Forthcoming in University of Western Australia Law Review – Special Edition on Causation in the Law (2021)

Law and Epidemiological Evidence: Double, Toil and Trouble

Per Laleng and Charles Feeny*

Abstract

In *Sienkiewicz v Greif (UK) Limited,* the Supreme Court discussed a doubles-the-risk test based on epidemiological studies for the proof of individual causation in toxic tort litigation in the United Kingdom. The issue was *obiter* in the Appeal. Differing views were expressed and the speeches cannot be interpreted as rejecting the test as a matter of law. Unsurprisingly, therefore, reference continues to be made to the test and the analogous argument that causation can be proved by a statistical likelihood of a better outcome in the absence of breach. It is generally accepted that risk-based epidemiological evidence is admissible in litigation. This raises the question of the continued forensic role of such evidence in English common law. We use a case study with variations to indicate a range of issues that may arise in the application of epidemiological evidence. The issues are multi-faceted and demonstrate why a simple formulaic rule based on doubling of the risk ('a relative risk of two') could never work. An arbitrary cut-off at a relative risk of two would lead to injustice. Whilst the epidemiological evidence is telling us something of relevance, it does not answer all the questions that are specific to a particular case at a particular moment in time. A better understanding of epidemiological evidence and how it can be applied in individual cases will assist, but it is reasonable to anticipate that considerable controversy will persist in clinical negligence and toxic tort litigation. For that reason, we propose a structured approach to the assessment and use of epidemiological evidence in litigation. This approach may assist decision-makers and others as they navigate the current muddles and misconceptions that surround the forensic role of such evidence.

Key words: tort law – proof of causation – epidemiological evidence – deep vein thrombosis

> In my view, it must now be taken that, saving the expression of a different view by the Supreme Court, in a case of multiple potential clauses, a Claimant can demonstrate causation in a case by showing that the tortious exposure has at least doubled the risk arising from the non-tortious cause or causes.

> *per* Smith LJ, Court of Appeal, *Sienkiewicz v Greif (UK) Limited*.[1]
>
> … there is no room ... for applying the approach laid down by Smith LJ in the Court of Appeal in the passage quoted ... above. The purported guidance to Courts in that passage should not be followed.
>
> *per* Lord Rodger, Supreme Court, *Sienkiewicz v Greif (UK) Limited*.[2]

Introduction

In 1932, at the inception of the modern tort of negligence[3], epidemiology as a scientific approach was essentially nascent. In 1848, Jon Snow had demonstrated through careful analysis that an outbreak of cholera in Soho could be traced to a polluted water pump.[4] His work was mainly credited with its contribution to an acceptance that cholera was waterborne and a dismissal of the miasma theory rather than an appreciation of the significance of his methodology. Whilst individual studies such as that of Jon Snow were well known, that epidemiology would develop into a systematic underpinning of mainstream medicine would not have been anticipated. Through the 20th Century epidemiology developed with a consequent understanding of risks that were not immediate in terms of causation as with water from a polluted pump. In relation to toxicity, risk came to be understood in relation to exposures over many years including long historic cigarette-smoking or employment involving asbestos. Epidemiology now considers risk factors which pre-date birth or even conception. The parallel extensions

---

* Per Laleng is a Senior Lecturer in Law at the University of Kent, UK. Charles Feeny is a barrister, mediator and legal analyst based in Liverpool, UK. He is Director of *Complete Counsel Ltd*. This article follows two seminars organized by Pro-VIDE Law exploring the issues arising. The first was held at Wadham College, University of Oxford with a follow-up event at DWF, London. We would like to thank the following people for their helpful comments on previous drafts: Erika Rackley, Professor of Law, University of Kent; Professor Jonathan Beard, Consultant Vascular Surgeon, Sheffield Vascular Institute; Maurice Zeegers, Professor of Complex Genetics and Epidemiology, Maastricht University; Sandy Steel, Associate Professor of Law, University of Oxford; Alan Thomson. We would also like to thank the anonymous peer reviewers for their time and comments. All comments have helped improve this article. The usual caveats apply.

[1] [2009] EWCA Civ 1159 at [23].
[2] [2011] UKSC 10 at [162].
[3] *Donoghue v Stevenson* [1932] UKHL 100.
[4] J. Snow, *On the Mode of Communication of Cholera, 2nd ed.* (John Churchill 1855)

of the tort of negligence and epidemiology resulted in an inevitability that epidemiological evidence would be used in court. Unsurprisingly this has proved troublesome given the clear difference in focus: epidemiology focusses on groups whereas litigation is concerned with individual redress. Equally unsurprisingly the English courts sought to resolve the issues by a formulaic rule which led to the articulation of the doubles-the-risk test by the Court of Appeal in *Sienkiewicz*.[5]

The doubles-the-risk test derived from epidemiology, a science that studies the occurrence of disease and injury in human populations.[6] An important measure used in many epidemiological studies is the relative risk. It expresses how much more likely an exposed group is to suffer the studied harm compared with an unexposed group. The rate of harm within an unexposed group is also known as the background rate. A relative risk of two suggests that the exposed group is twice as likely as the unexposed group to suffer the studied harm. If the relevant exposure is tortious, the tortious exposure has doubled the risk arising from the non-tortious cause or causes *ie* the background rate. To illustrate, let's compare two groups of 1000 people. One group has been exposed to a pathogen and the other has not. In the exposed group we observe 50 people with a disease. In the second unexposed group we find 25 people with the same disease. Assuming all else is equal, of the 50 cases of disease in the exposed group, 25 can be attributed to the background rate (*ie* the disease would have occurred without exposure). The other 25 cases can be attributed to exposure. The relative risk of contracting the disease after exposure is a proportional measure or ratio that compares the likelihood of an event (here, a disease) after an intervention (for example, exposure or treatment) compared with its likelihood in a control (non-exposed) group. In our example as there are 1000 people in each group, the ratio is simply fifty divided by twenty-five which is two. There are twice as many instances of the disease in the exposed group compared to the unexposed group. In short, the risk associated with exposure has been doubled: a relative risk of two. Put differently, if a person with the disease was chosen at random from the exposed group, then it is equally likely that that disease can be attributed to exposure or to the background rate.

---

[5] n 1.

[6] L.M. Bouter, G.A. Zielhuis and M.P.A. Zeegers, *Textbook of Epidemiology* (Houten: Bohn, Stafleu van Loghum 2018) 2.

A doubled risk appears to dovetail with the standard of proof on the balance of probabilities in civil cases. Whilst Lady Justice Smith said that a Claimant could prove causation by showing that tortious exposure had *at least* doubled the risk, she probably meant to say that exposure had *more than* doubled the risk. This is because a doubled risk means that a disease is equally likely to be attributable to exposure as to the background rate whereas a risk that is more than doubled would mean that exposure is associated with more than fifty per cent of the observed cases; that is, more likely than not. Superficially, therefore, Lady Justice Smith's proposed test for causation in multiple cause cases was attractive in its apparent simplicity of application. However, the formulaic melding of an epidemiological doubled risk with the legal 'more likely than not' standard of proof conceals the difficulties - if not the fallacy - of drawing an inference about an individual from aggregate data about groups.

