



The need for “gentle medicine” in a post Covid-19 world

Gabriel Andrade¹ · Maria Campo Redondo²

Accepted: 14 August 2021

© The Author(s), under exclusive licence to Springer Nature B.V. 2021

Abstract

As it has historically been the case with many pandemics, the Covid-19 experience will induce many philosophers to reconsider the value of medical practice. This should be a good opportunity to critically scrutinize the way medical research and medical interventions are carried out. For much of its history, medicine has been very inefficient. But, even in its contemporary forms, a review of common protocols in medical research and medical interventions reveal many shortcomings, especially related to methodological flaws, and more importantly, conflicts of interests due to profit incentives. In the face of these problems, we propose a program of “gentle medicine”. This term, originally formulated by philosopher Jacob Stegenga, describes a form of medicine in which physicians intervene less than they currently do. As part of this general program, we advance a series of reform recommendations that could be enacted both by medical staff in their everyday practice, but also by public health officials and policymakers.

Keywords Gentle medicine · Medical interventions · Conflicts of interests · Public health

Introduction

Despite its grim outcome, the Covid-19 pandemic may provide an opportunity for the improvement of medical practice. Nicholas Christakis (2020) has documented that there is a pattern of reflexive practice after pandemics are overcome. And part of that reflexive practice might consist in asking, what reforms are needed for the improvement of medicine?

In this article, we posit that, given the current state of medical practice, we may need *less* medicine, instead of more. This is on the basis of the thesis that medicine does not deserve the overwhelming positive reputation that it currently enjoys. In fact, there are sufficient reasons to be skeptical of the overall effectiveness of most areas of medical practice.

This particular thesis has had an important number of adherents in the past (Illich 1975; Foucault 2012), and it gave rise to a position that became known as “therapeutic

skepticism” in the 1970s (Brody 1989). This view is now gaining some new adherents, particularly philosopher Jacob Stegenga. But, Stegenga (2018, p. 21) has preferred to use the term “medical nihilism”, defined by him as “the view that we should have little confidence in the effectiveness of medical interventions.”

Stegenga’s wording is not altogether fortunate, because nihilism implies *nothingness*, meaning that medical nihilism implies that *no* feature of medicine is ever justified. This is certainly a strong claim that is not justified by the evidence, as many features of medicine are immensely beneficial. But, Stegenga does have a strong case in his assertion that a big chunk of medical procedures (if not the majority) are ineffective, for reasons that will be explained below. In that regard, although Stegenga’s choice of words is inadequate, his views are fundamentally correct, as indeed, there are plenty of reasons to have little confidence in the effectiveness of many medical interventions.

Much more adequate is Stegenga’s use of another term, “gentle medicine”. He defines this approach as the “proposal that physicians should intervene less, perhaps much less, than is presently the case, and we should try to improve health with changes to our lives and to our societies.” (Stegenga 2018, p. 35). The term “gentle medicine” is adequate to the extent that it manifests a sort of medical practice that is not needlessly aggressive, but rather gentle. It intervenes

✉ Gabriel Andrade
gabrielernesto2000@gmail.com

Maria Campo Redondo
mcampo@uaeu.ac.ae

¹ Ajman University, Ajman, United Arab Emirates

² United Arab Emirates University, Abu Dhabi,
United Arab Emirates

when it is necessary, but it wisely abstains from doing so when the harms outweigh the benefits.

A proposal for gentle medicine is warranted by an examination of the current state of medicine. As it happens, current medical practice suffers from many shortcomings, and these particular problems cast a big shadow over its real effectiveness. These problems have mostly to do with issues of interference of biases in medical research, overdiagnosis, and overtreatment. Consequently, in this article, we first examine some of the current problems faced by medical practice (and that justify a form of medical skepticism); then, as part of a “gentle medicine” approach, we propose some of the concrete reforms that might be put in place, so as to make medicine more efficient. This article will therefore make an additional contribution to the debate on the current status of medicine, by expanding Stegenga’s notion of “gentle medicine”, and relating it to data that is currently being discussed in various areas of medicine.

Historical reasons for medical skepticism

There are various reasons as to why our trust in medicine is disproportionate, and in turn, we need a more skeptical approach to it. A historical review of the data does seem to confirm that many medical therapies that at some point were believed to be effective, have actually been useless or even detrimental to patients’ health.

Indeed, given its many failures, in the history of medicine there has been a long history of skepticism. Perhaps this attitude is best encapsulated in Oliver Wendell Holmes’ 1860 phrase: “if the whole *materia medica*, as now used, could be sunk to the bottom of the sea, it would be all the better for mankind—and all the worse for the fishes” (Shojaina 2012).

A more thorough investigation has proven that, for most of medicine’s history, Holmes’ diatribe was largely justified. The definitive study of the failures of medicine in history has been carried out by David Wootton. In his assessment, “the long tradition that descended from Hippocrates, symbolized by a reliance on bloodletting, purges, and emetics, was almost totally ineffectual, indeed positively deleterious, except in so far as it mobilized the placebo effect” (Wootton 2007); medicine began to improve by 1865, and this only came about “when doctors began to count and to compare. They had to count the number of patients that lived and the number that died, and then compare different treatments to see if they resulted in improved survival rates” (Wootton 2007).

Not surprisingly, the history of medicine has been a long list of failures and procedures that ultimately, have done more harm than good. For example, mercury was typically used for allegedly therapeutic purposes in various strands of traditional medicine (Salon et al. 2017), but now we know

that it could have very toxic effects. There is evidence that mercury is linked to diseases like Alzheimer’s, Parkinson’s, lupus, and autism. In one study, it has been found that mercury can induce decreased performance in tasks related to motricity and memory in children, even when they have had prenatal exposure to seemingly safe levels at 10–20 µg/g (Grandjean et al. 1998).

Likewise, bloodletting practices were routinely performed (on the basis of humoral theories) (Greenstone 2010), leaving dangerous consequences as a result of decompensation (Lim et al. 2015).

As for psychiatry, Wootton (2007) writes that “the story of bad psychiatry would require at least a volume to itself.” Indeed, dubious diagnoses such as drapetomania (Willoughby 2018), the pathologizing of homosexuality (Goldberg 2001), and brutal and ineffectual procedures such as lobotomy (Anasthasia 1984), and the political use of psychiatry targeting dissidents (Andrade and Campo Redondo 2020), give weight to the argument that psychiatry has been mostly “bad medicine.”

Yet, it must be acknowledged that this skeptical approach has not always been justified in the history of medicine. Despite his harshness in approaching the history of medicine, Wootton frames his narrative under a Whig perspective, in which, ultimately, medicine does triumph and progress prevails. In Wootton’s (2007) assessment, “the key development that made modern medicine possible is the germ theory of disease. More specifically, the first breakthrough took place with the germ theory of putrefaction. The great puzzle here is the long delay before anyone formulated a germ theory that had a medical application.” Be that as it may, Wootton (2007) insists on the final triumph of medicine, by stating “the idea of progress now needs to be rescued.”

Admittedly, Wootton’s views must encounter some nuance, especially regarding the history of the germ theory of disease. As it happens, prior to the nineteenth century there were already approximations to such a theory. For example, the ancient Egyptians may have had some notion of it, although it wasn’t until the nineteenth century that it was completely accepted by physicians, in light of the invention of the microscope (Castiglioni 2019). Be that as it may, Wootton’s approach to the history of medicine is still open to debate, insofar as the relationship between medicine and science is concerned. For example, it is possible that medicine kept progress at the same pace as science, and in that regard, medical practice never truly lagged behind, but instead, may have actually been at the forefront of scientific innovation (Porter 2004). In any case, this historical debate is still ongoing, and while open to criticism, Wootton’s approach can be tentatively assumed as valid.

