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#### Explanatory pluralism in the medical sciences: Theory and practice

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#### Abstract:

Explanatory pluralism is the view that the best form and level of explanation depends on the kind of question one seeks to answer by the explanation, and that in order to answer all questions in the best way possible, we need more than one form and level of explanation. In the first part of this article, we argue that explanatory pluralism holds for the medical sciences, at least in theory. However, in the second part of the article we show that medical research and practice is actually not fully and truly explanatory pluralist yet. Although the literature demonstrates a slowly growing interest in non-reductive explanations in medicine, the dominant approach in medicine is still methodologically reductionist. This implies that non-reductive explanations often do not get the attention they deserve. We argue that the field of medicine could benefit greatly by reconsidering its reductive tendencies and becoming fully and truly explanatory pluralist. Nonetheless, trying to achieve the right balance in the search for and application of reductive and non-reductive explanations will in any case be a difficult exercise.

#### Keywords:

explanatory pluralism, reductionism, holism, medical sciences, geneticization, biochemicalization

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#### 1. Introduction

Ever since the advent of a mechanistic worldview, science has made important progress. Medicine has also benefited greatly from the growth in knowledge brought about by applying the new approach to human beings. This has led to ever increasing insights into ever smaller parts of the human body that can be intervened on to improve people's health. This progress has also resulted in the increasing impact on medical theorizing of reductionism, the "chief metaphysical presupposition of biomedicine" [1, p. 395].

Different kinds of reductionism should be discerned. In this article, we will focus on what James Marcum calls "methodological reductionism" [2, pp. 24-25]. A methodological reductionist argues that efficient research should dissect higher order phenomena into their constitutive components at the lower order. In other words, a methodological reductionist sees component-centered social science, psychology, biology, biomedical science, etc. as the most effective way of doing research. Methodological reductionism should be distinguished from ontological reductionism. For the ontological reductionist, the only real things in the world are subatomic particles and their interactions. Therefore, everything needs to be explained in terms of the laws of physics. In what follows, we will put reductive metaphysics between brackets (i.e., we do not presume that ontological reductionism is true, nor that it is false) and, instead, discuss the pragmatic value of explanations at different levels in the medical sciences.

The dominant approach to explanation in medicine is *methodological reductionism*, which claims that diseases should *always* be explained by reference to the constitutive components of their bearers. There are three possible alternatives to this view. The first is *methodological holism*—the view that a complete explanation in medicine should *always* take non-reductive explanatory factors into account (factors that do not refer to components), together with reductive ones (factors that do refer to components). The second is *methodological non-reductionism*—the view that medical phenomena should always be explained by reference to non-reductive explanatory factors only (leaving out reductive factors)<sup>1</sup>. The third alternative is *methodological explanation* depends on the kind of question one seeks to answer by the explanation and that one needs more than one form and level of explanation to answer all questions in the best way possible.

the label "methodological non-reductionism" throughout the paper strictly as defined here.

The term "non-reductionism" gets different interpretations in the philosophical literature. However, we do not want to refer to the extensive philosophical debates on non-reductionism (and/or anti-reductionism) but will use

Sections 2 and 3 form the first part of this paper. In section 2, we discern different kinds of explanation in medicine by way of two examples (skin cancer and lung cancer), which we further use in section 3 to show that, in theory, explanatory pluralism holds for the medical sciences. In the remaining sections, we focus on the situation in practice and explore to what extent methodological explanatory pluralism is actually a fact in medicine today. In section 4, we argue that medicine is moving in the right direction but is not fully and truly explanatory pluralist yet. In section 5, we show that the medical literature indirectly provides arguments for explanatory pluralism by drawing attention to epistemic interests calling for reductive explanations as well as to epistemic interests calling for non-reductive explanations. Section 6 illustrates two important forms of reduction in contemporary medicine, namely, biochemicalization and geneticization, by way of two case studies (ADHD and Alzheimer's disease). We further use these examples to claim that medicine should consider whether the great emphasis on reductive explanatory factors is justified in view of what could potentially be gained from an explanatory pluralist approach.

# 2. Macro-explanations, micro-explanations, and reductive explanations in the medical sciences.

In this article, we distinguish between reductive explanations and non-reductive explanations in the medical sciences. More specifically, we discern three kinds of explanation: non-reductive macro-explanations, non-reductive micro-explanations, and reductive micro-explanations. Thus, non-reductive explanations are of two kinds: macro- and micro-explanations. In contrast, reductive explanations are a kind of micro-explanation in which one additionally refers to properties that require decomposition.

Let us look at an example to clarify this. Suppose we want to explain a higher incidence of skin cancer in a group of Belgians spending their summer holidays each year in the Mediterranean, compared with a group of Belgians staying in Belgium during summer holidays. In this case, we can explain the difference in the incidence of skin cancer by referring to a higher exposure to sun rays in the group of people going on holiday in the Mediterranean. This would form a macro-explanation. In *macro-explanations*, we refer to a property that a whole population has in common and that is external to the individuals in the group. In other words, it concerns characteristics of a group as a whole, which individuals leaving the group and joining the other group will no longer possess.<sup>2</sup>

<sup>2</sup> One might, for example, think that the genetic make-up of Asians compared to those of Europeans is a group characteristic, and hence, one that can act as a macro explanatory factor. However, if an Asian moves to Europe

However, if we want to explain differences in the development of skin cancer within the group of people exposed to a higher amount of sun rays each year, we can, for example, refer to the fact that some of these people have a habit of protecting themselves using suntan lotion while others do not. Such an explanation, referring to differences among individuals within a group, is a *micro-explanation*. If a micro-explanation, as in this case, refers to behavior, lifestyle, habits, etc., then it concerns a non-reductive micro-explanation.

