Causation in Evidence Based Medicine

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Abstract

Evidence based medicine (EBM) offers an established framework for the generation, interpretation, and utilisation of information in medicine and the health sciences. Central to the practice of EBM is, I argue, the notion of causation. This thesis makes an original contribution to the philosophy of EBM through a unique identification of a causal theory in EBM, and then by demonstrating a reconceptualised theory of causation better suited to evidence based person centred care. PART 1 of this thesis demonstrates that a very specific idea of causation can be witnessed within the structure of EBM. This idea is typically Humean. Through a consideration of the structure and textual narrative of EBM, it is proposed that the framework substantiates central and canonical claims. These claims relate to the core activity of EBM being the informing of clinical decision-making through the transference of causal claims from prioritised research methods. I argue that a Humean notion of causation is problematic for the central and canonical claims, thereby presenting a paradox – EBM is structured to inform clinical decision-making about causation but is inhibited from doing so by the way this very structure conceptualises causation.

In PART 2 I argue for a reconceptualisation of causation that offers some solutions to the problems identified in PART 1. This theory relates to a dispositionalist ontology and takes causes to be derived from properties of an individual and as being things that merely tend towards an effect. Causes are seen as complex and context-sensitive, and whereby a traditional Humean account sees these factors as challenges to its epistemological reading, causal dispositionalism takes them as its starting point. To present this theory, desiderata are developed from existing narratives on EBM and elements of the theory set against these. In conclusion, I argue that if medicine and health care desire a framework of practice that is both evidence based and person centred, its causal theory must be reconceptualised. Causal dispositionalism offers an encouraging reconceptualisation.

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Published papers and conference presentations

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The central premises of the thesis were originally sketched out in:

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ERIKSEN T.E., KERRY R., MUMFORD S.D., NOER LIE S.A., ANJUM R.L. 2013. At the borders of medical reasoning: aetiological and ontological challenges of medically unexplained symptoms. *Philosophy, Ethics, and Humanities in Medicine*, 8:1-11.

ANJUM R.L., KERRY R., MUMFORD S.D. 2015. Evidence based on what? *Journal of Evaluation in Clinical Practice,* 21(6): E11–E12

Key reasoning and rationale for the background for *Chapter 2* came from:

KERRY R., MADOUASSE A., ARTHUR A., MUMFORD S.D. 2013. Analysis of scientific truth status in controlled rehabilitation trials. *Journal of Evaluation in Clinical Practice*, 19:617-625

MADDOCKS M., KERRY R., TURNER A., HOWICK J. 2016. Problematic placebos in physical therapy trials. *Journal of Evaluation in Clinical Practice*, doi: 10.1111/jep.12582

Elements of the arguments surrounding the positioning of Evidence Based Medicine and Person centred medicine (*Chapter 3*) were originally presented in:

TURNER A., BLAKEY J., KERRY R. 2014. Medicine in crisis, or a crisis in semantics? Working towards coalescence between evidence based medicine and person centred medicine. *European Journal of Person Centered Medicine*, 2: 81-83

KERRY R., ANJUM R.L., MUMFORD S.D. 2014. Causation as a way forward in person centred medicine. *European Journal of Person Centered Medicine*, 2:79-80

Notions of aspects of causation presented in *Chapter 4* and *Chapter 6* were included in:

EVANS D., LUCAS, N., KERRY R. 2016. Time, space and form: necessary for causation in health, disease and intervention? *Medicine, Healthcare and Philosophy*, 19: 207-213

EVANS D., LUCAS N., KERRY R. 2016. The anatomy of causation in health, disease and intervention. *Medicine, Healthcare and Philosophy*, In press

Book chapters

Detail and information regarding probability and risk (for example in *Chapter 1* and *Chapter 7*) relates to work presented in:

KERRY R. 2015. Communicating Risk, Chapter in: Jull G *et al* (eds) Grieve's *Modern Musculoskeletal Physiotherapy*, 4th Edition, Elsevier, London

Conferences

The ideas that form the central arguments of this thesis have been presented at the following conferences:

KERRY R. 2011. A counterfactual analysis of randomised controlled trials. *Causation in Science Conference (Biology)*, UMB, Ås, Norway

KERRY R. 2012. Ontology of causation in health science and evidence based practice. *Evidence and Causality in the Sciences conference*, University of Kent, Canterbury, UK

KERRY R. 2012. Ontological issues of causation in evidence based medicine. Invited symposium. *Evidence, Value and Practice Conference*, Manchester Metropolitan University, Manchester, UK

MUMFORD S.D., KERRY R. 2015. What is science and why do health professionals need to know? *Council for Allied Health Professions Research*, London, UK

KERRY R. 2015. The Methods. *CauseHealth Inaugural meeting*, Oslo, Norway

KERRY R., LOUGHLIN M. L., DE BIE R., LAMB S. 2015. "This house believes that in the absence of research evidence an intervention should not be used". Plenary session, *Chartered Society of Physiotherapy Congress, PhysioUK*, Liverpool, UK

KERRY R. 2016. What do clinical guidelines mean in person centred care? *Causal Reasoning and Evidence for Clinical Practice*, Oslo, Norway

KERRY R. 2016. Expanding our perspective on research in medicine. *International Federation of Orthopaedic Manipulative Physical Therapists Conference*, Glasgow, UK

List of abbreviations and acronyms

A	Abstract of a Treatise of Human Nature
EBM	Evidence Based Medicine
EBMWG	Evidence Based Medicine Working Group
EUH	An Enquiry Concerning Human Understanding
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
NICE	National Institute for Health and Care Excellence
OCEBM	Oxford Centre for Evidence Based Medicine
PCM	Person Centred Medicine
RCT	Randomised Controlled Trial
THN	A Treatise of Human Nature

A note on referencing Hume

Three texts of David Hume's are referred to in this thesis:

A Treatise of Human Nature, 1739

Abstract of a Treatise of Human Nature, 1740

An Enquiry Concerning Human Understanding, 1748

A Treatise of Human Nature (THN)

References are taken from the Oxford Philosophical Text - *David Hume: A Treatise of Human Nature*. 2000. Norton DF, Norton MJ (eds), Oxford, OUP.

The in-text referencing style for *Treatise* is:

Hume, 1739 THN Book.Part.Section.Paragraph

For example: "Hume, 1739 THN 1.3.16.20"

If a whole section is referred to then the paragraph will not be cited.

Abstract of a Treatise of Human Nature (A)

Source as above. The in-text referencing style for *Abstract* is:

Hume, 1740 A Paragraph

For example: "Hume, 1740 A 6"

An Enquiry Concerning Human Understanding (EUH)

References are taken from an electronic version based on *An Enquiry Concerning Human Understanding* (1748), OUP.

The in-text referencing style for *Enquiries* is:

Hume, 1748 EUH Section.Part.Paragraph

For example: "Hume, 1748 EUH 7.1.53"

Thesis Introduction

I have always had a worry about evidence based medicine. Not intentional, not cynical, not reactionary – just a worry. Of course, as a clinician, an educator, a scientific researcher, a patient, and a philosopher, I did and still do see much appeal in the compelling discourses and structures surrounding this scientifically driven framework. A framework whose intentions and strategies I take as genuine - a movement that aims to improve the health of as many people as possible in a cost-effective way. But this is precisely where my worry stems from: the proposed relationship between science and care. As a clinician I have always been enthused and motivated by the idea that therapeutic decisions could be based on best evidence – and as a scientist, especially so if that evidence originates from good science. But what is this *best evidence* and what is the *good science* that underpins it? And further still, how would such phenomena *translate* to clinical practice? Well, evidence based medicine has a substantial narrative about all of this. As a philosopher I remain worried. Hence this thesis.

This thesis relates evidence based medicine (EBM, henceforth) to the notion of causation. That is, how do causal claims established by the scientific research methods favoured by EBM – particularly those regarding therapeutic effectiveness – relate to individual instances of care,

or indeed policy? This in itself is not a unique concern. Indeed philosophers, scientists, researchers and the like have been challenged by this problem for centuries. It may, for example, be framed as a problem of induction; or an ecological fallacy; or relate to issues of external validity in health science, *et cetera*. However, throughout time and sectors, little resolution has been demonstrated with regards to this concern, and the space between research data and patient care is occupied by unsubstantiated assumptions and premises. Furthermore, approaching the issue through conceptual frameworks explicitly anchored to the notion of causation, especially at an ontological level, is something that is not visible within extant literatures surrounding EBM.

As such, this work is a philosophical thesis about the nature of causation in EBM. The thesis is one of applied philosophy, attempting to bear philosophical ideas directly on a practical concern. EBM is a challenging subject area because it is concerned with more than just scientific methods. The existing problems of causation are confounded by the way EBM is centred on the relationship between causal claims from scientific methods to their application in clinical decision-making. This thesis aims to make some sense of causation and science in a real world context, and asks the following questions:

- *What does a causal theory in EBM, as it stands, look like?*
- *Is this causal theory sufficient for the claims of EBM? and if not, then*
- *What should a theory of causation for EBM look like?*

In sum, the thesis argues that EBM presently conceptualises causation as a Humean idea, and that this is insufficient in respect of the core activity and claims of EBM. It then proposes a reconceptualisation of the nature of causation. This is based on a theory of causal dispositionalism. The thesis concludes that a dispositionalist account of causation can help address some of the fundamental challenges to the core activity of EBM.

But why causation?

What is it to say 'it works'? I take 'it works' as a causal term. In other words, we are saying something causes a change in another thing. In health care we are interested in knowing whether or not a therapeutic health intervention works, that is whether or not it causes a desired health effect. Thinking of causal relationships in this way signals what we understand of the processes that have generated sufficient knowledge to allow such a statement to be made. These processes have changed over time. Understanding what works was once a product of experience, or wisdom from a teacher perhaps. Modern health care sees these processes as insufficient and has developed specific research methods to generate knowledge of causal relationships. Formal observation and recording of patient behaviour as a response to interventions grew into what we now know as clinical epidemiology. A segue of observational studies into experimental-looking multi-condition trials was seen as a significant advancement of cause-claiming research methodologies. Randomised controlled trials (RCTs) were introduced in the 1950s with claims of epistemological superiority over other methods. This claim continues today and is witnessed by explicit notions of evidential hierarchies and

structures of what constitutes quality of evidence and strength of recommendations for practice. Almost parallel to the development in research methods was the re-framing of clinical epidemiology as a formal framework of EBM. (To note: when I talk about EBM I am talking about the 'post-1992' movement – which I will go on to define and explain in good time). This movement aimed to facilitate clinical decision-making by making best use of the evidence available. The evidence in this sense was normatively suggested to be multiple-sourced knowledge relevant to the clinical question:

> *"Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research"* (Sackett *et al*., 1996:71)

Depending on the nature of the clinical question, 'systematic research' would mean the best research for that particular question purpose. Questions of causation ('does this work?' questions) would appeal to methods of causation – that is, RCTs, or ideally systematic reviews of RCTs. Thus research methods are an inherent and immanent part of EBM, and findings from research should be used to directly inform clinical practice.

Since its introduction, EBM has been beset by scientists, researchers, clinicians, and philosophers debating its proposed merits and limitations. Epidemiology and RCTs seem to have been specifically focused on, with

issues of ethics, epistemology, pragmatics and morality commonly attended to. There is little doubt that how research findings relate to clinical practice is an emotive, sensitive, contentious notion, and of critical importance to best patient care. Philosophers in particular have found this area of notable interest. A recent health body funded research programme concluded with an explicit call for urgent attention to understand the richness and diversity of identified problems associated with establishing causal claims in epidemiology:

> *"The simplest and most direct way to satisfy this need [of addressing the academic problems of epidemiology] is to promote the philosophy of epidemiology as a distinct focus within the philosophy of science"* (Broadbent, 2011:15)

It is clear that the majority of philosophical concerns in this area have been associated with epistemological issues of research methods. Causation is talked of as a product of research methods, and philosophical quests have aimed to understand the best methods for producing causal claims. The issue of observational epidemiological studies versus RCTs is often used as a demonstration of epistemological differentiation. Most commonly, conclusions appeal for continued commitment to the experimental type comparative studies exemplified by RCTs. Appreciation of the ability of statistical analyses to compare group means against each other is linked to beliefs about the method's ability to differentiate correlation from causation. Observational studies can suffer from a lack of a comparable control group, a group so similar to the intervention group save one factor that any inferences drawn must be considered coincidental, not causal.

The ability of RCTs to create and control homogenous groups and manipulate interventions appeals to the scientist. If the groups are similar save one thing (the intervention), and a between-group difference in outcome is observed, then that difference must be due to the intervention. Causation, not correlation, can been claimed. Thus, when we state 'it works', we are saying something about the epistemological qualities of the research methods embedded in this framework of EBM. I will, despite what has just been said, eventually claim that EBM can be satisfied with causal claims from certain types of observational studies too, and in fact this holds the key to understanding the nature of causation in EBM, *as it stands*.

There are significant limitations with constraining philosophical analysis to epistemological concerns. 'It works' may well say something about epistemology. It also says something about what we understand of the nature of causation. Thus if we propose that epistemological concerns are of urgent priority to understanding best care, then ontological concerns also need to share that priority. Here is an example: I say 'it works' because I have attended to outcomes of epistemologically superior research methods (for causation at least). This exposes my appreciation of how knowledge is generated. However, I am also saying that what I mean by causation is that it is something inherently related to those methods in its nature. For example, I might genuinely believe that a causal relationship did not exist before it was 'produced' by the RCT, or whatever; or I might believe that the causal relationship did always exist but I didn't know of it and it took the RCT to 'expose' it; or I might say that I always strongly suspected a causal relationship but the findings of the RCT better 'justifies' my use of the intervention in some procedural sense.

Either way, what I am saying is that the nature of causation seems to be dependent on the research methods at hand.

There are now some problems. If evidential hierarchies are to be taken seriously, as is the normative stance, then causal ontology can be read from the hierarchy itself. That is, causation is something that is inherently related to the fact that groups are compared against each other, but not something that is part of 'lower level' evidential sources. This is a clear position that exposes how health science understands causation. I will use this normative stance as the basis of the majority of the analysis to follow.

The normative stance is sufficiently complex and challenging. However, the broad problem is exaggerated further by the descriptive stance. For example, causal claims are, in reality, made from multiple sources of evidence that may or may not include RCTs, for example, smoking causes cancer. But here is the problem: health science states that causation should exclusively be the domain of certain types of studies, and causation is dependent on and is characterised by that epistemology. However, causal claims are made otherwise. Therefore what causation is cannot be sustained on epistemological grounds. Further, epidemiology does not have a 'fall-back' epistemological position to widen the nature of causation.

Philosophers get beyond this problem by avoiding or deflecting ontological analysis. In fact, I am fully aware that attending to ontological matters of causation in EBM is not at all a popular or welcome thing to be doing, according to the sum of most philosophers of EBM. For example:

> *"EBM should not get entangled in ontological disputes but focus on the epistemological and inferential aspects of causation relevant for clinical practice"* (Strand and Parkkinen, 2015:533)

> *"Indeed, one might argue that it is preferable to remain neutral regarding methods for causal learning"* (Williamson, 2006:263)

More broadly, attempts have been made to draw any further philosophical discussion regarding EBM at all to a close - Djulbegovic *et al*. (2009) being a prime example. In this case, this is done by firstly spelling out what the philosophical underpinning of the movement is – with a distinct conclusory tone. Secondly, the issue of philosophical investigation is side-stepped by framing EBM not as a scientific or philosophical theory, but rather as a "*continuously evolving heuristic structure for optimizing clinical practice*" (Djulbegovic *et al*. (2009:158). Others have already sufficiently deconstructed the philosophical analysis of Djulbegovic *et al* (for example, Miles (2009b)), and I have no intentions of becoming embroiled in a debate about whether or not we should continue to think about what EBM is. I will simply take it that, in line with the majority of the extant literatures surrounding EBM, thinking and philosophising over this complex phenomenon is far from complete. Indeed, although intended to close the debate, a concluding statement from the above analysis simply serves to warrant urgent and deepened attention:

> *"Writing 30 years before the term "evidence based medicine" was coined, Tukey formulated the key challenge for the medical science and practice of medicine: how to move from estimation, with respect for "truthfulness" of evidence, to decisions in specific clinical situations. Clinical problem-solving and decision-making remain at the heart of EBM . . . The key challenge that needs to be tackled is how to elucidate a process of optimal decision-making. This includes the difficult task of defining rational decision-making for individuals and society and the application of evidence obtained from group observations at the patient bedside"* (Djulbegovic *et al.*, 2009:166)

I am confident therefore that for progress toward a meaningful philosophy of EBM to be made, philosophical (broadly) and ontological (specifically) attention is indicated. It does not seem enough to simply say *we shouldn't get entangled*, or *we should stay neutral*, or even that we should change what EBM is to avoid discussion. These defences seem vacuous and engineered to take the conversation away from uncomfortable questions such as "what *is* evidence?" Or even more fundamentally, what is the thing that our evidential elements are searching for?

I do have some sympathies with Djulbegovic *et al*.'s antagonists when their frustration is aired regarding the lack of development in understating what it is that is driving clinical decision-making and affecting the health and lives of millions:

> *"I re-iterate, then, that EBM remains, simply, the application of epidemiological data to clinical practice, nothing less and certainly nothing more. Nothing within Djulbegovic et al.'s inflated philosophical treatise can or does alter this basic fact. Another fact is this: medicine has entered a period of enormous and increasing complexity . . . And another fact is this: the continuing reductionism of EBM has,* ipso facto*, no place there"* (Miles, 2009b:928)

From this sort of dialogue my concern stems. And from that concern my position has developed to one of becoming increasingly inquisitive about the most fundamental things that we seek in order to understand how we can affect peoples' health - causes. An understanding of the nature of causation, I claim, independent of but supplementary to epistemological inquiries into research methods, will enhance and progress a philosophy of EBM.

Why causal dispositionalism?

The thesis makes it clear and is open about the fact that the framework for a reconceptualised account of causation is related to an idea of causal dispositionalism. That is, there is a single example of how causation might be reconsidered given the insufficiencies of EBM's current causal account. This means that the thesis is not concerned with an analysis on which of several possible alternative accounts in the world is best for the *new concept*. And, of course, there are other accounts on offer. Specifically,

causal pluralism, epistemic theories and critical realism have been put forward as alternative models in the prevailing literatures as ways to address the scientific and humanistic challenges presented by healthcare. So one option for me would have been to build on these ideas, rather than introduce a new one. But this is precisely one of the reasons why I have chosen this approach - because it *is* new. The thesis presents a unique account of how a dispositions theory of causation can be applied to the field of medicine and health care.

Of course, the theory itself is nothing new, but rather grounded in the tradition of philosophy to at least Aristotle. Having said that, the interpretation of the dispositional theory of interest is in fact something different to a classic sketch of dispositions. The term *causal disposition* (with its numerous suffixes) is one I will use throughout, and the term relates a specific account of dispositions given by philosophers Stephen Mumford and Rani Anjum. The detail and nuances of the theory will be presented within the thesis, particularly in the second half. In brief however, the theory is one that is based on an ontology of powers and sees causes as real entities that can only ever tend towards an effect. Causal dispositionalism takes the world and its causes to be complex and context-sensitive. Causation is considered a process, and something primitive – that is, causes are not things that can be analysed and reduced to something else like discrete events ('the cause' followed by 'the effect', for example). It is these fundamental features of the theory that, as a clinician at least, I found attractive. This leads on to the second reason why I have purposefully focused this thesis on causal dispositionalism. This is because I do genuinely anticipate that a dispositions account of causation will respond to many of the challenges set in the first part of this thesis more

satisfactorily than existing alternatives. I do not claim this with any bias on my part. Rather, there is a genuine recognition that the characteristic features of the theory intuitively appeal to many problems of health care that fundamentally seem to be related to complexity and variation (context). In particular, pluralistic and epistemic views will be positioned against the dispositions account as desiderata are addressed. Again, this positioning is neither intentionally combative nor comparative. More so it is to function as a framework to help understand the possible integration of a reconceptualised theory of causation into the world of health care.

I will not refer to critical realism in the same way, and I make no attempt to sketch out the similarities within and differences between this view of the world and that of causal dispositionalism. This is simply not a purpose of this thesis. I accept that there are many features of both world views that relate closely to each other, and dispositionalism is sympathetic to critical realism in many ways[1]. The primary focus of this thesis is however to work towards a reconceptualisation of causation. Although critical realism operates on a complex world and accepts generative mechanisms and powers in its ontology, for example, I think for the purpose of this thesis dispositions has the upper hand. Dispositions, I think, can relate to epistemological and methodological matters more readily and avoids both a commitment to a broad social theory, and a relativist stance – common criticisms of a critical realists view.

[1] Critical realism is used extensively as an analytical lens in medicine and health care literatures. However, for specific examples on methods and evidence, insightful realist critiques are provided by Connelly (2004) and Edgley et al. (2014).

As such, I am confident that a dispositions account of causation can respond more acutely and precisely to the sorts of matters raised in this thesis.

What this thesis is and is not

The parameters of this thesis are tight and the focus is clear. I want to know about the nature of causation in EBM. The thesis is therefore about causation, but its primary commentary is on EBM. So, although this is a philosophy project, it is applied; and although I will be using philosophical thought and ideas to recognise and problematise features of the subject domain, I do not make any aspirations to develop the philosophy itself. The unique developments are in a novel interpretation of an aspect of EBM, causation; and a novel consideration of a reconceptualised theory of causation, causal dispositionalism. I am not the first person to say that there is something Humean about the way medicine and health science operates (although explicit Humean accounts are rare), but this will be the first contribution that details precisely how and why this is so, and then to present this as a critical concern for EBM. Similarly, I make no allegations of a unique contribution to the theoretical work concerning causal dispositionalism. I am merely using existing work on this theory as an example of how causation could be reconceptualised in EBM. However, this will be a unique application of the theory. Throughout the thesis there will be explicit and implicit reference to the relationship between ontological and epistemological matters, and the thesis deals with an ontological reconceptualisation. Consequently it might feasibly be assumed that there may be a focus on reconceptualised

research methods, but this is not the case. The thesis does point towards possible reconsiderations of the sort of knowledge we read from existing methods, and statements regarding further research towards the development of new methods form part of the conclusions. However, research method development falls outside the current remit.

The emergent conclusions will detail the impact this thesis has on the current state of a philosophy of EBM. In sum, the work done by this thesis will represent an initial and significant stage in providing a substantial philosophical underpinning for an evidence based, person centred framework that is inclusive of multiple sources of evidence and embraces the complexity and context-sensitivity of humans and health.

I declare that there is an empirical background to the broad project here, but empiricism will play no part in this thesis. What I mean by this, from my perspective, is that I have observed with great interest for some time published data on the epistemic trajectory of research findings in medicine and health care. Particularly so the work of John Ioannidis *et al*. From Ioannidis' seminal publication on the accuracy and meaning of trial results (Ioannidis, 2005) I have been somewhat fascinated by what this says about research methods, and science in general. In fact, my inquisition led to our own project which attempted to extend Ioannidis' rationale to focus closer on study design quality and truth status in physiotherapy trials (Kerry *et al*., 2013). However this line of inquiry soon turned from empirical questions to philosophical ones - least of all due to a realisation of the

paradox of inquiry we were getting entrapped within. To reiterate, this thesis is one of philosophy, albeit very much applied.

The thesis is sympathetic to a number of contemporaneous emergent movements from health humanities with similar directions of travel. *Person Centred Medicine* is one such movement and will form an explicit part of the thesis narrative. Other 'shop-floor' movements such as the *Campaign for Real Evidence Based Medicine*, the *Evidence Based Medicine Renaissance Group*, the *Critical Physiotherapy Network*, for example, are equally concerned with developing a world where patients are seen as humans and are considered as central to, not subsequent to, science informed decision making. Although I will not be detailing the accounts of all of these movements, I will state that, in conclusion, I see this present work as a contribution to the philosophical justification of an EBM renaissance. It is with this in mind that I now present a somewhat unconventional aspect to this introductory chapter. The following section presents a clinical case study.

Case study

The sort of real-world dilemma that has served to inspire, motivate and problematise the critical and fundamental dimensions of this thesis is represented by a case study that is detailed in Appendix 1. There is nothing methodological or sophisticated about the use of a case study here, it is purely illustrative. It does not at all form part of my research approach, this is purely narrative. Furthermore, I will not even be referring to it within the main body of the thesis. I will only briefly return to it in the final chapter during the conclusions. However, I do feel the case

characterises and highlights many of the tensions, discords, and unsuccessfully resolved core elements of EBM. The story is one of a person narrating their experience of health care as a patient, and I will briefly report on the key meta-themes here. The narrator talks about frustration and confusion regarding the clinical decisions being made for her care. She often draws out the intended logic of her care, but then quickly positions this next to her own rationalisation as an individual human. The problems highlighted by the narrator could well be responded to with an EBM counter-claim for a call for better trials and more data that could increase opportunities for better external validity. But the case says so much more than this. The narrator refers to multiple sources of evidence, including mechanistic data, and the patient herself. It is difficult however to reconcile her humanistic rationale with the direction and structure of EBM. The following is an extract as an example. The narrator is reflecting on the decision regarding whether or not to take non-steroidal anti-inflammatory drugs, which could help with pain, but could also increase risk of gastro-intestinal (GI) bleeding, and delay bone healing:

> *"In randomised trials, post-surgical patients had a higher incidence of GI bleeding. So that's the objective evidence – we know that, we know that. Now let's look at the individualised evidence about this particular patient . . . Um, I've taken non-steroidals for 30-odd years, never had any problems with them. So that's the first bit of evidence. The second bit of evidence is that as part of my sports obsession, I think I'd call it when I was younger, I encountered several stress fractures, all of which healed very quickly indeed on non-steroidals. And in*

> *fact, healed rather more quickly than I was led to believe would be the natural history. So people would say, 'you're going to be off your sport for 6 weeks', I was only off for 3 weeks. So for me PERSONALLY, non-steroidals do not appear to delay MY bone healing"* Appendix 1:355-356

As stated, one approach would be to call for a better trial that included subjects more akin to this patient. But this is not what the story is here. What is being presented are the evidential elements that seem causally relevant. But the way EBM structures and defines its causation, there is no logical way to accept these as valid sources of evidence of causation. What is needed here is not better trials, but – in support of this thesis – an account of scientific causation which values multiple sources of information within the causal story. So then, when we say best evidence of therapeutic effectiveness we mean something quite different to what EBM would say now. I ask the reader to implicitly consider this case study during the reading of this thesis, and nothing more.

In conclusion then, this chapter has introduced a thesis concerned with a philosophical account of causation, but whose primary interest is in medicine and health care. The scholarly lacuna exists. Talk of causation in the philosophy of EBM is even frowned upon. Because of the lacuna and despite the frowns, it is anticipated that the thesis will offer an opportunity for the philosophy of EBM to develop, and promote a move towards a more holistic and person centred model of health care. The final section of this chapter presents an outline of the thesis content and structure through a synopsis of each chapter.

Structure of thesis and chapter synopses

In Hegelian terms, the dialectic is:

Thesis: The present understanding of causation in evidence based medicine (EBM) is insufficient to account for the central and canonical claims of EBM, that relate to the use of knowledge derived from prioritised evidential elements to inform clinical and policy decisions.

Antithesis: It is not necessary to be concerned about the nature of causation as robust methods are sufficiently able to establish knowledge regarding the efficacy, effectiveness and efficiency of therapeutic interventions. Even if causation was of importance, EBM as it stands has a satisfactory notion of causation.

Synthesis: Robust methods do offer something, but it is not necessarily evidence of therapeutic effectiveness that can be readily utilised in other contexts, that is clinical and policy decision-making. The essence of such methods are indeed causal, and so causal claims derive from them. However, this isn't, on the present understanding of causation, the sort of causation desired in the clinical/policy context, which is a complex, humanistic, person centred environment. A reconceptualisation of the nature of causation might provide a better account for how multiple evidential elements might relate to each other in complex and context-sensitive situations. In turn, a revised ontology might inform what we take from existing methods, and the development of new research methodologies.

The thesis is written in two parts: PART 1 sketches out the history and background of EBM together with the challenges faced in the core activity of EBM. It then continues to identify and problematise the Humean nature of causation within the operational structure of EBM, focusing on the prioritisation of particular evidential elements above others. PART 2 makes the move towards reconceptualising causation in dispositionalist terms. It introduces causal dispositionalism through vector modelling, and continues to develop the application of this theory through desiderata of what a theory of causation for EBM should look like. The main arguments of the thesis are summarised and conclusions drawn from emergent themes in the final chapter.

PART 1 (*Chapters 1 – 4*)

Chapter 1: This chapter aims to provide a focused, historical analysis on the origins of evidence based medicine (EBM). The purpose of this is to foreground *chapters 2 - 4* that attend in more detail to the causal characteristics of EBM as a movement. This chapter uses textual commentary on EBM as a source to develop the critical narrative. First, the development of EBM as a movement from early clinical epidemiology is considered. This is to give an understanding of the deep scientific foundations of the movement. I present this as being an important part of the background justification to warrant subsequent attention to the notion of causation in EBM. The idea is to elucidate what the causal intents of the movement are. The second part of the chapter deals with the statistical foundations of the dominant research methods used in EBM. Frequentism

is presented as the core statistical principle to which the majority of research approaches are anchored. This provides well for objectivity, but as a basis of a research programme aimed on clinical application, might also demonstrate significant limitations of inference.

Chapter 2: This chapter begins the search for a deep account of causation. It does this by examining the evidential structures of the movement through both textual narratives and analytical review. It is here where the central claim of EBM: *"evidence from study designs higher up the hierarchy more reliably informs therapeutic decisions"* (from La Caze (2008:361)) is used to develop a conceptual framework that will sit in the background for the remainder of the thesis. This conceptual framework is characterised by the idea that EBM can be reduced to two canonical claims:

> *Claim 1: Evidential priority is given to comparative research methods, utilising statistical estimates, above other elements of research and practice.*
> *Claim 2: Data from prioritised methods should determine clinical decision-making.*

Person centred medicine is proffered as a conceptual challenge to the tenets of EBM, and this will form part of the back-drop to the complexities of health care through which the causal account might be further challenged. This chapter is also where the essence of causation is first alluded to as something broadly Humean. A Humean account is apparent, I argue, due to the way EBM structures its sources of evidence. With this in mind, a paradox is noted: the very prioritisation of evidence elements for

use in clinical decision-making (*Claim 1*) prohibits use of this evidence in clinical decision-making (*Claim 2*).

Chapter 3: The thesis so far rests on the assumption that causation is something Humean in essence. This assumption gives an opportunity to warrant claims towards i) the idea that this understanding of causation is problematic for the central and canonical claims of EBM; and ii) a reconceptualisation of causation is therefore required. This chapter deals with the proposition that this necessary assumption might be fragile. It takes two challenges to the Humean account: i) there is a possible misinterpretation of the evidential structuring seen within EBM, and ii) deeper uncertainties as to precisely where within the EBM methods causation may actually be claimed. This chapter deals with these two challenges in turn. The first challenge is addressed via an essentialist account of evidential hierarchies and concludes that the only valid position to adopt with regard these hierarchies is that they must be read categorically in respect of epistemic prioritisation. The second challenge forces a deeper exploration into evidential elements to understand precisely whether or not causal claims indeed emerge exclusively from the assumed evidential sources identified in *Chapter 3*. It concludes that, in essence, causation in EBM as it stands is, and can only be, related to regularities. I conclude overall that consideration of these potential threats to the argument serves in fact to strengthen the proposed position.

Chapter 4: Mechanisms are framed as an analogy to Hume's *necessary connexion*. The problem of necessary connection has vexed philosophers throughout history in terms of its role in scientific discovery. EBM de-emphasises the causal value of mechanisms, but commentators on EBM have tried to juxtapose it with the traditional framework. I focus on

Howick and the Russo-Williamson Thesis as two exemplar commentaries on this challenge. I argue that they have been unsuccessful in doing so because of the fixed causal account in the traditional framework, hence further indication for reconceptualisation. This chapter then asks what should a theory of causation look like if it is to be relevant for EBM. It then sets out four desiderata as a conceptual framework for this.

PART 2 (*Chapters 5 – 7*)

Chapter 5: Causal dispositionalism is now introduced as a possible alternative theory of causation for EBM. The key features of the theory are sketched out through the notion of modelling. Vector models are preferred for dispositionalism, and these are summarized to highlight features relevant for this thesis. These features relate to the core ontological assumptions of dispositionalism, that is, causes only tend towards an effect and complexity and context-sensitivity are taken as a starting point for what causes are.

Chapter 6: This chapter is structured around the first two desiderata: D1) *Explain the causal role of content from particular research methods*, and D2) *Motivate a viable epistemology*. For D1, the dispositionalist response is straightforward: the content that is being referred to in the traditional Humean account is not of causation, but something else. The essence of causation has not been reached and as such, any explanation related to causation cannot be given. What dispositionalism offers is a view that sees causation within the core of the content itself. Dispositionalists see various causal factors that may or may not manifest in an effect. The causal role of these events for dispositionalism is the notion of how they manifest and how they may tend towards and away from anticipated thresholds.

Dispositionalists are unsatisfied with causal explanations that relate to frequentist interpretations of probability, as probability should be thought of in relation to the propensities held by causal factors. For D2, an argument is built against Williamson's provocation on the epistemic role of dispositions that states that a dispositionalist ontology fails to relate to an epistemology of causation because it takes causes as real entities. I claim that causes being real is in fact the position that allows a viable epistemology.

Chapter 7: This chapter considers the third and fourth desiderata: D3) *Account for causal processes in individual-level clinical decision-making*, D4) *Help understand and assess additional premises and assumptions needed to bridge the inferential gap between population-level evidence and clinical decisions*. D3 is approached through a reframing of external validity in terms of general and particular causal claims. Analysis of how different causal theorists see the relationship of these claims in relation to each other is provided, with specific reference to David Armstrong's realist theory on laws of nature. This leads to a proposition of how an understanding of general claims can be provided by particular instances. Causal dispositionalism sees value in both types of claims, but takes single instance (particulars) as its starting point to understanding causation. For EBM, the patient then becomes central to the causal process. A case study of low back pain is provided to highlight the features of a dispositions theory in respect of this desideratum. D4 represents the core concern of this thesis; that is, the translation of causal claims across spatiotemporal environments in line with the central and canonical claims of EBM. This desideratum stems from a direct rebuttal of a dispositionalist stance regarding causation in EBM from Strand and Parkkinen (2014). The defence is therefore framed

exclusively with this dialogue. I argue that Strand and Parkkinen make the mistake of considering causes to be either necessary (within probability bounds) or purely contingent. Causal dispositionalism offers a modality of *sui generis* that falls somewhere between necessity and contingency, and as such can respond well to many of the critical concerns towards the assumptions of inference.

The final chapter brings the thesis to a close by drawing out conclusory themes from the thesis' key arguments and identifying key questions that warrant further study.

PART 1

A Humean Interpretation of Causation in Evidence Based Medicine

Introduction to PART 1

This thesis sets out to provide a reconceptualisation of the nature of causation in EBM, or at least understand if such a move is warranted. The primary concern is whether the causal claims deriving from preferred or prioritised research methods offer the sort of information about causation that would be required during individual clinical decision-making or policy making at a population level. This concern is not unique. This is a philosophical thesis, but there are many non-philosophical approaches to this concern. The philosophical approach I am taking however is towards whether the way causation is understood in EBM is sufficient for the central and canonical claims of EBM. These claims are related to the use of information from prioritised evidential elements in other spatiotemporal environments, which are characterised by their complexity and person-centredness.

Before a reconceptualisation can be considered, it is obvious that an understanding of the present conceptualisation of causation in EBM is developed. This is the purpose and focus of PART 1. I take EBM for what it is: a complex, historically and logically rich movement that has the interests of the health of the world as its core concern. At its centre sits an intention to exploit the best of scientific methods to try and understand all

aspects of health care[2]. The exploitation of these methods is for the benefit of patients - that is knowledge from scientific methods should provide evidence of therapeutic effectiveness that is suitable for use in spatiotemporally removed environments.

EBM recognised the onerous nature of its task. It is this self-awareness that has helped develop EBM into much more than 'just' a scientific activity. The complexity of decision-making is recognised explicitly throughout the history of EBM, and models and tools have been developed accordingly to allow for and facilitate this. Thus, EBM seems humanistic and person-centred. It is this, paradoxically, that seems to be at the centre of the challenges for EBM. How does the holism and humanism of a person-centred intent relate to the reductionist and statistical rigor of its adopted scientific methods? I am suggesting that causation is critical to a complete philosophical account of this substantive area. During this first part of the thesis, I will develop an account of causation that is informed by what EBM is. This will necessitate a review of where EBM has come from, how it presently operates, how it structures itself, and how it considers the juxtaposition of discrete evidential elements. It is through this process that, I claim, the nature of causation in EBM can be understood. Or at least a visible framework of causation can be identified, through which the ontological aspects can be further considered: a task for PART 2.

I am talking about EBM as if it is some sort of discrete natural phenomenon. Of course, it is not. It is a socio-political movement

[2] I am particularly interested in how people get better; therefore this thesis primarily focuses on therapeutics (although some aspects of what causes disease will be considered at times).

developed by human beings. As such, accessing the essence of EBM is primarily through the textual account of the movement. It is equally important to then separate the logic and notions of the movement from the authoritative text. This is what PART 1 will attempt to do.

In sum, PART 1 offers the following contribution to the broad thesis: the way EBM structures its evidential elements - that are a consequence of its rich statistical and epidemiological history - exposes what EBM considers as being causation. This is essentially a Humean account of causation, following Hume's commitment to a regularities view of the relationship between events. This account is inconsistent with the central and canonical claims of EBM. Therefore, a reconceptualisation of causation in EBM is indicated.

PART 1 consists of four chapters:

Chapter 1 provides a historical review of the evolution of EBM. This sketches out the influences on the movement that in turn have served to influence the way it considers establishing causal claims. Some emphasis is given towards the detailed statistical approach observed within EBM. This is exclusively for the purpose of understanding the scientific intents of the movement, rather than some attempt to contribute to the debate on statistical inference.

Chapter 2 begins the search for a deep account of causation. It does this by examining the evidential structures of the movement through both textual narratives and analytical review. It is here where the central (from (La Caze, 2008) and canonical claims of EBM are committed to as a conceptual framework for the ensuing analysis. Also, this is where the essence of causation is first indicated to as something broadly Humean.

Person centred medicine is put forward as a conceptual challenge to the tenets of EBM, and this will form part of the backdrop to the complexities of health care through which the causal account might be further challenged.

Chapter 3 presents some challenges to a Humean account. An essentialist critique of evidential hierarchies stakes a claim that the epistemological essence of evidential hierarchies creates further ontological tension on the causal account. Only through analysis of the relationship between randomised and non-randomised (observational) studies is the final commitment to a Humean account provided.

Chapter 4 focuses on mechanistic science and mechanistic reasoning. It does so as an example of how traditionally de-emphasised sources of knowledge and reasoning have tried to be given causal warrant within existing structures. Mechanisms can also be seen as analogous to Hume's *necessary connexion*, and so are fitting when working on the Humean puzzle. These attempts have failed because of a fixed Humean stance.

PART 1 concludes that the limitations of how the traditional EBM stance reveals its causal theory call for a reconceptualisation of a causal theory. An alternative theory should be able to respond to desiderata informed by the extant literatures.

Chapter 1: A Historical and Evolutionary Account of Evidence Based Medicine

1.1. Introduction

I take the idea of Evidence Based Medicine (EBM) to mean the movement that emerged in the early 1990s as a result of the activity of the Evidence Based Medicine Working Group (EBMWG) at the Department of Clinical Epidemiology and Biostatistics, McMaster University, Ontario, Canada. The rationale for this is not that this movement has or had complete authority on the idea of EBM, nor is it because there is a belief that prior to this time medicine was not based on evidence. Rather, it is because this movement substantially represents (practically and intellectually) differentiating mechanisms of thought and practice to any previous or corresponding observed procedures of practicing healthcare, at least at that point in time. Further, this movement is the one most visibly represented in literature surrounding EBM, and the one that has most visibly infiltrated numerous dimensions of contemporary healthcare including teaching, research, and commissioning of healthcare provisions. Additionally, by virtue of its nature and real-world impact, this model has courted an unprecedented amount of controversies and critical attention during the past 20 or so years. Below is a focused history of the

development of this model. The intention is to provide a landscape by which the critical literature can be contextualised, and thought towards its philosophical and practical operations can be further developed.

As suggested, it would be erroneous to say that before what we now know as EBM[3], healthcare practice was not based on evidence. It always has been, it is simply that throughout the ages, the idea of what constitutes evidence has changed. Historically, clinical observations have formed the bulk of what clinicians may have referred to as evidence. To support such clinical observations, medical practice has relied heavily on understanding the causes of illness and health through systematic study of the scientifically observable mechanisms. Further, systematic observations of large groups of (ideally homogenous) patients receiving the same intervention have been considered valid procedures for understanding the effects of medical interventions. This relates to the notion of clinical epidemiology that serves as a natural starting point to the evolution of EBM.

1.2. Epidemiology: hunting for causes

Epidemiology can be defined as:

> *". . . the study of the distribution and determinants of disease and other health states in human populations by means of*

[3] From this point onwards, the acronym 'EBM' will be used to refer to the '1990+' notion of evidence based medicine, unless stated otherwise.

> *group comparisons for the purpose of improving population health"* (Broadbent, 2013a:1[4])

This definition serves two distinct purposes. First, it allows some initial analysis of the nature of methods and methodologies that seem to have evolved in EBM; second, it is sufficient to act as the informative procedural background to EBM.

To address the first purpose regarding the nature of these forms of inquiry, Broadbent sets out to identify a number of central themes that are characteristic of what he considers to be epidemiology. First is that epidemiology focuses on causation[5]. A causal intent is seen in the above definition through the words 'determinants' and 'improving' - both causal terms. The data acquired by epidemiologists is not primarily intended to develop grand theories of the world, nor used to justify the discovery of laws of nature. Epidemiology seems to have, rather, an urgent interest in trying to establish causal connections between two or more events:

> *". . . hunting for causes is an overriding characteristic of the most famous episodes in epidemiology and finding them is characteristic of its most famous successes. The discovery that drinking water contaminated with excrement from cholera*

[4] There is a vast literature on the structure and development of epidemiology over the last 50 years or so. For the purpose of this Chapter, I am interested in sketching out some philosophically relevant broad themes related to how epidemiology can be thought of. With this in mind, I will use Broadbent (2013a) as a sole reference source at this point. This is because this work reflects a comprehensive and contemporaneous philosophical commentary on epidemiology that is sufficient for exploring the underpinnings of EBM within the parameters of this Chapter.

[5] This (causation) is of course the core concern of the present thesis and as such forms the primary focus throughout.

> *sufferers caused cholera; the discovery that pellagra is not an infection afflicting those living in poverty but is caused by diet; the discovery that smoking causes lung cancer – these are epidemiological milestones, and they all involve the identification of causal connections between what epidemiologists refer to as "exposures" and "outcomes""* (Broadbent, 2013a:3)

If epidemiology is in some way to be related to EBM, then immediately the idea of EBM necessarily has something to do with causation. Precisely what causation is and how it is established are not things that are clearly visible in broad definitions and explanations of epidemiology. The detail and analysis of such questions comes only when there is a deconstruction of these broad principles. This will be returned to in *Chapters 3 and 4*. For now, laying-out the foundations of EBM is sufficient.

Next, Broadbent proposes that epidemiology is a-scientific in the sense that "*the standard philosophical images of science*" (Broadbent, 2013a:3) do not feature in the act of epidemiology. Although use of quasi-experimental designs is part of epidemiology, Broadbent is strict in his philosophical interpretations regarding use of interventions and controlling for all variables. Further, epidemiology is characterised by its lack of theory (Broadbent, 2013a:3-4). The discipline seems to be concerned solely with its methodologies and its discoveries, which again is clear in the definition.

Epidemiology concerns "*(the) study of the distribution and determinants"* (Broadbent, 2013a:2), and this seems to be to the exclusion of any faithful commitment to a specific domain. In other words, the methods of

epidemiology are suited and are of relevance to any domain that seeks to understand the sorts of relationships that epidemiology can offer, for example health, economics, education, *et cetera*. Broadbent's concern is with the possible implications of the unestablished and unpredictable limits of its use. Significantly, and particularly for this thesis, is that epidemiology is most visibly characterised by the centrality of population thinking, "*improving population health"* (Broadbent, 2013a:2). It assumes that populations are "*entities which can bear properties"* (Broadbent, 2013a:7), and that the health of a population has something to do with the health of individuals. Again, this is the core concern of the present thesis. Lastly, if epidemiology is to observe patterns of health determinants in populations with the intention of making grand inferences from these observations, then it is a high risk phenomenon. If health policy is to be determined through epidemiology, then we must have sufficiently high confidence in its methods. Can we be satisfied with its outcomes, or is the epistemic risk high enough to warrant additional caution to inferences from its methods?

This chapter now considers epidemiology, together with its associated problematised characteristics, and reviews its influences on the development of EBM. In line with this is a necessary review of other significant associated influential thoughts and works. To begin, the historical development of EBM as a movement is reviewed.

1.3. Evidence Based Medicine *as it was, as it is*

The term '*Evidence Based Medicine'* was first formally[6] introduced in the field of medical epidemiology in 1991 (Guyatt, 1991). In this brief eponymous editorial, the proposed difference between "*the way of the past*" and "*the way of the future*" is striking: "*The way of the future . . . depicts an important advance in the inclusion of new evidence into clinical practice*" (Guyatt, 1991:A-16). A simple case study is presented with the "*way of the past*" being the internist's reliance on her senior's knowledge (*ibid*). "*The future*" is a considered and critical appraisal of published population data, involving technical skills to correctly search for this information (*ibid*). There are suggestions here of an early formalised definition of EBM. In addition to information technology skills, Guyatt states that EBM:

> *". . . also requires judgement of the applicability of evidence to the patient at hand and systematic approaches to make decisions when direct evidence is not available"* (Guyatt, 1991:A-16).

Themes emerge in this initial monograph that are visible later in more developed and formalised definitions of EBM. It is clear that there is to be a shift in the source of evidence, in this case from the knowledge of experienced clinicians to published data. There is also a clear statement

[6] The term does actually appear sporadically throughout literature on medical statistics from the 1930s up to the 1990s. However, in line with using the '1990s' as the starting point for this review, I will consider Guyatt's 1991 paper as the formalised introduction of the term.

that this '*new*' evidence should be considered in the context of the patient for whom it is intended. Lastly, despite the proposed importance of published data as evidence, it is anticipated that there may not always be sufficient evidence. Therefore some form of contingency strategy is needed to facilitate decision-making. There are no allusions though to this strategy being a fall back to the '*way of the past*". The past is truly the past, it appears.

The idea of EBM was exposed to a wider community, and in more detail, a year later (Guyatt and EBMWG, 1992)[7]. This paper is the first to demonstrate the commitment of the *Journal of the American Medical Association* (JAMA) to the dissemination of the thoughts and workings of the EBMWG. The paper offers a development of the defining principles of EBM. There is a sense of greater confidence in what should constitute the operationalisation of the movement. The first part of the paper's introductory statement summarising the defining principles of EBM suggest reconsideration of traditional components of practice:

> *"Evidence based medicine de-emphasizes intuition, unsystematic clinical experience, and pathophysiological rationale as sufficient grounds for clinical decision-making "*
> (Guyatt and EBMWG, 1992:2420)

[7] Although Gordon Guyatt is often cited as the referred author in this publication, it is important to realise that he acted as the lead author of the Evidence Based Medicine Working Group that at the time included 30 members from McMaster University; University of Toronto; Queen's University, Ontario; University of North Carolina; University of Ottawa; University of Texas, as well as each establishment's associated clinical departments in Canada, North America, and Europe.

The paper attempts to anticipate any future *straw man* sabotages of the movement by explicitly clarifying what is meant by this statement. Although it is clear that the three components of practice stated in this sentence - intuition, clinical experience, and pathophysiology – are insufficient for decision-making, qualification of their role is provided. All three components are considered as *necessary but insufficient* in the focused context of best clinical decision-making for an individual patient. A call for clinicians to systematise their clinical observations and experiences is given, together with a caveat for avoiding reliance on non-systematised experiences and instincts. Regarding pathophysiological rationale, by which it appears the group are referring to basic mechanisms of disease, warnings are placed on the clinician's use of such knowledge in making diagnostic judgements and deterministic claims of efficacy[8] of treatment. The suggestion is that such knowledge, although important in explaining and understanding observations, can be misleading and result in inaccurate predictions[9].

[8] The terms *efficacy*, *effectiveness*, and *efficiency* will be used carefully to suit the intentions of the text. The meanings will be in line with original definitions given by Archie Cochrane (Cochrane (1972) as he meant them to relate to what would become the notion of EBM. These definitions were later contextualised and given a practical vernacular after the onset of EBM by Brian Haynes (Haynes, 1999), a leading EBM proponent. His terms follow the original definitions below.
Efficacy: Cochrane "The extent to which an intervention does more harm than good under ideal circumstances". Haynes "Can it work?"
Effectiveness: Cochrane "Does an intervention do more harm than good when provided under usual circumstances of healthcare". Haynes "Does it work in practice"
Efficiency: Cochrane "The effect of an intervention in relation to the resources in consumes". Haynes "Is it worth it?"
A caveat to this is if referring to specific work that has used one of the above words, I will use the term those authors have used with a note for clarity as needed.

[9] The role of pathophysiological mechanisms will only be alluded to briefly in this Chapter, and will be considered as a discrete matter in *Chapter 4*.

To replace these traditional pillars of practice, a second part to the defining principles is given: "*(EBM) stresses the examination of evidence from clinical research*" (Guyatt and EBMWG, 1992:2420). The tone of this paper assumes the reader's acceptance that *clinical research* is a better source of evidence than traditional sources (authority, experience, intuition, specialist knowledge in the form of pathophysiology, and so forth). No explicit argument is given towards justifying the supremacy of clinical research. Rather, attention is accelerated to the mechanisms by which clinicians can and should translate published clinical research into their decision-making. Such mechanisms are suggested as: refining lines of clinical inquiry (question formulation); improving information technology skills (search and retrieval of the best available evidence, and critical appraisal of the study methods to ascertain the validity of results), role modelling, education, and consideration of anticipated barriers to implementation (scepticism, lack of sufficient evidence, time pressures, threat to professional autonomy).

In sum, the two inaugural papers from Guyatt *et al* provide a clear intention of what EBM *should be*. The idea of a profession-impacting, and potentially de-professionalising , shift in the way healthcare is thought of and delivered is unambiguous. The intentions of the movement to re-order how much inferential value is placed on differing sources of evidence are bold and directed. Practical and professional limitations aside, there still remain some central questions regarding the evolution and justification for the movement[10]. First of all, what has led to the assumption that *clinical*

[10] *Chapter 3* provides a more detailed analysis of classic and philosophical criticisms of EBM.

research holds superior epistemic and predictive powers, and to what extent is a dramatic shift of values justified? Second, there are only implicit suggestions that within the scope of clinical research methods, certain ones should be given special emphasis, for example, controlled comparative studies above uncontrolled observations. Third, to what extent can a de-emphasis of pathophysiological rationale be justified? There is an over-arching proposal of concern, I propose, that relates to the EBM narrative so far, that is: if the new movement is intent on improving the way clinical decisions are made in order to achieve (cause) the best health outcomes possible, and the method of improvement is associated with the type of evidence source, then what is the relationship between that evidence source and the causal intentions of the clinical decision? In order to begin to address this, it is of significant importance to review the recent historical influences on the bold conjectures of the EBM initiative.

1.4. The Evidence Based Medicine blood-line

What methods does 'clinical research' refer to? The term *clinical research* is used throughout the inaugural papers on EBM, and forms a critical component of the EBM definition so far. Whatever the term means, there are at least two assumptions:

- That the methods are in some way superior in their epistemic and predictive capabilities than 'traditional' sources of evidence, hence the call for a 'new way'; and,

- That there are actually a range of methods with varying quality within and between them, hence the call for clinician training on how to best judge the quality and relevance of the evidence.

