

MAIMON WORKING PAPERS No. 8 JUNE 2021

ISPOR SCORES ITS TECHNOLOGY ASSESSMENT OWN GOAL: SIMULATION MODELS AND HUME'S PROBLEM OF INDUCTION

Abstract

The rejection of hypothesis testing in favor of creating approximate information in health technology assessment has been assiduously promoted by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) for many decades. Unfortunately, this embrace of invented information was dead on arrival; leading to the creation of claims for cost-effectiveness and product access based on assumption driven simulations. This decision overlooked, or more probably was blissfully unaware of, one of the most famous arguments in philosophy: Hume's problem or the impossibility of justifying future or unobserved expectations on the basis of past observations. If this problem of inductive inferences cannot be resolved – and continues to be unresolved – then there are no grounds for believing that simulation modelling in health technology assessment based on assertions and assumptions are anything but a succession of pointless exercises..

INTRODUCTION

Hume's problem, the impossibility of inductive inferences having any foundation other than wishful thinking or just guesses, is one of the most famous in philosophy with, for our purposes, particular reference to the philosophy of science ¹. Neglect of Hume's problem, renders any notion of predictions based on a vague concept of approximate information a travesty. Certainly, simulations can be constructed to make any unevaluable prediction based on assertions and assumptions. To argue that past experience justifies their choice is a step too far. We have no basis, nor will ever have, to come to conclusions that go beyond previous experience. The only basis is psychological; our belief, not in formal causal inference, but casual association.

It is unusual, indeed unique, for a game to be decided some 250 years before kick-off. In the language of the immortal game of soccer, the Institute for Clinical and Economic Review (ICER) and their mentor team, the world of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) scored their own-goal before the game had ever started. The game is a defense of simulation modelling; the creation of approximate invented information through models based entirely on assertions and inferred assumptions and with no pretense to provide anything other than non-empirically evaluable claims ². The own-goal is to uncritically embrace induction. Due to a lack of appreciation, indeed an outright rejection, of the rules of elementary logic, the ISPOR (and ICER) reference framework collapses. Certainly simulation models can be built, but we can never formally judge one model in any way superior to another with the common and fatal flaw that none conform to the standards of normal science. They are entirely constructs of the imagination; in some cases highly fertile imaginations with tools such as probabilistic sensitivity analysis to attach a likelihood to an imaginary claim decades into the future ³.

HUME'S PROBLEM

The problem raised by David Hume, originally formulated in *A Treatise of Human Nature* (1739), concerned the grounds for forming beliefs about the unobserved⁴. How are we able to justify expectations or predictions about observations not yet made? What is the status of inferences made from the observed to the unobserved, so called 'inductive inferences'? While such inferences are commonly made as part of everyday life, the question is how do rationalize this when we are faced with a dilemma that rules out the possibility of an inductive inference process to create knowledge.

The dilemma concerns causality; can there be a causal relation that links our experience to expectations? The experience of constant conjunction where if an object has always been associated with an effect other objects which are similar will always be associated with similar effects¹. This leads to a uniformity claim that instances of which we have no experience will resemble those of which we have experience. For Hume, there can be no reasoning behind this uniformity claim. Hume bases his argument on his distinction between what he calls relations of ideas and matters of fact. The former include propositions that can be affirmed without reference to external observations or facts. The latter are empirical observations. Hume argues that relations of ideas cannot demonstrate reasoning because they cannot be false. They are matters of proof. Empirical observations and associations also fail the test of reasoning, even if considered in probabilistic terms, as they are based on the supposition that is taken for granted that the future will be conformable to the past. There is no chain of reasoning which is not circular¹. We cannot justify, other than by belief, a psychological defense, any claim that the past will support a claim on the future. Imagination underpins inductive inferences.

In terms of simulation modelling, driven by assertion and assumption, we have no reasoned basis for believing that any claims for past associations (e.g., the utilities associated with a disease state) will hold in the future. Certainly they may be associated in the past, but may just be happenstance. There is no rational argument for claiming a future occurrence even if, for example, we argue on the grounds of a high probability given the many associations recorded. As Bertrand Russell notes: a chicken may have been fed regularly every morning for months to fatten it up, yet its expectation for its now last morning is dashed when its neck is wrung⁵. The chicken, presumably, was not aware of Hume's problem.

While considerable effort has been devoted to attempting a refutation or reformulation of Hume's dilemma, the most persuasive view is that of the inductivist skeptic; to accept the proposition that inductivist inferences cannot be justified by any rational argument¹. The issue is, of course, that in everyday life our mind makes inductivist conclusions and decisions. Given this, it seems appropriate to see Hume's problem of induction as one that arises at the philosophical level which makes it entirely appropriate as a fundamental argument to reject modelled lifetime imaginary simulations that rest on assumptions and assertions, and that are designed to generate claims that lack credibility, empirical evaluation and replication. This last caveat is important: it does not deny that both induction and deduction can play a role in formulating tests and testing credible hypotheses. The

scientific method does not rely on deduction alone; but we are not dealing with the standards of normal science. We are dealing with pseudoscience; with intelligent design not biological evolution. More importantly, the question of inductivist skepticism is not restricted to a philosophical problem but, more significantly, is an existential problem. Where inductivist claims are made based on data collection and modelling, the outcomes in simulation modelling, indeed the acceptance of the inductivist modelling paradigm, must be rejected out of hand. It should never have been considered in the first place as a believable alternative to hypothesis testing.