Indeed, in some aspects, there is a case to be made in favor of Wootton’s Whig approach. For, in some particular

periods, there have been significant innovations that have dramatically improved healthcare, and on the basis of these particular achievements, modern medicine has seemingly built its robust reputation.

Problems with the aggressive approach to medicine

These particular achievements are frequently referred to as “magic bullets” in medical parlance, and they are the foundations for the prestige of modern medicine. The term “magic bullet” was originally formulated by Paul Ehrlich, to designate those particular medical innovations that facilitated the treatment of hitherto untreatable diseases (Strebhardt and Ullrich 2008). Ehrlich was particularly interested in experimenting with the treatment for syphilis. In concordance with the medical mores of his times, this disease was treated with mercury—a very ineffective and dangerous method. Consequently, Ehrlich discovered a new possibility. As Winau et al. (2004) praise it, “Ehrlich envisaged a treatment of pathogens and toxins in the human body by means of a chemical substance, which, in analogy to the side chains, should be equipped with high affinity to the causative agent.” As it happens, this turned out to be a very effective treatment, and this particular innovation was called a “magic bullet”, to the extent that it would bind to the pathogen in order to kill it, without having to interfere with the rest of normal human physiology.

Now, despite the use by Ehrlich of this term, it must be still be acknowledged that in many important institutions of biomedical research and ethics committees, researchers and clinicians do not employ this term. Indeed, the case could be made that in most researchers’ reckoning, there is no quest at all to search for a magic bullet. This may actually be a distortion, as it is possible that the majority of labs are not concerned with “magic bullets” at all. Nevertheless, it is important to note that there is still a public perception (which, again, may or may not be accurate) that medicine *is* indeed in such a search. Perhaps authors are to blame for inaccurately using the term in many publications, without necessarily reflecting the actual attention given to it by clinicians. Be that as it may, in this article, on the basis of the available scientific literature, we will assume that some clinicians do rely on the magic bullet approach, although we admit that many clinicians do not use this term, and consequently, do not engage in any such search.

Another important breakthrough in medicine is penicillin (by targeting pathogens without interfering in the rest of normal physiology) (Gaynes 2017), and more recently, insulin for the treatment of Type 1 diabetes. The discoverers of the medical use of insulin, Frederick Banting and Charles Best, revolutionized medicine by applying this treatment to type

1 diabetes patient, who until that time, only had the option of being starved into coma (Simoni et al. 2002).

Wootton offers a sensible review of medicine’s past failures, but critics have accused him of naïveté when it comes to his overly optimistic Whig approach in regards to the present (Broadbent 2019). Medicine’s present state of affairs may not be as bright as it is made to be, and in fact, may resemble more the failures of its past. For that very reason, there may be plenty of motives to be skeptical of the current possibilities of success for medicine. Medicine as it is practiced today faces various shortcomings that have not yet been duly corrected for, and they may be foundations for the claim that, as it stands today, medicine does not deserve the reputation it enjoys.

In fact, the ultimate argument typically used in the triumphalist account of the history of medicine, is not robust. This argument appeals to the increase of average life spans. While it is true that life expectancy has dramatically increased worldwide to an average of 76.2 years (Riley 2001), it is by no means certain that this achievement is due to improvements in medical practice. Thomas McKeown (2014) has offered relevant studies documenting that increased longevity are more due to access to potable water, improved sanitation, better nutrition, and an overall rise in the standard of living. In his words, “the improvement of health during the past three centuries was due essentially to provision of food, protection from hazards, and limitation of numbers.”

Despite the obvious landmark advances of medicine in the last 150 years, for much of the history of medicine, when it comes to new pharmacological treatments, magic bullets are the exception, rather than the norm. And this seems to be particularly true in our current times. Indeed, the case could be made that the majority of drugs out in the market target particular symptoms or limited measures of some diseases, but are of little help in managing the disease itself (Stegenga 2011). Such drugs are far from being magic bullets, to the extent that their results are mixed at best, as compared to the real magic bullets of the past (e.g. penicillin or insulin).

As an example, consider statins. These particular drugs are very effective in reducing cholesterol levels, and in turn, they might reduce risks of heart disease (Armitage 2007). Consequently, pharmaceutical companies have managed to generate huge profits with the sales of statins. For example, the revenue in 2005 was US\$ 25 billion (Endo 2010). But the reduction of the risk in cholesterol level is quite minimal (although it is not zero), and in turn, they have risks of their own which, in a cost–benefit analysis, might actually offer negative results in terms of safety (Franco et al. 2005). Statins are clearly not magic bullets.

A particular problem with statins is that, very frequently, data is reported only on surrogate outcomes, thus skewing results. For example, in a study that reviewed 192 published randomized controlled trials comparing statins to other

drugs, 189 of such trials reported data solely on surrogate outcomes (Bero et al. 2007); this clearly affects the integrity of the information needed to decide on the effectiveness of statins.

As it happens, most drugs fall short in the treatment of diseases, as disease itself is a complex phenomenon that cannot be easily addressed by just targeting a particular aspect of it, as in the case of magic bullets. Being complex phenomena, diseases might remain unaffected by treatments (Naylor and Chen 2010), to the extent that these interventions only target one particular focus of the causal chain, and in turn, this might prove insufficient for the treatment of the disease as a whole.

The entanglement of pharmaceutical companies and its effect on medicine

The sheer complexity of disease would seem to be forever unmatched by our attempts to target its entangled network of causes, with particular treatments. Admittedly, modern medicine has offered awe-inspiring innovations that might give us sufficient confidence to believe that, in the not-so-distant future, our pharmacological interventions will match the complexity of disease itself. But, for the time being, it does seem more accurate to posit that we are not anywhere close to that prospect, and we remain very uncertain as to whether we will ever get there.

Be that as it may, there are good reasons to believe that, at least as it stands now, medicine has little chance of developing true magic bullets, not only because of the inherent complexity of disease, but also because of the very nature of medicine in modern society.

In its current state, most research in medicine has difficulty overcoming biases towards positive results. There are particular market and social conditions that favor experimenters' (both conscious and unconscious) inclinations towards results that confirm the effectiveness of particular drugs and treatments. This is understandable in many cases, not least of which is the Covid-19 pandemic. Given the alarming mortality of the current pandemic (and perhaps even more importantly, the devastating economic effects due to lockdown measures), there is a pressing need for emergency vaccines approvals in trials.

This gives rise to relevant ethical questions. As Dal Re and Caplan (2021) express their concern, the speedy approval of Covid-19 vaccinations "will not answer questions about long-term efficacy and safety, which requires more months of data. Moreover, early deployment could interfere with the acquisition of long-term data." So, just as in the case of Covid-19 vaccination trials there is an inadequate eagerness to get positive results, the whole pharmaceutical industry at large is characterized by this tendency.

The way research grants are allotted is also part of the problem. Few institutions will give out money to researchers who carry out experiments that fail to reject null hypotheses. Consequently, there is relentless pressure for researchers to design experimental designs so as to get positive results. Many medical journals are also complicit in this. As Richard Smith (2005) denounces, "medical journals are an extension of the marketing arm of pharmaceutical companies", eventually rigging trials to get the results they want.

