Variational Causal Claims in Epidemiology

Federica Russo

ABSTRACT This article examines definitions of *cause* in the epidemiological literature. Those definitions describe causes as factors that make a difference to the distribution of disease or to individual health status. In philosophical terms, they are "difference-makers." I argue that those definitions are underpinned by an epistemology and a methodology that hinge upon the notion of variation, contra the dominant Humean paradigm according to which we infer causality from regularity. Furthermore, despite the fact that causes are defined in terms of difference-making, this doesn't fix the causal metaphysics but rather reflects the "variational" epistemology and methodology of epidemiology. I suggest that causality in epidemiology ought to be interpreted according to Williamson's epistemic theory. In this approach, causal attribution depends on the available evidence and on the methods used. In turn, evidence to establish causal claims requires both difference-making and mechanistic considerations.

Epidemiology studies the distributions of diseases in and across populations and seeks to identify the factors determining those distributions. This broad characterization of epidemiological research raises issues of broad philosophical interest. One such issue concerns adopting an explicit causal stance. This is some-

Institut Supérieur de Philosophie, Université Catholique de Louvain, Belgium; Department of Philosophy, School of European Culture and Languages, University of Kent.

Correspondence: Department of Philosophy, SECL, Cornwallis Building, University of Kent, Canterbury CT2 7NF, United Kingdom.

E-mail: f.russo@kent.ac.uk.

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times avoided, perhaps as a consequence of scientific humility and a reluctance to claim to have found causal relations. As a result, a plain causal terminology is sometimes replaced with a less obvious and more confusing one, using terms such as *factors* or *determinants*, but not *causes* and *effects*. While this is certainly an important issue for investigation, I will here take for granted that an explicit causal stance is justifiable (let alone desirable) and will tackle another problem arising in causal reasoning in epidemiology.

Various definitions of cause can be found in the philosophical and scientific literature. Parascandola and Weed (2001) have identified five definitions of cause: production, necessary causes, sufficient-component causes, probabilistic causes, and counterfactual causes. Unfortunately, none of these has succeeded in attracting a consensus or in accounting for different causal scenarios in epidemiology. To illustrate, consider a "necessary" definition of cause. This definition fits the case of AIDS, for HIV infection is a necessary cause of AIDS; however, it does not seem to suit the case of cancer, for exposure to any carcinogenic substance is neither necessary nor sufficient to develop cancer. Parascandola and Weed conclude that the probabilistic account provides a better picture, both because it can encompass other definitions and because it accounts for the fact that different factors have a different impact on the disease. According to their definition, "A probabilistic cause increases the probability of its effect occurring. Such a cause need not to be either necessary or sufficient" (p. 906).

The literature offers other related definitions of *cause*:

> A determinant [of health] can be any factor, whether event, characteristic, or other definable entity so long as it brings about change for better or worse in a health condition. (Susser 1973, p. 3)
>
> . . . a factor is a cause of an event if its operation increases the frequency of the event. (Elwood 1988, p. 5)
>
> Being a cause is a special characterization of some state of affairs characterized by change, i.e. an event, a fact, a state or a deed: in medicine and epidemiology, a cause makes a disease happen or not happen. (Karhausen 2000, p. 59)
>
> 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. (Lagiou, Adami, and Trichopoulos 2005, p. 565)

In slightly different ways, all of these definitions say what a causal factor does, and what it does is to make changes, either in frequencies of disease or in the health status of individuals. In philosophical terms, according to those definitions, causes are "difference-makers."

This article offers a critical evaluation of definitions of *cause*, in order to discuss the kind of epistemology, methodology, and metaphysics of causation that underpin them. I argue that these definitions are supported by an epistemology

and a methodology of causality that hinge upon the notion of variation rather than regularity. The underlying metaphysics, however, is more complicated. Even though these definitions describe causes as difference-makers, this does not necessarily fix a "difference-making" causal metaphysics; rather, these definitions reflect the "variational" methodology and epistemology of epidemiology. I argue that causality is better interpreted according to Williamson's epistemic theory, an approach that explicates causality in terms of an individual's rational beliefs and provides constraints to forming causal beliefs upon available evidence.