However, we might also want to explain why some of the Belgians spending their holidays in the Mediterranean still develop skin cancer despite using suntan lotion to protect their skin. In that case, a possible explanation would be that genetic differences between people make some people more susceptible than others to risk factors such as excessive exposure to sun rays. In this case, we refer again to differences between individuals in a group and hence use a micro-explanation. However, the properties referred to (genes) require parsing an individual in terms of his or her biologic make-up rather than externally observable characteristics and behaviors. We call explanations referring to such categories *reductive* explanations.

Let us look at a second example, namely, the search for explanations of lung cancer. Clearly, the most straightforward explanation of lung cancer refers to one's individual lifestyle, most commonly, the habit of smoking. This explanation focuses on the most important risk factor of lung cancer at the nonreductive micro-level. However, other possible non-reductive microexplanations are left aside when focusing on smoking habits only. For example, people who lead a stressful life or get nervous easily might be more likely to start and/or continue smoking, thus becoming more susceptible to lung cancer. Such explanatory factors would also be of the micro-, non-reductive kind. However, none of these factors can explain why, for example, some smokers develop lung cancer while others do not. To explain this, reference to the role of "lung cancer genes" can be made. In 2008, three research teams reported the identification of specific gene variants that would make some smokers more susceptible to lung cancer than others [3-6]. These findings offer information that could figure in a reductive explanation of lung cancer. Lastly, we can also explain certain differences in the incidence of lung cancer between two groups of people by reference to, for instance, differences in the social acceptance of smoking behavior, differences in advertising policies, or differences in the

and takes a European nationality, he will still have the same genetic make-up. For this reason, reference to one's genetic make-up in an explanation makes for a reductive explanation, as we will further explain.

<sup>&</sup>lt;sup>3</sup> Non-reductive micro-explanations can sometimes easily be translated to the macro-level and the reverse. This depends on whether one focuses, for example, on unhealthy individual lifestyle choices or, rather, on the environmental factors that lead to these unhealthy lifestyles. This does not pose any problems because we can use the term "non-reductive explanation," which covers both types.

economic situation of their countries. These explanations would all be situated at the macro level. What all the above explanations have in common is that they explain lung cancer in one way or another. Nonetheless, they are all of a different kind.

#### 3. Explanatory pluralism in the medical sciences: Elaboration and defense.

As already mentioned, methodological explanatory pluralism consists in the claim that the best form and level of explanation depends on the kind of question one seeks to answer by the explanation and that in order to answer all questions in the best way possible, one needs more than one form and level of explanation. Suppose we wonder why x has property P at time t. Different, more specific questions—motivated by different epistemic interests—can underlie this general explanation-seeking question, even if all questions are assumed to be requests for causal explanations. For instance, why does x have property P, rather than the more desirable property P'? Is the fact that x has property P the predictable consequence of some other events? Is the fact that x has property P caused by a familiar pattern or causal mechanism? According to explanatory pluralism, these questions have different answers. Which answer provides the most adequate, efficient, and accurate explanatory information depends on the specific question one wants to answer (or, in other words, on the specific information that is requested in view of the explanatory purposes). Hence, making the specific question as explicit as possible is important for explanatory success. This account of explanatory pluralism makes use of the erotetic model of explanation developed by Bas Van Fraassen. He introduced the concept of relevance relation in order to deal with the fact that "verbally the same whyquestions may be a request for different types of explanatory factors" [8, p. 131]. His example (an adapted version of an example given by Aristotle in his *Posterior Analytics*) is the following:

Suppose a father asks his teenage son, "Why is the porch light on?" and the son replies "The porch switch is closed and the electricity is reaching the bulb through that switch." At this point you are most likely to feel that the son is being impudent. This is because you are most likely to think that the sort of answer the father needed was something like: "Because we are expecting company." But it is easy to imagine a less likely question context: the father and the son are re-wiring the house and the father, unexpectedly seeing the porch light on, fears that he has caused a short circuit that bypasses the porch light switch. In the second case, he is not interested in

<sup>&</sup>lt;sup>4</sup> The *adequacy*, *efficiency*, and *accuracy* of explanations are elaborated in Van Bouwel and Weber [7].

the human expectations or desires that led to the depressing of the switch. [8, p. 131]

This passage shows the importance of making explanatory requests, i.e., explanation-seeking why-questions, as explicit as possible since different epistemic interests might be motivating a seemingly similar explanatory request.

In earlier research, arguments have been developed in favor of explanatory pluralism in history, psychology, and the social sciences. It has been argued that the explanatory practices of scientists in these disciplines show how different epistemic interests might lead them to choose different forms of explanation at different levels.<sup>5</sup> Among the different epistemic motivations for providing an explanation, we encounter therapeutic and remedial motivations, prediction, straightforward curiosity, and explanations for the unexpected. In this article, we want to examine how this plays out in medicine. In arguing for explanatory pluralism, we will primarily focus on the role of different levels to which explanations in medicine refer.<sup>6</sup>

Let us look again at the lung cancer example. In this case, the rudimentary explanation-seeking question is, why did person P develop lung cancer? This formulation allows for many relevance relations. More specific formulations would be:

- (a) Why did person P, who smokes, develop lung cancer, while person P', who also smokes, did not?
- (b) Why did person P with behavior B develop lung cancer, while person P' with behavior B' did not?
- (c) Why did person P living in country C develop lung cancer, while person P' in country C' did not?