For example, in one study of 56 trials funded by providers of nonsteroidal anti-inflammatory drugs for arthritis, it was found that not even one of the published trials reported any result that were not favorable to the pharmaceutical company that funded the trial; indeed, all trials returned positive results (Rochon et al. 1994). This overwhelming tendency for favorable results makes it suspicious.

Nevertheless, it is important to make a distinction between the epistemological basis of responsibility in biomedical research, as opposed to the sheer corruption of research by the less-than-noble interests of pharmaceutical companies. It is entirely possible that some forms of epistemological injustices be at play, and consequently, they have an influence on the way conventional medicine is practiced.

In this regard, it is important to keep in mind the epistemological input provided by Thomas Kuhn (2012). In Kuhn's philosophy of science, the notion of paradigms shed light on how historically, biomedical (and all scientific research) has shifted its focus, depending on the prevailing assumptions of particular epochs. Consequently, it is entirely possible that some of the research propelled by the pharmaceutical industry is problematic, not only because of the pernicious influence of economic interests but also because contemporary Western medicine may itself rely on a set of paradigms that are detrimental to the proper and ethical conduct of research.

Indeed, there is sufficient reason to be concerned about the prevailing epistemic injustices in medical practice that may tilt the balance in favor of practices that have come to prevalent, not necessarily because of their scientific legitimacy, but rather, due to contingent factors related to power that ultimately result in epistemic injustice. This brings forth the pressing problem of so-called "knowledge asymmetries", in which practitioners ultimately have access to knowledge, and are able to determine what course patients must follow without giving much consideration to what patients themselves feel is best for them.

Carel and Kidd (2017, p. 336) eloquently point their finger towards the end results of epistemic injustice: "most practitioners can leave the world of illness, at the end of the day, physically and psychologically, experiencing it through the context of a professionalised domain... The power structures of healthcare systems can also indirectly affect the epistemic confidence and capacities of ill persons.

Many are vulnerable and fragile in various ways—physically, emotionally, socially—as a result of their condition and treatment, and the difficulties of life as an ill person in an often uncooperative, uncompassionate social world.”

This perspective sheds light on an encompassing phenomenon that is deeply rooted in the prevailing paradigm of medicine. Not only is there a danger of impure economic interests staining research and biomedical practice, but also the way the system itself is arranged, ultimately contributes to an unbalance of power that leads to deeper forms of injustice. Carel and Kidd (2017, p. 345) note that “certain conceptions of health may contain latent prejudices about nature of credibility, understanding, and explanation in medical and healthcare contexts... On this model, epistemic relevance is confined to science and scientifically trained HCPs in a way that may generate epistemic prejudices against patients.” This particular problem should give pause to think that, while the influence of big pharmaceutical companies must be limited, the problems at the heart of biomedical research and practice are much larger, and some more radical measures might be needed, oriented towards some form of paradigm change.

Additionally, the pharmaceutical industry has powerful lobbies that can find their way to bypass some of the stronger governmental regulations (Barber IV and Diestre 2019), and these lobbies can also directly target researchers and practitioners through contributions and gifts that compromise their integrity, and puts them in conflicts of interests that are not always reported (Patwardhan 2016).

The problem of lobbying in pharmaceutical companies has long concerned leading practitioners in biomedical sciences. For example, in her widely read work *The Truth About the the Drug Companies*, Marcia Angell (2005, p. xix) expresses deep concern over the fact that “instead of investing more in innovative drugs and moderating prices, drug companies are pouring money into marketing, legal maneuvers to extend patent rights, and government lobbying to prevent any form of price regulation.” It is especially troublesome that, as Angell (2005, xx) reminds us, “drug companies have the largest lobby in Washington [and other centers of power], and they give copiously to political campaigns. Legislators are now so beholden to the pharmaceutical industry that it will be exceedingly difficult to break its lock on them.” This as enabled the pharmaceutical companies to generate huge profits, inducing the consumption of all sorts of drugs. For example,

Indeed, much lip service is paid to the avoidance of conflicts of interests. But thorough examinations of the state of affairs in medicine, reveal that conflict of interests are extremely common, and they are not properly taken care of. For example, a comprehensive statistical examination of research findings by John Ioannidis (2005) has revealed that most of them are false, and in his assessment, this is

because “conflicts of interest are very common in biomedical research, and typically they are inadequately and sparsely reported.” Indeed, in Ioannidis’ (2016) estimation, such is the magnitude of the problem of conflicts of interests in medicine, that in his words, medical research does not “make a difference for health and disease outcomes.”

Methodological concerns in the design of experimental trials

Biomedical research also encounters other problems. For example, placebo effects may actually hamper the accuracy of particular drug trials (Enck et al. 2011). Traditionally, biomedical research has sought to solve this particular problem through the use of randomized control trials, which apart from tackling the placebo issue, attempt to minimize any bias. But, randomized trials have many shortcomings of their own. Suresh (2011) has shown that randomization usually falls short, as it increases the probability that some confounding variables may be more balanced in group distribution, but certainly not all confounding variables involved in the study can be properly distributed. Ultimately, researchers do have the flexibility to play around with experimentation, so as to design and interpret trials, and consequently obtain the results that match their preconceptions.

Likewise, metaanalyses, another common methodological technique frequently used in biomedical research, also falls short. In metaanalyses, quantitative methods are used to evaluate data obtained from multiple randomized control trials. But, if these trials are imperfect to begin with, then naturally their metaanalyses will also be skewed. As Stenga observes (2011), “meta-analysis fails to constrain assessments of medical interventions because numerous decisions must be made when performing a meta-analysis, which allow wide latitude for subjective idiosyncrasies to influence the results of a meta-analysis.” Furthermore, metaanalyses can be malleable so as to fit the researchers’ preconceived notions, to the extent that they allow for malleability in choice of primary evidence, choice of outcome measure, and choice of averaging technique (Stegenga 2011).

Typically, problems with these sorts of malleability account for the frequent disparity amongst trials. Interestingly, when independent investigations are carried out (i.e., financed with public funds, independent of big pharmaceuticals’ sponsorship), more negative results are reported (Ioannidis 2017).

This is particularly worrying in the case of antidepressants, a class of drugs that has had a massive increase in consumption over the last few decades. For example, in the United States, 10% of women and 4% of men consume antidepressants at any point during any month (Horwitz and Wakefield 2007). There is also the significant datum

that patients undergoing treatment for depression in 1997 were 4.5 times more likely to take some medicinal drug than in 1987; even more concerning is the fact that in the 1990s, the amount of money spent by consumers on antidepressants in the United States rose by 600% (Moynihan and Cassels 2005).

This is especially troubling, as the clinical efficacy of antidepressants is increasingly in question. For example, Ebrahim et al. (2016) report that research projects conducted by scientists related to the pharmaceutical industry are 22 times less likely to report negative side effects, than independent researchers.

A fundamental principle of scientific methodology is that theories are built on the basis of collected evidence. But surprisingly, this particular cornerstone is frequently sidestepped in clinical research. In many cases, particular hypothesis can be formulated so as to find data in order to support a particular study. This method is called “p-hacking”. In one particular study using text-mining methods (Head et al. 2015), it was shown that “p-hacking is widespread throughout science.” For example, in that study, the strength of p-hacking in the biomedical sciences presented as the proportion of p-values in the upper bin with one-tailed 95% confidence intervals was 0.5, suggesting that it is widespread.

