

Interpreting Causality in the Health Sciences

Federica Russo and Jon Williamson

We argue that the health sciences make causal claims on the basis of evidence both of physical mechanisms, and of probabilistic dependencies. Consequently, an analysis of causality solely in terms of physical mechanisms or solely in terms of probabilistic relationships, does not do justice to the causal claims of these sciences. Yet there seems to be a single relation of cause in these sciences—pluralism about causality will not do either. Instead, we maintain, the health sciences require a theory of causality that unifies its mechanistic and probabilistic aspects. We argue that the epistemic theory of causality provides the required unification.

1. Introduction

It is quite uncontroversial that the health sciences look for causes, namely for causes of disease and for effective treatments. This search for causes has a twofold objective. On the one hand, the health sciences pursue a *cognitive goal*, detecting causal factors and identifying mechanisms of disease—this aspect is related to explanation; on the other hand, they pursue an *action-oriented goal*, informing policies and guiding early diagnosis or treatment on the basis of causal knowledge—this aspect is related to inference.

However, this causal perspective is not always made explicit in the scientific literature, where causal terminology is frequently disguised—e.g., ‘cause’ is often replaced with less obviously causal terms such as ‘factor’, ‘determinant’, or ‘risk’—or is even claimed to be unnecessary and misleading. For instance, Lipton and Odegaard (2005) claim,

Our point is that although it is important to be able to use epidemiological research to predict and intervene at the public health level, to tell the best story possible about the research findings at hand, one doesn’t have to say that *X* causes *Y* to achieve such an outcome. In fact, one cannot definitively claim such a relationship. (Lipton and Odegaard 2005, 7)

Their paper aims to show that explicit causal terminology, as used in statement (1) ‘Smoking causes lung cancer’, does not convey more information than statement (2)

Federica Russo and Jon Williamson are at the Department of Philosophy, University of Kent.
Correspondence to: Department of Philosophy, SECL, University of Kent, Canterbury CT2 7NF, United Kingdom. E-mail: f.russo@kent.ac.uk, j.williamson@kent.ac.uk

'If you smoked two packs a day for X amount of years, your chance of getting lung cancer would be 10 times greater than a non-smoker', and, moreover, for statement (1) to be useful from an epidemiological or public health standpoint, information in statement (2) has to be made explicit. It is worth noting why this line of reasoning fails: statement (2) could be true while statement (1) is false (say if smoking and cancer are effects of a common cause). To intervene (e.g., by restricting tobacco advertising) requires statement (1) to be true as well.

Despite this attack on causal language, recent review articles try to extrapolate a concept of cause as it is used in scientific practice (Lagiou et al. 2005; Parascandola and Weed 2001). They isolate several, none of which seems to be fully satisfactory or attract a firm consensus. Parascandola and Weed (2001) isolate five different meanings of 'cause': production, necessary cause, sufficient-component cause, probabilistic causation, and counterfactual. None of these can alone account for all the possible ways in which causes operate. For instance, HIV infection is a necessary cause of AIDS, but a definition of cause in terms of necessity does not suit the case of exposure to carcinogenic factors, which are neither necessary nor sufficient causes of cancer.

This question of how causality is to be interpreted in health sciences is of crucial importance and deserves close philosophical attention. We shall argue that although causal relations are inferred from mixed evidence, including knowledge of mechanisms and of probabilistic relations, one ought not to confuse the causal relation itself with the types of evidence used to support putative causal relationships. Monistic accounts attempt to analyse causality solely in terms of one type of evidence, e.g., solely in terms of mechanisms or solely in terms of probabilistic relations, focusing only on one aspect they neglect and fail to account for the others. However, pluralistic accounts hold that there are different coexisting types of cause, e.g., a mechanistic relation and a probabilistic one. We will argue that the claim that there are at least two types of cause does not follow from the fact that there are at least two kinds of evidence for causal assertions.

The paper is organised as follows. Sections 2, 3, and 4 argue that the health sciences infer causal relations from mixed evidence: on the one hand, mechanisms and theoretical knowledge, and, on the other, statistics and probabilities. Statistics are used to show that the cause makes a difference to the effect, and mechanisms allow causal relationships to explain the occurrence of an effect. Section 5 evaluates the extent to which traditional monistic accounts (either mechanistic or probabilistic) provide a successful concept of cause; we argue that they cannot explain the dual-faceted epistemology of causality. Section 6 goes further in claiming that a pluralistic account won't do either, because health scientists use statistics and mechanisms to support a single causal claim, *not* to support *two different types* of causal claim. Finally, section 7 presents the epistemic theory of causality as a unified account, transcending the mechanistic and probabilistic accounts.