Given Lord Rodger's comment in the Supreme Court in *Sienkiewicz*, the reign of a doubles-the-risk test for causation in toxic tort litigation in the United Kingdom might have seemed destined to be short-lived. However, controversy over the correct approach and support for the test has lingered on. So, ten years after *Sienkiewicz*, in *Mather v Ministry of Defence*[7] the Defendant submitted on a preliminary issue that unless the Claimant's exposure was shown to have more than doubled his risk of developing multiple sclerosis, his claim must fail as "a matter of law". Similarly, as shown in clinical negligence cases such as *Schembri v Marshall,*[8] courts must toil with the argument that statistical evidence showing a better than fifty per cent prospect of avoiding injury in absence of breach *ipso facto* proves causation. This argument is analytically indistinguishable from the doubles-the-risk test. It has a beguiling apparent simplicity but can be shown to be deeply flawed. Understanding why such a formulaic test is inappropriate is instructive for an appreciation of how such evidence can be reasonably deployed in proof of causation. We discuss the issues with reference to a hypothetical case study. Whilst the case study refers to a particular disease, deep vein thrombosis, the analysis provided in this article is generalizable.

[7] [2021] EWHC 811 (QB).
[8] [2020] EWCA Civ 358.

Case Study

The case study centres upon the fortuitously named Donna von Trapp. Donna is a 30-year-old woman who had flown back from Bangkok. She took a direct 11 ½ hour flight. About a week after her return she noticed pain in her right thigh. On seeking medical attention, she was diagnosed as having developed a Deep Vein Thrombosis ('DVT'). Donna was otherwise healthy and investigation of her and her family's history revealed no known risk factors for DVT. Donna had the benefit of personal accident insurance and sought to claim in respect of the DVT, which caused her significant disability and loss of earnings. The insurers objected, arguing that the DVT had been caused by the long-haul flight. A term of the policy excluded compensation for DVT caused by a long-haul flight. There are various epidemiological studies which address the risk of DVTs associated with flying long-haul. For the case study, reference is made to a paper by Adi and others[9] that suggests a relative risk of 1.7. The first question is whether the insurance company can maintain the exclusion when the risk associated with the long-haul flight was not demonstrated to have been doubled. We introduce some variations on this case study later.

The case study and its variations will demonstrate why a doubled risk cannot be determinative of causation. Either way, it cannot - without more - establish causation, and a claim does not necessarily fail when epidemiological evidence shows that the relative risk is less than two. We provide a set of guidance questions to assist decision-makers and others considering the use of epidemiological evidence in the proof of causation in tort law. To understand the interplay of epidemiological and legal concepts, it would be useful to have a basic grasp of some of the epidemiological concepts that may be relevant to legal questions of causation.

Risks: relative and background

[9] Y. Adi, S. Bayliss, A. Rouse and R. S. Taylor, 'The association between air travel and deep vein thrombosis: Systematic review & meta-analysis' (2004) 4 BMC Cardiovasc Disord 7. doi: 10.1186/1471-2261-4-7. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC434500/ (last visited 3 December 2020).

A concept that is common to both law and epidemiology in this area is the concept of risk. As Rothman and Greenland note,

> In everyday language, risk is often used as a synonym for probability. It is also commonly used as a synonym for hazard, as in living near a nuclear power plant is a risk you should avoid. Unfortunately, in epidemiological parlance, even in scholarly literature, risk is frequently used for many distinct concepts: rate, rate ratio, risk, incidence, odds, prevalence and so forth. The more specific, and therefore more useful, definition of risk is probability of an event during a specified period of time.[10]

We adopt the more specific and useful definition for the purpose of our discussion. By reference to the case study, the risk of developing DVT is the probability of developing DVT within a set period (the duration of a long-haul flight and shortly thereafter). The case study refers to a relative risk of 1.7. As we have seen, relative risk is a comparative measure. Typically, it compares the risk associated with a type of exposure, say a long-haul flight, with the risk associated with no exposure (no long-haul flight). As such, it describes the proportional increase in the probability of an effect (DVT) of an event (long-haul flight) occurring to a group of long-haul fliers, as measured from a baseline of a comparison group of non-long-haul fliers. If there is no background risk within the baseline comparison group (that is, no DVT unless you have taken a long-haul flight), there can be no relative risk because there is nothing with which to make a comparison. Conversely, if there is a relative risk then there must also a background risk. That background risk is not associated with the exposure of interest (flying long-haul). It follows that if there is a background risk then some people may suffer harm even if they have not been exposed to the agent (long haul flight, toxin etc) of interest. Often, the cause of the background incidence of disease is unknown. Diseases caused by unknown factors are sometimes classified as idiopathic conditions.[11] Further, there may be unknown component causes within the causal mechanisms of a disease.[12] If the relative risk is greater than one then there is an increased

[10] K.J. Rothman, S. Greenland and T.J. Lash *Modern Epidemiology, 3rd Ed.* (Lippincott Williams & Wilkins, 2008) 10.
[11] E. Beecher-Monas, 'Lost in Translation: Statistical Inference in Court' (2014) 46(4) Ariz St LJ, 1057, 1063. The Supreme Court in *Sienkiewicz* n 2 above appears to have misunderstood the meaning of this word. See C. Feeny, 'The Dust Settles? *Fairchild* to *Williams*' (2013) 21 Tort L Rev 87, 88.
[12] K.J. Rothman, 'Causes' (1976) 104 Am J Epidemiol 587.

risk. If the relative risk is below one, then there is a decreased risk, and the exposure can be theorised to *protect* against the harm of interest. This might be the case if the intervention of interest is a vaccine. If the relative risk is greater two (or more simply RR > 2) then the risk of harm associated with the exposure is more than double the background risk.

The relative risk is an important and common measure used in epidemiological studies to analyse differences between groups. Although epidemiological studies may use different measures, relative risks derived from observational studies are commonly encountered in tort litigation. We therefore use the concept of relative risk for the purpose of our discussion. The relative risk is a measure of association. Statistical measurements are said to be associated when knowing something about the state of one variable, say a risk factor, tells you something about the state of the other variable, say a disease.[13] So, if Group A is exposed to a risk factor X (long-haul flying) and Group B is not and there is a greater incidence of disease Y (DVT) in Group A then, as we have seen, the relative risk will be higher in Group A than in Group B. It is in this sense that the relative risk is a measure of association where the association of interest is that between X and Y. That X and Y are associated does not necessarily mean that X (long haul flying) *causes* Y (DVT). To reach that conclusion, epidemiology adopts its own standards of causal inference.

Associations and causal inference

Observational epidemiology draws on several methods to transform an observed association into causal inference. Methods include the exclusion of alternative explanations such as systemic bias, confounders, or chance.[14] The well-known Bradford Hill criteria were explicitly formulated with this transformation in mind. As Hill wrote: "In what circumstances can we pass

[13] C.T. Bergstrom and J.D. West, *Calling Bullshit: The Art of Scepticism in a Data-Driven World* (Allen Lane, 2020) 51.

