

114. *See* Patrick M.M. Bossuyt, *Defining Biomarker Performance and Clinical Validity*, 30 J. MED. BIOCHEM. 193, 194 (2011) (noting "lack of progress in the methodology for biomarker evaluation"); Martin Latterich & Jan E. Schnitzer, *Streamlining Biomarker Discovery*, 29 NATURE BIOTECH. 600, 600 (2011) (observing that validation has been a "bottleneck").

115. *See* Bossuyt, *supra* note 114, at 194 (discussing analytical validity).

suspected cause-and-effect mechanism, and on the other, that a marker's absence demonstrates that the disease was caused by something other than the suspected cause.[116]

For the presence of a marker to establish specific causation more deterministically than is possible with today's evidence, the marker must link the exposure to the plaintiff's disease and exclude other causes. A marker might unambiguously show that a particular disease is present. That won't prove causation, however (except for the unusual disease that has been shown by other means to be a signature of a particular exposure, in which case the molecular marker would not be needed). A marker might even be able to distinguish that a particular case of disease was induced by an environmental toxin such as a carcinogen, instead of being "endogenous."[117] That might be definitive if human beings were lab rats living in controlled environments in which only the exposure of interest varied, but that is decidedly not the case.[118] Given the myriad of potentially harmful environmental agents to which we are all exposed, a biomarker's presence alone will suffice to prove a plaintiff's case only if the marker is specific to the exposure–disease combination.[119]

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116. This discussion addresses only the potential of biomarkers to show that exposure to a particular toxic agent caused disease, as opposed to some other toxic agent, a genetic or other endogenous cause, or an unknown cause. There seems to be no particular reason to believe that biomarkers would be at all helpful in identifying a cause among multiple purveyors of a single indistinguishable substance, which would add its own layer of causal indeterminacy.

117. *See* Henricksen v. ConocoPhillips Co., 605 F. Supp. 2d 1142, 1149 (E.D. Wash. 2009) (noting a distinction between environmentally-caused cases of leukemia and "de novo," "endogenous," "primary," or "idiopathic" cases).

118. *See* CTRS. FOR DISEASE CONTROL & PREVENTION, FOURTH NATIONAL REPORT ON HUMAN EXPOSURE TO ENVIRONMENTAL CHEMICALS (2009), http://www.cdc.gov/exposurereport/pdf/FourthReport.pdf (presenting data on blood and urine levels of 212 chemicals in a sampling of the American population); David Ewing Duncan, *The Pollution Within*, NAT'L GEOGRAPHIC, Oct. 2006, at 116, 126 (describing 165 potentially toxic chemicals identified in samples of author's body).

119. *See* Schulte & Perera, *supra* note 112, at 103 (explaining that a "specific" marker of exposure "attribut[es] negative results to a high percentage of unexposed persons"). For an example of the importance of marker specificity to a finding of causation, albeit in a different factual context, see Precourt v. Fairbank Reconstruction Corp., 856 F. Supp. 2d 327, 337 (D.N.H. 2012) (denying beef processor's motion for summary judgment on crossclaim against beef

Conversely, for the absence of a marker to disprove causation definitively, the marker must invariably be associated with disease caused by the suspect agent. This would imply that exposure produces the disease in question via a single biochemical pathway, that the pathway always produces the marker, and that the marker can always be detected after the disease has manifested.[120] Given the myriad of metabolic and mutagenic pathways by which some substances can cause illness, a biomarker's absence alone will suffice to disprove a plaintiff's case only if the marker is perfectly sensitive to the exposure–disease combination.[121]

In other words, the dream of certainty depends on the discovery of "signature" biomarkers that would connect harm to exposure in the same way that the handful of currently known "signature" diseases do.[122] Biomarker studies ordinarily accept a trade-off between sensitivity and specificity.[123] Biological and environmental complexity—of the human genome, the epigenome, metabolic and developmental processes, exposures, and their numbingly vast numbers of potential interactions—militate against the possibility that biomarkers of "signature"

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supplier because proof that bacteria from decedent was genetically identical to bacteria in supplier's meat did not exclude the possibility that plaintiff was infected by genetically identical bacteria from another source).

120. *See generally* Carl F. Cranor, *The Challenge of Developing Science for the Law of Torts*, *in* PERSPECTIVES ON CAUSATION, 261, 262–63 (Richard Goldberg ed., 2011) (distinguishing induction period from latency period of a disease and explaining that either or both may be long).

121. *See* Schulte & Perera, *supra* note 112, at 103 (noting that "sensitive" marker of exposure "pick[s] up a high percentage of individuals in the exposed group"). For an example in which the sensitivity of a marker was questioned, see Declaration of Martyn T. Smith, Ph.D. ¶¶ 25–26, Milward v. Acuity Specialty Prods. Grp., 664 F. Supp. 2d 137 (D. Mass. 2009), *rev'd*, 639 F.3d 11 (1st Cir. 2011), *cert. denied*, 132 S. Ct. 1002 (2012) (No. 07CV11944), 2008 WL 7425049 (asserting that the failure to detect a chromosome abnormality after benzene exposure did not exclude possibility that benzene caused the same disease by a different mechanism).

122. *See* Grodsky, *supra* note 110, at 1707 (discussing possibility of signature biomarkers).

123. *See, e.g.*, Sandhya Pruthi et al., *Evaluation of Serum Estrogen-DNA Adducts as Potential Biomarkers for Breast Cancer Risk*, 132 J. STEROID BIOCHEMISTRY & MOLECULAR BIOLOGY 73, 75–76 (2012) (explaining this general trade-off).

specificity and sensitivity are prevalent in our cells just waiting to be found.[124]

Some types of biochemical damage are thought to be common to numerous disease pathways or exposures. Oxidative stress is an example. Oxidation is thought to play a role in the genesis of cancer and other diseases,[125] but finding valid oxidative biomarkers for particular substance–disease links has proven difficult.[126] Oxidative damage from a given exposure may affect diverse biochemical components of human tissue;[127] conversely, many different exposures may cause harm through an oxidative mechanism.[128] Moreover, everybody's DNA is oxidized during life, so any putative oxidative biomarker must be found against a background incidence of oxidative damage, which is highly variable from person to person.[129] That background incidence and variability, whether it results from differences in genotype, environmental exposure, or both, makes it more difficult to find the type of specific and sensitive biomarkers needed for particularistic proof of toxic causation in individual cases.[130]

Some markers have proven to be less sensitive or specific than they at first seemed. For example, benzene is thought to cause certain leukemias by inducing relatively large-scale aberrations in chromosomes.[131] But although studies have found

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124. *See* Latterich & Schnitzer, *supra* note 114, at 602 (describing how study bias and genetic and epigenetic variability of patients, including gender, ethnicity, age, diet, and environmental factors, have contributed "to a level of biological complexity beyond the scope of what can be typically interrogated").

125. *See* Cosetta Minelli et al., *Interactive Effects of Antioxidant Genes and Air Pollution on Respiratory Function and Airway Disease: A HuGE Review*, 173 AM. J. EPIDEMIOLOGY 603, 603 (2011) (describing that oxidative stress is mechanism for air pollutants causing lung disease; Ward et al., *supra* note 79, at 1356 (stating that oxidative stress is believed to be carcinogenic mechanism)).

126. *See* Eileen D. Kuempel et al., *Carbon Black: Kuempel et al. Respond*, 119 ENVTL. HEALTH PERSP. 333, 333 (2011) (noting that "methodological challenges to the validation of oxidative stress biomarker assays remain").

127. Ward et al., *supra* note 79, at 1356.

128. *See* Minelli et al., *supra* note 125, at 603 (describing oxidative stress as a "mechanism of action common to all pollutants").

129. Ward et al., *supra* note 79, at 1356.

130. *Id.*

131. *See* Luoping Zhang et al., *Use of OctoChrome Fluorescence in Situ Hybridization to Detect Specific Aneuploidy Among All 24 Chromosomes in*

some chromosomal aberrations that occur at much higher frequencies in leukemias of patients with known occupational benzene exposure, they also occur in the control groups of these studies.[132] A number of different aberrations have been associated with benzene exposure.[133] The metabolism of benzene is complex;[134] several metabolites may be involved in the carcinogenic effect of benzene exposure, and benzene-caused carcinogenesis is likely a multi-step process.[135] Researchers do not know exactly how benzene causes chromosomal aberrations or exactly how those aberrations cause leukemia.[136] Despite the progress in chromosomal and genetic study of leukemia in people exposed to benzene, the search for a "signature" biomarker continues.[137]

Similar issues have dogged the search for smaller toxic signatures in DNA, such as mutations of individual genes. Investigators examined the DNA of persons with a type of kidney cancer called renal cell carcinoma (RCC), which is known to begin with the mutation of a particular gene. They observed that the tumors of RCC patients who had been occupationally exposed to

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Benzene-exposed Workers, 153–54 CHEMICO-BIOLOGICAL INTERACTIONS 117, 118 (2005) (explaining that benzene is an "established human leukemogen[,]" and its metabolites cause aberrant numbers of chromosomes).

132. *See* Zhang et al., *supra* note 91, at 6 (describing a study in which chromosome abnormalities were present in 100% of leukemia patients with benzene exposure but 54% of non-exposed patients).

133. *See* Luoping Zhang et al., *Chromosome-Wide Aneuploidy Study (CWAS) in Workers Exposed to an Established Leukemogen, Benzene*, 32 CARCINOGENESIS 605, 605 (2011) (finding that benzene-exposed subjects showed statistically significant increases in frequency of aberrations on eight chromosomes).

134. *See* Michael G. Bird et al., *International Symposium: Recent Advances in Benzene Toxicity*, 153–54 CHEMICO-BIOLOGICAL INTERACTIONS 1, 4 (2005) (describing benzene as an example of "metabolic multi-tasking").

135. Michael G. Bird et al., *BENZENE 2009—Health Effects and Mechanisms of Bone Marrow Toxicity: Implications for t-AML and the Mode of Action Framework*, 184 CHEMICO-BIOLOGICAL INTERACTIONS 1, 5 (2010); *see also* Eric S. Johnson et al., *A Critique of Benzene Exposure in the General Population*, 375 SCI. TOTAL ENV'T 183, 192–94 (2007) (listing potentially significant benzene metabolites and sources of exposure).

136. Zhang et al., *supra* note 133, at 610; *see also* Bird et al., *supra* note 134, at 3 (explaining that it is not known if chromosomal aberrations are random or which metabolites are responsible).

137. Zhang et al., *supra* note 133, at 610.

trichloroethylene (TCE) carried a pattern of mutations not observed in people who had not been exposed or whose cancer resulted from inherited alterations in the gene.[138] But fewer than half of the TCE-exposed study subjects showed that mutation pattern.[139] Another group of researchers could not replicate the finding of the purported signature mutation.[140]

RCC, moreover, is atypical in being traceable to mutations in a single gene. Much more commonly, cancer is characterized by many mutated genes, and sorting out causes from effects is difficult.[141] The recently published genomic atlases of colon and rectal cancer[142] and breast cancer,[143] for example, identified a large number of genetic changes in the studied sample of tumors. In colon and rectal cancer, some of those changes were found in a large proportion of the tumors.[144] That is good news from the perspective of treatment, because it suggests that a relatively

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138. Hiltrud Brauch et al., *Trichloroethylene Exposure and Specific Somatic Mutations in Patients with Renal Cell Carcinoma*, 91 J. NAT'L CANCER INST. 854, 854 (1999).

139. *Id.* at 859.

140. Barbara Charbotel et al., *Trichloroethylene Exposure and Somatic Mutations of the VHL Gene in Patients with Renal Cell Carcinoma*, 2 J. OCCUPATIONAL MED. & TOXICOLOGY 13, at *6 (2007), http://www.occup-med.com/content/pdf/1745-6673-2-13.pdf.

141. WILLS, *supra* note 54, at 23 ("Genetic mayhem at the gene and chromosome level can continue even after the cell becomes cancerous. This confuses the picture, covering up the traces of the original cancer-causing events."); The Cancer Genome Atlas Network, *Comprehensive Molecular Characterization of Human Colon and Rectal Cancer*, 487 NATURE 330, 330 (2012) [hereinafter *Human Colon and Rectal Cancer*] (identifying thirty-two recurrently mutated genes and many other genetic alterations in colon cancer); Guyton et al., *supra* note 109, at 233 (noting it is unlikely that all 1,149 somatic mutations found in a group of breast and colorectal cancers are key events); Yih-Horng Shiao, *Genetic Signature for Human Risk Assessment: Lessons from Trichloroethylene*, 50 ENVTL. & MOLECULAR MUTAGENESIS 68, 70 (2009) (stating that only some genetic alterations found in tumors are tumorigenic "drivers" while others are "passengers").

142. *Human Colon and Rectal Cancer*, *supra* note 141, at 330 (identifying "32 somatic recurrently mutated genes . . . in the hypermutated and nonhypermutated cancers").

143. The Cancer Genome Atlas Network, *Comprehensive Molecular Characterization of Human Breast Tumours*, 490 NATURE 61, 61 (2012) [hereinafter *Human Breast Tumours*] (identifying "619 mutations across 177 previously reported cancer genes").

144. *Human Colon and Rectal Cancer*, *supra* note 141, at 333–35.

small number of pathways drive the development of these cancers,[145] but it also suggests that finding pathways unique to individual carcinogens seems less likely. For breast cancer, the research described four major subtypes of the disease characterized by different sets of genetic and epigenetic changes, with some changes found frequently within a subtype and a few relatively common across subtypes.[146]

Changes in gene expression, a common subject of study by DNA microarrays, also often are similarly multifarious and may be mediated both by mutations and by epigenetic effects.[147] Their significance as markers is more limited than biologists first believed.[148]

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145. *See* Gina Kolata, *In Gene Study, a Map to Fight Colon Cancer*, N.Y. TIMES, July 19, 2012, at A3 ("The hope now is that the genetic alterations driving those 1,000 different tumors are operating through only a limited number of genetic pathways that can be targeted by a more manageable number of drugs.").

146. *Human Breast Tumours*, *supra* note 143, at 61–62 (reporting that somatic mutations at three genes occurred in more than ten percent of all tumors studies, but numerous genes were frequently mutated in particular subtypes of breast cancer).

147. *See* Paolo Vineis & Miquel Porta, *Causal Thinking, Biomarkers, and Mechanisms of Carcinogenesis*, 49 J. CLINICAL EPIDEMIOLOGY 951, 955 (1996) (noting that once people are sick it is hard to distinguish altered expression that shows they are sick from altered expression that causes sickness); *see also, e.g.*, Yoko Hirabayashi, *p53-Dependent Gene Profiling for Reactive Oxygen Species After Benzene Inhalation: Special Reference to Genes Associated with Cell Cycle Regulation*, 153–54 CHEMICO-BIOLOGICAL INTERACTIONS 165, 165 (2005) (determining that expression changes after benzene exposure may be masked by other genes); Sarah X.L. Huang et al., *Role of Mutagenicity in Asbestos Fiber-induced Carcinogenicity and Other Diseases*, 14 J. TOXICOLOGY ENVTL. HEALTH PART B 179, 214–19 (2011) (describing many gene expression changes in cancers of patients who had been exposed to asbestos).

148. Alan Dove, *Biomarker Hunters Probe the Proteome*, 329 SCI. 1373, 1373 (2010).

> [C]hanges in the RNA transcription levels of a gene are mere hints of what's actually happening in cells and tissues; the complex interactions between proteins downstream of the transcripts drive much of an organism's physiology. . . . [V]alidating a potential disease biomarker in the clinic turns out to be a much thornier problem than most investigators had realized.

Id. Very recently, an international consortium of researchers published findings showing that the large amount of human DNA that does not contain protein-encoding genes does include large numbers of DNA "switches" that are responsible for turning other genes on or off, and that may explain variable

Molecular complexes between possible carcinogens and DNA or proteins, known as addition products or adducts, are another potential toxic signature.[149] Because of the long latency of many diseases that result from toxic exposure, an adduct would have to be long-lasting and detectable after disease has emerged in order to provide definitive proof in litigation.[150] It also would have to be specific and sensitive: that is, a specific adduct would have to result only from the exposure at issue rather than from a metabolic pathway involving exposure to some other substance, and all metabolic pathways linking the accused exposure to disease would have to necessarily produce the adduct. Finally, perhaps most difficult, to satisfy this causal model the presence of the adduct would have to indicate causation and not merely exposure.[151] The presence or absence of adducts will not

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incidence of disease despite identity of genes. Gina Kolata, *Study Discovers Road Map of DNA, a Key to Biology*, N.Y. TIMES, Sept. 6, 2012, at A1. The consortium's findings are expected to "force a rethink of the definition of a gene and of the minimum unit of heredity." Ecker, *supra* note 107, at 52. Whether they herald biomarkers that will provide individualized proof in toxic tort cases, however, is far from clear. Legal use of any biomarkers that may be found in these genetic switches would face the same hurdles of specificity and sensitivity. The initial findings suggest that much complexity and interaction exist in the regulation of gene expression. *See id.* (describing findings of "poorly understood" regulation of genes by distant DNA regions); Wendy A. Bickmore, *Expression Control*, 489 NATURE 53, 53–54 (2012) (describing findings of more than 200,000 DNA "enhancers" per cell type and pairing of 500,000 enhancers with nearby target genes, which still "leaves more than 2 million putative enhancers without known targets"); Benjamin Vernot et al., *Personal and Population Genomics of Human Regulatory Variation*, 22 GENOME RES. 1689, 1689 (2012) ("We estimate that individuals likely harbor many more functionally important variants in regulatory DNA compared with protein-coding regions, although they are likely to have, on average, smaller effect sizes.").

149. *See* Frederica P. Perera, *Molecular Epidemiology: On the Path to Prevention?*, 92 J. NAT'L CANCER INST. 602, 603 (2000) ("[U]sing adducts as biomarkers has the theoretical advantage that they reflect chemical-specific genetic damage.").

150. This may be true for some, but not necessarily all, adducts. In one study, DNA adducts of the carcinogen acetaldehyde had a half-life of thirty-five hours. Kimiko Hori et al., *Stability of Acetaldehyde-derived DNA Adduct in Vitro*, 423 BIOCHEMICAL BIOPHYSICAL RES. COMM. 642, 644 (2012).

151. *See, e.g.*, Yongquan Lai et al., *New Evidence for Toxicity of Polybrominated Diphenyl Ethers: DNA Adduct Formation from Quinone Metabolites*, 45 ENVTL. SCI. TECH. 10,720, 10,726 (2011) (discussing a study that demonstrated adduct formation *in vitro* but acknowledged that *in vivo*

necessarily sharply distinguish cases of disease caused by a particular exposure from background cases caused by something else.[152]

What about viewing the gene–toxin interaction from the opposite direction: looking for genetic variations that increase susceptibility to the toxin, rather than seeking signs of the toxin's effect on genetic material? Such research must confront a staggering amount of variability.[153] Because of gene–gene or gene–environment interactions, individual genetic variants do not typically determine the occurrence of disease, either alone or in combination with exposure to toxic substances.[154] A review of studies of genetic susceptibility to health effects of air pollution, for example, observed that the studies produced conflicting results. The review examined seven potentially relevant genes involved in antioxidant activity, but noted that many other

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implications of markers are unknown); Menglong Xiang et al., *Chromosomal Damage and Polymorphisms of Metabolic Genes Among 1,3-butadiene-exposed Workers in a Matched Study in China*, 27 MUTAGENESIS 415 (2012) (characterizing DNA alterations as markers of exposure).

152. *See* Stephen M. Rappaport et al., *Protein Adducts as Biomarkers of Human Benzene Metabolism*, 153–54 CHEMICO-BIOLOGICAL INTERACTIONS 103, 104 (2005) (noting "significant background levels" of adducts in persons in control group); Vineis & Perera, *supra* note 59, at 1954 (stating that adduct studies have shown "overall correlations" between adduct levels and exposures).

153. *See supra* note 99 and accompanying text (describing the large number of variations found in human DNA).