2. Two Types of Evidence

The cognitive and action-oriented goals guiding research in the health sciences demand that phenomena be *systematised* and *explained*: these sciences need to provide

coherent and sensible stories about causation of disease and about effective treatments and policies. Evidence is constituted by two complementary elements: probabilities and mechanisms.

The probabilistic aspect is crucial because, in the health sciences, causal claims are used for prediction, diagnosis, and intervention; for these modes of inference to be possible, a cause needs to make a difference to its effects, i.e., there needs to be some appropriate probabilistic dependence. But the mechanistic aspect is required because mechanisms explain the dependencies, and in the health sciences causal relationships are also meant to be explanatory.

Moreover, the existence of a mechanism provides evidence of the stability of a causal relationship. If we can single out a plausible mechanism, then that mechanism is likely to occur in a range of individuals, making the causal relation stable over a variety of populations. If no mechanism were found, that may be because the correlation is particular to a specific sample population or a specific set of circumstances—i.e., it is a ‘fragile’ relationship—and not sufficiently repeatable. In other words, mechanisms allow us to *generalise* a causal relation: while an appropriate dependence in the sample data can warrant a causal claim ‘*C* causes *E* in the sample population’, a plausible mechanism or theoretical connection is required to warrant the more general claim ‘*C* causes *E*’. Conversely, mechanisms also impose negative constraints: if there is no plausible mechanism from *C* to *E*, then any correlation is likely to be spurious. Thus mechanisms can be used to differentiate between causal models that are underdetermined by probabilistic evidence alone—see section 4.

The health sciences provide explanations of disease. Explanation is here conceived of in a broad sense—we do not pretend to give an account of what a good explanation is. Bunge (2004, 182) claims that ‘to explain a fact is to exhibit the mechanism(s) that makes the system in question tick’, and he argues against the covering-law model of explanation: a fact is not explained by deducing it from a more general law, but only when the mechanism bringing about it is provided. Although we are with Bunge in saying that we need mechanisms, we do not commit to any particular account of mechanism.

To establish causal claims, scientists need the mutual support of mechanisms and dependencies. Witness for instance Hales and Barker (2001):

The thrifty phenotype hypothesis proposes that the epidemiological associations between poor fetal and infant growth and the subsequent development of type 2 diabetes and the metabolic syndrome result from the effects of poor nutrition in early life, which produces permanent changes in glucose-insulin metabolism. These changes include reduced capacity for insulin secretion and insulin resistance which, combined with effects of obesity, ageing and physical inactivity, are the most important factors in determining type 2 diabetes. (Hales and Barker 2001, 5)

The idea is that probabilistic evidence needs to be accounted for by an underlying mechanism before the causal claim can be established; both participate in the assessment as to whether the given phenotypes cause diabetes. In section 6 we shall argue that these two types of evidence do not support different causal claims but a single claim. In the remainder of this section and in sections 3 and 4 we shall describe some

precedents for the view that causal claims in the health sciences require two kinds of evidence.

In 1965 Bradford Hill, in his Presidential Address to the Section of Occupational Medicine of the Royal Society of Medicine, discussed nine issues that should be addressed when deciding whether an observed association is causal (see Hill 1965). The probabilistic and mechanistic aspects are already present in these criteria for causation. Hill put forward the following nine criteria:

- 1: Strength of Association. The stronger the relationship between the independent variable and the dependent variable, the less likely it is that the relationship is due to an extraneous variable.
- 2: Temporality. It is logically necessary for a cause to precede an effect in time.
- 3: Consistency. Multiple observations, of an association, with different people under different circumstances and with different measurement instruments increase the credibility of a finding.
- 4: Theoretical Plausibility. It is easier to accept an association as causal when there is a rational and theoretical basis for such a conclusion.
- 5: Coherence. A cause-and-effect interpretation for an association is clearest when it does not conflict with what is known about the variables under study and when there are no plausible competing theories or rival hypotheses. In other words, the association must be coherent with other knowledge.
- 6: Specificity in the causes. In the ideal situation, the effect has only one cause. In other words, showing that an outcome is best predicted by one primary factor adds credibility to a causal claim.
- 7: Dose Response Relationship. There should be a direct relationship between the risk factor (i.e., the independent variable) and people's status on the disease variable (i.e., the dependent variable).
- 8: Experimental Evidence. Any related research that is based on experiments will make a causal inference more plausible.
- 9: Analogy. Sometimes a commonly accepted phenomenon in one area can be applied to another area. (Frumkin 2006, 1)

Roughly, criteria 2, 4, 5, 8, and 9 involve mechanistic considerations, while criteria 1, 3, 7, and 8 involve probabilistic considerations. The sixth criterion seems to be problematic as the development of multi-causal models indicates that in many case diseases don't have merely one cause. Needless to say, while these criteria were intended as a guide in assessing causality, they do not ensure causality with certainty. Hill's criteria are still widely used in scientific practice as a rationale for evaluating causal relations. In occupational and environmental risk assessment, these criteria play a role analogous to that of Koch's postulates for microbiology.