[14] For examples of random and systematic errors see G.F. Craun and R.L. Calderon, 'How to Interpret Epidemiological Associations' (2006) 111 available at https://www.semanticscholar.org corpus ID: 12411134 (last visited 4 December 2020).

from ... [an] observed *association* to a verdict of *causation*? Upon what basis should we proceed to do so?''[15] The Hill criteria involve considering an epidemiological study in the context of other direct, mechanistic, or parallel evidence of causation.[16] Such evidence may include the temporal proximity of exposure and effect, any plausible biological or chemical mechanisms of action, or considering the extent to which epidemiological evidence fits with what is already known. As Dammann and others suggest,[17] the Hill guidelines can be read as a contribution to abductive reasoning - that is, inferential reasoning to the best explanation. The authors note that whilst causal inference from epidemiological evidence is complex, it remains important to determine causal relationships because public health can and should be improved. The Hill criteria help make the inference of causation from association more secure.[18]

As a result of causal inference, epidemiological studies have made important contributions to both public health policy[19] and clinical decisions made by medical practitioners.[20] Studies contribute to the evidence-base that justifies the implementation of public health policies aimed at preventing disease and other adverse health outcomes within populations. They also contribute to the development of evidence-based medicine: medical practitioners treating their patients regularly use evidence from clinical studies when treating their patients. More recently, the practice of forensic epidemiology has professionalised the application of epidemiological studies in litigation.[21]

Epidemiological evidence in law

[15] A.B. Hill, 'The environment and disease: association or causation?' (1965) 58 Proc R Soc Med. 295–300, 295 cited by O. Dammann, T. Poston and P. Thagard, 'How do medical researchers make causal inferences?' in Kevin McCain, Kostas Kampourakis (eds.) *What is Scientific Knowledge? An Introduction to Contemporary Epistemology of Science* (New York: Routledge, 2019) Chapter 3.
[16] D. Spiegelhalter, *The Art of Statistics: Learning from Data* (London: Penguin, 2020) 115.
[17] n 15.
[18] For a critique of the application of the Hill criteria in causal inference, see K.J. Rothman and S. Greenland, 'Causation and Causal Inference in Epidemiology' (2005) 95 Am J Public Health S144-150.
[19] A. Aschengrau and G.R. Seage III, *Essentials of Epidemiology in Public Health 3rd ed* (Burlington: Jones & Bartlett Learning, 2014).
[20] J.D. Potter, 'Epidemiology Informing Clinical Practice: From Bills of Mortality to Population Laboratories' 2005 2(12) Nat Clin Pract Oncol 625-634.
[21] S.A. Koehler and M.D. Freeman, 'Forensic Epidemiology: a method for investigating and quantifying specific causation' 2014 10(2) Forensic Sci Med Pathol. 217-22. doi 10.1007/s12024-013-9513-8.

Even though epidemiological studies are routinely used for disparate purposes, this does not resolve the underlying question: even if an epidemiological study evidences causation, how can studies that deal with the relationship between risk factors and the distribution of disease within groups apply to an individual? Whilst a premise of the public health approach to epidemiological evidence might be cast in terms that an intervention to remove or reduce risk factor X (flying long haul) will reduce or eradicate the incidence of disease Y (DVT) (because long haul flying plays a causal role in the development of some DVTs), epidemiology is not directly addressing the question of whether harm was caused to a specific individual.[22] This is a fundamental problem for epidemiology: it can never discover what would have happened to a specific exposed individual if they had not been exposed to a risk factor or vice versa. But it must also be remembered that epidemiology does not claim to be able to answer this question. Epidemiology is the self-avowed study of the occurrence of disease and injury in human populations.[23] Relatedly, Garstwirth notes that epidemiology is a science and is therefore interested in general phenomena.[24] In contrast, both medicine and tort law share a common interest in a particular individual. The medical practitioner is interested in identifying the disease that may be the cause of her patient's symptoms; the lawyer, is primarily interested in whether that disease can be attributed to the Defendant's acts or omissions.

If observational epidemiological evidence has little, if anything, to say about what caused harm in a specific individual, then how can it assist the court at all? The objectives and subject matters of law and observational epidemiology seem to be poles apart. And yet, epidemiological evidence is admissible in court. Whilst it is arguable that a majority of the Supreme Court in *Sienkiewicz* in *obiter* rejected an arbitrary bright-line rule relating to doubled risk, it does not follow that evidence of an increased risk cannot be adduced at all. On the contrary, courts have indicated that epidemiological evidence "may sometimes be very helpful".[25] Indeed, epidemiological evidence is already widely used in law. Beyond the areas to which we have already

---

[22] National Research Council, *Reference Manual on Scientific Evidence: Third Edition* (Washington, DC: The National Academies Press, 2011) 608. doi 10.17226/13163.

[23] 'Epidemiology' in *The Concise Encyclopaedia of Statistics*. (New York: Springer, 2008) https://doi.org/10.1007/978-0-387-32833-1_128 (last visited 4 December 2020).

[24] J.L. Gastwirth 'The role of Statistical Evidence in Civil Cases' 2020 7 Ann. Rev. Stat. Appl. 39.

[25] *per* Lord Toulson in *Williams v Bermuda Hospitals Board (NHS Litigation Authority intervening)* [2016] UKPC 4 at [48].

referred, such evidence is used in the context assessing life expectancy,[26] product liability,[27] causation in relation to civil[28] and criminal road traffic incidents;[29] even in cases on badger-culling[30] and (in Northern Ireland) decisions about the height of kerbs.[31] Given its use in norovirus cases,[32] it seems highly likely that such evidence will play a major part in the inevitable flood of Covid-related claims. In complex cases involving potentially competing causes of a disease, expert evidence is likely to be key, and that expert evidence can include epidemiological evidence. But just as courts should avoid the cognitive anchor caused by RR > 2, so too they must avoid being blinded by a false air of mathematical authority.[33] Just as epidemiologists are increasingly educating each other about how their work may be used in the forensic process,[34] so too lawyers and judges need to understand the power and limits of epidemiological evidence.

Epidemiological evidence and causal inference in law

It is our contention that epidemiological evidence can play a useful role in legal arguments about causation in personal injury litigation, and courts can approach such evidence using the traditional framework of legal principles of causal analysis. The traditional framework requires the trier of fact to draw an inference of causation on the balance of probabilities. Those probabilities are a non-mathematical belief probability. Belief probability is a vaguer notion than a mathematical probability. The danger of taking too mathematical an approach to the belief

[26] *Jones v MoD* [2020] EWHC 1603 (QB).
[27] *Gee v DePuy International Ltd* [2018] EWHC 1208 (QB).
[28] *Young v AIG Europe Ltd* [2015] EWHC 2160 (QB).
[29] *R v Wilson* [2018] EWCA Crim 1184.
[30] *R (on the application of Langton) v Secretary of State for Environment, Food and Rural Affairs* [2018] EWHC 2190 (Admin); *The National Farmers Union v Secretary of State for Environment, Food and Rural Affairs* [2020] EWHC 1192 (Admin).
[31] *Re Toner's Application for Judicial Review* [2017] NIQB 49
[32] *Gilmovitch and Others v Bourne Leisure Ltd* [2016] EWHC 3228 (QB).
[33] *per* Geoffrey Tattersall QC in *Bannister v Freemans plc* [2020] EWHC 1256 (QB) [174] echoing Lord Kerr in *Sienkiewicz* n 2 above [205]-[206].
[34] T. Christoffel and S.P. Teret, 'Epidemiology and the Law: Courts and Confidence Intervals' (1991) 81(12) Am J Public Health 1661-1666; Gastwirth n 24 above, 2; P.D. I Meilia, M.D.Freeman, Herkutanto and M.P. Zeegers, 'A review of causal inference in forensic medicine' (2020) 16 Forensic Sci Med Pathol 313-320. doi: 10.1007//s12024-020-00220-9.