154. *See* Liam R. Brunham & Michael R. Hayden, *Response*, 337 SCIENCE 911, 911 (2012) ("[R]esults . . . appear to support [Nebert & Zhang's] view as regards common diseases, as many studies have reported a large number of loci, each conferring a small risk of disease."); D.W. Nebert & G. Zhang, *Personalized Medicine: Temper Expectations*, 337 SCIENCE 910, 910 (2012) ("[O]ne can infer that accurate statistical predictions of a complex trait require identification of many small-effect variants . . . . For most complex traits, this is an unachievable goal."); Raffan & Semple, *supra* note 70, at 10 ("[I]t is extremely difficult in an individual patient confidently to link a disease to only one or two mutations."); Ward et al., *supra* note 79, at 1356 (asserting that the magnitude of genetic associations with toxic susceptibility "may be modest and involve multiple genes"); *see also, e.g.*, Stacey et al., *supra* note 99, at 1098 (noting that the gene with the greatest increased risk of basal cell carcinoma had odds ratio of 2.36); Olivia Fletcher et al., *Association of Genetic Variants at 8q24 with Breast Cancer Risk*, 17 CANCER EPIDEMIOLOGY BIOMARKERS & PREVENTION 702, 705 (2008) (explaining that a study, although statistically equivalent to 12,000 samples, had insufficient statistical power to detect modest gene–gene interactions).

potentially important genes exist and concluded that because antioxidant mechanisms are complex, it is unlikely that any one polymorphic gene has a large effect on susceptibility. Nongenetic factors also play a role, so three-way interactions (among a given gene, pollutants, and other genes or environmental factors other than pollution) are real possibilities.[155]

More generally, the Environmental Genome Project has identified nearly 90,000 variations in more than 600 genes believed to be involved in response to environmental exposures.[156] For carcinogens, "[a]ddressing the role of genetic susceptibility . . . is . . . important; however, the stable and reproducible associations are few."[157]

In sum, many genes and epigenetic factors may affect toxic susceptibility, toxins may affect people in many ways, and many effects may result from more than one toxin.[158] It would be foolish to predict that no signature biomarker will ever be found for any disease caused by any exposure, but the evidence so far does not seem to suggest that signature biomarkers are typical.[159]

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155. *See* Minelli et al., *supra* note 125, at 603–05, 609–13 (describing studies of three-way interactions and the difficulties involved).

156. Mark J. Rieder, *The Environmental Genome Project: Reference Polymorphisms for Drug Metabolism Genes and Genome-Wide Association Studies*, 40 DRUG METABOLISM REV. 241, 244 (2008); *see* Nebert & Zhang, *supra* note 154, at 910 (noting that "most examples of pharmacogenomic traits (adverse drug reactions, as well as drug efficacy) resemble complex diseases and other multi-factorial traits [that] reflect contributions from innumerable low-effect genes").

157. Ward et al., *supra* note 79, at 1356.

158. *See* Huang et al., *supra* note 147, at 213 (describing multiple carcinogenic mechanisms for asbestos); Latterich & Schnitzer, *supra* note 114, at 602 ("Many pathologies . . . are complex and have multiple etiologies, especially at the molecular level.").

159. *See* Guyton et al., *supra* note 109, at 231–32 (describing the necessity of evaluating multiple modes of action of carcinogens); Latterich & Schnitzer, *supra* note 114, at 602 (stating that "very few single biomarkers are likely to have the high sensitivity and specificity necessary to make diagnosis and treatment decisions," although combining multiple markers might improve sensitivity and specificity); Shiao, *supra* note 141, at 69 ("Some agents can produce more than one type of DNA damage."); Ward et al., *supra* note 79, at 1360 (noting that genomic advances "are likely to increase the challenges and complexities of carcinogen testing and evaluation" in part because most carcinogenic mechanisms are not simple and carcinogens may act through diverse pathways).

Toxicogenomics and molecular epidemiology are unlikely to undo the Gordian knot of specific causation in toxic torts.[160]

C. The True Promise and Its Implications

Advancing scientific understanding can assist in legal fact-finding even if science will not provide law's longed-for, conclusive post hoc answer to the question of what *did* make a particular plaintiff sick. But the law must understand how science can best contribute. That understanding begins with acceptance of the fact that bringing toxicological understanding to the molecular level will not bring causation to the individual level. Even toxicogenomics and molecular epidemiology produce data that ultimately are group-based, statistical, and probabilistic—much like the data available before genomics.

Thus, finding that a plaintiff does or does not have a genetic susceptibility to the disease-causing effect of a substance to which the plaintiff was exposed will provide probabilistic but not deterministic evidence of causation or its absence.[161] Toxic

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160. Such research, however, may be extremely probative with respect to general causation. Mechanistic insights can form part of the weight of the evidence supporting an inference of general causation. Milward v. Acuity Specialty Prods. Grp., 639 F.3d 11, 20–23 (1st Cir. 2011). A study of susceptible genotypes can provide evidence of general causation when classical epidemiology does not. Tomlinson et al., *supra* note 100, at 219.

161. As two researchers explained:

> Particularly in the case of low-dose toxicants, the interactions of susceptibility genes with specific environmental factors are probably the dominant cause of any res
>
> ultant human illness. However, the probability that an environmental exposure will cause illness is dependent on the capacity of the genetically-controlled metabolic machinery and repair mechanisms of the cell. . . . Thus, elucidating the cause of most chronic diseases will require an understanding of both the genetic and environmental contributions to their etiologies.

Kenneth Olden & Janet Guthrie, *Genomics: Implications for Toxicology*, 473 MUTATION RES. 3, 5 (2001); *see also* Radoje Drmanac, *Response*, 337 SCIENCE 910, 911 (2012) (predicting that in the long run, limitations on measurement of gene effects on disease "will be less important than unpredictable environmental and stochastic effects"); Ebony B. Bookman et al., *Gene-Environment Interplay in Common Complex Diseases: Forging an Integrative Model—Recommendations From an NIH Workshop*, 35 GENETIC EPIDEMIOLOGY 217, 218–19 (2011) (stating

susceptibility genes do not determine that an individual of a particular genotype will contract a specified illness if subjected to a given exposure.[162] Rather, "[t]hey modify risk."[163] So, for example, even though a particular genotype of the *NAT2* gene makes it much more likely that a woman smoker will develop breast cancer, not all women of that genotype who smoke end up with breast cancer; some women who smoke develop breast cancer even though they do not have that genotype; some women develop breast cancer even though they neither smoke nor have that genotype.[164] And multiple studies of toxic susceptibility genes are unlikely to give identical results because of the influence of other factors and of random chance.[165]

Biomarkers of exposure or effect similarly provide probabilistic rather than deterministic evidence. For example, it would be relevant to know if a plaintiff's kidney cancer had a mutation pattern that is found more often among patients who had been exposed to trichloroethylene, but the pattern could nevertheless be present without causation and vice versa.[166] The same is true of the chromosome aberrations associated with benzene exposure in leukemia patients.[167]

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that susceptibility to most human diseases "is complex and multifactorial" and describing difficulty of assessing risk contribution in gene–environment interactions).

162. *See, e.g.,* Bookman et al., *supra* note 161, at 218 (giving example of how variations in the *NAT2* gene alter relative risk of smoking-related bladder cancer).

163. Olden & Guthrie, *supra* note 161, at 5.

164. *See* Ambrosone et al., *supra* note 97, at 23 (providing a table with data showing that while cigarette smoking increases the risk of breast cancer in those with the *NAT2* gene, possessing that gene is not the sole determining factor).

165. *See, e.g.*, Xiang et al., *supra* note 151, at 419 (discussing how a particular genotype showed a 2.28-fold increase in a specific type of DNA damage after exposure, and the results differed from earlier studies).

166. *See* Brauch et al., *supra* note 138, at 856 (providing data showing that of kidney cancer patients in the study who had occupational TCE exposure, fewer than half displayed a putatively characteristic mutation pattern); *see also* Scesnaite et al., *supra* note 77, at 426–27 (noting that various epigenetic changes were found more frequently in subjects exposed to tobacco smoke, but still in fewer than half of them).

167. *See* Vineis & Perera, *supra* note 59, at 1956 (describing a study that found "increased . . . frequencies of aberrations . . . frequently seen in . . .

Biomarkers are thus most useful from a scientific perspective "at the population level."[168] Their specificity, sensitivity, and predictive value are population-based rather than individualized attributes.[169]

Toxicogenomics and molecular epidemiology are producing evidence about suspected exposure-disease links at finer and finer scales of resolution,[170] but they have not altered the essential nature of that evidence. What these sciences will do, however, is produce more such evidence. More agents will be investigated to see if they are associated with molecular consequences. More genes will be interrogated to see if they affect susceptibility to agents.[171] The data will still be about relative risk, but risk will be parsed more and more finely. As research discriminates among genotypes, coexposures, and other variables that cannot be addressed with classical techniques, new associations will be detected or known associations will be disaggregated in new ways. This process has already begun even for causal connections that were already relatively well-accepted.[172]

At the same time, the enormous number of possible combinations of potentially interacting causal factors—genes, epigenetics, other individual characteristics, and exposures—

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leukemias").

168. *Id.*

169. *See* Bossuyt, *supra* note 114, at 197 ("Like sensitivity and specificity, predictive values are essentially group based measures.").

170. *See* Ward et al., *supra* note 79, at 1360 ("Research gaps and opportunities have been identified that can help to resolve uncertainties. . . . We hope that this process will lead to well-planned epidemiologic and mechanistic studies for these agents . . . .").

171. *See id.* ("Use of omics techniques will accelerate the understanding of the cellular and molecular basis for biological responses to environmental and occupational exposures, and high-throughput technologies will increase the number of agents that can be tested."); Minelli et al., *supra* note 125, at 618 ("The study of genetic susceptibility can greatly improve our understanding of air pollution pathophysiologic mechanisms of action and allow identification of those pollution components with the highest potential for harm.").

172. *See, e.g.*, E. Brigitte Gottschall, *Taking a Retrospective Look at Asbestos-Related Thoracic Disease Produces Interesting Results*, 255 RADIOLOGY 681, 682 (2010) (discussing how polymorphisms in the gene for a certain enzyme appear to affect risk from asbestos).

makes it extraordinarily unlikely that complete risk characterization will ever be possible at an individual level.[173] In a scientific research paradigm that depends on *ceteris paribus*, there is real doubt over whether every important variable can be held constant—or even identified—for the foreseeable future, if ever. Scientists know that there is much they do not know, but the "unknown unknowns" may be even more important.[174]

With better data on multiple exposures,[175] more frequent classification of risk by genotype,[176] and increasing mechanistic knowledge, science will likely point toward multiple causal sets of genetic, epigenetic, and environmental factors that are associated with disease risk. Even if some of those combinations display strong associations with a particular toxic outcome, other combinations will display weaker ones.[177] The better the science gets and the larger the data sets it can assemble, the easier it will be to identify relatively small incremental contributions to risk.

The reality is that the available proof in the new world of biomarkers, toxicogenomics, and molecular epidemiology will look a lot like the proof that has been available until now in the world of differential diagnosis, toxicology, and classical epidemiology. These sciences will dramatically increase the quantity of scientific information available to the legal system but will not represent a qualitative change in the nature of the information available to address the question of ex post causal attribution.

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173. *See* Christopher S. Carlson et al., *Mapping Complex Disease Loci in Whole-Genome Association Studies,* 429 NATURE 446, 450 (2004) (explaining how allowing for gene–gene or gene–environment interactions presents "intractable" problems for studies seeking association of genes and disease).

174. *See* Raffan & Semple, *supra* note 70, at 60 (concluding that new, next-generation gene sequencing technology "now allows researchers to take an unbiased approach to gene discovery, and thus to look for 'unknown unknowns'"). (Apologies to Donald Rumsfeld).

175. *See* Lin, *supra* note 110, at 1470–72 (describing prospects for improved exposure assessment); Wang et al., *supra* note 81, at 126 (describing a study that used personal monitors to measure exposure to air pollutants).

176. *See* Muin J. Khoury, *Genetic Epidemiology and the Future of Disease Prevention and Public Health*, 19 EPIDEMIOLOGIC REVS. 175, 176 (1997) (predicting that genotype information "will routinely be sought in almost every epidemiologic study").

177. *See, e.g.*, Pharoah et al., *supra* note 69, at 2797, 2801 (explaining that common genetic variations confer small incremental risks).

For the most part, increased knowledge of toxicity at the genomic and molecular levels will simply provide an increasingly detailed description of probabilistic associations—population-based frequencies rather than deterministic certainties. To seek a determined causal answer in this world would be like trying to determine the weather in Seurat's *Sunday Afternoon* by looking very closely at a few points of color in a lady's parasol.

At a molecular level, many of the processes associated with toxicity and disease are simply random.[178] The "probabilistic description of the mutation process cannot be replaced by a deterministic one."[179] Experiments have shown that even genetically identical cells exposed to the same environmental conditions can display random variations in gene expression, leading to significant differences in the chemical and phenotypic characteristics of the cells.[180] Such "random phenotypic noise, consequent on stochastic epigenetic processes," could have substantial effects on biological outcomes.[181] "Nowadays it is commonly stated that disease is either genetic or environmental, when in reality stochastic events are equally important."[182]

In the end, toxic causation questions dwell in a world with a substantial stochastic component that does not fit well with a deterministic causal model. It does not matter whether the connection between exposure and disease is really random or whether it only looks random because a truly deterministic pathway is too complex to be fully specified. What matters is that for the reasonably foreseeable future, science will not be able to

178. *See* ANATOLY RUVINSKY, GENETICS AND RANDOMNESS 7, 33–35 (2010) (discussing how quantum uncertainty manifests in random genetic alterations).

179. *Id.* at 39.

180. *See* Mads Kaern et al., *Stochasticity in Gene Expression: From Theories to Phenotypes*, 6 NATURE REVS. GENETICS 451, 451 (2005) (describing the study, in which "[s]pecial emphasis is given to stochastic mechanisms that can lead to the emergence of phenotypically distinct subgroups within isogenic cell populations").

181. Davey Smith, *supra* note 75, at 548; *see also* Drmanac, *supra* note 161, at 911 (noting importance of stochastic effects in attempting to measure genetic contribution to disease risk).

182. Robin Holliday, *DNA Methylation and Epigenotypes*, 70 BIOCHEMISTRY 500, 503 (2005).

give law a deterministic answer. Look closely enough, and certainty dissolves into probability.

IV. An Alternative Vision: Probabilistic Causal Contribution

Courts' square-peg–round-hole frustration continues as they try to make causation judgments by applying an individual-based, deterministic model to population-level, frequency-based probabilistic evidence.[183] The realization that reductionist science is not likely to discover the legal system's way out of the toxic causation problem suggests that courts should be open to a different mental model of causation—one that treats cause and effect explicitly as probabilistic—and should reconsider alternative doctrinal approaches to suit.[184] Adapting some ideas from earlier reform proposals offered by scholars, but largely ignored by courts,[185] I propose that courts adopt an expressly probabilistic view of causation when the dominating evidence comprises population-based data of toxic effect. To frame the standard, an exposure should be considered a cause of disease if it was a contributing factor to the disease's occurrence. To be a contributing factor, an exposure would be shown by a

183. *See* Merck & Co. v. Garza, 347 S.W.3d 256, 264 (Tex. 2011) (reiterating the view that "frequency data . . . cannot indicate the cause of a given individual's disease [but the] use of scientifically reliable epidemiological studies and the requirement of more than a doubling of the risk strikes a balance between the needs of our legal system and the limits of science") (quoting Merrell Dow Pharm., Inc. v. Havner, 953 S.W.2d 706, 718 (Tex. 1997)); Sienkiewicz v. Greif, [2011] UKSC 10, [2011] 170 A.C. 229, [170] (Lady Hale) (contrasting use of risk data to advise individual patient before getting sick with use of risk data to infer causation of existing illness); *id.* [190]–[92] (Lord Mance) (describing tension between use of statistical evidence and law's "concern[ ] with the rights and wrongs of an individual situation" and expressing preference for use of epidemiology "in conjunction with specific evidence related to the individual circumstances and parties").

184. One clarification is essential. Although genomic data will not likely provide definitive particularistic proof of causation, such data could still be relevant to specific causation even if courts do not adopt probabilistic causal contribution, along with other evidence deemed relevant in the absence of deterministic proof.

185. Many of these are discussed in Michael D. Green, *The Future of Proportional Liability: The Lessons of Toxic Substances Causation, in* EXPLORING TORT LAW 352, 357–70 (M. Stuart Madden ed., 2005).

preponderance of the evidence—not limited to any single favored type of evidence—to have added incremental risk that the plaintiff would develop a disease that the plaintiff in fact developed. Damages should be apportioned to that contributing factor in proportion to its contribution to the plaintiff's risk.

A. A Metaphor

An illustration from the Third Restatement of Torts allows a metaphorical comparison of the deterministic causation model that fits typical cases and the probabilistic model that better fits most toxic torts. The illustration posits three defendants—Able, Baker, and Charlie—who negligently, independently, and simultaneously lean against a car. Collectively they provide enough force to send the car over a diminutive curb and down the side of the mountain. Any two of the actors together would have propelled the car over the edge, yet each actor alone is too weak to budge the car. Thus, no single actor's tort is either a sufficient or a necessary cause of the harm.[186]

The illustration addresses the problem of multiple sufficient causal sets, which are analogous only to a particular subset of toxic tort claims.[187] For present purposes, what matters is that

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186. The hypothetical is given in RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYSICAL & EMOTIONAL HARM § 27 cmt. f, illus. 3 (2010). *See id.* § 27 cmt. f ("In some cases, tortious conduct by one actor is insufficient . . . to cause the plaintiff's harm. Nevertheless, when combined with conduct by other persons, the conduct overdetermines the harm, i.e., is more than sufficient to cause the harm.").

187. The analogy is to several actors who contribute subthreshold doses of a toxin that exerts toxic effects only after a threshold dose is reached. *See id.* cmt. g ("Assuming that there is some threshold dose sufficient to cause the disease, the person may have been exposed to doses in excess of the threshold before contracting the disease. Thus, some or all of the person's exposures may not have been but-for causes of the disease."). The Restatement's quite proper rule, in both cases, is that at least until the threshold is reached, each contributor is a cause of the harm, even though causal sets that did not include that contributor would also have been sufficient to produce the harm. *See id.* cmt. f ("When an actor's tortious conduct is not a factual cause of physical harm under the [but-for] standard . . . only because one or more other causal sets exist that are also sufficient to cause the harm at the same time, the actor's tortious conduct is a factual cause of the harm."); *id.* cmt. g ("Nevertheless, each of the exposures prior to the person's contracting the disease . . . is a factual cause of the person's

the illustration works only because it fits an implicitly assumed mechanistic model of causation. Simple Newtonian physics describes the situation: we can compute the force required to overcome the car's inertia and the static friction of its tires on the parking surface. If we could reconstruct the accident, we might find that 300 pounds of force were required to move the car and that Able, Baker, and Charlie each provided 200 pounds. This knowledge, at least in qualitative terms, is implicit in the illustration's assumptions.

Suppose, however, that Able, Baker, and Charlie could not be described by Newtonian physics but only by quantum mechanics. On a mountaintop ringed with cars, the three charge around blindfolded. What is more, they are joined by undetectable sprites that also impart momentum to any object they strike. Sometimes Able, Baker, and Charlie hit a car, and sometimes the impact is powerful enough to tip the car down the hill. But this is a quantum world: if we know what they hit, we cannot tell how hard they hit it.[188] And we can't detect the sprite strikes at all. Every once in a while a car rolls down the hill. But the most science can tell us—if we can say whether Able, Baker, Charlie, or any combination of the three hit the car at some point before its descent—is the probability that they hit the car hard enough to make it move.

If Able, Baker, and Charlie represent independent risk factors for a disease, and the invisible sprites represent unknown causes, then the probabilistic metaphor fits a wide range of toxic tort cases. In fact, toxic tort plaintiffs with this much information—those who find some epidemiologic data that, despite being inherently group-based and probabilistic, connect their exposure with their disease—have been the lucky ones. Toxicogenomics and molecular epidemiology will make that type of information available in more cases and in a more tailored

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disease under the rule in this Section."); *see also* Jane Stapleton, *Two Causal Fictions at the Heart of U.S. Asbestos Doctrine*, 122 L.Q. REV. 189, 191 (2006) (discussing threshold toxic mechanisms).

188. This of course is a metaphorical modification of the uncertainty principle. *See* RUVINSKY, *supra* note 178, at 4 (explaining Heisenberg's uncertainty principle).

way, but they will not change the nature of the appropriate model.