CAUSAL EPISTEMOLOGY AND METHODOLOGY

The definitions mentioned above describe a cause in terms of what it does, namely producing changes in frequencies of disease or in individual health status. These definitions are supported by an epistemology and methodology of causality built around the notion of variation rather than regularity.

The epistemology and methodology of causality are concerned with how we come to know about causal relations—that is, with the notions involved in causal reasoning—and with problems of scientific method. In turn, problems of scientific method may concern developing successful means of discovering and confirming causal relationships, or for analyzing the conceptual issues behind those means. Although the borderline between epistemology and methodology is often blurred, it is still worth drawing a line between the two. For example, the epistemology of causality may be interested in how laypeople rather than scientists come to know about causal relations, in which case epistemology and methodology would not coincide. Moreover, the development of methods for the discovery and confirmation of causal relations is not, strictly speaking, an epistemological issue, but it surely ought to be driven by the scientists' epistemological stance about, for example, causality, probability, or induction.

The philosophical literature has not always been careful in distinguishing the epistemological from the methodological. Yet it does address a number of epistemological and methodological issues. Consider for instance the recent development of Bayesian networks (Pearl 2000; Spirtes, Glymour, and Scheines 1993; Williamson 2005). Customarily used in the everyday scientific practice and especially in artificial intelligence and data mining, Bayesian networks presuppose a number of epistemological questions. The most important and most debated perhaps is whether and when the so-called "causal Markov condition" allows us to interpret probabilistic dependencies as causal dependencies (see, for instance, Cartwright 2002; Hausman and Woodward 1999, 2004). Another epistemological question is whether there is epistemic access to causal relations other than correlations or randomization. This question is addressed, for instance, by philos-ophers such as Ducasse (1926, 1968) and by experimental psychologists such as Michotte (1962), who thought that causation was directly perceivable—a question followed

up in more recent psychological research too (see Cohen et al. 1998; Leslie and Keeble 1987; Muentener and Carey 2006; Twardy and Bingham 2002).

In many ways, answers offered in the philosophical literature are indebted to Hume (1748). Recent philosophical accounts within the Humean tradition usually referred to as "regularism" analyze causation as follows. (For one account, see Psillos 2002.) Simply put, an event *c* caused an event *e* if and only if events of type *E* regularly follow events of type *C*. For instance, in this account, smoking causes lung cancer because cancer-events steadily follow smoking-events; one might then infer that Harry's smoking caused him to develop lung cancer because lung cancer typically follows smoking. However, although the philosophical literature has frequently used this example, it has failed to recognize two flaws in the regularity approach. First, the intuition that "Harry's smoking caused him to develop lung cancer because lung cancer typically follows smoking" has some plausibility only because the relation between smoking and lung cancer—indeed, between smoking and many types of cancer—is well established (Vineis et al. 2004). Second, the issue of how we come to know about causal relations emerges more clearly once we consider more controversial (causal) relations. It is not because exposure to electromagnetic fields is regularly followed by cancer that epidemiologists (tentatively) establish a causal relation between the two, but because variations in exposure to electromagnetic fields are linked to variations in cancer rates.

So a central problem in epistemology is what notion or principle guides causal reasoning: independently of what causality (metaphysically) is, what notion guides our reasoning in making inferences to establish causal relations? This epistemological question is most relevant to methodology. Contrary to the dominant Humean paradigm, I have argued previously that model building and model testing in the social sciences turn around the notion of variation, not regularity (Russo 2006, 2008). Simply put, a causal model is built around meaningful co-variations between the variables of interest and tests are performed in order to establish which variations are causal. One requirement is that in large data sets the co-variation between variables also show some regularity. This does not mean that the scientist infers causal relations from regular successions à la Hume, but that the scientist requires co-variations to be regular enough to rule out accidental or spurious relations. In the following sections, I show that epistemology and methodology in epidemiology also crucially turn around the notion of "variation," *pace* Hume.