So first, what clues are available to determine the precise nature of the methods placed so centrally in EBM? In the 1991 paper, Guyatt states "*Evidence based medicine uses additional strategies, including quickly tracking down publications of studies that are* ***directly relevant to the clinical problem*** . . ." [emphasis added] (Guyatt, 1991:A-16), and then "*It may also involve applying the* ***scientific method*** *in determining the optimal management of the patient (3)"* [emphasis added] (*ibid*). Reference "(3)" in the last statement refers to a review (Guyatt *et al*., 1990) of 57 *N-of-1* randomised controlled trials concluding that the results supported the "*feasibility and usefulness of N-of-1 trials in clinical practice*"[11;12]. Therefore, it appears that *clinical research* is something to do with clinically relevant studies, based on the scientific method, which is manifest in randomised controlled trials.

This idea is made explicit in the 1992 paper. Following a suggestion that EBM represents a Kuhnian paradigm shift[13] , Guyatt *et al* state:

> *"The foundations of the paradigm shift lie in the developments in clinical research over the last 30 years. In 1960, the randomized clinical trial was an oddity. It is now accepted that*

[11] The notion and role of *N-of-1* trials will be detailed further in *Chapter 7*, §7.2

[12] These findings were based on a survey of physicians' actions following their awareness of a trial with a 'definitive statistical answer'.

[13] The idea that EBM truly represents a Kuhnian paradigm shift has been contended, for example Crawley (1993). This discussion, however, falls outside of the interests of this thesis.

> *virtually no drug can enter clinical practice without a demonstration of its efficacy in clinical trials"* (Guyatt and EBMWG, 1992:2420)

and:

> *"Meta-analysis is gaining increasing acceptance as a method of summarizing the results of a number of randomized trials, and ultimately may have as profound an effect on setting treatment policy as randomized trials themselves*" (Guyatt and EBMWG, 1992:2420)

Other than a brief reference to "*less dramatic, (crucial) methodological advances . . . in other areas*"(Guyatt and EBMWG, 1992:2420-1), the sole methodological approach representing *clinical research* is presented as the randomised controlled trial (RCT). As well as therapeutic (intervention, that would also inform on harm) and prognostic research, the RCT is also supported in its value for diagnostic research[14]. This commitment to a particular methodology is underlined with a statement regarding the background principles of such an approach - "*Proposals to apply the principles of clinical epidemiology to day-to-day clinical practice have been put*

[14] EBM practically classifies evidence into a number of categories, intended to facilitate its clinical application. Classically these are Therapeutics; Diagnosis; Prognosis; Risk/Harm. The focus of this thesis is Therapeutics. This is not to say other areas of practice are less important, but it is the area where I think the notion of causation is best examined.

forward"[15] (Guyatt and EBMWG, 1992:2421), bolstered further by a qualifying condition that it is the purpose and responsibility of the EBM user to ensure that the published research intended for clinical use is of sufficient methodological quality, "*high . . .methodological rigor*" (Guyatt and EBMWG, 1992:2421).

The shape of EBM at its inception has now become clear, in so much as its methodological commitments are concerned. Clinical research, the tool that is to supersede and support the de-emphasis of traditional sources of evidence on which practice has been based, is essentially high quality controlled comparative studies, based on the principles of clinical epidemiology.

1.5. What of epidemiology and Evidence Based Medicine?

The relationship between clinical epidemiology and EBM can be tracked through EBM's references to Sackett *et al's* earlier publications and thoughts on clinical epidemiology (Sackett *et al*., 1991). Further, there is an implicit yet obvious inspiration from two series' of articles by epidemiologist Alvan Feinstein in the 1960s. In 1964, Feinstein published a series of four articles in the *Annals of Internal Medicine* entitled "*The Scientific Methodology in Clinical Practice*"Feinstein (1964a), Feinstein (1964b), Feinstein (1964c), Feinstein (1964d).These four papers eventually formed the basis of Feinstein's 1967 book on clinical judgement (Feinstein,

[15] Reference "3" here is to David Sackett *et al's* 1991 book on clinical epidemiology (Sackett *et al.*, 1991). This book was later to be re-packaged and re-marketed in the form of possibly the best-selling book on EBM: (Sackett *et al*., 1997).

1967). This collection of thoughts closely reflects the intentions and principles of EBM. Feinstein's premise was that each patient encounter was analogous to a laboratory experiment, in so much as baseline measurements are taken, an intervention applied, and an outcome recorded. The key difference between the clinical encounter and a laboratory experiment however was, according to Feinstein, that the clinical encounter lacked a concurrent control group – something against which the clinician could judge the patient's response. The best control comparison a clinician could have was her awareness of similar patients in the past. This lay the process open to natural human biases of erroneous memory and perception – a recurring theme in the contemporary justification of scientific approach to clinical reasoning. Feinstein thus proposed methods for the clinician to adopt a more scientific approach to the humanistic process of clinical judgement. As long as a systematic and rigorous process was followed, clinical data, Feinstein argued, could be as valuable as laboratory data. Thus, the *art* of clinical medicine could be substantially complimented by the *science* of clinical practice. This fits well with Guyatt *et al's* proposals:

> *". . . systematic attempts to record observations in a reproducible and unbiased fashion markedly increase the confidence one can have in knowledge about patient prognosis, the value of diagnostic tests, and the efficacy of treatment"* (Guyatt and EBMWG, 1992:2421)

Feinstein's second contribution to the path towards EBM was in the form of three papers published in 1968 entitled '*Clinical Epidemiology*' (Feinstein

(1968a), Feinstein (1968b), Feinstein (1968c)), again leading to the publication of a book of the same matter in 1985 (Feinstein, 1985). The emphasis of this body of work was clearly on the ability of 'clinical epidemiology' – being the application of epidemiological methods to the study of clinically defined populations - to improve clinical practice: *". . . clinical epidemiology is concerned with studying groups of people to achieve the background evidence needed for clinical decisions in patient care. . . . [It thus] emphasizes issues of diagnosis, prognosis, therapy and other distinctly clinical judgments*" (Feinstein, 1985:1). Further parallels with EBM are obvious in Feinstein's commitment to precise areas of practice and principles associated with health care management: "*The foci of investigation are topics in the occurrence, distribution, causation, diagnosis, natural history, prognosis, prevention, and therapy of disease*" (Feinstein, 1985:3). It is also clear that the way Feinstein thought of epidemiology was in accordance with contemporary definitions, for example, Broadbent (Broadbent, 2013b). Further, Feinstein considered the methods of epidemiology to represent the rigor of basic scientific enquiry:

> *"The methods of clinical epidemiology are intended to bring clinical sophistication and scientific rigor to the difficult challenges of investigating phenomena that occur in free-living people, who often cannot be studied by experimental plans"* (Feinstein, 1985:8)

Again, in line with Broadbent, his idea of '*experimental plans'* was one of full control over all variables – a phenomenon accepted as impossible in the human sciences. The idea of rigorous investigation was thus reduced

to systematic observation of populations, with and without comparison groups. The complexity, variability and heterogeneity of human populations were things that Feinstein embraced and saw as an indication for rigorous scientific study, rather than a reason to avoid systematic study.

In 1969, Canadian medic David Sackett and future pioneer of EBM attempted to evoke the medical community into further embracing the notion of clinical epidemiology (Sackett, 1969). Like Feinstein, these thoughts were later developed significantly with the resultant publication of Sackett *et al's* handbook on clinical epidemiology (Sackett *et al*., 1991). Sackett's self-proclaimed definition of clinical epidemiology seems strikingly familiar: "*I define clinical epidemiology as the application, by a physician who provides direct patient care, of epidemiological and biometric methods to the study of diagnostic and therapeutic process in order to effect an improvement in health*" (Sackett, 1969:125). The drive to differentiate *clinical* epidemiology from a 'traditional' (apparently non-clinical) survey approach is manifest in Sackett's proposals:

> *"The traditional or "survey" epidemiologist, on the other hand, almost never has continuing exposure and orientation to patient care responsibilities. Even if he is a physician, upon initiating his epidemiologic training he almost always stops providing direct patient care"* (Sackett, 1969:125)

This background work on clinical epidemiology so far has clear and consistent themes that are represented in both the initiation of EBM, and a contemporary understanding of clinical epidemiology. These themes are:

an (initially implicit) de-emphasising of the role of 'traditional' (unsystematic) clinical experience and judgement; the development of an individual systematic and rigorous approach to cataloguing of clinical experiences and patient data; a conscious clinical commitment to knowledge and data from scientific population studies; and an integration of such data into individualised clinical decision-making. It is of no surprise then that the content and structure of one of the most commonly quoted definitions of EBM, stemming from Sackett *et al's* highly-cited 1996 *British Medical Journal* editorial reads as it does:

> *"Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research"* (Sackett *et al*., 1996:71)

1.6. What evidence is and what it isn't

From a range of post-1992 commentaries and opinions on EBM, Sackett *et al's* 1996 editorial (Sackett *et al*., 1996) specifically deserves focused attention. Due to its high profile referencing throughout the history of EBM, it would be of some academic interest to consider what it offers above the inaugural work of Guyatt and the EBMWG[16]. Sackett's editorial

[16] Interestingly, a more informative and instructional short paper was published the year before this by Sackett and colleague William Rosenberg which has received only around 5% of the citations of Sackett *et al* 1996. (Sackett and Rosenberg, 1995).

is sub-titled "*It's about integrating individual clinical expertise and the best external evidence*" (Sackett *et al*., 1996:71) reinforcing the propositions of Guyatt *et al* and the epidemiological forefathers of EBM. Sackett's presentation and explanation of EBM demonstrates a professional integrity, and above-all, a broad-minded and holistic approach to clinical decision-making, visible in the definition quoted above.

By 'best evidence' these authors allude to clinically relevant research from patient-centred studies, whose findings could be used in a clinical decision-making process in harmony with clinical expertise and experiences. Sackett *et al* chose to refer to this sort of evidence as *external evidence*, a term that might serve a perfunctory role given the need to grapple with the juxtaposition of multiple sources of information. There is an apparent desire to support the complex and holistic process of integrating *external evidence* whist explicitly attempting to avoid any obvious denigration of clinical experience and expertise: "*by individual clinical expertise we mean the proficiency and judgement that individual clinicians acquire through clinical experience and clinical practice*"(Sackett *et al*., 1996:71), and "*External clinical evidence can inform, but can never replace, individual clinical expertise*" (*ibid*:72).

However, there is some confusion with this stance, as the authors have already boldly stated that, "*External clinical evidence both invalidates previously accepted diagnostic tests and treatments and replaces them with new ones which are more powerful, more accurate, more efficacious, and safer*" (*ibid*). Therefore, if considering clinical research (external evidence) and clinical experience as two independent sources of evidence - although there may be some validity in experience acting as evidence - it is clear that external evidence trumps experience. It may, however, be that the intention was

never to set these discrete dimensions of health care against each other in the battle for the best source of evidence. Rather, there are clues from Sackett *et al* that perhaps what clinical experience means for EBM is something other than a source of evidence on which to base future decisions, "*. . . it is this expertise that decides whether the external evidence applies to the individual at all and, if so, how it should be integrated into a clinical decision*" (*ibid*). So the value of clinical experience is not necessarily in its utility as a valid source of evidence, but rather as a necessary medium for contextualising external evidence. This is an important and informative move on Sackett *et al's* part.

1.7. What is *best available* evidence?

What do Sackett *et al* offer to an understanding of what should and should not be considered as best available evidence? It has already been suggested that clinical research (external evidence) should act as *the* source of evidence on which to base clinical decisions. Other than appreciating that the research generating this evidence should be 'patient-centred', it is still not clear what this entails. Sackett *et al* seem to loosen the parameters of what constitutes clinical research compared to earlier proponents of EBM. Whereas previous propositions seem to have been strictly focused on well-controlled comparative studies, Sackett *et al* make it clear that EBM is not "*restricted to randomised controlled trials*" (*ibid*). They provide a brief summary explaining that the type of research should be relevant to the type of clinical question. For example, cross-sectional studies should be sought if the accuracy of a diagnostic test was queried; follow-up studies for prognostic questions *etcetera*. This has utility in terms of sectioning-out

methods within each category of EBM (therapeutics, diagnostics, prognosis, risk/harm), but still does not inform on what constitutes the *best* evidence within each such category. Although Sackett *et al* comment on alternatives in the absence of randomised controlled trials for example, there is no attempt to inform on how quality judgements should be made on the different types of methods that may be suited to a particular category. For example, are controlled studies 'better' than non-controlled studies? This is an issue that is formally addressed by developments within the EBM movement over the next few years, and still to the present day. It is also of practical and intellectual importance to examine this concern from a deeper historical review. All that is established thus far is that rigorous, systematic, population-based clinical research should be prioritised over traditional justifications for clinical decisions. It has been implied why such traditional sources of 'evidence' are insufficient and should be de-emphasised (or not considered a source of evidence at all), but so far, EBM is lacking a rationale to robustly support, or at least explain, clinical research methods as a prioritised source of evidence.

1.8. The randomised controlled trial

In *Effectiveness & Efficiency: Random Reflections on Health Services*, Archie Cochrane wrote, "*The general scientific problem, with that we are primarily concerned is that of testing a hypothesis that a certain treatment alters the natural history of a disease for the better*" (Cochrane, 1972:20). Here, Cochrane was attempting to review medical practice and cast some sense of order on the different methods clinicians had used to understand whether or not a treatment did in fact alter disease outcomes. He seemed concerned with

two fundamental problems: one, the overuse of clinical opinion as a source of evidence to inform this (type of) hypothesis; and two, the misuse of the concept of 'experiment'. Cochrane indicted clinical opinion for its lack of quantitative metric, and the failure to understand what the outcome might have been had the patient not received treatment. Together with biases in human assessment, these reasons seem to be sufficient for Cochrane's consideration of clinical opinion as the "*simplest (worst) type of observational evidence*" (Cochrane, 1972:21). By misuse of the concept of experiment, it seems that Cochrane was referring to the reliance on large-scale observational studies to test the hypothesis that a treatment has an effect. Acknowledging that such observational evidence was "*clearly better than opinion*" (Cochrane, 1972:21), in terms of understanding the efficacy or effectiveness of a treatment intervention, this method remained "*thoroughly unsatisfactory*" (Cochrane, 1972:21). The landmark shift in testing hypotheses of efficacy and effectiveness, and the one that truly reflected an experimental approach to clinical medicine, was, according to Cochrane, the randomised controlled trial. For Cochrane, the RCT was a "*very beautiful technique*" (Cochrane, 1972:22), which would address the issues of measurement, quantification, and bias. It is clear that this thought influenced the priorities of EBM, but is at odds, to some degree, with the general principles of clinical epidemiology that place values of judgment of effectiveness on non-randomised observational studies. The challenges of understanding the relative values of observational versus RCT methods will be dealt with in some detail in *Chapter 3*. Likewise, the technicalities of study design must be explored if a meaningful account of their fitness for purpose is to be given. This too will be addressed in *Chapter 3*. For now, the historical narrative of how and why comparative (experimental)

methods should feature with such prominence and priority in the EBM movement is considered further. This is undertaken in line with a brief history of the statistical approaches to group comparisons that are now most commonly used in contemporaneous research.

This historical narrative is provided so that a sense of context can be developed as to how EBM is now operationalised. It should make some sense that a good, or 'fair', way to evaluate a therapeutic intervention is through group comparisons. For the purpose of this thesis, it is of some importance to understand the nature of the specific statistical approaches used in comparative studies. Quite simply this is because the clinician is expected to use data associated with these statistical methods in their clinical decision-making. I am making no grand commentary or claims towards the intricacies and controversies surrounding statistical analysis and inference – this is not a thesis of statistics. However, if the relationship between research activity and clinical decision-making is to be critically considered, then some appreciation of the underpinning mathematical concepts is necessary. Specifically, any analysis of matters of causation arising from and within the research and EBM framework will naturally entail some thought on the probabilistic nature of such causal claims. Thus, understanding the statistical nature of this probability will be of some critical value.

1.9. Comparing groups

The idea of comparing groups to make inferences about the effect of a controlled variable is in no way novel. Practical examples have been recorded throughout history. Daniel of Judah, according to the Hebrew

Book of Daniel, reports on a process that has component parts of a comparative controlled trial, including a claim towards inference from the trial:

> *"(12) Please test your servants for ten days: Give us nothing but vegetables to eat and water to drink. (13) Then compare our appearance with that of the young men who eat the royal food,* ***and treat your servants in accordance with what you see****"* [emphasis added] (Daniel, 600BC)

In the 16th Century, French surgeon Ambroise Paré reported on a trial that compared a *digestive medicament* – a paste made of gun-powder and onions - with boiling oil for cauterisation, claiming the efficacy of the former (Paré, 1575). In the 1720s, Scottish surgeon Charles Maitland initiated a series of trials with a report on the efficacy of inoculation for smallpox (Maitland, 1722). Famously, and of direct influence on the contemporary curating of information on 'fair tests'[17], Scottish naval surgeon James Lind published his *Treatise of the Scurvy*. Lind was committed to basing his work on '*observable facts*', as opposed to the authoritative medical opinion of the time (Lind, 1753; Chalmers, 2003). His 18th century reports on a number of trials showed an intuitive devotion to controlling variables and systematically recording outcomes[18].

[17] The James Lind Library: Explaining and illustrating the development of fair tests of treatment in health care. http://www.jameslindlibrary.org/index.html

[18] From what is reported in his text, Lind 'systematically reviewed' literature of what was known of treatments for scurvy at the time. He then conducted trials involving 12 sailors who were at similar stages of the disease, controlling for basic diet and environment. He randomly assigned the groups of men (six groups of n=2) to one of six most commonly used treatments: 1.1 litres of cider; twenty-five millilitres of elixir vitriol (dilute sulphuric

Sackett *et al* (Sackett *et al*., 1996) state that the *philosophical origins* of EBM extend back to the mid-19th century and earlier. It is likely that they are referring to the activity of French surgeon, Pierre Charles Alexandre Louis who, in addition to publishing trials on blood-letting, progressed the field of scientific inquiry in healthcare by developing the *la méthode numérique* (Kulkarni, 2005) – possibly the closest forerunner to clinical epidemiology noticed in history. His *numerical method* was the first sign of explicit attention to use group averages in determining decisions on future individual cases of the same disease. He supported – what would become – the *epidemiological* notion of using data from large populations to influence decisions on individuals on the basis that over time, individual patients would 'average out'. This notion took a long while to gain traction, and it was not until some decades into the 20th century that specific exploitation of both the historical backdrop of comparing groups, and the Louisian notion of inferring beyond the trial sample, began to manifest in published reports.

What could be considered the first detailed published RCTs in modern medicine began with an investigation of the efficacy of streptomycin in the treatment of pulmonary tuberculosis (MRC, 1948), closely followed by a series of RCTs published in the early 1950s (for example, Daniels and Hill (1952); MRC (1951); MRC (1952)). Sir Austin Bradford Hill (a member of all the above teams) is considered a significant instigator and proponent of

acid); 18 millilitres of vinegar three times throughout the day before meals; half a pint of sea water; two oranges and one lemon continued for six days only (when the supply was exhausted); and a medicinal paste made up of garlic, mustard seed, dried radish root and gum myrrh. At 14 day follow-up he concluded "The most sudden and visible good effects were perceived from the use of oranges and lemons". http://www.jameslindlibrary.org/illustrating/articles/who-was-james-lind-and-what-exactly-did-he-achieve

the RCT, following up a number of early trials with a seminal essay published in the *New England Journal of Medicine* extolling the virtues of the RCT (Hill, 1952). These works have served to function as exemplars of innovative research practice, changing understanding in the world of medicine, in terms of what interventions were effective.

In medicine, the defining and differentiating quality or essence of the RCT seems to be in its ability to compare two or more groups with each other to make some sort of judgement of the effect of a variable. The inability of other sources of evidence to compare groups in such a way seems to provide a strong rationale for their de-emphasis within EBM and 'pre-EBM' arguments for best tests of interventions (for example, clinical opinion through to large-scale non-controlled observational studies). Again this reflects early thoughts:

> *". . . it is difficult to determine through clinical impressions whether or not a drug is quite useless or of some slight but undoubted value, and that it is even more difficult to determine with uncontrolled and unco-ordinated (sic) observations . . . "*
> (Hill, 1952:118)

The above cited trials from the 1940s and 50s, together with Hill's monologue (Hill, 1952), specifically highlight this as the critical feature that provides superior evidence of treatment effect:

> *"The essence of such a trial is comparison. To the dictum of Helmholtz that "all science is measurement," we should add,*

> *Sir Henry Dale[19] has pointed out, a further clause that "all true measurement is essentially comparative""* (Hill, 1952:115)

Some years earlier, Hill had published a primer on '*the statistical method'* in medicine's leading journal *The Lancet* using examples of group data to demonstrate the value of statistics in experimental medical methods (Hill, 1937. Further, the purpose, it seems, was to convince the clinician of the values of statistically analysed population data in clinical practice. It is clear that the injection of the statistical method into medicine was directly influenced by the work of statistician R.A. Fisher: first, that the methods presented by Hill were decidedly Fisherian; and second Fisher's *The Design of Experiments* was the only referenced material in this paper in support of his thoughts on the experimental method[20]. There is little doubt on the relationship between EBM, experimental methods, and their associated statistics. If this is the case, then the nature and development of the type of statistics that has found its way into the EBM model is worthy of brief exploration. This may assist as background knowledge in the analysis of the how EBM's research methods are considered as sources of evidence for causation, especially if that evidence is intended for use in clinical decision-making[21].

[19] Hill is referring to Dale (1951), *Measurement in Medicine*.
[20] Hill does in fact begin the paper with a quotation from Professor Major Greenwood's earlier essay on medical statistics in the first volume of the same journal. However, the methods report by Greenwood are overtly Fisherian (Greenwood, 1921).
[21] in line with other commentators on the philosophy of medical research and practice, (for example, Broadbent (2013b); Howick (2011)), I fully acknowledge that statistics and the philosophy of statistics are subject areas in their own right and hold significant and important questions regarding inference and causation. I have no intention of exploring such questions of statistics. This is done remarkably well elsewhere, for example, Cox (2006); Bandyopadhayay and Forester (2011). However, I do feel that a conceptual

By definition, statistics deal, in a scientific way, with large quantities of numerical data. The defining characteristic is one of inferring proportions in a whole from those in a representative sample[22]. Hill moulded a classical definition to highlight further its fitness for purpose in medical research, with particular emphasis on its ability to deal with complexities and variances of clinical practice:

> *"The essence of the statistical method lies in the elucidation of the effects of (these) multiple causes . . . 'methods specifically adapted by a multiplicity of causes'"* (Hill, 1937:41).

The types of comparative studies of concern, that is, those that are relatively privileged for their ability to determine effects of a treatment intervention, use statistical methods to compare two or more sets of data (sample means) to decide if one set differs significantly from the other. Statistical models, together with trial designs, are developed with great thought to allow the user to make a decision on how likely that difference is due to the fact that each sample is derived from separate populations (the hypothesis), or that any difference is due to sampling error, or chance. If it can be confidently judged that the difference is not due to error or chance, then the user can infer that the difference is due to something that happened in one sample, but not the other (for example, a treatment

understanding of the development and broad nature of the statistical model prevalent in contemporary health research care research will facilitate an understanding of philosophical questions regarding causation.

[22] For example, Oxford English Dictionaries, *statistics*. http://www.oxforddictionaries.com/definition/english/statistics

intervention under test). This structure and interpretation of statistics and probability integral to this approach is overtly *frequentist* (Sim and Wright, 2000). The approach seems to be some sort of hybrid of Fisherian ideas on experimental design and the type of hypothesis testing associated with the Neyman-Pearson lemma (Cox, 2006). What follows is a condensed historical overview of the contemporary development of statistical inference that is needed to understand why and how this model is utilised so readily in health science research[23].

Pierre-Simon Laplace (1749-1827) is a natural starting point for this analysis as his prediction of planetary motion differed from any previous statistician because he suggested the concept of error: previously, statisticians thought their calculations were wrong if they were not exact. This would serve as a portal for a whole new way of considering prediction. Of significant interest is that Laplace used terms such as *flat priors* and *inverse probabilities*. Laplace was born in 1749, and Thomas Bayes died in 1761. Although there is some uncertainty as to Bayes original publications, it is quite likely that Laplace had read Bayes' work, and this terminology reflects that[24]. Carl Freidreich Gauss (1777-1855) continued a Laplacian approach to statistics, but with an obvious frequentist

[23] Multiple sources of reference text have been used to establish this narrative for example, Good (1988); McCloskey and Ziliak (1996); Salsburg (2002); Bellhouse (2004); Elliott and Granger (2004); Spiegelhalter et al. (2003); Cox (2006 Ziliak and McCloskey (2008); as well as original texts such as Student (1908); Fisher (1925); Fisher (1935); Fisher (1956); Neyman (1967).

[24] The debate between frequentists and Bayesians regarding the best statistical approaches to experimental design is ongoing. Bayesians see their interpretation of probability more reflective of complex, humanistic environments – contextualising experimental data in an *a priori* estimation of probability for the truth of the hypothesis. Strict frequentists on the other hand reject this 'soft' approach on the grounds of lack of objectivity to the prior distributions necessary for Bayesian analysis. For example: Spiegelhalter et al. (2003); Cox (2006); Howson and Urbach (2007).

interpretation to Laplace's ideas. His text *Arthimeticae* rarely considers a Bayesian notion, and the idea of a distribution based on frequency of occurrence is introduced (that is, the Gaussian bell-curve for normally distributed data). A further criticism of flat priors, and a reinforcement of a frequentist idea was given by George Boole (1815-1864), whose ideas were developed again by Isaac Todhunter (1820-1884). The fascination with probability theory was evident at this time with Todhunter often being considered a major instigator of statistical thought on probability. Next, a new era developed, considered a '*statistical revolution*'. Karl Pearson (1875-1936) became the editor of *Biometrika* and developed a research programme that essentially involved his workers collecting large amounts of data - seemingly on any conceivable subject. Pearson used this data to demonstrate how many things in life were distributed in a particular way: normally. Most phenomena had an average, with a symmetrical spread of reducing frequency either side of it. Pearson would produce *Gaussian curves* to represent this data, and it seem like this was the primary intent of *Biometrika* at this time. Pearson was strictly frequentist, as was his younger contemporary, Ronald Alymer Fisher (1890-1962). Influential and often considered a genius, Fisher was also strictly anti-Bayesian. He developed the concepts of analysis of variance, estimation and distribution, likelihoods, and conditional inference. His seminal texts in these areas were hugely influential to scientists and research workers. Fisher presented the idea of hypothesis testing, but it was Jerzy Neyman (1894-1981) and Karl Pearson's son, Egon Pearson (1890-1962) who are most commonly credited with this concept, to become known as the *Neyman-Pearson theory*, or lemma. It is of some relevance to note that all the above statisticians shared knowledge and friendship with a less assuming

character, William Sealy Gossett (1876-1937). It is evident that Gossett originally presented the notions of i) sampling from large and small populations, and ii) testing multiple sets of data in order to see if one was 'better' than the other (Student, 1908). It is likely that Fisher popularised Gossett's intellect. If Gossett was the real intellect behind this major statistical advancement, there is a major concern due to Fisher's interpretation. Gossett – under the pseudonym 'Student' - was explicit in his warnings regarding the limitations, and potential errors and dangers of the concept of statistical significance and using the standard error to inform analysis outside of the dataset. Especially so in relation to informing decisions where the *statistical* regularity between sample and population cannot be guaranteed: "*Now any series of experiments is only of value in so far as it enables us to form a judgment as to the* ***statistical constants*** *of the population to that the experiments belong*." [emphasis added] (Student, 1908:1). These caveats are not so obvious in Fisher's work, and certainly seem to have been diluted as statistics have become utilised in areas outside its historical intentions (for example, health). This, in-spite of contemporary statisticians still reinforcing the unique and discrete purpose of statistics:

> *"The object (of statistical inference) is to provide ideas and methods for the critical analysis, and, as far as feasible, the interpretation of empirical data arising from single experimental or observational study. . . The extremely challenging issues of scientific inference may be regarded as those of synthesising very different kinds of conclusions if possible into coherent whole or theory and of placing specific*

> *analyses and conclusions within that framework"* (Cox, 2006:200).

It seems like medical and healthcare science has readily adopted a specific statistical approach to help it understand the effects of therapeutic interventions, among other things. This approach is frequentist by nature, and is a hybrid of Fisherian experimental design and significance testing, and Neyman-Pearson hypothesis testing. There is a rich historical background as to why this should be the case, but there are also some well-known limitations. Statisticians themselves have been explicit in highlighting that problems associated with conflating statistical and scientific (outside of the data-set) inference. Seeing as EBM directly sets-out to relate one notion to the other, it is of use to consider some conceptual underpinnings of this chosen approach a little further. The following section on frequentism serves to underline and complete this first chapter that has explored historical and conceptual underpinnings of the present day EBM movement. To be clear, the purpose of the following brief analysis on a frequentists approach to statistics is simply to draw-out any features of the process that may be relevant to the thesis. By no means is this analysis either a) something that focuses on the limitations of the approach to act as a straw man against EBM. Although limitations will be drawn out, so will its strengths. Only by doing this will any relevant features be identified, or b) any attempt at all of a sophisticated and complete analysis of statistical inference. This thesis has no direct concern or ambitions towards advancing the arguments on statistical inference. Simply, I am attempting to present the most fundamental conceptual key that serves as the root for all causal claims (regarding therapeutic

interventions) within EBM. I see this as being the most basic level of statistical analysis observable in the process of health science research. What I mean by this is that there are numerous statistical tests and process available to the healthcare researcher, depending on the precise nature of the research question. However, at the core of all of these (most commonly) used approaches is the simple idea of observing data, but in a specific way, with specific principles in mind. This, I suggest, is of some importance for a critique of causation, especially in a model where there are complex expectations of the causal claims, that is to be meaningful for a purpose other than their original statistical intent, and to hold in a spatiotemporally removed environment. With this in mind, I have just one question: what sort of evidence of observed data does our most commonly used statistical approach provide? The following chapters will deal with what this means in terms of causal claims. One final note is that although I will refer very briefly to a Bayesian approach, I am doing this simply to highlight that other approaches do exist, and these may address some of the limitations of a frequentists approach. I am making no grand claim as to which is best, or proposing that all research science should start adopting Bayesian methods, *et cetera*. However, fundamentally, Bayesian approaches may sit more comfortably in a dispositionally reconceptualised notion of causation. For now, frequentism, in the briefest way possible.

1.9.1. Frequentism[25]

The appeal of a frequentist approach to statistical analysis for healthcare scientists could well have been its overt commitment to objectivity. The background concerns for the early proponents of epidemiology and EBM were generally related to unsystematic biases and errors of judgement from a variety of existing sources of information, for example expert opinion, unsystematic observations, and so forth. Thus subjectivity needed to be eradicated in order to understand the 'true' effects of treatment. Frequentism could offer the objectivity being looked for, and objectivity is the defining characteristic of a frequentists approach. The primary advantage of a frequentist approach therefore, compared to alternative statistical approaches, for example Bayesian, is "*. . . its apparent separation of the evidence from subjective factors"* (Spiegelhalter *et al*., 2003:123). However, with the quest for objectivity come some limitations. Again, it is of use to briefly revise the conceptual principles of frequentism if the role of statistical outcomes is to be given consideration in the analysis of EBM.

First, frequentism relies on a specific and self-defined theory of objective probability, namely *frequentist probability*. This thesis talks about

[25] This brief analysis is my own attempt to synthesise the process and detail of a frequentists approach to statistical inference. This is not a forgiving task, but I hope it is accurate. My synthesis has been informed by numerous texts and other people's own attempts at summarising this highly complex phenomenon. Namely, I have been influenced by the likes of David Spiegelhalter; David Cox; and David Freedman, and to balance things with a Bayesian perspective, also Colin Howson and Peter Urbach. Unpublished analysis from Adam La Caze's PhD thesis has also served as an inspiring background, and although I think my final comments align with his conclusions, there are some points of difference in the way we both get there. I have also been lucky enough to have personal communications with David Cox, David Spiegelhalter, Philip Dawid, and Adam La Caze that has helped form my personal perception of some detail within the broad field of statistical analysis and probability.

causation, and causal claims. To pre-empt any misunderstandings of what I mean when I use these terms – at least in the analysis of causation as it presently seems in EBM – I am not saying that a causal claim within or deriving from any research activity means that a cause will produce an effect in any deterministic way[26]. Of course, there is always a probabilistic rider such to say '*a* causes *b*' really means '*p*(*a* causes *b*), depending on the underpinning theory of probability. This is still a causal claim however. It is just that the *likelihood* of the cause is being referred to. The cause is still the central issue. As it stands, a frequentist theory of probability seems to be at play. Simply, this means that the probability of an event occurring is defined relative to a sequence of outcomes in a repeatable set of conditions ((Howson and Urbach, 2007:202). In other words, if I toss a coin 100 times and it lands heads 51 times, I would say of a random toss in future time that the probability of it landing heads is 0.51 (51%). For frequentists, probabilities are inherent properties of the observed data. When a causal claim is made from group comparisons (for example, RCTs), it is essentially saying event *b* occurred n_1-times as a result of intervention a^i (group 1) and n_2-times as a result of control a^c (group 2), say. The statistical approach that deals with these frequencies is briefly described below. Both statistics and EBM use a suite of tools and associated vernacular to interpret and try to make some sense of these base-frequencies, for example *p*-values, confidence intervals, absolute risk ratios (for example, numbers-needed-to-treat), relative risk ratios (for example, odds-ratios), likelihood ratios, *et cetera*. Although some of these tools have the appearance of embracing alternative statistical approaches, for example

[26] The ideas of determinism and necessity are dealt with in *Chapter 7,* specifically §7.3.

likelihood ratios incorporate prior probability in their calculations, all probabilistic interpretation and communication regarding comparative study outcomes is fundamentally frequentist. Thus, frequentist probability theory - essentially describing the rate of regularly occurring events – sits at the heart of research methods associated with EBM (Bland and Altman, 1998), at least for the evaluation of the effects of therapeutic interventions[27].

The probabilistic principles of a frequentist approach relate directly to its statistical principles. First, it is by virtue of random sampling – or at least a technique that ensures homogenous baseline grouping - that a frequentists approach to statistical analysis can be used. Hence, frequentism is based on *sampling theory* and assumes sample populations to be identical save for the variable of interest in order for proper analysis to be undertaken. Central to frequentism is that observed data (say x), represented by a test statistic (for example, a mean, say X) is used to estimate something about the relative support given to an unknown parameter, say θ, (for example, the effect of the intervention). X is derived from x. Assumptions are made about X that are essentially commentaries on its performance as a *long-run* estimator in an *infinite number of trials*. For example, X must be a *good* estimator of θ - that is X must equate to θ, X must converge on θ as the sample size increases, X must have smaller variances than its alternatives, X must contain all the information about θ. X is also assumed to be normally distributed, especially so that the sampling distribution can be fully specified. The evidence about X is summarised against a specified null hypothesis (H^{null}) by a Fisherian value

[27] Some diagnostic research utilises Bayesian approaches.

(a *p*-value, for example) that expresses the chance of getting a result as extreme as *X*, *given the truth* of H^{null}. Thus, it is the case that frequentism assumes the truth of H^{null}. It must be remembered that as the underpinning probabilistic theory relates to increasing confidence with increasing repetitions, commentaries on values such as a *p*-value should formally be followed by the caveat: 'in the long run', or 'in an infinite number of trials'.

Specific types of errors are accounted for within the statistical principles. The chance of incorrectly rejecting the H^{null} (Type I error, α, for example 5%), or of not detecting the alternative hypothesis (H^1) (Type II error, β, for example 80%) are fixed during the study design (pre-intervention) in line with the Neyman-Pearson lemma. Judgements towards the significance (informing which hypothesis is accepted) of whether or not observed data are from the sample population are dictated by the values of α and β. Hence decisions for declaring where significance should fall are made pre-study, and outside of the observed data.

As θ can never actually be the case, given that it is a probabilistic estimate and its true value is unknowable, interval estimates are formulated to allow judgment on the probability of the range of values from the observed data covering the true value of θ. For example confidence intervals might be set at 95%, meaning that in 95% of situations *in an infinite number of trials*, these intervals will contain the true value of θ. In sum, if t_1 and t_2 represent the estimate limits, then an expression of its associated confidence coefficient (1 - α) would be:

$$1 - \alpha = p(t_2 \leq \theta \leq t_1)$$

As stated, the defining strength of a frequentists approach to statistical analysis is undeniably its objectivity, meaning its ability to separate the (apparent) evidence in the data from subjective factors. Analysis and inference is focused on the observed data. Study design, hypothesis testing, and probabilistic inference are centred on the estimation of an unknown parameter represented by a test statistic deriving from the observed data. The underpinning probabilistic theory means the probabilities are properties of the observed data. There are a number of criticisms with this, mainly revolving around notions of an approach that deals with the *long-run* and its relevance for specific instances, and that probabilistic properties are contained within the data.

These aside, there is one further peculiarity. The 'rules' for decision-making on hypothesis acceptance or rejection are made pre-study and do not belong to the observed data. To some this is a serious flaw that violates a fundamental principle of statistical inference, the likelihood principle. The likelihood principle states that all the information that the data provide about a parameter is contained in the likelihood (Berger *et al*., 1988). Briefly, as the principle states that only the observed data should influence the conclusions (exclusively through likelihood) and the interpretation of *p*-values (through α and β) depend on what would have happened had something else been observed (because the truth of H^{null} is assumed, then it has to be x that is variable), then the process is nonsensical.

The simplest expression of frequentism as a statistical approach is fundamentally:

$$p(x/H^{null})$$

that is, the probability of x being the case, given the truth of H^{null}, noting, of course, that inferences about x rely on sampling distributions for X.

As a very brief contrast, should we be inclined to think that all statistical analysis has to be constrained by the same limitations as frequentism, a Bayesian approach offers some direct responses: First, Bayesian approaches consider outside context, that is prior probabilities. This means that not all the probabilistic properties are contained within the observed data. Second, the statistical theorem of a Bayesian approach relies on observed x directly, and does not assume the truth of a hypothesis. Thus, the opposite to frequentism:

$$p(H/x)$$

that is, what is the probability of H being the case, given the observed data, x? x is fixed (through observation) and is used to test the hypothesis. It considers an *a prior* probability of the likelihood of the hypothesis, but pitches this against the experimental findings, so Bayes Theorem is equivalent to:

$$p(H/x) = p(x/H) \times (p(H)/p(x))$$

I do not need to go any further with this statistical narrative, only to summarise some points that are, or at least will become, relevant to the thesis.

Statistics are an integral and necessary component of the scientific undertaking of rigorous comparative research studies. However, the inference made from these statistical models is formally restricted to robust statistical constants within the models. Inferring outside of these parameters has been warned against since the onset of the discipline of statistics. The statistical approach at the heart of most contemporaneous population study designs, frequentism, is applauded for its objectivity but criticised for its fundamental concern with infinite long-runs of events, and violating a core principle of statistics. However, clinical research distributions are fundamentally interpreted around this concept and indeed the integration of clinical research data into decision-making is a central requirement of EBM. On the one hand, there is a rich and appealing historical development of epidemiological approaches to understanding health that underpins the foundations of EBM. On the other hand there are some fundamental questions related to how, precisely, can data from such approaches be integrated into clinical decision-making.

In sum, and to answer the question I set of this brief analysis: the favoured statistical approach of healthcare scientists offers something. It offers an objective account of observed data, conforming to tight statistical constructs. We can believe the outcomes of such an analysis, at least as far as its commentary on the observed data. What can be taken away from here is that scientific activity in healthcare research offers something that has an intuitive appeal – in which a thorough, systematic, objective process has been undertaken to achieve an outcome. What this means to EBM and clinical decision-making is another matter.

1.10. Conclusion

What EBM puts forward is undeniably sensible and uncontroversial – that healthcare practice should be based on the best evidence. The foundations for EBM lay in clinical epidemiology, and the idea of experimental-like research approaches to establish the effects of a therapeutic intervention. EBM uses these notions as an argument for what constitutes *best evidence*. EBM argues that the clinical research methods associated with these founding principles can improve – to a significant degree – on controlling for the biases present in traditional sources of evidence, namely clinical experience, expertise, and observations. Specifically, the biases it refers to relate to judgement on causal associations. Reviewing clinical epidemiology as a construct serves to allow investigation into both the nature of its research methods, and the structure of EBM. It is characterised by *real-world* investigations (human populations), and by its purposeful intention of improving health. This second characteristic reflects the core purpose of EBM being that clinical research outcomes should be used to inform clinical decisions. This implies, strongly, that the relationship between research outcome and future patient-centred decisions is stable. In other words, the inferential properties of clinical research are as trustworthy as the methods themselves.

Experimental like approaches, for example group comparisons, have been advocated throughout recent medical history by healthcare workers and medical statisticians alike. There is a consistent commentary associated with these cases that suggests that the emergent knowledge from such methods is better than what was previously obtainable. However, other than appeals to common intuitions about what happens

when groups are compared, there is little additional rationale for this claim. The notion of group comparison methods is anchored in specific principles of statistics that are overtly frequentist in nature. There are tight restrictions in these models that caution against non-statistical inference.

The rich epidemiological foundations of EBM have a central theme of causation. The history of both experimental (comparative) methods and their associated statistical approaches are clearly concerned with establishing 'what works' – a deeply causal notion. EBM is then concerned with improving (causing) the health of an individual (or a population) based on the causal evidence from clinical research. So far, EBM has not offered *what* it means by causation, nor has there been a commitment to *how* causation established in research relates to clinical decision-making. What is now of interest is to wonder if the type of causation established in clinical research is the type of causation desired with an individual patient (or population of patients). This is the subject matter of the following chapter.

Chapter 2: Searching for Causation in Evidence Based Medicine

2.1. Introduction

The development of EBM as a discrete movement is predicated on a rich history of clinical epidemiology, in the sense that it intends to identify patterns of diseases and determinants and the effects of interventions, through large-scale population studies. The resultant data is intended to be used in clinical decisions focused on the improvement of people's health. As a movement, it advances itself on from epidemiology by choosing comparative studies as a primary tool for its clinical research. This is principled on the ability of statistical models to make objective judgments on the likelihood of error in any estimation of group differences. This, it is claimed, is better than using traditional sources of evidence that are more prone to systematic biases of judgement in informing future clinical decisions. At inception, EBM's main function was to re-order sources of evidence and give clinical research some form of priority. In doing so, it would de-emphasise the evidential role of other elements of health care practice and science. Its secondary function was to facilitate clinicians in integrating research data into clinical decision-making. In line with these functions, it might be said that EBM has a form

of *central claim* that reads something like "*evidence from study designs higher up the hierarchy more reliably informs therapeutic decisions*" (La Caze, 2008:361). I will use this *central claim* as a core element of the conceptual framework developed throughout the following two chapters. The early definitions of EBM, for example Sackett's much-quoted 1996 slogan on "*conscientious, judicious and explicit use. . .*"(Sackett *et al*., 1996:71), reinforce the stance that EBM takes in placing responsibility on the clinical decision-maker to use the best of evidence. These slogans may be dismissed as rhetoric - in so much as there is an implied morality issue should anyone disagree – who would *not* want healthcare to be based on best evidence? As such, more *falsifiable* definitions have been proposed, a prime example being:

> *"the use of mathematical estimates of the chance of benefit and the risk of harm, derived from high-quality research on population samples, to inform clinical decision-making"* (Greenhalgh and Donald, 2003:469)

This definition exposes EBM's *central claim* and its component parts more clearly, and allows more challenging stances to be adopted that may oppose such claims, that is: i) that clinical decisions might not be best made using mathematical predictions, ii) that population samples might not directly map onto individual patients, iii) that clinical decision-making might not be fully reflective of clinical practice.

It is with these challenges in mind that the conceptual framework of this part of the thesis is developed. Given the early definitions and intentions of EBM, its historical make-up, re-interpretations reflecting its *central claim*,

and forthcoming commentaries notwithstanding, it seems that what EBM *is* can be reduced to two canonical claims:

> *Claim 1: Evidential priority is given to comparative research methods, utilising statistical estimates, above other elements of research and practice.*
>
> *Claim 2: Data from prioritised methods should determine clinical decision-making.*

These claims relate to the *processes* inherent within the movement. It is taken that the intended *product* of the movement is, in sympathy with its forefathers, the most effective and efficient healthcare possible. The way, of course, that *process* relates to *product* is in the assumption that *if* both *Claim 1* and *Claim 2* hold, then healthcare is likely to be as effective and efficient[28] as possible. However, there must also be something that relates the two claims to each other, that is, the evidence obtained according to *Claim 1* must hold for *Claim 2*. If we are talking about evidence of effectiveness, then what is considered to be effective according to *Claim 1*, should also be effective in the context of *Claim 2*. There are several ways to describe this relationship. For example, in clinical research this is referred to as *external validity,* or *generalisability,* meaning that the findings of some population based clinical research should have "*relevance to patients in*

[28] For simplicity and relevance, I shall now talk about **effectiveness** alone as the *product* of EBM, or its associated elements. Although efficiency is of course part of 'best care', for the purpose of this thesis – on its core concern of causation - it is clinical effectiveness that is the most relevant aspect of healthcare to talk about. Further, as most ideas will be in-mind of Phase III-type trials, *efficacy* will be left aside as far as the core ideas of the thesis are concerned.

future clinical practice" (Lees *et al*., 2006:48). The standard discourse on external validity is unsettled[29] , and refers to necessary assumptions on which findings can be generalisable. This is further discussed below. However, there are also philosophical concerns about this relationship and again these are at the core of the thesis. In outline, this thesis takes *effectiveness* as a causal term, such that the research methods referred to in *Claim 1* set out to establish some sort of relationship between variables that can be considered causal in nature. This is usually in the sense of the therapeutic intervention under investigation being the cause of a health change in a group of patients. For *Claim 2*, causation is also present. This is in the sense that a decision-making process between, for example, a clinician and a patient say, is causal in nature such that all stakeholders would desire a consequence of the decision to be an alteration of the health status of the patient. Therefore the intervention of choice has been beneficial. Again, there are ways to argue against this being conceptualised in causal terms. I will again hope to show the limitations of non-causal interpretations. If it can be accepted that causation *is* central to both *Claims 1* and *2*, then it would be hoped that causation in both claims is consistent. That is, what is meant by causation in *Claim 1*, is the same as what is meant by it in *Claim 2*. Empirically, this can be judged in terms of outcomes related to the strength of external validity, that is, the health effect found in population studies as a consequence of the intervention of interest is also seen in future individual patients. This factive empirical account of EBM, however, does not offer insight to the movement's

[29] This is considered below. However, for immediate reference, Rothwell (2005) and Knottnerus and Tugwell (2014) provide informative commentary on this.

philosophical underpinnings. I argue that a stable grounding of the *nature* of the phenomena at play is required. The phenomenon in this case being *causation*. I assume a stance at this point that suggests that what we mean by causation in *Claim 2* is substantially different from what we mean it to be in *Claim 1*. 'It works' according to EBM's prioritised research methods is not necessarily the same as 'it works' for a patient in future clinical practice.

The causal conceptualisation of the basis of EBM through the central and canonical claims, together with consideration of the intended broad product of the movement, allows a way forward for philosophical analysis. Clarifying the stance of EBM gives further exposure of what is in fact meant by 'evidence', and a paradoxical challenge for EBM's underpinning philosophy of evidence.

There are fundamental intuitive challenges to the position of EBM, some operational: *how* is research data integrated into decision-making?, and some philosophical: *what* is the nature of the evidence being talked about? Of course, there are relationships between these concerns insomuch as understanding the nature of the evidence might inform how such information can physically and intellectually be utilised. Beyond these intuitions lie textual criticisms of the movement. The main concern of this chapter is towards the philosophical questions regarding the nature of evidence at play within EBM. To offer support to a philosophical investigation, the textual criticisms can be examined in an attempt to understand whether there are any broad themes of concern emerging following the inception of EBM. My claim is that there is in fact one consistent theme of concern to both critics and proponents of EBM, and this is the notion of causation. This is at the heart of the movement, and at

the heart of the underpinning predecessor components of EBM, namely clinical epidemiology and its statistical methods. At times the idea of causation is hidden behind the mechanics of the process of EBM, at times it is ignored, and at times it is assumed. There is however, a discrete body of philosophical literature that takes causation in EBM as its primary subject matter, which of, course is of central relevance to this thesis. However, I claim that the idea of causation as represented in the literature, and as a philosophical concern emergent from the literature, is problematic for the canonical claims of EBM. This is not to say that the literature is unclear about how it considers causation. In fact, both the literature and the structure of EBM offer apparently clear notions of what EBM means by causation. Paradoxically, it is this that offers the most serious challenge to a philosophy of EBM. The intent of this chapter is to therefore draw from both the literature, and the operational structures of EBM, an idea of how causation is represented in this movement. What will then follow is a problematisation of these representations.

2.2. Textual responses to Evidence Based Medicine

A recent essay in the *British Medical Journal* was somewhat controversially entitled "*Evidence based medicine: a movement in crisis*" (Greenhalgh *et al*., 2014). The essayists provide a summary of twenty years-plus of EBM, pointing to some successes and limitations of the movement. They indicate five key concerns: misappropriation of the EBM 'quality mark', an unmanageable volume of evidence, marginal clinical relevance of statistically significant trial results, EBM induced management driven care,

and failure of evidence based guidelines to adequately reflect complex comorbidity. They conclude:

> *"Much progress has been made and lives have been saved through the systematic collation, synthesis, and application of high quality empirical evidence. However, evidence based medicine has not resolved the problems it set out to address"* (Greenhalgh *et al*., 2014:g3729)

They also make explicit recommendations for a return to the movement's founding principles and for the operationalisation of *". . . individualised evidence and share(d) decisions through meaningful conversations in the context of a humanistic and professional clinical-patient relationship*" (Greenhalgh *et al*., 2014:g3729). So, what Greenhalgh *et al* seem to be claiming is that the founding principles of EBM were, and still are, valid - in some professional sense at least. One key learning point is for the founding principles to be better contextualised in a patient-centred approach to healthcare. I am sure that this is also what the original proponents of the movement meant, and am fully sympathetic to this position. However, this polemic exaggerates a conceptual disjoint that makes it unclear as to *how* evidence from prioritised sources can be contextualised in patient-centred care. The disjoint is characterised by two questions: i) how do the evidential claims of respective sources relate to each other? ii) how do the evidential claims from prioritised sources relate to future clinical decisions? The tone of these conceptual concerns is represented in a range of earlier responses to the movement since its inception, and reflected in the canonical claims. Briefly, examples of responses and criticisms follow.