Kundi, commenting on Hill's criteria, says

The Bradford Hill criteria were established such that, in the case they are met for a specific factor, this would increase our confidence in this factor being causally related to the disease. However, they were not intended to dismiss a factor as potentially causing the disease. (Kundi 2006, 970)

Thus the criteria are not necessary for causation, but they are a valuable tool since they consider both mechanistic and probabilistic aspects. To illustrate, let's see how Hill's criteria can be applied to the classic case of smoking and lung cancer:

- 1) *Strength of association*. The lung cancer rate for smokers was quite a bit higher than for nonsmokers (e.g., one study estimated that smokers are about 35% more likely than nonsmokers to get lung cancer).
- 2) *Temporality*. Smoking in the vast majority of cases preceded the onset of lung cancer.
- 3) *Consistency*. Different methods (e.g., prospective and retrospective studies) produced the same result. The relationship also appeared for different kinds of people (e.g., males and females).
- 4) *Theoretical plausibility*. Biological theory of smoking causing tissue damage which, over time, results in cancer in the cells was a highly plausible explanation.
- 5) *Coherence*. The conclusion (that smoking causes lung cancer) 'made sense' given the current knowledge about the biology and history of the disease.
- 6) *Specificity in the causes*. Lung cancer is best predicted from the incidence of smoking.
- 7) *Dose-response relationship*. Data showed a positive, linear relationship between the amount smoked and the incidence of lung cancer.
- 8) *Experimental Evidence*. Tar painted on laboratory rabbits' ears was shown to produce cancer in the ear tissue over time. Hence, it was clear that carcinogens were present in tobacco tar.
- 9) *Analogy*. Smoking induced in laboratory rats showed a causal relationship. It, therefore, was not a great jump for scientists to apply this to humans. (Frumkin 2006, 2)

The crucial and equal importance of probabilistic and mechanistic considerations is recognized by the International Agency for Research on Cancer (IARC), one of the major agencies for cancer research. IARC scientists review published studies and evaluate the weight of evidence for the claim that a factor is a possible cause of cancer. Criteria, procedures and principles guiding their evaluations are stated in IARC (2006). Assessment of causality depends on the presence of a plausible mechanism and on probabilistic evidence, i.e., on cancer frequency in a population or on relative risk.

Consequently in the health sciences it is now a commonplace that both mechanistic and probabilistic evidence are required to substantiate causal claims. Thus, for instance, Dalton et al. (2002) sum up their study as follows:

We have reviewed the evidence for an association between major life events, depression and personality factors and the risk for cancer. ... The generally weak associations found, the inconsistency of the results, the unresolved underlying biological mechanism and equivocal findings of dose-response relationships prevent a conclusion that psychological factors are established risk factors. (Dalton et al. 2002, 1)

In the next two sections we shall discuss these two types of evidence in turn.

3. Probabilistic Evidence

The probabilistic evidence required in the health sciences mainly consists of observed dependencies in a range of similar studies. A single study is not enough—several studies of the same putative causal relation need to be performed and to give coherent results (positive, negative, or absence of dependency). These correspond to the consistency and coherence criteria in Hill's list. Although, as is well known, correlation does not prove causation, strong correlations can be good evidence for the presence of a causal relation. Structural models require tests for the stability of parameters of interest, and the reliability of results also depends on the chosen significance level. Statistics are thus a key feature of almost all research studies in the health sciences, in order to discover both biological and social components of diseases.

It is uncontroversial that mechanistic evidence on its own can not warrant a causal claim, as it may be the case that the purported cause, although prior to the effect and mechanistically connected to it, actually makes little or no difference to it. Of course, without evidence of some dependence there may not be enough warrant for the mechanistic claim in the first place. The case of the discovery of the transmission of cholera is a clear example of this (Snow 1855). In 1849 Snow suspected that cholera infection was caused by a living organism that contaminates drinking water by proximity to sewage. Although he had hit upon the mechanism, the causal claim wasn't accepted until he found, in 1854, that the incidence of cholera was dependent on the source of water.

4. Mechanistic Evidence

A biomedical mechanism may involve chemical reactions, electric signals, alterations at the cellular level, etc. Exactly what constitutes such mechanisms will not concern us here—some view mechanisms to be processes transmitting conserved physical quantities; others claim that mechanisms are composed of chains of probabilistic or counterfactual dependencies, others that they are composed of chains of theoretical explanations.