VARIATIONAL EPISTEMOLOGY

A case for a variational epistemology can be made by appealing to the goals of epidemiology. Epidemiologists usually claim that their goal is to study the variability of disease due to the variability of exposure. A number of epidemiologists

have explicitly supported this idea (for instance, Jewell 2004; Lilienfeld and Stolley 1994; Susser 1973; Timmreck 1994). Isolated and independent voices are brilliantly summarized by Bhopol (1997, 1999), who carried out a systematic review of epidemiology textbooks and came to the following conclusion: "Certain beliefs—that epidemiology is about the study of health and disease in populations, that there is a *population group variation in disease that is worth of scientific study*, and that such variation is important to public health policy and practice—were common to virtually all textbooks" (Bhopol 1999, p. 1162; my emphasis). Bhopol summarizes very well the aspect of epidemiology I am concerned with: that epidemiologists are interested in how the disease varies across individuals, time, space, and so forth. In other words, epidemiology seeks to establish causal claims by studying variations in exposure and in disease. It is worth pointing out that if this were merely a platitude about epidemiology, it would not be a noteworthy and widespread belief. Causal epistemology is concerned with how we come to know about causal relations, and the answer here is that we will know about causes of disease by investigating whether some specific variations in exposure lead to variations in disease.

This is definitively what the definitions of cause cited earlier point to: causal factors are responsible for variations in the distribution of disease or in individual health status and they can be established by studying the population group variation in disease. Hence, the definitions of cause are underpinned by a variational epistemology.

Causal epistemology in epidemiology is variational, *pace* Hume. Let me develop this point further. The conceptual background pervading philosophy of science and scientific thinking generally is a paradigm of regularity, a heritage of the Humean conception of causation (Hume 1748, sec. VII). However, if the regularity paradigm were the correct one in epidemiology, Bhopol would be misinterpreting the "common beliefs" of epidemiologists. But perhaps Bhopol is right, and instead Hume is misleadingly called to support causal reasoning in epidemiology. Witness Karhausen (2000):

> This paper attempts to charter [sic] some of the territory of the concept of causation in epidemiology and its potential interactions with logic and scientific philosophy. David Hume looms large in this matter . . . . Being a cause is a special characterization of some state of affairs characterized by change, i.e. an event, a fact, a state or a deed: in medicine and epidemiology, a cause makes a disease happen or not happen. (p. 59)

Karhausen then points to several misunderstandings of the Humean doctrine in both the philosophical and the epidemiological literature. For instance, he says that some authors took Hume as claiming that causal inference is a subjective process, or that causes are not real, or that induction does not exist. Two remarks are in order. The first is that Karhausen, in the quote above, also misunderstands Hume. In fact, Karhausen claims that Hume contributes to the definition of

causes as "some state of affairs characterized by change." But this is a patently wrong reading of Hume. Hume's influence is in the definition of a cause as an object displaying regular behavior, not one producing changes. Furthermore, Karhausen's definition is underpinned by a variational epistemology of causality, whereas Hume believed that we infer causation from regular successions of events.

This issue is controversial, and dissent with the regularist paradigm also comes from the health sciences. For instance, Elwood (1988) complains that the paradigm of regularity is not well suited to medicine. The view that a certain event always and invariably follows another event might well fit physics, because the causal agent is sufficient, the time lag between the cause and the effect is short, and experimental conditions allow for the replication of causal relations. However, most situations in the health sciences do not fulfill these criteria. Elwood may or may not be right about the simplicity of situations in physics, but he is surely right about epidemiology.

VARIATIONAL METHODOLOGY

According to the causal epistemology sketched above, in epidemiology we find out about causes by examining the variability of disease due to the variability of exposure. Methodology is concerned with how this is practically done. What I want to show next is that definitions of cause in epidemiology are also underpinned by a variational methodology.