B. Contributing Factor Causation

The first step toward a different model of causation is to acknowledge frankly the irreducible indeterminism of post hoc causal assessments. A few courts that decided relatively early toxic tort cases, recognizing that the traditional "logical model . . . does not suit the toxic tort explanandum," seemed to move toward such an alternative model.[189] These courts used "substantial factor" as their anchor.[190] *Allen v. United States*[191] remains a leading example and stands in analytical counterpoint to the Tenth Circuit's decisions in *June* and *Wilcox*.[192]

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189. Elam v. Alcolac, Inc., 765 S.W.2d 42, 174 (Mo. Ct. App. 1988).

190. The Third Restatement explained *Elam* as an instance in which "substantial factor" was invoked to deal with multiple sufficient causes. RESTATEMENT (THIRD) TORTS: LIAB. PHYSICAL & EMOTIONAL HARM § 26 cmt. c, reporters' note (2010). *Elam* discussed multiple-sufficient-cause situations, but the issue on appeal was whether plaintiffs' evidence proved that defendant's chemical releases caused injury to plaintiffs at all. *Elam,* 765 S.W.2d at 174, 183. The court invoked "substantial factor," but never suggested that it believed the evidence showed more than one sufficient cause had operated to produce plaintiffs' conditions. *See id.* at 174 (determining that the substantial factor test suited toxic exposure cases where harm may result from a "confluence of causes"); *id.* at 187 n.63 ("[T]he substantial factor rule of causation . . . applies to [toxic tort] cases."); *id.* at 195 (referring to many different possible causes).

191. Allen v. United States, 588 F. Supp. 247 (D. Utah 1984), *rev'd on other grounds*, 816 F.2d 1417 (10th Cir. 1987).

192. *Compare id.* at 429–43 (applying the substantial factor rule to the plaintiffs), *and Elam*, 765 S.W.2d at 174–77 (distinguishing but-for from substantial factor), *with* June v. Union Carbide Corp., 577 F.3d 1234, 1241 (10th Cir. 2009) (determining that but-for causation was appropriate), *and* Wilcox v. Homestake Mining Co., 619 F.3d 1165, 1168 (10th Cir. 2010) (agreeing with *June*). *See also* James v. Bessemer Processing Co., 714 A.2d 898, 908–09 (N.J. 1998) ("To prove medical causation, a plaintiff must show 'that the exposure [to each defendant's product] was a substantial factor in causing or exacerbating the disease.'") (citation omitted); *id.* at 913 (holding, without ever referring to "but-for" causation, that plaintiff, who worked at a drum reconditioning facility, had produced sufficient evidence of causation to withstand motion for summary judgment despite inability to prove the number or specific contents of drums from various defendants).

In *Allen*, twenty-four plaintiffs contended that radiation from above-ground nuclear weapons tests caused their cancers. As in *June* and *Wilcox*, general causation was indisputable, but specific causation was another matter. The plaintiffs' various "non-specific" cancers[193] might have been caused by the accused bomb-test radiation, by radiation from other sources, or by something other than radiation. The impossibility of proof led the court to eschew but-for causation. Instead, *Allen* concluded that

> [w]here it appears from a preponderance of the evidence that the conduct of the defendant significantly increased or augmented the risk of somatic injury to a plaintiff and that the risk has taken effect in the form of a biologically and statistically consistent somatic injury, i.e., cancer or leukemia, the inference may rationally be drawn that defendant's conduct was a substantial factor contributing to plaintiff's injury.[194]

Allen's creative move was the deft elision of risk augmentation with injury causation. The court's inference from one to the other was "rationally drawn" because the scientific evidence needed to prove causation was, and could be, framed only in risk terms. Nevertheless, *Allen* broke new ground.[195] Its statement of the standard for proof of causation followed a lengthy discussion of creative common law solutions to other problems of causal indeterminacy, but none of those re-envisioned causation in probabilistic terms based on risk augmentation.[196]

The closest parallel is a sixteen-year-old opinion by the California Supreme Court in a worker's compensation case, *McAllister v. Workmen's Compensation Appeals Board*.[197] In

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193. *Allen*, 588 F. Supp. at 406. Presumably, by "non-specific" the court meant that the cancers were not uniquely associated with a particular exposure, i.e., they were not "signature" diseases. *Id.*

194. *Id.* at 428. The court allowed the defendant to defeat the inference if "the facts [were] proven otherwise by sufficient evidence." *Id.*

195. *See id.* at 415 ("A remedial framework can certainly be fashioned to meet the circumstances and requirements of the parties and issues now before this court in this action.").

196. *Id.* at 406–10. *Allen* cited alternative liability cases, multiple sufficient cause cases, and idiosyncratic cases in which absence of evidence makes the post hoc counterfactual inference especially difficult. *Id.*

197. McAllister v. Workmen's Comp. Appeals Bd., 445 P.2d 313 (Cal. 1968).

McAllister, a firefighter's widow claimed that her husband's on-the-job exposure to smoke caused his fatal lung cancer, although he had also smoked cigarettes for decades.[198] The opinion prefigured the factual causation issues that would come to bedevil toxic tort litigation:

> Given the present state of medical knowledge, we cannot say whether it was the employment or the cigarettes which "actually" caused the disease; we can only recognize that both contributed substantially to the likelihood of his contracting lung cancer. . . . Future scientific developments will tell us more about lung cancer. Ultimately it may be possible to pinpoint with certainty the cause of each case of the disease. But the Legislature did not contemplate years of *damnum absque injuria* pending such scientific certainty.[199]

To avoid that result, *McAllister* invoked precedent holding that a worker could obtain benefits if the employment was a "contributing cause" of an injury.[200] How could one tell whether exposure to smoke while firefighting was a "contributing cause" of lung cancer in a long-term tobacco smoker? By considering whether "the *likelihood* of contracting lung cancer from the smoking was so great that the *danger could not have been materially increased* by exposure to the smoke produced by burning buildings."[201]

Thus, in different contexts and with dramatically different amounts of evidence to work with, both *McAllister* and *Allen* recognized that scientific indeterminacy of specific causation justifies a risk-based, probabilistic reconceptualization of cause-

198. *Id.* at 314.

199. *Id.* at 319.

200. *Id. McAllister* went far beyond the precedent it relied on, which simply recognized that an event could have more than one cause. Emp'rs Mut. Liab. Ins. Co. of Wis. v. Indus. Accident Comm'n, 263 P.2d 4, 6 (Cal. 1953) (holding that injury could arise out of employment even if employment was not "the sole cause" but only "a contributory cause").

201. *McAllister*, 445 P.2d at 319 (emphasis added). *McAllister* also held that there was sufficient evidence to establish what is now known as general causation, even though there was no proof of exactly how smoke from building fires caused cancer. *Id.*

in-fact. But *McAllister* remained obscure and *Allen*'s causation analysis garnered little attention.[202]

To address a different but related problem of inherent causal indeterminacy, however, courts in both the United States and the United Kingdom have much more prominently linked evidence of risk creation to inferences of causation. In *Rutherford v. Owens-Illinois, Inc.*,[203] the California Supreme Court confronted the "indeterminate defendant" problem typical of many asbestos cases.[204] Mr. Rutherford had died of lung cancer after being tortiously exposed to asbestos fibers by numerous defendants, including his former employer and the manufacturers of asbestos-containing products that he had used at work.[205] Science could not interrogate the cancer to determine the source of the asbestos fiber or fibers that caused the malignancy.[206] The trial court instructed the jury on alternative liability, shifting the burden of proof on causation to the defendants.[207] The California Supreme Court held that doctrine inapplicable, but not because the

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202. Just a handful of California worker's compensation cases and two dissenting opinions outside of California have cited *McAllister*. Only *Elam v. Alcolac, Inc.* cited *Allen* in the course of adopting a causation standard anything like *Allen*'s. *See* Elam v. Alcolac, Inc., 765 S.W.2d 42, 174 (Mo. Ct. App. 1988) ("The substantial factor standard . . . is particularly suited to injury from chronic exposure to toxic chemicals where the sequent manifestation of biological disease may be the result of a confluence of causes.").

203. Rutherford v. Owens-Ill., Inc., 941 P.2d 1203 (Cal. 1997).

204. *See id.* at 1218 ("[A]sbestos-related cancer would, under the single-fiber theory of carcinogenesis, be an example of alternative causation, i.e., a result produced by a single but interminable member of a group of possible causes.").

205. *Id.* at 1207.

206. *See id.* at 1206 (implying that plaintiff could not "prove with medical exactitude that fibers from a particular defendant's asbestos-containing products were those, or among those, that actually began the cellular process of malignancy").

207. *See id.* at 1206–08. ("This instruction shifts the burden of proof to defendants in asbestos cases tried on a products liability theory to prove that their products were *not* a legal cause of the plaintiff's injuries , provided the plaintiff first establishes certain predicate facts . . . ."). Mr. Rutherford also had been a smoker, adding the possibility that the cancer had really been caused by tobacco smoke rather than asbestos. *See id.* at 1209 ("Undisputed evidence indicated that smoking sharply increases the risk of lung disease, including lung cancer, and works 'synergistically' with asbestos exposure to enhance the severity of resulting damage to the lungs."); *infra* notes 268–69 and accompanying text.

plaintiff could (and therefore must) establish which of the tortfeasors had delivered the fiber that actually caused his cancer.[208] Rather, the court held, "no insuperable barriers" prevented the plaintiff from proving causation without relying on the alternative causation doctrine—if causation were appropriately understood in the circumstances of the case.[209]

The most important of those circumstances was the "irreducible uncertainty" of determining which defendants' asbestos fibers actually contributed to the cellular development of cancer.[210] Despite that uncertainty, the court observed, every exposure to asbestos increased plaintiff's risk of disease.[211] The court therefore conceived all of the exposures as concurrent rather than alternative causes.[212] Left implicit in this conceptual shift was rejection of the deterministic model of causation as inappropriate.[213] Implementing that rejection, the court held that a particular product would be a "substantial factor in causing or bringing about the disease" if "it was a substantial factor

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208. *See Rutherford*, 941 P.2d at 1223 ("In an asbestos-related cancer case, the plaintiff need *not* prove that fibers from the defendant's product were the ones, or among the ones, that actually began the process of malignant cellular growth.").

209. *Id.* at 1206.

210. *Id.* at 1218.

211. *See id.* at 1209 ("[The defendant's] own medical expert . . . testified . . . that if a worker had occupational exposure to many different asbestos-containing products, each such exposure would contribute to the risk of contracting asbestos-related lung cancer . . . ."). As Michael Green pointed out to me, if any exposure occurred *after* the malignant transformation, that exposure did not in fact contribute to the risk of developing the tumor that plaintiff actually developed. Determining which exposures occurred before and after the malignancy began, however, is also impossible. Moreover, it is at least possible that continued exposure presents an additional carcinogenic risk even after a particular tumor has begun to grow.

212. *Id.* at 1220–21, 1223.

213. *Cf. id.* at 1218 (stating that the mechanism of cancer causation by asbestos remained a debated scientific issue, the resolution of which could affect legal conclusions regarding causation in cases of exposures from multiple sources). *But cf.* Jane Stapleton, *The Two Explosive Proof-of-Causation Doctrines Central to Asbestos Claims*, 74 BROOK. L. REV. 1011, 1029 (2009) (stating that *Rutherford*'s concurrent causation approach is based on "a fiction[] that every asbestos fiber was involved in the cancer mechanism").

contributing to plaintiff's or decedent's risk of developing cancer."[214]

A year after *Rutherford*, the New Jersey Supreme Court issued an opinion that was consistent with *Rutherford*'s reasoning, although it did not explicitly equate risk augmentation and causation.[215] Mr. James worked in a drum reprocessing facility where he was exposed to different types of chemical and petroleum residues in drums from many companies. His widow alleged that these residues caused Mr. James's fatal stomach and liver cancer.[216] Witnesses testified about which companies' drums were processed during Mr. James's employment, and expert witnesses testified that residues these companies shipped were carcinogenic.[217] But a lack of records made it impossible to prove how much of which residues from which companies Mr. James had come in contact with.[218] The court nevertheless decided that the evidence of causation against some defendants was adequate to survive summary judgment.[219] To establish "medical causation," the New Jersey Supreme Court held, a plaintiff like Mr. James must prove two things: (1) sufficient exposure to defendant's products and (2) "medical and/or scientific proof of a nexus between the exposure and the plaintiff's condition."[220] This is another way of saying that the defendant augmented the plaintiff's risk of disease.[221]

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214. Rutherford v. Owens-Ill., Inc., 941 P.2d 1203, 1220 (Cal. 1997).

215. James v. Bessemer Processing Co., Inc., 714 A.2d 898 (N.J. 1998).

216. *Id.* at 901.

217. *Id.* at 904–06.

218. *Id.* at 903, 913.

219. *Id.* at 913–14.

220. *Id.* at 911. To test sufficiency of exposure the court adopted the criterion of "frequent, regular and proximate exposure" borrowed from many asbestos cases. *Id.*

221. The close relation of risk augmentation to the *James* description of medical causation is evident in the court's description of the way a defendant might avoid joint and several liability under New Jersey's Comparative Negligence Act. Once "deemed [a] substantial factor[] in causing James's cancer," the court held, a defendant would bear the burden of proving a basis for apportioning fault. *Id.* at 916. "[E]ach defendant may seek to reduce its individual percentage of fault by submitting proof that its products . . . were *less carcinogenic* . . . or that James's exposure to its products was *more limited* . . . ." *Id.*

Courts in the United Kingdom reached a similar result by a path that began with a decision in a somewhat odd case, *McGhee v. National Coal Board*.[222] Mr. McGhee became covered in dust and sweat while cleaning out brick kilns and had to bicycle home in that condition because his employer did not provide washing facilities.[223] He developed dermatitis and sued his employer.[224] The medical experts agreed that the presence of the irritating dust on skin made vulnerable by perspiration caused Mr. McGhee's dermatitis.[225] The rub was that only the lack of a shower that extended the exposure to the dust, and not the working conditions that first deposited the dust on Mr. McGhee's skin, was held negligent.[226] Longer exposure increased the risk, but no expert could say whether Mr. McGhee would have avoided dermatitis had he showered at his workplace.[227] Therefore, the trial and intermediate appellate courts concluded, Mr. McGhee could not prove by a preponderance of the evidence that the employer's negligence had caused his dermatitis.[228] The losing plaintiff[229] appealed to, and prevailed in, the House of Lords.[230]

Four of the five members of the panel reasoned that in the circumstances of the case, to establish causation, it was sufficient that Mr. McGhee had shown that his employer's negligence had

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222. McGhee v. Nat'l Coal Bd. [1972] 3 All E.R. 1008, [1973] 1 W.L.R. 1 (H.L.).

223. *Id.* at 3–4 (Lord Reid).

224. *Id.* at 3.

225. *Id.*

226. *Id.*

227. *See id.* at 5 (Lord Wilburforce) ("The experts could [determine the cause of dermatitis], but had to admit that they knew little of the quantity of dust or the time of exposure necessary to cause a critical change.").

228. *See McGhee*, 1 W.L.R. at 3–4 (Lord Reid) ("It was held in the Court of Session that the appellant had to prove that his additional exposure to injury . . . caused the disease in the sense that it was more probable than not that this additional exposure to injury was the cause of it.").

229. The British cases refer to the party seeking relief as the pursuer or claimant, and to the party from whom relief is sought as the defender. For simplicity and ease of reading, I use the familiar American terms plaintiff and defendant (including survivors of decedents).

230. *See id.* at 13 ("Appeal allowed.").

materially increased his risk of disease. Lord Salmon's speech was representative:

> [W]hen it is proved, on a balance of probabilities, that an employer has been negligent and that his negligence has materially increased the risk of his employee contracting an industrial disease, then he is liable in damages to that employee if he contracts the disease notwithstanding that the employer is not responsible for other factors which have materially contributed to the disease . . . . In the circumstances of the present case, the possibility of a distinction existing between (a) having materially increased the risk of contracting the disease, and (b) having materially contributed to causing the disease may no doubt be a fruitful source of interesting academic discussions between students of philosophy. Such a distinction is, however, far too unreal to be recognised by the common law.[231]

The House of Lords revived *McGhee*'s reformulation of the concept of causation when it confronted a case similar to *Rutherford*, in which each claimant or decedent had developed mesothelioma after being exposed to asbestos by multiple defendants.[232] In *Fairchild v. Glenhaven Funeral Services Ltd.*,[233] the Lords allowed the appeals of three claimants who had lost below for failure to establish but-for causation.[234] The committee members differed in their analyses and in the limits they would impose on the doctrine being announced.[235] They were

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231. *Id.* at 12–13 (Lord Salmon); *see also id.* at 5 (Lord Reid) ("From a broad and practical viewpoint I can see no substantial difference between saying that what the respondents did materially increased the risk of injury to the appellant and saying that what the respondents did made a material contribution to his injury."); *id.* at 8 (Lord Simon of Glaisdale) ("'[M]aterial reduction of the risk' and 'substantial contribution to the injury' are mirror concepts in this type of case.").

232. *McGhee*'s formulation needed to be revived because intervening cases had cast doubt on the interpretation of *McGhee*. *See* Sanders, *supra* note 1, at 23–28 (tracing the discussion of the relation between risk contribution and causation in United Kingdom cases).

233. Fairchild v. Glenhaven Funeral Servs. Ltd., [2002] UKHL 22, [2002] 1 A.C. 32.

234. *See id.* [1] (Lord Bingham of Cornhill) ("[I]t was announced that these three appeals would be allowed.").

235. *See id.* [35]; [45] (Lord Nicholls); [118] (Lord Hutton); [170] (Lord Rodger).

unanimous, however, on the implication of the "rock of uncertainty"[236] that made it impossible for each claimant to prove which asbestos fiber(s) had invaded the cell from which the fatal mesothelioma grew.[237] In light of that scientific indeterminacy, a material contribution to risk should be considered a "sufficient degree of causal connection" to support a finding of causation.[238] The panel members noted the parallels with *Rutherford*,[239] and all but one openly acknowledged that *Fairchild* embraced a legal standard of causation different from the deterministic but-for model.[240]

These cases, from *McAllister* to *Allen* to *Rutherford* to *James* to *Fairchild,* groped toward a redefinition of specific causation in cases in which scientific indeterminacy rendered it impossible to prove by a preponderance of the evidence that a particular exposure was a but-for cause of a plaintiff's harm. Treating risk creation as causal contribution is appropriate when a plaintiff can prove that tortious conduct "materially increased the risk of him contracting a particular disease and the disease occurred, but where in the state of existing medical knowledge he is unable to prove by medical evidence that the [conduct] was a [but-for] cause of the disease."[241]

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236. *Id.* [7] (Lord Bingham of Cornhill).

237. *See id.* [7] (Lord Bingham), [49] (Lord Hoffmann), [77] (Lord Hutton), [120] (Lord Rodger) (acknowledging that current medical knowledge is insufficient to determine which asbestos fiber caused the cancer).

238. *Id.* [42] (Lord Nicholls of Birkenhead); *accord id.* [34] (Lord Bingham); *id.* [47] (Lord Hoffmann); *id.* [108]–[09] (Lord Hutton); *id.* [168] (Lord Rodger of Earlsferry).

239. *See id.* [31] (Lord Bingham), [73] (Lord Hoffmann), [105] (Lord Hutton), [161] (Lord Rodger) (noting that the court was asked to apply the rule from *Rutherford* that "the causal requirements of the tort were satisfied by proving that exposure to a particular product").

240. *See id.* [9] (Lord Bingham), [41], [43] (Lord Nicholls), [56], [63] (Lord Hoffmann), [168] (Lord Rodger) (variously characterizing the *Fairchild* holding as a variation, relaxation, or policy-based deviation from traditional rules of factual causation); *but see id.* [109] (Lord Hutton) (taking the view that in *McGhee* and *Fairchild* the plaintiffs succeeded based on judicial inference that but-for causation had been established more likely than not, though acknowledging that this interpretation makes "little practical difference").

241. *Id.* [108] (Lord Hutton). This formulation, by the one member of the Appellate Panel who declined to deviate expressly from traditional but-for causation, is almost indistinguishable from the way the other members of the

It is immediately apparent that this general statement of principle need not be restricted to asbestos cases or even to indeterminate-defendant cases,[242] despite the courts' tendency to do so.[243] The same type of indeterminacy afflicts a wide range of toxic tort claims that have two salient characteristics: (1) general causation is reasonably well-established (for example, by appropriately confirmed epidemiologic data showing increased risk associated with exposure); and (2) science cannot specify the cause of an individual case of disease. As explained above, molecular science is likely to increase the prevalence of the first characteristic without greatly decreasing the prevalence of the second. Thus, increasingly, a probabilistic conception of causation based on risk contribution will be needed to conform legal doctrine to the realistically available evidence.