probability was vividly illustrated by *Re A (Children) (Care Proceedings: Burden and Standard of Proof)*.[35] In that case, a local authority applied for care orders in respect of five siblings after a ten-year-old sibling was found dead in the family home. She had died of neck injuries and had suffered genital injuries inflicted less than 24 hours previously. The judge considered that there were three possible causes of death: suicide, an accident, or a perpetrated act. He aggregated the probability of suicide, which he put at 10 per cent, with the probability of accident, which he put at 45 per cent, and concluded that he was not satisfied on the balance of probabilities that the child had died because of a perpetrated act. The Court of Appeal ruled that it is for the trier of fact to assess and weigh all the evidence and to decide on the preponderance of that evidence - rather than on possibilities or probabilities - whether a case is made out. If a judge is blinded by the quantitative evidence, the distinction between the two types of probability may become unhelpfully blurred. As Steel has observed, quantitative evidence may provide decision-makers with a better evidential reason to believe in causation than not,[36] but it should not overwhelm the decision-maker's judgement. Quantitative evidence is simply one type of evidence amongst other types of evidence that may inform the decision about causation. On the assumption that the epidemiological evidence has passed appropriate thresholds of epidemiological validity, then that evidence should be treated as circumstantial evidence which forms at least a "strand in the cable"[37] in the process of causal inference in law.

To what extent, then, can such circumstantial epidemiological evidence be used in tort litigation? In the Supreme Court in *Sienkiewicz*, Lord Rodger said

> where there is a strong epidemiological association between a drug and some condition which could have been caused in some other way, that evidence along with evidence that the Claimant developed the condition immediately after taking the drug may well be enough to allow the Judge to conclude, on the balance of probability, that it was the drug that caused the Claimant's condition.[38]

[35] [2018] EWCA Civ 1718.
[36] S. Steel, *Proof of Causation* (Cambridge: Cambridge University Press, 2015) 94.
[37] *per* Spigelman CJ in *Seltsam Pty Ltd v McGuiness* (2000) NSWCA 29 at [89], [91] and [98].
[38] *Sienkiewicz* n 2 at [163].

Using the example of a drug-related condition, Lord Rodger specifies three conditions: If (1) Disease Y could have been caused by exposure X or by some other cause, and (2) there is epidemiological evidence suggesting a strong association between exposure X and disease Y, and (3) there is evidence showing that disease Y occurred immediately after exposure, then a judge could conclude on the balance of probabilities that disease Y was caused by exposure X. In our case study, (1) Donna has suffered DVT which may have been caused by the long-haul flight or by some other unknown cause. A question here might ask whether long-haul flights can cause DVT in general. A second question might ask: does it matter that the other cause is unknown or idiopathic? (2) There is epidemiological evidence suggesting an association between long-haul flights and DVT. A question here might ask whether a relative risk of 1.7 counts as a "strong epidemiological association". From a fairness point of view, it might be supposed that since long-haul flights have been found to be associated with an increased risk of DVT - quantifiable at 70 per cent - it would be unfair to prevent the insurer from arguing that Donna's DVT was caused by the long-haul flight. However, there is by no means universal agreement between epidemiologists that an increased risk of 70 per cent, in general, amounts to a strong association. (3) Donna suffered symptoms of DVT a week after her long-haul flight. Does this satisfy Lord Rodger's immediacy condition? There is clearly a close temporal association, but arguably no immediacy.

As we have seen, the main difficulty with Lord Rodger's second point lies in the fact that epidemiological studies address the risk or incidence of disease in populations not in individuals. They do not address the question of the cause of an individual's disease which is the law's ultimate interest. One focus in epidemiology is on whether a type of exposure can cause harm. This is sometimes – especially in the US - referred to as general causation and which an individual litigant must also prove. Epidemiological studies therefore lead to a dichotomy between general and specific causation[39] where specific causation refers to the cause of an individual's disease. In short, an epidemiological study cannot say whether a specific individual's disease

[39] M.D. Green, 'All You Ever Wanted to Know About Adequate Proof of Causation in Tort Law' (2018) 9(3) JETL 308, 317.

was caused by the exposure of interest or would have happened anyway because the individual is one of the victims of the unavoidable background causes. As mentioned earlier, this relates to the fundamental problem of causal inference in epidemiology. As noted by Goldberg,[40] the impossibility of applying statistics from epidemiological studies directly to individuals was the main reason why the pursuer failed to prove specific causation in the lung cancer cigarette-smoking case of *McTear v Imperial Tobacco Ltd*.[41] However, once it is recalled that whilst epidemiologists are cautious about making causal claims, this does not mean that they will never make such claims. If there are other consistent epidemiological studies, standards of validity have been met and/or there is other evidence (for example toxicology or experimental evidence) then an epidemiologist might be inclined to make a causal claim. It remains a claim about general causation, but the technique of combining epidemiological evidence with other evidence is a technique with which courts are very familiar and is the general approach we advocate.

A cautionary note about the strength of association

To move from a claim about general causation to specific causation, the *US Reference Manual on Scientific Evidence*[42] is a useful starting point. The authors open by noting that "before an association or relative risk is used to make a statement about the probability of individual causation, the inferential judgment ... that the association is truly causal rather than spurious is required."[43] The authors of the *Manual*, like Lord Rodger above, suggest that strength of association is a guideline for drawing an inference of causation from an association. But no specific threshold is required. That said, some care must be taken here because there are different ways to think about the strength of the association. For instance, if a relative risk is used as a measure of the strength of association it must be remembered that the relative risk depends on the background rate. The background rate is crucial for providing context to

[40] R. Goldberg, 'Epidemiological uncertainty, causation and drug product liability' (2014) 59(4) McGill L J 777, 805.
[41] [2005] CSOH 69.
[42] n 22.
[43] ibid 611.

the relative rate. To illustrate: it might be tempting to conclude that a relative risk of, say, five represents a strong association and is therefore strong evidence of causation. But a relative risk of five might mean that in two groups of one thousand people exposure has increased the incidence of a disease from one to five people in a thousand. Or it might be that a background rate of fifty cases has increased to two hundred and fifty in a thousand. Depending on the nature of the disease, the difference in the expected frequencies may have some relevance to the *practical* significance of the risk. If the disease is something innocuous like unexplained sneezing for twenty-four hours after exposure, one might be tempted to conclude that the relative risk of five is only strong evidence in the second example and not in the former.

To use a different example, in *The Art of Statistics*, David Spiegelhalter relates the story of the *Daily Record*'s 2015 headline "Bacon, Ham and Sausages Have the Same Cancer Risk as Cigarettes Warn Experts." [44] The report was based on the World Health Organisation's International Agency for Research in Cancer ("IARC") announcement that the consumption of fifty grams of processed meat a day was associated with an increased risk of bowel cancer of 18 per cent. An identical 18 per cent increased risk of mesothelioma was identified in *Sienkiewicz*. Based on expert evidence in that case, the judge found that the deceased's exposure to asbestos over her working life at the defendant's factory had increased the background risk of environmental exposure to asbestos by 18 per cent. That increased risk was found to be a material increase in risk under the *Fairchild/Barker* rules[45] for proof of causation. An increased risk of 18 per cent is a relative risk of 1.18. But the *practical* effect of the increased risk is in fact very different in the two cases.