Savitz (2003) notes that epidemiology is primarily interested in establishing statements such as "the risk of disease is x times greater among exposed persons than unexposed persons" (p. 35). Such claims contribute to establishing causal relations through comparative statements, which are in fact the bulk of a variational methodology. This idea can also be found in Susser (1973), who says that epidemiology is all about comparing and interpreting group exposure and response. Notably, comparisons involve establishing whether factors make a difference—that is, whether distributions of disease differ conditionally on exposure, or whether relative risks are greater for exposed individuals than for non-exposed individuals.

Epidemiology is more often concerned with observational than with experimental data. It is apparent that the methodology of experimentation—for example, in randomized clinical trials—is variational because the idea is just this: to see what changes occur by making certain interventions. In fact, in experimental studies we estimate certain predetermined outcomes of a well-defined intervention that is deliberatively administered to certain individuals, and we compare results with outcomes in individuals that have not been administered the intervention. No doubt the most direct tests for causation would be experimentation and intervention; however, much debate turns on the question of whether randomized controlled trials really are the gold standard. A thorough

discussion of this issue falls beyond the scope of the paper and I will not reiterate arguments given elsewhere (Cartwright 2007a; Elwood 1988; Glasziou et al. 2007). Glasziou et al. (2007) defend the idea that observational evidence can indeed support causal claims, and then provide a significant number of historical examples where convincing causal inferences have been performed without resorting to randomized trials. Timmreck (1994) goes as far as claiming that observational studies provide many more insights into the effects of diseases. The reason is that they deal with population groups, whereas experimental studies deal with individuals or smaller treatment or experimental groups, and therefore the inference to relations in large populations is limited. Of course, questions remain concerning the problem of confounding or the use of frequentist rather than Bayesian statistics, but those are separate issues.

What I want to show next is that observational studies rely on a variational methodology too. Timmreck (1994) expresses this idea clearly: "Observational method of study is based on the concept that changes which are observed in one trait or variable can cause changes in another characteristics or variable, and those changes occur without the event being altered by the epidemiologist or without intervention by a researcher" (p. 326). That observational methods in epidemiology are variational in character is clear from the fact that they are all comparative. Cohort studies compare individuals exposed to the putative cause with individuals that have not been exposed. Case-control studies compare individuals with the disease with individuals that do not have the disease. In cross-sectional studies, data are collected at a specific point of time and comparisons are made for that specific moment. It is not my goal here to evaluate the strengths, weaknesses, or applicability of those type of studies. I wish only to stress their comparative aspect.

CAUSAL METAPHYSICS

It is perhaps obvious that causal methods hinge upon the notion of variation and that the definitions of cause cited at the beginning indeed reflect a variational methodology. Fair enough. But the metaphysical import of such definitions is perhaps less obvious.

Epidemiologists are interested in studying variations of disease due to variations in exposure. But to what extent does a variational epistemology and methodology also determine the causal metaphysics we adopt? Although the definitions of cause all point to difference-making, they do not fix a "variational" or "difference-making" metaphysics; rather, they reflect of the variational epistemology and methodology of epidemiology.

The metaphysics of causality seeks to know what causality in fact is, what kind of entities causes are, and what we mean when we say that "A causes B." Those tasks can be achieved in a number of ways. Philosophers of causality have pro-

vided analyses of the concept of causality (e.g., Hall 2004), accounts of the kind of entities causes are (e.g., Cartwright 1989), and have developed sets of conditions under which relations between variables are causal (e.g., Woodward 2003).

The philosophical literature is vast. Broadly speaking, "traditional" philosophical theories fall into two families: those analyzing causality in terms of difference-making, and those analyzing causality in terms of production or mechanisms. Probabilistic theories and counterfactual theories are examples of the former sort: in probabilistic approaches, causes, whether positive or negative, are difference-makers as they change (increase or decrease) the probability of their effects (see, for example, Eells 1991; Hitchcock 1995; Suppes 1970). In Lewis's (1986) counterfactual analysis causes are also difference-makers as if the cause had not been, the effect would not have been either. Examples of theories focused on production or mechanisms include the account developed by Cartwright (1989), where causes are capacities having the ability or disposition to produce or bring about an effect; the process-based approach (Dowe 2000; Salmon 1998), where causes are linked to effects via physical processes that intersect and interact; or the mechanist approach (Machamer, Darden, and Craver 2000; Glennan 2002; Craver 2007), where "A causes B" means that there is a suitable mechanism linking the two.