2.2.1. Early responses

Despite its provocative manifesto, the initial response to EBM was considerably accepting and largely uncritical. 1992 – 1999 saw a range of commentaries that were either focused on reinforcing early messages[30], offering tools for implementation of EBM[31;32], or demonstrating general support and applying the model to different areas of health care[33]. Beyond this, there were subtle signals of disquiet[34]. From several early critics there were some demonstrations that signal the sort of concern that I am interested in regarding the precise nature of EBM's intentions. Conceptualising the premises of EBM as the *outcomes movement*, Sandra Tanenbaum considered how the traditional reasoning skills of physicians that would *". . . draw on all their knowledge, including their own experiences of patients and laboratory-science models of cause-and-effect"*(Tanenbaum, 1993:1269) could be juxtaposed with a movement that *". . . undermines confidence in the physician's ability to act wisely in the face of inevitable uncertainty" (ibid*:1270). Tanenbaum is uncomfortable with the propositions of EBM for some sort of wholesale improvement in the way healthcare operates. There is an implication that EBM is somehow missing the point

[30] For example: Sackett and Rosenberg (1995), Rosenberg and Donald (1995a), Rosenberg and Donald (1995b), Hooker (1997).
[31] For example: Farkouh et al. (1993), Jaeschke et al. (1994), Oxman et al. (1993).
[32] In 1993, *JAMA* began to publish a series of *User's Guides to the Medical Literature* written by members of the EBMWG. These guides were based around EBMs 'triple tenets' of finding, evaluating, and applying evidence in clinical practice and were written to facilitate these processes for busy clinicians. In all, between 1993 and 2000, 25 guides were published that were eventually collated in two volumes of books of the same name (2002).
[33] For example: Hersh (1996), McCarthy (1996), Partridge (1996).
[34] Some general examples of early critics and challenges to EBM: Anonymous (1995), Polychronis et al. (1996a), Polychronis et al. (1996b), Horwitz (1996); Maynard (1996), Shuchman (1996), Walker and Labadarios (1996), Feinstein and Horwitz (1997).

of what healthcare is: "*By mistaking a part of medical knowledge for the whole, the outcomes movement devalues clinical expertise and ultimately medicine itself" (ibid*:1270)[35]

Whilst acknowledging how "*spectacularly successful*" randomised (controlled) trials have been in answering some specific hypothesis of average efficacy, Alvan Feinstein showed concern over some misappropriation of clinical research methods and their tendency to distract from other sources of knowledge (Feinstein, 1994). In the advent of the EBM movement, Feinstein - supporting his early work - strengthens his case for the value of 'subjective' judgement, and basic science in the architecture of a healthcare knowledge base. Feinstein's concerns seem to grow and a few years later he sets out a clear distinction between what EBM counts as best evidence – the *contents* of EBM - and the application - or *practice* - of EBM. By EBM conflating these two phenomena, Feinstein sees a variety of problems. In particular, and in response to EBM's claims of *integrating sources of evidence*, Feinstein points out an obvious limitation: "*. . .the EBM "textbook". . . offers no guide or instruction for the pathophysiological or clinical judgemental reasoning used in clinical decisions"* (Feinstein and Horwitz, 1997:533). I do not think Feinstein is referring to a 'method' or some practical way of joining up different sources of evidence here, but rather some sort of theoretical principle in which differing, and

[35] The notion of healthcare craftwork has previously been described, for example Sennett (2008). Carmel (2013:742) describes such craftwork (in the context of critical care) as *"a practical, interpretative orientation to different kinds of knowledge… require[ing] embodied skills to be mastered".* Sennett (2009) has considered the demise of such medical 'craft' at the hands of numerous neo-liberal reforms of the NHS. He claims that nursing and medical craftwork traverses a "*liminal zone between problem solving and problem finding*" utilising a continuous interchange between tacit knowledge and explicit awareness (Sennett, 2009:48).

potentially conflicting, sources of evidence might be integrated. A more cynical reading of the early EBM proposals might conclude that it was in fact never the intent to integrate de-emphasised components to act as *sources of evidence* as Sackett had already alluded (Sackett *et al*., 1996). This gives a further indication of *what* in fact the evidence talked about is *of*. What I mean by this is that so far the EBM movement itself has not offered an explicit way what they mean when they talk about *evidence*. Only from starting to understand some of the challenges can a sense be gained that there must be a single notion serving as the central object that the evidence (as talked about in EBM) is concerned with. Again, I say this is causation. And in particular, some type of causation that is able to be transferred between different spatiotemporal environments. Tanenbaum talks about clinical research being a component part of medical practice, with a worry that traditional components of practice will be undermined in an *outcome measures* environment. But this would only be the case if those traditional components were thought of as sources of evidence of causation. If clinical experience was considered as something other than a source of evidence – a mechanism by which research data is transferred to the patient, say - then there would be no reason for it to be undermined, indeed it could be further valued. Feinstein also worries about the integration of varying sources of evidence. Again, if what EBM truly means is that 'de-emphasised' sources are not actually sources of evidence at all, then any problems of integration become redundant. Likewise, Feinstein's concerns about the conflation of the *content* and *practice* of EBM become less worrisome as these two notions are no longer conflicting, and have the potential to be complementary. A response in *The Lancet* to Tanenbaum's defence of clinical experience and pathophysiological mechanisms

provided sympathetic support for her holistic concern: *". . . let us agree that good medicine will always blend the art of uncertainty with the science of probability*" (Naylor, 1995:841). The prioritisation of EBMs central claim is, however, soon reinforced "*But let us hope that the blend can be weighted heavily towards science, whenever and wherever sound evidence is brought to light" (ibid*:841-2). This mix of sentiment is typical within EBM but offers little in understanding what the role of de-emphasised sources should be. I suggest that the problem can be represented by two distinct positions, also noted by others, in particular Tonelli (2006b):

i) 'De-emphasised' components of EBM are evidentiary: they *can* act as valid sources of evidence (of causation) in the absence of 'higher level' evidence.

If so, why would they be de-emphasised in the presence of higher-level evidence?

ii) 'De-emphasised' components of EBM are non-evidentiary: they are *not* to be considered as sources of evidence (of causation) at all, but rather a medium for the skilled transference of research data (should it exist) to clinical decision, or something else.

If so, then why does EBM talk about them as evidence sources at all?

My view is that position i) is the most likely case. With the brief suggestion by Sackett aside, the opposite view is not at all reflective of what EBM actually states. Further, thinking of 'de-emphasised' components as non-

evidentiary might work for clinical experience, but is troublesome for methods of basic science of pathophysiological mechanisms. These methods possess a scientific intent that could be nothing other than to develop knowledge of causation. If this is the case, then there are further problems. EBM prioritises certain methods based on their scientific and statistical rigor that serves to reduce systematic biases present in de-emphasised levels of evidence. If the evidence we are talking about is indeed evidence of causation, then EBM has now developed 'rules' for establishing causation, *viz* that the best evidence of causation comes from prioritised methods of *type X*. But in the absence of *type X* methods, de-emphasised sources of *type Y* can serve as adequate in terms of evidence for causation, for example: "no RCTs exist for this situation, but my clinical experience and knowledge of pathomechanics will allow me to make this clinical prediction". But the sources do not confer to the rules set for evidence, so how can this be so? This situation might be grounded in practicalities of clinical practice – a decision has to be made regarding treatment, regardless of the level of evidence available – but presents a philosophical challenge if EBM is to substantiate itself as a robust and trustworthy model of practice. I propose that the source of the problem is in understanding not just that the evidence talked about is evidence of causation, but, if so, what *is* the causation, and how can it serve to satisfy the intentions of EBM, *that is*, transcend methods, sources, and environments?

The ongoing response to EBM found in relevant literature to date offers a dynamic narrative of the continued evolution and development of the movement. This narrative is perhaps best exemplified by focused attempts to engage proponents of EBM into deep discourse on traditional and

emerging phenomena[36]. Frequently, the arguments set up by EBM's critics centre around particular challenges, for example commonly cited are operational challenges such as limited time and resources, organisational and professional constraints, or the need to develop new skills (Straus and McAlister, 2000). I see these as challenges that are not necessarily unique to EBM, nor deeply problematic. They are most likely self-limiting or easily resolvable in a practical way, if there is the capacity to do so. Beyond such practical concerns lie deeper conceptual ones, which I see as constituting more of a fundamental challenge to EBM. These conceptual concerns seem to relate consistently to three key areas[37;38]:

i) The philosophical basis of the movement[39],

ii) The ordering of sources of evidence (prioritising and de-emphasising),

iii) The relationship between data from prioritised evidential sources and individual patients.

[36] For example, the *Journal of Evaluation in Clinical Practice* has published special issues of discussion papers on EBM in 2010 and 2012.

[37] These themes can be found throughout the literature base, and are often categorised in reviews of criticisms of EBM, for example, Straus and McAlister (2000); Cohen et al. (2004); Lambert (2006).

[38] For specific textual examples of points ii) and iii), see Haynes (2002); Gupta (2003); Porta (2004); Miller and Jones-Harris (2005); De Vreese (2011); Muckart (2013); Bouffard and Reid (2012); Seshia and Young (2013a); Seshia and Young (2013b); Rees (2012); Thorgaard and Jensen (2011).

[39] I am thinking of these as commentators who provide broad analyses of the underpinning philosophical basis of EBM, rather than those who have focused in detail on specific dimensions of EBM, e.g. mechanisms. For examples of broad philosophical commentaries, see Shahar (1997); Charlton and Miles (1998); Harari (2001); Ashcroft (2004); Kulkarni (2005); Worrall (2010b); Hjorland (2011); Howick (2011); Solomon (2011).

These three areas serve to further underpin the basis of this thesis. Of course, the textual concerns regarding point i) relate well to the primary purpose of the thesis, which is to provide a contribution towards a more substantial philosophical grounding for evidence based healthcare. In this case, the philosophical focus of this thesis is on a particular dimension – causation – rather than to provide a wholesale philosophy of EBM as a challenge to, say Howick (2011). This said, I would claim that an exploration and revision of what causation could be in evidence based healthcare will undoubtedly influence a re-analysis of a broader range of conceptual, epistemological, methodological and practical dimensions of EBM.

Points ii) and iii) are again in line with the canonical claims, and are considered throughout this section in varying contexts and dimensions. For example, point ii) relates broadly to the focus on evidence hierarchies, point iii) relates broadly to the discussion on evidential relevance and external validity. Before going further however, it is worth considering two specific areas in isolation as they raise some of the arguably most interesting and pressing concerns related to this thesis. First, a propositional challenge of the person-centredness of EBM (§2.3), second, analysis of the broader structure of EBM, and what this reveals about the nature of causation (§2.4).

2.3. Person centred medicine

That EBM could be anything other than person centred might seem counter-intuitive given its core intents. However, considering the emergent themes witnessed so far in the literature, a dialogue regarding

the person-centredness of the movement might seem valid. Indeed, explicit alternative movements of health care purpose themselves with just such dialogue. This section focuses on the positioning of one such movement, *Person Centred Medicine* (PCM).

The dialogue and the movement is best characterised by a specific line of narrative found in the literature, examples being Miles and Loughlin (2006), Loughlin (2009), Miles (2009c), Miles (2009a), Miles (2009b), Miles and Loughlin (2011), Miles and Mezzich (2011), Miles and Loughlin (2011), and Miles and Mezzich (2012). Further, specific journals have emerged as a vehicle for this response, for example, *The International Journal of Person Centered Healthcare*, and the *European Journal of Person Centered Healthcare*[40]. Recently, a focused call for active and progressive dialogue has been made (Miles and Mezzich, 2012), (Miles and Ashbridge, 2014). What these authors mean by PCM is explicated:

> *"(PCM is) an affordable biomedical and technological advance to be delivered to patients within a humanistic framework of care that recognises the importance of applying science in a manner that respects the patients as a whole person and takes full account of his values, preferences, aspirations, stories, cultural context, fears, worries and hopes and thus that recognises and responds to his emotional, social and spiritual necessities in addition to his physical needs"*
> (Miles and Mezzich, 2012:219)

[40] And further still, a recently instituted *European Society for Person Centered Healthcare.*

PCM builds on an earlier 'landmark' casuistic framing of how EBM should be considered (Tonelli, 2006a). Signposting to the evolution of a biopsychosocial framework of care (Engel, 1977) is conducted via a historical background of care related to both Francis Peabody's *The Care of The Patient*, and Paul Tournier's *Medicine de la Personne* [41]. Referring to Engel's rejection of a *monistic or reductionist* approach to clinical practice, the sentiments of PCM are clear:

> *"In doing so, he [Engel] directly laid the foundations of the thinking that now recognises the importance of complexity theory in medical practice and that illustrates that clinical phenomena are generally far too complex to be understood solely through the use of linear cause-effect models"* (Miles and Mezzich, 2012:210)

.

PCM sketches out its emergence from a developing EBM movement and a general idea of historical 'good care' referred to as patient-centred care. The difference between the *patient* and the *person* is emphasised in sympathy to a '*deep respect for patients as unique living beings*' (Epstein and Street, 2011:100). PCM gives a substantial and focused account of a 'crisis' of knowledge, care, compassion and costs in modern medicine (Miles and Mezzich, 2012). Its claim is that an over-emphasis of scientific and scientistic medicine has resulted in the depersonalisation of care. In response, it proposes an emergent humanistic model of clinical practice

[41] See: Peabody, F. W. (1927). The Care of the Patient. Journal of the American Medical Association 88, 877 – 882.; Tournier P. (1940) Médicine de la Personne, Neuchatel, Switzerland: Delachaux et Niestlé.

grounded in holism and complexity. There is an easy and intuitive response to this, that EBM does not in fact 'depersonalise' care at all. EBM proponents have indeed suggested how EBM has led to the sophisticated articulation of the proper role that patients' values and circumstances play in clinical decision-making, for example, Montori and Guyatt (2008), Montori *et al*. (2013). Further, it may be that the PCM argument sees EBM as a rigid strategy for the practicalities of clinical decision-making (always do what is supported by the best evidence). This might not be a fair characterisation of EBM because of the tension it artificially creates between facts and individual values. However, despite these intuitive responses, it is still unclear to see how the relationship between facts (data, say) and values (clinical context, patient values) might actually develop whilst maintaining the grounded principles of holistic person centred care. This, as I see it, is a challenge that is exacerbated rather than eased by the first canonical claim of EBM. Likewise, regarding the possible misinterpretation of EBM, it seems there are limited ways to interpret the movement, and dimensions of these will be considered in detail in *Chapters 3* and *4*. In brief, although *other ways* of viewing EBM might be considered, the challenges set by PCM do not dissolve. Whether EBM is thought of as a 'rigid structure', an 'epistemological guide', or a 'practical heuristic', there are still inherent components that make it unclear as to how the tenets of EBM can in fact be operationalised, and on what conceptual basis this can be done.

The general idea of PCM is one that this thesis is aligned to, and in some humble sense this thesis might offer a form of thought related to how PCM might best develop. It is not, however, the intention of this thesis to dismiss the valuable role that science and systematic research play in

healthcare. Thus, I have little interest in using EBM as some form of straw man by which to pronounce "the new way".

PCM searches for *a rational form of integration* between EBM and PCM. It shows concern about a possible danger of this being a wholesale shift towards obliging to care for patients on their own terms, with the clinician being a "*simple provider of goods*" (Miles and Mezzich, 2012:219). I take this as a serious and warranted worry. An ill-considered response to the 'crisis' has the potential to dismiss knowledge from valid sources of evidence and revert practice to some form of behaviour, thought about in terms of clinical freedom, for example Hampton (2011). A position where coalescence is achievable is something that is desirable. The claim is that for this position to exist, examination of the fundamental notions on which health care is based is now necessary. This is opposed to the numerous existing proposals of practice reform that centre on the re-cycling of unexamined existing notions of health and health science[42].

All aspects of health including disease processes, diagnosis, scientific evidence, effects of interventions, patient values and so on have a common ground: causation. No aspect of health care and its associated science can escape this notion. If the present dialogue is about the coalescence of two discrete models of medicine, it must now be asked how they relate to each other with respect to fundamental notions such as causation. How is the type of causation we think of in individualistic cases of PCM represented

[42] Many authors have offered alternatives to the EBM model that I do not think offer a change in the fundamental principles of the movement as it is. This is not to say these theses are not valuable, it is just not what I am after at this point in time. Examples that come to mind are Harald Walach's 'circular not triangle' re-structuring of evidential elements (Walach *et al*., 2006), and Susan Horn's challenge of RCTs with 'clinical practice improvement' approaches (Horn e*t al*., 2005). Interesting commentary is offered by such models, but the fundamental idea of causation is unchanged.

in its associated sciences? Proponents of EBM might be tempted to stake dismissive claims about the utility of attending to understanding the nature of causation. EBM seems to be moving towards an exclusive interest in establishing "what works" through the process of, for example, systematic reviews of RCTs. What causation is, therefore, might be seen as unimportant. The outcomes of trials show an effect and that is all we need to know. This position however, explicitly states an accepted understanding of what causation is: it is something to do with the structures of research methodologies. "What works" is a causal term firmly embedded in this particular scientific process. Development of coalescence must therefore have something to do with uniting the meaningfulness of individualistic causation with the scientific process of investigation. Or at least the outcomes of existing scientific research methods must be read with reference to person-centred causation.

I consider the PCM movement to be a sharp prompt for dialogue between approaches to healthcare that is being undertaken in a sophisticated and refreshing way. Its quest for coalescence of models seems valid and is likely to have the best chance of success in pushing the issue at hand. There is a risk however that through such coalescence, traditional and unexamined fundamental notions of healthcare will be let slip. Progress in the understanding and evolution of how healthcare should best be thought of should avoid being impeded by the reluctance to challenge historic and dated notions of healthcare and health science. It is with this worry in mind that this thesis takes the sympathies of both EBM and PCM and attempts to search for some sort of unifying principle, at least as far as the idea of causation is concerned.

The next section begins an attempt to further unravel some of the detail and complexities of the inherent structure and associated challenges of EBM. It begins with a brief re-focus on the background issue of external validity and some of its philosophical dimensions. I see external validity as a core concern, but as stated earlier, one that goes beyond the simple practical interpretation that is the issue of homogeneity between the trial subjects and future patients. By making some abstract dimensions of external validity more visible, further support to the framing of the structural challenges of EBM can be given. This section, and the chapter itself, will conclude with a commentary of the hierarchical structures of EBM and what they might mean for how EBM constructs its notions of causation.

2.4. Evidence where? The space between here and there

As a concerned geriatrician, J Grimley Evans questioned the appropriateness of outcome data from prioritised research methods – RCTs – to individual patients, reflecting *Claim 2*:

> *"Such problems as 'off legs', 'confused', 'wobbly', may be too heterogeneous and ill-defined for collective study, but an RCT on a small definable subset of patients with such afflictions could give a result that would harm the majority if extrapolated to them"* (Evans, 1995:461)

As indicated above, the notion of *external validity* is a long recognised and extensively debated worry within health research, as well as in philosophy. A recent editorial in the *Journal of Clinical Epidemiology* demonstrates that the concern about the clinical significance of medical research is still far from resolved (Knottnerus and Tugwell, 2014). In 2005, Peter Rothwell – an original and continual proponent of EBM - made it clear in a special series in *The Lancet* that the generalizability of findings from RCTs represented significant problems in the operationalisation of EBM:

> *"RCTs. . . are the most reliable methods of determining moderate treatment effects, but external validity is inevitably less than perfect. . . because the aim is not to measure the benefit that will be derived from treatment in clinical practice"*
> (Rothwell, 2005 :83)

However, beyond the standard discourse on external validity, what are Evans and others saying? It seems again that the relationship between population study and individual patient provides an indication as to what, or what not, EBM means by evidence. This is a clear example[43] of a prioritised method providing an outcome of which EBM would want to be used in clinical decision-making, but the value and role of which is altered in an individual clinical situation. So the evidence established at source (RCT) fails to hold when future patients ('extrapolated to them*')* are

[43] I am not talking about empirical examples here, but alluding to conceptual underpinnings of what EBM is proposing.

considered. This may well be simply about heterogeneity, and the 'wrong' patients are being represented in a trial, but there is also a signal to a deeper conceptual issue: the prioritised method has produced *something*, but what is the value and stability of that *something*?[44] Indeed what is the foundational nature of that *something*? I could repeat now that this *something* is evidence of causation, but that does not move the debate forwards because at this juncture, the word *causation* is vacuous. We need to look closer at the structure of the process and products of methods in order to gain ground with assessing the nature of causation.

Nancy Cartwright has been vocal in the philosophical discourse on *external validity.* By framing outcomes of RCTs as gold standards for predicting effectiveness, the central issue of EBM becomes one of external validity, so Cartwright claims (Cartwright, 2011b). She draws attention to the difference between 'it-works-somewhere' (efficacy) claims, and 'it-will-work-for-us' (effectiveness) claims, and sees RCTs as establishing the former, but insufficient for prediction of the latter. There is nothing substantially different about this concern to the standard research discourse on external validity so far. The idea is that RCTs should reflect the population of interest as best as possible. However, Cartwright provides a terminology for this that allows us to develop a greater appreciation of some of the inherent limitations of EBM in permitting outcomes to be readily transferred from study to patient. For example, following Cartwright and Munro (2010) *T* is the established causal factor of outcome *O*, from a robust trial (or series of trials) in study population *X*.

[44] As an example of this concern: recently, a *Fragility Index* has been developed to better indicate the confidence readers (presumably users) of RCTs can have when extrapolating RCT results to clinical decisions, Walsh *et al*. (2014).

The problem of external validity is simply under what conditions *T* will cause *O* on any new population *θ*. In order to draw causal conclusions between *T* and *O*, Cartwright sets the following sufficient conditions: i) the causal laws for *O* in *θ* are identical to those in *X*, ii) or at least a causally homogenous subpopulation is present in both *X* and *θ*. The same restrictions would apply when "*back(ing) off" (ibid*:261) from causal conclusions and rather looking at the stability of effect sizes (probabilistic) between *X* and *θ*. In fact, notions of causation are still present as the probability of *O* being fixed relies on assumptions of *causal fixing (ibid*:261). What Cartwright has offered, I think, is a focused exposure of the implicit *messy* ground between clinical research outcome and clinical decision (for a patient or for policy). Not that this was ever a concern of EBM from the start, but the EBM literature, at least initially, implied that the journey between 'it-works-somewhere' and ''it-will-work-for-us' would be smoother than the last twenty years or more of clinical research and analytical discourse have suggested. The crux is in the *causal laws* at *θ*. To initiate a move towards resolution in the issue, Cartwright starts to talk about *capacities* (a word she uses synonymously with *powers*[45]) (Cartwright, 2011a). *Capacities* being a kind of causal claim that goes something like *T reliably promotes* [46] *O* across a given range of conditions:

> *"Effectiveness predictions are always dicey. Use of scientific evidence makes them far less so. But to use this evidence we need to tackle, not ignore, the messy issue of "theoretical"*

[45] More to come on this in *Chapter 5*.
[46] *Reliably promotes* - meaning that there will be more cases of O with T than there would be without T.

> *warrant for capacities in medical and social contexts"*
> (Cartwright, 2011a:1401)

This seems similar to Greenhalgh *et al*. (2014): evidence from robust scientific research forms a central role in clinical practice, but its use in decision-making (outside of the study) is highly context-sensitive. Under what conditions does *T* cause *O*? What are the causally relevant factors at play in a humanistic and professional clinical-patient relationship (or health policy)? Within which research data is to be integrated? What does this context-sensitivity say of the type of causation being established by prioritised research methods?

2.5. The structure of Evidence Based Medicine

We have clearly seen that, in accordance with canonical *Claim 1*, some research methods are prioritised as sources of evidence. Fundamentally, these are comparative methods utilising statistical approaches that derive from a history of trials of efficacy and effectiveness, and clinical epidemiology. The most favoured method is the RCT. The justification so far is that these methods offer substantially more rigor in collecting and analysing data from populations samples than could ever be hoped for by traditional sources of evidence, namely clinical experience and basic sciences investigating pathophysiological mechanisms of disease (*mechanisms*). Accordingly they are able to control for subjectivity and humanistic biases associated with clinical experiences. Played-off against mechanisms, they offer data on clinically meaningful outcomes related to

health and living, whereas basic sciences focus on pathophysiological outcomes that might not relate directly to clinical status[47]. However, although RCTs have so far been held up as the exemplar of sources of evidence – "(*they have) become the "gold standard" for judging whether a treatment does more good than harm"* (Sackett *et al*., 1996:72) - there are a range of clinical research methods that EBM also valued at its inception, with even closer associations with clinical epidemiology, namely observational studies[48]. EBM talks in terms of outcomes, and the pragmatic values of comparing or observing groups. This is framed as a clinically and politically useful function in terms of making broad (population) or individual (patient) decisions. At this point, the commitment to the substance of evidence ceases. There are no claims from either epidemiology nor EBM about precisely *what* is being established – for example epidemiology's open claim of being atheoretical (Broadbent, 2013a:6). However, I propose that the substance of the evidence is unconditionally causation, and this is most clearly demonstrated in the area of therapeutics. The prioritised clinical research methods, I claim then, are concerned with establishing what intervention *causes* a change in a patient's health status. *Efficacy* and *effectiveness* are both causal terms. At this juncture I am merely conceptualising 'causation' as something in line with a lay interpretation of the term, for example '*the act of causing something*', '*the relationship between cause and effect*', '*the product of an effect*'. In this sense, the methods being discussed are ones whereby the effect of a therapeutic intervention is observed and, for comparative methods,

[47] Discussed in *Chapter 4*.

[48] 'Observational studies' meaning epidemiological approaches to health determinants such as cohort studies, 'outcome' research, case-control studies, case-series studies.

compared against another observed effect by another intervention. Thus the intervention/s is/are considered as the cause, and the process witnessed has been one of causation. There are simple stances against this position, that is, that causation is not central to EBM's claims. These are considered below, in the context of the hierarchical structure of EBM's elements.

2.5.1. Hierarchies: a clue to a theory of causation

The commitment to prioritise some research methods as sources of evidence over others is best illustrated in evidence hierarchies. An evidence hierarchy is a partially-ordered set in which the ordering of the elements is based on the property of the individual element's ability to, in this case, control for systematic bias. The origin of evidence hierarchies in relation to how EBM should be seen to provide certain levels of evidence stems from early-EBM 'guidebooks' aimed at facilitating best decision-making[49], and their use was promoted with a crisp confidence:

> *"The hierarchy implies a clear course of action for physicians addressing patient problems: they should look for the highest available evidence from the hierarchy"* (Guyatt and Rennie, 2002:13)

Hierarchies of evidence are sympathetic to claims of the evidential superiority of discrete methods. They are concerned with effectiveness of intervention and in line with the historical underpinnings of EBM, they

[49] For example, Sackett *et al*. (1997); Guyatt and Rennie (2002).

most commonly place systematic reviews of RCTs, and then single RCTs, above other forms of research methods, see Figure 1 for example.

There is therefore explicit evidential superiority claimed for methods towards the top of the hierarchy. In this sense, hierarchies provide EBM's "*rules of evidence*" (La Caze, 2008:356). The favoured position seems to be that hierarchies should be given an epistemological reading. This is what has been referred to as the *categorical interpretation* (La Caze, 2008): thus, any given source of evidence will always give more evidential support than a source from lower down the hierarchy.

In this case, RCTs will always 'trump' observational studies, for example. If the central issue truly is one of causation, then we can say that RCTs provide a better level of causal evidence than sources below, including observational studies and basic science research. For now, this type of categorical interpretation will be assumed. The problems of interpreting hierarchies in this way, and consideration of alternatives, are dealt with specifically in *Chapter 3*. Once again, the challenge of EBM's commitment to the precise role of de-emphasised components arises. In this case, what is the normative stance for observational studies?

Do they have a causal role in the absence of higher levels of evidence? If so, how can this be the case given EBM's self-imposed epistemological *rules of evidence*? Part of the answer to this is to move closer to understanding the structural differences between elements to try and identify at what point, or points, there are substantive changes that influence the epistemological value of each element. Intuitively, it would

Level of Evidence	Therapy / Prevention, Aetiology / Harm
1a	SR (with homogeneity*) of RCTs
1b	Individual RCT
1c	All or none **
2a	SR (with homogeneity) of cohort studies
2b	Individual cohort study (including low quality RCT, e.g., <80% follow-up)
2c	"Outcomes" Research, Ecological studies
3a	SR (with homogeneity) of case-control studies
3b	Individual Case-Control Study
4	Case-series (and poor quality cohort and case-control studies
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"***

SR: Systematic Review; RCT: Randomised Controlled Trial
*From OCEBM (2011): "By homogeneity we mean a systematic review that is free of worrisome variations (heterogeneity) in the directions and degrees of results between individual studies. Not all systematic reviews with statistically significant heterogeneity need be worrisome, and not all worrisome heterogeneity need be statistically significant. As noted above, studies displaying worrisome heterogeneity should be tagged with a "-" at the end of their designated level."** From OCEBM *(ibid)*: "Met when all patients died before the Rx became available, but some now survive on it; or when some patients died before the Rx became available, but none now die on it". *** "physiology, bench research or "first principles"" are what I will eventually be referring to as *mechanistic* research in later chapters.

Figure 1: Evidence hierarchy in health science research for decisions on therapeutic interventions, prognosis, or harm.[50;51]

[50] Extracted from the latest modification of evidence hierarchies from the Oxford Centre for Evidence Based Medicine (OCEBM) http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/, accessed 11/11/14

[51] Figure 1 is a typical, and representative, example of what health care sees as an evidence hierarchy. There are others, but the features are similar in so much as RCTs and systematic reviews of RCTs are placed high in the hierarchy, above non-controlled studies and other types of research or sources of evidence. *For example,* a review of a report for the Agency for Healthcare Research and Quality of the US Department of Health and

seem that the transition between observational studies (and all elements below) and RCT-based elements is an area of utmost interest. That intuition is based on the facts that EBM, and its adopted hierarchies, grew from an epidemiological (non-controlled) stance and developed by adopting statistical methods of comparison (controlled); and that RCT-based elements consistently hold higher levels in all hierarchies. The hierarchical form itself is tempting commentary on what is at play between these two key elements. If EBM epistemologically prioritises RCTs, then why? If EBM still values observational studies (and below), then why and for what reasons? These points are addressed below in §3.2 where a form of essentialist critique of the hierarchy structure will be offered. For now however, what can hierarchies offer in terms of an understanding of causation?

2.5.2. Hierarchies expose health sciences view of causation

In the categorical interpretation of hierarchies, RCTs offer causal claims. So what do RCTs provide to the causal account that is apparently lacking in correlational based observation studies, or below? I do not wish or intend to cover much-trodden ground about the whys and wherefores of RCTs and other research design. However, I do need to present some basic structuring to allow the development of the reconceptualisation of what RCTs and other designs mean in terms of a causal theory.

Human Services found 34 different systems for evaluating bodies of clinical evidence demonstrating similarities in the prioritisation of sources of evidence (West *et al.,* 2002).

In reiteration of some thoughts from *Chapter 1*, RCTs are proposed to be able to make causal claims based on their methodological structure. Randomisation provides closely matched groups, say, an intervention group who would receive the variable of interest (active treatment *t*), and a control (or comparison) group (*c*)[52], by whom the effect of the variable of interest, *t*, is compared. The controlled manipulation of variables ensures that one group differs from the other by the variable of interest *t* alone. Matching groups for known variables can be done without randomisation[53].

The additional value of randomisation is that it supposedly also matches the groups for unknown variables. Thus, any differences in outcome recorded between the groups have to be due to the variable of interest *t*. This is the characteristic difference between RCTs and observational studies. Therefore, if RCTs are considered as providing evidence of causation whereas observational studies might not, then it is on this characteristic that the understanding of causation lays - this is what makes the claim causal. In line with the frequentist approach to statistical hypothesis testing and estimation (as detailed in *Chapter 1*), this structure might be expressed in terms of the effect that *t* has on the primary clinical endpoint, or an outcome represented by a test statistic X, that has a function - an unknown parameter θ. θ_{dif} is the difference in rate of occurrence of the endpoint between groups *t* and *c*, so $\theta_{dif} = Xt - Xc$. Estimation provides some form of clinically intended utility by allowing judgment on the probability of the range of observed values covering the

[52] Placebo

[53] See arguments by Worrall, for example (Worrall, 2010a)

true value of θ . This summary merely re-sketches the principle that RCTs offer causal claims because they control for confounding variables and use robust statistical analysis to test hypotheses regarding group differences.

Philosophically, there is a limited way of understanding this, which is to treat such causation as a broadly 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 EUH 7.1.60)

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 condition. The counterfactual account is developed by many, but perhaps David Lewis offers a comprehensive modern philosophical treatment of the conditional (Lewis, 1973b). In sum: "*$A \mathrel{\square\!\!\rightarrow} C$ is nonvacuously true iff C holds at all the closest A worlds*."[54] (Lewis, 1973a:561). Cartwright also represents counterfactual conditions in experimental-like trials by saying:

[54] Lewis uses the symbol "$\square\!\!\rightarrow$" as the counterfactual operator. For Lewis then: "*Given any two propositions A and C, we have their counterfactual $A \mathrel{\square\!\!\rightarrow} C$: the proposition that if A were true, then C would also be true. **The operation $\square\!\!\rightarrow$ is defined by a rule of truth**, as follows. $A \mathrel{\square\!\!\rightarrow} C$ is true (at a world w) iff either (1) there are no possible A-worlds (in which case $A \mathrel{\square\!\!\rightarrow} C$ is vacuous), or (2) some A-world where C holds is closer (to w) than is any A-world where C does not hold*" [emphasis added] (Lewis, 1973a:560)

> *"...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)

that is, p(O/T)>p(O/¬T)

Accordingly, the counterfactual state (control or comparison group) is in fact the truthmaker of causation: that is 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 – at least as EBM desires it to be by *Claim 1* and as exposed by the hierarchical structure of its sources of evidence - is then counterfactually dependent. This is a secure position if elements below RCTs are to be considered non-evidentiary. However, as suggested, this seems not to be a favoured position and evidential claims for causation do exist in relation to non-controlled (non-counterfactual) observational studies, for example smoking causes cancer. So if the rules of evidence differentiate controlled methods as being constitutive of causation due to their structural characteristics, but causal claims still arise from non-controlled methods, then counterfactual dependency cannot be a sufficient account for the theory of causation in healthcare science.

The structure and function of observational studies requires some expansion if the essence of causation is to be considered further. For the

purpose of this step, observational studies[55] will be thought of simply as that collection of methodologies embedded in the tradition of epidemiology whose intention is to investigate associations between determinants of health and health outcomes[56]. They do this by observing large groups of patients, in various ways[57]. The differentiating characteristics of observational studies from RCTs are that "*investigators neither allocate patients to receive an intervention,* [nor] *administer an intervention*" (Howick, 2011:40). As such, observational studies suffer from "*nearly intractable problems of 'confounding by indication'"* (Vandenbroucke, 2008:e67), or as Howick summarises:

> *"The main problems with observational studies are that they suffer from (i) self-selection bias, . . . (ii) allocation bias, and (iii) performance bias"* (Howick, 2011:40)

So, for the purpose of searching for their causally evidential basis, we can surmise that although observational studies do indeed follow-up and identify patterns of associations in large groups of people over-time, controlling for confounding and systematic biases are absent. The *closest possible A world* does not exist. How then can we read causation into these elements given the counterfactual conditional asserted by Hume? Well, Hume allowed that causation could be wholly represented in fact by

[55] Meaning those types of methodological approaches referred to in Figure 1 between Levels 2b and 4.
[56] More of observational studies in *Chapter 3*, particularly their intentions of discovery and explanation. For now, the conceptual basis will suffice.
[57] A more detailed and contextualised analysis of the role of observational studies on conceptualising a causal theory is given in *Chapter 3*.

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, 1740 A 9)

Thus, if an observational study can demonstrate that the cause always precedes the effect (*a* precedes *b* in time), that the effect is consistently close to the cause (*a* and *b* are spatiotemporally contiguous), and that the association is repeatedly and constantly observed (events like *a* are invariably followed by events like *b*), we can in fact still claim causation in a Humean sense (*a* causes *b*), but not counterfactually. This *regularity view of causation* offers a better philosophical stance for supporting causal claims from observational studies, in the sense of capturing how evidential frameworks view causation. The regularities view is still embedded with a counterfactual make-up: trials simply compare the difference between two or more regularly occurring events. In this sense, the counterfactual condition can thus be seen as some sort of 'add-on' to strengthen a belief in the observer's impression of the comparative rates of events. So, we can say that at least two independent, and sometimes inter-related, causal concepts are evident in discretely categorised research methods: *counterfactual dependency* and *regularity*. Both, however, are richly Humean notions.

Let us consider a further dimension to understanding what causation might be here. This relates to EBM's de-emphasis of evidence from

mechanistic science and mechanistic reasoning. This, I say, further supports the notion of causation in EBM being considered as something Humean, or probably more accurately, neo-Humean. Take this 'on the idea of a *necessary connexion*' from Hume's *Enquiry*:

> *"The impulse of one billiard-ball is attended with motion in the second. This is the whole that appears to the outward senses. The mind feels no sentiment or inward impression from this succession of objects: consequently, there is not, in any single, particular instance of cause and effect,* ***any thing*** [sic] ***which can suggest the idea of power or necessary connexion****"* [emphasis added] (Hume, 1748 EUH 7.1.50)

So, neo-Humeans have a strict interpretation of this. Briefly, for the present purpose, we can use Lewis' *Neo-Humean Supervenience* programme as a helpful example of such neo-Humeanism:

> *"... all there is to the world is a vast mosaic of local matters of particular fact, just one little thing and then another. ... We have geometry: a system of external relations of spatiotemporal distances between points. Maybe points of space-time itself, maybe point-sized bits of matter or aether or fields, maybe both. And at those points we have local qualities: perfectly natural intrinsic properties that need nothing bigger than a point at which to be instantiated. For short: we have an arrangement of qualities.* ***And that is all. There is no difference without***

> ***difference in the arrangement of qualities. All else supervenes on that***" [emphasis added] (Lewis, 1986:IX)

Thus, the world according to neo-Humeans is simply a vast collection of local matters of facts with all else supervening on the mosaic of facts. The facts themselves however are "*devoid of any intrinsic nomic, causal, or modal character*" (Jacobs, 2011:81). In neo-Humean terms then, EBM seems to have no concern with understanding causes as anything more than regularities of facts. That is, there is nothing internal to the causal process that relates to a cause producing an effect, for example, some sort of real force or compulsion. Causation is just one thing followed regularly by another. EBM seems not to claim that causation is itself observable in either RCTs or observational studies. It is only the regularities of one event being followed by another that is observable.

Although neo-Humeans (and EBM) might be happy with this stance as a complete account of causation, health science and healthcare 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, healthcare itself is constructed of clinical experiences, patient values and social contexts. Indeed all of these elements are explicitly embraced and showcased in EBM's manifesto. If a Humean stance is to be taken, then what is there to be said of remaining knowledge, experiences, patient input, and contexts? The EBM framework determines that clinical decisions – entailing causal intentions – should integrate as much of this knowledge as possible. A neo-Humean commitment seems not to allow such background conditions a role in the understanding of a precise nature of causation in health care, thus an

ontological tension seems to exist. This tension exists in at least two places: First, tension within the research methods themselves. Although broadly Humean, there are some difficulties in understanding the relationship between comparative trials (counterfactual dependency) and observational studies (regularities) in terms of the causal claims made by EBM. When is it acceptable for a causal claim to be contingent on observational studies, for example? This matter aligns to the first canonical claim of EBM and will be explored in detail in *Chapter 3*. Second, tension is deepened in respect of *Claim 2* by EBM's proposed alignment to a neo-Humeanist metaphysic that the world is a vast collection of particular facts with no *substance* to connect or account for the relationships between such facts. This makes it troublesome to understand how observed facts (supported or otherwise by a counterfactual condition) can remain stable through their transition to spatiotemporally removed environments. What is holding the facts together in order for them to remain stable during their transference and operationalisation in the complex and context-sensitive situations of clinical decision-making for individuals and populations? This is an essential and critical component to the thesis. However, it will be left aside for now whilst the structuring of EBM is dealt with further, specifically as to whether or not a Humean account of causation in EBM is a valid interpretation.

2.6. Conclusion

To summarise the central concern: EBM -when referring to therapeutic interventions - clearly prioritises certain methods in terms of establishing causal associations between interventions and health outcomes. In doing

so, it de-emphasises other elements as 'sources of evidence', but still values them in some unexplained way. It seems, however, that there is some normative evidential role for de-emphasised elements.

The claim here is that the concern cannot be sufficiently satisfied because there is a paradox related to the logic of canonical claims of EBM. The paradox is that *the very prioritisation of evidential elements for use in clinical decision-making (Claim 1) prohibits use of this evidence in clinical decision-making (Claim 2)*. There is an implication here, in causal terms, that the causation established through prioritised research methods does not align with the causal intentions of clinical decisions with future patients.

This has led to an exploration of what EBM seems to think is constitutive of causation. It has been possible to do this through examining the structural make-up of evidential elements found within EBM. I have claimed that a Humean account of causation can be revealed through this examination. However, the precise nature of what causation is seems to be inconsistent, entailing at least counterfactual and regularity theories. Further, what this causation is prohibits the integration of de-emphasised elements - including mechanistic evidence, clinical experience, patient values, and social contexts - into decision-making related to causation. However, with a Humean account in the background, I can afford a conjecture that what causation is in relation to canonical *Claim 1* does not seem to relate to the desired causation inherent in canonical *Claim 2*: that events occur with some regularity does not necessarily entail a cause of health status change in some future patient. Causation in EBM, as exposed by its own hierarchy and structures, is insufficient to sustain its own central and canonical claims.

Of course, the premises underpinning this conjecture need to be more confidently established. This task is now undertaken below.

Chapter 3: Hierarchies & Observations

3.1. Introduction

The previous chapter proposed that through a considered structuring of evidential elements valued in health science, clues towards the nature of causation that serve to underpin scientific inferences are given. A Humean account of causation was proposed, and it is this account that now sits central to any further reconceptualisation of the fundamental nature of causation, as proposed in this thesis. Before such conjecture can proceed however, there are potential challenges to a Humean account that need to be dealt with. These challenges relate to i) a possible misinterpretation of the evidential structuring seen within EBM, and ii) deeper uncertainties as to precisely *where* within the EBM methods causation may actually be claimed. This chapter deals with these two challenges in turn. I conclude that consideration of these potential threats to the argument serves in fact to strengthen the proposed position. As such, a philosophical reconceptualisation of the nature of causation in EBM is permitted. PART 1 has so far served to provide a focused exploration of the central concerns of a scientific movement that has intentions towards causal claims. This exploration has sufficiently provided a rationale for warranting a reconceptualisation of a fundamental component of the movement. It has

done this by exposing a major challenge of the central claim of EBM, a challenge steeped in a paradox between its two canonical claims. The premises on which the argument for identifying a specific account of causation have now been established.

The hierarchical structure seems a sensible attempt to organise how EBM sees a range of elements that may serve as sources of evidence - sensible in that it serves as a convenient tool for the user of such evidence. The structuring has also served a philosophical purpose, as introduced in the previous chapter. There are still some unfounded assumptions and potential challenges to the argument so far. As implied above, this chapter aims to deal with what may be seen as the main ones. These, as will be explained, relate to the assumptions I have made towards evidential hierarchies, and the detailed role of observational studies.

First, hierarchies. Assumptions have been made so far on the hierarchical structuring that stem from a categorical interpretation view point. In what follows, alternative interpretations of the structuring are considered. However, I will argue that it is difficult to accept that a reading of the hierarchies can be reduced to anything other than something epistemological. Thus, it is always the case that some elements will be seen to provide better evidence than others. The background questions related to this position have so far been concerned with understanding precisely what the elements are evidence of, and what can the organisation of the elements tell us about the nature of that evidence. I have suggested that i) the elements are evidence of causation, and ii) clues as to the nature of that causation are revealed by the structuring and prioritising of methods. As such, a Humean stance has been offered that defines a conceptual framework for judging causation. This is to say that

there are clear signals towards, and examples of, a regularity view of causation within EBM's organisation of evidence. Observational studies align to Humean 'regularity' criteria of spatiotemporal contiguity, temporal prioritising, and constant conjunction. Further, a counterfactual theory underpins the interpretation of causal claims from EBM's prioritised sources of evidence - RCTs. The premise being developed is that the Humean framework for causation is sufficient to judge causation in relation to population research, and indeed this is the strongest stance that serves to indicate a theory of causation.

I have also stated that the two canonical claims of EBM, despite their synergistic intents (best evidence (*Claim 1*) to be used for clinical decision-making (*Claim 2*) resulting in best practice) offer a paradox: *it is the very prioritisation of evidential elements for use in clinical decision-making (Claim 1) that prohibits use of this evidence in clinical decision-making (Claim 2)*. This forces the issue beyond one of external validity. External validity, at least as per the standard discourse, examines the generalisability of data from prioritised methods. Here, there is a push towards a deeper dimension of the matter at hand, that being causation. Put in causal terms, what I am saying is that what is meant by causation in relation to prioritised research (as revealed by the prioritising) is not what is meant by causation in relation to individual clinical decision-making. So far the narrative has been asymmetrical in that primary attention has been given to 'causation in research methods' and the idea of 'causation in clinical decision-making', despite a brief reference to person centred medicine (§2.3), is yet to be addressed. The balance will be suitably redressed in due course. Briefly though, the clinical decision-making environment is something that is assumed to be complex and context-sensitive, in such a way that the

causal claims from population research, if indeed Humean by nature, do not readily hold.

3.1.1. Exploring causation further

So far we have accepted, albeit implicitly, some underpinning ontological groundings of what causation is, as witnessed through a Humean lens. In order to begin to make these intuitions explicit, we need to sketch out a distinction between causal frameworks or approaches (in this case, the Humean stance), and a deeper causal theory or ontology on which such frameworks are understood and causation is interpreted. Such ontology can be witnessed via the Humean framework. I suggest then that the ontological grounding of the way EBM presently sees causation – I will call this the *traditional* ontology – is one that is fundamentally based in a regularities view of causation. As highlighted in counterfactual instances, it relates to a *difference-making* notion of causation that is reliant upon a frequentist interpretation of probability. This traditional ontology does not support a fluency of causal notions between research approaches and clinical decision-making. These ideas of difference-making and frequentist probability are neither neutral nor philosophically unchallenged. Further, the traditional ontology forms the basis of the problematisation of external validity, and is therefore fundamental to the challenges of the central and canonical claims of EBM. With this in mind, the intentions of *Chapter 5 – 7* are to present an alternative causal ontology. This is an unpopular stance in the philosophy of EBM and epidemiology, and it is often seen as unnecessary, for example, again, Howick (2011). However, it seems that all existing philosophical treatments of the issues at hand, which are fixed to a

traditional causal ontology, are making little progress. That is not to say that such treatments have not been useful. Extremely valuable contributions have been made that have provided clarity and developments towards the understanding of many aspects of the philosophy of EBM[58]. However, I suggest that these treatments are, and always will be, restricted in developing meaningful progress on the relationship between *Claim 1* and *Claim 2*. Again, this is because of the commitment to a traditional causal ontology. We can only move forward, I argue, by revising the causal ontology. First, however, there is further groundwork to be done. There are still unexamined details of the propositions underpinning this stance.

The proposition of a necessary revision of EBM's causal ontology is essentially dependent on the credibility of a Humean framing of causal interpretation within EBM as it stands. This is because the Humean framework acts as a portal for us to view the deeper causal ontology at play. If a Humean account cannot be considered credible, then perhaps any worries about the existing ontology are unfounded or, at the least, different worries would develop. So, the first task here is to examine in further detail how the component parts of EBM can be thought of to see *how* Humean the causal picture really is. The Humean problem developed so far looks like this: EBM is concerned with causation and although many elements are included in EBM as sources of evidence, there are key

[58] For example John Worrall on the necessity, or not, for randomisation; Nancy Cartwright on RCTs and evidential relevance; Jeremy Howick on a broad philosophy of EBM; Alex Broadbent on a philosophy of epidemiology and causation; Federica Russo and Jon Williamson on a mechanisms thesis; Adam La Caze on a development of understanding EBM hierarchies, to name a few. The works of these, where relevant, are represented in the subsequent analyses of key steps in this chapter.

elements that are considered epistemologically superior. The reason they are considered superior is because of their specific methodological structures (for example RCTs compare closely matched groups; observational studies carefully record events over time). These structures thereby reveal what EBM sees as causation. The structures of prioritised elements best align to Humean ideas about causation, specifically a regularity view and counterfactual dependency. Causation that is counterfactually dependent or is a consequence of regularly occurring events is not something that readily relates to a clinical decision that would cause a health change in future patients. Further, it is not clear to see how this framework tolerates other acknowledged adjuncts of EBM, namely the integration of mechanistic levels of evidence, patient values, clinical experiences, and so forth – none of which are intuitively Humean ideas.

So, Humean causation may be a suitable account of EBM's prioritised research methods, but it does not seem to be the sort of causal event we are seeking when making a clinical decision with patients in spatiotemporally distant environments. Or at least if it is, a number of additional assumptions must be met. In many ways, existing philosophical treatments have been challenging these assumptions for some time. As expected, the assumptions centre on the core concerns of this thesis: what type of evidence is being established by population research, and how this relates to clinical decision-making. To be able to accept that the existing situation is adequate for satisfying the central and canonical claims of EBM, we need to assume that first of all, population research entails suitable causal claims, and second of all, these causal claims are somehow transferrable to spatiotemporally distant situations. The proposition has

already been made that the first assumption above may be in place - population studies are anchored in a strong statistical and epidemiological tradition and are logically appealing regarding their quest for causal associations of the matter at hand, statistically at least. However, the second assumption is weak. There is no intuitive process by which it can be understood how or if the causal claims of interest are readily transferrable to environments outside of the statistical model or of the research process. This relates to many general philosophical worries, and might be referred to as the problem of induction, causal inference, the causal interpretation problem, prediction, *et cetera*. Although this list of philosophical areas are all subtly (but substantially) different, they all share the same concern of understanding how evidence in one sense holds in other situations. These are also examples of philosophical treatments restricted by an implicit adherence to a fixed ontology of causation. It is of some importance to rehearse some of the most relevant features of these arguments, and this is done below. First, there are the two aforementioned interim steps that need to be taken.

Step one: the argument presented is based on a categorical interpretation of the evidence hierarchy. If there are alternative ways to interpret the hierarchy that might prove more credible, then the argument need not go any further. Non-categorical viewpoints for evidence hierarchies are examined below. I will claim that however hierarchies are viewed, they will always be reduced to some sort of epistemological categorisation. It is through this categorisation that causation is read.

Step two: is to present some situation that, if credible, would make a revision of the ontological status of causation unnecessary. I have stated that it is by virtue of the fact that a Humean framework emerges from the

structure of EBM that alerts us to an ontology that is insufficient for the intentions of EBM. So, if there are situations regarding the EBM structure that lead us to believe that a Humean stance is not credible, then our worries dissolve, or at least change.

These two steps will now be dealt with in turn. Step one will be addressed through a brief analysis of alternative readings of evidence hierarchies (§3.2). Step two will be approached through a consideration of whether or not observation studies can truly generate causal claims, the sort of which are desired by EBM at least (3.3). If so, then a looser interpretation of the traditional ontology might be applied and an urgent revision avoided.

3.2. Can hierarchies be read non-categorically[59]?

Of central importance to the thesis is that evidence hierarchies are *the* clue to the nature of causation with EBM. This relies on hierarchies giving away at least some sort of epistemological information. If an alternative interpretation can be accepted, then the premise that hierarchies expose the nature of causation is destabilised. The purpose of this section is to understand whether or not a non-categorical reading of evidence hierarchies is a feasible interpretation, and if so, is it a better interpretation than a categorical one? So far, I have assumed a categorical interpretation, which may be critiqued as a naïve view. Certainly it has been questioned

[59] A reminder of a definition of categorical interpretation of hierarchies: Any given source of evidence will always give more evidential support than a source from lower down the hierarchy, from La Caze (2008).

whether in fact anyone actually does (or ever did) hold this view. Proclamations are common that the stance is frequently proffered as straw man by which to (falsely) expose philosophical weaknesses of EBM - for example, Borgerson (2009), Djulbegovic *et al*. (2009), Goldenberg *et al*. (2009), Howick (2011). I claim, however, that the view is valid - or at least the essence of the view is valid. That is that hierarchies have epistemically informative content. Thus, the most convincing interpretation of evidence hierarchies remains problematic for the philosophical underpinnings of EBM. The dialectic on whether or not anyone did (or does) hold the view is largely irrelevant. In place, a consideration of the fundamental intentions of EBM and possible alternative interpretations of its methods are needed to meaningfully appreciate the function of evidence hierarchies. Once this has been undertaken, and the most credible interpretation established, confidence can be developed in a richer understanding of what the nature of the evidence in EBM is.

Alternatives to a categorical interpretation to evidence hierarchies that avoid an epistemic reading of ranked research methods are considered below. These are intuitively appealing. One such view - a *heuristic* view - in fact, is provided by the Oxford Centre of Evidence Based Medicine (OCEBM) and seems to be presented as some sort of contemporaneous 'official' stance towards how evidence hierarchies should be read (OCEBM, 2011). I argue, however, that despite seemingly strong propositions, and despite these views giving the appearance of being in some way contra and progressive to a categorical reading, there is still epistemological content to be found within the evidence hierarchies. Thus, the structuring of sources of evidence remains a credible and key indicator to the nature of causation in EBM. This being said, an essentialist

exploration of alternative views provides a significant development of the problematisation of EBM and reinforces the proposed tension between *Claim 1* and *Claim 2*. It does this by demonstrating that neither the categorical interpretation nor its alternatives are independently robust views.