To the extent that p-hacking “occurs when researchers collect or select data or statistical analyses until nonsignificant results become significant”, it constitutes a form of confirmation and selection bias, and it is alarmingly common in biomedical science.

When it comes to drug experimentation, it has long been a matter of concern that harmful side effects have been underreported. This is in fact a structural problem, as the agency that supervises trials and approval of drugs, the FDA (Foods and Drugs Administration), is not sufficiently independent of the pharmaceutical industry. As Light et al. (2013) state it, “the pharmaceutical industry has corrupted the practice of medicine through its influence over what drugs are developed, how they are tested, and how medical knowledge is created.” Most worrying is the fact that in the United States, the approval of the Prescription Drug User Fee Act (PDUFA) in 1992, allowed the FDA to collect fees from drug manufacturers to fund new drug approval processes. This accelerated the approval of drugs, but clearly at the expense of safety (Zelenay 2005).

And, even many drugs that are approved, go on to be quickly withdrawn, as a result of concerns over safety. This has been the case with valdecoxib; for that drug, in a trial of 1671 patients who had undergone bypass grafting, cardiovascular events were more frequent in patients taking valdecoxib than in the placebo group (risk ratio 3.7, with a confidence interval of 95%) (Cotter and Wooltorton 2005).

In a German study with 1100 patients, aprotinin was riskier in routine coronary bypass graft surgery (Spiess 2010), thus raising concerns about the safety of that drug, and thus being withdrawn. Similar concerns were raised with clobutinol (Rottlaender and Hoppe 2008) and rofexoxib; for that particular drug, one study reported a worrying increase in the risk of myocardial infarction (relative risk 5.00, with a 95% confidence interval; 1.72–14.29) (Dieppe et al. 2004).

While it is a positive feature that these drugs were eventually removed, most likely they should have never been approved in the first place, anyways. Instead, they were probably approved because of researchers’ biases and pressures from lobbies.

Even worse, there are still approved drugs in the market whose safety is far from being established. For example, rosiglitazone purportedly helps in the treatment of diabetes, but a thorough study by Nissen and Wolski (2007) had demonstrated that the drug increases risk of myocardial infarction and death from cardiovascular causes. In that study of 42 trials, in comparison to the control group, patients taking rosiglitazone had odds ratio for myocardial infarction of 1.43 (95% confidence interval, from 1.03 to 1.98); for death due to cardiovascular causes, the odds ratio was 1.64 (95% confidence interval, from 0.98 to 2.74). Nevertheless, the drug remains in the market, largely because new trials have shown better results. But, a key feature of these trials has been the exclusion of participants are most likely to react adversely to the drug.

Concerns over the mongering of disease

Apart from problems with faulty designs and conflicts of interest, medical practice frequently engages in what some critics have come to call “disease-mongering”. As Moynihan and Henry (2006) define it, “disease mongering is the selling of sickness that widens the boundaries of illness and grows the markets for those who sell and deliver treatments.” This sale of sickness is particularly prominent in psychiatric medicine. While the claims of anti-psychiatry crusaders such as Thomas Szasz (1960) are too extreme in regarding mental illness as a myth, it is nevertheless true that some particular diagnoses are highly questionable. For example, the diagnostic criteria of Attention Deficit Hyperactivity Disorder are not sufficiently clear, and in fact, an increasing number of critics posit that the DSM-5’s guidelines pathologize normal children’s behavior (Hinshaw 2018), to the point that now it is claimed that 1.6 million children in the United States suffer this condition, a number that defies reasonable expectations (Gottlieb 2002).

Since the treatment for this particular condition is pharmacological, it has been posited that the pharmaceutical industry has played an important role in disease mongering

in this diagnosis (Saddichha 2010). Similar concerns have been raised for diagnoses such as erectile dysfunction, with 152 million cases worldwide in 1995 (Ayta et al. 1999; Lexchin 2006).

The fact that diagnoses of halitosis (85 million cases in 2007) has increased on par with mouthwash sales (a US\$ 2 billion industry in the United States) (Dal Rio et al. 2007) has shed some doubts on the way this is diagnosed (Iroegbulem 2020); the same concern exists for restless leg syndrome (Woloshin and Schwartz 2006), and social anxiety disorder (Wolinsky 2005).

And for those disorders that are real, the medical industry also constantly emphasizes the need for screening. According to the conventional narrative, preventive care is very important, and screening asymptomatic persons can solve potential illnesses. But, the case could be made that these procedures themselves are largely ineffectual, and consequently, they are profitable for companies that manufacture and sell the procedures’ equipment, but do not contribute significantly to any improvement in public health.

False positives are a pressing problem in many preventive screening procedures, and they can have detrimental impacts on people’s lives. For example, in a study of false positive screening mammography, it was found that “3 years after a false-positive finding, women experience psychosocial consequences that range between those experienced by women with a normal mammogram and those with a diagnosis of breast cancer” (Brodersen and Siersma 2013). Likewise, many screening procedures may detect particular anomalies, but in doing so, may engage in overdiagnosis, to the extent of pathologizing a feature that would not cause harm on its own. This is frequently the case in cancer screening. For example, in a study of cancer screening, Black (2000) considers that overdiagnosis has effectively become an “under-recognized cause of confusion and harm.” In the same manner, in an analysis of the impact of overdiagnosis on public health, Bulliard and Chiolerio (2015) conclude that “treating an overdiagnosed condition bears no benefit but can cause harms and generates costs. Overtreatment also diverts health professionals from caring for those most severely ill.”

Indeed, when it comes to four of the leading causes of death in many industrialized countries (heart disease, cancer, respiratory disease and diabetes), Saquib et al. (2015) found that “among currently available screening tests for diseases where death is a common outcome, reductions in disease-specific mortality are uncommon and reductions in all-cause mortality are very rare or non-existent.” That does not imply that screening is completely useless, as Saquib et al. (2015) acknowledge that “screening may still be highly effective (and thus justifiable) for a variety of other clinical outcomes, besides mortality”, but when it comes to screening for mortality risks, most procedures are not effective. In

a cost–benefit analysis, it would appear the balance inclines more towards the costs.

What, then, can be done? The need for gentle medicine

The criticisms discussed above should in no way be used as a justification of alternative medicine. Although conventional medicine may be overrated for many of the reasons already alluded to, that does not imply that alternative medicine is any better. For, proponents of alternative medicine frequently also engage in confirmation bias, and in many cases, there is a profit incentive in many of their alleged research endeavors, as alternative medicine is an industry of its own (McLennan et al. 2002). Furthermore, there is also overtreatment in alternative medicine, to the extent that the goal is not to abstain from medical practice, but rather, to use alternative methods that can also be costly and provide very little therapeutic value, such as acupuncture, homeopathy or chiropractic treatments.

The problems presented above should place limits on medicine, but it should not lead to the position that no medical intervention is ever justifiable. As complement to the concept of “gentle medicine”, Stegenga uses the phrase “medical nihilism” to describe his views on medicine, but recall that this phrase is inadequate, as certainly, the ideal approach is to point out some of medicine’s shortcomings, but not to throw the baby out with the bathwater. Despite its limitations, medicine remains a worthwhile endeavor.

The ideal situation, rather, is to put in place “gentle medicine”, precisely as what the name implies: a soft approach that applies medical interventions only when deemed really necessary, and as part of this process, abstains from using medical procedures that are very costly (in all terms, not only financial) and with virtually null benefits.

