Causation and evidence-based practice

An ontological review

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INTRODUCTION

If a complete philosophy of evidence-based practice (EBP) is intended, then attention to the nature of causation in health science is necessary. We identify how health science currently conceptualises causation by the way it prioritises some research methods over others. We then show how the current understanding of causation serves to constrain progress in the field of EBP. An alternative, dispositionalist account of causation is offered. By understanding causation from a dispositionalist stance, many of the processes within an evidence-based practice framework are better accounted for. Further, some of the problems associated with health research, e.g. problems of induction and external validity of causal findings, dissolve. This paper provides a review of causal ontology as it appears in present health science, with specific reference to evidence-based practice frameworks. It is not the intention here to provide a complete theory of dispositionalism but, rather, to review present ontologies and their limitations, allowing for a focused introductory sketch of how dispositionalism might respond. This will provide a background for further attention to causal ontology in health science and EBP.

PHILOSOPHY OF EVIDENCE-BASED PRACTICE IS INCOMPLETE

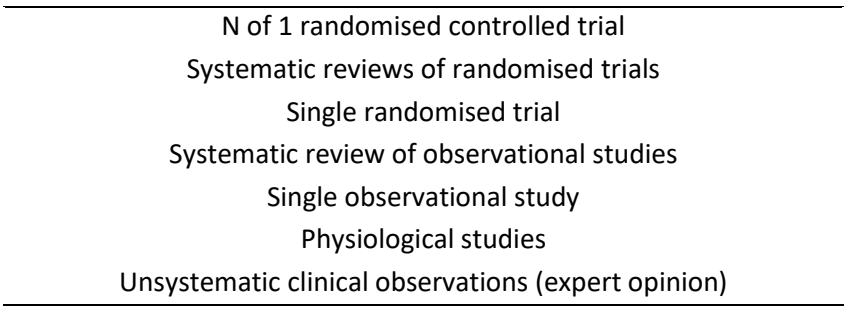
The broad context of this paper is set in two operational frameworks firmly embedded in health care: evidential categorization of research methods, and evidence-based practice (EBP). Briefly, EBP is taken as the integration of the best of research knowledge with clinical experience and patient values [1]. Thus, each clinical decision taken by a health care practitioner should be informed by multiple sources of knowledge [2]. There has been contention surrounding this framework since its high profile induction in the early 1990s e.g. [3-13]. In summary, proponents believe this is a sensible, professional advancement of clinical decision making which tracks exponential progress in

data production from rigorous research processes [14]. Opponents offer arguments based around, among many things, the apparent disproportionate weighting given to epidemiologically-derived data e.g. [15-25]. Many arguments focus on the problems faced with statistical inference and generalisability of population-based research findings to particular instances of clinical decision making [16-26]. We take this as serious challenges to EBP and ground much of our arguments in this issue. However, this paper is not interested in rehearsing or developing arguments associated with statistical inference, and takes these as read. We also accepted that EBP and evidential frameworks hold an established procedural role in the delivery of health care. This political and administrative functional fitness should not drive attention away from the nature of the phenomenon. The growing influence and institutionalization of the evidential frameworks makes it more important than ever to ask fundamental questions about what kind of evidence we have. The matter of causation is prevalent in existing philosophical literature related to both research methods and the discrete notion of EBP. However, existing literature seems to be exclusively focused on epistemological matters and the current view of the nature of causation seems to be fixed, with no apparent criticisms of the way EBP understands causation [27]. Our claim is that it is this fixed stance on causal nature which is central to both the philosophical unrest in EBP, and limitations on its inherent scientific progress.

CATEGORICAL INTERPRETATIONS OF EVIDENCE

By categorical interpretation, a given piece of evidence always gives more evidential support to a claim than evidence from lower down the hierarchy [28-29]. In order to develop thought regarding causal ontology, it is first necessary to understand how evidence is interpreted. It seems apparent that since the inception of EBP, a categorical interpretation has been supported [29]. Until recently, research methods associated with investigating treatment interventions were categorized within hierarchical forms. A common example is seen in work of some of the originators of the EBP movement [30] (Figure 1). Its essence is that methods are ordered by their epistemic strength [29]. For treatment interventions, associated research methods are primarily concerned with establishing causal associations between intervention and health effect. Thus, an epistemic reading of evidential hierarchies assumes that methods higher up the hierarchy generate stronger causal claims than the ones lower down.