In the bacon example, Spiegelhalter shows that ordinarily around six people in a hundred are expected to suffer bowel cancer in their lifetime. An 18 per cent increase would mean that one more person in a hundred might be expected to get bowel cancer in their lifetime. If you eat fifty grams of processed meat daily your lifetime risk will increase from about six per cent

[44] D. Spiegelhalter *The Art of Statistics: Learning from Data* (Penguin Random House 2019) 31.
[45] *Fairchild* v *Glenhaven Funeral Services* [2002] UKHL 22; *Barker* v Corus (UK) plc [2006] UKHL 20; *Sienkiewicz* n 2 above; and see generally P. Laleng '*Sienkiewicz* v *Greif (UK) Ltd* and *Willmore* v *Knowsley Metropolitan Borough Council*: A Material Contribution to Uncertainty?' (2011) 74(5) MLR 777-793. *The Trigger Litigation: Durham v BAI (Run Off) Limited (In Scheme of Arrangement)* [2012] UKSC 14.

to seven per cent. As he points out, the 18 per cent increased risk sounds more frightening than one more person in a hundred being subject to the risk.

In *Sienkiewicz*, the 18 per cent increase in risk raised the absolute risk from a background rate of 24 cases of mesothelioma *per million* to 28.39 cases per million.[46] In other words, the occupational exposure meant that the deceased's lifetime risk of developing mesothelioma increased from 0.0024 per cent to 0.0028 per cent. When put in these terms one might wonder whether the court was right to hold that the increased risk was "material". An increased risk of 18 per cent sounds much more material than a difference of 0.0004 per cent. Perhaps this is what Lord Toulson had in mind in *Williams v The Bermuda Hospitals Board* when he said "… inferring causation from proof of heightened risk is never an exercise to apply mechanistically. A *doubled tiny risk* will still be very small [emphasis added]."[47] Further, as the strength of association is predicated on observed effects, it is questionable whether the strength of an association in *Sienkiewicz* could ever be measured at this level of precision: you would need at least two groups of one million people for such a study to detect the effect. And such a small practical effect could well be explained by noise. Conversely, it might be concluded that the bacon example - which increases the lifetime risk by 1% - is material in a way that the asbestos example is not.

Of greater relevance to our case study, in early April 2021, the UK Health Minister announced that the level of risk from a blood clot possibly linked to the Oxford/AstraZeneca COVID-19 vaccine "is the same as taking a long-haul flight."[48] What is unclear from the Minister's statement is whether he made a comparison of relative risks or whether he ignored a background rate of blood clots without the vaccine being administered. The distinction is crucial. If he ignored the background rate of blood clots in the general population then the vaccine could potentially be interpreted as being protective. In any event, up to the end of March 2021, there had been 79 reported cases of blood clots following the administration of more than 20

[46] n 2 [60].
[47] n 25 [48].
[48] *The Times* 8 April 2021.

million doses of the Oxford/AstraZeneca vaccine.[49] The patients developed thrombotic thrombocytopenia. This condition has been theorised to be associated with some vaccines.[50] The condition can be inherited or acquired. Sometimes, the condition is idiopathic *ie* of no known cause.[51] This implies that there must be a background rate. One epidemiological study from 2014 that pre-dates any Covid vaccine found that the population incidence of immune thrombocytopenia in France was 2.9 / 100,000. Sevety-nine cases in more than 20 million works out at less than 1 / 250,000. If the France study describes the background rate (which it probably does not because it concentrated on people in hospital) then the relative risk is less than 0.15. This implies that there is a *decreased* risk associated with taking the Astra-Zeneca vaccine. If we ignore the possibility of any background rate, then 1 / 250,000 equates to 0.0004 per cent.[52] Coincidentally this is the same level of 'increased' risk as the court in *Sienkiewicz* found to be material for the purpose of the *Fairchild* test for causation. If there is a background rate for thrombotic thrombocytopenia, then the practical increased risk associated with the vaccine must be even smaller than this. What this example illustrates is that reaching a conclusion on general causation that the Oxford/AstraZeneca vaccine can cause blood clots is based on very small numbers. The relative risk may look superficially high, but the expected practical frequencies, as Lord Toulson said in *Williams*, are tiny. Yet, causation appears to be provisionally accepted on the basis that the clot appears soon after the jab. This once more has echoes Lord Rodger's approach in *Sienkiewicz* cited above.[53]

Risk and individual causation

Assuming that the court finds that an association is truly causal rather than spurious, then the court must decide whether the evidence of general causation (*ie* that exposure is capable of causing the harm of interest) can support a finding of specific causation in an individual

[49] https://www.bmj.com/content/373/bmj.n954 (last visited 16 April 2021).
[50] A. Greinacher, T. Thiele, T.E. Warkentin, K. Weisser, P.A. Kyrle and S. Eichinger, 'Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination' (2021) N Engl J Med. DOI: 10.1056/NEJMoa2104840.
[51] https://www.nhlbi.nih.gov/health-topics/thrombocytopenia (last visited 16 April 2021).
[52] https://www.gov.uk/government/news/mhra-issues-new-advice-concluding-a-possible-link-between-covid-19-vaccine-astrazeneca-and-extremely-rare-unlikely-to-occur-blood-clots (last visited 16 April 2021).
[53] n 36 above.

Claimant's case. In this context it is relevant to recall that epidemiological evidence of relative risk is not designed to be a means of establishing causation in an individual case. As Lady Hale stated in *Sienkiewicz*:

> I … agree with Lord Roger that doubling the risk is not an appropriate test of causation in cases to which the *Fairchild* exception does not apply. Risk is a forward-looking concept - what are the chances that I will get a particular disease in the future? Causation usually looks backward, what is the probable cause of the disease which I now have?[54]

Further, as many - if not most - causal relations cannot be observed directly, individual causation must be inferred from the available evidence.[55] As Lord Justice Toulson said in *Nulty v Milton Keynes BC*:

> In deciding a question of past fact the court will, of course, give the answer which it believes is more likely to be (more probably) the right answer than the wrong answer, but it arrives at its conclusion by considering on an overall assessment of the evidence (ie on a preponderance of the evidence) whether the case for believing that the suggested event happened is more compelling than the case for not reaching that belief …[56]

As we have discussed, the probabilities here are non-mathematical. As he went on to explain:

> The chances of something happening in the future may be expressed in terms of percentage. Epidemiological evidence may enable doctors to say that on average smokers increase their risk of lung cancer by X%. But you cannot properly say that there is a 25% chance that something has happened.[57]

Therefore, the epidemiological evidence does not tell us once the event has occurred how likely it is that the relevant risk factor was the cause of the specific event. This is the general problem of epistemic uncertainty[58] which afflicts all causal questions both within and outside law. Whilst there is *a* cause - or more likely several causal components within one or more

[54] n 2 [170].
[55] Steel n 36, 66-7.
[56] [2013] EWCA Civ 15 at [37].
[57] Ibid.
[58] For a helpful discussion about the distinction between epistemic and aleatory uncertainty, see n 44 above at 240 and 306.

causal mechanisms involved in a particular disease,[59] in many cases we simply do not know with sufficient cogency what the cause is. And yet, a judge cannot avoid reaching a practical judgement about causation in an individual case. This issue must be analysed by reference to the whole factual matrix of that case; and identifying the risk from epidemiological evidence is only one factor. Provided the epidemiological evidence is admissible then it should be placed in the balance with other evidence and might support a finding of individual causation.

