# Pragmatic Progress and the Improvement of Medical Knowledge for Global Health

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## Abstract

The paper presents an epistemological argument on the crisis in medical knowledge today, first identifying a fundamental problem of the crisis, i.e., the *epistemic gap*, and then introducing the concept of *pragmatic progress* as a tool for understanding what is needed for pharmaceutical research to solve pressing epistemic and public health problems. This (new) analysis can contribute to identifying at least one mechanism needed to close the epistemic gap in current medical knowledge, which in turn could serve as a criterion for filtering current and future proposals. In order to do this, first, I show that the drug market has led to a significant *epistemic gap* between the knowledge needed to address pressing public health issues and the knowledge produced following the demands of the global market. Second, using the notion of pragmatic progress, I suggest a reading of the crisis in medical knowledge, which emphasizes the problems that clinical research is set to solve. Then I present two alternative ways to restructure medical research to fulfill this aim, illustrating how each can be implemented through real-world examples. The last section addresses a possible objection to the argument and exemplifies how the criterion can be used to filter undesirable proposals.

**Keywords:** Medical Knowledge, Pragmatic Progress, Commercialization of Research, Epistemic Gap, Biomedical R&D, Philanthrocapitalism.

## Introduction

The globalized privatization of scientific research has been both rampant and vicious for evidence-based medicine and the production of medical knowledge. Pharmaceutical companies now control the performance and funding of the majority of clinical trials and drug development strategies worldwide, and have strong financial incentives to keep unfavorable results confidential, squeeze patent revenues, and prompt doctor prescriptions through massive marketing campaigns. A number of scholars agree that there is something fundamentally wrong in the way Big Pharma conducts scientific research today (Sismondo, 2009; Carpenter, 2010; Dumit, 2012; Goldacre, 2012; Mirowski, 2013; Homedes and Ugalde, 2014; Whitaker and Cosgrove, 2015; Harris, 2017; Moynihan et al., 2019), but less consensus is found regarding the main causes of this crisis, and even less regarding the best way to move forward.

While some blame the culture of secrecy in Big Pharma and demand more transparency (Goldacre, 2012), others attack the patent system

as inappropriate for medical innovation (Light and Maturo, 2015), and still others identify the problem as one of institutional corruption (Whitaker and Cosgrove, 2015). Proposed solutions range from different paths towards Open Science (Nielsen, 2011; OECD, 2015), including open access to trial data and publications (Phelps et al., 2012; Goldacre and Gray, 2016), through strengthening the public and independent funding of medical research (Light et al., 2013; Lexchin, 2016), to a diversity of strategies for democratizing clinical research and making it more inclusive (Epstein, 1995; Grasswick, 2010; Harding, 2015). One analysis of the problem (Moynihan et al., 2019), examines how different organizations, e.g., governments, professional associations, medical journals, etc., are implementing strategies to move away from commercial influence in three broad areas, i.e., research, education, and practice.

More recently, a number of alternative approaches to pharmaceutical research and development (R&D) have emerged, especially in areas of market failure, such as research on neglected tropical diseases (NTDs), establishing public-private partnerships and new communities of collaboration (Lezaun and Montgomery, 2015). Many have argued for a 'delinkage' of the price of medicines, and thus market profitability, from the financial investment in R&D; and different financing mechanisms (such as the so called 'pushing' and 'pulling' strategies) have been proposed and implemented with this goal in mind (Greenberg and Kiddell-Monroe, 2016; Suleman et al., 2020). But are these 'delinking' mechanisms good enough to solve the crisis in medical knowledge today? And if not, how can we improve medical knowledge for global health given the current state of medical R&D?

The aim of the paper is not to provide further diagnosis about the particular factors that have led evidence-based medicine to where it is today, nor to provide an empirical evaluation of the proposed alternatives. Instead, in this paper, I offer an epistemological argument on the crisis in medical knowledge today, first identifying what I consider to be a fundamental problem of the crisis, i.e., what I call the 'epistemic gap', and then introducing the concept of 'pragmatic progress' as a tool for understanding what is needed for pharmaceutical research to solve pressing epistemic and public health problems. This (new) analysis can contribute to identifying at least one mechanism needed to close the epistemic gap in current medical knowledge, which in turn could serve as a criterion for filtering current and future proposals. In other words, thinking about pragmatic progress can help us identify whether or not the strategies found in the literature and described in the previous paragraphs can actually serve the medical knowledge crisis.

The paper in divided in the following sections. In the next section, I question the idea that the free-market provides the best possible framework to produce scientific knowledge, showing instead that the drug market has led to a significant epistemic gap between the knowledge needed to address pressing public health issues and the knowledge produced following the demands of the global market. Once this epistemic gap is understood, the following section examines two competing notions of scientific progress and suggests a new reading of the crisis in medical knowledge, which emphasizes the problems that clinical research is set to solve. The lesson is that for medical knowledge to progress towards public health goals, i.e., to close the epistemic gap, research cannot be set to solve commercial problems primarily, but epistemically and socially relevant ones. Then I move on to present two alternative ways to restructure medical research to fulfill this aim, illustrating how each can be implemented through real-world examples. Last, I address a possible objection to the argument and exemplifies how the criterion can be used to filter undesirable proposals.