DIGGING A HOLE

A common aphorism is that if you are in a hole, stop digging. Unfortunately ISPOR (and its attendant acolyte ICER) have, in the continued affirmation of the gold standard paradigm of 'approximate information' modelled simulation for creating evidence, made the hole that more deep. The starting point is the commitment by ICER, following the standards of health technology assessment established by groups such as ISPOR, to the creation of approximate information. This was a short-cut, to avoid a more extended program of the discovery of new facts, to create evidence to support imaginary claims for cost-effectiveness rather than deductive modelling and hypothesis testing. Formulary committees would be presented with modelled claims, from assumption driven simulation models, and asked to factor these into pricing negotiations, proposals for prior authorization and access. Recipients are asked to take these recommendations at face value, including media companies, without any understanding of the wacky inductivist basis on which the simulations were built.

Despite continued criticism in terms of the failure of the simulation models to meet the standards of normal science, notably in respect of measurement theory, the defense has been extended to the mathematically impossible QALY⁶. The QALY is still centerpiece; indeed in the ICER reference case the complete dependence on the QALY with its need for inductivist preference scores, usually from no more than one published paper or a conference presentation, together with the need to create a stream of direct medical costs, emphasizes the dependence on inductivist claims. To this is added the opportunity with the ICERAnalytics cloud-based inductivist modelling game, for model assumptions and assertions to be varied and new imaginary claims created. In the case of ICER, the only glue to hold this inductivist house of cards together is the fact that it is the basis of ICER's business case. This must be defended at all costs despite arguments deconstructing the reference case⁷

CONCLUSIONS

Alone among the physical sciences and the mature social sciences such as economics, health technology assessment as practiced by ISPOR and ICER rejects the standards of normal science in favor of creating imaginary approximate information; a claim on the future. This was matter of convenience; instead of a process of evidence discovery it was easier and more lucrative to invent it. Unfortunately, creating lifetime imaginary simulation models based on assumptions and assertions involved a rejection of Hume's problem; the impossibility of basing claims for the future on

observations from the past. It is not a question of the credibility of assertions and assumptions to support simulations but the fact that this is a waste of time.

This does not deny that assumptions play a role in even the simplest scientific test. But these assumptions can be tested if questions arise as to the validity of test results (e.g., an unanticipated false positive). The test can be replicated, even with slightly different assumptions as to the standards of the equipment used and the quality of the inputs. This is impossible in imaginary simulations. Certainly assumptions can be varied through sensitivity analysis but there can be no existential appeal. The assumptions and claims are non-evaluable as they relate to an unknowable future. The only defense falls into Hume's trap: we cannot appeal to prior observations to justify one assumption over another. We cannot make the absurd claim that one set of assumptions is more 'realistic' of the future than another as they have been in the past. All non-evaluable claims on the future have, if this is not a contradiction, equal merit (or demerit). This applies across the board to all assumptions that underpin the model from its structure to the choice of parameters and distributional assumptions in sensitivity analysis.

While ignorance of logic or indeed the standards of normal science are not a defense for producing, as ISPOR does, imaginary simulations to create evidence, clinging to these beliefs is pointless. The implications produce a major downside for patients, caregivers and physicians. The fact is that those recipients of ICER's modelled claims who take these at face value is more than unacceptable; it is a waste of time. It is as though claims for cost-effectiveness, pricing and access were decided by the reading of a Tarot card pack to assess the likelihood of cost-effectiveness or just the toss of a coin.

REFERENCES

¹ Henderson L. The Problem of Induction. Stanford Encyclopaedia of Philosophy. March 21, 2018
<https://plato.stanford.edu/entries/induction-problem/>

² Neumann PJ, Willke R, Garrison LP. A Health Economics Approach to US Value Assessment Frameworks – Introduction: An ISPOR Special Task Force Report. *Value Health*. 2018;21:119-123

³ Drummond M, Sculpher M, Claxton K et al. *Methods for the Economic Evaluation of Health Care Programmes*. 4th ed. New York: Oxford University Press, 2015

⁴ Hume D. *A Treatise of Human Nature*. 1739

⁵ Russell B. *The Problems of Philosophy*. London: Williams and Norgate, 1912

⁶ Langley P. The Great I-QALY Disaster. *InovPharm*. 2020; 11(3): No 7
Press<https://pubs.lib.umn.edu/index.php/innovations/article/view/3359/2517>

⁷ Langley P. Peter Rabbit is a Badger in Disguise: Deconstructing the Belief System of the Institute for Clinical and Economic Review in Health Technology Assessment. *InovPharm*. 2021;12(2):No. 20
<https://pubs.lib.umn.edu/index.php/innovations/article/view/3992/2855>