To be clear, the categorical interpretation is about an epistemological ordering of certain elements of evidence included in the wide context of EBM. As already discussed in previous chapters, EBM's self-defined *rules of evidence* carve the way for a clearly epistemic intention of its hierarchies. This is justified on the basis of the varying levels that different elements control for bias and confounding. In turn, this has a rich history of scientific logic and statistical robustness. This intention is characterised by remarks such as:

> *"If the study wasn't randomised, we suggest that you stop reading it and go on to the next article in your search (Note: We can begin to rapidly critically appraise articles by scanning the abstract to determine if the study is randomised; if it isn't we can bin it). Only if you can't find any randomised trials should you go back to it"* (Strauss *et al*., 2005:118)

Thus, although it is clear that EBM values a range of sources of evidence, its ranking of these sources relates to what it considers as 'best' evidence (La Caze, 2008). As the matter at hand is one of understanding effectiveness of therapeutic interventions, it is difficult to think of the structuring as none other than some form of epistemological prioritisation - that is that elements give rise to the most believable ('best') evidence.

RCTs trump observational studies, for example. La Caze summarises the position of a categorical stance succinctly: "*All the results of a randomised study are always superior to the results of studies from lower down the hierarchy. . . How else could it be appropriate to 'bin' all non-randomised studies. . .*" (La Caze, 2008:358). A categorical interpretation makes, for many, uneasy reading. There are intuitive problems, some already referred to, some to come. For example, that randomisation as a process serves as a key differentiator is viewed as inherently problematic by some, (Worrall (2007)). For now, it is acceptable to let this go as a specific issue as all we are concerned with is the general idea of different elements giving different levels of evidence. There are further reactions related to the issue of total evidence – the idea that the basic sciences should be relied on to support population claims (more of this below also) for example Bluhm (2005), Grossman and Mackenzie (2005). Briefly, if this is the case and EBM de-emphasises basic sciences (mechanisms), then how should the application and integration of varying (epistemologically different) elements be undertaken?

The problem of external validity is highlighted in the context of a categorical interpretation, and this relates well to the canonical claims. If RCTs are prioritised as the 'best' source of evidence, and this evidence is intended for use in clinical decision-making, then the fact that RCTs relate only to averages of groups restricts the extrapolation of such findings to individuals (Bluhm, 2005). Clearly, this is a central issue to this thesis, and although undeveloped here, the issue of transference of causal claims is dealt with elsewhere. Here, it is presented simply as an example of the sort of problems associated with the categorical interpretation.

There are three further specific problems for the categorical interpretation. Two of these relate to the relationship between effect size and the hierarchy, and the third relates to quality of study design. First, effects sizes. The argument appears simple: if a categorical interpretation is taken, then it is difficult to rationalise how observations of interventions with dramatic effects (or dramatic lack of effects) can count as evidence. Jeremey Howick refers to this as the 'paradox of effectiveness' (Howick, 2011:39). Using Howick's examples, neither the Heimlich manoeuvre nor parachutes (Smith and Pell, 2003) have been subject to testing by RCTs, but observation of these events would count as sufficient evidence of their effectiveness. The problem with small effects is that the probability of false positive results increase despite study design[60].

The issue with study design is that the categorical interpretation could be taken literally, especially given La Caze's statement about "***All*** *the results of a randomised study are* ***always*** *superior…"* [emphasis added] (La Caze, 2008:358). This would mean that a poorly designed RCT carries more evidential value than a well-designed observational study. This latter point is not too much of a challenge as a simple caveat clarifying that the discussion is about the ideal, not the actual, would suffice. However, the two former points prove problematic for a categorical interpretation. Having sketched out a background for warranting alternative approaches, two possible such alternatives are now summarised: a heuristic interpretation and an interpretation based on comparative internal validity.

[60] Thank you to Andrew Turner for highlighting this problem. Leibovici's (now seemingly infamous) prayer study is a light-hearted example of this (Leibovici, 2001).

3.2.1. A heuristic interpretation

The OCEBM group suggest that hierarchies should be read heuristically, not epistemically (OCEBM, 2011). They state that the 2011 Levels of Evidence hierarchy[61] is *"Designed so that it can be used as a short-cut for busy clinicians, researchers, or patients to find the likely best evidence"* (Howick *et al*., 2011:1), "*The Levels is NOT intended to provide you with a definitive judgment about the quality of evidence*" (*ibid*:2), "*The Levels will NOT PROVIDE YOU WITH A RECOMMENDATION"* [original emphasis] (*ibid*:2). There is a clear emphasis towards the hierarchy being used in a time-limited clinical environment as a "*fast and frugal*" (*ibid*:2) search tool to make quick decisions. There is also a clear intention to avoid extracting any meaningful epistemic content from the hierarchy. This view of the process has also been supported by strong proponents of EBM in their attempts to clarify a philosophical position for EBM, for example "*. . . we should consider EBM as a continuously evolving heuristic structure for optimizing clinical practice*" (Djulbegovic *et al*., 2009:158). The OCEBM set-out clear instructions together with examples of using hierarchies. They present a 'pick-a-box' imagery to assist the clinician in rapidly identifying best evidence. Each box representing a research approach: systematic review of RCTs, RCTs, cohort studies, case series, mechanistic reasoning. A question is presented: "*If you have limited time, where do you begin searching for*

[61] The OCEBM revised what they refer to as 'Levels of Evidence' in 2011. The system relates to Figure 1, with design changes in the presentation. Conceptually, 'levels' is synonymous with 'hierarchy'. This is the introductory statement from the Centre's website for levels: "*Hierarchies of evidence have been somewhat inflexibly used, and criticised, for some decades. The CEBM "levels of evidence" were first produced in 1998 for Evidence Based on Call to make the process of finding appropriate evidence feasible and its results explicit. We have revised the "levels" in light of new concepts and data*" (OCEBM, 2011).

evidence?" (Howick *et al*., 2011:1). So, it seems the scenario is that a busy clinician would not have time to search all boxes, so she makes a rapid decision to search the box that is likeliest to give information that best approximates with the total evidence, which is the summary of evidence resulting from a thorough, unrestricted search of all boxes. Again, this approach has clearly been a direct reaction to the problems identified in a categorical interpretation. It seems that by emphasising a heuristic reading, all problems associated with a categorical (epistemic) reading dissolve. The heuristic approach promotes a probabilistic mindset, "*. . . to find the likely best evidence" (ibid*). Thus, the overly deterministic suggestion of the categorical interpretation ("***All*** *the results of a randomised study are* ***always*** *superior. . .")* is elided. As the hierarchies become a purely heuristic tool, any worries regarding epistemological matters (integration of effect sizes, quality of study design in relation to a causal claim, randomisation, external validity) lose their relevance.

Cleary there is a problem. The heuristic view offers a shortcut between accessing the evidence and making a clinical decision. If the intention of the healthcare process is to make the best clinical decision from a range of possible decisions, then by definition (according to EBM) that decision would need to be based on the best evidence. Asking the clinician to rapidly choose a box is essentially asking them to rapidly commit to what they consider to be the best evidence, which is an epistemic notion. The probabilistic caveat serves no purpose. This just changes the vernacular from 'is the best evidence' to 'likely to be the best evidence'. The matter of concern is still 'best evidence', regardless of whether it is deterministically so, or if it is likely to be so. The documentation from OCEBM gives explicit

clues that a categorically epistemic undertone is still present in the heuristic reading, for example:

> *"There are five boxes each containing a d*ifferent *type of evidence: which box would you open first?* ***For treatment benefits and harms, systematic reviews of randomized trials have been shown to provide the most reliable answers, suggesting we begin by searching for systematic reviews of randomized trials****"* [emphasis added] (Howick *et al*., 2011:1)

> *"Systematic reviews are better at assessing strength of evidence than single studies. . . and should be used if available"* (Howick *et al*., 2011:2)

In fact, the term 'best evidence' is used throughout the supporting documentation, and the very use of 'Levels' (*sic*) in the title to the approach is overtly suggestive of categorisation based on studies' ability to say something epistemically meaningful about a treatment effect. The only alternative is to insist that the approach is purely pragmatic, and make explicit claims that decisions should not at all relate to the ability of a research approach to provide a certain level of information regarding treatment effect. This would make the process wholly vacuous and be in complete contrast to what EBM is fundamentally based on – that is, using the best of the evidence to inform the best clinical decision. I am sure that this is not what proponents of a heuristic view truly intend. Thus, it seems the heuristic interpretation is simply a categorical interpretation with a

built-in process to encourage best use of time for the busy clinician. The heuristic interpretation remains overtly epistemically informative.

3.2.2. Hierarchy of comparative internal-validity

Evidence hierarchies characterise the intentions of EBM in two ways: first they set out a ranking of methods based on each element's ability to estimate treatment effects, then they signpost users (clinicians/policy-makers) towards the best evidence for use in clinical decision-making. As already discussed, a key area of contention in the hierarchy is the transition zone between non-randomised (observational) studies and randomised studies. For the present purpose, this gives a clue towards causation. Others have also used this to deconstruct the interpretation of the hierarchies. It is again a concern to some that this distinction is so influential in the operationalisation and interpretation of the methods and process of EBM. It is clear that the hierarchical ranking of elements is based on the methodological properties of each research design. The methodological properties relate solely to reducing the risk that the effect seen is due to chance, and the higher ranked methods do this by controlling for the systematic errors and biases witnessed in 'lesser' methods. La Caze sees this as the clue to understanding how hierarchies should be interpreted (La Caze (2008), La Caze (2009)).

The methodological improvements seen in the ascendency of the hierarchy all point to a single aim: increasing the likelihood of the results of the study being true for the participants of the study. Thus, the hierarchy has a central concern regarding *internal validity*. Although clues towards this are seen at each juncture in the hierarchy – for example

cohort studies having higher internal validity than case-control - the methodological mechanics indicating improvements in internal validity are best witnessed at the randomised/non-randomised transition. The defining strengths of randomisation are that it controls for all (known and unknown) confounding, and prevents biases that are known to influence the likelihood of the treatment effect being due to chance, particularly selection bias (Wang and Bakhai (2006), Jadad and Enkin (2007), La Caze (2009)). La Caze states that it is important to be clear as to what the distinctions between levels are an argument for. Given the details of methodological properties, the argument can only be for internal validity. Thus, La Caze proposes, hierarchies associated with EBM should be seen as hierarchies of comparative internal validity (La Caze, 2009). This then begs the question, "*What kinds of claims does the argument substantiate for EBM?*" (La Caze, 2009:11). By understanding hierarchies in terms of internal validity, significant constraints are placed on what should be drawn from the resultant evidence of the methods in question. The statistical analysis necessary to ensure high internal validity makes it essential to appreciate that optimal warrant is given only to the primary hypothesis, and is applicable only to the sample population in the trial ((*ibid*:14) and La Caze (2008)). Further, the methodological constraints required for reduction of bias although improving internal validity, reduce external validity. Thus, outcomes from methods with good internal validity are not synonymous with good evidence for therapeutic decisions. The claims of EBM then, from its chosen methods, given a reading of comparative internal validity, should be restricted to comments about the confidence of an outcome being due to the variable under trial in the study

population (Cartwright' *efficacy* claims). Claims of evidence of therapeutic *effectiveness* are not warranted.

It is however clear to see how La Caze's interpretation addresses the central problems of a categorical interpretation: the paradox of effectiveness becomes redundant because there are no effectiveness claims. Likewise, issues related to small effect sizes dissolve as there are no evidential claims regarding therapeutic effect. La Caze puts a *ceteris paribus* clause throughout his claim, such that he is referring to ideal, not actual studies, so issues of bad implementation of poor study design are also avoided.

Although a robust proposition, and possibly the most rationalised way of interpreting hierarchies, for EBM's central and canonical claims, understanding hierarchies in these terms does not seem to render EBM's research methods fit for purpose.

3.2.3. Summary of views

A categorical interpretation is the most referred to view of evidence hierarchies, and one that seems to fit the early intentions and remit of the EBM movement. The view is one that, due to the ranking of elements based on their methodological strengths, determines that results from a study higher in the hierarchy always give more (better) support to a given hypothesis than those from a study lower down the hierarchy. Given that the idea of EBM is to inform clinical decision-making, the hypotheses of interest are intended to be clinically relevant. Thus, results from studies in the higher tiers are thought of as providing better evidence for therapeutic effectiveness. The problems associated with this view have been outlined,

and two alternative views presented. A heuristic view makes the claim that the hierarchies are of no epistemological interest and merely serve as a time saving tool for the busy clinician. I have proposed that this is not a credible stance and that to strip away any epistemological content from the hierarchies would leave them vacuous in relation to the central and canonical claims of EBM. A second view based on comparative internal validity has also been presented. This view claims that the only defensible position is for hierarchies to be read as a tool for understanding the level of confidence in whether a research outcome is due to the variable under trial in the study population. This is not synonymous with evidence for the effectiveness of a therapeutic intervention.

I propose that hierarchies must always possess some epistemological interest in order for them to be non-vacuous. A traditional categorical interpretation is overly problematic and is based on unexplained assumptions that fail to stand up to philosophical analysis. The most convincing view is for hierarchies to be read as a table of comparative internal validity. It is quite plausible, of course, for this to have some heuristic value, but only in understanding the level of internal validity of any particular element. La Caze concludes: "*Interpreting EBM's hierarchy as one of comparative internal validity makes the challenge of external validity explicit*" (La Caze, 2009:17). I would say that the analysis has done more than this. External validity is only one component of the transition between *Claim 1* and *Claim 2*. Further, it is a component fixed in the Humean ontology of how we presently understand causation in EBM. That is, causal claims arise for set methods, and some are better at producing these than others – those that are better at identifying robust patterns of regularly occurring events. External validity is the expectation

that such claims, as they are, will hold in spatiotemporally different environments. La Caze has highlighted that claims from EBM's chosen research methods are not synonymous with evidence for therapeutic effectiveness. In causal terms, the type of causal claim developed in the research activity of EBM is not the same sort of causation desired in clinical decision-making. An enhanced appreciation of how evidence hierarchies and their content can be seen has served to further destabilise EBM's central claim of *evidence from study designs higher up the hierarchy more reliably informs therapeutic decisions*. In turn, the tension between the canonical claims has increased: the *nature* of the prioritising of research methods (*Claim 1*) is further compounding the difficulties with the integration of information in clinical decision-making (*Claim 2*).

For a philosophy of EBM to be sustainable and sufficiently explanatory, a more consistent ontological basis of causation is desired. It is the ontological basis that I suggest is of core concern here. The relationship between *Claim 1* and *Claim 2* is governed by the nature of the matter of interest, which is causation. There may be different ways to view evidence hierarchies, some more credible than others. Ultimately, there has to be some epistemological content seen. This epistemological ranking again strengthens a Humean understanding of what causation is, or at least it seems to. By analysing alternative views of the hierarchies, not only do issues of external validity become more explicit, so do issues of causation. The nature of causation, as indicated through all possible readings of evidence hierarchies, does not seem sufficient to satisfy either the central or canonical claims of EBM.

This essentialist critique of hierarchies seems to have strengthened the Humean account of causation in EBM. This is because of the

epistemological prioritisation given to certain methods, particularly RCTs and observation studies above others, for example, mechanistic reasoning. A Humean account of causation is principled on regularly occurring events. Counterfactual conditions form a part of Humean causation. Both of these principles are characterised in prioritised research methods. Hume was troubled by causation being something other than observed regularities, and neo-Humeans have taken this strictly to mean that *necessary connexion* forms no part of causation. This principle manifests in EBM's de-emphasis on mechanistic science. This latter point with be dealt with more clearly in *Chapter 4*. For now, it seems that a Humean account of causation befits what EBM has to offer. However, a problem has emerged.

The worry is this: if there truly is some epistemological ordering of methods, and RCTs truly do take priority in the sense that causal claims from anything below (observation studies and down) are not warranted, then it has to be the counterfactual condition that is the central defining feature of causation in EBM. This has been discussed already, with much detail and emphasis being put towards the idea of comparative studies. We have seen what logical and statistical value they provide over their uncontrolled epidemiological cousins. So far, The Humean proposition has been grounded on the facts that EBM *generally* favours population studies *such as* RCTs *and* observation studies, rather than less trustworthy evidential elements with higher risks of bias such as mechanistic science and experiential judgements. The proposition I have made has been to the effect that *both* RCTs *and* observational studies are epistemologically valued by EBM and *both* demonstrated Humean elements of causation:

> *"So, we can say that there are at least two independent, and sometimes inter-related, causal concepts evident in discretely categorised research methods; counterfactual dependency and regularity. Both, however, are richly Humean notions"* (§2.5.2:102)

However, since then more ground has been trodden and a firmer commitment to the understanding of what evidential hierarchies are representing has been made. It is at this juncture that the problem emerges. If evidential hierarchies are to be seriously considered as a tool for judging comparative internal validity, then I am not convinced that the premises for the Humean account are sufficiently substantial. Perhaps proposing that a range of methods representing "*independent, and sometimes inter-related, causal concepts*" is too vague? Maybe the Humean-hand was thrown down too early? Maybe what EBM offers as constitutive of causation is not Humean at all? What I am getting at is this:

> *"Here is a billiard ball lying on the table, and another ball moving towards it with rapidity. They strike; and the ball, that was formerly at rest, now acquires a motion.* ***This is as perfect an instance of the relation of cause and effect as any that we know****, by sensation or by reflection"* [emphasis added] (Hume, 1740 A 9)

The Humean account may well embrace and encourage, counterfactual conditions, but it by no means insists on such. At the centre of the account sits *the perfect instance of causation*. To commit to a Humean account is to

commit to an understanding of a causation that in essence is *just one little thing and then another*. For Hume, event A followed by event B is what constitutes causation. If this is the case, then what of the counterfactual? Are comparative, controlled studies offering some additional constitution to the causal account? It was proposed early, in line with Lewis, that "*the counterfactual state (control or comparison group) is in fact the truthmaker of causation*" (§2.5.2). For Hume, I am not sure this is so. And for EBM, following the critique of evidential hierarchies, I am also not sure.

For a brief reflection, why is this important? Of course there are numerous philosophical accounts of causation, many of which could explain what is happening in EBM. Previous authors have also aligned EBM to Humean causation[62], but so far a detailed justification for doing so is absent. I have no vested interest in committing to a Humean account, although it is intuitively appealing. A Humean account does, however, readily offer some openings for analysis and progression. All this aside, what I do say is of utmost importance is that at least *some* account of causation on EBM is identified. The quest of this thesis is a philosophical reconceptualisation of the nature of causation in EBM. To do this, I need to understand, as best as possible, how causation is presently conceptualised. So far, the Humean account looks promising. However, there has since been a stricter commitment to hierarchies demonstrating comparative internal validity, as far as epistemic outcomes are concerned. RCTs sit above observation studies, and if the commitment is genuine, we must try

[62] In fact, anyone who has cared to relate the processes of health care research to some philosophical ideas of causation usually ends up with something at least vaguely Humean in their analysis, whether they are aware of it or not. A Humean influence can be traced even in those who begin an analysis with, say Hill's Aspects of Causation. Morabia (2013) gives an informative review of this notion.

and understand why this is so. I suggest that, given this commitment, it is no longer satisfactory to conflate RCTs and observation studies into a single 'population studies' typology and stamp some vague Humean interpretation on them. A more microscopic examination of the juxtaposition between RCTs and observation studies is needed. What is it that truly differentiates them? Is there really something beyond the statistical offerings? Does the idea of causation serve as the differentiating characteristic? This is what I propose: if the differentiator is something causal, then the Humean account is vulnerable. The Humean account should be satisfied with causation being related to what observation studies have to offer, event A followed by event B. If we are genuinely saying that causation in EBM is something other than this, and in fact it *is* related to RCTs then Humeanism will not suffice. I suggest that this proposition can be addressed by asking a familiar question: can observation studies make causal claims? If the answer is 'yes', then a Humean account can finally be seen as a credible one. If the answer is 'no', then it cannot.

It is also timely to remember that what is at stake here is a philosophical account of causation, not *just* a statistical, probabilistic, nor scientific account. I say this because the question of causation and observation studies has already been exposed to analysis[63]. However, the existing

[63] As referred to previously, and below. However, Jan Vandenbroucke offers extensive and accessible commentary on this; for example Vandenbroucke (2004); Vandenbroucke (2008).

analysis has focused on the statistical and scientific logic of observation studies. Further, it has been restricted to the internal mechanism of the study design. What I am interested in is EBM, and the role of observation studies within that. I see it as a different matter to consider discrete methodologies within the broader system. As we know, EBM is a complex, evolutionary rich, clinical, scientific and socio-political framework in which multiple sources of information are intended to inform complex and context-sensitive clinical decisions. So, what I am interested in is a qualified question of 'can observation studies make causal claims *within EBM?*' I see this as a different question to the one that existing analysis has focused on. With this in mind, the approach to this question, should again be to use the textual commentaries regarding EBM on this matter. This, I claim, will offer a portal towards the philosophical underpinnings, which will be considered further in *Chapter 5*. For now, a consideration of the role of observation studies, and their relationship with RCTs with the EBM framework is given.

3.3. Can observational studies make causal claims?

As stated, I am not concerned here with rehearsing arguments that are commonly linked to a discussion on 'randomised v non-randomised' studies, for example the paradox of effectiveness (Howick, 2011:56-59). In this sense, I am by no means using the debate to hold randomised trials up as a straw man with that to berate EBM. In fact, the opposite is true. Having examined the scientific quality and values of RCTs, their strengths (credible causal claims through high internal validity) and limitations

(poor external validity) can be used to consider the role of other methods. Not in any evaluative way, but rather to inform how causal claims may or may not be obtained from non-randomised studies. This analysis is for the sole purpose of understanding the nature of causation in EBM. Of course, the analysis might be considered redundant if Howick's *non-causal* interpretation of EBM were to be accepted (Howick, 2011:Ch5). To briefly review the argument in the context of observational studies: Simply, Howick's defence against EBM methods - particularly RCTs - being concerned with causation is pitched against attacks that anchor their argument on RCTs establishing genuine causation due to their control of *all* confounding, for example Worrall (2007). This makes a counter-claim easy: EBM never set out to state that RCTs align perfectly with classical hypothesis testing (in which *all* confounding is controlled for) and therefore causal claims are not being established. In this sense, observational studies can inform clinical decisions in certain conditions. For Howick, the conditions are when the effect size seen in observational studies outweigh the combined effect of plausible confounders (Howick, 2011:59). Thus it seems that the judgement on the utility is dependent on the observed effect, rather than the methodological properties themselves. However, the devil is in the detail. First, it is once again difficult to see how causation is not at the heart of the argument. Despite Howick's reluctance to frame EBM in causal terms, there seems no escaping the issue, for example: "*At the same time, in many cases strong relative (but small absolute) effects can provide strong evidence support for the causal hypothesis*"(Howick, 2011:57). Second, I am not sure that the issue is about effect size more than methodology. In working towards a bold conclusion on his *rule of evidence*, Howick reveals clues as to what might really be the

important dimension at hand : "*A **carefully controlled** observational study with a large effect could provide stronger evidence than a **confounded** randomized trial with a small effect*" [emphasis added] (Howick, 2011:57). Although effect size may act as a clue to the credibility of observation studies providing causal evidence, it is the methodological quality that is important. The phenomena of re-evaluating the utility of elements that sit above and below each other in traditional hierarchies, as is being pointed to by Howick, are detailed in recent developments amongst EBM proponents. The phenomena are important in their role for further understanding of what we can mean by causation in EBM, and these are discussed below.

3.3.1. Levelling the hierarchies: can observational studies be 'up-graded'?

There are two notable exceptions that differentiate themselves to traditional evidence hierarchies as, for example, detailed in Figure 1. These are the GRADE system[64], and a revised OCEBM system[65,66]. They do so on the basis of providing additional conditions whereby *grading* of evidence is made on *quality of evidence* and *strength of recommendation*. This structure addresses an obvious limitation of hierarchical structures: that hierarchical

[64] *Grading of Recommendations Assessment, Development, and Evaluation* (GRADE). A series of guidelines published in the *Journal of Clinical Epidemiology* from 2011 – present (15 separate guidelines at present) detail the GRADE system.
[65] OCEBM Levels of Evidence Working Group. "The Oxford 2011 Levels of Evidence". Oxford Centre for Evidence Based Medicine. http://www.cebm.net/index.aspx?o=5653, accessed 12/11/14.
[66] As these two systems are conceptually similar in respect of the dimension I am interested in, I will treat them as one. For clarity then, I shall only refer to GRADE from now on.

structures do not accommodate judgment on quality of methods. That is, a poor RCT is better than a well conducted observational trial (as considered above). For interventions, the GRADE strength of recommendation is still weighted towards RCTs, albeit high quality RCTs. Only pragmatic concerns seem to have been addressed. The epistemological concerns remain the same. As GRADE does not seem to have altered the philosophical stance of EBM, it will be considered - for purposes of clarity – that the hierarchical structure of EBM is still, in fact, the core focus of concern.

Since 2000, the GRADE Working Group have been developing a system to facilitate the summary of evidence (Guyatt *et al*., 2011a). The motivation for this was the way (clinical) guideline developers created summaries of evidence seemed inconsistent. This is suggested to have presented challenges for guideline users when attempting to interpret evidential summaries (Guyatt *et al*., 2008a) . It is necessary to consider the work of GRADE in the context of evidence hierarchies on at least some pragmatic basis. The work of GRADE is of importance to the landscape of understanding evidence. GRADE can be seen as a multi-national, influential group that includes key authors responsible for original models of EBM, and there is a growing worldwide adoption of the GRADE system by health institutes and policymakers (Guyatt *et al*., 2011a:2). Politics and pragmatism aside however, conceptually, although the self-proclaimed advantages over 'traditional' systems are largely organisational (Guyatt *et al*., 2008a), the system may have additional things to say regarding an epistemological reading of different sources of evidence.

Of relevance to this analysis, there appears to be two main conceptual differentiators between traditional systems of assessing evidence (for

example, hierarchies) and the GRADE system. First, GRADE initially treats *quality of evidence* and *strength of recommendation* as discrete and separate notions in order to ultimately understand how they pragmatically relate to each other. Second, there are explicit criteria within the GRADE system for downgrading and upgrading quality of evidence ratings. Again, these are presented as transparent and pragmatic administrative processes for going about the business of summarising evidence. However, there still seems to be something of philosophical interest regarding how health care should interpret what GRADE are saying about the epistemic value of research methods within this re-systemisation of evidence. The question now therefore is one of whether or not the GRADE system has altered the way evidential sources should be considered in terms of epistemic value. For this question to be answered, a brief revision of the proposed conceptual differentiators is required.

GRADE's definition of quality of evidence comes in two parts. First, quality of evidence refers to a default position based on research method: simply, RCTs are high quality, observational studies are low quality (Guyatt *et al*., 2008b). This reflects traditional positions on evidential quality. It is also based on an assumption that outcomes from discrete methods should not be used to make recommendations on practice. As such, this part of the definition is qualified by a statement that the quality of evidence arising from a discrete method "*reflects the extent of confidence that an estimate of effect is correct*" (Guyatt *et al*., 2008b:995). The second dimension to the definition is that quality of evidence is relative to the specific context in which the evidence is to be used. In sum, quality of evidence therefore reflects the extent to which confidence in an estimate of the effect is adequate to support recommendations in a specific context.

Despite the default positioning of RCTS as 'high-quality', and assuming this has at least something to do with controlling for bias, GRADE insist that quality means more than risk of bias (Balshem *et al*., 2011). When considering a body of evidence, confidence in effect estimates may be compromised by imprecision, inconsistency, indirectness and publication bias. GRADE present clear strategies for making judgment on these. It is now this concept that relates to the second conceptual differentiator of upgrading and downgrading.

Quality of evidence can be lowered if there are at least serious limitations in either of the quality criteria stated above. Thus, an RCT could start at its default 'high quality' position and be downgraded based on these criteria. The same applies to observational studies although their default position is already low (Guyatt *et al*., 2011b). Conversely, evidential quality of a rigorous observational study can be upgraded dependent on the presence of a large effect size, a dose-response gradient, and/or when plausible residual confounding supports (increases confidence in) estimated effect (Guyatt *et al*., 2011c).

GRADE suggest the value of their system is not only in the way evidential quality is judged, but also in its facilitation of making clinical recommendations. The system offers two grades of recommendation of interventions, 'strong' or 'weak'. This recommendation is based on four principles: quality of evidence as discussed, certainty about the balance between desired and undesired effects, certainty in values and patient (or policymakers) preferences, and certainty of whether or not the intervention represents a wise use of resources (Guyatt *et al*., 2008a).

So what does GRADE appear to be saying about the epistemic role of discrete research methods? Well, there is the default epistemic assumption

that RCTs are superior to observational studies, and this is clear in their position regarding quality of evidence. This aligns to traditional models of evidential quality. However, there is a dimension imposed by GRADE that suggests that the quality of evidence can be altered by consideration of factors other than those related to risk of bias. This offers something in terms of the epistemological view. The defining characteristic of RCTs in traditional models is their ability to control for bias. This appears to be the feature that transcends the space between correlation and causation. If this is downplayed, could this destabilise what we previously thought to be the epistemic differentiator? This would be the case if an observational study was upgraded to at least the level of an RCT based on its ability to demonstrate a large effect size, dose-response and support from residual confounders. These are factors that are not necessarily related to methodological rigor and could be observed purely because that is how those interventions behave. Thus they are chance factors. It is possible that an RCT can be downgraded even with good control for bias: it may contribute to a body of evidence that is considered imprecise, inconsistent, indirect, or suffer from publication bias. Thus, through no fault of its own (that is, it could be very good at controlling for bias), if the overall body of evidence is downgraded, an upgraded observational study could be considered better than the discrete RCT. Therefore, the epistemological reading would be that better evidence of causation has arisen from an observational study that has been upgraded on chance findings than from a well-controlled, but poorly contextualised RCT. It seems then that the pragmatics of summarising evidence has created further turbulence in the epistemic reading of evidential quality.

The rationale for upgrading still appears confusing. Both Howick and GRADE claim that the primary reasoning is related to 'external' matters, and specifically effect size. Yet within both of their explanations there are suggestions that methodological quality can influence an 'upgrade' to a credible causal claim. This is an important issue but any answer will still be unsatisfactory toward contributing to any resolution of the problem of causation in EBM. However, the manner in which it fails to contribute is still of interest as it will allow further commentary on the nature of our causal understanding. I propose that the most credible rationale for 'upgrading' observational studies is in fact more to do with their methodological rigour. And here is why: Let us say that the defining strength of randomisation is its ability to control for confounding via better allocation concealment (reducing selection bias). The random sampling leads to increased group homogeneity that then allows the use of specific statistical approaches (based on frequentist probability) concerned with accurately expressing the degree of chance that would account for any differences found between groups, by way of a measure of variance, for example confidence intervals. There are, at least, two (interrelated) ways to use this as a platform for re-examining the methodological properties of observational studies in relation to their (potential for) causal claims.

First, Vandenbroucke (2004) for example, notes that there are circumstances when the allocation process can match that of a randomised trial, namely when it can be assessed whether the exposure allocation is unrelated to the outcome, for example adverse or unexpected events - smoking causes cancer, oral contraception protects from ovarian cancer, and so forth. In such circumstances, statistical approaches can be used to

measure the effect of confounders in each group, for example regression analysis. These approaches are still founded on frequentist probability and will, conceptually, allow a similar confidence in interpretation as that used in randomised trials. Thus, in certain circumstances, the methodological properties of observational studies can make causal claims from observational studies as credible as those from randomised studies. This is also at the heart of the argument from Worrall, for example Worrall (2002), Worrall (2010b).

Second, Vandenbroucke's reference to a relationship (or lack of) between the outcome and exposure, or subject characteristics, is directly related to the concern of causation. That is, causation from randomised studies is anchored to the idea of homogenous groups wherein known and unknown confounders are distributed as equally as possible. Because there is no known *a priori* association between patient characteristic and outcome, the groups are said to be 'exchangeable', and it is this that justifies a causal claim – that is, conceptually, any subject can move group but will always obtain the outcome of the group (Hernan, 2004; Hernan and Robins, 2014). This aligns to some extent with a counterfactual theory. In randomised studies, it is chance that results in exchangeable groups. For observational studies, other mechanisms are required, as noted by Vandenbroucke (2004). Vandenbroucke restricted his conditions to a limited range of circumstances and clinical questions. This may indeed be the case, but others have suggested that the identification of an *instrumental variable* has been proposed to be feasible in more observational studies than perhaps first thought, for example Dekkers (2011). An instrumental variable is an identified variable that determines the probability of treatment, but is not in any other way associated with

the outcome, thus mimicking the randomisation process. There are additional criteria to be met of course: the instrumental variable should only affect the outcome by the treatment, and it should also predict the intervention (for example, Rassen *et al*. (2009a), Rassen *et al*. (2009b), Hernan and Robins (2014)). Dekkers (2011) uses Smets *et al*. (1999) study on two types of kidney transplant as an example. Habitation area was a suitable and sufficient instrumental variable as the two interventions under test happened to be performed independently and exclusively in two geographically distant centres.

The purpose of revising the contemporaneous perspectives on how randomised and non-randomised might be positioned, together with some focused points on methodological properties, has been to gain further insight into an ontological basis of causation in EBM. Prior to this section, a Humean idea of causation was proposed, but was questioned following a commitment towards hierarchies being interpreted epistemologically on their ability to compare discrete methods related to internal validity. I claimed that if non-randomised methods could not establish credible causal claims, then this proposal might be destabilised.

There are examples of credible causal claims by observational studies, for example, that smoking causes cancer. Further, an authoritative voice of EBM formally proposes a mechanism by which observational studies can be upgraded to the causal status of randomised studies. There is a veneer of rationality that suggests the drawing of causal claims and the upgrading of observation studies is related to large effect sizes. However, it seems

that the effect size rationale is only a component part of the process of upgrading. More fundamental is a review of the requirements of methodological properties of observational studies in order for any causal utility to be considered. It appears that observational studies can be seen as causally credible if they address some aspects of study design that relate to their controlling of biases, especially confounding.

3.3.2. GRADE and context

There is one other informative adjunct emerging from exploration of the GRADE framework. That is an explicit consideration of the potential context-sensitivity of research data. An outline of this adjunct can be sketched out as follows.

The relationship between quality of evidence and strength of recommendations might give further insight into what we might say about the value of discrete methods. In essence, the journey between quality of evidence and recommendation is analogous to causal inferences from particular instances, that is, generalisation of research findings. The problem of inference is core to this thesis. Thus, if advances are made here, some seemingly important concerns might be dismissed. On the one hand it seems like advances are suggested in the sense that the pathway between research and practice has been strengthened by the rigour with which GRADE have considered precisely what evidence should make this transition. A perennial problem for philosophers might thus be lessened. Cartwright talks of the road between 'it works somewhere' (that is, in the research method) and 'it works for us' (in practice), as discussed in §2.4. Her concern is with the *evidential relevance* of the research output, and a

focus for progress is, partially, on the contextualisation of findings. What GRADE offers looks somewhat like contextualisation. A theoretical example might be that prior to considering the dimension of strength of recommendation, theoretical findings from a (rigourous) RCT that showed causal efficacy of, say, Warfarin in stroke reduction could have meant that Warfarin became clinically recommended. However, by considering the status of certainty of balance between desired and undesired effects, the GRADE system would facilitate consideration that Warfarin also increases the chance of bleeding. Thus, a recommendation of an effective intervention is weakened because of context. This seems to be the first time since the development of EBM hierarchies that the movement itself has explicitly concerned itself with not just the external validity of specific data, but the more general idea of the context in which the data may or may not fit. A strong move towards the context-sensitivity of how causal claims hold is demonstrated, and observational studies have a role in that.

3.3.3. Summary of observational studies

In sum, a review of the GRADE framework with reference to its perception of observational studies pushes an understanding of the epistemological landscape of EBM a little further. Although with GRADE the default position regarding the ranking of research methods is fundamentally unchanged, that is RCTs are assumed to offer better evidence for therapeutic decisions than non-randomised studies *ceteris paribus*, another dimension is introduced. By allowing upgrading of observational studies under certain conditions, the epistemological stance seems to have shifted, subtly but critically.

If observation study design quality is sufficiently robust, and the observed effect-size large enough, emergent causal claims start to seem credible. In other words, some observational studies can be judged as able at identifying when event As are followed by event Bs. Hence a Humean account of causation in EBM is supported.

In relation to the causal *truthmaker*, it seems like this analysis has gone someway to exposing a critical feature of the nature of causation in EBM. Earlier it was suggested that, given an initial understanding of evidential hierarchies (RCTs trump observation studies, *de facto*), the counterfactual condition was the causal truthmaker. However, I now advance the proposition as follows.

There is something intuitively Humean about EBM. At a cursory examination, it might have been satisfactory to conflate all population studies to a kind from which causation emerges and say they were essentially Humean. Following a more detailed analysis of evidential hierarchies, it seemed necessary to consider the relationship between different types of population studies closer to see where, in fact, causation is anchored. As it is at least theoretically possible for observation studies to make credible causal claims, causation cannot be something exclusive to the counterfactual condition. It must be something to do with a common feature of both RCTs and observation studies. I propose that this common feature is the correlation between events A and events B found in a single group.

To demonstrate this, consider the following. Figure 2 illustrates a typical, simple comparative study (for example, an RCT). The left hand group is the intervention group (A). The right hand is the counterfactual (¬A). In the intervention group a level of outcome is observed, B(x). In the

counterfactual group, outcome B(y) is obtained. The Randomisation and Allocation stages provide the strict counterfactual conditions. If the truthmaker was the counterfactual, then causation is B(x) – B(y). This satisfies that A→B. Without y, and therefore without ¬A, there could be no claim to causation. Figure 3 shows a typical methodological structure from an observational study.

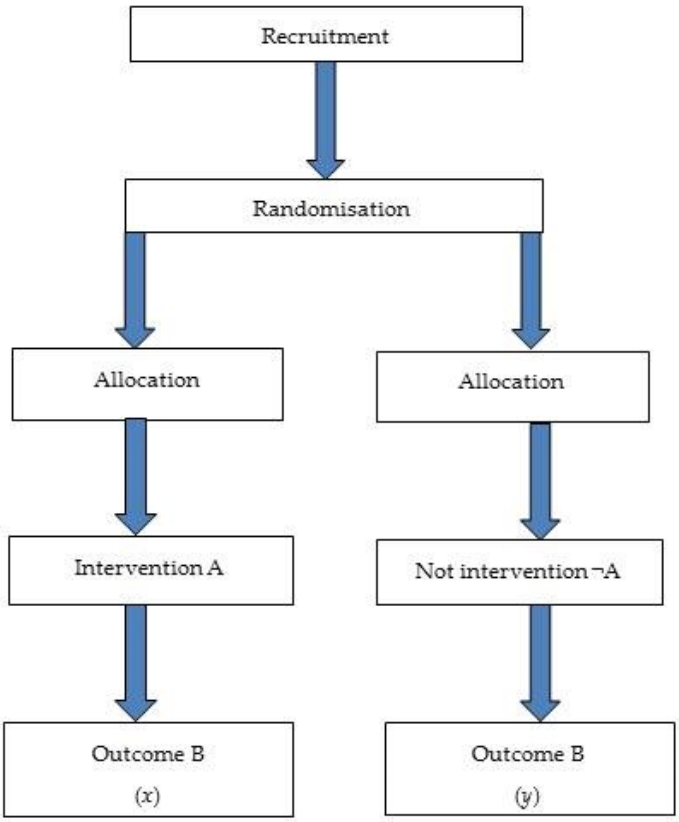

Figure 2: Randomised Controlled Trial methodology. The randomisation and allocation processes create the counterfactual conditions by which B(x) – B(y) would, under a counterfactual account of causation, constitute a causal claim. However, causation is happening in each group, irrespective of the other group.

In Figure 3, the strict counterfactual conditions are absent. The non-randomised selection and distribution processes are characteristic of observational studies and, as discussed already, expose this method to selection, allocation and performance biases. So although comparisons can be made between the two groups, causation cannot be related to a counterfactual condition.

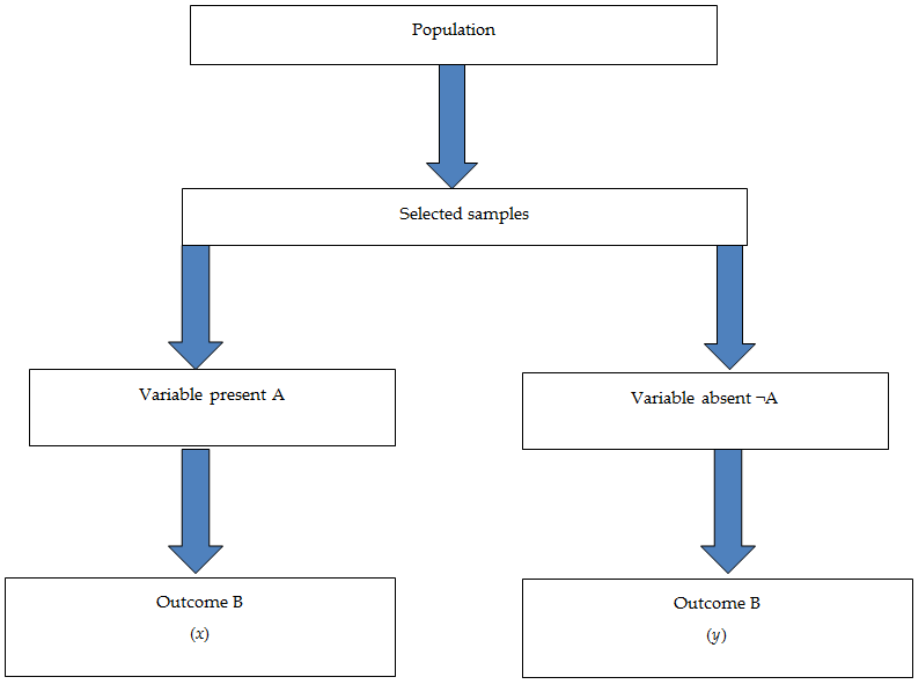

Figure 3 Observational methodology. Counterfactual conditions are absent. Causation is still present in Group A.

As per GRADE, the rationale for drawing causation from observational studies is based on features such as methodological quality (in terms of robustness of group observation), effect size, exchangeability, *et cetera*. These are not necessarily features that strengthen the counterfactual

properties of the method, but rather the overall quality of observation. If causation is drawn from this method, it must be related to non-counterfactual aspects of the method. It seems that the common causal truthmaker in both RCTs and observational studies is the observation of regularly occurring events A and B in a single group, group A. Group ¬A does something, but it is not something that can be part of causation itself. Rather, it is external to causation, and most likely something to do with the psychological mindset that merely increases our confidence that A→B. The causal work can only be done in the single group. This is where health status change occurs, not in ¬A, nor in the space between the groups. Counterfactually characterised methods, that is RCTs, cannot be seen as constitutive of causation. Only, perhaps, symptomatic.

3.4. Conclusion

At the start of this chapter it seemed like understanding causation in EBM as something broadly Humean was a reasonable stance. This stance was taken following analysis of the historical and evolutionary dimensions of contemporary health care research approaches, and how the characteristics of these approaches have, in turn, helped to shape what we now see as EBM. A Humean interpretation seemed reasonable as this account of causation relates to much of what we intuitively understand as causation in the world. That is, that ordered and regularly occurring events in close proximity to each other lead us to believe that one event causes the other. Although Hume spoke of counterfactuals, and Humean proponents have since developed this account of causation, at the heart of Humean causation is regularity. Hume also asserted that there was no *necessary*

connexion in causation, and EBM's de-emphasis of mechanistic approaches to evidence aligns to this, although this will be dealt with in further detail in the next chapter. This initial stance was based on a specific set of assumptions about how EBM organises its elements of evidence. A Humean stance was under threat if non-epistemological interpretations of evidential hierarchies seemed credible. I suggested they were not, but in doing so exposed a further risk to the causal analysis; that a strict epistemological reading of hierarchies based on the internal validity (scientific robustness for efficacy claims) of methods pointed towards the counterfactual condition being the causal truthmaker. If this were to be the case, then a revision of a causal account would be necessary. However, reanalysis of contemporary commentary on how EBM sees the relationship between non-randomised methods and causation highlighted that causation may be drawn from observational studies in terms of claims of clinical effectiveness. This being so, I have proposed that the causal truthmaker is not indeed the counterfactual condition, but rather the regularly occurring events in a single group of a study – the common feature between randomised and non-randomised methods.

As an adjunct, emergent themes from reviewing the GRADE framework support this thesis in that a further and wider analysis of causation could help provide a more satisfying philosophy of evidence, which is research data should explicitly be considered in the context of its intended use. A strengthening of the initial account of causation merely serves to exaggerate the background problems relating to the central and canonical claims of EBM. The ontological tension suggested to exist within EBM is highlighted further. On the one hand there is an urge to value statistical and methodologically robust counterfactual approaches to establishing

causal claims. But the ontological basis of this urge is questioned by a parallel proposal that causation can be drawn from non-counterfactual conditions. Although a satisfactory Humean regularity framework has been revealed that identifies a common causal truthmaker, inconsistencies in the deep causal account are still apparent and problematic. All we can say is this: an account of causation in EBM, as it stands, is one based on regularly occurring events. These events are identified in the types of methods associated with EBM's canonical *Claim 1*. Although there are indications towards causation being influenced by a wider context-specific clinical situation, the identified causal framework does still not account for how this can happen. The challenges associated with the theoretical space between *claims 1* and *2* remain unresolved.

Chapter 4: Mechanisms

4.1. Introduction

The broad remit of this chapter is to move towards the development of an alternative theory of causation that is relevant for EBM. Within this, the chapter has two discrete but related aims, and is structured in line with these. The first, and by far the most prominent, is an investigation into the relationship between *mechanisms* and the Humean account of causation in EBM. Having identified through the example of mechanisms that the traditional account of causation appears problematic for the claims of EBM, the second aim - that concludes §4.3 - is to consider what an alternative theory of causation *should* look like.

Consideration is given to the role of seemingly important but de-emphasised evidential elements from within the EBM framework - specifically, mechanistic science and reasoning. This is not to say that other de-emphasised elements are not worthy of commentary, in fact the opposite. One dimension of the conceptual framework integral to the development of the causal theory to come in *Chapter 5* includes complexity and context-sensitivity. These components are defined by the input of multiple sources of information, such as patient values, clinician experience, and so forth, to the context within which EBM operates. For the purpose of demonstrating the difficulties in attempting to account and include 'other' sources of information, this chapter will be solely

concerned with mechanisms. The idea of *mechanisms* (defined fully below, §4.2) represents a feature of Hume's thoughts about causation - *necessary connexion*[67,68]. The analogising of EBM's *mechanisms* with Hume's *necessary connexion* is around the position they have in a causal account. We now know Hume's constituents of his regularities view of causation: spatiotemporal contiguity, temporal priority, and constant conjunction. However, Hume was tormented by a fourth constituent, *necessary connexion*. At times, he placed this central to his account of causation: "*The necessary connexion betwixt causes and effects is the foundation of our inference from one to the other"* (Hume, 1739 THN 1.3.14.21). But ultimately because the idea fell outside the realms of sense experience, he could bargain no place for it: "*What! The efficacy of causes lie in the determination of the mind!"*

[67] For clarity, I will use Hume's wording and spelling *necessary connexion* (italicised) when referring directly to Hume's text, and within quotations. For general reference to the notion, I will use non-italicised convention spelling: "necessary connection".

[68] Hume asks "*What is our idea of necessity, when we say that two objects are* ***necessarily connected*** *together*?" (Hume, 1739 THN 1.3.14.1) [emphasis added]. To define the idea of *necessary connexion* then: the basic idea is that events are tied together (connected) in some way that allows some type of *a priori* reasoning as to the causal inference of events (necessity). There are many conflated notions within this term, and throughout both *Enquiries* and *Treatise* Hume talks of "powers", "energy", "efficacy", "force", *et cetera*, synonymously with *necessary connexion*. The ideas of "necessity" and "determination" are also related and conflated. For example, Hume says "*For a frequent repetition, I find, that upon the appearance of one of the objects, the mind is* ***determin'd*** *by custom to consider its usual attendant. . . 'Tis this impression, then, or determination, that affords me the idea of necessity."* [original emphasis] (*ibid*). The relationships between "connections", "powers", "necessity" and "determination", are of importance to the details of causal theories with regards to this thesis. These will be appropriately considered throughout PART 2 of the thesis as causal theories are examined.

With regards to this chapter, I am using scientific mechanisms as an analogy for *connexions*, within an idea of *necessary connexion*. This is not to support an idea that knowledge of mechanisms might guarantee some sort of causation, but for a much broader remit. I am interested, as explained in the main text, whether contemporary theses on mechanisms allow some solutions to the traditional problems raised by Hume in his discourse on *necessary connexion* and causation.

(*ibid*: 1.3.14.26). This torment is now briefly expanded on, as it is of central relevance for this chapter.

Earlier, in his Enquiries, Hume gave a sense of the background for his understanding between constant conjunction and connection:

> *"Necessity may be defined in two ways, conformably to the two definitions of cause, of which it makes an essential part. It consists either in the constant conjunction of like objects, or in the inference of the understanding from one object to another"* (Hume, 1748 EUH 7.2.20)

There are some relationships here that provide us with a key to understanding not only the present dialogue on mechanisms, but also further problems of necessity and inferences - the problem of induction, These are addressed in due course (specifically in *Chapter 7*). In brief, necessary connection relates to us having some knowledge of the necessity of causal connections to permit an *a priori* understanding of what exists between cause and effect. As such, causal inferences would be permitted. Without such knowledge, there is a problem of induction.

Despite his assertions of an intuitive and obvious compulsion that something of substance should exist between causal events – "*the foundation of our inference"* – Hume could not, however, legitimise a place for necessary connection in his conclusory account of causation. Necessary connections were beyond our sense impressions, experiences, and composition of ideas, and belonged elsewhere:

> *"The efficacy or energy of causes is neither placed in the causes themselves . . . but belongs entirely to the soul, which considers the union of two or more objects in all past instances. It is here that the real power of causes is placed along with their connexion and necessity."* (Hume, 1739 THN 1.3.14.23)

As Hume's conclusions on causation are towards a regularities account with no place for necessary connection, there is a problem of induction.

> *"I shall venture to affirm, as a general proposition, which admits of no exception, that the knowledge of this relation is not, in any instance, attained by reasonings a priori; but arises entirely from experience, when we find that any particular objects are constantly conjoined with each other."* (Hume, 1748 EUH 4.1.20)

EBM's response to this problem, as we have seen in *Chapter 1* and will return to in *Chapter 7*, is a reliance on probabilistic inferences from the observation of regularly occurring events. This is premised on an assumption that in nature, uniform laws of some sort exist (again, addressed further in *Chapter* 7):

> *"That instances of which we have had no experience, must resemble those of which we have had experience, and that the course of nature continues always uniformly the same."* (Hume, 1739 THN 1.3.6.5)

However, such a principle cannot be proved in any way, inductively or deductively[69]. As such, Hume would say that this cannot be what drives causal inference. Another contender for driving such inferences - that preferred by EBM - is probability:

> *"'Tis therefore necessary, that in all probable reasonings there be something present to the mind, either seen or remember'd; and that from this we infer something connected with it, which is not seen nor remember'd"* (Hume, 1739 THN 1.3.6.6)

However, this is immediately problematised:

> *". . . probability is founded on the presumption of a resemblance betwixt those objects, of which we had experience, and those that we have had none; and therefore 'tis impossible this presumption can arise from probability"* (*ibid*, 1.3.6.7)

With the ideas of natural laws and probability being dismissed, such inferences therefore must be driven by something else, which can only be an understanding of the necessary connections between events. As this cannot be legitimised however, then the problem of induction remains. This is all, of course, just another expression of the core concern of the thesis – the relationship between prioritised methods and clinical decision-making.