## The epistemic gap in current medical knowledge

As a result of the pharmaceutical industry's influence in medical research, we currently have a significant epistemic gap between the knowledge needed to address pressing public health issues (by which I mean health problems, such as access to medication and proper treatment, for society's most vulnerable), and the knowledge produced following the demands of the global market. Profitable medical knowledge does not necessarily

coincide with the knowledge needed to improve public health, to combat health inequality, or to prevent health hazards. Expert scholars have repeatedly shown that, contrary to what companies argue, market incentives do not produce better medical knowledge.

To illustrate this point, consider the following three examples. First, market incentives promote the use of placebos instead of the best available therapy in clinical trials, since new treatments are more likely to outperform placebos than outperform the best available therapies, although outperforming placebos does not constitute a real epistemic gain if we already have better therapies (Barbui et al., 2007; Homedes and Ugalde, 2016).

Second, market incentives encourage companies to maintain failed trials and trials with unfavorable outcomes confidential, so that results do not have a negative impact on the marketing process and future profits, although this practice is clearly detrimental from an epistemic point of view, since only a biased portion of the knowledge produced is available and thus no sound conclusions can follow from it (Goldacre, 2012; Wieseler et al., 2013).

Moreover, by exclusively focusing on conducting randomized clinical trials for the production of new drugs, the pharmaceutical industry is completely centered in the evidence-based knowledge paradigm, which only accounts for a partial epistemology of medicine, leaving aside core epistemic issues regarding the causal mechanisms involved in disease development and drug interactions (Solomon, 2015). This is even the case for some of the main alternatives to RCTs. For instance, Adaptive Design Trials (ADTs) have emerged to provide flexibility as a response to market and financial pressures that RCTs have not been able to tackle, leaving untouched, or even worsening, the epistemic limitations of RCTs (Helgesson and Lee, 2017). In a similar vein, Pragmatic Clinical Trials (PCTs), which aim at conducting biomedical research in real-world settings with patients undergoing medical treatments, and thus obtaining results from actual medical settings, have been criticized precisely for not questioning the RCT model as the gold standard for research (Rushforth, 2015).[1]

And these are only three of a myriad of epistemically worrisome practices that Big Pharma has put in place following market incentives (for a summary of other problems see Bero and Rennie, 1996; Moynihan et al., 2019).

Thus, as scholars of science, technology, and medicine have been arguing for some time now (see, e.g., McGarity and Wagner, 2012; Mirwoski, 2013; Whitaker and Cosgrove, 2015) and contrary to what free-market fundamentalists might say (Oreskes and Conway, 2010), market incentives have not rendered better knowledge. Not only because we can easily identify epistemic problems that need to be fix, but also because we can imagine many different ways in which medical knowledge could better address social needs, e.g., by addressing neglected tropical diseases, developing affordable treatments, aiming at de-medicalizing patients, etc; and, more importantly, because we have good examples of alternative frameworks, such as the Mario Negiri Institute or the Cochrane Center, different from the commercial framework, in which the production of medical knowledge does not suffer from the epistemic flaws we find in Big Pharma. Thus, instead of producing better medical knowledge, market incentives have created an epistemic gap between the medical knowledge society needs and the medical knowledge actually being produced.

This epistemic gap becomes even more salient when we examine the attempts at fixing market incentives through democratizing strategies, i.e., strategies to increase citizen participation, make research more inclusive and diverse, or merely taking into account stakeholders, which have been for the most part unsuccessful, as market incentives rapidly corrupt the laudable aims of these strategies. Good examples that illustrate this point are the recruitment of diverse subjects in global clinical trials (Fernández Pinto, 2019) and the way private companies have learned to steer health advocacy organizations (Fernández Pinto, 2018). As it will become clear in the next section, even philanthropic initiatives, such as the Bill and Melinda Gates Foundation (BMGF), with their apparent aim at epistemic redistribution, i.e., procuring medical knowledge for the most needed, fail to keep financial conflicts of

interest at bay (Birn, 2014; McGoey and Thiel, 2018; Fernández Pinto, 2022). In all these cases, strategies to democratize the process of medical knowledge production do not seem to contribute to making research more inclusive or diverse, or even to render better results to treat the more vulnerable. Instead, it seems that market incentives are likely to corrupt the goals of such strategies, which only accentuates the significance of the epistemic gap in medical research today.

## Scientific progress as problem-solving

In this paper, I would like to shed a new light on the problems for medical knowledge stemming from the current organization of medical research led by pharmaceutical companies worldwide and guided by market incentives. But first, the analysis requires a small philosophical detour.