As we mentioned in the previous section, a straightforward explanation of lung cancer refers to one's individual lifestyle, namely, the habit of smoking. This explanation in fact answers the more specific question (b). That smoking causes lung cancer has been an established fact for decades. For our epistemic interest in the prevention of lung cancer at the individual level, this explanation is clearly useful. However, other explanations are also useful in view of other more specific questions. For example, the knowledge of lung cancer gene variants,

<sup>&</sup>lt;sup>5</sup> See Vanderbeeken and Weber [9], and Weber and Vanderbeeken [10] for a defense of explanatory pluralism in psychology. For explanatory pluralism in history and the social sciences, see Weber and Van Bouwel [11], Van Bouwel and Weber [7, 12], and Van Bouwel [13].

<sup>&</sup>lt;sup>6</sup> Although different levels of explanation might be connected to the use of diverse forms of explanation-seeking questions, we will not focus on forms in this paper but rather on levels.

figuring in a possible answer to question (a), is supposed to meet the epistemic interests of *curiosity to know* and *individual prevention*:

The new results allow researchers to construct a better picture of how cigarette smoking affects the body, and how the active agents in cigarettes, including nicotine, alter the normal growth and development of cells in the lung. That could lead to improved and individualized smoking-cessation drugs and programs, which are currently successful only 25% of the time. [3]

Nonetheless, an explanation at the genetic level does not deliver adequate and efficient information in view of the epistemic interest of public health policy. For this purpose, macro-explanations answering questions like question (c) are probably most adequate.

This lung cancer example demonstrates that researchers and practitioners cannot freely select one or the other of the more specific questions to answer the rudimentary question. Instead, something needs to guide them toward their choice. Good scientists think thoroughly about what kind of information they need, and which of the possible more specific explanation-seeking questions will deliver the most adequate, accurate, and efficient explanation in view of their needs. Different epistemic interests will guide medical researchers and practitioners to different kinds of explanation-seeking questions and thus to different kinds of explanations in different explanatory contexts. This means that, in theory, explanatory pluralism holds for the medical sciences.

The lung cancer example also constitutes an argument against methodological reductionism on the condition that (1) questions (b) and (c) cannot adequately be answered by a reductive explanation and (2) that these questions are legitimate. That the first condition is satisfied was argued above and in the previous section. But what about the legitimacy of the questions? Let us put it this way: exclusively focusing on one kind of question at the expense of others might have disastrous consequences. This is, for example, demonstrated by Pearce's arguments with respect to tobacco smoking as a cause of disease:

It is one thing to discover that tobacco smoke is the major cause of lung cancer, but redressing this situation is a different problem entirely....

Moreover, it can be argued that the fundamental problem of tobacco lies in its production rather than in its consumption. The limited success of legislative measures in industrialized countries has led the tobacco industry to shift its promotional activities to developing countries, so that more people are exposed to tobacco smoke than ever before.... [W]hen a public health problem is studied in individual terms (e.g., tobacco smoking) rather

than in population terms (e.g., tobacco production, advertising, and distribution, and the social and economic influences on consumption), then it is very likely that the solution will also be defined in individual terms and the resulting public health action will merely move the problem rather than solve it. [14, p. 680]

Let us recapitulate. We have an argument against methodological reductionism, but methodological non-reductionism and methodological holism still stand as theoretically possible rivals for methodological explanatory pluralism. However, our examples can also be used in an argument against methodological non-reductionism: a methodological non-reductionist must reject the legitimacy of questions like, why did person P, who smokes, develop lung cancer, while person P', who also smokes, did not? and why do some people who protect themselves with suntan lotion nevertheless get cancer of the skin? Such questions are nonetheless legitimate scientific questions in view of our quest for knowledge and the prevention and treatment measures that might follow from such knowledge, as we argued above. Hence, here again, we would end up in a situation where focusing on one kind of question at the expense of others would have disastrous consequences. History has proven that reductive explanations are often very useful in view of preventive measures and treatment decisions in medicine.<sup>7</sup> Without all this knowledge, medicine would not have been so powerful in preventing and treating diseases as it is today.

What about methodological holism? This view overlooks an important point about explanation, namely, that general questions like, why did person P develop lung cancer? are too vague to be answered, while more specific questions usually require only one type of explanatory factor. Always focusing on the whole, irrespective of one's precise epistemic aims and needs in a given context, would—if even possible—unnecessarily complicate matters and even paralyze medical research and decision-making. In other words, methodological holists do not offer an *efficient* alternative for an explanatory pluralist approach.

The account of explanatory pluralism developed here differs from other accounts of pluralism in the literature. A prominent one is Sandra Mitchell's [15,16]. Unlike our approach, Mitchell claims that the integration of the different levels (population, individual, genetic make-up, etc.) is always a necessary condition in providing a *satisfactory explanation*: "The 'levels of analysis' framework describes the territory of pluralistic investigations, but it is only by integration of the multiple levels and multiple causes, including attention to the diverse contexts in which they occur, that satisfactory explanations can be generated" [15, p. S78]. Mitchell does not take into account

<sup>&</sup>lt;sup>7</sup> We will further discuss arguments for the usefulness of reductive explanations in section 5.

the efficiency criterion and her account of pluralism ends up defending "satisfactory" explanations that are far too cumbersome, less efficient, and less adequate than possible alternative explanations (defended by our account). Philosophical views on the explanation of complex biological systems such as Carl Craver's [17, 18] also fail to account for the pragmatics that underlie the search for diverse explanatory factors. These theories often allow for the explanatory relevance of different organizational levels. In this sense, they are compatible with our view. However, they do not aim at accounting for the necessity and usefulness of explanatory pluralism for scientific practice, which is precisely what we argue for.