[69] See Vickers (2016) for contemporaneous analysis on this, within a Humean framework.

So where does this leave us? What I am curious about is whether or not contemporary analyses in health science can offer some solution to part of the problem by legitimising a role for something analogous to necessary connections: that being mechanisms. To note, the analogy here is with the *connections* element of the Humean notion. This chapter avoids entanglement with the *necessary* component, which is attended to specifically in *Chapter 7*, §7.3 . The science and reasoning of mechanisms appear to have rich causal information at hand. If mechanisms can be legitimised in the causal account, then there could well be progress towards solving some of the deep problems of causation.

Others have also considered the evidential role of mechanisms and how a mechanistic element might be included in the EBM framework. I will explore two dominant theses on this matter: one from Howick (Howick *et al*., 2010), and second in the Russo-Williamson Thesis (Russo and Williamson, 2007). I argue that despite these works being a significant contribution to EBM literature, they are not successful in developing an understanding of what EBM means by causation. Further, the theses highlight the restrictions that a Humean account puts on a theory of causation for EBM. This argument is then used to conclude the idea that an alternative causal theory might be better suited to EBM.

With this in mind, the second aim is to present an image of what any proposed causal theory should look like if it were to be relevant for EBM. This is done through the development of a desiderata informed by the concerns highlighted through the central and canonical claims of EBM,

together with direct challenges from detractors of non-Humean accounts of causation.

Presentation of these desiderata will form the link to PART 2 of the thesis. *Chapter 5* will present an outline of the characteristic features of the proposed alternative causal theory, causal dispositionalism. This will be initially conducted through a brief presentation of how causation can be graphically modelled. Doing this provides a clear, visual sketch of the key differentiators between traditional causal theories and dispositionalism. The outline sketches will give the relevant foregrounding for the further development of a dispositional theory of causation in *Chapters 6* and *7*.

4.2. Mechanisms: an example of *other* evidence of causation

I am using the term 'mechanisms' to express a concept that relates to the scientific activity *and associated inferences* of understanding and explaining how parts of a system relate to each other. The conflation of 'scientific activity' and 'associated inferences' is purposeful and facilitates clarity. In this case then, what I mean by *mechanisms* seems similar to what others mean by it, for example Clarke *et al*. (2014). This thesis has so far purposefully neglected attention towards the role of mechanistic science and reasoning in the causal story. This is because it has been important to shine the light on the critical methods that EBM *as its stands* considers as most causally important: population studies searching for statistical differences. In turn, this has allowed analysis of the causal account thus far. What we know so far is that, *as it stands*, EBM de-emphasises the role of mechanisms. There have been reasons for this provided throughout the

development of EBM, primarily that reliance on mechanistic levels of evidence can lead to a misappropriation of causal associations. Also, of course, the clinical appeal of comparative studies together with the outcomes movement have served to support the prioritisation of population data, which has often conflicted with the findings of mechanistic science.

But what about mechanisms? There are arguments for a better consideration of mechanisms in the EBM causal story, particularly as we move towards a dispositional account of causation. Below I will use two of the most prolific and convincing stances for the inclusion of mechanisms in a causal account. The first comes from Howick, which is in essence aligned to the position of the OCEBM[70]. The second is the Russo-Williamson Thesis (RWT)[71]. To reinforce the rationale for attending to matters of mechanisms at this stage: first, we need to examine how attempts to include a 'de-emphasised' element into an established causal account might look, and how it might change that causal account; second, attending to mechanisms may serve to foreground a reconceptualisation of causation towards a theory that in essence is inclusive of mechanistic science and reasoning. For this second reason, this section merely provides some existing thought and vocabulary on what EBM sees as mechanisms. I finish this chapter with a conclusion that the two prevailing arguments have both provided some insight into the possible role of mechanisms into the causal story. However, both arguments fall short of making any

[70] The detail presented in §5.3.1 is an attempt to extract the core argument from various sources of Howick's work, for example: Howick *et al*. (2010); Howick (2011); Howick *et al*. (2013a); Howick *et al*. (2013b). The core argument of Howick is represented in later commentaries such as Clarke *et al*. (2014), so I will treat these as similar.
[71] Based on Russo and Williamson (2007).

serious headway in development of the underpinning causal account with EBM. This in turn amplifies the challenge: the arguments for the inclusion of mechanisms as causally relevant elements within EBM are honest and grounded in fundamentals of scientific discovery. However, the overriding causal theory on which EBM exists prohibits the inclusion of such elements in any meaningful way. These arguments for mechanisms are in fact similar. They both support the premise that mechanisms might have a role in understating causal associations with health science. However, they cannot move beyond this due to the fixed Humean stance on what causation is that is now evident in the philosophical underpinnings of EBM. I therefore use this as further rationale for considering a reconceptualisation of causation in EBM. In addition to EBM's traditional causal account being paradoxically restrictive in relation to its own central and canonical claims, it also prohibits the inclusion of fundamentally rich scientific data and logic in the understanding of causal associations in healthcare research and practice. Now to outline the two dominant commentaries on mechanisms in EBM.

4.2.1. The Howick Thesis: Mechanisms *could* be part of causation

In line with the definition above, *mechanisms* is what Howick and OCEMB mean by 'mechanistic reasoning' or 'mechanism-based reasoning' (Howick, 2011:126-128, (OCEBM, 2011). The OCEBM class mechanisms as Level 5 evidence, the lowest level of evidence for therapeutic benefit from an intervention (as originally presented in Figure 1). Following an appreciation of why comparative population studies should be prioritised

(in line with the main themes of the present thesis), Howick develops a philosophy of EBM with an attempt to better understand how mechanisms could feature in a causal set-up related to both causes of disease and therapeutic effectiveness[72].

Mechanistic scientific research is focused on understanding the arrangements and regularity of relationships between parts and features of a system, that is 'inputs and outputs' (Howick, 2011:126). Simple examples include the way that (*a*) inhaled cigarette smoke (*b*) destroys airway cilia that leads to (*c*) exposure to cancer-inducing agents that leads to (*d*) aberrant cell-division that leads to (*e*) cancer[73]. For interventions, mechanistic science has allowed an interpretation of related events to influence clinical treatment decisions. For example, with low back pain: local tissues are (*a*) innervated, such as facet joint capsules, and (*b*) specific activities might (*c*) strain these tissues; but (*d*) passive mobilisation by a therapist might (*e*) change local mechanical and chemical properties which can lead to (*f*) less pain and dysfunction. With this example, (*a*) to (*c*) represent mechanistic scientific activity whilst (*d*) to (*f*) represents the associated inferences (mechanistic reasoning) made from known mechanisms to a relevant patient outcome. This is therefore an account of mechanisms with inherent causal intent.

The issue at hand is one of the actual causal importance or otherwise of mechanisms in the EBM framework. Of course, Hill's 'aspects of causation'

[72] For example, Howick (2011:Ch10)
[73] From Russo and Williamson (2007) (pathology information corrected herewith for accuracy)

consider mechanisms[74], but as we know, EBM de-emphasises them. There seems, however, to be an intuitive attraction towards the utility of Hill's claims, and those of others who see mechanisms as having a prominent role in the causal account. The EBM stance of de-emphasising mechanisms should first be considered. EBM proponents defend their position by pointing towards well-rehearsed cases where mechanisms have led us astray, with dramatic and fatal consequences. These arise in at least two forms: one is when mechanisms, or at least the full mechanistic story, are often unknown but seemingly rational connections are made to develop a story. For example, the famous case of Dr Spock's advice on an infant's sleeping position to reduce risk of sudden infant death syndrome (SIDS). *Mechanism*: (*a*) vomiting whilst asleep is related to SIDS, therefore (*b*) avoiding baby sleeping on back will avoid (*c*) aspiration of vomitus. Population studies later found that SIDS occurred less in groups of babies who slept on their backs, whilst Dr Spock's advice of sleeping on their front increased risk of SIDS, for example Taylor *et al*. (1996). 'Unknown' of course is the level of evidence behind each component link of the mechanistic chain. Howick claims that in much (all) of medicine, for example, mechanistic chains are complex with varying levels of evidence, so the full mechanistic story is unlikely to ever be complete (Howick *et al*., 2010) and (Howick, 2011:137-140).

The second form of mechanistic fallibility highlighted by Howick is developed from the idea that therapeutic interventions activate more than one mechanism (often a *"complex web"* (Howick, 2011:141)), and do so

[74] Five out of nine of Hill's aspects of causation relate directly to mechanistic considerations, rather than probabilistic ones.

stochastically. This jeopardises reasoning based on mechanisms, even if one mechanism is known. This issue is compounded further by the complexities of known and unknown paradoxical responses to treatments, and side-effects (Smith *et al*., 2012). In accordance with the causal stance of EBM, Howick offers mechanisms as a 'black box' between the interventions and outcomes observed in comparative studies. Their utility is fragile, but *could* support a causal claim (arising from comparative studies) should at least two criteria be satisfied: first that knowledge of the full mechanistic pathway (for a particular disease or intervention) is complete, and second that an explicit account of the probabilistic and complex nature of mechanisms is considered when making inferences to claims of therapeutic outcome.

In all practicalities, given the low positioning of mechanisms in evidential hierarchies, the necessary connections purportedly being offered by mechanisms seem superfluous to the causal account. They may exist, but they are not part of the fundamental causal make-up. How they contribute to causal claims then, is tenuous. In the Lewisian view of a richly Humean world of a mosaic of particular facts (intervention, outcome), all else (mechanisms) supervene on it. Howick's position seems to be then that mechanisms are correctly de-emphasised, but *could* (given challenging conditions) support causal associations obtained from population studies. Others, however, do not see this as satisfactory and set out to challenge the de-emphasis of mechanisms further.

4.2.2. The Russo-Williamson Thesis: Mechanisms *should* be part of causation

Russo and Williamson (2007) provide a response to the EBM *status qua*:

> *The Russo-Williamson Thesis (RWT): "In order to establish that A is a cause of B in medicine one normally needs to establish two things. First, that A and B are* ***suitably correlated*** *. . . (probabilistically dependent) . . . ; Second, that there is some underlying* ***mechanism*** *linking A and B which can account for the difference that A makes to B"* [emphasis added]. Adapted from (Clarke *et al*., 2014)

The fundamental position of RWT is that what unites different sources of evidence is their *epistemic role*, and it is this that will ground inductive inferences. The thesis emerges from the argument that if health science uses multiple sources of evidence to infer causal relations[75], then traditional epistemological accounts of causality fail[76]. Monistic accounts, for example, by definition cannot tolerate that causality is inferred from multiple sources of evidence. Pluralistic accounts on the other hand fail on

[75] Let us say we know of at least two accounts of *sources* of evidence by now: i) a statistical difference-making account, as per the bulk of the history and practice of EBM. This would include regularity, probabilistic, and counterfactual theories. Despite the varying conceptualisations, their processes are all concerned with identifying a difference or change; ii) a mechanisms account, as proposed by, for example Russo and Williamson.
[76] Russo and Williamson premise their argument on the background that much philosophical literature on causation can be considered in terms of two broad notions of causality: causal monism and causal pluralism. Monistic theories provide that there is just a single notion of cause. Pluralistic theories claim that we have more than one concept of cause (*conceptual* pluralism), or there is more than one type of causal relation (*ontological* pluralism). More on this matter in §6.4.

two counts: count one, because health science uses multiple sources of evidence to support a single causal claim, for example, difference-making accounts and mechanistic studies support the *single claim* that smoking causes cancer; count two, because the epistemological problems of monism remain, that is pluralism still cannot *explain* the variety of evidence for a single claim. This framing is helpful: an ontology of mechanisms (explanatory evidence) and probabilistic elements (evidence of systemisation and difference-making) assist in conceptualising multiple evidence sources, and adhere well to the policy-making and clinical requirements of health science. This thesis, however, is one that understands causal relationships in terms of rational beliefs. The epistemic causality central to RWT dictates that the causal relationship itself is determined by causal epistemology. Causal beliefs, however, are constructed from the totality of evidence – of which mechanisms are necessary. Thus, the theory is monistic – there is a single notion of causality (difference-making) - but allows integration of multiple evidence sources, not through any form of reconceptualised epistemic or ontological account, but by appeal to rationality.

This account might capture the full complexity of causal evidence, but it also exposes resistant and important limitations in a philosophy of evidence. By "complexity", Russo and Williamson mean multiple sources of evidence. For their account, complexity in this sense seems to have been captured. And this relates well to thinking about the goals of health science at a public health policy level. However, complexity of health care *per se*, and of individual clinical decision-making has not been captured. Compare, for example, with the previously described concerns of person centred medicine (§2.3). Thus, Russo and Williamson's premises and

conclusions seem to rest on at least three assumptions: first, that causal beliefs derived from total evidence are stable and law-like; second, that causal beliefs derived from total evidence are the same in general and particular situations; third, that an epistemic reading of evidential hierarchies can either be ignored, or is at least a separate matter to the concern of this theory. The stability of these assumptions is affected by the level at which full complexity has been captured. The epistemic theory has indeed allowed some progress with a philosophy of evidence. However, more analysis of these underlying assumptions would be necessary if the thesis was to be better understood. Further, an emergent notion from the epistemic theory is that causal claims are constitutive of causality itself. This idea gives a signal to how such a theory actually sees causal relationships[77].

I see it that the positions marked out by both RWT and Howick are, in fact, similar. Their philosophies offer some account of evidence that (appears to) consider total evidence. However, I do not see much progress made towards advancing a theory of causation, despite this being the intention of at least the RWT. To align them then: Howick offers an honest account of mechanisms that is in line with the evidential structuring of EBM, that is, mechanisms may be an unnecessary supervening phenomena on a Humean world of regularities. Despite its best efforts, I do not see how the RWT has impacted on this stance. The only difference is one of degree of conditionality: Howick says mechanisms *could* play a causal role, RWT says they *should*. Mechanisms in both cases perform the same causal

[77] But this seems inconsistent with Russo and Williamson's introductory claims about *causality* and *evidence of causality* not being conflated (*ibid*:158).

function: they support the causal claims of statistical correlations. This means that there is still admittance to the preference and supremacy of comparative population studies over mechanisms. It still seems then, that in this world at least, mechanisms can be nothing more than a supervening phenomenon.

The limitations to progression of a causal theory in EBM are now clear. Despite best efforts to address fundamental concerns of EBM - that is to provide a causal theory that would allow the central and canonical claims of EBM to be satisfied - it is the fixed commitment to a Humean account of causation which is itself inhibiting development.

4.3. Where are we now?

At this point, a summary of the situation at hand should be presented. This is to serve at least two purposes: first and foremost it is to exaggerate the characteristic features of the causal account established so far with regards to EBM. Second, a subtle but necessary shift in vernacular is highlighted to align the discussion so far with that of the forthcoming philosophical reconceptualisation. I will outline these in turn.

The thesis has to this point been explicitly concerned with using the methods and structure of EBM to identify what might be meant by causation. It is these very methods and structures that have indeed allowed the pinpointing of sites of emergence of causal claims. In doing this, an account for what causation might actually be – that is, to identify a theory of causation - was hoped for. Of course, this whole process has been based on a belief that the undertaking of scientific activity that sets out to look for a cause - which I have argued as being the core purpose of

medical science - does so with a presupposition of what causation is. More often than not, science itself has no overt or ongoing concern with this, and such ontological matters are often largely tacit and left unexamined. However, such an understanding forms the very basis of what is, or can be, accepted as evidence of causation. This understanding is reflected in the scientific methods. More than merely guaranteeing the quality of research, scientific methods serve to define what counts as evidence, and as such what counts as a cause.

In this exploration, it has been proposed that large-scale population studies, including observational studies and RCTs, offer evidence of causation. RCTs offer a counterfactual condition, which increases confidence in causal claims, and thus acts as the strongest evidence of causation. However, we have seen that any causal work is actually being done in single groups, independent of a counterfactual condition. Thus, studies with non-homogenised (or at least less so homogenised) groups may also lead to causal claims. There is rich debate concerning the role of mechanisms as sources of evidence. EBM, as it stands, de-emphasises such approaches to its lowest levels. It has been these components that have enhanced a commentary of what EBM might mean by causation. I have proposed that this is something essentially Humean. Hume thought we could only understand causation as a relation of regularity between discrete, essentially unconnected types of event – and this is an image we see in EBM and its associated scientific methods. So when we say 'intervention *x* works (in producing some effect *y*)', what EBM essentially means is that there have been more instances of observations of intervention *x* being followed by event *y* than those where such regular relationships have not been observed, probabilistically. The Humean

account has allowed some insight into the underpinning substance of causation.

With regards to terminology, we can relate the Humean account to something based on a *difference-making* notion of causation that is dependent on a frequentist interpretation of probability. Within this, causation is associated to the identification of *robust correlations* and is fixed to the notion that the same cause always produces the same effect. The terms *difference-making* and *robust correlations* are linked to the positioning of observational studies and RCTs. *Difference-making* is an intuitively plausible way to think about causation – we would want a cause to make a difference after all – and this is what counterfactual conditions set out to identify. RCTs are in essence saying 'what difference would it make if this factor was changed'. The intuition is that if we are looking for a cause, then we look for the difference-maker. *Robust correlations* refers to the checks that are made within EBM's methods to ensure that correlating patterns of events observed in studies are not a result of confounding, nor some non-causal relationship. The correlation[78] is seen in the data set, but the 'robust' checking is through randomisation or, in the case of non-randomised studies, internal and external factors influencing study design. Thus, correlation in itself does not imply causation, but the conditions under which it is judged allow confidence in causal claims. This paradigm is tacitly accepted in many scientific methodologies, but viewing the activities within a broader framework of

[78] In line with Clarke *et al*. (2014) 'correlation' is being used not to refer to the simplistic statistical linear coefficient between two continuous variables, but rather in the much broader sense of a probabilistic dependence between arbitrary variables.

EBM has exposed limitations, primarily that this probabilistic evidence fails to facilitate the central and canonical claims of EBM.

We should acknowledge that although correlation (in sum: $A \rightarrow B$), and difference-making (in sum: $\neg A \rightarrow \neg B$) are both underpinned by a Humean notion of *regularities*, and are both typically Humean concepts, they are different conceptions of cause.

EBM is principled on the idea that what is true of a given population should be directly applicable to individual clinical decisions. What works for most people should also work for this patient. Such external validity only holds if we assume that individual propensities can be derived directly from statistical frequencies. Further, EBM assumes that the same treatment should be given to all. But what does that mean? Is there a rational basis for the claim that the same intervention in two different patients is the same treatment? Further, what of the presupposition that the same intervention will have the same effect in different patients? EBM's hierarchical structure reveals a commitment to the unsustainable and largely unquestioned orthodoxy that singular causal truths are derived from general causal laws. The direct transfer of probabilistic results from population-level studies to individual patients remains, however, philosophically troublesome.

What we have seen is that from a seemingly simple process of favouring particular sources of evidence, there is in fact many expressions of the way the scientific methods used in medicine and health relate to their causal claims. Further, the way EBM wishes for these claims to be utilised is far

from what the methods themselves will allow. Although an account of causation has been developed, a substantive theory about what causation *is* is still not apparent. The hope of a coherent ontological basis that would allow us to be confident in stating what evidence *is actually of* has not been realised. The ontological tension at play in the Humean world is now revisited. This is for the purpose of explicitly problematising the tension so that clarity can be given towards a way out of some of the Humean traps, traps exposed by the complex and holistic intentions of EBM as a decision-making framework.

4.3.1. What should a theory of causation look like?

The Humean understanding of causation is one of quantifying regularities. Hume believed that causation itself was not a primitive matter and the only way that some judgement on causation could be made was to observe the regularly occurring events *C* and *E*. He saw relationships of time and space, but none of a causal substance. Hume did not believe in necessary connections in nature. This mirrors well the image of scientific practice in healthcare and medicine, especially when considering the clinical effects of therapeutic interventions.

The Humean account conflates the ideas of necessary connection and powers[79]. By rejecting necessary connection in an account of causation,

[79] Detail as to what this thesis means by 'powers' follows in *Chapter 5*. However, in brief, from this point onwards the word 'powers' is used to refer to the substance of an object or notion. At a basic level, the words *powers, substance, properties, capacities,* and *dispositions* can be thought of synonymously. Later, I will discuss how subtle differences in the use of these terms help define differences in broad dispositional theories. But for now, we can simply consider the idea that worldly things possess powers that, according to a certain metaphysic, have a critical role in how the world should be understood. In the case of causation, that things possess powers is what motivates a theory of causation. Further,

Hume also rejects the existence of powers. If you believe in powers, you believe in necessary connection. As anything can follow anything else, there can be no necessary connection, therefore there can be no powers.

If a reconceptualisation of a causal account in EBM is truly intended, then what better way to start than to face Hume head-on: that powers are in fact where causes come from. But Hume has a strong case, as we have seen, backed by a historical account, centuries-old, whereby science has operated on Humean terms. Hume has many supporters, and his opponents have failed to provide substantial alternative accounts. Many challenges to Hume have however begun with the acceptance of powers as central to the causal account. This has led to arguments for necessity in causation. However, given the strength of Hume's rejection of necessity, many such alternatives have failed. But what of a theory that saw powers not as necessitating their effects, but rather as a disposition that is less than necessity, but more than contingent? Something that *tends* towards an effect, but does not guarantee it? This immediately avoids the Humean trap of necessary connection[80]. After all, health science has a wealth of

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the events witnessed in a Humean world, that is event *C* followed by event *E*, are merely *changes produced when powers exercise themselves* (Mumford and Anjum, 2011b:2). Powers, for example, can be things such as mass, velocity, fragility and so on (*ibid*). Thus, a glass pushed from a table (event *C*) that then shatters (event *E*) on the stone floor is not simply a story of events C and E, but rather one of the properties held by the glass (fragility, weight, mass, *et cetera*), and the properties of the environment (gravity, hardness of stone floor, *et cetera*) being exercised and partnered with one another in order to manifest in a particular observable way. Powers are the substances that although Hume accepted, he could not see, and therefore rejected them from his account of causation.

[80] This 'Humean trap', for clarity, is such that Hume saw no part in causation for *necessary connexion*, but left an account of causation intuitively incomplete. What I mean by this is that there is something appealing as humans to think that there *must* be something more to causes than mere regularity. For example, when I eat, by hunger subsides. I, as a human, think this story is more than two discrete events: 'eat' and 'hunger'. My intuition is that they are related by some causal substance. With this, philosophers have endeavoured to solve Hume's problem (for typical review of such: Miller (2012)). The trap

mechanistic scientific data at its disposal that most likely never set out with intentions of some sort of proof of necessity. Further, clinical context, complexity of disease, and patient presentation also make the motion of necessity challenging.

EBM, however, is wary of using this data and rationale as evidence of a causal phenomenon. This wariness has emerged from deep Humean intuitions. But it might be that this data, together with other elements of a complex framework, could be used not to make a case for some $\forall x(Cx \rightarrow Ex)$[81] implying necessity, but rather to understand how a cause disposes towards its effect. Such a theory has indeed been offered - the theory of causal dispositionalism, and this will be introduced in *Chapter 5*. Therewith, my intention is to use the dispositional theory as a test in providing some form of a reconceptualised notion of causation in EBM.

At the heart of concern in this thesis still lie the canonical claims of EBM. I have proposed that the way EBM presently conceptualises causation does not satisfy these claims. As a reminder, the proposed canonical claims are:

> *Claim 1: Evidential priority is given to comparative research methods, utilising statistical estimates, above other elements of research and practice;*

has been one of falling at the first hurdle. On trying to account for a *necessary connexion*, the temptation and custom has been to account for necessity. Hume's strength of argument against necessity wins each time.

[81] This is a universal quantification of particular instances, saying that it is universally true ($\forall$) of x that in all particular instances where x is C, x is also E. Put in health research terms, whenever a particular intervention is applied, a particular outcome will result, to a probabilistic level.

Claim 2: Data from prioritised methods should determine clinical decision-making.

These relate to EBM's *central claim* that evidence from study designs higher up the hierarchy more reliably informs therapeutic decision. These claims must inform at least some conditional part of any new theory of causation if that theory is to be of relevance for EBM. Beyond this there should be related conditions that help to further advance the relationship between *claims 1* and *2*. This is an area where, with the exception of a procedural concern over external validity, EBM as it stands has been particularly silent. To help with understanding the shape and conditions of a causal theory for EBM I shall borrow directly from two opponents of dispositional theory. Both parties have seemingly developed conditional terms to specifically demonstrate the insufficiencies of an alternative (non-Humean) account of causation.

First, Strand and Parkkinen (2014) in a reply to an inaugural proposition of a dispositional causal account for EBM[82] agree with the core challenge to EBM set out in this thesis, that is:

"The complexity of disease aetiology and individual heterogeneity in causally relevant detail block direct inference from population-level evidence to results of treatments performed on individuals. ***Consequently, substantial***

[82] This proposition was presented in a ontological review of EBM whereby the key features of the causal account in EBM were sketched out in line with the present thesis (Kerry *et al*., 2012). A dispositional account, namely *Causal Dispositionalism*, was introduced in this paper in relation to medicine and health science.

> ***assumptions are needed in order to justify such inferences****. Philosophical accounts of causation and causal knowledge are pertinent to EBM when they shed light on such inferential problems"* [emphasis added] (Strand and Parkkinen, 2014:981)

The understanding of such assumptions (as emphasised) should therefore be something that a philosophical account of causation is able to provide. In their challenge, Strand and Parkkinen (*ibid*) confidently claim that a difference-making (Humean) account of causation is able to show the kinds of substantial assumptions needed when making inferences from population-level comparative studies to individual decision-making. Of course, they also claim that a dispositional account falls short of providing for addressing this condition:

> *"In contrast [to a Humean account[83]], the dispositionalism of Kerry* et al. *provides, at best, only gestures as to how the inferential aspects of causal knowledge can be assessed."* (Strand and Parkkinen, 2014:982)

I see the best move now as being to take this as a head-on challenge and suggest that this component[84] of Strand and Parkkinen's considered

[83] Strand and Parkkinen use the terms 'difference-making' and 'dependency' to refer to the Humean features that they succinctly characterise EBM as being constructed of.
[84] Strand and Parkkinen (*ibid*) also set out a primary condition that a causal account should explain the role of causal knowledge in EBM's sources of evidence. This is something that I have already considered as an emerging requirement from the analysis so far and will be represented in the forthcoming desiderata at the end of this chapter.

response to a dispositional account should directly inform the conditions of any causal theory. It should be obvious from the analysis of EBM thus far that I would take the opposite stance to Strand and Parkkinen and state that a Humean world does not in fact provide for an understanding of the sort of assumptions implied here. I will, of course, consider whether or not a dispositional account can do a better job.

One feature of the argument presented in Kerry *et al*. (2012) that Strand and Parkkinen highlight is the (apparent) disjoint between ontological aspects of causation and the more practical epistemological concerns of generating and systematising knowledge.

> *"EBM should not get entangled in ontological aspects of causation that transcend the issues of causal inference and causal epistemology . . ."* (Strand and Parkkinen, 2014:981)

> *"What is needed, however, is an explicit epistemology of causal knowledge, especially of its evidence conditions and relations to practical inference."* (*ibid*:983)

and

> *"Such an epistemology does not flow from the dispositionalist ontology, and is not provided by Kerry et al."* (*ibid*:983)

This is also the concern of second voice of opposition to a "non-epistemic" account of causation, Jon Williamson, from whom I will also borrow a condition for a causal theory. Williamson states: "*it is not enough for a*

philosophical theory of causality to take the form 'causality is X'" (Williamson, 2006:262). Williamson proposes an *epistemic theory of causality* and attempts to show (*ibid*) that this theory makes up for what a metaphysic of capacities[85] fails on. Like Strand and Parkkinen, Williamson sees greater value in providing a theory of causation where epistemological matters are the primary concern (as already seen in discussion on the RWT in §4.2.2). Williamson seems to be more tolerant of the inclusion of an ontological aspect to a grand theory, but identifies the problems associated with claiming an ontological account as sufficient. It is clear that both parties are concerned with the relationship between 'real world' epistemology and the metaphysical accounts on the nature of causation. This is also a concern of mine, but I think that the relationship can be seen as something other than the view of these two commentators. Williamson says that Cartwright's dispositional account is "*not altogether conclusive*" (*ibid*:267) in linking the epistemology of causality to her metaphysics of capacities. I see Williamson's insistence that a philosophical theory of causality should inform something epistemological as a healthy move, and one that should inform the conditions of a causal theory.

With the above in mind, some desiderata can be set. A theory of causation, to be relevant for EBM, should at least:

> *D1: Explain the causal role of content from particular research methods.*
>
> *D2: Motivate a viable epistemology.*

[85] Williamson plays off his epistemic theory against Cartwright's dispositional account of causality, within which she uses the term 'capacities' for what I have called, and will continue to call, 'powers'.

D3: Account for causal processes in individual-level clinical decision-making.

D4: Help understand and assess additional premises and assumptions needed to bridge the inferential gap between population-level evidence and clinical decisions.

Each of these desideratum should now seem like valid areas of inquiry. They relate to the core issues of this thesis, those being the nature and function of causes, and the ability for a theory to relate evidential sources to their intended spatiotemporal distant instances. Desiderata 1) and 2) relate to the nature of the content deriving from the scientific methods used in medicine and healthcare, and what can be known from that. Desiderata 3) and 4) relate to the inferential issues of data and what causation could mean in individual instances. The desiderata are therefore clearly integrated with the central and canonical claims of EBM, as defined herewith. In order to ensure a tight relationship with existing key concerns of the possibility of an alternative account of causation, the desiderata are a combination of emergent themes from the broad body of literature (D1 and D3), and specific requests from the most contemporaneous of opponents to a reconceptualised ontology (D2 and D4). D2 being a criterion from Williamson (2006:260), and D4 being a direct call from Strand and Parkkinen (2014:981). Of course these authors have other concerns, but these chosen desiderata are the ones most reflective of and relevant to the core focus of this thesis. I anticipate that if any proposed alternative theory can respond well to these desiderata, substantial progress will have been made as to the possibility of a viable reconceptualised account of causation in EBM.

These desiderata will form the structure and framework for PART 2 of the thesis where development of a reconceptualisation of causation in EBM will be given.

4.4. Conclusion

Mechanisms, as defined in this chapter, represent a traditionally de-emphasised evidential element in the EBM structure. There are reasons for this de-emphasis, given by EBM theorists and proponents, such as the dramatic failure of reliance on mechanism as a source for causal evidence (Dr Spock and such like). This chapter could have focused on any number of de-emphasised sources of evidence, such as expertise, patient values, case studies, *et cetera*. However, the appeal for this thesis was that mechanisms seem more obviously and visibly related to what Hume might have meant by *necessary connexion*, the causal substance, the causal process. Therefore mechanisms seem rightly suited to have no part in the constitution of causation. However, there are philosophers of EBM who seem to think there *is* something causally evidential about mechanisms. Something intuitive perhaps about this dimension of science and rationalising that makes us wonder more about causation. Perhaps understanding a mechanisms of action makes us more scientifically and clinically confident in a causal claim arising from population data. A number of authors have provided theses that attempt to include mechanisms into an account of what counts as evidence in EBM. Specifically, I focused on two of the most prolific accounts, from Howick and from Russo-Williamson. I have argued that both of these theses make some headway into understanding the relationship between population

data and mechanisms. However, I conclude that both attempts fall short of a satisfactory account of causation that could be inclusive of mechanisms because both accounts remain fixed to a Humean interpretation of what causation is.

From this, I have presented desiderata that a theory of causation, to be relevant for EBM, should be able to respond to. This is the concern of PART 2 of the thesis.

Summary of PART 1

This thesis is focused on a reconceptualisation of the nature of causation in EBM. In order for this to happen, I have considered it necessary to first conceptualise what holds as causation in EBM *as it stands*. By doing so, characteristics of causation in EBM have been exposed. These characteristics will in turn support a drive for reconceptualisation. I have attempted to develop a conceptual framework by which to place the present account of causation in some meaningful sense. This framework has developed around the core tenets of the EBM movement. Namely, I have reduced EBM to two fundamental and canonical claims:

> *Claim 1: Evidential priority is given to comparative research methods, utilising statistical estimates, above other elements of research and practice.*
>
> *Claim 2: Data from prioritised methods should determine clinical decision-making.*

The background for these claims has been presented and relates to a central claim of EBM given previously by La Caze (2008): *"evidence from study designs higher up the hierarchy more reliably informs therapeutic decisions"*. The statistical and epidemiological history has provided a

backdrop from which to understand the precise scientific approach that EBM has invested in. There is indeed a stable and convincing historical and logical rationale for the chosen preferences of EBM towards robust comparative studies. EBM itself however must be seen for what it is: a complex and multi-faceted movement that has at its heart the best of scientific activity. However, its fundamental purpose is to inform clinical decision-making with the best evidence possible. The positioning of scientific activity, evidence, and best practice is not readily confluent, nor philosophically unchallenging. We have seen that the ideas of scientific activity and evidence cannot be conflated. This is best witnessed through a reappraisal of evidential hierarchies that privilege robust population studies for establishing 'what works'. The most rationalised interpretation of this phenomenon is that evidential hierarchies are best seen as heuristics for comparative internal validity of specified research methods. This is not synonymous with claims for efficacy of therapeutic interventions. The stability of the relationship between *Claim 1* and *Claim 2* is, on this account, problematic. The canonical claims of EBM become inherently paradoxical: *the very prioritisation of evidence elements for use in clinical decision-making (Claim 1) prohibits use of this evidence in clinical decision-making (Claim 2).*

The broad aim of PART 1 was to identify an account of causation found within the structure, narrative, and logic of EBM. Some have argued this is not necessary. I have argued it is. If causal claims about health care interventions are made that are to have direct clinical and political influence, then, I say, the causal account on which such claims are developed is critical in defining what those claims mean. A Humean regularities account has emerged that reduces causation to constituent parts of spatiotemporal contiguity, temporal priority (*c* always before *e*),

and constant conjunction. These constituents are visible through analysis of the prioritised research methods found in EBM. I have claimed that because of this account, the central and canonical claims of EBM are fragile. Hence, placing causation as a central concern of EBM, it is the account of causation itself that is undermining what EBM is.

So what is missing in the traditional account? The broad context of this thesis is set in two operational frameworks firmly embedded in health care: evidential categorisation of research methods, and the operational structure of EBM itself. We have seen the background to this together with analysis of arguments and the textual narratives. In sum, proponents of EBM believe it to be a sensible, professional advancement of clinical decision-making that tracks exponential progress in data production from rigorous research processes. However, more data does not necessarily lead to an increased understanding of causal knowledge. Opponents, therefore, offer arguments based around, among many things, the apparent disproportionate weighting given to epidemiologically-derived data. Many arguments focus on the problems faced with statistical inference and generalisability of population-based research findings to particular instances of clinical decision-making. So far, I have taken these as serious challenges to EBM and grounded much of the argument in this issue. As already stated, I am not interested in rehearsing or developing arguments associated with statistical inference, and take these as read. I also accept that EBM and evidential frameworks hold an established procedural role in the delivery of health care. However, this political and administrative functional fitness should not drive attention away from the nature of the phenomenon. In fact, the growing influence and institutionalisation 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 EBM. However, this 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 EBM understands what causation is. A core claim to my argument is that it is this fixed stance on causal nature that is central to both the philosophical unrest in EBM, and limitations on its inherent scientific progress.

So far, multiple causal concepts have been identified but all seem to be underpinned by an essentially Humean view of causation. The explicit preference towards randomised methods leads us to think that causation is something to do with the differences seen between homogenous groups, *ceteris paribus*. However, the idea that causal claims can obtain from non-randomised methods gives us a clue as to precisely *where* the causation is at play – that is, within a single group. Comparing with homogenous groups is indeed a good way of identifying a difference between groups, and counterfactually reassuring, in some psychological sense. However, it makes sense to say that although randomised methods may provide good evidence of a test of a primary hypothesis related to the inherent experimental-type qualities of the method (internal validity), they do not constitute causation itself. We should, however, take counterfactual dependency as something of importance to the causal story. Presently though, its role and interpretation is being dictated by the traditional Humean account.

The broad assumption is that causal claims are made based on regularly occurring events. Within this, different theories can be identified. The

different theories are also of course Humean in nature. These are, in summary, the Humean concepts of correlation (A→B), and difference-making (¬A→¬B). These theories are implicit within different aspects of evidential frameworks, those being observational studies and RCTs respectively.

It is not obvious then that the different methods found in health science research, and central to EBM, 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. For example, what is claimed from RCTs and observational studies say, as it stands, different things about causation. RCTs say that there is something happening in a group and it is because of the counterfactual condition that we can obtain something causal from that. Observational studies say that causal claims obtain from comparisons of non-randomised groups, but due to factors both internal and external to the methodology, we have causal confidence in the observational of regularly occurring events. Health science seems to be operating with several ideas of causation and thus ontological tension exists. What is meant by 'tension' is that although there might be a coherent framework for causation - a Humean regularities view – at an ontological level, the different methods point towards different causal concepts. It seems then, given the way EBM has developed and is structured, the ontological groundings of its central concern are being shaped by its epistemology. Indeed, this is in line with prolific commentators on causality in the health sciences, for example: "*Thus causality itself is determined by causal epistemology*" (Russo and Williamson, 2007:167, referring to Williamson (2005), Williamson (2006), Williamson (2007a), Williamson (2007b)).

I have used PART 1 of this thesis to approach the background analysis in a linear manner. That is to say that I have looked at EBM, together with its history, evolution, structures and nuances, considered its defining strengths and limitations, and said, 'this is where and how we see causation'. PART 2 of the thesis takes an about-turn. What if from now on our starting point was in fact causation, and we looked back at EBM from this point? What if we had a different understanding of what causation could be? Perhaps a causal world unfamiliar to the one Hume examined. How would EBM then look? What could we make of the methods and evidential elements of EBM if we were to pin-point historical and emergent limitations of a Humean world and replace it with an account of causation that could respond to the complex and multi-faceted challenges of EBM and health care in general? Could we indeed find such an account, and would that account be able to fill the space between the claims of EBM? Can a reconceptualisation of causation mean that what we establish in our scientific activities relates much closer to what we mean by causation in clinical and policy-making practice? These are the sorts of questions that PART 2 of the thesis is now concerned with. During the next part of the thesis each of the stated desiderata shall be addressed. It should become apparent that a more robust philosophical account of a discipline is given when explanations of causal content from methods relate to both general and particular instances of causation. It should be visible as well that epistemological matters emerge when the ontological grounding of a theory is explicit and stable. Thus, a credible account of the nature of causation in EBM should possess functions of explaining and influencing how knowledge obtained from its methods is read, and how these factors relate to matters of causation at individual levels.

PART 2

Towards a Dispositions Theory of Causation in Evidence Based Medicine

Introduction to PART 2

This second and final part of the thesis establishes a foundation for the reconceptualisation of a theory of causation in EBM. A theory of causation based on an ontology of powers is introduced as an alternative account. Specifically, this will be centred on a theory of causal dispositionalism. This account is defended by showing its relevance and importance for the scientific practices within EBM. No attempt is made to defend the account on general metaphysics grounds. That is beyond the parameters and necessity of this thesis. As such, I will take many metaphysical assumptions of this account as accepted.

It is proposed here that a powers based account of causation offers meaningful solutions to the problems identified in PART 1. As set out in the introduction, this thesis is not concerned with the idea of comparing alternative causal accounts against each other. Rather, it takes as a starting point that causal dispositionalism is an account sufficiently ready for examination through a test of fitness-for-purpose, rather than comparison.

It will be demonstrated that dispositional readings of evidential frameworks show how causation can be better understood relative to existing scientific methods than the traditional causal account. Further, a dispositional account re-emphasises the importance of background conditions in understanding causes. Specifically, the roles of single instance cases and mechanistic science are central to understanding causes

dispositionally. The relationship of causes to individual situations in an EBM framework is also explained. A sketch of the relevant characteristics of dispositionalism is given before attending to specific components of the evidential frameworks. This sketch is provided in the context of highlights of the characteristic features of the Humean account. These features are drawn out within brief summaries of the ontologically relevant dimensions of the Humean account, namely regularities and counterfactuals. The purpose of doing this will be to allow some introductory commentary regarding a dispositional theory that will hopefully appear to have some direct relevance to the identified areas of concern.

PART 2 consists of three chapters:

Chapter 5 provides an introduction to causal dispositionalism. This is undertaken through a lens of causal modelling. Doing this provides a clear and direct introduction to some key characteristics of an account of causation based on a powers ontology, and how these differ from the traditional account. Traditional modelling of causal theory is conventionally provided with neuron graphs. Causal dispositionalism sees this as problematic and illustrative of the limitations of a traditional account. Dispositionalism offers vector models as a solution. I have used these ideas on modelling to provide a structural platform on which to develop an alternative causal account.

Chapter 6 begins to develop detail of how a theory of causal dispositionalism might respond to the desiderata stated in §4.3.1. This chapter deals with the first two desiderata, which are broadly concerned

with the nature of causal knowledge and the meaning that a revised ontology would have on a causal epistemology. To remind:

> *D1: Explain the causal role of content from particular research methods.*
> *D2: Motivate a viable epistemology.*

Humeans are content that observations of frequently occurring events sufficiently explain the causal role of research content and act as the causal truthmaker. To the dispositionalist, this is unsatisfactory, and they can provide an explanation that sees causation within the core of the content itself. Similarly, that dispositionalism takes causes as real entities, a key to a causal epistemological framework is identified.

Chapter 7 attends to the inferential gap between population data and individual clinical decision-making – the very core concern of the thesis and one positioned tightly to the central and canonical claims of EBM. The final two desiderata represent this concern in a number of dimensions. To remind:

> *D3: Account for causal processes in individual-level clinical decision-making.*
> *D4: Help understand and assess additional premises and assumptions needed to bridge the inferential gap between population-level evidence and clinical decisions.*

A Humean theory – *the traditional stance* – can only account for causal process at an individual level by reliance on universal laws and

probabilistic rationale. For the dispositionalist, the individual is the very starting point of the causal account. Likewise, despite a narrative from proponents of the traditional stance, the assumptions and premises needed to bridge the inferential gap are problematic for Humeans. A traditionalist's reliance on methodological structure and deductive logic is surpassed by the dispositionalist acceptance of causes only tending towards an effect. The dispositionalist theory can also account for the fact that predictions are fallible and defeasible – a key function of a causal theory.

PART 2 concludes with an understanding of the characteristic features of causal dispositionalism and an ontology of powers, and how these features facilitate progressive responses to the desiderata in question.

Chapter 5: Introducing Causal Dispositionalism

5.1. Introduction

Dispositionalism, broadly, views the world not as *loose and separate* distinct events as did Hume, but rather as one admitting a category of power or capacity (Mumford, 2009:265). That is to say that where Hume saw no *necessary connexion* in nature (Hume, 1748 A 7), (Hume, 1739 THN 1.3.14), a dispositions ontology asks at least if there are real causal connections. Thus, dispositions are what Hume rejects. This seems immediately problematic for a reconceptualisation of any theory responding to such an established account of causation. But there are ways in which dispositionalism can respond. The more detailed responses will be the concern of *Chapters 6* and *7*, as the desiderata are addressed. For now, an introduction to causal dispositionalism is given in a context of highlighted limitations of the traditional Humean theory of causation.

First, some brief attention to clarify the Humean position with regards to a dispositions ontology. Above I stated 'dispositions are what Hume rejects'. There is an important commentary here that is worthy of at least some acknowledgement when trying to establish the background position for a move from one account of causation to another. Dispositions works on an ontology of powers. Powers have already been introduced in §4.3.1,

and more attention will also be given below. However, for now, powers can be thought of as the causally important component of the properties of things - something more fundamental than just the substance of an object or phenomenon. Using an analogy of a glass, we might say that a wine glass has a disposition of fragility. So we could say that the glass consists of certain properties that could causally explain it breaking, the material it is made of, *et cetera*. But beyond these physical elements lie the real causal reasons that provide it with a disposition of fragility – the powers of the properties that give them the capability of breaking. With powers we move beyond causal relata towards a much more fundamental causal ontology. So when we say 'dispositions are what Hume rejects', it is an ontology of powers we are referring to. Hume accepts only the events that can be experienced following the exercising of such powers[86]:

> *". . . the distinction, that we often make betwixt* ***power*** *and the* ***exercise*** *of it, is equally without foundation"* [original emphasis] (Hume, 1739 THN 1.3.14.34)

> *"It has been observ'd in treating of the understanding, that the distinction, which we sometimes make betwixt a* ***power*** *and the* ***exercise*** *of it, is entirely frivolous, and that neither man nor any other being ought ever to be thought possessed of any*

[86] To reinforce: when this thesis refers to Hume on causation, it refers to the *standard view* of Hume on causation – that causation is nothing more than regular succession. The reminder here is particularly timely as one point of contention within contemporaneous non-standard views is about Hume's belief in causal powers, for example Strawson (2008:Ch18 David Hume: Objects and Power).

> *ability, unless it be exerted and put in action"* [original emphasis] (*ibid*: 2.1.10.4)

But what does this actually say about Hume's account of powers? If Hume was forgiving about powers we might say that a revised account of causation in EBM might just be to keep it essentially as it is, but emphasise some detail about powers. I suggested in *Chapter 4*, for example, that theses on mechanisms fail because of the Humean account. If Hume allows powers, we may have to revise this conclusion. However, it is most likely the case that Hume is certain about his position on powers, and as such we will not need to backtrack at this point. But what is the nature of this certainty? Neo-Humeans think Hume gave a reductionist account of powers, that is that they can be reduced to events with regularity and constant conjunction, for example Lewis (1973a). However, what Hume seems to actually be saying is that because the distinction between powers and their exercising is "*without foundation*" or "*frivolous*" and "*that neither man nor any other being ought ever to be thought possessed of any ability, unless it be exerted and put in action*", then it is only the exercising (experienced events) that are part of causation. Rather than powers being reduced to events, powers are being eliminated from the causal account. Thus, Hume seems to offer an eliminativist account of powers. If this is the case then, according to causal dispositionalism, Hume is eliminating something that is essential to the world. As such, a reconceptualisation of a causal account cannot simply be a revised Humean account. Causal dispositionalism offers an account with a fundamentally different grounding – an admission of powers and the reality of causes.

It should be noted that the attempt to address the concerns emerging from the traditional causal account is not a patent attack on the theory and methods that exist in EBM as it is, in fact, much the opposite. Whereas a Humean account rejects *a priori* what dispositionalism may have to offer, dispositionalists accept the outcomes of 'Humean' scientific methods. But dispositionalists think there will be regularities, counterfactually-derived and probabilistic dependencies and so forth, not because this is what constitutes causation, but rather because there are real causal connections in nature. Thus a subtle shift in the way such outcomes may be read is apparent: instead of the methods *establishing* causal claims, the outcomes of such population studies may be seen as *symptomatic* of some real causal notion. However, they are only one symptom of many, and indeed that symptom may sometimes lead to a misdiagnosis. There are, for the dispositionalist, other ways to consider causation at play.

The above are the broad and general features of dispositionalists' accounts across the board. Beyond this, constructions of a theory of causation based on dispositions are varied. It is not at all the intention of this thesis to provide historical or critical analysis of these different theories. As stated, I will commit straight away to the most contemporaneous dispositionalist theory of causation - causal dispositionalism - from Mumford and Anjum (2011b). There may be times in the following chapters where it is necessary, or simply of interest, to point to some differences between dispositional theories. However, although a matter of importance for thick philosophical analysis of dispositionalism, this thesis will avoid most of the inter-theory nuances for the sake of the development of a subject-specific thesis. Having said this

much, there are a couple of key priorities that should be identified in order to depict the shape of causal dispositionalism.

The first priority is to declare a vocabulary. Dispositionalism admits to powers and capacities. Dispositions are powers, powers are capacities. Causal dispositionalism uses with equivalence the terms 'powers' and 'dispositions'. Cartwright, for example, prefers the term 'capacities'. When it becomes necessary to clarify semantic differences, this will be done. There is a subtlety by which powers should be thought of in this theory. A power may be "*something that has possible manifestations, but may nevertheless still exist unmanifested"* (*ibid*:4-5). This is in contrast to more common readings of powers, for example Fara (2005) that see powers and dispositions as related, but separate terms and entities[87].

Causal dispositionalism does reserve the term *tendency* to describe powers that reliably and frequently manifest. Other terms to describe other types of powers are used, such as *abilities*, to describe advantageous dispositions; *liabilities*, for those powers that it would be a disadvantage to have, *et cetera*.

In line with these semantic differentiators, it is worth highlighting that causal dispositionalism takes some assumptions from existing dispositional theories, especially pandispositionalism[88], such that i) powers are real (against categoricalism[89]), ii) powers are not properties, but

[87] That is, disposition is a term used for powers that manifest. Causal dispositionalism on the other hand is happy with the equivalency of the terms, and would say that something could have unmanifested dispositions, for example.

[88] Causal dispositionalism relates to pandispositionalism, that can be thought of as a: ". . . *thesis about the properties of the entities studied in the empirical sciences*." (Tugby, 2010:12).

[89] Categoricalism is the view that all fundamental natural properties are categorical — they have no nomic or causal essences (from Bird (2007:Ch4)). Dispositionalism is the opposing view to this: "*On this view, the nature of a property is exhausted by its nomic dispositional role(s). Properties are nothing more than dispositions.*" (Tugby, 2014:1147-1148).

properties are not not-powers; properties are 'bundles' of powers, iii) *all* properties are powerful, that is there cannot be properties that are not powerful; and as such iv) dispositions are not to be conceived as a kind of property, and properties are not categorical: powers are irreducible to any other ontological category (against categoricalism). Now, further detail of causal dispositionalism will be presented. This, again, is to help foreground development of the theory for EBM.

There are a number of ways in which the fundamental characteristics of causal dispositionalism could be presented. In order to keep this brief, focused and to avoid being overly descriptive, I will sketch out the detail of causal dispositionalism through the way in which causes are commonly modelled. This will have the two-fold effect of i) expressing details of the theory, and ii) introducing a novel approach to modelling causes. §5.2 now presents causal dispositionalism firsty through a brief review of traditional modelling (neuron models) that will further highlight the key characteristics and limitations of the traditional Humean theory. Then an introduction to modelling causes through vectors will provide the necessary backdrop by which development of causal dispositionalism towards EBM can begin.

5.2. Modelling causal theories

One critical feature of causal dispositionalism that advances dispositionalism from existing causal theories is in the way in which causes are modelled. Again, this is worth highlighting at this point as it will shape the way some of the approaches towards satisfying the desiderata are taken. Further, I see the difference between *traditional* and

causal dispositional modelling as an explanatory visualisation of the shift between Humean thinking and the way by which causal dispositionalism would like to represent the causal world.

5.2.1. Neuron models

Conventionally, causes are modelled as neurons, for example Figures 4 - 10 (adapted from Mumford and Anjum (2011b:20-22). This works well for modelling a world of discrete events. Figure 4 is the simplest example of neuron modelling. It shows two nodes representing relata - for example, events - in this case, *a* and *b*. The nodes are shaded, which indicates their occurrence. The causal connection[90] is represented by the arrow. If both nodes are shaded, then the connection can be considered as *stimulatory.*

Figure 4: The simplest example of a neuron graph for causation. If one event *a* occurs, and it is causally connected to another event *b*, then b must also occur.

Further, the 'firing' of *b* could in turn stimulate another event, *E*, depicting a causal chain (Figure 5).

[90] It is important to note that neuron models are used to express various ideas of causation, so 'causal connection' may mean different things to different people.

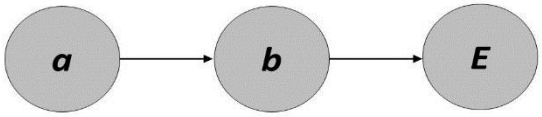

Figure 5: A simple causal chain. *a* could explain *E* through a specific line of causal connections, which in this example goes via *b*.