### *Pragmatic progress*

Traditionally, scientific progress is understood in terms of achieving or moving towards a general epistemic goal, such as truth or knowledge. However, the idea of science progressing in this sense has been the target of various critiques, among other reasons, because of the linear and cumulative picture of scientific practice and knowledge production that it presupposes.[2] Thomas Kuhn famously opposed this view of science:

> We are all deeply accustomed to seeing science as the one enterprise that draws constantly nearer to some goal set by nature in advance. But need there be any such goal? Can we not account for both science's existence and its success in terms of evolution from the community's state of knowledge at any given time? Does it really help to imagine that there is some one full, objective, true account of nature and that the proper measure of scientific achievement is the extent to which it brings us closer to that ultimate goal? If we can learn to substitute evolution-from-what-we-do-know for evolution-toward-what-we-wish-to-know, a number of vexing problems may vanish in the process. (Kuhn, 1962: 171)

Contrary to the linear and cumulative view of science, Kuhn had in mind a history of deep ruptures in the scientific world view, which he famously called scientific revolutions. However, even with this radically different conception of scientific practice, Kuhn also had an account of scientific progress: not a cumulative view, but an evolutionary one. As he (Kuhn, 1962: 171) says in the previous quote: "Can we not account for both science's existence and its success in terms of evolution from the community's state of knowledge at any given time?"

Here, Kuhn is following the steps of American pragmatist philosopher John Dewey, with whom he shared a naturalist view of scientific progress. For Dewey, progress is pragmatic in character. It is not the transition towards some ultimate goal, but the organized solution to an end-in-view or a problem at hand:

> The aim set up must be an outgrowth of existing conditions. It must be based upon a consideration of what is already going on; upon the resources and difficulties of the situation. Theories about the proper end of our activities (…) often violate this principle. They assume ends lying outside our activities; ends foreign to the concrete makeup of the situation; ends which issue from some outside source. (Dewey, 1915: 112)

For Dewey, the notion of progress in human action is tied to the possibility of improving current circumstances: "The value of a legitimate aim, on the contrary, lies in the fact that we can use it to change conditions. It is a method for dealing with conditions so as to effect desirable alterations in them" (Dewey, 1915: 113). In this account, aims are situated, local, i.e., they respond to contextual practical needs. Accordingly, scientific progress occurs when the research process, which is an organized and ordered process, improves present conditions. Philosopher Philip Kitcher illustrates this kind of pragmatic progress using the example of transport technology:

> Progress in transport technology is not to be understood in terms of decreasing distance towards some ideal goal—there is no ideal system of transportation towards which we are converging—but as progress away from problematic situations: we make progress by solving problems, by introducing or refining devices that fulfill the pertinent functions. (Kitcher, 2012: 316)

In sum, there is a notion of scientific progress stemming from the American pragmatist tradition in which progress is not understood teleologically, i.e., as the movement towards an ultimate goal, but pragmatically or evolutionarily, i.e., as solving a particular problem at hand. I will now use this idea of pragmatic progress to shed light on the epistemic gap of medical knowledge today.

### *What problems is pharma trying to solve?*

The idea of *pragmatic progress* is useful to our purposes because it is closer to current scientific practice, where research projects need to be self-contained and have clearly set goals, achievable in a reasonable amount of time. Pharmaceutical research might be an extreme case of such constraints, where time pressure and well-defined problem-solving guides the whole research process. Accordingly, we can now ask, what problems is pharmaceutical R&D trying to solve?

The question becomes a crucial one because research outcomes directly depend on the problems research is set up to solve in the first place. If the problems that commercialized medicine is set up to solve are fundamentally different from the public health problems one would expect it to solve, then, not surprisingly, research results need not render solutions to the latter. Pharmaceutical research today is a problem-solving enterprise, structured to solve in the most efficient way an array of problems that arise at different stages of the research process. The main problem is how to get a drug quickly into the market to benefit the most from patent-protected revenues. This problem is then meticulously fragmented into smaller efficiency problems along the research process: how to recruit research subjects quickly, how to comply with government regulations, how to design and conduct trials to obtain significant results, how to write and publish scientific papers to get the most recognition and coverage, how to give patients information about diseases and treatment, etc.

The problems are set in a commercial framework and are for the most part commercial in character.[3] If they target any epistemic or social goals, it is only instrumentally, i.e., for the sake of further commercial gain. For example, as some have argued, commercial research can benefit from being methodologically rigorous, given that obtaining good quality results would lead to good quality products that consumers will favor (Carrier, 2009). However, here we can see that solving the epistemic problem is just instrumental to solving the commercial problem. And, as it happens, whenever solving the epistemic problem does not contribute to solving the commercial problem, or when the commercial problem can be solved more efficiently some other way, then the epistemic problem is easily set aside.