Two asserted bases for limiting this view of causation to asbestos indeterminate-defendant cases merit discussion. The first argues that this concept of causation should apply only if the competing possible causes of plaintiff's illness all contributed to risk in the same way, e.g., by exposing a plaintiff to the same substance (i.e., asbestos).[244] The second argues that this concept

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panel expressed the rule. *See also* Barker v. Corus UK Ltd., [2006] UKHL 20, [2006] 2 A.C. 572, [77] (Lord Rodger) (noting that *McGhee* held "that, in the particular circumstances, by proving that the defenders had materially increased the risk of injury, the pursuer had proved that they had materially contributed to his injury").

242. *See* Fairchild v. Glenhaven Funeral Servs. Ltd., [2002] UKHL 22, [2003] 1 A.C. 32, [163] (Lord Rodger) (noting that although *Rutherford* limited its holding to asbestos cases, "the reasoning itself develops from the impossibility of proof inherent in those cases").

243. Sanders, *supra* note 1, at 32–33 (describing reticence of courts, including California courts, to extend the *Rutherford* "risk rule" to contexts beyond asbestos); *but cf.* Green v. Alpharma, Inc., 284 S.W.3d 29, 35–40 (Ark. 2008) (using "substantial factor" formulation, frequency-regularity-proximity test from asbestos cases, and testimony about leukemogenic risks of arsenic, to reverse summary judgment for poultry producers, each of which contributed an unknown amount of plaintiff's exposure to arsenic-laced chicken litter).

244. *See Fairchild*, [2002] UKHL 22, [115], [118] (Lord Hutton) (arguing that risk contribution model is inappropriate if multiple possible causal agents exist); Green, *supra* note 94, at 546 ("[A]ny risk contribution scheme should be limited to a single toxic substance whose risk profile is established (asbestos is surely that) and in which multiple defendants contributed to the risk but plaintiff is unable to prove which one(s) is the actual cause of her harm.").

of causation should apply only if all of the sources of plaintiff's exposure to enhanced risk are tortious.[245] From a theoretical perspective, neither argument is persuasive.

The first argument seems rooted in a concern for being reasonably certain of the substance that caused the disease and for being able to compare various risk contributions. It fails because exposure to an additional risk factor, and not only exposure to more of a single risk factor to which the plaintiff was already exposed, may increase a plaintiff's risk. As Lord Hoffmann noted in *Fairchild*, "what if [a plaintiff] had been exposed to two different agents—asbestos dust and some other dust—both of which created a material risk of the same cancer and it was equally impossible to say which had caused the fatal cell mutation? I cannot see why this should make a difference."[246] Lord Hoffmann later tweaked this view, explaining that the *substance* to which a plaintiff was exposed need not be the same, but the *mechanism* of disease causation must be the same for all of the exposures at issue.[247] The latter distinction, however, is equally untenable. The justification for the "risk rule"[248]—the inability to tell which of multiple exposures caused a given case of illness—is just as strong when the exposures increase the risk of a disease in different ways, if after the plaintiff is sick it is impossible to tell which mechanism operated to cause the illness.

Further, if identity of mechanism were crucial, then *defining* mechanism would become critical. That definition would depend on both the state of scientific knowledge and on judicial line-

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245. *See Barker*, [2006] UKHL 20, [14]–[16] (Lord Hoffmann) (acknowledging though disagreeing with the argument that a risk-based conception of causation should not apply if one of the sources of exposure was not tortious); *id.* [128] (Baroness Hale) (opining that rationale for imposing liability on those responsible for all asbestos exposures is absent or weakened if not all exposures were tortious).

246. *Fairchild*, [2002] UKHL 22, [72] (Lord Hoffmann).

247. *See Barker*, [2006] UKHL 20, [24] (Lord Rodger) ("It may have been different in some causally irrelevant respect, as in Lord Rodger's example of the different kinds of dust, but the mechanism by which it caused the damage, whatever it was, must have been the same.") *Cf. id.* [17] (referring ambiguously to exposure to "the same risk"); *see also* Sanders, *supra* note 1, at 29 (calling Lord Hoffmann's revision "a delightful piece of self-reinterpretation").

248. The nomenclature is Joseph Sanders's. Sanders, *supra* note 1, at 11.

drawing.[249] For Lord Hoffmann, asbestos and some other hypothesized "dust" were similar enough, but asbestos and tobacco smoke were not.[250] For the California Supreme Court in 1968 (when the mechanism of lung carcinogenesis was completely mysterious) smoke was smoke, whether it came from cigarettes or burning buildings.[251] If two substances are shown to cause the same histological form of cancer, should the law treat them as acting by the same mechanism? What if it can be shown that both are capable of altering DNA? Or must each be shown to increase cancer risk by turning off a tumor suppressor gene? Must it be the same tumor suppressor gene? What if both of them are shown sometimes to turn off the same tumor suppressor gene, and other times to turn off another tumor suppressor gene, and both genes are turned off in the patient's cancer? If the mechanisms by which two or more substances cause a disease were distinct, specific, and determinable after the fact—the false promise—then specific causation would be scientifically knowable, and there would be no need to conceptualize causation in probabilistic terms. In any other situation, however, mechanistic understanding at smaller scales will make it harder for two exposures to look the "same" but will not solve the indeterminacy problem that led to the *Fairchild* solution.[252]

The second argument, that a probabilistic, risk-augmentation view of causation should be limited to cases in which all the contributors of increased risk are tortious, seems rooted in the view that the only justification for modifying causation rules in

249. *See id.* at 36 (noting that such limits are both arbitrary and subject to change as science learns more).

250. *See Barker*, [2006] UKHL 20, [24] (Lord Rodger) ("I do not think that the exception applies when the claimant suffers lung cancer which may have been caused by exposure to asbestos or some other carcinogenic matter but may also have been caused by smoking . . . .").

251. *See* McAllister v. Workmen's Comp. Appeals Bd., 445 P.2d 313, 318–19 (Cal. 1968) ("We cannot doubt that the more smoke decedent inhaled—from whatever source—the greater the danger of his contracting lung cancer. . . . Given the present state of medical knowledge, we cannot say whether it was the employment or the cigarettes which 'actually caused the disease . . . .'").

252. It is true, however, that exposure to multiple risk factors may present formidable factual complexities. *See infra* notes 274–75 and accompanying text (discussing the possibility of the same solvent in materials produced by two different manufacturers).

the face of indeterminacy is the relative moral position of an "innocent" plaintiff and multiple "wrongdoers."[253] It also fails, as can be seen even in the context of asbestos mesothelioma cases.

The fact that each claimant in *Fairchild* had been exposed to asbestos by multiple employers distinguished each claim from what would have been an easy case if only one entity had been responsible for the exposure. But what distinguished these claimants from the general population of the United Kingdom was the fact that they were exposed to asbestos on the job. The source of the other exposure did not logically affect the determination of whether the tortious exposure contributed materially to the risk. The House of Lords recognized this in *Barker v. Corus UK Ltd.*,[254] which applied *Fairchild* to hold defendant employers liable to a claimant even though one of the claimant's material exposures to asbestos was entirely his own fault.[255]

The same reasoning would apply regardless of the competing source of exposure or risk. Thus, the Supreme Court of the United Kingdom reaffirmed this aspect of the logic of *Barker* in *Sienkiewicz v. Greif (UK), Ltd.*,[256] which involved two women with mesothelioma who had been exposed to relatively small amounts of asbestos at their respective workplaces.[257] The defendants

253. *See Barker*, [2006] UKHL 20, [128] (Baroness Hale) (making this argument).

254. Barker v. Corus UK Ltd., [2006] UKHL 20, [2006] 2 A.C. 572.

255. *See id.* at [17] (Lord Hoffmann) ("These distinctions may be relevant to whether and to whom responsibility can also be attributed, but from the point of view of satisfying the requirement of a sufficient causal link between the defendant's conduct and the claimant's injury, they should not matter."); *id.* [58]–[59] (Lord Scott) (asking how the *Fairchild* principle would apply to a case involving a claimant's exposure to multiple sources and determining that this would make no difference); *id.* [97] (Lord Rodger) ("Having reserved my opinion on the point in *Fairchild*, I would now hold that the rule should apply in that situation."); *id.* [117] (Lord Walker) (agreeing, except still believing that "the *Fairchild* principle [should apply] to cases where less than 100% of the risk has been caused by employers or occupiers guilty of breaches of duty"); *id.* [128] (Baroness Hale) (explaining that because *Barker* imposed only several liability based on risk contribution, "[t]he victim's own behaviour is only relevant if he fails to take reasonable care for his own safety during a period of tortious exposure by a defendant.").

256. Sienkiewicz v. Greif, [2011] UKSC 10, [2011] 2 A.C. 229.

257. *See id.* [2]–[4], [59]–[60], [115], [117]–[19], [124]–[25] (describing the

argued that each woman's exposure to asbestos in the ambient air exceeded her incremental exposure at work, and therefore it was more likely than not that the ambient exposure, rather than the workplace exposure, had caused her disease.[258] The Supreme Court unanimously rejected the argument, holding that so long as the negligent employer's contribution to the risk of mesothelioma had been "material," that negligence would be considered a cause of the claimant's mesothelioma.[259] Similarly, it should not matter if the competing exposure was not created by human agency at all, such as exposure to radiation by naturally occurring radioisotopes as in *Allen*, *June*, and *Wilcox*.[260]

Allen shows that the traditional "substantial contributing factor" formulation of the causal connection opens the possibility of reformulating causation in risk-creation terms to address specific causation in toxic torts. The treatment of asbestos indeterminate-defendant cases in California and the United Kingdom shows that the reformulation can be credibly applied. "At the very least," it proves "that it is not necessarily the hallmark of a civilised and sophisticated legal system that it treats cases where strict proof of causation is impossible in exactly the same way as cases where such proof is possible."[261]

C. Risk as Cause, Not as Harm

A probabilistic model of specific causation in toxic torts, as opposed to deterministic but-for causation, is best supported by

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facts).

258. *See id.* [60]–[61] (Lord Phillips) ("[T]he judge . . . heard expert evidence which quantified this exposure and compared it to the environmental exposure that would be experienced by everyone. . . . It was on the basis of this finding that the judge held that the claimant's case on causation had not been made out.").

259. *See id.* [107]–[09] (Lord Phillips) (determining what constitutes a "material risk" and applying that determination to this case).

260. *See* Sanders, *supra* note 1, at 40 ("[A]ll of the distinctions designed to rein in the reach of the risk rule feel arbitrary.").

261. Fairchild v. Glenhaven Funeral Servs., Ltd., [2002] UKHL 22, 168, [2002] 1 A.C. 32, [168] (Lord Rodger). The appropriate scope of liability in such cases is discussed *infra* Part IV.E.

existing and developing scientific evidence—but not in the sense that some particularistic trait of an individual's disease allows a direct estimate of the likelihood that his or her case was caused by a particular exposure.[262] Rather, an individual's combination of genetic makeup and exposure increases the likelihood of the disease relative to genetically similar individuals not exposed.[263] The exposure, accordingly, is considered a risk factor for the disease. The courts that decided *Allen*, *Rutherford*, *McGhee*, and *Fairchild* all recognized that in light of causal indeterminacy, it is appropriate to treat proof of contribution to risk as proof of contribution to cause.

In *Barker*, however, the House of Lords adopted a different conceptual framework to explain its *Fairchild* holding. According to the *Barker* majority, the *Fairchild* defendants were held liable not because the tortious augmentation of a plaintiff's risk was a contributing factor to the plaintiff's harm of mesothelioma, but because the tortious exposure of a plaintiff to asbestos caused the plaintiff's harm of increased risk of developing mesothelioma.[264] This reformulation extended *Fairchild* considerably with respect to the harm element of a tort.[265] With respect to causation

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262. The reasoning process known as differential etiology (usually—though inaccurately—called differential diagnosis) may seem to approach a direct estimate of a probability of causation in an individual case. Differential etiology attempts to prove that but-for causation is more likely than not, by ruling out other possible causes of the plaintiff's disease. It could be fully determinative if a set of deterministic causes of plaintiff's disease were fully characterized (e.g., if an infection were caused only by a known virus or a known bacterium, and exposure to one were ruled out). More often, however, the disease in question is characterized by several risk factors and a residuum of disease incidence unaccounted for by any known risk factor. Ruling out some risk factors may allow a more refined estimate of risk, but that estimate still would be derived ultimately from population-based studies.

263. Other traits besides genetics and exposure may be pertinent, such as exposures to additional toxins, environmental factors (e.g., nutrition or weather), or personal factors (e.g., age).

264. *See* Barker v. Corus U.K. Ltd., [2006] UKHL 20, [2006] 2 A.C. 572, [35]–[36] (Lord Hoffmann), [59]–[62] (Lord Scott), [126] (Baroness Hale) (noting that the defendants in *Fairchild* were not found to have ultimately caused the harm but that they were liable for creating the risk).

265. As Lord Rodger noted in dissent, the majority took pains to limit the extension, without convincing rationale, to the context of multiple asbestos exposures and mesothelioma. *Id.* [85] (Lord Rodger).

doctrine, however, it implicitly retreated to the comfortable confines of but-for: each material exposure to asbestos, tautologically, was a but-for cause of the increment of risk associated with that exposure.

Although the increased risk caused by a tortious toxic exposure could be considered sufficient harm to support a cause of action,[266] reconceptualization of causation-in-fact as proposed here has advantages over recognizing liability for a new tort based on creation of risk alone. The latter would invite the objection that many negligent or otherwise wrongful acts create risk of harm, but tort law ordinarily does not, and practicably

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266. *See id.* [71] (Lord Rodger) ("[T]he majority of the House proceeded on the simple basis that the creation of a material risk of mesothelioma was sufficient for liability."). The *Barker* majority's attempt to reframe *Fairchild* was unconvincing. The majority labeled the equation of risk creation with contribution to injury a "fiction" and cited passages from *Fairchild* rejecting reliance on legal fictions, but those passages rejected a different fiction—that proof of material contribution to risk permitted an inference of but-for causation. *Compare id.* [31]–[34] (Lord Hoffmann) (arguing that the *Fairchild* Court did not rely on the fiction that creation of a material risk constitutes material contribution to contraction of disease), *with id.* [80]–[83] (Lord Rodger) (countering that Lord Hoffmann's view that *Fairchild* "did not proceed on the basis that a defendant who had created a material risk of mesothelioma was deemed to have caused . . . the disease" was true only of Lord Hoffmann's own speech in *Fairchild* but not true of the *Fairchild* majority). This reframing was used to justify the conclusion that each defendant should be liable only severally for its proportionate share of risk contribution, rather than for the plaintiff's full damages as United Kingdom law would otherwise have required. *See id.* [2], [31] (Lord Hoffmann), [60]–[62] (Lord Scott), [112]–[13] (Lord Walker) (concluding that if tort consisted of exposure to risk then several liability proportionate to risk would be appropriate). *Barker* held that fairness demanded that result. *See id.* [127] (Baroness Hale) ("It seems to me most fair that the contribution [that defendants in a *Fairchild*-type situation] should make [to plaintiff's compensation] is in proportion to the contribution they have made to the risk of that harm occurring."). Parliament promptly reversed that policy judgment. Compensation Act, 2006, c. 29, § 3(1)(a), (c), (2) (U.K.). The Supreme Court, with some justices holding their noses, later adhered to the precedent that material contribution to risk was sufficient causal connection despite the statutory requirement of joint and several liability. *E.g.*, Sienkiewicz v. Greif, [2011] UKSC 10, [2011] 2 A.C. 229 [167]–[68] (Baroness Hale). In the United States, risk contribution as a tort is the premise underlying some claims for medical monitoring. *E.g.*, Donovan v. Philip Morris USA, Inc., 914 N.E.2d 891 (Mass. 2009). This Article takes no position on whether claims for medical monitoring should be permitted upon proof of toxic exposure even absent manifest illness.

could not, compensate every person exposed to such risks.[267] The *Barker* majority answered this objection, despite holding that the harm caused by tortious asbestos exposure was creation of a risk of mesothelioma, by holding that tortfeasors would be liable only if the harm of mesothelioma had materialized. It imposed this limit by assertion rather than by reasoning, however.[268]

By contrast, if risk augmentation is recognized as a cause of injury within a model of probabilistic causal contribution, a

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267. Another problem soon led the United Kingdom's Supreme Court to repudiate the risk-as-harm formulation. A group of employers' liability insurers balked at covering liabilities owed to employees who developed disease long after their workplace exposures to asbestos. *Cf.* Jeffrey W. Stempel, *The Insurance Policy as Statute,* 41 MCGEORGE L. REV. 203, 209–10 (2010) (recounting history of similar litigation in United States). The insurers argued that their policies covered only liability for disease that became manifest during the policy period, not for disease that became manifest after the policy period even if it had been caused by exposure during the policy period. BAI (Run Off) Ltd. v. Durham, [2012] UKSC 14, 3 (Lord Mance). The justices unanimously rejected this argument. *Id.* 76 (Lord Clarke) ("Like other members of the Court, I agree . . . [that] for the purposes of the . . . policies, mesothelioma is 'sustained' or 'contracted' when the process that leads to the disease is initiated" by exposure to asbestos). Lord Phillips, however, would have held nevertheless that the insurance was not triggered. He argued that *Barker* correctly interpreted *Fairchild* as imposing liability for risk creation alone, and that because no one could tell which employer's fiber actually caused a plaintiff's mesothelioma, liability based on risk creation did not satisfy the insurance policies' requirements of causation and injury. *Id.* 124, 134–35. The majority, however, disagreed. *Id.* 65 (Lord Mance) ("[I[t is impossible, or at least inaccurate, to speak of the cause of action recognized in *Fairchild* and *Barker* as being simply 'for the risk created by exposing' someone to asbestos."); *id.* 82 (Lord Clarke) (*Barker* "cannot have intended to hold, without more, that the basis of liability was the wrongful creation of the risk . . . because there would be no liability at all but for the subsequent existence of the mesothelioma.") I am indebted to Sandy Steel for calling my attention to the insurance trigger litigation.

268. *See Barker*, [2006] UKHL 20, [48] (Lord Hoffmann) ("Although the *Fairchild* exception treats the risk of contracting mesothelioma as the damage, it applies only when the disease has actually been contracted."); *id.* [61] (Lord Scott) ("If, in the event, the victim does not contract the disease, no claim can be made for the trauma of being subjected to the risk."); Chris Miller, *Liability for Negligently Increased Risk: The Repercussions of* Barker v. Corus UK (PLC), 8 LAW, PROBABILITY & RISK 39, 42 (2009) (emphasizing distinction between liability for creating risk of harm and liability for creating risk that eventuates in actual harm). Courts that accept "lost chance" doctrines similarly limit their application by pronouncement. *See generally* David A. Fischer, *Tort Recovery for Loss of a Chance*, 36 WAKE FOREST L. REV. 605 (2001) (discussing possible limiting principles for application of lost chance doctrine).

plaintiff would still need to establish an injury.[269] The mechanistic view of causation deems a cause-in-fact of that injury to be any necessary element of a sufficient causal set. A stochastic model of causation would imply that in any particular toxic tort case it is impossible to tell whether even a known risk factor fits that description. The causal set that matters, instead, is a set of factors that increased the probability of the plaintiff's injurious result. Each element of this set should be considered a cause-in-fact of the harm the plaintiff experienced.

Jane Stapleton has called such reasoning a "fiction" in asbestos cancer cases because, so far as is known, asbestos-related lung cancer or mesothelioma does not result only if aggregate asbestos exposure exceeds some threshold and is not made more severe by additional exposure. Thus, she reasoned, a tortfeasor who contributed part of the plaintiff's total exposure can in no factual way be said to have "caused" just a "part" of the plaintiff's disease.[270]

Professor Stapleton's careful distinctions among cumulative, threshold, and non-threshold mechanisms of toxic injury are valuable and informative. But probabilistic causal contribution is a fiction only in relation to assumed scientific[271] and legal models

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269. Jamie Grodsky argued that injury itself could be reconceptualized to include detectable sub-clinical cellular or biochemical changes. Grodsky, *supra* note 110, at 1671–74. Although this Article takes no position on that suggestion, there is nothing about Professor Grodsky's suggestion that is inconsistent with this Article's proposal.

