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2018.

MEDICAL NIHILISM



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Medicine has enjoyed a chequered history. Peak discoveries, such as penicillin and insulin, have alternated with bogus treatments, such as bloodletting or mercury. General trust in medicine has also waxed and waned, although somewhat independently from medical efficiency. Bloodletting inspired more trust than handwashing later did. Nowadays, vaccines are far from being universally accepted and homeopathy has vocal defenders. More generally, defiance surrounds a number of treatments that are otherwise strongly supported by scientific data. Or are they? In 'Medical Nihilism', Jacob Stegenga precisely defends the eponymous thesis that our confidence in medical interventions is too high and less warranted by science than we typically think. This is a timely endeavour, for medicine has perhaps never been more threatened than now by vested interests and industrial influences. This calls for a careful assessment of its results. At the same time, Stegenga is walking a fine line here. By explicitly addressing philosophers, medical professionals and the public simultaneously (p.7), he needs to remain clear enough to avoid his theses being misinterpreted and seized upon by anti-science movements. In this respect, he only partly succeeds, or so we will argue (among other things).

Stegenga defends the 'radical position' (p.3) that is medical nihilism by way of a 'master argument', which is fuelled by a variety of conceptual, methodological and empirical considerations. Nonetheless, the book also spans a number of more classical topics in the philosophy of medicine. Its first part is conceptual. Drawing on the traditional debate about the concepts of health and disease, Stegenga endorses a hybrid account, where disease possesses both a causal and a normative basis. Stegenga insists that this conceptual framework is indispensable for defining the effectiveness of medical interventions. In the hybrid account of disease, it follows that an intervention is effective if it targets the causal and/or normative conditions, which, in his terms, should provide 'cure', 'care' or both (p.36). In addition, effectiveness is to be primarily understood at a microphysiological level in relation to particular patients. It should be noted that among the conceptions of disease discussed in chapter 1, the hybrid account is the most demanding one. In conjunction with Stegenga's focus on interventions aimed at treating diseases, this contributes to a narrowing of the scope of the analysis, allowing him to avoid inflationary risks due to disease-mongering or overdiagnosis (which do not target diseases in the hybrid sense), which would taint our assessment of medical efficiency. However, more traditional medical interventions (such as cosmetic surgery, abortion or contraceptives) are also excluded (p.52). In chapter 4, Stegenga turns to the gold standard of medical intervention that is the 'magic bullet' model. Magic

bullets are interventions that are both highly effective and specific – that is, they successfully target a disease and nothing else (hence the avoidance of side effects). Unfortunately, as Stegenga argues, very few contemporary pharmaceuticals come close to approximating this ideal (p.61) because of the lack of specificity of pharmaceuticals and of the complexity of organic systems – that is, for empirical as well as conceptual reasons. This is particularly important, as the dearth of magic bullets is one of the main reasons why we should adopt medical nihilism: we are unduly confident in medicine because we wrongly expect treatments to be magic bullets.

The second part (the best of the book in our view) deals with the methods that are used to test medical interventions and assess their effectiveness. In chapter 5, Stegenga argues against the epistemic usefulness of hierarchies of evidence. Medicine relies on various types of evidence, which are typically hierarchically ordered (first meta-analyses, then randomized controlled trials – RCTs – etc.). However, hierarchies lead to utter neglect of some possibly relevant, lower-level evidence. Moreover, rankings may feature evidence tokens at best because quality varies too much within evidence types. RCTs also suffer from drawbacks. For instance, they rarely warrant causal inference and their results are difficult to extrapolate to specific individuals. Meta-analyses hardly fare any better as they can turn out to be highly malleable, giving leeway to what does or does not count as primary evidence, or how outcomes should be measured and averaged. In short, 'meta-analysis allows unconstrained choices to influence its result' (p.67). In this context, it is of prime importance to be able to assess the quality of medical studies. This is what quality assessment tools aim to do (QATs). However, as chapter 7 shows, they do not succeed in securing objective assessments. Both inter-rater and inter-tool reliability are weak, and we lack a theoretical basis to adjudicate between the available QATs. In short, evidence and evidential significance are underdetermined by theory. Stegenga then turns to issues concerning how the effectiveness of medical interventions is measured. Here, too, his diagnosis is bleak. Measuring instruments, such as depression questionnaires, lack specificity; formal measures usually report relative effects, while absolute effects are typically very small; effectiveness assessments are difficult to extrapolate, due to the numerous differences between test subjects and ordinary patients; finally, regulations regarding drug approval are too weak and usually allow one to disregard unfavourable evidence. Overall, these factors conspire to have us overestimate the effectiveness of medical interventions. At the same time, chapter 9 argues, harmful effects are systemically underestimated by medical research. A major problem is that phase