A good example is the case of surrogate endpoints in clinical trials. Surrogate endpoints or markers that correlate with real-world outcomes, the true research targets, are frequently used as a substitute during clinical trials. Surrogates are useful for clinical research whenever the real-world outcome is undesirable or when there is a methodological barrier to reading the endpoint (e.g., when trying to prevent heart attacks or death). However, surrogate markers can also render unreliable results, when benefits on surrogate endpoints do not correlate with benefits on real targets. A clear example that illustrates this point is the development of anti-arrhythmic drugs to prevent sudden death after myocardial infarction. Heart arrhythmias post-infraction seemed to increase the risk of sudden death, which led researchers to believe that preventing such arrhythmias, a surrogate marker, would lead to lower the risk of sudden death. As the infamous CAST study illustrates (Echt et al., 1991), preventing abnormal heart rhythms did not correlate with preventing sudden death. Quite the contrary, anti-arrhythmic drugs increased the risk of death and had to be pulled out of the market (Goldacre, 2012: 133). A crucial mistake was made because arrhythmia was used as a surrogate.

Even though the use of surrogate endpoints is a great tool for investigating possible treatments that could not be investigated otherwise, one should not underestimate the difficulty of using this tool appropriately. Among others, a strong relationship between the surrogate endpoint and the 'real' endpoint should be established, as well as the biological plausibility of the causal relation between changes in the surrogate marker and changes in the 'real' marker and a strong biological justification for using

such a surrogate marker (Lonn, 2001). When any of this fail, surrogate endpoints in clinical trials might provide completely mistaken results, as in the anti-arrhytmic drugs case. And even if the surrogate endpoint appropriately correlates with the 'real' endpoint, there is also the risk of unexpected secondary effects that can only be identified in trials specifically designed for this purpose (Lonn, 2001: 504).

Accordingly, if surrogate endpoint trials are carried out without the precautions needed to establish the validity of the surrogate marker as well as its possible side effects, both of which entail strict epistemic conditions, then one would have reasons to claim that the proper epistemic interests of scientific research are being set aside in favor of other, perhaps commercial, interests.

Now, as previously mentioned, it has been widely accepted that there is a crisis in medical knowledge today, and that the current business model for pharmaceutical R&D is less than optimal. Accordingly, a number of strategies have emerged as a response to this challenge. Acknowledging the epistemic gap left behind by the Big Pharma model, philanthropic foundations, such as the Bill and Melinda Gates Foundation (BMGF), Bloomberg, the Clinton Foundation, and the Carso Health Institute, have channelled billions of dollars into biomedical research, have collaborated with governments in low and middle income countries (LMICs) in developing public health initiatives, and have reshaped global health policy and aid (Reubi, 2018). In general, these philanthropic initiatives favor public-private partnerships (PPPs), bringing together international organizations, local governments, pharmaceutical companies, and NGOs (Reubi, 2018). The BMGF, perhaps the most influential of them all, also has the capacity to line up other rich donors to support their biomedical R&D projects overseas (Birn, 2014).

Despite ear-marking R&D that has been left aside by the pharmaceutical market (e.g., research on malaria and other NTDs has been at the front of philanthropic initiatives), these foundations are organized and execute their research plans under a clear business model. They foster PPPs to attract private companies so that they invest in areas in which they would not normally invest. The underlying principle is the same that in the traditional Big Pharma model: the market is infallible, so business models will give us the best solutions to social problems, including global health problems (Birn, 2014: 15). This new wave of philanthrocapitalism (Bishop and Green, 2008; Edwards, 2010) has not detached commercial interests from biomedical R&D but, on the contrary, it has created new commercial incentives for private companies to get involved in these previously neglected areas of research (Birn 2014; McGoey and Thiel 2018). As Birn states, "When PPP benefits such as direct grant monies, tax subsidies, reduced market risk, reputation enhancement, expanded markets, and IP rights are taken into account, the net result is that most PPPs channel public money into the private sector, not the other way around" (Birn, 2014: 14). So in the case of philanthropic initiatives, pretty much as in traditional biomedical R&D, commercial aims are involved in setting research agendas, collaborating with local governments, channelling tax-payers money, opening new markets, etc. The epistemic and social goals of biomedical research get, once again, compromised by commercial interests.

Thus, in order to solve particular epistemic and public health problems, research should be set to achieve those goals, and not other competing commercial targets. So now we have to ask: What are the problems that medical research ought to solve? What should count as medical progress?

## Pragmatic progress to improve medical knowledge

The emphasis on the pragmatic progress of science uncovers the close connection between the particular problems research is set to solve and the direction research achievements follow. Hence, it is not coherent to expect research to solve pressing public health issues, as some of us would like, if research is trying to provide solutions to commercial problems. The preliminary conclusion is that in order to achieve pragmatic progress regarding public health issues or particular epistemic problems, research should be set to solve those and not other problems. A corollary of this conclusion is that any attempt at solving the large epistemic and social flaws of commercial medical research today should pay attention

and provide alternatives to the way commercial science operates to solve commercial problems. Solutions that maintain research focus on commercial targets will not render the relevant results. As shown previously, attempts at democratizing science through inclusion of citizens and members of marginalized groups, or philanthrocapitalist initiatives, have failed to achieve progress for public health causes precisely because they have not challenged the commercial goals research is set up to meet.