270. Stapleton, *supra* note 187, at 191. *See generally* Wagner v. Bondex Int'l, Inc., 368 S.W.3d 340, 349, 353 (Mo. Ct. App. 2012) (attempting to harmonize requirement of but-for causation with reality of indeterminacy by ruling that based on testimony of "cumulative nature of mesothelioma," a reasonable juror could conclude that asbestos in defendant's product "contributed to cause" plaintiff's mesothelioma and death).

271. I do not mean to suggest that mesothelioma may be a cumulative disease like asbestosis or that asbestos can only cause mesothelioma after a threshold exposure is achieved. At bottom, however, the assertion that contributing-factor causation is a legal fiction depends on the scientific model that assumes that the interaction of one asbestos fiber with one cell causes mesothelioma. This may well be true, although, curiously, the Supreme Court of the United Kingdom asserted, without citation, that "[t]he single fibre theory has . . . been discredited." *Sienkiewicz*, [2011] UKSC 10, 102 (Lord Phillips). It is clear, at least, that more than one molecular change is necessary for a mesothelium cell to become malignant. Huang, et al., *supra* note 147, at 180–81.

of causation. The deterministic legal model assumes that one and only one source of asbestos exposure should be treated as "the" cause of the plaintiff's entire illness: that as a matter of historical fact, the physical tumor in the plaintiff's body originated with a cellular alteration initiated by a particular defendant's fiber,[272] which could be identified if only science were omniscient. Even if reality matches this assumption, the counterfactual inference required by the but-for test does not necessarily follow. We cannot say that if only plaintiff had been protected from inhaling this one fiber, plaintiff would not have mesothelioma today, because it is quite plausible that if this fiber had not turned this cell malignant, some other fiber would have—or would have enabled another cell, already mutated multiple times, to evade the body's defenses and take the last step to cancer.[273] A probabilistic view of causation acknowledges this uncertainty. Moreover, the lack of omniscience alters the balance between historical fact and legal fiction. We can know as a fact that a particular defendant's tortious exposure of the plaintiff to asbestos increased the risk that the plaintiff would develop cancer. We can make some type of estimate of that risk contribution as compared to other risk contributions. We cannot know, as a fact, which fiber is the one without which plaintiff's

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Even the possibility that more than one fiber may be involved (which could, indistinguishably, come from more than one source) would weaken the scientific basis for the legal assumption that one and only one source of asbestos was the cause of a plaintiff's mesothelioma. More fundamentally, even if the model of how a fiber causes a mesothelioma is accurate, the best scientific model of which source the fatal fiber came from is, at present, a stochastic one.

272. I say "defendant's fiber" for ease of reference. The party responsible for the exposure in a given case might not be a defendant for any of a variety of reasons (insolvency, worker's compensation bar, inapplicability of any theory of tort liability, inability to identify the source of an ambient exposure).

273. *See* Noel F.C.C. de Miranda et al., *Role of the Microenvironment in the Tumourigenesis of Microsatellite Unstable and MUTYH-associated Polyposis Colorectal Cancers*, 27 MUTAGENESIS 247, 247 (2012) (explaining that after accumulating genetic alterations, various clones of tumor cells compete against one another for growth and space). In theory, a similar argument could be made about any tort: how can we say that, if the pedestrian plaintiff's leg had not been broken by impact with the negligently driven car, it would not have been broken by something else? The difference is that in the ordinary case no reason exists to suppose that at the time of plaintiff's injury some other cause created a material risk of the same injury.

disease would not have developed. To preclude recovery as a result would embrace a legal fiction that the defendant did no harm.

To think of causation in risk-creation terms requires a shift in the legal mindset, despite the centrality of risk creation to many parts of tort theory. Lawyers customarily think of risk as "a forward-looking concept" while "[c]ausation usually looks backwards."[274] But even in traditional counterfactual causal inference, the causal generalizations that support the inference derive from experience that associates the event we call a cause with the occurrence that is the result of interest. We do not speculate that the pedestrian plaintiff's broken leg might have resulted from something other than impact with the negligently driven car because common experience tells us that such impacts break legs that otherwise normally remain intact. In other words, impact with vehicles is an extremely powerful risk factor for broken legs.[275] The difference in toxic torts is that scientific indeterminacy makes the reasoning from ex ante risk creation to ex post injury causation both more explicit and more necessary. Despite the doubts some courts have expressed about causal proof based on population-based estimates of relative risk,[276] such measures are relevant to individual cases—even though they do not directly measure the probability of causation in an individual case.[277] Because such measures will continue to be the type of

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274. *Sienkiewicz*, [2011] UKSC 10, [170] (Lady Hale).

275. The inference is strengthened because of the typical absence of competing strong risk factors that might have caused the broken leg. Yet I strongly suspect that even a plaintiff with a diseased leg that might spontaneously fracture at any time would be able to obtain a factual finding of causation, and certainly would be able to reach a jury.

276. This skepticism has manifested in various ways. In *Sienkiewicz*, some members of the Supreme Court of the United Kingdom questioned whether population-based relative risk data were at all useful to causal judgments about an individual case. *Id.* The Texas Supreme Court, by contrast, acknowledged that epidemiologic data could be relevant, but its skepticism led it to impose the doubling+ rule and other unrealistic requirements. *See* Merrell Dow Pharm., Inc. v. Havner, 953 S.W.2d 706, 719 (Tex. 1997) (justifying doubling+ rule and other requirements as "strik[ing] a balance" allowing acceptance of epidemiologic proof).

277. *See* Sander Greenland & James M. Robins, *Epidemiology, Justice, and the Probability of Causation*, 40 JURIMETRICS 321, 322 (2000) (noting that

evidence that science can provide, it is time for a corresponding probabilistic contributing-factor model of causation.

D. The Question of Substantiality

Probabilistic causal contribution begins with the idea that when causal evidence is population-based, the law should treat risk factors as contributing causal factors despite the inability to infer but-for causation. In the United States, however, the prevailing verbal formulation of causation in tort has been the "substantial factor" test of the Second Restatement.[278] In light of the Third Restatement's decisive rejection of "substantial factor" as vague and analytically inchoate, it may seem contrarian to propose a "contributing factor" concept of causation. Probabilistic causal contribution can avoid the biggest problems of "substantial factor" simply by jettisoning the requirement of substantiality.

That *Allen v. United States* relied on the then-current Second Restatement's "substantial factor" formulation is hardly surprising, but this reliance exemplified some of the confusion that led to the next Restatement's rejection of "substantial factor."[279] *Allen* held that to be deemed a "substantial factor" in causing a plaintiff's illness, the defendant must have "significantly" increased that plaintiff's risk.[280] The court's interpretation of "significance," therefore, had a dispositive effect. In that regard, *Allen* considered but rejected adopting the doubling+ rule.[281] Yet, apparently because of a heuristic view of "significant" risk contribution, the outcome of each plaintiff's case

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"equating the probability of causation to the attributable fraction [derived from relative risk] leads to systematic underestimation" of probability of causation); *see also* Steve C. Gold, Note, *Causation in Toxic Torts: Burdens of Proof, Standards of Persuasion, and Statistical Evidence*, 96 YALE L.J. 376, 379–82 (1986) (distinguishing population-based from individually applicable probability concepts).

278. RESTATEMENT (SECOND) OF TORTS § 431(a) (1965).

279. *See* RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYSICAL & EMOTIONAL HARM § 26 cmt. j ("The substantial-factor test has not, however, withstood the test of time, as it has proved confusing and been misused.").

280. Allen v. United States, 588 F. Supp. 247, 428 (D. Utah 1984).

281. *Id.* at 416–18.

closely mirrored what might have been expected with a doubling+ requirement.[282]

Thus, *Allen*'s use of "substantial factor" served two purposes. First, the court treated "substantial factor" as an alternative test of factual causation that better fit the nature of the available evidence. Second, the court used "substantial factor" to narrow the alternative test it had created. The latter use, more policy judgment than factual determination, is problematic because it so closely tracks the doubling+ version of but-for causation, when doubling+ always was an inappropriate test of cause-in-fact and will become more so as risk characterization improves.

Rutherford, too, used the word "substantial" to describe the risk contribution that would be required for an exposure to be considered a cause of a plaintiff's illness.[283] *Rutherford* cautioned, however, that the "substantial factor standard . . . requir[es] only that the contribution of the individual cause be more than negligible or theoretical."[284] Similarly, throughout the development of the mesothelioma case law in the United Kingdom, only exposures creating "material" increases in risk have been considered causative,[285] but in that context "material" simply means "not de minimis."[286]

In an analogously difficult situation requiring proof of causation, a federal district court[287] applied a "contributing factor" standard to a claim for damages arising under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA).[288] The government plaintiffs alleged that

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282. *See id.* at 429–40 (describing the specific details and outcome of each plaintiff's case).

283. *See* Rutherford v. Owens-Ill., Inc., 941 P.2d 1203, 1223 (Cal. 1997) (holding that "a substantial factor contributing to plaintiff's . . . risk" would be deemed a "substantial factor in causing or bringing about the disease").

284. *Id.* at 1219.

285. Fairchild v. Glenhaven Funeral Servs., Ltd., [2002] UKHL 22, 64, [2002] 3 All E.R. 305 (Lord Hoffmann).

286. *See Sienkiewicz*, [2011] UKSC 10, 107–12 (Lord Phillips) (holding "material" an asbestos exposure increasing mesothelioma risk by 18% above background).

287. *In re* Acushnet River & New Bedford Harbor, 722 F. Supp. 893 (D. Mass. 1989).

288. 42 U.S.C. §§ 9601–9675 (2006).

defendants were liable for damages for "injury to, destruction of, or loss of natural resources" caused by defendants' releases of PCBs to New Bedford Harbor.[289] The defendants claimed, however, that some releases had been "federally permitted" and were therefore exempt from liability.[290] Commingled in the harbor, the PCBs from allegedly exempt and non-exempt releases could not be distinguished *in situ*.[291] The court considered the question: what would the government need to prove to establish that the non-exempt releases caused injury?[292]

The court held that the non-exempt releases would result in liability if shown to be "a contributing factor to an injury to natural resources."[293] The court specifically considered and rejected requiring a showing of a "substantial contributing factor," noting appellate precedent holding that defendants could be liable—even jointly and severally liable—for CERCLA response costs despite a lack of proof that their contribution to hazardous substance releases had been "substantial."[294]

An injury to natural resources provides a useful analogy: it is essentially a toxic tort committed on an ecosystem.[295] In that

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289. *Acushnet*, 722 F. Supp. at 900; *see also* 42 U.S.C. § 9607(a)(4)(D) (2006) (creating a cause of action for such damages).

290. *Acushnet*, 722 F. Supp. at 897; *see also* 42 U.S.C. § 9607(j) (2006) ("Recovery . . . for response costs or damages resulting from a federally permitted release shall be pursuant to existing law in lieu of this section.").

291. *Acushnet*, 722 F. Supp. at 897.

292. *Id.* at 897–98.

293. *Id.* at 897.

294. *Id.* at 897 n.8 (citing O'Neil v. Picillo, 883 F.2d 176, 179 n.4 (1st Cir. 1989)). In *O'Neil*, the trial judge held that defendants, who asserted they had arranged for disposal of only a relatively small portion of the hazardous substances at a dump, were jointly and severally liable for the full cleanup costs. O'Neil v. Picillo, 682 F. Supp. 706, 730–31 (D.R.I. 1988); *see also* 42 U.S.C. § 9607(a)(4)(A) (creating a cause of action for recovery of government response costs). On appeal, defendants contended that Restatement (Second) of Torts § 433B required the government to prove that each defendant was "a 'substantial' cause of the harm." *O'Neil*, 883 F.2d at 179 n.4. The court of appeals rejected that contention, observing that to require proof of substantial contribution would impose an "almost impossible task" on the government, in conflict with statutory objectives. *Id.*

295. The *Acushnet* court announced a legal standard for proof of causation but did not have to determine whether the evidence satisfied the standard. The particular harm allegedly inflicted on New Bedford Harbor—the concentration

context and in indeterminate-defendant toxic tort cases, courts have successfully eliminated the substantiality requirement for contributing factors. With only a sensible exclusion for *de minimis* contributions,[296] "contributing factor" defined by increases in risk fits well with the causal world that toxicogenomics and molecular epidemiology are in the process of revealing.

E. Discounted Recoveries

The preceding discussion showed that a "contributing factor" standard of causation, based on risk contribution, can be used to implement a stochastic, probabilistic model of causation that better fits the realities of proof of specific causation in many toxic tort cases—even, perhaps especially, in light of the anticipated results of continued research at the genomic and molecular scales. This proposed standard will face an easily anticipated objection: that tortfeasors will overpay if held liable for full damages for all harms of which they created incremental risk, no

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of PCBs in water, fish and shellfish above the maximum allowed for consumption, *Acushnet*, 722 F. Supp. at 898 n.12, is similar to a disease that appears if a threshold dose of toxin is administered but that does not get worse with larger doses. Nevertheless, *Acushnet*'s discussion is not limited by a particular fact-bound causal model. For example, the court considered the possibility that the non-exempt releases alone might *not* have been a contributing factor to *any* harm, *id.* at 897 n.11, which would seem impossible if the harm inhered solely in exceeding a threshold quantity of PCBs. *Cf.* RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYSICAL & EMOTIONAL HARM § 27 cmt. g.

296. Rejecting causal attribution for *de minimis* risk contributions would reduce some of the complexity that a probabilistic causal contribution model could introduce to toxic tort litigation. It would take some care, however, to apply this sensible limit sensibly. A common scenario in CERCLA cases involves many contributors of small fractions of a hazardous substance release that, as a whole, requires response action. An analogous situation in toxic torts—many exposures, each of which adds a small increment of risk—is plausible and may become increasingly apparent with improved ability to characterize both risk and exposures. Eliminating liability for each contributor as *de minimis* would allocate the loss entirely to the victim. Thus, *de minimis* ultimately must be a matter of relative contribution rather than an arbitrarily fixed absolute proportion of risk contribution. *See also infra* notes 319–20 and accompanying text.

matter how small their (non-*de minimis*) risk contribution. The objection impinges, in different ways, on both corrective justice and efficiency rationales for tort liability. And, in different ways, the objection may be overcome by a carefully designed system of discounted recoveries in proportion to the degree of risk created by the tortious exposure, a suggestion that has recurred in the literature in various forms since the early 1980s.[297]

The corrective justice or fairness argument is that contributing factor causation would unjustly hold some defendants liable for illnesses they did not cause. That criticism tautologically depends on the deterministic model of causation and the assumption that specific causation is knowable. If specific causation is not deterministically knowable, but population-based data are available, the deterministic all-or-nothing model would allow two outcomes that are different from contributing factor causation. The first possible outcome would be to deny recovery in every case because measures of relative risk are insufficient to establish specific causation. That would offend corrective justice and fairness just as much as contributing factor causation, but in the opposite direction. The second possible outcome would be to take specific causation as true only if the relative risk exceeded some threshold (e.g., doubling+). That, however, is internally inconsistent with the deterministic model's insistence that each affirmative finding of causation represents a belief about what would probably have happened to the particular plaintiff had the plaintiff not been exposed. The doubling+ rule simply glosses over the fact that each group of exposed and sick plaintiffs—whether they prevail or not—necessarily includes some whose litigation outcomes would have been different but for the irreducible scientific indeterminacy.

The efficiency argument takes a population perspective from the outset, contending that contributing factor causation would make tortfeasors overpay—and thus be over-deterred—by holding defendants liable for an aggregate amount in excess of the total amount of harm the defendants could have prevented. Discounting recoveries to reflect risk contribution is, at least

297. For a thorough survey of prior proportional liability proposals, see Green, *supra* note 185, at 357–70.

theoretically, a complete response to that objection. The claim that such discounting would produce optimum deterrence has figured prominently in arguments for proportional liability schemes.[298]

From the perspective of a probabilistic model of causation, discounted recoveries would be a form of causal apportionment that would cohere conceptually with the available evidence on specific causation in many toxic torts. Consider a relatively simple yet paradigmatic hypothetical case. The plaintiff worked for many years at a job that entailed daily inhaling vapors of some solvent. After the appropriate latency period, the plaintiff's doctors diagnosed a particular cancer. Undisputed, peer-reviewed scientific research shows that: (1) cells of this cancer almost always have mutations in a particular set of genes; (2) DNA treated with the solvent *in vitro* is statistically significantly more likely than untreated DNA to contain mutations in at least some of those genes; (3) the frequency of this cancer among exposed individuals with a specific susceptible genotype is slightly, but statistically significantly, greater than among unexposed individuals of similar genotype; and (4) no other specific risk factors for this cancer have yet been identified, so the vast majority of cases are considered unexplained or idiopathic. This hypothetical evidence of both biological mechanism and statistical association should suffice to support a reasonable factual finding of general causation.

Assume that genetic testing showed that the plaintiff's tumor has mutations in the usual genes and the plaintiff has the susceptible genotype. Under the contributing factor standard of probabilistic causal contribution, the evidence of specific causation would be sufficient for submission to a fact-finder. The fact-finder would be asked to determine by a preponderance of the evidence whether the exposure caused the cancer; cause would be defined as a non-trivial increase in plaintiff's risk of developing cancer. Upon an affirmative answer, the fact-finder

298. *See, e.g.*, David Rosenberg, *The Causal Connection in Mass Exposure Cases: A "Public Law" Vision of the Tort System*, 97 HARV. L. REV. 849, 868 (1984); Steven Shavell, *Uncertainty over Causation and the Determination of Civil Liability*, 28 J.L. & ECON. 587, 589 (1985).

would estimate, as a percentage, the extent to which the solvent exposure contributed to the plaintiff's risk of the cancer. The fact-finder would also determine the plaintiff's total damages under the jurisdiction's damages rules. The court would enter judgment for the determined percentage of the total damages.

The preceding hypothetical deliberately did not specify a value for the relative risk estimated by molecular epidemiologic investigation, in order to avoid the suggestion of automatic equivalence between observed relative risk and causal apportionment in a particular case (i.e., relative risk of 2 equates to 50% risk contribution, relative risk of 1.5 equates to 33.33% risk contribution, etc.). A fact-finder might rationally apply such reasoning, but also might, for various reasons, reach a different result. The biological assumptions implicit in such reasoning might be disputed.[299] The significance and weight to be assigned multiple studies that reported different relative risk values might be disputed. The fact-finder might understand the reported relative risk(s) not as point values but as estimates of a parametric value as indicated by a statistical confidence interval, and might find a central tendency in overlapping confidence intervals of multiple studies. Or facts particular to the case at hand—characteristics of the plaintiff, the exposure, or both, as compared to the study subjects—might prompt the fact-finder to make a causal apportionment greater or less than implied by the study's relative risk. Adjustments for these reasons are appropriate and are, or should be, part of the fact-finding process under the but-for mechanistic model of causation as well.

The hypothetical can be made more complicated by assuming that two or more parties contributed to the solvent exposure. The analysis would depend on the nature of the multiple contributions and on what is known about the effect on risk of increasing amounts of exposure. A solvent manufacturer that failed to warn that its product should not be inhaled and a company that used the product without taking reasonable precautions to prevent inhalation, for example, would both be

299. *See* Greenland & Robins, *supra* note 277, at 325 (discussing, as an example, the independence-of-background assumption and explaining that many plausible disease mechanisms do not satisfy this assumption).

but-for causes of the same exposure under traditional causation analysis; therefore each should be treated as fully causally responsible for the share of damages attributed to the solvent exposure.[300] By contrast, if the plaintiff was exposed to the same solvent in products made by two different manufacturers, the question of causal attribution between the manufacturers would resemble the mesothelioma indeterminate-defendant cases, with the important difference that the causal link between plaintiff's cancer and the overall solvent exposure would be treated probabilistically.[301] Assuming that the amount of risk created by the solvent exposure was somehow proportional to the amount of exposure,[302] the logic of probabilistic causal contribution implies division of the solvent's causal contribution in proportion to each source's contribution of solvent exposure. In some cases this rule would invite fine parsing of whether multiple exposures truly involved the same agent; that assessment would best be tailored to the available evidence in particular circumstances.