Figure 1 Typical hierarchy of strength of evidence for therapeutic interventions



Commonly, it is taken that randomised controlled trials (RCTs) are able to claim causal associations, whereas epidemiological studies (e.g. observational studies) are not [31]. This stance has given rise to a discrete area of philosophy of epidemiology, concerned largely with understanding whether causation can be established with lower-level methods [32]. The claim that smoking causes cancer, for example, is an epidemiological one. A defence for such claims is that in fact causation is not the concern for such methods, only statistical trends which allow probabilistic judgment on treatment efficacy. However, it is not easy to remove causal implications from statistical trends. To say that the health status of x% of subjects changed in a particular study group is causal by definition: something caused an effect. Further, if inferences to singular clinical decisions are to be informed from such trends, as is the purpose of EBP, then it would be nonsensical to offer a treatment if an effect was not intended. Therefore we do not accept that issues of causation are avoided on probabilistic accounts of statistical trends.

Evidential hierarchies are further characterized by the de-emphasizing of clinical experience and pathophysiological mechanisms of potential treatment effects. This immediately appears at odds with the structure of EBP frameworks which intend to facilitate the integration of research outputs with clinical experience. This implies that clinical experience has little to do with causation. More contentious is the idea that pathophysiological mechanisms say little about causal claims.

There are two recent developments which respond to some of the issues raised above. One is a recent monograph of the philosophy of EBP [33]. Although providing further philosophical justification for the epistemic supremacy of RCTs, Howick attempts to provide a rationale for considering coherent findings from different methods when making judgment on recommendation for treatment. In other words, if multiple levels of evidence supporting a single hypothesis provide coherent output, the strength of the causal claim can increase. Howick's work incorporates and reflects the contemporaneous stance of the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) Working Group [34-43]. In brief, GRADE set to address some problems raised by evidential hierarchies. The GRADE statement builds on the original hierarchy by focused consideration of methodological robustness, as opposed to the methodological approach *per se*. Thus, rigorous observational studies can be upgraded to the status of RCTs. From the GRADE perspective, high-quality epidemiology is indeed capable of making causal claims. The *de facto* stance for RCTs within the GRADE system remains, however, that they take epistemic supremacy. GRADE has little to say about traditionally lower levels of evidence, or Nof1 trials.

In sum, a categorical interpretation of evidence is seen clearly in conventional evidential hierarchies and this categorization is premised on the epistemic reading of discrete research methods. Further, epistemic emphasis and de-emphasis of discrete research methods is still apparent in revised contemporaneous models. This interpretation of evidence gives insight into the way health science understands causation. To say that evidence in health science is not related to causation is mistaken: the categorical interpretation is related to the ability of methods to establish causation. This itself provides evidence for the fact the EBP is in reality very much relying on a concept of causation.

CAUSATION

Within evidential frameworks, multiple causal concepts can be identified. It is not obvious that the different methods fit a unified concept of causation: epistemologically we can say that in one instance causation means such a thing, and in another it means something else. Health science seems to be operating with several ideas of causation and thus ontological tension exists. The broad assumption is that causal claims are made based on regularly occurring events. Within this, three different theories can be identified: interventionism, counterfactual dependency, and regularity. These three theories are implicit within different aspects of evidential frameworks.

In interventionism, causation is related to adding to a situation, for example in treatment studies: the effect of adding a drug to the sample population. This clearly relates to the structure and purpose of RCTs and observational studies. It also accounts for how methods at the top (Nof1 trials) and bottom (case studies; mechanistic research) might relate to causal claims. In this sense, change as a result of intervening is the focus of scientific observation. However, interventionism is an incomplete and insufficient account of causation when a categorical interpretation of evidence is considered. This is implicit within evidential frameworks by their de-emphasis of lower-level methods, and the exclusion of Nof1 trials from impact on recommendations. If interventionism was a complete and sufficient account, then methodological emphasis would be better balanced. However, evidential frameworks suggest causation as something other than what can be drawn from interventionism alone. It is now necessary to consider dominant research methods central to evidential frameworks which relate to causal claims. From this, further causal accounts can be drawn.