Old-fashioned medical wisdom is relevant in this regard. An old maxim in medicine is “good surgeons know how to operate, better ones when to operate, and the best when not to operate” (Schaller and Leonardi 2006). As it happens, this maxim is not true only for surgery, but rather, for medicine as a whole. Sometimes, the best treatment is non-treatment. Medical education needs to emphasize this, and medical schools ought to train physicians so as to know when they have the duty to intervene, but also when they have the duty *not* to intervene.

This discussion can be framed in the context of the main principles of medical ethics. Whereas nowadays there seems to be great emphasis on the principle of beneficence (doing good), the principle of non-maleficence is (abstaining from doing harm) has always had priority in medical ethics (Pellegriano 1993). *Primum non nocere* (first, do no harm) is the phrase that best expresses this principle (Yeo 1989).

Criticisms of medicine and an awareness of its shortcomings should lead to a reaffirmation of this principle, so as to learn how to recognize the many cases in which medicine presents more harms than benefits. In the current state of affairs, as Smith and Moynihan (2002) point out, there is “too much medicine”, but that does not imply that there should be no medicine whatsoever.

A good way to finding a balance so as to be in the path of gentle medicine, is to move away from overtreatment. Here, the term “gentle medicine” becomes very meaningful, to the extent that, as a general rule, treatment needs to be less aggressive. In fact, amongst medical ethicists, there seems to be a growing recognition of this. For example, in the United Kingdom, the Academy of Medical Royal College has launched a “Choosing wisely” campaign, which seeks to create awareness that medicine can indeed become excessive, and that when it comes to choosing treatment, it must be done wisely (Malhotra et al. 2015).

In the absence of aggressive medical intervention, whose efficacy is far from completely proven (due to the shortcomings of medicine explained above), a program of gentle medicine would attempt to reduce the amount of medications that are prescribed by physicians. The opioid epidemic in the United States has already made many practitioners aware that painkiller medication has great potential for abuse, and consequently, less aggressive forms of pain treatment ought to be sought, especially if they reduce the risk of opioid addiction (Blendon and Benson 2018).

In fact, there are good reasons to believe that, in many cases, drugs can be discontinued without adverse consequences. For example, one study done by Avorn et al. (1992) in nursing homes reported that patients who were taking psychoactive drugs could be successfully tapered off in a gradual program. The study concluded that “an educational program targeted to physicians, nurses, and aides can reduce the use of psychoactive drugs in nursing homes without adversely affecting the overall behavior and level of functioning of the residents.”

Restructuring medical research to global needs

This move towards a less aggressive medicine should also be reflected in research priorities. If the prospects of gentle medicine become more hopeful in the years to come, more efforts should also be devoted to investigating the possible beneficial effects of reducing medical treatments. In particular, researchers should be more active investigating the effects of drug discontinuation. Based on the prevailing current paradigms, drug discontinuation is assumed to produce harmful effects, but in fact, little research has been done as to whether this might actually be the case.

As a replacement of many of the drugs that are used in overtreatment, gentle medicine would emphasize the need for more basic perspective, such as a humane approach of dignified treatment in doctor-patient relationships. As part of this endeavor, instead of focusing on the prospects of magic bullets, medical research should investigate more the possibilities of larger societal variables at play, which ultimately may have a greater impact on public health.

For example, there are many hints that social inequality impacts health standards in society. One particular review of the empirical evidence concludes that “reducing income inequality will improve population health and wellbeing” (Pickett and Wilkinson 2015). Marmot (2006) also makes the intriguing observation that in developed countries, “people do not die from lack of clean water and sanitary facilities or from famine—and yet, persistently, those at the bottom of the socioeconomic scale have worse health than those above them in the hierarchy.” This suggests that inequality impacts health significantly, a phenomenon that Marmot terms the “status syndrome”.

In order to target this particular problem, gentle medicine needs to focus less on finding particular magic bullets for disease, and instead, it needs to embrace forms of social activism so as to enable societal changes at large, that lead to better income distribution, and ultimately, improvements in health conditions.

This is a particular dimension of gentle medicine that needs further development in public health policies, so as to reflect a more robust public health ethics. This conceptual model has already been proposed by relevant figures in the field. For example, in his seminal work *Just Health Care*, Norman Daniels (1985) emphasized the importance of achieving meaningful equality in accessibility to healthcare. Likewise, Amartya Sen has written extensively on the need for a capability approach, which places its focus on the ethical significance of people’s capability of reaching the sort of lives that they come to value. In Sen’s (1992, p. 39) account, “the well-being of a person can be seen in terms of the quality (the ‘well-ness’, as it were) of the person’s being. Living may be seen as consisting of a set of interrelated ‘functionings’, consisting of beings and doings”; and in order for society to get to this state of affairs, a radical reconsideration of inequality must be enacted.

Likewise, environmental approaches can also serve the cause of gentle medicine. Instead of focusing on magic bullets for particular respiratory diseases, gentle medicine could focus its attention on reducing air pollution levels. It has been well-established that air pollution has significant effects on health (Kampa and Castanas 2008), and consequently, by embracing environmental movements, a gentle medicine approach would target the root causes of many respiratory diseases, thus reducing the need for aggressive treatments.

This also holds true for the current challenges of the Covid-19 pandemic. Although vaccines apparently do have an impact on reducing the spread of the virus, a focus on non-medical interventions could be of immense value in combatting the disease, without the need to engage in some of the medical practices that present some of the problems alluded to before. For example, a greater focus on the non-medical practice of social distancing, and basic procedures such as routinely washing hands (and educating people about the need to do so), would likely be very efficient in flattening the curve.

As mentioned above, gentle medicine does not imply embracing alternative medicine or complete medical nihilism. Research about drug treatments must continue. But, keeping in mind that most drugs are not magic bullets, medicine needs to reframe its priority about what drugs to focus on when it comes to research. Drugs that come much closer to the medical bullet model (such as antibiotics) should be given priority in research, since so much hinges upon their effectiveness.

For the most part, pharmaceutical companies offer very little interest in the further development of antibiotics. One possible explanation for this phenomenon is that, given that antibiotic treatments are not long-lasting, pharmaceutical companies do not have the incentive to invest research funds into drugs that will only be taken by patients for a few days, as opposed to drugs that are typically prescribed for much longer terms (such as antihypertensives or antipsychotics).

Private initiatives may not provide sufficient incentives for the development of medications that are most needed. Precisely for that reason, a gentle medicine approach would recommend governments to step in, and provide public funding so as to carry out the truly necessary research that needs to be done, in order to target diseases that are most common worldwide.

As it happens, currently there is a fundamental inequality of research priorities. Many resources are invested in drugs that target particular rich markets that are not necessarily bulks of population. In contrast, many of the diseases of large portions of world population are left unattended in research. Vidyasagar (2006) reports that “currently... less than 10% of global funding for research is spent on diseases that afflict more than 90% of the world's population.” Epidemiologists refer to this phenomenon as the 10/90 gap (Ramsay 2001), further contributing to the inequality that has an impact on health levels in the first place. A gentle medicine approach would recommend what Reiss and Kitcher (2009) call a “fair-share principle”, in which “the proportions of global resources assigned to different diseases should agree with the ratios of human suffering associated with those diseases.” There is no clear path about how to accomplish this fairness, but as with any redistributive endeavor, some degree of government action

and regulation is needed, so as to prevent the concentration of research funding in diseases that afflict only a very small percentage of the overall population.