The next complication adds other proven, non-*de minimis* contributing risk factors. As noted above, conceptually it does not matter whether the plaintiff's exposure to additional risk factors required human agency or not, whether it was tortious, or whether it was created by a defendant or the plaintiff or a third party. If multiple risk factors apply to a plaintiff, a court's first

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300. This illustration assumes that all other requisites of liability are satisfied for both these parties. Applicable comparative fault and scope-of-liability rules would determine whether judgment would be entered against each tortfeasor for the full amount of this apportioned share.

301. In the mesothelioma cases, by contrast, it was not in dispute that asbestos, rather than something else, caused the disease.

302. This critical biological assumption might be well established in some cases (e.g., asbestos-mesothelioma) and in other cases might reasonably be treated as an acceptable approximation. It should be subject to factual dispute, however. For example, the available data might show any of the following: increased risk only after exposure exceeded a threshold amount; increased risk relatively insensitive to dose (perhaps after dose exceeded a threshold); increased risk in some way proportional to dose up to a limit beyond which increasing dose adds no increment of risk. Perhaps the most likely scenario, even in molecular epidemiology studies, would be insufficient data to assess the assumption, i.e. studies that simply compared relative risk among "exposed" and "unexposed" groups. In that scenario the reasonableness of the proportionality assumption could be a subject for expert debate.

instinct might be to ask the fact-finder to assign percentages to all of them, but strictly speaking it would not be necessary to quantify the proportion assigned to any individual non-defendant risk factor. The crucial assessment would be what causal share to attribute to each of the exposures for which any defendant was liable. The non-defendant risk factors could be treated, collectively, as part of that plaintiff's "background" risk, although of course they could elevate that plaintiff's background risk value above the background risk faced by somebody not affected by any known risk factors.

Proof that the plaintiff had been exposed to multiple risk factors would present significant factual complications, however. If each risk factor independently added incremental risk, a fact-finder could relatively easily assign causal contributions by comparing the risk increments to one another. But risk contributions from diverse factors might not be independent of one another, and if they were not, they could interact in a variety of ways.[303] The best-known example is the synergistic effect of tobacco smoking and occupational asbestos exposure on the risk of lung cancer.[304] Exposure to both carcinogens increases lung cancer risk far more than the sum of the risk contributions of each acting alone.[305] Although some courts have tried to divide the additional risk resulting from the synergy between the two contributing factors, there is no entirely satisfying way to do so.[306] An alternative would be to assign the additional risk resulting from a synergistic interaction to each of the interacting risk factors. The latter approach would mean that, as compared to a

303. Susan R. Poulter, *Science and Toxic Torts: Is There a Rational Solution to the Problem of Causation?*, 7 HIGH TECH. L.J. 189, 233–34 (1992).

304. Huang et al., *supra* note 147, at 203.

305. Sanders, *supra* note 1, at 35.

306. *See, e.g.*, Dafler v. Raymark Indus., Inc., 611 A.2d 136, 145–56 (N.J. Super. 1992), *aff'd*, 622 A.2d 1305 (N.J. 1993) (affirming a jury verdict that appeared to apportion the synergistic risk in proportion to the amount of risk added by exposure to each carcinogen separately and independently); *see also* V. McCormack et al., *Estimating the Asbestos-Related Lung Cancer Burden from Mesothelioma Mortality*, 106 BRIT. J. CANCER 575, 575 (2012) ("Quantifying the asbestos-related lung cancer burden is difficult in the presence of this disease's multiple causes."). *But see* Green, *supra* note 94, at 545 ("[V]arious plausible, yet complicated, methods for determining risk contribution exist . . . .").

case of independent and additive risk factors, in a case of synergy the proof of plaintiff's exposure to an additional risk factor would have less effect on the causal share assigned to the risk factor contributed by defendant(s).[307]

The quality of evidence concerning potential interaction of multiple risk factors will likely vary from case to case. In some cases the effect of combined exposure will itself have been the subject of scientific study designed to assess the independence or interaction of risk contributions. Even then, factual issues such as the extent of exposure to the various risk factors might affect the causal attribution. In other cases each risk factor might have been studied independently, with the attendant possibility of confounding by the other risk factor(s), leaving the experts to battle over whether an assumption of independence or of synergy best fit the available data. Toxicogenomic and molecular evidence about the mechanism of toxicity for the various risk factors could inform that debate.

In a probabilistic causal contribution model, a plaintiff seeking to prove a risk contribution need not exclude other risk factors, unlike a plaintiff using differential diagnosis in a deterministic causation model. Thus, defendants should be assigned the initial burden of production of evidence that plaintiff was exposed to additional risk factors and of general causation with respect to those risk factors. There would be no justification, however, for shifting the ultimate burden of persuasion: plaintiff must persuade the fact-finder by a preponderance of the evidence

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307. Susan Poulter used the asbestos-tobacco-lung cancer example to show how under this approach, if the relative risk jointly created by two exposures is the product rather than the sum of the relative risks of each acting individually, the fraction of cases attributed to each exposure in the population exposed to both is exactly the same as the fraction attributed to each in the population exposed only to it. *See* Poulter, *supra* note 303, at 233–34, n.215. (This handy result obtains only if the synergistic risk exactly equals the product of the individual risks, but applying this approach to any synergistic interaction will result in attributable shares closer to the individual shares than would be the case if the risks were additive.) Because this approach assigns overlapping parts of the synergistic risk to both exposures, the sum of the assigned risk fractions would exceed one. *See also* Susan R. Poulter, *Genetic Testing in Toxic Injury Litigation: The Path to Scientific Certainty or Blind Alley?*, 41 JURIMETRICS 211, 223–31 (2001) (describing possible interactions among genetic and environmental causes of disease).

that defendant increased plaintiff's risk of disease with evidence that will permit the fact-finder to make some estimate of a percentage causal contribution (even if, as will usually be true, the scientific evidence does not produce a single point value for that contribution).

Undeniably, in these cases the proof, and the fact-finders' task, will be complicated. One can imagine cases as complex as one cares to: exposures to many different risk factors, from tortious, non-tortious human, plaintiff, and natural sources, with each tortious exposure including contributions of multiple tortfeasors. A premise of this Article is that toxicogenomics and molecular epidemiology will make these cases more, rather than less, complex. Nonetheless, it is possible to exaggerate the concern about complexity. The adversary system, the human decision-making process, the reduced importance of additional risk factors in cases of synergy, and the *de minimis* limitation on risk factors that "count," all will tend to focus litigation on the most salient tortious conduct and alternative causes. In any event, complexity of the facts is not a good excuse for oversimplification of the law.

Here, too, an analogy from CERCLA is instructive, demonstrating that causal apportionment is feasible even if factually difficult. A defendant liable for the government's response costs incurred under CERCLA is jointly and severally liable, unless the defendant shows, on a purely causal and not equitable basis, that the environmental harm to which it contributed is reasonably capable of apportionment.[308] The statute makes liable several qualitatively different classes of actors.[309] Information about their relative contributions is often

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308. Burlington N. & Santa Fe Ry. Co. v. United States, 556 U.S. 599, 613–14 (2009) (following RESTATEMENT (SECOND) OF TORTS § 433A (1965)). The decision expresses what is required to justify apportionment in at least three ways: whether the harm is "capable of apportionment," whether "a reasonable basis for apportionment exists," and whether the harm is "a single, indivisible harm." *Id.* at 1881. The Court emphasized that the analysis is purely causal, invoking none of the equitable factors courts use to allocate responsibility among jointly and severally liable parties. *See id.* at 1882 n.9; United States v. Hercules, Inc., 247 F.3d 706, 718–19 (8th Cir. 2001); United States v. Twp. of Brighton, 153 F.3d 307, 318–19 (6th Cir. 1998).

309. *See* 42 U.S.C. § 9607(a)(1)–(4) (2012) (listing "covered persons" as

scant. Apportionment may require substantial amounts of assumption and inference. Nevertheless, the Supreme Court upheld a trial court's use of data that were extremely limited—in type, in clarity of causal significance, and in precision—to apportion liability.[310]

The Maryland Court of Special Appeals required causal apportionment in another different yet analogous context. The plaintiffs in *CSX Transportation, Inc. v. Bickerstaff*[311] sued their employer railroad under the Federal Employers' Liability Act (FELA).[312] They alleged that they suffered osteoarthritis of the

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including the owner and operator of a vessel or facility, any person who owned or operated a facility at the time of disposal of a hazardous substance, any person who arranged for disposal, treatment, or transport for disposal or treatment of hazardous substances at a facility owned by another person, and any person who accepted substances for transport to a disposal or treatment facility selected by that person).

310. *See Burlington Northern*, 556 U.S. at 619 (concluding that "the District Court reasonably apportioned the Railroads' share of the site remediation costs at 9%"). The trial court apportioned liability among three parties that owned or operated a facility when hazardous substances were disposed of there: an agricultural chemical distributor that spilled toxic chemicals during its operations and two railroads that jointly owned a piece of property that the distributor leased. *Id.* at 1874–76. By the time the United States sued to recover more than eight million dollars in response costs, the distributor was defunct. *Id*. at 1876. The railroads' parcel was only a portion of the land the distributor used, was used for only a portion of the time during which the distributor operated, and was used to handle only two of the three chemicals that were the subject of the cleanup. *Id.* The district court concluded that the product of these three fractions represented a reasonable apportionment of the harm, and then increased the computed share by a 50% fudge factor to account for uncertainty. *Id.* at 1882. The Supreme Court acknowledged that the district court had received little evidence on the apportionment issue, that one could question the assumption that the harm was proportional to geographic area and years of operation, and that little record evidence supported the conclusion that the two chemicals handled on the railroads' parcel were responsible for two-thirds of the harm. *Id.* at 1882–83. Nonetheless, the Court upheld the apportionment as reasonable with only one justice dissenting. *Id*.; *see also* United States v. Bell Petrol. Servs., 3 F.3d 889, 903 (5th Cir. 1993) (reversing judgment of joint and several liability because, although it was "not possible to determine with absolute certainty the exact amount of chromium each defendant introduced," the evidence sufficed for "reasonable and rational approximation of each defendant's individual contribution to the contamination").

311. CSX Transp., Inc. v. Bickerstaff, 978 A.2d 760 (Md. Ct. Spec. App. 2009), *cert. denied*, 984 A.2d 244 (2009).

312. 45 U.S.C. §§ 51–60 (2012).

knee because CSX negligently used mainline ballast—relatively large rocks—as a walking surface in the rail yards where they worked.[313] The trial court instructed the jury on comparative negligence, and the jury returned verdicts assigning some fault to the plaintiffs but larger shares to the defendant.[314] The defendant contended that in addition to the parties' negligence, "other significant causes such as obesity, smoking, other pre-existing medical conditions, and age,"[315] as well as genetics,[316] had contributed to causing the plaintiffs' injuries. The appellate court agreed that the trial court should have treated such alleged causes separately from the plaintiffs' own negligence.[317]

On appeal, the defendant did not argue that any of these other factors was a but-for cause of plaintiffs' injuries and the ballast was not.[318] Rather, CSX relied on evidence that osteoarthritis is "multifactorial, meaning that there are many factors involved in contributing to it."[319] A defense expert had defined a "risk factor" as "something that would cause or lend someone to have a certain problem or condition."[320] The appellate court treated these risk factors as concurrent causes and held that the trial court should have instructed the jury to apportion any fraction of damages the jury found "attributable" to these "other causes and factors."[321]

So, in addition to the House of Lords's application of causal apportionment to asbestos indeterminate-defendant cases in *Barker*,[322] American courts have held that causal apportionment

313. *Bickerstaff*, 978 A.2d at 770.

314. *Id.* at 770–71, 793.

315. *Id.* at 793.

316. A defense expert testified that a "small percentage of osteoarthritis" is hereditary, and argued (without presenting genomic evidence) that one plaintiff's inherited bowleggedness was a significant cause of that plaintiff's injury. *Id.* at 797, 799.

317. *Id.* at 799.

318. The trial judge seemed to think this the only proper use of evidence of such non-negligent causes. *See id.* at 794–95 (summarizing the transcript of the trial judge's ruling).

319. *Id.* at 798 (quoting plaintiffs' expert witness).

320. *Id.* at 797 (quoting defendant's expert witness).

321. *Id.* at 799 n.22.

322. Some American courts have used comparative fault to achieve results

can work in a CERCLA case in which multiple defendants were liable in different ways and in a FELA case in which plaintiffs bore non-negligent risk factors for their injuries.[323] These examples show that causal apportionment is a practicable approach that has received judicial imprimatur, even when facts are complex and data limited.[324] Causal apportionment, via a probabilistic causal contribution model as described here, can work in toxic tort cases more generally. Although imperfect, it is the best available solution to the problem of liability disproportionate to the contribution to risk.

To apply probabilistic causal contribution correctly, however, courts will need to take care to avoid duplicate reductions of plaintiff's damages through comparative responsibility regimes.

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similar to *Barker*'s. *See, e.g.*, Barnes v. Owens-Corning Fiberglas Corp., 201 F.3d 815, 822–23 (6th Cir. 2000) (applying Kentucky comparative fault statute); Green, *supra* note 185, at 353 (distinguishing apportionment based on relative culpability from determining and apportioning liability based on probabilistic assessments).

323. Each of these holdings may be criticized for undermining a joint and several liability scheme that fosters core objectives of the statute involved. *See* Norfolk & W. Ry. Co. v. Ayers, 538 U.S. 135, 165–66 (2003) (holding that under FELA, "an employee who suffers an 'injury' caused 'in whole or in part' by a railroad's negligence may recover his or her full damages from the railroad"); United States v. NCR Corp., No. 12-2069, 2012 WL 3140191, at *8 (7th Cir. Aug. 3, 2012) (agreeing with defendants that under *Burlington Northern*, "apportionment calculations need not be precise. To the contrary, the [Supreme] Court upheld a district court's rather rough, sua sponte calculation of apportionment. . . . But we do not agree that . . . lower courts must always take such an approach"). This Article takes no position on whether *Burlington Northern* and *Bickerstaff* correctly applied CERCLA and FELA, respectively.

324. *See, e.g.*, Loui v. Oakley, 438 P.2d 393, 396–97 (Haw. 1968) (requiring instruction that if the jury "is unable to determine by a preponderance of the evidence how much of the plaintiff's damages can be attributed to the defendant's negligence" in causing one of two entirely separate auto accidents that injured plaintiff, the jury "may make a rough apportionment"); Campione v. Soden, 695 A.2d 1364, 1375 (N.J. 1997) (holding that a comparative negligence statute required apportionment of damages for injuries caused in part by each of two auto accidents occurring in rapid succession, although the "absence of conclusive evidence concerning allocation . . . will necessarily result in a less precise allocation"). *See generally* RESTATEMENT (THIRD) OF TORTS: APPORTIONMENT OF LIAB. § 26 cmt. h (discussing the difficulty of apportioning harm on causal grounds). The Restatement endorsed placing the burden of proof on a party seeking to avoid responsibility for an entire injury, but relaxing such a party's burden of production of evidence. *Id.*

Consider three hypothetical workers with lung cancer, each of whom was exposed to an asbestos product made by a manufacturer that negligently failed to warn of the product's dangers. Each worker contributed to his or her elevated risk of lung cancer in a different way. Worker #1 negligently failed to use a protective respirator provided by the worker's employer. Worker #2 negligently inhaled fibers from a similar product (made by an unidentifiable manufacturer) during a home renovation project. Worker #3 negligently smoked cigarettes. Worker #1 would be causally responsible for the same increment of lung cancer risk as the manufacturer; the only apportionment between them would be based on comparative fault. Worker #2 would be causally responsible for an apportioned share of the fraction of lung cancer risk causally attributed to asbestos exposure; after the causal apportionment, further reduction in the plaintiff's damages based on a share of fault would be inappropriate, as the plaintiff bore no fault for the portion of risk attributed to the manufacturer. Worker #3, for the same reason, would recover damages subject to causal apportionment (with appropriate treatment of the asbestos/tobacco synergy), but not further reduced by comparative fault.

Critics of apportionment (whether causal or fault-based) argue that joint and several liability appropriately places the risk that some tortfeasors will be insolvent on other tortfeasors rather than on injured plaintiffs.[325] There is much to this argument, particularly as applied to situations like asbestos, where the total harm caused was so great that many liable parties entered bankruptcy.[326] In the controversy over specific causation in toxic torts, however, the real choice frequently will not be between joint and several liability for full damages or only several liability for apportioned damages—it will be between liability based on probabilistic causal contribution and no liability at all based on deterministic models of but-for causation. Moreover, as the

325. *E.g.,* Mark M. Hager, *What's (Not!) in a Restatement? ALI Issue-Dodging on Liability Apportionment*, 33 CONN. L. REV. 77, 95–96 (2000); Richard W. Wright, *Allocating Liability Among Multiple Responsible Causes: A Principled Defense of Joint and Several Liability for Actual Harm and Risk Exposure*, 21 U.C. DAVIS L. REV. 1141, 1185–86 (1988).

326. Sanders, *supra* note 1, at 13.

variety of state comparative fault regimes demonstrates, acceptance of apportionment need not dictate the allocation of the risk of insolvency.[327] Courts or legislatures could, despite the tension with the theoretical rationale for probabilistic causal contribution, make the policy choice that a tortious risk contributor should bear all or part of the portion of risk contributed by another tortfeasor that is insolvent. That choice would make a party liable for a risk the person did not cause, but not necessarily for a harm the person did not cause (which cannot be determined).

F. Boundaries

Commentators on the components of probabilistic causal contribution—treating risk contribution as causation and discounting recoveries in proportion to relative contribution of risk—often question whether, once accepted in one class of cases, these doctrines can sensibly be restricted to that class.[328] Limiting doctrinal reform to asbestos mesothelioma cases, for example, has been criticized as arbitrary.[329]

I propose probabilistic causal contribution as a response to a particular problem of causal indeterminacy that will be exacerbated rather than solved by scientific advances. Although it is tempting to say that if the concept is appropriate in some cases it could be applied in every case, the boundaries of the solution need not extend beyond the boundaries of the problem.[330]

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327. *See* RESTATEMENT (THIRD) OF TORTS: APPORTIONMENT OF LIAB. § 10 cmt. a (describing five variously adopted "tracks").

328. *See* Jonathan Morgan, *Causation, Politics and Law: The English—and Scottish—Asbestos Saga*, *in* PERSPECTIVES ON CAUSATION, *supra* note 1, at 57, 64–65 (despairing that judicially-imposed limits can withstand "common law's ineluctable method of reasoning by analogy"); *see also* Sanders, *supra* note 1, at 39 (expressing concern that the scope of risk rule could be difficult to limit).

329. *See* Sanders, *supra* note 1, at 36 (expressing concern that the scope of the risk rule could be difficult to limit).

330. *See generally* BIC Pen Corp. v. Carter, 346 S.W.3d 533, 545 (Tex. 2011) (distinguishing toxic tort cases and refusing to allow plaintiff to apply doubling+ rule and statistical evidence of increased risk to support claim that defect in cigarette lighter caused injury).

And the boundaries of the problem can be defined, if not precisely, then reasonably well.[331]

Once again a metaphor from the physical sciences is helpful. At a quantum scale, the behavior of elementary particles is inherently random and unpredictable.[332] But the behavior of millions of particles in a beam is not.[333] Quantum mechanics did not render Newtonian physics useless for describing the motion of billiard balls. But a probabilistic view is required to describe the motion of the electrons of the atoms of which those balls are made.[334]

Causation is always an inference, and all evidence of causation can be conceived as probabilistic.[335] But in most cases a fact-finder can comfortably fit that evidence to an inferential process grounded in the deterministic model, deciding whether the proof leads it to a level of belief in but-for causation that satisfies the standard of persuasion.[336] The mechanistic model fails when proof of causation rests on evidence derived from

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331. Probabilistic causal contribution would hardly be the first doctrinal adjustment to recognized difficulties of proof. Professor Green gave as examples res ipsa loquitur, market share liability, the rationale for strict products liability, *see* Escola v. Coca-Cola Bottling Co. of Fresno, 150 P.2d 436, 461–63 (Cal. 1944) (Traynor, J., concurring) (citing plaintiff's inability to refute evidence of due care as grounds for strict liability), and the sufficiency standard for the magnitude of damages caused by a defendant's wrongdoing. Michael D. Green, *Pessimism About* Milward, 3 WAKE FOREST J.L. & POL'Y (forthcoming 2013) (on file with author).