The causal link between smoking and lung cancer was hotly disputed by the eminent Sir Ronald Fisher, who argued that a genetic factor might be a common cause of smoking and cancer (Fisher 1957, 1958). Probabilistic evidence did not on its own distinguish this common-causal claim from the claim that smoking causes lung cancer. A decision between the two hypotheses required evidence of a plausible physiological mechanism, as well as evidence of the correlation between the two variables. We now know how the physiological mechanism operates in the lungs. The hair-like cilia in the lungs, which beat rhythmically to remove inhaled particles, are destroyed by smoke inhalation; thus the lung cannot cleanse itself effectively. Cancer-producing agents in cigarette smoke are therefore trapped in the mucus. Cancer then develops when these chemical agents alter the cells, in particular, cell division. This is a simplified example of a biomedical mechanism. The mechanism invoked in the case of smoking and lung cancer involves a physiological mechanism, but it is also a chain of theoretical explana-

tions of the correlation between smoking and cancer. Moreover, this mechanism can be used to rule out Fisher's hypothesis.

The history of medicine presents many cases in which causal claims made solely on the basis of statistics have been rejected until backed by mechanistic or theoretical knowledge. For instance, in 19th-century Austria, the risk of puerperal fever after childbirth was extremely serious. In 1833 the Vienna Maternity Hospital was divided into two clinics, and statistics on births and deaths due to puerperal fever were collected. One of the two clinics showed a significantly higher death rate, of which Ignaz Semmelweis, an assistant physician at the hospital, wanted to find the cause. After having considered several hypotheses, Semmelweis came up with the idea that puerperal fever was caused by contamination of 'cadaverical' particles. In fact, after having carried out autopsies, doctors and medical students failed to wash their hands well enough to eliminate any possible source of contamination; they subsequently infected their patients when examining them. In spite of the extensive statistics gathered corroborating this hypothesis, Semmelweis' claim about cadaverical contamination and puerperal fever was accepted only after the germ theory of disease was developed and the *Vibrio cholerae* had been isolated by Robert Koch, establishing a viable mechanism (see Gillies 2005; Kundi 2006).

To give another example, quite recently researchers discovered the bacterium responsible for gastric ulcer. Although there was significant probabilistic evidence pointing to *Helicobacter pylori* as a cause of ulcers, the medical community was sceptical in accepting this hypothesis because, according to available theory, the stomach is too acidic an environment for a bacterium to survive. We now know that *H. pylori* produces ammonia, which neutralizes stomach acid and allows it to survive in the stomach walls. Although the causal relation was first hypothesised on the basis of probabilistic evidence (see Warren and Marshall, quoted in Thagard 1998, 115), the causal relation was only accepted after further evidence was gathered; this evidence was *probabilistic* (in particular, covariation between presence of helicobacter and ulcer and covariation between recoveries resulting to antibiotics) but also *mechanistic* (researchers found that this bacterium can survive in acid environments by secreting ammonia).

It is worth pointing out that we are not concerned, here, with how scientists came up with (controversial) causal hypotheses (as in the case of puerperal fever or of the discovery of *H. pylori*) but rather with how those hypotheses have become accepted by the medical community. In the case of Semmelweis, it is not clear whether he hypothesised the relation between cadaveric contamination and puerperal fever on the basis of statistical evidence alone, but what matters is that this claim was not accepted until backed up by mechanistic evidence, i.e., until the germ theory had been developed. Also, both historical cases—Semmelweis and *H. pylori*—have been discussed (see, for instance, Gillies 2005; Thagard 1998) to make a point about change of paradigm or hypothesis formulation in the biomedical sciences. Our point, instead, is a *theoretical* but not an historical one: two different *types of evidence*—probabilistic and mechanistic—are at stake when deciding whether or not to accept a causal claim.

5. Against Causal Monism

The debate on causality has recently turned to the question of whether a pluralistic or a monistic view of causality ought to be adopted. Do different notions of cause fit different contexts or does a single notion account for causal relations in all domains? Here we will be concerned with the question of whether *the health sciences* require a pluralistic or a monistic account.

In the philosophical literature two types of monistic account have traditionally been advanced: (i) a mechanistic approach; and (ii) a difference-making approach.

The mechanistic approach holds that causal connections are to be understood in terms of physical processes. Perhaps the primary example of this type of account is the Salmon-Dowe process theory (Dowe 2000; Salmon 1998). This theory uses concepts of process and interaction and appeals to laws of nature (e.g., conservation of energy and momentum). Physical processes are the key because they supply the link between the causes and the effects; processes intersect with one another in interactive forks, in this interaction they are modified and changes persist after the point of intersection. Processes and interactions are *physical* structures, and their properties cannot be characterised in terms of relationships among probability values alone. Salmon (1990) clearly states that physical processes and interactions will explicate causality even in domains outside physics—e.g., in the social sciences, where complex socio-political processes are at stake. Thus, the process theory qualifies as a monistic approach.