Gentle medicine would also need to find a way to remove the profit element that, ultimately, gets big pharmaceutical companies in the way of non-biased research programs. One possible way of achieving that goal is by doing away with intellectual property statuses for medical interventions. If such intellectual property legislations disappear, pharmaceutical companies and their lobbies would not have the same level of motivation in skewing research results, so as to market new drugs. Consequently, researchers would feel less pressure to tamper with results (and would be less likely to unconsciously fall for confirmation biases), and laboratories would only approve drugs that truly work as magic bullets, instead of drugs that seem to work, but in fact, their effectiveness is based on flawed methodology.

Admittedly, many philosophers and social scientists have pointed out that innovation requires incentives (Scotchmer 2004). If intellectual property protection is removed, so the argument goes, no experimenter would invest efforts in finding new treatments. But this may actually be a form of what Eric Johnson (2011) calls the “incentive fallacy”. Johnson states that it is perfectly possible that “natural and intrinsic motivations will cause technology and the arts to flourish even in the absence of externally supplied rewards.”

This would appear to be the case in many of the great innovations in the history of medicine. Most of the great advances in medicine (e.g. Jenner's vaccine, Fleming's discovery of penicillin, Morton and Warren's discovery of anesthesia) were done without the profit incentives that the current financial system offers. Although each case is different, there does seem to emerge a pattern of genuine humanitarianism, and intrinsic scientific curiosity, rather than pure monetary incentive. This fact supports the argument that for medical science to keep advancing, not much of a profit incentive is needed, and consequently, in the realm of medical research, intellectual property laws do more harm than good.

Finally, another important aspect in the endeavor to reduce the preponderance of the distortion of research due to profit incentives, is to ensure that pharmaceutical companies do not have control of testing protocols in research. This would imply that institutions that have the task of testing new drugs, preserve autonomy from companies that ultimately produce and market the drugs or medical procedures. Furthermore, in order to avoid p-hacking distortions, protocols should require researchers to publicly register the working hypothesis before collecting data, so as to prevent *a-posteriori* modifications that ultimately skew results.

Conclusion

The Covid-19 experience once again made one of Hippocrates' observations very relevant: "to do nothing is also a good remedy" (Agus 2014). Especially in the initial days of the pandemic, before the development of vaccines, the best medical advice in order to stop the spread of the virus was precisely that: do nothing and stay home. If this particular advice were at first more closely followed in the early days of the pandemic, probably we would be in a better position today. For, as the virus was spreading, going to a hospital was itself a risk. Alas, hospital infections are relatively common, and in the United States alone, 99,000 people die of hospital infections each year (Healthline 2021).

This should give occasion to think that in deciding to pursue a medical procedure, a more thorough cost–benefit analysis must be done, as risks are always involved. Due to some methodological flaws, and some interference from profit incentives in the way research is conducted, medicine tends to overestimate the benefits and underestimate the costs of medical interventions.

In the face of these issues, the program of "gentle medicine" is a much-needed approach. There are good enough reasons to be skeptical of many of the claims of medicine's success. That does not imply that critics must throw the baby out with the bathwater, and embrace a full-blown medical nihilism. But, it does imply that medicine must be subject to a greater critical scrutiny, and in so doing, we must come to the conclusion that a more effective and humane medicine will require less aggressive treatments, more restrictive diagnoses, and stricter controls in research protocols.

There is also the surprising implication that medicine may have to come to terms with some linguistic reform. For too long, biomedical practice has been embedded in metaphors and expressions that are too reminiscent of militaristic terms, and this has even proven detrimental to the wellbeing of many patients, who feel an enormous pressure to "combat" so as to become "survivors", otherwise they would "lose a war". For example, Susan Sontag (2001) in her seminal work *Illness as Metaphor* (a deeply personal indictment of militarist language in medicine) laments that "the controlling metaphors in descriptions of cancer are, in fact, drawn not from economics but from the language of warfare: every physician and every attentive patient is familiar with, if perhaps inured to, this military terminology. Thus, cancer cells do not simply multiply; they are "invasive."

In turn, this language has enabled a more aggressive approach to medicine. Under this paradigm, pursuing

gentler forms of medicine (or simply doing nothing) is interpreted akin to a naïve pacifism, or even worse, a defeatist approach that lets the "invader" take over the body. Although military metaphors can be useful to the extent that they can allow patients to feel empowered, they can ultimately also fuel an overly aggressive medicine that incurs in many of the difficulties that we have so far approached. For that reason, some balance in the use of metaphor must be obtained. As Parsi (2016) argues, "allowing a certain level of pluralism with the kinds of metaphors we use is appropriate. What's troubling is when one metaphor (in this case, the military metaphor) becomes the only or dominant way we interpret various illnesses."

The Covid-19 experience is a good illustration of how military metaphors may actually be counterproductive. In the wake of the pandemic, many governments were prompted to respond as if it were some sort of military emergency, and public health operations were referred to as if they were wars (Kalkman 2021). The use of military language in addressing the pandemic conditions people to believe that the only way to deal with this emergency is by embracing aggressive medicine programs. But, as previously mentioned, that is not necessarily accurate. If a softer language devoid of military metaphors were used, then perhaps there would have been a wider acceptance that the best approach to Covid-19 was meeting social distancing protocols, instead of aggressively pursuing actions of questionable efficacy.

In light of all the lines of criticism approached above, at this point some nuance must also be considered, especially concerning the specificity of each medical field. While this has been a critique of biomedical research and practice as a whole, it must still be pondered how each specialty differs. Future ethical engagement with the paradigm of gentle medicine should induce ethicists to consider how each medical field relates to it. For example, might surgery be less or more exposed to the line of criticism discussed in this article? Tentatively, we may argue that unnecessary surgery remains a problem in medicine (Leape 1989); but even within this field, there are differences between, say, cosmetic surgery and orthopedic surgery, as the former has a far greater risk of being subject to many of the economic and social pressures already alluded to (Diamond and Garland 2014). Nevertheless, even if it is certainly true that not all specialties of medicine are prone in the same degree to excessively aggressive medicine, all healthcare professionals (regardless of their specialty) must seriously consider the ethical obligations to consider whether treatments are truly effective, and in what cases it may actually be a better approach to engage with more gentle forms of treatment.