one trials (first-in-human studies) are often not published (Stegenga speaks of 95%) and are sometimes kept secret. The issue is that when a researcher is unaware of past evidence of harm, this leads to a misleading impression of prior probability in terms of how harmful the molecule under investigation is, making the probability lower than it should be. This effect is compounded by a selection bias (test subjects are typically healthier and more uniform than ordinary ones) and the fact that harms are typically provided by disregarded types of evidence (e.g., case studies). As a result, the probability of harmful effects is underestimated 'for all drugs'. Note that the arguments in this chapter could apply to pharmaceutical procedures not aimed at the treatment of diseases (such as contraceptives or pain-killers).

The third and last part of the book provides the finishing stroke and makes the case for medical nihilism, before offering a possible way forward. Stegenga first reviews the many biases that can affect evidence in medical research, many of which are mentioned in previous chapters. Confirmation bias is ubiquitous and insufficiently controlled for (as illustrated by blind-breaking issues). Even the best designs fail to mitigate instrument or recruitment biases and post-hoc analysis (for instance, the much-debated practice of 'p-hacking') is widespread. Finally, publication itself is often biased. Although it is difficult to estimate their frequency, cases of deliberate fraud do exist. In any case, deliberate deception relying on the many existing biases is common. Such practices may be driven by unresolved conflicts of interest, and their upshot is to raise the probability of evidence of effectiveness, whereas less biased methods would lower it. In chapter 11, Stegenga finally gathers most of the book's insight into one general, formal argument – his 'master argument' – in favour of medical nihilism, which mixes empirical, conceptual and methodological considerations. The argument is worth presenting in some detail, both because of its importance and the coherence it brings to the book. Let H be the claim that a given intervention is effective and E the evidence we have regarding this intervention. We want to know the probability that H is true given the evidence, that is, to assess $P(H|E)$. Bayes' rule teaches us that obtaining such evidence depends on the prior probability $P(E)$ – the prior probability $P(H)$ that the intervention is efficient, and the probability $P(E|H)$ that we would have such evidence were the intervention efficient, as per the following formula: $P(H|E) = P(E|H) \cdot P(H) / P(E)$. But $P(E)$ is high because of biases, fraud, harm underestimation and the malleability of methods. $P(H)$ is low because of the ubiquity of past rejected medical interventions and because magic bullets are expected to be rare for conceptual reasons. Finally, $P(E|H)$ is low because of discordant evidence and small effects, which are widespread in medicine but should not be strongly expected for truly effective interventions. As a result, $P(H|E)$ is low: we should have low trust in the effectiveness of any intervention given the available evidence. This is medical nihilism. Potential objections are dismissed: our perception that medicine is 'awesome' is misguided; regulation and peer-review are insufficient safeguards; the argument is not anti-science but asks for better science.

How? In his final chapter, Stegenga claims that we should

preregister trials before collecting data, pre-specify outcomes and make trial details public. But 'tweaking methodological details' will not be enough. The regulation of medical interventions should be strengthened and procedures leading to the commercialization of new drugs may be revised. One may also think of more global changes, targeting the patent system or private funding of most pharmaceutical research. An even better strategy, Stegenga argues, would be to change our research priorities and move away from the magic bullet model. Stegenga gives a few suggestions: focusing on socio-economic disparities and their impact on health; defining research priorities, depending on their probability of success (following Ioannidis' work, already largely cited in the bias and fraud chapter); and finally redirecting research towards what he calls 'gentle medicine'. This excludes aggressive treatments and includes lifestyle interventions, such as better nutrition, sport and the like (p.191).

It is remarkable that Stegenga manages to pack so much into an otherwise reasonably short book. It blends a wealth of examples and epistemological considerations into a coherent, impressive, formally backed-up argument. Nonetheless, it invites discussion on a number of points. Firstly, the choice of title. This enables Stegenga to make his work part of a long history, browsed in the introduction, of scepticism with regard to medicine. However, an important feature of Stegenga's main thesis does not fit well with the radicalness of 'nihilism': for his medical nihilism is a *relative* thesis. Although one can find more radical formulations in the book (in the introduction in particular), it argues that our confidence in the effectiveness of medical interventions should be lower (maybe much lower) than it currently is. Stegenga does not mean to show that this confidence should be low in absolute terms. The title also suggests – and the book claims, for that matter – that we should adopt nihilism in all medical interventions. However, the arguments given in the book essentially concern pharmaceutical drugs. Not only are other interventions, such as surgical interventions, rarely mentioned, but much of the argumentation does not apply to such cases, specifically because RCTs are not in order. Conversely, most of what Stegenga claims would hold for drugs that do not aim to treat diseases, for instance, contraceptive drugs or painkillers. In short, 'Medical Nihilism' here refers to a form of relative nihilism regarding some type of pharmaceutical interventions.