Now the relevant question is how to organize or structure medical research to solve epistemically and socially relevant problems instead of mainly commercial problems; a task presumably attainable in different ways.

I will not consider radical or ideal scenarios, such as banning for-profit research and supporting medical research exclusively through public funding (e.g., Kitcher, 2001), which have already been questioned for not being realistic enough (Fernández Pinto, 2015) in a world in which the privatization and commercialization of science has been increasing since the 1980s, and where Big Pharma has taken over the market. Instead, I would like to examine alternative ways of conducting medical research, which have already proved to be viable or have been proposed for implementation in real world scenarios. Pragmatic progress to fulfill public health goals does not need to come from big structural changes in the current organization of science. Given that pragmatic progress is achieved through solving localized problems, research can be set to solve these problems in a localized manner.

Alternatives can be divided into two main groups. First, strategies to reorganize parts of medical research without commercial goals in mind, locally encouraging research that is not for profit. An example of this type of strategy is the Drugs for Neglected Diseases Initiative (DND*i*). Second, strategies to change the financial scheme of drug development, so that commercial profit is not directly tied to commercial problem-solving. An example to illustrate this case is the Health Impact Fund (HIF). Both types of strategies have something in common: they try to change financial incentives to protect public health problem-solving from commercial diversions. Shifting financial incentives to other places in the research process, breaks the link between the cost of research and the profitability of the end product. Accordingly, money is no longer tied to commercial problem-solving during the research phase, and local public health and epistemic issues can be prioritized.

Before reviewing how these strategies have been implemented, let me clarify that my aim is not to directly defend the examples that follow. As many other proposals to counteract the epistemic gap in medical knowledge, they have different pros and cons. My aim is rather to emphasize the way in which both examples break the link between the research process and the solution of commercial problems. This is the particular feature I am interested in here.

### *The Drugs for Neglected Diseases Initiative (DNDi)*

The Drugs for Neglected Diseases Initiative is a good example of how medical research can be reorganized to target public health goals without commercial interference. This patient's need-driven initiative seeks to improve the quality of life and health of people suffering from NTDs, such as hepatitis C, Chagas diseases, sleeping sickness, and leishmaniasis, and of neglected patients, such as those suffering from malaria and pediatric HIV. DND*i* seeks to develop new drugs or new formulations of existing drugs in collaboration with the international scientific community (DND*i,* 2014). Focusing on neglected diseases and patients, allows DND*i* to target localized populations and specific diseases, delimiting the public health problems medical research is set to solve.

An initiate from Médecins Sans Frontières (MSF), the DND*i* was established in 2003 to fill a research gap in the drug market, where less than 1.1% of new drugs were approved for the treatment of neglected diseases (Trouiller et al., 2001). Given that drug development for neglected diseases was particularly unattractive for Big Pharma, the DND*i* was a welcomed alternative R&D model for solving major public health problems in low and middle-income countries. More than a decade later, DND*i* has become a game-changer in the fight against NTDs:

> Within 10 years and with a budget of approximately EUR 182.5 million, the initiative has delivered six new treatments for neglected diseases and established a solid drug development pipeline, including 12 new chemical entities (NCEs) in preclinical and clinical development. Over 350 collaborations in 43 countries, including nearly 20 pharmaceutical and biotechnology companies, and over 50 universities and research institutes have been put into action. (DND*i,* 2014: 2)

DND*i* depends on both public and private donations to finance their projects. Donations go to an unrestricted core fund, which is then allocated to specific projects after a careful decision-making process, which requires the approval of a Scientific Advisory Committee. The independence of the organization is balanced through a diverse pool of donors, ensuring that no one contributes over 25% of the overall funding (DND*i,* 2006). In this sense, the DND*i* is an example of a "push mechanism" in which direct funding for biomedical R&D is given in advance to incentivize treatment development in areas of limited commercial potential (Suleman et al., 2020).

DND*i* collaborates with a number of research partners, including pharmaceutical and biotech companies, universities, research institutes, government organizations, and CROs. In this sense, it follows the PPP model. However, given the organization's goal of addressing urgent patient needs, collaborations require licenses that are royalty-free, sub-licensable, and non-exclusive, while guaranteeing worldwide coverage and disclosure of information (DND*i,* 2014: 4). In this way, DND*i* negotiates directly with partners to ensure that IP is not used to obstruct affordable access or further research. Breaking the link between commercial revenue and research development, DND*i* has been able to reorganize medical research, shifting the financial incentives to upfront contracts, and prioritizing public health problem-solving at the research stage.