#### 4. Explanatory pluralism and actual medical research and practice.

In the previous sections, we defended explanatory pluralism in medicine from a theoretical point of view. In what follows, we will focus on the situation in practice. Our leading question is, "to what extent is methodological explanatory pluralism a fact in medicine today?" Looking at the situation in practice will not only put flesh on the theoretical bones, but will also force us to recognize that, in practice, medical science is moving in the right direction, but is not fully and truly explanatory pluralist yet.

As Marcum argues, medical knowledge is traditionally expressed in terms of mechanistic or bottom-up causation, focusing on the diseased body (parts) and trying to identify the physical causes or entities and processes that are responsible for the onset of a disease [1, p. 396]. Consequently, the preferred treatments are often based on chemical or physical interventions on these lower-level mechanisms by means of drugs or surgery. Hence, the traditional and dominant biomedical model relies on a reductive presupposition, as a result of which reductive explanations attract all the attention within this approach. Marcum is not the only one emphasizing the dominant role of the reductionist biomedical model in medicine. Many papers describe the historical evolution through which the biomedical model became dominant, and influenced even those domains of medicine that were originally concerned with higher-level explanations of disease.<sup>8</sup>

However, after a long reign of a strict biomedical approach in Western medicine, recent decades have seen an increasing number of calls for a wider perspective on human health and disease, opening up our minds for the significance of higher-level explanatory factors. The attention to non-reductive factors as causes of disease has started to rise because of the growing attention to

<sup>&</sup>lt;sup>8</sup> See, e.g., [14, 19, 20].

chronic rather than infectious diseases over the course of the twentieth century. Among them also are some diseases for which the underlying pathology remains unclear, such as chronic fatigue syndrome, fibromyalgia, unexplained chronic pain, irritable bowel syndrome, etc. Different holistic approaches plead for more attention to both non-reductive micro-explanations (the psychological explanatory factors for disease) and macro-explanations (the social, cultural, and environmental explanatory factors for disease).

The best-known alternative to the biomedical model is the biopsychosocial model, introduced by George Engel in 1950. Engel argued that human suffering, disease, and illness should be understood as the product of multiple levels of organization, from the societal to the molecular. In other words, one can only adequately understand and respond to human suffering if it is understood in terms of its biological, psychological, and social dimensions. He criticized the dualistic nature of the biomedical model and the excessively materialistic and reductive orientation of medical thinking. He argued that although mental and social phenomena depend on more basic physical phenomena, they cannot necessarily be explained by them. Engel's new perspective gave great impetus to research seeking to elucidate psychological and/or social causes of disease as well as their interaction with biological factors [21]. For example, health psychology [22], medical sociology, and sociological epidemiology [23-24] became increasingly important domains for research into the psychological and social causes of health and illness, respectively.

However, the biopsychosocial model has also been criticized for continuing to compartmentalize the patient, such that physicians address the biomedical symptoms separately from the psychologists and psychiatrists who address the psychosocial elements. This led to the development of integrative models, which promoted an even more holistic approach to medical problems [25]. Indeed, as Diez Roux [26] argues, models for the integration of social factors have evolved from viewing social factors as antecedents to biological processes, to viewing them as modifiers of biological effects, and then to viewing them as an integral part of the causal pathways leading to disease. The former step in this evolution can be illustrated by the development of genetic determinism into an approach in terms of gene-environment interactions [27-29]. The latter can be illustrated by the development of the systems approach [26, 30].

The turn of attention toward non-reductive explanatory factors of health and disease is also clear in the late history of epidemiology, which is precisely the branch of medicine that focuses on the search for causes of and risk factors for the onset of disease. Whereas epidemiology traditionally focused on the causes of disease and health at the population level, it turned toward risk factor epidemiology in the previous century, focusing increasingly on the individual

level. However, this evolution has often been criticized in the last two decades and calls have been launched for redirecting the field towards the population-level—by including societal and ecological factors in the analyses:

Epidemiology has largely ceased to function as part of a multidisciplinary approach to understanding the causation of disease in populations and has become a set of generic methods for measuring associations of exposure and disease in individuals. This reductive approach focuses on the individual, blames the victim, and produces interventions that can be harmful. We seem to be using more and more advanced technology to study more and more trivial issues, while the major causes of disease are ignored. Epidemiology must reintegrate itself into public health and must rediscover the population perspective. [14, p. 678]<sup>9</sup>

Many case studies that try to establish the benefits of attending to psychological, social, cultural, ecological and/or environmental points of view in tackling certain specific diseases can be found in the recent medical literature.<sup>10</sup>

In a period of change, medicine is searching for the right mindset with which to approach medical problems in research and practice. The general impression one gets from the above survey is that medicine is moving in the right direction: away from methodological reductionism and toward a more pluralist approach. The advantage of this recent tendency is that non-reductive explanations are defended as important in addition to reductive explanations, unlike methodological reductionism, which defends reductive explanations at the expense of other kinds of explanations. In other words, methodological non-reductionism is not actually defended in the medical literature. Some of the pluralist approaches, nonetheless, tend to the other extreme, namely, a methodologically holistic approach, arguing that the most effective way of doing research and of reasoning in medicine always takes the whole range of explanatory factors into account. Although it is important to think about the big picture once in a while, a methodologically holistic approach does not seem feasible in specific research and practice contexts. 11 Medicine further does not need an "overall approach" in which one always considers the same kinds of explanatory factors (always reductive explanations, or always non-reductive explanations, or always the whole picture). In writing this article, we want to propose an alternative approach that does not lapse into extremes, but adopts a middle course that combines the advantages of different approaches in a flexible and context-sensitive whole. We argue that the best way for medicine to be in the future is not reductionist, nor holist, but

<sup>&</sup>lt;sup>9</sup> see also [26, 31-34]

<sup>&</sup>lt;sup>10</sup> see, e.g., Fee and Krieger [35] with respect to AIDS, Smith and Ruiz [36] with respect to Coronary Heart Disease, Vinetz et al. [37] with respect to Leptospirosis, and Chaufan [29] with respect to Diabetes type 2.