The US Reference Manual on Scientific Evidence suggests some conditions of admissibility for epidemiological evidence. For example, the study and risk estimate must be valid (that is, no random error, bias, or confounding); there must be similarity between study subjects and the Claimant in relation to other risk factors (that is the Claimant is representative of the reference population and is not exposed in different way); there must be non-acceleration of disease (that is harm would never have occurred but for exposure. Few diseases are like this, but birth defects fall into this category. If there is acceleration, then the relative risk is an underestimate). The harmful agent operates independently (not synergistically), and the agent is not responsible for other fatal diseases apart from the one of interest, and it does not provide protective effect. [60] If admissible, the epidemiological evidence can play various roles in the proof of specific causation.

Can causation by reference to epidemiological evidence alone be established? The majority in *Sienkiewicz* thought not and that epidemiological evidence could only prove a probability, not a fact. Lord Rodger was probably most sceptical about proof by epidemiological evidence alone. Yet, his comments in *Sienkiewicz* cited above, arguably amount to proof of causation on this basis. Whilst reference is made to the temporal association, this association has relevance only if it is accepted that there is a significant likelihood that the drug could cause the condition, which in the absence of any other evidence would rest solely on epidemiological evidence.

---

[59] K.J. Rothman and S. Greenland 'Causal Inference in Epidemiology' (2005) 95(S.1) Am. J. of Public Health S144. K.J. Rothman, S. Greenland and T.L. Lash *Modern Epidemiology, 3rd Ed*. (2008, Lippincott Williams & Wilkins) especially Chapter 2.

[60] n 22 above 612-614.

Despite the careful discussion in *Sienkiewicz*, many judges still seem to find the distinction between proof of fact and proof of probability elusive.[61] If on a purely numerical basis the Claimant proves that it is most likely that the Defendant was responsible, this is nothing more than proof of prevalence as in the famed red cabs / yellow cabs example.[62] This at best establishes proof of probability but not a fact. Proof of a fact becomes more plausible if there is already evidence such as a breach of duty and acceptance of an elevated risk.

In practice, Courts regularly infer causation in individual cases from epidemiological evidence alone but only where the relative risk is demonstrated to be so high as to rule out any other reasonable conclusion. The classic example of this is causation by asbestos exposure in mesothelioma claims. Given the long latent period from exposure to asbestos until the development of mesothelioma, it is common for there to be no pathological evidence of asbestos exposure, specifically raised asbestos fibre counts in a victim's lungs. However, mesothelioma is a rare tumour and an exceptionally rare tumour in the absence of asbestos exposure. Research by Peto and others[63] has suggested that a joiner born in the United Kingdom in the 1940s had a one in fifteen chance of developing mesothelioma, which is to be contrasted with the usually quoted risk within the population of one in one thousand. This massively elevated risk (a relative risk of 66.7) for such joiners is accounted for by the significant use of asbestos insulation board in the UK, in particular during the 1960s and 1970s. If a court was considering a claim by such a joiner with a history of asbestos exposure who had developed mesothelioma, a Court would readily infer causation even though there was no other proof that the mesothelioma had been caused by asbestos. Clearly RR > 2 would be insufficient for these purposes. In analysing such questions, it will be important to identify whether other significant known risk factors can be identified. A court is likely to be more willing to infer causation from a risk factor when this is in practical terms the only risk factor identified. This resonates with the distinction

[61] For two examples at first instance, see *Garner v Salford City Council & McGuinness & Co Ltd* [2013] EWHC 1573 (QBD); *Morrison v Liverpool Women's Hospital NHS Foundation Trust* [2020] EWHC 91 (QBD).

[62] R. Schmalbeck, 'The Trouble with Statistical Evidence' (1986) 49(3) Law and Contemporary Problems 221-236. doi:10.2307/1191634.

[63] J. Peto, C. Rake, C. Gilham and J. Hatch, 'Occupational, domestic and environmental mesothelioma risks in Britain: A case-control study' (London: Institute of Cancer Research and London School of Hygiene and Tropical Medicine Research Report RR 696 for Health and Safety Executive, 2009).

between single agent and multi-agent cases, where although epidemiological evidence was not directly addressed, the same difficulty was perceived.[64]

So, where does doubling of risk fit into all this? Given that it was proposed as a formulaic rule of causation, the surprising answer is probably nowhere in particular. As Steel has observed,

> If the RR = 1, there is the same number of cases of disease in the unexposed population. Conversely, there is no specific > 1 at which an association is automatically deemed to be causal. Rather, the move from an observed association of a particular strength to a claim about causation involves the exercise of judgement.[65]

The converse also applies. At first instance in *Schembri v Marshall*, Mr Justice Stewart reasonably directed himself that

> The court must also be wary of relying on the statistical evidence in the literature which has a number of variables. Had the statistical evidence, in conjunction with the expert evidence, have led to the conclusion that Mrs Marshall's chances of dying would have assessed on presentation as only slightly better that 50-50, I would have found for the Defendant.[66]

Therefore, a court cannot infer causation simply because a doubling of risk had been provided from epidemiological evidence without more. On the other hand, the fact that the relative risk is demonstrated to be less than two should not of itself cause a claim to fail. As with epidemiological evidence demonstrating RR > 2, a decision on individual causation will be based on an overall assessment of the evidence. As King LJ said in *In re A (Children) (Care Proceedings: Burden of Proof),*[67]

> The court arrives at its conclusion by considering whether on an overall assessment of the evidence (ie on a preponderance of the evidence) the case for believing that the suggested event happened is more

[64] See, for example, the discussion by Lord Hoffmann in *Fairchild* n 45 above at [70]-[73].
[65] n 36, 71.
[66] [2019] EWHC 283 (QB) at [146]
[67] [2018] EWCA Civ 1718

> compelling than the case for not reaching that belief (which is not necessarily the same as believing positively that it did not happen) and not by reference to percentage possibilities or probabilities.[68]

The suggested event in the case study is whether the DVT was caused by the long-haul flight. This is a question of past fact like any other. Proving causation in an individual case is best achieved by identifying additional factors to the relative risk from epidemiological evidence and, if possible, excluding other known or competing causes whether by way of differential aetiology or otherwise. Eliminating other causes increases the likelihood that an individual's disease was caused by the exposure to interest.[69] The court assesses the position as a whole and, according to Australian authorities such as *Seltsam Pty Ltd v McGuiness,*[70] drawing on Wigmore's simile referred to *Shepherd v R,*[71] considers epidemiological evidence to be "a strand in the cable." It would also be open to judges to place less weight on epidemiological evidence if there is sufficient evidence to demonstrate that the victim is closer to one group than another as happened in the lung cancer case of *Benhaim v St-Germain*[72] considered by the Supreme Court of Canada.

A structured approach to epidemiological evidence?