A tangible example of the DND*i* model was the development of the artesunate-amodiaquine combination therapy for the treatment of malaria, ASAQ Winthrop, commercialized as Coarsucam™ by the pharmaceutical Sanofi-Aventis at $1 per treatment in 2007 (Cassier, 2021). A year later, in 2008, ASAQ received a prequalification by WHO and became available for production by generic manufacturers (Lezaun and Montgomery, 2015). ASAQ was the result of the Fixed-Dose Artesunate Combination Therapy (FACT) consortium, established by the DND*i* in 2002 with the goal of developing new pharmaceutical technologies for the treatment of malaria, and which included Farmanguinhos/Fiocruz (Brazil), Tropival of the Bordeaux II Victor-Segalen University (France), Oxford University (UK), Universiti Sains (Malaysia), Mahidol University (Thailand), the Special Programme for Research and Training in Tropical Diseases WHO/TDR (Switzerland), and the Centre National de Recherche et de Formation sur le Paludisme (Burkina Faso) (Bompart et al., 2011). Funding for FACT came from the European Union, the Agence Française de Développement, the Swiss government, and philanthropic organizations, primarily MSF and the DND*i*. The pharmaceutical Sanofi-Aventis stepped in later on for the industrialization and registration process, as well as the completion of the clinical trials, which were initiated by the FACT consortium (Cassier, 2021: 334-335).

Sanofi-Aventis agreed not to file a patent on the results of the collaboration, in exchange of market exclusivity before registration or WHO prequalification, which came only after one year. Sanofi-Aventis also agreed to pay the DND*i* 3% of market profits in the private sector for a period of seven years, a revenue that the DND*i* decided to invest in a Risk Management Plan for ASAQ. In addition, to ensure that those who most needed the malaria treatment had access to the new medication, the agreement also established a low price to market of US$1 for an adult treatment and US$0.5 for a child's treatment in the public sector (Bompart et al., 2011).

For our purposes, the crucial part in this case is the fact that Sanofi-Aventis agreed to produce and market a treatment without patent protection and extreme price control. In this way, the DND*i* was able to break the link between biomedical R&D and commercial revenue. For sure, most of the initial investment came from public sources (51%), a good amount also came from MSF and the DND*i* (32%), and only a small portion came from the industry (17%) (Cassier, 2021). But precisely because the main initial investment and risk was

not carried by the pharmaceutical company, this PPP allowed the DND*i* to successfully develop a much needed biomedical treatment and make it accessible to patients in LMICs.

### *The Health Impact Fund (HIF)*

The Health Impact Fund illustrates a second strategy to achieve pragmatic progress towards public health goals in medical research. Unlike DND*i*, HIF does not get rid of potential commercial profit from medical research, but shifts commercial interests to another place of the drug development process to break the relation between patent protection and future profit. One of the main goals of the HIF is to reward companies for the actual social impact of the treatments they develop, or what they call a "pay-for-performance mechanism".[4] In this sense, the HIF is an example of a "pull mechanism," in which rewards are delivered after certain milestones or goals are achieved, normally some time after a treatment hits the market (Suleman et al., 2020).

The basic idea behind the HIF is to create a fund, supported by national governments, with a fix sum of money per year (the initial suggestion is 6 billion dollars). Pharmaceutical companies and other drug developers can choose between the traditional drug market or registering with HIF, which would make them eligible for HIF rewards during a ten-year period. Rewards are set as a percentage of the fund and will be proportional to the health impact of the registered treatment. Health impact will be assessed according to a unified measure, such as the Quality-Adjusted Life Year (QALY) or the Disability-Adjusted Life Years (DALY), but the process is open to better indicators when available. Payments are also sensitive to increasing improvements compared to alternative treatments, ensuring that new drugs are evaluated against the best available treatments. In return, drug developers are required to sell their product at the cost of production, wherever is needed, and to sublicense the patents to generic manufacturers after the ten-year reward period (Pogge, 2011).

The HIF seeks to incentivize medical research for health treatments suffered by patients in LMICs, who cannot afford medications at a high price, while securing financial incentives for pharmaceutical companies:

> This approach will make it profitable to develop medicines for heretofore neglected diseases as well as medicines with global impact. And these medicines will be sold at low prices all over the world, while still generating a return for the shareholders of innovative pharmaceutical companies. (Incentives for Global Health, 2008: 3)

Even though the HIF strategy does not eliminate commercial interests, it is after all a "market-based solution," it ties profits to the treatment's overall health impact, while mainiting prices at cost of production and ensuring the possibility of generic manufacturing after ten years, thus prioritizing both accessibility of treatments for the most vulnerable and the proper solution of public health problems. In other words, "The HIF instead promotes a system in which competitors are rewarded based on their success in fixing a problem of global social injustice" (Botti, 2013). Pharmaceutical companies have an incentive to register with the HIF particularly in the development of treatments for the diseases that disproportionally affect patients in LMICs, who are not able to afford high medication prices. In this way, the HIF seeks to contribute to ameliorate the global burden of disease.