Stegenga's main ambition is a unificatory one. He intends to show how various reasons for scepticism about the efficiency of medical drugs (some of which are not original) can be rigorously articulated to form one coherent argument. This effort towards clear argumentation is, in places, obscured by the many cross-references contained in the book. It is, in fact, sometimes hard to exactly locate the arguments. There may also be a concern, in the context of Stegenga's unificatory project, with the definitions of disease that are discussed in chapter 2. It is not immediately clear why an argument concerning the effectiveness of drugs should rely on a definition of disease. However, that Stegenga opts for hybridism is illuminating here. Choosing the most restrictive concept of disease is a way to be maximally liberal as to what counts as a treatment for a disease: if a disease has both a causal and

normative basis, then it is sufficient to target one of these to qualify as a treating intervention. As a consequence, Stegenga's medical nihilism seems to leave room for his optimistic stance on gentle medicine: the arguments he develops essentially deal with interventions targeting the causal basis of disease, but it may be that interventions targeting their normative basis fare better. In combination with the focus on interventions aimed at treating diseases, hybridism also makes irrelevant for medical nihilism all the evidence and doubts we may have concerning treatments of conditions that are not pathological. Stegenga thereby gives up on an artificially easy way to make his point. Apart from chapter 2 as a whole, there are smaller passages whose relevance to the overall argument is disputable. In section 11.3 for instance, Stegenga's insistence on the fact that the drugs he discusses are (or have been) extensively used, however suggestive it may be, does not support his point that 'for many medical interventions, the best evidence available today suggests that they are barely effective, if at all' (p.171).

Stegenga also has ambitions for the proposed argument itself. It is meant to be general, holding for any medical intervention whatsoever, and not to be a merely inductive argument drawing on the enumeration of evidence that specific drugs are not as effective as one might have thought. The latter is necessitated by the fact that some bits of the argument, specifically the one dealing with magic bullets, are conceptual. Although some of its empirical premises are inductively established, the master argument, to which we now turn, is a Bayesian argument. Under its formal guise, it is not as clear-cut as it seems. To recall, our evidence-based trust in an intervention, $P(H|E)$, should be low partly because $P(E|H)/P(E)$ is low, which in turn stems from the fact that $P(E)$ is high and $P(E|H)$ is low. However, these two claims appear to envisage distinct evidential scenarios. $P(E)$ is claimed to be high because we should expect biases, fraud and malleable methods to provide positive evidence for the effectiveness of any intervention whatsoever. So, for any intervention, the evidence will be favourable and likely to show significant effects. $P(E|H)$, however, is estimated as being low in reference to cases where E is evidence of small effects or discordant evidence. These cases are frequent, the argument goes, but unlikely if the intervention is effective. So, the two claims are hard to square. If the evidence E is strongly favourable, then $P(E)$ is high, but $P(E|H)$ should be high too, as it is the probability that evidence indicates the effectiveness of a truly effective intervention. If the evidence is discordant, then, following Stegenga, $P(E|H)$ will be low – but $P(E)$ should be too! We should not expect much discordant evidence in a world plagued by vested interests, biases and malleable methods. More generally, the point is that $P(E)$ and $P(E|H)$ will rise and fall *together* as the evidence becomes more or less favourable.

This does not mean that medical nihilism is false, for even if the two probabilities are dependent, $P(E|H)$ may still be lower than $P(E)$ in general. The foregoing argument, if correct, only establishes that the general value of $P(E|H)/P(E)$ is indeterminate. We would need to quantitatively estimate $P(E|H)$ and $P(E)$ to issue a verdict. This is a daring and pos-

sibly difficult task to achieve for all cases. Still, the value of $P(E|H)/P(E)$ may turn out to be low in many or even most contexts. Moreover, as long as it is not too high, medical nihilism may follow from the claim that $P(H)$ is low. This is the point that if our confidence in the effectiveness is very low to begin with, it would remain low even after a reasonable amount of evidence has been gathered. So, a general case for medical nihilism can be as strong as the motivations for a low $P(H)$, namely, the inductive argument that past effective interventions have been uncommon and the conceptual argument that magic bullets should be hard to come by.