Observational studies record data from large groups representing populations of interest. It is possible to observe the effects of different interventions or conditions in such groups. However, the conventional contention is that despite the size and rigor of such groups, any claim made cannot be truly causal, only correlational. What is meant by this? Certainly, the claim is that correlation is something different from causation. In the categorical interpretation, RCTs offer causal claims. So what do RCTs provide to the causal account which is apparently lacking in correlation? RCTs are proposed to be able to make causal claims based on their methodological structure. Randomization provides closely matched groups and controlled manipulation of variables ensures that one group differs from the other by the variable of interest alone. Thus, any differences recorded between the groups have to be due to the variable of interest. This is what makes the claim causal. There is a limited way of understanding this, which is to treat causation as a Humean concept. Hume claimed:

> "we may define a cause to be *an object, followed by another, and where all the objects similar to the first are followed by objects similar to the second.* Or in other words *where, if the first object had not been, the second never had existed.*" (Hume, 1748: VIII:56 [44])

This should be read in two parts: first Hume states that a cause is a form of regularity, one object regularly followed by another. He then asserts a condition that the regularity should be confirmed by the fact that the second event did not occur when the first object did not exist. This aligns to a counterfactual conditional. The counterfactual account is developed by many

others e.g. Lewis who offers a comprehensive modern philosophical treatment of the conditional [45], and Cartwright who says:

> "...if two groups have identical distributions, save one (T) and a probabilistic difference obtains (O occurs in 'T' group only) then T is causally related to O" (Cartwright, 2007 [46])

Accordingly, the counterfactual state (control or comparison group) is in fact the truthmaker of causation, i.e. the proposition cannot be true in itself; it is the counterfactual that is making it true. We can observe a series of events following each other, but we only read causation into the observation if the same regularity is absent in another condition. Causation in health science is, then, counterfactually dependent. There remains the problem of accounting for casual claims based on observational studies, e.g. smoking causes cancer, which could be the case according to the GRADE statement based on possible upgrading of such studies. How can we read causation into this given the counterfactual conditional asserted by Hume? Hume allowed that causation could be wholly represented in fact by adherence to three criteria: temporal priority, contiguity and constant conjunction.

> "Every object like the cause, produces always some object like the effect. Beyond these three circumstances of contiguity, priority, and constant conjunction, I can discover nothing in the cause." (Hume, 1739 p. 409 [47])

Thus, if an observational study can demonstrate that the cause always precedes the effect, that the effect is consistently close to the cause, and that the association is repeatedly and constantly observed, we can in fact still claim causation in a Humean sense. This regularity view of causation offers the best philosophical stance for supporting causal claims from observational studies, in the sense of capturing how evidential frameworks view causation. So, we can say that there are at least two independent causal concepts evident in discreetly categorised research methods; counterfactual dependency and regularity.

Health science seems not to claim that causation is itself observable. It is only the regularities of one event being followed by another which is observable. In Humean terms, health science has no concern with understanding causes as anything more than regularities. That is, there is nothing internal to the causal process which relates to a cause producing an effect, e.g. some sort of real force or compulsion. Causation is just one thing followed regularly by another. Although neo-Humeans are happy with this stance as a complete account of causation, health science and practice might not be. Health science in one sense seems rich with a history of informative science ranging from laboratory studies through to large scale clinical trials. Further, health care itself is constructed of clinical experiences, patient values and presentations. If a Humean stance is to be taken, which seems the only plausible philosophical account of causation in health science so far, then what is there to be said of remaining knowledge, experiences and patient input? The EBP framework determines that clinical decisions – entailing causal intentions – should integrate as much of this knowledge as possible. A Humean commitment seems not to allow such background conditions a role in the understanding of a precise nature of causation in health care.

PROBLEMATISING ONTOLOGICAL TENSION

The interventionist account provides a back-drop for the proposed ontological tensions. Health science research methods seem to be concerned with understanding the effect of an intervention. Thus causation is what is added to a situation that interferes and changes the outcome. If only intervention counts as causation, then no causation is happening before the intervention. But often an intervention seems to be the primary cause because it is what takes the situation out of equilibrium, such as sugar increasing the insulin level in the body. The rest of the system was already doing its causal work before the intervention. It is not clear how an interventionist account deals with subtractive cases. For example, the reason for having a headache is that adequate water wasn't drunk. There is a further counter-example of multiple causes intervening with each other: two billiard balls that interrupt each other's natural course would result in the conclusion that neither or both are a cause [48].