As with the DND*i*, the HIF breaks the link between biomedical R&D and direct commercial revenue from prices. According to Towse and his colleagues, the HIF works as other "pulling" strategies in that: "underlying this proposal is the idea that the cost of R&D should be 'de-linked' from the price of the product." However, the HIF differs in that rewards are tied to patients' health outcomes: "A prize fund would again be used as the 'draw' from innovation, but in this case the developer would not be rewarded until it could demonstrate that the resulting product has health value for the intended patients" (Towse et al., 2011: 327). In this particular way, the HIF would be able to break the link between R&D and revenues from pricing, while securing low prices and epistemic success (i.e., actually evaluating whether the treatment is medically successful and better than other available therapies). In other words, the HIF presents a mechanism that ensures we attain the

medical knowledge we need to face global health problems.

In sum, strategies to restructure medical research in order to prioritize public health problems instead of prioritizing commercial interests exist and have been implemented in different ways (for a survey of alternatives to biomedical R&D, see Kiddell-Monroe et al., 2016; Greenberg and Kiddell-Monroe 2016). Some strategies, such as DND*i*, reject the commercial development of medical treatments and instead support a non-for-profit patient-centered framework. Other strategies, such as the HIF, work within the global drug market to incentivize research on treatment that are not particularly attractive for pharmaceutical companies. Both of these strategies shift the place of financial incentives to avoid conflict with solving public health problems, so that these can be prioritized in the research process, fomenting pragmatic progress towards public health goals.

Notice also that the fact that these strategies work as "pulling" or "pushing" mechanisms is not really important for our purposes. Pushing or pulling strategies can be implemented to serve epistemic and social goals as much as they can be implemented to serve commercial goals. What is important here is the fact that both the DND*i* and the HIF are able to break the link between R&D and revenues from pricing, thus prioritizing the search for the relevant knowledge to serve public health goals.

## Pragmatic progress as a filter for large scale proposals

Both of the strategies examined in the previous section are local, and target specific types of medical issues related to tropical neglected diseases or health conditions that affect low and middle-income countries. Some might argue that these strategies can only work in parallel with the neoliberal organization of pharmaceutical research, insofar as they have searched for gaps in the market and played with financial incentives precisely where pharmaceutical companies are not interested to invest. However, the argument goes, they do not deal with the core of the crisis in medical knowledge, since they do touch the pharmaceutical market in high income countries, where most revenues come from.

The argument is right that none of these strategies aims to restructure pharmaceutical research in the large scale, and thus they do not present a complete alternative to current biomedical R&D (Greenberg and Kiddell-Monroe, 2016). However, by reorganizing research incentives to find treatments relevant the most vulnerable, who for the most part live in LMICs, both of these strategies built bridges to close the epistemic gap in current medical knowledge. As a result, real solutions to pressing health issues are developed, addressing a core aspect of the crisis.

Furthermore, the general reading of the crisis in terms of the pragmatic progress of research offers a clear criterion to evaluate whether possible strategies to reorganize pharmaceutical research to assess global health needs are promising or not. If proposed strategies maintain the link between the research process and the solution of commercial problems, we have good reasons to believe these strategies will not prioritize public health issues in the long run. If, on the contrary, strategies break the link, they would seem more promising.[5]

Even if the criterion does not suggest an actual solution, it proves useful to filter proposed strategies. I have already shown two promising strategies that pass the filter. Now let me show a negative case. MIT professors of financial engineering, José María Fernández, Roger Stein, and Andrew Lo (2012), have made a bold proposal to restructure the financial schemes in pharmaceutical research through securitization techniques. The proposal consists in creating a Megafund (3-15 billion dollars), funded through capital markets by securitized debt and equity, including low-risk bonds with a 5-10% annual revenue, attractive to venture capitalists, but also to pension funds, 401ks, and the like. The Megafund will provide capital to pharmaceutical companies in exchange for returns similar to a diversified debt portfolio: high risks from investments with low chance of success will be minimized by a sufficiently diverse and large portfolio, where the chance of one drug to be successful is high (The Economist, 2013). In this way, the risks involved in pharmaceutical research will not be taken by pharmaceutical

companies, but absorbed by capital markets. Pharmaceutical market failures and successes would balance each other out.

In the aftermath of the financial crisis where securitization techniques dramatically failed, the Megafund has received serious critiques. But without getting into the financial objections, we already have a good reason to believe that the Megafund will not address public health issues as expected. Even though the proposal shifts financial risks from pharma companies to markets, financial incentives remain tied to the research process, since only treatments that prove to be successful in the market will pay off. Accordingly, pharmaceutical research is still linked to solving commercial problems tied to efficiency: recruiting research subjects quickly, designing and conducting trials to obtain significant results, writing and publishing scientific papers to get the most recognition and coverage, and so on. Not surprisingly, solving public health problems is not likely to be a priority in this scheme. The expected progress is not appropriately directed, and thus the proposal does not pass the filter.