A number of criticisms may be raised against these traditional accounts. Usually, counterexamples are construed in order to show that none of them is able to provide *the* answer to what causality is. In fact, counterexamples to each of the above positions can be easily construed—Reiss (2009) offers a detailed overview and discussion of stock examples. Hence, slowly but surely, due to the failures of traditional philosophical theories of causation, pluralistic stances have come into range as the most promising solution. (For a discussion on pluralism see, among others, Campaner and Galavotti 2007; Cartwright 2007b; De Vreese 2006; Godfrey-Smith n.d.; Hall 2004; Psillos n.d.; Reiss 2009; Russo and Williamson 2007; Weber 2007.)

Simply put, pluralists say that causality has many aspects, not just one, and that causal claims have many meanings, not just one. Hall (2004), for instance, maintains that causation involves "dependence" as well as "production." Since dependence and production are usually defined in terms of "difference-making" and "mechanisms" respectively, this pluralist stance requires that causes make a difference to the effect *and* that causes be linked to the effect via a mechanism. Alternatively, pluralists may maintain that the right concept in terms of which causality has to be identified depends on the context. Thus, Weber (2007) suggests that an analysis in terms of difference-making is suitable for the generic level ("smoking causes lung cancer"), while an analysis in terms of mechanism is suitable in the single-case ("Harry's smoking caused him to develop lung cancer").

But what kind of metaphysics should epidemiologists adopt? Is disease causation intrinsically difference-making or mechanist? Or a combination of the two?

VARIATIONAL METAPHYSICS?

Definitions of cause consistently describe causes as difference-makers. Does it follow that epidemiologists should endorse a difference-making metaphysics? The straight answer is no, because, I will argue, causality in epidemiology is better interpreted according to Williamson's epistemic theory (Williamson 2005, 2006).

Williamson's epistemic theory is, in essence, a metaphysical account of causation. However, it differs from other proposed accounts in significant respects. First, while traditional accounts explicate causality in terms of "probability raising," "physical process," "mechanism," or "capacity," Williamson explicate causality in terms of an individual's beliefs formed upon available evidence. Second, under Williamson's theory, causal relations are not real but rather "representational": causality is not a feature of the physical world, but a feature of an individual's set of rational beliefs about a phenomenon. What Williamson is ultimately suggesting is that the issue is not to find the "secret connection," but to provide methods and principles to decide whether a relation is causal. Causal relations do happen in the world: viruses cause disease in real patients, throwing a stone at a window causes it to break. But Williamson is interested in how and under what conditions an individual deems those relations to be causal. It is in this sense that causation is "in our head" rather than "out there."

Let us now consider a specific individual, the epidemiologist. The epidemiologist's job is to decide, for instance, what are the causes of a given disease or what levels of exposure to a given substance are more likely to cause the disease. What kind of metaphysics should the epidemiologist adopt? Does this mean that causality is reduced to probabilities or to mechanisms?

Let me use the International Agency for Research on Cancer (IARC) procedures to illustrate. IARC procedures evaluate carcinogenic risks to humans, and the monographs provide extensive descriptions of the procedures for the evaluation of carcinogenicity (IARC 2006). Simply put, this is the problem of deciding whether and to what extent an agent causes cancer (in humans or in animals). An agent will be deemed carcinogenic depending on what evidence supports such a claim. The point at stake here is that the claim "the agent X is carcinogenic to humans" is the judgment or causal beliefs of the IARC panel representing the evidence, methods, and evaluation procedures used to come to such a conclusion. Causation is not metaphysically reduced to difference-making or to mechanisms; instead, it refers to the causal beliefs that scientists form on the basis of the evidence and methods at their disposal. It is in this sense that causation, under Williamson's epistemic theory, is representational. It is worth emphasizing, however, that this does not make causation idiosyncratic to scientists' tastes and preferences: Williamson's theory states that, in principle, if two agents disagree as to causal relations, at least one of them must be wrong (Williamson 2005, ch. 9). This, of course, has to be taken as an "asymptotic" principle: in practice, the scientific community has procedures to decide whether and

to what extent to regard results as reliable and sound. Thus, through IARC procedure the scientific community aims to reach an agreement about what causes what. It goes without saying that this isn't easy nor always the case, but Williamson's epistemic theory offers principles in order to avoid arbitrariness in causal beliefs.