Neuron modelling can be developed in an attempt to represent causal complexity. For example, Figures 6 - 7. Figure 6 demonstrates a case of prevention modelled with neurons. *b* is an inhibitor of *E* (the arrow end is a large dot), thus *E* does not occur (unshaded). *a* is still represented as an active event with a causal connection to *E*. Figure 7 illustrates a problem case of pre-emption[91] modelled with neurons. Both *a* and *b* are causes of *E*.

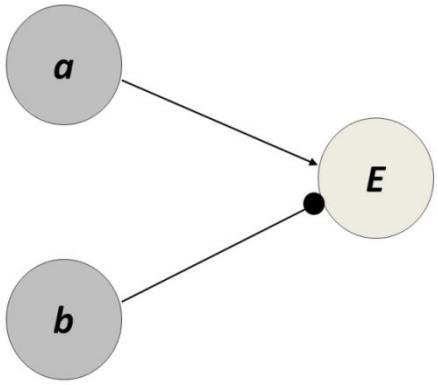

Figure 6: Prevention: *b* is an inhibitor that prevents *a* from causing *E* (now unshaded).

[91] Pre-emption: "*One of the two potential causes did cause the effect, the other one did not. Call the one that did a* ***pre-empting*** *cause of the effect; call the other one a* ***pre-empted*** *alternative, or backup*"[original emphasis] (Lewis, 2000:182)

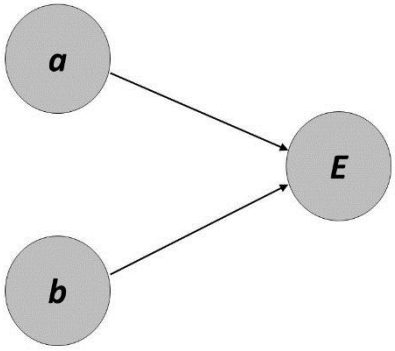

Figure 7: Pre-emption: both *a* and *b* are a cause of *E*.

Relationships between events that have multiple and related causal roles may also be depicted by neuron modelling. Figure 8 demonstrates that both *a* and *b* are causes of *E*, but *a* can also prevent *b*, so also prevents *E*. For example: *a* = contraceptive pill, *b* = pregnancy, *E* = thrombosis. The contraceptive pill prevents pregnancy that is a cause of thrombosis, but the contraceptive pill itself is also a cause of thrombosis. In this case, the contraceptive pill is both a cause and preventer of thrombosis.

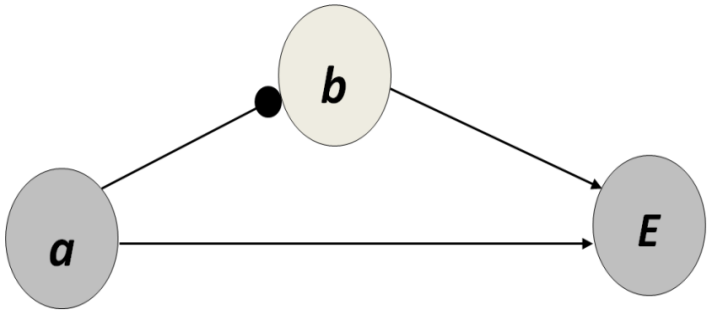

Figure 8: Multiple and related causal roles of *a* and *b*. *a* is both a cause and inhibitor of *E*.

Neuron modelling has been utilised in specific graphical theories of causation that are underpinned by mathematical expressions of causality. The most commonly referred to of these is perhaps Judea Pearl's use of *directed acyclic graphs* (DAG) as an expression of a "structural equation model" for causality[92]. Here is a brief example of how a causal account represented mathematically can be expressed graphically with neuron modelling. In this case, the causal account is counterfactuals. Figure 9 represents a counterfactual problem with neuron modelling in the form of directed acyclic graphs based on a structural equation mathematical expression of a counterfactually-founded case of late pre-emption: $a = 1$; $b = 1$; $b = E$; $e = d + \sim b$; $E = b \vee d$

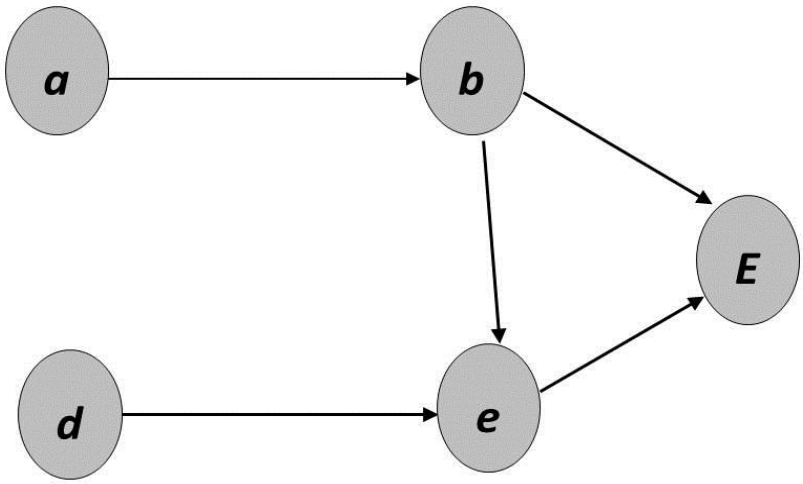

Figure 9: Counterfactual situation of late pre-emption. A graphical representation of a structural equation mathematical expression.

[92] DAGs graphically represent non-parametric structural equation models, synthesised and generalised to develop powerful graphical syntax for causal inference (Pearl, 2000).

This graph tells us that *E* is a function of *b* and *e*, that *e* is a function of *d* and *b*, and that *b* is a function of *a*. In this sense, the graph is informative about counterfactually complex causal relationships.

In summary, it seems that graphical representations of causal theory using neuron modelling allow informative, visual conveyance of, at least, causal chains, prevention, pre-emption, and counterfactuals. The reason for presenting these examples of neuron modelling for causation in this section is simply to prepare some ground that will serve to first provide a justification for an alternative modelling approach by allowing a brief commentary on the limitations of neuron modelling. Second, these models can highlight in a visual way some critical characteristic differences between traditional accounts of causation and a dispositional account. This, I am hoping, will allow a clearer initial appreciation of what causal dispositionalism entails.

5.2.2. Vectors: an alternative model for causal dispositionalism

First then, why not continue to model a dispositions account of causation with neuron graphs? Some have tried. Figure 10 is adapted from Hiddleston (2005)[93].

[93] Hiddleston provides a 'work-up' of models to represent a causal powers theory from Cheng (1997). My interpretation (Figure 10) is adapted from Hiddleston for simplicity. Some details of Cheng's powers theory are different to causal dispositionalism, however, these neuron models are attempts to represent features that are similar in most dispositions theories, which is how powers combine.

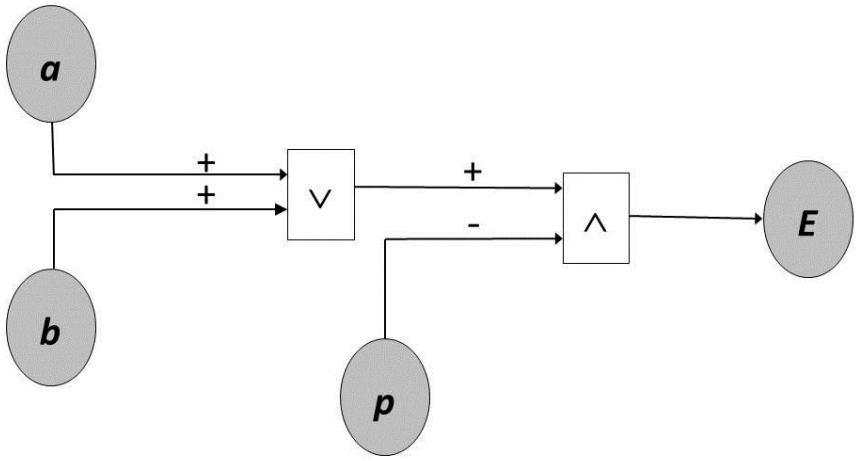

Figure 10: Modelling a dispositonal theory of causation with neuron graph.

Figure 10's attempt to capture the idea that dispositionalism is overtly concerned with how powers combine towards an effect. In this case, *a* and *b* are independent causes of *E,* for example if *E* = lung cancer, let *a* = smoking, and *b* = asbestos exposure. In this modelling, Hiddleston refers to *a* and *b* as *generative*[94] powers (+). Although disjunctive, *a* and *b* can combine probabilistically. That is, there are specific chances that *either a* or *b* produce *E.* In this model, these powers combine in the disjunction (or,∨) box to give a probabilistic output that remains generative. *p* represents a *preventative* power (-), say a genetic disposition that acts against the development of lung cancer. The generative and preventative powers combine in the conjunction (and, ∧) box to give a resultant output to the chance of *E* occurring. Whether or not the resultant output to *E* is generative or preventative is dependent on known probabilities attached

[94] This is what causal dispositionalism calls *additive*.

to each node. This example seems, at some level, to represent what it sets out to. There are however some limitations in neuron modelling, especially when representation of the real essence of causal dispositionalism is intended.

It is clear that neuron modelling relates to a Humean view of causation. This makes it immediately problematic to use in representing non-Humean ideas of causation. The nodes give us an idea of discrete events that are related only by a representational arrow indicating direction. This set-up aligns to discrete events having some form of contiguity and temporal ordering. The very notion of there being nodes and arrows in the first place suggests that this is a representation of a causal situation that is typical of a regularly occurring sequence of events, hence the need for modelling. These models therefore contain "*certain tacit ontological commitments about the way causation works"* (Mumford and Anjum, 2011a:55).

Events *a, b, c,* and so forth are entirely self-contained and stand independent of each other but for a chance firing given particular upstream activity. Event *a* is event *a* regardless of its stimulation of a downstream event, *b*. This points again to a Humean ideal of a world of discrete events that remain *loose and separate* (Hume, 1748 EUH 8.2.58). This might satisfy a committed Humean, but is problematic for a theory of causation that seeks to offer more content on the nature of relationships between events. If these features are fundamental commitments of neuron modelling, then attempting to use neurons as a way of expressing a causal theory based on an ontology of real powers is clearly an aberrant move.

What is also problematic is that neuron modelling is overtly suggestive of necessitarianism. That is to say that the firing of one neuron *must* result

in the firing of the downstream neuron to that it bears a stimulatory connection (assuming it is a *generative*, or +ve, connection). This is problematic for both the Humean and the non-Humean. For the Humean, it should be satisfactory to have discrete events related only by contingency, yet the model supports a feature whose existence Hume was certain did not form part of causation - necessary connections. For a non-Humean, and particularly for a dispositionalist, this raises challenges and opportunities. The challenges are presented in the suggestion that these models depict causes as both necessary and entirely sufficient for their effect. Dispositionalism responds directly to this challenge, as per below. The opportunities presented by this anomaly in the model is that a clear pathway is opened for the introduction of an alternative model that can demonstrate unambiguously how causes – for dispositionalists - should be thought of, that is as something "*weaker than pure necessity, yet stronger than pure contingency"* (Mumford and Anjum, 2011a:56).

On causal dispositionalism, a cause does not necessitate its effect but rather tends towards it. Smoking disposes to 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, that is, 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. For health care, it is intuitive from this that immediately the patient becomes of utmost importance in the causal process. This key shift, from understanding causes and effects as discrete events to understanding

causes as disposing *and only* disposing towards their effects, requires an alternative model to represent its essence. A vector model has been proposed as an alternative[95], and I will now briefly sketch out what this is and what it can help provide us with in terms of introducing a theory of causal dispositionalism.

The vector model represents the basic idea that causation is about dispositions. That is, rather than causation being something about a contingent or necessary relationship between discrete events, causation is the process of something occurring when powers are exercised. On this, causes tend, and *only* tend, towards producing their effect. The background set-up to which causal dispositionalism is committed can be represented by a quality space[96]. Figure 11 illustrates such a space within which a movement of events can occur. Causes are represented by vectors in the quality space. In this example, *a* is a power with a disposition towards B. T is a threshold beyond which dispositions are manifest. Say that A = the worsening of low back pain (LBP), B = improvement in LBP, *a* = therapeutic exercise; T is a threshold of successful management of the LBP (whatever that may be). In this example, *a* disposes towards B but the threshold is not reached.

The first key feature and conceptual difference here is obvious. If this same phenomena were to be modelled with neurons (as per Figure 12), it would present as *a* having no effect on *B*. The only way neuron modelling can represent this is to treat *a* as an inhibitory neuron. Here, *a* fires, but there is no subsequent firing of downstream neuron *b.* Given the

[95] (Mumford and Anjum, 2011b:19-46).
[96] From Lombard (1986).

assumptions of necessitation with neuron modelling, *a* is not sufficient to cause *b*. The vector model (Figure 11) shows something else though. It shows at least some movement within the quality space of a disposition (*a*) in a certain direction. This cannot be satisfactorily represented in a neuron model.

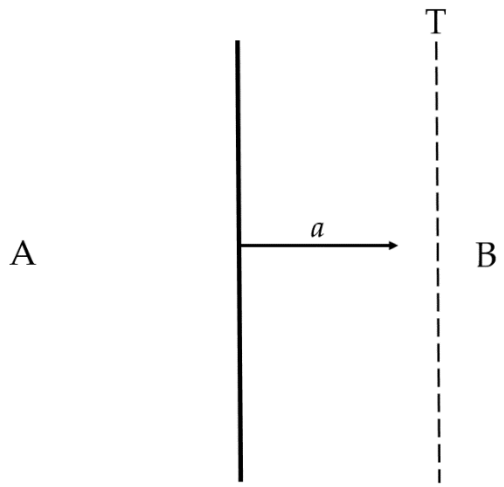

Figure 11: One dimensional quality space with a disposition *a* toward B. T is a threshold past which causes manifest.

Figure 12: *a* does not have a stimulatory connection with *b*. Therapeutic exercise does not cause improvement in low back pain.

Another anomaly of the neuron model is that *b* is represented as inactive, that is, it does in fact not exist, but is still represented, "*that is a strange idea in itself*" (*ibid*:21). Translating this back to epistemological matters, what we can say is that the neuron model represents a Humean idea of causation that, say, stems from the findings of RCTs; that is, in this example, that therapeutic exercise is not effective for LBP. It can now be appreciated that what the vector diagram offers is something more. There may be other sources of evidence that have allowed a dispositional reading of therapeutic exercise, for example, observational studies, mechanistic reasoning, therapist experience, patient report, and so forth. These collated sources might allow that there is *some* contribution of therapeutic exercise in managing LBP, but it is not singularly sufficient to produce a specific predetermined outcome, as tested in an RCT. In Humean terms, this intervention would not be considered a cause of health improvement. However, we can see through the vector model that there is something causally active about the intervention. We now need to understand more about *what* this causal property is and how dispositions such as this act out in an alternative causal theory.

From this, the vector model has two features that make it a suitable tool for representing causes: direction and intensity. Direction is binary (at least in one-dimensional spaces[97]), and intensity is represented by the length (spatial extension) of the vector arrow. Both of these features are relevant when considering a further critical feature of causal dispositionalism, the composition of powers.

[97] Multi-dimension vector models can represent causal activity in more than one direction.

On causal dispositionalism, powers combine (compose together) to tend towards a resultant effect. This again is built on an idea that vectors stand for dispositions to bring about a possible causal outcome. Figure 13 shows powers composing with a resultant effect. Say that *b* = manual therapy. Thus, the composition of therapeutic exercise and manual therapy becomes sufficient to obtain a threshold (dashed-line T) of, in this case, a predetermined therapeutic outcome. *a* and *b* compose to become a *resultant* vector, *R*.

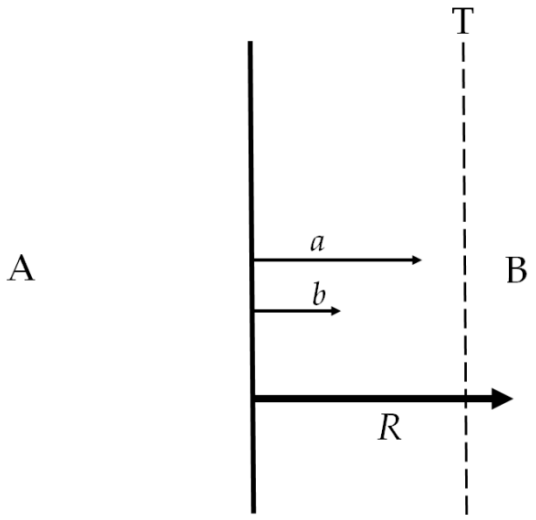

Figure 13: two powers *a* and *b* disposing towards B. *R* = resultant vector.

Again, to draw from common research methods, we might have an RCT that trials such a combination of interventions. This would tell us, in Humean terms, that therapeutic exercise plus manual therapy is effective for LBP (or rather the combined interventions and the outcome are related in terms of constant conjunction, temporality, and contiguity). What a

dispositional enquiry into this data would search for is the make-up of this composition in terms of the relative intensities of each power, and, of further importance, *how* these powers compose and what is the meaning of the powers coming together.

Dispositionalism is also concerned with the influence of powers that dispose away from an effect. Figure 14 shows how the previous situation might be influenced by a power with a disposition towards A. *c* in this case might be some biomechanical constraint on a subject's daily activity, for example, sitting for long periods. So, although that patient may be doing relevant therapeutic exercise, and receiving manual therapy, that they sit all day at a computer will influence the causal activity of the powers disposing towards improvement. The addition of a threshold in the *A* space represents the onset of LBP. As per known epidemiology of LBP, sitting for prolonged periods has not been identified as a cause of LBP. However, it can be seen that representing sitting dispositionally as a power in a vector model, there is at least some influence toward a causal set-up of what now seems to be growing complexity.

There is now another critical feature of a dispositions theory that vector modelling can assist in demonstrating. This has to do with the way a dispositions account of causation thinks of chance. This of course has central relevance to EBM as the background for information concerning clinical decisions is thoroughly invested in studies that use probability as their driving tool for knowledge, as detailed in *Chapter 1*.

The Humean account is explicitly committed to a specific interpretation of probability, frequentism. There are alternative views of probability of course and in *Chapter 1* conditional probability was referred to in a

Bayesian guise as a valid alternative, or at least supplement, to classic frequentist methods.

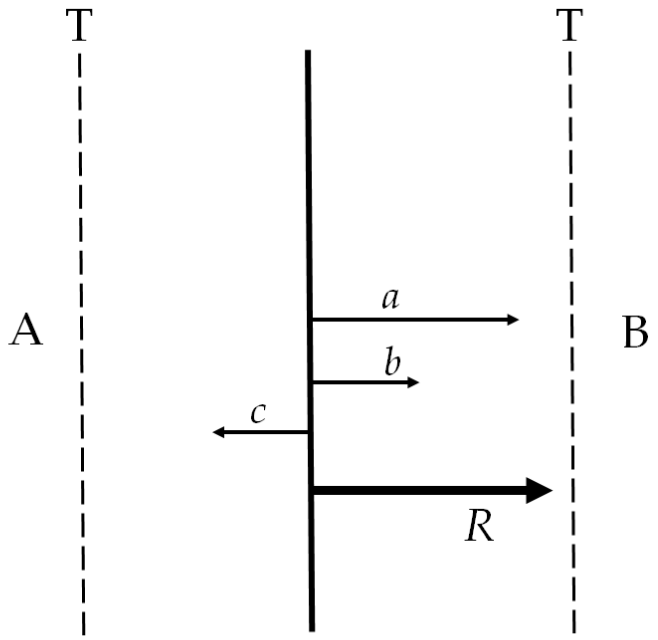

Figure 14: Composition of multiple powers. *c* disposes towards *A*. The resultant vector *R* fails to reach the therapeutic outcome threshold.

At this point, for clarity, I will highlight that although a Bayesian view seems to offer more tolerance of context and complexity (the chance of an event occurring is conditional on any number of other factors), it is still wedded to Humean ideals. This is because it still represents causation in terms of discrete events. Indeed, the Bayesian form clearly expresses this:

$$p(H/x) = p(x/H) \times (p(H)/p(x))$$

x has a chance of occurring because of *H*. *x* is still just an occurrence. This of course can be analysed away to something other than causation, that is, regularity, just as occurrences in a frequentist framework can. Dispositionalism sees these higher-level accounts of probability as unsatisfactory in terms of dealing with causation, especially complex and context-sensitive causation, that dispositions takes all causes to be. So a dispositions account has another view of probability, which in fact eventually becomes easier to understand without referring to it as a probabilistic concept at all, but something more fundamental. This is an idea of propensities. What is meant by this? Well, a simple and classic example would be a coin toss. A fair coin could land either on heads or tails. We could say there is a 50% chance of either, but where do we get that idea from? One might be from observations of repeated occurrences, as suggested in *Chapter 1*. This would be a frequentist idea of probability. But for a propensities account, we can say that the properties of the coin are the real clue as to why there is an equal chance of heads or tails, and the frequentist methods are redundant in this calculation.

This is a further insight into how causes are part of the individual process, and not reduced to external phenomena (regular occurrences). Of course, the two views might coincide, that is to say that a frequentist might observe 50 out of a 100 occurrences of heads and conclude with a "50% chance" of heads. A propensity view might conclude the same, but from understanding the coin. However, having faith on the coincidence might not be something we would like to rely on as scientists, and it might not often be the case. The contraceptive example helps again. A 1 in 1000 occurrence of venous thrombosis with oral contraceptive use, say, is uninformative for the one person who has a thrombosis. Yet with a

propensities view, we can learn something about causation here. Not just from the one person who has a thrombosis, but from cases where a thrombus does not develop. We would then have a different causal story about venous thrombosis to 'oral contraceptives do not cause thrombosis'.

There is another aspect of dispositions and propensities that reveals more still about the ontology, and this is where dispositions starts to move away from talking about probabilities at all. Dispositionalism talks about tendencies, not probabilities. But it is challenging to see how these two notions differ, even with an understanding of propensities – indeed we have already framed propensities as a view of probability. There is a difference however, and modelling can help explain it. So, a frequentist (or Humean) would say an event either occurs or it does not, to degrees of probability. Thus, their measure of causation is occurrence (or non-occurrence). In terms of neuron modelling, they would still have to commit to a binary outcome, albeit with a probabilistic caveat. This is because the Humean is constrained by the bounds of calculus in the probabilistic framework. Probability theory works on the terms that things happen somewhere between 0 and 1, but there can be nothing beyond these bounds. The chance of heads is 0.5, but if the coin was slightly weighted on one side, that chance might rise to 0.7. If there was some way of ensuring the coin could never land on tails, the chance of heads would be 1. But the chance could never be more than 1. This seems an abstract way of representing the world however[98]. Can causes be something that go beyond an abstract mathematical notion of 1? A feature of tendencies is

[98] Thank you to Stephen Mumford for explaining his thoughts on this "bounds of calculus" idea.

that they can, and an informative way to understand this is through the idea of *overdisposing*. This can be represented on a vector diagram (Figure 15) as tendency (*a*) going horizontally *beyond* the threshold, T, *over*disposing towards B. For example, *a* could represent therapeutic exercise for LBP again.

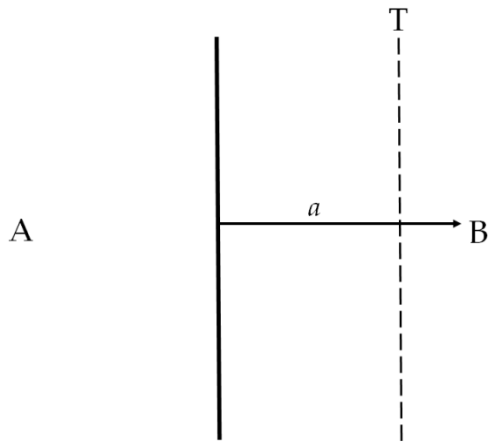

Figure 15: Overdisposing. *a* represents a tendency beyond a threshold.

The patient has suffered from particularly disabling LBP that has meant time off work and loss of earnings, something that he does not want to happen again. Following clinical advice, he understands that some basic movement exercises should help him improve. However, he is a previously fit and strong athlete and would like to ensure the best chance of recovery and prevention. He therefore chooses an exercise programme with elements of strengthening and endurance, as well as basic movement.

Conceptually, the exercises he has chosen are *overdisposing* him to recovery – he is doing *more than he needs to* in order to recover. The idea of overdisposing is not being presented here as some sort of causal tool that

we should aim to utilise in aspects of life, in this case health – although there may be times when this is desired, being over cautious with the management of critical and infectious diseases, say. In fact, in life, we might want to mainly seek to avoid overdisposing as it seems inefficient. Rather, the function of understanding overdisposing is to get a little closer to what dispositions see the nature of causes being. If a cause can go beyond the calculus bounds of classic probability, then what does this mean about causes in general? Are causes anything at all to do with probability? Dispositional tendencies and probability might be coincidentally related, but tendencies offer something more fundamental to the causal story. They are the substance of causation rather than a symptomatic feature of it.

To sum up this introduction to dispositions by demonstration of vector modelling, I see this difference in the visual representation of what a cause may be as something that characterises the key differentials between the traditional Humean account, and that proposed by an account of causation based on an ontology of powers. That is, for clarity, the traditional account would consider an event as a cause if, together with its effect, it aligned to Hume's constituents for a regularities view of causation that *c* causes *e iff* a) *c* is spatiotemporally contiguous to *e*, b) *e* succeeds *c* in time, and c) all events of type *C* are constantly conjoined with all events of type *E*. If this is the case, then neuron modelling will show node *e* as active, that is *e* and *c* share a stimulatory connection. If these conditions fail to be met, then there will be no stimulatory connection between events. Vector modelling is able to represent an event as causally relevant, however, even if the event does not achieve a resultant threshold (comparable to an active neuron). Thus, the ontology underpinning the vector model must consider causal events

as something quantitatively and qualitatively different to the way a traditional account does.

What is critical here is that on the Humean account, causation reduces to non-causal facts. The three constituent parts of Humean causation are not causal facts in themselves, they are features of observed correlations.

At this point I do not think it is necessary to use modelling further in order to express additional features of causal dispositionalism. The general picture is emerging, and we now have a sense of what an ontology of causal powers in terms of causal dispositionalism might look like. During PART 2, the features of causal dispositionalism needed to respond to desiderata for a reconceptualisation of causation will be focused on and drawn out in more detail as necessary. For now, we can bring to a close this introductory section on causal dispositionalism by very briefly describing three further features and views of causal dispositionalism that will form part of the application of the theory in PART 2. For now, we simply need to be aware of the dispositionalist stance on causal primacy, complexity and context-sensitivity, and how a dispositionalist might begin to think about a problem of induction – something central to this thesis.

Causal primacy: Causal dispositionalism takes causation to be a primitive and singular matter (Mumford and Anjum, 2011b). It is primitive in the sense that causation cannot be reduced to non-causal facts, such as regularity or counterfactual dependence. The present Humean account of causation in EBM, by self-admission, does not talk about causation in itself. 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.

Complexity and context-sensitivity: 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, for example, complex regression analysis of multiple variables, sensitivity analysis, randomisation producing homogeneity in unknown confounders, *et cetera*. 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 that may be understood from single instances.

Induction: On causal dispositionalism, because causation involves tendencies towards an outcome, rather than a guarantee of an outcome, the traditional problem of induction dissolves. The problem of induction concerns how we can know from past regularities that future cases are guaranteed to be the same. But if we understand causation in dispositional terms then there should be no rational grounds to make that inference. It is always possible that the disposition does not manifest in some future case.

5.3. Conclusion

The purpose of this chapter was to begin the move towards reconceptualising the notion of causation in EBM. The starting point of this chapter was at the conclusion of PART 1 of this thesis. This represented a position that has been proposed - that given the structure, history, process, narrative, and logic of EBM, the account of what EBM means by causation is philosophically aligned to a Humean account of causation. In sum, this means that causation is a matter of regularity, which can be quantified statistically. Underpinning this is a notion of probability related to a theory of frequentism. For EBM then, causation is constituted by discrete events that are spatiotemporally contiguous, have temporal priority, and are constantly conjoined. That EBM prioritises methods that rely on randomised and controlled groupings for counterfactually-grounded comparisons of outcomes does not affect the underlying account of causation. Causation exists in the regularities found within observed groups. What the counterfactual conditions do add to the Humean causal story is a layer of rational belief in what is being observed. The philosophy of the scientific activity remains within groups.

This background has allowed commentary towards how this account of causation relates to the real world intentions of the holistic EBM framework, represented by the central and canonical claims proposed in PART 1. It has been argued that it is because of the way EBM has shaped its idea of causation, that in fact the clinical and political intentions of EBM cannot be readily satisfied. The causation obtained through prioritised research methods, acting as evidential elements, is not what is meant by

causation at a clinical or political level. Person centred medicine has acted as an example framework for demonstrating this.

The core challenge of this chapter was to introduce an alternative theory of causation that has an intuitive appeal to address the exposed limitations of the Humean account. This is a theory of causal dispositionalism. The theory is developed and exposed to critical analysis in *Chapters 6* and *7*. This present chapter presented key characteristic differences between a Humean account and a dispositionalists understating of causation through the means of visual modelling. Traditionally, and conventionally, neuron modelling is used to represent causal theory. This is distinctively Humean and so was used to demonstrate a Humean world of discrete events, and the key limitations within this – particularly necessitation. Although neuron modelling has been used to try and represent complex causal networks, and even dispositional accounts of causation, it fails because, once again, it works from an *a priori* Humean commitment. To begin to understand non-Humean ideas of causation, a different approach to modelling is required. Vector models have been proposed to provide a richer and progressive understanding of what causal dispositionalism means for causation. Brief examples of how a dispositional account of causation might progressively work towards a causal account were presented, namely causal primacy, the problem of induction, and complexity.

In summary, this chapter has shaped the way for a critical and detailed proposal of how causal dispositionalism might be a relevant theory of causation for EBM, meaning that it could better support the central and canonical claims of EBM.

Chapter 6: Causal Content and a Viable Epistemology: Desiderata 1 & 2

6.1. Introduction

The broad context of this chapter is still of two operational frameworks firmly embedded in health care: evidential categorisation of research methods, and the wider context of EBM. In line with EBM's claims, clinical decision-making is central to the whole process of the framework. In this sense, relevant causal knowledge relates to inferences about expected results of treatments. This knowledge should then consist of an understanding of the sorts of causal claims obtained by specific sources of evidence, and the inferences they do or do not entail. It has been a central feature of this thesis so far that the pathway from population study to clinical decision is not straight forward. In part, this thesis works on an idea that causally relevant detail is held in the complexity of multiple factors that form part of the health care process, for example disease, environment, and so forth, and also within the context in which causal inferences are intended. As such, a philosophical account of causation would need to relate to and illuminate the assumptions needed to justify and facilitate the ideas of causal content and causal inferences at play. As detailed in the previous chapter, it is these sorts of concerns that have

given rise to specific desiderata. This chapter attends specifically to concerns surrounding causal content of methods and what we can read from such methods. To do this, the chapter addresses the first two stated desiderata in turn:

> *D1: Explain the causal role of content from particular research methods.*
> *D2: Motivate a viable epistemology.*

Before setting to on this task, §6.2 provides a 'work-up' to further understand the desired shape of a causal theory. The chapter concludes with comments on how a dispositions account of causation is able to respond to these two desiderata with some promise. This is primarily due to the idea that dispositions take causes to be primitive and real features of the world. As such, causal content of methods is readily visible, and the ontological stability facilities a multi-method epistemological framework, contrary to commentaries from the traditional stance.

6.2. Shaping a theory of causation

A philosophical account of causation that aspires to have relevance for and impact on EBM should answer to the desiderata set. In the words of others, philosophical accounts of causation are pertinent to EBM when they help us understand, evaluate and optimise the role of causal knowledge in inferences from evidence to clinical decisions (Strand and Parkkinen, 2014).

In contrast to others however (for example Howick, Strand and Parkkinen), it is taken here that a grasp of the ontological issue of what causation *is* is a necessary component of a full understanding of the philosophy of health science and practice. As suggested as early as in the Introduction to this thesis, it seems that the strongest argument against disputing ontological arguments is that it is simply *not* necessary in order to develop a philosophical appreciation of causation in EBM. This is certainly the stance of Strand and Parkkinen (2014, 2015). The argument is premised on the idea that a relevant account of causation for EBM is sufficient if it is, in essence, able to "*shed light on epistemological and inferential aspects of causation*" (Strand and Parkkinen, 2015:2). For proponents of this stance, critically assessing epistemological matters alone is sufficient. However, once again, this is strikingly limited by the epistemological set-up. Strand and Parkkinen make the case that the sorts of things an ontological enquiry is concerned with can be addressed without appeal to fundamental ontology. For example, causal relations, manipulation/control of effects via causes, context-sensitivity of causal relations, fallibility of assumptions, causes combining, *et cetera*. This is, however, a self-limiting process. In this argument there is an *a priori* assumption of a Humean understanding of causation. So when Strand and Parkkinen, for example, say something like "*The crucial*[99] *point, however, is that we do not need to settle this philosophical* [ontological] *issue in order to understand the complexities involved in causal epistemology and inference in EBM"* (*ibid*), what they mean is that the idea of causation is already defined by the epistemology. Indeed, "*causal relations give support to*

[99] It is not at all clear in the argument to see why this point is crucial.

counterfactual claims" (*ibid*). These causal relations themselves have been established through counterfactual conditions, so how can they do anything else? So, despite their insistence that "*EBM should not get entangled in ontological disputes but focus on the epistemological and inferential aspects of causation relevant for clinical practice.*"(*ibid*), it is clear that these proponents *are already* entangled in ontological disputes. It is just that their ontology is being read from their epistemology, and as such any progress in a philosophy of science in EBM is limited by its own science. I argue against this and propose that in order to systematise the best possible evidence for causation and then infer to clinical decisions, it is the very nature of causation itself that should necessarily be re-examined. It is the view of the nature of causation that determines what can be taken to be its evidence.

If one takes a cause to be a difference-maker, for example, then RCTs constitute good evidence of a cause and inform clinical decisions. But a dispositional theory supposes a cause is not simply a difference-maker. That, in turn, affects how we understand the importance of, say, RCTs. It is taken that ontological considerations about the nature of causation can guide our methodology and epistemology in the right direction. This chapter aims to enhance this dimension of the thesis by responding directly to the first two desiderata set out above. Consideration of these two points will help not only the development of the relationship between a discipline's ontology and epistemology, but also serve to enrich the understanding of how a reconceptualised theory of causation might influence our interpretation of causal content from research methods used within a scientific activity.

6.3. Desideratum 1: Explain the causal role of content from particular research methods

A Humean account does indeed go some way to providing explanation for the role of causal knowledge (content) from particular research methods, and this is essentially what has been examined thus far in the thesis. However, reframing the Humean argument for the purpose of this desideratum is a useful exercise at this juncture. The case for a Humean account of causation with regards to its explanatory role is fundamentally based on its commitment to a difference-making account, manifested through the notions of regularity, and perhaps more obviously, counterfactual dependency. The argument trades exclusively on this difference-making notion, which immediately points towards its ontological interests. This, indeed, has already been attended to. There is a clinical appeal to this, as clinical decision-making is centred on choice of therapeutic interventions that are judged to make the biggest positive difference in health status[100]. However, some focused reappraisal is informative.

For difference-making accounts, causation is analysed in terms of the dependency relations resulting from particular research methods. The meaning of a causal claim is therefore written by hypothetical interventions such that *A is a cause of B iff there is a possible intervention on A that would lead to a change in B* (Strand and Parkkinen, 2014:982).

[100] If that is the requirement of the decision. Of course, I am simplifying the notion here to draw out the philosophical concern. Decision-making is also concerned with multiple other factors such as cost, as already discussed.

This looks weak as an analysis because (among other reasons) the notion of *leading to* that is invoked itself looks causal, hence assuming the notion itself is meant to be analysed, and this is problematic. To analyse causation into something else – in this case difference-making under possible intervention - is very difficult, and does not have an intuitive appeal as a theory of causation - it is most likely a theory of something else. It seems however, that this is the essence of explanation of causal knowledge from a Humean account.

Critically, the explanatory framework at play here relies on an interventionist theory that sees causation as what is added to a situation that interferes with and changes the outcome. An interventionist theory is, of course, one of counterfactuals[101]. As such, it is exposed to the same problems as those highlighted for counterfactuals. For these reasons at least, although a seemingly fundamental characteristic of a Humean account of causation on EBM, a typically interventionist theory does not sufficiently provide additional support for a thorough appreciation of what a cause might be, or what sufficient explanation can be provided for causal knowledge, even at some semantic level.

There are some further problems with this for the dispositionalist. If intervention counts as causation, then no causation is assumed to be happening before the intervention. 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. It assumes then that the rest of the system was not already doing its causal work before the

[101] For example, Reutlinger (2012) makes the claim 'there is a possible intervention' to have a clear relation to possible worlds semantics, that is, there is a possible intervention "$I = i$ on X" which can be true *iff* $I = i$ is an intervention on X in at least one possible world.

intervention. Also, it is not clear how an interventionist account deals with subtractive cases. For example, the reason for having a headache is that adequate water was not drunk. Furthermore, while most causes do make a difference, not all do - for example, not in cases where effects are overdetermined by more than one sufficient cause.

Dispositions, however, can relate to an interventionist theory 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.

Given the above limitations of the Humean attempt to provide sufficient explanation of causal knowledge content, there is at least some conceptual gap between our notions of *cause* and *difference-maker*.

To look a little closer now at what a regularities account contributes to explaining causal knowledge. There are two counter-examples for regularity 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, for example, water is H_2O, humans are mortal. If causation is equated with regularity then too much comes out as causal.

Dispositionalism relates to regularities because there is a real causal power that tends towards the effect. This tendency might be strong, that 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[102]. 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, but when taken in combination tend towards raising blood pressure[103]. Conversely however, causation is not read directly from the correlation, and as such correlation itself is neither necessary nor sufficient for causation.

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, and so forth, 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

[102] Necessity is addressed specifically in §7.3.
[103] Example from Mumford and Anjum (2011b:91).

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 Humean. 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 (as first suggested in *Chapter 2*). 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 and so forth, 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[104]. This would mean however that birth is a cause of death, and having a back is a cause of low back pain - that is the counterfactual condition in each of these examples demonstrates that if you had not been born, you would not have died; if you did not have a back, you would not have low back pain. Further, 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 an 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 - that is: $(C1 \rightarrow E) = (C2 \rightarrow E)$. However, neither $C1$ nor $C2$ can be counterfactually defended. There are seemingly intuitive responses to this in the context of RCTs: first, conduct separate trials for $C1$ and $C2$, both against another control group (time or placebo). Let us say that in each of these separate trials, both $C1$ and $C2$ outperform their control. Thus, in each separate trial, both $C1$ and $C2$ have a counterfactual defence and causal claims may be drawn such that in trial 1, $C1$ works, and in trial 2, $C2$ works. However, because both $C1$ and $C2$ have a similar causal effect on E, it is still not clear what is the true cause of E, and the original problem of overdetermination remains.

[104] This thought is attended to in more detail in below, and in *Chapter 7*. Briefly though, although Hume denied necessary connection as being part of causation, what is meant here is that an effect will necessarily (to a probabilistic level) happen if the constituents of causation are in place.

Further still, known challenges surrounding assumptions of conditionality and biconditionality compound the stability of causal readings from RCTs[105]. For conditionals, there is a Humean intuition that when a causal relationship exists between *C* and *E*, so does the conditional $C \rightarrow E$. Thus *C* is a necessary condition for *E*, and $C \rightarrow E$ is a necessary condition of a causal relationship between *C* and *E*. How, then, are cases of $C \rightarrow \neg E$ accounted for? Rather than a problem, we can look at this as something characteristic of causation. For biconditionals we cannot determine whether the causal story is such that (*C* caused *E*) *iff* (*C* counterfactually depends on *E*) or whether (*C* counterfactually depends on *E*) *iff* (*C* caused *E*).

Do counterfactually-derived causal claims infer necessity? There seems to be a deep claim to necessity hidden inside the probabilistic 'get-out clause' related to counterfactually dependent causal claims. This serves as a 'selling feature' of RCTs, and their role within EBM, but it is also a problem. That all deductively sound (counterfactually dependent) observations of $C \rightarrow E$ in a series of trials should be a valid path to a general causal truth of the form $\forall x(Cx \rightarrow Ex)$ would justify, for example, the implementation of clinical guidelines and policy, and address the central and canonical claims of EBM. In this sense then, EBM assumes necessity. If necessity of this sort were to be accepted, then inductive inferences as sketched above would be supported. This of course is the core concern of this thesis and so far, many dimensions of this issue have been considered. Framing this problem in terms of a traditional problem of necessity will

[105] *Conditionals* and *biconditionals* simply as per classic (propositional) logic. *Conditionals*: "if *P* then *Q*" ($P \rightarrow Q$). *Biconditionals*: "*P* if and only if *Q*" ($P \leftrightarrow Q$), or (*P iff Q*).

again help to provide a route for progress with the causal ontology. The heuristic basis of counterfactually dependent RCTs does not seem secure. Again, it would look like RCT outcomes do say something evidential about causation, but this is not constitutive of the causation at work.

Dispositionalism relates to counterfactuals in so much as counterfactual truths have dispositions as their truthmakers. Thus, counterfactually derived outcomes (for example, 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 is 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, 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 does not, is not merely a statistical nor probabilistic fact. For each individual who smokes, the propensity towards cancer will be different. Someone who smokes and has genetic predispositions 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. It is a critical feature of a dispositional account of causation that the underpinning notion of probability is related to a propensity theory, rather than one of frequentism (as per §5.2.2).

To sum up the response to D1: It has been suggested that a traditional Humean account of causation offers some explanation as to how causal claims are developed from research methods. Humeans are able to discuss such claims in terms of either frequencies of occurrence of events, or the degree of differences between two frequencies, or both. Proponents of the Humean account are satisfied that this sufficiently explains the causal role of research content, specifically highlighting that this avoids unnecessary matters of ontology. The dispositionalist response is straightforward: the content that is being referred to here is not of causation, but of something else. The essence of causation has not been reached, and as such any explanation related to causation cannot be given. The truthmaker of causation within traditional accounts is removed from where causation itself is most likely to be found. What dispositionalism offers is a view that sees causation within the core of the content itself. Changes are seen within groups, and these changes occur as a result of multiple events tending towards and away from effects. Whereas Humeans consider single and necessary causes by proxy of frequently occurring observed events, dispositionalists see various causal factors that may or may not manifest in

an effect. The causal role of these events for dispositionalism is the notion of how they manifest and how they may tend towards and away from anticipated thresholds. Dispositionalists are unsatisfied with causal explanations that relate to frequentist interpretations of probability, as probability should be thought of in relation to the propensities held by causal factors.

The response to D1 has allowed some appreciation of the way that causal content from research methods might be thought of in relation to different ideas about causation. A criticism of a dispositions ontology however is that it fails to satisfy requirements of a theory that desire to understand the way things can be known. I now argue against this, and propose that a dispositions theory of causation determines the way knowledge from research methods is thought of, and therefore a dispositional ontology for causation is able to satisfactorily motivate and account for an epistemology of causation.

6.4. Desideratum 2: Motivate a viable epistemology

Having considered what an ontological background might look like 'epistemology down', the concern is now to develop an ontology in its own right and then examine how causal knowledge might be taken from this. The undertone throughout this thesis has concerned the relationship between ontological and epistemological matters. There have been attempts to argue that not only are these two dimensions necessary in providing a complete philosophical account of scientific activity, but that ontological matters should be the starting point of such an enquiry. This is

in contrast to proponents of EBM who have suggested that that commentators on the philosophy of EBM "*should not get entangled in ontological aspects of causation*" (Strand and Parkkinen, 2014:981). Indeed, the textual and intellectual accounts of EBM throughout its history have avoided such abstract matters. Despite this, and having confidence in the argument concerning the importance of a causal ontology in EBM, I have so far attempted to draw an ontological account of causation out of the epistemological and pragmatic structuring of EBM's scientific activity. This, I claim, has served a purpose in exposing what EBM might best mean by causation, but it is not ideal. Rather, it is preferable for an ontology to inform epistemological thought and practice. There is, of course, the opposite view of the EBM methodologists, such that an ontology should have no business in trying to inform an epistemology. Indeed, from Williamson:

> *"Some metaphysicians might advocate the view that it* ***is*** *enough to give a coherent theory of the nature of causality. Indeed, one might argue that it is preferable to remain neutral regarding methods for causal learning"* [original emphasis] (Williamson, 2006:263)

However, Williamson does talk of the potential errors of divorcing metaphysics from practice, least alone the impact of the utility of metaphysics (*ibid*). More relevant than this is that to create a relationship between the metaphysical understanding of causation and its methods for causal learning allows a way for judgement on the 'best-fit' theory; hence this desiderata. Though causal methods might be of type *x*, there is a risk

of under-determination given the countless causal theories underpinning the reading from such methods. Thus, it seems like the role of a theory of causation is not merely to say 'causation is *this*', but also to offer a way to learn about causal facts in the most practical of senses. This is the stance that I take: a theory of causation should have something substantial to say how about causal relationships can be known. To obtain data from research methods is only one part of understating causal associations in healthcare. It is important for us to understand that when we use certain methods, we are in fact learning about a particular type of causation - without an ontology, the data is vacuous.

Having helped us reach this point, Williamson now throws out a challenge to a dispositional ontology. He claims that a dispositionalist account[106] of causation is unsuccessful in linking the epistemology of causality to its metaphysic. This is to set-up the argument for a theory of *epistemic causality*[107] as being a 'better-fit' theory of causation of course. Now to take-up Williamson's challenge.

Williamson's argument goes something like this: Cartwright argues that capacities (powers) are required to understand the model building and experimental methods used by scientists in pursuit of causal claims. This is on the commitment to the reality of such capacities. However, as models and experimental set-ups are representational devices within scientific

[106] Williamson uses Cartwright's dispositional account of causality (found for example within Cartwright (1983) and Cartwright (1989) to demonstrate that such a metaphysic cannot do the job of relating sufficiently well to an epistemology. Although there are characteristic differences between Cartwright's account on that of causal dispositionalism, for the purpose of this argument they are sufficiently similar in that they are both realists about causal powers (capacities).

[107] As attended to in §4.2.2.

activity, they do not need to correspond to reality "*to permit successful inferences*" (Williamson, 2006:267).

Cartwright argues that the demarcation between the representational and the things we accept as real is not epistemologically defined. That is, we learn about the two things in the same way, the reality of all things is to be either accepted or rejected. Williamson thinks this is some sort of backward reasoning, claiming that the reality of some things is unproblematic - using Williamson's examples, chairs, tables, *et cetera*. Other things, however, *are* problematic, such as causality. Williamson therefore sees the demarcation between representational and real as ontological, not epistemological. Being problematic or not seems to serve as an ontological tool for demarcation for Williamson, and as such, Cartwright's defence is unstable.

Williamson's alternative is to present a theory of epistemic causality as one that does not commit to the reality of causation at all, and so its relationship to epistemological matters is straightforward. According to this theory, a causal belief (taken from experimental data, say) is a rational one - a *"transition of the imagination"* (*ibid*:275) - about the epistemic qualities of the data that are a mere representation of some other notion. It is not a belief about that notion itself. The beliefs are rationalised by patterns of predictability, *et cetera*. So the relationships that are learnt about through the process of science are not of 'some other notion'; rather they are of an epistemic causality. Williamson thus avoids the *"fallacious projection of causality onto reality"* (*ibid*:275) and in doing so side-steps the critical problems faced by a theory that commits to the reality of causes.

The dispositionalist account has no problem with causal realism, and takes this as one of its central tenets *"causation is a feature of the world and*

not just our thinking about it" (Mumford and Anjum, 2011b:16). Not only does causal dispositionalism not consider its commitment to the reality of causes as a problem, it sees it as the key to a robust epistemological reframing of scientific inquiry. In sum, the argument between Williamson and Cartwright above reduces down to a standard discourse on the relevance of ontology, and (if an ontology is of relevance) a call for what a dispositions account can offer. With these matters in mind, this chapter will draw to a close by presenting a case for how a theory of causation based on dispositions ontology can satisfactorily motivate a convincing epistemological framework for EBM, contrary to Williamson's stance.

We will see in the following chapter that the modality of dispositionalism is a unique one - a *sui generis* - that falls somewhere between necessity and contingency. The modality is also monistic and primitive. This means that causation is one thing, and cannot be analysed into anything else. This is in contrast to the position of Williamson, among others, who commit to ideas of causal pluralism. Within the pluralist view is the notion that causation can be many things. Dispositionalism is not sympathetic to this view at all, and I will return to why this is so below. For now though, it is worth considering the conventional positioning of pluralism *vs* monism.

Williamson, for example, uses a pluralist theory as a background to his eventual epistemic account of causality (that is, the RWT (Williamson (2007a)). What this means is that the different methods used in science identify different causal notions. For example, Ned Hall (Hall, 2004) talks about how difference-making approaches (RCTs in our case) relate to a counterfactual theory of causation, whereas mechanistic approaches (say, laboratory studies) can account for more fundamental ideas of causation,

like processes. This is justified by an assumption that different causes do different things. Not all causes make a difference, *et cetera*. So each approach does a specific job in searching for a specific type of causation, but neither can do the job of the other. This motivates pluralistic accounts to conclude that causation must be more than one thing.

This type of argument usually arises as a result of highlighting limitations of causal monism, and the argument seems simple. Conventional monistic accounts would allude to the idea that we have a range of causal indicators, say observations, experiments, trials, mechanisms, guesses, *et cetera*. Each of these indicators would relate to a single causal theory, trials might relate to a difference-making account, for example. But, whereas the pluralist would now say causation must be more than one thing, the monist would say it is one thing or the other, but not more than one thing. The pluralist is then in a good position to counterclaim this and refer to the complexity of the world and 'real facts' that show that causation arises from more than one indicator. For example, if a monistic theory is committed to, say, difference-making, then we would have trouble reconciling a causal claim of smoking causes cancer from observational studies. This inability to explain how other indicators can also count as evidence presents an apparent, and possibly critical, challenge to monistic theories that have led pluralists to question the epistemological viability of the position (Williamson, 2006:70).

It should be clear now that the Humean interpretation of EBM represents an essentially monistic account of causation, favouring a regularities theory and failing to account for causal claims arising from other research or clinical methods. However, I stated above that part of the dispositions modality is causal monism, so how can we commit to the

idea that a cause is a single thing (so avoiding a pluralist theory), yet offer opportunities for epistemological viability given the case against monism?

But first, why not just accept pluralism? Then, in terms of epistemology, we can account for claims arising from different methods, and this would seem to address the problems identified with the Humean account. There may be some progress to be made in being pluralist, and this seems the favoured stance within the philosophy of EBM. A contemporaneous example is an advocation of methodology of causal explanatory pluralism in the diagnostic workup and clinical management of medically unexplained physical symptoms (Cournoyea and Kennedy (2014) utilising a pluralist theory from De Vreese *et al*. (2010)). The grounds on which pluralism is favoured in this example are indeed appealing: that the best explanation depends on the question, it contextually privileges one strategy (method) over another, it avoids reductivism, *et cetera*. However, and this is the key, these authors – and pluralists in general - make an explicit reference here, as with other pluralists, that the position does not attempt to make metaphysical claims about its theory or its subject matter, that is, causation. Causation can be analysed to something other than what is epistemically evident. The Humean example: causal claims arising from trials can be analysed and reduced to something other than causation, that is two discrete events occurring one after the other. However, pluralists will say that causes cannot be analysed down to just one thing, because there is not one single thing that is found in all cases of causation. This is seen as an advantage to such theoretical positions, and reflects the background discourse between ontology and epidemiology. That is, if there are robust methods that align with a theory of causation then there is

no need to worry any further about the nature of the causation. This is also, of course, the same for the traditional monist.

So pluralism seems to have the upper hand with regards to inclusivity of methods, and appreciation of complexity and context (to a degree), but still favours an epistemologically driven reading that is analytical of causes and sees them as reducible to epistemic facts. What they see as a strength, dispositionalism sees as a downfall and an opportunity to intervene. The most obvious retort to avoiding an ontological commitment is simply to say that in order to find causation, we first need to know what it is. And this is indeed the starting point for the dispositionalist retort to the question of epistemological viability.