332. RUVINSKY, *supra* note 178, at 4–6.

333. *Id.* at 6.

334. *See id.* at 4 (explaining that Heisenberg's uncertainty principle means that position and speed of elementary particles "is always characterized by a probability distribution").

335. *See* Rosenberg, *supra* note 298, at 870 (suggesting that particularistic evidence is no different than statistical evidence in that it "offers nothing more than a basis for conclusions about a perceived balance of probabilities"); *see also* Gold, *supra* note 277, at 384 n.42 (agreeing with Rosenberg that "all evidence . . . involves inference from observed probability patterns," but acknowledging the "power of particularistic proof to generate belief probabilities regardless of known fact probabilities").

336. In a civil case "preponderance of the evidence" is routinely described as proof leading the fact-finder to believe that the fact is more likely than not, but Professor Wright has argued that to find a fact proven, legal fact-finders actually require a degree of belief much higher than belief that the fact and its negative are equally likely. Wright, *supra* note 19, at 201–02.

population-based data on the association of disease and exposure, or of disease and genotype and exposure, or of exposure and disease-related biomarkers. In such cases the fact-finder must test its belief in a frequentist-probability value supported by evidence of risk contribution. Probabilistic causal contribution is therefore the appropriate model to apply. Advances in toxicogenomics and molecular epidemiology will make such evidence available more often than it has been in the past.

Sometimes, of course, such evidence will not be available although other evidence exists that might support an inference of general causation. To require relative risk data as proof of specific causation in every case is to ask too much. Compelling cases may exist in which such data are unavailable for perfectly good reasons. *Zuchowicz v. United States,*[337] in which epidemiologic study was implausible because both the disease and the exposure were exceptionally rare, is an example.[338] Or a plaintiff may have adequate mechanistic evidence of general causation, as in *Milward v. Acuity Specialty Products Group, Inc.*[339] Most likely the best that can be done in such cases is to muddle through under the all-or-nothing, but-for causation rule, as courts have been doing.[340] It is ironic that a plaintiff who succeeds without relative risk data would receive a full recovery while a plaintiff with "better" evidence would recover only a discounted award, but then again, the absence of relative risk data would in most cases make success substantially more difficult for the plaintiff.

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337. Zuchowicz v. United States, 140 F.3d 381 (2d Cir. 1998).

338. *Id.* at 384–85, 391 (affirming a verdict that negligent prescription of endometriosis drug at a dose that "very, very few women" had ever received had caused plaintiff's "very rare" disease).

339. *See* Milward v. Acuity Specialty Prods. Grp., Inc., 639 F.3d 11 (1st Cir. 2011), *cert. denied*, 132 S. Ct. 1002 (2012) (reversing summary judgment for defendant because the trial court abused its discretion in excluding plaintiff's expert testimony on general causation). Because general causation was addressed before other issues in the case, *id.* at 13, the decision does not address how plaintiffs intended to prove specific causation.

340. *See generally* Sanders, *supra* note 20, at 1375–80 (discussing admissibility standards for specific causation testimony in toxic tort cases in which the plaintiff presents adequate evidence of general causation).

V. Probabilistic Causal Contribution and Tort Goals

Toxicogenomics and molecular epidemiology will strengthen the argument for reenvisioning specific causation in toxic tort cases, but the indeterminacy at the core of that argument was understood even in the pre-genomic era. Nevertheless, American courts, as in *June* and *Wilcox*, have generally continued to insist on rules that assign all-or-nothing liability depending on whether there is more-likely-than-not proof of but-for causation.[341] Michael Green has noted that this insistence seems to buck two tides: a general trend away from an all-or-nothing rule in tort law and a "striking consensus" among academic writers (from which Professor Green dissented) in support of proportional liability.[342] Although courts have not typically explained their resistance by reference to the goals of tort law recognized by scholars, it is worth assessing probabilistic causal contribution against those goals.

A. Deterrence Goals: Is Probabilistic Precision Probable?

Legal economists have argued that using probabilities to discount recoveries, across a population of exposed and sick claimants, would produce an economically efficient deterrence signal in which the aggregate amount of awarded damages matched the value of the harm actually caused.[343] Professor

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341. The view in other countries is less monolithic. *See* Ken Oliphant, *Uncertain Factual Causation in the Third Restatement: Some Comparative Notes*, 37 WM. MITCHELL L. REV. 1599, 1624–30 (2011) (comparing the tort principles of several European nations).

342. Green, *supra* note 185, at 352 (noting that modern tort law is "more receptive" to apportioning liability); *id.* at 357 (scholarly consensus); *id.* at 397 ("[T]here is good reason for the courts' unwillingness."); *see also* Michael D. Green, *Introduction: The Third Restatement of Torts in a Crystal Ball*, 37 WM. MITCHELL L. REV. 993, 995 (2011) (saying he has been "critical of the pro-proportional liability literature").

343. *See, e.g.*, Green, *supra* note 185, at 354–55 (noting that proportional liability to acknowledge probabilistic uncertainty in fact-finding, "the argument goes, would, through more accurate outcomes, provide more fine-tuned deterrence incentives"); Mario J. Rizzo & Frank S. Arnold, *Causal Apportionment in the Law of Torts: An Economic Theory*, 80 COLUM. L. REV. 1399, 1427–28 (1980); Rosenberg, *supra* note 298, at 867.

Green questioned how well epidemiologic reality would match economic theory. He pointed out that when epidemiologists repeatedly investigate a suspected association between exposure and disease, the resulting relative risk values generally vary considerably. This real-world variability derives in part from random sampling error but also from the inherent difficulty of epidemiologic study design. With the possible exception of very large and expensive studies, any two epidemiologic investigations are likely to be conducted in ways that create different biases and confounding factors that can affect the results. Because the notion of a single, knowable quantitative measure of risk contribution is illusory, Professor Green noted, so too is the notion of an accurately modulated optimum deterrence signal based on risk contribution.[344]

The improbability of probabilistic precision is indisputable. Significant variation in measured relative risk characterizes even some of the strongest and most accepted substance-disease links uncovered by classical epidemiology.[345] Even if repeated studies could be designed to be perfectly comparable in avoiding bias and confounding, sampling error would frustrate any hope of replicating relative risk values. For claims involving rare diseases, uncommon exposures, or small toxic effects, an epidemiologic study's a priori statistical power will be relatively low, and the statistically computed sampling error relatively high.[346]

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344. Green, *supra* note 185, at 371–84, 395–96.

345. *See, e.g.*, W.C. HUEPER, OCCUPATIONAL AND ENVIRONMENTAL CANCERS OF THE URINARY SYSTEM 118–19, 156 tbl.48 (1969) (describing studies reporting relative risk of bladder cancer ranging from 8.7 to 17 in aniline dye industry workers). Estimates of the fraction of mesothelioma cases that occur absent known exposure to asbestos range from less than ten percent to upward of thirty percent. *Compare* Mark A. Behrens, *What's New in Asbestos Litigation?*, 28 REV. LITIG. 501, 527 (2009) (asserting that "there is wide agreement that a significant number (by some estimates, twenty to thirty percent) of mesotheliomas are not asbestos-induced"), *with* Troyen A. Brennan, *Environmental Torts*, 46 VAND. L. REV. 1, 15 (1993) (noting that "well over ninety-percent" of mesothelioma deaths are attributable to asbestos exposure). *See also* Becker v. Baron Bros., Coliseum Auto Parts, Inc., 649 A.2d 613, 618 (N.J. 1994) (reporting that plaintiff's witness testified that fifteen percent of cases "have no known cause," and defendant's witness testified that twenty to forty percent of cases have "unknown causes").

346. David H. Kaye & David A. Freedman, *Reference Guide on Statistics*, *in*

Shifting epidemiologic analysis to the molecular level will improve this situation. In past epidemiologic studies, undetected genetic differences contributed to the variability of results (because the research subjects were not all equally susceptible to the toxic effect under study or not equally at risk for the disease even without exposure).[347] Assessing relative risk by genotype will reduce that variability. Biomarkers of exposure will enable finer calibration of the very rough distinctions between "exposed" and "unexposed" samples to which epidemiologists have previously been limited. Biomarkers of effect or pre-clinical biomarkers of disease (even if not associated with toxic exposure) will similarly allow more precise delineations.[348]

Nonetheless, toxicogenomics and molecular epidemiology will not produce quantitative precision for the legal system's convenience. Their results will inherently be probabilistic, statistical, and variable. Molecular epidemiologists will be able to account for more causes of variation than classical epidemiologists could, but they will not be able to control for all sources of bias and confounding.[349] The legal system must understand that neither classical nor molecular epidemiology is likely to satisfy a norm of mathematical precision.

But where does that norm come from? Why should it be the norm? And why does it apply to causal findings but not to other elements of a tort claim?

To a large extent, the precision norm arises directly from the economic efficiency rationale. Critics ask: If optimal deterrence is the sole rationale for abandoning all-or-nothing causation rules,

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REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 211, 253–54 (Fed. Judicial Ctr. ed., 3d ed. 2011); *see also* Michael D. Green et al., *Reference Guide on Epidemiology*, *in* REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 549, 582–83 (2011) (describing application of statistical power concept in epidemiology).

347. *See* Marchant, *supra* note 53, at 7–8 ("[E]ach person is unique in his or her susceptibility to toxic agents, further complicating the inquiry into what caused illness in that individual.").

348. *See id.* at 18–27 (discussing potential use of biomarkers to prove or disprove exposure, as well as general and specific causation); Grodsky, *supra* note 85, at 181–87 (defining biomarkers of exposure, susceptibility, and effect).

349. Paolo Boffetta, *Biomarkers in Cancer Epidemiology: An Integrative Approach*, 31 CARCINOGENESIS 121, 125 (2010) (asserting that molecular epidemiology studies "fit into the same framework" as classical epidemiology).

but optimization is impossible because of inadequate data, why forgo the perceived accountability advantages of traditional *sine qua non* causation?[350]

The argument that probabilistic precision is illusory, however, applies also to factual determinations under the but-for test. This is especially true in jurisdictions that apply bright-line doubling+ relative risk standards for specific causation.[351] Even absent bright line rules, the all-or-nothing but-for causation model forces a fractional statistical probability to either 1 or 0. As Professor Green acknowledged, no one can say that those errors balance each other out.[352] Probabilistic causal contribution may not be able to discriminate finely between, say, a 40% risk contribution versus 35% or 45%. But even with limited accuracy, its results would more closely match the available risk evidence than the all-or-nothing test of but-for causation. It would avoid the under-deterrence problem that results when claims against tortious exposures to known risk factors fail because the but-for test cannot be satisfied, and it would provide some compensation and accountability in such cases.[353] At the same time, it would

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350. *See* Green, *supra* note 185, at 395–96 (doubting that proportional liability would enable "tort law to provide a liability signal precisely calibrated to the costs of accidents worth avoiding"); Klein, *supra* note 53, at 44 (asserting that although class-based, proportional liability schemes theoretically might provide optimal deterrence, Agent Orange experience suggests otherwise).

351. The arbitrary effects of the doubling+ rule have been felt in real cases. *See, e.g.*, Merck & Co. v. Garza, 347 S.W.3d 256, 267 (Tex. 2011) (rejecting plaintiff's expert's reliance on epidemiologic study with reported relative risk of 1.92); Estate of George v. Vt. League of Cities & Towns, 993 A.2d 367, 382 (Vt. 2010) (affirming the exclusion of plaintiff's expert testimony when epidemiologic results varied, some relative risks exceeded 2.0, and plaintiff's expert testified to "summary risk estimate" of 1.51).

352. Green, *supra* note 185, at 396. The net effect of all-or-nothing causation in toxic tort cases is a subject of debate. *Compare Estate of George*, 993 A.2d at 396 ("[T]here is reason to believe that the current system does not systematically underdeter."), *with* Lin, *supra* note 110, at 1442 (stating that causation proof problems and litigation costs cause "systematic undercompensation of environmental tort victims and the systematic underdeterrence of polluters").

353. Professor Green also argued that epidemiology cannot detect relatively small increases in risk as accurately as needed for proportional liability, and questioned the legal system's ability to assess the causal significance of a weak association between exposure and disease. Green, *supra* note 185, at 375–87, 392–95. Molecular epidemiology and toxicogenomics are likely to alleviate

reduce the over-deterrence of the "all" part of all-or-nothing rules.[354]

Large swaths of tort law are, to put it charitably, highly approximate. It is somewhat ironic to criticize causal apportionment of damages as imprecise when the amount of damages itself contains a large heuristic component and when significant components even of seemingly objectively calculable economic damages are computed by informed probabilistic estimates. Furthermore, comparative fault regimes that divide up liability and thus affect deterrence signals have become nearly universal. Of course, apportioning among liable parties "on the basis of a normative judgment about relative culpability or responsibility is different from employing probabilistic assessments of the existence of an element of a *prima facie* case to determine the liability of a party and the damages for which the party is liable."[355] But both processes ask fact-finders to divide liability for a harm into pieces. Probabilistic causal contribution, although an imprecise fraction based on imprecise data, would at least be based to *some* degree on quantitative evidence. It is incongruous to let fact-finders hear all the evidence about the parties' conduct and then carve up the liability based

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(though not completely eliminate) the problem of weak associations by disaggregating them into relatively strong associations for susceptible individuals and very weak or nonexistent associations for resistant individuals. Ofer Shpilberg et al., *The Next Stage: Molecular Epidemiology*, 50 J. CLINICAL EPIDEMIOLOGY 633, 637 (1997); *see also* Perera, *supra* note 149, at 608 (noting that "new molecular epidemiologic and other data invalidate the assumption of population homogeneity" with respect to toxic susceptibility). The need to decide whether an epidemiologic association is causal, which addresses general rather than specific causation, arises in every case in which a plaintiff relies on epidemiologic evidence, even under but-for causation. The decision requires consideration of the "aspects" of an association that epidemiologists use to assess the causal significance of an association, only one of which is the association's strength. *See* Hill, *supra* note 18, at 295. Probabilistic causal contribution would be applied to specific causation only if the evidence were sufficient to support an inference of general causation.

354. Because of incomplete claiming, over-deterrence may in many cases be more theoretical than real. *See* Dan Markel, *Reply: Punitive Damages and Private Ordering Fetishism*, 158 U. PA. L. REV. PENNUMBRA 283, 284 & n.4 (2010), http://www.pennumbra.com/responses/05-2010/Markel.pdf (noting "widely known problems of tort underenforcement").

355. Green, *supra* note 185, at 353.

on a normative judgment,[356] but prevent them from using relative risk as an apportionment tool because epidemiology is imprecise.

In the CERCLA context, the Supreme Court accepted the division of millions of dollars of liability based on very indirect measures of causal contribution.[357] Tort law tolerates the imposition of full liability based on a belief that each element of the claim is "more likely than not." It tolerates the extremely rough justice of comparative fault. Why should it demand a higher level of accuracy for causal apportionment? Getting it right is important, but the presence of scientific evidence should not fool us into thinking the law can or must get it exactly right—especially when the alternative is acknowledged over-deterrence in some cases and under-deterrence in many others.[358] Detailed toxicogenomic and molecular information, to the extent available, will improve a fact finder's ability to assign a causal share to a defendant's toxic substance as opposed to all other contributors to the risk of a plaintiff's disease. We should recognize this as an improvement—without feeling a need to pretend that such information will allow courts to impose theoretically perfect amounts of liability.

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356. *See* Wright, *supra* note 325, at 1144–45 (stating that comparative responsibility is assessed "not according to any detailed formula but rather through rational commonsense judgment").

357. Burlington N. & Santa Fe Ry. Co. v. United States, 556 U.S. 599, 612 (2009) (affirming liability allocation under CERCLA even though "the evidence adduced by the parties did not allow the court to calculate precisely the amount of hazardous chemicals contributed by the Railroad parcel to the total site contamination or the exact percentage of harm caused by each chemical.").

358. *Martin v. Owens-Corning Fiberglas Corp.*, 528 A.2d 947 (Pa. 1987), illustrates the tensions inherent in all-or-nothing rules. The court rejected a jury verdict apportioning a plaintiff's disability between his asbestos exposure and his tobacco smoke exposure. *Id.* at 950–51. Two dissents argued that apportionment should have been permitted using "rough approximation," *id.* at 951 (Nix, J., dissenting) without requiring "[m]athematical exactitude," *id.* at 954 (Hutchinson, J., dissenting). The first complained that apportionment was essential to avoid the "unconscionable" result of no recovery (presumably because the plaintiff's own actions vitiated but-for causation by the defendant). *Id.* at 951 (Nix, J., dissenting). The second complained that apportionment was essential to avoid the "unjust" result of full liability (presumably because plaintiff's and defendants' acts would be treated as multiple sufficient causes). *Id.* at 954 (Hutchison, J., dissenting).

Another deterrence-based critique argues that causally-based apportionment of damages will provide inadequate deterrence because defendants will have incentives to hunt for extra risk factors to blame—and finding them would, perversely, reduce the liability of each wrongdoer as more wrongdoers (or at least risk factors) are found.[359] Yet defendants have every incentive to conduct this hunt under an all-or-nothing but-for model of causation as well. The difference is that under the current regime a defendant that successfully posits additional risk factors as independent alternate causes has a good chance of avoiding liability altogether, while under probabilistic causal contribution the defendant would bear at least some liability even if many cases of the plaintiff's disease have no known cause.[360] Probabilistic causal contribution would also shift the onus with respect to alternative risk factors. Under current law, plaintiffs often must attempt to "rule out" other possible causes to leap the "more likely than not" hurdle and obtain a finding of but-for causation. Under probabilistic causal contribution, if a plaintiff proves that the exposure for which a defendant is responsible increased the plaintiff's risk, a defendant seeking to use another risk factor to reduce its own liability would have to justify that reduction by showing that the plaintiff was exposed to the other risk factor and consequently faced a greater risk than would have been the case with only the exposure for which the defendant was responsible.

Moreover, the premise of the under-deterrence argument, that the tortfeasor caused the whole injury but is being held liable for only part of it, fits poorly with the reality of

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359. *See, e.g.*, David A. Fischer, *Proportional Liability: Statistical Evidence and the Probability Paradox*, 46 VAND. L. REV. 1201, 1211–14 (1993) (arguing that the "probability paradox" means that "probabilistic causation requires people to use the least care when the world is the most dangerous").

360. If the evidence shows that the risk factors interact to create risk, the defendant is less likely to prevail under an all-or-nothing regime but also likely to pay a larger share under probabilistic causal contribution. *See supra* note 273 and accompanying text. And in an all-or-nothing regime, even in the case of a synergistic interaction, a defendant might be able to convince a fact-finder that only the other risk factor was a "more likely than not" cause, depending on the strength of the interaction and the risk characteristics of the individual exposures.

indeterminate specific causation. Because that indeterminacy is the rationale for probabilistic causal contribution, exposure to multiple independent risk-contributing factors *should* matter: the additional risk factors reduce the relative role of a defendant's risk factor. The deterrence signal of a discounted recovery, even if less than that of a full recovery, would still be higher—and therefore theoretically would produce greater investment in safety—than the signal that would result if but-for causation rules precluded any recovery.[361] And if the hunt for alternative risk factors leads to legitimate scientific research, it will help society learn the truth and perhaps make better decisions about what products create risks that are not worth their benefits and vice versa.[362]

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361. David Fischer's contrary argument misapprehended the nature of epidemiologic data. Professor Fischer hypothesized seven known carcinogens, exposure to each of which posed a thirty percent risk of developing lung cancer. Fischer, *supra* note 359, at 1213. He argued that under proportional liability a plaintiff tortiously exposed to just one of them would probably receive a 90% recovery because there would be no other plausible cause, while if each of seven equally culpable defendants exposed the plaintiff to a different carcinogen, each defendant would be liable only for one-seventh of the damages. *Id.* The premise of a 90% recovery from the single tortfeasor, however, assumed that the seven known carcinogens are the only possible causes, so if the plaintiff was exposed to only one, that exposure must have been the cause—which is inconsistent with the hypothesized fact that *ceteris paribus*, exposure to that one carcinogen only explained 30% of the incidence of the disease. A court applying all-or-nothing but-for causation and the doubling+ rule would not let the hypothesized single-tortfeasor case be tried. Under probabilistic causal contribution, the single tortfeasor would appropriately be liable for 30% of the damages. The seven-defendant case would be more complicated, because the hypothetical treated the carcinogens independently but the hypothesized facts ruled out the possibility of independent additive risk contributions: the seven carcinogens could not together account for 210% of the risk of lung cancer. Based on equal relative risk values for each carcinogen, a fact-finder might attribute a one-seventh share to each, but evidence of the degree of confounding in the various studies, the similarity or differences of the carcinogens' biological mechanisms, or studies of the interactions of multiple exposures might alter that result.