But why are pluralist approaches not suitable? Pluralist philosophers have argued, in slightly different ways, that causality is a multifold concept involving difference-making and mechanisms. There is, however, a deep mistake in such analysis: pluralists are confusing the *concept* of causality with the *evidence* to establish a causal claim. In other words, from the fact that we have multiple sources of evidence, it doesn't follow that should have a multifold concept of causality. The full argument and examples of how pluralists confuse evidence concept of causation is given in Russo and Williamson (2007). Simply put, in the epistemic theory, the concept of causality is explicated in terms of belief. In turn, causal beliefs are formed upon evidence; in order to establish whether a factor or a relation is causal, evidence has to involve difference-making *and* mechanistic considerations. The evidence for causal relations is certainly complex—it involves, in fact, both difference-making and mechanistic considerations—but the concept isn't. Russo and Williamson (2007) offer various arguments for the claim that mixed evidence is needed in the health sciences: (1) pluralist stances are fallacious exactly because they confuse the concept of causality with the types of evidence to establish causal claims; (2) history of medicine has paradigmatic cases where causal claims have not been accepted until *both* difference-making and mechanistic evidence have been provided to support a causal claim; and (3) the need for difference-making and mechanistic evidence is current practice in the health sciences, as required, for instance, by IARC procedures to evaluate studies on carcinogenic factors.

Adopting the epistemic theory brings many advantages. One is that the epistemic theory answers the worries of those who argue against an explicit causal terminology on the ground that the notion of cause is metaphysical—in other words, obscure and untestable. Lipton and Ødegaard (2005), for example, state 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" (p. 7). Lipton and Ødegaard's anti-causal stance is motivated by the belief that metaphysical causal claims are independent of, and even not needed for, the "use value" of research findings for prediction and intervention. The two sentences "smoking causes lung cancer" and "smoking two packs a day increases the risk of lung cancer by ten times," according to Lipton and Ødegaard, do not merely differ as to their semantics. The former—they claim—resorts to a "metaphysical and unsupported" notion of cause, while the latter already tells a causal story, and

it uses a language that allows practical applications, such as prediction and interaction. The "metaphysical and unsupported" notion of cause they refer to is Anscombe's (1981) notion, which is explicated in terms of necessary connection and instantiation of an exceptionless generalization. Historical considerations about the reception of and the critiques to Anscombe's thought in the philosophical literature and about the advancements in the philosophy of causality after Anscombe are beyond the scope of this article. However, Lipton and Ødegaard's point of concern dissolves once the epistemic theory is adopted, for epistemic causality is not metaphysically obscure (rational beliefs can be characterized precisely in probabilistic terms, as in decision theory) nor untestable (difference-making evidence, for instance, is subject to statistical testing).

The epistemic theory is not far from the position defended by Vineis (2003), who says that we believe that smoking causes lung cancer on the basis of various sources of evidence, such as observations in humans, experiments in animals, and knowledge about DNA damage in carcinogenesis. But this does not force epidemiologists to a "realist" position, according to which "empirical observations do refer to some reality in the external world (independently of theoretical models)" (p. 85).

Another advantage is that the epistemic theory encompasses different modus operandi of the cause. Recall Parascandola and Weed's (2001) five possible definitions of cause, none of which attracts consensus nor can account for causes in all domains. Consider causes as necessary factors. The view that all causes must be necessary for their effects (traditionally associated with the germ theory of disease) has been discarded. While some causes aren't necessary for the effect, some indeed *are*—for instance, tuberculosis is caused by an infectious agent, which is necessary for the development of the disease. Under the epistemic theory, necessary and probabilistic causes can peacefully live together; also, since causality is not physical, causes can be variables, particular entities, events, properties or facts, depending on the context.