References

- Agus, D.B. 2014. *A short guide to a long life*. New York: Simon and Schuster.
- Anastasia, K. 1984. History of frontal lobotomy in the United States, 1935–1955. *Neurosurgery* 14 (6): 765–772.
- Andrade, G., and M. Campo-Redondo. 2020. The ethics of psychiatrists’ political involvement: A reassessment in the Trump era. *Ethics, Medicine and Public Health* 15: 100554.
- Angell, M. 2005. *The truth about the drug companies: How they deceive us and what to do about it*. New York: Random House.
- Armitage, J. 2007. The safety of statins in clinical practice. *The Lancet* 370 (9601): 1781–1790.
- Avorn, J., S.B. Soumerai, D.E. Everitt, D. Ross-Degnan, M.H. Beers, D. Sherman, and D. Fields. 1992. A randomized trial of a program to reduce the use of psychoactive drugs in nursing homes. *New England Journal of Medicine* 327 (3): 168–173.
- Ayta, I.A., J.B. McKinlay, and R.J. Krane. 1999. The likely worldwide increase in erectile dysfunction between 1995 and 2025 and some possible policy consequences. *BJU International* 84 (1): 50–56.
- Barber, B., IV., and L. Diestre. 2019. Pushing for speed or scope? Pharmaceutical lobbying and Food and Drug Administration drug review. *Strategic Management Journal* 40 (8): 1194–1218.
- Barnett, R. 2018. Type 1 diabetes. *The Lancet* 391 (10117): 195.
- Bero, L., F. Oostvogel, P. Bacchetti, and K. Lee. 2007. Factors associated with findings of published trials of drug–drug comparisons: why some statins appear more efficacious than others. *PLoS Medicine* 4 (6): e184.
- Black, W.C. 2000. Overdiagnosis: An underrecognized cause of confusion and harm in cancer screening. *Journal of the National Cancer Institute* 92 (16): 1280–1282.
- Blendon, R.J., and J.M. Benson. 2018. The public and the opioid-abuse epidemic. *New England Journal of Medicine* 378 (5): 407–411.
- Broadbent, A. 2019. *Philosophy of medicine*. Oxford: Oxford University Press.
- Brodersen, J., and V.D. Siersma. 2013. Long-term psychosocial consequences of false-positive screening mammography. *The Annals of Family Medicine* 11 (2): 106–115.
- Brody, H. 1989. Ethics and therapeutic skepticism. *Journal of Family Practice* 29 (6): 611–613.
- Bulliard, J.L., and A. Chiolerio. 2015. Screening and overdiagnosis: Public health implications. *Public Health Reviews* 36 (1): 1–5.
- Carel, H., and J. Kidd. 2017. Epistemic injustice in medicine and healthcare. In *The Routledge handbook of epistemic injustice*, ed. I. Kidd, J. Medina, and G. Pohlhaus. New York: Routledge.
- Castiglioni, A. 2019. *A history of medicine*. New York: Routledge.
- Christakis, N. 2020. *Apollo’s arrow: The profound and enduring impact of coronavirus on the way we live*. New York: Little.
- Cotter, J., and E. Woollorton. 2005. New restrictions on celecoxib (Celebrex) use and the withdrawal of valdecoxib (Bextra). *CMAJ* 172 (10): 1299–1299.
- Dal Rio, A.C.C., E.M.D. Nicola, and A.R.F. Teixeira. 2007. Halitosis—an assessment protocol proposal. *Brazilian Journal of Otorhinolaryngology* 73 (6): 835–842.
- Dal-Ré, R., A.L. Caplan, C. Gluud, and R. Porcher. 2021. Ethical and scientific considerations regarding the early approval and deployment of a COVID-19 vaccine. *Annals of Internal Medicine*. 8: 3.
- Daniels, N. 1985. *Just health care*. Cambridge: Cambridge University Press.
- Diamond, M., and J. Garland. 2014. Evidence regarding cosmetic and medically unnecessary surgery on infants. *Journal of Pediatric Urology* 10 (1): 2–6.
- Dieppe, P.A., S. Ebrahim, R.M. Martin, and P. Jüni. 2004. Lessons from the withdrawal of rofecoxib. *BMJ* 329: 867.
- Ebrahim, S., S. Bance, A. Athale, C. Malachowski, and J.P. Ioannidis. 2016. Meta-analyses with industry involvement are massively published and report no caveats for antidepressants. *Journal of Clinical Epidemiology* 70: 155–163.
- Enck, P., S. Klosterhalfen, K. Weimer, B. Horing, and S. Zipfel. 2011. The placebo response in clinical trials: More questions than answers. *Philosophical Transactions of the Royal Society B: Biological Sciences* 366 (1572): 1889–1895.
- Endo, A. 2010. A historical perspective on the discovery of statins. *Proceedings of the Japan Academy, Series B* 86 (5): 484–493.
- Foucault, M. 2012. *The birth of the clinic*. New York: Routledge.
- Franco, O.H., A. Peeters, C.W. Looman, and L. Bonneux. 2005. Cost effectiveness of statins in coronary heart disease. *Journal of Epidemiology & Community Health* 59 (11): 927–933.
- Gaynes, R. 2017. The discovery of penicillin—new insights after more than 75 years of clinical use. *Emerging Infectious Diseases* 23 (5): 849.
- Goldberg, A. 2001. Depathologizing homosexuality. *Journal of the American Psychoanalytic Association* 49 (4): 1109–1114.
- Gottlieb, S. 2002. 1.6 million elementary school children have ADHD, says report. *BMJ* 324 (7349): 1296.
- Grandjean, P., P. Weihe, R.F. White, and F. Debes. 1998. Cognitive performance of children prenatally exposed to “safe” levels of methylmercury. *Environmental Research* 77 (2): 165–172.
- Greenstone, G. 2010. The history of bloodletting. *BC Medical Journal* 52 (1): 12–14.
- Head, M.L., L. Holman, R. Lanfear, A.T. Kahn, and M.D. Jennions. 2015. The extent and consequences of p-hacking in science. *PLoS Biology* 13 (3): e1002106.
- Healthline. 2021. 99,000 Americans die of healthcare-acquired infections every year. <https://www.healthline.com/health-news/aging-healthcare-acquired-infections-kill-nearly-a-hundred-thousand-a-year-072713>
- Hinshaw, S.P. 2018. Attention deficit hyperactivity disorder (ADHD): Controversy, developmental mechanisms, and multiple levels of analysis. *Annual Review of Clinical Psychology* 14: 291–316.
- Horwitz, A., and J. Wakefield. 2007. *Loss of sadness: How psychiatry transformed normal sorrow into depressive disorder*. New York: Oxford University Press.
- Illich, I. 1975. *Medical nemesis*. Sydney: Australian Broadcasting Commission, Science Programmes Unit.
- Ioannidis, J.P. 2005. Why most published research findings are false. *PLoS Medicine* 2 (8): e124.
- Ioannidis, J.P. 2016. Why most clinical research is not useful. *PLoS Medicine* 13 (6): e1002049.
- Ioannidis, J.P. 2017. Defending biomedical science in an era of threatened funding. *JAMA* 317 (24): 2483–2484.
- Iroegbulem, V. C. 2020. Disease Mongering: How Sicknes Sells. Augustuna Student paper. <https://digitalcommons.augustana.edu/ethicscontest/20/>
- Johnson, E.E. 2011. Intellectual property and the incentive fallacy. *Fla. St. UL Rev.* 39: 623.
- Kalkman, J.P. 2021. Military crisis responses to COVID-19. *Journal of Contingencies and Crisis Management* 29 (1): 99–103.
- Kampa, M., and E. Castanas. 2008. Human health effects of air pollution. *Environmental Pollution* 151 (2): 362–367.
- Kuhn, T.S. 2012. *The structure of scientific revolutions*. Chicago: University of Chicago Press.
- Leape, L.L. 1989. Unnecessary surgery. *Health Services Research* 24 (3): 351.
- Lexchin, J. 2006. Bigger and better: how Pfizer redefined erectile dysfunction. *PLoS Medicine* 3 (4): e132.
- Light, D.W., J. Lexchin, and J.J. Darrow. 2013. Institutional corruption of pharmaceuticals and the myth of safe and effective drugs. *The Journal of Law, Medicine & Ethics* 41 (3): 590–600.