In contrast, proponents of difference-making accounts see the concept of causation as involving the notion of change, rather than mechanism. Examples of such accounts include probabilistic, counterfactual and agency theories of causality (Lewis 1986 [1973]; Price 1991; Suppes 1970). Probabilistic theories of causality, for instance, have been developed in a variety of ways by different authors in the last decades. Despite significant differences among them, a core of agreement can be found in the basic idea of a probability-changing requirement: *ceteris paribus*, causes change the probability of their effects. Causes are often assumed to precede their effects in time, and other conditions may be imposed to ensure that dependency of *E* and *C* is not spurious or due to a common cause.

Unfortunately, both types of account fail to handle the dual aspect of causal epistemology. Neither the mechanistic nor the difference-making approach can adequately account for the need for two types of evidence—mechanistic and probabilistic—for a single causal claim. On the one hand, the proponent of the mechanistic theory can't account for the widespread use of probabilistic data and methods in causal analysis even where the underlying mechanism is uncontroversial, and, on the other, the proponent of the probabilistic theory can't account for the fact that mechanisms are required even when appropriate probabilistic associations are well established.

The search for the nature of causality is pursued not only by philosophers. As mentioned in section 1, a number of review articles in epidemiology have recently tried to single out the definition of cause that best fits the health sciences. A probabilistic notion is perhaps the leading contender. Witness, for instance, Lagiou et al. (2005) who propose a probabilistic understanding of cause:

The following definition of a cause applies to all diseases, whether defined on the basis of a particular exposure (for example, many infectious and occupational diseases) or documented by specified laboratory or clinical findings (for example, malignant tumors, connective tissue disorders, psychoses, etc.): a factor is a cause of a certain disease when alterations in the frequency or intensity of this factor, without concomitant alterations in any other factor, are followed by changes in the frequency of occurrence of the disease, after the passage of a certain time period (incubation, latency, or induction period). (Lagiou et al. 2005, 565)

In the same vein, Kundi (2006) claims,

In this pragmatic sense disease cause can be defined as follows: Consider two or more populations of subjects that are sufficiently similar for the problem under study, then a disease cause is a set of mutually exclusive conditions that increase the probability of the disease. (Kundi 2006, 7)

This probabilistic account suffers from the epistemological problem highlighted above. This definition of cause only appeals to a difference-making requirement; it does not require that there be any plausible mechanism backing up this probabilistic evidence. Thus it makes the need for mechanistic evidence a mystery. Denying the need for mechanistic evidence is a dangerous move—it would allow an increase in the number of storks to be considered a cause of an increased birth rate, given an appropriate dependency.

6. Against Causal Pluralism

If monistic theories fail to provide an adequate account of cause in the health sciences, one might hope that pluralistic accounts will succeed. On the contrary, we will argue, only a single notion of cause is used in the health sciences. More specifically, health scientists use two types of evidence for a *single causal claim*, ‘*C causes E*’, not for two different types of causal claim, *C-causes₁-E* and *C-causes₂-E*. Because only *one* notion of cause is used in the health sciences, pluralism is false.

Note that causal pluralism takes two forms. *Conceptual* pluralism is the view that we have more than one concept of cause, while *ontological* pluralism is the view that there is more than one type of causal relation in the world. Conceptual pluralists normally hold that each concept of cause picks out a different causal relation—i.e., conceptual pluralism normally presupposes ontological pluralism. However, it is possible to be an ontological pluralist without being a conceptual pluralist by maintaining that there are two causal relations ambiguously picked out by a single concept of cause. Both varieties of pluralism are, we argue, implausible.

While studies don’t often adopt explicit causal vocabulary, where they do they use ‘cause’ in a single sense. They do not use one word to equivocate between two things, but use one word to isolate one relation, albeit a relation that admits more than one type of evidence. For instance, in Hwang et al. (2003), we read,

Malignant neoplasms in the lung and bronchus are the leading causes of cancer related deaths in the United States and in many developed countries. ... Cigarette

smoking, the most extensively studied lifestyle-related risk factor for disease, is causally associated with these cancers. (Hwang et al. 2003, 238)

The words ‘causes’ and ‘causally’ in this passage are used in the same sense—to refer to one relation which is associated with both mechanisms and dependencies, not to different relations, one mechanistic and one probabilistic. There are not two varieties of cause but two types of evidence. Similarly, Maruyama and Aoki (2006) say,