<sup>11</sup> S. Nassir Ghaemi, for example, nicely describes in his recent book how the methodologically holistic stance of the biopsychosocial model made the approach unfeasible in practice by being too general and too vague [38].

explanatory pluralist. We think that an explanatory pluralist approach provides a useful, pragmatic answer to the current reductionism versus holism debate in medicine. An explanatory pluralist approach has the potential to reduce the controversy and, meanwhile, to remove the blinders imposed by a one-sided approach. Medical literature underpins this indirectly by drawing attention both to epistemic interests that call for reductive explanations and to epistemic interests that call for non-reductive explanations.

# 5. Epistemic interests in medicine support non-reductive and reductive explanations.

We clearly do not support a methodologically holistic approach. Nonetheless, the shift of attention towards holism in medicine has played a significant role in drawing attention to non-reductive explanations, and the arguments for holism include arguments for the pragmatic value of non-reductive explanations that we are endorsing. These are some of the recurring arguments for searching for and applying non-reductive explanations: they are necessary for a more complete understanding of the causation of human disease; they can lead to long-term rather than short-term solutions; they can lead to more efficient strategies for the prevention of disease at the population/policy level; they provide whole societies with help rather than only those individuals that are able to afford healthcare; they can lead to a general improvement of people's health rather than tackling each single health problem separately when it arises; they can lead to spectacular reductions in the society's costs for healthcare. In general, the leading epistemic interest for the implementation of non-reductive explanations in research and practice is effective *prevention*<sup>12</sup> of disease at the macro-level.

There are also cogent pragmatic epistemic values that drive us to the search for reductive explanations in scientific practice. One is *simplicity*: why complicate matters if the biomedical approach has shown its usefulness for the advancement of medicine? Reductive explanatory factors are often thoroughly understood and make up a consistent body of knowledge on the development of diseases, but with higher-level explanatory factors, it is often much less clear precisely how they influence disease processes. This brings us to a second, and probably the most important, pragmatic epistemic value: the reductive approach leads to quick fixes, unlike the non-reductive one. In other words, it often enables intervention in terms of an easy and efficient treatment, and hence, instant care for diseased individuals. A third pragmatic epistemic value is that these are also very useful for diagnosis, which is clearly an important goal of

<sup>&</sup>lt;sup>12</sup> Although prevention and treatment can be interpreted as two forms of the broader epistemic interest of intervention/manipulation, the usefulness of distinguishing between the two in the context of medicine will become clear from what follows. In medical research, each of these epistemic interests may indeed lead to a different approach to the same research topic, possibly even focusing on different levels of explanation and, consequently, intervention.

practicing doctors. Furthermore, the ability to *predict* disease development and disease progress at an individual level (sometimes as a means to timely intervention) drives medicine toward reductionism. A final epistemic value is, of course, simple *curiosity* about how the human body develops disease.

Notwithstanding the growing attention to non-reductive explanations, methodological reductionism is still dominant in medicine. A reductive approach is often seen as a straightforward choice, even though this should not be the case. The epistemic interests leading to reductive explanation-seeking questions seem to play an important role in the ongoing dominance of reductionism in medicine. In the next section, we will illustrate this by discussing in more detail two familiar forms of reductionism in the biomedical sciences in relation to certain diseases, the first being *biochemicalization* with respect to ADHD, and the second being *geneticization* with respect to Alzheimer's disease. In addition, we will demonstrate what medicine can gain by an explanatory pluralist approach in these cases.

#### 6. Two case studies

#### Drugging deficits

Probably the most important form of reduction in the biomedical sciences can be labeled *biochemicalization*<sup>13</sup>. Following a biochemical reduction, the explanation of diseases or "inappropriate" behavior invokes a pharmacological response (chemicals are used to influence the biochemical processes in the human body), rather than a social or psychological remedy. This approach has proven its usefulness in treating many diseases and is therefore often hardly questioned. However, the choice to biochemicalize the explanations for some diseases and to pharmacologize their treatments cannot be considered self-evident but should be a matter of well-considered interests and related explanation-seeking questions. One example of such a disease is Attention Deficit Hyperactivity Disorder (ADHD).