## Conclusion

The aim of the paper was to offer an epistemological argument on the crisis in medical knowledge today, specifically in clinical research controlled by the pharmaceutical industry. In order to do so, I first identified a fundamental problem of the crisis, i.e., the 'epistemic gap' that the current globalized privatization of biomedical R&D has left. I then introduced the concept of 'pragmatic progress' as a tool for understanding what is needed for pharmaceutical research to solve pressing epistemic and public health problems. I concluded that we need to find alternatives to biomedical R&D financialization which stop prioritizing the solution to commercial problems, and instead clearly prioritize epistemic and public health problems. While this can be achieved in different ways, the fourth section examined two alternative strategies, illustrated by the DND*i* and the HIF, which have already been considered in the current global medical market. The last section addressed a possible objection to the proposed reading, and showed how the concept of 'pragmatic progress' can be used to evaluate and discard proposals for restructuring pharmaceutical research.

In this way, I aimed to show that the concept of pragmatic progress can be used as a tool for evaluating when a proposed alternative truly contributes to the delinkage of investment in biomedical R&D from commercial profit, thus prioritizing the solution to epistemic and public health problems over commercial ones. Accordingly, the main contribution of the paper can be understood as hermeneutical in character, exploring new conceptual resources for understanding the crisis of medical knowledge today and providing guidelines to move forward. In this sense, the paper aims to contribute to a growing literature in the social studies of science and technology which focuses on the epistemic dimensions of the globalized privatization of science, including the practices of ignorance production that neoliberal strategies in biomedical research are encouraging (see, e.g., Sismondo, 2009; McGarity and Wagner, 2012; Mirowski, 2013; Gross and McGoey, 2015; Whitaker and Cosgrove, 2015). More, however, still needs to be said about how the concept of pragmatic progress can illuminate such issues.

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## Appendix 1. Abbreviations

BMGF: Bill and Melinda Gates Foundation
CAST: The Cardiac Arrhythmia Suppression Trial
CRO: Contract Research Organization
DALY: Disability-Adjusted Life Years
DND*i*: Drugs for Neglected Diseases Initiative
FACT: Fixed-Dose Artesunate Combination Therapy
HIF: Health Impact Fund
LMICs: Low and Middle Income Countries
MSF: Médecins Sans Frontières
NCEs: New Chemical Entities
NGO: Non-Governmental Organization
NTDs: Neglected Tropical Diseases
PCT: Pragmatic Clinical Trial
PPP: Public-Private Partnership
QALY: Quality-Adjusted Life Year.
RCT: Randomized Controlled Trial
R&D: Research and Development

## Notes

1 Pragmatic Clinical Trials are called "pragmatic" for being conducted in the midst of medical practice with patients who are undergoing medical treatment and teams (doctors, nurses, and administrators) who are embedded in medical settings. In this sense, PCTs can be understood as cross-disciplinary fostering the co-construction of medical knowledge (Rushford, 2015: 1286). Despite their flexibility and their goal of conducting research in more realistic scenarios, most PCTs follow the basic methodological structure of RCTs. Even though there is a similarity in the sense in which these trials are "pragmatic" and the "pragmatic" progress I argue for in this paper, insofar as both refer to practical and not idealistic or abstract aims, PCTs should not be considered necessarily conducive to pragmatic progress just because of this terminological overlap.

2 The literature on scientific progress is large and goes beyond the scope of this paper. For those interested in the philosophical debate, see Laudan (1977), Douglas (2014), and Niiniluoto (2015).

3 Some have characterized this broader framework as the *financialization* of pharmaceutical R&D. Epstein defines financialization as "the increasing role of financial motives, financial markets, financial actors and financial institutions in the operation of the domestic and international economies" (Epstein, 2005: 3). This financialization certainly defines the structural conditions and logical possibilities for pharmaceutical R&D today. Special thanks to one anonymous reviewer for pointing out this connection.

4 To date, the HIF has not been implemented, but a pilot of the program has been designed. Accordingly, we do not have real examples of drug development by the HIF. For more information, see: https://healthimpactfund.org/pdf/HIF_pilot_proposal_2019_11.pdf

5 Notice that I am not denying the possibility that commercial and social interests align in ways that are both profitable and socially beneficial. The development of antiretroviral drugs for the treatment of HIV (Epstein, 1995), and even the recent development vaccines for the treatment of COVID-19 could be seen as examples of such alignment (Fernández Pinto 2023). However, the vast amount of evidence showing the corrupting effects of commercial interests in medical research (for a good summary see, Moynihan et al., 2019) clearly give us good reasons to favor breaking the link between the research process and the solution of commercial problems.