Within a dispositions account, the causal set up and the manifesting effects are irreducible and the causation cannot be analysed. The causation is the causal process, and cannot be anything less. This is causal primitivism - a defining modal strength of a dispositional theory of causation. So in this sense, causation is just one thing, hence dispositionalism being monistic. However this is an *ontological* monism, not an *epistemic* one. So where a traditional monist commits to a singular theory being attached to a particular method, which is problematic, dispositionalism merely states that causation is one thing and has no commitment to a singular method. It also avoids cumbersome explanations offered by integrative pluralistic views that are committed to merging different causal theories together to make sense of the world. This stance is also against pluralism on the grounds that causation is irreducible, and if it cannot be analysed at all, then it cannot be analysed into many things either. So once we have a sense of a singular notion of

causation, and once we understand that it is irreducible, we know what we are looking for: a most basic and fundamental singular thing of the world.

But there are still challenges in terms of defining an epistemological framework. Part of the dispositions ontology of course is that causes neither necessitate an effect nor are they purely contingent – causes tend towards an effect in complex and extremely context-sensitive ways. Therefore, reliance on a single method with an expectation to reliably find causation cannot be a feature of the epistemological account of causation. There must be more indicators of causation, but all pointing to the same thing. So we can have pluralism, but not epistemic pluralism. The dispositions plurality is with its methods, not with what causal theory those methods relate to. We might therefore speak of a methodological pluralism, and not causal pluralism[108].

We now need to examine the epistemic role of methods a little closer to appreciate the relationship between what dispositionalism says causation is, and what comes from scientific methods. Because causes escape analysis, we cannot even say that there are reliable markers of causation. If we could, we would say that as long as methods identify this marker, we can know causation, but that is not the case. One mistake that perhaps existing scientific theories have made is to assume that scientific methods are somehow constitutive of causation. So, for example, RCTs making causal claims and us rationalising that this means there *is* causation, rather

[108] To declare: the idea of *methodological pluralism* became much clearer to me following a talk by Stephen Mumford (Council of Allied Health Profession Research evening lecture, November 2015, London). My talk then tried to relate the idea (that was then referred to as *evidential pluralism*) to physiotherapy research. Since then, I have thought that this idea is most likely one of the key emergent directions from this thesis for future inquiry and development.

than something else like correlation or chance. We would then say that RCTs are a representational component of causation. But if causation cannot be analysed and reduced to something else, how can this be so? Further, if the given theory of causation operates in the absence of a robust ontology, then how can we even say what the causation is? One way to reconsider the information given from methods is to again think of their outcomes as symptomatic, rather than constitutive, of causation. So trials, for example, might give us a good understanding of where to look for causation, but they do not know that what they find is causation. Of course, symptoms might appear without any related phenomena, so again reliance on a single method is far from ideal. Conversely, because dispositionalism takes causes as complex, it is more likely that causes have many symptoms and so multiple methods are required to complete a scientific picture of a particular case of causation. These symptoms may relate to parts of causation such as difference-making, probability raising, mechanical process, *et cetera*. But these are not committed theories, they are just types of manifestation. For example, *X* just happened to manifest in a change in *Y*.

Accepting causation as an irreducible process casts more light on this story. If causation is something more fundamental than a series of discrete events, we in fact have more to see, and the possibility of more symptoms. This was discussed in a recent publication (Evans *et al*., 2016) where we presented a concept of causation (edging towards dispositionalism) being a process from disease through intervention to health, with common features (namely time, space, and form) transcending the whole process. The symptoms of this process are multiple, and the methods required to see them would be varied. Much causal information would come from

indicators of causation such as mechanistic pathways and patient narrative. RCTs, for example, could be sensitive to some of the causal symptoms during particular parts of the process, say, when considering intervention. But this information would only be meaningful if other parts of the process were understood through other indicators, again, say mechanisms and narrative.

So the motivation for a viable epistemology comes from dispositions' commitment to an ontology of the reality of causes, and the understanding that those causes are the most basic and fundamental features of the world. These are the very things that pluralist and epistemologically focused theories say are the reasons dispositionalism fails to account for an epistemology of causation. Although others have spoken about multiple methods, (Williamson of course, and Howick's views on mechanisms as per *Chapter 4*) they struggle to conclude with a convincing epistemology due to their Humean commitments. Framed by epistemological matters, these attempts have been instances of identifying the problems of a traditional monistic account, but trying to resolve these with either pluralistic accounts, or epistemologically driven theories. This is unsatisfactory on two counts: one that there is confusion and conflict between competing theories of causation; and two that in refusing to commit to an ontology of causation, it is not even possible to identify what the methods are searching for. A theory of dispositions has clearly defined what causation is, and is confident that a methodological pluralistic framework, whereby all methods point to the same thing, offers a satisfactory account of its causal epistemology.

6.5. Conclusion

This chapter has dealt with two of the four desiderata that were developed as a conceptual framework to inquire into the viability of a reconceptualised theory of causation, which can be relevant for EBM. A common element in the dispositionalist response across the two desiderata has been the primacy of causation in a dispositions account. Causes are assumed as fundamental and real features of the world with dispositions. This has been something that has been used in critical responses against dispositionalism. However, it has been shown here that this is a feature of the ontology in fact strengthens its candidacy as an alternative theory.

That causes are primitive and real has allowed commentary on both how causal content of methods can be explained, and how a viable epistemology can be motivated. Humeans struggle with explaining causal content because they admit to causation being nothing more than supervening phenomena in a world of discrete events. All they can say is that causation is regularity, represented through a frequentist interpretation of probability. Dispositions on the other hand take causes as real entities and so can describe and explain precisely their content. As causes can only ever tend towards an effect, dispositionalism does not have to represent causes through frequencies. Rather, a probabilistic theory based on individual propensities offers deeper explanation of the causal content.

Dispositionalism is confident that its visible ontology with its commitment to ontological monism prepares the ground well for talking about and accounting for a reconceptualised causal epistemology. Its reference to methods being symptomatic rather than constitutive of

causation facilitates a methodological pluralist stance whereby information from multiple methods and sources may reveal parts of the causal process. These sources can include indicators of causation such as mechanistic science and patient narrative. Dispositionalists do not need to worry about the cumbersome and ultimately unsuccessful reconciliation of multiple theories of causation, because causes are only one thing.

In sum, a dispositions account of causation, based on an ontology of powers, seems to be standing up well to the proposed desiderata. What follows now is a continued examination of this alternative theory, played off against its Humean counterpart. The final two desiderata relate to the problems associated with the transference of scientific data and causal knowledge from source to target. These desiderata have been developed to ensure sufficient attention is given to the individual human-centred decisions that should sit at the heart of evidence based clinical reasoning.

Chapter 7: How do Causes get to Individuals? Desiderata 3 & 4

7.1. Introduction

This chapter deals directly with the central issue of the thesis, the starting place of my original worry about EBM: that is the relationship between one source of information and its intended target. In EBM terms, the inferences from study data to clinical decision-making. The two desiderata developed to provide a framework for this discourse are:

> *D3: Account for causal processes in individual-level clinical decision-making.*
>
> *D4: Help understand and assess additional premises and assumptions needed to bridge the inferential gap between population-level evidence and clinical decisions.*

As stated earlier, D3 is an emergent call from existing analysis of the literatures and asks us to consider how causation is represented at an individual level. D4 is a direct demand from some of the most visible opponents of a dispositions account of causation and relates to the dominant question of inference. Clearly both desiderata relate to each

other, but each offer a unique opportunity to address subtly different dimensions of the inferential problem.

The broad problem highlighted can be framed practically and epidemiologically as a problem of external validity, which has already been alluded to. This thesis however is concerned with the deeper philosophical and ontological accounts of how knowledge from one source relates to its role in a spatiotemporally removed environment. This issue is one of critical concern for a theory of causation if it is to be judged as relevant for EBM. The concern relates to inferences, prediction, induction and so forth, but there also needs to be some account of the actual process of causation at its intended environment. In the case of EBM, this is the patient and the clinical context in which individual clinical decisions are made. The core concern of this thesis is the suspicion that the nature of causation found in the prioritised evidential elements is not the same causation that we seek in patients at an individual level, and this forms the backdrop to this chapter.

§7.2 deals with the third desiderata: *Account for causal processes in individual-level clinical decision-making*. In sum, there is a play-off between the Humean account that I propose can only speak to the individual level through a probabilistic translation, and a dispositions account that takes the individual case as the essence of where causation lies. A short case study of non-specific low back pain (§7.2.1) is utilised as part of the explanation for expressing the difficulties in understanding precisely where and how methods see – or do not see - causation.

§7.3 takes the fourth and final desiderata: *Help understand and assess additional premises and assumptions needed to bridge the inferential gap between population-level evidence and clinical decisions.* There is attention here to the

problem of induction. Proponents of a Humean view see the solutions coming from more robust methodologies. Their arguments against dispositionalism related to a failure for dispositions to properly account for defeasibility. There is some confusion in the Humean argument surrounding necessity, determinism, and probability. This allows them to set up a straw man. Clarity is given on these issues from a dispositionalist account, and because causes only ever tend towards an effect, necessity is never part of the causal story. As such, dispositions offers a built-in explanation to defeasibility. Further, the problem of induction is dissolved in a dispositions account because dispositions see causes as things that tend towards a manifestation, but never guarantee (even probabilistically) such.

The chapter takes issue once more with claims about the futility of an ontological enquiry, characterised again by the likes of: "*. . . an epistemology does not flow from the dispositionalist ontology*" (Strand and Parkkinen, 2014:983). Through addressing these final desideratum, it will be further demonstrated that epistemological concerns are intrinsically related to an ontological position. This chapter concludes that causal dispositionalism is able to relate well to these two final desiderata in comparisons to the traditional stance, whose only ammunition is to invest further in robust population methods and hope that the strength of these data eventually reach the individual. Dispositionalism offers something more convincing for the issue of inference in a real world defined by complexity.

7.2. Desideratum 3: Account for causal processes in individual level clinical decision-making

Given the regularities account, causation exists when we observe the occurrence of two events associated with each other, for example, smoking is associated with cancer. This is the premise for all methods based on a regularities account - that is the prioritised methods of EBM: high quality observational studies and RCTs. However, the logic of the argument is most clearly seen through a simple account of correlational associations, especially cases of weak associations where causation in a Humean sense is unsupported. Weak associations (low correlations) 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 – that is, 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, yet 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, for example, 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 – a frequentist interpretation that an individual's chance of having the event of 1 in 1000 is uninformative. However, probabilities can be related to classification of kinds[109]. 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, that is a 100% chance (as the 1 in the 1000 did), or they will not, that is a 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. We therefore seek a theory of causation that can comment on and account for individual cases and individual clinical-decisions. This should be a theory that is not reliant on the passive probabilistic translation of causation through time and space, but one that takes single, individual instances of causation as its core matter. This is the province of causal dispositionalism.

Before a dispositionalist commentary on this desideratum, there is a case from within a traditional EBM framework that so far I have (purposefully) not considered, that of the N-of-1 trial. This has

[109] Examples throughout Mellor (2005), for example.

conventionally at times, sat high on traditional evidential hierarchies[110]. Its position there is based on its ability to provide a strong counterfactual condition. N-of-1 trials are RCTs with a single subject. The conditions (interventions) are randomly allocated in temporal sequence and the individual acts as his own control. Although these are counterfactually robust, N-of-1 trials are commonly rejected in policy and clinical decision-making due to their limits of external validity, that is, the causal claim is established in one individual and therefore only generalisable to that one individual. 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 N-of-1 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. However, there does seem to be something causally appealing about such cases of singularity. In these cases, if nurtured instincts about population causality can be ignored for just a moment, something causal has definitely happened. The Humean argument fails to account for this, but I am uncertain whether such instances should be excluded from an understanding of what causation can be in terms of health effects. Singular instances such as N-of-1 studies, and every clinical encounter, should be able to offer something to a theory of causation.

[110] See Lillie *et al*. (2011) for a review of N-of-1 trials and their role in hierarchies.

So how can causal dispositionalism respond to this desideratum? First of all, causal dispositionalism takes causes to be mutually manifesting partners whose resultant effect is highly context-sensitive. The vector diagrams (§5.2.2), for example, display how causal partners relate to each other. An underpinning assumption of causal dispositionalism is that each situation in which causation occurs offers a unique set of causally relevant partners (powers). It is the composition of these partners that a dispositionalist theory of causation is interested in. That is, the resultant effect (or not) of a causal set-up is sensitive to the unique context in which possible causes exist. A regularities (and difference-making) account acknowledges that this may be the case and as such attempts to deal with the phenomenon. But it does so from afar, probabilistically. The process of randomisation, for example, aims to provide homogeneity between groups with respect to both known and unknown confounding variables. The philosophical implication here is that the purpose of randomisation is to create situations whereby the context of each individual instance within the study is as identical as possible. Good randomisation can produce groups with high degrees of homogeneity, but only in a probabilistic sense. That is, there are high levels of probability that any single instance is causally similar to another. With known confounders, this is done with statistical tests of the probability of difference between group characteristics (at baseline). With unknown confounders, it is an assumption of the process that because known confounders have 'evened out', it is *just as likely* that unknown variables will have done so also. Furthermore, the very process of statistical analysis based on *averages* of aggregated data rests on the assumption that effects are variable, even in very high levels of homogeneity. This again points to a notion that at

individual levels, there has to be something causally informative that is unique to that instance. A traditional ontology might see this as a perpetual challenge to causation. Dispositionalism however sees this as an opportunity to reach closer to understanding what causation is. It does this by accepting single instances not as a threat to causation, but rather as the starting point from which a theory of causation can be derived. As such, causal dispositionalism does not merely attempt to account for individual instances; it is embedded in the very notion.

The essence of causal dispositionalism – that causes tend - provides a backdrop for appreciating the position of individual causation. For 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, that is, 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.

For causal dispositionalism, single cases provide fundamentally important matter towards what causation is. Such instances will be referred to as *particular causal claims* from this point on. We can think of two kinds of causal claims: *general* and *particular*. Analogous to general causal claims for this thesis are, of course, claims from population studies, 'exercises help improve low back pain, in population *X*'. Particular causal

claims are related to individual cases of clinical intervention and outcome, 'patient *x* responded well to these exercises'.

Causal dispositionalism, uniquely, sees both of these kinds of claims as being important for a theory of causation. It is more common that one kind of claim is given metaphysical priority over the other. For example, those of a non-dispositional stance accept that general claims (or *universals*) are not only real, but form a central part of the scientific world. David Armstrong presents a strong view on this in his realist thesis on laws of nature, for example (Armstrong, 1983:77-110). This thesis has some appeal, as it seems to offer an encouraging non-Humean alternative to understanding the nature of causation. The difference between Armstrong and Hume is this: Hume says the world is a mosaic of discrete events conjoined only by observed association, and all else supervenes upon it. There are no laws that offer *a priori* explanations to the observed associations (no *necessary connexion*). What Armstrong offers is an account of the world that begins with accepting the existence of laws of nature. These laws are real features of the world, and are the relations between general claims. A law-like relation is of course one of necessitation[111], hence contra-Hume: "*it adds the necessity missing from the regularity theory*" (Mumford, 2004:85).

To add to a regularities theory, a new theory would have to offer something beyond how a regularities theory sees a law, which would be in the form of a universal quantification over particular cases: $\forall x(Cx \rightarrow Ex)$. This universal quantification relates to particular and not general claims,

[111] Again, this necessitation can be probabilistic. See Armstrong on nomic probabilification (Armstrong, 1978:158-9), from Mumford (2004:85). This will be considered further in §7.3.

of course. The expression is of a world of discrete events. As such it is exposed to the problems of a Humean world, as already presented. Armstrong's move to a commitment in law-like relations looks to respond to some of these problems, specifically the problems of induction and counterfactual threats: without necessity, there is no account by which $Cx_1 \rightarrow Ex_1, Cx_2 \rightarrow Ex_2, Cx_3 \rightarrow Ex_3 \ldots Cx_n \rightarrow Ex_n$ could entail $Cx_{n+1} \rightarrow Ex_{n+1}$, nor $Cx \rightarrow \neg Ex$. Necessity, however, can indeed entail $\forall x(Cx \rightarrow Ex)$, but not vice versa. Law-like relations of general claims is therefore the added interest from Armstrong's metaphysic. Mumford, however, identifies a problem with Armstrong's prioritising of general claims (Mumford, 2004:83-104). The problem is anchored, paradoxically, in how the attempted prioritising of general claims positions the role of particular claims.

The way particular claims are considered by Armstrong is by an indirect concern with the law through which particular cases instantiate the properties of the law. As a realist account, the general claims can only exist in particular instances. From such an account, this is how causation is explained: if *c* causes *e* in a particular instance, it is only because *c* and *e* fall under a general law. The problem, for Armstrong at least, is that general claims are therefore only understood through examples of their instantiations - that is, particular claims: "*Hence, we know of the nomic relation through knowing causes*" (*ibid*:86). Further, it becomes clear how the defining feature of Armstrong's theory – necessitation – is governed by particular cases. Recall that in order for progress, a law must be more than what a regularities view (if laws did exist in such a view) sees it; that being nothing more than "*mere collections of necessitation holding in the individual case"* (Armstrong, 1983:78); that is, $\forall x(Cx \rightarrow Ex)$. So Armstrong needs to add to the idea of 'necessitation' such that necessitations become something

more than mere collections. He does this by proposing that there must be some feature in each particular that defines that particular's identity. This is the crucial step in provision for an ontological ground that responds to the regularities view.

> *"For then, and only then, can we say that* ***being an*** *F necessitates* ***being a*** *G and,* ***because*** *of this, each individual F must be a G. But this is to say that the necessitation involved in a law of nature is a relation between universals"* [original emphasis] (Armstrong, 1983:78)

So again, the understanding of universals (general claims) and their relationship to laws of nature is provided through the understanding of particulars (single claims). Although a problem for universal realists, for causal dispositionalism this 'anti-dispositionalist' metaphysic in fact helps an appreciation of the value of particular causal claims: through individual cases of patient encounters we might better understand general causal claims.

Other causal theorists have provided accounts contra to the above type of projects, which are realist about universals. That is, that *general* causal claims supervene on singular instances thus giving priority to *particular* causal claims. Such a stance is again by definition anti-Humean. If Hume says – in line with population level evidence – we can only experience discrete events and not any necessary connection between them, then this leaves causation as constant conjunction, *et cetera*. However, constant conjunction "*allows no sense of causation in the single case*" (Mumford, 2009:275). Therefore, understanding causation through particular claims

cannot be something Hume had in mind. As an example, for a general claim such as 'exercise helps improve low back pain', Hume would mean that 'exercise' and 'improvement in low back pain' were two discrete events conjoined through non-causal facts such as constant conjunction, *et cetera*. To prioritise the particular, then the general claim 'exercise help improve low back pain' is considered as an ascription of capacities[112].

Causal dispositionalism is sympathetic to a singularist view as sketched out above, and takes particular causal claims (singular instances) to be where causation lies. However, the dispositionalist ontology moves quickly beyond a world of discrete events. The relata for causal relations are not discrete events or facts (for example, event *C* (exercise) and event *E* (improvement in LBP)), but the powers and properties of things (for example, the disposition of exercise and the disposition of a patient with low back pain). At the same time, dispositionalism sees general claims as having a role to play in a theory of causation, especially when particular circumstances are not yet known. General claims allow us to be "*armed for future actions*" (*ibid*:14). Once again, however, the truth of any general causal claim is substantiated by the properties or powers of such claims, and not associations of discrete events and the statistical facts that relate to such. The relationship between general and particular causal claims will be demonstrated further below with a case example (§7.2.1). The particular instance, however, that is able to stand separate from a general claim, allows further insight into what causation is. For now, we can focus on what particular instances offer us, in isolation.

[112] Nancy Cartwright, for example, presents an ontology whereby singular causes come first (Cartwright, 1989).

If causal relata are the properties of things, then immediately there is a glimpse of the essence of what causation might be. Causation is now something primitive. That is, it is not something that can be analytically reduced to something else, such as non-causal facts about (repeated) observed associations between events. The singular nature of the event itself has pulled us away from such analytical attempts through a lack of constant conjunction at the very least. Particular instances provide a notion that the modality of a dispositionalist account is neither one of contingency (that is, the probability or possibility of an effect happening), nor of necessity (that the effect will (or will not) happen). What dispositions can say about a particular instance is that there is a modality that is unique - a *sui generis* (*ibid*:175). A cause is something that disposes towards its effect that cannot be reduced to the logical modes of contingency and necessity. In this sense, the dispositional modality might seem weakened by the idea that it is irreducible to logical notions. However, the strength of a modality lying somewhere between contingency and necessity might be seen elsewhere. Indeed, it is because of this modality that causation can be thought of as something that does not need to rely on logical analysis. Rather, it is something that can be understood directly through experience. The following section now typifies these ideas by way of a simple clinical case study of low back pain.

7.2.1. Case study: non-specific low back pain

Let us take low back pain as an example of how the relationships with individual cases differ between a Humean account of causation, and that of causal dispositionalism.

Non-specific low back pain (NSLBP) is of significant concern to health care science due to its complexity and high prevalence (Hoy *et al*., 2014). Lifetime prevalence has been reported at up to 84%, representing significant costs to society (Airaksinen *et al*., 2006). By definition, NSLBP is not attributable to a known specific cause (Balague *et al*., 2012). But what does this mean? This brief case study focuses on what it is to say 'no cause', and takes this to be an epidemiological statement grounded in a Humean understanding of what causation is. However, this is of little use for clinical decision-making at an individual level. This case study should highlight what a dispositional view can offer in terms of reconceptualising causation with particular instances at its centre.

Evidence regarding the progression and intervention response for NSLBP is grounded in uncertainty. Uncertainty regarding all aspects of NSLBP can be accounted for by its seemingly inherent complexity. However, the persistence of this uncertainty seems at odds with the vast amount of scientific research focused on the phenomena over several decades. With reference to its aetiology, a brief review of epidemiological science exposes the limits of knowledge of causal responsibility. NSLBP is traditionally hypothesised to be causally related to mechanical stresses on the body created through, for example, posture and lifting that may induce aberrant muscle responses and subsequent pain experiences. However, mechanical factors including lifting, standing, walking, occupational postures, bending, twisting, carrying, and manual handling have been reported as non-causative through systematic epidemiological study[113].

[113] For example, Roffey *et al*. (2010a); Roffey *et al*. (2010b); Roffey *et al*. (2010c); Roffey *et al*. (2010d); Roffey *et al*. (2010e); Wai *et al*. (2010a); Wai *et al*. (2010b); Wai *et al*. (2010c).

What this means is, although there are cases within the data whereby one or more of the factors mentioned above would have had an association with the onset of NSLBP, overall, there would not have been enough cases to warrant a general causal claim. That is, the data fail to fulfil Hume's conditions for causation, especially that of constant conjunction. We can now look at this a little closer.

Varying degrees of statistical associations have been reported between NSLBP and activity levels, obesity and deconditioning, but none of these variables can be considered causal (Shiri *et al*., 2010a; Verbunt *et al*., 2010). The same can be said for factors such as smoking, mood, and hypothesised genetic factors, such as Interleukin-1 gene cluster polymorphisms[114]. Structural changes identifiable on imaging have also been considered as causal factors but although some studies demonstrate significant associations between pain and lumbar disc degeneration and disc space narrowing (Cheung *et al*., 2009; de Schepper *et al*., 2010), meta-analyses do not support causal claims (Endean *et al*., 2011). Further, pathophysiological factors associated with tissue structure and pain mediation, for example nerve growth factor and tumour necrosis factor α, are also weak causal agents (Wang *et al*., 2008; Yamauchi *et al*., 2009).

It is apparent that NSLBP is a complex phenomenon. Furthermore, given the variation of epidemiological responses in different studies and different sub-groups, NSLBP can be considered as highly context-sensitive in terms of any potential causal factor. High proportions of the population

[114] For example, Battie *et al*. (2007); Kalichman and Hunter (2008a); Kalichman and Hunter (2008b); Karppinen *et al*. (2009); Tegeder (2009); Dai *et al*. (2010); Riemann *et al*. (2010); Shiri *et al*. (2010b).

experience NSLBP and associate it with a cause – for example, bending or lifting. Equally, clinicians listening to and assessing people with NSLBP find it difficult to disassociate the effect from some cause (Kent and Keating, 2004; Jeffrey and Foster, 2012). A patient may state, for example, that they bent to lift something and felt a sudden onset of back pain, and since that event they have continued to have back pain. There is a deep intuition here for both the patient and the clinician to consider the lifting event as causal to the pain. Yet this intuition is not satisfied by a Humean idea of causation - this is far from supported by epidemiological studies. Epidemiologically and aetiologically, NSLBP does not have a cause. In each single case however, there clearly is some cause.

What is seen in this case study is that health science accepts the complexity of a certain condition. It sets about exploring this complex phenomenon by using its most powerful tools to search for invariances in the causal make-up of the condition. The methods have had some success in so much as they provide evidence of a test of a primary hypothesis related to some *a priori* assumptions regarding cause. However, the theory of causation that underpins this process dictates what should be considered as a cause. In this case, there is no such cause. For the individual however, this makes no sense. As such, a Humean theory of causation fails to relate to individual instances of particular causal claims.

This is not the case for a dispositionalist. Causal dispositionalism sees value in the 'limit cases': that smaller proportions of data that Humean's dismiss on lack of regularity. Where Humean's look for stability in the

effect of a single (or combination of) factor(s), dispositionalists will look at cases where an effect did occur, but not frequently enough for the Humean. This is where causation can best be explored. In line with this, dispositionalists are wary of strong correlations (as started earlier), as there is no guarantee that this is causation at work: having a back is strongly correlated with low back pain, *et cetera*. As such, dispositionalism is interested in the behaviour of a potentially causal factor in single, or limited, cases because dispositionalism sees a single causal factor as having a vast number of possible manifestations due to the vast number of manifestation partners it might work with. Which effect it contributes to will depend entirely on what context it appears in. A sudden, forceful movement will have the power to cause pain, but whether it will succeed in doing so will depend on the other causal powers involved. Some people have better motor control, for instance, but even this is entirely dependent on context: in periods of stress, for example, we might have altered motor strategies, or aberrant pain beliefs. Whether pain is influenced by movement or not also depends on the precise type of movement, its intensity, repetition, and so on. It should therefore be no surprise that two people can have vastly different effects from a particular movement.

NSLBP acts as a sensitive measure of the scientific limitations underpinned by a Humean idea of causation. This is not to say that population studies in themselves are limited. It is clear that a massive amount of knowledge of health processes has been derived from such studies. However, it is what this knowledge means to an individual that is the concern here.

In trying to identify the essence of causation, considering cases where an effect did not occur as being of no causal interest is a mistaken view.

Typical for dispositions is that they can exist unmanifested. A woman can be fertile without ever becoming pregnant and one can have a genetic predisposition for a disease without ever developing it. When a sugar cube dissolves, for instance, it is because it has a real causal power of solubility that is 'released' when it meets the appropriate mutual manifestation partner, water. Taken in isolation, a disposition might not ever do any causal work. Only through interaction with other dispositions will a causal process be initiated. Furthermore, a disposition can contribute to bring about a number of effects. What effect a disposition contributes to produce will therefore depend on the causal context. Heat, for instance, can causally produce a burn, boiling, steam, melting, explosion, drought, fire, growth, health, death, and many other effects depending on the manifestation partners.

In sum, this section has dealt with a desideratum concerned with causal processes at an individual level. A Humean theory of causation has difficulties accounting for this and any attempts it makes to do so rely on fragile notions of probabilistic inference and universal laws. Dispositionalism approaches the challenge with ease because, whilst accommodating both general and particular causal claims, it sees single instances as where causation lies. The essence of causation is found at the individual level. The next section will develop this line further whilst considering additional challenges associated with the inferential gap.

7.3. Desideratum 4: Help understand and assess additional premises and assumptions needed to bridge the inferential gap between population level evidence and clinical decisions

This desideratum stems from a direct rebuttal of a dispositionalists stance regarding causation in EBM. It has been set up as a condition by which to demonstrate the limitations of a dispositional ontology for causation. I see this then as a firm test with which to apply to the present thesis on two counts: i) that those opposed to a dispositional account, and indeed to attempts at developing an ontological account in relation to causal matters in EBM at all, see this as a strict condition for a causal theory and one that a dispositional account fails to speak to; and ii) that this desiderata represents the core concern of this thesis - that is, the translation of causal claims across spatiotemporal environments, in line with the central and canonical claims of EBM.

The challenge I have laid out should be now be clear: despite its best intentions, EBM cannot satisfy its central and canonical claims due to the way it structures its preference for particular evidential elements. The challenge has become ontological as I have proposed that the above problem exists because of the way that EBM has constructed a concept of causation through its hierarchical structure. As such, a possible move towards developing solutions for this problem is an ontological reconceptualisation of what causation is. As outlined in the introduction to the thesis, and referred to again presently, there are opposing arguments

to this approach: that the concern is not ontological, but something more practical and epistemological. I conceptually defended the ontological approach when introducing this thesis. In this section I shall provide a detailed account of how I think the ontological concerns play a central role in addressing the core worry of the thesis, that is how prioritised scientific evidence relates to individual clinical decision-making. I shall again use the arguments of Strand and Parkkinen as a backdrop for this section as I take their account to be the strongest, most direct, and most relevant refutation of the dispositionalist stance with regards this matter. Further, I see their account as representative of others in this area[115]. In sum, however, the conclusion to this response will be familiar. That is, that there is a single line of fire from the antagonists in attempting to meet this desideratum. This comes from the Humean arsenal. The only possible move to be made is to invest heavily in a regularities account of causation. This entails hope that probabilistic inferences forced from robust population studies somehow survive the inferential gap in the absence of any explanatory logic to support their transition. By avoiding 'ontological entanglement' in favour of focusing on causal inference and causal epistemology, the contemporary response to this desideratum offers nothing new over the traditional problems of induction, inference, prediction and so forth, all of which are associated with a Humean account of causation.

The dispositionalist's response to this desideratum is grounded once again in a framework drawn up by the relationship between general and

[115] For example Howick, Russo and Williamson *et al.*, as previous.

particular claims. Within this, causal dispositionalism relies on the ideas of necessity, causal tendencies, modal primacy and probability interpretation to understand how it could meet this desideratum. These features are considered below. However, it is clear that these same features have acted as catalysts for opponents of dispositionalism to re-stake their Humean claims. In this section I seek to further develop the dispositional response to this desideratum. In doing so I will see how far the traditional stance[116] can be pushed, specifically in relation to one critical feature of this argument: necessity in causation.

Before this, I will attend to the broad concern of this desideratum in relation to the conventional vocabulary of EBM. This entails further consideration of the issues of external validity and the problem of induction with relation to the inferential gap highlighted by this desideratum.

7.3.1. The broad problem: the inferential gap

Again, the problem set out in this desideratum is not unique. In fact, it is possibly one of the longest standing and most vexing problems within both philosophy of science and healthcare research itself - *"the despair of philosophy"* (Whitehead, 1925:35): how knowledge is inferred from one instance to another. In antiquity:

[116] Again, to be clear, what I am calling the 'traditional stance' is one expressed by, for example, Strand and Parkkinen (2014, 2015). The stance (for the purpose of this desideratum) characterises the necessary features of a Humean account of causation, and represents the most common position held by other contemporary commentators on this aspect of EBM.

> *"Your appeal to past experience decides nothing in the present case . . . Why from this experience we form any conclusions beyond those past instances, of which we have had experience?"* (Hume, 1739 THN 1.3.6.10)

and in modern thought:

> *"For many people believe that the truth of these universal statements is '**known by experience**'; yet it is clear that an account of experience – of an observation or the result of an experiment – can in the first place be only a singular statement and not a universal one"* [original emphasis] (Popper, 1959:27)

For EBM, this problem sits behind, but is often conflated with, the issue of external validity. I will take it that what we are talking about here is the philosophical challenge of logical induction in spite of issues of external validity. That is to say that we can assume the external validity is accounted for procedurally by ensuring the best possible level of homogeneity between research subject and patient, if there ever was such a thing. Further, we need to consider the problem beyond the epistemological account of searching for methods that can differentiate 'good' and 'bad' inductions, or offer alternatives. This is a fruitless pursuit in the absence of a robust ontology. The challenge therefore is to consider

the problem at an ontological level[117]. At this level the broad problem stems from something like:

P1: All observed *C*s have also been *E*s

P2: *a* is a *C*,

C: Therefore (or, it is therefore probable that[118]), *a*, not yet observed, is also an *E*[119].

Hume's argument was, essentially, that this logic was consistent with some causal necessity and as causation was not an objective feature of the world, then such inferences could not be the case. In place, such conclusions were a result of our habits of the mind, and not objective experiences:

> *"First, We may argue, that the supposition,* ***that the future resembles the past****, is not founded on arguments of any kind, but is deriv'd entirely from habit"* [original emphasis] (Hume, 1739 THN 1.3.12.9)

The problem with this being:

[117] Popper's response is essentially about epistemology. Rejecting induction as part of the scientific process, Popper proposed methods for the falsification and corroboration of hypotheses (for example, Popper (1959:Ch10). I will not go any further into Popper and induction as this will add little to the present discussion.

[118] The inference may well be, and is in the case of healthcare research, contingent, and as such the conclusion comes with a probability rider. We will see below that the notion of probability has little impact on the issues at hand.

[119] This, of course, relates to universal quantification as discussed above, so the base of the problem can also be expressed as $\forall x(Cx \rightarrow Ex)$.

> *". . . this determination [habit], tho' full and perfect in itself, presents us with no steady object, but offers us a number of disagreeing images in a certain order and proportion"* (*ibid*:1.3.12.10)

The challenge is now to assess what theory of causation can best relate to the assumptions that inferences from population research to individual clinical instances rest upon. The only such assumptions that can exist for the Humean interpretation of EBM are ones appealing to the structural qualities of inherent research methods. For example, Strand and Parkkinen (2014) set out three case-specific assumptions that should hold if inferences from population studies were to be confidently obtained. First, that the values of Y are determined independently of the way Ys are assigned to treatment groups; second, that treatment outcomes are independent of the timing of treatments and measurements; and third, that the value of Y in an individual is assumed to be independent from prior exposure to treatment conditions (*ibid*:983).

These all relate to quality and control issues of trial design, and as such are matters of epistemology. The traditional stance, by its very nature, can address the assumption for inference only by matters of epistemology. The limitations of these responses have already been witnessed throughout this thesis, and are what lie at the core of the central problem. Paradoxically then, the traditional stance's approach to this desideratum is to simply re-state the assumptions that are in fact the essence of the problem - that is, it is because of the way EBM has structured its methods, and thereby its account of causation, that has been critical in instigating the problems related to the central and canonical claims of EBM.

Causal dispositionalism can relate more meaningfully to the issues emerging from this desideratum because, first, it does not see the relationship between general and single causal instances in the same way that the traditional stance sees it; second, it sees causes as tendencies and not as things that necessitate their effect.

To expand on the first notion of general and single claims then. This has already received some attention above, but there are elements of this that are useful to return to at this point. Earlier, it was proposed that dispositions value both general and single instance claims, but what is unique about a dispositions account is that it is in single instances where the true substance of causation can be found. It was also discussed as to how general and single claims relate to each other from the perspective of accounts that have tried to make-up for the Humean restrictions related to patterns of conjoined discrete events. For example, in §7.2 the ideas of universals and laws of nature were presented and noted to be insufficient to get to the real essence of causation in single instances. What is needed now is some further commentary on the relationship between general and single instances that responds to the way this desideratum has so far been framed, that is in terms of an inferential gap and the problem of induction.

The dispositionalist response is quite simple: there is not a problem of induction. The problem of induction is dependent on there being some element of necessity in causal claims. Note though that the primary defence for EBM against dispositionalism is predicated on the idea that necessity is not a part of what EBM means by causation. This is discussed in detail below, but in sum, this defence does not hold. So, conventionally, the problem of induction relates to: 'general claim *C* causes *E* = single claim *c* (necessarily) causes (to some level of probability) *e*'. As causal

dispositionalism rejects necessity as part of causation (see below), this set-up does not hold. Dispositionalism takes causes as tendencies that at most dispose towards an effect, so the set-up becomes more like: 'general claim *C* disposes towards *E* = single claim *c* disposes towards *e*, but the manifestation of *e* is context-dependent on the particular case of *e*'. Because causes only tend towards their effect, the hard line of guaranteeing some form of repetition of events between general and single instances is dissolved. As such, causal dispositionalism makes no claims towards there ever being a process of inductive inference. All a general claim has done is to identify that *C* disposes towards *E*. As there is no statement of necessity, there can be no claim that this will be the case again in the future, and no suggestion of *c* and *e* probably being the case.

This stance might, however, be seen as somewhat evasive in terms of the pragmatic aspirations of healthcare research. If the purpose of population level research is to inform future decisions, and a disposition account of causation shows little interest in the inference of causal claims, then of what utility can such an account provide? The utility can be seen when we sketch out a contrast between the traditional EBM framework, and one underpinned by a dispositions ontology. Traditionally, in essence, the central driver to data-informed decision-making has been the linear trajectory from hypothesis to clinical decision, that is: generate hypothesis → test hypothesis (with population-level group comparisons) → make statistical inferences to clinical decisions (singular). As we have seen, the assumptions required from stage two to three in this trajectory appear not to be sufficiently accounted for by the traditional stance. Dispositions does not rely on this linear, functional trajectory however. Hence the relationships and the assumptions between general and

particular claims are qualitatively different to the ones promoted by the traditional stance. Whereas the traditional stance sees population data as a tool for informing spatiotemporally removed decisions via the identification of patterns of conjunction between discrete events, dispositions sees the value of population data in providing information about possible causes and the factors that influence their tendencies towards their effects. This can also be seen in single instances as well, as per §7.3. Thus, as already presented, dispositions does not commit to any metaphysical prioritising of one over the other (for example, general claims over particular claims). As dispositions sees general claims - let us say the outcomes of a review of RCTs - as *symptomatic* of causation rather than *constitutive* of it, it will take single instances as 'tokens' of the 'type' of causal claim pointed towards by a general claim. Thus the relationship between the general and particular is one of 'token-type', that is that the two claims share an identity through the dispositions at play – "*You can't have one without the other*" (Mumford and Anjum, 2011b:15). This is what brings the two forms of causal claims together, and provides assumptions and accounts that are inherently more robust than those relying on inductive inference from the general to the particular. The truth of a general causal claim from a traditional stance derives from within the process leading to that claim, for example the quality of the research design to establish the nature and strength of any association identified. Such a truth holds no epistemological or ontological relationship with any spatiotemporally distant particular instances for whom it is intended. Dispositionally, on the other hand, views the truth of a general claim as derived from the token-type relationship it has with particular instances. Immediately, such truths are intrinsically embedded in both parties to this

relationship through their shared dispositional identity. This makes a general claim of, say, 'exercise improves low back pain' true even if there are some single cases whereby exercise does not improve a person's back pain. Exercise, in this example, would still hold a disposition to improve a single person's low back pain, but given that causes can be prevented or interfered with, a richer appreciation of the context and complexity of the single instance is indicated. Therefore, once again, the complex environment of the individual person sits at the heart of what causation is.

We have established that the broad problem with respect to this desideratum is the inferential gap between general and particular causal claims. This problem is not unique and has existed at the core of philosophy of science throughout its history. It seems that the restrictions put in place as a result of committing to a traditional Humean account of causation prevent a solution to this problem. Because dispositions see causes as tendencies only, that can be prevented or interfered with, such an account of causation is able to dismiss notions of inference and induction as problematic. The relationship between general and single causal claims with a dispositional ontology is through a shared identity of dispositions, which can be present in either claim. This provides a clearer and stronger relationship between particular and general claims than any other theory that relies on inferring truths formed exclusively in the processes of general claims. Dispositional truths are identified equally by both general and single instances. A lack of manifestation of an effect in a

single case serves to better understand the complex conditions under which causes can best do their job.

Of course, this argument need not be readily accepted, by Humean proponents at least. Especially because the argument assumes that necessity is a firm part of causation in the Humean account. The following section (§7.3.2) will consider the strongest and most visible reactions to a dispositionalist position for this desideratum. This reaction is characterised specifically in a direct rebuttal from Strand and Parkkinen (2014) and Strand and Parkkinen (2015). Because Strand and Parkkinen offer the most serious and well-considered attack on dispositions, I shall again use their work as the platform for further testing the dispositional account. Strand and Parkkinen propose – as always - that first, the issue at hand is an epistemological one, with little need for an ontological account of causation. Specifically, they then argue that necessity is not, in fact, part of a Humean idea of causation. I argue that they are mistaken on both grounds and conclude by stating that the traditional stance cannot escape the idea of necessity, but necessity should have no part in causation. This reinforces the dispositionalist account that is anti-necessitarian, as causes are only ever seen as tendencies[120].

[120] NB: On necessity, for clarity again. Although Hume saw no place for a *necessary connexion* as part of causation, what is being referred to here as necessity is the notion that a cause necessarily results in an effect.

7.3.2. Causal inference and causal epistemology: traditional stance

It seems that opponents to an ontological project for EBM are so because they see a disjoint between the practical matters of causal epistemology and the intellectual theorising of a metaphysical commentary: "*EBM should not get entangled in ontological disputes but focus on the epistemological and inferential aspects of causation relevant for clinical practice*" (Strand and Parkkinen, 2015:533). This stance resonates with earlier and ongoing discussions on the relationship between ontological and epistemological projects, with opponents explicitly trading on the stance that it is the role of an ontology to "*accommodate and explain"* (*ibid*:532) epistemologically grounded facts of causation, rather than *vice versa*. This 'difference' view on philosophical methodology may well be a primary source of disagreement in attempting to progress towards a solution for this key area. This should be kept in mind throughout, but for the immediate task this helps in understanding the seemingly fixed stance of the opponents.

There are, I claim, two dimensions to the traditional view that cause it to be problematic for this desideratum. The first is that, as stated above, this continues to be fixed to a Humean account of methods and causation; the second is that there are some erroneous interpretations of key notions of a dispositionalist theory. First, the Humean traps.

In attempting to meet this desideratum, there is an argument that an account of causation can explain the assumptions necessary for extrapolating population data to individual instances with exclusive appeal to matters of causal inference and causal epistemology. The argument reinforces a Humean commitment and seems to recycle a logic

that already exists in the way that EBM speaks about using population data. In summary, the case is set out as follows.

We can assume first of all that causal inference drawn from population data is by no means a given process, and as such relies on a number of causal assumptions. It would be unusual to think otherwise. Strand and Parkkinen set out to make these assumptions explicit in order to evaluate clinical effectiveness at a particular instance (Strand and Parkkinen, 2015; Strand and Parkkinen, 2014).

The first appeal to explicate any assumptions is on the grounds of biological complexity. For causal inference to withstand extrapolation from population to individual, supporting knowledge of biological mechanisms should be sought: for example,

> *"This [an explicit epistemology of causal knowledge] should bring clarity, for example to how research aimed at discovering biological mechanisms might support or undermine specific causal claims that are based on population evidence"* (Strand and Parkkinen, 2014:983)

This is the precise argument regarding mechanisms from Howick, and more so, the one that characterises the RWT (§4.2.2).

The second appeal is towards the level of robustness as to how a general causal claim is established. High quality conditions for counterfactual dependency under interventions[121] "*. . . ground inferences to probability*

[121] Strand and Parkkinen explicitly support an interventionist account of counterfactuals, specifically in line with Woodward (Woodward, 2003).

estimates in clinical predictions of expected effect on individuals" (Strand and Parkkinen, 2015: 533). This is provided as an assumption for inference in itself.

In sum, the traditional stance seems to rely on two appeals in order to explicate the necessary assumptions for understanding the relationship between population data and individual instances of clinical decision-making. The first is to consider mechanistic levels of evidence to support claims derived from comparative studies; the second is to ensure that the counterfactual conditions under which a general causal claim is established are robust. This sounds very familiar and does not seem to have added to the issue at hand. It is clear that certain assumptions have been laid out – ensure some mechanistic evidence and have good quality trials – but this stance has gone no further to *account for* or *understand* these assumptions. They are left vacuous. Trapped in a Humean landscape of discrete events - cursorily supervened upon by mechanistic information - and anchored to a frequentist understanding of probability in the blind hope that the void between population and patient will be navigated successfully, we are still no better informed towards this desideratum. Again, there is a further unexamined assumption that frequentist probabilities relate to individual instances. The stance is truly traditional. What it does offer however is a reinforcement of the fact that no matter how hard a Humean tries to take causation (or rather the non-causal facts that it has been reduced to) from the place it emerged to a another place in space-time, they are prevented in doing so by the very essence of what causation has become. But what can a dispositional account offer in terms of understanding better the relationship between population data and individual clinical instances?

A primary concern for the dispositionalist is that the assumptions laid out by the traditional stance seem not to adequately account for the defeasibility in prediction, if prediction is the basis for clinical decisions. The best that the traditional account can offer, as stated above, is pointing to various assumptions and stating that they are fallible. This fallibility being related to both issues of external validity (hence the requirement for robust and representative studies), and the complexities and context-sensitivity of individual instances that are in turn impacted on by the complexity of biopsychosocial mechanisms. Within this dialogue is a further opportunity for dispositionalism to step in, and also a chance to highlight some mistaken interpretations of ideas that seem to have been made in a traditional stance.

As presented earlier, the modality of causal dispositionalism is one of *sui generis,* falling somewhere between contingency and necessity. Causes are more than chance, yet do not guarantee an effect - rather, they tend towards their effects. The dispositionalist claim towards how the traditional stance does not account for defeasibility in prediction is anchored in the notion of necessity. Causal dispositionalism says that the inferences from general causal claims made by the traditional stance entail necessity, and therefore by definition cannot account for fallibility. If this is so, then the traditional stance is limited to the extent to which it can explain inferential practices. Dispositionalism, on the other hand, can show why prediction is defeasible and, although reliable to some degrees, is not reliable entirely. What dispositionalism means by necessity is related to the traditional stance's explicit investment in a regularities account in which causation is analysed in terms of dependency relations, such as variation under intervention: intervene on one variable and another alters

with it. This trades on the intuitive, yet explicated, idea that causes make a difference: "*A is a cause of B if and only if there is a possible intervention on A that would lead to a change in B.*" (Strand and Parkkinen, 2014:982). Of course, this notion was utilised in earlier in §6.3 for the Humean case on causal content, and the dispositionalist response is similarly repeated: '*this fails as an analysis because the invoked notion of lead(ing) to looks causal in itself, hence assuming the notion it is meant to analyse'* (§6.3:226). While most causes do make a difference, not all do - not in cases where effects are overdetermined by more than one sufficient cause; or where a cause is prevented from happening, as prime examples. Investing in difference-making commits to an idea of necessity that in turn fails to account for when causes do not occur. As such, fallibility in prediction is unaccounted for by the traditional stance. There is, again, at least some conceptual gap between our notions of *cause* and *difference-maker*.

A mistaken counter-claim to this is, once more, to appeal to probability – presented as an alternative to necessity - as the actual intended position for the traditional stance. For example, the traditional stance, in reference to assumptions about variation through replication, state (that acknowledging this assumption): "*…does not require a commitment to determinism; the effect under study might well be probabilistic, as is typically the case in medical trials"* (Strand and Parkkinen, 2015:532). There is no dispute that probability is at the centre of the argument here. As set out already, the statistical models adopted by healthcare science in their prioritised research methods are inherently probabilistic. Dispositionalism accepts probabilistic causation but, of critical difference to the traditional stance, does not see this as an argument against necessity in causation. The difference in approach here is most likely one of interpretation of the ideas

of probability and necessity. To appeal to probability as a way of accounting for fallibility in causal claims is a mistaken move.

The traditional stance's argument is thus weakened on at least two grounds: first, probability in this argument is played off against determinism. Dispositionalism does not see determinism and necessity as being the same thing, and as such the traditional stance is mistakenly playing off probability against the wrong notion. If this is the case, then the traditional stance's only option is to admit to either genuine necessity *or* probability in causal claims. This exposes a second weakness of this argument: that it is a mistake to think of probability as an alternative to necessity; what dispositionalism means by necessity is not something that is a-probabilistic. These two notions are considered further below.

First of all then, *necessity not determinism*: The traditional stance mistakenly conflates the ideas of necessity and determinism. Dispositionalism does not claim that causes necessitating their effects are an expression of determinism[122]. A commitment to causal necessity is not at all one to a deterministic world view. What causal necessity means to dispositionalism is something in line with the account of difference-making, as above. That is to say that if there is one thing (a cause) then there has to be a second thing (an effect); being necessary makes one thing a sufficient condition for the next thing to occur. Determinism, however, sees the future world fixed by the past[123]. To relate causal necessity to determinism would entail an assumption that somehow necessary causes

[122] For example, Mumford and Anjum (2011b:74-76)

[123] More formally, say: "*Determinism*: *The world is governed by (or is under the sway of) determinism if and only if, given a specified way things are at a time t, the way things go thereafter is fixed as a matter of natural law*" (Hoefer, 2016).

are a "*means by which determinism does its work*" (Mumford and Anjum, 2011b:75). This means that determinism could be explained by causation. One response to this is simply to claim that determinism may be true in the absence of any causation occurring at all. As such, if the traditional stance truly has interpreted necessity as determinism – and I would state that this is indeed the case – then the argument that the traditional idea of causation does not require a *commitment to determinism* may be valid. However, it is one of little relevance to the discussion in hand, namely causal dispositionalism's accusation that the way the traditional stance sees causation is anchored in a notion of necessity, not determinism.

This then leads to the second aberrant view that *necessity is a-probabilistic*. More specifically, that an appeal to probability acts as an argument against necessity. To take the second part of the above-mentioned defence: ". . . *the effect under study might well be probabilistic, as is typically the case in medical trials"*(Strand and Parkkinen, 2015:532). Dispositionalism would, once again, agree. Indeed, the dispositions theory seeks to be consistent with probabilistic causation (assuming now that what is meant by determinism here is in fact necessity[124]). However, this is not a sufficient defence against the claim that the way the traditional stance considers causal claims is grounded in necessity. Necessity is not an idea that is considered as something a-probabilistic.

It would seem that what the traditional stance has presented is an idea whereby a cause need not necessitate its effect at all, but rather something that raises the probability of that effect happening. This *probability-raising*

[124] For clarity, of course it is much easier to pitch determinism against probability. That is, probability is by definition indeterministic, for example Salmon (1980).

theory of causation relates well to the statistical foundations of EBM's prioritised methods, steeped in a frequentist interpretation of probability. It is easy to see how it can be utilised to argue against a position that accuses EBM of holding a necessitarian ontology. This idea has a rich intellectual history[125] perhaps summed up by Cartwright's proposition that *C* is a cause of *E iff* "*. . . C increases the probability of E in every situation which is otherwise causally homogenous with respect to E*" (Cartwright, 1979:423). Thus, a cause is firmly fixed to the idea of probability. The question now is how does this relate to the idea of necessity? Further, in relation to this desideratum, how does this commitment relate to the inferential gap between population and individual cases?