362. *See* MICHAEL D. GREEN, BENDECTIN AND BIRTH DEFECTS 332 (1996) (noting that Bendectin litigation spurred scientific research into the drug's effects).

B. Corrective Justice Goals: Is Causation Different?

The Third Restatement of Torts acknowledged widespread adoption of comparative responsibility and apportionment principles. It embraced a theoretical distinction, however, between apportionment based on cause and apportionment based on fault or other norm-based conceptions of responsibility.[363] Apportionment based on cause, according to the Third Restatement, may be appropriate in limited circumstances when "legally culpable conduct . . . was a legal cause of less than the entire damages for which the plaintiff seeks recovery" and a fact-finder can determine "the amount of damages separately caused by that conduct."[364] Other than straightforward enhanced-injury cases, however (as where a defendant negligently causes an accident that injures a plaintiff who is then further injured by medical malpractice), the Third Restatement did little to illustrate when such a situation might arise, noting that very little case law provides clear analysis of the problem.[365]

The Third Restatement thus took a clear position that but-for causation is a prerequisite for any fault-based apportionment. The basis for this choice was the principle that "[n]o party should be liable for harm it did not cause."[366]

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363. RESTATEMENT (THIRD) OF TORTS: APPORTIONMENT OF LIAB. § 26 (2010).

364. *Id.* § 26(b); *see also, e.g.*, RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYSICAL & EMOTIONAL HARM § 28 cmt. d (2010) (discussing circumstances under which harm is "causally divisible"); *id.* cmt. l (distinguishing circumstance when each one of multiple actors causes all of a plaintiff's harm from circumstances in which each actor causes part of a plaintiff's harm). Under the Third Restatement, liability for what the Second Restatement called distinct "harms," RESTATEMENT (SECOND) OF TORTS § 433A (1)(a) (1965), would be assigned to each defendant whose conduct was a but-for cause of the separate harms, with any apportionment to be determined by the jurisdiction's scope of liability rules. RESTATEMENT (THIRD) OF TORTS: APPORTIONMENT OF LIAB. § 26(b) (2010). The Third Restatement appeared to abandon the Second Restatement's concept of single harms for which there is a reasonable basis for apportionment, or "divisible" harm. *Compare* RESTATEMENT (SECOND) OF TORTS § 433A (1)(b) & cmt. d (1965), *with* RESTATEMENT (THIRD) OF TORTS: APPORTIONMENT OF LIAB. § 26 cmt. a, c (2010).

365. RESTATEMENT (THIRD) OF TORTS: APPORTIONMENT OF LIAB. § 26 cmt. a (2010) ("[F]ew if any cases provide much analysis.").

366. *Id.*

Andrew Klein relied heavily on the same principle in his argument for a strong requirement of *sine qua non* causation even in toxic torts. Professor Klein argued that requiring but-for causation is compelled by corrective justice principles.[367] He also noted that to hold defendants liable for damages they did not "cause" undermines confidence in the legal system and bolsters calls for replacing tort law altogether.[368] The powerful intuitive notion that cause is a yes-or-no phenomenon that cannot be divided up[369] thus fits tightly with corrective justice theories of tort.[370]

The principle that persons should be liable only for damages they cause, depends, however, on the meaning of "cause." In the uncertain molecular world of toxic causation, if a substance is a risk factor for disease then that substance is causing injury to someone, but science does not let us identify that person in the routine, familiar way.[371] Reliably attributing a particular plaintiff's harm to a particular defendant's conduct—were it possible—would be more satisfying than basing causation on contribution to risk, realized injury, and discounted recovery. But in the face of irreducible uncertainty, a discounted recovery provides at least some redress and is a better measure of corrective justice than no recovery at all.[372] Probabilistic causal contribution thus can restore some degree of accountability that has been eroded by narrow judicial interpretations of the

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367. *See* Klein, *supra* note 53, at 9–13 (discussing the value of *sine qua non* causation in terms of corrective justice principles).

368. *Id.* at 30.

369. *See* Sanders, *supra* note 1, at 26 (noting that mesothelioma is an indivisible injury not susceptible to apportionment, "[a]t least not apportionment based on causation").

370. MICHAEL S. MOORE, CAUSATION AND RESPONSIBILITY 5 (2009).

371. Richard Delgado described this as the problem of the "indeterminate plaintiff." *See generally* Richard Delgado, *Beyond* Sindell*: Relaxation of Cause-in-Fact Rules for Indeterminate Plaintiffs*, 70 CALIF. L. REV. 881 (1982).

372. *See* John Makdisi, *Proportional Liability: A Comprehensive Rule to Apportion Tort Damages Based on Probability*, 64 N.C. L. REV. 1063, 1073–74 (1989) ("While it is true that those who are actually injured by the tortious conduct do not receive their compensation in full and the others receive compensation to which they are not entitled under traditional tort theory, a fairer distribution of the damages is not possible given the uncertainty of causation.").

admissibility and sufficiency of causation evidence.[373] It is also better than allowing full recovery, which in the aggregate (assuming sufficient claiming) would force a defendant to pay for more harm than its actions created.

The theoretical purity of but-for causation has already been diluted to some extent by comparative responsibility regimes. Fact-finders must, and do, weigh the incommensurate all the time in comparative responsibility cases, which may entail a quantitative comparison of behavior found blameworthy (i.e., negligent) to behavior that is fault-free but nevertheless gives rise to liability.[374] Who is more responsible for the truck that backed up into its driver: the strictly liable auto manufacturer that designed the defective transmission that mis-shifted, or the negligent driver who exited the car without disengaging the ignition?[375] It is fanciful to think jurors view such questions through polarized lenses that transmit no light on relative causal contribution. Judgments of blameworthiness incorporate causal judgments too. When a drunk driver runs a stop sign and injures another driver who could not avoid the crash because a mechanic erred when repairing her brakes, the drunk driver gets a greater share of liability not just because the conduct is worse, but also because of the sense that the brakes would not have been needed absent the drunk driving, even though the bad brakes were a but-for cause of the accident.

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373. *See* Christopher H. Schroeder, *Corrective Justice and Liability for Increasing Risks*, 37 UCLA L. REV. 439, 444–45 (1990) (arguing that liability for imposing risks is consistent with corrective justice). *See generally* Thomas O. McGarity, *Proposal for Linking Culpability and Causation to Ensure Corporate Accountability for Toxic Risks*, 26 WM. & MARY ENVTL. L. & POL'Y REV. 1, 5–14, 38–41 (arguing that toxic tort causation doctrine has contributed to an "accountability crisis").

374. New Jersey's statute is exemplary: "In all negligence and strict liability actions[,]" the fact-finder must determine the "extent, in the form of a percentage, of each party's negligence or fault." N.J. STAT. ANN. § 2A:15-5.2.a (West 2002). The statute provides for only several liability for any party less than 60% "responsible" for the damages, subject to a partial exception for environmental tort actions. *Id.* §§ 2A:15-5.3.b, 5.3.d.

375. *See* Gen. Motors Corp. v. Sanchez, 997 S.W.2d 584, 598 (Tex. 1999) (holding that the plaintiff's actual recovery would be reduced by the "jury's finding of fifty percent comparative responsibility").

Current doctrine requires fact-finders to engage in *sub silentio* causal attribution in some toxic tort cases as well. As noted above, data show that exposure to both tobacco smoke and asbestos synergistically increases the risk of lung cancer above the sum of each product's independent risk enhancement.[376] Yet manufacturers of tobacco and asbestos products routinely name each other as the cause of lung cancer in plaintiffs exposed to both products. Even if fault dominates fact-finders' thinking in such cases, it seems extraordinarily unlikely that they pay no attention to the risk data and other causal issues, such as the relative amounts of exposure, when they assign comparative responsibility.[377]

A related view, prominently espoused by Richard Wright, relies on a sharp distinction between ex ante risk and ex post causation. The argument holds that statistical data derived from studies of populations provide insufficient information to satisfy corrective justice norms for a causal finding in an individual case; instead, particularistic evidence should be required to support a specific causal inference.[378] If, however, particularistic evidence means evidence of some characteristic that distinguishes an exposure-caused case of disease from any other, this would imply that no plaintiff relying on epidemiologic or similarly population-based evidence could ever prevail, even in the post-genomic era. Professor Wright has acknowledged the normative appropriateness of forms of proportional liability to avoid this harsh result, at least in some circumstances in which it is impossible to prove "who actually caused the plaintiff's injury."[379]

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376. *See supra* Part III.A.2.

377. *See* Sanders, *supra* note 1, at 38 (noting blending of causal and normative concepts in comparative responsibility instructions).

378. *See, e.g.*, Wright, *supra* note 19, at 196, 206–08 ("Legal fact-finders are not told that they merely need to place a bet on the existence of some fact, but rather are instructed that they must determine whether the fact actually existed."); Wright, *supra* note 24, at 1312–14; Wright, *supra* note 5, at 1049–50.

379. Wright, *supra* note 5, at 1072; *see also* Green, *supra* note 185, at 362–63 (discussing Professor Wright's views on proportional liability); Wright, *supra* note 19, at 214 (approving of market-share liability in DES cases and the proportional liability imposed in *Barker*, though disagreeing with *Barker*'s risk contribution theory).

When the causation evidence inherently must be statistical, however, probabilistic causal contribution is not just a second-best approach; it is the approach that best fits knowable truth.[380] The indeterminacy of toxic tort causation is different from the familiar example in which the knowledge that one company operates a large majority of buses on a route will not suffice to hold that company liable when an unidentified bus runs a car off the road.[381] The intuitive discomfort with holding the bus company liable arises not because of the statistical nature of the evidence that it was the most probable owner of the errant bus. Rather, we do not really believe that the statistic accurately reflects the probability. To say that the bus company probably caused the accident is to say that one of its drivers was probably at fault and we are loath to do that without more information.[382] Despite reductionist neurobiology, we don't treat momentary lapses of attention as the result of random molecular movements in the driver's brain. The statistical frequency of motor vehicle accidents per vehicle mile traveled is well known, yet most people think they can avoid accidents—indeed most people think they are above-average drivers.[383] Instinctively we believe that road accidents, especially accidents caused by bad driving, are not

380. *See* Makdisi, *supra* note 372, at 1100–01 (when a causal link "is believed by a factfinder to be probable rather than actual, the willingness to consider this probability and allocate proportional relief reflects a more complete and accurate notion of cause"). *But cf.* Wright, *supra* note 19, at 214 (describing the market-share scheme as a "second best liability doctrine").

381. Sargent v. Mass. Accident Co., 29 N.E.2d 825, 827 (Mass. 1940) (quoted in Wright, *supra* note 19, at 201); *see also* Smith v. Rapid Transit, 58 N.E.2d 754, 754–55 (Mass. 1945).

382. *See* Makdisi, *supra* note 372, at 1079 (arguing that *Smith v. Rapid Transit* is partly explained because it is normatively "more offensive to attribute to a potentially innocent defendant a wrongdoing harm that he may not have caused").

383. *See generally, e.g.*, Leilani Greening & Carla C. Chandler, *Why It Can't Happen to Me: The Base Rate Matters, But Overestimating Skill Leads to Underestimating Risk*, 27 J. APPLIED SOC. PSYCH. 760 (1997); Mark S. Horswill et al., *Drivers' Ratings of Different Components of Their Own Driving Skill: A Greater Illusion of Superiority for Skills That Relate to Accident Involvement*, 34 J. APPLIED SOC. PSYCH. 177 (2004).

randomly distributed, and that bad drivers may not be randomly distributed across bus companies either.[384]

There is no morality to the molecule. In toxic torts, once a fact-finder concludes that *general* causation has been established by the available evidence,[385] no reason exists to suspect anything other than randomness for specific causation.[386] Or, at least, science usually won't be able to distinguish the "actual" cause in a given case from the probability distribution of causes.[387] In such cases, insisting upon particularistic evidence to protect

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384. When causation turns on statistical data but issues of fault are resolved without statistical evidence, as in alternative and market-share liability cases, courts have been less likely to require particularistic evidence of causation. *But cf.* RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYSICAL & EMOTIONAL HARM § 28 cmt. j (2010) (noting that courts are less willing to apply alternative causation when evidence connecting particular defendants to even the possibility of harm is absent, perhaps because exculpation is too difficult or plaintiffs are insufficiently diligent).

385. Professor Wright agrees that evidence of statistical associations may bear on general causation. Wright, *supra* note 19, at 206, 215.

386. *See* RUVINSKY, *supra* note 178, at 153 ("[Q]uestions such as what is the cause for this mutation . . . do not have answers.").

387. Michael Green pointed out that the distinction between particularistic ex post proof of causation and population-based ex ante proof of risk collapses if an epidemiologic study is the only evidence available. He wondered how Professor Wright would respond to a hypothetical in which a plaintiff proved exposure to an agent presenting a very high statistical risk of disease but a witness "claims to have observed the plaintiff contract the disease from an alien bite." Green, *supra* note 185, at 362 n.38, 363. Professor Wright responded that the hypothetical was fallacious because it did not really involve competing causes but instead depended on an implicit assumption that the alien bite could not cause disease: "If . . . there is no proven or accepted alien-bite causal generalisation and no other possibly applicable causal generalisation, then" the toxic agent is "the only possibly applicable causal generalisation [the known statistical risk] with at least some particularistic instantiation [the known exposure] . . . which fact could support the formation of a belief that it was the causal process actually at work in the particular situation." Wright, *supra* note 19, at 210 n.67. If proof of exposure could satisfy the demand for particularistic proof, that demand would present only a small obstacle to reliance on population-based data (even though proving exposure is sometimes difficult). But if exposure constitutes sufficient particularistic proof only when "no other possibly applicable causal generalisation" exists, then it will never be sufficient. No one can ever exclude every possible alternative cause, *see* Stubbs v. City of Rochester, 124 N.E. 137, 140 (N.Y. 1919), and frequently the competing cause is not a specific risk factor but rather "unknown causes." *See, e.g.*, Henricksen v. ConocoPhillips Co., 605 F. Supp. 2d 1142, 1149 (E.D. Wash. 2009).

defendants from paying for harm they did not cause rings hollow; probabilistic causal contribution requires them to pay for the harm that they did cause.[388]

Toxicogenomics and molecular epidemiology will continue to undermine the appropriateness of the deterministic model of but-for cause in toxic tort cases. Corrective justice would be better served by using a more appropriate causation model. With but-for and toxic torts, if it doesn't fit, abandon it.

C. Truth-Seeking Goals: Wrong All the Time?

In their helpful catalogue of "vices" of proportional recovery, Ariel Porat and Alex Stein include an epistemological problem: although all-or-nothing rules may produce erroneous results in some cases (either wrongly attributing causation where it did not actually exist or wrongly failing to attribute causation where it did actually exist), a rule that assigns a fractional recovery will produce a result at variance with historical truth in each individual case, because it will never be true that a tortious exposure caused *x%* of a plaintiff's harm but not the remainder.[389] This is indisputable for a non-cumulative disease in a deterministic causal model when only population-based evidence is available.[390] Any all-or-nothing rule, however, also accepts the existence of some erroneous adjudications, and further accepts that the aggregate result across a population of cases will be

388. *See* Makdisi, *supra* note 372, at 1073–74.

389. Ariel Porat & Alex Stein, *Liability for Future Harm*, *in* PERSPECTIVES ON CAUSATION, *supra* note 1, at 221, 227–28. Porat and Stein, who are generally sympathetic to probability-based compensation, argued that probabilistic recovery for the chance of future harm avoids this and some of the other "vices" of probability-discounted recovery for past harms. *See generally id.* at 226–33 (describing how different characteristics of the causal indeterminacy problem for past and future harms affect the strengths and weaknesses of using proportional liability to address the indeterminacy).

390. To say that there is an *x*% probability that a randomly-selected exposed individual with a disease will be a "true" causation case, is not the same as saying that the individual's case is *x*% probable of having "true" causation, even though many courts equate the two statements. *See* Gold, *supra* note 277, at 390 n.72.

wrong.[391] It is not clear why having a lower count of errors is epistemologically superior to reducing the overall magnitude of the consequences of the errors.[392] More fundamentally, if we adopt a probabilistic view of causation at the individual level—even if that model is only a concession to the limits of scientific understanding—then probabilistic causal contribution gets it roughly right in every case, and the epistemological problem that Porat and Stein identified disappears.

D. Administration of Justice Concerns: Too Much Information?

In a thoughtful essay, Joseph Sanders emphasized a number of "practical, administration-of-justice" problems that he concluded outweighed the "persuasive substantive arguments" in favor of the "risk rule" of *Rutherford* and *Barker*.[393] Professor Sanders expressed concern about the level of complexity that risk-based causal attribution would bring to toxic tort litigation,[394] although he acknowledged that toxicogenomics could actually alleviate some of that concern by providing a more finely-grained understanding of causal mechanisms.[395]

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391. Not everybody who has experienced both illness and exposure will sue, which adds a further element of unpredictability to the fact-finding accuracy of all-or-nothing rules. If the probability of claiming were strongly positively correlated with the probability of "true" causation (e.g., because only people with obvious exposures or known genetic susceptibility are likely to sue), but the applicable all-or-nothing rule bars recovery, the frequency of false negative errors among cases actually brought could approach 100%.

392. *See* Makdisi, *supra* note 382, at 1065, 1074 (arguing that proportional liability is more accurate and fair).

393. Sanders, *supra* note 1, at 34, 36.

394. *See id.* at 34 (doubting feasibility of identifying risk proportions in multi-agent cases); *id.* at 40 ("[R]isk rule introduces a substantial degree of conceptual complexity and uncertainty."). Michael Green expressed similar concerns but suggested that apportionment based on risk contribution would be less of a "litigative quagmire" than apportionment based on comparative responsibility. Green, *supra* note 94, at 540–41. Andrew Klein has argued that administrative concerns justify the doubling+ rule with proportional recovery. Andrew R. Klein, *A Model for Enhanced Risk Recovery in Tort*, 56 WASH. & LEE L. REV. 1173, 1195–96 (1999).

395. Sanders, *supra* note 1, at 36.

The concern is well-founded. Probabilistic causal contribution does not have the virtue of simplicity. Courts will be challenged to administer cases in reasonable time, at reasonable cost, and with appropriate levels of scrutiny of expert testimony, which will be offered by all parties. But even if courts adhere to a deterministic "more-likely-than-not but-for" causation model, they will still be confronted with toxicogenomic and molecular epidemiologic data and all of the complexity such evidence will entail. As I've said elsewhere, that train is coming, and courts cannot get off the tracks.[396]

The complexity courts will face will reflect the complex world that science reveals. If toxicogenomics, molecular epidemiology, and related sciences fulfill their potential, they will show us an elaborate landscape of toxic risks and variable genetic susceptibility to those risks, many of them relatively small but still significant. If, in the name of simplicity and reduced administrative expense, courts impose on that landscape the same all-or-nothing rules now in effect, the law will willfully blind itself to the truth, will too frequently fail to redress harm truly caused, and will impose too much liability for the harm it does redress. Such outcomes would be neither efficient nor just.

VI. Conclusion

Paradoxically, the emergence of toxicogenomics and molecular epidemiology promises to increase our understanding of the effects of toxic exposures while simultaneously highlighting the fundamental uncertainty of any individual claim. These scientific advances strengthen, rather than weaken, the case for reform of causation doctrine.

The deterministic model of but-for causation does not fit toxic tort cases that depend on population-based data—even if the data come from studies at a molecular scale. Worse, it produces results that are inefficient and unjust. Commentators have recognized this for a quarter-century, but with few exceptions the courts have not responded. In the post-genomic era, it is time for the

396. Gold, *supra* note 3, at 397.

courts to adapt,[397] and to adopt a probabilistic causal contribution model in toxic tort cases.

397. *See* Donovan v. Philip Morris USA, Inc., 914 N.E.2d 891, 901 (Mass. 2009) (recognizing a medical monitoring claim for increased risk resulting from toxic exposure).