The health risk of dioxins and dioxin-like compounds to humans was analyzed quantitatively using experimental data and mathematical models. To quantify the toxicity of a mixture of three dioxin congeners, we calculated the new relative potencies (REPs) for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), 1,2,3,7,8-pentachlorodibenzo-p-dioxin (PeCDD), and 2,3,4,7,8-pentachlorodibenzofuran (PeCDF), focusing on their tumor promotion activity. We applied a liver foci formation assay to female SD rats after repeated oral administration of dioxins. The REP of dioxin for a rat was determined using dioxin concentration and the number of the foci in rat liver. A physiologically based pharmacokinetic model (PBPK model) was used for inter-species extrapolation targeting on dioxin concentration in liver. Toxic dose for human was determined by back-estimation with a human PBPK model, assuming that the same concentration in the target tissue may cause the same level of effect in rats and humans, and the REP for human was determined by the toxic dose obtained. (Maruyama and Aoki 2006, 188)

Here causal language is used (‘the same concentration in the target tissue may cause the same level of effect in rats and humans’); the scientists are clearly looking for mechanisms (hence the physiological model) and for difference-making, too (‘relative potencies’). Likewise, when Kuhl (2006, 680) says ‘About 10% of breast cancers are “hereditary”, i.e., caused by a pathogenic mutation in one of the “breast and ovarian cancer susceptibility genes” (BRCA)’ the word ‘caused’ is associated both with a genetic mechanism and with making a difference to 10% of breast cancer patients. That mechanism and difference-making are closely bound up in a single notion of cause in the health sciences is also supported by the causal language of Italiano (2006):

Colorectal cancer (CRC) is the second leading cause of cancer death in the western world. Even with the significant improvement in traditional chemotherapy, there remain limitations with this treatment. One of the most promising new targets in the treatment of CRC is the epithelial growth factor receptor (EGFR). Agents that inhibit the EGFR have demonstrated clinical activity as single agents and in combination with chemotherapy and the most promising of these agents is cetuximab, which blocks the binding of EGF and transforming growth factor- α (TGF- α) to EGFR. Thus, the finding that monoclonal antibodies against EGFR caused a response in patients, and reversed resistance to chemotherapy, was exciting news. However, expression of EGFR did not correlate with clinical benefit. Clearly, the search for markers of response to treatment against EGFR must go on. (Italiano 2006, 161)

We see then that pluralism about the nature of causality faces a crucial problem—it can not account for the homogeneity of causal language. But there is a second problem that besets pluralism, namely, that it inherits the difficulties of monistic accounts. This problem affects the pluralist who notes that there are two types of evidence for causal claims—mechanistic and probabilistic—and concludes that there are two types of

causal claim, mechanistic and probabilistic. This is clearly a fallacious inference, and, worse, opens the pluralist up to the objections of section 5.

Suppose that the pluralist advocates two notions of cause, a mechanistic, *cause*₁, and a probabilistic, *cause*₂. Take any *particular* causal claim, e.g., ‘smoking causes cancer’, that the pluralist cashes out in terms of one or other of these notions but not both (there must be some such claim, for otherwise she is not a pluralist but rather takes causality to be one thing that has two aspects or components). Now the evidence for this claim is multi-faceted, consisting of observed dependencies and mechanistic/theoretical considerations. But the pluralist’s analysis of this claim will be single-faceted, say ‘smoking is a *cause*₁ of cancer’. But then the pluralist opens herself up to the epistemological problems of monism. If this particular use of ‘cause’ is mechanistic, *cause*₁, then how can it be that, even when the mechanism is established and uncontroversial, further probabilistic evidence is cited in support of the causal claim? However, if the use is probabilistic, *cause*₂, why are mechanisms invoked as evidence, even when there is ample probabilistic evidence? The pluralist can’t explain the variety of evidence for the claim: if pluralism is right, it should be possible that the evidence just be mechanistic, or just be probabilistic.

So, while the pluralist may say that different uses of the word ‘cause’ can refer to different relations, some particular use must refer to a single relation. If that single relation is understood in terms of mechanisms on the one hand, or difference-making on the other, then with respect to that particular use of the word ‘cause’, it is subject to the problems of section 5.

7. Epistemic Causality

It may seem that our understanding of causality in the health sciences is stuck between a rock and a hard place: on the one hand monistic accounts—both mechanistic and difference-making—face epistemological problems (section 5); on the other, pluralism faces similar problems, plus the difficulty of explaining why we seem to have one concept of cause when in fact we have several, or why we seem to be talking about one causal relation when in fact there are several (section 6). But there is a way out of this dilemma. We have not exhausted the space of theories of causality, because the standard partition of monistic accounts into mechanistic and difference-making is a false dichotomy. False, because there is a third way: the *epistemic theory* offers a monistic conception of causality which is neither a purely mechanistic account nor a purely difference-making account—it involves aspects of the two types of approach. In this section we shall see how this type of integrated account does justice to the two-fold epistemology of causality in the health sciences.