Next we address a regularity view of causation in health care. We can say, given the regularities account, that causation exists when we observe the occurrence of two events associated with each other, for example, smoking is associated with cancer. Weak associations (low correlations), however, may be regarded as non-causal. But what does this say about the few cases in which something did happen? Causation must have occurred in these cases, but not in a Humean sense. The negative outcomes of low correlation studies relate to a Humean account – i.e. there has not been sufficient regularity observed to warrant a causal claim. But this can only be stated if referring to the population of the study as a whole, not as a collection of individuals. The clinical recommendation would be that the intervention does not cause the change in health (effect). So what did happen in the proportion of individuals who improved? This phenomenon cannot be accounted for by the way health science presently structures its understanding of causation. The only valid statement is one about a population. This does not serve to inform singular clinical decisions. A regularity account would still be unable to provide for causation in low-prevalence observations with strong mechanistic support, e.g. oral contraceptives and venous thrombosis. We could only say that oral contraceptives do not cause thrombosis. This would be correct for a population, but is uninformative for an individual. A probabilistic defence in this case in unsatisfactory. In low rate events – say a 1 in 1000 prevalence – a frequentist interpretation that an individual's chance of having the event is 1 in 1000 is uninformative. Probabilities are related to classification of kinds [49]. Thus, the chance of the event will increase as the classification characteristics of the individual move closer to the kind that will have 100% chance of the event. However, it is incorrect to talk of continuous probabilities in such cases; when framed in causal terms, the division is binary – either an individual will experience the event, i.e. 100% chance (as 1 in the 1000 did), or they will not, i.e. 0% chance (as 999 of the 1000 did). Regression to kind will only inform an instance of that kind. For example, sub-grouping from data to identify responders will only inform the sub-group, not members within the sub-group. Regression will continue until the smallest kind is reached - in the case of health care, the single patient.

There are two further counter-examples for correlation as causation: first, causation versus accidents. If causation is nothing but regularity, we cannot distinguish pure accidental

correlations and those that are genuinely causal, hence the progression in health science from epidemiology to RCTs. Second, the most robust correlations seem to indicate something other than causation, e.g. water is H_2O; humans are mortal. It causation is equated with regularity then too much comes out as causal.

Similar problems exist with a counterfactual account. In two groups, A (the intervention) and B (the control), there will be a certain proportion who achieve the outcome of interest, say 58% in group A and 42% in group B. Depending on the research question, power of the study, etc, statistical analysis will be performed to determine the significance of this difference. If significant difference is established, then the recommendation would be that, thus far, A is the preferred intervention compared to B. In other words, there will be a greater causal effect from A than B. But what does this say about the 42% of subjects who responded just as well with B? Again, the issue is that it looks like something causal did in fact happen to 42% of subjects in Group B, but this cannot be accounted for by the way health science considers causation. There is a further, simplistic issue surrounding the counterfactual stance. As stated earlier, the counterfactual conditional determines that the counterfactual (control group) is the truthmaker. In the above example, this would translate in the following way: if this were an uncontrolled observational study observing outcomes in Group A only, then the same result would obtain: 58% of the group achieved the outcome of interest. Depending on the research question, statistical modelling etc, this might not be considered satisfactory for a causal claim to be made. If the study was then changed into a counterfactual study by adding Group B and the same 42% obtains in this group, causation in Group A is then claimed, assuming significant difference. Therefore, Group B (the counterfactual) has acted as the truthmaker. If we now reverse this story, the truthmaker looks fragile: if we remove the counterfactual (Group B), reverting the study to an uncontrolled observation, then how can we accept that there is no causation in Group A? Something causal did happen in Group A. The causal work was in operation all along in Group A, so can we now refer to the factual, rather than the counterfactual as the truthmaker? This is an unacceptable proposition for the Humean account. It is clear, however, that the counterfactual conditional fails to get to the essence of what causation is.

