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Evidence Based On What?

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At 21 years old, evidence-based medicine (EBM) is an established central pillar of modern healthcare. The model continues to intentionally develop its structure and meaning on an almost monthly basis (Guyatt et al. 2011). In-line with this, an untiring body of literature aims to analyse its strengths and limitations: often provocatively (Cartwright 2011, Seshia and Young 2013), sometimes sympathetically (Djulbegovic and Guyatt 2009, Cipriani 2013). Studies have also examined the quality of data being used in EBM, questioning its value and trustworthiness (Ioannidis 2005, Pereira and Ioannidis 2011, Kerry et al. 2013). Further, there have been moves to suggest alternative modes of practice, specifically person-centred medicine (Miles and Mezzich 2011, Miles and Asbridge 2013).

Conceptually, the vast majority of the critique is focussed on either EBM's epistemology (what methods produce what evidence) or its mechanics (what's the best ways to implement it). After two decades of witnessing successes and limitations, it is now both possible and timely to consider the very foundations of EBM and how fit-for-purpose these are. Such an inquiry will promote and facilitate future development of the model, especially regarding translating population data to individual cases, and the relationship between epidemiological and mechanistic data – both central and stubborn concerns of EBM critics (Muckart 2013, Clarke et al. 2012).

It is uncontroversial that health care practice should be based on evidence. But on what is this evidence based? And what is it evidence of? The first question concerns methods: evidence could be based on correlation data, randomised controlled trials (RCTs) or mechanistic knowledge, for instance. The second question is conceptual and concerns causation: an unavoidable matter in healthcare research, e.g. what causes disease; what causes people to get better, etc. Paradoxically, in EBM there is a tradition of avoiding matters of causation and accepting only the statistical facts, from which a type of causation is often inferred (Thompson 2010). From a philosophical perspective, there is a contested theoretical basis for sticking to correlation data (Cox 1992). Existing methods of medical research to a large extent cohere with an understanding of causation dating back to David Hume's 1739 *Treatise*. According to Hume, causation is nothing more than correlation or regularity. Others have since argued that it is something more (Lewis 1973). The corresponding debate can be seen in medicine, where the different approaches to causation are reflected in the hierarchical ranking of evidence: evidence for an intervention's effectiveness is considered stronger when derived from comparative studies like RCTs, than from mere population studies (Balshem et al. 2011).

Irrespective of one's commitment to causal interpretations of data, evidence-based medicine rests its evidence extensively on large scale population data. Such statistical studies are thought to

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provide the relevant evidence for guiding medical practice. But is this type of evidence generally justified? This viewpoint offers an alternative perspective, both conceptually and methodologically.

From a conceptual perspective, instead of focusing on correlation data and observed regularities derived from population studies, it is proposed that evidence needs to be evidence of causation, and causation should be understood in terms of tendencies (Mumford and Anjum 2011). Typical for such tendencies is that they can be counteracted by others, which means that all causal processes can be interfered with, or even prevented. Arguably this fits better with scientific practice. Tendencies come in degrees and are not a matter of all or nothing. Oral contraception causes thrombosis but the tendency is only small, affecting around 1 of 1,000 women (Stegeman et al. 2013). If we look for robust correlations, we would have to explain how causation could fail in 999 of 1,000 cases.

There is also a methodological concern about how the various approaches relate. If medical practice ought to be based on evidence gathered by a range of research methods, then these methods had best give evidence of the same thing. Arguably though, different methods do not give the same results. Rather than pointing in the same direction, different methods commit us to different concepts of causation (Kerry et al. 2012).

To consider uncontrolled observational studies as solid sources of evidence for causation commits us to a Humean regularity view. To test such correlations further, we rely on controlled comparative studies or RCTs. RCTs allow comparisons of two or more groups to see whether an intervention makes a difference. This is to commit to a difference-making concept of causation. A fundamental assumption in both regularity theory and difference-making theory is that the same cause will produce the same effect. If a treatment works for a group of patients, we expect that it will also work for other patients that fall under the same group. It here becomes essential that a patient is defined under the right sub-group. If a treatment does not work after all, we assume that this is because of a causally relevant difference. When this causal factor is taken into account, this should suffice to infer that if a patient falls under that sub-group, the response to the treatment will be the same. This line of reasoning can continue indefinitely. The aim is to narrow down the sub-group sufficiently to be able to make a qualified inference about all members of the sub-group. A problem with this strategy is that the most relevant sub-group is always the N-of-1 group.

When perfect correlations are not found, population data can be interpreted probabilistically. We might find that a certain intervention has an effect on 3 out of 10 people. EBM is premised on such data being a fundamental empirical basis for guiding and informing individual clinical decisions. But how does it do so? Is it a 0.3 chance that the patient belongs to a sub-group where there is a 100 percent effect? If causation is a matter of all or nothing, as the regularity theory suggests, then specifying the right sub-group is essential. Alternatively, we can give a stochastic interpretation, saying that this patient has a 0.3 chance of responding to the intervention. This commits us to a probability-raising theory of causation. A statistical frequency is then directly transferrable to the individual patient. However, such a population-informed ascription of individual probabilities continues to be problematic (Robinson 2009).

The concept of causation is, at least, linked to the idea of probability. There are various theories of probability, and the theory on which health care population studies are grounded is that of

frequentism (Whitehead 1993). On this view probabilities are determined by the distribution of outcomes over a sequence of trials. But then a question is whether the sequence of trials is a representative sample. A coin could land heads 6 out of 10 times but we do not infer from this that the coin has a 60:40 chance of landing heads. A second theory of probability is a propensity one, linking probability to intrinsic properties of an individual or situation. Saying that a coin has a 60:40 chance of landing heads would on a propensity theory mean that the coin is biased.

One concept of probability does not automatically transfer to the other. When making a clinical decision about an individual treatment, it matters to the patient at least whether he has a genuine propensity of responding to the treatment or whether it is just a statistical fact that many others in the group have responded. Placing the individual at the centre of clinical decision-making seems intuitive, but is counter to contemporary trends towards health care being driven by population study data. By taking causation to be tendencies, and such tendencies as providing an ontological basis for propensities, we argue that causation occurs in the particular instances. Since no two instances will be exactly identical, we should not expect that the same intervention will always have the same effect, even in broadly similar cases. This gives ontological and conceptual support to N-of-1 trials over large-scale population data, and to person-centred medicine. It also gives support to mechanistic and experimental approaches.

If this is correct we need a reinterpretation of what type of evidence existing methods can offer: population studies of statistical data could indicate causal tendencies; RCTs may reveal the strength of those causal tendencies; knowledge of sub-groups could indicate how these tendencies compose with various other causal factors. Evidence of true causation however would be established through mechanistic studies, and by understanding the relevant features of individual patients. This means that, on our preferred model of causation, all methods could point to evidence of the same thing and evidence can have a more stable base.

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