- Lim, W.H., S.H. Kim, H.L. Kim, K.H. Kim, S.H. Na, H.J. Lee, and M.A. Kim. 2015. Recurrent acute decompensated heart failure owing to severe iron deficiency anemia caused by inappropriate habitual bloodletting. *Journal of Cardiovascular Ultrasound* 23 (4): 253.
- MacLennan, A.H., D.H. Wilson, and A.W. Taylor. 2002. The escalating cost and prevalence of alternative medicine. *Preventive Medicine* 35 (2): 166–173.
- Malhotra, A., D. Maughan, J. Ansell, R. Lehman, A. Henderson, M. Gray, S. Bailey, et al. 2015. Choosing Wisely in the UK: The Academy of Medical Royal Colleges' initiative to reduce the harms of too much medicine. *BMJ* 350: 1.
- Marmot, M.G. 2006. Status syndrome: A challenge to medicine. *JAMA* 295 (11): 1304–1307.
- McKeown, T. 2014. *The role of medicine: Dream, mirage, or nemesis?* New York: Princeton University Press.
- Moynihan, R., and A. Cassels. 2005. *Selling sickness: How the world's biggest pharmaceutical companies are turning us all into patients.* Vancouver: Greystone Books.
- Moynihan, R., and D. Henry. 2006. The fight against disease mongering: generating knowledge for action. *PLoS Medicine* 3 (4): e191.
- Moynihan, R., and R. Smith. 2002. Too much medicine? Almost certainly. *BMJ* 324: 859.
- Naylor, S., and J.Y. Chen. 2010. Unraveling human complexity and disease with systems biology and personalized medicine. *Personalized Medicine* 7 (3): 275–289.
- Nissen, S.E., and K. Wolski. 2007. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. *New England Journal of Medicine* 356 (24): 2457–2471.
- Parsi, K. 2016. War metaphors in health care: What are they good for? *The American Journal of Bioethics* 16 (10): 1–2.
- Patwardhan, A.R. 2016. Physicians-pharmaceutical sales representatives interactions and conflict of interest: challenges and solutions. *INQUIRY: the Journal of Health Care Organization, Provision, and Financing* 53: 597.
- Pellegrino, E.D. 1993. The metamorphosis of medical ethics: A 30-year retrospective. *JAMA* 269 (9): 1158–1162.
- Pickett, K.E., and R.G. Wilkinson. 2015. Income inequality and health: A causal review. *Social Science & Medicine* 128: 316–326.
- Porter, R. 2004. *Blood and guts: A short history of medicine.* New York: WW Norton & Company.
- Ramsay, S. 2001. No closure in sight for the 10/90 health-research gap. *The Lancet* 358 (9290): 1348.
- Reiss, J., and P. Kitcher. 2009. Biomedical research, neglected diseases, and well-ordered science. *THEORIA. Revista De Teoría, Historia y Fundamentos De La Ciencia* 24 (3): 263–282.
- Riley, J.C. 2001. *Rising life expectancy: A global history.* Cambridge: Cambridge University Press.
- Rochon, P.A., J.H. Gurwitz, R.W. Simms, P.R. Fortin, D.T. Felson, K.L. Minaker, and T.C. Chalmers. 1994. A study of manufacturer-supported trials of nonsteroidal anti-inflammatory drugs in the treatment of arthritis. *Archives of Internal Medicine* 154 (2): 157–163.
- Rottlaender, D., and U.C. Hoppe. 2008. Risks of non-prescription medication. Clobutanol cough syrup as a recent example. *Deutsche Medizinische Wochenschrift (1946)* 133 (4): 144–146.
- Saddichha, S. 2010. Disease mongering in psychiatry: Is it fact or fiction? *World Medical & Health Policy* 2 (1): 267–284.
- Sallon, S., Y. Dory, Y. Barghouthy, T. Tamdin, R. Sangmo, J. Tashi, and T. Bdoah-Abram. 2017. Is mercury in Tibetan Medicine toxic? Clinical, neurocognitive and biochemical results of an initial cross-sectional study. *Experimental Biology and Medicine* 242 (3): 316–332.
- Saqib, N., J. Saqib, and J.P. Ioannidis. 2015. Does screening for disease save lives in asymptomatic adults? Systematic review of meta-analyses and randomized trials. *International Journal of Epidemiology* 44 (1): 264–277.
- Schaller, B.J., and M. Leonardi. 2006. Invited comments. *Neurology India* 54 (1): 57–57.
- Scotchmer, S. 2004. *Innovation and incentives.* Boston: MIT Press.
- Sen, A. 1992. *Inequality reexamined.* Oxford: Oxford University Press.
- Shojania, K.G. 2012. Deaths due to medical error: jumbo jets or just small propeller planes? *BMJ* 21 (9): 1.
- Simoni, R.D., R.L. Hill, and M. Vaughan. 2002. The discovery of insulin: The work of Frederick Banting and Charles Best. *Journal of Biological Chemistry* 277 (26): e15–e15.
- Smith, R. 2005. Medical journals are an extension of the marketing arm of pharmaceutical companies. *PLoS Medicine* 2 (5): e138.
- Sontag, S. 2001. *Illness as metaphor and AIDS and its metaphors.* New York: Macmillan.
- Spieß, B.D. 2010. Pro: The practice of cardiac anesthesia has changed after the withdrawal of aprotinin. *Journal of Cardiothoracic and Vascular Anesthesia* 24 (5): 875–878.
- Stegenga, J. 2011. Is meta-analysis the platinum standard of evidence? *Studies in History and Philosophy of Science Part c: Studies in History and Philosophy of Biological and Biomedical Sciences* 42 (4): 497–507.
- Stegenga, J. 2018. *Medical Nihilism.* Oxford: Oxford University Press.
- Strehhardt, K., and A. Ullrich. 2008. Paul Ehrlich's magic bullet concept: 100 years of progress. *Nature Reviews Cancer* 8 (6): 473–480.
- Suresh, K. P. 2011. An overview of randomization techniques: an unbiased assessment of outcome in clinical research. *Journal of human reproductive sciences* 4 (1): 8.
- Szasz, T.S. 1960. The myth of mental illness. *American Psychologist* 15 (2): 113.
- Vidyasagar, D. 2006. Global notes: The 10/90 gap disparities in global health research. *Journal of Perinatology* 26 (1): 55–56.
- Willoughby, C.D. 2018. Running away from drapetomania: Samuel A Cartwright, medicine, and race in the Antebellum South. *Journal of Southern History* 84 (3): 579–614.
- Winau, F., O. Westphal, and R. Winau. 2004. Paul Ehrlich—in search of the magic bullet. *Microbes and Infection* 6 (8): 786–789.
- Wolinsky, H. 2005. Disease mongering and drug marketing: Does the pharmaceutical industry manufacture diseases as well as drugs? *EMBO Reports* 6 (7): 612–614.
- Woloshin, S., and L.M. Schwartz. 2006. Giving legs to restless legs: A case study of how the media helps make people sick. *PLoS Medicine* 3 (4): e170.
- Worrall, J. 2002. What evidence in evidence-based medicine? *Philosophy of Science* 69 (S3): S316–S330.
- Wottoon, D. 2007. *Bad medicine: Doctors doing harm since Hippocrates.* Oxford: Oxford University Press.
- Yeo, M. 1989. Primum non nocere: The ethics of teaching medical ethics. *Teaching Philosophy* 12 (1): 23–34.
- Zelenay, J.L. 2005. The prescription drug user fee act: Is a faster Food and Drug Administration always a better Food and Drug Administration? *Food and Drug Law Journal* 60 (2): 261–338.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.