The medical world clearly prefers to treat children suffering from ADHD with methylphenidate (MPH)—with apparent success—rather than supporting pedagogical remedies, such as different teaching techniques, or advocating preventive measures, such as avoidance of smoking, alcohol, and drugs during pregnancy. Although ADHD is diagnosed on the basis of the apparent deviant *behavior* of children as described by the DSM-IV criteria, the currently predominant scientific model of ADHD locates the origins of the disease in *neurobiological* dysfunctions [39]. Pharmacological treatment is considered an

<sup>13</sup> The most debatable form of which is neurobiochemicalization, where biochemical processes in the brain are influenced by means of a pharmacological intervention.

effective means to influence the undesired effects of the neurobiological deficits involved in ADHD. Consequently, medication treatment rates are increasing rapidly [40]. Nevertheless, neither the precise neurobiological pathways leading up to ADHD, nor the neurochemical pathways through which methylphenidate and similar stimulant medications exert their positive effects on deficient neurobiological pathways are well-known [40, 41]. However, the justification for using stimulant medication is straightforward: "the medication works!" As Hawthorne [39] argues, physicians favoring neurobiochemicalization of the disease are clear in their reasoning: since ADHD is a morbid and potentially devastating condition, and given that medication works, why should one want to let children suffer unnecessarily? It is true that there is convincing evidence that psychostimulant medication is highly effective in the short-term reduction of the core symptoms of ADHD [39, 42]. This information is also communicated to the public, for example, via informative websites which often list medical treatment as the first and most common of the available therapies. Other therapies (such as behavioral parent training, behavioral classroom interventions, social skills training, dietary treatment, etc.) are also listed. However, usually, none of these get as much support as the treatment by stimulant medication.

Effective treatability drives physicians and researchers, as well as parents and school teachers, to support the neurobiochemicalization of ADHD. An effective treatment is, in this case, expected to lead to a short-term and profound change in what is perceived as a child's misbehavior. Pharmacological treatment makes an easy intervention possible, in this case, even without a detailed account of the causation of the disease. Even if one holds the uncommon view that ADHD should primarily be explained by reference to the peculiarities of our modern society<sup>14</sup>—rather than situating the most important causes of the disease in the suffering individuals themselves—the epistemic interest in an effective short-term intervention can form a valid pragmatic argument for preferring to intervene at the lower level. 15 Indeed, reducing the causes of ADHD seems to make it more easily "treatable," which can be a first and well-considered epistemic interest of the researchers and physicians involved. A related epistemic motivation underlying neurobiochemical reduction might be parsimony: the neurobiochemical reduction is more parsimonious (proposing a one-pill-fits-all treatment) than non-reductive explanations that invoke childspecific, customized behavioral (or even family) therapies.

Hence, we agree that well-considered epistemic goals can be justified motives for choosing to adopt a reductive approach in treating ADHD.

<sup>&</sup>lt;sup>14</sup> This would suggest that prevention of the disease should involve changes at these higher levels.

<sup>&</sup>lt;sup>15</sup> Hence, arguing for the primacy of the sociocultural explanation does not automatically entail the denial of reductionist aspects in the etiology of the disease. However, the importance of the reductionist aspects for prevention and intervention, for example, can be discussed and the weight given to them can differ depending on the context.

However, the ADHD case also demonstrates that it is pertinent to ask whether it is not just generalized and unfounded methodologically reductive presuppositions rather than well-considered epistemic goals that often guide us towards reductionism in medicine. Merely the *conviction that* (still to be found) neurobiochemical problems cause the disease 16—for example, on the basis that the medication seems to work<sup>17</sup>—is then treated as a sufficient justification for a reductive approach; but it is doubtful that such convictions are in fact sufficient. Another pertinent question is to what extent unjustified epistemic interests guide research and practice towards a reductive approach. For example, the patentability of an explanation and remedy might play an important role. Would a researcher look for an explanation that can support the development of a patentable pill to cure a disease or look for a less lucrative, non-patentable method (e.g., physical exercise, healthy foods, and education) to prevent a disease? Also, simplicity might be, in some cases, an unjustified epistemic concern: focusing on a behavioral and social level intervention, rather than pharmacological treatments, means choosing the more difficult approach that will indeed be much more demanding of the time and effort of children, their parents, their teachers, etc. However, this in itself is not necessarily enough reason to prefer a reductive approach. 18

The emphasis on a reductive explanation leads to a denial of the lack of reasons to reduce the search for an explanation of ADHD to individual dysfunctions. After all, no convincing clues for such a reductive explanation have been found yet. Meanwhile, it leaves other important explanation-seeking questions aside. Does the mother's lifestyle during pregnancy play a role in the onset of ADHD in the child? Does the child's lifestyle play a role? Can changes

<sup>&</sup>lt;sup>16</sup> The *conviction that* a reductive explanation will be found in the future and that such an explanation will support a reductive approach—rather than the fact that an *actual* reductive explanation justifies the reductive approach—seems to form a sufficient ground for medicine to base the bulk of the research and preferred treatments on these still to be found reductive explanatory factors, for example, in the case of ADHD. This contrasts sharply with, for example, the arguments given by Scheidt [43] for not translating the findings on psychological explanatory factors into clinical practice measures. His argument is the current lack of knowledge about the precise mechanisms whereby psychological issues cause or potentiate disease. In view of such arguments with respect to non-reductive causes, it is remarkable that knowledge of the precise mechanisms, whereby reductive elements cause or potentiate disease, is not always requested, for example, when administering stimulant drugs to treat ADHD.

<sup>&</sup>lt;sup>17</sup> In fact, that stimulant medication could treat what we now know as ADHD was discovered before the addressed problematic behavior of children was actually conceptualized as a disease [44].