The epistemic theory understands causal relationships in terms of rational beliefs as follows. First, it gives primacy to an account of how an agent’s evidence determines which causal beliefs she should adopt. Second it analyses the causal relation to be the set of causal beliefs that an agent with *total* evidence should adopt. Thus causality itself is determined by causal epistemology (Williamson 2005, chapter 9, 2006, 2007a, b).

How, then, does evidence constrain rational causal beliefs? Roughly speaking, an agent's causal belief state should satisfy the following conditions: (i) her causal beliefs should account for all known dependencies that are not already accounted for by known non-causal relationships; (ii) her causal beliefs should be compatible with her other knowledge (including knowledge of mechanisms); and (iii) she should not have any causal beliefs that are not warranted by her evidence. The details of how this causal epistemology is to be fleshed out, and why the resulting causal beliefs are deemed rational, need not concern us here—see Williamson (2005, 2007a) for one kind of account. What is important for our purposes is to note that there are a variety of indicators of causality, including dependencies and mechanisms, and that under the epistemic account the full variety will have a role in determining rational causal beliefs and hence causal relationships themselves.

Causal relationships are to be identified with the causal beliefs of an omniscient rational agent. This gives a view of causality that is analogous to the objective Bayesian view of probability, according to which probabilistic beliefs are determined by an agent's evidence, and probabilities themselves are just the beliefs that an omniscient agent should adopt. It might be thought that such a view renders causal relationships unknowable, for none of us can be omniscient, but it is quite plausible that, roughly, the more we know, the closer our rational causal beliefs will correspond to the causal facts, i.e., correspond to the causal beliefs of an omniscient rational agent. If so, then causal knowledge is possible.

The epistemic theory of causality can be applied to the health sciences (Nagl et al. 2007, sec. 20; Williams and Williamson 2006). In the health sciences it is clear that there are a variety of kinds of evidence. For example, in cancer science one might have a dataset containing clinical observations relating to past patients, another containing observations at the molecular level, some knowledge of the underlying biological mechanisms, some knowledge about the semantic relationships between variables provided by medical ontologies, and so on. All these types of evidence will shape causal beliefs about cancer: the datasets provide statistical evidence concerning difference-making; mechanisms provide evidence of stability; semantic relationships may provide evidence against causal connection (two dependent variables that are ontologically but not mechanistically related do not require a causal connection to account for their dependence). The epistemic theory of causality can account for this multi-faceted epistemology, since it deems the relationship between the various types of evidence and the ensuing causal claims to be constitutive of causality itself. Causality just *is* the result of this epistemology. On the other hand, a monistic account of causality in terms of just one of its indicators will struggle to explain why the other indicators are so important. A pluralistic account will struggle to explain the apparent unity to our concept of cause and how any particular causal claim can have multi-faceted evidence.

8. Conclusion

The health sciences pursue both a cognitive goal and an action-oriented goal in looking for causes of disease and for effective treatments and public health policies. In this

paper we raise the question of how causality ought to be interpreted in this domain. We argue that monistic theories—either mechanistic or probabilistic—don't give a successful account of causation, because they confuse the *evidence* from which causal relations are drawn with the very notion of cause. However, pluralistic accounts won't do either because a *single* notion of cause is used in the health sciences, not different ones depending on the type of evidence. Instead, an epistemic account of causality is required to capture the full complexity of causal evidence.

Although in this paper we restrict our scope to the health sciences, our point about interpreting causality can be generalised to other domains. For instance, evidence in the social sciences is very diverse too. The social sciences look for mechanisms, which can be social, biological or mixed, and for dependencies between variables of interest. Also, background knowledge of various types, e.g., the socio-political context, previous studies, economic or demographic theories, and field knowledge are used to draw inferences about causal relations. Yet in using both mechanistic and probabilistic evidence scientists do not aim at establishing different causal claims.

In the natural sciences the case is not as clear cut. There, many claim that a single experiment is enough to establish a causal claim. If so, that is perhaps because the experiment establishes the mechanism and the dependency at the same time, in which case there is a certain homogeneity about causality throughout the sciences. Clearly, the viability of an epistemic interpretation for all causal statements, not just those in the health sciences, would be worth investigating further—Williamson (2007a) takes a step in this direction by looking more closely at epistemic causality and causal pluralism from a general perspective.

Acknowledgements

This research forms a part of the project Causality and Probability in the Social and Health Sciences. We are grateful to the British Academy and to the Fonds Spécial de Recherche (Université catholique de Louvain) for funding this project.