This happens all the time in biomedical contexts. Consider the two causal claims "exposure to asbestos dust causes lung cancer" and "the bacteria streptococcus causes irritation and inflammation of the throat." The first involves variables as causal relata, and the cause thereby operating is probabilistic. The second involves different kinds of relata (bacteria are microorganisms, and irritation and inflammation of the throat is an event describing health status), and the cause is of type sufficient-component. It follows that necessary and probabilistic definitions of cause are not mutually exclusive definitions. Williamson's epistemic theory does not need to fix what entity a cause is; the point is that we deem some relations to be causal, so that causality lies exactly in this epistemic activity of evaluating the available evidence. Other metaphysical accounts are wanting in this respect. (For instance, probabilistic accounts typically define causal relations as relations between variables or events, which doesn't obtain when we say that "the bacteria streptococcus causes irritation and inflammation of the throat.")

Thus, the question to address is: why are causes consistently defined in terms of difference-making? The temptation would be to infer that those definitions are underpinned by a difference-making metaphysics, namely that this is what causality is—to make a difference to the effect. But this is a fallacious inference. Some causes may *not* be difference-makers. For instance, the pillar causes the building to stand, but it is not a difference-maker. (For a discussion about causes of states and difference-making, see Russo 2008, ch. 3.) Additionally, difference-making is *evidence* to establish whether a factor is causal, but it does not coincide with the *concept* of causation.

The reason why definitions of cause prominently display difference-making considerations is that they reflect the variational epistemology and methodology discussed earlier: difference-making definitions of cause reflect how we come to know whether something is a cause, and the "how" question is answered by methodology and epistemology. Whether we deem something a cause is still an epistemic activity, and in epistemic terms, causality simply results from epistemology and methodology. Williamson's epistemic account of causation not only provides sufficient conditions for the action-oriented goals of epidemiology—to inform public health and medical interventions—but it also provides normative principles on the basis of which to take (or not to take) action (Williamson 2005, 2006, 2007).

CONCLUSION

Causal issues are extremely important in epidemiology. The definitions of the concept of cause found in the epidemiology literature share a common feature: they say that a cause brings about changes in the distribution of disease or in individual health status.

The causal epistemology in epidemiology hinges upon the notion of variation rather than regularity. Therefore, the definitions of cause are underpinned by a variational epistemology. Similarly, because causal methods in epidemiology are essentially comparative, methodology in epidemiological research is variational too. This overtly goes against the dominant Humean paradigm that instead hinges upon the notion of regularity. The result is important to epidemiologists because it clarifies the meaning of their working definition of cause and of their methods, and it disproves the erroneous use of the notion of regularity to the detriment of the notion of variation. The point is conceptual, but, arguably, only by using the right concepts can we improve the quality of methods and of empirical research.

Those definitions of cause are also not underpinned by a variational metaphysics. Causality in epidemiology is best interpreted according to Williamson's epistemic theory, where it is understood not as a physical property of things or of the world, but rather as a representation of the rational beliefs of the individual, in our case the epidemiologist. A key feature of epistemic causality is that it

clearly distinguishes between the concept of cause and the evidence needed to establish causal claims. This confusion is the source of a questionable approach in the philosophy of causality, causal pluralism. Definitions of cause in epidemiology consistently point to difference-making because this is crucial evidence for disease causation. In fact, it reflects the way epidemiologists come to know about causal relations, namely the variational epistemology and methodology of epidemiological research. However, difference-making is not, by itself, sufficient evidence. Thus, the distinction between evidence and concept and a causal metaphysics in terms of rational belief are essential conceptual tools that working epidemiologist have to use when they establish causal relations, as in empirical research or in the evaluation of evidence for carcinogenic agents.

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