The traditional stance, then, claims that this removes any commitment to saying that causes necessitate their effects. But this is not the case. The first consideration is that although the ideas of cause and probability are now conjoined, this is not to say that probability need be part of what causation is. That is, the probability-raising theory of causation is not an analysis of causation itself. As Cartwright herself states: "*obviously CC*[126] *does not provide an analysis of the schema C→E, for exactly the same schema appears on both sides of the equivalence*" [127] (Cartwright, 1979:424). As such, what causation is is something other than probability (we can relate back to discussion on propensity in §5.2.2, for example). Probability is a non-causal component of the epistemological and factive understanding of what might bring about effects. In our case, the understanding is informed

[125] For example, Suppes (1970); Cartwright (1979); Mellor (1988)
[126] Causal Condition, referring to the earlier proposition.
[127] The equivalence, for clarity: *C* causes *E iff P(E/CK) > P(E/K)* for all states *K* of the *E*'s other causes that are not between *C* and *E*.

from population research data. A second consideration, that reinforces the above view, is perhaps best expressed by considering John Mackie's thesis on causes as INUS conditions (Mackie, 1974:62-87)[128]. This looks like a reaction to the probability-raising theory that adds to a traditional regularities view of causation by considering causal complexity whilst attempting to provide an anti-necessitarian stance. Somewhat paradoxically however, it is a thesis that serves to further highlight that there cannot be an escape from necessity in causation if fixed to a Humean stance. For Mackie, causes are at least an *insufficient* but *non-redundant* part of an *unnecessary* but *sufficient* condition for the effect. Mackie sees causes as complex 'clusters' of factors that although being sufficient for an effect can be, but do not need to be, necessary[129]. There does seem therefore to be some room to allow for non-necessity in causes. The paradoxical element of this thesis however - as seen by dispositionalists at least - is that *sufficiency* still suggests that an effect is brought about. Even though it might not have been *necessary* for that particular cluster to cause the effect – that is, there could have been an alternative cluster that could equally cause the same effect – the effect still happened. This condenses what dispositionalism means by necessity: that whether factually probabilistic or merely sufficient, when causes are talked about in the traditional (Humean) way, they are done so with a commitment to there being some effect. Necessity remains at the core of Humean causation and as such this theory of causation is unable to account for defeasibility. In healthcare

[128] The first letters of the italicised words form the acronym 'INUS'.

[129] For example, adapted from Psillos (2009:151): *A* can be considered an INUS condition *iff* it exists in the form: '*AX* or $Y \leftrightarrow E$'. That is, *A* is non-redundant part of a condition (*AX*) which itself is sufficient (it can cause *E*), but unnecessary (*Y* can also cause *E*).

there are many cases of 'causes' not working, for example non-responders to interventions, and a theory of causation should be able to account for such cases. The traditional stance cannot account for such assumptions of fallibility that arise between population studies and individual cases. It is difficult therefore to accept such a theory as being satisfactory for the purpose of EBM, by this desideratum at least.

Because the traditional stance holds a commitment to necessity in causation, then at this level the stance fails to satisfy this desideratum. So, how does dispositionalism explain defeasibility? It does so once again with relative ease. Already I have stated that a dispositions theory brings with it a *sui generis* modality – a modality more than pure contingency but less than necessity. This modality represents the key to explaining defeasibility. Less than necessity, dispositionalism sees causes as tendencies towards an effect. The important feature of such tendencies is that they can always be *prevented* or *interfered* with. Thus, causes are inherently fallible. In this respect, a cause can never necessitate its effect because it can always be prevented from doing so. This does not mean however that the cause is not a cause.

Consider the contrast again with the traditional stance, framing RCTs in their logical form as an example. The logical form of the RCT is inherently deductive, that is to say that the premises (P) within the trial necessarily entail the conclusions (C). For example, P1: if two groups are identical save one factor (the intervention), P2: greater change is observed in the intervention group, then C: that change was due to the intervention. The necessity of the conclusion gives appeal to causal prediction and explanation. And this is what Humean proponents exploit in their defence.

Indeed, this is precisely what Stand and Parkkinen highlight in their argument for the traditional stance:

> *"On this method, one isolates a factor of interest in a system and proceeds to vary it in specific ways, while detecting whether the putative effect changes as a result"* (Strand and Parkkinen, 2014:982)

However, how does this deductive model account for failure of an effect? For example, non-responders, as stated. In logical terms, such defeasibility is accounted for by the truthfulness of the premises. If the conclusion is wrong, then it has to be because the premises were false. Again, on a traditional account the assumptions for prediction and inference rest within methodological structure. This seems, however, like a poor account of real world inference. By definition, the trial set up can only ever be an abstract representation of the real world, hence "*isolates a factor of interest in a system and proceeds to vary it in specific ways"* (*ibid*), *et cetera*. As such, the logical form operates independently of factors that may exist in the real world. Therefore, although the premises can be changed, their *form* cannot - neither can their logic.

This is unsatisfactory for the dispositionalist who sees the world as complex and context-sensitive: "*. . . the basic form of one of the premises is always mistaken and inappropriate*" (Mumford and Anjum, 2011b:139). The trial could never be an accurate representation of the real world because, on dispositionalism, no causal process necessitates its effect. Because causes are highly context-sensitive and thus only tend towards an effect, the premises within a trial could only ever represent the dispositions of a

subject, not the necessity of them. Whereas the traditional stance offers a(n unsuccessful) methodological and abstract account of defeasibility, dispositions offer a rich, real world account because causes can always be prevented. For an example, consider the low back pain and exercise trial. On a traditional account, non-responders could be explained by the relevance of the exercise in respect of their physical attributes, say. Thereafter, a new trial with a different exercise, or different inclusion criteria (adjusting the premises) could be developed. However, on a dispositionalist account, failure of response could be explained by the complex composition of powers in individual cases. Such composition would influence the tendencies of the person's dispositions, for example they may be physical capable of performing the exercise, but still hold fearful beliefs about their pain and in fact the aching from the exercise is reinforcing their aberrant pain beliefs.

Causes are clearly not to be understood as factors that have exactly the same effect in every context in which they appear, therefore. Causes that have been identified through RCTs carried out to perfectly acceptable standards, and clearly suggestive of a certain prediction and clinical intervention, could nevertheless fail to produce their expected effect. When one looks to the ontological matters of causation, one sees that this further consideration, concerning context and composition, can be highly significant. Adding together a combination of drugs, for instance, each of which has been found to have a safe, positive effect in RCT, in theory could possibly produce a 'cocktail effect' that is unsafe. Again, this

explains why causal inferences are fallible. They are based on an assumption of a finite number of operating factors. An unknown factor could effectively be an additive interferer, for some expected effect. Worse still, it might be a factor that composes nonlinearly with the presence of the other factors to produce an antipathetic effect.

The predictive value of such dispositional reasoning might, however, be questioned by those schooled in (probabilistic) deductive necessity – at least robust methods might have *some* predictive utility within a traditional account, it might be claimed. However, dispositionalism is not relativism and prediction is a feature of causal dispositionalism. It is not that dispositions denies deductivism, although it does judge it to be "*over-ambitious*" (Mumford and Anjum, 2011b:140). The difference is subtle but clear: whereas the traditionalist would say 'if *A*, then necessarily *B* (to a degree of probability)', the dispositionalist would say 'if *A*, then *B* is disposed to happen'.

7.4. Conclusion

This chapter has concentrated on the inferential aspects of causal knowledge. Proponents of the traditional stance say that their difference-making theory explains those causal inferences while the dispositional account does not. They argue for this conclusion without considering the ontological issues at stake. Indeed, the traditional stance suggest those considerations are not even relevant. An ontological inquiry would, I have argued, be beneficial in unveiling some of the shortcomings of current causal models for the complexities of medical phenomena.

The core of the discussion in this chapter has been centred on the relationship between general and particular instances of causes. The third desideratum asked of a causal theory to *account for causal processes in individual-level clinical decision-making*. The traditional stance had limited options and utility with regards to this, either appealing to a rationalised faith in probabilistic inference, or some claim to universal laws. Dispositionalism can respond with ease to this desideratum. Although it has no deep ontological commitment to the priority of either general or particular instances, dispositionalism does take the single instance as to where causes are. From this, the theory can account for general causes as being signals as to where causation might lie. There is no commitment needed to universal laws, and the account avoids problems associated with probability and induction.

The fourth and final desideratum then: *Help understand and assess additional premises and assumptions needed to bridge the inferential gap between population-level evidence and clinical decisions*. The traditionalists' response was simply to assert that if prioritised methods are conducted correctly - without experimental error - then predictions should be forthcoming that are simple, exact and unfailing. We know this to be false. Any account of causal inferences has to respect the obvious datum that predictions are fallible and defeasible. Dispositionalism offers an explanation of prediction and inference within a fallibilist's framework in which dispositions tend to produce their effects but might not always do so. Strand and Parkkinen are thus wrong to say that an epistemology of causal knowledge "*does not flow from the dispositionalist ontology*". What does not flow is an epistemology in which inferences can be drawn with deductive certainty, which seems to be exactly as it should be.

Summary of PART 2

The aim of this final part of the thesis was to establish a foundation for the reconceptualisation of a theory of causation in EBM. To do this, a conceptual framework was established through the formation of desiderata that a theory of causation, to be relevant for EBM, should be able to respond to. These were:

> *D1: Explain the causal role of content from particular research methods.*
> *D2: Motivate a viable epistemology.*
> *D3: Account for causal processes in individual-level clinical decision-making.*
> *D4: Help understand and assess additional premises and assumptions needed to bridge the inferential gap between population-level evidence and clinical decisions.*

A foreground to this part was provided by the ontological tension existing in the way health science presently considers causation. A dimension to PART 2 was that it is arguable that existing research methods can be read dispositionally. The thesis as a whole had no *a priori* intentions towards a wholesale rejection of current methods. The methods of EBM simply form a part of the story by which a reconceptualisation of theory

can develop. We have learnt something about the relationship between theory and methods. 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. Prioritised research methods can again indicate causal processes. However, the causal work is being done within each group and thus it is the groups themselves, not the regularities or counterfactuals, which act as the truthmakers. Robust population studies 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 dispositions ontology, scientific research should focus on the interaction of causal partners and not be dominated singularly by the pursuit for statistical invariance in large groups. For the clinician, the relationship between research findings and individual clinical decisions becomes clearer. Despite those who reject the utility of anything other than epistemological analyses, an ontological review allows the notion of EBM to be re-evaluated from bottom-up. One of the foundational intentions of this thesis was to work towards a philosophical underpinning of EBM that would better support what already happens in clinical practice. This bottom-up approach relates well to clinical practice. Least of all because a dispositionalist account of causation takes the human and the therapeutic interaction, with all that is known about the process of disease and interventions as its starting point for an account of causation.

The ontological locus of dispositionalism allows the theory to escape commitments to - and therefore shortcomings of - proxy truthmakers, universal laws, necessity, probabilistic inference, and restrictive logical forms. A causal theory based on causal dispositionalism is well positioned to account for the problems represented by the central and canonical claims of EBM, and furthermore has an appealing commentary on a causal epistemological framework.

Thesis Conclusion

This thesis has examined the nature of causation in evidence based medicine and health care. The naïve question that inspired the thesis was along the lines of 'in an age of evidence based medicine (EBM), what is it to say something (a treatment) works?' Despite the core business of EBM being to find out 'what works', there did not seem to be a convincing account in the extant literatures that would philosophically satisfy this sort of question. This thesis has contributed to a better understanding of causation in EBM, and of causation more generally. Additionally, it seeks to inspire thought and further investigations into a reconceptualisation of a causal theory for EBM, particularly with regards to a theory related to a dispositions ontology of powers. The thesis has been concerned with three cardinal questions:

- *What does causation in EBM, as it stands, look like?*
- *Is this causal theory sufficient for the claims of EBM? and*

if not, then:

- *What should a theory of causation for EBM look like?*

In sum, the answers to these questions are that within EBM, as it stood until now, causation could be understood as a Humean notion that in fact is reduced to something non-causal - observed regularities. This, I propose, is not sufficient for the claims of EBM, in fact a paradox, whereby the claims of EBM cannot be satisfied because of this account, is apparent. As such, a reconceptualisation of a causal theory was approached, and specific desiderata developed to identify precisely what a theory of causation, if relevant for EBM, should look like. The outcome of this is that, to satisfy the claims of EBM, causation is best thought of within an account characterised by complexity and context-sensitivity, such as causal dispositionalism. The main body of this chapter will attend to the concluding position of the thesis with regards these findings.

In this final chapter I will summarise key arguments within the thesis and identify the meaning of these arguments in the context of a revised understanding of causation, and how this might warrant future work in this area. The thesis has been presented in two parts, preceded by an introductory chapter that set the landscape and justification for this enquiry. PART 1 was primarily concerned with identifying what it is that EBM, as it stands, considers causation to be. The framing for PART 1 was provided by the reduction of EBM to three specific and inter-related claims, which I referred to as the central and canonical claims of EBM. PART 2 was where the move towards a reconceptualisation of a causal account was made, deeming a theory of causal dispositionalism as relevant. This part was framed by desiderata emerging from narratives within the subject literatures.

The analytical dimensions of this conclusory chapter are evident throughout, but are most significant in the final section which draws on

the emergent themes of each of the two parts of the thesis. Bringing these themes to coalescence will draw to a conclusion the narrative that has permeated this work.

From this introduction, the primary importance of this subject should have been clear: medicine and health care are practices fundamentally concerned with enhancing the health of people. Therefore, to understand 'what works' is a necessary feature of enhancing health. These professions have set about this task with a renewed vigour since the onset of EBM. However, whilst there was something scientifically appealing about the progress being made in clinical research – a primary source of evidence - I remained unconvinced that the sort of causal notions arising from this were what was actually sought in guiding management of patients. This was profiled via a case study that identified components of a human narrative pointing towards a person centred approach to therapeutic decision-making (appendix 1). This early suspicion reflected much philosophical and health domain literatures on the same subject, although this was often cloaked in non-causal terms. Of course, framing my worries in terms of causation was always going to be a contentious stance. I hope I have accounted for this stance by demonstrating that, in fact, if we are interested in affecting the health status of individuals, then how else can we talk about things? To have an effect, then there must be a cause. On the other hand, Jeremy Howick among others, would say that for a therapeutic decision to be made, then we can rely on comparative population data showing the level of therapeutic effectiveness, for example data from randomised controlled trials (RCTs). He would say that the nature of any underlying notion like causation is not at all something to be concerned with. I suggested however, that for the philosopher and

the person seeking to change their health status at least, it is. By simply talking about effectiveness, we are talking about causation. Having gone through the process of this philosophical inquiry, I am still convinced that this is the case. For the sake of a complete philosophy of EBM, understanding something about what we mean by causation should be of critical importance. But more than this, the impact that this ontological account could have on the epistemological readings of research outcomes, and perhaps even the development of unique research methodologies must be developed. Such aspirations were always outside the remit of this thesis, but I am encouraged, at this point, that future investigations of this nature are indicated.

For now however, the concluding position is presented. This is done with reference to Figures 16 and 17 shown below. These figures portray the key arguments of each chapter represented in the vertical columns, together with emerging themes stated in horizontal rows that transcend these arguments. The final two sections (for PARTS 1 and 2 respectively) provide analysis of the key arguments from each chapter, followed by attention to emergent horizontal themes. The last section develops the final concluding commentary given the coalescence of these themes.

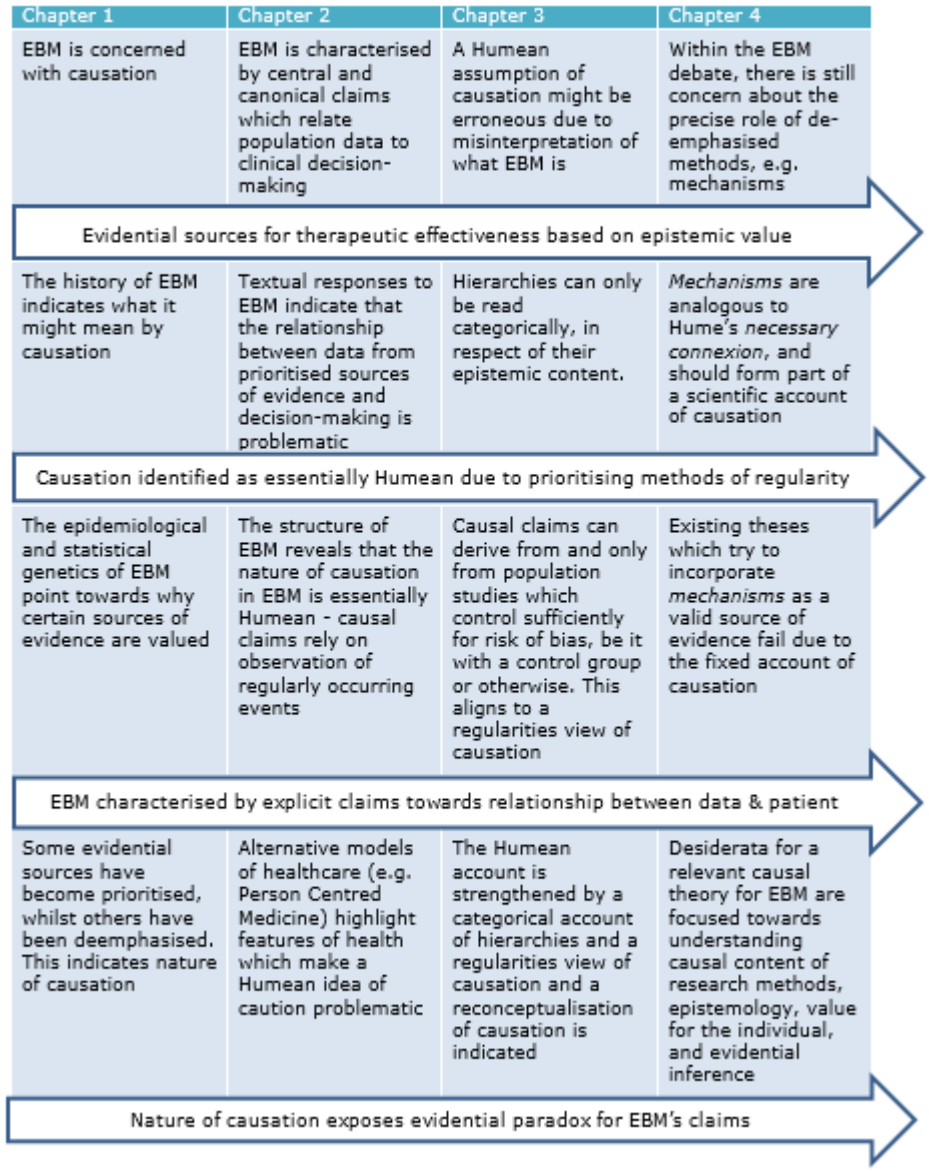

Figure 16: Vertical arguments and horizontal themes for PART 1

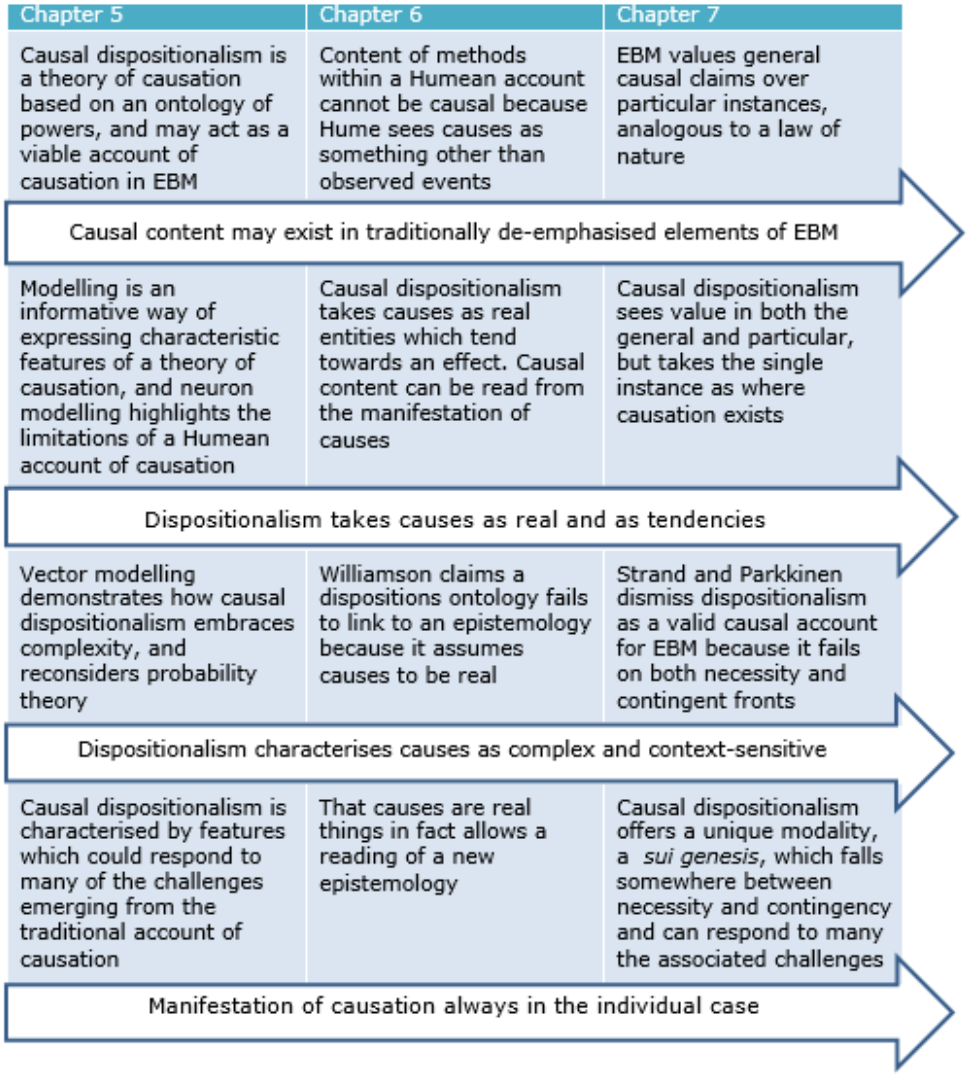

Figure 17: Vertical arguments and horizontal themes for PART 2

Key arguments of PART 1: Chapters 1 to 4

Chapter 1 introduced the post-1992 EBM movement as an opportunity to explore what health care means by 'it works'. One of the challenges was to identify the causal intentions, if any, of EBM from literatures that rarely talked in explicit causal terms. Much of the EBM literatures refer to 'best evidence for therapeutic decisions', 'most effective', 'comparative effectiveness' and so forth, even making explicit statements that causation is not even on the EBM agenda. However, to further support the causal propositions made in *Chapter 1*, my claim was that the terms used within EBM are mostly causal, and the fundamental intentions of EBM are strictly causal, for example: what causes disease, what causes people to get better. Effectiveness is a causal notion. This was backed up by the rich epidemiological history of EBM that - despite claiming to be atheoretical - seemed more open about its causal intentions. Perhaps EBM has always been conscious of the complexity, contentions and contradictions that exist in the study of causation *per se* and would rather avoid an open declaration that causation was at its core. It might be easy to side-step causation and talk about probabilities and comparative effectiveness instead. I hope I have made it clear here and elsewhere that such terms, especially probability, do not escape the problematisation of causation.

The statistical modelling and frequentist idea of probability inherent within the research approaches adopted by EBM further portrayed the causal intents of the movement. Attempts to reduce systematic error, controlling for confounding, reproducibility of methods and so forth all point towards an attempt to identify a relationship between variables that declares that in the presence of one (say, a therapeutic intervention), then

another (say, a health effect) will (to a level of probability) occur, and this occurrence is more likely because of that intervention than any other variable. This, again, is an overtly causal notion.

So causation was immanent, but without any identified theory of what was intended by causation. This was something that could now only be implied and interpreted through further analysis, which led eventually onto *Chapters 3* and *4*. This analysis utilised the hierarchical structuring of EBM to 'tease out' and understand precisely what causation was. The fact that methods that best controlled for risk of bias (those with good internal validity) were prioritised, whilst other more nuanced evidential sources were de-emphasised, would lead to a commitment of a causal theory.

So what of this? What the arguments of this chapter raise are questions about the validity and utility of endeavouring to force causal thinking onto a research and practice framework. Was this the right thing to do? Does the possibility of a causal theory matter? Could a philosophical inquiry into EBM be satisfactory without attention to the nature of its causation? One conceivable response might be to suggest that whilst some thoughts regarding the nature of causation might be possible, it is in fact inconsequential because causation is something that is not real. But this would mean taking an essentially eliminativist stance that committed to a denial of the existence of causation. I do not think that this is something even the strongest of EBM proponents would wish to admit to. After all, there is universal interest in, at least, whether something has an effect. It may be that the antithesis to this chapter is simply to continue with a denial of causation line. Having examined the history and statistical construct of EBM's methods, it seems that to actively avoid the idea of causation is at worst a denial, and at best a misinterpretation of what the

core research activity of EBM is about: effectiveness is causal, best evidence implies causal intents, probability is still a causal concern, *et cetera*. So at this stage, I found it hard to consider that a philosophy without causal attention could represent a complete philosophy of EBM. Indeed, the activities and intentions of EBM have yet to be provided with a substantial philosophy, and if validation of the movement is anticipated, then a philosophical account of its core activity is necessary. Accepting that causation is a necessary line of inquiry within a philosophy of EBM then, the conclusions of *Chapter 1* warranted further analysis of what a theory of causation looks like. This became the focus of *Chapter 2*.

Chapter 2 highlighted that EBM makes it explicit as to what it values as best evidence, and affirms a relationship between this evidence and therapeutic decisions. Indeed, the prioritisation of particular evidential sources and the recommendations for use of resultant data in clinical decision-making are the defining features of EBM. EBM, then, was characterised by its own the central and canonical claims that were focused around the idea that prioritised population studies are better placed to inform therapeutic decisions than other sources of evidence. Again, I saw this relationship as one wedded to the notion of causation – what causes an effect in populations and what causes an effect in a person. Yet this relationship has little explicit justification provided by either EBM itself, or philosophers concerned with this subject. The structure of EBM gave way to an analysis of causation from which I concluded that causation could be nothing more than regularly occurring events – a Humean view of causation. And this I saw as the crux of the problem.

This problem might not have been immediately apparent, but the consideration of what health care might truly want to be - a holistic world

that places the individual at the heart of its care – does exaggerate it. If person centred medicine represents a holistic vision of medicine and health care, then it gives a framework in which to cast some degree of judgement on a causal theory. If causation is not causation at all, but merely a mosaic of conjoined events on which all else supervenes, then what does this say about the values, preferences, aspirations, stories, cultural context, fears, worries and hopes of a human, or how does it recognise and respond to (their) emotional, social and spiritual necessities in addition to (their) physical needs? How does the statistical average representing high numbers of associated events speak to the individual and the clinician who cares for that individual? Is the causation exposed by EBM's hierarchical structure the same causation we want at the level of the individual? These sorts of questions led to a paradox whereby EBM intends particular methods to inform decision-making, but it is these very methods that expose a causal account that prohibits (philosophically) the use of their outcomes in individual decision-making: a wicked problem of sorts. This is because the Humean account does not see causes as real entities. However, if clinicians desire to affect the health of their patients, cause(s) need to be part of the therapeutic interaction.

Furthermore, the prioritisation of particular methods, I claimed, seemed to define and restrict what could be considered as causally relevant. For example it became apparent that mechanistic science and patient values could not easily be part of a strict Humean account. Although EBM de-emphasises these elements, it still implies that they should have a part in decision-making, but how can that be so if the causal account prevents their inclusion?

Chapter 3 served two functions. Its primary purpose was to strengthen the premises of the argument so far; its second was to enhance the landscape and detail of the critical features of the causal account defined by EBM. In terms of the argument, to this point the thesis rested on two broad assumptions. One was that evidential hierarchies have some epistemological function, and the other was that the population studies of sorts held the key to what EBM defines as the nature of causation, as it currently stands. There was still a chance that these assumptions were false and therefore supposing a Humean account of causation might also be wrong due to a misinterpretation of what EBM actually is. I set about enquiring into both background assumptions and initially presented an essentialist critique of evidential hierarchies, concluding that an epistemological-driven categorical reading of such was the only plausible stance. This was followed by a deeper inquiry into observational studies that indeed served to strengthen the position that causal claims derive from observations of well controlled regularly occurring discrete events, and as such the Humean account of causation was further validated as an interpretation of what sits at the core of EBM. This being the case, it now became even more of an interest to wonder about the role and position of the evidential elements that are de-emphasised in the framework. If the commitment truly is towards Humean ideals, then how should we think about sources of information (it now seems difficult to refer to them as evidential sources) that do not have a clear function in regularity? The thesis could have taken a number of directions at this point, and an appealing one would have been to focus on the function of the patient, and what patient and person values mean in a Humean account. Consideration of clinical experience, expertise, intuition, and case studies had equal

fascination. However, as much as the person is central to my being as a clinician, for this thesis I was always interested in research methods. It seemed peculiar to me that in the world there are numerous ways of deriving scientific knowledge, yet EBM had placed particular values on some but not others – for all the reasons elucidated so far. As such, I was minded to focus on types of scientific activity that seem to offer causal knowledge, but by virtue of the Humean idea within EBM, cannot do so. Namely, I was thinking about various types of mechanistic science and the intellectual rationale based on this type of research. Were we to completely dismiss mechanistic science as part of a causal story? By strict adherence to the Humean interpretation, it seemed so. Earlier in the thesis, I alluded to thoughts from Howick, and Russo and Williamson who, it seemed, had provided some commentary that could help with this problem. It seemed that now was the time to interrogate these commentaries more thoroughly. It may be that there was indeed a solution, and there was some way in which EBM's causal account could be inclusive of de-emphasised elements – particularly mechanistic science – whilst preserving all the valuable features of a Humean ontology. Further, it could be that the inquiry into mechanisms could act as a portal for reconceptualisation of the causal account in medicine and health care, should such be warranted. Mechanisms then, acted as the focus for *Chapter 4*. This built on the problematic detailed earlier, and edged towards further justification for an alternative understanding of causation in EBM.

Chapter 4 provided a commentary on mechanisms that represented an exit point for the analysis of the traditional stance. By now there was enough of a case to move towards a consideration of an ontological reconceptualisation. Mechanisms were put forward as a domain specific

example of Hume's *necessary connexion*, but where Hume could see no necessary connection, commentators on the philosophy of EBM think at least there should be some place for mechanisms in the causal story of EBM. Normatively, mechanisms could (Howick) or should (Russo-Williamson) have a causal role. Both of these aforementioned theses offered compelling arguments for the inclusion of mechanisms, but their pathway was repeatedly blocked by the very fact that all commentators still explicitly commit to Humean ideals. The theses still concede, when pushed, to accept that prioritisation of methods does exist. It becomes difficult, therefore, to understand precisely what utility is to be placed on de-emphasised evidential elements. Does this mean that mechanisms can be taken as causally informative in the *absence* of data from prioritised methods, or *with* such data? And what about situations when contradictory data exists? Are we to trust the prioritised methods then? But what then if such methods eventually reveal confirmatory findings of the original mechanistic science? It seems like, in both theses, causal utility from mechanistic studies is dependent on something external to the science itself. Even the compelling causal pluralism of Russo-Williamson falls short of satisfying answers related to what precisely we mean by causation from mechanisms, and how it can be accounted for in a Humean idea of causation. Consequently this review of philosophical thought concerning mechanisms, led to a point where we cannot move forwards without attention towards a reconceptualisation of the causal ontology, for it is the fixed adherence to a Humean account that is preventing progress. *Chapter 4* concluded with a declaration of desiderata for a causal theory relevant to EBM. These desiderata would form the framework for PART 2.

Key arguments of PART 2: Chapters 5 to 7

The move from what causation in EBM looks like *as it stands* (or stood) – the traditional stance – to the possibility of a reconceptualisation of causation was made in *Chapter 5*. The choice of causal dispositionalism as a possible alternative ontology was discussed and rationalised during the thesis introduction. Of course there are other alternatives. PART 2 was where the detail of causal dispositionalism could be played out in relation to what a causal theory for EBM should look like. The attraction of causal dispositionalism was that it explicitly assumes a conceptual framework of complexity and context-sensitivity. At face validity, the ontology sounds appealing for the messy world of medicine and health care. The characteristic feature of causal dispositionalism were presented in *Chapter 5* through graphical representation, in this case playing off vector modelling against traditional neuron modelling for causation. This served as an introduction. What became apparent was that a theory of causation based on an ontology of powers seemed, at this stage, to offer some answers to the emergent challenges from the traditional stance. It was now important to understand if a dispositions alternative could respond to the most direct challenges as expressed by the set desiderata.

The first two desiderata were addressed in *Chapter 6*. These were concerned with an explanation of the causal role of content from methods, and the relationship between a causal theory and an epistemology. The play-off with Strand and Parkkinen was always going to involve the unravelling of their argument to constantly reveal the same Humean limitations due, again, to a fixed idea of what constitutes causation. Whilst their explanations of causal content were concerned with the robustness of

comparative methods used in population studies, their argument did in fact offer little new in terms of progress of a relevant causal theory. The response of causal dispositionalism was fairly straightforward. Causal dispositionalism takes causes as real entities, and so explanations surrounding examples of causation are read directly from the manifestations themselves. Further, causal dispositionalism is not dismissive of existing methods, and relates well to varying views of causation. It is just that a dispositions ontology does not see these methods as constitutive of causation. That is something else.

That causes are real was also a stance for the second desiderata on epistemology. Although Williamson has used this exact stance as a case against a dispositions account, it offers a way in to consider and underpin a notion of evidential pluralism, as well as allowing a reconceptualised reading of outcomes from, say, population studies.

The final two desiderata were considered in *Chapter 7*. These were both concerned with the relationship between population data and individual-level clinical cases. The way EBM explicitly values population data was set up to be analogous with a commitment to the existence of laws of nature. Within this brief analysis, dispositionalism was offered as an account that is able to value both general and particular instances, but clearly differentiates itself from the traditional stance by taking single instances as the place where real causation exists. This aligns more suitably to aspirations for a person centred medicine, and is something that starts to look like the constituents of a person centred notion of 'what works'. Opponents have tried further to reject a non-Humean (and specifically dispositional) causal account on the grounds that an ontology not invested in something predominantly frequentist must fail in accounting for the

assumptions needed to successfully traverse an inferential gap from data to patient because its ontology commits to neither necessity nor contingency. This is a mistaken stance, and serves only to offer an opening to demonstrate that a dispositional ontology is unique as a causal account as it possess a *sui generis* modality, falling somewhere between necessity and contingency. In this way it avoids many problems associated with inference, especially, for example, the problem of induction. The response to the final desiderata gave a way to consider the essence of what dispositionalism takes causes to be: something that *tends* towards a manifestation, but never guarantees (probabilistically) such.

Having now drawn some conclusions from the summary of key arguments of each chapter, the thesis will end by considering a coalescence of the emerging themes from each of its two parts. This coalescence will allow a final conclusion to the thesis to be made through the exposure of a metanarrative. Within this, comments are given as to what work the thesis has done, together with directions for future research and analysis.

Final conclusions

To talk about the ontology of causation in EBM was never anticipated an easily navigable path. Least of all because the vast majority of literatures within EBM have not considered it a viable or necessary approach to the EBM narrative. I have claimed, however, that the issue of causation is central to EBM and the relevance is visible throughout the history and structure of EBM. A central theme to PART 1 was that in terms of therapeutic effectiveness, evidential sources are organised based on their epistemic value. However, within the analysis and reconceptualisation of a

causal account, it was proposed that causal content may exist in traditional de-emphasised evidential sources, the example in this thesis being mechanistic science. As such, there seems to now be an indication that the epistemic worth of numerous components to the therapeutic decision-making process might be reconsidered. This reconsideration has been permitted by the possibility of a change of view of what we might now mean by causation. I am now inclined to conclude that the type of story presented in Appendix 1 can be better understood, philosophically, with a revised account of what causation might be. Framing the clinical story in causal terms is not usual practice, but for the purpose of philosophical exploration it serves a critical function. When the patient is talking about interpretation of ('higher level') evidence in the context of the patient narrative, what we can say is that there are elements of that narrative, and the associated mechanistic background (in this case, say, bone healing and non-steroidals) that are causally relevant phenomena. Dispositionalism has offered a notion of evidential pluralism. Contextualising each possible element of evidence, if allowed to be thought of as causally relevant, aligns with how dispositionalism thinks of causes when they mutually manifest to reach a threshold. This is the clinical method, but the clinical method has difficulty surviving in the EBM structure. Rather than talking of cases that fail to fit the predictions from prioritised methods as atypical, or rather than talking about external validity and so forth, we can now understand such cases as being the very key to what causation is and where it exists. The Humean world exposed by evidential prioritisation does not even allow a conversation about singular causes because it does not take causation to be real. Yet people change, diseases happen, health states improve. The acceptance of the reality of causes in a dispositions

ontology at the very least allows us to work out and explain how a singular case behaved irrespective of the most relevant population data.

The relationship between these data and the patient was always at the centre of the thesis. Indeed, EBM is characterised by its explicit claims towards this relationship. Dispositionalism has offered a way out of many of the traditional challenges to the assumptions and premises required to bridge the inferential gap. This is because a causal account based on dispositions would make no inferential claims anyway, causes can only tend towards an effect. And the strength of that tendency is related to the complex interactions of many causal factors. Further, the manifestation of an effect is highly context-sensitive. With this in mind, dispositions take the single case as the starting point for the causal story – this is where causally important substance exists. As such, there is no gap to bridge. Of course, dispositions relates to population data from varying methods, but does not see such structures as being constitutive of causation, rather, symptomatic. In our case study, the patient narrative was the desired starting point. Resistance due to the traditional stance made this troublesome throughout, and furthermore could not account for the favourable patient response. How was our patient being viewed? From the population data downward, as a patient. Have we been looking through the telescope the wrong way? Have we been looking at patients with no causal agency, rather than people with the key to causation?

The evidential paradox inherent within the traditional structure of EBM need not be so. The epistemic reading from traditionally prioritised methods need not restrict the relationship between that data and the individual. Manifestation of causation is, according to a dispositional account, always in the individual case.

So where now? I am confident that this thesis has answered the questions it set out to. We now know what causation in EBM looks like, we know that this interpretation is insufficient for EBM to meet its own claims, and we know that there is a possibility for a reconceptualisation of a causal theory within EBM. This work contributes to the extant literatures within the philosophy of EBM because it takes a bold move to begin a conversation about ontological matters in a field where such a conversation has been repeatedly stamped out due to obstinate Humean commitments. The dialogue between the features of this thesis and Strand and Parkkinen is an example of the unique conversation that can now be allowed to develop. The current philosophy of EBM is incomplete. The most striking contention is in the field of causation. This work has problematised the traditional philosophy and made advances towards an alternative discourse. The implications of this relate to the alignment between a thesis on causal ontology that places the human at the centre of the scientific framework, and corresponding activity regarding person centred care. This comes in numerous guises such as the *person centred medicine* movement referred to in the thesis, and also 'shop-floor' movements such as a *campaign for real evidence based medicine*. This thesis goes a significant way to offering part of a philosophical explanation and justification for such movements.

There are, as expected, more questions than answers. This thesis has merely glanced at the idea of reconceptualisation of a fundamental notion in a particular area of real-world science. Further research is thus, of course, indicated. This should now be focused towards the continued development, analysis, and testing of the causal theory; a considered approach on working towards a restructuring of evidential frameworks;

and furthermore, a rather ambitious programme that might entail the development of unique scientific methods that embrace, rather than control for, the complex and context-sensitive causal worth of multiple person-centred clinical factors.

The ambitious programme would be to further prepare the philosophical ground for a possible paradigm shift in medicine and health sciences. This would have impact on how we understand human health as a complex, genuinely emergent, and individually unique matter. As a result of further research, new methods and guidelines would need to be developed for EBM and related health care disciplines. Future work should focus not only on ontological dimensions of a theory of causation, but from this point onwards be prepared to address concerns related to conceptual, methodological and practical aspects of a broader programme.

We have had, at the very least, two and half centuries of causal thinking on Humean terms. To change how we conceptualise causation is a major task. But medicine and health care offer us an opportunity. When I worry about 'what works', I instinctively worry about the person in front of me and their story. This is not a reaction that relates to 'what works' for Hume the philosopher. However, we as people may hold the key to a world where causes are real. Maybe Hume the person thought the same.

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Appendices

Appendix 1: Case Study

This is a transcribed narrative from a patient talking about their experiences within the health care system.
Original source: Real vs rubbish EBM: what is the state of evidence based medicine, and is it broken?
https://www.youtube.com/watch?v=qYvdhA697jI

[segment] "Now I'm going to give you a case example. People have been saying to me today, 'God you've had a difficult year, haven't you? How's your neck, how's your whatever?' So I thought I'd use myself as a case. I would say that although I'm going to challenge, and in fact directly criticise some of the management that I had, this is not intended as a complaint against people who were managing me. This is intended as a fairly in depth discussion of a case to ask, 'what can we learn from this? What can we learn about EBM? What can we learn about the use of guidelines?' Cos I was certainly managed according to guidelines. Um, those of you who follow me on Twitter might have seen this tweet (Tweet reads: Bad bike smash. In hospital 2 broken arms, on today's 'trauma list'. Thanks to kind bystanders and #NHS. Sorry will be out of action UFN). I certainly got quite a few dozens of replies when I tweeted that I'd fallen off my bike, I was in hospital with 2 broken arms and I was on the trauma list.

Um I tweeted lots of pictures of my bruises, um I tweeted pictures of me being patched up by nice happy nurses, I tweeted pictures of my physiotherapy, and finally a month after it all I was feeling quite a bit better. So that was my case. Um, let's start off then, as I think we should always start off by having a history from the patient, a subjective narrative. I was riding my racing bike along the towpath. I was going about 20 mph, it was a bright sunny day, um something got caught in my front wheel, perhaps it was pushed, but perhaps it just rolled in. The whole bike went up in the air and somersaulted and I came down very heavily on concrete, landing very heavily on my arms and also the back of my head. I was very dazed, but I don't think I was knocked out. Both my arms were deformed and completely useless and I had marked numbness in the fingers of my hands and my helmet was split. This history was distilled into a couple of sentences from a junior doctor. On the ward round the next day: '55 year old female. Fell off bike' (laughter). And I was channelled into the falls algorithm (laughter). Now the irony of that is, when I fell off the bike I was only 54 (laughter), but by the time the ward round came round 2 days later, I had become, I had met the criteria for being in the evidence based guidelines for falls prevention that happens the day you turn 55, that unfortunately was the day that I was in there. And so, this is actually from the CDC in America and actually the particular falls prevention guideline that was used on me was not this one, but it was one remarkably similar and I can report that what happens when you're lying in a hospital bed, wondering how you're going to eat the food they've put on the trolley in front of you cos your arms don't work. Um, you get a nice lady coming in, in a white coat with a clipboard and the first question she asks you is, (shouts) 'can you hear me?' (laughter). And I was offered a home visit to

make sure that the rugs were taped down, um and that there was a rail to help me get out of the bath and all that kind of thing which I politely declined. Now I hope you can see the mismatch between the narrative here, and the guideline that I found myself channelled into, although I met the criteria. I WAS a 55 year old female who had had a fall. Let me give you now some more objective um data on what happened. I had, over the next 4 months, 7 operations to put the bits of bone back, put in metal, get metal out. The numbness in the fingers persisted and I went along to out-patients and was reassured by a very confident junior doctor, 'look dear, you did break your arms, you will expect to have numb fingers.' Um at 6 months I had another review, actually with another doctor at another hospital, I'd decided to change by then. I had wasting of the muscles in both hands and was also noted to have heaviness, clumsiness and hyperreflexia in the legs, including quite marked ankle clonus that was shown to the medical students. Um no one was more surprised than me. I was sent off for an MRI scan that showed severe cervical disc prolapse at 2 levels and 2 collapsed vertebrae. Now we will never know whether those vertebrae were fractured at the time of the bike crash or whether they collapsed subsequent to the disc prolapse. Um, I went along and had a very successful cervical disc replacement at 2 levels. Here is another guideline. This is the NICE guideline for selection of adults for imaging of the cervical spine (Slide shows NICE guideline with section highlighted): Adults presenting to the Emergency Department who have sustained a head injury. Um, now my helmet was split so I think I can definitely say I came down on my head. Now I fit the criteria here (slide shows second highlighted section): Dangerous mechanism of injury, fall from greater than 1 metre or 5 stairs. Well I can tell you I was right up in the air and

flipped over, so definitely more than… and an interesting piece of… this ejection from motor vehicle (read from 3rd highlighted section on slide). Well my vehicle wasn't motorised but I was certainly motoring along and I was ejected. Now it's a very good example I think of the interpretation of the guideline, (sarcastically) 'well hang on a minute, it didn't have an engine so it doesn't count as an ejection'. Or would you look at that guideline and think, 'hmmm, it would be a good idea to x-ray this patient's cervical spine'. The learning point here is it takes judgement to decide which guideline to follow, and how to follow it. An over-55 year old female with a fall may also be an athlete with a high impact hyperflexion injury of the cervical spine. I would encourage you to get hold of this interesting book by Bowker and Star. One of the chapters in the book, they take apart I think what was then the ICD9's (now the ICD10, that's probably ICD11 by now) International Classification of Diseases and what they say is, we create classification schemes. Another classification scheme is you know 'old ladies'. Well 'old ladies' is over-55 and once you're in that um once these classification schemes become enshrined in guidelines and protocols they ossify and reproduce our assumptions and prejudices. Furthermore it makes those assumptions and prejudices appear scientific. Um and Bowker and Starr demonstrate that by creating these categories um we then channel our prejudices in particular directions and it's then quite hard to draw back from them. There are at least three people at this conference, and I'm really sorry to these people because they're kind of my friends as well, but I'm sorry I'm going to use you as an example… um who said to me, 'hang on, you didn't need that operation. There's been randomised trials which have shown that in cervical disc lesions, the surgical groups didn't do any better. So

really, you shouldn't have had that operation.' They said that without taking a history, without finding out what the examination showed, without looking at the MRI findings and without acknowledging what the inclusion or exclusion criteria were for the trials. And it's a good job they did because I think it was a great example of rubbish EBM. Sorry guys. Let's have a look at those trials. Here's one. Um surgery versus non-surgery in cervical radiculopathy (which is what I had). Um prospective, randomised, ticks the methodological boxes and it showed that initially the surgical patients did better, but then after two years you know the medically treated patients caught up with them so why bother having the operation in the first place? And so it says, 'structured physiotherapy should be tried before surgery is chosen.' But look at the exclusion criteria: obvious myelopathy, slight intermittent signs of myelopathy even in the absence of objective findings, a history of neck distortion… um so those who were saying… oh and these patients hadn't had any physiotherapy. I'd had four months of physiotherapy! So wait a minute guys! This I think is a classic example of the use of evidence, this is Grimley Evans, you must know this quote, 'in the manner of the fabled drunkard who's searched under the street lamp for his door key because that's where the light was, even though he'd dropped the key somewhere else'. Um and again Grimley Evans was writing that in the 1990s – we do it too much! Let's go on. So having decided that my operation was actually going to be evidence based, you know this is my jugular vein and carotid artery we're talking about, I DID look up the evidence before I signed the consent form. Um, the surgeon advised me not to take NSAIDs for a month following surgery because he said, 'there's SOME evidence of delayed healing of the bone repair, AND the risk of bleeding is higher in the post-op period'. So this

was a very simple question for me. I don't want to bleed, I don't want delayed healing, but I don't fancy going round in pain, and people who've had this operation, it's pretty painful for a few weeks afterwards. So of course I got onto Twitter. It's great, you should join Twitter, it's absolutely fantastic! So this is me (screen shows Twitter feed: 'Anyone got an evidence base for 'don't take NSAIDs when recovering from disc replacement surgery? Or indeed for the counter-argument?'). Um, and speaking as a patient, I didn't tell them that, but you know whatever… So somebody tweets back, and this is a really good example of this rubbish EBM coming from the EBM community (screen shows responses to TG's original tweet): 'if you're not worried about the evidence for disc replacement, then don't worry about the non-steroidals'. But he also says, 'actually the evidence is pretty weak, the evidence on healing blah, blah, blah'. Other people were saying, 'no, I routinely prescribe non-steroidals after a discectomy, very good painkillers, opioid sparing, they get you up and about.' So good reasons. This is again interpretation of the evidence. And I like this one (new tweet shown on screen). This one really made me think. This is someone who, I'm not sure who this person is. 'Lumbar discs, yes take non-steroidals, cervical discs, ACDF, anterior cervical discectomy and fusion, not in the first 24 hours because when and if they bleed, the airway is often compromised'. So suddenly, yeah, it's not very likely that you're going to bleed, but if you do it might be catastrophic. So this is kind of scary, so I started looking up the evidence. I'm not going to give you very many of these cos there's dozens and dozens of these studies. This is just one of many (screen shows study abstract with highlighting). Look at the pink bits, this is an animal study. So they go in and they take rats and deliberately break their legs and then they put some

on non-steroidals and some not. Um and sure enough, if you treat rats like that, and you put them on non-steroidals, they're less… they have delayed healing. Um, then there's sort of retrospective case controlled studies of patients with a different kind of fracture who have had non-union. Looking back they have been more likely to have taken non-steroidals. Loads of studies like that. Okay, let's get a decent systematic review. I love this conclusion in this systematic review (screen shows abstract with highlighted section): 'animal and in vitro studies present such conflicting data that even studies with identical parameters have opposing results.' So the evidence is an absolute mess. But they say, well in the absence of better evidence, you're probably better off not prescribing non-steroidals blah, blah, blah… All right, let's have a more up-to-date systematic review, and they go back and they simply say 'more research is needed'… So this isn't getting us very far. We've got this mountain of evidence that is methodologically flawed, it's small, it's under-powered, it's goodness knows what. What do I do? And this is the point I want to make. So many people then conclude we need to start all over again, with another enormous trial. But let me show you what happens. If you take a more detailed analysis of the patient in front of you. So what we've got here is the objective evidence: non-steroidals inhibit the same kind of prostaglandins that are involved in bone healing, animals given non-steroidals showed slower healing of induced fractures, people with delayed healing were more likely to have taken non-steroidals. This is all pretty low down the hierarchy of evidence. In randomised trials, post-surgical patients had a higher incidence of GI bleeding. So that's the objective evidence – we know that, we know that. Now let's look at the individualised evidence about this particular patient (screen shows slide

detailing individualised evidence about this patient). So the first thing about this patient is I was, I am an ex-elite athlete. Anyone who has done sport at any kind of level knows that your coach is paid to train you to within an inch of your life and then to fill you up with non-steroidals to cover the pain in your recovery period so you can get back up the next day and do even more training. Um, I've taken non-steroidals for 30-odd years, never had any problems with them. So that's the first bit of evidence. The second bit of evidence is that as part of my sports obsession, I think I'd call it when I was younger, I encountered several stress fractures, all of which healed very quickly indeed on non-steroidals. And in fact, healed rather more quickly than I was led to believe would be the natural history. So people would say, 'you're going to be off your sport for 6 weeks', I was only off for 3 weeks. So for me PERSONALLY, non-steroidals do not appear to delay MY bone healing. I don't know about you, but for me… And we do know that with some confidence. (Reads from the slide on the screen): This patient has had adverse reaction to opiods in a dose-dependent way. So in this patient, the option of jacking up the opiate dose isn't an option. This patient has had a particularly difficult operation – the surgeon came in quite late at night after the operation, was absolutely exhausted, was going to go home to bed, had cancelled his evening thing because the whole operation had taken several hours and he said this was a very, very difficult operation. 'You will probably be in considerable pain'. So I said, 'well I already am in considerable pain'. And, I think Fi's in the room, I'd had a call from Tony D, this was Monday, and I'd had a phone call from him saying, 'look, if you're off sick with that operation, could you just do us an editorial and get it to me by Friday' (laughter). So that had to be… and I did! In conclusion, in this particular patient, it's all

much easier now isn't it? Now that we know this patient based evidence. Given the history, given the clinical picture, and given the equivocal nature of the evidence, the benefit-harm balance appears to be in favour of non-steroidals, especially after the first 24 hours. So I, in consultation with my surgeon said, 'right, I'll stick it out for 24 hours and then I'm going to go on non-steroidals' which I did, and I healed absolutely fine. So let me conclude, this is the uncontroversial conclusion, and I think it's uncontroversial. Whenever managing a patient, ask yourself, 'is my management of THIS PATIENT in THESE CIRCUMSTANCES an appropriate or inappropriate application of the principles of EBM?' I also think it's fairly uncontroversial, and quite important, that EBM experts, most people in this room probably call themselves that, should avoid pulling rank on experienced clinicians by citing irrelevant randomised trials, out of context where they don't know the patient. And I mean that very, very seriously. Um, but here's a more controversial, and I think more interesting, conclusion. If we practice patient-focused, individualisation of the evidence – that is 'real' EBM – we will often find that more research is not needed. Perhaps the uncertainty in science is inherent. And this is a philosophical point. Um, perhaps we need to return a bit more to old-fashioned clinical method and use EBM slightly less comprehensively."