Still, are there not ways to assess some probabilities that do not rely on painstaking review and study of past interventions? Stegenga gestures towards one in his chapter on bias and fraud, where he argues that $P(E)$ increases with the number of biases that plague medical research. Here, too, his argument is probabilistic, and here, too, it is debatable. Supposing E is some evidence that an intervention is effective, then $P(E)$ can be calculated according to the principle of total probability, as the sum of the $P(E|X_i).P(X_i)$ for all possible hypotheses X_i that may explain E , which include, say: that the intervention is indeed effective (Hx); that the evidence was obtained by chance (Hc); that it was due to a bias B_1 or to another one B_2 . Now suppose we discover another bias, B_3 , which may explain E as well: $P(E)$ now equals the sum of its previous value and of a new term, $P(E|B_3).P(B_3)$, which is always positive; so, $P(E)$ will increase. However, the conclusion does not hold. For the principle of total evidence applies to situations in which all possible alternatives are envisaged: the sum of the probabilities of Hx , Hc , B_1 and B_2 has to be one. So, when B_3 is brought in with a positive probability $P(B_3)$, the probability of at least one previous hypothesis will decrease, and the new $P(E)$ will, therefore, amount to the sum of $P(E|B_3).P(B_3)$ with a value that is lower than the initial $P(E)$. There is thus no guarantee that $P(E)$ will increase; again, only a context-sensitive analysis could tell. (As an aside, the principle of total probability applies when the various possibilities are independent, although there is no reason for biases to be so; and the fact that even unknown biases should typically favour the overestimation of effectiveness, as also assumed in appendix 5, is debatable.) Overall, there is doubt that a formal take was the best way to spell out the book's argument.

Finally, Stegenga seems to understand his defence of 'gentle medicine' as an important consequence of 'medical nihilism'. Firstly, what is 'gentle medicine'? Stegenga co-opts the French words *la médecine douce*. Rhetorically, this is not an obvious move. Stegenga does not argue for complementary or alternative medicine – he himself admits that much alternative medicine is not 'gentle' because it entails physical manipulation. So, what does the expression mean? Stegenga writes that 'gentle medicine is concerned with attending to what it is like to be a person confronting disease' (p.191). However, his later description of 'gentle medicine' does not target the experience of illness. Rather, Stegenga lists medical interventions that he considers as 'gentle'. They are, in his words, 'targeting the normative' (p.51) and they are thus particularly wide-ranging. They go from pharmaceutical painkillers and palliative care to 'simply caring' and lifestyle interventions

(e.g., promoting physical activities or decreasing stress levels), all the way to societal changes. Are such interventions 'gentle' though? Why presuppose that interventions are aggressive when targeting the causal basis of disease, yet gentle when targeting the normative one? Painkillers have led to addictions; lifestyle changes can be distressing and societal changes unruly. Conversely, public health measures and socio-economic factors may target the 'causal basis' and not solely the 'normative basis' of disease (for instance, whether a population has access to enough food is not a normative factor). In other words, the distinction between 'gentle' and 'aggressive' does not seem to track the distinction between the 'causal basis' and the 'normative basis' of disease.

This lack of a clear-cut distinction between gentle and aggressive interventions is not problematic in itself, since, in his closing section, Stegenga chiefly aims to indicate possibly fruitful avenues for future medical research, for which a heterogeneous list is certainly well-suited. However, this has an unfortunate consequence, as gentle medicine is now threatened by nihilism as well. Note firstly that there is nothing to prevent us from applying most of Stegenga's arguments to the normative basis of disease (as medical nihilism is partly supported by the underestimation of harms and some treatments targeting the normative basis are pharmaceutical drugs). Secondly, the effectiveness of lifestyle interventions is notoriously difficult to measure, as is measuring welfare in

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general. But why not expect the effects of diet or physical activity to be as small as those of 'aggressive' treatments? Why expect biases to be less pervasive? This suggests that we have no reason not to consider gentle medicine (however ethically preferable it may be) to be epistemologically on a par with its aggressive counterpart. This does not mean it is not worth exploring further; but other alternatives might also be worth pursuing, such as multiple therapies based on the accumulation of small effects, for instance, which might have been mentioned as well.

This discussion does not detract from the book's value. If anything, it is testimony to the many debates it is likely to generate, firstly, because it spans a wide array of topics in the philosophy of medicine and, secondly, because of the clarity of the careful scrutiny of various scientific methods, which the book provides. Indeed, regardless of the cogency and scope of Stegenga's main unifying argument, it is difficult not to be affected by his relentless streak of negative conclusions – the lists of failed interventions, of forgotten or buried studies, of loose methods, of undetected harms and manipulated data. In other words, it is difficult not to feel that there really is something to medical nihilism. In this, Stegenga succeeds. That there are things to discuss in the book does not diminish the urgency with which medical research should evolve – whether this entails it becoming gentler or something else entirely.

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