<sup>&</sup>lt;sup>18</sup> The relation between epistemic motivations and non-scientific interests is in any case interesting enough to be further explored. The role of non-scientific interests is discussed in Gannett [45, p. 370] with respect to geneticization: "The context in which genes are chosen as the best 'handles' among these parts are not just scientific and clinical but economic and political. Geneticization finds a friendly home in a society less and less willing to commit resources to solving complex social problems.... Genetically engineered solutions make private investors money; serious attempts to counter poverty, environmental degradation, and tobacco, alcohol, and drug addiction just costs taxpayers money. The appreciation of the pragmatic dimensions of genetic explanations, and hence their contingency, not only provides good reason to be sceptical of what geneticization has to offer but, by forcing attention to context, asks us to examine the aims, interests, and orientations that lie behind the choices that are being made."

in society at large (e.g., in the way children are educated) make up for a change in the incidence of ADHD? Do Western societies have a higher incidence of ADHD than non-Western societies? If so, what can explain these differences? Gathering much more knowledge on such explanatory factors than we have now might lead to important insights with respect to preventive and non-pharmacological treatment measures, making it possible to lower the number of children who need medication to treat their ADHD.

In any case, it is true that the treatability of the disease through interventions at non-reductive levels seems much more cumbersome than pharmacological responses. Even people arguing against the reduction of the problem of ADHD realize this. For example, Brock and Fernette Eide [46] argue against our tendency to adapt the abilities of ADHD children to our expectations by means of medical treatment and plead for adapting our demands to the peculiarities of these children's brains. Yet, they have to admit that

Of course, such an approach—better chemistry through living—is more demanding than writing prescriptions for Ritalin. And we are not naïve enough to believe that every child will ever get access to the best brain-based teachers and therapists, or that parents will become experts in brain-based learning. Yet we do believe that the time has come to move beyond the behavioral approach, to lessen our dependence on pharmacotherapy, and to seek more precise ways to help struggling kids. [46, p. 59]

To conclude, it is clear that scientists and physicians will often have a difficult job in weighing the pros and cons of a reductive approach. However, this is no argument for considering neurobiochemicalization to be the straightforward choice. Scientists and practitioners should at least think about what can potentially be won by an explanatory pluralist approach instead of a reductive approach.

## A genetic disease?

Another important form of reduction in the medical sciences for which the justification is not always clear, is *geneticization*. Geneticization can be defined as "a process in which differences between individuals are reduced to their DNA codes" [cf. 47, p. 235]. One can distinguish strong geneticization from weak geneticization. The strong variant implies methodological reductionism: it presupposes that the reduction will shed a light on the comprehensive causal web that leads to a disease. This ends in viewing complex traits, such as cancer, schizophrenia and alcoholism, narrowly as "genetic diseases," although other significant environmental and other "non-genetic" contributions have been

identified in the past and have explanatory relevance in view of certain epistemic interests. Earlier successes of finding *the* gene causing a trait or disease, for example, Huntington's disease, have installed a traditional model of deterministic monocausality in the popular imagination. This model presupposes that for many traits and diseases, *the determining gene* could be found—rather than the gene(s) that is/are in some way involved in the development of a trait or disease. This led, among other things, to research looking for *the* gay gene [48]. Monocausality has made place for multicausality in the explanation of most traits nowadays, but the tendency to pay a lot of attention to genetic explanations is still present. However, while the strong variant of geneticization causes the term "geneticization" to have a pejorative undertone in the literature, geneticization is not necessarily negative as the following examples of weak geneticization demonstrate.

Dekkers and Rikkert [49] have analyzed the research on Alzheimer's disease. Their paper clearly illustrates how geneticization is at work in medical research. In their discussion of the causes of Alzheimer's disease (AD), Dekkers and Rikkert present the complex causal web leading up to forms of AD—a web in which neurological and genetic factors figure. Moreover, the authors notice that the current definition and classification of AD does not mention any genetic factors [49, p. 278]. Notwithstanding this, they discuss two examples in which researchers do geneticize. The first example deals with a successful experience of Preimplantation Genetic Diagnosis for early-onset AD, in which only V717L mutation-free embryos were implanted in a 30-year-old woman with no signs of AD but who carried the V717L mutation [50]. A second example refers to the injection—with mixed success—of genetically modified skin cells that produce a protein called nerve growth factor, which prevents cell death in the brain [51]. Dekkers and Rikkert defend the search for a genetic explanation by these authors <sup>19</sup> by concluding that: "[d]octors and researchers in the above examples are interested in one particular causal factor that they can influence in order to prevent AD (case 1) or to relieve the symptoms of AD (case 2)" [49, p. 281; italics added].

In terms of our framework for explanatory pluralism, Dekkers and Rikkert argue in their paper that the work of these scientists is driven by certain specific epistemic motivations that explain their choice. The specific epistemic motivations that can be met by reducing the complex trait to a lower level (DNA) explanation are (a) prevention (at the individual level) and (b) treatability (the relief of symptoms) via (c) decomposition and re-composition of

<sup>&</sup>lt;sup>19</sup> Since scientists hardly justify their choice to search for an explanation at a certain level, it is not possible to figure out whether or not these (and other) scientists just follow a general tendency to try to reduce everything to the level of the genes, or whether their work is grounded in the conviction that their results will serve specified epistemic interests.

brain cells. Both surveys are based on a weak form of geneticization in which the reduction does not intend to shed a light on the comprehensive causal web or all of the causal connections involved. Weak geneticization does not imply methodological reductionism but hopes to find an adequate answer at the genetic level, addressing specific epistemic interests. The completeness of such an explanation depends on the adequacy of the answer to the explanation-seeking question rather than on some ideal explanatory text (invoking all—*possible*—causes) involving all relevant levels.