The doubles-the-risk test illustrates the instinctive attraction of a formulaic rule which avoids the need to consider technical evidence in detail. This heuristic approach results from the superficial similarity between the relative risk of two and the legal test of proof of balance of probabilities causation. Similarity does not connote equivalence and on analysis the test was shown to be flawed. But the demise of this test should not result in a situation where epidemiological evidence is nothing more than a backdrop to intuitive judicial engagement. A fairer, more nuanced, application of epidemiological evidence could be achieved. Whilst courts in this country have not followed the analytical approach of those in the US in terms of

[68] ibid at [57]
[69] n 22, 617. For a similar point, see Steel n 36, 83-4.
[70] n 37 at [91].
[71] (1990) 170 CLR 573, 579.
[72] [2016] SCC 48.

a strict distinction between general causation and specific causation, nonetheless proof of general causation, that is that the agent in question is capable of causing the injury in question, must be the starting point. Notwithstanding the eccentricity of the approach in Texas,[73] it is obvious that proving general causation does not necessitate proving RR > 2.

Courts have considerable assistance in relation to general causation. Firstly, the validity and strength of studies can be analysed by reference to a method such as a Cochrane analysis.[74] Further, whether a study shows causation as opposed to just association is subject to accepted and valid approaches such as the Bradford Hill criteria.[75] These criteria examine the plausibility of causation as opposed to just association through a number of different scientific prisms. With appropriate expert evidence, there can be confidence that courts will reach reasonable decisions as to whether general causation is established. The much more problematical issue is the application of general causation to the facts of a specific case. At this stage the relative risk is neither irrelevant nor determinative. Applying a relative risk of just over two in a mechanistic way assumes that the individual was one of a group of say 51 individuals who would contract the relevant condition because of the risk as opposed to one of the 49 who wouldn't. Without further analysis, this is an unwarranted assumption of fact.

We suggest that the approach could be reduced to the following questions which would reasonably inform the process of identifying individual causation. Question 1: Is the relative risk so high that it would be reasonable to infer causation, and (i) no other known risk factors are identified; and (ii) individual causation has bio-pathological and factual plausibility? If the answer to Question 1 is yes, then causation is established. If the answer to Question 1 is no, then ask the following sub-questions for Question 2: (a) does the relative risk identify a real possibility of causation; (b) can other risk factors be excluded with confidence; and (c) does the causal connection have bio-pathological and factual possibility? If the answer to each sub-question of Question 2 is yes, then causation is established. This approach could be considered more of a rubric rather than a template. Each issue clearly raises subsidiary questions that do

[73] *Merck & Co v Garza* 347 S.W.3d 256, 265 (Tex. 2011) which requires proof of a doubling of risk for both general and specific causation.
[74] See Cochrane Library at https://www.cochranelibrary.com
[75] For a helpful summary of the criteria in the context of tort law, see Steel n 36, 72.

not have an immediate binary answer. The questions may nevertheless be set out in a decision tree as suggested in Figure 1 below. The approach can be considered analogous to routes to verdict in criminal cases to assist judges in reaching their decisions.

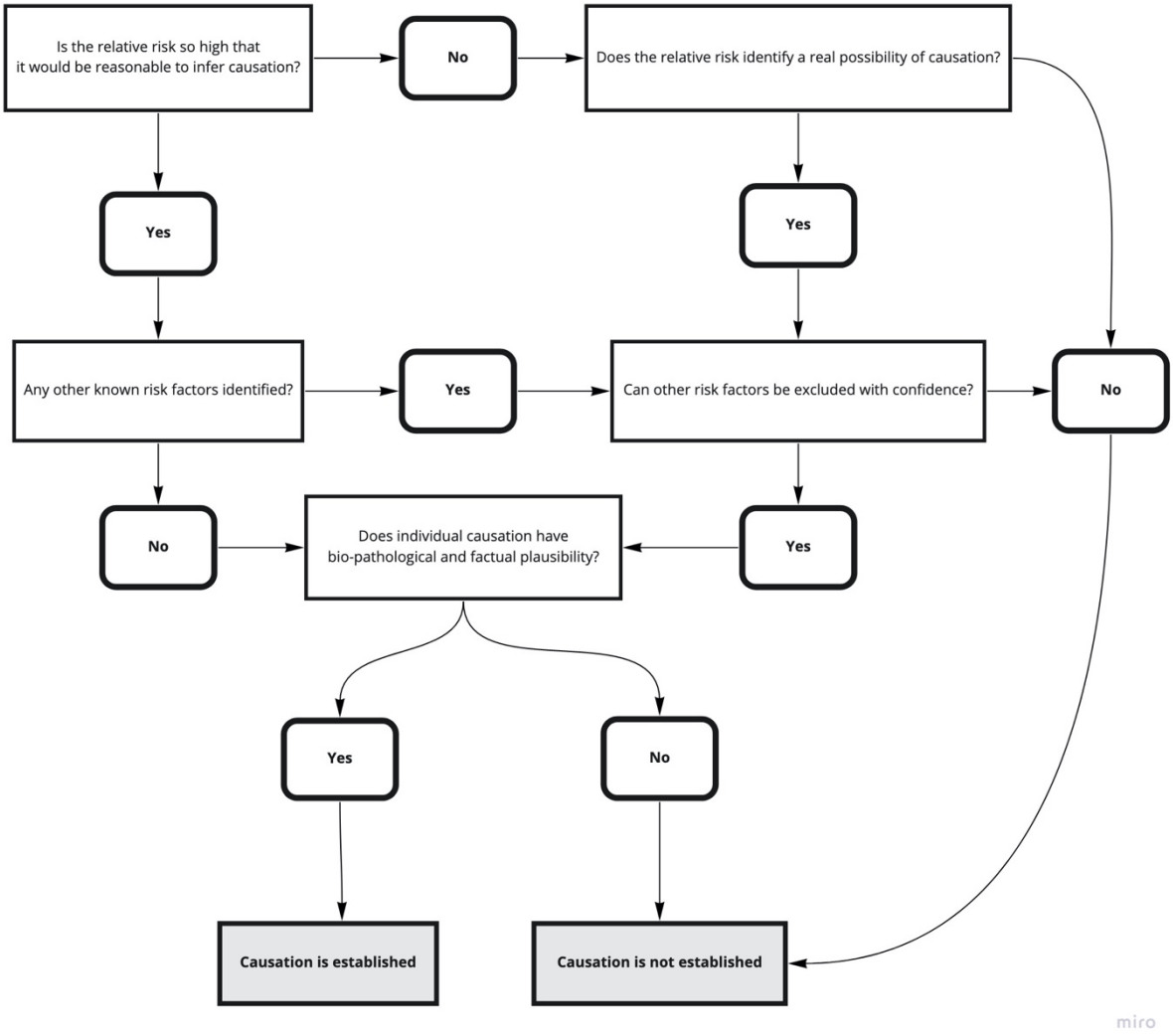

Figure 1: The routes to proving individual causation in toxic tort and other cases using epidemiological evidence.