References

- Bunge, M. 2004. How does it work? The search for explanatory mechanisms. *Philosophy of the Social Sciences* 34: 182–210.
- Dalton, S., E. Boesen, L. Ross, I. Shapiro, and C. Johansen. 2002. Mind and cancer: Do psychological factors cause cancer? *European Journal of Cancer* 38: 1313–1323.
- Dowe, P. 2000. *Physical causation*. Cambridge: Cambridge University Press.
- Fisher, R. 1957. Alleged dangers of cigarette smoking. *British Medical Journal* 2: 297–298.
- . 1958. Lung cancer and cigarettes. *Nature* 182: 108.
- Frumkin, H. 2006. 'Causation in medicine'. Rollins School of Public Health, Emory University, Available from <http://www.aoc.org/CEEM/methods/emory2.html>; INTERNET.
- Gillies, D. 2005. Hempelian and Kuhnian approaches in the philosophy of medicine: The Semmelweis case. *Studies in History and Philosophy of Biological and Biomedical Sciences* 36: 159–181.
- Hales, N., D. Barker. 2001. The thrifty phenotype hypothesis. *British Medical Bulletin* 60: 5–20.
- Hill, B. 1965. The environment of disease: association or causation? *Proceedings of the Royal Society of Medicine* 58: 295–300.

- Hwang, S.-J., C. L. Shu-Chung, G. Lonzano, C. Amos, X. Gu, and L. Strong. 2003. Lung cancer risk in germline *p53* mutation carriers: Association between an inherited cancer predisposition, cigarette smoking, and cancer risk. *Human Genetics* 113: 238–243.
- IARC (International Agency for Research on Cancer). 2006. 'Preamble to the IARC monographs'. IARC. Available from <http://monographs.iarc.fr/ENG/Preamble/index.php>; INTERNET.
- Italiano, A. 2006. Targeting the epidermal growth factor receptor in colorectal cancer: Advances and controversies. *Oncology* 70 (3): 161–167.
- Kuhl, C. 2006. Familial breast cancer: What the radiologist needs to know. *Rofo-Fortschritte auf dem Gebiet der Rontgenstrahlen und Dereoleol Bildgebenden Verfahren* 178 (7): 680–687.
- Kundi, M. 2006. Causality and the interpretation of epidemiological evidence. *Environmental Health Perspectives* 114: 969–974.
- Lagiou, P., Adam, H.-O., and Trichopoulos, D. 2005. Causality in cancer epidemiology. *European Journal of Epidemiology* 20: 565–574.
- Lewis, D. K. 1986 [1973]. Causation. In Lewis, *Philosophical papers*, vol. 2, 159–213. Oxford: Oxford University Press.
- Lipton, R., and T. Odegaard. 2005. Causal thinking and causal language in epidemiology. *Epidemiological Perspectives and Innovations* 2: 8. Available from <http://www.epi-perspectives.com/content/2/1/8>; INTERNET.
- Maruyama, W., and Y. Aoki. 2006. Estimated cancer risk of dioxins to humans using a bioassay and physiologically based pharmacokinetic model. *Toxicology and Applied Pharmacology* 214: 188–198.
- Nagl, S., M. Williams, and J. Williamson. 2007. Objective Bayesian nets for systems modelling and prognosis in breast cancer. In *Innovations in Bayesian networks: Theory and applications*, edited by D. Holmes and L. Jain. New York: Springer.
- Parascandola, M., and D. Weed. 2001. Causation in epidemiology. *Journal of Epidemiology and Community Health* 55: 905–912.
- Price, H. 1991. Agency and probabilistic causality. *British Journal for the Philosophy of Science* 42: 157–176.
- Salmon, W. C. 1990. Causal propensities: statistical causality vs. aleatory causality. *Topoi* 9: 95–100.
- 1998. *Causality and explanation*. Oxford: Oxford University Press.
- Snow, J. 1855. *On the mode of communication of cholera*. London: John Churchill.
- Suppes, P. 1970. *A probabilistic theory of causality*. Amsterdam: North-Holland.
- Thagard, P. 1998. Explaining disease: Correlations, causes, and mechanisms. *Minds and Machines* 8: 61–78.
- Williamson, J. 2005. *Bayesian nets and causality: Philosophical and computational foundations*. Oxford: Oxford University Press.
- 2006. Dispositional versus epistemic causality. *Minds and Machines* 16: 259–276.
- 2007a. Causal pluralism versus epistemic causality. *Philosophica* (in press).
- 2007b. Causality. In *Handbook of Philosophical Logic*, vol. 14, edited by D. Gabbay and F. Guenther, 89–120. New York: Springer.
- Williams, M., and Williamson, J. 2006. Combining argumentation and Bayesian nets for breast cancer prognosis. *Journal of Logic, Language and Information* 15: 155–178.