As stated above, the tendency to pay a lot of attention to the search for genetic explanations is still present. Much research in the biomedical sciences focuses on the role of genes. Often this tendency has been interpreted as a consequence of scientists subscribing (in official and public contexts) to the *fundamental* theory within molecular genetics which sees genes as the fundamental units responsible for guiding all basic life processes. However, since many philosophical arguments have been formulated against this theory [cf. 53, p. 90], why is it being upheld? One answer might be that scientists still *believe* in genetic determinism. Another, more plausible, answer is that so much biomedical research is centered on genes and DNA because it is believed that genes can be used as handles to manipulate biological processes; they are supposed to serve several epistemic interests better than "non-genetic" approaches do. Again, epistemic interests cause researchers to adopt a reductionistic approach.

What is the upshot of all this? First, it should be clear that an explanatory pluralist approach is not compatible with strong geneticization but is compatible with weak geneticization, where the choice to geneticize is motivated by specific epistemic interests. Consequently, the question is not whether geneticization as such is justified but whether the effort invested in the search for a genetic

<sup>&</sup>lt;sup>20</sup> The *fundamental theory* should be distinguished from the *basic theory*. While the basic theory is more modest in answering the question, "What do genes do?"—i.e., that they "code for" or "determine" the linear sequences in RNA molecules and polypeptides synthesized in the cell—the fundamental theory is bolder, claiming that genes are "fundamental" entities that "direct" the development and functioning of organisms by "producing" proteins that in turn regulate all the important cellular processes [52].

<sup>&</sup>lt;sup>21</sup> Cf. Keller [54], Waters [52, 53]. "In the case of molecular genetics, it is investigative pragmatics, not fundamental theorizing, that drives scientific research. The basic theory suffices to explain the investigative utility and results of gene-centered approaches. The fundamental theory is, in an important sense, epiphenomenal with respect to the design and implementation of gene-centered research. On this view, the role of the fundamental theory should be understood in Latourian terms... as a platform for rallying the troops and bringing resources to research endeavors. The design of the laboratory experiments and the reason why the experiments work, can be explained in terms of broad investigative strategies, the basic causal theory of molecular genetics, and the details of the experimental contexts" [52, sec. 6]. Lisa Gannett [45], too, explains the increasing geneticization as driven by pragmatic dimensions, especially manipulability: "[the change brought about by geneticization] lies not in using newly acquired technological prowess to confirm the truth of long standing suspicions about the primacy of genes. I suggest, instead, that we understand geneticization in pragmatic terms: the increasing focus on genes as causes mirrors the increasing ability to manipulate DNA in the laboratory and in the clinic in furtherance of what are perceived to be desirable ends" [45, p. 369-370].

explanation is justified in these and other specific cases, given the epistemic interests that were supposed to be served. Hence, the crucial question that practitioners, researchers and funding agencies should pose becomes, what are the epistemic interests we want to serve, and given these epistemic interests, is the genetic level the level where we can reasonably hope to find the most adequate and accurate explanations? Whether or not one should answer the latter part of the question in the affirmative cannot be evaluated from a general stance towards geneticization but should be considered on a case-by-case basis. In any case, it is clear that not all medical researchers are convinced that the epistemic value of genetic research into the causes of disease is always well-considered:

The quest for understanding complex diseases, attitudes or behaviors by scrutinizing genes severely distorts not merely psychological and social issues, but biological ones as well. While human societies, psyches, and bodies have to be compatible with our genes, much as they have to be compatible with the subatomic particles constituting matter, it does not follow that genetics or quantum physics will provide an "instruction book for human biology...," much less illuminate anything interesting about the human condition. Further research should investigate how the genetic paradigm exerts its fascination on intellectuals themselves. Failure to challenge it on its own term matters because it leaves beliefs about its "potential" (or its imagined dangers) alive, legitimizing claims that grab the collective imagination and driving resources away from urgently needed social, economic, and public health policies. [29, p. 1739]

What Chaufan actually argues here—if translated to our framework—is that focusing on genes as explanatory factors, at the expense of other explanatory factors, often does not provide the adequate, efficient, and accurate answers to the rudimentary explanation-seeking questions that are used as a basis for this research into genes. Rather, she argues, this focus on genes distracts the attention from the search for non-reductive explanations, which are important because of the pressing epistemic needs of society. To conclude, it is an important task for medicine to consider thoroughly whether its inclination to attach great importance to research into genetic explanatory factors is always justified.

#### 7. Conclusion

Cogent reasons clearly exist for preferring a reductive approach in certain medical contexts, given certain interests and goals. However, no reason exists to assume that a reductive approach is always the most adequate, efficient, and accurate. That is why we argued that methodological reductionism should be rejected as a regulative ideal for medicine. The same holds for methodological

non-reductionism and methodological holism: while convincing reasons do exist to search for, and make use of, non-reductive explanations in certain medical contexts, no reason exists to assume that a non-reductive or holistic approach will always deliver adequate, efficient, and accurate answers to our rudimentary explanation-seeking why-questions. Hence, all kinds of medical explanations generally have potential pragmatic value, but none of them have pragmatic value in every explanatory context. Different specific epistemic interests in different explanatory contexts will lead to different kinds of explanation-seeking questions, thus leading to different kinds of explanations. That is why we are convinced that explanatory pluralism holds for medicine.

Nonetheless, methodological reductionism is still dominant in medicine; therefore, as our examples demonstrate, medical researchers and practitioners seem to presuppose too easily and too often that the rudimentary explanation-seeking why-question can only be answered adequately in reductive terms. Although medicine slowly shows more interest in non-reductive explanations nowadays, it still has a long way to go to become fully and truly explanatory pluralist in practice. However, achieving the right balance will be a difficult exercise for the medical sciences.

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