Counterfactual theories, although Humean in essence, take causes to be the same as necessary conditions [45,50]. This would mean however that birth is a cause of death, and having a back is a cause of low back pain, i.e. the counterfactual condition in each of these examples demonstrates that if you hadn't been born, you would not have died; if you didn't have a back, you would not have low back pain. Counterfactuals notoriously struggle with cases of overdetermination: if only necessary conditions are causes, then if there are two causes that are each sufficient for the effect, then neither is necessary, thus neither is a cause. If a RCT failed to show a significant difference between two intervention groups, but in both groups a treatment effect was observed, then the counterfactual stance would have to support the statement that neither intervention caused the effect. The heuristic basis of counterfactually dependent RCTs does not seem secure. It seems that RCT outcomes do say something evidential about causation, but this is not constitutive of the causation at work.

There is a case which has yet to be considered, that of the Nof1 trial. This has conventionally sat at the pinnacle of traditional evidential hierarchies and its position there has been based on its ability to provide a strong counterfactual condition [28-29]. Nof1 trials are randomised controlled trials with a single subject. The conditions (interventions) are randomly allocated in temporal sequence and the individual acts as his own control [29]. Although these are counterfactually robust, Nof1 trials are commonly rejected in policy and clinical decision making due to their limits of external validity, i.e. the causal claim is established in one individual and therefore only generalisable to that one individual [29]. Group comparisons (RCTs) are claimed to have external validity based on their sample's ability to represent a population of interest. This differentiation, however, is rejected with a Humean account of causation as populations are considered as a single unit. Therefore, if external validity is compromised in Nof1 trials, then the same must be said for group trials: generalisability is per group, not per single instance within that group. Single instance cases of causation appear to have difficulty holding in a Humean account of causation.

INTRODUCING DISPOSITIONS

A dispositional account of causation is now introduced as an alternative causal ontology for evidence-based practice. It is proposed that such an account offers some solution to the problems identified above. It is also demonstrated that dispositional readings of evidential frameworks show how causation can be better understood relative to existing methods and causal accounts. Further, a dispositional account re-emphasises the importance of background conditions in understanding causes. Specifically, the role of single instance cases and mechanistic science is central to understanding causes dispositionally. The relationship of causes to individual situations in an EBP framework is also explained. A focused summary of the relevant characteristics of dispositionalism is given before attending to specific components of the evidential frameworks.

Dispositionalism takes causation to be a primitive and singular matter [50]. It is primitive in the sense that causation cannot be reduced to non-causal facts, such as regularity or counterfactual dependence. The health research methods of interest (RCTs and observational studies) make causal claims, but they are trading on a Humean sense in which causation is merely an observed series of regular events, plus or minus counterfactual support. The causal matter is reduced to associations of discrete events. Hence these methods say little about the essence of what causation is, beyond its regularity.

On causal dispositionalism, a cause does not necessitate its effect but rather tends towards it. Smoking disposes or tends towards cancer, but not everyone who smokes gets cancer. A tendency can be stronger or weaker. Low rate occurrences of causal connections are better understood from this dispositional account. The account has little interest in causal partners being considered as discrete events, i.e. a 'cause' and an 'effect'. Rather, partners interact with each other with far greater intimacy and simultaneity than the Humean account allows. An effect is manifested when there is sufficient interaction of mutually accountable causal partners. Immediately, the patient becomes of utmost importance in the causal process.

Because causation involves tendencies towards an outcome, rather than a guarantee of an outcome, then the traditional problem of induction is dissolved. The problem of induction concerned how we could know from past regularities that future cases are guaranteed to be the same. But if we understand causation in dispositional terms then there should indeed be no rational ground to make that inference. It is indeed always possible that the disposition does not get manifested in some future case.

Causal complexity is characteristic of a dispositions ontology. An effect is typically a result of many causal factors taken in combination. Complexity is not an immediate challenge for observational studies and RCTs. Study designs can tolerate it, e.g. complex regression analysis of multiple variables; randomisation producing homogeneity in unknown confounders. However, it is again evident that the type of causation read from these methods is saying very little about the essence of complex and context-sensitive causation, and how this relates to single instances. In this sense, translating probabilities from large-groups to individuals is failing to utilise and harness the richness of causal processes which can be understood from single instances.