It is suggested that the relative risk must be significantly higher than two to make it reasonable to infer causation in answer to Question 1. Equally, a relative risk of less than two should not of itself mean that causation is not established if the further conditions in Question 2 are satisfied in the Claimant's favour. The concepts of bio-pathological and factual plausibility are illustrative but not restrictive. The essential requirement is plausibility. Bio-pathological plausibility connotes identifying how the eventuation of a risk factor can be understood medically as seen in the lack of plausibility in the varicose vein example set out in Variation 3 below. Factual

plausibility is best illustrated by temporal coincidence. As such, these concepts have echoes of the Hill criteria. They also resonate with Lord Rodger's example in *Sienkiewicz* of suffering a known side effect of a drug immediately after ingesting the same. One example from the case study is the temporal closeness of the DVT to the long-haul flight. There are examples in cases where causation has been established: Whilst the relative risk in most mesothelioma claims would be sufficient on its own to establish causation, nonetheless in cases of slight exposure, knowledge that the condition developed after the characteristic latent period of 30-40 years can bolster the finding whilst recent exposure to asbestos would point in the opposite direction. Similarly, in relation to the thalidomide victims, the birth defects were shown by medical evidence to be likely to have been caused by an insult at the stage of pregnancy when the drug was taken.[76]

It will no doubt be observed that this approach does not make any reference to unidentified risk factors. It might be argued that for this reason it is simply basing causation on material increase in risk: *Fairchild* in disguise. However, the approach is justified because of the requirement of factual and bio-pathological plausibility and because individual Claimants' cases will be scrutinised in much greater detail than would occur in the context of individuals forming the cohort group in any epidemiological study. Exclusion of risk factors in epidemiological studies is essentially by questionnaire and it is reasonable to accept that were these individuals subject to the same degree of investigation as occurs in litigation, several other known risk factors would be identified. On this basis, it is reasonable to argue that where general causation is established, if the existence of other risk factors is reasonably excluded in an individual case, and the circumstances of the injury have factual and bio-pathological plausibility in relation to the agent in question, causation could be established on the balance of probabilities.

[76] N. Vargesson, 'The teratogenic effects of thalidomide on limbs' (2019) 44(1) J Hand Surg Eur Vol. 88-95. doi: 10.1177/1753193418805249. N, Vargesson, 'Thalidomide-induced teratogenesis: history and mechanisms' (2015) 105(2) Birth Defects Res C Embryo Today 140-56. doi: 10.1002/bdrc.21096. W. Lenz, 'A short history of thalidomide embryopathy' (1988) 38(3) Teratology203-15. doi: 10.1002/tera.1420380303. R.W. Smithells and C.G. Newman, 'Recognition of thalidomide defects' (1992) 29(10) CG. J Med Genet. 716-23. doi: 10.1136/jmg.29.10.716.

Applying this reasoning further to the case study's variations could raise various approaches.

VARIATION 1

In this variation, the facts are the same except that it is shown that Ms von Trapp had a known risk factor, a family history of venous thrombosis. In a paper by Bezemr[77] it was suggested that a positive family history would increase the risk of venous thrombosis more than twofold and up to fourfold where there was more than one relative affected. At face value, the family history indicates a greater degree of risk than the long-haul flight. However, the nature of the family history must be considered, in particular the number of relatives who constitute the family history. The family history in itself does not prove the presence of a causative risk factor, *ie* an underlying hereditary thrombophilia. In other individuals in the family, it may be shown that their history of thrombophilia is accounted for by more obvious risk factors, such as obesity, cigarette smoking or cancer, which are not present in the case of Ms von Trapp. Further, it must be considered whether the family history is a risk factor independent of the long-haul flight. The family history might indicate a susceptibility on Ms von Trapp's part, but this is not inconsistent with the actual occurrence being precipitated by the immobility of a long-haul flight.

VARIATION 2

In this variation it is shown that Ms von Trapp has just started taking the combined oral contraceptive pill ('OCP'), which contains oestrogen and progesterone. A paper in the British Medical Journal in 2015 indicates that the combined OCP creates a relative risk of 2.97 for DVT.[78] Again, the risk from the contraceptive pill appears to be higher than that for the long-haul flight. However, the temporal association may be important. Further consideration would have to be given as to whether these risk factors were independent of each other.

---

[77] I.D. Bezemer and F.R. Rosendaal, 'The Value of Family History as a Risk Indicator for Venous Thrombosis' (2009) 169 (6) Arch Intern Med, 610.

[78] Y. Vinogradova, C. Coupland and J. Hippisley-Cox, 'Use of combined oral contraceptives and risk of venous thromboembolism: nested case-control studies using the QResearch and CPRD databases' (2015) 350 BMJ h2135.

VARIATION 3

In this variation Ms von Trapp is known to have been suffering from varicose veins for several years. A paper by Chang and others[79] indicates that the relative risk for DVT in persons suffering from varicose veins (expressed as the absolute risk difference) is 5.32 However, this raised risk may not be applicable to Ms von Trapp who has no prior history of DVT. The raised risk in the Chang paper is shown to correlate with patients who have had such a history; the varicose veins in these cases are on analysis secondary to DVT, the converse of the causation issue in point. The temporal association is particularly important in this variation because the risk from varicose veins has been present for a number of years, yet the DVT occurred within one week of the flight.

Considering the case study and its variations with reference to this approach, it is likely that in each case causation by the long-haul flight will be established. Consistent with Lord Rodger's example, the temporal association appears determinative. This remains the case when other risk factors are introduced. On analysis they might be better described as apparent risk factors. They are longstanding by way of contrast with the immediacy of the long haul-flight. Their pathological relevance can be questioned; Ms Von Trapp may not have the risk factors accounting for the family history or her presentation of varicose veins might not be associated with DVT. It is likely the risk factors do not operate independently of each other. So, risk factors can be discounted even when RR > 2 and significantly higher than the relative risk which is accepted as being causative. However, it should be borne in mind that an apparent temporal association can deceive as with Andrew Wakefield's discredited study on the MMR vaccine and autism.[80]

The DVT case study is an easy example and is being used to illustrate the simple proposition that a relative risk of two has no special application in proving causation, either general

[79] Shyue-Luen Chang *et al* 'Association of Varicose Veins with Incident Venous Thromboembolism and Peripheral Artery Disease' (2018) 319(8) JAMA 807-817. doi:10.1001/jama.2018.0246.

[80] T. S. Sathyanarayana Rao and C. Andrade 'The MMR vaccine and autism: Sensation, refutation, retraction, and fraud' (2011) 53(2) Indian J Psychiatry 95-96. doi: 10.4103/0019-5545.82529

or individual. The issues become much more complicated where risk factors are historic and operate independently of each other. So, for example, bladder cancer can be caused by either toxic chemical exposure or cigarette smoking.[81] The pathological presentation is identical. Proving that the relative risk from chemical exposure is greater than two and/or greater than the risk from cigarette smoking does not prove individual causation unless the risk from smoking is so low it can be discounted, or some other evidence can be identified which makes chemical exposure a more plausible cause.

Conclusion

The case study and the variations indicate a range of issues which arise as to the application of epidemiological evidence. These issues are multi-faceted and demonstrate why a simple formulaic rule based on doubling of the risk is troubling and could never work. To have an arbitrary cut off at RR > 2 would lead to injustice. In particular, it would lead to a situation where a number of individuals who had in fact been harmed by an exposure where the relative risk was less than two would never succeed (unless they had other evidence) and conversely, Defendants would be compensating some Claimants whose harm they had not in fact caused even though the relative risk exceeded two. Whilst the epidemiological evidence is telling us something of relevance, it is not answering all the questions that are specific to the particular case at a particular moment in time. A better understanding of epidemiological evidence and how it can be applied in individual cases will assist, but it is reasonable to anticipate that considerable controversy will persist in clinical negligence and toxic tort litigation where such issues arise. For that reason, we have proposed a structured approach to the assessment and use of epidemiological evidence. This structured approach may assist decision-makers and others to navigate the current muddles and misconceptions that surround the forensic role of such evidence.

[81] *Novartis Grimsby Ltd v Cookson* [2007] EWCA Civ 1261.