Variety, Reliability Confirmation and Drug Safety

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1 Background

While Randomised Controlled Trials (RCTs) reign supreme in the Evdience Based Medicine (EBM) paradigm for the determination of efficacy of drugs, the role of "lower level" evidence – such as mechanistic evidence – is significantly enlarged for safety assessments. An ever growing number of philosophers of science argue also for a more prominent role of "lower level" evidence for efficacy considerations.

There are a number of reasons for the more prominent role of "lower level" evidence for drug safety within the EBM paradigm. The most compelling reason is in my mind a numbers argument. Side effects occurring in one of ten thousand patients may be deemed unacceptable, see Food and Drug Administration (2009). Since RCTs have – almost always – much fewer than 10.000 patients in the treatment arm(!), RCTs are much too small to pick up rare but severe side effects. Furthermore, it is unethical to ask patients to take part in a study to establish the *harmfulness* of a drug.

To assess the (un-)safety of drugs it is hence imperative to take into account every bit information which could possibly offer insights into possible side effects. This presents the challenge to amalgamate statistical data and mechanistic evidence to form a view informed by *all the evidence* on the (un-)safety of a drug.

2 Evidence Amalgamation

Frequentist statistics has no principled means to amalgamate evidence from trials and mechanistic evidence. The Bayesian approach to scientific hypothesis con-

firmation, e.g., Bovens and Hartmann (2003), does offer such a mean and it has been adapted for the assessment of adverse drug reactions in Landes et al. (2017).

Not only does this framework allow for a principled approach to evidence amalgamation, it also allows an analysis of epistemological value of different kinds of evidence. Philosophers have long pondered the epistemological thesis that ceteris paribus, varied evidence speaking in favor of a hypothesis confirms it more strongly than less varied evidence, Horwich (1982); Earman (1992); Wayne (1995); Steel (1996); Myrvold (1996); Fitelson (1996); Bovens and Hartmann (2003); Claveau (2013).

3 Vested Interests

Evidence for medical inferences is often produced by researchers which have (financial) ties to pharmaceutical companies. Such evidence needs hence to be evaluated in light of the reliability on attaches to the evidence. The frequentist approach does not possess principled means to take assessed reliabilities into account. By contrast, the Bayesian approach of Landes et al. (2017) effortlessly incorporates assessed reliabilities.

4 This Talk

In this talk, I investigate the notions of *varied evidence* and *reliability*, their interplay and their contributions towards hypothesis confirmation within the framework of Landes et al. (2017). In particular, I shall show how one can explicate the notion of *varied evidence*, how too much positive evidence leads to a sharp drop in assessed reliability (too-good-to-be-true evidence) and whether the hypothesis of interest or biases are more likely given the available evidence.

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