Counterfactuals

Dispositionalism relates to counterfactuals in that counterfactual truths have dispositions as their truthmakers. Thus, counterfactually derived outcomes (e.g. findings from RCTs) are seen as informative but only in the sense that they are symptomatic of causation, and not constitutive of it. The causal work was done entirely in the factual case. Counterfactual dependency cannot be a complete theory of causation because it fails to include cases of overdetermination where there is more than one tendency towards the effect. This is unproblematic for a dispositional account, as multiple tendencies moving both towards and away from the effect are core to the ontology.

Counterfactual dependency also entails that the total history of an outcome will be a cause for this, while a dispositional account only counts as causes those factors that tend towards the outcome. It does not for instance include having a back as a cause of lower back pain, since this (although being a necessary condition) neither tends towards nor away from having lower back pain.

Considering causes as tendencies allows dispositionalism to reject the idea that the same cause always gives the same effect. Again, it is clear that a Humean ontology seems to be in search of the invariance associated with this relationship. An example of two smokers, one getting cancer while the other not, is not merely a statistical or probabilistic fact. For each individual who smokes, the propensity towards cancer will be different. Someone who smokes and has genetic pre-dispositions towards cancer has a higher risk of getting cancer than a smoker who also has no family history of cancer. The causation appears to be embedded in the process of the activity of smoking and its associated various physiological responses, not a distant statistical outcome. Variance is tolerated in a dispositional account.

Regularities

Dispositionalism relates to regularities because there is a real causal power that tends towards the effect. This tendency might be strong, which means that there is a discernible regularity from cause to effect, such as from smoking to cancer. But a tendency is less than necessity because it is never wholly sufficient to produce an effect. Whether or not the effect will occur will typically depend on which other causal factors are involved. An instance where the cause occurs but the effect does not will thus not be a counterexample to dispositionalist causation. For instance, some causes interact in nonlinear ways, which means that the same cause in two different contexts can contribute to produce two different outcomes. Clonidine and betablockers taken separately, for example, tend to lower blood pressure when taken in combination tend towards raising blood pressure. Conversely however, causation is not read directly from the correlation. As such, correlation itself is neither necessary nor sufficient for causation.

Interventionism

Dispositions relate to interventionism because to add something to a situation is to add a new tendency, hence intervention might causally affect the situation. However, interventionism fails to account for why this addition is causally efficient. On dispositionalism, the added factor is causally powerful only insofar as it is causally related to at least some of the causal factors involved, either by counteracting or adding to a causal process that is already present before the intervention. Cases of subtractive causes are easily accounted for dispositionally. When a contributing cause is removed, the remaining dispositions can take a situation out of equilibrium.

CONCLUSION

The idea of evidence-based practice has gained more and more support. Epistemically supreme evidential methods, e.g. RCTs, are thought of as gold-standard methods for establishing efficacy of interventions and as such have vast and deep influences on our health and the way the health-system works. We have tried to ask the question about causation in health sciences in the light of ontology. We have pointed to weaknesses in the current prevailing regime and suggested a better ontological understanding of causation and hence of evidence, and what would be evidence-based. Ontological tension exists in the way health science presently considers causation. It is arguable, however, that existing research methods can be read dispositionally. Less-than-perfect correlations indicate something causal occurring, but are by no means irrefutable evidence of some consistent or generalisable causal trend, however strong the correlation. RCTs can again indicate causal processes. However, the causal work is being done within each group and thus it is the groups themselves, not the counterfactuals, which act as the truthmakers. RCTs may be very good at displaying symptoms of causation, but they are not constitutive of causation. The greatest causal work can be seen in single instance cases. This is where the real nature of causation is witnessed. The interaction between causal agents; subtractive and additive forces tending towards and away from an effect; causal powers being passed from one partner to another. For the dispositionalist, the essence of causation becomes apparent. In a dispositional ontology, scientific research should

focus on the interaction of causal partners and not be dominated by the pursuit for statistical invariance in large-groups. For the clinician, the relationship between research findings and individual clinical decisions becomes clearer. An ontological review allows the notion of evidence-based practice to be re-evaluated.

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